Studies in sulphoxide chemistry

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Metadata Record: https://dspace.lboro.ac.uk/2134/35550

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STUDIES IN

SULPHOXIDE CHEMISTRY

by B. CROWHER

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A thesis submitted
in partial fulfilment of the
requirements for the degree of

DOCTOR OF PHILOSOPHY

of

LOUGHBOROUGH UNIVERSITY OF TECHNOLOGY

March 1972
To my wife

and

to my parents
I should like to thank Dr. J. B. Lee for his help and his insight into the many problems met during this research. His supervision is gratefully acknowledged.

I am also indebted to Mr. I. M. Downie for his supervision in the absence of Dr. Lee during the last year of this period of research.

The provision of a CAPS award from the S.R.C. and the consequent time spent at "Boots Pure Drug Company" Laboratories is acknowledged.

A final acknowledgement is necessary for the opportunity of working in the organic chemistry laboratories of Loughborough University and the assistance provided by the technicians of the department.
SUMMARY

The effect of further stabilisation on the generation of sulfoxide carbanions, under milder conditions than those commonly employed by the generation of dimethylsulphoxide carbanion, has been briefly investigated. Both dibenzyl sulfoxide and diphenylsulphinylmethane failed to react sufficiently under milder conditions.

Attempts to secure the Michael addition of DMSO$^-$ to a wide variety of conjugated systems has proved successful in most cases.

Thus a wide variety of $\alpha$-phenylcinnamionitriles, formed by condensation of benzyl cyanide with substituted benzaldehydes, has given DMSO adducts in good yield. These adducts have shown interesting features in their mass spectral breakdown patterns explicable in terms of Hammett coefficients.

Other sulfoxides such as dibenzylsulphoxide and dipropyl sulfoxide have also been successfully added.

The synthetic utility of these adducts has been demonstrated in pyrolysis and reduction reactions.

The reaction of DMSO$^-$ with 1,1-dicyanoethylene proved complex and structures are postulated for the product isolated.
A detailed study has been made of the addition of DMSO\textsuperscript{−} to substituted chalcones. Previous knowledge of conjugated ketone chemistry has been verified and a variety of adducts has been obtained either by 1,2 or 1,4 addition. This is the first instance of the successful addition of DMSO\textsuperscript{−} to a conjugated ketone.

The reaction of the postulated dicarbanion of DMSO with the chalcone system has also been investigated. The adduct obtained has been shown by degradation to be a 6-membered ring as postulated by previous workers.

Addition to conjugated nitro compounds in DMSO did not occur, but in liquid ammonia addition went readily and interesting new synthetic routes have been investigated.

The addition of the dicarbanion of DMSO to benzil has been shown to give 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide with the hydroxy groups orientated in a cis manner. In contrast another class of dicarbonyl compounds investigated, the quinones did not react.

The preparation of cyclic $\beta$-ketosulphoxides by several routes has been investigated and the first synthesis of a cyclic $\beta$-ketosulphoxide is reported. A thiazolidin-4-one, one of an interesting biological group of compounds, has been converted to the S-oxide which contains a cyclic $\beta$-ketosulphoxide grouping.
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INTRODUCTION

PREVIOUS WORK

Little is known about the chemical reactivity of carbanions substituted by a single alkylsulphinyl group although it does appear that this group produces appreciable stabilisation of an adjacent negative charge \(^1\), \(^2\), \(^3\) by a combination of coulombic effects and sulphur d-orbital resonance. The polar sulphur-oxygen bond has a bond order\(^4\) in the region of 2 and the electron density at the oxygen atom causes it to exhibit nucleophilicity. In dimethylsulphoxide, a typical sulphoxide, the activating effect on the alpha protons is not very great and the pKa has been found\(^5\) to be 32.9. The acidity of dimethyl sulphoxide is less by \(10^7\) than that of acetone and \(10^3\) less than that of diphenylmethane. Very basic reagents are thus needed to induce ionisation. A further consequence of the strong carbon hydrogen bond is the resistance to free radical attack, so that dimethyl sulphoxide is a good solvent for free radical polymerisation.

Interest in sulphoxide carbanions was stimulated by the use of DMSO as a solvent for many inorganic and organic compounds. The solvent properties of dipolar aprotic solvents are now well understood and have been reviewed by Parker.\(^6\) The effect of DMSO is to increase the basicity of alkoxides and hydroxide ion dissolved in it. Elimination reactions\(^7\) and particularly base-
catalysed elimination reactions are frequently run in DMSO. Both the high dielectric constant of DMSO and the enhanced base activity means that eliminations may be run at lower temperatures and in some cases successful eliminations may be achieved even with poor leaving groups such as the -SII group.

Alkoxides of large cations in DMSO are $10^{12}$ to $10^{14}$ times more basic than in the corresponding alcohols. This is the case for potassium and caesium alkoxides; small cations such as sodium and lithium give less basic solutions because of ion-pair formation.

Solutions of potassium t-butoxide in DMSO are the most strongly basic solutions in organic chemistry. This has led to their extensive use. It has since been shown that the t-butoxide ion/DMSO system exists in equilibrium with the conjugate base of DMSO.

$$\text{Bu}_3\text{OK} + \text{CH}_3\text{SOCH}_3 \underset{\text{K}^+}{\overset{\text{CH}_2\text{SOCH}_3 + \text{Bu}^+\text{OH}}{\rightleftharpoons}}$$

The existence of the conjugate base of DMSO, now commonly termed the "dimsyl ion", was first demonstrated by Corey by its reaction with benzophenone.

$$\text{Ph}_2\text{CO} + \text{CH}_3\text{SOCH}_2^- \rightarrow \text{Ph}_2\text{C}^- + \text{CH}_2\text{SOCH}_3 \rightarrow \text{Ph}_2\text{C}^- + \text{CH}_2\text{SOCH}_3^+$$
Generation of Dimethylsulphoxide Carbanion

The conjugate base of DMSO is conveniently generated by heating finely powdered sodium hydride with anhydrous DMSO under nitrogen. Sodium hydride is obtained commercially as a 50/50 dispersion in oil and is readily isolated by repeated washing with dry petroleum ether. When heated at 70-80°C reaction takes approximately one hour, at lower temperatures solution takes longer. Longer periods of heating at higher temperatures cause decomposition of the carbanion. The complex thermal decomposition of DMSO has been the subject of a recent paper. There are reports of the potential hazards of this decomposition. Completion of the reaction is easily observed by the cessation of hydrogen evolution and the formation of a glassy, pale grey solution. By this means fairly concentrated solutions of the carbanion may be formed (e.g. in the region of a 3 M. solution). Sodamide or alkyl lithiums may be used as an alternative to sodium hydride. Use of lithium alkyls permits the formation of lithium methylsulphinyl carbanion in solvents other than DMSO e.g. THF, benzene, ether, and dimethoxyethane. However, some decomposition of DMSO can occur and the preparation is difficult. With lithium hydride the low density of the hydride (\(\rho = 0.78\)) causes it to float in DMSO. In order to effect complete dissolution, prolonged heating and high speed stirring is required giving an extensively decomposed solution with little synthetic application. In a similar fashion, n-butyl lithium yields highly decomposed
solutions of DMSO. It may be that there is a large conversion of n-butyl lithium by DMSO to give DMS in a similar way to the reduction of aromatic alkyl sulphoxides by phenyl lithium.\textsuperscript{16}

Dimeyl ion has been generated using sodium or potassium but in both cases methyl sulphonate ion is also formed and the reactions are exothermic. Lithium metal does not react with DMSO. Other metal salts have not as yet been prepared. Solutions of the carbanions are fairly stable and a highly stable solution has been made utilising an ultra-sound generator to cause sodium hydride to react with DMSO at \(50^\circ\).\textsuperscript{17}

Equilibrium concentrations of the anion occur with the systems potassium \(\pm\)-butoxide/DMSO and sodium methoxide/DMSO. Russell makes a distinction between the use of the reversible and irreversible formation of methylsulphinyl carbanion.

There is speculation over the formation of a dicarbanion of DMSO.\textsuperscript{19,20} Following his work on the ionisation of dibenzyl sulphone in liquid ammonia, Hauser\textsuperscript{19} has postulated the existence of the dicarbanion in its reaction with aliphatic bromides

\[
{\text{-CH}_2\text{SOCH}_2^-} + 2\text{Br}^- \rightarrow \text{RCH}_2\text{SOCH}_2\text{R} + 2\text{Br}^-
\]

The actual existence of the dicarbanion has not however been adequately proved.
Reactions of the Carbanion

The methylsulphenyl carbanion reacts rapidly with oxygen, carbon dioxide and water. As anticipated the anion is an extremely strong base as is shown by its rapid reaction with triphenylmethane to produce a deep red solution of the triphenyl-methane carbanion. Study of this reaction has shown that in 2:1 THF/DMSO as solvent the methylsulphenyl carbanion is $10^2$ or $10^3$ more basic than the trityl anion. Many of the reactions of dimethyl carbanion are typical nucleophilic reactions but occasionally the high basicity of the reagent interferes with the expected reaction. The great synthetic utility of the reagent is not only in the formation of new sulphoxides but also in the further transformations which they can undergo to sulphur free products.

Reactions with Ketones and Aldehydes

Methylsulphenyl carbanion adds readily to non-enolisable ketones and aldehydes to form $\beta$-hydroxy sulphoxides. In the case of acidic ketones enolate formation occurs, but there are cases intermediate between the two extremes e.g. cyclohexanone gives 17% adduct together with 80% recovery of starting material. The extent of addition varies with solvent and cation with both aromatic ketones and aromatic aldehydes and aromatic aldehydes. Aliphatic carbonyl compounds, particularly non-enolisable ketones, tend to undergo cleavage to carboxylic acids and alkanes. $\beta$-Hydroxy sulphoxides may be pyrolysed to form substituted ethylenes.
As mentioned previously, benzophenone reacts with DMSO\textsuperscript{−} to give a hydroxy sulfoxide. Depending upon the reaction conditions various other products may result.\textsuperscript{9,13}

\[
\begin{align*}
\text{Epoxide Formation (80°)} & : \quad \text{Ph}_2\text{C} - \text{CH}_2\text{-SO}_3^- \rightarrow \quad \text{Ph}_2\text{C} - \text{CH}_2 \\
\text{Olefin Formation (80°)} & : \quad \text{Ph}_2\text{C} - \text{CH}_2\text{-S} - \text{CH}_3 \quad 0\text{-S-O}_3^- \\
& \quad \rightarrow \quad \text{Ph}_2\text{C} = \text{CH}_2 \\
& \quad \downarrow \\
& \quad \text{Ph}_2\text{C} = \text{CH}_2 \quad + \text{CH}_3\text{SO}_2^- 
\end{align*}
\]

The potassium t-butoxide/DMSO system containing some water has been used as an effective way of cleaving non-enolisable ketones and is a useful alternative to the Haller-Bauer\textsuperscript{28} reaction which uses sodamide in benzene. Thus nortricyclanone under these conditions is cleaved to the isomeric bicyclic acids.\textsuperscript{26} Epoxides in an analogous fashion to carbonyl compounds, condense with DMSO\textsuperscript{−} to yield 8-hydroxysulphoxides.\textsuperscript{29,30}

**Reaction with Esters**

Reaction of DMSO\textsuperscript{−} with esters gives \(\beta\)-keto sulphoxides which are intermediates of exceptional usage. Two equivalents of DMSO\textsuperscript{−} are required in their formation since the \(\beta\)-keto sulphoxide formed
initially is readily ionised.

\[ \text{RCO}_2\text{R}^* + \text{CH}_3\text{SOCH}_2^- \rightarrow \text{RCOCH}_2\text{SOCH}_3 + \text{R}^*\text{O}^- \]

\[ \text{RCOCH}_2\text{SOCH}_3 + \text{CH}_3\text{SOCH}_2^- \rightarrow \text{RCOCH}_3\text{SOCH}_3 + \text{CH}_3\text{SOCH}_3 \]

The original application of this reaction was limited to reactions with aromatic esters.\textsuperscript{9,31,32} Optimum yields were obtained using KOBu\textsuperscript{+}/DMSO with the exception of \textbf{p}-toluates, which due to acidic aromatic methyl protons, self-condense.\textsuperscript{33} However, with NaH/DMSO the \(\beta\)-ketosulphoxide was obtained.\textsuperscript{15}

The reaction has been extended to aliphatic esters\textsuperscript{34,35,36} and in these laboratories to the esters of sugar acids.\textsuperscript{37} Variation of the sulphoxide instead of the ester increases the synthetic potential of the reaction. An application is found in the synthesis of ecdysone.\textsuperscript{38}

Reduction of \(\beta\)-ketosulphoxides with aluminium amalgam in aqueous tetrahydrofuran is a convenient route to methyl ketones. Other sulphoxides may be utilised to form substituted ketones.

\(\beta\)-Ketosulphoxides may be oxidised, reduced, alkylated, and rearranged to a host of sulphur containing and sulphur free products.
Becker and Russell\textsuperscript{39} have utilised the reactions of esters with DMSO\textsuperscript{−} in a synthesis of ninhydrin.

\[
\text{ester} + \text{DMSO}^{-} \xrightarrow{\text{NaOH}} \text{products}
\]

Reactions with Halides and Tosylates

As mentioned previously DMSO\textsuperscript{−} is a powerful basic system and, in general, reaction with halides and tosylates produces a mixture of olefins, by E\textsubscript{2} elimination, and ethers, by S\textsubscript{N}\textsuperscript{2} substitution. The relative extent of these reactions depends on the alkyl or aryl residue on the halide or tosylate, the leaving group, and whether the DMSO\textsuperscript{−} used is made by a reversible or irreversible reaction.\textsuperscript{40,41,42,43}

Aromatic halides appear to react via a benzyne intermediate with DMSO\textsuperscript{−}; chlorobenzene reacts with DMSO\textsuperscript{−} to give a mixture of benzyl methyl sulphoxide and benzhydryl methyl sulphone.\textsuperscript{9,13} With a large excess of DMSO\textsuperscript{−} little benzhydryl methyl sulphone is obtained.
Polybromo aromatics react with KOBu/DMO by selective loss of bromine atoms. Hexabromobenzene gives a mixture of 1,3,5 - tribromobenzene and 1,2,4,5 - tetrabromobenzene.\(^4^4\)

With 1,2,4 - tribromobenzene under similar conditions, 1,4 - dibromobenzene is formed.\(^4^5\) The mechanism postulated in these reactions involves the postulated formation of the little known bromodimethylsulphoxide. However no product from the bromosulphoxide was detected. Non-aromatic cyclic bromides such as 1,2,5,6 - tetrabromocyclooctane give elimination products the nature of which depends on the DMSO\(^-\) system used.\(^4^6\)
The difference between reversibly formed and irreversibly formed DMSO$^-$ has been reviewed.$^{47}$

Aliphatic bromides give good yields of the substituted sulphoxide. Pyrolysis of the products gives terminal olefins.$^{48}$ With tosylates and mesylates dimethyl sodium can behave as a carbon nucleophile, a sulphur nucleophile or a hydrogen nucleophile according to the nature of R in ROTs or ROMes.

Broxton et. al.$^{49}$ have obtained high yields of substitution products with long chain aliphatic tosylates but phenyl tosylate gives sodium phenoxide (82%) and p-tolylsulphenylmethylenesulphonylmethane (23%).

\[
\text{n-C}_{12}\text{H}_{25}\text{OTs} + \text{NaCH}_2\text{SOCH}_3 \rightarrow \text{n-C}_{12}\text{H}_{25}\text{CH}_2\text{SOCH}_3 \quad (83\%)
\]

\[
\text{PhOTs} + \text{NaCH}_2\text{SOCH}_3 \rightarrow \text{PhONa} + \text{CH}_3\text{SOCH}_2\text{Ts}
\]

With R = cyclohexyl, elimination rather than substitution takes place and cyclohexene is formed.
A number of sulphonate esters in carbohydrate\textsuperscript{50} and steroidal\textsuperscript{51,52} systems have been shown to undergo sulphur-oxygen cleavage with bases in DMSO.

Reactions with Aromatic and Olefinic Systems

DMSO\textsuperscript{−} may be added to olefinic bonds in both aliphatic and aromatic systems if there is stabilisation of the intermediate carbanion. The further reactions of this carbanion depend upon the experimental conditions.

Thus 1,1-diphenylethylene reacts rapidly with DMSO\textsuperscript{−} at room temperature to give, after hydrolysis, a quantitative yield of 1,1-diphenyl-2-methylsulphinylethane.\textsuperscript{53} When the temperature is raised to 70\textdegree a series of equilibria arise and a variety of products may be obtained.
Protonation of the carbanion formed initially gives the straightforward addition product. A process of $\beta$-elimination of methanesulphenic acid yields 3,3-diphenylpropene which isomerises to the more stable olefin by a base catalysed isomerisation. This type of elimination has been shown by Hofmann et. al.\textsuperscript{54,55} to occur with a wide variety of sulphotides.

An alternative $\gamma$-elimination has also been observed to yield 1,1-diphenylcyclopropane by elimination of methane sulphenate.\textsuperscript{56} The ratio of $\beta$ to $\gamma$ elimination has been studied for a number of 2-alkyl-3-phenylpropylsulphoxides in DMSO\textsuperscript{7}/DMSO and KN\textsubscript{2}/Et\textsubscript{3}N.\textsuperscript{57} The initial sulphoxides were prepared by adding DMSO\textsuperscript{7} to $\beta$-alkylstyrenes.

Methylation may be achieved by adding DMSO\textsuperscript{7} to an olefinic system, eliminating methanesulphenic acid and finally isomerising to give the methylated product. There are several reported examples of this.\textsuperscript{58,59} Stilbazoles and trans-stilbenes gave methylated products in good yield. The methylation of some 1,3-dienes has been observed. Thus butadiene gave a mixture of cis and trans 1,3-pentadienes which on further reaction with DMSO\textsuperscript{7} gave a mixture of isomeric hexadienes.\textsuperscript{59}

A number of aromatic systems have been successfully methylated.\textsuperscript{59,60} However benzene, pyridine, phenazine and thianaphthene failed to give methylated products.
A stepwise mechanism similar to aliphatic methylations is likely.

\[
\begin{align*}
A & \xleftarrow{\text{DMSO}^-} B \xrightarrow{\text{H}^+} C \\
 & \downarrow \\
D & \xleftarrow{\text{DMSO}^-} E
\end{align*}
\]

Miscellaneous Reactions of DMSO

Iwai and Ide have successfully added DMSO\(^{-}\) to phenylacetylene to give a mixture of the cis and trans adducts.\(^{61}\)

\[
\text{Ph}-\equiv-\text{CH} \xrightarrow{\text{DMSO}^-} \text{Ph}-\equiv-C\equiv-\text{H} + \text{Ph}-\equiv-\text{C}-\equiv-\text{CH}_2\text{SOCH}_3
\]

Lactones are opened with the formation of \(\beta\)-ketosulphoxides.\(^{62}\)

House and Larson utilised the reaction of DMSO\(^{-}\) in DMSO/THF in the synthesis of bicyclo (3.2.1.) octane systems.
Previous work in these laboratories has confirmed the
generality of this reaction. \( \alpha \)-Butyrolactone gave, after
desulphurisation, 5-hydroxy-pentan-2-one.\(^{37}\)

\[
\begin{align*}
\text{O} & + \text{Na}^+\text{CH}_2\text{SOCH}_3 \rightarrow \text{HO(CH}_2)_2\text{COCH}_2\text{SOCH}_3 \\
& \downarrow \\
& \text{HO(CH}_2)_2\cdot\text{COCH}_3
\end{align*}
\]

Only one example of a reaction with imines has been reported.
Benzalaniline reacted readily at 25\(^\circ\) in a manner analogous to
benzaldehyde to give a mixture of diastereoisomeric \( \beta \)-anilino-
sulphoxides.\(^{13}\)

\[
\text{PhN} = \text{CHPh} \xrightarrow{\text{DMSO}^-} \text{PhNHCHPh} \\
\downarrow \text{CH}_2\text{SOCH} \_3
\]

In Reissert Chemistry DMSO\(^-\) has been used as a reactive base for
novel reactions.\(^{63,64}\)
During the course of studies on the phenoxide ion catalysed benzilic acid rearrangement of benzil, Trisler et al. have found that there was an equilibrium of phenoxide ion with DMSO\(^-\).\(^65\),\(^66\)

\[
\text{PhO}^- + \text{DMSO} \quad \xrightleftharpoons{\text{PhOH + DMSO}^-}
\]

Trisler has postulated a mechanism involving attack of DMSO\(^-\) on one of the carbonyl groups of benzil as a key step in the formation of products not incorporating sulphur (scheme \(\text{I}\)). The products obtained from the reaction were: 3-Benzoyl-2,4,5-triphenylfuran, cis-\(\alpha\beta\)-dibenzoyl-styrene, benzoic acid, and benzilic acid. This reaction is discussed in context when the reaction of benzil in liquid ammonia with DMSO dicarbanion is considered.

Isolated examples of new reactions of DMSO\(^-\) continue to occur. Recently Russell and co-workers, whilst extending the scope of the synthetic utility of \(\beta\)-ketosulphoxides, have reported the addition of DMSO\(^-\) to a nitrile. When DMSO\(^-\) was reacted with benzonitrile under normal conditions a tar resulted. The use of lithium iodide however gave good yields of the expected ketosulphoxide, the imine formed by addition of DMSO\(^-\) hydrolysing prior to isolation.\(^15\)

\[
\text{PhCN} + \text{CH}_3\text{SOCH}_2^- \quad \rightarrow \quad \left[ \begin{array}{c} \text{PhC} \equiv \text{NH} \\ \text{CH}_2\text{SOCH}_3 \end{array} \right] \\
\downarrow \quad \text{PhCOCH}_2\text{SOCH}_3
\]
SCHEME I

\[
\text{PhCOCOPh + DMSO}^- 
\]

SCHEME II

\[
\text{PhCOCOPh + DMSO}^- 
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Many reactions involving bases have been improved with the use of DMSO\(^{-}\). Thus a modification\(^{67}\) of the Wittig reaction based on DMSO\(^{-}\) frequently gives higher yields and shorter reaction times than more conventional means.

Styrene oxide, a typical epoxide, has been reacted with DMSO\(^{-}\) to yield 3-methylsulphonyl\(-1\)-phenylpropanol.\(^{15}\)

\[
\text{Ph-CH=CH}_2 + \text{CH}_3\text{SOCl}_2 \rightarrow \text{PhCH(OH)CH}_2\text{SOCH}_3
\]

Attempts to isolate the pure product resulted in low yields.

Whilst this introduction was in preparation there were several further interesting publications on sulphoxide carbanion chemistry. Bravo\(^{68}\) has shown that o-aminobenzophenone reacts with DMSO\(^{-}\) at room temperature to give 3-phenylindole according to the reaction scheme 2.

Truce has recently added phenylbenzylsulphoxide to carbon disulphide and methylated the intermediate in situ with methyl iodide.\(^{69}\) In this case KOBu\(^{+}\)/DMSO was the base used.
Pharmacological aspects of Sulfoxide Chemistry

Organosulphur compounds have a long history of use as insecticides, fungicides, bacteriostats and for general therapeutic use. Most attention has been applied to the sulphone and sulphonate groups as in the important antibiotic drugs which are sulphonamide derivatives. However, several sulphoxide compounds have been patented. Insect repellants have been patented utilising bis-(2-aminoethyl]-sulphoxide and bis [(3-dimethylamino) propyl] sulphoxide. Bis-alkylsulphinyl aliphatic acid derivatives of the type \((RSO)_2CHCH_2CO_2R\) have been used as bacteriocides and fungicides. Many more examples exist.

A considerable boost to therapeutic sulphoxide chemistry was given by the use of dimethyl sulphoxide in medicine. Because of systemic penetration and ability to combine with other drugs, its wide range of potential uses has been demonstrated as a penetrant carrier and "translocutor" of dyes and fungicides, diuretics, tranquillisers and central-nervous-system depressants. It produces dramatic effects in acute muscular-skeletal inflammation by topical application. Absorption is rapid and a garlic taste can be detected due to breakdown in the body to dimethyl sulphide. DMSO has been shown to alter tissue permeability and to increase membrane permeability to a number of compounds. The pharmacodynamic mechanism remains unknown. It appears that the penetration of DMSO is a function of the sulphoxide moiety. Hence it appeared of
interest to synthesise sulphoxide containing molecules and subject them to a biological screening process. This was done in co-operation with "Boots Pure Drug Company".

Up to the present time no detailed biological leads have emerged, although some DMSO adducts have shown slight fungicidal activity. Some intermediates in their formation have also shown activity but none have proceeded to final stages of screening. Recently a book on DMSO has been published giving a detailed account of the medical uses of DMSO and includes a comprehensive bibliography up to 1969.
PRELIMINARY SURVEY

At the commencement of this work the major objectives were as follows: From a pharmaceutical point of view it was desirable to synthesise several new classes of compounds incorporating at least one sulfoxide group. If possible a range of other functional groups should also be introduced. Chemically the activating influence of the sulfoxide group was of interest in a number of aspects, and arising from this the exploration of the extent to which the derivable carbanions followed better known carbanions in their behaviour. Attention was focussed on the Michael addition as a typical carbanion process, and a study commenced of the factors affecting the behaviour of the dimethyl sulfoxide ion in such reactions. Having established that reactions of this type were feasible an additional interest was maintained in obtaining routes to sulfoxide heterocycles.

Interest in the carbanion of DMSO led us to study whether other sulfoxide carbanions could be generated under milder conditions if extra stabilising groups were present.

Dibenzylation of sulfoxide would be expected to form a more stabilised carbanion than DMSO since the carbanion formed would be further stabilised with a phenyl group. Several reactions were performed using ethyl benzoate to trap any carbanion formed as shown below.
A variety of bases were used to try and generate the carbanion including the methoxide and t-butoxide ions. However, the absence of any addition was indicated by the absence in the product of any carbonyl absorption in the IR at 1690 cm\(^{-1}\). The methylene protons of benzyl methyl sulphoxide have been shown to exchange with deuterium in NaOD/D\(_2\)O which suggests some stability of the carbanion.

In our case the concentration of carbanion must also be very small and the equilibrium must be well to the left.

\[
\text{PhCH}_2\text{SOCH}_2\text{Ph} + \text{Bu}^\text{tO}^- \rightarrow \text{PhCH}_2\text{SOCH}_2\text{Ph} + \text{Bu}^\text{tOH}
\]

It was found that the carbanion can be readily generated under similar conditions to DMSO\(^-\) and this is discussed later in this thesis.

The stabilisation of a carbanion by two sulphoxide groups was investigated using diphenylsulphinylmethane as an example. Ethyl benzoate and diphenylsulphinylmethane failed to react even at reflux temperature when sodium ethoxide in ethanol was used as base.

\[
(\text{PhSO})_2\text{CH} + \text{PhCO}_2\text{Et} \rightarrow (\text{PhSO})_2\text{CHO}\text{Ph} + \text{EtO}^-
\]
In view of these observations it was concluded that generation of the carbanion under these conditions was not practicable.

Before investigations were begun using the DMSO⁻/DMSO system initial experiments were performed to confirm the correctness of the experimental conditions. Attempts were made to prepare some β -ketosulphoxides both to check the experimental conditions and also obtain some examples for biological screening. The reaction of ethyl benzoate with DMSO⁻ was carried out under conditions which differed somewhat from those employed by Corey¹³ and by Russell. The ester was added in solution in DMSO rather than THF, and the base used to generate DMSO⁻ was sodium hydride.

Under these conditions a high yield of the β -ketosulphoxide was still obtained and corresponded in its physical data with that obtained by Corey.¹³

\[
\text{PhCO}_2\text{Et} + \text{CH}_3\text{SOCH}_2^- \rightarrow \text{PhCOCH}_2\text{SOCH}_3^- + \text{EtO}^-
\]

It was found that the period of drying of DMSO with calcium hydride was a crucial factor in obtaining a good reaction yield.

A number of attempts to obtain the β -ketosulphoxide from ethylphenylacetate under the same conditions failed.

\[
\text{PhCH}_2\text{CO}_2\text{Et} + \text{CH}_3\text{SOCH}_2^- \rightarrow \text{PhCH}_2\text{COCH}_2\text{SOCH}_3^- + \text{EtO}^-
\]
During one of these attempts phenylacetic acid was obtained in good yield. This indicates that proton transfer from the α-carbon atom of the ester to DMSO⁻ predominates over carbonyl addition of the carbanion because of the high acidity of the ester relative to the carbanion. After this work was performed a recent publication by Otsuji has described the same occurrence and an almost quantitative yield of phenylacetic acid was obtained.

Corey has previously reported that this proton transfer reaction can predominate when there is high acidity of the ester or because of strong steric hindrance to carbonyl addition.

In an attempt to obtain a cyclic ketosulphoxide diethyl oxalate was reacted with excess DMSO⁻.

However no product was isolatable. Russell has obtained a similar result using KOH/IMSO as the source of DMSO⁻. Having satisfied ourselves that the experimental conditions were satisfactory, work was commenced in trying to add DMSO⁻ to conjugated systems.

Until this work commenced addition of DMSO⁻ to unsaturated systems had only involved addition to carbon-carbon double bonds.
activated by a phenyl group. A previous attempt to add DMSO\(^{-}\) to pent-3-en-2-one yielded only high-boiling polymeric products.\(^{23}\) Low molecular weight \(\alpha/\beta\) unsaturated ketones are well known to be unstable in the presence of base. The simplest \(\alpha/\beta\) unsaturated ketone methyl vinyl ketone polymerises on standing.\(^{74}\) Hence pent-3-en-2-one was an unfortunate choice of substrate.

It was thought that a suitable conjugated system for investigation was that provided by an extensively conjugated Schiff base such as that formed by the condensation of cinnamaldehyde with aniline.

\[
\text{PhNH}_2 + \text{PhCH} = \text{CHCHO} \rightarrow \text{Ph-N} = \text{CH - CH = CIPh}
\]

Corey had previously shown that the simple Schiff base benzaline reacts with DMSO\(^{-}\) in high yield to give the expected adduct.\(^{13}\)

It was thought that the formation of an intermediate nitrogen stabilised anion (1) would provide a driving force for conjugate addition to take place.

\[
\text{Ph-N} = \text{CH - CH = CIPh} \xrightarrow{\text{DMSO}^{-}} \text{PhN} - \text{CH} = \text{CH-CHPh} \quad \text{(1)}
\]

However when the reaction was performed a complex oily tar was obtained. Examination by TLC showed the presence of at least a dozen coloured components. Attempts to obtain any well defined products by PLC failed.
Attention was then directed to \( \alpha/\beta \) unsaturated nitriles and the possibility of a Michael addition occurring with \( \alpha \)-phenylcinnamionitriles was examined.

The Michael condensation\(^{75}\) in its original sense involves the addition of the conjugate base of the carbonyl compound (2) to an activated carbon-carbon double bond such as that in (3).

\[
\begin{align*}
\text{CH} - \text{C} = \text{O} & \quad + \quad \text{C} = \text{C} - \text{C} = \text{O} \\
\text{base} & \quad \quad \rightarrow \quad \text{O} = \text{C} - \text{C} - \text{C} - \text{C} - \text{C} = \text{O}
\end{align*}
\]

(2) (3)

The condensation occurs with alkaline reagents, usually alkoxides. As now understood, the Michael condensation includes a variety of addends and acceptors. In the case of \( \alpha \)-phenylcinnamionitriles it might be expected that they would form suitable acceptors since a highly stabilised carbanion results from the addition of a nucleophile.

A variety of \( \alpha \)-phenylcinnamionitriles are readily available by the condensation of equivalent amounts of benzyl cyanide and an aromatic aldehyde in ethanol in the presence of base. The usual base is sodium ethoxide but it was found here that aqueous sodium hydroxide was sufficient to effect condensation. If 2 \( \text{mol.} \) of benzyl cyanide to one of aldehyde are used a propane derivative (4) arises by Michael addition to the expected product.\(^{76}\)
It has been observed\textsuperscript{77} with \( \alpha \)-hydroxy benzaldehydes that coumarin formation occurs. Either the intermediate unsaturated nitrile (5) is hydrolysed to the corresponding acid (6) which then cyclises to 3-phenyl-7-methoxycoumarin (7) or attack upon the nitrile yields the iminolactone which subsequently hydrolyses. (scheme 3).

By proper control of conditions the \( \alpha \)-phenylcinnamionitriles were obtained as highly crystalline solids in high, often quantitative yield. Derivatives were prepared of the general structure (8) where \( R = H; 4\text{MeO}; 3,4\text{-MeO}; 3,4\text{CH}_2\text{O}; 2\text{Cl}; 4\text{Cl}; 4\text{NMMe}_2; 4\text{Me}; \)

(8)

The \( \alpha \)-phenylcinnamionitriles showed a characteristic band in the IR at 2,220 cm\(^{-1} \) typical of an \( \alpha/\beta \)unsaturated nitrile. In all NMR spectra the olefinic proton was sufficiently deshielded to resonate under the aromatic envelope.

It would be expected that addition of a nucleophile to \( \alpha \)-phenylcinnamionitriles would produce a highly stable carbanion stabilised by a phenyl group and a nitrile group. In view of this it is surprising that little work appears to have been done with them in Michael additions. So far as the author is aware the only previous examples are the additions of nitromethane and nitroethane\textsuperscript{78} using diethylamine as catalyst.
SCHMME III
The reaction of DMSO\textsuperscript{−} with the unsaturated nitrile was investigated using DMSO or DMSO/THF as the reaction medium. In all cases a deeply coloured solution was obtained. The products, obtained as more or less crystalline white solids, were shown to be the Michael addition product as discussed below.

In order to facilitate comparison between different R groups, standard reaction conditions were used although yields could no doubt be improved. Initial experiments with α-phenylcinnamionitrile established that a reaction time of between 5 min. and 30 min. was optimal. The reaction is envisaged as attack of the DMSO\textsuperscript{−} ion on the planar trans olefin.

\[
\begin{array}{c}
\text{CH}_3\text{SOCH}_2 \quad \text{Ph} \quad \text{CN} \\
\text{H} \quad \text{Ph} \quad \text{H} \quad \text{Ph}
\end{array} \rightarrow \begin{array}{c}
\text{CH}_3\text{SOCH}_2 \quad \text{CN} \\
\text{Ph} \quad \text{Ph} \quad \text{H}
\end{array}
\]

(9)

It is quite likely that the intermediate adduct (9) is further stabilised by either intramolecular electrostatic interactions or intermolecular interactions with DMSO. This is illustrated by the fact that protonation with water is not instantaneous but takes several seconds and is much quicker with H\textsuperscript{+}. Protonation of (9) can occur from either side to form a mixture of diastereoisomers.
The adduct, obtained after purification, is a high melting white solid insoluble in non-polar solvents. TLC showed the presence of diastereoisomers as a pair of overlapping spots. Recrystallisation from ethanol gave one of the isomers with a sharp melting point.

Support for the assigned structure came from spectroscopic data. Infra-red absorption at 2,260 cm\(^{-1}\) showed the presence of a non-conjugated nitrile group. Furthermore there was no trace of any absorption attributable to an ethylenic group in the region 1600 - 1700 cm\(^{-1}\). The strongest absorption in the spectrum was found at 1055 cm\(^{-1}\) and may be assigned to the sulphur-oxygen stretch of the sulphoxide group. Similar IR spectra were obtained with the other adducts obtained. The NMR spectrum was readily assignable. The methine proton adjacent to the nitrile group occurred as a doublet at 5.47. Except for a sharp singlet at 7.47 due to the methyl group adjacent to the sulphoxide group, the rest of the protons formed a complex multiplet from 6.0 to 7.07.

The mass spectrum showed a molecular ion at the appropriate mass number. Several interesting features were found in the mass spectra of the nitrile adducts. The expected fragment ion formed by cleavage of the molecular ion at the \(\alpha\)-position to the sulphoxide group was found in all samples investigated and formed from 10 - 20\% of the major ion at M - 63. A typical example, the 4-dimethylamino adduct is shown on page 28.
### Mass Spectra of Nitrile Adducts

<table>
<thead>
<tr>
<th>Hammett σ- Value</th>
<th>Ratio of Abundance of Ions *</th>
<th>Substituent R</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.8</td>
<td>H</td>
</tr>
<tr>
<td>-0.17</td>
<td>0.1</td>
<td>4-Me</td>
</tr>
<tr>
<td></td>
<td>1.7</td>
<td>3,4-CH$_2$O</td>
</tr>
<tr>
<td>-0.27</td>
<td>3.3</td>
<td>4-MeO</td>
</tr>
<tr>
<td></td>
<td>6.2</td>
<td>3,4-MeO</td>
</tr>
<tr>
<td>-0.83</td>
<td>13.0</td>
<td>4-NMe$_2$</td>
</tr>
</tbody>
</table>

* Ratio $= \frac{[\text{R-CH=CH}_2]}{[\text{PhCHCN}]}$  

![Graph showing the relationship between Hammett σ- and the ratio of the abundances of ions.](image-url)
There was also evidence of $\beta$-elimination of methylsulphenic acid. Entwhistle et al. have observed a similar phenomena in the mass spectrometry of alkyl sulphoxides at a source temperature of $100^\circ$. In our case the $M - 64$ peak was in the majority of cases stronger than the $M - 63$ peak.

The notable feature of the spectra was that the major ion was found to be either $[\text{PhCHCN}]^+$ (10) or an ion resulting from breakdown of the molecular ion to a styrene $[\text{PhCH} = \text{CH}_2]^+$ (11).

$$[\text{PhCH} - \text{CH(Ph)CN}]^+ \rightarrow [\text{PhCHCN}]^+ \quad m/e 116 \quad (10)$$

$$[\text{PhCH} = \text{CH}_2]^+ \rightarrow [\text{PhCH} = \text{CH}_2]^+ \quad m/e 104 \quad (11)$$

The actual mechanism operating in the breakdown is open to speculation. It seems feasible to postulate a McLafferty type rearrangement $^{79}$ of the molecular ion (12).
By varying the nature of the group R in (8) the relative amounts of (10) and (11) may be varied. Electron releasing groups show an increasing tendency, depending upon their ability to donate electrons, to stabilise breakdown to the substituted styrene (11) and thus increase its abundance in the mass spectrum. This effect is subject to a rough quantitative application of Hammett’s sigma coefficient (table and graph page 28). Other groups such as the methylenedioxy group cannot have a Hammett coefficient directly applied to them but do show an effect consistent with their electron donating properties. Unfortunately, no further examples of electron withdrawing groups were available at the time.

Additions to Other Conjugated Nitriles

With simpler unsaturated nitriles e.g. cinnamonnitrite a more complex reaction occurred. Instead of a clean addition the reaction gave black tarry products. Examination by IR showed that conjugation had been removed. Probably anionic polymerisation occurs under the strongly basic reaction conditions.

Attempts to obtain a facile preparation of unsaturated long chain nitriles resulted in the formation of isomers. Nonaldehyde condensed with cyanoacetic acid in the presence of piperidine gave a mixture of the conjugated (13) and non-conjugated (14) nitriles in the ratio 3:1 respectively, as indicated by NMR. Gas chromatographic analysis also indicated a 3:1 ratio.
This is substantiated by previously published work.\textsuperscript{80,81} Attempts to add DMSO\textsuperscript{−} to systems of the type \( R-\text{CH} = \text{CH} - \text{CN} \) were consequently abandoned.

Compounds containing furan and thiophene residues are of interest in the drug industry. A preliminary examination was made of the addition of DMSO\textsuperscript{−} to (15) which is readily prepared by the Knoevenagel condensation of furfuraldehyde with benzyl cyanide.

\[
\begin{align*}
\text{CH}_3(\text{CH}_2)_7\text{CHO} + \text{CNCH}_2\text{CO}_2\text{H} \rightarrow \quad & \text{CH}_3(\text{CH}_2)_7\text{CH} = \text{C(Ph)CN} + \text{CH}_3(\text{CH}_2)_6\text{CH} = \text{CHCH}_2\text{CN} \\
\text{(13)} & \quad \text{(14)}
\end{align*}
\]

When (15) was reacted with DMSO\textsuperscript{−} at room temperature an intractable tar was produced. This is somewhat surprising since furans are known to be stable under basic conditions and only unstable under acidic conditions. Since the conditions of the reaction are highly basic it appears that a rationalisation may be made by considering the subsequent reactions of the adduct formed. Addition may occur to furans via a direct or indirect mechanism.\textsuperscript{82}
Either (16) or (17) may undergo addition to a further molecule of the conjugated nitrile. Polymerisation probably occurs in this case because of the facile carbanion attack on the furan ring in contrast to the smooth addition of DMSO$^-$ to other less polyfunctional molecules. Possible breakdown of (17) may be envisaged as below.

The breakdown product (18) would be expected to lead to extremely complex products.

It is of interest to note that Corey$^{13}$ successfully obtained a high yield (71%) of the ketosulphoxide from methyl$\alpha$-furcote without observing any tar formation which supports the view that the basic reaction conditions are not responsible for the complex
reactions occurring. The possibility of 1,6 addition with DMSO\textsuperscript{−} was investigated using the conjugated nitrile (19) from the condensation of cinnamaldehyde and benzyl cyanide.

\[
\text{PhCH} = \text{CH} - \text{CHO} + \text{PhCH}_2\text{CN} \rightarrow \text{PhCH} = \text{CH} - \text{C(Ph)CN} \quad (19)
\]

Little published work exists on 1,6 Michael additions. Crotylideneacetone yields with diethyl malonate, in the presence of sodium methoxide, a mixture of products resulting from 1,6 and 1,4 addition, the former predominating.\textsuperscript{83}

The addition of (19) to DMSO\textsuperscript{−} at room temperature gave a mixture of unchanged (19) and one other product in low yield. Spectral data confirmed this as the 1,4-adduct (20).

\[
\begin{align*}
\text{PhCH} = \text{CH} - \text{CH} - \text{CH(Ph)CN} \\
\text{CH}_2\text{SOCH}_3
\end{align*}
\]

(20)

The synthetic utility of the addition of DMSO\textsuperscript{−} to conjugated nitriles lies in its applicability to various other sulphoxides as well as transformation of the adducts.

Dibenzyl sulphoxide monocarbanion generated in DMSO with sodium hydride was added to the 4-methoxy derivative (21) of \(\alpha\)-phenylcinnamonnitrile in fair yield to give the adduct (22).

\[
\text{PhCHSOCH}_2\text{Ph} + \text{MeO} \rightarrow \text{PhCH} = \text{C(Ph)CN} \quad (21)
\]

\[
\begin{align*}
\text{PhCHSOCH}_2\text{Ph} + \text{MeO} \rightarrow \text{PhCH} = \text{C(Ph)CN} \\
\text{PhCHSOCH}_2\text{Ph}
\end{align*}
\]

(22)
Steric repulsions due to the attack of a bulky carbanion may account for the lowered yield. Wallace\textsuperscript{84} has shown that decomposition of dibenzyl sulphoxide in KOBu\textsuperscript{+}/DMSO to 1,2-diphenylethylene occurs only in 8% yield at 80\textdegree C over a period of 20 hours, hence decomposition of the carbanion is a minor factor in accounting for a lowered yield. The applicability of this reaction to simple alkyl sulfoxides other than DMSO is difficult under similar conditions. Higher alkyl sulfoxides such as dipropyl sulfoxide would be expected to give a carbanion which is less stable than DMSO\textsuperscript{−} due to the electron donating properties of the alkyl group. Hence the equilibrium between DMSO\textsuperscript{−} and dipropyl sulfoxide carbanion would be expected to lie largely to the left.

\[ \text{CH}_3\text{SOCH}_2^- + \text{CH}_3\text{CH}_2\text{SOCH}_2\text{CH}_2\text{CH}_3 \rightarrow \text{CH}_3\text{SOCH}_3 + \text{CH}_3\text{CH}_2\text{SCHSOCH}_2\text{CH}_2\text{CH}_3 \]

An alternative practical method would be to generate the carbanion using the parent sulfoxide as the solvent. This method however, would be expensive and wasteful. There is also a limited availability of higher alkyl sulfoxides.

The generation of the carbanion from dipropyl sulfoxide was investigated in liquid ammonia using sodamide as base. A low yield of the adduct (23) from \(\alpha\)-phenylcinnamoneitrile was obtained under these conditions.
PhCH = C(Ph)CN $\xrightarrow{\text{Pr}_2\text{SO}}$ PhCH - CH(Ph)CN $\xrightarrow{\text{NaNH}_2}$ EtCHSOPr$^n$

The adduct (23) gave absorptions in the IR at 2,250 cm$^{-1}$ and an unusually weak one at 1,020 cm$^{-1}$. The methine proton $\alpha$ to the nitrile group absorbed in the NMR at 5.4 $\tau$ exactly the same position as found in the DMSO adduct. The mass spectrum showed a very weak molecular ion and a breakdown pattern that was consistent with those of the DMSO adduct.

Other polyfunctional sulphoxides have also been added to conjugated nitriles. Whilst this work was in progress Bergmann and Diller$^{85}$ added a $\beta$-keto sulphoxide to acrylonitrile and showed its synthetic utility by several transformations of the adduct (24)

PhCOCH$_2$SOCH$_3$ $\xrightarrow{\text{CH}$_2$=CHCN}$ PhCOCH$_2$SOCH$_3$

$\xrightarrow{\text{Cl}_2\text{CH}_2\text{CH}}$ $\xrightarrow{\text{H}^+/\text{H}_2\text{O}}$

PhCO(CH$_2$)$_3$CO$_2$H $\xleftarrow{\text{PhCOCH$_2$SOCH$_3$}}$ CH$_2$CH$_2$CO$_2$H

Vig et. al.$^{86}$ have also added the $\beta$-keto sulphoxide (25) produced from the reaction of isovaline ester with DMSO$^{-}$ to acrylonitrile. Reduction of the adduct (26) gave 1-cyano-6-methyl-heptan-4-one (27).
Undoubtedly there remains wide scope in the addition of other polyfunctional sulfoxide carbanions to conjugated nitriles.
REATIONS OF NITRILE ADDUCTS

The adducts of DMSO with conjugated nitriles form the basis of potential intermediates in the synthesis of other compounds. An investigation was made of some reactions of the adducts.

Reduction

Chaser\(^ {87}\) on reporting the use of sodium borohydride/cobaltous chloride for reducing sulfoxides to sulphides states that no general method is available which accomplishes the reduction in high yield under mild conditions with common laboratory reagents. It was found that reduction of 2,3-diphenyl-4-methylsulphinyl-butyronitrile with aluminium amalgam gives the corresponding sulphide in good yield although some sulphone remained. Separation by PLC was facilitated by the vast difference in \(R_f\) of sulfoxides and sulphides.

\[
\begin{align*}
\text{PhCH} &\text{-CH(Ph)CN} \quad \xrightarrow{\text{Al/Hg}} \quad \text{PhCH} &\text{-CH(Ph)CN} \\
\text{CH}_2\text{SOCH}_3 &\quad \text{CH}_2\text{SCH}_3
\end{align*}
\]

Under these mild conditions the nitrile group remained intact. The use of aluminium amalgam for cleaving activated sulfoxides is well known. Its use as a mild and possibly selective reducing agent for sulphone reductions does not seem to be well known.
In the reduction of the thiazolidone-1-oxide (28) with aluminium amalgam, as reported elsewhere in this thesis, a high yield of the sulphide (29) was obtained without any competing reactions and retention of the carbonyl group.

\[
\begin{align*}
\text{p-CH}_3\text{-Ph} & \quad \text{CO} \\
\text{CH}_2 & \quad \text{CHPh} \\
\text{SO} & \quad \text{S} \\
\text{(28)} & \quad \text{(29)}
\end{align*}
\]

The use of aluminium amalgam in this area warrants more detailed study.

**Pyrolysis**

Two convenient methods are available for the direct conversion of sulphoxides to olefins viz. base catalysed \(\beta\)-elimination\(^{88}\) and simple pyrolysis. Thermal elimination requires a somewhat higher temperature but is potentially a cleaner reaction. The only examples which have been studied in detail are aryl and alkyl sulfoxides by Kingsbury and Crem.\(^{89}\) Stereospecific cis-elimination is observed at 80\(^\circ\) and a less stereospecific process at higher temperatures.

\[
\begin{align*}
\text{RCH}_2\text{CH}_2\text{SOR} \quad \rightarrow \quad \text{R} - \text{CH} \quad \rightarrow \text{CH}_2 \rightarrow \quad \text{R} - \text{CH} = \text{CH}_2 + \text{HOSR}
\end{align*}
\]
Walling and Bollyky have studied in detail the pyrolysis of adducts of DMSO$^-$ with aryl conjugated olefins. They conclude that the reaction is quite general and provides an alternative to the number of better known olefin syntheses via a thermal $E_i$ mechanism.

It was of interest to examine the pyrolysis of an example of the adducts obtained in this work. Pyrolysis of 2,3-diphenyl-4-methylsulphinylbutyronitrile in refluxing diglyme gave, after purification, a 74\% yield of a white crystalline solid. Absorption in the IR occurred strongly at 2,220cm$^{-1}$ suggesting a conjugated nitrile. A strong singlet in the NMR at 7.5$^\circ$ in the region characteristic of a methyl group adjacent to an olefinic bond indicated that the compound was 2,3-diphenylacrylonitrile (31). The intermediate non-conjugated olefin (30) undoubtedly formed initially, must isomerise to give the more stable conjugated olefin (31).

$$\begin{align*}
\text{PhCH} - \text{CH(Ph)CN} & \quad \xrightarrow{\text{CH$_2$SOCH$_3$}} \quad \left[ \begin{array}{c}
\text{PhC} - \text{CH(Ph)CN} \\
\text{CH$_2$}
\end{array} \right] \\
\text{(30)} & \quad \xrightarrow{} \quad \text{PhC(CH$_3$)=C(Ph)CN} \\
\text{(31)}
\end{align*}$$

Surprisingly perhaps there is no evidence of this olefin having been prepared before. A number of carbanion condensations are known to occur less readily with ketones and the simple condensation between acetophenone and benzyl cyanide may be a case in point. A synthesis via the pyrolysis of the sulfoxide adduct appears to be a new route to olefins of this type.
It is difficult to conclusively assign a cis or trans structure to the olefin from the spectral data. The cis and trans analogues of α-phenylcinnamonitriles show absorption in the UV; the cis at 224 nm. \((\log E 4.36)\) and 295 nm. \((\log E 4.22)\) whilst the trans absorbs at 227 nm. \((\log E 4.27)\) and 312 nm. \((\log E 4.41)\).\(^9\) The olefin obtained \((31)\) absorbed in the UV at 289 nm. \((\log E 3.95)\).

Since a double bond migration is involved it is most likely to be the thermodynamically most stable olefin (i.e. trans) that is formed. The formation of the more stable trans conjugated olefin in pyrolysis has been observed by Hunter and Cram.\(^9\) in elimination reactions of 2,3-diphenyl-1-methylsulphinyl propane \((32)\).

\[
\text{PhCH}_2\text{CH(Ph)CH}_2\text{SOCH}_3 \rightarrow \text{PhCHC(Ph) = CH}_2 \quad 1.2\% \\
(32)
\]

\[
\begin{array}{c}
\text{Ph} \\
\text{C} = \text{C} \\
\text{Ph}
\end{array} \quad \begin{array}{c}
\text{CH}_3 \\
\text{C} = \text{C} \\
\text{H}
\end{array} \quad \begin{array}{c}
\text{Ph} \\
\text{C} = \text{C} \\
\text{Ph}
\end{array} \quad \begin{array}{c}
\text{Ph} \\
\text{CH}_3 \\
\text{H}
\end{array} \\
\text{86.3\%} \quad \text{12.5\%}
\]

As far as is known the pyrolysis of polyfunctional sulphoxides has not yet been systematically studied.
REACTION OF DMSO⁻ WITH 1,1-DICYANOETHYLENES

As an extension of the work with conjugated nitriles the addition of DMSO⁻ to substituted 1,1-dicyanoethylenes was investigated.

Malononitrile is one of the most reactive methylenic compounds in the Knoevenagel condensation. Condensation of benzaldehyde with malononitrile gave the required substituted 1,1-dicyanoethylene (33) in good yield in the presence of ammonium acetate.

\[ \text{PhCHO} + \text{CH}_2(\text{CH})_2 \rightarrow \text{PhCH} = \text{C(CN)}_2 \quad (33) \]

However, the condensation of benzophenone with malononitrile, using ammonium acetate as the condensing agent in the method described by Campagne et al. failed to give the required cyanoethylene (34).

\[ \text{Ph}_2\text{CO} + \text{CH}_2(\text{CN})_2 \rightarrow \text{Ph}_2\text{C} = \text{C(CN)}_2 \quad (34) \]

A mixture of benzophenone and malononitrile was recovered. The reaction of alkylidene and aryldene malononitrile derivatives with basic reagents is often extremely complex and has been reviewed. Simple addition of nucleophiles is rare. Malononitrile has been added to ethylidenemalononitrile (35) using piperidine to generate the carbanion.
The reaction of the dicyanoethylene (33) with DMSO\(^-\) at room temperature gave a tarry material. Column chromatography gave a small yield of a yellow crystalline material. The yellow colour suggested extensive conjugation which was confirmed by the UV spectrum (\(\lambda_{max} 352\ \text{nm}, \log\varepsilon 5.10\)). The evidence for the structure of this material was somewhat conflicting. Elemental analyses were in excellent agreement with the formula \(\text{C}_{16}\text{H}_{12}\text{N}_2\), supported by mass spectral evidence (ions of mass 256, 255, 254).

The IR indicated the presence of a conjugated nitrile, while a moderately strong bond at 1615 cm\(^{-1}\) could be indicative of aromatic \(\text{C} = \text{C}\) or \(\text{C} = \text{NH}\). Some support for this formula also came from the NMR spectrum, which showed one proton as a doublet, just clear of the aromatic H signal, and apparently coupled with a second proton underneath the aromatic envelope. The high coupling constant indicated a vicinal olefinic pair of protons. On this basis a structure such as (36) could be proposed.

\[
\text{CH}_3\text{CH} = \text{C(CN)}_2 + \text{CH(CN)}_2 \longrightarrow \text{CH}_3\text{CH}[^{\text{CH(CN)}}_2]_2
\]

(35)

An alternative structure (37) would also be in agreement with most
of the evidence except the NMR, where it is difficult to explain the apparently high coupling constant, unless special factors are operating.

Partial support for either of these structures comes from the mass spectral data. Schemes 4 and 5 may be drawn to rationalise some of the main breakdown fragments.

It is possible to rationalise the formation of the compounds (36) and (37) as depicted on the next page. The mechanistic pathway for the dimer (37) involves a 6 membered transition state compared to a 4 membered one for the isomer (36). Although the NMR is difficult to explain for compound (37) the mechanism strongly supports this structure for the product isolated.
POSTULATED MASS SPECTRAL BREAKDOWN OF ADDUCTS (36) and (37)

**ADDUCT 36**

\[ \text{Ph} \quad \begin{array}{c} \text{H} \\ \text{H} \end{array} \begin{array}{c} \text{CN} \\ \text{CN} \end{array} \rightarrow \text{PhC} = \text{C} = \text{CH} + \text{PhC} = \text{CN} + \text{HCN} \]

\[ m/e \ 102 \quad m/e \ 127 \quad m/e \ 27 \]

\[ m/e \ 256 \quad \rightarrow \quad m/e \ 153 \]

**ADDUCT 37**

\[ \text{Ph} \quad \begin{array}{c} \text{H} \\ \text{H} \end{array} \begin{array}{c} \text{C} = \text{N} \\ \text{CN} \end{array} \rightarrow \text{PhCH} = \text{C} = \text{C} = \text{NH} - \text{H} \rightarrow m/e \ 128 \]

\[ m/e \ 129 \quad + \quad \text{PhC} = \text{C} = \text{CN} \quad m/e \ 127 \]

\[ \text{Ph} + \text{HC} \equiv \text{C} - \text{C} \equiv \text{N} \]

\[ m/e \ 77 \quad m/e \ 51 \]

\[ \text{Ph} \quad \begin{array}{c} \text{H} \\ \text{H} \end{array} \begin{array}{c} \text{CN} \\ \text{CN} \end{array} \rightarrow \text{PhC} = \text{C} = \text{CN} + \text{PhC} = \text{C} = \text{H} + \text{HCN} \]

\[ m/e \ 127 \quad m/e \ 102 \quad m/e \ 27 \]

(The location of the positive charge is omitted)
POSTULATED FORMATION OF ADDUCTS (36) and (37)

Scheme 4

\[
\text{PhCH} = \text{C} (\text{CN})_2 + \text{DMSO}^- \rightarrow \text{PhCH} - \text{C} (\text{CN})_2 \rightarrow \text{PhCH} - \text{C} (\text{CN})_2 + \text{HCN}
\]

(36)

Scheme 5

\[
\text{PhCH} = \text{C} (\text{CN})_2 + \text{DMSO}^- \rightarrow \text{PhCH} - \text{C} (\text{CN})_2 \rightarrow \text{PhCH} - \text{C} (\text{CN})_2 + \text{HCN}
\]

(37)
ADDITION TO CONJUGATED KETONES

It seems appropriate at this point to discuss the effect of steric and electronic factors in Michael additions since these will be discussed in considering the addition of DMSO to the chalcone system (38).

\[
\begin{align*}
\begin{array}{c}
\text{CH} = \text{CH} - \text{CO} \\
\text{CH} = \text{CH} - \text{CO}
\end{array}
\end{align*}
\]

As will be discussed later in this section interest is centred round indirect or conjugate addition to unsaturated ketones. The presence of a carbon-carbon multiple bond attached to a carbonyl group allows the electron deficiency of the carbonyl group to be partially transferred to a more remote position. An excellent review on this subject is found in "The Chemistry of the Carbonyl Group".\(^5\)

For instance, methyl vinyl ketone can react with hydrogen cyanide in two ways; at low temperatures direct addition (1,2) takes place to give the cyanohydrin (39) whilst at room temperature conjugate addition (1,4) gives the \(\gamma\)-ketovaleronitrile (40).

\[
\begin{align*}
\text{CH}_2 = \text{CHOCH}_3 + \text{HCN} \xrightarrow{\text{RT}} \text{NCCCH}_2\text{CH}_2\text{COCH}_3 \\
\text{CH}_2 = \text{CHOCH}_3 + \text{HCN} \xrightarrow{\text{RT}} \text{CH}_2 = \text{CHC} - \text{CH}_3 \quad (39)
\end{align*}
\]
On the other hand, chalcone undergoes only conjugate addition

\[
\text{PhCH} = \text{CHOOPh} \quad \xrightarrow{\text{HCN}} \quad \text{PhCOCH}_2\text{CH(CN)Ph}
\]

Bond energy calculations for 1,2 and 1,4-addition processes indicate that 1,4-addition should be favoured by a considerable amount. Despite this, 1,2-additions are frequently observed. Thus mesityl oxide reacts with methylamine via conjugate addition but with ethyl magnesium bromide via direct addition.

\[
\begin{align*}
\text{(CH}_3\text{)}_2\text{C} - \text{CH} = \text{C}(-\text{O}^-)\text{CH}_3 \\
\text{(CH}_3\text{)}_2\text{C} = \text{CHOOCCH}_3 \\
\text{EtMgBr} \quad \xrightarrow{\text{CH}_3\text{NH}_2} \quad \text{(CH}_3\text{)}_2\text{C} = \text{CH} - \text{C} - \text{CH}_3 \\
\end{align*}
\]

There is a tendency for strong nucleophiles such as Grignard reagents and metal alkyls to undergo 1,2-addition and weaker nucleophiles such as methylamine to undergo 1,4-addition. For a given nucleophile the extent of the type of addition will be governed by steric and electronic factors. This is shown with ethyl cinnamate which adds methyl magnesium bromide in a direct fashion whereas ethyl benzalmalonate undergoes conjugate addition.

\[
\begin{align*}
\text{PhCH} = \text{CHO}_2\text{Et} \quad \xrightarrow{\text{CH}_3\text{MgBr}} \quad \text{PhCH} = \text{CHC(CH}_3\text{)}_2\text{OH} \\
\text{PhCH} = \text{C(O}_2\text{Et)}_2 \quad \xrightarrow{\text{CH}_3\text{MgBr}} \quad \text{PhCH(CH}_3\text{)}\text{CH(O}_2\text{Et)}_2
\end{align*}
\]
The reactivities at the carbonyl carbon and the $\beta$-carbon may also be sensitive to subtle changes in the nucleophile. For example, chalcone reacts with phenyl magnesium bromide to give 88% of the 1,2-adduct but with ethyl magnesium bromide only 40% of 1,2-adduct is formed and 60% of 1,4-adduct.

Several generalisations can thus be made for direct addition versus conjugate addition.

(1) Conjugate addition product increases with decreasing "carbonyl character" of the carbonyl group.

(2) Conjugate addition increases with increasing steric hindrance at the carbonyl group.

(3) Direct addition product increases with increasing strength of the nucleophile.

(4) Direct addition product increases with increasing steric hindrance at the $\beta$-position.

Previous work has shown that DMSO$^-$ adds readily to simple non-enolisable ketones to give the $\beta$-hydroxysulphoxide.$^9$ With the exception of one attempt to add DMSO$^-$ to methyl vinyl ketone no study has been made of the Michael addition of sulphoxide carbanions to $\alpha\beta$-unsaturated ketones.
The introduction of aromatic residues into the terminal positions of the system $C = C - C = C$ appears to increase its polar character and therefore its tendency to undergo the Michael condensation. In consequence of this benzylidene acetophenone (chalcone) seemed an excellent system to study. Its high molecular weight would be expected to produce a high melting solid readily isolated in the normal reaction procedure.

In fact chalcone has been the subject of numerous Michael condensations involving a wide range of addends e.g. diethylmalonate, ethyl acetoacetate, ethyl cyanoacetate, benzyl cyanide, deoxybenzoin, nitromethane, etc. A sulphenyl carbanion from p-tolylmethysulphone has also been added.

Chalcone itself is prepared in high yield by the base catalysed condensation of acetophenone with benzaldehyde. The condensing agent is usually aqueous sodium hydroxide. Some instances exist where acid catalysed condensations using $BF_3$ have been used. It was necessary for this work to have available a number of substituted chalcones. These were usually prepared using conditions similar to those suggested by Vogel. The chalcones were all low melting highly crystalline solids and were usually of a light yellow colour. Chalcones, as usually formed, show absorption in the IR characteristic of $\alpha,\beta$-unsaturated ketones in an $\alpha$-trans configuration, e.g. chalcone (41).
The absorption position of the carbonyl group was found to be greater than that of the olefinic group. The NMR did not show separate olefinic absorptions; the olefinic protons are sufficiently deshielded to resonate under the aromatic envelope.

Chalcone added as a 1:1 molar equivalent to DMSO\(^{-}\) at room temperature gave a dark brown solution. After 30 min, the reaction was quenched with ice and dilute HCl to give a yellow syrup which on trituration with ether gave a white solid shown to be homogeneous upon TLC. Recrystallisation from benzene gave white crystals which analysed for \(\text{C}_{17}\text{H}_{18}\text{O}_2\text{S}\) corresponding to the addition of one molecule of DMSO. Addition was shown to be 1,2 (42) by the absence of any absorption in the IR at 1690 cm\(^{-1}\) corresponding to a carbonyl group and the presence of a strong band at 3,390 cm\(^{-1}\) corresponding to a hydroxyl group. This was shown to be a tertiary hydroxyl group by repeating the NMR in DMSO-\(d_5\). Whilst this work was in progress Gautier et al.\(^{106}\) obtained the same result using DMSO\(^{-}\) generated in liquid ammonia.

\[
\begin{align*}
\text{PhCH} = \text{CHOOPh} \quad &\xrightarrow{\text{DMSO}^-} \quad \text{PhCH} = \text{CH} - \text{C} - \text{Ph} \\
\quad &\uparrow \quad \uparrow \\
&\quad \text{CH}_2\text{SOCH}_3
\end{align*}
\]
This was at first a surprising result since the vast majority of additions to the chalcone system result in 1,4-addition. To some extent the mode of addition can be controlled by temperature as mentioned in the introduction. However, in this case addition is 1,2 at -33° and also at 25°.

At this point mention may be made of the methods used to determine whether an adduct is 1,2 or 1,4. Examination of the crude reaction product (which is obtained as a white solid indicating that conjugation has been removed) was performed routinely by NMR, IR, and TLC before purification. In all cases only one adduct was detected. In the IR the presence of a peak at 1690 cm.⁻¹ indicated the 1,4-adduct, and in the NMR, absorption in the olefinic region indicates the 1,2-adduct. Besides TLC these criteria were used to determine which adduct was formed.

In an attempt to obtain 1,4 addition either the nucleophile or the chalcone system may be varied. Initial attempts were made by modifying the chalcone system.

It has been mentioned that conjugate addition is favoured by steric hindrance at the carbonyl group. In chalcone this can be achieved by substituting the ortho hydrogen atoms for example by methyl groups. The sterically hindered chalcones 2',4'-dimethylchalcone and 2',4',6'-trimethylchalcone were readily prepared from the readily available corresponding acetophenones. Reaction of DMSO⁻ with 2',4'-dimethylchalcone gave material (in
22% yield) identified as the 1,4-adduct (43), showing absorption in the IR at 1690 cm$^{-1}$ and 1020 cm$^{-1}$.

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

This was the first successful example of a Michael addition to $\alpha/\beta$ unsaturated carbonyl compounds with DMSO. Gautier, who since this work began has added DMSO$^-$ to a variety of chalcones has failed to obtain a 1,4-monoadduct. The inertness of the carbonyl group in 2',4'-dimethylchalcone is attributable to the fact that the carbonyl group is forced out of the plane of the adjacent phenyl ring by the ortho methyl group as may readily be seen with Dreiding models.

When a further methyl group was introduced no significant increase in yield was observed. Thus reaction of 2',4',6'-trimethylchalcone with DMSO$^-$ gave 31% of the 1,4-adduct (44).

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

It might be however that the inductive effect of the methyl groups causes a significant effect. This point is discussed later.
There appears to be no detailed investigation of the mode of addition of a nucleophile to a variety of substituted chalcones. The few cases that exist show no effect on the mode of addition by variation of the chalcone used. Thus Seter\textsuperscript{108} observed 1,4-addition only, of various nitroparaffins to 3-nitro and 3'-nitro chalcones.

It was thus of interest to see if 1,4 addition could be induced by manipulating the electron density at the olefinic bond. The effect of substituents on the addition of Br\textsuperscript{+} to double bonds is well known.\textsuperscript{109} Hence with the chalcone system an electron withdrawing group on ring A should decrease the electron density at the \(\alpha\)-carbon atom of the double bond and make it more susceptible to attack by a nucleophile. A similar effect should be observable with substituents on ring B.

Hence when 4-chlorochalcone was reacted with DMSO\textsuperscript{-} the adduct formed was the 1,4 Michael product. The product, although showing a moderate carbonyl absorption in the infra red at 1695 cm.\textsuperscript{-1}, gave a strong peak in the mass spectrum at m/e 105 attributable to PhCO\textsuperscript{+}.

This mode of addition is in accord with the fact that the \(+M\) effect of the chloro group is much less than the \(-I\) effect as witnessed by the pKa of 4-chlorobenzoic acid.\textsuperscript{110} The symbol \(+M\) designates those groups that, by resonance effects, supply electron
density to conjugated systems and those groups as -M that withdraw electron density from such systems. An analogous nomenclature applies to +I and -I.

This rationalisation assumes that a thermodynamic effect predominates since the pKa is a thermodynamic function; however a kinetic effect may upset the balance. 4-Fluorochalcone with DMSO gave a product that showed no carbonyl absorption and further spectral data showed it to be the 1,2 adduct. This apparently anomalous result is explained by the +I effect of the fluoro group being nearly equivalent to its -I effect as shown again by the pKa of p-fluorobenzoic acid.

Attempts to obtain addition to 4-nitrochalcone led to the formation of intractable tars. The effect of the nitro group on DMSO additions is dealt with elsewhere.

With 2-chlorochalcone and 2-bromochalcone 1,2 adducts were obtained. It is difficult to decide whether a steric or electronic effect predominates in this case. Kadesch has observed that the olefinic bond in chalcone, even when the adjacent phenyl group is substituted with two ortho methyl groups, has been shown to undergo 1,4 addition with HCl. Substitution of ring A by electron releasing groups would be expected to give similar results to those observed with chalcone. When 4-dimethylaminochalcone and 4-methoxychalcone were used as substrates 1,2 adducts were obtained as expected. Gautier et al. obtained similar products from the reaction of DMSO in liquid ammonia with these two chalcones, but
gave no spectral data on the adducts.

The NMR spectrum of both products showed interesting features. The olefinic protons gave an AB quartet with $J = 15$ Hz, indicating a trans configuration. This is to be expected since the starting chalcones themselves are also of trans configuration. What is of interest is the appearance of the methylene group as a singlet. It is well established that the sulphoxide group is chiral and that a prochiral methylene group gives an NMR absorption typical of an AB system. Indeed, in all compounds containing the system $-\text{CH}_2\text{SO}-$ examined in this work, this effect has been observed. The methylsulphinyl group absorbs at the usual position of 7.4 ppm. Intermolecular bonding as in (45) has been observed previously producing equivalent methylene protons.

![Diagram](45)

The actual explanation of the NMR pattern needs examination by variable temperature NMR.

4-Acetamidochalcone gave an enolate anion (46) with DMSO$^-$.

![Diagram](46)
An examination of the substituent effects in the B ring of the chalcone system was also made.

The methoxy group in 4'-methoxychalcone would be expected to deactivate the carbonyl group to nucleophilic attack and this is observed. The 1,4 adduct produced gives the expected PhCO absorption at 1690 cm⁻¹ in the IR spectrum. On the other hand 4'-chlorochalcone gives the 1,2 adduct. An unusual occurrence is observed with a methyl group in the 4' position. The presence of this single methyl group is sufficient to alter the mode of addition from 1,2 to 1,4. It has been noted that an alkyl substituent gives rise to an influx of electrons to the benzene ring by both inductive and hyperconjugative mechanisms.¹¹⁶ To see if a hyperconjugative mechanism was the predominant factor 4'-t-butylchalcone was made and reacted with DMSO⁻ under the same conditions. Friedel-Craft acetylation of t-butylbenzene (47) gave 4-t-butylacetophenone (48) which was condensed with benzaldehyde to give the chalcone (49).

\[
\begin{align*}
&\text{Bu}^t \quad \text{CH}_3\text{COCl} \quad \text{Bu}^t \quad \text{PhCHO} \\
&(47) \quad \text{COCH}_3 \quad \text{COCH} = \text{CHPh} \\
&(48) \quad (49)
\end{align*}
\]

Again solely 1,4 adduct was obtained thus ruling out a hyperconjugative mechanism. It thus appears that the weak inductive effect of the methyl group is sufficient to alter the electron
distribution in the molecule to give a complete reversal of addition. This result indicates that additions to chalcone with DMSO\(^{-}\) are delicately poised and that minor changes in the molecule are important. It is thus no surprise, in view of this reaction, that addition always occurs completely in one direction. The effects of a methyl group in altering the rate of aromatic reactions is well known, but such dramatic effects as above are exceptional.

A study was subsequently made of the interaction of steric and electronic factors. Previous attempts in the literature to obtain highly substituted chalcones have usually relied on the Friedel-Crafts reaction of substituted cinnamoyl chlorides with alkyl benzenes. However the normal base catalysed condensation was found to be effective although the yield was low. Thus 4-methoxy-2',4',6'-trimethylchalcone (50) was prepared using sodium hydroxide as base.

\[
\begin{align*}
\text{COCls}_3 + \text{MeO} &\xrightarrow{\text{HO}^-} \text{CHO} \\
\end{align*}
\]

In (50) the methoxy group encourages 1,2 addition and the ortho methyls 1,4 addition. With DMSO\(^{-}\) (50) gave solely 1,4 adduct. Hence it appears that the steric effect is much stronger than the electronic effect.

- 56 -
Confirmation of the structure of the adduct from (50) was provided by Raney nickel reduction to the sulphur free product (51).

\[ \text{PhCH} = \text{CHOOPh} \xrightarrow{\text{Ni/H}_2} \text{PhCH} = \text{CHCOPh} \]

Besides variation of the chalcone structure an investigation was made of the variation of the sulphoxide carbanion. Increasing the bulk of the substituents on the carbanion should promote 1,4 addition by an analogous argument to that discussed previously. Hence when dibenzyl sulphoxide was reacted with chalcone in DMSO the 1,4 adduct (52) was obtained. Confirmation of this structure was provided by reduction to the known ketone (52A) which was synthesised from the addition of benzyl magnesium bromide to chalcone.

\[ \text{PhCH} = \text{CHOOPh} \xrightarrow{(\text{PhCH}_2)_2\text{SO}} \text{PhCHCH}_2\text{COOPh} \xrightarrow{\text{Ni/H}_2} \text{PhCHSOCH}_2\text{Ph} \]

PhCH = CHOOPh \xrightarrow{\text{PhCH}_2\text{MgBr}} PhCHCH_2COOPh \xrightarrow{(A)} PhCH

The IR spectrum of (52A) synthesised via route A was identical to that from route B. However the NMR spectra, although similar, were not superimposable indicating differences in their stereochemistry.
With 4-methoxychalcone the 1,4 adduct was obtained again. As before the steric effect seems to outweigh the electronic effect and despite the increased electron density at the olefinic bond reaction occurs to give the Michael adduct exclusively.

The use of other \( \alpha/\beta \) unsaturated ketones has not been fully investigated in this work. Difficulties might be expected to arise in the use of enolisable ketones. Thus when cholest-4-en-3-one was reacted with DMSO\(^{-}\) no addition product was observed. Enolate anion formation occurs to the exclusion of addition.

![Diagram](attachment:image.png)

It may be that the use of Li\(^{+}\)\( \text{CH}_2\text{SOCH}_3 \) will encourage addition as has been observed with simple ketones.

A summary of the additions of DMSO\(^{-}\) to chalcones is found on the next page.
### Chalcone Adducts

<table>
<thead>
<tr>
<th>Substituent</th>
<th>Addition Type</th>
<th>Yield</th>
<th>M.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>1,2</td>
<td>64%</td>
<td>149-50°</td>
</tr>
<tr>
<td>2Cl</td>
<td>1,4</td>
<td>20%</td>
<td>202-6°</td>
</tr>
<tr>
<td>4Cl</td>
<td>1,4</td>
<td>13%</td>
<td>212-4°</td>
</tr>
<tr>
<td>4'Cl</td>
<td>1,2</td>
<td>21%</td>
<td>142-4°</td>
</tr>
<tr>
<td>4F</td>
<td>1,2</td>
<td>53%</td>
<td>206-7°</td>
</tr>
<tr>
<td>2Br</td>
<td>1,4</td>
<td>33%</td>
<td>195-7°</td>
</tr>
<tr>
<td>4MeO</td>
<td>1,2</td>
<td>73%</td>
<td>136-8°</td>
</tr>
<tr>
<td>4'MeO</td>
<td>1,4</td>
<td>28%</td>
<td>300°</td>
</tr>
<tr>
<td>4Me₂N</td>
<td>1,2</td>
<td>28%</td>
<td>168-9°</td>
</tr>
<tr>
<td>2',4' Dife</td>
<td>1,4</td>
<td>21%</td>
<td>120-2°</td>
</tr>
<tr>
<td>2',4',6' TriMe</td>
<td>1,4</td>
<td>31%</td>
<td>111-2°</td>
</tr>
<tr>
<td>4'Me</td>
<td>1,4</td>
<td>58%</td>
<td>202-4°</td>
</tr>
<tr>
<td>4'Bu⁺</td>
<td>1,4</td>
<td>10%</td>
<td>236-8°</td>
</tr>
<tr>
<td>4Me</td>
<td>1,2</td>
<td>16%</td>
<td>143-6°</td>
</tr>
<tr>
<td>Me</td>
<td>1,2</td>
<td>32%</td>
<td>168-9°</td>
</tr>
<tr>
<td>4Meo; 2',4',6' TriMe</td>
<td>1,4</td>
<td>50%</td>
<td>150-2°</td>
</tr>
</tbody>
</table>

* Reaction in Ammonia
CYCLIC ADDUCTS WITH CHALCONE

One of the main objectives of this work has been to open up new approaches to novel sulfoxide systems especially cyclic ones. The chalcone adducts described in the previous section seemed to have high potential as intermediates in the formation of cyclic sulfoxides.

Previous work with the chalcone system has shown its potential for forming cyclic systems. Thus ethylacetoacetate gives an unsaturated cyclohexanone (53).

\[
\text{CH}_3\text{OOCCH}_2\text{CO}_2\text{Et} + \text{PhCH} = \text{CHOPh} \rightarrow \text{Ph} \quad \text{(53)}
\]

Cyanoacetamide gives a ketopiperidine (54). A means of obtaining cyclic sulfoxides lies in the use of the dicarbanion of DMSO.

Kaiser and Beard have demonstrated that reactions typical of DMSO\(^{2-}\) may be performed; thus a ratio of benzophenone to DMSO\(^{2-}\) of 2:1 gives a di-adduct (55).

\[
2\text{Ph}_2\text{CO} + \bar{\text{CH}}_2\text{SOCH}_2 \rightarrow \text{Ph}_2\text{C(CH)}\text{CH}_2\text{SOCH}_2\text{C(OH)Ph}_2 \quad \text{(55)}
\]
Whether a dicarbanion is actually formed is open to dispute since a sulphoxide group is not a very good stabiliser of adjacent carbanions. However, reactions typical of DMSO$^{2-}$ are observed using a 2M equivalent of sodamide in ammonia to one of DMSO. In contrast to this we have noted that even though a large excess of sodium hydride in DMSO is used, reactions where there is a subsequent ionisation of the second methyl group of DMSO are not observed.

Whilst similar work was being planned with chalcone a group of pharmaceutically biased French workers led by Gautier reacted chalcone with DMSO$^{2-}$. In their publication they presented evidence for the cyclic sulphoxide (56).

![Chemical Structure](image)

However, from our previous work it is apparent that chalcone gives a 1,2 adduct with DMSO$^-$ generated in either DMSO or ammonia. If this is so, then the 1,2 adduct would be expected to cyclise preferentially to give a 5-membered ring (58) via the more stable carbanion (57).

![Chemical Structure](image)

- 61 -
Gautier's compound (56) was described as a crystalline solid with a melting point reported as 218°C and not as a range as would be expected. The mass spectral data quoted did not seem to conclusively favour (56).

Repetition of Gautier's work under the same conditions gave a crystalline solid melting over the range 202-12°C after one recrystallisation. TLC gave one spot and the mass spectrum was completely identical to that obtained by Gautier. When recrystallised the compound was not soluble enough in CDCl₃ to obtain an NMR spectrum. The NMR spectrum in DMSO-d₆ unfortunately is obscured in the region of 7.4 T and cannot be used to strongly support either (56) or (58).

To conclusively determine the formation of either a 5 or 6 membered ring the reaction of DMSO²⁻ with either α or β methyl substituted chalcones was attempted. The α methyl chalcone dypnone (59) was made by the AICl₃ catalysed condensation of acetophenone according to Calloway and Green usando methylene dichloride as solvent and not CS₂ as they state.

\[ 2\text{PhCOCH}_3 \rightarrow \text{PhC(Ch)} = \text{CHOOPh} \]  

(59)

Reaction with DMSO²⁻ can give either the 5 ring compound (60) or the 6 ring compound (61).
In the case of (60) the methyl signal would be expected to appear as a doublet in the region of $8 - 9 \tau$ and in (61) as a singlet in the same region, assuming there are no anisotropic effects from the conformations of the phenyl and sulphoxide groups.

When the reaction was performed there was a low yield of a crystalline solid which was readily deduced from the spectral data as the 1,2 adduct (62).

\[
\text{PhC}(\text{CH}_3) = \text{CHOOPh} \xrightarrow{\text{DMSO}^2-} \text{PhC} = \text{CH} - \text{C} - \text{Ph} \\
\text{CH}_2\text{SOCH}_3
\]

With $\beta$-methylchalcone a similar result was obtained, the 1,2 adduct being obtained in 30% yield. Both compounds were obtained by Gautier in a subsequent publication by reacting the chalcones with DMSO$^-$ generated in liquid ammonia. Consequently the cleavage of the cyclic adduct by Raney nickel was examined. (56) would be expected to give the alcohol 2-hydroxy-2,4-diphenyl-pentane (63) and (58) the alcohol 2-benzyl-3-hydroxy-4-phenyl-butane (64).

\[
\text{(56)} \xrightarrow{\text{Ni/H}_2} \\
\text{(58)} \xrightarrow{\text{Ni/H}_2}
\]

Cleavage of the adduct gave an oil which did not show a sulphoxide
absorption in the IR showing complete cleavage had occurred.
PLC gave one major product which showed an hydroxyl group
absorption in the IR. The NMR assignment was consistent with
structure (63).

\[
(7.8 - 8.2^\circ C)
\]

\[
\begin{align*}
\text{Ph} & \quad \text{OH} (s, 8.2^\circ C) \\
(d, 9.1^\circ C) & \quad (s, 8.4^\circ C) \\
\text{Ph} &
\end{align*}
\]

(63)

The 2 methyl groups are readily assignable. The singlet at 8.2 \( ^\circ C \)
was removed on deuteration. The methylene group is adjacent to
2 chiral centres and should appear as an AB quartet coupled to
the adjacent benzylic proton. Two overlapping AB quartets may
be detected in the region 7.8 - 8.2 \( ^\circ C \), broadened by coupling.

The minor product from PLC showed no OH group absorption in
the IR and deuteration had no effect on the NMR spectrum. It
seemed likely this product would be 2,4-diphenylpentane (65) from
reduction of (63).

\[
\begin{align*}
\text{Ph} & \quad \text{OH} \\
\text{Ph} & \quad \text{Ni/H}_2 \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

(63) \quad (65)

This is substantiated by the mass spectrum which gave a molecular
ion at m/e 224 and fragment ions at m/e 119, 105 and 91 as depicted
below.
The NMR of 2,4-diphenylpentane has been extensively studied for both the dl and meso compounds by Dostokilova and Schneider.\textsuperscript{120} It is difficult to assign our compound as either the meso or dl. Examination of the region around 8.8 \textsuperscript{7} shows 3 separate peaks whereas in the meso and dl forms there are 2 in each case. The 3 peaks may be interpreted as the overlapping of the doublets from the meso and dl compounds. This is consistent with a mixture of the meso and dl forms.

Hence we can conclude that the substituted thiane oxide (56) is a mixture of diastereoisomers with the phenyl groups cis and trans. It is of interest to note that Johnson\textsuperscript{121} has shown that in 4-substituted thiane-1-oxides the isomer bearing the axial oxygen is more stable. There appears to be little work however on the equilibration of thiane-1-oxides substituted in other positions, and whether this rule applies in these cases. The conformational situation in similar systems is worthy of more detailed investigation.

Thus it is established that a six membered ring is formed when DMSO\textsuperscript{2-} is reacted with chalcone in liquid ammonia. Gautier has since prepared a series of similar cyclic compounds and has
also obtained further 1,2-mono-adducts. As stated previously with chalcone DMSO\(^{-}\) in DMSO or liquid ammonia produces the 1,2 adduct. When the 1,2 adduct was reacted with an excess of sodamide in liquid ammonia the expected 5 ring compound was not obtained. Analysis of the highly crystalline product showed the absence of sulphur and an empirical formula (C\(_{15}H_{12-14}O\))\(_n\). Material identical in m.p. and IR and NMR spectra was obtained by reaction of chalcone with NaH in DMSO. The IR spectrum of this material indicated absence of hydroxyl, presence of aryl and alkyl groups, a carbonyl bond at 1690 cm\(^{-1}\), and in a generally uncomplicated spectrum strong absorption at 700 cm\(^{-1}\), indicative of a mono-substituted phenyl ring, with, however no band in the 770 - 730 cm\(^{-1}\) region, usually associated with this in alkyl substituted benzenes, although caution is needed in making assignments in the presence of polar substituents. The NMR showed the presence of aromatic and aliphatic protons in a ratio of 21:5. The aliphatic signals in the region of 5 - 6 were poorly resolved into two one proton triplets, plus possibly a 2 proton doublet or two one proton singlets, with a further unresolved broad one proton signal.

All of these signals are too low for a simple CH - CO - Ar system, and would indicate either direct substitution by an O - R residue, or disubstitution by olefinic or similar groups. The evidence seems to favour a dimeric structure of formula C\(_{30}H_{26}O_2\) (67) which is in good agreement with the analysis figures also, and would suggest that some hydride transfer was involved in its
formation. Since reaction of DMSO\(^-\) does not lead to formation of this material, whereas NaH/DMSO does, this hydride addition may well have occurred. Its formation in the sodamide reaction could indicate either that it derives from the α-hydroxy α-methylsulphinyl compound directly, or that under these conditions dissociation occurs to regenerate chalcone.

It is difficult to formulate a structure on the present evidence. Tentatively the sequence (66) to (67) is postulated, but clearly more work is needed to elucidate the structure of this material.

\[
\begin{align*}
\text{PhCH} = \text{CHOPh} & \quad \overset{\text{DMSO}^-}{\longrightarrow} \quad \text{Ph} - \text{C} - \text{CH}_2\text{COPh} \\
\text{Cl}_2\text{SOCH}_3 & \\
\downarrow & \\
\text{PhCH} = \text{CHOPh} & \quad \overset{\text{H}_2\text{O}}{\longrightarrow} \\
\end{align*}
\]

\[
\begin{align*}
\text{PhCH} = \text{CHOPh} & \quad \overset{\text{DMSO}^-}{\longrightarrow} \quad \text{Ph} - \text{C} - \text{CH}_2\text{COPh} \\
\text{Cl}_2\text{SOCH}_3 & \\
\downarrow & \\
\text{PhCH} = \text{CHOPh} & \quad \overset{\text{H}_2\text{O}}{\longrightarrow} \\
\end{align*}
\]
There remains the question of the formation of the cyclic adduct. Since the mono-adduct can be obtained by limitation of the amount of base, it would seem reasonable to assume that this is formed intermediately. This is contradicted by the failure to cyclise the mono-adduct on further treatment with base. It would seem unlikely that a dinsyl dianion could form, with subsequent concerted addition, or that addition of extra base should alter the initial mode of addition from 1:2 to 1:4, yet clearly, initial 1:4 addition with cyclisation is the most satisfactory explanation in theory.
NITRO ADDUCTS

Conjugated nitrocompounds are readily available by the Knoevenagel condensation of nitroalkanes with aldehydes. Their preparation is not as simple as that mentioned for chalcones and α-phenylcinnamalonitriles. Normally they were prepared by refluxing an ethanolic solution of a nitroalkane with an aromatic aldehyde using n-butylamine as the basic catalyst.

\[ R\quad \text{CHO} + \quad \text{CH}_2\text{CH}_2\text{NO}_2 \quad \xrightarrow{n\text{-BuNH}_2} \quad R\quad \text{CHO} + \quad \text{CH} = \text{C} \quad \text{NO}_2 \]

Attention was focussed on aromatic aldehydes in this reaction since aliphatic aldehydes do not give the nitro olefin, only the hydroxy nitro compound is isolated as discussed in a comprehensive review on condensations of aliphatic nitro compounds by Hass and Riley.\textsuperscript{122}

Initial attempts to induce Michael addition of DMSO\textsuperscript{-} to unsaturated nitro compounds in DMSO failed. For example, when 1-methyl-1-nitrostyrene was treated with DMSO\textsuperscript{-}/DMSO at room temperature an intractable tar was obtained. It seemed from our earlier work that compounds containing a nitro group tended to give tarry products. Previous experiments with 4-nitrochalcone (68), 2-(4-nitrophenyl)-3-phenylacrylonitrile (69), and 2-phenyl-3-2-(4-nitrophenyl)-acrylonitrile (70) had similarly given intractable products.
There are a number of references in the literature to the behaviour of unsaturated nitrocompounds which are pertinent to these observations.

Leseticky and Prochazka\textsuperscript{123} have observed that 1-nitro-alk-1-enes \textsuperscript{(71)} are isomerised to 2-nitro-alk-1-enes \textsuperscript{(72)} in KOBu\textsuperscript{+}/IMSO, and in addition unidentified polymers are obtained.

\[ \text{(71)} \quad \xrightarrow{\text{R}} \quad \text{(72)} \]

In an attempt to prepare nitrosubstituted ninhydrins, nitrophenaline esters have been reacted with CH\textsubscript{3}O\textsuperscript{-}/IMSO\textsuperscript{124}

\[ \text{(73)} \quad \xrightarrow{\text{(71+)} \text{NO}_2} \quad \text{(74)} \]

Products \textsuperscript{(73)} and \textsuperscript{(74)} not incorporating sulphur were obtained.
There appears a further complication in the addition of DMSO\textsuperscript{-} to unsaturated nitrocompounds. The postulated intermediate in the addition of DMSO\textsuperscript{-} to 1-methyl-1-nitro-styrene (75) is the nitro stabilised carbanion (76).

\[
\begin{align*}
\text{PhCH} = C \overset{\text{Me}}{\text{\scriptsize NO}_2} & \xrightarrow{\text{DMSO}^-} \text{PhCH} - C \overset{\text{Me}}{\text{\scriptsize NO}_2} \overset{\text{CH}_2\text{SOCH}_3}{\text{\scriptsize Me}} \\
(75) & \quad (76)
\end{align*}
\]

It is known that nitro stabilised carbanions can undergo the Nef reaction when neutralised with strong acids\textsuperscript{125} to give a ketone. Thus the carbanion (76) may be expected to give the ketone (77).

\[
\begin{align*}
\text{Me} & \quad 0 \\
\text{PhCH} - C = N & \quad H^+ \\
\text{CH}_2\text{SOCH}_3 & \quad \text{PhCHCOMe} \\
(76) & \quad (77)
\end{align*}
\]

The crude tar obtained from our reaction showed the presence of a weak absorption band in the IR at 1710 cm\textsuperscript{-1} indicating the partial occurrence of the Nef reaction. Attempts to isolate the Nef product with sodium bisulphite failed.

In view of this series of possible side reactions an extremely complex reaction seemed inevitable. However it was thought that some difficulties of the reaction might be overcome by the use of liquid ammonia as the reaction medium. Liquid ammonia has been
shown to be an excellent solvent for Michael additions although its use has not been extensive in this field. The lower temperature might be expected to minimise competing side reactions, and protonation by the weaker NH₄⁺ ion should be expected to minimise the Nef reaction.

This was borne out in practice. DMSO⁻ was generated with NaNH₂ at -33°C to -50°C and the nitro-olefin was added in dry ether. Neutralisation of the reaction mixture with excess ammonium chloride and evaporation of the solvent gave a sticky white residue. There was an absence of tar formation. Work up in the normal way gave a viscous colourless oil.

The NMR showed the oil to be a mixture of diastereoisomers of the DMSO adduct (78).

\[
\text{PhCH} = \text{C} \quad \xrightarrow{\text{DMSO}^-} \quad \text{PhCH} - \text{CH} \quad \xrightarrow{\text{Me}} \quad \text{Me}
\]

(75) (78)

The methylsulphinyl signal appeared as two singlets at 7.5 ppm. Similar evidence for the presence of diastereoisomers was presented by the rest of the spectrum.

A solution of the oil, in either toluene or acetone, kept at -30°C for several days deposited one of the diastereoisomers as a crystalline precipitate.
Addition was also successful with the nitrostyrene (79) formed from the condensation of phenyl nitromethane and benzaldehyde.

\[
\text{PhCH}_2\text{NO}_2 + \text{PhCHO} \rightarrow \text{PhCH = C} \begin{array}{c}
\text{Ph} \\
\text{NO}_2
\end{array} + \text{H}_2\text{O}
\]

(79)

The adduct obtained (80) was isolated in good yield.

\[
\text{PhCH = C} \begin{array}{c}
\text{Ph} \\
\text{NO}_2
\end{array} \xrightarrow{\text{DMSO}^-} \text{PhCH - CH} \begin{array}{c}
\text{Ph} \\
\text{NO}_2
\end{array} \begin{array}{c}
\text{CH}_2\text{SOCH}_3
\end{array}
\]

(79) (80)
REACTIONS OF THE NITRO ADDUCTS

The DMSO adducts of unsaturated nitrocompounds appear to have potential as intermediates in the synthesis of various compounds.

A preliminary experiment with the adduct (76) showed that the Nef reaction is capable of being applied to the nitro adducts in the novel synthesis of γ-ketosulphoxides. Thus treatment of the adduct (76) with aqueous KOH gave a solution of the potassium salt (81) which when acidified gave material having spectral data consistent with the structure (82).

\[
\begin{align*}
\text{PhCH} - \text{CH} & \quad \text{KOH} \\
\text{CH}_2\text{SOCH}_3 & \quad \xrightarrow{\text{KOH}} \quad \text{PhCH} - \overset{\text{K}^+}{\text{CH}} \\
\text{NO}_2 & \quad \xrightarrow{\text{HCl}} \quad \text{PhCH} - \text{COCH}_3 \\
(76) & \quad (81) & \quad (82)
\end{align*}
\]

Thus the oil obtained absorbed in the IR at 1710 cm\(^{-1}\) and the NMR was consistent for the impure ketone (82) showing a singlet at 7.9 \(\tau\) attributable to \(\text{CH}_3\)-CO.
It was considered that non-enolisable β-diketones would be suitable intermediates for the formation of cyclic sulfoxides via the postulated DMSO dicarbanion.

Benzil, a typical β-diketone is readily available commercially. With bases e.g. CN⁻ or HO⁻ benzil undergoes the benzilic acid rearrangement, but with strong nucleophiles such as Grignard reagents, addition normally takes place without rearrangement. Numerous examples of these additions are known. Occasionally, and particularly with hindered Grignard reagents, rearrangements do occur. Thus 2-methyl-phenylmagnesium bromide with benzil gives 70% of the normal adduct (83) and 30% of the rearranged product (84).

![Chemical diagram]

Similar results are observed with mesityl magnesium bromide. The addition of carbonyl-stabilised carbanions to benzil is well known. In the synthesis of tetraphenyl cyclopentadienone (86) the intermediate hydroxy compound (85) dehydrates spontaneously to form the stabilised conjugated olefin.
An example in sulphur chemistry is the Hinsberg thiophene synthesis\textsuperscript{128} e.g.

The intermediate (87) dehydrates to give a product (88) stabilised by extensive conjugation over the phenyl rings and the carbethoxy groups.

Preliminary investigation of the reaction of DMSO\textsuperscript{-} with benzil at room temperature was disappointing. Work up of the reaction in the normal way gave a brown tarry oil. Whilst this work was in progress it was found that previous work on a similar system had been reported by Trisler et al. In Trisler's case benzil had been reacted with phenoxide ion in DMSO to give several products (see scheme I in the introduction). Although the mechanism invoked involved the addition of DMSO\textsuperscript{-} to benzil no products involving
sulphur were obtained. The following scheme illustrates the formation of \( \alpha/\beta \)-dibenzoylstyrene (89).

\[
\begin{align*}
\text{PhCOOCOPh} + \text{DMSO}^- &\rightleftharpoons \text{PhCO} - \overset{\text{O}^-}{\mid} \overset{\text{Ph}}{\mid} \overset{\text{CH}_2\text{SOCH}_3}{\mid} \\
\text{HO}^- + \text{PhC} = \text{CHOOPh} &\rightarrow \text{PhCOOCOPh} \quad \text{base} \quad \text{PhCO}_2\text{C}_2\text{Ph} \\
&\rightarrow \text{PhCO} - \overset{\text{O}^-}{\mid} \overset{\text{Ph}}{\mid} \overset{\text{CH}_2\text{SOCH}_3}{\mid} \\
\end{align*}
\]

(89)

The same products were also obtained when DMSO\(^-\), made by the irreversible reaction of sodium hydride with DMSO, was reacted with benzil, with coincident tar formation.

With DMSO\(^2-\) in liquid ammonia benzil reacted smoothly to give a low yield of a white solid. Absorption in the IR at 1020 cm\(^{-1}\), 3540 cm\(^{-1}\) and 3,300 cm\(^{-1}\) indicated the presence of the groups SO and OH. The NMR showed 2 slightly separated singlets which were removed on deuteration and 2 superimposed AB quartets in the region of \(-\text{CH}_2\text{-SO}-\) absorption. The presence of adducts of the type (90) and (91) are discountable in the absence of any methylsulphinyl absorption at 7.4 \(\delta\).

\[
\begin{align*}
\text{PhCO} - \overset{\text{O}^-}{\mid} \overset{\text{Ph}}{\mid} \overset{\text{CH}_2\text{SOCH}_3}{\mid} \\
\text{CH}_3\text{SOCH}_2 - \overset{\text{C}^-}{\mid} \overset{\text{O}^-}{\mid} \overset{\text{Ph}}{\mid} \overset{\text{CH}_2\text{SOCH}_3}{\mid} \\
\end{align*}
\]

(90) (91)
At this stage an apparent deduction would be that the product was a mixture of the *cis* (92) and *trans* (93) substituted tetrahydrothiophene-s-oxide.

![Chemical structures](image)

Desulphurisation by the action of Raney nickel in boiling ethanol gave the desulphurised product as a crude oil. PLC gave a crystalline solid which gave spectral data consistent for a 2,3-diphenylbutan-2,3-diol (94).

![Chemical structure](image)

This diol has been extensively studied in its meso and dl forms. Cram and Kopecky\(^{129}\) were able to assign a configuration on the basis of IR data. The meso form absorbed at 1335 cm.\(^{-1}\), 1129 cm.\(^{-1}\) and 1111 cm.\(^{-1}\) all of which were absent in the IR of the dl form which gives characteristic peaks at 1356 cm.\(^{-1}\) and 1143 cm.\(^{-1}\).

In our case examination of the IR spectra of both crude and purified material showed absorption characteristic of the meso configuration but not the dl.
Further evidence is provided by the position of the hydroxyl resonance in the NMR. Agahigian et al.\textsuperscript{130} have shown that the meso form differs in its NMR spectrum from the dl form. Observation of the NMR of our compound supported assignment of a meso configuration.

Recrystallisation of the material raised the melting point to 117-8\textdegree in agreement with the literature value for the meso compound. Hence the cyclic sulphoxide has a cis configuration of the hydroxyl groups. The NMR spectrum of the products can thus be explained as an approximate 1:1 mixture of structures (95) and (96).

Further confirmation of structures (95) and (96) is provided by their facile cleavage with sodium metaperiodate. From the work of Criegee\textsuperscript{131} and others it is well established that cis-1,2-glycols are attacked more rapidly than the trans isomers. With the similar compound 1,2-dihydroxycyclopentane the cis isomer reacts 3,000 times faster than the trans isomer.\textsuperscript{132} Thus cleavage of the sulphoxide (95) or (96) gave the 1,5-diketone (97).
The diketone (97) showed strong absorption in the IR at 1690 cm\(^{-1}\). In the NMR the methylene protons gave an unresolved broad signal and not a sharp AB quartet as might be expected.

Attempts to form an isopropylidene derivative (98) from acetone and the sulphoxide (95) failed.

\[
\begin{align*}
\text{HO} & \quad \text{OH} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

\[
\begin{align*}
\text{SO} & \quad \text{(CH}_3\text{)}_2\text{CO}
\end{align*}
\]

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

\[
\begin{align*}
\text{SO} & \quad +\text{H}_2\text{O}
\end{align*}
\]

The condensing agent used was p-toluenesulphonic acid.

Oxidation of a sulphoxide to a sulphone removes the chirality at the sulphoxide centre. In our case the NMR spectrum should be simplified by coalescence of the separate AB quartets corresponding to structures (95) and (96) and thus verify our interpretations.

Despite repeated attempts with hydrogen peroxide as oxidising agent no sulphone was obtained either in neutral or acidic conditions. It appears that attack of hydrogen peroxide at the sulphur atom is prevented by steric hindrance of the hydroxy and phenyl groups. Construction of models supports this as a possible explanation.
It is surprising perhaps that dehydration of the sulphoxide (95) to the stabilised thiophene-1-oxide (99) does not occur during the formation of the former.

\[
\text{Ph} \quad \text{Ph} \quad -2\text{H}_2\text{O} \quad \text{Ph} \quad \text{Ph}
\]

(95) (99)

No dehydration was observed during the attempted oxidation of (95) in acetic acid.

Although with the corresponding ketone dehydration occurs during formation to give the stabilised cyclopentadienone no enhanced stability is gained by forming a conjugated sulphoxide.

The scope of the reaction of DMSO\(^2\)- with benzil as a means of preparing further substituted tetrahydrothiophene oxides was investigated by studying the reaction of other sulphoxides with benzil. Variation of the groups R and R' in the sulphoxide \(\text{RCH}_2\text{SOCH}_2\text{R'}\) would be expected to give tetrahydrothiophene oxides substituted in positions 2 and 5.

\[
\text{Ph} \quad \text{Ph} \quad \text{R} \quad \text{R'} \quad \text{SO}
\]

- 81 -
With dibenzyl sulphoxide no adduct was formed and starting material was largely recovered. The bulk of the substituents on the sulphoxide group apparently prevent reaction, as in the case of the chalcone series where attempts to form a cyclic system from chalcone and dibenzyl sulphoxide also failed. It is unlikely that the weaker nucleophilicity of dibenzyl sulphoxide carbanion is a major factor in the failure of addition.

The addition of dipropyl sulphoxide is currently under investigation. Cyclic addition has occurred and the structure of the product(s) is being determined.

As well as varying the nature of the sulphoxide carbanion a short study was also made of substituted benzils. Benzils are readily available via the benzoin condensation and subsequent oxidation of the benzoin (100).

\[
\begin{align*}
\text{2PhCHO} & \rightarrow \text{PhCH(OH)COPh} & \text{[O]} & \rightarrow \text{PhCOCOPh} \\
\end{align*}
\]

(100)

Anisoin (4,4'-dimethoxybenzoin), furoin and 4,4'-dichlorobenzoin were oxidised smoothly and in high yield by copper acetate/ammonium nitrate in boiling acetic acid according to the method described by Vogel.\textsuperscript{133}

The reaction of anisil with DMSO\textsuperscript{2-} gave no adduct and anisil was largely recovered. The electron donating methoxy groups appear
to be sufficient to deactivate the two carbonyl groups to nucleophilic attack.

Furoin under similar conditions gave a tar showing a continuous streak on TLC. The extensive decomposition of furan derivatives with DMSO\(^{-}\) has been discussed on page 31.

Another class of dicarbonyl compounds investigated were quinones. Quinone itself has some reactions typical of an unsaturated ketone. However, there are examples where non-conjugate addition to the quinone carbonyl group occurs. Thus it has been observed\(^{134}\) that quinone gives a di-adduct \((101)\) with two moles of sodium acetylide.

\[
\begin{align*}
\text{\text{0}} & \quad \text{+2Na}^{+} \quad \text{C} \equiv \text{CH} \rightarrow \\
\text{\text{0}} & \quad \text{\text{o}} \quad \text{C} \equiv \text{CH} \\
\text{\text{0}} & \quad \text{\text{o}} \quad \text{C} \equiv \text{CH}
\end{align*}
\]

\((101)\)

It was thought that DMSO\(^{2-}\) might form a bridged compound \((102)\) by di-addition with a quinone.

\[
\begin{align*}
\text{\text{0}} & \quad \text{DMSO}^{2-} \quad \rightarrow \\
\text{\text{0}} & \quad \text{\text{o}} \quad \text{SO} \quad \text{0}^{-} \\
\text{\text{0}} & \quad \text{\text{o}} \quad \text{C} \equiv \text{CH}
\end{align*}
\]

\((102)\)
When 1,4-naphthaquinone was reacted with $\text{DMSO}^{2-}$ no reaction was observed after a period of 5 hr., the naphthaquinone being recovered unchanged. A similar result was obtained with anthraquinone.

Carbocyclic systems of the type (103) are "well known" and the replacement of the central carbon atom by sulphur should not produce instability

\[ \text{(103)} \]

It may be that the addition of $\text{DMSO}^{2-}$ is reversible and the intermediate (104) does not cyclise

\[ \text{(104)} \]

The planar configuration is energetically stable and may not allow the methyl sulphinyl group to approach within a reasonable bonding distance of the other carbonyl group.
SYNTHESIS OF CYCLIC $\beta$-KETOSULPHOXIDES

As mentioned in the introductory survey $\beta$-ketosulphoxides have extensive utility in synthetic organic chemistry. However, no study has been made of the preparation and reactions of cyclic $\beta$-ketosulphoxides.

Cyclic $\beta$-ketosulphones have been known for a long time. The thianaphthene-1-dioxide (106) was prepared in 1926 by peroxide oxidation of the corresponding sulphide (105).\(^{135}\)

\[
\begin{align*}
&\text{(105)}

&\text{H}_2\text{O}_2

&\text{(106)}
\end{align*}
\]

Truce and Knospe\(^{136}\) have obtained tetrahydrothiopyran-3-one-1-dioxide (108) from the cyclisation of ethyl $\beta$-methylsulphonyl-butyrolactone (107) with sodium ethoxide.

\[
\begin{align*}
&\text{CH}_3\text{SO}_2(\text{CH}_2)_3\text{CO}_2\text{Et} \quad \text{NaOEt}

&\text{(107)}

&\text{(108)}
\end{align*}
\]

Examples of cyclic $\beta$-ketosulphoxides are few. Those that do exist have other functional groups present.
Schroeder and Dodson during the study of pyrimidothiazines obtained a pyrimidothiazine-S-oxide (110) by perbenzoic acid oxidation of the corresponding sulphide (109).

Recently Glue et al. oxidised 2,2-dialkyl-1,3-oxathiolan-5-ones, made by the acid catalysed removal of water from an aliphatic ketone and thioglycollic acid, to the corresponding sulphoxide (111).

In this case hydrogen peroxide in acetic acid was used as the oxidant.

There are several possible synthetic routes to cyclic β-ketosulphoxides. The method used by Truce for β-ketosulphones is of limited applicability for sulphones and would be of little use for sulphoxides since more basic conditions would be needed forming a variety of competing ions.
A possible route is by the cyclisation of the DMSO nitrile adduct (9) described previously, to give an imine (112) which on hydrolysis would give the ketone (113)

This reaction sequence was attempted using the \( \omega \)-phenylcinnamonnitrile to generate the adduct (9) \textit{in situ} with DMSO\(^{-2} \) in liquid ammonia. A white crystalline solid was obtained which had spectral data inconsistent with either of the structures (112) and (113). Thus the IR spectrum showed a non-conjugated nitrile absorption at 2240 cm\(^{-1} \) and a strong sulphoxide absorption at 1040 cm\(^{-1} \). An elemental analysis, although poor for C and H, was accurate for S and N, and indicated a dimer. The mass spectrum substantiated this deduction showing peaks in the region m/e 300 - 400. Two dimeric structures (114) and (115) are feasible by mechanistic schemes depicted below.
Structure (115) was confirmed by NMR. There was an absence of a singlet at 7.4 \( \tau \) attributable to \( \text{CH}_3\text{SO} \) and the integration ratio of aromatic to aliphatic protons confirmed a dimeric structure. Two pairs of doublets centred at 5.6 \( \tau \) and 5.75 \( \tau \) were consistent with the methine protons \( \alpha \) to the nitrile groups.

Attempts to cyclise the adduct (9) directly with excess sodamide in liquid ammonia failed, the unchanged starting material being recovered. Presumably ionisation occurs \( \alpha \) to the nitrile group without further reaction.

The simplest and probably the most convenient synthesis of cyclic \( \beta \)-ketosulphoxides is the oxidation of the corresponding \( \beta \)-ketosulphide. Investigations were commenced with thiazolidinones, an interesting class of compounds which contain a cyclic \( \beta \)-keto-sulphide residue. Thiazolidinones have been reviewed by Brown and are of pharmacological interest. Kumar et. al\textsuperscript{140} have investigated the anticonvulsant properties of thiazolidinones of the type (116) where \( R' = 2 \text{ or } 4\text{-chlorophenyl and } R' = \text{furfuryl} \)

\[ \text{(116)} \]

\[
\begin{align*}
\text{O} & \quad \text{N} \quad \text{S} \\
\text{R} & \quad \text{N} = \text{CHR'} \\
\end{align*}
\]

Fungistatic thiazolidinones of the type (117) have been successfully screened against Aspergillus niger by Choubey and Singh\textsuperscript{141}.
The method of Surrey\textsuperscript{142} was adopted for the preparation of 4-thiazolidinones.

4-thiazolidinones have been oxidised previously but in all cases the product isolated was the sulphone. Thus several 4-thiazolidinones of the type (118), where \( R' \) is an alkyl or substituted alkyl group and \( R \) was phenyl or substituted phenyl, have been oxidised with hydrogen peroxide.\textsuperscript{143}

\[
\begin{align*}
\text{R} & \quad \text{N} & \quad \text{O} \\
\text{S} & \quad \text{N} & \quad \text{O} \\
\text{H}_2\text{O}_2 & & \\
\text{R'} & \quad \text{N} & \quad \text{O} \\
\text{S} & \quad \text{R} & \quad \text{SO}_2
\end{align*}
\]

(118)

Similar results were obtained with potassium permanganate.\textsuperscript{144}

Thus if the sulphone were to be produced care would have to be taken to choose a suitable oxidising agent.

Since the first recorded synthesis of a sulphone by Marcker\textsuperscript{145} in 1865 numerous methods have been developed for the transformation of sulphides to sulphones. Leonard and Johnson\textsuperscript{146} have shown the wide applicability of sodium metaperiodate as a suitable reagent for
this transformation. The oxidation probably proceeds via a cyclic mechanism analogous to that observed for oxidation of $\alpha$-glycols with the same reagent.

\[
S + IO_4^- \rightarrow S \xrightarrow{O} I \xrightarrow{O^-} S = O + IO_3^-
\]

A preliminary experiment with tetrahydrothiophene (119) and sodium metaperiodate gave a good yield of the oxide (120).

With 2-phenyl-3-$p$-tolythiazolidin-4-one (121) oxidation proceeded smoothly to the S-oxide (122) in 73% yield.

The S-oxide (122) was obtained as a highly crystalline solid showing strong absorption in the IR at 1710 cm$^{-1}$ and 1060 cm$^{-1}$. The methylene group appeared as a single AB quartet in the NMR centred at 6.3 $\tau$. No over-oxidation to the sulphone was observed and no amine oxide was formed.
Oxidation of the thiazolidinone (121) with hydrogen peroxide gave the expected sulphone (123)

\[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{S} & \quad \text{N} \\
\text{Me} & \quad \text{Ph} \\
\end{align*}
\]

An attempt to cleave the thiazolidinone-S-oxide (122) to the corresponding ketone failed with aluminium amalgam. Instead reduction to the sulphide (121) occurred in high yield.

Using a more powerful reducing agent such as Raney nickel desulphurisation occurred to give the disubstituted acetamide (124).

\[
\begin{align*}
\text{Ph} & \quad \text{SO} \\
\text{N} & \quad \text{C} \\
\text{Me} & \quad \text{Ph} \\
\end{align*}
\]

The acidic methylene group in thiazolidinones has been extensively utilised for carbanion reactions. With the novel thiazolidinone-S-oxide ring system there exists the potential of building up various structural units via a carbanion stabilised by both a carbonyl group and a sulfoxide group.
The thiazolidinone system was a convenient starting point for the formation of a cyclic \( \beta \)-ketosulphoxide. However it was thought that a compound containing just the \( \beta \)-ketosulphoxide grouping should be prepared to study the chemistry of cyclic \( \beta \)-ketosulphoxides.

As stated previously the best starting point for the preparation of a cyclic \( \beta \)-ketosulphoxide is the corresponding sulphide. 3-ketothiacyclohexane (125) was obtained by a similar method to Leonard and Figueras.\(^{147}\)

\[
\begin{align*}
\text{CH}_2\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Me} \quad \text{NaS} \quad \text{CH}_2\text{CO}_2\text{Et} \quad \text{CO}_2\text{Et} \\
\text{CH}_2 & \quad \text{Cl} \quad \text{Cl} \quad \text{CO}_2\text{Me} \quad \text{CO}_2\text{Me} \quad \text{OR} \\
\text{(125)} & \quad \text{OR} \quad \text{CO}_2\text{H} \quad \text{CO}_2\text{Me}
\end{align*}
\]

Oxidation of 3-ketothiacyclohexane with sodium metaperiodate in methanol/water gave a low yield of the ketosulphoxide (126).

\[
\begin{align*}
\text{(125)} & \quad \text{NaIO}_4 \quad \text{(126)} \\
\end{align*}
\]
The low yield is surprising since periodate oxidations usually occur in high yield. Probably the highly polar molecule being of low molecular weight is tightly retained in the aqueous phase during work up. The ketosulphoxide (126) is readily characterised in the NMR by the methylene group in the 2 position appearing as an AB quartet \((J = 14 \text{ Hz.})\) at 6.2 \(\tau\) sufficiently deshielded not to be included in the methylene envelope.
EXPERIMENTAL

Unless otherwise stated the following conditions apply.

Melting points were measured on a Kofler hot stage apparatus and are uncorrected.

Infra red spectra were determined using a chloroform or carbon tetrachloride solution for solids, or using thin films in the case of liquids, on Perkin-Elmer 237 or 257 grating spectrophotometer.

Ultraviolet spectra were determined in methanolic or ethanolic solutions on a Unicam S.P. 800 spectrophotometer.

N.m.r. spectra were measured with a Perkin-Elmer 60 MHz instrument. Resonance lines are reported in (ppm) units; tetramethyldisilane was used as the internal reference. Unless otherwise stated, the ppm-value quoted for a doublet (or multiplet) is the mid-point of the doublet (or multiplet).

Mass spectra were obtained on an A.E.I. MS12 spectrometer.

The majority of elemental analyses were carried out by Beller, Microanalytisches Laboratorium Gottingen. The remainder were determined at Hatfield Polytechnic and Nottingham University.

Thin layer chromatography (t.l.c.) was carried out with silica gel GF 254 (0.25 mm. layers). Spots were detected by iodine vapour or UV light. Preparative thin layer chromatography (p.l.c.) was performed on plates, 20 cm. x 20 cm. (1.0 mm. layers) spread with silica gel PF 254.
Dimethyl sulfoxide was dried over calcium hydride for a minimum of 3 days and distilled in vacuo for immediate use. Sodium hydride, obtained as a 50/50 dispersion in oil, was washed at least three times with twice its volume of dry petroleum ether before use.

Diethyl ether and petroleum ethers were dried with sodium wire.

The following abbreviations are used in the text:

- s = singlet
- d = doublet
- t = triplet
- q = quartet
- m = multiplet
- b = broad
- w = weak
- sh = shoulder

Unless otherwise stated NMR were determined in deuterochloroform.
Attempted Reaction of Dibenzyl Sulphoxide with Ethyl Benzoate

(a) Using Sodium Methoxide

A solution of dibenzyl sulphoxide (1.2 g., 0.05 mol.) in methanol (25 ml.) was added to a stirred solution of sodium (1.2 g., 0.05 mol.) in methanol (50 ml.). After 30 min. ethyl benzoate (0.75 g., 0.05 mol.) was added. No colour change took place and the solution was heated under reflux for 1 hr., cooled to room temperature, and left overnight. The solution was evaporated to dryness and the resulting residue taken up in chloroform. The chloroform solution was washed with dilute hydrochloric acid, dried and evaporated in vacuo to give a white solid (1.2 g.) after trituration with ether. The IR spectrum was identical with that of dibenzyl sulphoxide.

(b) Using Potassium t-Butoxide

t-Butanol was distilled from sodium before use. Dibenzyl sulphoxide (2.3 g., 0.1 mol.) in t-butanol (25 ml.) was added to a solution of potassium (3.9 g., 0.1 mol.) in t-butanol (100 ml.) and stirred for 1 hr. Ethyl benzoate (1.5 g., 0.1 mol.) was added to the stirred solution which was then heated at 80-90°C overnight. The reaction mixture was then cooled to room temperature and poured in to dilute hydrochloric acid (50 ml.). The mixture was extracted with chloroform and the organic phase dried and evaporated down to an oil which when triturated with ether gave a white solid. The IR spectrum was identical with that of dibenzyl sulphoxide.
Attempted Reaction of Diphenylsulphinylmethane with Benzophenone

A solution of diphenylsulphinylmethane (284 mg., 0.001 mol.) and sodium methoxide (108 mg., 0.002 mol.) in anhydrous methanol (50 ml.) was left for 30 min. Benzophenone (182 mg., 0.001 mol.) in methanol (10 ml.) was added and the solution left to stand overnight. Methanol was removed in vacuo and the residue triturated with ether. The white solid obtained (150 mg.) had an identical IR spectrum to that of diphenyl sulphinylmethane.

Reaction of DMSO\(^{-}\) with Diethyl Oxalate

DMSO\(^{-}\) (0.08 mol.) was reacted at room temperature with diethyl oxalate (5.8 g., 0.04 mol.) for one hour to give a dark solution. Work up according to method A with dilute hydrochloric acid gave a dark oil. Backwashing with water 6 times gave an oil (2.0 g.) shown by IR to be DMSO.

Reaction of DMSO\(^{-}\) with Ethyl Benzoate

Ethyl benzoate was dried over magnesium sulphate and distilled in vacuo before use. Use of ethyl benzoate (7.5 g., 0.05 mol.) and DMSO\(^{-}\) (0.1 mol.) in the general procedure gave a yellow reaction mixture. After 30 min. the reaction mixture was quenched with ice and adjusted to pH 4-5 with dilute hydrochloric acid. The mixture was extracted with chloroform, washed with sodium bicarbonate solution, and evaporated down to an oil. Trituration with ether gave \(\mu\)-methylsulphinyl-
acetophenone (7.0g., 80%). m.p. 81-3°. Further washing with ether raised the melting point to 84-5° (lit. 9, 86-86.5°). ν\text{max.} (nujol) 1680(s), 1040(s), 1025(s) cm\textsuperscript{-1}. τ 1.8-2.6 (m,5H), 5.55 and 6.0Hz. (q, 2H, J=13.5 Hz), 7.2 (s,3H).

**Reaction of Ethyl Phenylacetate with DMSO\textsuperscript{-}\)**

DMSO\textsuperscript{-} (0.05 mol.) reacted with ethyl phenylacetate (8.2g., 0.05 mol.) at room temperature for one hour, was quenched with dilute hydrochloric acid to produce a yellow oil. Work up according to the one described on page 99 gave a white solid on trituration with ether. Recrystallisation from ethanol gave white plates of phenylacetic acid, m.p. 76-7° (lit. 148 77°). τ (CCl\textsubscript{4}): -2.1 (S,1H), 2.7 (S,5H), 6.5 (S,2H).

**Preparation of Aniline-N-cinnamylidene**

Crude aniline-N-cinnamylidene was obtained as a student preparation from the reaction of aniline with cinnamaldehyde. Recrystallisation from ethanol gave yellow crystals m.p. 106-8° (lit. 149 109°). ν\text{max.} 1640(s), 1615(s), 1590(s) cm\textsuperscript{-1}.

**Reaction of Aniline-N-cinnamylidene with Methylsulphinyl Carbanion**

Use of aniline-N-cinnamylidene (2.1g., 0.01 mol.) and DMSO\textsuperscript{-} (0.01 mol.) in the general method described later gave a dark coloured reaction mixture. The mixture was poured on to ice and
neutralised with acetic acid. Extraction with chloroform gave a brown-black solution which was washed with water, dried and evaporated down to a black viscous oil. Chromatography on neutral alumina using ether gave a lighter coloured oil. Examination by T.L.C. indicated the presence of at least six components and the experiment was abandoned.

General Procedure for the Preparation and Reaction of Dimethylsulphoxide Carbanion

Sodium hydride (50% mineral oil dispersion) was weighed under dry distilled petroleum ether (b.p. 40 - 60°C) and added as a slurry to a three-necked round-bottomed flask. The hydride was washed 3 times with further quantities of petroleum ether by swirling, allowing the hydride to settle, and decanting the liquid portion in order to remove the mineral oil. The flask was then fitted with a nitrogen gas inlet and a mineral oil ”bubbler” to allow the nitrogen to escape. The remaining neck was fitted with a 100 ml. pressure-compensated funnel.

DMSO, distilled immediately prior to use from calcium hydride, was quickly poured into the nitrogen filled flask. At the same time the substrate was dissolved in some distilled DMSO and placed in the dropping funnel. The NaH/DMSO mixture was then heated, with magnetic stirring using an oil bath. The temperature of the oil bath was kept below 70°C to avoid decomposition of the sulfoxide carbanion. Usually a mixture of sodium hydride (0.05 mol.) and DMSO (50 ml.)
required 45 min. to 60 min. for complete reaction to give a somewhat cloudy, pale yellow-grey solution of the sodium salt.

After cooling the solution to room temperature or slightly below, the substrate was added dropwise with stirring. After a period of time the reaction was quenched by pouring the reaction mixture (usually highly coloured) on to ice. When a precipitate was not formed excess dilute hydrochloric acid was added. When an ill defined precipitate was formed it was filtered and taken up in chloroform. If no precipitate was obtained the mixture was extracted with chloroform. The chloroform solution was back-washed with water several times, dried and evaporated down to an oil which was triturated with ether or stored under ether at -30° to initiate solidification.

Preparation of Substituted \( \alpha \)-Phenylcinnamionitriles

General Procedure

The substituted benzaldehyde (0.1 mol.), dissolved in a minimum amount of alcohol, was mixed with benzyl cyanide (0.1 mol.) and sodium hydroxide (10 ml., 10% sol.) added with shaking. The precipitate produced was recrystallised from aqueous ethanol.

3-(4-dimethylaminophenyl)-2-phenylacrylonitrile

4-Dimethylaminobenzaldehyde (14.9g., 0.1 mol.) and benzyl cyanide (11.7g., 0.1 mol.) gave yellow plates (23.9g., 96%)
m.p. 136-9° (lit., 150 136°), ν max. 2220 cm. -1 (s), 2.3-2.8 (m, 5H), 2.15 and 3.3 (q, JAB = 12Hz.), 7.1 (s, 6H).

3-(3,4-methylenedioxyphenyl)-2-phenylacrylonitrile

Piperonaldehyde (15.0g., 0.1 mol.) and benzyl cyanide (11.7g., 0.1 mol.) gave fine white needles (22.4g., 90%) m.p. 121-2° (lit., 151 122°), ν max. 2220 cm. -1 (s), 2.2-2.9 (m, 6H), 3.1 (s, 1H), 3.2 (s, 1H), 4.0 (s, 2H).

3-(4-chlorophenyl)-2-phenylacrylonitrile

4-Chlorobenzaldehyde (14.0g., 0.1 mol.) and benzyl cyanide (11.7g., 0.1 mol.) gave white plates (19.1g., 80%) m.p. 102-3° (lit., 152 108°), ν max. 2230 cm. -1 (s), 2.1-2.8 (m).

3-(3,4-dimethoxyphenyl)-2-phenylacrylonitrile

Veratraldehyde (16.6g., 0.1 mol.) and benzyl cyanide (11.7g., 0.1 mol.) gave small yellow needles (22.8g., 86%) m.p. 85-7° (lit., 77 88°), ν max. 2220 cm. -1 (s), 2.2-2.8 (m, 7H), 3.1 (s, 1H), 3.3 (s, 1H), 6.1 (s, 3H), 6.15 (s, 3H).

3-(4-methoxyphenyl)-2-phenylacrylonitrile

4-Methoxybenzaldehyde (13.6g., 0.1 mol.) and benzyl cyanide (11.7g., 0.1 mol.) gave yellow needles (20.1g., 80%) m.p. 95-6°
3-(4-methylphenyl)-2-phenylacrylonitrile

4-Methylbenzaldehyde (12.0 g., 0.1 mol.) and benzyl cyanide (11.7 g., 0.1 mol.) gave white prisms (11.1 g., 54%) m.p. 59-60° (lit., 154 51°), \(v_{\text{max.}}\) 2220 cm\(^{-1}\) (s), \(\tau\) 2.1-2.9 (m, 10H), 7.7 (s, 3H).

3-(2-chlorophenyl)-2-phenylacrylonitrile

2-Chlorobenzaldehyde (14.0 g., 0.1 mol.) and benzyl cyanide (11.7 g., 0.1 mol.) gave long white needles (17.7 g., 74%) m.p. 167° (lit., 155 167-8°), \(v_{\text{max.}}\) 2230 cm\(^{-1}\) (s), \(\tau\) 1.8-2.8 (m).

2-phenyl-3-(2-furyl)-acrylonitrile

Furfuraldehyde was distilled from anhydrous magnesium sulphate before use. Furfuraldehyde (9.6 g., 0.1 mol.) and benzyl cyanide (11.7 g., 0.1 mol.) gave pale cream needles (13.1 g., 68%) m.p. 44-6° (lit., 153 42-3°), \(v_{\text{max.}}\) 2230 (s) cm\(^{-1}\), \(\tau\) 2.1-2.9 (m, 8H), 3.45 (m, 1H).

3-(\(\beta\)-styryl)-2-phenylacrylonitrile

Cinnamaldehyde (13.2 g., 0.1 mol.) and benzyl cyanide (11.7 g., 0.1 mol.) gave bright yellow plates (12.4 g., 54%) m.p. 121-2° (lit., 156 118-9°), \(v_{\text{max.}}\) 2220(s) cm\(^{-1}\), \(\tau\) 2.0-3.2 (m).
Attempted preparation of Undec-2-en-nitrile

A mixture of nonaldehyde (7.1g., 0.05 mol.), cyanoacetic acid (4.3g., 0.05 mol.) and piperidine (2 ml.) in pyridine (40 ml.) was heated under reflux for 5 hrs. After cooling, removal of solvents in vacuo gave a yellow oil which was taken up in chloroform (100 ml.). The solution was washed successively with saturated solutions of sodium bisulphite and sodium bicarbonate, dried, and evaporated to an oil. Fractional distillation gave a colourless oil (6.0g., 75%) b.p. 170-80°C/0.8 mm., \( \lambda_{\text{max}} \) 2260(\( \nu \)) cm.\(^{-1} \) and 2230(\( \nu \)) cm.\(^{-1} \). Examination of the oil by VPC on a PEGA column at 200°C showed two peaks in the ratio 3:1 with retention times 2.25 min. and 4.12 min. A similar ratio was obtained from the N.M.R. integration.

Reaction of Methysulphinyl Carbanion with Conjugated Nitriles

All reactions of DMSO\(^{-} \) with conjugated nitriles were accomplished by a procedure similar to that employed for the preparation of 2,3-diphenyl-4-methysulphinylbutyronitrile, which is described in detail.

Preparation of 2,3-diphenyl-4-methysulphinylbutyronitrile

A solution of 2,3-diphenylacrylonitrile (6.15g., 0.03 mol.) in DMSO (50 ml.) was added dropwise to a magnetically stirred solution of DMSO\(^{-} \) (0.03 mol.) prepared as previously described (page 99).
The mixture, which changed colour from green to red and then black, was stirred at room temperature for approximately 15 min. The reaction mixture was then poured on to ice to give a red-white sticky precipitate. The precipitate was taken up in chloroform (100 ml.), washed with water (2 x 100 ml.), and dried over anhydrous magnesium sulphate. Removal of the solvent in vacuo gave a viscous oil. Trituration with ether gave a white solid (1.7 g., 40%). Recrystallisation from ethanol gave very fine white needles m.p. 194-5° (Found: C, 71.95; H, 6.07; N, 5.00; C\textsubscript{17}H\textsubscript{17}NOS requires C, 72.06; H, 6.05; N, 4.94%). V\textsubscript{max.} 3010(s), 2250(m), 1610(m), 1500(m), 1460(s), 1060(s) cm\textsuperscript{-1} \mathcal{C} 2.4-3.0 (m,10H), 5.4 (d,1H, J=5Hz.), 6.0-7.0 (m,3H), 7.45 (s,3H).

Preparation of 3-(4-dimethylaminophenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(4-dimethylaminophenyl)-2-phenylacrylonitrile (5.8 g., 0.023 mol.) in T.H.F. (20 ml.) and DMSO\textsuperscript{-} (0.025 mol.) in the general procedure gave 3-(4-dimethylaminophenyl)-4-methylsulphinyl-2-phenylbutyronitrile (4.9 g., 65%). Recrystallisation from ethanol gave white crystals m.p. 209-10° (Found: C, 69.79; H, 6.60; N, 8.70. C\textsubscript{19}H\textsubscript{22}N\textsubscript{2}OS requires C, 69.92; H, 6.79; N, 8.58%). V\textsubscript{max.} 3010(m), 2250(w), 1620(s), 1530(s), 1365(m), 1050(s) cm\textsuperscript{-1} \mathcal{C} 2.5-2.9 (m,5H), 2.9 and 3.2 (q, J=8.5Hz.), 5.5 (d,1H, J=5Hz.), 6.2-6.9 (m,3H), 7.1 (s,6H), 7.4 (s,3H); m/e 326.
Preparation of 3-(3,4-methylenedioxyphenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(3,4-methylenedioxyphenyl)-2-phenylacrylonitrile (7.5g., 0.03 mol.) in T.H.F. (10 ml.) and DMSO\(^-\) (0.03 mol.) in the general procedure gave 3-(3,4-methylenedioxyphenyl)-4-methylsulphinyl-2-phenylbutyronitrile (5.0g., 51%). Recrystallisation from ethanol gave white needles m.p. 195-6\(^\circ\). (Found: C,69.8; H,5.6; N,4.31. \(\text{C}_{19}\text{H}_{19}\text{NO}_{2}\text{S}\) requires C,70.14; H,5.89; N,4.31%).

\[\text{\textsuperscript{\text{v}}}_{\text{max.}} 2795(\text{w}), 2260(\text{w}), 1620(\text{m}), 1490(\text{s}), 1450(\text{s}), 1380(\text{m}), 1230(\text{w,b}), 1030(\text{s}), 935(\text{s}) \text{ cm}^{-1}. \text{\textsuperscript{\text{T}}}_{2.4-2.8} (\text{m,5H}), 3.1-3.4 (\text{m,3H}), 4.1 (\text{s,2H}), 5.5 (\text{d,1H, J=5Hz.}), 6.0-6.9 (\text{m,3H}), 7.4 (\text{s,3H}); \text{m/e} 327.

Preparation of 3-(4-chlorophenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(4-chlorophenyl)-2-phenylacrylonitrile (8.5g., 0.035 mol.) in T.H.F. (10 ml.) and DMSO\(^-\) (0.035 mol.) in the general procedure gave 3-(4-chlorophenyl)-4-methylsulphinyl-2-phenylbutyronitrile (3.8g., 32%). Recrystallisation from benzene/pet. ether (b.p. 60-80\(^\circ\)) gave white crystals m.p. 126-31\(^\circ\). An analytical sample had m.p. 148-50\(^\circ\). (Found: C,64.01; H,5.00; N,4.38. \(\text{C}_{17}\text{H}_{16}\text{ClNOS}\) requires C,64.25; H,5.04%).

\[\text{\textsuperscript{\text{v}}}_{\text{max.}} 3020(\text{m}), 2250(\text{w}), 1600(\text{w}), 1500(\text{s}), 1460(\text{m}), 1420(\text{m}), 1100(\text{m}), 1050(\text{s}), 1020(\text{m}) \text{ cm}^{-1}. \text{\textsuperscript{\text{T}}}_{2.5-3.1} (\text{m,9H}), 5.4 (\text{d,1H, J=5Hz.}), 6.1-7.0 (\text{m,3H}), 7.4 (\text{s,3H}).]
Preparation of 3-(3,4-dimethoxyphenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(3,4-dimethoxyphenyl)-2-phenylacrylonitrile (7.9 g,, 0.03 mol.) and DMSO\textsuperscript{-} (0.03 mol.) in the general procedure gave 3-(3,4-dimethoxyphenyl)-4-methylsulphinyl-2-phenylbutyronitrile (5.2 g,, 50%). Recrystallisation from ethanol gave very fine white needles m.p. 179-80\textdegree C. (Found: C,66.38; H,6.30; N,3.93.

C\textsubscript{1g}H\textsubscript{21}NO\textsubscript{3}S requires C,66.46; H,6.16; N,4.08%). ν\textsuperscript{max.} 3000(m), 2250(w), 1600(m), 1510(s), 1470(s), 1460(m), 1455(m), 1420(m), 1260(s), 1150(s), 1030(s), 940(w), 800(m) cm\textsuperscript{-1}. ν 2.6-3.0 (m,5H), 3.3 (m,2H), 3.6 (m,1H), 5.5 (d,1H, J=5Hz), 6.2 (s,3H), 6.3 (s,3H), 6.3-7.0 (m,3H), 7.4 (s,3H); m/e 343.

Preparation of 3-(4-methoxyphenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(4-methoxyphenyl)-2-phenylacrylonitrile (11.0 g,, 0.05 mol.) and DMSO\textsuperscript{-} (0.05 mol.) in the general procedure gave 3-(4-methoxyphenyl)-4-methylsulphinyl-2-phenylbutyronitrile (9.4 g,, 64%). Recrystallisation from ethanol gave white crystals m.p. 178-80\textdegree C. (Found: C,69.13; H,6.07; N,4.47. C\textsubscript{18}H\textsubscript{19}NO\textsubscript{2}S requires C,68.99; H,6.11; N,4.47%). ν\textsuperscript{max.} 2850(m), 2250(m), 1620(s), 1590(s), 1500(m), 1460(m), 1310(s), 1240(b,s), 1180(m), 1025(s), 960(m), 930(m) cm\textsuperscript{-1}. ν 2.6-3.2 (m,3H), 5.5 (d,1H, J=5Hz), 6.25 (s,3H), 6.1-7.0 (m,3H), 7.45 (s,3H); m/e 313.
Preparation of 3-(4-methylphenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(4-methylphenyl)-2-phenylacrylonitrile (8.8g., 0.04 mol.) and DMSO⁻ (0.045 mol.) in the general procedure gave 3-(4-methylphenyl)-4-methylsulphinyl-2-phenylbutyronitrile (5.2g., 44%). Recrystallisation from ethanol gave white crystals m.p. 205-6°. (Found: C,72.30; H,6.55; N,4.68. \( \text{C}_{18}\text{H}_{19}\text{NOS} \) requires C,72.70; H,6.44; N,4.71%). \( \nu \) max. 3000(m), 2250(w), 1610(m), 1500(m), 1460(m), 1240(b,m), 1050(s), 960(w), 940(w) cm⁻¹ \( \tau \) 2.6-3.2 (m,9H), 5.5(d,1H, J=5Hz.), 6.2-7.0 (m,3H), 7.45 (s,3H), 7.7 (s,3H); m/e 297.

Preparation of 3-(2-chlorophenyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of 3-(2-chlorophenyl)-2-phenylacrylonitrile (10g., 0.042 mol.) and DMSO⁻ (0.050 mol.) in the general procedure gave 3-(2-chlorophenyl)-4-methylsulphinyl-2-phenylbutyronitrile (3.8g., 32%). Recrystallisation from benzene gave white needles m.p. 168-70°. (Found: C,64.13; H,5.34; Cl,11.2; N,4.37. \( \text{C}_{17}\text{H}_{16}\text{ClNOS} \) requires C,64.24; H,5.04; Cl,11.2; N,4.41%). \( \nu \) max. 3000(m), 2250(w), 1600(w), 1500(m), 1480(m), 1300(w), 1040(s) cm⁻¹ \( \tau \) 2.6-3.0 (m,9H), 5.2-6.8 (m,2H), 6.85 (broad doublet, 2H, J=7Hz.); m/e 317 (for \( ^{35}\text{Cl} \)).
Attempted Preparation of 3-(2-furyl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of the general method with 2-phenyl-3-(2-furyl)acrylonitrile (9.8g., 0.05 mol.) and DMSO$^-$ (0.05 mol.) gave a viscous black tar. T.l.c. on silica using chloroform as solvent showed a continuous streak.

Attempted Preparation of 3-phenyl-4-methylsulphinylbutyronitrile

Use of the general method with cinnamonic acid (12.9g., 0.1 mol.) and DMSO$^-$ (0.10 mol.) gave a black tar. $V_{max}$ 2230 cm.$^{-1}$ and 2200 cm.$^{-1}$. T.l.c. gave a continuous spot.

Preparation of 3-(2-styryl)-4-methylsulphinyl-2-phenylbutyronitrile

Use of the general method with 3-(2-styryl)-2-phenylacrylonitrile (6.3g., 0.03 mol.) and DMSO$^-$ (0.03 mol.) gave a viscous yellow oil. An ether solution of the oil kept at 0°C for several days deposited: 3-(2-styryl)-4-methylsulphinyl-2-phenylbutyronitrile (500 mg., 6%). Recrystallisation from benzene gave fine white needles m.p. 175-7°C. (Found: C, 73.34; H, 6.02; N, 4.52. $C_{19}H_{19}NOS$ requires C, 73.76; H, 6.19; N, 4.53%). $V_{max}$. 3020(m), 2260(w), 1615(m), 1500(s), 1465(s), 1080(m), 1030(s), 970(w) cm.$^{-1}$. $\delta$ 2.4-2.9 (m, 10H), 3.0-3.2 (m, 2H), 5.8 (d, 1H, J=8.5Hz.), 6.8-7.4 (m, 3H), 7.5 (s, 3H); m/e 309.
Preparation of 3-(4-methoxyphenyl)-4-benzylsulphinyl-2,4-diphenylbutyronitrile

Use of the general method with 3-(4-methoxyphenyl)-2-phenylacrylonitrile (7.0g., 0.03 mol.) and dibenzyl sulphoxide (6.9g., 0.03 mol.) in MSO⁻ (0.03 mol.) gave a sticky yellow precipitate. An ether solution of the precipitate deposited 3-(4-methoxyphenyl)-4-benzylsulphinyl-2,4-diphenylbutyronitrile (1.8g., 13%) as a white solid. Recrystallisation from ethanol gave fine white needles m.p. 202-3⁰. (Found: C, 78.01; H, 5.93; N, 3.07. \(C_{30}H_{27}N_{2}O_{2}S\) requires C, 77.41; H, 5.81; N, 3.01%). \(\nu_{\text{max}}\) 2960(m), 2260(w), 1620(s), 1590(m), 1500(m), 1460(s), 1310(m), 1230(b, s), 1030(s), 920(m) cm⁻¹. 2.3-3.5 (m, 19H), 5.9-6.6 (m, ca. 8H). The compound was too involatile to obtain a mass spectrum.

Preparation of 2,3-diphenyl-4-propylsulphinylhexanitrile

The preparation was carried out using the procedure described later for additions to conjugated nitro compounds. Dipropylsulphoxide was dried over calcium hydride before use; a warm oil bath ensured that the dipropylsulphoxide remained molten. A sample for use was obtained by pipetting from the container flushing the system with dry nitrogen. An IR spectrum showed the absence of water. Use of 1,2-diphenyl-1-cyanoethylene (4.1g., 0.02 mol.), dipropylsulphoxide (2.7g., 0.02 mol.) and excess sodamide (0.8g., 0.04 mol.) in ammonia (200 ml.) in the general method gave a colourless oil. The oil was taken up in ether and storing at -30⁰C for
several days gave a white precipitate of 2,3-diphenyl-4-propylsulphinylhexanitrile (198 mg., 3%) m.p. 239-40°. Recrystallisation from ethyl acetate gave white crystals m.p. 248-50°. (Found: C, 74.02; H, 7.35; N, 4.10. C_{21}H_{25}NOS requires C, 74.31; H, 7.42; N, 4.13%).\[\nu_{\text{max}} \text{(KBr)} = 3080(\nu), 3040(\nu), 2930(\nu), 2890(\nu), 2250(\nu), 1610(\nu), 1500(s), 1460(s), 1410(m), 1300(s), 1290(s), 1240(\nu), 1130(s), 1080(m), 1030(\nu), 770(s), 760(s), 720(s), 700(s) \text{ cm}^{-1}\] The NMR was complex and ill defined in the region of absorption of the alkyl groups and cannot be interpreted. However, the methine proton gave a characteristic doublet. \[\tau = 2.5-3.2 \text{ (m, 10H), 5.4 (d, 1H, J=5Hz), 6.2-8.0 (s, A), 8.6-9.1 (s, B)}\]. The ratio of the integrated multiplets A and B was 1.3:1 (calculated 1.3:1).

**REACTIONS OF NITRILE ADDUCTS**

**Reduction of 4-methylsulphinyl-2,3-diphenylbutyronitrile**

4-methylsulphinyl-2,3-diphenylbutyronitrile (283 mg., 0.001 mol.) dissolved in aqueous THF (20 ml., H_{2}O 5 ml.) and magnetically stirred with aluminium amalgam prepared from aluminium (0.45g.) according to Fieser.\(^{157}\) After 15 hr. the mixture was filtered and the filtrate extracted with chloroform. The extract was washed with water, dried, and evaporation of the solvent gave a white solid. Chromatography of the solid on silica plates in chloroform gave 4-thionethyl-2,3-diphenylbutyronitrile (150 mg., 68%). Recrystallisation from ethanol gave white crystals m.p. 89-91°.
Pyrolysis of 2,3-diphenyl-4-methylsulphinylbutyronitrile

2,3-diphenyl-4-methylsulphinylbutyronitrile (1.05 g., 0.004 mol.) was refluxed in anhydrous diglyme (100 ml.) for 14 hrs. The solution was cooled and diglyme removed in vacuo, final traces being removed at 0.5 mm. Solidification occurred giving 2,3-diphenyl-3-methylacrylonitrile (0.6 g., 74%) after trituration with cold ether. Recrystallisation from ethanol gave white crystals m.p. 80-20°C (Found: C, 87.98; H, 6.39; N, 6.39%). $\nu_{\text{max.}}$ 2220(s), 1600(s), 1580(m), 1490(s), 1440(s), 1330(s), 1310(s), 965(s), 920(s) cm.$^{-1}$, $\tau_{\text{max.}}$ 289 nm., log $\varepsilon$ 3.85, $\tau$ 2.7-2.9 (m, 10H), 7.5 (s, 3H); m/e 219.

DINITRILES PREPARATION AND REACTIONS

Preparation of Malononitrile

Malononitrile was prepared according to the method described in Organic Syntheses$^{158}$ on a 0.2 scale. Distillation of the crude reaction product gave malononitrile (76 g., 38%) m.p. 29-30°C, $\nu_{\text{max.}}$ (liquid film) 2280(s) cm.$^{-1}$, $\tau$ 6.4(s)
Preparation of 1,1-dicyano-2-phenylethylene

A solution of benzaldehyde (10.6 g., 0.1 mol.), malononitrile (9.4 g., 0.12 mol.), ammonium acetate (0.8 g.), and acetic acid (2.4 ml.) in benzene (100 ml.) was heated under reflux overnight using a Dean-Stark trap to remove water formed during the reaction. The solution was cooled, washed with water, dried, and evaporated to dryness. Recrystallisation from ethanol gave white needles (6.5 g., 42%) m.p. 44.5° (lit. 92, 46-70°), \( \nu_{\text{max}} \) 2240(s) cm.\(^{-1}\) \( \tau \) 2.0-2.5 (m).

Reaction of 1,1-dicyano-2-phenylethylene with DMSO\(^-\)

Use of 1,1-dicyano-2-phenylethylene (6.2 g., 0.04 mol.) and DMSO\(^-\) (0.04 mol.) in the general procedure gave a dark oily tar. Chromatography on alumina grade 1 with benzene and chloroform as elutants gave a green oil which partially solidified on standing. Recrystallisation from ethanol gave light yellow plates (250 mg., 24%) m.p. 117-8°. (Found: C, 84.53; H, 4.87; N, 10.94. \( \text{C}_{18}\text{H}_{12}\text{N}_{2} \) requires C, 84.35; H, 4.72; N, 10.93%), \( \nu_{\text{max}} \) 2230(s), 1615(s), 1580(m), 1530(m), 1350(s), 1315(w), 1110(w), 1005(w), 970(s) cm.\(^{-1}\) \( \tau \) 2.4-2.8 (m) and signals at 2.3, 3.0 and 3.3; \( \lambda_{\text{max}} \) 352, logε 5.10.

Attempted Preparation of s-Diphenyldicyanoethylene

The method of Campagne et. al.\(^{92}\) was adopted. A solution of benzophenone (18.2 g., 0.1 mol.), ammonium acetate (0.8 g., 0.01 mol.),
malononitrile (9.4g., 0.12 mol.) and acetic acid (2.4 ml.) in benzene (150 ml.) was heated under reflux for 9 hrs. The solution was evaporated to dryness and the residue taken up in chloroform. The chloroform solution was washed with water, sodium bicarbonate solution, dried and evaporated down to an oil. Repeated attempts to solidify the oil failed. Distillation in vacuo gave an oil shown by NMR and IR to be a mixture of benzophenone and malononitrile. Examination of the residue by IR did not indicate the presence of any s-diphenyl-dicyanoethylene.

PREPARATION OF CHALCONEs

General Procedure

The method described by Vogel159 was adopted with slight modifications. The substituted benzaldehyde (0.1 mol.) was dissolved in ethanol (ca. 50 ml.) and the substituted acetophenone (0.1 mol.) in ethanol (50 ml.) was added. A 10% solution of sodium hydroxide (10 ml.) was added and the mixture left to stand until precipitation had occurred. Recrystallisation was from aqueous ethanol. If precipitation of a solid did not occur the mixture was neutralised with dilute hydrochloric acid and extracted with chloroform. Removal of the solvent gave a yellow oil which was triturated with ether and/ or cooled to 0°C to give the chalcone. Recrystallisation was as above.
Chalcone

Acetophenone (12.0 g., 0.1 mol.) and benzaldehyde (10.6 g., 0.1 mol.) gave pale yellow crystals of chalcone (15 g., 90%) m.p. 57-8°C (lit. 160°), \( \nu_{\text{max}} \) 1670(s), 1645(m), 1610(s) cm\(^{-1}\), \( \tau \) 1.8-2.8 (m).

2',4'-dimethylchalcone

2,4-Dimethylacetophenone (14.8 g., 0.1 mol.) and benzaldehyde (10.6 g., 0.1 mol.) gave yellow needles of 2',4'-dimethylchalcone (22 g., 85%) m.p. 71-2°C (lit. 161°, 71-2°C), \( \nu_{\text{max}} \) 2930(s), 1670(s), 1645(s), 1615(s) cm\(^{-1}\), \( \tau \) 2.3-3.0 (m,1OH), 7.6 (s,3H), 7.7 (s,3H).

2',4',6'-trimethylchalcone

2,4,6-Trimethylacetophenone (16.2 g., 0.1 mol.) and benzaldehyde (10.6 g., 0.1 mol.) gave pale yellow crystals of 2',4',6'-trimethylchalcone (8.9 g., 36%) m.p. 59-60°C (lit. 162°, 63°C), \( \nu_{\text{max}} \) 1670(sh,s), 1650(s), 1600(sh,s) cm\(^{-1}\), \( \tau \) 2.4-3.4 (m,9H), 7.8 (s,3H), 7.9 (s,3H).

4-chlorochalcone

4-Chlorobenzaldehyde (14.1 g., 0.1 mol.) and acetophenone (12.0 g., 0.1 mol.) gave glistening yellow crystals of 4-chlorochalcone (22 g., 91%) m.p. 113-4°C (lit. 163°, 113-4°C), \( \nu_{\text{max}} \) 1670(s), 1650(s), 1610(s) cm\(^{-1}\), \( \tau \) 1.9-2.1 (m,2H), 2.3-2.8 (m,3H).
**4-methoxychalcone**

Anisaldehyde (13.6g, 0.1 mol.) and acetophenone (12.0g, 0.1 mol.) gave yellow needles of 4-methoxychalcone (20.1g, 84%) m.p. 75-6°C (lit. 164°, 77-8°C), $\nu_{\text{max}}$ 1665(s), 1640(m), 1600(s) cm.$^{-1}$, $\tau$ 2.0-3.2 (m,11H), 6.3 (s,3H).

**4-dimethylaminochalcone**

4-Dimethylaminobenzaldehyde (14.9g, 0.1 mol.) and acetophenone (12.0g, 0.1 mol.) gave orange-yellow plates of 4-dimethylaminochalcone (11.8g, 47%) m.p. 110-12°C (lit. 165°, 114°), $\nu_{\text{max}}$ 1655(m), 1600(s), 1590(s) cm.$^{-1}$, $\tau$ 2.0-2.9 (m,9H), 3.35 (s,1H) and 3.5 (s,1H), 7.1 (s,6H).

**2-chlorochalcone**

2-Chlorobenzaldehyde (14.0g, 0.1 mol.) and acetophenone (12g, 0.1 mol.) gave yellow needles of 2-chlorochalcone (3.6g, 15%) m.p. 54°C (lit. 166°, 52-3°C), $\nu_{\text{max}}$ 1670(s), 1650(s), 1610(s) cm.$^{-1}$, $\tau$ 1.7-2.9(m).

**4-nitrochalcone**

4-Nitrobenzaldehyde (7.5g, 0.05 mol.) and acetophenone (6.0g, 0.05 mol.) gave pale yellow crystals of 4-nitrochalcone (10.1g, 82%) m.p. 164-5°C (lit. 167°, 164°), $\nu_{\text{max}}$ 1675(s), 1650(sh,m), 1620(s), 1605(s) cm.$^{-1}$, $\tau$ 1.6-2.7 (m).
2-bromochalcone

2-Bromobenzaldehyde (9.2g., 0.05 mol.) and acetophenone (6.0g., 0.05 mol.) gave yellow needles of 2-bromochalcone (3.5g., 25%)
m.p. 45-7° (lit.168, 72°), $\gamma_{\text{max}}$. 1670(s), 1650(s), 1610(s) cm.$^{-1}$,
$\tau$ 1.7-2.9 (m).

4'-methoxychalcone

4-Methoxyacetophenone (15.0g., 0.1 mol.) and benzaldehyde (10.6g., 0.1 mol.) gave yellow crystals of 4'-methoxychalcone (10.2g., 43%)
m.p. 108-9° (lit.169, 106-7°), $\gamma_{\text{max}}$. 1670(s), 1615(s), 1600(s) cm.$^{-1}$,
$\tau$ 2.2-2.9 (m,7H), 1.95 and 3.05 (q,4H, J=8Hz.), 6.2 (s,3H).

4'-chlorochalcone

4-Chloroacetophenone (15.5g., 0.1 mol.) and benzaldehyde (10.6g., 0.1 mol.) gave 4'-chlorochalcone (4.0g., 16%). Recrystallisation from acetone/pet. ether (60-80°) gave yellow needles m.p. 98-99° (lit.170, 101°), $\gamma_{\text{max}}$. 1670(s), 1645(s), 1610(s) cm.$^{-1}$, $\tau$ 1.9-2.8 (m).

4'-methylchalcone

4-Methylacetophenone (13.4g., 0.1 mol.) and benzaldehyde (10.6g., 0.1 mol.) gave pale yellow needles of 4'-methylchalcone (8.8g., 40%)
m.p. 53-4° (lit.167, 59-60°), $\tau$ 2.0-2.8 (mllH), 7.5 (s,3H).
Preparation of tert.-butylacetophenone

Tert.-butylacetophenone was prepared according to the Perrir modification of the Friedel-Crafts Reaction.\(^{171}\) Acetyl chloride (92.0 g., 1.16 mol.) was added dropwise to a stirred mixture of aluminium chloride (156 g., 1.16 mol.) and carbon tetrachloride (600 ml.) over a period of 15 min. Tert.-butylbenzene (134 g., 1.0 mol.) was then added over a period of one hour, keeping the temperature below 5°C. with an ice bath. After a further 1 hr, the mixture was poured on to excess ice and dilute hydrochloric acid. The organic layer was separated, washed successively with dilute hydrochloric acid, a solution of sodium bicarbonate, and water. Removal of the solvent in vacuo gave a mobile liquid. Distillation at 90-100°C/0.2 mm. gave tert.-butylacetophenone (121 g., 80%), \(^{17}2.2 \text{ and } 2.6 \ (q, 4H, J=8.5Hz.)\), 7.55 (s, 3H), 8.7 (s, 3H), \(\nu_{\text{max.}}\) (liquid film) 2960(s), 2870(m), 1685(s), 1610(s), 1465(w), 1410(s), 1360(s), 1320(s), 1190(m), 1110(m), 1010(m), 960(s), 835(s) cm\(^{-1}\).

4'-tert-butylichalcone

4'-t-Butylacetophenone (35.2 g., 0.2 mol.) and benzaldehyde (21.2 g., 0.2 mol.) gave yellow crystals of 4'-t-butylichalcone (11.4 g., 22%) m.p. 96-98°C (lit.\(^{172}\) 98°C), \(\nu_{\text{max.}}\) 1665(s), 1610(s), 1600(sh, s) cm\(^{-1}\), \(\tau\) 2.0-2.8 (m, 11H), 8.7 (s, 3H).
4-methoxy-2',4',6'-trimethylchalcone

Anisaldehyde (6.8 g., 0.05 mol.) and 2',4',6-trimethylacetophenone (8.1 g., 0.05 mol.) gave yellow crystals of 4-methoxy-2',4',6'-trimethylchalcone (8.6 g., 60%) m.p. 90-10 (lit. 173, 103-10), υ_{max.} 1670 (m), 1650 (s), 1610 (s) cm⁻¹, Ζ 2.4-3.4 (m, 8H), 5.2 (s, 3H), 7.7 (s, 3H), 7.8 (s, 6H).

4-fluorochalcone

4-Fluorobenzaldehyde (5.0 g., 0.04 mol.) and acetophenone (4.8 g., 0.04 mol.) were dissolved in boron trifluoride etherate BF₃·2Et₂O (20 ml.). After five days the mixture was poured into a saturated solution of sodium acetate giving a precipitate of 4-fluorochalcone (6.2 g., 68%). Recrystallisation from aqueous ethanol gave yellow needles m.p. 79-80 (lit. 174, 85-70), υ_{max.} 1670 (s), 1645 (m), 1610 (s) cm⁻¹, Ζ 1.8-3.1 (m).

α-methylchalcone

Using the method of Calloway and Green 175 acetophenone (2.4 g., 0.2 mol.) and aluminium chloride (10.7 g., 0.08 mol.) were dissolved in methylene dichloride (100 ml.) and allowed to stand for a week. The reaction mixture was then poured on to ice, the organic layer separated and the aqueous layer extracted with chloroform (3 x 25 ml.). The combined extracts were washed with water, dried, and evaporated down to an oil. Fractional distillation gave dypnone b.p. 180-90
A sample of \( \beta \)-methylchalcone supplied by "Boots Pure Drug Co." had b.p. 120-30\(^\circ\)/0.1 mm. (lit., \(176\)\(^\circ\) 128-30\(^\circ\)), \(\gamma_{\text{max}}\) (liquid film) 1670(s), 1650(sh,s), 1610(s) cm.\(^{-1}\), \(\tau\) 2.1-3.0 (m,11H), 7.75 (d,3H, \(J=\text{ca.} 1.5\text{Hz.}\)).

\(\beta\)-methylchalcone

4-acetamidochalcone

4-Acetamidobenzaldehyde (16.3g., 0.1 mol.) and acetophenone (12.0g., 0.1 mol.) gave glistening yellow plates of 4-acetamidochalcone (20.0g., 75%) m.p. 178-9\(^\circ\) (lit.\(177\), 179\(^\circ\)), \(\gamma_{\text{max}}\) 3440(b,s), 3330(b,m), 1700(s), 1670(s), \(\tau\) 1.8-2.8 (m,11H), 7.8 (s,3H), 8.3 (s,1H, exchangeable NH).

REATIONS OF METHYLSULPHINYL CARBANION WITH CHALCONES

General Method

The method employed with chalcones is essentially the same as that with conjugated nitriles. The reaction with chalcone is described at length to illustrate the general procedure.
Preparation of 2,4-diphenyl-1-methylsulphinylbut-3-en-2-ol

A solution of chalcone (6.2g., 0.03 mol.) in DMSO (20 ml.) was added dropwise to a magnetically stirred solution of methylsulphinyl carbanion (0.03 mol.) at room temperature. After 10 min. the reaction was quenched by pouring on to ice and dilute hydrochloric acid. The white-yellow precipitate formed was taken up in chloroform, the solution washed with water, dried and evaporated down to a white solid which was triturated with cold ether giving 2,4-diphenyl-1-methylsulphinylbut-3-en-2-ol (5.5g., 64%). Recrystallisation from benzene gave fine white needles m.p. 149-50°. (Found: C, 72.5; H, 6.16. C_{17}H_{18}O_{2}S requires C, 72.46; H, 6.08%). \( \nu_{\text{max.}} \): 3390(b, s), 3000(m), 1610(m), 1585(w), 1500(s), 1450(s), 1410(s), 1310(m), 1070(s), 1020(s), 990(s), 970(s), 935(m) cm\(^{-1}\).

Preparation of 1-methylsulphinyl-2-phenyl-3-(2,4,6-trimethylbenzoyl)-propane

Use of 2',4',6'-trimethylchalcone (7.5g., 0.03 mol.) and DMSO\(^-\) (0.03 mol.) in the general procedure gave 1-methylsulphinyl-2-phenyl-3-(2,4,6-trimethylbenzoyl)-propane (3.1g., 31%). Recrystallisation from benzene/pet. ether b.p. 60-80° gave fluffy white crystals m.p. 111-2°. (Found: C, 73.0; H, 7.41. C_{20}H_{24}O_{2}S requires C, 73.14; H, 7.37%). \( \nu_{\text{max.}} \): 2920(m), 1700(s), 1620(s), 1500(m), 1460(m), 1410(m), 1300(m), 1020(s), 985(m), 960(m), 850(m) cm\(^{-1}\), \( \gamma \): 2.7 (s, 5H), 3.2 (s, 2H), 5.9-6.4 (m, 1H), 6.8-7.1 (m, 4H), 7.5 (s, 3H), 7.8 (s, 3H), 8.05 (s, 6H).
Preparation of 3-(2,4-dimethylbenzoyl)-1-methylsulphinyl-2-phenylpropane

Use of 2',4'-dimethylchalcon (7.1g., 0.03 mol.) and DMSO\(^{-}\) (0.03 mol.) in the general procedure gave 3-(2,4-dimethylbenzoyl)-1-methylsulphinyl-2-phenylpropane (2.0g., 21%). Recrystallisation from benzene/pet. ether b.p. 60-80\(^{\circ}\) gave colourless, glistening plates m.p. 120-2\(^{\circ}\). (Found: C,72.4; H,6.98. C\(_{19}H_{22}O_{2}S\) requires C,72.59; H,7.05%), \(\nu\) max. 2940(m), 1690(s), 1570(m), 1500(w), 1300(m), 1020(s), 990(m) cm\(^{-1}\), \(\tau\) 2.4-3.1 (m,8H), 6.0-7.1 (m,5H), 7.55 (s,3H), 7.7 (s,3H), 7.75 (s,3H).

Preparation of 3-(4-chlorobenzoyl)-1-methylsulphinyl-2-phenylpropane

Use of 4-chlorochalcone (9.7g., 0.04 mol.) and DMSO\(^{-}\) (0.04 mol.) in the general procedure gave 3-(4-chlorobenzoyl)-1-methylsulphinyl-2-phenylpropane (1.7g., 13%). Recrystallisation from chloroform gave floculent white crystals m.p. 212-4\(^{\circ}\). (Found: C,63.42; H,5.36. C\(_{17}H_{17}ClO_{2}S\) requires C,63.65; H,5.30%), \(\nu\) max. 2980(w), 1695(m), 1610(m), 1500(s), 1450(w), 1100(s), 1020(s), 950(w) cm\(^{-1}\).

The compound was not sufficiently soluble in chloroform or DMSO to obtain a suitable NMR spectrum.
Preparation of 4-(4-methoxyphenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol

Use of 4-methoxychalcone (7.2g., 0.03 mol.) and DMSO\(^-\) (0.03 mol.) in the general procedure gave 4-(4-methoxyphenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol (2.9g., 31%). Recrystallisation from benzene gave flocculent white crystals m.p. 136-8\(^\circ\). (Found: C,68.35; H,6.29. \(C_{18}H_{20}O_3S\) requires C,68.34; H,6.37\%). \(\nu_{max}\) 3380(b,v), 2850(m), 1655(w), 1610(s), 1580(m), 1500(m), 1470(m), 1450(m), 1410(m), 1310(s), 1250(b,s), 1110(m), 1020(b,s), 985(s), 970(s), 930(m) cm.\(^{-1}\), \(\tau\) 2.3-2.8 (m), 3.25 and 3.45 (q,2H, J=10Hz.), 4.85 (bs,1H, exchangeable OH), 6.7 (bs,2H), 7.4 (s,3H).

Preparation of 4-(4-dimethylaminophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol

Use of 4-dimethylaminochalcone (7.5g., 0.03 mol.) and DMSO\(^-\) (0.03 mol.) in the general procedure gave 4-(4-dimethylaminophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol (2.8g., 28%). Recrystallisation from benzene gave small white crystals m.p. ca. 174\(^\circ\) with decomposition. A satisfactory analysis could not be obtained. \(\nu_{max}\) 3380(b,m), 2820(w), 1650(w), 1610(s), 1520(s), 1450(m), 1360(m), 1200(b,s), 1035 (b,s), 990(m), 970(m), 930(m) cm.\(^{-1}\), \(\tau\) 2.3-2.8 (m), 3.4 and 3.7 (q, ca. 2H, J=15Hz.), 4.95 (s,1H, exchangeable OH), 6.65 (s,2H), 7.1 (s,6H), 7.4 (s,3H).
Preparation of 3-(2-chlorobenzoyl)-1-methylsulphinyl-2-phenylpropane

Use of 2-chlorochalcone (3.2g., 0.013 mol.) and DMSO\(^-\) (0.013 mol.) in the general procedure gave 3-(2-chlorobenzoyl)-1-methylsulphinyl-2-phenylpropane (830 mg., 20%). Recrystallisation from ethanol gave small clumps of needles m.p. 206-8\(^0\). (Found: C,63.45; H,5.26. \(\text{C}_{17}\text{H}_{17}\text{ClO}_2\text{S}\) requires C,63.65; H,5.30). \(\nu_{\text{max.}}\) (KBr) 3260(bs), 3060 (w), 2940(w), 1600(w), 1580(w), 1490(m), 1480(s), 1450(s), 1395(s), 1310(w), 1290(w), 1230(s), 1130(m), 1120(w), 1060(s), 1020(m), 990(vs), 950(s), 910(m), 770(s), 750(s), 720(m), 700(s) cm\(^{-1}\). The compound was not sufficiently soluble in CDCl\(_3\) to obtain a spectrum.

Reaction of 4-nitrochalcone with DMSO\(^-\)

Use of 4-nitrochalcone (5.1g., 0.02 mol.) and DMSO\(^-\) (0.02 mol.) in the general method gave a black viscous oil which proved intractable.

Preparation of 4-(2-Bromophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol.

Use of 2-bromochalcone (2.90g., 0.01 mol.) and DMSO\(^-\) (0.01 mol.) in the general method gave a sticky yellow oil. Chromatography on neutral alumina in chloroform and methanol gave 4-(2-bromophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol (1.2g., 33%). Recrystallisation from benzene gave white crystals m.p. 195-7\(^0\).
Preparation of 3-(4-methoxybenzoyl)-1-methylsulphinyl-2-phenylpropane

Use of 4'-methoxychalcone (7.2 g., 0.03 mol.) and DMSO\textsuperscript{-} (0.03 mol.) in the general method gave 3-(4-methoxybenzoyl)-1-methylsulphinyl-2-phenylpropane (2.7 g., 28%). Recrystallisation from acetone gave fine white crystals m.p. 300°. (Found: C, 67.97; H, 6.31. C\textsubscript{18}H\textsubscript{20}O\textsubscript{3}S requires C, 68.34; H, 6.37%), ν\textsubscript{max.} 3000 (w), 2840 (w), 1690 (m), 1600 (s), 1580 (m), 1510 (m), 1450 (w), 1300 (m), 1260 (s), 1170 (s), 1030 (m), 980 (m) cm\textsuperscript{-1}, τ 2.6-3.4 (m, 5H), 2.3 and 3.55 (q, 4H, J = 8Hz.), 5.2-6.0 (m, 3H), 6.2 (s, 3H), 6.4 (s, 2H), 7.85 (s, 3H).

Preparation of 4-(4-chlorophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol

Use of 4'-chlorochalcone (3.6 g., 0.015 mol.) and DMSO\textsuperscript{-} (0.015 mol.) in the general procedure gave 4-(4-chlorophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol (1.0 g., 21%). Recrystallisation from benzene/pet. ether b.p. 60-80° gave white crystals m.p. 142-4°. (Found: C, 63.50; H, 5.32. C\textsubscript{17}H\textsubscript{17}ClO\textsubscript{2}S requires C, 63.65; H, 5.30%).
$\nu_{\text{max.}}$ 3480 (b, m), 3000 (m), 1610 (m), 1500 (s), 1455 (w), 1430 (m), 1410 (m), 1095 (s), 1020 (s), 990 (m), 975 (m), cm$^{-1}$, $\gamma$ 2.4-2.9 (m, 9H), 3.3 and 3.4 (q, 2H, $J = 85$ Hz.), 4.65 (s, 1H, exchangeable OH), 6.7 (s, 1H), 6.8 (s, 1H), 7.4 (s, 3H).

**Preparation of 3-(4-methylbenzoyl)-1-methylsulphinyl-2-phenylpropane**

Use of 4'-methylchalcone (8.5 g., 0.038 mol.) and DMSO$^-$ (0.038 mol.) in the general procedure gave 3-(4-methylbenzoyl)-1-methylsulphinyl-2-phenylpropane (6.7 g., 58%). Recrystallisation from benzene/pet. ether b.p. 60-80$^\circ$ gave white crystals m.p. 202-4$^\circ$.

(Found: C, 71.99; H, 6.68. C$_{18}$H$_{20}$O$_2$S requires C, 71.98; H, 6.71%).

$\nu_{\text{max.}}$ 3000 (w), 1680 (s), 1610 (s), 1570 (w), 1500 (m), 1455 (m), 1410 (m), 1180 (s), 1110 (w), 1020 (m), 990 (m) cm$^{-1}$, $\gamma$ 2.2-3.4 (m, 9H), 6.2-7.3 (m, 5H), 7.5 (s, 3H), 7.6 (s, 3H).

**Preparation of 1-methylsulphinyl-2-phenyl-(4-t-butylbenzoyl)-propane**

Use of 4'-tert-butylchalcone (7.8 g., 0.03 mol.) and DMSO$^-$ (0.03 mol.) in the general procedure gave 1-methylsulphinyl-2-phenyl-(4-t-butylbenzoyl)-propane (1.05 g., 10%). Recrystallisation from benzene gave white crystals m.p. 236-8$^\circ$.

(Found: C, 73.10; H, 7.51. C$_{21}$H$_{26}$O$_2$S requires C, 73.66; H, 7.66%). $\nu_{\text{max.}}$ 3010 (m), 2900 (s), 2920 (w), 2880 (w), 1690 (s), 1610 (s), 1500 (m), 1460 (m), 1410 (m), 125
1370(m), 1270(m), 1110(m), 1020(b,s), cm$^{-1}$, Τ 2.0-3.0 (m,9H),
6.0-7.5 (m,5H), 7.55 (s,3H), 8.7 (s,3H).

Preparation of 2-(4-methoxyphenyl)-1-methylsulphinyl-3-(2,4,6-trimethylbenzoyl)-propane

Use of 2',4',6'-trimethyl-4-methoxychalcone (5.6g., 0.02 mol.)
and DMSO$-$ (0.02 mol.) in the general procedure gave 2-(4-methoxyphenyl)-1-methylsulphinyl-3-(2,4,6-trimethylbenzoyl)-propane (3.6g., 50%). Recrystallisation from benzene/pet. ether b.p. 60-80° gave white crystals m.p. 150-2°. (Found: C,80.79; H,8.23. C$_{20}$H$_{24}$O$_{2}$ requires C,81.04; H,8.16%). V$_{\text{max}}$ 3000(s), 2950(m), 1705(s),
1620(s), 1590(w), 1520(s), 1470(m), 1450(m), 1430(m), 1360(m),
1250(s), 1180(m), 1035(s) cm$^{-1}$, τ 2.7-3.3 (m,6H), 6.3 (s,3H),
6.7-7.1 (m,5H), 7.55 (s,3H), 7.8 (s,3H), 8.05 (s,3H).

Preparation of 4-(4-fluorophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol

Use of 4-fluorochalcone (3.5g., 0.015 mol.) and DMSO$-$ (0.015 mol.) in the general procedure gave 4-(4-fluorophenyl)-1-methylsulphinyl-2-phenylbut-3-en-2-ol (2.5g., 53%). Recrystallisation from ethyl acetate gave flocculent white crystals m.p. 206-7°.
(Found: C,66.85; H,5.61. C$_{17}$H$_{17}$FO$_{2}$S requires C,67.1; H,5.6%). V$_{\text{max}}$. 3340(b,m), 3000(w), 1610(m), 1510(s), 1450(m), 1160(m),
1100(w), 1020(s) cm$^{-1}$, τ (dmsod$_6$) 2.2-3.0 (m,ca.11H), 4.2(s, 1H, exchangeable OH), 6.7 (s,3H), 6.1 and 6.9 (q,2H, J = 12Hz).
Preparation of 3-Benzoyl-1-benzylsulphinyl-1,2-diphenylpropane

Use of dibenzyl sulphone (2.3g., 0.01 mol.), chalcone (2.1g., 0.01 mol.) and DMSO (0.01 mol.) in the general procedure gave a viscous oil. Trituration with ether gave 3-Benzoyl-1-benzylsulphinyl-1,2-diphenylpropane (1.4g., 32%). Recrystallisation from benzene gave white crystals which change structure at ca. 215° and then do not melt below 300°. (Found: C, 79.36; H, 5.91. \( \text{C}_{29}\text{H}_{26}\text{O}_2\text{S} \) requires C, 79.45; H, 5.94%). \( \nu_{\text{max.}} \) 3000(m), 1690(s), 1610(s), 1500(s), 1460(s), 1030(b, s) cm.\(^{-1}\). The N.M.R. was complex and no splitting patterns could be identified. The spectrum was consistent with a mixture of diastereoisomers. \( \tau \) 2.4-3.1(m), 5.6-7.0(m). The ratio of the integrated multiplets was found to be 3.4:1 (Calculated 3.3:1). The compound was too involatile to obtain a mass spectrum.

Preparation of 3-benzoyl-2-(4-methoxyphenyl)-1-methylsulphinyl-1-phenylpropane

Use of dibenzyl sulphoxide (2.3g., 0.01 mol.), 4-methoxy chalcone (2.4g., 0.01 mol.) and DMSO (0.01 mol.) in the general procedure gave a yellow, viscous oil. Chromatography on alumina (neutral grade I) with successively benzene, chloroform and methanol gave 4-methoxychalcone and 3-benzoyl-2-(4-methoxyphenyl)-1-methylsulphinyl-1-phenylpropane (1.6g., 34%) as a white foam. Recrystallisation from acetone gave white needles m.p. 188-9°. (Found: C, 77.15; H, 6.04. \( \text{C}_{30}\text{H}_{28}\text{O}_3\text{S} \) requires C, 77.90; H, 6.02%). \( \nu_{\text{max.}} \) (KBr) 1690(s), 1615(m), 1600(s), 1570(s), 1450(m), 1410(m), 1300(m), 1255(s), 1180(m), 1040(b, s), 700(m), cm.\(^{-1}\).
Reaction of 4-acetamidochalcone with DMSO⁻

Use of 4-acetamidochalcone (5.3 g., 0.02 mol.) and DMSO⁻ (0.04 mol.) in the general procedure gave a yellow solid shown by IR and NMR to be identical to the starting chalcone.

Reaction of Cholest-4-en-3-one with DMSO⁻

Cholest-4-en-3-one (500 mg., 0.0013 mol.) and DMSO⁻ (0.006 mol.) in the general procedure gave a colourless oil after back-washing the chloroform extract six times with water. The oil gave an IR spectrum superimposable with that of cholest-4-en-3-one.

Raney Nickel Reduction of Some 1,4 Adducts

Reduction of 1-methylsulphinyl-2-phenyl-3-(2,4,6-trimethylbenzoyl)-propane

A solution of 1-methylsulphinyl-2-phenyl-3-(2,4,6-trimethylbenzoyl)-propane (545 mg., 0.0166 mol.) in ethanol (100 ml.) with Raney nickel, prepared from aluminium nickel alloy (5 g.) according to the method described by Vogel,¹⁷⁸ was heated under reflux overnight. The mixture was filtered hot through a layer of celite and the nickel washed with hot ethanol (2 x 25 ml.). Removal of the solvent gave a yellow tinged mobile oil which was filtered through a small alumina column with chloroform to give 2-phenyl-1-(2,4,6-trimethylbenzoyl)-propane (320 mg., 72%), [α]²⁶^₀ 1.547.
Reduction of 3-(2,4-dimethylbenzoyl)-1-methyloxiphényl-2-phenylpropane

Use of 3-(2,4-dimethylbenzoyl)-1-methyloxiphényl-2-phenylpropane (257 mg., 0.0082 mol.) in the general method described above gave 1-(2,4-dimethylbenzoyl)-2-phenylpropane (200 mg., 95%). \( \nu \) max. (liquid film): 2970 (s), 2940 (s), 2880 (m), 1685 (s), 1620 (s), 1500 (s), 1460 (m), 1380 (m), 1290 (m), 1140 (m), 990 (s), 700 (s) cm\(^{-1}\). \( \nu \) 2.5-3.2 (m, 8H), 6.2-7.1 (m, 3H), 7.7 (s, 3H), 7.8 (s, 3H), 8.75 (d, 3H, J=6Hz).

Reduction of 2-(4-methoxyphenyl)-1-methyloxiphényl-3-(2,4,6-trimethylbenzoyl)-propane

Use of 2-(4-methoxyphenyl)-1-methyloxiphényl-3-(2,4,6-trimethylbenzoyl)-propane (284 mg., 0.0011 mol.) in the general method gave 2-(4-methoxyphenyl)-1-(2,4,6-trimethylbenzoyl)-propane (298 mg., 91%), \( \nu \) max. 1.547. (Found: C, 80.79; H, 8.23.)
\( \text{C}_{20}\text{H}_{24}\text{O}_2 \) requires C, 81.04; H, 8.16%.

\( \nu_{\text{max.}} \) (liquid film)

2950(s), 2850(s), 2750(m), 1700(s), 1620(s), 1590(m), 1515(s),
1470(s), 1380(m), 1310(m), 1230(b, s), 1180(s), 1160(m), 1120(m),
1030(s), 990(s), 855(s), 830(s) cm\(^{-1}\), \( \nu 2.7-3.3 \) (m, 6H), 6.3 (s, 3H),
6.4-6.9 (sextuplet, 1H), 7.1 (ca d, J=7Hz.), 7.8 (s, 3H), 8.0(s,5H),
8.7 (d, 3H, J=7Hz.).

Reduction of 3-Benzoyl-1-benzylsulphinyl-1,2-diphenylpropane

A solution of 3-Benzoyl-1-benzylsulphinyl-1,2-diphenylpropane
(377 mg., 0.00086 mol.) in ethanol with Raney nickel, prepared from
nickel aluminium alloy (4g.) was heated under reflux overnight.
Work up in the usual way gave a colourless oil which was purified
by PLC on silica with chloroform. Attempts to solidify the
purified 3-benzoyl-1,2-diphenylpropane (191 mg., 74%) failed.
The I.R. spectrum was superimposable with that of an authentic
sample of 3-benzoyl-1,2-diphenylpropane. \( \nu_{\text{max.}} \) 3020(s), 2940(w),
2860(w), 2410(w), 1690(s), 1605(m), 1590(w), 1500(m), 1450(m),
1210(s), 930(m) cm\(^{-1}\). The N.M.R. spectrum was not superimposable
with the authentic sample although it integrated correctly, and was
similar. This indicates the stereochemistry of the authentic
sample differs from that of 3,4-diphenyl butyrophenone prepared
as above, \( \nu 2.4-3.2 \) (m,15H), 6.5-7.1 (m,5H).
Preparation of 3-Benzoyl-1,2-diphenylpropane

A solution of benzyl chloride (12.7g., 0.1 mol.) in ether (50 ml.) was added dropwise to iodine-activated, ether-covered magnesium (5.8g., 0.24 mol.). When the mixture finished boiling it was heated under reflux for 1 hr. A solution of chalcone (20.8g., 0.1 mol.) in ether (100 ml.) was then added to the refluxing mixture. When addition was complete the mixture was heated under reflux for a further 2 hr. The mixture was poured into excess ammonium chloride solution and extracted with chloroform (3 x 100 ml.). The extract was washed with water, dried and evaporated down to a white solid. Recrystallisation from aqueous ethanol gave white crystals (20.1g., 67%), m.p. 115-7°C (lit. 179 112-3°C), V max. 3020(m), 2940(w), 2860(w), 1690(s), 1605(m), 1590(w), 1500(m), 1450(m), 1210(s), 930(m) cm⁻¹, 7 2.0-3.1 (m, 15H), 6.1-6.6 (m, 1H), 6.75 (d, 2H, J=7Hz.), 7.05 (d, 2H, J=7Hz.).

REACTIONS IN LIQUID AMMONIA

Reactions were carried out in a similar method to the procedure described below.

Preparation of 3,5-diphenyl-3-hydroxy-thiane-1-oxide

A solution of sodamide (2.3g., 0.06 mol.) and DMSO (2.4g., 0.03 mol.) in ammonia (200 ml.) was stirred for one hour. Chalcone (6.2g., 0.03 mol.) in ether (50 ml.) was added to the magnetically
stirred solution for a period of one hour. After a further
period of 3 hrs. excess ammonium chloride was added. Removal
of solvents gave a yellow oil. Trituration with cold ether gave
3,5-diphenyl-3-hydroxy-thiane-1-oxide (2.5g., 29%). Recrystal-
ensation from ethanol gave white needles m.p. 202-12°C (lit. 118,
218°C), \( \nu_{\text{max.}} \) (KBr.) 3250(b.s), 1610(s), 990(b,s) cm\(^{-1}\),
\( \nu \) (dms'-d\(_6\)) 2.2-3.1 (m,10H), 4.2 (s,1H, exchangeable OH),
evidence of half an AB quartet centred at 6.1 calculated 6.05
and 7.05, (J = 13.5Hz., 2H). There remains a multiplet from
6.5 to ca. 7.4

Preparation of 1-Methylsulphinyl-2,4-diphenyl-pent-3-en-2-ol

Use of \( \alpha \)-methylchalcone (2.9g., 0.013 mol.), sodamide (1.0g.,
0.026 mol.) and DMSO (1.0g., 0.013 mol.) in the general method gave
1-methylsulphinyl-2,4-diphenyl-pent-3-en-2-ol (645 mg., 16%).
Recrystallisation from ethanol gave small colourless needles m.p. 144-6°C
(Found: C, 71.88; H, 6.68. \( \text{C}_{18}\text{H}_{20}\text{O} \) requires C, 71.98; H, 6.71%),
\( \nu_{\text{max.}} \) 2380(b,s), 3000(s), 1540(w), 1600(w), 1500(m), 1450(m),
1410(m), 1300(w), 1310(m), 1040(b,s), 1020(b,s), 985(m), cm\(^{-1}\),
\( \nu \) 2.3-2.9 (m,1OH), 3.75 (b,s,1H), 5.15 (s,1H, exchangeable OH),
6.6 and 6.8 (q, 2H, J = 14Hz.), 7.5 (s,3H), 8.0 (d, 1H, J = ca. 1.5Hz.)

Preparation of 1-Methylsulphinyl-2,4-diphenyl-3-methyl-but-3-en-2-ol

Use of \( \beta \)-methylchalcone (4.4g., 0.02 mol.), sodamide (1.6g.,
0.04 mol.) and DMSO (1.6g., 0.02 mol.) in the general procedure gave
1-methylsulphinyl-2,4-diphenyl-3-methyl-but-3-en-2-ol (1.9g., 32%).
Recrystallisation from ethyl acetate gave white needles m.p. 169-70°. (Found: C, 71.91; H, 6.71. \( \text{C}_{18}\text{H}_{20}\text{O}_2 \) requires C, 71.98, H, 6.78%).

\( \nu_{\text{max.}} \) 3380(b,s), 3000(s), 1650(w), 1600(m), 1490(m), 1450(m), 1410(m), 1220(b,m), 1040(b,s), 1020(b,s), 985(m), 950(m) cm\(^{-1}\). \( \tau \) 2.2-3.0 (m,1OH), 3.3 (m,1H), 4.7 (s,1H, exchangeable OH), 6.55 (d,2H, \( J = \text{ca.} 3.5\text{Hz.} \)), 7.35 (s,3H), 8.25 (d, 3H, \( J = \text{ca.} 1\text{Hz.} \)).

Desulphurisation of 3,5-diphenyl-3-hydroxy-thiane-1-oxide

A solution of 3,5-diphenyl-3-hydroxy-thiane-1-oxide (200 mg., 0.0007 mol.) in ethanol (50 ml.) was heated under reflux overnight with Raney nickel prepared from aluminium nickel alloy (2.0 g.). Work up as described previously gave a colourless oil (163 mg.). T.L.C. on silica using chloroform indicated two components. PLC gave 2-hydroxy-2,5-diphenylpentane (107 mg., 64%) as an oil. \( \nu_{\text{max.}} \) 3620(m), 3450(b,m), 3070(w), 2980(m), 2940(m), 2880(w), 1610(m), 1500(s), 1460(sh,s), 1450(s), 1380(m), 1310(w), 1120(w), 1070(m), 1030(m), 1010(w), 900(m) cm\(^{-1}\). \( \tau \) 2.4-3.1 (m,1OH), 7.0-8.0 (m,3H), 8.2 (s,1H, exchangeable OH), 8.45 (s,3H), 9.2 (d, 3H, \( J = 7\text{Hz.} \)). Measured mass 240.1518, \( \text{C}_{17}\text{H}_{20}\text{O} \) requires 240.1514.

The faster running component was identified as 2,4-diphenylpentane (26 mg., 16%). \( \nu_{\text{max.}} \) 2970(sh,s), 2930(s), 2860(sh,s), 1610(m), 1500(s), 1450(s), 1380(m) cm\(^{-1}\). \( \tau \) (CCl\(_4\)) 2.7-3.1 (m,1OH), 7.0-8.0 (m,4H), 8.6-8.9 (superimposed doublets \( J = \text{ca.} 7\text{Hz.} \)).

MS. m/e 224, 119, 105, 97, 91, 85, 83, 71, 69, 57, 55.
Attempted Cyclisation of 1-Methylsulphinyl-2,4-diphenylbut-3-en-2-ol

Using the general method, 1-methylsulphinyl-2,4-diphenylbut-3-en-2-ol (3.7 g., 0.013 mol.) and excess sodamide (1.6 g., 0.040 mol.) in ammonia (200 ml.), gave a sticky white residue. Trituration with ether gave a white solid (2.0 g.). Recrystallisation from ethanol gave white needles m.p. 278-80°. (Found: C, 86.20; H, 5.72%), \( \nu_{\text{max.}} \) 3095(w), 3070(w), 3040(w), 1690(s), 1600(m), 1580(m), 1490(m), 1460(m), 1450(m), 1270(s), 980(w) cm\(^{-1}\), \( \gamma \) 2.2-3.2 (m\(_{A}\)), 4.9-6.2 (m\(_{B}\)). The ratio of \( n_{A} \) to \( n_{B} \) was 4.6:1.

Preparation of \( \omega \)-Methyl-\( \omega \)-nitrostyrene

The method of Hans et. al.\(^{180}\) was adopted. A solution of benzaldehyde (10.6 g., 0.1 mol.), nitroethane (7.5 g., 0.1 mol.) and \( n \)-butylamine (0.5 ml.) in ethanol (100 ml.) was refluxed for 8 hr. The solution was reduced to small bulk and cooled in ice giving a yellow crystalline precipitate of \( \omega \)-methyl-\( \omega \)-nitrostyrene (3.6 g., 22%). Recrystallisation from ethanol gave yellow needles m.p. 64-5\(^{\circ}\) (lit.\(^{180}\), 65\(^{\circ}\)), \( \nu_{\text{max.}} \) 1670(s), 1610(w), 1580(m), 1510(s), 1450(s), 1400(s), 1330(s), 1300(m), 985(s) cm\(^{-1}\), \( \gamma \) 2.1 (s,3H), 2.7 (s,5H), 7.7 (s,3H).
Attempted reaction of \( \mu \)-methyl-\( \mu \)-nitrostyrene with Methylsulphinyl carbanion

Use of \( \mu \)-methyl-\( \mu \)-nitrostyrene (1.5 g., 0.0092 mol.) and DMSO\(^-\) (0.0092 mol.) in the general method previously described gave a viscous dark coloured oil (2.0 g.) contaminated with DMSO. \( \nu \)\(_{\text{max.}}\) (liquid film) contained a medium absorption band at 1710 cm\(^{-1}\).

Preparation of 1-Methylsulphinyl-3-nitro-2-phenylbutane

A solution of sodium (2.0 g., 0.05 mol.) and DMSO (3.9 g., 0.05 mol.) in ammonia (200 ml.) was stirred for 1 hr. \( \mu \)-Methyl-\( \mu \)-nitrostyrene (8.2 g., 0.05 mol.) in ether (50 ml.) was added and the solution stirred for a further 4 hr., during which a pale orange colour developed. The solution was neutralised with excess ammonium chloride and the solvent evaporated to leave a sticky, viscous oil. The oil was taken up in hot toluene and stirred at \(-30^\circ \text{C}\) for several days depositing a mixture of stereoisomers of 1-methylsulphinyl-3-nitro-2-phenylbutane (3.1 g., 26%). Recrystallisation from toluene/pet. ether b.p. 60-80\(^\circ\) gave white crystals m.p. 126-31\(^\circ\). (TLC indicated two diastereoisomers). (Found: C, 54.65; H, 6.16. \( \text{C}_{11}\text{H}_{15}\text{NO}_{3}\text{S requires C, 54.76; H, 6.27%}\). \( \nu \)\(_{\text{max.}}\) 3000(m), 1610(w), 1555(s), 1500(w), 1460(m), 1390(m), 1360(m), 1300(w), 1040(b,s), 970(m) cm\(^{-1}\). \( \tau \) 2.5-3.0 (s, 5H), 5.1 (p, 1H, \( \int = 7\text{Hz.}\)), 6.0-6.5 (m, 1H), 6.7-7.1 (m, 2H), 7.5 (s, 3H), 8.45 (d, 3H, \( \int = 7\text{Hz.}\)).
Preparation of 1,2-diphenyl-3-methylsulphinyl-1-nitropropane

Use of sodamide (0.8g., 0.02 mol.), DMSO (1.6g., 0.02 mol.) and 6-phenyl-6-nitrostyrene (4.5g., 0.02 mol.) in the method described above gave 1,2-diphenyl-3-methylsulphinyl-1-nitropropane (1.6g., 26%). Recrystallisation from ethanol gave white crystals m.p. 218-20°. (Found: C,63.61; H,5.55. C_{16}H_{17}NO_{3}S requires C,63.35; H,5.65%), \(\nu_{\text{max.}}\) (KBr) 3020(m), 2940(m), 1610(w), 1590(w), 1550(s), 1520(w), 1500(m), 1460(m), 1400(s), 1360(s), 1300(w), 1200(w), 1080(m), 1030(s), 970(m), 870(w), 790(m), 760(s), 730(m), 700(s) cm.\(^{-1}\), \(\gamma\) (material m.p. 175-80° mixture of diastereoisomers in DMSO-d\(_6\)) 2.2-2.9 (m,1OH), 3.5-6.1 (m,3H), 5.5-7.0 (m,3H), 7.7 (s,3H).

The Nef Reaction of 1-Methylsulphinyl-3-nitro-2-phenylbutane

1-Methylsulphinyl-3-nitro-2-phenylbutane (120 mg., 0.0005 mol.) was dissolved in 10% potassium hydroxide (5 ml.) on a steam bath. The solution was cooled to room temperature and poured on to a mixture of excess ice and dilute hydrochloric acid. The mixture was extracted with chloroform (3 x 20 ml.) and the extract washed with water and sodium bicarbonate solution. The solution was dried and evaporated down to a crude oil (78 mg.). Absorption in the IR was observed at 1710(s) cm.\(^{-1}\) and in the NMR at \(\gamma\) 7.9. No further purification was attempted.
Preparation of some Dicarbonyl Compounds

4,4'-Dimethoxybenzil

Using the method described by Vogel a mixture of anisoin (4,4'-dimethoxybenzoin) (81.6g., 0.3 mol.), ammonium nitrate (40g., 0.5 mol.), and cupric acetate (0.8g.) in acetic acid (200 ml.) and water (50 ml.) was heated under reflux for 90 min. On cooling the solution 4,4'-dimethoxybenzil was deposited. Recrystallisation from ethanol gave yellow needles (57.3g., 71%) m.p. 133-4°C (lit. 131, 133°C) \( \nu_{\text{max}} \) 1695(sh, w), 1670(s), 1600(s), 1575(s) cm\(^{-1}\), \( \tau \) 2.05 and 3.0 (q, 8H, J = 8.5Hz.), 6.1 (s, 6H).

\( \alpha \alpha \)-Furil

Using the same method as described above furoin (11.5g., 0.06 mol.), ammonium nitrate (5g., 0.063 mol.), and cupric acetate (0.1g.) in acetic acid (100 ml.) and water (10 ml.) gave, after recrystallisation from benzene, \( \alpha \alpha \)-furil (7.0g., 61%) m.p. 165-6°C (lit. 182, 166°C), \( \nu_{\text{max}} \) 1695(s), 1670(s) cm\(^{-1}\).
Preparation of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide

A solution of sodamide (3.9g., 0.1 mol.) and DMSO (3.9g., 0.05 mol.) in ammonia (200 ml.) was magnetically stirred for 1 hr. Benzil (10.5g., 0.05 mol.) in ether (50 ml.) was added dropwise over a period of 30 min. and the solution stirred for a further 3 hr. Removal of solvents gave a sticky white residue. Trituration with ether gave 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide (466 mg., 3.5%). Recrystallisation from ethanol gave white crystals m.p. 174-6°. (Found: C,66.52; H,5.48. C₁₆H₁₆O₃S requires C,66.67; H,5.55). \( \nu_{\text{max.}} \) 3540(b,s), 3500(b,m), 3010(m), 1610(w), 1500(m), 1450(w), 1390(w), 1170(w), 1065(s), 1020(b,s) cm⁻¹.
The NMR was consistent with the presence of 2 isomers: \( ^2J = 2.8-3.3 \) (m,1OH), 4.2 and 4.25 (s,2H, exchangeable OH), 2 superimposed AB quartets 5.9 and 6.5 (q, 4H, \( J = 14 \text{Hz} \)).

Reaction of 4,4'-dimethoxybenzil

Using the general method sodamide (2.3g., 0.06 mol.), DMSO (2.3g., 0.03 mol.), and 4,4'-dimethoxybenzil (8.1g., 0.03 mol.) gave a yellow solid. Recrystallisation gave 4,4'-dimethoxybenzil (6.0g., 75% recovery) with an identical I.R. to that of the starting benzil.

Attempted Reaction of Dibenzyl sulfoxide with Benzil

A solution of dibenzyl sulfoxide (5.75g., 0.025 mol.) and sodamide (2.0g., 0.05 mol.) in ammonia (200 ml.) was magnetically
stirred for 1 hr. Benzil (5.25 g., 0.025 mol.) in ether (50 ml.) was added and the solution stirred for a further 4 hr. Evaporation of solvents gave a sticky white residue. Trituration with ether gave a white solid (5.0 g.) having an identical IR to that of dibenzyl sulphoxide. The NMR was also identical to that of dibenzyl sulphoxide.

Reactions of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide

(a) Periodate cleavage

A solution of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide (144 mg., 0.0005 mol.) and sodium metaperiodate (200 mg., 0.00094 mol.) in aqueous methanol (25 ml. MeOH, 5 ml. H2O) was magnetically stirred for 8 hr. The mixture was filtered to remove sodium iodate and the filtrate extracted with chloroform (3 x 25 ml.). The solution was dried and evaporated down to an oil. TLC with chloroform on silica gave diphenacylsulphoxide (64 mg., 45%) as an oil. A solution of the oil in ethanol gave small white crystals m.p. 96-97° (lit.183, 98°) \( \nu_{\text{max}} \) 3000(w), 1680(s), 1600(s), 1580(m), 1450(s), 1320(m), 1280(s), 1180(m), 1050(b,m), 1000(sh,m), 990(s) cm.\(^{-1}\), \( \gamma \) 1.8-2.5 (m,10H), 4.9-5.6 (m,4H).

(b) Raney nickel reduction

3,4-Dihydroxy-3,4-diphenylthiolane-1-oxide (122 mg., 0.00042 mol.) was heated under reflux with Raney nickel, prepared from
aluminium nickel alloy (4.0g.), in ethanol (50 ml.) for 4 hr.

Work up in the usual way gave a colourless oil. PLC on silica with chloroform gave 2,3-dihydroxy-2,3-diphenylbutane (50 mg., 49%). Recrystallisation from ethanol gave white crystals m.p. 117-8° (lit. 129, 116.2-117.8°). √ (CCl₄) 3600(b,m), 3000(m), 1600(s), 1495(m), 1450(s), 1370(m), 1335(b, m), 1170(w), 1125(m), 1110(m), 1070(m), 1025(m), 900(m) cm.⁻¹

(Δ (c Cl₂): 2.75 (s, 1OH), 7.7 (b, s, 2H, exchangeable OH), 8.4 (s, 6H) (lit. 130) (acetone d₆): 2.4-2.9 (m, 1OH), 6.1 (s, 2H, exchangeable OH), 8.5 (s, 6H). (lit. 130).

(c) Attempted oxidation with hydrogen peroxide

1. A solution of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide (144 mg., 0.0005 mol.) in methanol (25 ml.) was stirred with hydrogen peroxide (2 ml., 30% H₂O₂) overnight. The solution was diluted with excess water and extracted with chloroform (3 x 25 ml.). The extract was washed with water, dried, and evaporated to a white solid (110 mg.) having the same R_f as the starting material. An IR of the solid was superimposable with that of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide.

2. Use of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide (144 mg., 0.0005 mol.) in acetic acid (25 ml.) in the procedure described above with hydrogen peroxide (2 ml., 30% H₂O₂) gave an 84% recovery of starting material.
(d) **Attempted formation of an isopropylidene derivative with acetone**

A solution of 3,4-dihydroxy-3,4-diphenylthiolane-1-oxide (144 mg., 0.0005 mol.) and acetone (2 ml.) in benzene (50 ml.) together with a crystal of p-toluenesulphonic acid was heated under reflux for 2 days. Removal of solvent gave a crude white solid having the same $R_f$ as the starting material. An IR spectrum of the solid was identical with that of the starting material.

**Attempted Reactions with Quinones and "Dimethylsulphoxide Dicarbanion"**

1. **9,10-Anthraquinone**

   Use of 9,10-Anthraquinone (5.2 g., 0.025 mol.), sodamide (2.0 g., 0.05 mol.) and DMSO (2.0 g., 0.025 mol.) in the general method gave a cream coloured solid (2.0 g.) having an IR superimposable on that of 9,10-Anthraquinone.

2. **Naphthaquinone**

   Use of 1,4-naphthaquinone (3.9 g., 0.025 mol.), sodamide (2.0 g., 0.05 mol.) and DMSO (2.0 g., 0.025 mol.) in the general method gave an 80% recovery of 1,4-naphthaquinone identified by its IR and NMR.
Preparation of 2-Phenyl-3-p-tolylthiazolidin-4-one-l-oxide

A solution of 2-phenyl-3-p-tolylthiazolidin-4-one (2.6 g., 0.01 mol.) and sodium metaperiodate (2.9 g., 0.01 mol.) in aqueous methanol (MeOH, 100 ml.; H₂O, 20 ml.) was magnetically stirred at room temperature overnight. Sodium iodate was removed by filtration and the filtrate extracted with chloroform (3 x 25 ml.). The extract was washed with water, dried and evaporated to an oil. Trituration with ether gave 2-phenyl-3-p-tolylthiazolidin-4-one-l-oxide (2.0 g., 73%). Recrystallisation from methanol gave glistening white crystals m.p. 180-1°. (Found: C, 65.66; H, 5.79. C₁₆H₁₅NO₃S requires C, 65.70; H, 5.34%). \( \gamma \) max. 3000(m), 1710(s), 1620(w), 1510(s), 1495(m), 1455(m), 1390(m), 1370(s), 1320(m), 1290(m), 1265(s), 1130(m), 1110(m), 1060(b,s), 1020(w), 1000(w) cm⁻¹, \( \tau \) 2.5-3.0 (m, 9H), 4.05 (s, 1H), 6.15 and 6.45 (q, 2H, \( J = 17\text{Hz.} \)) 7.75 (s, 3H).

Preparation of 2-Phenyl-3-p-tolylthiazolidin-4-one-l-dioxide

A solution of 2-phenyl-3-p-tolylthiazolidin-4-one (2.6 g., 0.01 mol.) and hydrogen peroxide (100 vol., 4 ml.) in acetic acid (50 ml.) was left overnight. The solution, stored at 0° for several days, deposited crystals of 2-phenyl-3-p-tolylthiazolidin-4-one-l-dioxide (1.9 g., 63%). Recrystallisation from methanol gave glistening white crystals m.p. 185-7°. (Found: C, 63.86; H, 5.29; N, 4.71. C₁₆H₁₅NO₃S requires C, 63.78; H, 5.02; N, 4.65%). The IR shows a large number of absorption peaks and only the strong absorptions are
recorded. $\nu_{\text{max.}}$ (KBr) 2940, 1715(b), 1520, 1380, 1330, 1220, 1130, 1820, 700 cm$^{-1}$, $\tau$ 2.5-3.1 (m,9H), 4.1 (s,1H), 6.2 (s,2H), 7.8 (s,3H).

Reduction of 3-phenyl-3-p-tolylthiazolidin-4-one-1-oxide

(a) Aluminium amalgam

A solution of 3-phenyl-3-p-tolylthiazolidin-4-one-1-oxide (640mg., 0.0022 mol.) in aqueous THF (25 ml. THF, 5 ml. $H_2O$) was magnetically stirred with aluminium amalgam prepared from aluminium (2g.) as previously described. After 2 hrs. the mixture was filtered and the filtrate extracted with chloroform (3 x 25 ml.). The chloroform solution was washed with water, dried and evaporated to yield a white solid. Recrystallisation from ethanol gave 3-phenyl-3-p-tolylthiazolidin-4-one n.p. 127-8°. The IR and NMR spectra were identical to those of an authentic sample.

(b) Raney nickel

A solution of 3-phenyl-3-p-tolylthiazolidin-4-one-1-oxide (420mg., 0.0015 mol.) in ethanol (50 ml.) was heated under reflux with Raney nickel, prepared as previously described, from aluminium nickel alloy (3g.). After 4 hrs. the mixture was cooled and filtered; the filtrate was extracted with chloroform (3 x 25 ml.). The solution was dried and evaporated down to an oil. PLC on silica with chloroform gave N-benzyl-N-p-tolylacetamide (240 mg., 60%) as an oil. A satisfactory
analysis could not be obtained. \( \nu_{\text{max.}} \) 3700(w), 3640(m), 3020(s),
2980(m), 2400(s), 1650(m), 1520(m), 1480(m), 1430(m),
1220(b,s),
1050(s), 930(s)cm\(^{-1}\) \( \tau \) 2.6-3.2 (m,3H), 5.1 (s,2H), 7.7 (s,3H),
8.1 (s,3H).

**Preparation of 3-Ketothiacyclohexane**

3-Ketothiacyclohexane was prepared adopting Leonard and
Figueras' method.\(^1\)\(^4\)\(^7\) Ethyl \( \delta \)-chlorobutyrate (62.3g., 0.414 mol.)
and methyl thioglycolate (43.9g., 0.414 mol.) gave an overall yield
of 19% of 3-ketothiacyclohexane (9.4g.) b.p. 60\(^0\)/1.5 mm. (lit.\(^1\)\(^4\)\(^7\)
80\(^0\)/4.0 mm.) \( \nu_{\text{max.}} \) (liquid film): 2930(s), 2860(m), 1710(b,s),
1430(s), 1420(s), 1410(s), 1350(m), 1320(s), 1260(m), 1230(s), 1200(m),
1160(m), 1060(m), 1030(m), 940(m), 890(m), 850(w), 760(m) cm\(^{-1}\),
\( \tau (\text{CCl}_4): 6.9 \text{(s,2H)}, 7.1-7.4 \text{(m,2H)}, 7.4-7.7 \text{(m,4H)} \).

**Preparation of 3-Ketothiacyclohexane-1-oxide**

A mixture of 3-Ketothiacyclohexane (2.3g., 0.02 mol.) and
sodium metaperiodate (4.3g., 0.02 mol.) in aqueous methanol (50 ml.
MeOH, 5 ml. H\(_2\)O) was magnetically stirred overnight. Sodium iodate
was filtered off and the filtrate extracted with chloroform (3 x 25 ml.)
The solution was dried and evaporated down to a yellow tinged oil;
there was the absence of any smell due to 3-ketothiacyclohexane. PLC
on silicil with chloroform gave 3-ketothiacyclohexane-1-oxide (500 mg.,
19%) as a colourless oil. Recrystallisation from ethanol gave well
defined crystals m.p. 83-9\(^0\) \( \text{(Found: C}, 45.36; \text{H}, 5.01.} \)

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$C_{32}H_{26}N_2O_S$ requires $C, 78.7\%$; $H, 5.74\%$; $N, 5.74\%$; $S, 6.56\%$; $\nu_{\text{max}}$ (KBr) $3040(w)$, $2360(w)$, $2240(w)$, $1610(w)$, $1500(s)$, $1460(s)$, $1400(b, s)$, $1080(w)$, $1030(b, s)$, $760(m)$, $700(s)$ cm$^{-1}$, $\tau = 2.6-3.2$ (m$\alpha$), 5.6 and 5.75 (2 superimposed doublets, $J = 9$ Hz., ca. 2H), 6.2-7.0 (m$\beta$). The ratio of multiplets $m_\alpha:m_\beta$ found 3.6:1 calculated 3.3:1.
REFERENCES


42. C.H. Snyder, *Chem. and Ind.*, 1963, 121.


145. C. Marcker, Annalen, 1865, 136, 75.


153. H.V. Frost, Annalen, 1889, 250, 156.


183. E. Frohne, Annalen, 1912, 394, 290.