SYNTHETIC APPLICATIONS OF THE SHAPIRO REACTION

A thesis submitted by

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CONTENTS

ABSTRACT

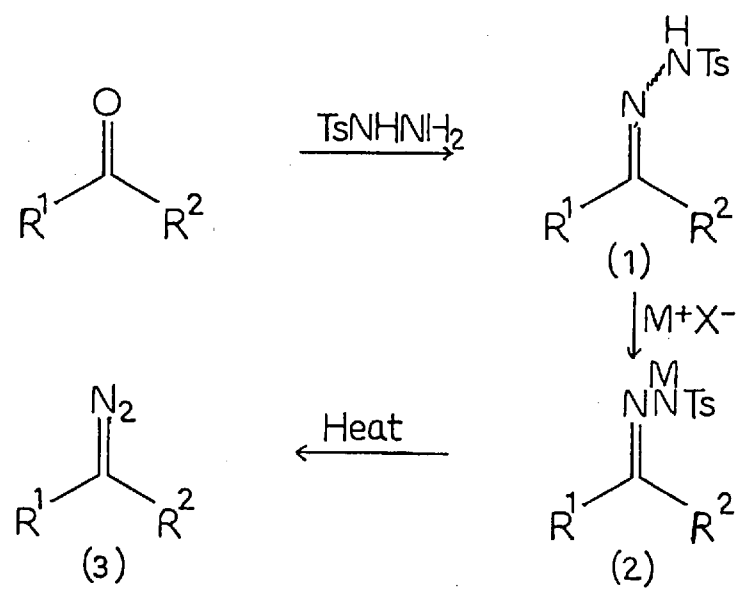
The Shapiro reaction is reviewed. The mechanism and synthetic applications of the characteristic reaction intermediates are discussed.

A new concise preparation of 3-methylenetetrahydrofuran-2-ones derived *via* the Shapiro reaction is described; two ketones (or ketone plus aldehyde) and carbon dioxide are shown to be the synthetic equivalent of the α-methylene-γ-lactones. The basic reaction has been extended to the preparation of the novel 3,5-dimethylenetetrahydrofuran-2-one and 3,6-dimethylenetetrahydropyran-2-one systems. Studies towards the preparation of obtusilactone derivatives, *via* a novel carbonyl stabilised vinyl carbanion,are reported. The preparation of 3-methylene-azetidin-2-ones is described.

Some unusual reaction products, including a novel sultone derived from 2,4,6-tri-iso-propylbenzenesulphinic acid, are described.

INTRODUCTION

Toluene-4-sulphonylhydrazine has been shown to react with ketones to form toluene-4-sulphonylhydrazone derivatives in high yield. These substrates (1) reacted with mild bases to form a metallated derivative (2) which upon heating produced a diazo compound (3)[51] by the α-elimination of the metal arylsulphinate (Scheme 1). The fate of the diazo

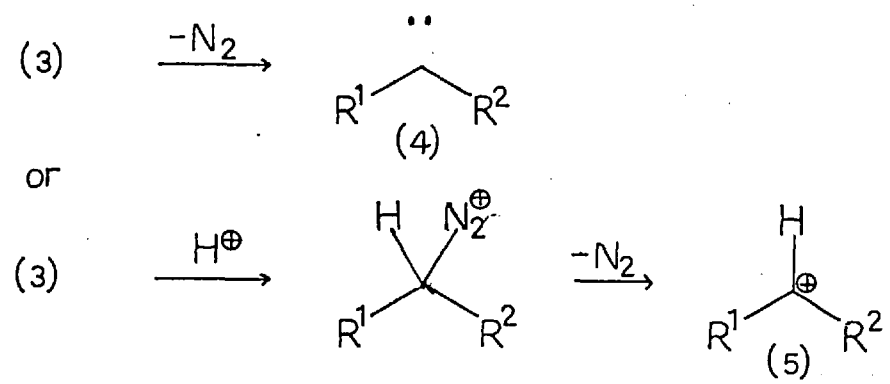


Ts = toluene-4-sulphonyl

SCHEME 1

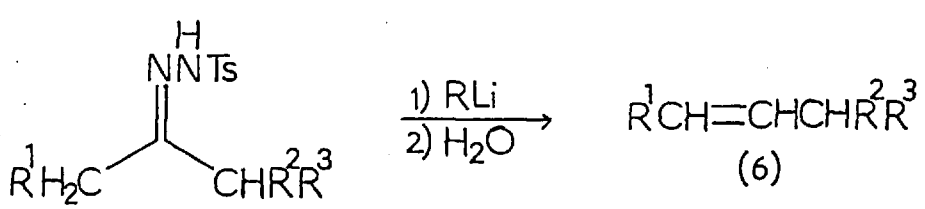
compound (3) in the presence of excess base was largely dependent upon the nature of the solvent. If no proton source was available or if the available proton source reacted too slowly with the diazo intermediate, molecular nitrogen would be eliminated and a carbene (4) generated. If, however, proton donation was faster than nitrogen elimination, a diazonium ion was formed. The diazonium ion could lose nitrogen, giving a carbonium ion (5) which would expel a proton with or without previous rearrangement[51] (Scheme 2). These reactions are known as the aprotic

and protic Bamford-Stevens reactions respectively.



SCHEME 2

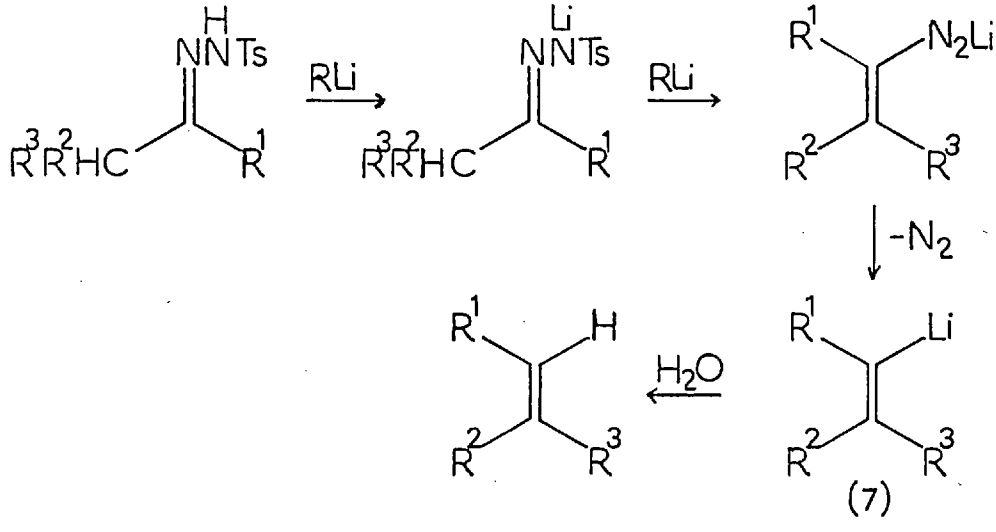
With an alkyllithium reagent[1,2,4] ketone toluene-4-sulphonylhydrazones with an α-hydrogen atom, were found to react to form the least substituted, unrearranged alkene (6) (Scheme 3). This reaction is termed the Shapiro reaction.



SCHEME 3

SECTION I : THE MECHANISM OF THE SHAPIRO REACTION

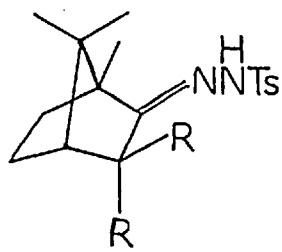
In his introductory communication[1], Shapiro suggested that the Shapiro reaction proceeded by a carbanion mechanism (Scheme 4) involving the approach of the alkyllithium reagent at the least hindered and most acidic proton. Other base induced toluene-4-sulphonylhydrazone decompositions are comparable[48,50].



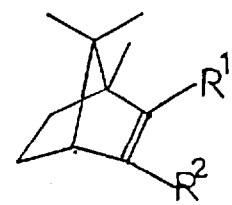
SCHEME 4

Formation of the vinyl carbanion (7) was consistent with capture by deuterium oxide for a limited number of arylsulphonylhydrazone derivatives[1,3]. For example[1], the reaction of camphor toluene-4-sulphonylhydrazone (8) with greater than two equivalents of n-butyllithium at room temperature in hexane, followed by deuterium oxide quenching, gave 2-deuterio-2-bornene (10). The position of the deuterium atom was confirmed by nmr spectroscopy. However[1], the reaction of 5α-androstan-17-one toluene-4-sulphonylhydrazone (13) with methyllithium in diethyl ether at room temperature gave, on deuterium oxide quenching, the Δ^{16}

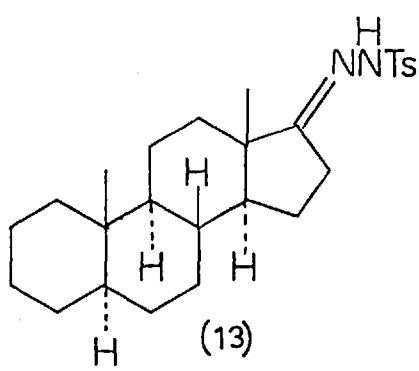
androstene containing 60% mono-deuterio-alkene (14). More surprisingly[1], the reaction of camphor toluene-4-sulphonylhydrazone (8) with methyllithium in diethyl ether and subsequently with deuterium oxide gave the 2-bornene (10) with only 10% deuterium incorporation. Shapiro concluded that the vinyl carbanion (7) was a reaction intermediate,



(8) R=H
(9) R=D



(10) R^1=D, R^2=H
(11) R^1=H, R^2=D
(12) R^1=Li, R^2=H



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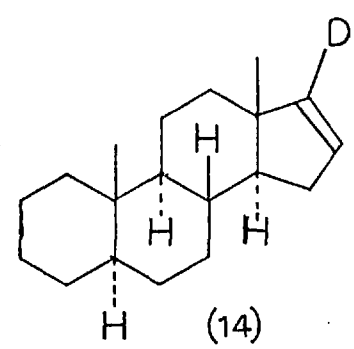
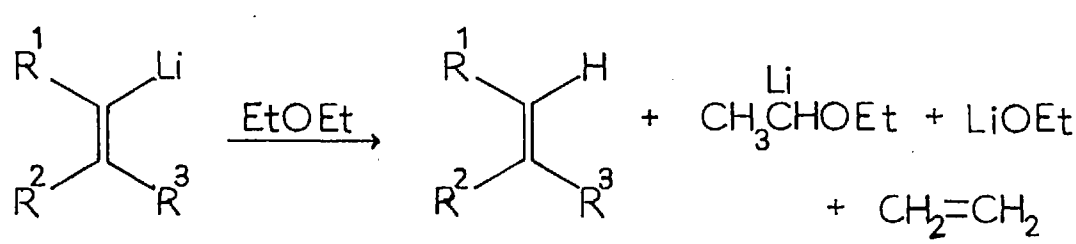


(14)

plausibly partially protonated by solvent prior to the additon of the deuterium oxide quench (Scheme 5). Indeed, Shapiro was able to identify

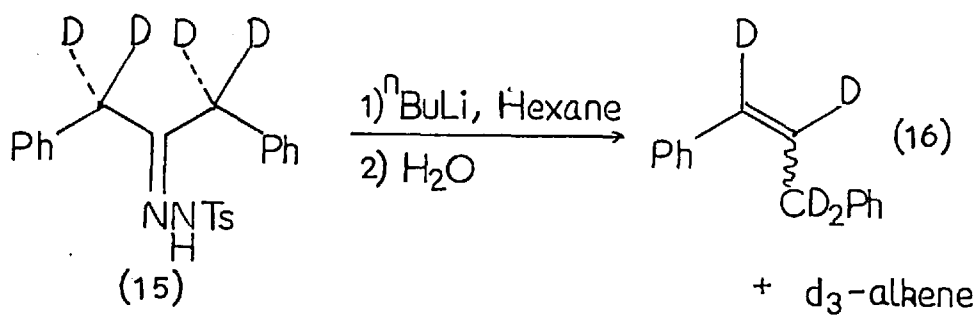


SCHEME 5

ethanol in the reaction mixture, and quantitative gas determination[1] showed that greater than three equivalents of gas (nitrogen and methane) were produced in his ethereal experiments.

Shapiro[1] was also able to show that α-proton abstraction had occurred. The reaction of 3,3-dideuteriocamphor toluene-4-sulphonylhydrazone (9) with alkyllithium reagents gave 3-deuterio-2-bornene (11).

In an attempt to clarify the solvent effect, Shapiro[11] conducted further experiments using hexane as reaction solvent. He found that 1,3-diphenylacetone toluene-4-sulphonylhydrazone gave 1,3-diphenylpropene and an undefined mono-deuteriopropene derivative under usual reaction conditions, followed by deuterium oxide quenching. The reaction, however, was heterogeneous. More significantly 1,1,3,3-tetradeuterio-1,3-diphenylacetone toluene-4-sulphonylhydrazone (15) gave both a tetradeuterio-(16) and a trideuterio-alkene product under the same sequence followed by a water quench (Scheme 6). The product (16) could only have

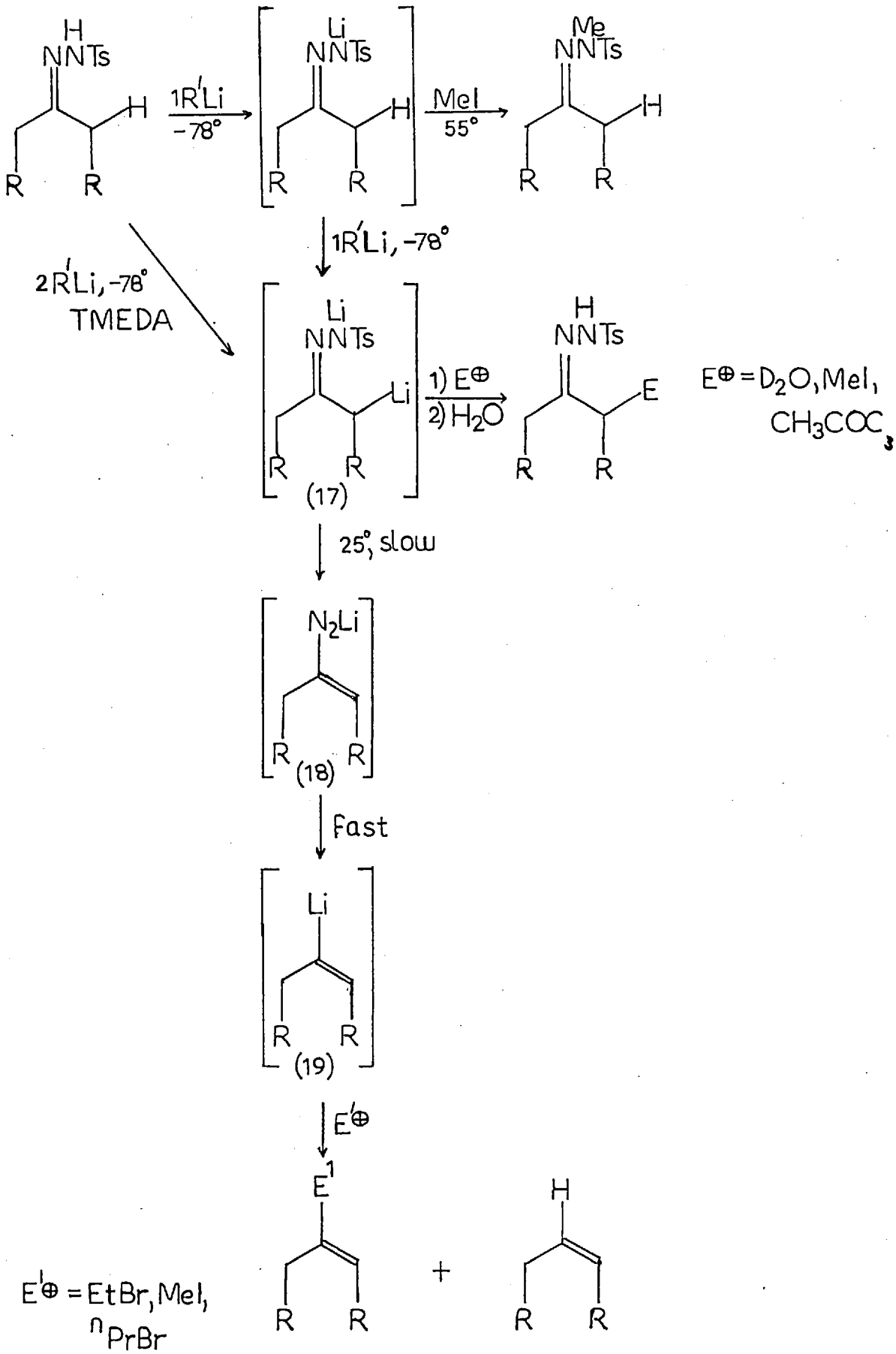


SCHEME 6

resulted from the reaction of a vinyl carbanion intermediate (7) with the initial substrate, or its monoanion derivative. This result indicates that Shapiro's initial choice[1] of camphor toluene-4-sulphonylhydrazone (8) as a model compound was not representative; 2-lithio-2-bornene (12) would be particularly hindered and unlikely to abstract an α-proton from a substrate molecule (or its monoanion equivalent). Hence the vinyl carbanion (12) could be quenched by external deuterium oxide. The steric hindrance of electrophilic attack on 2-lithio-2-bornene (12) has been shown in subsequent experiments[19,23]. Reaction of carbanion (12) with other electrophiles, N,N-dimethylformamide and chlorotrimethylsilane, gave only 10-15% yields of the trapped products.

In further, more rigorous experiments, Shapiro was able to substantiate his mechanistic proposals. Treatment of a ketone toluene-4-sulphonylhydrazone in diethyl ether at -78° with one equivalent of methyllithium[15,51], followed by the addition of methyl iodide and warming to 55°, gave monomethylation on nitrogen. If the ketone toluene-4-sulphonylhydrazone[15] was treated with two equivalents of methyllithium at low temperature, a discrete dianion (17) was formed which was trapped by electrophiles, deuterium oxide, methyl iodide and acetone on carbon. Warming of the dianion species (17)to room temperature gave the vinyl carbanion intermediate (19) and nitrogen. If N,N,N',N'-tetramethylethylenediamine (TMEDA), with or without benzene[15] as cosolvent, was used as reaction solvent, then addition of electrophiles (E'^{+}) after gas evolution gave products derived from the vinyl carbanion intermediate (19) in addition to the normal Shapiro olefin product (Scheme 7).

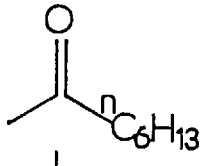
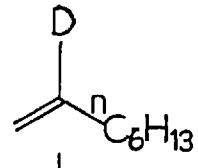
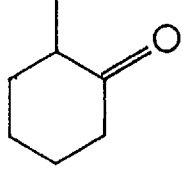
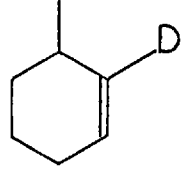
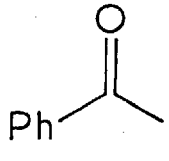
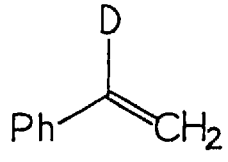
Shapiro[15] also claimed to have trapped the vinyl diimide anion (18) in low yield, however, no evidence was offered.


H
NNTs
R
R
H
1R'Li
-78°
Li
NNTs
Mel
55°
Me
1R'Li, -78°
2R'Li, -78°
TMEDA
1) E⊕
2) H2O
E
E⊕ = D2O, Mel, CH3COCl
(17)
25°, slow
N2Li
(18)
Fast
(19)
E'⊕
E'
E'⊕ = EtBr, Mel, nPrBr
+

SCHEME 7

In an accompanying publication, Bond[14] demonstrated that vinyl carbanion intermediates (7) could also be generated by the reaction of ketone benzenesulphonylhydrazones in TMEDA with four equivalents of n-butyllithium at -50°, followed by warming to room temperature. Subsequent addition of deuterium oxide gave deuterio-olefins in high yields with high deuterium incorporations (Table 1).

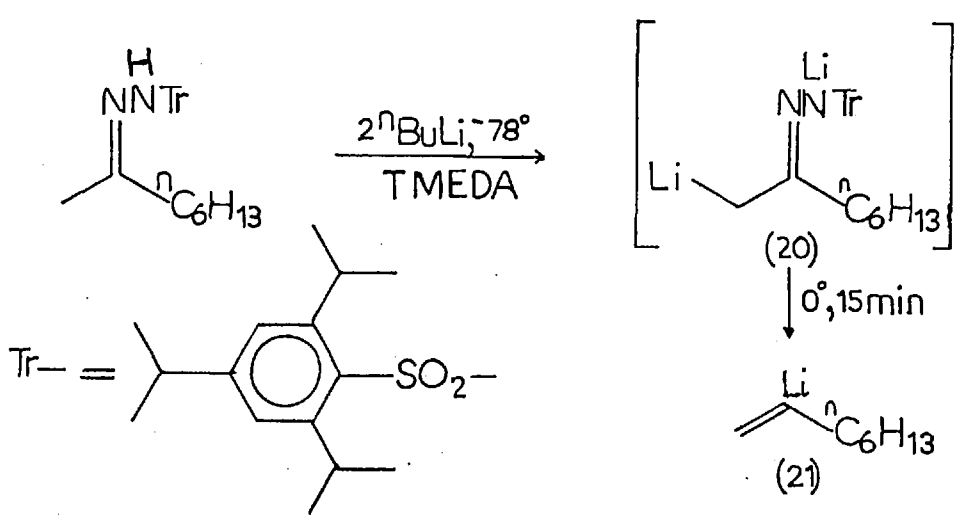
TABLE 1

Ketone	Product	Yield (%)	Deuterium incorporation (%)
		100	91
		98	93
		96	94

Furthermore, Bond[20] has shown that the vinyl carbanion intermediate (7), generated from a ketone toluene-4-sulphonylhydrazone with three and a half equivalents of alkyllithium reagent in TMEDA, could be trapped with a variety of electrophiles, ketones, alkyl halides, carbon dioxide and aldehydes, in moderate to high yields.

The superiority of Bond's[14, 20] method over Shapiro's[15] lies in the amount and reactivity of the alkyllithium reagent used. Indeed, Bond[20,33] indicated that when octan-2-one toluene-4-sulphonylhydrazone was treated with three equivalents of n-butyllithium in TMEDA at -78°, warmed to 0° and quenched with deuterioacetic acid, the recovered octan-2-one toluene-4-sulphonylhydrazone was labelled with deuterium in the aromatic ring at the ortho-position (Section IIIc). Shapiro's conditions[15] provided only two equivalents of alkyllithium reagent for dianion formation. On warming, a vinyl carbanion intermediate (7) was formed which was partially quenched by the ortho-proton of a toluene-4-sulphonyl-residue. The use of excess alkyllithium[14,20] removed this proton source before a vinyl carbanion intermediate (7) was formed and hence the vinyl carbanion (7) was efficiently trapped by external electrophiles.

Later, Bond[33] was able to demonstrate that ketone 2,4,6-tri-iso-propylbenzenesulphonylhydrazones could be used to generate stable vinyl carbanions (21) from stoichiometric amounts of alkyllithium reagents. Clearly ortho-metallation was blocked and the dianion intermediate (20) underwent fragmentation to the vinyl carbanion intermediate (21) at a lower temperature; relief of steric congestion brought about this more facile cleavage (Scheme 8).



SCHEME 8

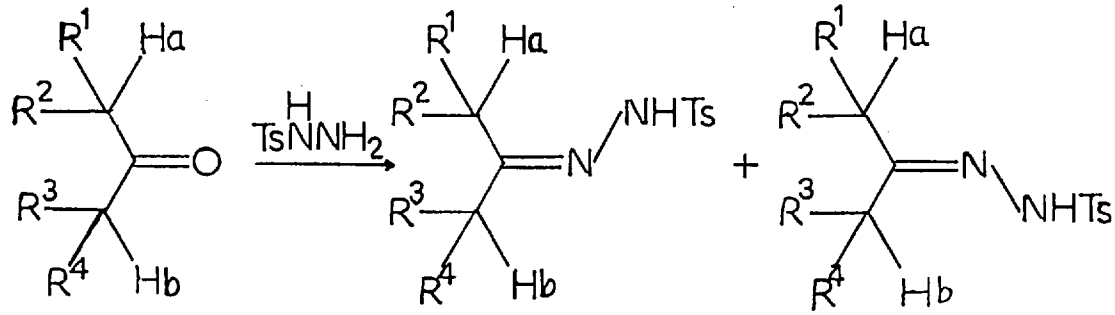
SECTION II: THE SYN-DILITHIO EFFECT

One of the most puzzling results of the Shapiro reaction is the high Z:E ratio of the normal alkene product[5,51]. For example Shapiro[5] was able to demonstrate the predominance of the Z-isomer in most cases (Table 2).

TABLE 2

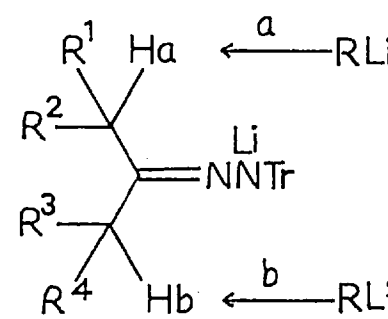
Ketone	Alkyllithium	Solvent	Product	Z/E ratio
$PhCH_2COCH_2Ph$	MeLi	diethyl ether	$PhCH_2CH:CHPh$	86:14
PhCOEt	MeLi	" "	PhCH:CHMe	76:24
$PhCOCH_2CH_2Ph$	MeLi	" "	$PhCH:CHCH_2Ph$	48:52

Furthermore, Shapiro[51] showed that phenylacetone toluene-4-sulphonylhydrazone reacted to form allylbenzene as the only alkene. Later Dauben[31] was able to offer evidence that the second deprotonation was the rate determining step in the reaction leading to the dianion intermediate (17). Hence it is clear that steric effects must be very important during this deprotonation. A ketone toluene-4-sulphonylhydrazone will consist of a mixture of both E- and Z-isomers, the isomeric composition depending upon the steric nature of the initial ketone (Scheme 9). Upon treatment with one equivalent of an alkyllithium reagent at low temperature, nitrogen monoanions were rapidly produced; these have been shown to be geometrically stable.[31] Typically, ethers or hydrocarbons were used as reaction solvents and in these solvents



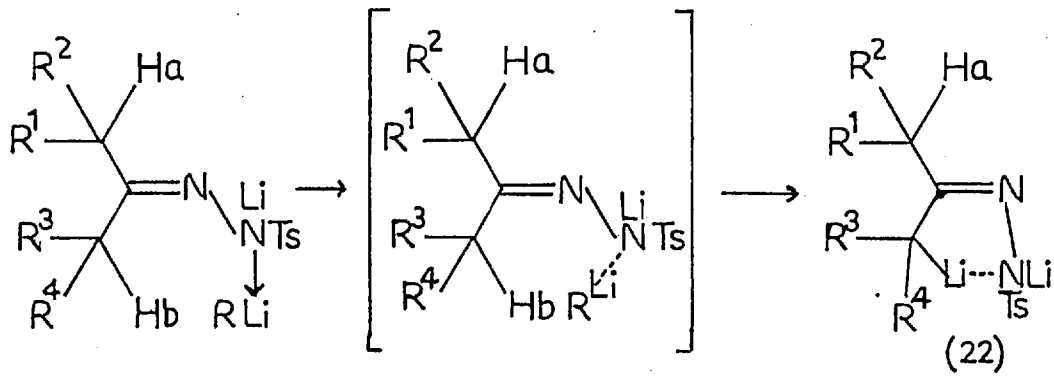
SCHEME 9

alkyllithium reagents are known to be highly aggregated[53]. Probably the rate determining dianion formation is controlled by the attack of a bulky alkyllithium species on the hydrogen atom α- to the imine carbon atom (Ha, Hb - Scheme 10).



SCHEME 10

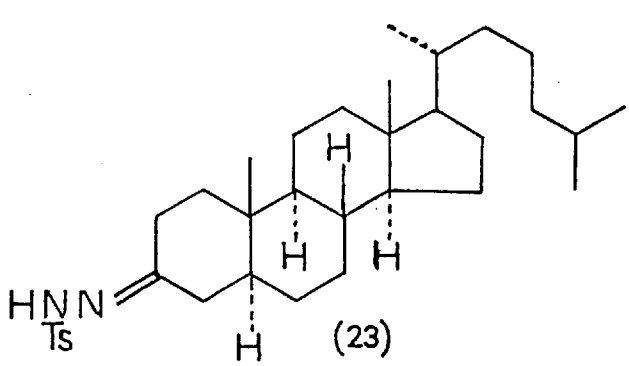
However, the nitrogen anion was able to complex the incoming alkyllithium reagent, decreasing the aggregation and increasing its reactivity[53]. The alkyllithium reagent was thus held in the correct position to remove the syn-α-proton (Hb, Scheme 11) to produce a syn-dianion (22).

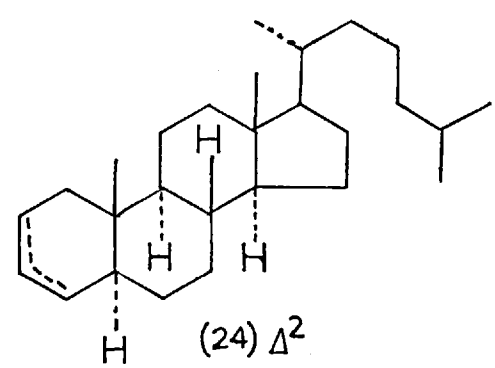


SCHEME 11

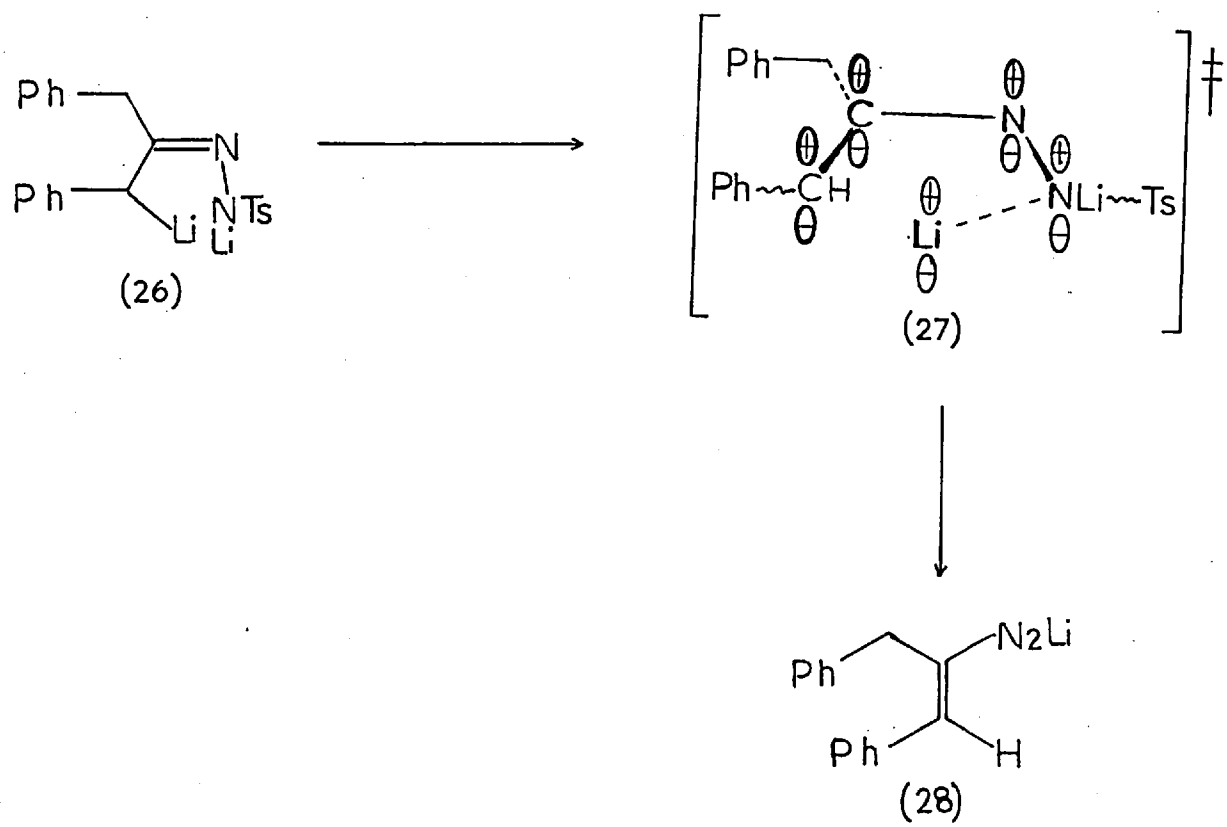
Syn-dianion formation was first suggested by Shapiro[15] since the dianion of phenylacetone toluene-4-sulphonylhydrazone could only be trapped with electrophiles on the carbon atom syn to the arylsulphonyl group.

Clearly the subsequent fragmentation reaction would form different constitutional alkenes depending upon which proton was removed during dianion formation. This was controlled exclusively by the geometry of the starting hydrazone. For example, E,Z-5α-cholestan-3-one toluene-4-sulphonylhydrazone (23) gave a mixture of the Δ^2-(24) and Δ^3-(25) 5α-cholestenes[8].



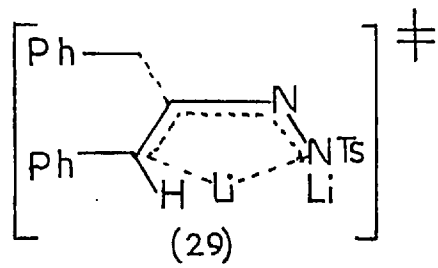


However, this rationale fails to explain why 1,3-diphenylacetone toluene-4-sulphonylhydrazone reacted to form a 86:14 Z:E mixture of 1,3-diphenylpropene (Table 1). For this hydrazone derivative, both nitrogen anions were identical due to symmetry, and the resulting dianion intermediate would have structure (26). Indeed, Shapiro[21] has quenched this dianion (26) with deuterium oxide to give the starting hydrazone derivative (83%) with 97% mono-deuterium incorporation, specifically on the carbon atom syn to the toluene-4-sulphonyl group. The dianion intermediate (26) decomposed to the vinyl diimide anion (28), most reasonably via a planar five centre, six electron heterocyclic transition state (27), the electrons being delocalized through the 2p-orbitals of the five atoms (Scheme 12).

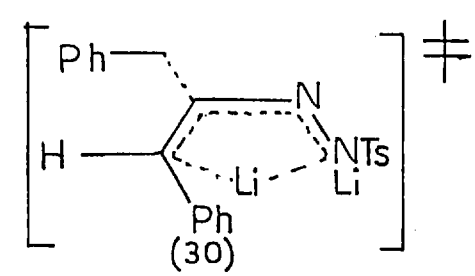


SCHEME 12

The transition state (27) could have existed as two planar heterocycles (29) and (30). Clearly due to steric congestion between



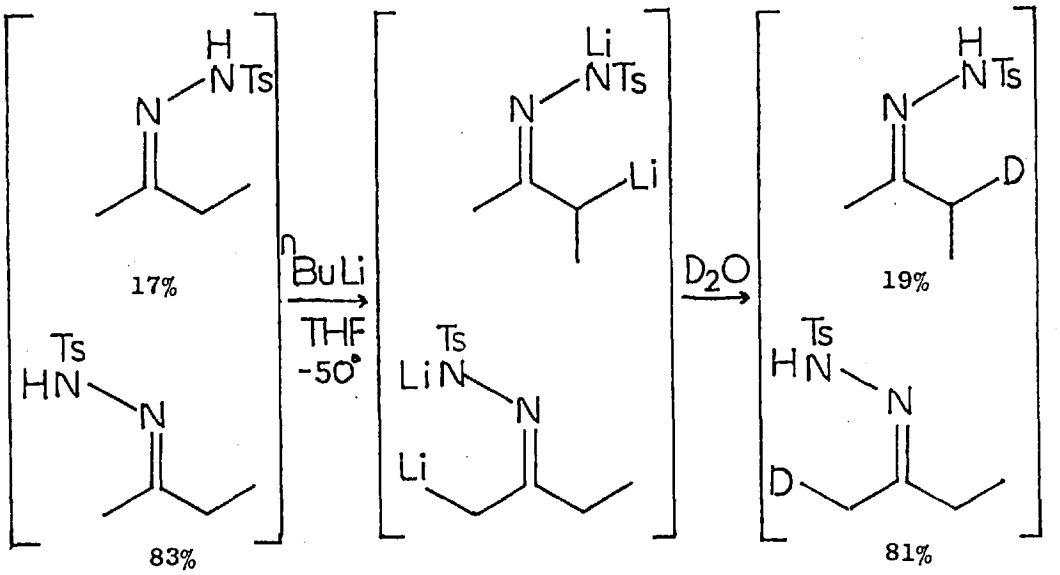
(29)



(30)

the phenyl and lithium, transition state (30) would be of higher energy than (29). Thus, the lower energy pathway gave rise to Z- 1,3-diphenylpropene, the major isolated product (86%). The minor (14%) trans isomer may have arisen from an alternative pathway or by isomerisation of the kinetic product.

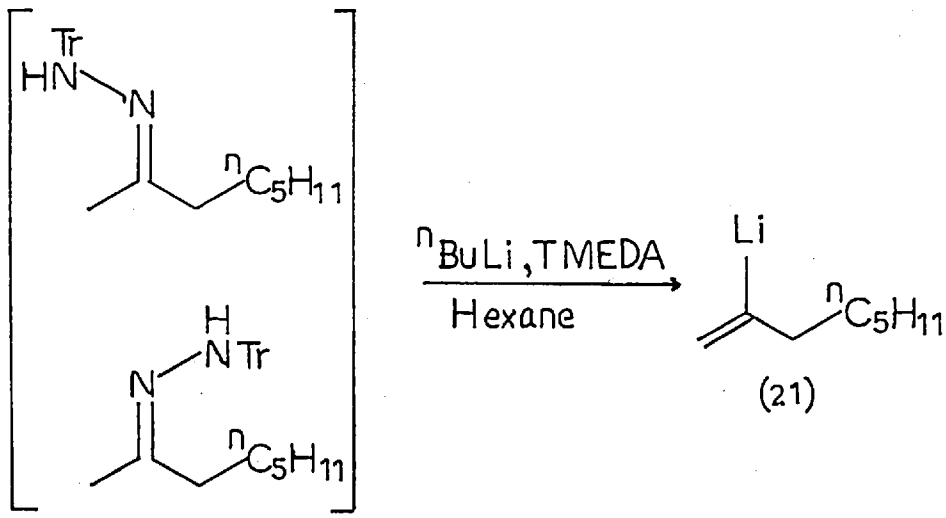
The syn-dilithio effect has literature precedent in other systems: the deprotonation of oximes[43a,b] and the asymmetric syntheses of aldehydes from chiral hydrazones[24] mimic the above mechanisms. Further evidence for the syn-dilithio effect in ethereal or non polar solvents can be found in Shapiro's[21] work on unsymmetrical toluene-4-sulphonylhydrazones. For example butanone toluene-4-sulphonylhydrazone has been shown by n.m.r. analysis[21] to exist as a Z:E (17:83) mixture of isomers. Treatment with n-butyllithium in tetrahydrofuran (THF) followed by deuterium oxide quenching gave a kinetic product which contained 81% deuterium label on the syn-methyl group and 19% label on the syn-methylene group (Scheme 13). In general, a sterically hindered dianion intermediate is produced by substrates which show pronounced syn-



SCHEME 13

dilithio effects. Shapiro[21] has demonstrated that these dianion intermediates (17) can be readily trapped on carbon with methyl iodide but not with other alkyl halides.

Syn-proton abstraction from toluene-4-sulphonylhydrazones only occurred when ethereal or non polar solvents were used. If the highly chelating TMEDA was used as solvent or cosolvent, then this reagent would break up the alkyllithium aggregates[53] to form monomeric alkyllithium complexes. The solvent was a far superior chelating ligand for the alkyllithium reagent than the hydrazone monoanion and, hence, the syn-proton abstraction effect would break down. For example,[30,33] the equilibrium mixture of octan-2-one 2,4,6-tri-isopropylbenzenesulphonylhydrazone isomers E:Z (4:1) reacted with n-butyllithium in hexane and TMEDA to form exclusively the least substituted alkenyllithium reagent (21) by abstraction of the most acidic proton (Scheme 14). This result was found to be applicable to the corresponding benzenesulphonylhydrazone derivatives[14]. However, the effect of TMEDA only appeared to be applicable for alkyllithium reagents. Shapiro[26] has shown that a mixture of octan-2-one toluene-4-sulphonylhydrazone isomers,

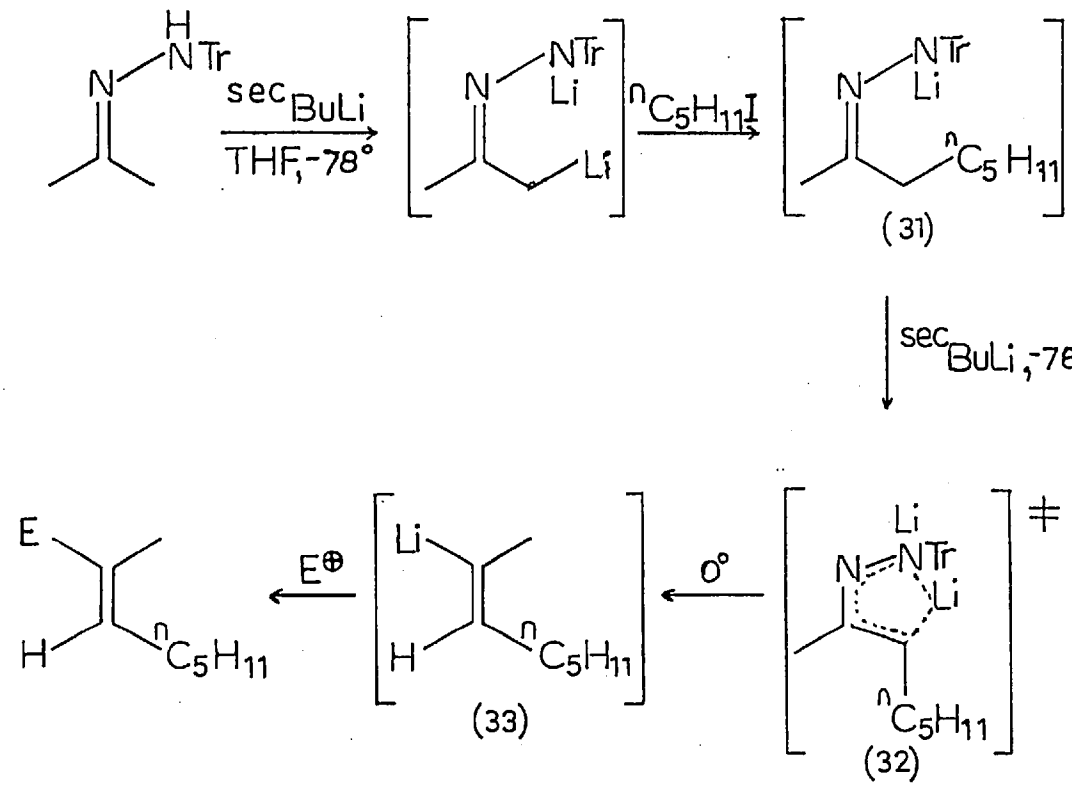


SCHEME 14

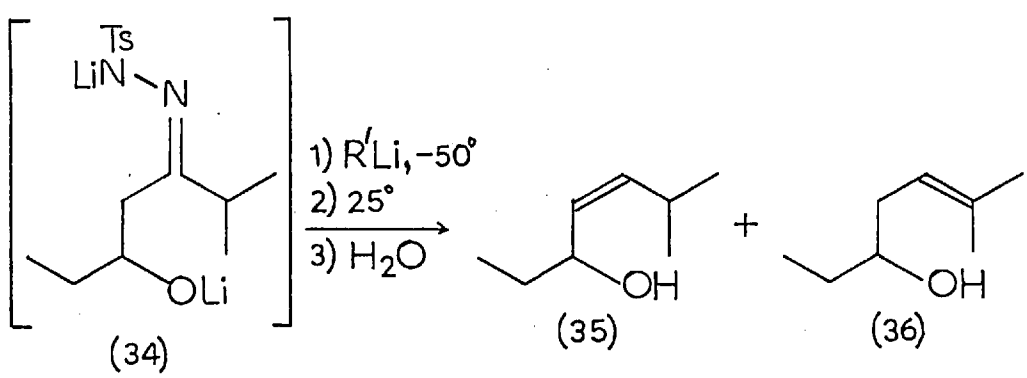
E:Z (76:24), reacted with lithium di-iso-propylamide in TMEDA to produce a mixture of oct-1-ene (80%) and oct-2-ene (20%); a ratio strongly in agreement with control by the syn-dilithio effect.

One of the most elegant applications of the syn-dilithio effect has been described by Bond [30]. Treatment of acetone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone with sec-butyllithium in THF at -78° produced a syn-dianion intermediate which trapped 1-iodopentane on carbon. Retreatment *in situ* with sec-butyllithium gave a second syn-dianion intermediate which decomposed exclusively to the Z-2-alkenyl-lithium reagent (33) via the most stable five centered, six-electron transition state (32) (Scheme 15).

An unusual syn-dilithio effect has been described by Shapiro[21]. Reaction of the dianion intermediate, obtained from 3-methylbutan-2-one toluene-4-sulphonylhydrazone (mostly E-isomer) and alkyllithium, with propanal gave the dianion (34). Alkyllithium addition to (34), then warming, gave a mixture of allylic (35) and homoallylic alcohols (36) (Scheme 16). The products were shown not to be interconvertible and



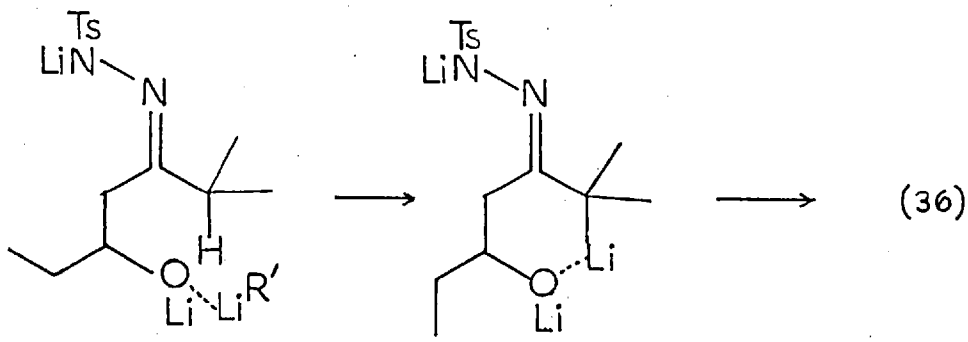
SCHEME 15



SCHEME 16

Shapiro suggested that they were derived by either syn-proton removal or by anti-proton removal from the intermediate (34). Undoubtedly, product (35) arose by this mechanism despite the unfavourable inductive effect of the oxygen atom. However, product (36) probably arose from deprotonation of (34) being directed by the oxygen atom, which was able to

complex the alkyllithium reagent and thus hold it in a position suitable for anti-proton abstraction (Scheme 17).



(36)

SCHEME 17

SECTION III: IMPORTANT FACTORS RELATING TO THE SHAPIRO REACTION

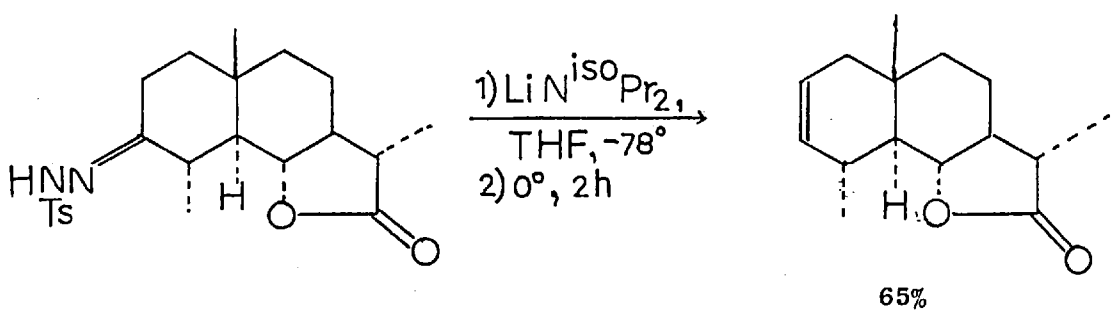
(a) THE SIGNIFICANCE OF CORRECT BASE CHOICE

For certain hindered ketone arylsulphonylhydrazones, bases such as lithium hydride[55], sodium hydride[50], sodium amide[50] or lithium aluminium hydride[42] have been used to produce alkenes. However, these bases did not always bring about the formation of olefins. Sodium hydride has been shown[52a,b] to produce carbenic products, whilst lithium aluminium hydride[42], sodium borohydride[49] and sodium cyanoborohydride[44] have been shown to reduce ketone arylsulphonylhydrazones to alkanes. Fortunately, alkyllithium reagents have been shown to react smoothly with ketone arylsulphonylhydrazones to produce olefins and these reagents are clearly superior. Typically, methyllithium, n-butyllithium, sec-butyllithium

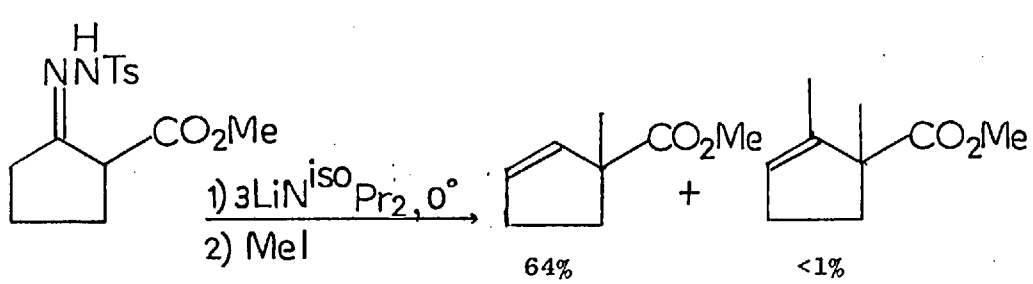
and t-butyllithium have been used. Since solvent deprotonation has been found to be a problem, especially with the more reactive alkyllithiums, the hydrazone solutions were cooled prior to the alkyllithium addition. Reactions at room temperature or above were less likely to be successful.

Certain other bases have been found useful for the Shapiro reaction; of these lithium di-iso-propylamide and lithium 2,2,6,6-tetramethylpiperidide have found most application. These bases cannot, however, be used for the preparation of simple unstabilized vinyl carbanions; the amine conjugate acids quenched the carbanions.

Lithium di-iso-propylamide has been used for the production of an olefin in the presence of a lactone[38] (Scheme 18) and for the production of β,γ-unsaturated esters[25] (Scheme 19)

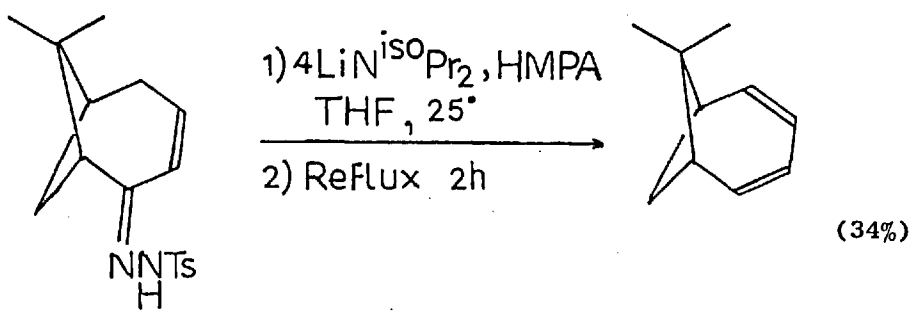


SCHEME 18



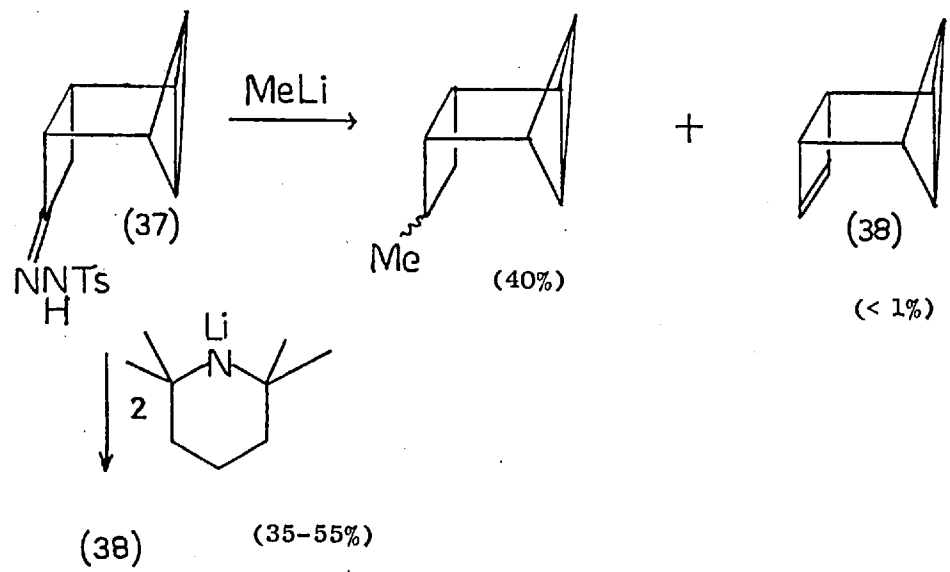
SCHEME 19

Lithium di-iso-propylamide has found application for the difficult tertiary α-proton removal. For example, Shapiro[26] has shown that 2-methyl-1-phenylpropan-1-one toluene-4-sulphonylhydrazone reacted with alkyllithium reagents with substitution at the imine carbon atom. The use of lithium di-iso-propylamide, however, resulted in normal Shapiro reaction yielding 2-methyl-1-phenylprop-1-ene (57%). Lithium di-iso-propylamide has also brought about a γ-proton abstraction[17] when normal α-proton abstraction was difficult (Scheme 20).



SCHEME 20

Lithium 2,2,6,6-tetramethylpiperidide has found application in circumstances where normal reaction produces undesirable products. For example, the introduction of a double bond into a cyclobutane ring system using normal Shapiro methodology was found to be difficult, and the alkyllithium added to the imine bond[12,39]. The use of lithium 2,2,6,6-tetramethylpiperidide, however, permitted conversion of the hydrazone derivative (37) into the substituted cyclobutene (38) (Scheme 21).



SCHEME 21

(bi) THE DYNAMIC EFFECT OF DIFFERING SOLVENTS

For the normal Shapiro olefin reaction, careful choice of reaction solvent is not necessary. However, for alternative electrophilic addition reactions to the vinyl carbanion intermediate (7), the choice of solvent is critical. The solvent defines the alkyllithium aggregation; the less polar the solvent the more aggregated and less reactive it is [53]. The bidentate legand TMEDA forms a 1:1 complex with alkyllithium reagents and this chelation vastly increases the base strength[53]. An increased base strength ensures that dianion formation (Scheme 7) is complete at a lower temperature than vinyl carbanion formation. Hence, when the vinylic carbanion is formed it would not be able to abstract a proton from the substrate monoanion (Scheme 6).

A bulky aggregated alkyllithium reagent is more likely to subject to a syn-dilithio effect (Section II) than a monomeric alkyllithium reagent. However, for hindered ketone arylsulphonylhydrazones, the solvent effect on the syn-dilithio effect was found to be more complicated[33].

If the Shapiro reaction is conducted under heterogeneous conditions then vinyl carbanion stabilization cannot be achieved as the vinyl carbanion would react with other reaction species (Scheme 6). Hence a solvent of suitable solubilizing power must be chosen. The solvent must be stable to the vinyl carbanion intermediate at the temperature of its formation otherwise alkenes might be formed. A vinyl carbanion intermediate has a similar stability to a phenyl carbanion on the basis of pKa values[54]. Gilman [47a,b] has shown that phenyllithium was reasonably stable in THF solution ; the reagent was only 33% decomposed after 10 hours at 25°. However, in diethyl ether or 1,2-dimethoxyethane, alkyllithium reagents have been shown to be unstable, rapidly decomposing to alkanes with the formation of alkoxide anions (Scheme 5).

(bii) SPECIFIC SOLVENTS

Hydrocarbons

Hexane has been used to generate the hindered carbanion (12) from camphor toluene-4-sulphonylhydrazone (8). However, reactions in hexane were generally found to be heterogeneous, and vinyl carbanion intermediates were quenched by the reaction systems[3,11] (Scheme 6).

Diethyl ether

Diethyl ether was, until recently, the most common solvent used for the production of alkenes from the Shapiro reaction[1, 51, 35i,s,w]. The solvent has been found to protonate the vinyl carbanion intermediate

(Scheme 5).

Dimethyl ether

Bond[14] examined dimethyl ether as a reaction solvent, arguing that it should be both sufficiently solubilizing and stable to carbanions, as it lacked β-protons. However, at the boiling point of the ether (-24°C) decomposition of the dianion intermediate to form a vinyl carbanion (7) was slow. Thus, reaction yields were lower (40-60%) although high deuterium incorporations, from deuterium oxide quenches, confirmed the solvent stability of the vinyl carbanion (7).

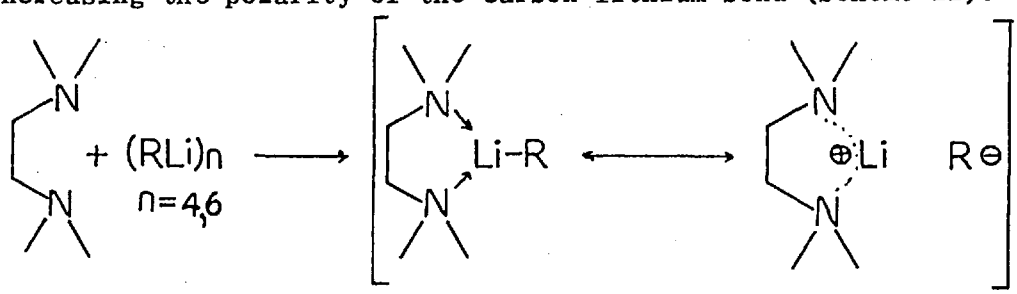
Tetrahydrofuran (THF)

THF has been used not only for normal olefin formation[35b], but also for stabilised vinyl carbanion (7) preparations, providing that a ketone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone was used[30] (Scheme 15).

In general, ethereal solvents show pronounced syn-dilithio effects[5,51].

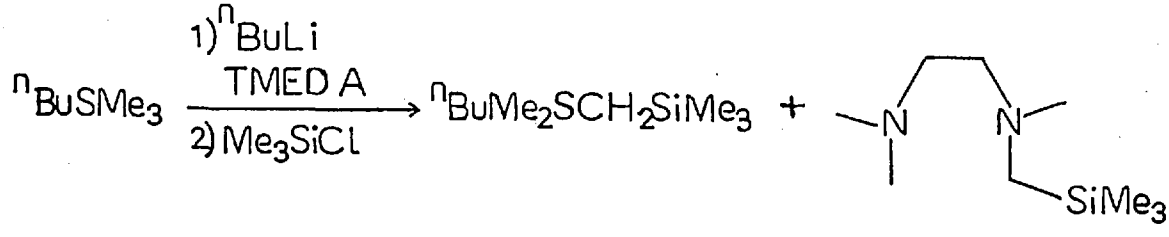
N,N,N',N'-Tetramethylethylenediamine (TMEDA)

TMEDA has been used either as a neat solvent or as cosolvent to form stabilised vinyl carbanion intermediates[14,16,19,20]. The superiority of this reagent probably lies in its ability to form a 1:1 complex with alkyllithium reagents[53]. The solvent thus increases the base strength of the alkyllithium reagents by decreasing aggregation and by increasing the polarity of the carbon lithium bond (Scheme 22).



SCHEME 22

Increasing the base strength was found to result in dianion formation at a low temperature, hence aiding vinyl carbanion stability. TMEDA has been found to destroy[14,30] the syn-dilithio effect; E,Z-octan-2-one phenylsulphonylhydrazone gave products derived from both 2-lithio-oct-1-ene (98%) and 2-lithio-oct-2-ene (< 2%). However, the definitive experiment in which both pure E- and Z- isomers are separately treated with alkyllithium in TMEDA has not been carried out. Reaction products derived from metallation[45] have been shown to be a complication in a different context (Scheme 23). However, it is questionable



(18%)

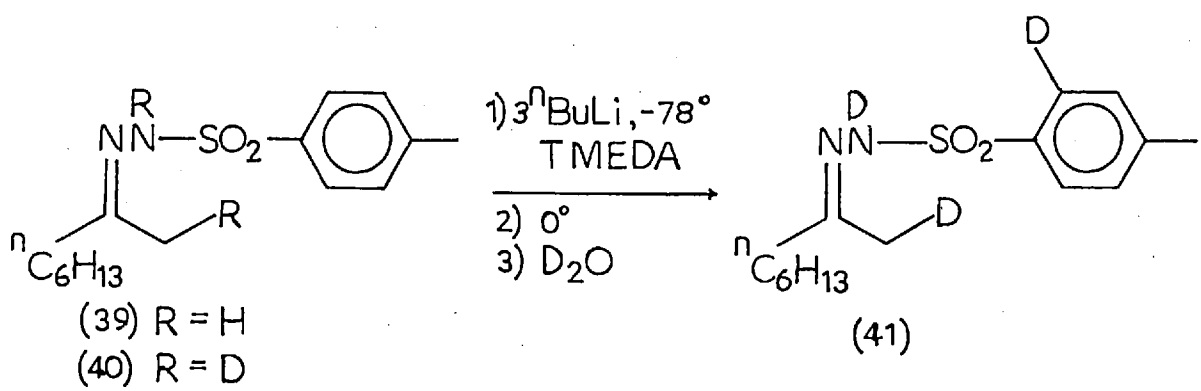
SCHEME 23

whether a vinyl carbanion (7) would be reactive enough to metallate TMEDA.

(c) COMPARISONS OF DIFFERENT ARYLSULPHONYL-RESIDUES

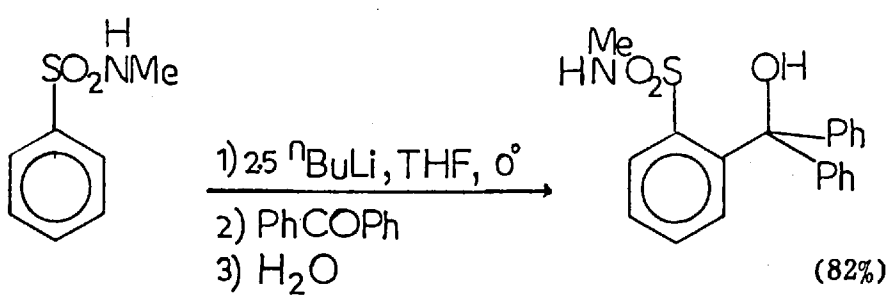
The early work on the Shapiro reaction was performed upon toluene-4-sulphonyl- or benzenesulphonylhydrazone starting materials. These reagents could be readily used for alkene formation[1,2,35], but to produce a stable vinyl carbanion (7), excess amounts of alkyllithium reagents needed to be used[16,37,20,33]. Indeed, Bond[20] suggested that excess alkyllithium was necessary due to metallation in the aromatic ring. Earlier, Vedejs[10] had suggested aromatic metallation to explain an unusual dianion rearrangement reaction. Later, Bond[33] was able to show that if a 2,4,6-tri-iso-propylbenzenesulphonylhydrazone was used,

then only the stoichiometric two equivalents of alkyllithium reagent were required for vinyl carbanion formation. Bond[33] explained these results after conducting a series of experiments on octan-2-one toluene-4-sulphonylhydrazone (39). Treatment of the hydrazone (39) with three equivalents of n-butyllithium in TMEDA and hexane at -78° followed by quenching with deuterium oxide gave a dideuterio-toluene-4-sulphonylhydrazone (40). However, if the reaction mixture was warmed to 0° prior to quenching, then a trideuterio-toluene-4-sulphonylhydrazone (41) was formed (Scheme 24).



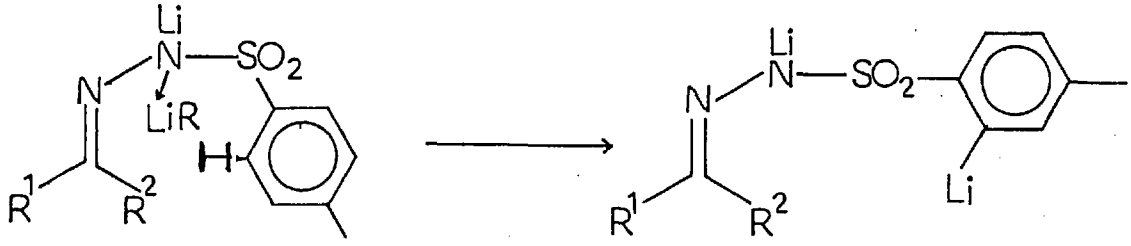
SCHEME 24

N.m.r. examination indicated that aromatic metallation had occurred in the ortho-position. Such ortho-metallations have been shown[46] to occur in other arenesulphonyl systems (Scheme 25). This was probably



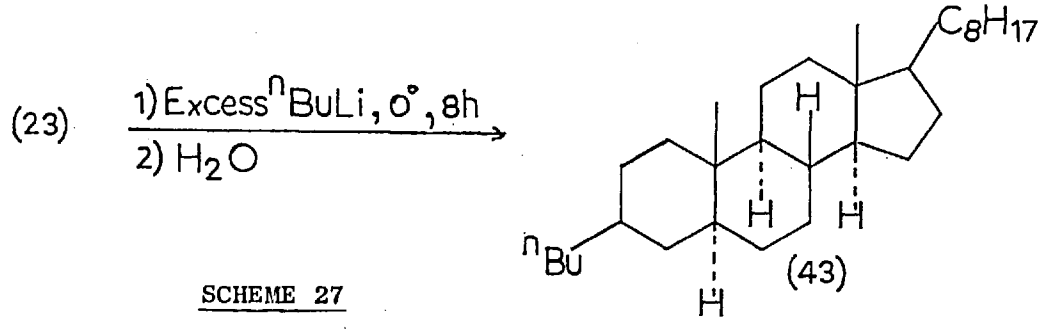
SCHEME 25

the result of both an inductive and a directed syn-proton abstraction effect (Scheme 26). Ortho-metallations are the probable explanation for



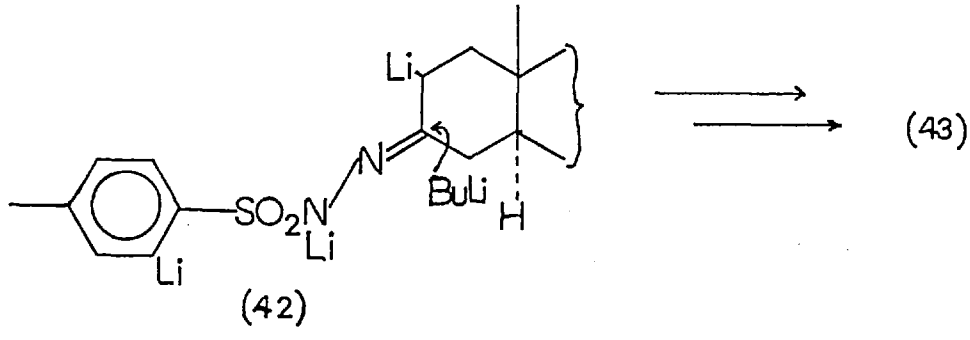
SCHEME 26

formation of the unusual alkane observed by Hertz[7,9] (Scheme 27). At the reaction temperature (0°) decomposition of the presumed trianion



SCHEME 27

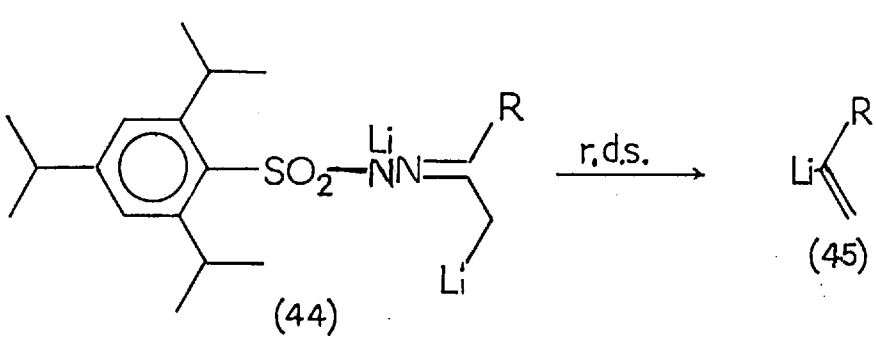
(42) to give the normal vinyl carbanion was slow. Hence n-butyllithium was presumably able to attack the trianion (42) to produce product (43) (Scheme 28).



SCHEME 28

Clearly a typical Shapiro reaction using stoichiometric amounts of alkyllithium reagents with a benzene- or toluene-4-sulphonylhydrazone derivative at low temperature would result in normal dianion formation (Scheme 7). As the mixture is warmed, fragmentation would occur, forming a vinyl carbanion intermediate (7) and a lithium arylsulphinate salt. This salt could act as a proton source (ortho-position) for the vinyl carbanion (7). If excess alkyllithium reagent was used then the ortho-position was probably metallated prior to vinyl carbanion (7) formation[33]. Hence a stable vinyl carbanion (7) was formed upon fragmentation.

Recently,[33] 2,4,6-tri-iso-propylbenzenesulphonylhydrazones have been found to be synthetically superior to both benzene- and toluene-4-sulphonylhydrazones. Firstly, since the ortho-position is already blocked, only the stoichiometric amount of alkyllithium reagent was needed for vinyl carbanion (7) formation, and hence by-product formation was minimized. Secondly, the increased bulk of the 2,4,6-tri-iso-propyl-benzenesulphonyl group facilitated fragmentation of the dianion (44) to the vinyl carbanion (45) (Scheme 29). Thus, vinyl carbanion (45) formation occurred at a lower temperature due to relief of steric congestion in the rate determining fragmentation step. For example[33],



(44) (45)

SCHEME 29

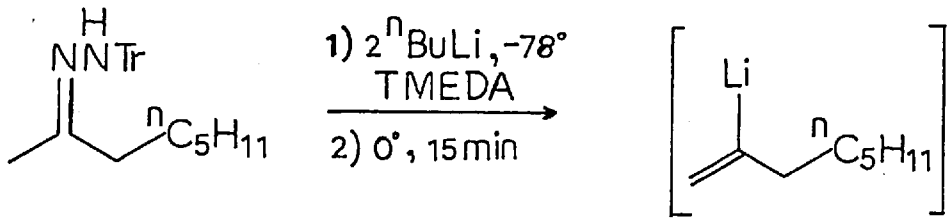
octan-2-one toluene-4-sulphonylhydrazone reacted with greater than three equivalents of n-butyllithium in TMEDA and hexane at low temperature, followed by warming to room temperature for four hours to produce 2-lithio-oct-1-ene. However, octan-2-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone reacted with two equivalents of n-butyllithium in TMEDA and hexane at -78°, followed by warming to 0° for 15 min to produce the same vinyl carbanion. Clearly, since the carbanion intermediate was unstable to prolonged storage in solvent, then the lowest possible fragmentation temperature must be used. Bond[30] has used a ketone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone in THF to produce a vinyl carbanion which was reasonably stable at 0°. The facile decomposition of a 2,4,6-tri-iso-propylbenzenesulphonylhydrazone monoanion in an aprotic Bamford-Stevens reaction has been demonstrated by Bond[34].

(d) THE SIGNIFICANCE OF THE STRUCTURE OF THE KETONE PRECURSOR

The selective deprotonation of a ketone arylsulphonylhydrazone during low temperature dianion formation controls the regiospecificity of the Shapiro reaction. If non-polar or ethereal solvents were used, then deprotonation was controlled largely by the geometry of the starting hydrazone due to the syn-dilithio effect (Section II). If TMEDA is used as solvent, then the least substituted α-proton will be removed to form the most stabilized dianion intermediate (Section II, and III (bii)). However, the conditions required for the second proton abstraction during dianion formation will depend upon the structure of the ketone precursor of the hydrazone derivative .

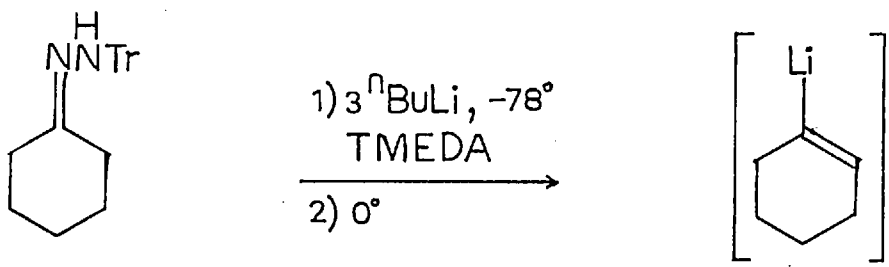
For primary α-proton removal from a 2,4,6-tri-iso-propylbenzenesulphonylhydrazone derivative, Bond[33] has shown that two equivalents

of n-butyllithium were required (Scheme 30). For secondary α-hydrogen[33]



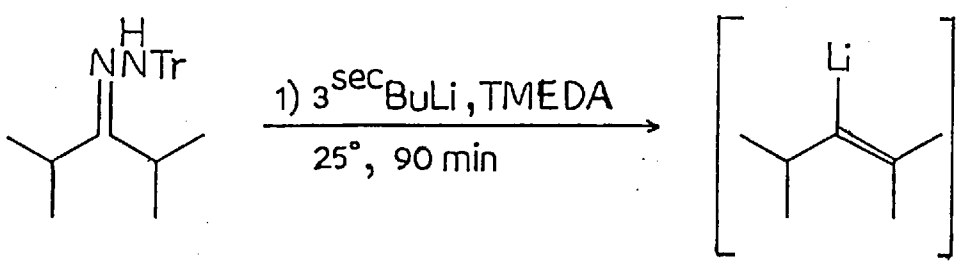
SCHEME 30

abstraction, two equivalents of the stronger base sec-butyllithium or three equivalents of n-butyllithium were necessary (Scheme 31). Similar



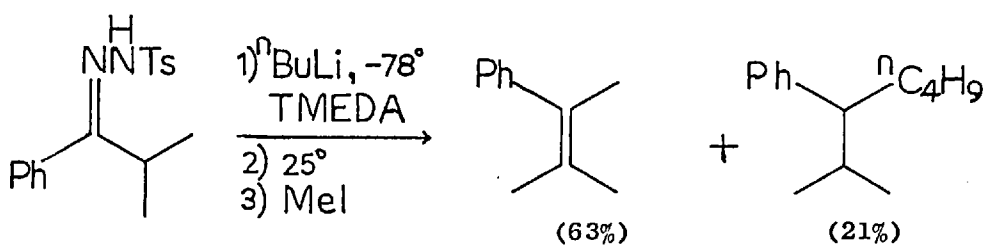
SCHEME 31

conditions were required for secondary proton removal from ketone toluene-4-sulphonylhydrazones[1,51]. For tertiary proton abstraction[33] from a ketone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone, three equivalents of sec-butyllithium at room temperature were essential (Scheme 32).



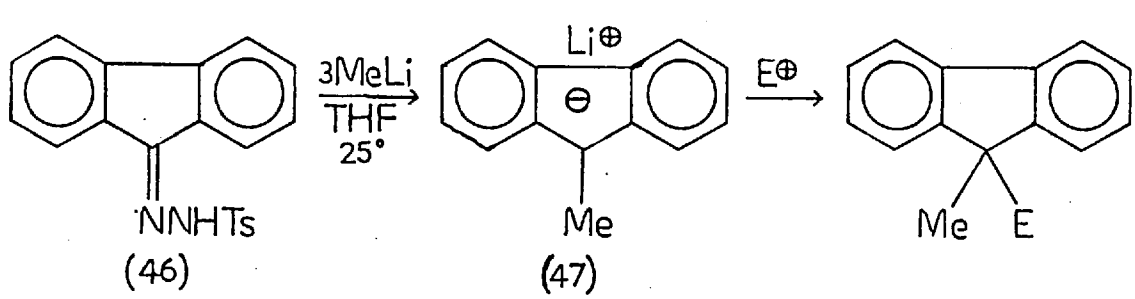
SCHEME 32

Alkene formation by primary or secondary α-proton abstraction from a ketone toluene-4-sulphonylhydrazone generally required the use of methyl- or n-butyllithium. Tertiary α-proton removal was more difficult[6], but Shapiro[15] has shown that TMEDA could be used to increase the rate of proton abstraction. However, substitution at the imino carbon was found to be a competing pathway (Scheme 33). Shapiro[26] has also shown that lithium di-iso-propylamide was a suitable base for tertiary proton abstraction (Section III(a)).



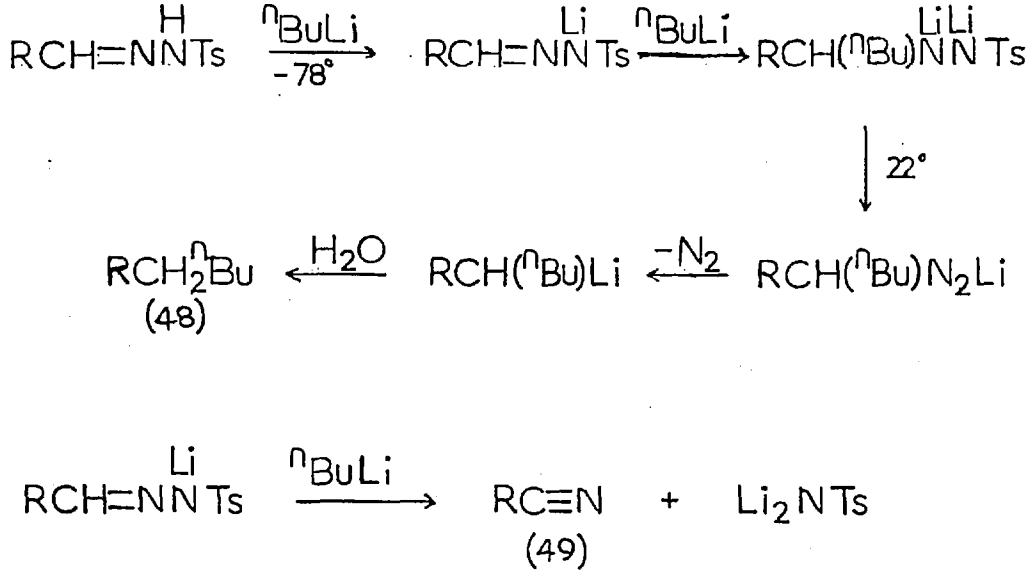
SCHEME 33

Molecules lacking acidic α-protons cannot form normal dianion intermediates and undergo alkyllithium addition to the imine bond. Fluorenone toluene-4-sulphonylhydrazone (46) reacted with methyllithium to form a stabilised carbanion (47) which was trapped with various electrophiles[13] (Scheme 34).



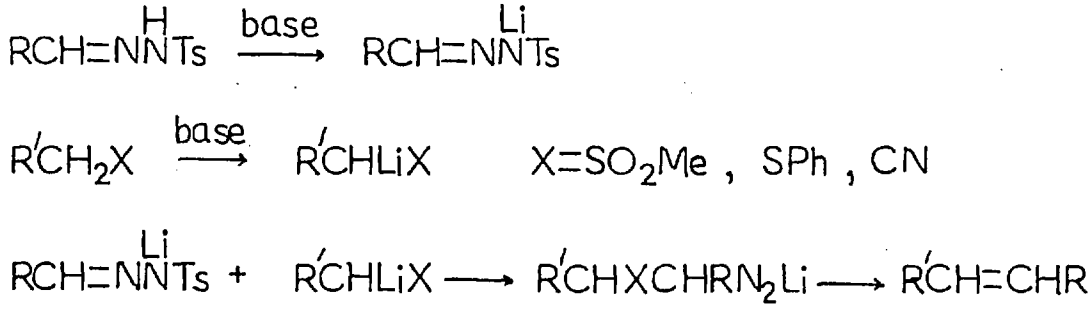
SCHEME 34

Aldehyde arylsulphonylhydrazones have been shown not to undergo the usual Shapiro reaction[3,20]. Indeed, Vedejs [22] has found that nucleophilic addition at the imino carbon was a more favourable process; alkanes (48) or nitriles (49) were thus formed (Scheme 35). More recently, Vedejs[27] has found that an aldehyde toluene-4-sulphonylhydrazone reacted with a stabilized carbanion to form an adduct which underwent



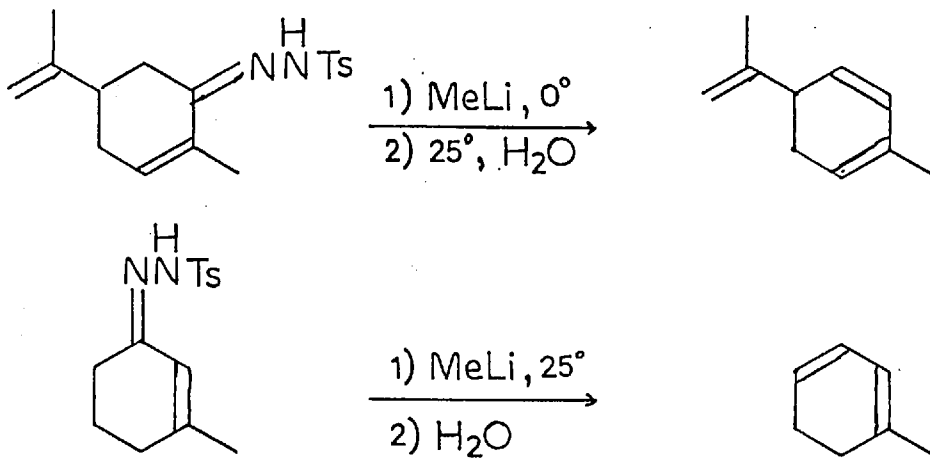
SCHEME 35

elimination to form an alkene (Scheme 36). The group (X) that stabilised the carbanion reagent had to be a good leaving group for a successful reaction.



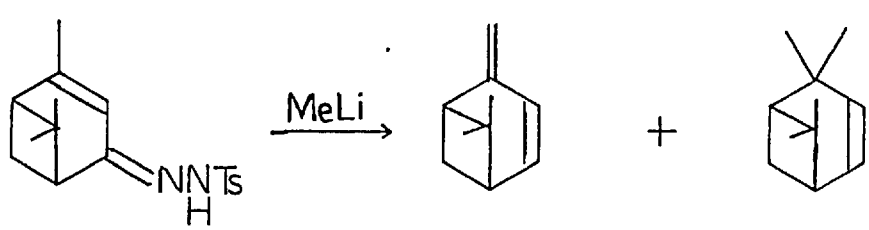
SCHEME 36

α,β-Unsaturated ketone arylsulphonylhydrazones have been reported by Shapiro[3] and Cargill[41] to produce dienes by a non conjugative elimination mechanism (Scheme 37). Conjugative elimination occurred when



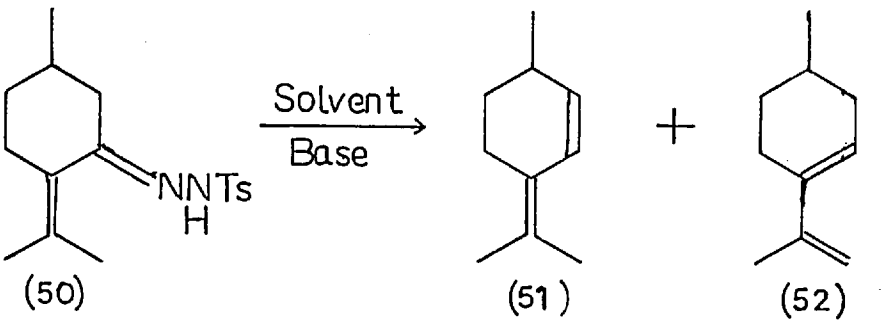
SCHEME 37

α-proton abstraction was difficult[17,36] (Schemes 20 and 38). Dauben[18,31] has shown that conjugative versus non conjugative elimination can depend



SCHEME 38

on both the substrate geometry, the reaction solvent and the alkyllithium reagent used (Table 3). The predominance of the product (51) from the E-isomer of (50) was probably due to a syn-dilithio effect (Section II). The increasing production of product (52) from the Z-isomer of (50)

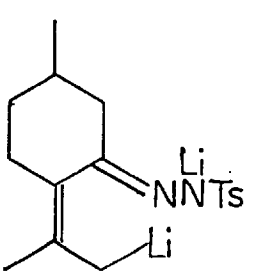


(50) (51) (52)

TABLE 3

E/Z Geometry of (50)	Solvent	Base	Ratio of products (51):(52)
E	PhH	n-BuLi	> 98:2
Z	PhH	n-BuLi	3:1
E	PhH:Et_2O(1:1)	MeLi	> 99:1
Z	PhH:Et_2O(1:1)	MeLi	2:3
E	TMEDA	n-BuLi	1:0
Z	TMEDA	n-BuLi	1:9

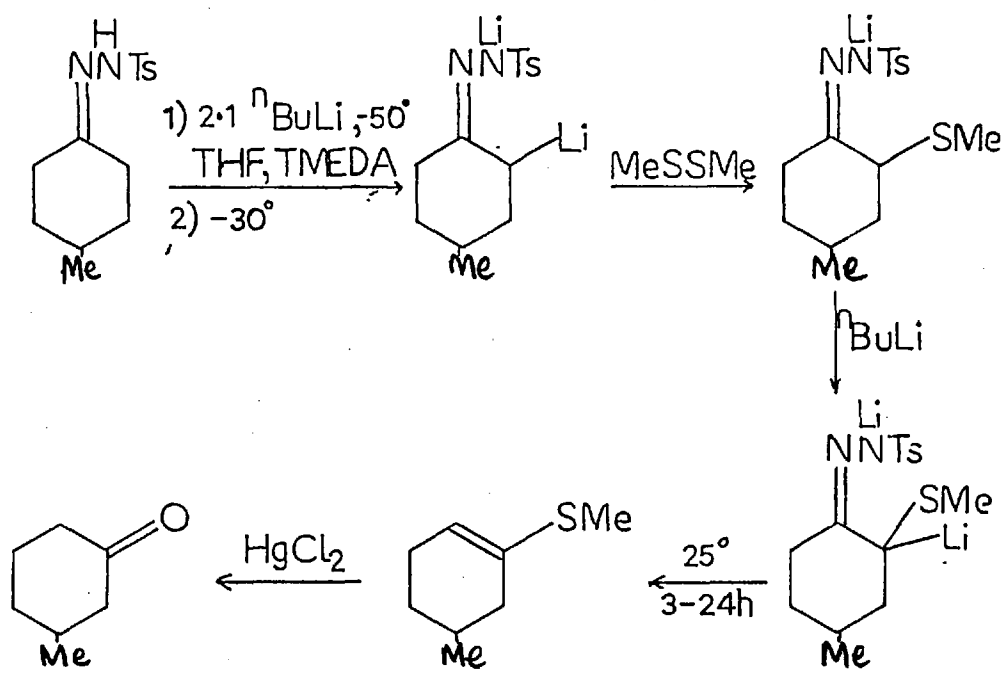
as the base strength increased was probably due to production of the most stabilised dianion (53) under these conditions.



(53)

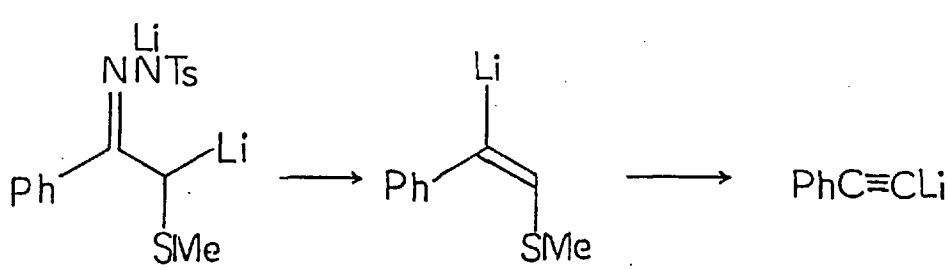
SECTION IV: RECENT ADVANCES IN THE APPLICATION OF THE SHAPIRO REACTION

The formation of alkenes from toluene-4-sulphonylhydrazones has been reviewed by Shapiro[51] and the extension of the reaction to the alternative functionalisation of vinyl carbanions (7) has been admirable described by Bond[33]. More recently, a number of authors have exploited the Shapiro reaction and its characteristic intermediates. Nakai[28] has shown that 1,2-carbonyl transposition reactions can readily be achieved by Shapiro reaction methodology (Scheme 39). However, Kano[32,40] has



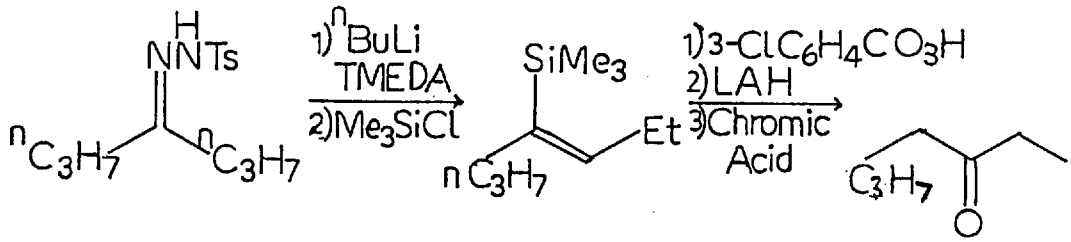
SCHEME 39

indicated that the above reaction was only general for cyclic ketone-arylsulphonylhydrazones. If an aliphatic ketone arylsulphonylhydrazone was used, then acetylenes were formed (Scheme 40).



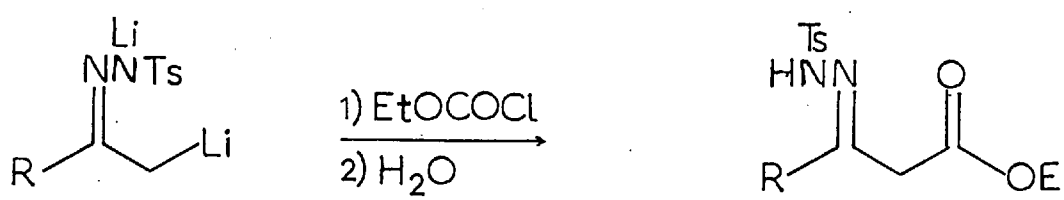
SCHEME 40

To compliment this work Paquette[29] has shown that alicyclic vinyl carbanions can be trapped with chlorotrimethylsilane and the resulting vinylsilane converted to a ketone with effective 1,2-transposition (Scheme 41).

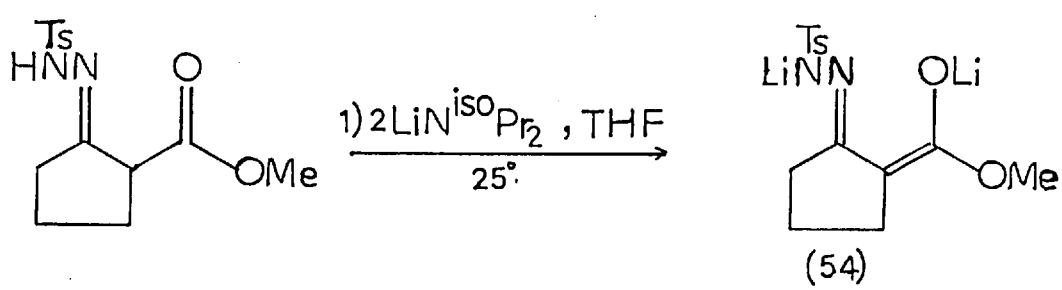


SCHEME 41

Fuchs[25] has conducted a study on the reactions of β-ketocarboxylic ester arylsulphonylhydrazones with strong bases. These compounds, available from the reaction of a ketone arylsulphonylhydrazone dianion with ethyl chloroformate[21] (Scheme 42), reacted with two equivalents of lithium di-iso-propylamide at room temperature to produce a stabilised dianion intermediate (54) (Scheme 43), which could be alkylated on carbon with methyl iodide. Alternatively, further treatment of the stabilised

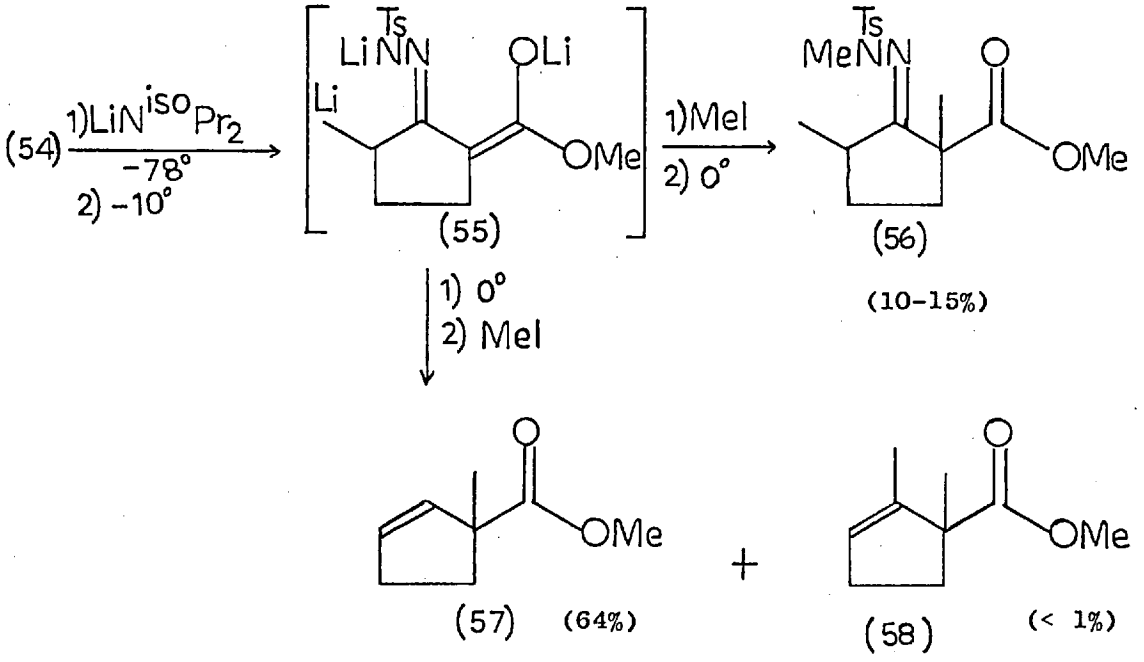


SCHEME 42



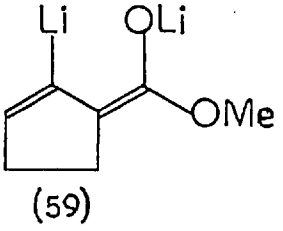
SCHEME 43

dianion intermediate (54) with lithium di-iso-propylamide and warming to -10°, produced a trianion intermediate (55) which was trapped in low yield (10-15%) with methyl iodide (Scheme 44).



SCHEME 44

The low yield of the trapped intermediate (56) strongly suggested low trianion (55) stability. By warming to 0°, fragmentation occurred and subsequent quenching with methyl iodide gave products (57) and (58) (Scheme 44). The low yield of the ester (58) indicated the instability of the assumed vinyl carbanion intermediate (59).

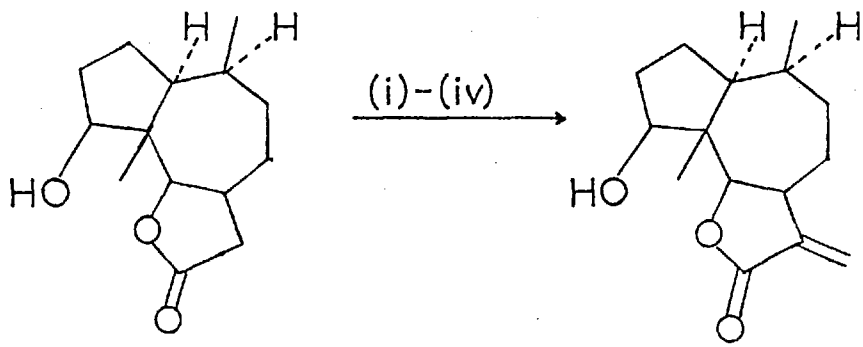


(59)

RESULTS AND DISCUSSION

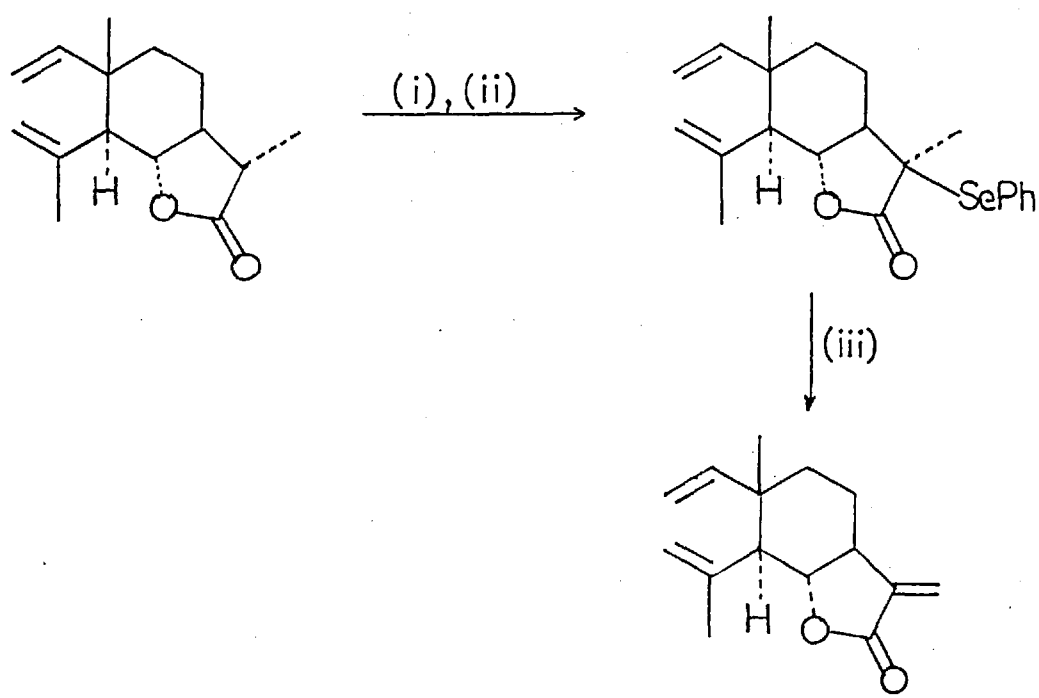
SECTION V: FORMATION OF α-METHYLENE-γ-LACTONES BY APPLICATION OF THE SHAPIRO REACTION

Standard methods for the preparation of α-methylene-γ-lactones (62) involve the α-methylenylation of preformed lactones[56] (e.g.[56b] Scheme 45) or the oxidation of α-methyl lactones[57,38] (e.g.[38] Scheme 46).



(i), $LiN^{iso}Pr_2$; (ii) $CH_2=O$; (iii) $MeSO_2Cl$; (iv) DBU

Scheme 45

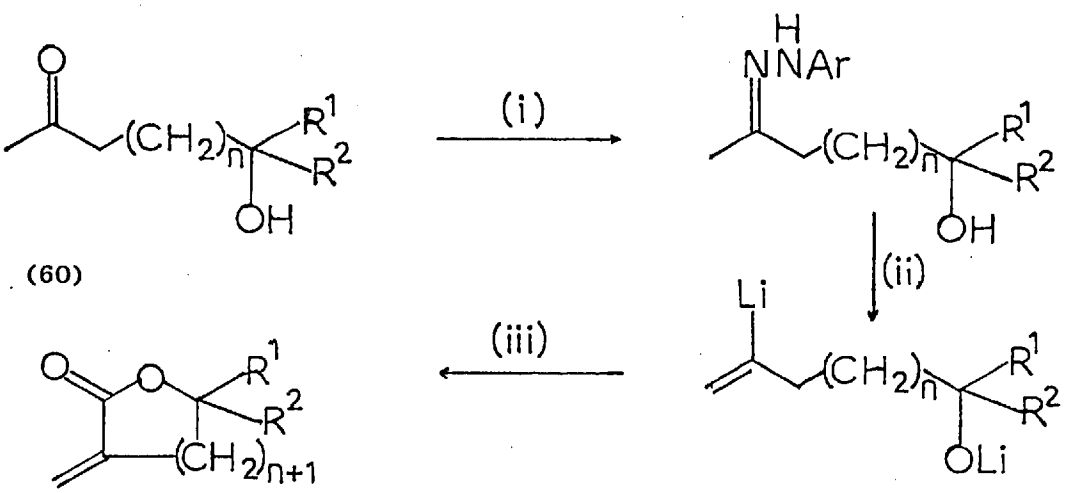


(i) $LiN^{iso}Pr_2$; (ii) PhSeSePh; (iii) H_2O_2

Scheme 46

Alternative procedures exist[58], some of which are synthetically less versatile on account of low yields and/or multistage reactions.

We argued that α-methylene lactones (62) should be available simply from the reaction of an alkoxy-vinyl dianion (61) with phosgene or an alkyl chloroformate. The alkoxy-vinyl dianion (61) should be available from the Shapiro reaction (Scheme 47), and cyclisation to form the lactone (62) has ample precedent[66,67,68].



(60)

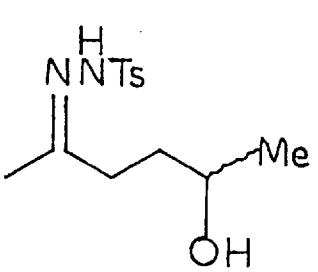
(62)

(61)

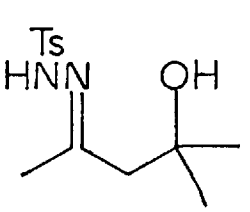
(i) $ArNHNH_2$; (ii) ^nBuLi; (iii) $COCl_2$ or RO.CO.Cl;

Scheme 47

Initially, we conducted a study of the Shapiro reaction to test its suitability as a method of discrete vinyl carbanion generation. Preliminary experiments involving attempted electrophilic trapping of the vinyl carbanion (61) prepared from the hydrazones (63) or (64) proved unsuccessful.

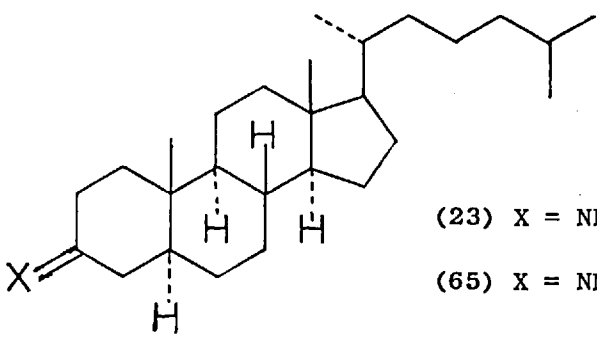


(63)



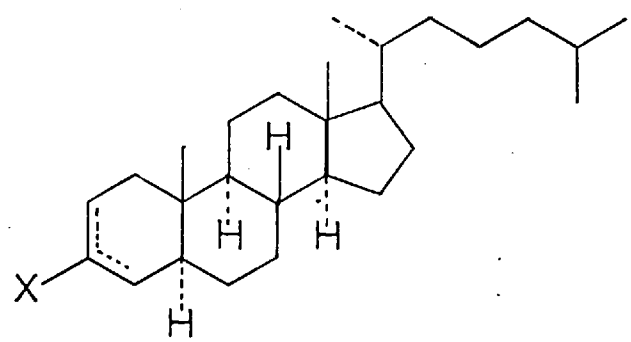
(64)

However, the more simple derivative 5α-cholestan-3-one toluene-4-sulphonylhydrazone[55] (23) reacted smoothly with methyllithium in TMEDA, N,N-dimethylformamide and 2,4-dinitrophenylhydrazine in sequence to form the α,β-unsaturated aldehyde derivative (70) (57%). Unfortunately, similar experiments using phosgene or ethyl chloroformate as electrophiles gave the olefin[61] (67) and no α,β-unsaturated acid (71). Presumably, these electrophiles reacted with TMEDA to provide a proton source which quenched the vinyl carbanion (66).



(23) X = NNHTs

(65) X = NNHTr



(66) X = Li

(67) X = H

(68) X = D

(69) X = CHO

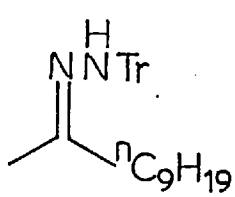
(70) X = CH=NN(H)–C$_6$H$_3$(NO$_2$)$_2$

(71) X = CO_2H

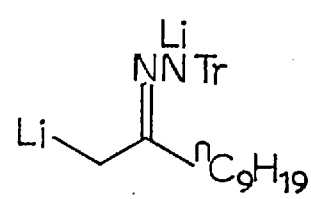
Other systems were examined (Table 4). Reactions of the hydrazone (23) in THF, diethyl ether or pentane gave the olefin (67), in agreement with literature results, whilst reactions in dimethyl ether were inefficient

due to the slow fragmentation (23→66) at the solvent boiling point (-24°). Similarly disappointing was the reaction of the 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (65) with n-butyllithium in dimethoxymethane. The Shapiro olefin (68) isolated showed only 6% deuterium incorporation on a deuterium oxide quench. However, undecan-2-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (72) reacted smoothly with n-butyllithium in 1,2-dimethoxyethane (DME), N,N-dimethylformamide and 2,4-dinitrophenylhydrazine in sequence to form derivative (77) (43%). A similar sequence followed by deuterium oxide quenching of the vinyl carbanion (74) gave the deuterio-olefin (75) (<99%) with 83% deuterium incorporation. The olefin product (75) was characterised as its isoxazoline derivative (79), formed by reaction[65] with 2,4,6-trimethylbenzonitrile oxide.

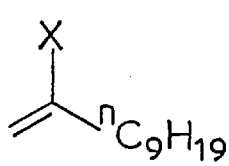
Reaction of the hydrazone (65) with sec-butyllithium in DME gave the vinyl carbanion (66), which on N,N-dimethylformamide or deuterium oxide

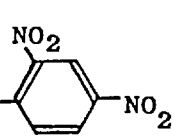


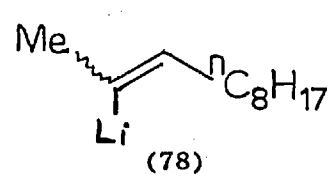
(72)



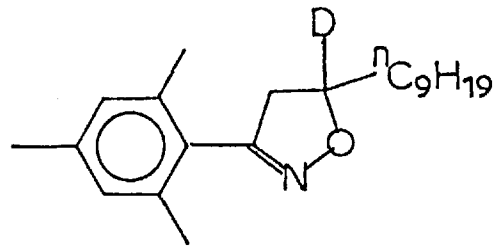
(73)



(74) X = Li
(75) X = D
(76) X = CHO
(77) X = CH=NNH- 

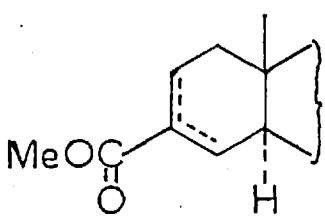


(78)

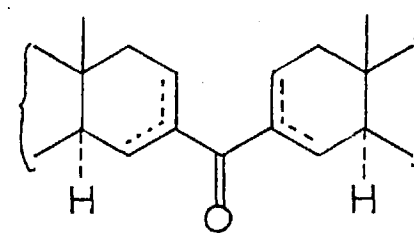


(79)

quenching gave the derivative (70) (58%) and the olefin (68) (75%, 78% d_1) respectively. Inverse addition of the vinyl carbanion (66) to methyl chloroformate gave a mixture of the Shapiro olefin (67) (33%), the methyl ester (80) (24%) and the disteroidal ketone (81) (4%).



(80)



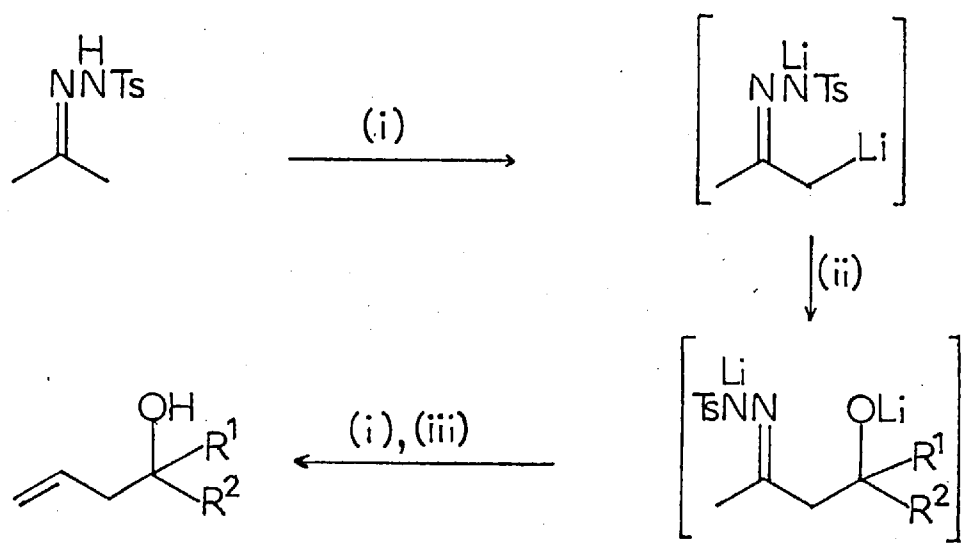
(81)

The reactions performed in DME were easily followed by change in colour. Addition of two equivalents of alkyllithium at low temperature gave a golden coloured dianion. Warming to 0^{o} resulted in fragmentation, nitrogen evolution and a loss of colour intensity to form a vinyl carbanion (7).

Although convinced of its suitability for formation and electrophilic quenching of the vinyl carbanion (7), we were unsure of the effect of DME on the syn-dilithio effect (Section II). The position (Δ^2 and/or Δ^3) of the double bond in products (67), (70), (80) and (81) was not determined, neither was the geometric purity of the hydrazones (23) or (65). However, products isolated from the mainly E-hydrazone (72) in DME were

derived from the least substituted vinyl carbanion (74), in agreement with a possible syn-dilithio effect. No products derived from the vinyl carbanion (78) were isolated, plausibly due to their inherent low yields.

The preparation of homoallylic alcohols[21] (Scheme 48) prompted us to examine the chemistry of the low temperature Shapiro dianion intermediate. Acetone reacted with 2,4,6-iso-propylbenzenesulphonylhydrazine[70] (108b) to form (82). Treatment with n-butyllithium (2.2 equiv.) in DME

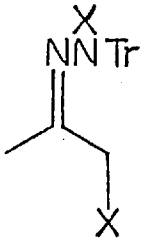


(i) RLi, -70°; (ii) $R^1.CO.R^2$; (iii) 25°, H_2O;

Scheme 48

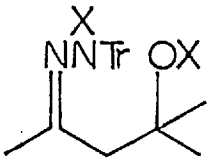
at -70° gave a golden coloured dianion (83) which was quenched with acetone to yield the dianion (84). Quenching with water initially gave only a single isomer of the hydroxy-hydrazone (85) (95%). The hydroxy-hydrazone (85) was independently synthesised from 4-hydroxy-4-methylpentan-2-one[60] and 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (93%) as a

mixture of the E-and Z-isomers. From t.l.c. and n.m.r. analysis it appeared that only the thermodynamically unstable Z-isomer of the hydrazone (85)



(82) X = H

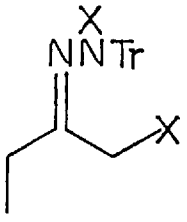
(83) X = Li



(84) X = Li

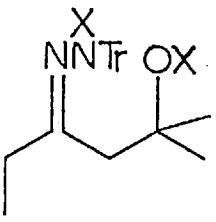
(85) X = H

was initially formed from the dianion (83) reaction. The Z-isomer of the hydrazone (85) readily isomerised in solution to a mixture of both E- and Z-isomers. Similarly, butanone trisylhydrazone (86) reacted with n-butyllithium to form a golden dianion (87). The addition of acetone gave a colourless solution containing the dianion (88), which was quenched with water to form mainly the Z-hydroxy-hydrazone (89) (90%). Again, this confirmed the geometric stability of dianion intermediates and the operation of the syn-dilithio effect.



(86) X = H

(87) X = Li

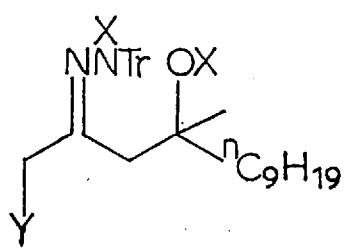


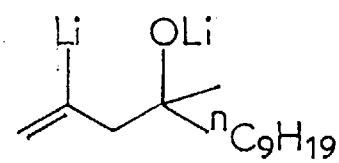
(88) X = Li

(89) X = H

Treatment of the dianion (83) with undecan-2-one gave a colourless solution of the dianion (90). Subsequent readdition of n-butyllithium

gave an orange coloured solution of the trianion (91) which on warming to -3^{o} faded and gave the vinyl carbanion (92) as a pale yellow solution. Quenching with deuterium oxide gave 2-deuterio-4-hydroxy-4-methyltridec-1-ene which was characterised by isoxazoline formation with 2,4,6-trimethylbenzonitrile oxide[65]. The isoxazoline derivative (93) was isolated in 85% yield with 90% deuterium incorporation. The regioselective deprotonation of the dianion (90) to the trianion (91) has precedent[21] and the use of 2,4,6-tri-iso-propylbenzenesulphonylhydrazones in DME was

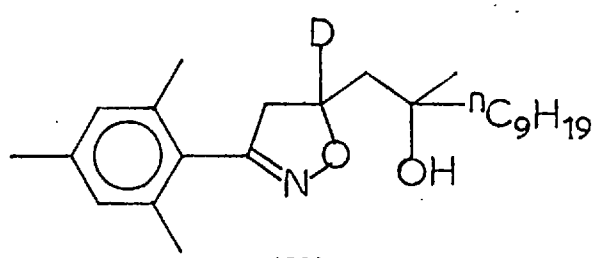




(92)

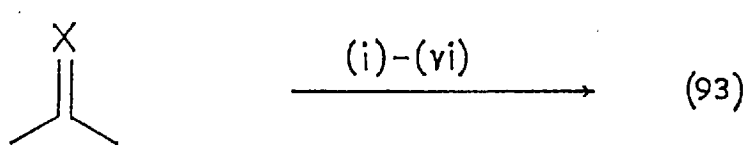
(90) Y = H, X = Li

(91) X = Y = Li



(93)

demonstrated to be superior to either a trisylhydrazone in THF or a tosylhydrazone in DME (Table 5).



(82) X = NNHTr

(94) X = NNHTs[21]

TABLE 5

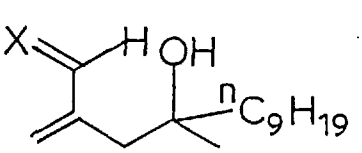
Hydrazone	Solvent	(iv)	Yield (deuterium incorporation)
82	DME	-3	85 (90% d_1)
82	THF	+15	80 (84% d_1)
94	DME	+3	3 (80% d_1)

(i) $^{n}BuLi$, -78^{o}, solvent (ii) $CH_3CO^{n}C_9H_{19}$

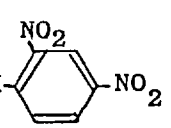
(iii) $^{n}BuLi$, (iv) T^{o},

(v) D_2O (vi) 2,4,6-trimethylbenzonitrile oxide

Treatment of the vinyl carbanion (92) with N,N-dimethylformamide gave a low yield of 4-hydroxy-4-methyl-2-methylenetridecanal (95a), characterised as its 2,4—dinitrophenylhydrazone derivative (95b) (14%). Attempted oxidation of the α,β-unsaturated aldehyde (95a) with activated manganese dioxide was unsuccessful. However, quenching of the vinyl carbanion (92)

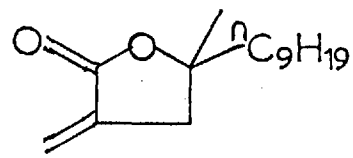


(95a) X = O



(95b) X = NNH-

with carbon dioxide gas at -78^{o} followed by warming to 25^{o} and acidification in sequence gave the α-methylene lactone (96). Using this methodology, a general one-pot synthesis of α-methylene-γ-lactones was developed. Typically, n-butyllithium (2.2 equiv.), the ketone or aldehyde (97)

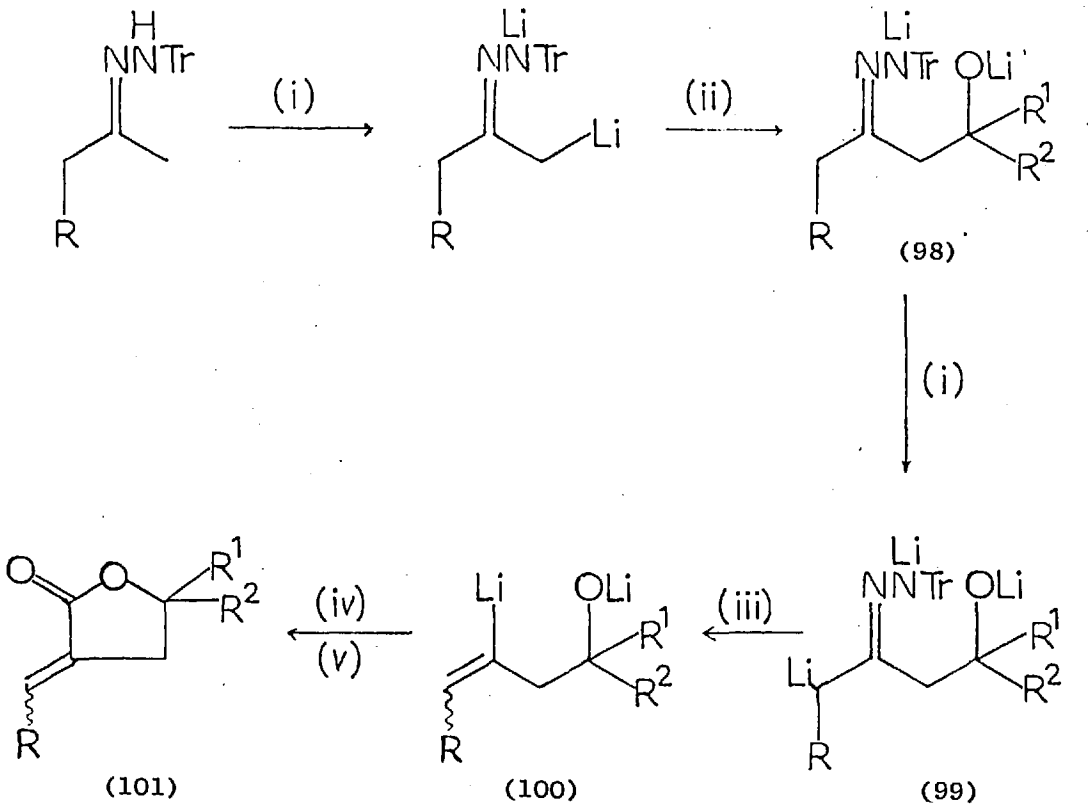


(96)

(1.2 equiv.) and n-butyllithium (1.2 equiv.) were added in sequence to the ketone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (82) or (86) (1.0 mmol) in DME at -78°. After warming to -3° and recooling to -78° the mixture was quenched with carbon dioxide gas. Work up, acidification and chromatography gave the α-methylene-γ-lactone (101) (Scheme 49, Table 6).

Typically, yields were good (40-60%). Alternatively the methylene lactone (101f) (74%) was prepared from the sulphonylhydrazone (85), n-butyllithium and carbon dioxide in sequence. In a similar way, the lactone (101c) (41%, E:Z (9:32)) was prepared from the sulphonylhydrazone (89).

The intermediacy of the trianion (99a) was confirmed by a series of quenching experiments. Treatment with acetone and acetic acid in sequence gave the dihydroxy-hydrazone (102) (31%) and the hydroxy-hydrazone (85) (36%). Similarly, reaction of hydroxy-hydrazone (85) with sec-butyllithium in DME or sec-butyllithium in DME and TMEDA gave, on acetone quenching, the dihydroxy-hydrazone (102) in 30% and 24% yield respectively. Although a discrete entity, the trianion (99a) was either not quantitatively formed or it was partially protonated by the electrophile. This second alternative was unlikely and indeed treatment of the hydroxy-hydrazone (85) with n-butyllithium, hexadeuterio-acetone and 0.1 M, pH 6.5 phosphate buffer in sequence gave the hexadeuterio-derivative (103) (16%) and the hydroxy-hydrazone (85) (80%). This confirmed that the trianion (99a) was not quantitatively formed. Shapiro[21] claims that a β-hydroxy-ketone toluene-4-sulphonylhydrazone does not afford a discrete trianion upon



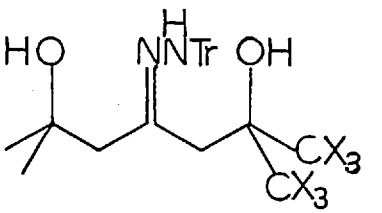
(i) ^{n}BuLi, -70°; (ii) R^1COR^2 (97); (iii) -3°; (iv) CO_2; (v) H^+.
Products (99), (100) a; R = H, $R^1 = R^2$ = Me.

Scheme 49

Table 6

Lactone (101)	R	R^1	R^2	Yield (%)
b	H	H	Et	45
c	Me	Me	Me	E:Z (2:35)
d	H	Me	^{n}hexyl	61
e	H	Me	^{iso}Bu	66
f	H	Me	Me	57
g	H	Me	Et	61
h	H	H	^{n}Pr	62
j	H	$-(CH_2)_5-$		40
k	Me	Me	^{iso}Bu	E:Z (5:12)

reaction with an alkyllithium reagent.



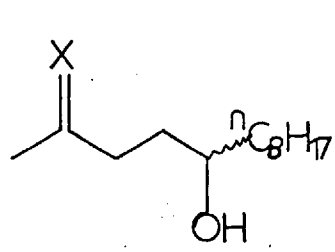
(102) X = H

(103) X = D

Our early results had suggested that the hydrazone (82) reacted with n-butyllithium in DME to produce the syn-dianion (83). We argued that the rate of the third deprotonation of the hydroxy-hydrazone (85) would depend upon the geometry of the hydrazone. Indeed, treatment of the pure Z-hydroxy-hydrazone (85) with n-butyllithium in DME at -65° followed by acetone quenching gave the dihydroxy-hydrazone (102) (30%) and the starting hydrazone (85) (43%). However, treatment of the pure E-hydroxy-hydrazone (85) in the same sequence gave the dihydroxy-hydrazone (102) (51%) and the starting hydrazone (85) (29%). Clearly, a syn-dilithio effect (Section II) was operating for the E-isomer. We applied these observations to the preparation of the α-methylene-γ-lactone (101f) and found that treatment of the Z-hydroxy-hydrazone (85) with n-butyllithium, carbon dioxide and acid in sequence gave the lactone (101f) (49%), in a similar yield to the "one-pot" method (Scheme 49). However, an identical sequence performed upon the pure E-isomer (85) gave the lactone (101f) in superior yield (78%). Clearly, these results indicated the importance and synthetic potential of the syn-dilithio effect, inherent to reactions performed in DME solvent.

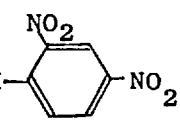
We anticipated that 3-methylenetetrahydropyran-2-ones (107) would be available from a γ-hydroxy ketone using our methodology. Reaction of 5-hydroxytridecan-2-one (105a) with 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b), n-butyllithium, carbon dioxide and trifluoroacetic

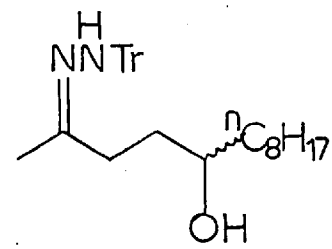
acid in sequence gave the lactone (107a) (23%). The intermediate hydrazone (106a) was unstable at 25°, decomposing with the loss of 2,4,6-tri-iso-propylbenzenesulphinic acid (108a). Treatment of the stable, crystalline γ-hydroxy-tosylhydrazone (63) in the same sequence gave no α-methylene-lactone (107b). The dianion (83) was found to be too unreactive to open an epoxide.



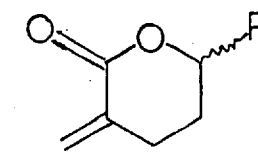
(105)

a; X = O

b; X = NNH- 



(106a)



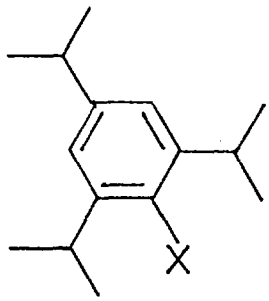
(107)

a; R = $^{n}C_{8}H_{17}$

b; R = Me

SECTION VI: SULTONE FORMATION FROM 2,4,6-TRI-ISO-PROPYLBENZENE-SULPHINIC ACID

The purification of the α-methylene-γ-lactones (101) (Section V) by standard chromatographic techniques was often found to be troublesome owing to the presence of a minor aromatic compound (109) of similar polarity. For example, during the preparation of 5,5-dimethyl-3-methylenetetrahydrofuran-2-one (101f) (57%) from acetone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (82), a low yield (2%) of the compound (109) was obtained. N.m.r. analysis indicated the presence of an intense singlet (δ_H 1.80) and we were most curious as to the composition of this product.



(108) a; X = SO_2H

b; X = SO_2NHNH_2

c; X = SO_2Cl

d; X = SO_2^+

e; X = SO^+

f; X = S^+

g; X = SO_2I

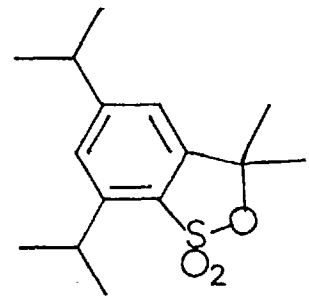
h; X = $SO_2\cdot$

i; X = $S(=O)-OEt$

j; X = SO_3Et

k; X = $S(=O)-P(=O)(OEt)_2$

l; X = $SO_2OO\cdot$

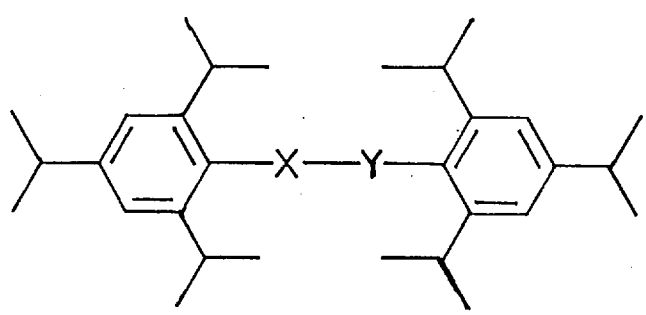


(109)

2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b) was slowly decomposed by treatment with triethylamine. Acidification after five days gave, on work up, a crystalline solid, m.p. 124-7°. Both the microanalysis and the mass spectrum ($M^{+\cdot}$, 282.1294) were consistent with a composition of $C_{15}H_{22}O_3S$. The i.r. spectrum demonstrated the lack of an OH function, but implied the presence of the $-SO_2-O-$ unit (1330 and 1190 cm^{-1}). The ^1H and ^{13}C n.m.r. spectra were most helpful for the elucidation of the structure of compound (109). Clearly the molecule possessed only two isopropyl functions [δ_H 1.33 (12H, 2 overlapping d, J 7Hz), 3.03 (1H, septet, J 7Hz), and 3.60 (1H, septet, J 7Hz); δ_C 23.29 (q), 23.67 (q), 29.58 (d), and 34.54 (d)], and was unsymmetrical. The low-field methyl resonance [δ_H 1.80 (6H, s), δ_C 89.89 (s)] indicated an ortho-fused isopropyloxysulphonyl function. Thus, formulation as the sultone (109) was unambiguous. Most proba-

bly the sultone (109) arose *via* aerial oxidation of the sulphinic acid (108a).

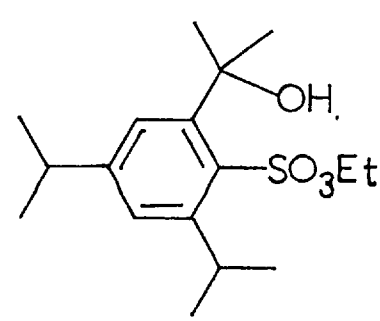
Zinc dust reduction[71] of 2,4,6-tri-iso-propylbenzenesulphonyl chloride[70] (108c) gave, on acidification, the sulphinic acid (108a). Identity and purity were confirmed by microanalysis, spectral characteristics, and by comparison with the literature data[70,71]. The mass spectrum showed ions derived from the thiosulphonate (110a) and the disulphide (110b), clearly arising from decomposition in the probe. Of note, ions at m/e 267 (108d), 251 (108e), 235 (108f) and 203 ($C_{15}H_{23}^{+\bullet}$) were observed. The sulphinic acid [λ_{max} 273 (ε 1400) and 282 nm (1200)] and 2,2-azobis-[2-methylpropionitrile] (herein after referred to as the initiator) [λ_{max} 345 nm (ε12)] were photolysed (> 316 nm[72]) under argon for three hours. Purification of the residue gave the disulphide (110b) (6%) and the thiosulphonate (110a) (58%). Assignment of structures followed from microanalysis, spectral data, and by comparison with literature data[73]. Further experiments are tabulated (Table 7, p. 53) and only selected examples are fully described in the experimental section.



(110) a; X=S, Y=SO_2

b; X=Y=S

c; X=Y=SO_2



(111)

TABLE 7

Reactions of 2,4,6-tri-iso-propylbenzenesulphinic acid (108a), S-2,4,6-tri-iso-propylphenyl 2,4,6-tri-iso-propylbenzene-thiosulphonate (110a) and 2,4,6-tri-iso-propylbenzenesulphonyl chloride (108c)

Reaction	Starting material (mmol)	Time	Reaction conditions[a]	Isolated products
1	0.99	3h	O_2, initiator (2.1 equiv.), hν	sultone (109) 34%
2	0.69	3h	Ar, hν	thiosulphonate (110a) 53%, disulphide (110b)7%
3	0.99	3h	Ar, initiator (2.1 equiv.), hν	thiosulphonate (110a) 58%, disulphide (110b)6%
4	0.60	2h	O_2, hν	sultone (109) 29%
5	0.38	2h	O_2	sultone (109) 23%
6	0.40	16h	O_2	sultone (109) 33%
7	1.00	(a)15 min (b)2h	(a) N_2, $NaHCO_3$ (1 equiv.), I_2 (1.06 equiv.) (b) O_2, hν	sulphonylsulphone (110c) 20%
8	1.00	(a)15 min (b)2h	(a) N_2, $NaHCO_3$ (1 equiv.), I_2 (1.00 equiv.) (b) O_2, hν	sultone (109) 8%, sulphonylsulphone (110c) 6%
9	0.99	3.5h	O_2, initiator (2.1 equiv.), $(EtO_3)P$ (4.7 equiv), hν	sultone (109) 11%, hydroxysulphonate (111)11% sulphinate (109i) 9%
10	0.52	2d	O_2, $(EtO)_3P$ (11.7 equiv)	sultone (109) 9%, sulphonate (108j) 41%, phosphate (108k) 13%, sulphinate (108i) 9%

/continued...

TABLE 7/continued

Reaction	Starting material (mmol)	Time	Reaction conditions	Isolated products
11	0.076	4.5 h	O_2, initiator (1.5 equiv.), hν	sultone (109) 51%, thiosulphonate (110a) 20%
12	0.18	2d	air, CF_3CO_2H (14 equiv.)	thiosulphonate (110a) (98%)
13	0.10	4h	O_2	thiosulphonate (110a) (100%)
14	0.46	9.5h	O_2, initiator (3.7 equiv.) hν	sulphonyl chloride[70] (108c) 78%
15	0.88	7d	air, DBU (1.3 equiv.)	sulphonyl chloride[70] (108c) 24%

a

Reactions 1-10 refer to the sulphinic acid (108a), reactions 11-13 to the thiosulphonate (110a) and reactions 14-15 to sulphonyl chloride (108c). In reaction 11 the yield of sultone (109) refers to a 1:1 stoichiometry. All reactions were carried out in the dark unless stated to the contrary; photolysis conditions are described in the Experimental section. The reactions were conducted whilst bubbling oxygen (O_2), argon (Ar), nitrogen(N_2) or air through the solutions. Reactions 1-6 and 9-15 were carried out in benzene as solvent; reactions 7 and 8 in water:benzene.

Photolytic decomposition (> 312 nm)[72] of the sulphinic acid (108a) under argon gave the disulphide (110b) (7%) and the thiosulphonate (110a) (53%). Most probably, the thiosulphonate arose *via* the well known disproportionation[74] mechanism. In the presence of oxygen, initiated or normal photolysis of the sulphinic acid (108a) gave the sultone (109), (34%) and (29%) respectively. Similarly, prolonged reaction in the dark, under oxygen, gave the sultone (109) (33%). In no instance, however, was the sultone (109) formed under anaerobic conditions. Clearly the presence of oxygen was vital for the formation of the sultone (109).

We argued that an arylsulphonyl radical (108h) might be an intermediate in the sultone (109) forming reaction. The radical (108h) should also be available from homolysis[75] of 2,4,6-tri-iso-propylbenzenesulphonyl iodide (108g). Reaction of the sulphinic acid (108a) with sodium hydrogencarbonate and iodine gave an intermediate (t.l.c.) presumably the arylsulphonyl iodide (108g). Subsequent photolysis under oxygen gave in low, but variable yield, the sultone (109) and a new compound (110c). From microanalysis and spectral data, the new compound was identified as the disulphone (110c). Presumably the arylsulphonyl radical (108h) was unable to abstract a hydrogen atom efficiently *via* an intramolecular pathway.

We argued that an alkyl hydroperoxide might also be a reaction intermediate during the formation of the sultone (109). These species are known to react with triethyl phosphite to give products derived from cleavage of the peroxide linkage. Indeed, in the presence of the initiator, triethylphosphite and oxygen, photolysis of the sulphinic acid (108a) gave the sultone (109) (11%), a more polar alcohol (111) (11%) and the sulphinate (108i) (9%). Similarly, reaction of the sulphinic acid (108a) with triethyl phosphite in the dark, under oxygen, gave the sultone (109) (9%), the sulphinate (108i) (9%), the sulphonate (108j) (41%), and *O*,*O*-diethyl *S*-(2,4,6-tri-iso-propylphenyl)thiophosphate (108k) (13%). Assignment of

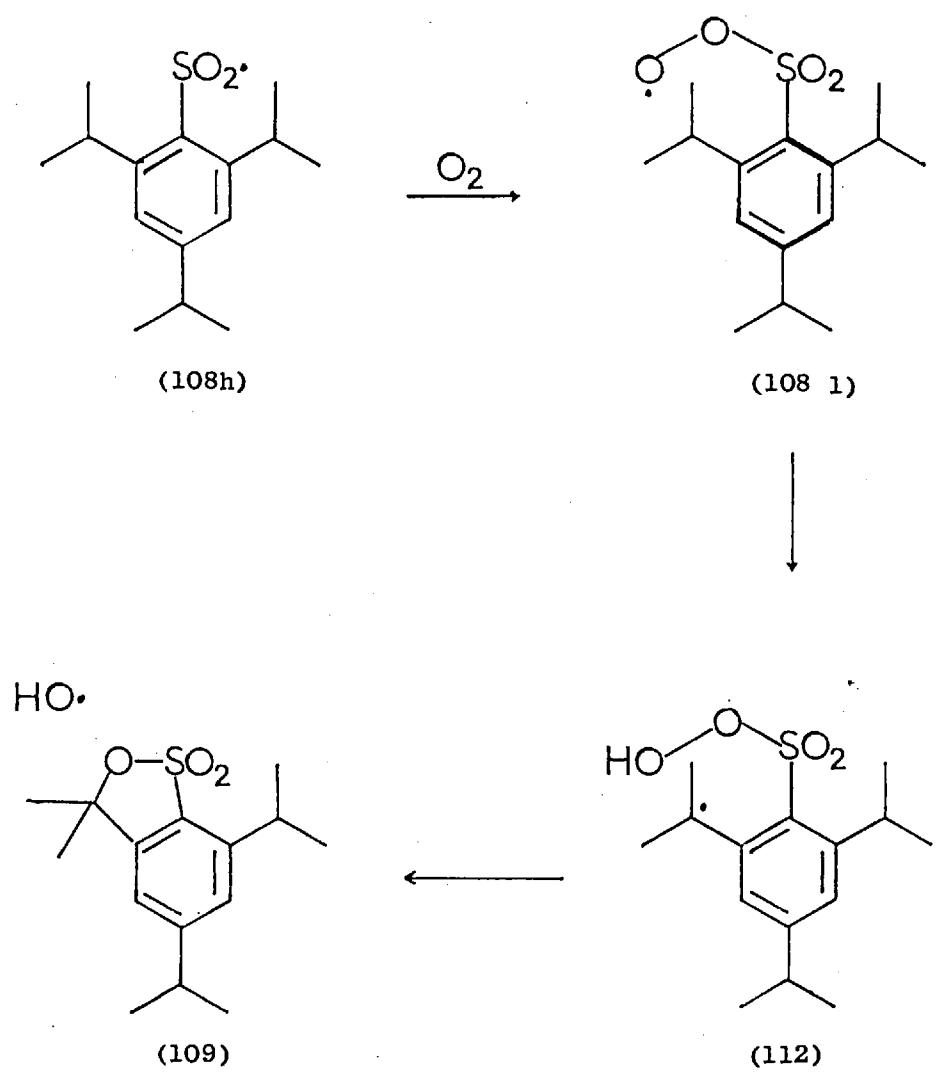
structures followed from both microanalyses and spectral data. Presumably both the sulphinate (108i) and the thiophosphate (108k) arose via the thiosulphonate (110a) and an Arbusov-like reaction. This has precedent in the literature[76]. Alternatively, ethylation of sulphonate anions would give rise to the ethyl arylsulphonates (108j) and (111). The introduction of the hydroxy function of the sulphinate (111) was consistent with a mechanism involving interception of an alkyl hydroperoxide by triethyl phosphite.

In the absence of the initiator, the thiosulphonate (110a) was shown not to be an intermediate of the sultone forming reaction. It was recovered unchanged upon exposure to trifluoroacetic acid and/or oxygen. However, photolysis of the thiosulphonate (110a) in the presence of initiator and oxygen, gave the sultone (109) (51%) and unreacted (110a) (20%).

The sulphonyl chloride[70] (108c) was examined as a model precursor of the sultone (109). Photolysis in the presence of the initiator and oxygen gave the starting sulphonyl chloride (108c) (78%) as the only isolable material. Similarly, reaction of the sulphonyl chloride (108c) with DBU for seven days, gave the starting material (108c) (24%) and no other isolable product.

The conversion of benzenesulphinic acid into benzenesulphonic acid by oxygen has been reported by Basedow[77]. The reaction was accelerated by photolysis. Basedow[77] postulated a chain-radical pathway involving a benzenesulphonyl radical and peroxybenzenesulphonic acid. Intermediacy of the peroxybenzenesulphonic acid was consistent with in situ oxidation of dibenzyl sulphide to the corresponding sulphoxide. Consistent with these observations and the results in Table 7, sultone (109) most probably arose by a radical pathway. In the absence of initiator, radical (108 1) is capable of intramolecular hydrogen atom abstraction to give the 2-aryl-

propyl radical (112) (Scheme 50). Hydrogen atom abstraction via a 7-membered transition state has precedent[78]. Subsequent ring closure of the radical (112) would give the sultone (109) (Scheme 50).



(108h) (108 1) (112) (109)

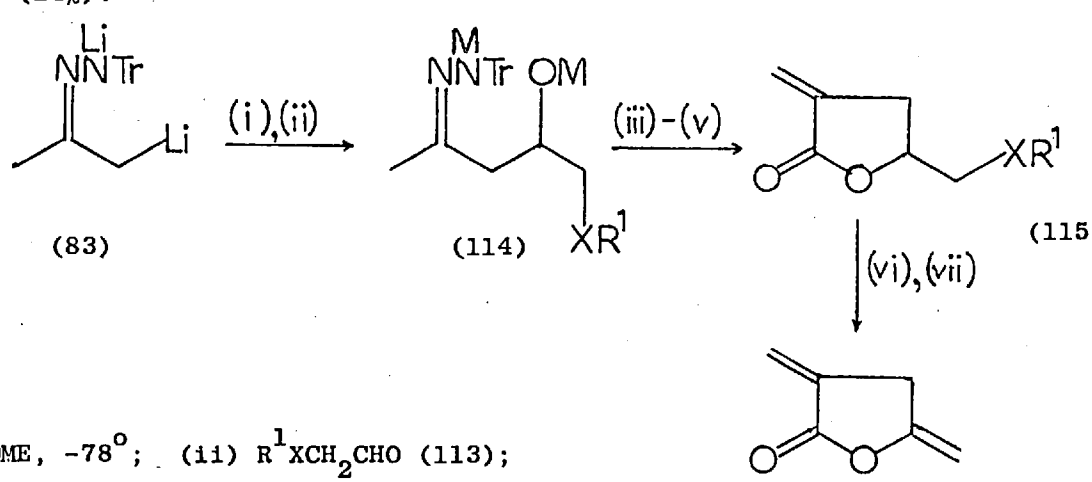
Scheme 50

SECTION VII: NOVEL SYNTHESES OF DIMETHYLENE LACTONES

(a) Novel Synthesis of 3,5-Dimethylenetetrahydrofuran-2-one

Derivatives of the 3,5-dimethylenetetrahydrofuran-2-one (116) unit occur naturally in the obtusilactones and malhubenolides.[79,80] We argued that this unit should be available by modification of the methodology described in Section VI. Treatment of a sulphonylhydrazone dianion [e.g. (83)] with a ketene equivalent [e.g. $PhSeCH_2CHO$ (113b)] , n-butyllithium, carbon dioxide and acidification in sequence should give the lactone (115b). β-Elimination of benzeneselenic acid from the lactone (115b) to form the dimethylene lactone (116) has precedent[128] (Scheme 51).

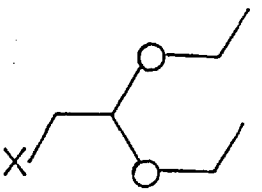
Phenylthio-acetaldehyde (113a) was chosen for initial study. Reaction of 2-bromo-1,1-diethoxyethane (117) with sodium thiophenoxide gave the thioacetal (118) (97%) and subsequent hydrolysis of the acetal with hydrochloric acid gave phenylthio-acetaldehyde (113a) (75%). Purity of the aldehyde was confirmed by spectral data and microanalysis. Reaction of the dianion (83) with the aldehyde (113a) at -65° gave, on work up, the hydroxy-hydrazone (114a) (24%).



(83) (114) (115) (116)

(i) DME, -78°; (ii) R^1XCH_2CHO (113);
(iii) ^nBuLi; (iv) CO_2; (v) H^+; (vi) oxidation;
(vii) $-(R^1XOH)$. For (113) and (115) a; R^1 = Ph, X = S;
b; R^1 = Ph, X = Se; c, R^1 = Me, X = Se; d, R^1 = ^nBu, X = Se;
(114) a, R^1 = Ph, X = S, M = H; b, R^1 = Ph, X = Se, M = H.

Scheme 51



(117) X = Br

(118) X = PhS

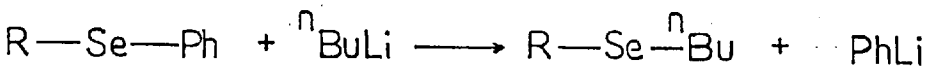
(119) X = PhSe

(121) X = MeSe

Plausibly, the aldehyde was acting as a proton source as well as an electrophile. Treatment of the hydroxy-hydrazone (114a) with alkyllithium, carbon dioxide and acetic acid in sequence failed to yield the methylene lactone (115a). Similarly, reaction of the dianion (83) with the aldehyde (113a), n-butyllithium, carbon dioxide and acidification in sequence gave no methylene lactone (115a). As each reaction was warmed to -20^{o}, an uncharacteristic red coloured intermediate was formed.

Somewhat discouraged, we tried phenylseleno-acetaldehyde (113b) as the ketene equivalent. Reaction of diphenyl diselenide with sodium borohydride and the bromo-acetal (117) in sequence gave the seleno-acetal (119) (95%), which was hydrolysed to phenylseleno-acetaldehyde(113b) (79%). Purity was confirmed by spectral data and microanalysis; the aldehyde (113b) has recently been synthesised by Baudat[81]. Treatment of the dianion (83) with the seleno-aldehyde (113b) gave, on work up, the selenosulphonylhydrazone (114b) (59%) and we were encouraged by this higher yield of trapped product. Reaction of the dianion (83) with the seleno-aldehyde (113b), n-butyllithium, carbon dioxide and acidification in sequence gave the selenolactone (115d) (1%) and benzoic acid (17%). Again a red solution was formed at -20^{o} during the reaction. Even a repeated reaction which was maintained at -25^{o} prior to being recooled to -78^{o} and quenched

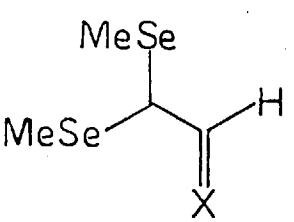
by carbon dioxide, gave the selenolactone (115d) (2%) and benzoic acid (17%). Presumably, benzoic acid and the lactone (115d) arose via transmetallation at selenium (Scheme 52). Such reactions at selenium have precedent[82].



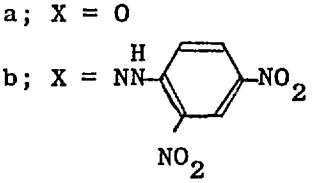
Scheme 52

We argued that if a methyl carbanion, rather than a phenyl carbanion was the potential leaving group (Scheme 52), then transmetallation at selenium would be thermodynamically less likely to occur. This required the preparation of methylseleno-acetaldehyde (113c). Reaction of dimethyl diselenide[83] (120) with sodium borohydride and the bromo-acetal (117) in sequence gave the seleno-acetal (121) (81%). Acidic hydrolysis gave both methylseleno-acetaldehyde (113c) (27%) and dimethylseleno-acetaldehyde (122a) (17%) in an unoptimised reaction. However, treatment of the dianion (83) with methylseleno-acetaldehyde (113c), methyllithium, carbon dioxide and acetic acid in sequence gave no methylene lactone (115c). Thus, we abandoned this route.

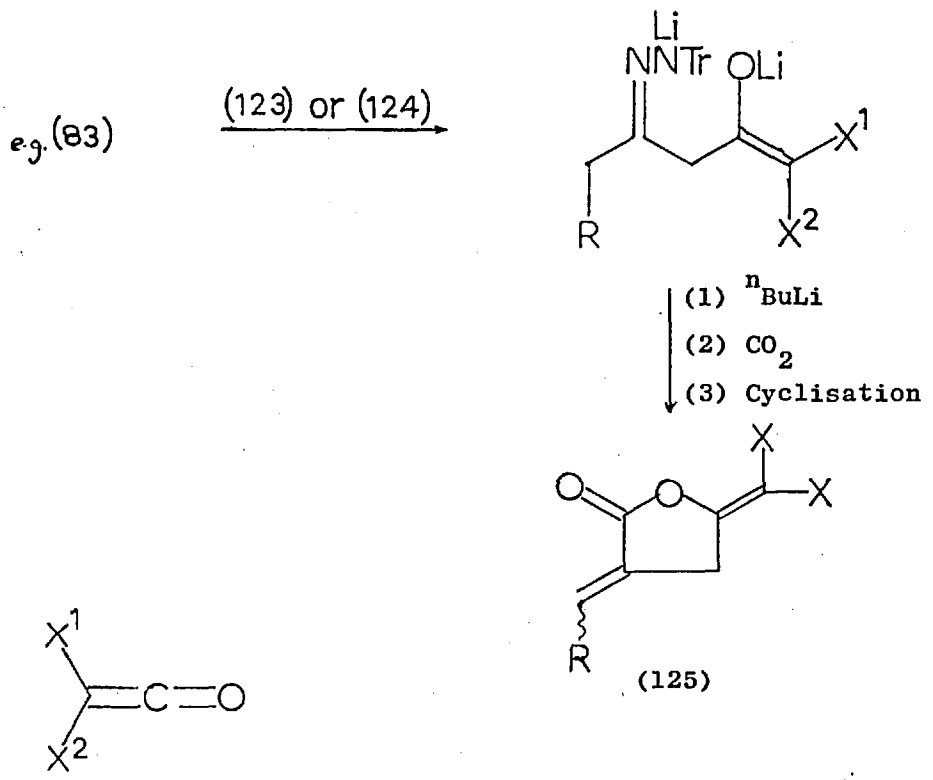
(120)



(122) a; X = O

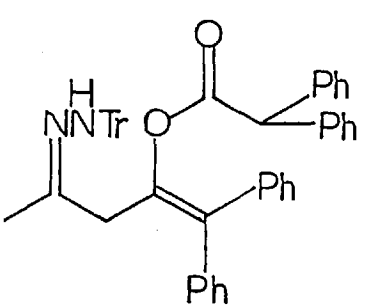
b; X = 

Dimethylene lactones (125) should also be available from the Shapiro reaction provided a ketene was used to quench the dianion of a sulphonylhydrazone (Scheme 53). However, reaction of the dianion (83) with diphenylketene (123) gave, on work up, the diacylated derivative (126)



Scheme 53

(25%) as the major isolated product. Presumably, the ketene was too reactive an electrophile. Similarly, reaction of the dianion (83) with tri-



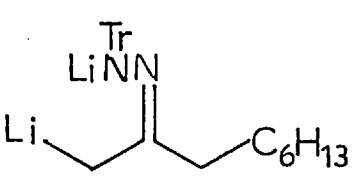
(126)

methylsilylketene[87] (124) at -65° proved unsuccessful. On work up, the starting hydrazone (82) (80%) and no major trimethylsilyl-containing compounds were isolated. Indeed reaction of the hydrazone (65) with sec-butyllithium at -65°, trimethylsilylketene[87] (124) (-78° to 0°) and deuterium oxide in sequence gave the olefin (67) (38%) and the starting

material (65) (60%). Neither product contained deuterium.

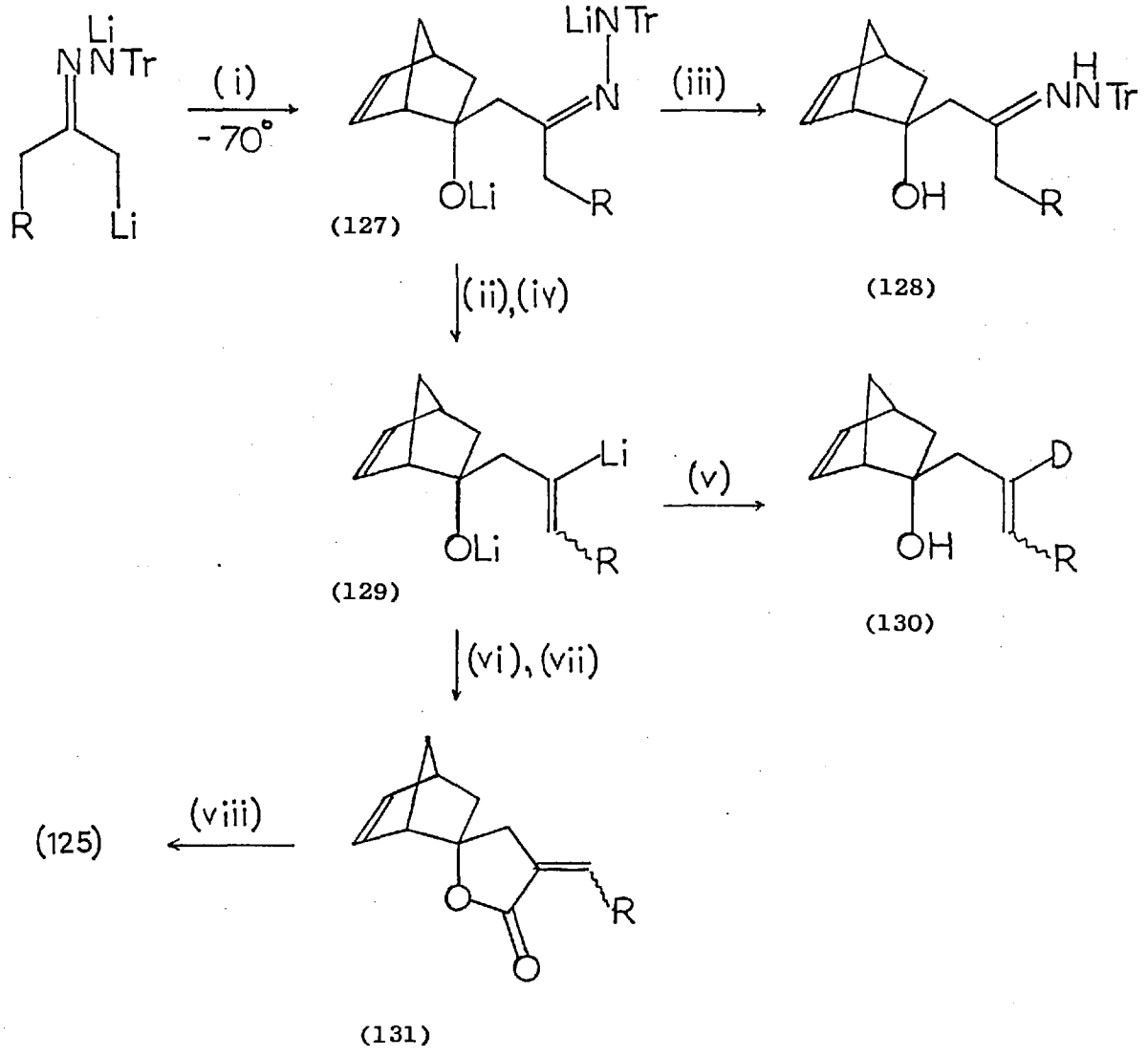
Dimethylene lactones (125) should also be available by a retro-Diels Alder reaction of the α-methylene-lactone (131a). This reaction has precedent[84]. The lactone (131a) should be available from the Shapiro reaction (Scheme 54). Indeed reaction of the dianion (83) with bicyclo [2.2.1] hept-2-en-5-one,[88] n-butyllithium, carbon dioxide and acetic acid in sequence gave the methylene lactone (131a) [61% from the hydrazone (82)]. Acetic acid was found to be best for the cyclisation of the intermediate hydroxy-acid to the methylene lactone (131a). Trifluoroacetic acid gave lower yields, presumably due to competitive rearrangement. The product lactone (131a) was stereochemically homogeneous (^{1}H and ^{13}C n.m.r. and t.l.c. analysis) and plausibly resulted from exo-carbanion attack.[85] Intermediacy of the dianions (127a) and (129a) followed from, respectively, trapping with acetic acid and deuterium oxide, which gave the hydrazone (128a) [56% from the hydrazone (82)] as an E,Z-mixture, and the olefin (130a) [70% from the hydrazone (82), 91% deuterium incorporation]. The lactone (131a), on flash vacuum pyrolysis at 550° and 10^{-4} mmHg, gave 3,5-dimethylenetetrahydrofuran-2-one (116) (83%).

In a similar way, the Z-lactone (131b) (16%) was obtained from the dianion of octan-2-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (132). Presumably the low yield was due to instability of the vinyl carbanion



(132)

(129b). Indeed quenching of the carbanion (129b) with deuterium oxide

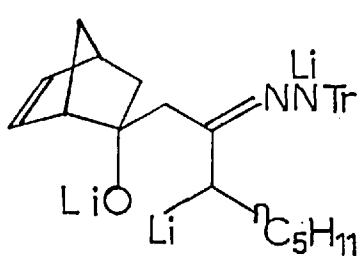


(131)

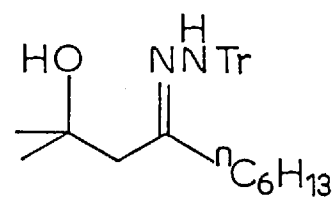
(i) bicyclo[2.2.1] hept-2-en-5-one; (ii) ^{n}BuLi, -78°; (iii) HOAc, -78°; (iv) -3°; (v) D_2O; (vi) CO_2, -78°; (vii) HOAc, CH_2Cl_2, 20°; (viii) 550°, 10^{-4} mmHg. For structures 127-131: (a) R = H; (b) R = $^{n}C_5H_{11}$.

Scheme 54

gave a crude olefin (130b) with only 70% deuterium incorporation. Formation of the trianion (99a) from the hydroxy-hydrazone (85) has already been shown to be incomplete at low temperature (Section V). Presumably, deprotonation of the dianion (127b) to the trianion (133) would be even harder to achieve due to inductive destabilization of the carbanion by the alkyl substituent. If formation of the trianion (133) was not maximised prior to generation of the vinyl carbanion (129b), then the vinyllithium (129b) could compete with the alkyllithium as base for the deprotonation of the dianion (127b). We tried several experiments involving increasing the base strength of the alkyl-



(133)

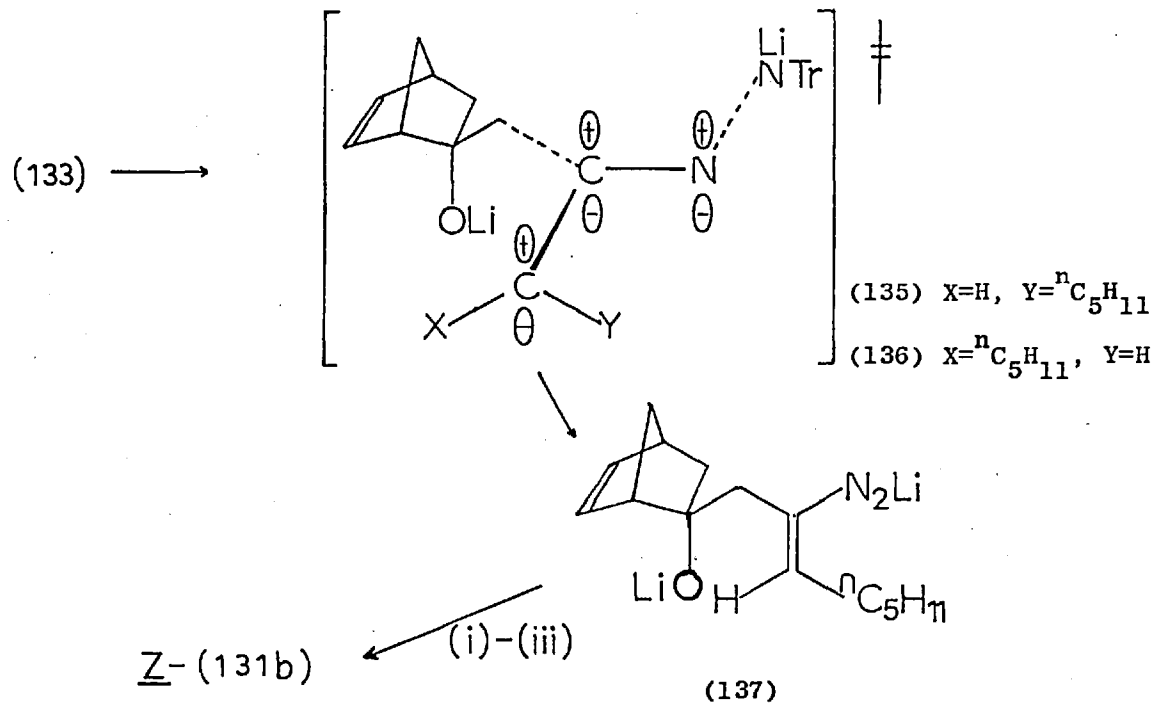


(134)

lithium reagent in an attempt to secure trianion formation at the lowest possible temperature, thus increasing the vinyl carbanion (129b) yield. Bases such as n-butyllithium in HMPA or n-butyllithium in 12-crown-4 gave the olefin (130b) with only 10% and 0% deuterium incorporations. Similarly n-butyllithium with potassium t-butoxide or t-butyllithium gave only low yields of the vinyl carbanion (129b). Attempted isomerisation of the hydrazone (128b) or the hydrazone (134) (with acid, by standing or heating in solution) to their corresponding more polar E-isomers proved unsuccessful. It was expected that the syn-dilithio effect in the E-isomer would have facilitated trianion formation (Section V).

In each α-alkylidene-γ-lactone (101c), (101k),(131b) prepared from

the Shapiro reaction, the Z-isomer was predominantly formed. Presumably, fragmentation of the trianion, e.g. (133), occurred via the lower energy transition state (135 not 136) (Scheme 55).

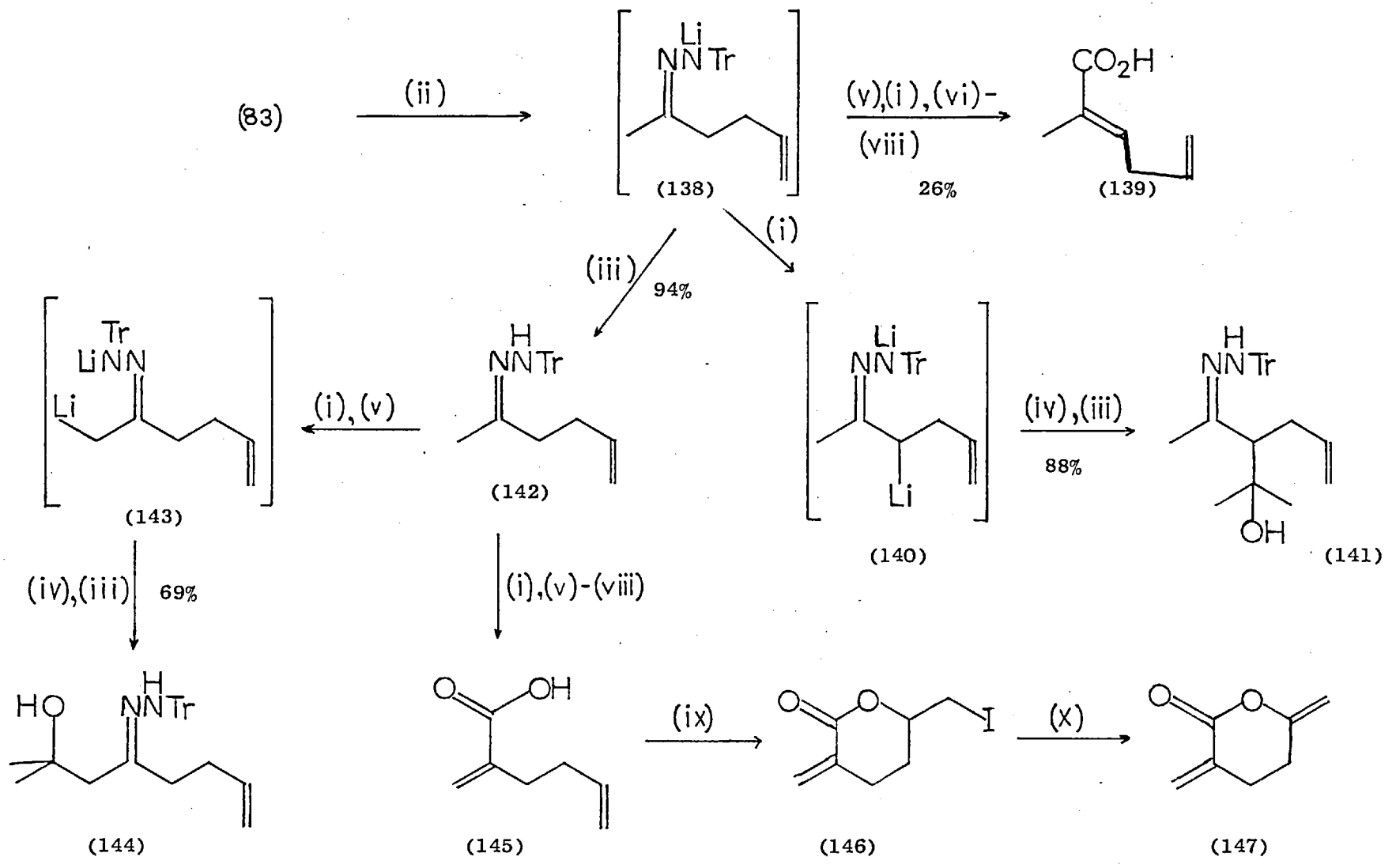


(i) -3°; (ii) CO_2; (iii) H^+;

Scheme 55

(b) Novel Syntheses of 3,6-Dimethylenetetrahydropyran-2-ones

Although not naturally occurring, we believed that 3,6-dimethylenetetrahydropyran-2-ones may show interesting chemical and biological activities. The parent compound, 3,6-dimethylenetetrahydropyran-2-one (147) should be available via iodolactonisation of 2-methylenehex-5-enoic acid (145). This reaction has ample precedent.[86] Treatment of the dianion (83) with allyl bromide gave the anion (138). Subsequent treatment with alkyllithium *in situ* gave the syn-dianion (140) as evidenced by an acetone quench, which gave the alcohol-hydrazone (141) (88%). Similarly, treatment of the anion (138) with TMEDA, alkyllithium (-78°) and carbon dioxide (-3°) gave



Scheme 56

/continued...

Scheme 56/continued...

All reactions, except (ix) and (x), were carried out in DME.

(i) $^{n}BuLi$, -78^{o}; (ii) $CH_2=CHCH_2Br$, 60^{o}; (iii) HOAc, -78^{o} to -50^{o};

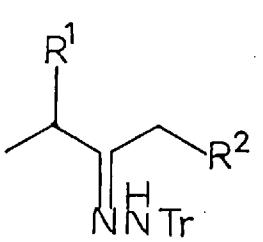
(iv) Me_2CO, -78^{o}; (v) $Me_2NCH_2CH_2NMe_2$ -78^{o}; (vi) -3^{o},

(vii) CO_2, -78^{o}; (viii) CF_3CO_2H; (ix) CH_2Cl_2, H_2O, $NaHCO_3$, KI_3, 20^{o};

(x) PhH, 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU), 74^{o}.

The hydrazones (141), (142) and (144) were of syn-stereochemistry on initial isolation but isomerised at room temperature. At equilibrium the hydrazone (142) was ca. 15:85 Z:E. In the sequences (142)→(144) and (142)→(145) the syn-isomer gave rise to minor side products.

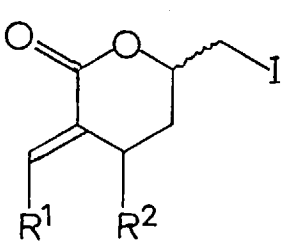
on acidification, the acid (139) (26%). Presumably, the regioselective deprotonation of (138) was being controlled by the syn-dilithio effect. We argued that if the anion (138) was protonated and the product warmed to 25°, then the resultant hydrazone (142) would equilibrate to the thermodynamically more stable E-isomer. Deprotonation of the hydrazone (142), controlled by the syn-dilithio effect, should now predominantly give the dianion (143). Indeed, treatment of the dianion (138) with acetic acid and warming, in sequence, gave the E:Z- (85:15) hydrazone (142) (94%). Reaction of the hydrazone (142) with n-butyllithium and TMEDA at -78° gave the least substituted dianion (143). An acetone quench gave the hydroxy-hydrazone (144) (69%). More pleasingly, treatment of the hydrazone (142) with TMEDA, n-butyllithium (-78 to -3°) and carbon dioxide, in sequence, gave upon acidification the acid (145) which was iodolactonised to the fully characterised iodolactone (146) [50% from the hydrazone (142)]. Subsequent reaction with DBU gave the novel 3,6-dimethyl-enetetrahydrofuran-2-one (147) (64%) (Scheme 56). Similarly, butanone trisylhydrazone (86) was allylated to a mixture of hydrazones (148a > 148b). Subsequent reaction with n-butyllithium, carbon dioxide and acidification in sequence, gave on work up a crude acid mixture. Iodolactonisation gave both the lactones (149a) (39%) and (149b) (6%). Dehydrohalogenation of the lactone (149a) with DBU gave the dialkylidene lactone (150) (71%)



(148)

(a) R^1 = H, R^2 = $CH_2CH{=}{=}CH_2$

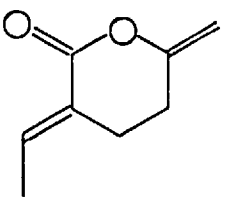
(b) R^1 = $CH_2CH{=}CH_2$, R^2=H



(149)

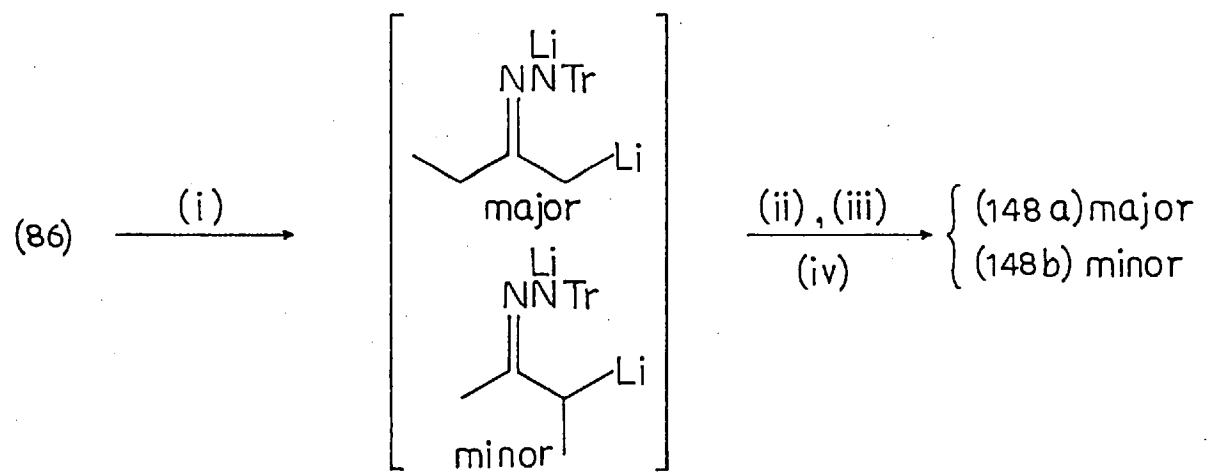
(a) R^1 = Me, R^2 = H

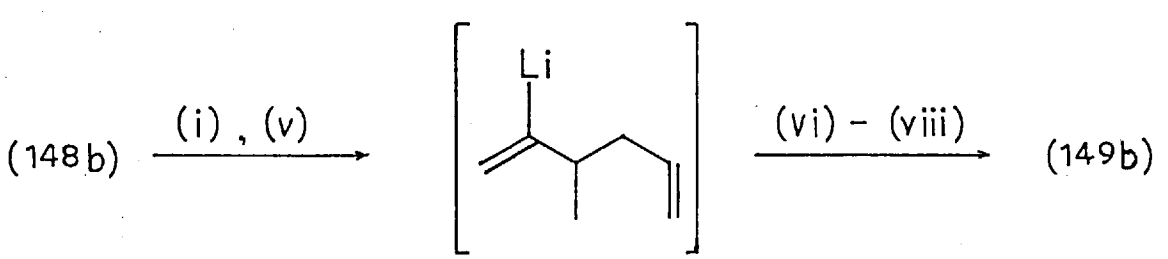
(b) R^1 = H, R^2 = Me



(150)

Formation of the lactone (149b) was indeed strong evidence for a syn-dilithio effect in DME solution (Scheme 57). The lactone (149b) arises from the minor hydrazone (148b), itself derived from the hydrazone (86) via a syn-dilithio effect.

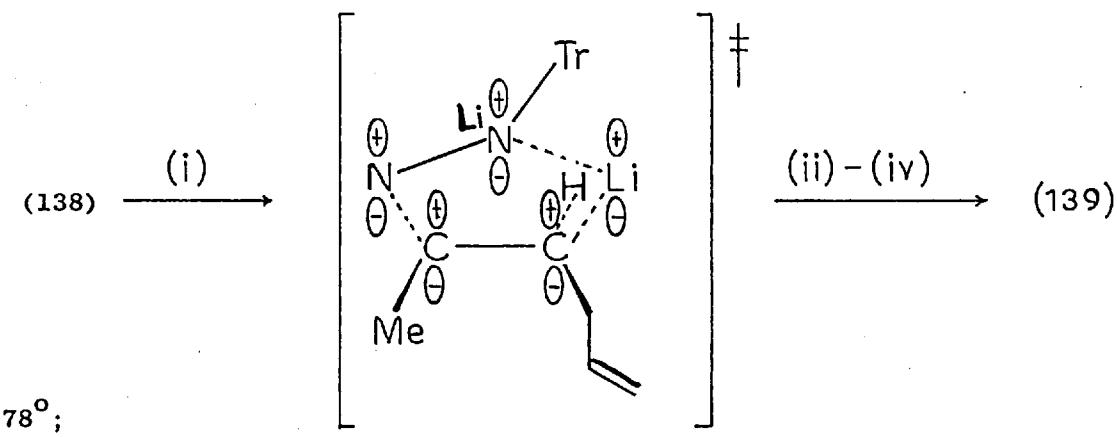




(i) $^{n}BuLi$, -78^{o}; (ii) $CH_2 = CHCH_2Br$, -65^{o}; (iii) HOAc; (iv) 25^{o}, (v) -3^{o}; (vi) CO_2; (vii) H^{+}; (viii) I_2;

Scheme 57

Exclusive formation of the E-acid (139) from the anion (138) and the E-lactone (149a) from the hydrazone (148a), indicated that the dianions fragmented through the more stable transition state (e.g. Scheme 58).

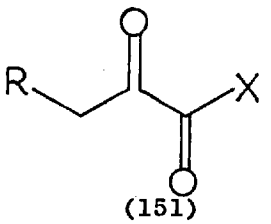


(i) -78^{o};
(ii) -3^{o};
(iii) CO_2
(iv) CF_3CO_2H

Scheme 58

SECTION VIII: PREPARATION OF STABILISED VINYL CARBANIONS

Direct formation of a vinyl carbanion adjacent to a stabilising carbonyl group by the Shapiro reaction has not been reported in the literature. We believed that α-ketocarbonyl compounds (151) would act as suitable precursors and the product vinyl carbanion would be stabilised by delocalisation (Scheme 59). Thus, high yields of products (156) with electrophiles were anticipated. Due to the anticipated stability of the vinyl carbanion (155), we believed it would not competitively deprotonate the anion (153) in the presence of reagent alkyllithium. We hope to apply such stabilised vinyl carbanions to the preparation of obtusilactones[79, 80] (157).



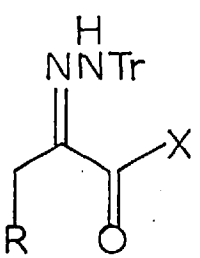
(151)

(a) X = OH

(152) $\xrightarrow{(i)}$ (153) $\xrightarrow{(i)}$ (154) $\longrightarrow$ (155) $\xrightarrow{(ii)}$ (156)

(i) R^3Li; (ii) E^+

Scheme 59



(152)

(a) X = OH, R = H

(b) X = OH, R = $^nC_{13}H_{27}$

(c) X = OH, R = $^nC_8H_{17}$

(d) X = OEt, R = H

(e) X = NH_2, R = $^nC_4H_9$

(f) X = NH-c-C_6H_{11}, R=H

(g) X = NH-c-C_6H_{11}; R = $^nC_4H_9$

(h) X = NH-c-C_6H_{11}; R = $^nC_{13}H_{27}$

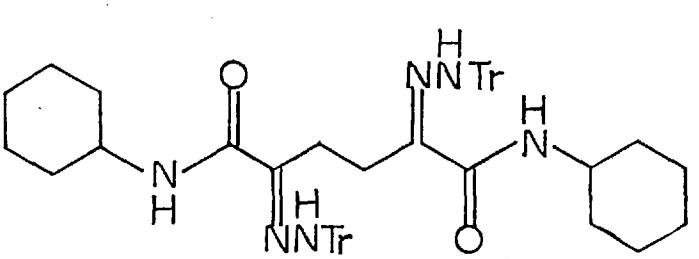
(i) X = NHMe; R = H

(j) X = NHMe; R = $^nC_4H_9$

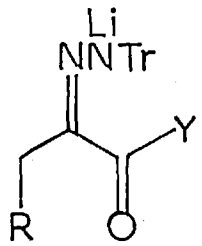
(k) X = NHMe; R = $^nC_{13}H_{27}$

(l) X = NH-c-C_6H_{11}; R = $^nC_3H_7$

(m) X = NH-c-C_6H_{11}; R = OH

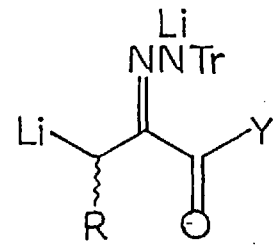


(152n)



(153)

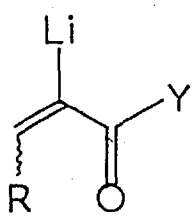
(a) R = H, Y = OEt



(154)

(a) R = H, Y = OEt

(b) R = H, Y = $\overset{Li}{N\text{-}\underline{c}\text{-}C_6H_{11}}$



(155)

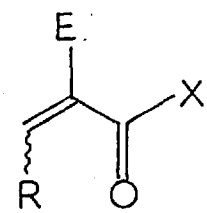
(a) R = H, Y = OEt

(b) R = H, Y = NLi-$\underline{c}$-C_6H_{11}

(c) R = H, Y = OLi

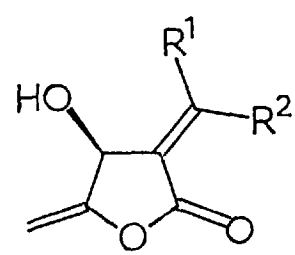
(d) R = ^{n}Bu, Y = NLi-$\underline{c}$-C_6H_{11}

(e) R = ^{n}Bu, Y = NLiMe



(156)

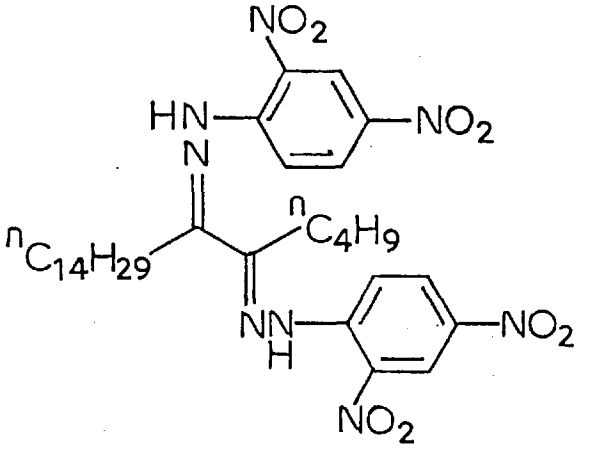
(a) X = NHR



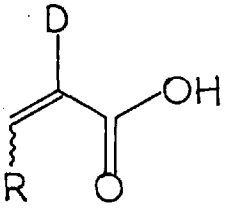
(157)

α-Ketoacids (151a) were examined as precursors. Pyruvic, 2-oxo-undecanoic[89] and 2-oxohexadecanoic acids[89] were chosen for the initial study. The keto-acids were converted to their corresponding 2,4,6-tri-iso-propylbenzenesulphonylhydrazones in good yields. However, reactions involving the acid hydrazone (152a) were unsuccessful. Treatment of the acid hydrazone (152a) with alkyllithium at low temperature, warming to 0^{o} or 25^{o} and attempted quenching of the vinyl carbanion (155c) with the electrophiles, benzyl bromide,

acetone, or 5α-cholestan-3-one, gave no isolable trapped products. Alkyl analogues of the vinyl carbanion (155c), prepared by a different method are reported in the literature.[102] Reaction of the acid hydrazone (152b)with n-butyllithium at -78°, followed by warming to 25° and quenching with deuterium oxide, gave a ketonic product (ν_{max} 1720 cm^{-1}). Reaction with 2,4-dinitrophenylhydrazine[63] gave plausibly the osazone derivative (159). Clearly the reagent alkyllithium had attacked the carboxylate anion. A reaction using lithium di-iso-propyl-



(159)

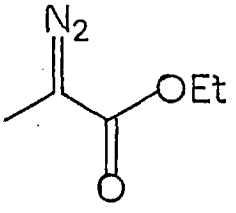


(158) R = $^{n}C_{13}H_{27}$

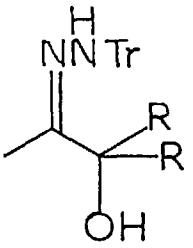
(160) R = $^{n}C_{8}H_{17}$

amide as base gave no deuterio-acid (158). Similarly, treatment of the acid hydrazone (152c) with sodium hydride, sec-butyllithium and deuterium oxide in sequence gave no deuterio-acid (160).

α-Keto-esters were also considered as potential precursors for the preparation of stabilised vinyl carbanions (155a). Treatment of the ester hydrazone (152d) with lithium di-iso-propylamide at -70°, followed by 1-bromohexane gave, on work up, the starting material (152d) (7%)and an unstable, volatile green oil. Spectral analysis indicated that the oil was probably the diazo-ester (161). Presumably the base was insufficiently strong for normal dianion (154a) formation, and loss of lithium 2,4,6-tri-iso-propylbenzenesulphinate from the substrate monoanion (153a) gave the diazo-ester (161).



(161)

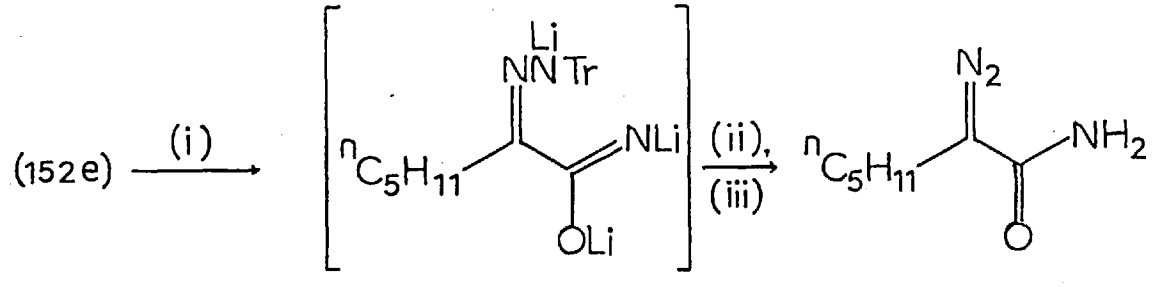


(162) R = ^{t}Bu

(163) R = ^{n}Bu

Attempts at increasing the base strength by the addition of t-butyllithium or n-butyllithium to the reaction mixture after the addition of lithium di-iso-propylamide were unsuccessful. The alkyllithium reagents reacted with the ester to produce carbinols (162) (31%) and (163) (32%) respectively.

Production of an amide anion from the reaction of a primary or secondary amide with base is a known method[90] for the prevention of alkyllithium attack at the carbonyl group. We believed we could utilise this effect to prepare the compounds (156a). This required a facile preparation of α-keto-amides. Reaction of n-hexanoyl chloride with copper (I) cyanide and acid hydrolysis of the intermediate acyl cyanide, gave in unoptimised yield, 2-oxoheptanamide (19%) which was smoothly converted to its corresponding 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (152e) (95%). However, reaction with n-butyllithium in DME or even sec-butyllithium in DME and TMEDA at -78°, followed by warming to 25° gave, on quenching with deuterium oxide,the fully characterised diazo-amide (165). Plausibly, the trianion (164) was formed, and the diazo compound formed by subsequent loss of lithium 2,4,6-tri-iso-propylbenzenesulphinate (Scheme 60).



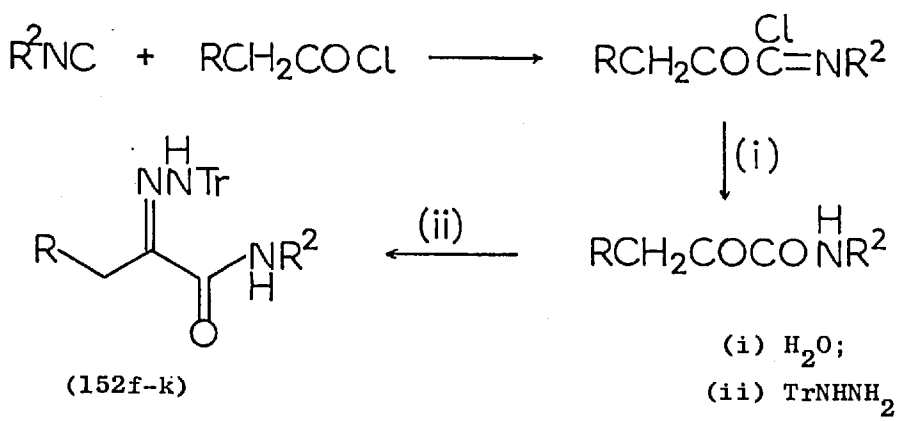
(164)

(165)
54%

(i) ^{n}BuLi; (ii) -LiTs; (iii) H_2O;

Scheme 60

The reaction of isonitriles with acid chlorides and subsequent hydrolysis of the intermediate imidoyl chlorides is a standard method[91] for the preparation of secondary α-keto-amides in good yield. We found that the keto-amides could be conveniently isolated as their crystalline 2,4,6-tri-iso-propylbenzenesulphonylhydrazone derivatives (152 f — k), normally in a "one pot" method (Scheme 61, Table 8).



Scheme 61

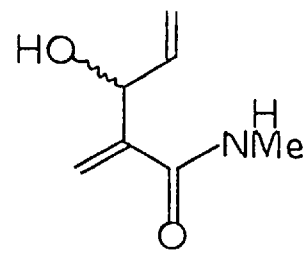
Table 8

R^2NC	RCH_2COCl	Product	(%)
R^2=c-C_6H_{11}	R = H	(152f)[a]	93
R^2= "	R = $^nC_4H_9$	(152g)[b]	85
R^2= "	R = $^nC_{13}H_{27}$	(152h)[a]	92
R^2= Me	R = H	(152i)[b]	55
R^2= "	R = $^nC_4H_9$	(152j)[b]	91
R^2= "	R = $^nC_{13}H_{27}$	(152k)[b]	65

a Yield from the intermediate keto-amide

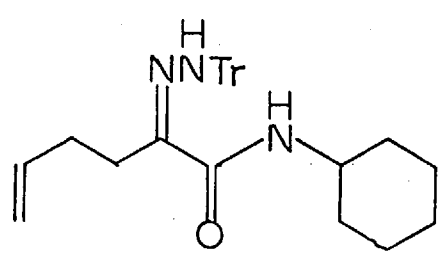
b Yield from the isonitrile

Reaction of the amide hydrazone (152i) with n-butyllithium in DME and TMEDA at -78°, warming to 25° and quenching with acrolein in sequence gave the hydroxy-amide (166) in poor yield (8%). However, reaction of the amide

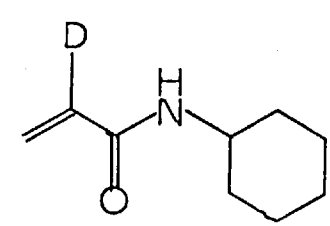


(166)

hydrazone (152f) with di-iso-propylamide in DME and n-butyllithium at -69° gave the trianion (154b). Reaction with allyl bromide gave the C-allyl derivative (167) (70%). On warming to 0° for 35 min the trianion (154b) gave the vinyl carbanion (155b). Addition of deuterium oxide gave the deuterio-amide (168) (54%) with ca. 100% deuterium incorporation. More simply, the trianion (154b) was obtained by treatment of the amide hydrazone (152f) with n-butyllithium in DME. Warming to 25° gave the vinyl carbanion (155b) which was

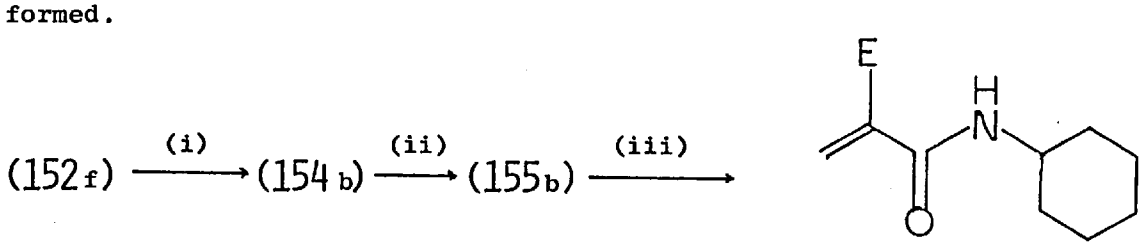


(167)



(168)

was efficiently trapped with various electrophiles (Scheme 62, Table 9). Optimised yields were obtained when 3.2 equivalents of n-butyllithium were used. In most reactions, a small amount (ca. 5%) of hydrazone, possibly (152n) was formed.

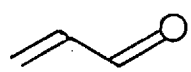
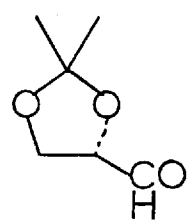
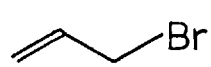


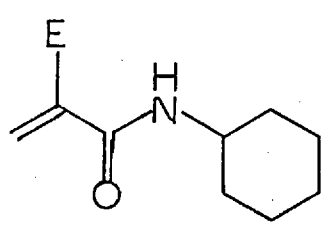
Scheme 62/continued

For Scheme 62

(i) 3.2 ^{n}BuLi, -78°, DME; (ii) 25°, (iii) E^{+}

Table 9

E	Product	Yield
D_2O	168	82 (ca. 100% d_1)
CH_3COCH_3	169	59
	170	81
$(CH_2\text{-}O)_n$	171	59
HCOEt	172	80
	173a	46
	173b	14
	none	-

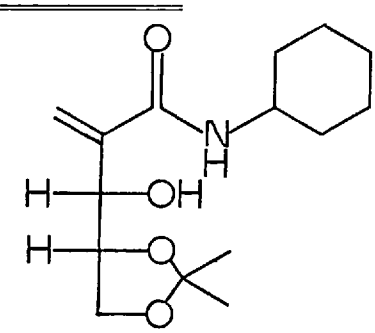


(169) E = $C(CH_3)_2OH$

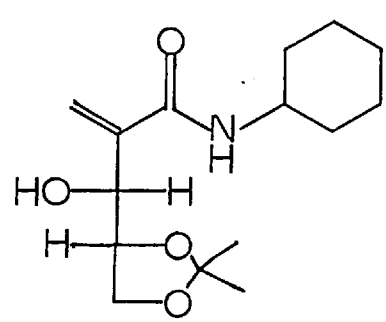
(170) E = $CH(OH)CH{=}CH_2$

(171) E = CH_2OH

(172) E = CH(OH)Et

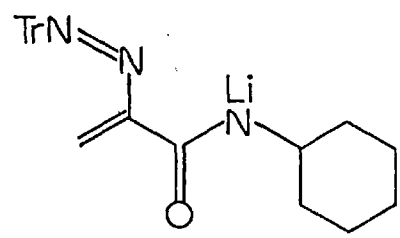


(173a)



(173b)

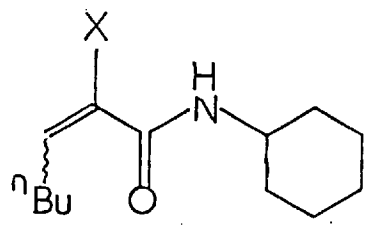
The trianion (154b) was found to react with 1-iodopropane to give the expected hydrazone (152 l) (38%), the starting hydrazone (152f) (46%) and an unexpected hydroxy-sulphonylhydrazone (152m) (14%). A similar reaction of the trianion (154b) with 1-iodotridecane gave the starting hydrazone (152f) (66%) and the hydroxy-sulphonylhydrazone (152m) (18%). Clearly, the trianion was not quantitatively formed at low temperature, or it was slow to react with alkyl iodides. The unusual product (152m) probably arose *via* electron transfer from the trianion (154b) to adventitious iodine, oxygen, or the alkyl iodide, thus generating the azaene (174) which was intercepted by water on work up.



(174)

The amide hydrazone (152g) was reacted with n-butyllithium (4.8 equiv.) at -78° and the reaction mixture then warmed up to 25° to yield the vinyl carbanion (155d). Addition of deuterium oxide gave the deuterio-amide (175) (62%) with *ca.* 100% deuterium incorporation. The product (175) was obtained predominantly as the *E*-isomer [δ_H 6.75 (1H, t, *J* 6Hz, *H*C=)]. Optimised yields of the deuterio-amide were obtained from an excess (*ca.* 5 equiv.) of alkyllithium. Reaction of the vinyl carbanion (155d) with acrolein (-78°) gave the *E*,*Z*-hydroxy-amide (176) (51%). Quenching the vinyl carbanion (155d) with acetone gave both the hydroxy-amide (177) (21%) of predominantly *Z*-geometry [δ_H 5.63 (1H, t, *J* 7Hz, *H*C=)] and the amide (178) (39%) of predominantly *E*-geometry [δ_H 6.78 (1H, dt, *J* 15, 7Hz, 3-C*H*)]. Presumably acetone was functioning both as an electrophile and as an acid. A similar reaction with hexadeuterioacetone gave the hydroxy-amide (179) (38%) of predominantly *Z*-geometry

[δ_H 5.64 (1H, t, J 7Hz, HC=)] and the deuterio-amide (175) (24%) of predominantly E-geometry [δ_H 6.75 (1H, t, J 6Hz, HC=)].



(175) X = D

(176) X = $CH(OH)CH=CH_2$

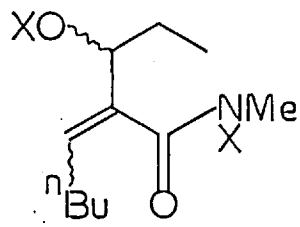
(177) X = $C(Me)_2OH$

(178) X = H

(179) X = $C(C^2H_3)_2OH$

Reaction of the amide-hydrazone (152j) with excess n-butyllithium in DME at -78° and warming to 25° gave the vinyl carbanion (155e). The addition of propanal at -78° gave the dianion (180), which on quenching with water at +25° gave the E:Z-(2:1) hydroxy-amide (181) (55%). Similarly, the dianion (180) on warming to 25° for 16 h before quenching with water, gave the hydroxy-amide (181) with identical geometry (n.m.r.). Thus the geometric stability of the dianion (180) was confirmed. On quenching with acrolein, the vinyl carbanion (155e) gave the hydroxy-amide (182) (50%). This was mostly of the E-geometry [δ 6.40 (1H, t, J 7Hz, HC=)]. Similarly, treatment of the vinyl carbanion (155e) with acrolein (-78°) and methyl iodide in sequence gave the E:Z-(2:1) methoxy-amide (183) (59%). Hydrogenation of the amide (183) gave the same product (184) as dimethylation of the dianion (180).

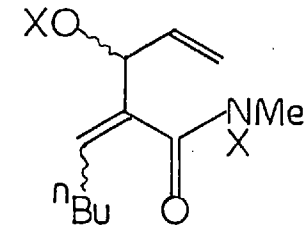
The vinyl carbanion (155e) on quenching with 4R-2,2-dimethyl-1,3-dioxolan [92a] gave the Z-amide [92] (185a) (21%) and an inseparable mixture of isomeric amides (185b). Earlier, we showed that the reaction of the vinyl carbanion



(180) X = Li

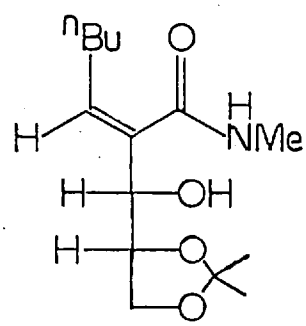
(181) X = H

(184) X = Me

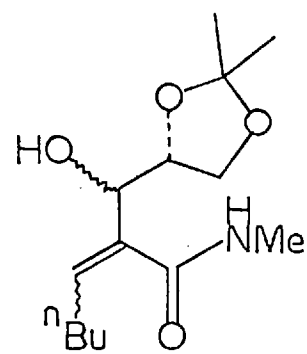


(182) X = H

(183) X = Me



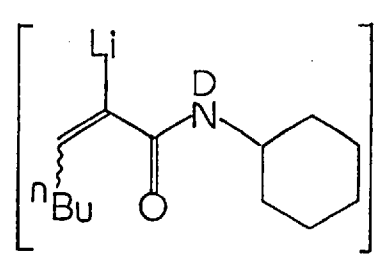
(185a)



(185b)

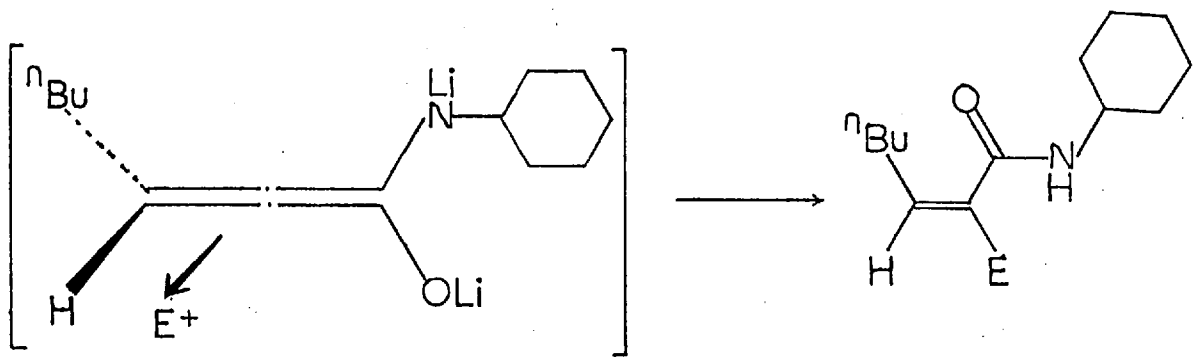
(155b) with 4R-2,2-dimethyl-1,3-dioxolan gave the 3S,4R-amide (173a) (46%) and the 3R,4R-amide (173b) (14%). Analogy[92b] was used in support of assignment of the major isomer (173a) as the Cram addition product.

Our results can tentatively be explained by assuming that the stabilised vinyl carbanions (155d or 155e) possess some allenic character. Treatment with deuterium oxide gave the more stable E-products (e.g. 175). Presumably, at -78° the vinyl anion (155d) was quenched on nitrogen or oxygen firstly, to give a more stable monoanion (186) which reacted to form the thermodynamically favoured product (175). However, reaction with the more bulky electrophile acetone, gave predominantly a Z-hydroxy-amide (177). This presumably



(186)

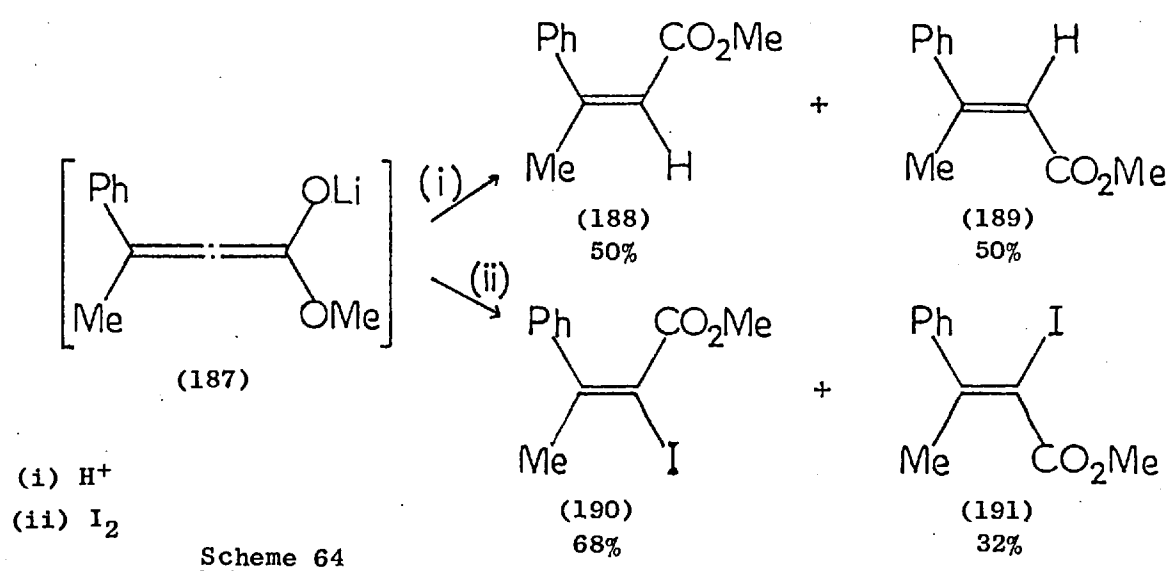
resulted from the approach of the electrophile from the least hindered face of the allenic dianion (Scheme 63). Electrophiles such as acrolein, propanal



Scheme 63

and 4R-2,2-dimethyl-1,3-dioxolan ,being intermediate in size,gave both E- and Z- products.

Klein[101] has shown that an anion (187) can be generated by treatment of methyl 3-phenylprop-2-ynoate with dimethylcopperlithium and methyllithium in sequence. The anion showed allenic character (ν_{max} 1900 cm^{-1}) and reacted with a proton (small electrophile) to yield a 50:50 mixture of the E- (189) and Z- (188) α,β-unsaturated esters. However, treatment with iodine (more bulky electrophile) gave a mainly Z-product (190) (68%) (Scheme 64).



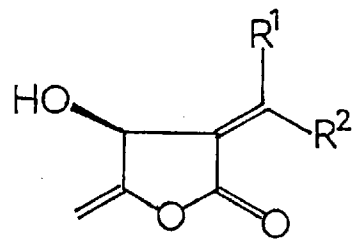
(i) H^+
(ii) I_2

Scheme 64

SECTION IX: SYNTHETIC APPLICATIONS OF STABILISED VINYL CARBANIONS

(a) Studies towards the Preparation of Obtusilactones

Obtusilactones (157) have recently been reported in the literature[79,80]. Katzenellenbogen[80] has described the α-methylenylation of the 5-methylene-



(157)

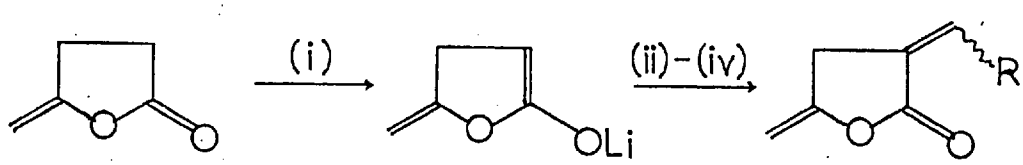
(a) $R^1 = (CH_2)_9CH=CH_2$, $R^2=H$

(b) $R^1 = H$, $R^2 = (CH_2)_9CH=CH_2$

(c) $R^1 = (CH_2)_{12}CH_3$, $R^2 = H$

(d) $R^1 = H$, $R^2 = (CH_2)_{12}CH_3$

tetrahydrofuran-2-ones as a method for the preparation of deoxyobtusilactones (Scheme 65). Reaction yields were modest (ca. 30%).

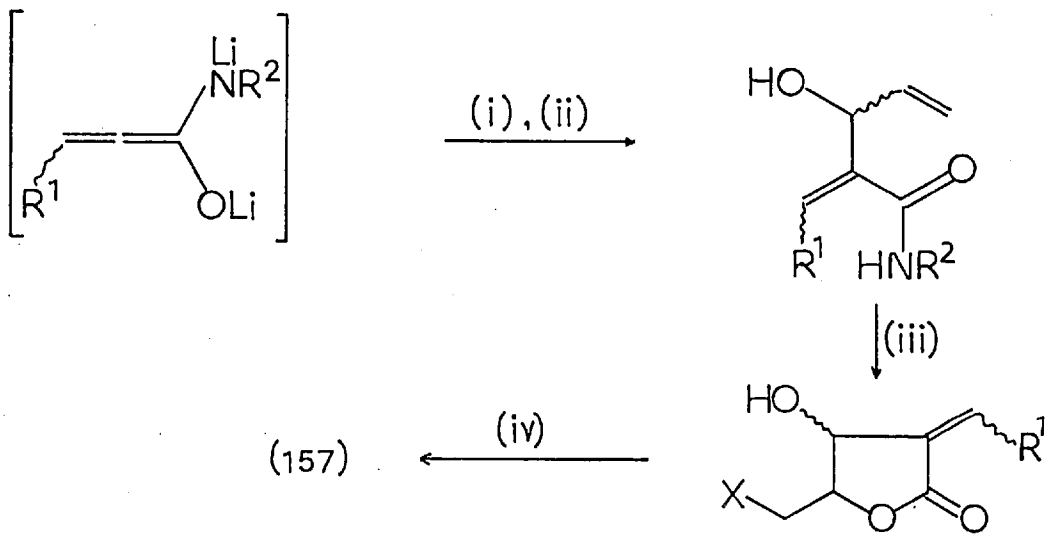


(i) $LiN^{iso}Pr_2$; (ii) RCHO; (iii) $MeSO_2Cl$; (iv) DBU

Scheme 65

We argued that the obtusilactones (157) should be available from a stabilised vinyl carbanion and acrolein (Scheme 66). Cyclisation of the amide *via* oxygen onto the double bond was anticipated with either iodine or a phenylselenium electrophile. Hydrolysis of the amide function of the adducts

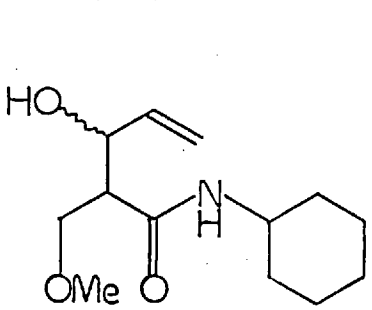
[(170), (182), (185a)] were unsuccessful. It was anticipated that acids would be ideally suited for iodolactonisation[93a]. Thus, reaction of the hydroxy-



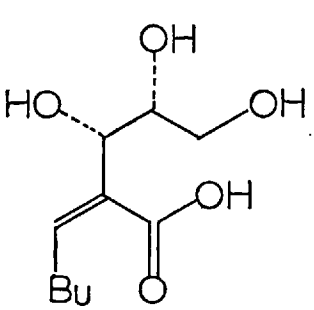
(i) CH_2=CHCHO; (ii) H_2O; (iii) PhSeCl or I_2; (iv) -(HX)

Scheme 66

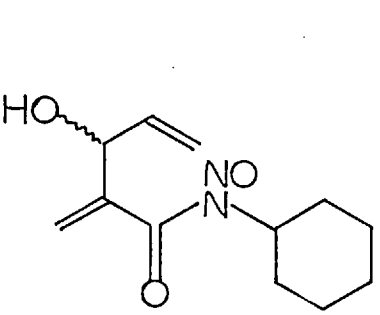
amide (170) with excess potassium hydroxide in methanol at 25° gave the 1,4-adduct (192) (72%). Similarly, treatment of the amide (182) with potassium t-butoxide and water[94] gave no isolable acidic product. Attempted acid hydrolysis of the hydroxy-amide (185a) and *in situ* cyclisation of the intermediate hydroxy-acid (193) was unsuccessful. Attempted N-nitrosations of the amide (170) were unsuccessful. It was anticipated that the product N-nitroso-amide (194) would readily saponify.



(192)



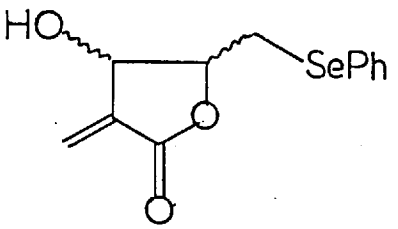
(193)



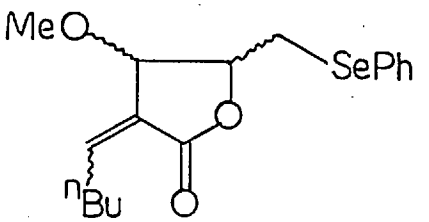
(194)

Reaction of the amides (170) or (183) with phenylselenyl chloride[93b], N-phenylselenylphthalalide [93c] or phenylselenyl hexafluorophosphate[95] (196),

under anhydrous conditions, gave on aqueous work up, neither lactone (195) nor (197) respectively.



(195)

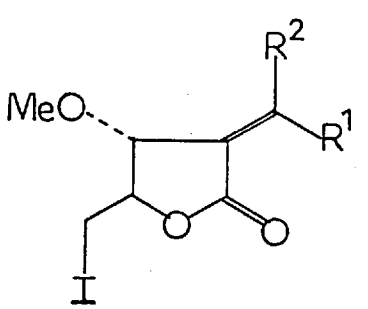


(197)

$PhSePF_6$

(196)

Reaction of the amide (170) with iodine under anhydrous conditions gave a variety of non-lactonic products. More significantly, reaction of the amide (182) with iodine in wet THF gave an unidentified product, ν_{max} 1705 s, presumably arising from amide cyclisation *via* nitrogen. Fortutiously, reaction of the *E*:*Z*-(2:1)-amide (183) with iodine in wet THF[97] gave the *E*-iodolactone (198) (22%) and the *Z*-iodolactone (199) (10%) [yields from the hydrazone (152j)]. Clearly by n.m.r. spectroscopy, both lactones (198 and 199) were of the trans configuration .

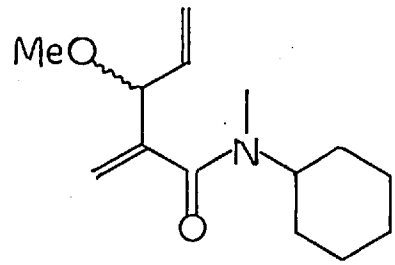


(198) $R^1 = H$, $R^2 = {}^nC_4H_9$

(199) $R^1 = {}^nC_4H_9$, $R^2 = H$

A similar reaction performed in anhydrous THF gave, on aqueous work up no iodolactones (198), (199). Reaction of the *N*-cyclohexyl - *N*-methyl-amide (200) with iodine in wet THF gave only a poor yield (<6%) of an uncharacteri-

sed iodolactone.

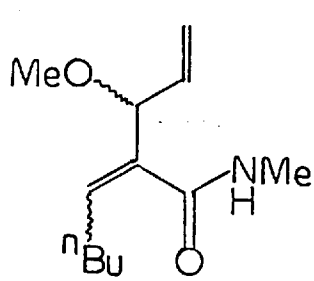


(200)

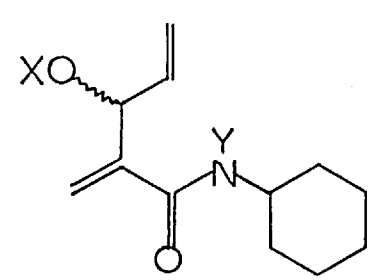
These results suggest the following criteria for the intramolecular iodolactonisation of α,β-unsaturated amides: (1) tertiary amides must be used to achieve cyclisation via oxygen; (2) N,N-dimethyl-amides are best suited for cyclisation, presumably due to steric interaction with the adjacent alkylidene function; (3) prolonged aqueous conditions are necessary, presumably to drive the reaction equilibria over to the iodolactone.

Attempted conversions of the iodolactones (198) or (199) to the methoxy-species (207a) were unsuccessful. Reaction with silver fluoride[96] in the dark for 10d gave only recovered starting material. Treatment with DBU resulted in decomposition, involving the loss of the methoxy function. Attempted SN_2 displacement of the iodine atom of the iodolactones (198) or (199) with the phenylseleno anion gave an uncharacterised product, derived from the loss of the methoxy function.

Reaction of the hydroxy-amide (182) with potassium t-butoxide and methyl-iodide in sequence gave the methoxy-amide (201) (55%). Clearly the alcohol



(201)

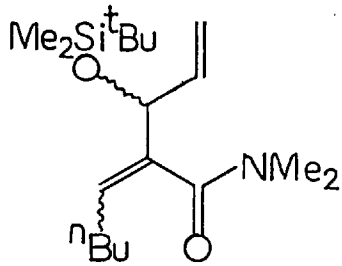


(202) X = Y = Li

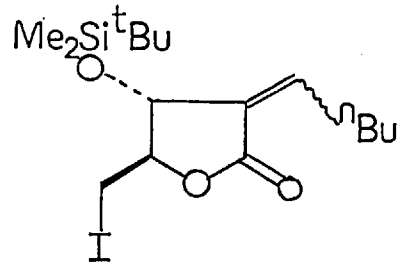
(203) X = Si^{t}BuMe$_2$, Y = H

(204) X = Si^{t}BuMe$_2$, Y = Me

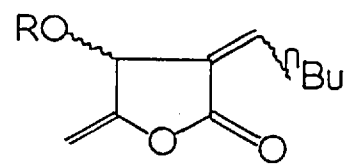
could be selectively functionalised. Indeed, reaction of the dianion (202) with t-butylchlorodimethylsilane gave the O-silyl-amide (203) which was smoothly converted with sodium hydride and methyl iodide to the O-silyl tertiary amide (204) [80% from the amide (169)]. An identical sequence applied to the hydroxy-amide (182) gave the O-silyl-amide (205) [77% from the amide (182)]. Cyclisation with iodine in wet THF gave the E,Z-iodolactones (206) (70%). Disappointingly treatment of the iodolactone (206) with silver fluoride or DBU gave no



(205)



(206)



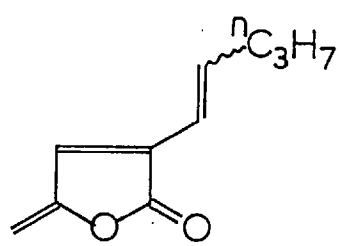
(207)

(a) R = Me

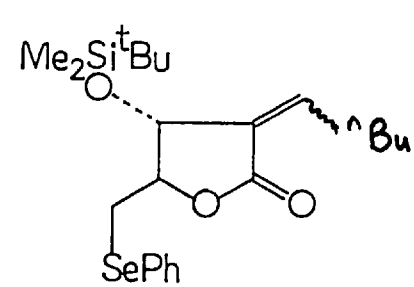
(b) R = Si ^{t}BuMe$_2$

desired dimethylene lactone (207b). With DBU an unstable product, possibly (208) derived from the loss of the silyloxy function was obtained. This product (208) possessed an enol lactone function [ν_{max} 1790 s cm^{-1}, δ 4.80 (1H, d, J 2.5 Hz) and 5.10 (1H, d, J 2.5 Hz)] and rapidly polymerised at 25°.

Attempted cyclisation of the amide (205) with phenylselenyl chloride in wet THF[98] gave a low yield (<9%) of a seleniferous lactone, presumably (209).



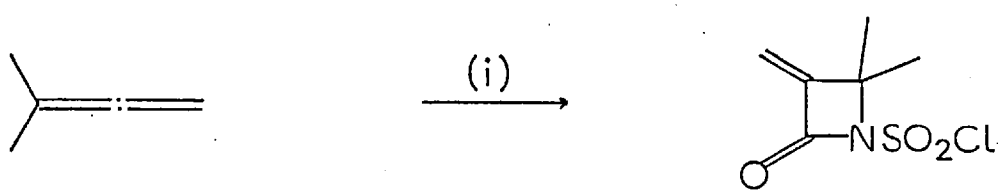
(208)



(209)

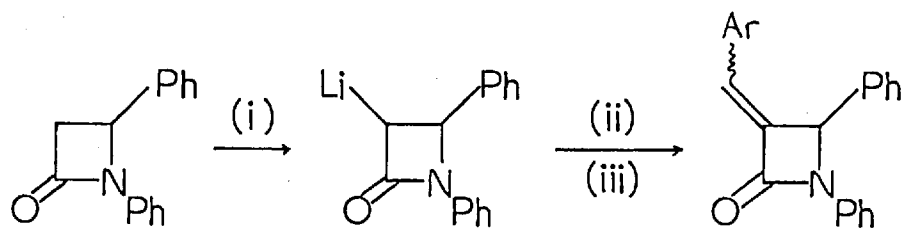
(b) The Preparation of α-Methylene β-Lactams

α-Methylene β-lactams have been reported in the literature[99]. Standard methods of preparation involve the reaction of chlorosulphonyl isocyanate (CSI) with allenes[99b,c] (Scheme 67), the α-methylenylation of the parent azetidinone[99d] (Scheme 68) or by phase-transfer catalysed cyclisation of 3-bromo-2-(bromomethyl)propionamides[99a] (Scheme 69). We argued that methylene



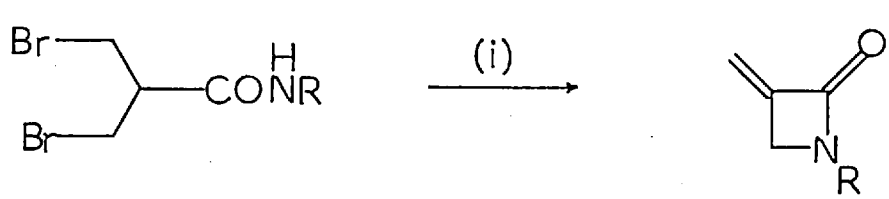
(i) CSI

Scheme 67



(i) $LiN^{iso}Pr_2$/THF; (ii) ArCHO; (iii) $-H_2O$

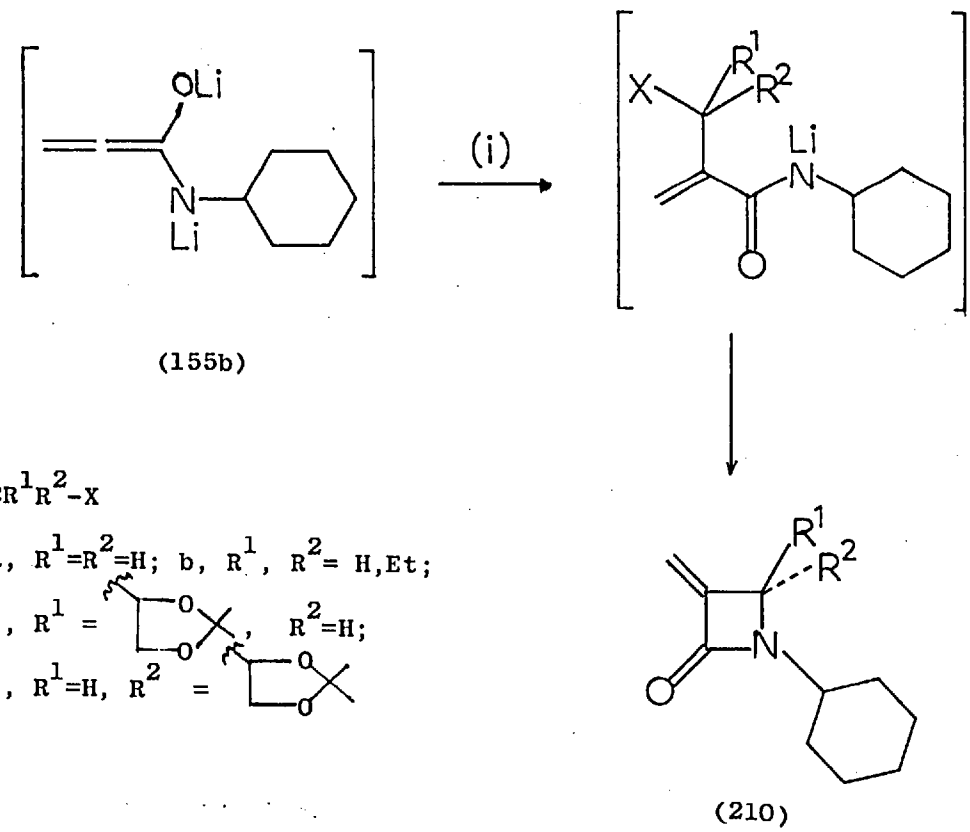
Scheme 68



(i) 40% NaOH-CCl_4, $C_5H_{11}NEt_3Br$, 25°, 18h.

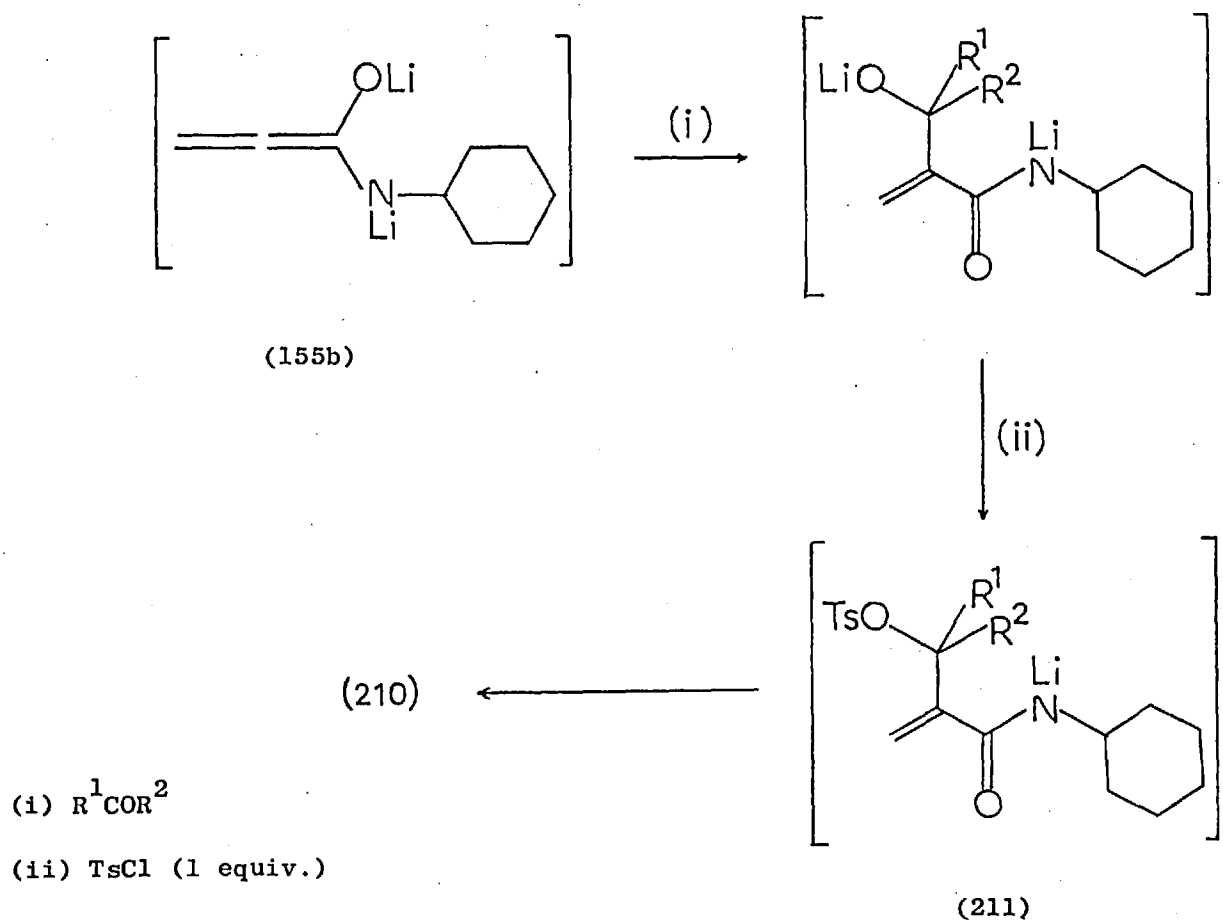
Scheme 69

β-lactams (210) could be prepared from a stabilised vinyl carbanion and a dielectrophile (Scheme 70). However, reaction of the vinyl carbanion (155b) with either di-iodomethane or benzal chloride gave no methylene β-lactam (210a).



Scheme 70

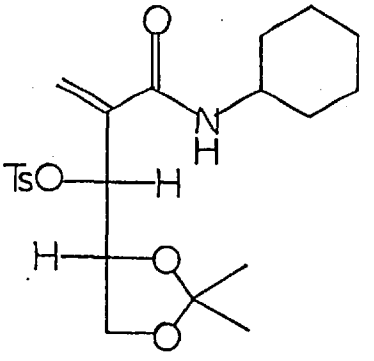
Having already shown that the dianion (202) reacted exclusively on oxygen with t-butylchlorodimethylsilane, we argued that specific O-toluene-4-sulphonylation could also occur. The oxygen function would now be a good leaving group and nitrogen attack by the amide anion, would give the methylene β-lactams (210) (Scheme 71). Indeed, reaction of the hydroxy-



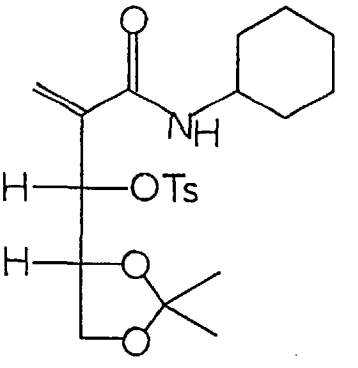
Scheme 71

amides (171), (172) with two equivalents of n-butyllithium and one equivalent of toluene-4-sulphonyl chloride in sequence gave the methylene β-lactams (210a) (60%) and (210b)(68%) respectively. Similarly, the hydroxy-amide (173a) gave the methylene β-lactam (210c)(65%), presumably with the natural configuration at C 4. However, an identical sequence performed upon the hydroxy-amide (173b) gave mainly the amide tosylate (212) [δ 5.20 (1H, d, J 6Hz, 3-CH)]. Cyclisation was achieved by reaction with excess sodium hydride, yielding the

methylene β-lactam (210d) (19%). The methylene-β-lactams (210c) and (210d) gave distinctly different n.m.r. spectra. Reaction of the hydroxy-amide (173a) with n-butyllithium, toluene-4-sulphonyl chloride (25° for 10 min) and water in sequence, gave the amide-tosylate (213) (43%), [δ 5.25 (1H, d, J 7Hz, 3-CH)].



(212)



(213)

Attempts to 1,4-add benzyl alcohol or benzylamine to the methylene β-lactam (210a) were unsuccessful.

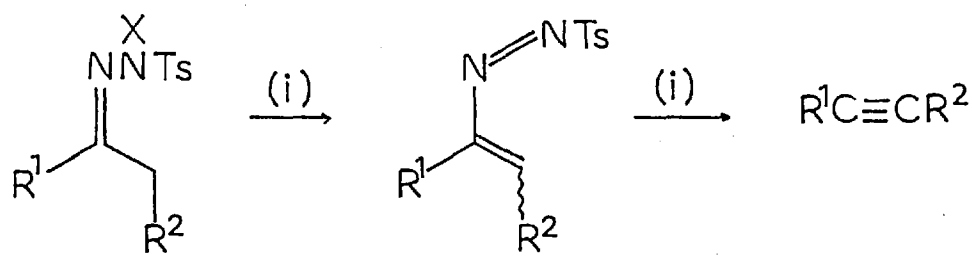
The application of this methodology to the preparation of methylene β-lactams is currently active at Imperial College[100].

SECTION X: SOME OTHER APPLICATIONS OF THE SHAPIRO REACTION

(a) The Preparation of Acetylenes

Acetylenes should be available from a sulphonylhydrazone providing the precursor molecule possesses two good leaving groups (Scheme 72). We found

that acetophenone di-(toluene-4-sulphonyl)hydrazone(214) reacted with n-butyllithium to produce an alkene (216) arising from nucleophilic addition to the

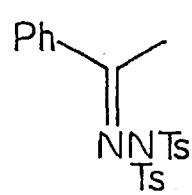


(215)

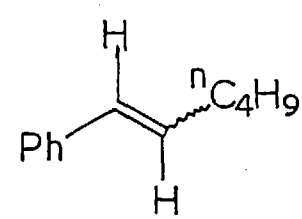
(i) Base

Scheme 72

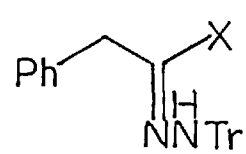
intermediate azaene (215). This reaction has literature precedent[103]. Similarly, reaction of deoxybenzoin toluene-4-sulphonylhydrazone with N-bromosuccinimide and triethylamine in sequence gave no desired acetylene.



(214)



(216)

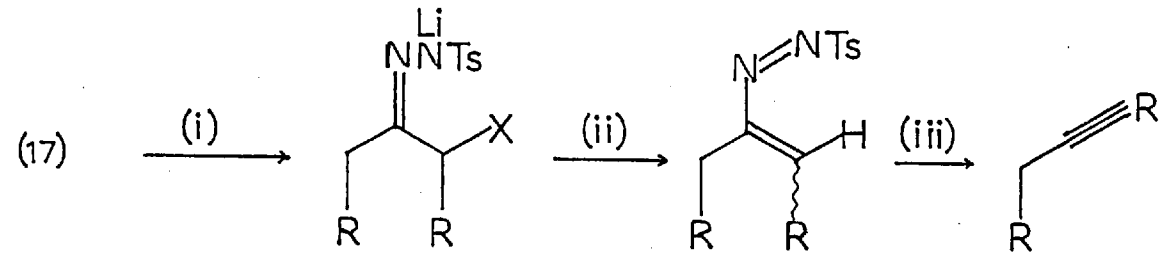


(217) X = Ph

(218) X = CH_2Ph

Acetylenes have been prepared from the reaction of α-haloketones with toluene-4-sulphonylhydrazine[104]. The mechanism probably involved elimination of halogen halide followed by fragmentation, and hence acetylenes

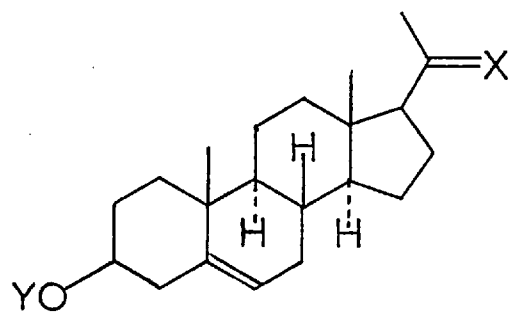
should be available from the dianion (17) (Scheme 73). Typically, treatment



(i) X-X; (ii) -LiX; (iii) -HTs

Scheme 73

of the hydrazone (217) with n-butyllithium (-65°), iodine (or bromine) and warming in sequence gave diphenylacetylene (18-19%) in a heterogeneous reaction. Similarly, the hydrazone (218) gave 1,3-diphenylpropyne (8%), also in a heterogeneous reaction. The pregnenolone trisylhydrazone (219c), however, gave no detectable acetylene derivative.

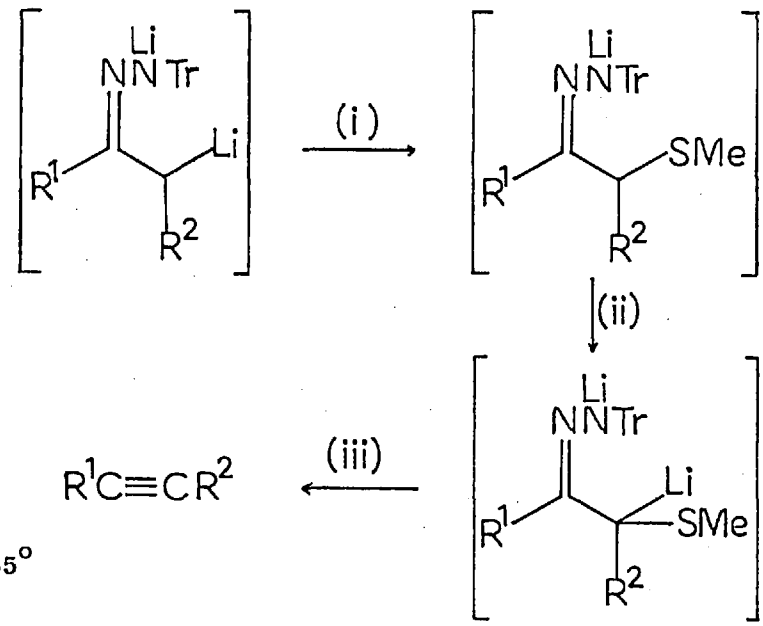


(219) (a) Y = H, X = O

(b) Y = ^{t}BuMe$_2$Si; X = O

(c) Y = ^{t}BuMe$_2$Si; X = NNHTr

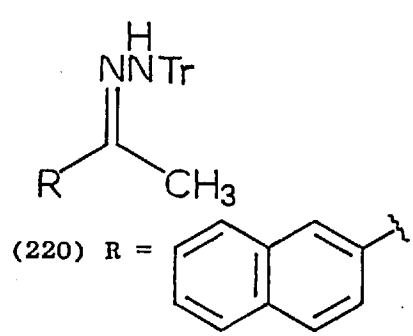
A report by Kano[32,40] drew our attention to the use of α-(methylthio)-ketone toluene-4-sulphonylhydrazones for the generation of acetylenes. We found that the trisylhydrazone dianions could be quenched at low temperature with dimethyl disulphide. Retreatment with alkyllithium and warming to 25° gave acetylenes (Scheme 74). For example the hydrazones (220), (72) and (221) gave the acetylenes (222)(74%), (223) (<59%) and (224) (47%)[105].



(i) MeSSMe, -65°
(ii) ^{n}BuLi
(iii) 25°

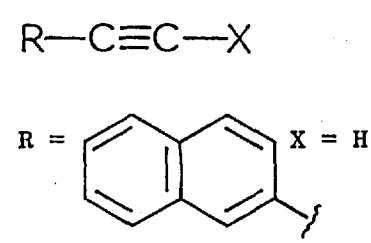
Scheme 74

However, the hydrazone (218) gave no 1,3-diphenylacetylene under this sequence. The mechanism probably involved the trans-elimination of lithium thiomethoxide from the vinyl carbanion (227). Such geometry was probably



(220) R =

(221) R = Ph

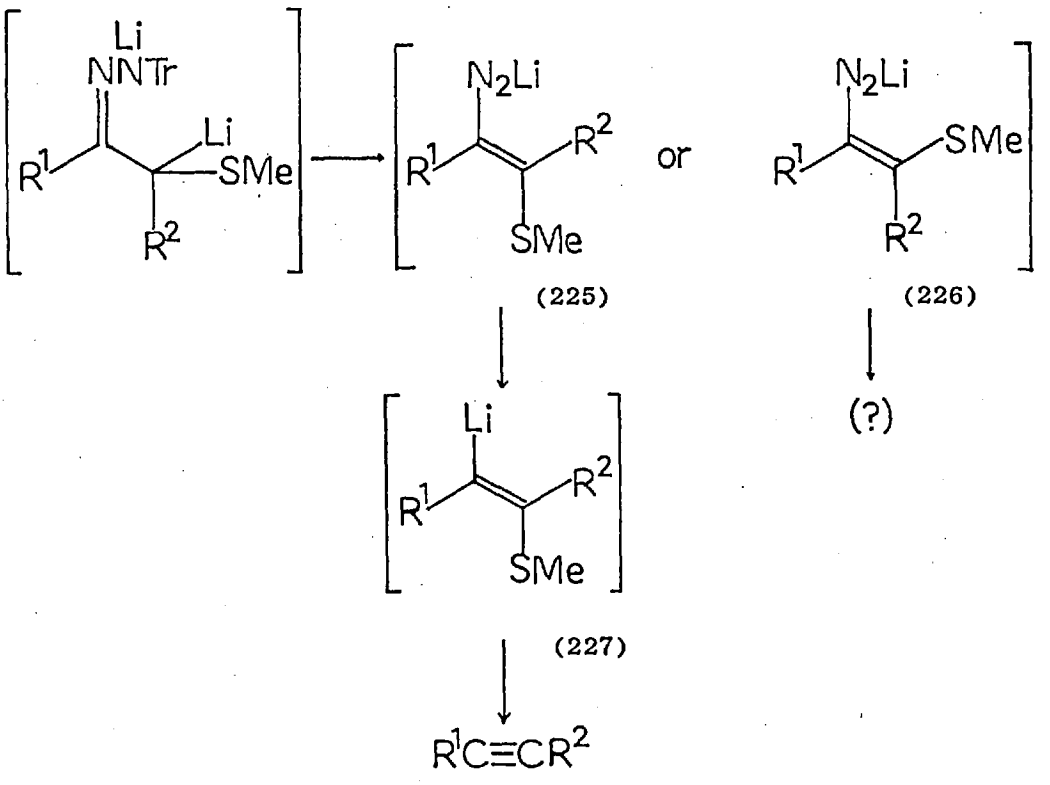


(222) R = X = H

(223) R = $^{n}C_9H_{19}$, X = H

(224) R = Ph, X = $C(CH_3)_2OH$

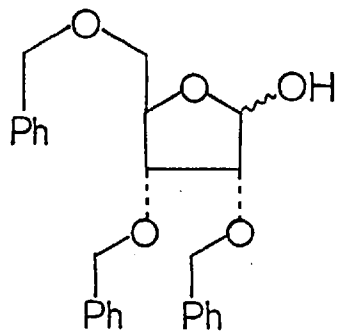
controlled by fragmentation to the vinyl diimide anion (225) occurring through the lowest energy transition state (Scheme 75).



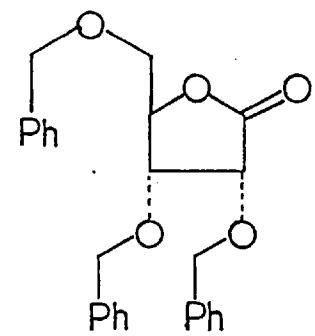
Scheme 75

(b) Some unexpected results observed during Sulphonylhydrazone forming reactions

In the preparation of 3-methylenetetrahydropyran-2-one derivatives (107), our methodology required the use of a γ-hydroxy-ketone trisylhydrazone. However, the reaction of 5-hydroxytridecan-2-one with 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) under neutral or acidic conditions gave an unstable derivative (106a) (t.l.c. analysis) which decomposed rapidly at 25° to a variety of uncharacterised products. We believe that the instability of the hydrazone (106a) arose from an intramolecular attack of the hydroxy function at the imine carbon atom. Indeed, reaction of 2,3,5-tri-O-benzyl-D-ribofuranose[126] (228) with 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) gave the ribofuranolactone derivative (229)[113] (59%).

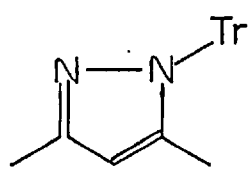


(228)

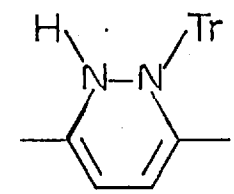


(229)

Reaction of pentan-2,4 -dione and hexan-2,5-dione with 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) gave the heterocycles (230) (63%) and (231) (75%) respectively.



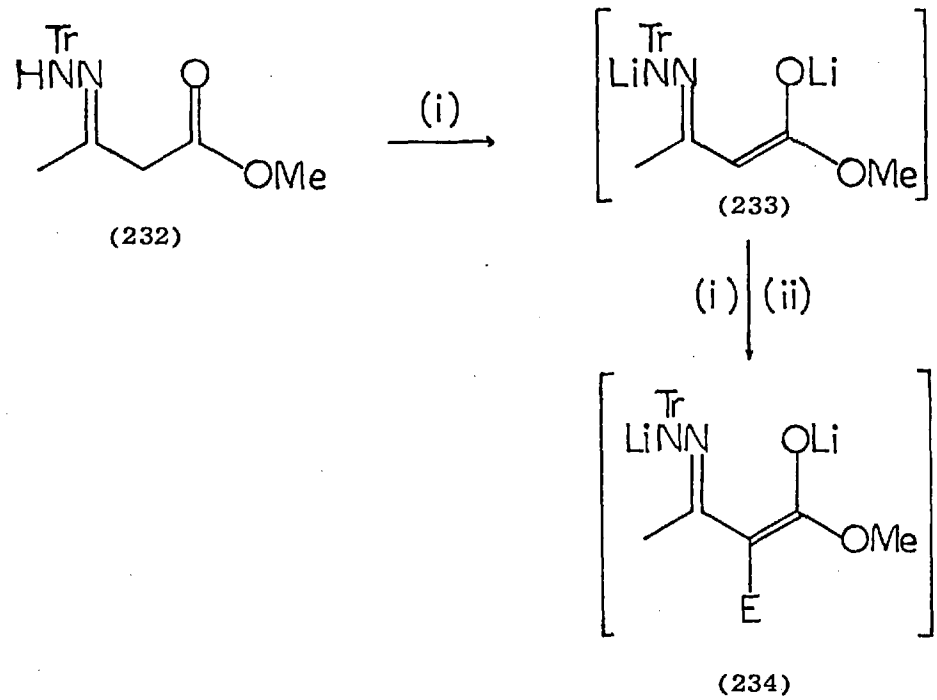
(230)



(231)

(c) Reactions of Methyl Acetoacetate 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone

Methyl acetoacetate 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (232) should react with base to form a stabilised dianion (233). Electrophilic quenching and retreatment with base *in situ* could provide a regiospecific second dianion (234) (Scheme 76). n-Butyllithium was found to be too reactive, adding to the ester function. However, treatment with lithium di-iso-propylamide at -65° followed by attempted quenching of the dianion (233) with acetone gave the starting hydrazone (232) (78%). Presumably, the dianion (233) was too unreactive. Recently, Fuchs[25] has published his own results in this field of research (Scheme 44).



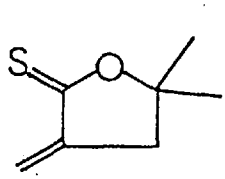
(232) (233) (234)

(i) Base (LiX); (ii) E^+

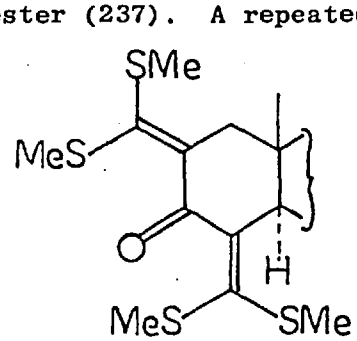
Scheme 76

(d) Reaction of the Vinyl Carbanions with Carbon Disulphide

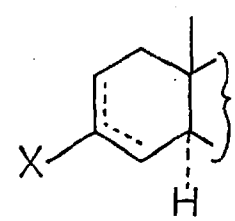
3-Methylenetetrahydrofuran-2-thione derivatives should be available via the Shapiro reaction if the alkoxy-vinyl dianion (61) was quenched with carbon disulphide. However, reaction of the hydroxy-hydrazone (85) with n-butyllithium, carbon disulphide and acid in sequence gave no detectable thiolactone (235). Similarly, reaction of the hydrazone (65) with sec-butyllithium (2.5 equiv.), carbon disulphide (0^o) and methyl iodide in sequence gave 5α-cholest-2(3)-ene (67) (74%), the ketone (236) (15%) and no isolable thio-ester (237). A repeated reaction using sec-butyllithium



(235)



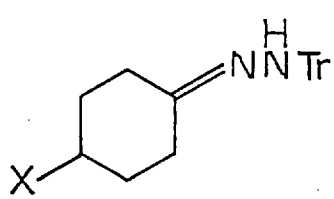
(236)

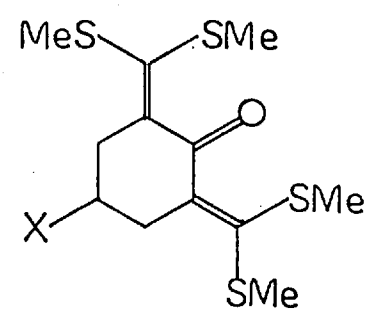


(237) X = CS.SMe
(238) X = S.CS.SMe

(2.9 equiv.) gave the olefin (67) (21%), the ketone (236) (2%) and the tri-thio-steroid (238) (19%). Similarly, reaction with sec-butyllithium (2.5 equiv.) followed by warming to -16° and quenching with carbon disulphide gave the olefin (67) (48%), the ketone (236) (8%) and the tri-thio-steroid (238) (25%). Presumably the product (238) arose from attack of the vinyl-lithium (66) on the sulphur atom of carbon disulphide. Reductive desulphurisation[106] followed by hydrogenation ($PtO_2/H_2/25°$) gave 5α-cholestane (83%).

Reaction of cyclohexanone trisylhydrazone (239) with n-butyllithium, carbon disulphide and methyl iodide in sequence gave a low yield (<6%) of the corresponding ketone (240)[114]. Similarly, reaction of the hydrazone (241) with n-butyllithium (-78° to -16°), carbon disulphide and methyl iodide gave the ketone[127] (242) (20%).





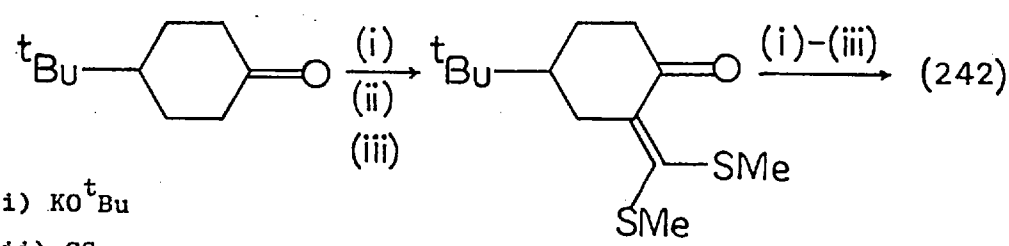
(239) X = H

(241) X = ^tBu

(240) X = H

(242) X = ^tBu

These ketonic products (236), (240), (242) are known in the literature[107, 114, 127]. Indeed, a modification of Shahak's[107] procedure gave the ketone (242) (34%) from 4-t-butylcyclohexanone (Scheme 77).



(i) KO^tBu

(ii) CS_2

(iii) MeI

Scheme 77

EXPERIMENTAL

Reactions were performed under a dry argon atmosphere at room temperature unless otherwise stated. Temperatures were measured in degree Celcius (^{o}C); low reaction temperatures were recorded as bath temperatures. n-Butyllithium (in hexane), sec-butyllithium (in cyclohexane), tert-butyllithium (in pentane) or methyllithium (in diethyl ether) were added dropwise during 5 to 10 min. Reaction times are recorded in seconds (s), minutes (min), hours (h) or days (d). Reactions were studied by t.l.c., i.r., or n.m.r. analysis prior to work up. Ultra-violet inactive compounds on t.l.c. were visualised either with iodine or by concentrated sulphuric acid charring. Steroids were visualised on t.l.c. by PAN's reagent [p-methoxybenzaldehyde:sulphuric acid:methanol (1:1:18)] spray followed by heating to 80^{o}. Carbonyl compounds or their equivalents, were visualised on t.l.c. with Brady's reagent [DNPH:sulphuric acid:methanol (1:1:18)]. Reaction mixtures were evaporated at 25^{o} or below on a Büchi Rotavapor R110; involatile compounds were further evaporated (< 2 mmHg). Crude reaction mixtures were worked up by the following methods:

(A) evaporated, extracted with solvent and brine, the organic phase separated, re-extracted with brine, dried, filtered and evaporated;

(B) evaporated, extracted with solvent and water, the aqueous phase separated, re-extracted with solvent, the organic layers combined, dried, filtered and evaporated;

(C) evaporated, extracted with solvent and water, the aqueous phase separated, re-extracted with solvent, acidified, saturated with sodium chloride or sodium sulphate, re-extracted with solvent, the final organic extracts combined, dried, filtered and evaporated.

Organic extracts were dried over sodium sulphate. Both t.l.c. and p.l.c. were carried out on Merck Kieselgel GF_{254}, developing solvents are given

in parentheses. Eluted products are listed in order of increasing polarity on t.l.c. M.p.s. were determined on a Kofler hot stage. Optical rotations were recorded on a Perkin-Elmer 141 polarimeter. I.r. spectra were recorded as nujol mulls (solids) or films (oils) on a Perkin-Elmer 257 instrument unless otherwise stated. Only broad (br), medium (m) or strong (s) bands were reported. U.v. spectra were recorded on a Unicam SP 800A spectrophotometer. N.m.r. spectra were recorded as deuteriochloroform solutions on a Varian T60, Perkin-Elmer R32, Varian XL 100 or Brucker WM 250 instruments using tetramethylsilane as internal reference unless otherwise stated. Multiplicities were recorded as br broad peak, s singlet, d doublet t triplet, q quartet and m multiplet. Mass spectra were recorded by the Mass Spectral Laboratory, Imperial College; only molecular ions, fragments from molecular ions, and major peaks were reported. Deuterium incorporations were judged from the heights of the appropriate ion peaks of a conventional mass spectrum. Microanalyses were recorded by the Microanalytical Laboratory, Imperial College. Solids were recrystallised and oils purified by p.l.c. prior to microanalysis.

All starting materials and reagents[60] were purified (t.l.c., n.m.r., i.r.) and dried unless otherwise stated. Common solvents, dichloromethane, diethyl ether, and light petroleum (b.p. 40-60°) were redistilled prior to use. For organometallic reactions the following solvent drying techniques were employed: TMEDA was dried by refluxing with potassium and benzophenone and distillation of the blue solution onto fresh sodium wire; DME was dried by refluxing with sodium wire for 2 h and distillation from potassium onto fresh sodium wire; diethyl ether and dimethyl ether were dried by refluxing with potassium and 18-crown-6 and distillation of the blue solution. Reagents were purified according to Perrin[62] unless otherwise stated. Acrolein was freshly distilled from anhydrous calcium sulphate

prior to use. 4R-2,2-Dimethyl-4-formyl-1,3-dioxolan was freshly distilled prior to use. Carbon dioxide gas and argon were purified by passage through chromium (II) chloride solution, concentrated sulphuric acid and calcium chloride (s) in sequence. n-Butanal and propanal were distilled from anhydrous magnesium sulphate. Di-iso-propylamine and DMF were refluxed with 4 Å molecular sieves and distilled onto 4 Å molecular sieves. DBU was distilled from molten sodium onto 4 Å molecular sieves. Alkyl iodides were dried with 4 Å molecular sieves in the dark. Acetone and butanone were dried by distillation from phosphorus pentoxide. Methyl chloroformate was purified by repeated freeze-thawing and distillation.

Photolyses were carried out using Pyrex apparatus with an externally cooled 125-W high pressure mercury arc lamp; a 10 mm 0.1 M solution of naphthalene in petroleum (b.p. 60-80°) cut out radiation below 316 nm[72].

ABBREVIATIONS

DBU - 1,5-Diazabicyclo[5.4.0]undec-5-ene

DME - 1,2-Dimethoxyethane

DMF - N,N-Dimethylformamide

DMM - Dimethoxymethane

DNPH- 2,4-Dinitrophenylhydrazine

MME - Dimethyl ether

Preparation of Acetophenone Toluene-4-sulphonylhydrazone (245)

Acetophenone (5.00 g) and toluene-4-sulphonylhydrazine (7.70 g) were dissolved in methanol (20 ml). Concentrated hydrochloric acid (3 drops) was added, the mixture refluxed for 1 h, cooled to 25° and evaporated to half-volume. Filtration gave the sulphonylhydrazone[21] (245) (11.09 g, 93%) m.p. 147-8.5°, ν_{max} 3215 m (N-H), 1400 m, 1340 m ($-SO_2-N<$), 1315 m, 1300 m, 1160 s($-SO_2-N<$), 752 m, 694 m, and 670 m cm^{-1}, δ 2.16 (3H, s, MeC=N), 2.36 (3H, s, aryl-Me), and 7.25-8.50 (10 H, m, aryl-H, NH), m/e 288 ($M^{+\cdot}$) (Found: C, 62.51; H, 5.58; N, 9.77. Calc. for $C_{15}H_{16}N_2O_2S$: C, 62.54; H, 5.58; N, 9.70%).

Preparation of *5-Hydroxyhexan-2-one Toluene-4-sulphonylhydrazone* (63)

5-Hydroxyhexan-2-one[59] (2.00 g) and toluene-4-sulphonylhydrazine (3.13 g) were dissolved in THF (20 ml) and the solution stirred overnight. Evaporation and recrystallisation from chloroform at 0° gave the *hydroxysulphonylhydrazone* (63) (3.82 g, 80%) m.p. 128-9.5°, ν_{max} 3350 m (O-H, N-H), 3040 m, 1600 m (C=C), 1415, 1340 m ($-SO_2-N<$), 1310 m (O-H), 1227 m, 1187 m, 1167 s ($-SO_2-N<$), 1072 m, 1040 m (C-O), 925 m, 905 m, 875 m, 810 m (aryl-H), 750 m, 745 s, and 660 m cm^{-1}, δ (d_6-DMSO) 0.90 (3H, d, J 6 Hz, 6-CH_3), 1.10-1.60 (2H, m, 4-CH_2), 1.70 (3H, s, 1-CH_3), 2.10 (2H, t, J 8 Hz, 3-CH_2), 2.30 (3H, s, aryl-Me), 3.40-4.00 (2H, br, 5-CH, OH), 7.30-7.90 (4H, m, aryl-H), 9.60 (1H, br, NH), m/e 285 ($M^{+\cdot}$ + H), 284 ($M^{+\cdot}$, weak), 267, 139, 111 (base), 99, and 91 (Found: C, 55.02; H, 7.13; N, 9.95; S, 11.59; ($M^{+\cdot}$ + H), 285.1264. $C_{13}H_{20}N_2O_3S$ requires C, 54.91; H, 7.09; N, 9.85; S, 11.28%, ($M^{+\cdot}$ + H), 285.1273).

Preparation of *4-Hydroxy-4-methylpentan-2-one Toluene-4-sulphonylhydrazone* (64)

4-Hydroxy-4-methylpentan-2-one (1.50 g) was added dropwise to a

solution of toluene-4-sulphonylhydrazine (2.0 g) in methanol (3 ml) and water (2 ml) at 60°. The solution was cooled to 0° overnight and the solid filtered off. Three recrystallisations from ethanol and water gave the *hydroxy-sulphonylhydrazone* (64) (2.74 g, 90%) m.p. 133-4° (lit.,[21] 134.0-5.5°), ν_{max} 3425 s (O-H), 3100 s(N-H), 1600 m (C=C), 1493 m, 1420 s, 1410 s (O-H), 1340 s ($-SO_2-N<$), 1305 m, 1290 m, 1220 s, 1165 and 1150 s ($-SO_2-N<$), 1120 m (C-O), 1093 m, 1053 s, 1018 m, 960 m, 918 s, 908 s, 841 s, 821 s (aryl-H), 772 m, 705 s, and 670 s cm^{-1}, δ (d_6-DMSO) 0.92 (6H, s, 4-Me), 1.88 and 1.92 (3H, 2 s, 1-CH_3), 2.18 (2H, s, 3-CH_2), 2.36 (3H, s, aryl-Me), 4.26 (1H, s, OH), 7.22-7.90 (4H, m, aryl-H), and 10.00 (1H, s, NH), m/e 285 ($M^{+\cdot}$ + H), 284, ($M^{+\cdot}$, weak), 269 ($M^{+\cdot}$ - Me), 226 (base), 157, 91, and 59 (Found: C, 54.78; H, 7.09; N, 9.81, S, 11.40. $C_{13}H_{20}N_2O_3S$ requires C, 54.91; H, 7.09; N, 9.85; S, 11.28%).

General Procedures for the Preparation of Ketone 2,4,6-Tri-iso-propylbenzenesulphonylhydrazones

The ketone and 2,4,6-tri-iso-propylbenzenesulphonylhydrazine (108b)[70] (0.95-1.05 equiv.) were dissolved in solvent (diethyl ether, dichloromethane, methanol). Acid [(A) concentrated hydrochloric acid (2 drops), (B) Amberlite IR-120 (H) resin, or (C) none] was added and the mixture stirred at 25° [or (D) 40°] until complete reaction had occurred. Evaporation gave the crude ketone 2,4,6-tri-iso-propylbenzenesulphonylhydrazone.

Acetophenone 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (221) [Method (A)] (93%) was recrystallised from methanol and water, m.p. 140, 158-60°, ν_{max} 3245 m (N-H), 1602 m (C=C), 1332 m ($-SO_2-N<$), 1168 s and 1156 m ($-SO_2-N<$), 1058 m, 1038 m, 912 m, 760 m, 750 m (Ph-), and 663 m cm^{-1}, δ 1.27 (18H, overlapping d, J 7 Hz, $CHMe_2$), 2.18 (3H, s, MeC=N), 2.90 (1H, overlapping septets, J 7 Hz, p-$CHMe_2$), 4.23 (2H, overlapping septets,

J 7 Hz, o-CHMe$_2$), 7.05-7.75 (6H, m, Ph-H, NH), and 7.17 (2H, s, aryl-H), m/e 400 ($M^{+\cdot}$), 235, 189, 134, 133, 120, 104, and 91 (base) (Found: C, 69.16; H, 8.19; N, 7.05. $C_{23}H_{32}N_2O_2S$ requires C, 68.96; H, 8.05; N, 6.99%).

Acetone 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (82) [Method (C)] (92%) was recrystallised from methanol and water, m.p. 136-8° (lit.,[30] 130-2°), ν_{max} 3250 s (N-H), 1600 m (C=C), 1570 m, 1333 s (-SO_2-N<), 1305 m, 1270 m, 1175 and 1160 s (-SO_2-N<), 1085 m, 1080 m, 1065 m, 945 m, 910 m, 887 m, 815 m, and 670 s cm^{-1}, δ 1.26 (18 H, 2 overlapping d, J 7Hz, CHMe$_2$), 1.80 (3H, s, MeC=N), 1.94 (3H, s, MeC=N), 2.90 (1H, overlapping septets, J 7Hz, p-CHMe$_2$), 4.27 (2H, overlapping septets, J 7Hz, o-CHMe$_2$), 7.05-7.60 (1H, br, NH), and 7.18 (2H, s, aryl-H), m/e 338 ($M^{+\cdot}$), 267 (108 d, base), 203, 139, 121, 91, 71, and 58 (Found: C, 63.82; H, 8.97; N, 8.24. Calc. for $C_{18}H_{30}N_2O_2S$: C, 63.87; H, 8.93; N, 8.27%).

2-Acetylnaphthalene 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (220) [Method (A)] (66%) was recrystallised from ethanol and water, m.p. 151-2°, ν_{max} 3240 s (N-H), 1602 m (C=C), 1428 m, 1332 s (-SO_2-N<), 1308 m, 1164 and 1153 s (-SO_2-N<), 1075 m, 912 m, 860 m, 705 m, and 658 m cm^{-1}, δ 1.27 (18 H, overlapping d, J 7Hz, CHMe$_2$), 2.28 (3H, s, MeC=N), 2.90 (1H, overlapping septets, J 7Hz, p-CHMe$_2$), 4.43 (2H, overlapping septets, J 7Hz, o-CHMe$_2$), 6.80-8.70 (8H, br, naphthyl-H, NH), and 7.17 (2H, s, aryl-H), m/e 450 ($M^{+\cdot}$), 251, 233, 189 (base), 161, 128, 105, and 91 (Found: C, 71.68; H, 7.65; N, 6.25. $C_{27}H_{34}N_2O_2S$ requires C, 71.96; H, 7.60; N, 6.22%).

Butanone 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (86) [Method (C)] (93%) was recrystallised from ethanol and water, m.p. 115-21°, ν_{max} 3250 s (N-H), 1605 m (C=C), 1325 s (-SO_2-N<), 1300 m, 1170 and 1155 s

($-SO_2-N<$), and 660 s cm^{-1}, δ 0.95 (3H, 2 overlapping t, J 7Hz, $MeCH_2$), 1.30 (18H, 4 overlapping d, J 7Hz, $CHMe_2$), 1.77 and 1.82 (3H, 2 s, MeC=N), 2.10 (2H, 2 overlapping q, J 7Hz, $MeCH_2$), 2.83 (1H, 2 overlapping septets, J 7Hz, p-$CHMe_2$), 4.24 (2H, 2 overlapping septets, J 7Hz, o-$CHMe_2$), 7.10 (2H, s, aryl-H), 7.50-8.40 (1H, br, NH), m/e 352 ($M^{+\cdot}$), 267, 203, 86, 85, 72, and 56 (base) (Found: C, 64.68; H, 9.15; N, 7.94. $C_{19}H_{32}N_2O_2S$ requires C, 64.73; H, 9.15; N, 7.95%).

4-t-Butylcyclohexanone 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (241) [Method (B)] (88%) was recrystallised from methanol and water, m.p. 130-2°, ν_{max} 3170 s, (N-H), 1645 m (C=N), 1600 m (C=C), 1565 m, 1318 s ($-SO_2-N<$), 1310 s, 1305 s, 1285 m, 1265 m, 1260 m, 1161 and 1152 s ($-SO_2-N<$), 1133 m, 1041 m, 1028 m, 1020 m, 1010 m, 938 m, 932 m, 914 s, 882 s, 762 m, and 665 s cm^{-1}, δ 0.88 (9H, s, ^tBu), 1.30 (18 H, 2 overlapping d, J 7Hz, $CHMe_2$), 1.70-3.50 (10H, br, 4-CH, 2,3,5,6-CH_2, p-$CHMe_2$), 4.38 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 7.28 (2H, s, aryl-H), and 7.70-8.20 (1H, br, NH), m/e 434 ($M^{+\cdot}$, weak), 204, 189 (base), 161, 105, 91, and 57 (Found: C, 69.02; H, 9.79; N, 6.42. $C_{25}H_{42}N_2O_2S$ requires C, 69.08; H, 9.74; N, 6.44%).

5α-Cholestan-3-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (65) [Method (B)] (94%) was recrystallised from methanol and water, m.p. 137-8°, ν_{max} 1345 m, 1325 m ($-SO_2-N<$), 1177 s ($-SO_2-N<$), 685 m, and 665 m cm^{-1}, δ 0.50-2.50 (46H, br), 1.28 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.90 (1H, septet, J 7Hz, p-$CHMe_2$), 4.30 (2H, septet, J 7Hz, o-$CHMe_2$), and 7.20 (3H, s, aryl-H, NH), m/e 370, 235, 204, 189 (base), and 161 (Found: C, 75.74; H, 10.84; N, 4.16; S, 5.08. $C_{42}H_{70}N_2O_2S$ requires C, 75.62; H, 10.58; N, 4.20; S, 4.81%).

Cyclohexanone 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (239)

[Method (B)] (88%) was recrystallised from methanol and water, m.p. 133-5° (lit.,[33] 123-4°), ν_{max} 3250 s (N-H), 1605 m (C=C), 1340 m, 1330 s ($-SO_2-N<$), 1320 m, 1308 m, 1170 and 1158 s ($-SO_2-N<$), 1020 m, 943 m, 925 m, and 668 s cm^{-1}, δ 1.24 (18H, 2 overlapping d, J 6Hz, $CH\underline{Me}_2$), 1.44-1.76 (6H, br, 3,4,5-$C\underline{H}_2$), 2.00-2.40 (4H, br, 2,6-$C\underline{H}_2$), 2.89 (1H, 2 overlapping septets, J 6Hz, p-$C\underline{H}Me_2$), 4.24 (2H, 2 overlapping septets, J 6Hz, o-$C\underline{H}Me_2$), 7.16 (2H, s, aryl-H), and 7.20-7.56 (1H, br, N$\underline{H}$), m/e 378 ($M^{+\cdot}$), 221, 204, 189 (base), 161, 91, 67, and 65 (Found: C, 66.88; H, 9.15; N, 7.46. Calc. for $C_{21}H_{34}N_2O_2S$: C, 66.63; H, 9.05; N, 7.40%).

Deoxybenzoin 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (217)

[Method (A)] (94%) was recrystallised from methanol and water, m.p. 144-6°, ν_{max} 3190 m and 3165 m (N-H), 1605 m (C=C), 1498 m, 1322 m ($-SO_2-N<$), 1298 m, 1165 and 1154 s ($-SO_2-N<$), 883 s, 760 m, 732 m, 700 m, 690 m, and 658 s cm^{-1}, δ 1.24 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 2.88 (1H, overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 3.64 and 4.02 (2H, 2 s, $PhC\underline{H}_2$), 4.14 (2H, septet, J 7Hz, o-$C\underline{H}Me_2$), and 7.10-7.80 (13 H, m, aryl-H, N$\underline{H}$), m/e 477 ($M^{+\cdot}$ +H), 476 ($M^{+\cdot}$), 461 ($M^{+\cdot}$-Me·), 211, 180 (base), 105, and 91 (Found: C, 72.83; H, 7.61; N, 5.92. $C_{29}H_{36}N_2O_2S$ requires C, 73.07; H, 7.61; N, 5.88%).

1,3-Diphenylacetone-2,4,6 Tri-iso-propylbenzenesulphonylhydrazone (218) [Method (A)] (70%) was recrystallised from ethanol and water, m.p. 150-2°, ν_{max} 3245 s (N-H), 1605 m (C=C), 1330 s ($-SO_2-N<$), 1260 m, 1170 and 1160 s ($-SO_2-N<$), 1030 m, 885 m, 745 m (Ph-), 698 s (Ph-), 670 s, and 655 m cm^{-1}, δ 1.26 (18H, overlapping d, J 7 Hz, $CH\underline{Me}_2$), 2.92 (1H, overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 3.38 and 3.44 (4H, 2 s, $PhC\underline{H}_2$), 4.26 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 6.80-7.35 (12H, m, aryl-H), and 7.60-7.80 (1H, br, N$\underline{H}$), m/e 491 ($M^{+\cdot}$ + H), 490 ($M^{+\cdot}$), 274 , 233, 210, 194 (base), 193, 139, 116, and 91 ($PhCH_2^+$) (Found: C, 73.63; H, 7.94;

N, 5.78. $C_{30}H_{38}N_2O_2S$ requires C, 73.43; H, 7.81; N, 5.71%).

Ethyl 2-Oxopropanoate 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (152d) [Method (B)] (86%) was recrystallised from ethanol and water, m.p. 135-7°, ν_{max} 3230 s (N-H), 1710, 1705 s (C=O), 1598 m (C=C), 1330 s and 1320 m ($-SO_2-N<$), 1166 and 1153 s ($-SO_2-N<$), 1100 s (C-O), 1035 m, 908 m, 884 m, 858 m, 688 s, and 653 m cm^{-1}, δ 1.20-1.40 (3H, obscured, $MeCH_2$), 1.30 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.05 (3H, s, MeC=N), 2.95 (1H, overlapping septet, J 7Hz, p-$CHMe_2$), 4.05-4.55 (4H, m, o-$CHMe_2$, CH_2Me), 7.22 (2H, s, aryl-H), and 8.45 (1H, br, NH), m/e 396 ($M^{+\cdot}$) 236, 221, 189 (base), 161, 149, and 128 (Found: C, 60.54; H, 8.28; N, 7.20. $C_{20}H_{32}N_2O_4S$ requires C, 60.58; H, 8.13; N, 7.06%).

E,Z-*4-Hydroxy-4-methylpentan-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (85) [Methods (C) and (D)] (93%) was recrystallised from ethanol and water, m.p. 125-7°, ν_{max} 3580-3350 m (O-H), 3255 m (N-H), 1320 m ($-SO_2-N<$), 1265 m (O-H), 1165 and 1155 s ($-SO_2-N<$), 1135 m (C-O), and 670 m cm^{-1}, δ 1.05 and 1.30 (6H, 2 s, 4-Me), 1.24 (18H, 4 overlapping d, J 7Hz, $CHMe_2$), 1.85 and 1.97 (3H, 2 s, 1-CH_3), 2.34 and 2.45 (2H, 2 s, 3-CH_2), 2.83 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.25 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 7.15 and 7.17 (2H, 2 s, aryl-H), 7.40-7.55 and 9.75-9.85 (1H, 2 br, NH), m/e 396 ($M^{+\cdot}$, weak), 381 ($M^{+\cdot}$-Me·), 379 (M^+-OH·), 378 (M^+-H_2O), 269, 267, 189, 111 [$M^+-(H_2O + ArSO_2^{\cdot})$, base], and 59 (Found: C, 63.52; H, 9.30; N, 7.05; S, 7.96. $C_{21}H_{36}N_2O_3S$ requires C, 63.60; H, 9.15; N, 7.06; S, 8.08%).

Methyl 3-Oxopropanoate 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (232) [Method (B)] (89%) was recrystallised from methanol and water, m.p. 120-3°, ν_{max} 3240 m, (N-H), 1755 s (C=O), 1600 m (C=C), 1332 m ($-SO_2-N<$), 1300 m, 1262 s (C-O), 1172 s and 1155 m ($-SO_2-N<$), 1076 m, 940 m, 921 m,

and 665 m cm^{-1}, δ 1.26 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.86 and 1.98 (3H, 2s, 4-$C\underline{H}_3$), 3.00 (1H, overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 3.20 and 3.32 (2H, 2 s, 2-$C\underline{H}_2$), 3.60 and 3.68 (3H, 2s, O$\underline{Me}$), 4.20 (2H, overlapping septet, J 7Hz, o-$C\underline{H}Me_2$), 7.12 (2H, s, aryl-$\underline{H}$), and 7.40-7.60 (1H, br, N$\underline{H}$), m/e 396 ($M^{+\cdot}$), 381 (M^{+}-Me·), 365 ($M^{+\cdot}$ - OMe·), 337 ($M^{+\cdot}$ - CO_2Me·), 267, 189 (base), 161, and 116 (Found: C, 60.62; H, 8.19; N, 7.07. $C_{20}H_{32}N_2O_4S$ requires C, 60.58; H, 8.13; N, 7.06%).

4-Methylpent-3-en-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (243) [Method (A) and (D)] (70%) was recrystallised from methanol and water m.p. 94-6°, ν_{max} 3255 m (N-H), 1605 m (C=C), 1380 m, 1365 m, 1330 and 1320 m (-SO_2-N<), 1165 and 1155 s (-SO_2-N<), and 670 m cm^{-1}, δ 1.28 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.50-2.10 (9H, m, 1-$C\underline{H}_3$, 4-$\underline{Me}$), 2.80 (1H, overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 4.28 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 5.30-5.60 (1H, br, $\underline{H}$C=), and 7.20 (2H, s, aryl-$\underline{H}$), m/e 378 ($M^{+\cdot}$), 363 (M^{+}-Me·), 189, 161, 111 (M^{+}-($ArSO_2$·), base), 97, 82, and 67 (Found: C, 66.91; H, 9.18; N, 7.21. $C_{21}H_{34}N_2O_2S$ requires C, 66.63; H, 9.05; N, 7.40%).

Octan-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (244) [Methanol (B)] (96%) was recrystallised from ethanol and water, m.p. 87-9° (lit.,[33] 87-88°), ν_{max} 3245 m (N-H), 1637 m (C=N), 1604 m (C=C), 1328 s (-SO_2-N<), 1306 m, 1260 m, 1167 and 1155 s (-SO_2-N<), 1105 m, 1060 m, 1036 m, 940 m, 912 m, 880 m, and 662 s cm^{-1}, δ 0.70-1.00 (3H, br, 8-$C\underline{H}_3$), 1.10-1.60 (8H, br, Me($C\underline{H}_2$)$_4$), 1.24 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.74 (3H, s, 1-$C\underline{H}_3$), 1.80-2.30 (2H, br, 3-$C\underline{H}_2$), 2.86 (1H, overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 4.24 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 7.10 (2H, s, aryl-$\underline{H}$), and 7.30 (1H, br, N$\underline{H}$), m/e 408 ($M^{+\cdot}$), 393 (M^{+}-Me·), 267, 251, 202, 189, 141 (base), 128, 72, and 70 (Found: C, 67.60; H, 10.08;

N, 6.90. Calc. for $C_{23}H_{40}N_2O_2S$: C, 67.60; H, 9.87; N, 6.85%).

2-Oxohexadecanoic Acid 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (152b) [from the ketone[89] and method (A)], was obtained as an oil (ca. 100%) containing solvent, ν_{max} 3700-2500 m br (O-H), 3400 m, 3200 s (N-H), 2958 s, 2925 s, 2850 s, 1695 s (C=O), 1602 s (C=C), 1569 m, 1465 s, 1428 s, 1380 s, 1364 s, 1337 s ($-SO_2-N<$), 1302 m, 1265 m, 1258 m, 1194 s, 1170 and 1154 s ($-SO_2-N<$), 1124 s (C-O), 1105 s, 1072 m, 1060 m, 1038 m, 940 m, 900 m, 882 m, 800 m, 770 m, and 663 s cm^{-1}, δ 0.70-1.00 (3H, br, $MeCH_2$), 1.10-1.70 (42H, br, $CHMe_2$, $Me(CH_2)_{12}$), 2.30-2.70 (2H, m, $CH_2C=N$), 2.95 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.20 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 7.14 and 7.20 (2H, 2s, aryl-H), and 8.35-8.55 and 8.75-8.85 (2H, br, OH, NH), m/e 268, 251 (base), 235, 233, 189, 149, and 91. A sample was repurified by p.l.c. (Found: C, 67.58; H, 9.93; N, 5.05. $C_{31}H_{54}N_2O_4S$ requires C, 67.59; H, 9.88; N, 5.08%).

2-Oxopropanoic Acid 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (152a) [Method (C)] was recrystallised from diethyl ether and light petroleum although the material could not be obtained pure, m.p. 142°, ν_{max} 3250-3190 m (N-H), 3200-2300 br (O-H), 2720 m, 2595 m, 1700 s(C=O), 1615 m (C=N), 1600 m (C=C), 1565 m, 1428 s, 1338 s ($-SO_2-N<$), 1308 m, 1180 s, 1175 s and 1155 m ($-SO_2-N<$), 1116 s (C-O), 1070 m, 1055 m, 1032 m, 940 m, 930 m, 925 m, 895 m, 878 m, 800 s, 678 s, and 650 m cm^{-1}, δ 1.30 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.10 (3H, s, MeC=N), 2.90 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.20 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 7.30 (2H, m, aryl-H), and 8.75-9.25 (2H, br, OH, NH), m/e 323 (M^+ - $CO_2H^\cdot$, weak), and 189 (base) (Found: C, 58.02; H, 7.82; N, 7.23. $C_{18}H_{28}N_2O_4S$ requires C, 58.67; H, 7.66; N, 7.60%).

2-Oxo-undecanoic acid 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone

(152c) [from the ketone[89] and method (A)], was recrystallised twice from dichloromethane and light petroleum to give the less polar isomer, m.p. 105-6°, ν_{max} 3500-2300 m br (O-H), 3250 s (N-H), 1696 s (C=O), 1602 s (C=O), 1570 m, 1340 s ($-SO_2-N<$), 1300 m, 1280 s, 1260 s, 1223 m, 1200 m, 1170 and 1160 s ($-SO_2-N<$), 1120 s (C-O), 1060 m, 1040 m, 940 m, 910 m, 880 s, 825 m, 680 s, and 655 s cm^{-1}, δ 0.75-1.00 (3H, br, 11-CH_3), 1.10-1.70 (12H, br, $Me(CH_2)_6$), 1.30 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.70-2.20 (2H, br, 4-CH_2), 2.30-2.75 (2H, br, 3-CH_2), 2.95 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.25 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 7.25 and 7.30 (2H, 2 s, aryl-H), and 9.25-9.75 (2H, br, OH, NH), m/e 251, 235, 187 (base), 151, 149, and 91 (Found: C, 65.10; H, 9.34; N, 5.86. $C_{26}H_{44}N_2O_4S$ requires C, 64.96; H, 9.23; N, 5.83%).

Undecan-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone (72) [Method (A)] (98%) was purified by chromatography on Kieselgel H and obtained as an oil, ν_{max} 3235 m (N-H), 2960 s, 2930 s, 2860 s, 1605 s (C=C) 1570 m, 1460 s, 1430 s, 1385 s, 1365 s, 1325 s, ($-SO_2-N<$), 1267 m, 1260 m, 1197 m, 1165 and 1155 s ($SO_2-N<$), 1073 m, 1062 m, 1040 m, 940 m, 915 m, 883 m, 740 m, and 665s cm^{-1}, δ 0.80-2.50 (19H, br, $^nC_9H_{19}$), 1.28 (18H, overlapping d, J 6Hz, $CHMe_2$), 1.76 and 1.88 (3H, 2s, 1-CH_3), 2.90 (1H, overlapping septets, J 6Hz, p-$CHMe_2$), 4.28 (2H, overlapping septets, J 6Hz, o-$CHMe_2$), 7.14 (2H, s, aryl-H), and 7.40-7.70 (1H, br, NH), m/e 325, 267, 235, 209, 187 (base), and 91 (Found: C, 69.31; H, 10.32; N, 5.91. $C_{26}H_{46}N_2O_2S$ requires C, 69.29; H, 10.29; N, 6.21%).

Preparation of *2-Oxoheptanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152e). Anhydrous copper (I) cyanide (3.60 g) was suspended in acetonitrile (16 ml). n-Hexanoyl chloride (2.80 ml) was added, the solution refluxed for 20 min, evaporated, the residue was extracted with diethyl ether (150 ml) and the extracts evaporated. The crude acyl cyanide was

dissolved in diethyl ether (20 ml) and the solution saturated with hydrogen chloride gas. Water (0.36 ml) was added and the solution was stirred for 30 min. Light petroleum (40 ml) was added and the mixture evaporated to half volume. Filtration gave 2-oxoheptanamide (530 mg, 19%) m.p. 106-7° (lit.,[115] 106-7°), ν_{max} 3400 s (N-H), 3300m (N-H), 3218 m (N-H), 1725 s (C=O), 1676 s (C=O), and 1610 m cm^{-1}.

2-Oxoheptanamide (515 mg), 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (1.07 g) and concentrated hydrochloric acid (1 drop) were dissolved in dichloromethane (15 ml) and the solution stirred for 30 min and evaporated. Recrystallisation of the residue from methanol and water and washing with light petroleum gave the E,Z-*amide sulphonylhydrazone* (152e) (1.45 g, 95%), m.p. 141-7° (from methanol and water), ν_{max} 3475 m (N-H), 3255 m (N-H), 3200 m (N-H), 1695 s (C=O), 1608 m (C=C), 1340 s ($-SO_2-N<$), 1308 m, 1168 s and 1160 m ($-SO_2-N<$), 1120 m, 1108 m, 1040 m, 788 m, and 667 s cm^{-1}, δ 0.70-0.95 (3H br, 7-CH_3), 1.10-1.60 (4H, br, 5,6-CH_2), 1.25 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.65-2.10 (2H, br, 4-CH_2) 2.35-2.65 (2H, br, 3-CH_2), 2.91 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.18 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 5.50-5.80 and 6.50-6.70 (2H, br, $CONH_2$), 7.18 (2H, br s, aryl-H), and 8.70-9.00 (1H, br, NNH), m/e 268, 251, 233, 204, 189 (base), 161, 98, and 91 (Found: C, 62.65; H, 8.99; N, 10.00. $C_{22}H_{37}N_3O_3S$ requires C, 62.38; H, 8.80; N, 9.92%).

Preparation of N-*Cyclohexyl-2-oxopropanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152f). N-Cyclohexyl-2-oxopropanamide[91] (471 mg), 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (0.836 g) and Amberlite IR-120 (H) resin were suspended in dichloromethane (20 ml) and the mixture stirred for 2 h. Filtration, evaporation and recrystallisation from methanol and water gave the *amide sulphonylhydrazone* (152 f) (1.17 g,

93%) m.p. 161-3°, ν_{max} 3410 m (N-H), 3155 s (N-H), 1655 s (C=O), 1605 m (C=C), 1518 s (C=O), 1342 s ($-SO_2-N<$), 1195 m, 1170 m and 1158 s ($-SO_2-N<$), 1104 s, 1072 m, 1060 m, 1038 m, 892 m, 885 m, 848 m, 686 s, and 662 m cm^{-1}, δ 1.00-2.20 (10H, br, $(CH_2)_5$), 1.28 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.02 (3H, s, 3-CH_3), 2.90 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 3.40-3.90 (1H, br, HCN), 4.24 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 6.40-6.80 (1H, br, HNCO), and 7.18 (2H, br s, aryl-H), m/e 449 ($M^{+\cdot}$), 268, 251, 204 (base), and 110 (Found: C, 64.04; H, 8.82; N, 9.36. $C_{24}H_{39}N_3O_3S$ requires C, 64.11; H, 8.74; N, 9.35%).

Preparation of N-*Cyclohexyl-2-oxoheptanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152 g). n-Hexanoyl chloride (1.36 g) and cyclohexyl isonitrile[91] (1.09 g) were stirred together at 65° for 50 min. The solution was cooled to 0°, treated with acetone (6 ml) and water (6 ml) and allowed to warm up to 25° over 2 h. General work up [(B) diethyl ether] and azeotropic evaporation with toluene (2 x 10 ml) gave the crude N-cyclohexyl-2-oxoheptanamide. 2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (2.98 g), concentrated hydrochloric acid (1 drop) and dichloromethane (25 ml) were added, the solution was stirred for 1 h and evaporated. Recrystallisation of the residue from ethanol and water and washing with light petroleum gave the *amide sulphonylhydrazone* (152g) (4.30 g, 85%) m.p. 140-3°, ν_{max} 3380 m (N-H), 3130 m (N-H), 1637 s (C=O), 1600 m (C=C), 1520 s (C=O), 1330 m ($-SO_2-N<$), 1300 m, 1170 s and 1120 m ($-SO_2-N<$), 1100 m, 1070 m, 1035 m, 680 m, 657 m, and 610 m cm^{-1}, δ 0.60-2.00 (19H, br, $(CH_2)_5$, ^nBu), 1.26 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.10-3.10 (3H, br, 3-CH_2, p-$CHMe_2$), 3.30-3.90 (1H, br, HCN), 4.15 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 6.40-6.70 (1H, br, HNC=O), 7.15 (2H, s, aryl-H), and 8.30-8.60 (1H, br, NNH), m/e 267, 251, 233, 204, 189 (base), 161, and 71 (Found: C, 66.50; H, 9.51; N, 8.35. $C_{28}H_{47}N_3O_3S$ requires C, 66.50; H, 9.37; N, 8.31%).

Preparation of N-*Cyclohexyl-2-oxohexadecanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152h). n-Pentadecanoic acid (1.396 g) and sodium hydride (145 mg) were suspended in dichloromethane (40 ml) and the suspension stirred for 10 min. Oxalyl chloride (0.50 ml) was added and the mixture stirred for 72 h at 25°. The solution was evaporated, the residue dissolved in THF (5 ml) and pentane (15 ml), treated with cyclohexyl isonitrile[91] (0.96 g) and heated at 60° for 2h. The solution was cooled to 0°, THF (25 ml) and water (25 ml) were added and the suspension was stirred for 2 h. General work up [(B) dichloromethane, diethyl ether] and chromatography on Kieselgel H (22 g) [eluant light petroleum-dichloromethane (1:0-3:1)] gave N-cyclohexyl-2-oxohexadecanamide (436 mg, 22%), ν_{max} 1725 s, and 1660 s cm^{-1}. 2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (358 mg), concentrated hydrochloric acid (1 drop) and diethyl ether (25 ml) were added and the solution was stirred for 30 min. Evaporation and recrystallisation of the residue from ethanol and water gave the *amide sulphonylhydrazone* (152h) (0.695 g, 92%) m.p. 74-6°, ν_{max} (CCl_4) 3415 s (N-H), 3150 s (N-H), 2920 s, 2850 s, 1655 s (C=O), 1605 m, 1510 s(C=O), 1410 s, 1340 s ($-SO_2-N<$), 1320 m, 1300 m, 1257 m, 1250 m, 1195 m, 1170 and 1155 s ($-SO_2-N<$), 1086 s, 1037 m, 940 m, 922 m, 905 m, 890 m, 880 m, 850 m, 842 m, 682 s, and 652 s cm^{-1}, δ 0.70-2.10 (37H, br), 1.24 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 2.10-2.70 (2H, br, 3-$C\underline{H}_2$), 2.70-3.20 (1H, br, p-$C\underline{H}Me_2$), 3.40-3.90 (1H, br, $\underline{H}CN$), 4.16 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 6.30-6.60 (1H, br, $\underline{H}NCO$), 7.20 (2H, s, aryl-$\underline{H}$), and 7.80-8.10 (1H, br, $NN\underline{H}$), m/e 254, 250, 189 (base), 161, 83 ($C_6H_{11}^+$), and 55 (Found: C, 70.40; H, 10.52; N, 6.55. $C_{37}H_{65}N_3O_3S$ requires C, 70.32; H, 10.37; N, 6.65%).

Preparation of N-*Methyl-2-oxoheptanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152j). Methyl isonitrile[116] (0.63 g) and n-hexanoyl chloride (1.35 g) were stirred together at 60° for 1 h and then cooled to 0°. Water (5 ml) and acetone (5 ml) were added, the mixture stirred for 2 h

whilst warming up to 25°, evaporated, the residue redissolved in toluene (3 x 5 ml) and the solution re-evaporated. 2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (3.00 g), dichloromethane (100 ml), methanol (100 ml) and concentrated hydrochloric acid (2 drops) were added, the solution stirred for 40 min and evaporated to 1/4 volume. Precipitation with water, filtration of the solid derivative and washing with light petroleum gave the *amide sulphonylhydrazone* (152j) (3.95 g, 91%) m.p. 174-80° (from methanol and water), ν_{max} 3390 m, (N-H), 3130 m (N-H), 1658 s (C=O), 1656 s (C=O), 1598 m (C=C), 1540 m (C=O), 1425 m, 1410 m, 1337 m, 1322 m 1172 s and 1154 m ($-SO_2-N<$), 1100 m, 1102 m, 1078 m, 1038 m, 940 m, 882 m, 690 m, and 660 m cm^{-1}, δ 0.70-1.00 (3H, br, 7-CH_3), 1.10-1.70 (6H, br, $Me(CH_2)_3$), 1.27 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.30-3.10 (3H, br, 3-CH_2, p-$CHMe_2$), 2.77 (3H, d, J 4.5 Hz, NMe), 4.20 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 6.40-6.80 (1H, br, HNCO), 7.18 (2H, s, aryl-H), and 9.50 (1H, br s, NNH), m/e 438 (M^+ + H), 267, 251, 233, 204, 189 (base), 161, and 91 (Found: C, 63.25; H, 9.12; N, 9.56. $C_{23}H_{39}N_3O_3S$ requires C, 63.12; H, 8.98; N, 9.60%).

Preparation of N-*Methyl-2-oxopropanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152i). Methyl isonitrile[116] (0.46 g) and acetyl chloride (813 mg) were dissolved in dichloromethane (1 ml), the solution refluxed for 30 min and recooled to 0°. Tetrahydrofuran (7.5 ml) and water (7.5 ml) were added and the solution stirred for 70 min. Methanol (20 ml), 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (3.07 g) and concentrated hydrochloric acid (2 drops) were added and the solution stirred for 70 min. Water was added, the product filtered off and washed with water and light petroleum. Purification by chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-0:1)] and recrystallisation from methanol and water gave the *amide sulphonylhydrazone* (152i) (2.15 g, 55%) m.p. 174°, ν_{max} 3415 m (N-H), 3050 m, 1667 s (C=O), 1628 m, 1608 m (C=C),

1558 m (C=O), 1432 m ($-SO_2-N<$), 1210 m, 1175 s, and 1158 m ($-SO_2-N<$), 1100 m, 1042 m, 912 m, 885 m, 840 m, 693 s, and 655 m cm^{-1}, δ 1.27 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 2.00 (3H, s, 3-$C\underline{H}_3$), 2.70-3.20 (1H, br, p-$C\underline{H}Me_2$), 2.77 (3H, d, J 5Hz, N$\underline{Me}$), 4.20 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 6.50-6.80 (1H, br, $\underline{H}NCO$), 7.18 (2H, s, aryl-$\underline{H}$), and 8.37 (1H, br s, $NN\underline{H}$), m/e 268, 251, 233, 204, 189 (base), 161, 105, and 91 (Found: C, 59.76; H, 8.27; N, 10.99. $C_{19}H_{31}N_3O_3S$ requires C, 59.81; H, 8.19; N, 11.01%).

Preparation of N-*Methyl-2-oxohexadecanamide 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (152k). n-Pentadecanoyl chloride (2.07 g), dichloromethane (2 ml) and methyl isonitrile[116] (0.60 g) were refluxed together for 50 min and cooled to 0°. Acetone (4 ml) and water (4 ml) were added, the solution stirred for 4 h whilst warming up to 25°, evaporated, the residue was redissolved in toluene (3 x 5 ml) and the solution re-evaporated. Dichloromethane (30 ml), methanol (50 ml), 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (2.37 g) and concentrated hydrochloric acid (3 drops) were added, the solution stirred for 2 h, evaporated to half volume, the product precipitated with water and filtered off. Washing with water and light petroleum gave the *amide sulphonylhydrazone* (152k) (2.93 g, 65%), m.p. 158-62° (from diethyl ether and ethanol at -20°), ν_{max} 3400 m (N-H), 3110 m (N-H), 1670 s (C=O), 1545 m, 1412 m, 1338 and 1322 m ($-SO_2-N<$), 1175 and 1165 s ($-SO_2-N<$), 1070 m, 1062 m, 680 m, 652 m, and 612 m cm^{-1}, δ 0.80-1.10 (3H, br, $\underline{Me}CH_2$), 1.28 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.10-1.45 (24H, br s, $Me(C\underline{H}_2)_{12}$), 2.30-2.70 (2H, br, 3-$C\underline{H}_2$), 2.60-3.10 (1H, br, p-$C\underline{H}Me_2$), 2.80 (3H, d, J 4.5Hz, N$\underline{Me}$), 4.20 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 6.60-6.90 (1H, br, $N\underline{H}$), and 7.20 (2H, s, aryl-$\underline{H}$), m/e 268, 251, 233, 204, 189 (base), 175, 161, 149, 105, and 91 (Found: C, 67.94; H, 10.34; N, 7.44. $C_{32}H_{57}N_3O_3S$ requires C, 68.16; H, 10.19; N, 7.45%).

Preliminary Alternative Electrophilic Additions to the Vinyl Carbanions (66) or (74)

In a typical experiment, the substrate sulphonylhydrazone was dissolved in dry solvent V_1 (ml) under a dry argon atmosphere and the solution cooled to T_1. Alkyllithium reagent RLi (mmol) was added, the solution was warmed to T_2, stirred for m_1 (min) and recooled to T_3. Electrophile E_1 (mmol) was added and the products isolated by standard methods. Table 4 shows details of individual experiments (page 116).

Preparation of *3-Formyl-5α-cholest-n-ene (n=2,3) 2,4-Dinitrophenylhydrazone* (70) from the hydrazone (23) using TMEDA as solvent. Sulphonylhydrazone (23)[55] (420 mg) was dissolved in TMEDA (10 ml) and the solution cooled to -45°. Methyllithium (2.88 mmol) was added, the solution warmed to 25° and transferred to a solution of DMF (20 mmol) in THF (22 g) at -78° during 5 min. General work up [(A) diethyl ether, glacial acetic acid] gave the crude aldehyde (69). Reaction[63] with 2,4-dinitrophenylhydrazine (0.147 g) and washing of the precipitate with light petroleum (3 x 50 ml) gave the *title hydrazone* (70) (249 mg, 57%) m.p. 252-4°, ν_{max} (dichloromethane) 1620 s (C=N), 1600 m (C=C), 1520 m (C-NO_2), and 1330 m (C-NO_2) cm^{-1} δ 0.50-2.60 (44H, br), 5.80-6.20 (1H, br, HC=), 7.20-8.20 (3H, m, aryl 5,6-H, HC=N), and 9.10 (1H, d, J 3Hz, aryl 3-H). A sample was recrystallised twice from ethyl acetate m.p. 254-6°, m/e 578 ($M^{+\cdot}$), 561 ($M^{+\cdot}$-OH), 517, 238, 71, and 57 (Found:C, 70.41; H, 8.74; N, 9.58. $C_{34}H_{50}N_4O_4$ requires C, 70.56; H, 8.71; N, 9.68%).

Preparation of the 2,4-Dinitrophenylhydrazone (70) from the Sulphonylhydrazone (65) using DME as solvent

Sulphonylhydrazone (65) (0.700g) was dissolved in DME (5 ml) and the solution was cooled to -78°. sec-Butyllithium (2.88 mmol) was added, the

TABLE 4

Run	Sulphonyl-hydrazone	mmol	V_1 (ml)	RLi (mmol)	T_1	T_2	M_1	T_3	E_1 (mmol)	Product		Yield
1	(23)	0.72	TMEDA (10)	MeLi (2.88)	-45°	25°	0	-78°	DMF (20)[c]	phenylhydrazone	(70)	57[a,d,e]
2	(23)	1.02	THF (10)	^{n}BuLi (3.97)	-78°	25°	0	-78°	$COCl_2$ (4.7)[c]	olefin	(67)	49[a,e]
3	(23)	0.90	TMEDA (9)	^{n}BuLi (3.71)	-78°	25°	0	-78°	$COCl_2$ (4.9)[c]	olefin acid	(67) (71)	major[b] none[b]
4	(23)	1.09	TMEDA (10)	MeLi (4.41)	-45°	25°	0	-78°	EtO.COCl (27)[c]	olefin	(67)	major[b]
5	(23)	0.84	MME (15)	^{n}BuLi (3.30)	-78°	-24°	390	-78°	DMF (26)	olefin aldehyde	(67) (69)	9[a] 32[a]
6	(65)	1.16	DMM (10)	^{n}BuLi (6.65)	-60°	25°	60	0°	DMF (26)	olefin aldehyde	(67) (69)	51[a,d,e] 5[b]
7	(65)	0.76	DMM (8)	^{n}BuLi (3.08)	-78°	0°	30	-78°	D_2O (excess)	deuterio-olefin	(68)	55[a,e] 6.3[g]
8	(72)	1.16	DMM (5)	^{n}BuLi (4.62)	-78°	0°	20	0°	DMF (6.4)	phenylhydrazone	(77)	26[a,d,e]
9	(72)	1.35	DMM (5) TMEDA (0.2)	^{n}BuLi (4.06)	-78°	0°	30	0°	DMF (6.4)	phenylhydrazone	(77)	37[a,d,e]
10	(72)	1.05	DMM (5) DME (0.15)	^{n}BuLi (3.50)	-78°	0°	20	0°	DMF (7.7)	phenylhydrazone	(77)	32[a,d,e]
11	(72)	1.05	DMM (5) DME (0.15)	^{n}BuLi (3.28)	-78°	0°	20	0°	D_2O (excess)	deuterio-olefin	(75)	<79[a,e] 92[g]
12	(72)	1.03	DME (5)	^{n}BuLi (3.04)	-78°	0°	20	0°	DMF (6.4)	phenylhydrazone	(77)	43[a,d,e]
13	(72)	0.93	DME (5)	^{n}BuLi (2.80)	-78°	0°	20	0°	D_2O (excess)	isoxazoline	(79)	65[a,d,f,e] 83[g]
14	(65)	1.05	DME (5)	^{sec}BuLi (2.88)	-78°	0°	20	0°	DMF (6.4)	phenylhydrazone	(70)	58[a,d,e]
15	(65)	1.00	DME (5)	^{sec}BuLi (2.53)	-78°	0°	20	0°	D_2O (excess)	deuterio-olefin	(68)	75[a,e] 78[g]

TABLE 4/ continued...

Footnotes:

a Isolated yield;

b Estimated yield by t.l.c. or i.r. analysis;

c Inverse addition of electrophile;

d Product isolated as its 2,4-dinitrophenylhydrazone derivative[63];

e Major isolated compound;

f Compound characterised by reaction with 2,4,6-trimethylbenzonitrile oxide to form an isozaxoline derivative[65];

g Deuterium incorporation (%).

solution stirred for 1 h, warmed to 0° over 50 min and stirred for 20 min. DMF (6.4 mmol) was added dropwise during 5 min. General work up [(A) diethyl ether, glacial acetic acid] and chromatography on Kieselgel H (15 g) [eluant light petroleum-diethyl ether (1:0-4:1)] gave the crude aldehyde (69). Reaction[63] with 2,4-dinitrophenylhydrazine (0.133 g) gave the 2,4-dinitrophenylhydrazone derivative (70) (352 mg, 58%) m.p. 252-4°, t.l.c. and i.r. as before.

Preparation of *2-Methylene-undecanal 2,4-Dinitrophenylhydrazone (77)*. Sulphonylhydrazone (72) (0.463 g) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (3.04 mmol) was added, the solution stirred for 75 min, warmed to 0° over 45 min and stirred for 20 min. DMF (6.4 mmol) was added dropwise during 5 min and the solution stirred for an hour. General work up [(A) diethyl ether, glacial acetic acid] and chromatography on Kieselgel H (15 g) [eluant light petroleum-diethyl ether (1:0-4:1)] gave the crude aldehyde (76) (305 mg). Reaction[63] with 2,4-dinitrophenylhydrazine gave the *title hydrazone* (77) (160 mg, 43%) m.p. 114-7°, ν_{max} (CCl_4) 2930 m, 1620 s (C=N), 1600 m (C=C), 1510 m (C-NO_2), 1340 s (C-NO_2), 1325 s (C-NO_2), and 1140 m cm^{-1}, δ 0.70-1.08 (3H, br, Me-), 1.10-1.70 (14H, br, Me(CH_2)$_7$), 2.24-2.72 (2H, br, 3-CH_2), 5.48 (1H, m s, CH_2=), 5.58 (1H, m s, CH_2=), 7.70-8.50 (3H, m, aryl 5,6-H, HC=N), and 9.16 (1H, d, J 2Hz, aryl 3-H). A sample was recrystallised from ethanol m.p. 122-4°, m/e 362 (M^+), 345 (M^+-OH), 330 (M^+-O_2), 327, 250, and 183 (base) (Found: C, 59.72; H, 7.24; N, 15.43. $C_{18}H_{26}N_4O_4$ requires C, 59.65; H, 7.23; N, 15.46%).

Preparation of 3-Deuterio-5α-cholest-n-ene (n=2,3) (68). Sulphonylhydrazone (65) (0.670 g) was dissolved in DME (5 ml) and the solution cooled to -78°. sec-Butyllithium (2.53 mmol) was added, the solution stirred for 90 min, warmed to 0° over 60 min and stirred for 20 min.

Deuterium oxide (0.50 ml) was added and the solution stirred for 15 min. General work up [(B) light petroleum] and chromatography on Kieselgel H (15 g) (eluant light petroleum) gave the crude deuterio-alkene (68) (304 mg, <82%). Recrystallisation from diethyl ether and acetone gave the deuterio-alkene (68) (278 mg, 75%) m.p. 59-61° (lit.,[64] 5α-cholest-2-ene 75-6°), ν_{max} (CS_2) 3020 m (vinyl-H), 2900 s, 1380 s, 1365 s, 1300 m, 1280 m, 1170 m, 960 m, and 940 m cm^{-1}, δ 0.50-2.80 (44H, br), and 5.25-5.55 (1H, br, HC=), m/e 371 (M^+), 370, 356 (M^+-Me), 355, 316, 258, and 57 (base), 78% mono-deuteriated.

Preparation of 2-Deuterio-undec-1-ene (75). Sulphonylhydrazone (72) (0.417 g) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.80 mmol) was added, the solution warmed to -65°, stirred for 30 min, warmed to 0° over 30 min and stirred for 20 min. Deuterium oxide (0.50 ml) was added and the solution stirred for 15 min. General work up [(B) light petroleum] and chromatography on Kieselgel H (15 g) (eluant light petroleum) gave the slightly impure deuterio-alkene (75) (142 mg, <99%) as an oil, ν_{max} (CS_2) 3080 m (vinyl-H), 2900-2840 s, 1620 m (C=C), 1380 m, 907 s (CH_2=), 840 m, 765 s, and 720 m cm^{-1}, δ (CCl_4) 0.60-2.30 (19H, br), and 5.00 (2H, s, CH_2=), m/e 155 (M^+), 154 and 43 (base), 83% mono-deuteriated.

A sample of the deuterio-olefin (75) (76 mg) and 2,4,6-trimethylbenzonitrile oxide[65] (79 mg) were dissolved in THF (2 ml)and the mixture stirred for 5 d. Evaporation and chromatography on Kieselgel H (16 g) [eluant light petroleum-dichloromethane (1:0-0:1)] gave *5-deuterio-5-(n-nonyl)-3-(2,4,6-trimethylphenyl)- (2)-isoxazoline* (79) (102 mg, 66%) as an oil, ν_{max} 2970 s, 2940 s, 2870 s, 1470 m, 1450 m, 1335 m, and 855 s cm^{-1}, δ 0.80-1.00 (3H, br, $MeCH_2$), 1.20-2.00 (16H, br, $Me(CH_2)_8$), 2.22 (6H, s,

o-Me), 2.28 (3H, s, p-Me), 2.65 + 3.10 (2H, ABq, J 16Hz, 4-CH_2), and 6.83 (2H, s, aryl-H), m/e 316 ($M^{+\cdot}$), 203 ($M^{+\cdot} - {}^{n}C_8H_{17}\cdot$), 189 ($M^{+\cdot} - {}^{n}C_9H_{19}\cdot$, base), 159, 119 ($C_9H_{11}^{+}$), 101, and 69 (Found: C, 79.41; H, 10.58; N, 4.43. $C_{21}H_{32}{}^{2}H_1NO$ requires C, 79.69; N, 4.42%).

Attempted Quenching of the Vinyl carbanion (66) with Methyl Chloroformate. Sulphonylhydrazone (65) (0.593g) was dissolved in DME (5 ml) and the solution cooled to -78°. sec-Butyllithium (2.24 mmol) was added, the solution stirred for 1h, warmed to 0° over 25 min and stirred for 20 min. The solution was transferred dropwise during 5 min to a solution of methyl chloroformate (6.5 mmol) in pentane[62] (5 ml) at -78°. The solution was warmed to 25° and stirred for 1 h. General work up [(B) diethyl ether] and chromatography on Kieselgel H (15 g) [eluant light petroleum-dichloromethane (1:0-0:1)] gave 5α-cholest-n-ene (n = 2,3) (109 mg, 33%), m/e 370 ($M^{+\cdot}$); and the impure steroids (80) and (81) (271 mg). Three recrystallisations of the latter mixture from diethyl ether and acetone at 0° gave *di-3-(5α-cholest-n-enyl)ketone (n=2, and or 3)* (81) (15 mg, 4%) as white plates, m.p. 213-5°, ν_{max} (CCl_4) 2940 s, 2870 m, 1635 m (C=O), 1470 m, 1435 m, 1380 s, and 1355 s cm^{-1}, λ_{max} 239 nm, δ (weak) 0.60-2.45 (88H, br) and 5.80-6.80 (2H, br, HC=), m/e 766 ($M^{+\cdot}$, base), 751 ($M^{+\cdot}$ - Me·), 653 ($M^{+\cdot} - C_8H_{17}\cdot$), 393, 369, and 287 (Found: C, 86.26; H, 12.11. $C_{55}H_{90}O$ requires C, 86.09; H, 11.82%). Purification of the mother liquors by p.l.c. [one development with light petroleum:dichloromethane (10:3)] and recrystallisation from dichloromethane and acetonitrile at 0° gave *3-methoxycarbonyl-5α-cholest-n-ene (n=2,3)* (80) (91 mg, 24%) as white crystals, m.p. 63-5°, ν_{max} (CCl_4) 2920 s, 2860 s, 1720 s (C=O), 1652 m (C=C), 1470 s, 1445 s, 1435 m, 1385 s, 1365 s, 1315 s, 1250 s (C-O), 1190 m, 1150 s, 1125 m, 1095 m, 1085 m, and 1050 m cm^{-1}, δ (CCl_4) 0.60-2.50 (44H, br), 3.68 (3H, s, MeO), and 6.40-7.00 (1H, br, HC=), m/e 428 ($M^{+\cdot}$, base), 413 ($M^{+\cdot}$ - Me·), 397 ($M^{+\cdot}$ - MeO·), 369 ($M^{+\cdot} - CO_2Me\cdot$), and 366 (Found:

C, 81.44; H, 11.28. $C_{29}H_{48}O_2$ requires C, 81.25; H, 11.28%).

Quenching of the Dianion (83) with Acetone. Sulphonylhydrazone (82) (466 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (3.08 mmol) was added, the golden solution stirred for 15 min, warmed to -50° over 20 min, quenched with acetone (1.9 mmol) until colourless, and warmed up to 25°. General work up [(A) diethyl ether, glacial acetic acid] gave 4-hydroxy-4-methylpentan-2-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone (85) (520 mg, 95%) m.p. 95-8°, mainly as the less polar Z-isomer by t.l.c. analysis, ν_{max} 3460 s (O-H), 3080 s (N-H), 1600 m (C=C), 1570 m, 1325 s ($-SO_2-N<$), 1295 m, 1260 m, 1235 m, 1195 m, 1165 m and 1155 s ($-SO_2-N<$), 1135 s, (C-O), 1105 m, 1055 m, 1040 m, 1015 m, 945 m, 720 m, 690 m, and 660 m cm^{-1}, δ 1.05 and 1.32 (6H, 2 s, MeCO), 1.26 (18H, overlapping d, $CHMe_2$), 1.86 and 1.94 (3H, 2 s, 1-Me), 2.42 (2H, br s, 3-CH_2), 2.90 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.20 (2H, overlapping septets, J 7Hz o-$CHMe_2$), 7.12 (2H, br s, aryl-H) and 9.95 (1H, br, NH).

Attempted Quenching of the Dianion (87) with Acetone. Sulphonylhydrazone (86) (1.06 g) was dissolved in DME (8 ml) and the solution cooled to -78°. n-Butyllithium (7.20 mmol) was added and the orange solution warmed to -65° over 10 min. Acetone (6.9 mmol) was added dropwise during 2 min, the clear solution quenched with glacial acetic acid (8.3 mmol) in water (2 ml) at -60°, and warmed to 25°. General work up [(A) diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane] and recrystallisation from methanol and water gave *Z-5-hydroxy-5-methylhexan-3-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone* (89) (1.11 g, 90%) m.p. 132-4°, ν_{max} 3470 s (O-H), 3080 m (N-H), 1325 s ($-SO_2-N<$), 1165 and 1155 s ($-SO_2-N<$), 1125 m (C-O), 1035 m, 912 m, 885 m, and 655 m cm^{-1}, δ 1.00 (3H, t, J 7Hz, 1-Me), 1.25 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.32

(6H, s, MeCO), 2.22 (2H, q, J 7Hz, 2-CH_2), 2.44 (2H, s, 4-CH_2), 3.00 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.20 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 7.10 (2H, s, aryl-H), and 10.10 (1H, br, NH), m/e 410 ($M^{+\cdot}$), 395 (M^+ - Me·), 352 [$M^{+\cdot}$ - (C_3H_6O)], 204, 189 (base), and 161 (Found: C, 64.49; H, 9.39; N, 6.87. $C_{22}H_{38}N_2O_2S$ requires C, 64.35; H, 9.33; N, 6.82%).

Preparation of *5-Deuterio-5-(2-hydroxy-2-methylundecyl)-3-(2,4,6-trimethylphenyl)-2-isoxazoline* (93) from the Sulphonylhydrazone (82) Using DME as Solvent.- Sulphonylhydrazone (82) (399 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.40 mmol) was added, the orange solution stirred for 10 min and warmed to -50° over 20 min. Undecan-2-one (1.45 mmol) was added, the clear solution recooled to -78° and treated with further n-butyllithium (1.56 mmol). The red solution was stirred for 10 min, warmed to -3° over 1 h and quenched with deuterium oxide (0.50 ml). General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) (eluant dichloromethane) gave crude 2-deuterio-4-hydroxy-4-methyltridec-1-ene (340 mg), m/e 213 ($M^{+\cdot}$). A sample (171 mg) and 2,4,6-trimethylbenzonitrile oxide[65] (129 mg) were dissolved in THF (5 ml) and the solution stirred for 10 d. Evaporation and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] gave the *isoxazoline* (93) (189 mg, 85%) as an oil, ν_{max} 3430 m (O-H), 2950 s, 2850 s, 1615 m (C=N), 1460 s, 1435 m, 1380 m (O-H), 1330 m, 910 m, 850 m, and 730 m cm^{-1}, δ 0.70-1.00 (3H, br, $MeCH_2$), 1.05-1.70 [19H, br, $Me(CH_2)_8$, MeCO], 1.70-3.40 (5H, m, 4-CH_2, 1'-CH_2, OH), 2.20 (6H, s, o-Me), 2.23 (3H, s, p-Me), and 6.80 (2H, s, aryl-H), m/e 374 ($M^{+\cdot}$), 359 (M^+ - Me·), 247 ($M^{+\cdot}$ - $^nC_9H_{19}$·), 188 ($M^{+\cdot}$ - $C_{12}H_{26}O$·, base), 159, and 145, 90% mono-deuteriated (Found: C, 76.72; H, 10.64; N, 3.63. $C_{24}H_{38}{}^2H_1NO_2$ requires C, 76.96; N, 3.74%).

Preparation of the Isoxazoline (93) from the Sulphonylhydrazone (82) using THF as Solvent. Sulphonylhydrazone (82) (344 mg) was dissolved in THF (10 ml) and the solution cooled to -78°. n-Butyllithium (3.00 mmol) was added and the yellow solution warmed to -65° over 10 min. Undecan-2-one (2.2 mmol) was added and the clear solution recooled to -78°. n-Butyllithium (3.60 mmol) was added, the orange solution warmed to 0° over 75 min and to 15° over a further 80 min. Deuterium oxide (2.0 ml) was added and the solution warmed to 25°. A similar work up and reaction with 2,4,6-trimethylbenzonitrile oxide[65] gave the isoxazoline (93) (80%) identical [t.l.c., n.m.r., and m/e (84% mono-deuteriated)] with an authentic sample.

Preparation of *4-Hydroxy-4-methyl-2-methylenetridecanal 2,4-Dinitrophenylhydrazone* (95b). Sulphonylhydrazone (82) (386 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.52 mmol) was added, the orange solution stirred for 10 min and warmed to -50° over 25 min. Undecan-2-one (1.94 mmol) was added, the suspension warmed to -40° and recooled to -78°. n-Butyllithium (1.89 mmol) was added, the orange solution stirred for 15 min and warmed to 0° over 40 min. DMF (6.5 mmol) was added dropwise during 2 min, the solution stirred for 40 min and warmed to 25°. General work up [(A) diethyl ether, glacial acetic acid], reaction[63] of the residue with 2,4-dinitrophenylhydrazine (226 mg), chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] and p.l.c. [one development with dichloromethane:diethyl ether (9:1)] gave the *2,4-dinitrophenylhydrazone* (95b) (66 mg, 14%) m.p. 122-3° (from dichloromethane and methanol at 0°), ν_{max} ($CHCl_3$) 2925 m, 1620 s (C=N), 1600 s, (C=C), 1500 m (C-NO_2), 1335 and 1325 s (C-NO_2), and 1140 m cm^{-1}, δ 0.70-1.05 (3H, br, 12-Me), 1.10 (3H, s, 4-Me), 1.10-2.00 (16H, br, $(CH_2)_8$), 2.30 (1H, s, OH), 2.70 (2H, s, 3-CH_2), 5.72 (2H, s, CH_2=), 7.80-8.60 (3H, m, aryl 5,6-H, HC=N), 9.25 (1H, m, aryl 3-H), and 11.00 (1H, br, NH), m/e 420 ($M^{+\cdot}$), 403 ($M^{+\cdot}$-OH·), 293 ($M^{+\cdot}$ - $^{n}C_9H_{19}$·), 238 [$M^{+\cdot}$ - ($C_6H_4N_3O_4$)], 223,

171 ($C_{11}H_{23}O^+$, base), 55, 43, and 41 (Found: C, 60.23; H, 7.72; N, 13.24. $C_{21}H_{32}N_4O_5$ requires C, 59.98; H, 7.67; N, 13.32%).

General Preparation of the α-Methylene-γ-lactones (96), (101)

The ketone 2,4,6-tri-isopropylbenzenesulphonylhydrazone was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (B_1, mmol) was added, the solution warmed to T_1 and treated with ketone or aldehyde ($R^1.CO.R^2$ mmol). The clear solution was recooled to -78°, treated with n-butyllithium (B_2, mmol), stirred for m_1 (min), warmed to T_2 over m_2 (min) and recooled to -78°. Quenching the mixture with carbon dioxide gas for 1 min, warming to 25°, general work up (C), chromatography on Kieselgel H and p.l.c. in sequence gave the α-methylene-γ-lactone (96) or (101). Individual experiments are recorded in Table10, page 125.

5-Methyl-3-methylene-5-(n-nonyl) tetrahydrofuran-2-one (96) (111 mg, 33%) as an oil, ν_{max} 2925 s, 2860 s, 1770 s (C=O), 1470 m, 1385 m, 1285 s (C-O), 1120 m, 1100 m, 1065 m, 940 s (CH_2=), and 905 m cm^{-1}, δ 0.75-1.05 (3H, br, $\underline{Me}CH_2$), 1.15-1.50 (16H, br, $(\underline{CH_2})_8$), 1.35 (3H, s, 5-$\underline{Me}$), 2.70 (2H, q, $\underline{J}$ 2.5 Hz, 4-$\underline{CH_2}$), 5.50 (1H, dd, $\underline{J}$ 3,3Hz, =$\underline{CH_2}$), and 6.13 (1H, dd, $\underline{J}$ 3,3Hz, =$\underline{CH_2}$) m/e 239 (M^+ + H), 223 (M^+ - Me·), 195 (M^+ - Pr·), 154 [$(M^+ + H)-{}^nC_6H_{13}\cdot$], 126 [$(M^+ + H)-{}^nC_8H_{17}\cdot$], 111 [$M^+ - {}^nC_9H_{19}\cdot$, base], and 55 (Found: C, 75.16; H, 10.97. $C_{15}H_{26}O_2$ requires C, 75.58; H, 10.99%).

3-Methylene-1-oxaspiro[4.5]decan-2-one[117] (101j) (66 mg, 40%) as an oil ν_{max} 2940 s, 2875 m, 1765 s (C=O), 1290 s, 1280 s (C-O), 1265 m, 1240 m, 1193 s (C-O), 1130 m, 1104 s, 1033 s, 961 s, and 938 m cm^{-1}, δ 1.10-2.10 (10H, br, $(\underline{CH_2})_5$), 2.64 (2H, t, $\underline{J}$ 2.5 Hz, 4-$\underline{CH_2}$), 5.40-5.60 (1H, m, =$\underline{CH_2}$), and 5.96-6.14 (1H, m, =$\underline{CH_2}$), m/e 166 (M^+), 123, 111, 97 (base), and 68

Run	Sulphonyl-hydrazone	(mmol)	B_1(mmol)	T_1	$R^1.CO.R^2$ (mmol)	B_2(mmol)	M_1(min)	T_2	M_2(min)	Acid (g)	α-methylene-γ-lactone	Yield %
1	(82)	1.41	2.94	-50	undecan-2-one (1.55)	1.54	15	0°	60	CH_3CO_2H 0.2	(96)	33
2	(82)	1.00	3.00	-60	cyclohexanone (2.14)	3.60	3	-3°	60	CF_3CO_2H 1.5	(101j)	40
3	(82)	1.28	3.00	-50	octan-2-one (1.92)	2.40	5	-3°	120	CH_3CO_2H 0.5	(101d)	61
4	(82)	1.01	2.40	-66	butanone (1.70)	2.40	5	-3°	60	CF_3CO_2H 1.0	(101g)	61
5	(82)	1.01	2.40	-70	^{n}butanal (1.62)	3.00	5	-3°	50	CF_3CO_2H 1.3	(101h)	62
6	(82)	0.99	2.40	-70	propanal (2.76)	2.40	5	-3°	60	CF_3CO_2H 1.3	(101b)	45
7	(82)	1.15	2.16	-65	4-methylpentan-2-one (1.36)	2.16	10	-4°	50	CF_3CO_2H 1.2	(101e)	66
8	(82)	1.00	2.40	-50	acetone (1.77)	1.80	8	-5°	40	CF_3CO_2H 0.4	(101f)	57
9	(86)	1.02	2.64	-65	4-methylpentan-2-one (1.68)	2.97[a]	3	-3°	180	CF_3CO_2H 1.5	E-(101k) Z-(101k)	5 12
10	(86)	1.00	2.40	-65	acetone (2.04)	3.60	15	-5°	60	CF_3CO_2H 1.3	E-(101c) Z-(101c)	2 35

TABLE 10

[a] Sec-butyllithium used

(Found: C, 72.37; H, 8.69. Calc. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%).

5-(n-Hexyl)-5-methyl-3-methylenetetrahydrofuran-2-one (101d) (154 mg, 61%) as an oil, ν_{max} 2925 s, 2855 m, 1762 s (C=O), 1280 s (C-O), and 940 m (=CH_2) cm^{-1}, δ 0.75-1.10 (3H, br, MeCH_2), 1.10-1.80 (10H, br, (CH_2)$_5$), 1.32 (3H, s, 5-Me), 2.58-2.76 (2H, br, 4-CH_2), 5.58 (1H, m, =CH_2), and 6.05 (1H, m, =CH_2), m/e 197 (M^+ + H), 181 (M^+ - Me·), 111 (M^+ - $^nC_6H_{13}$·, base), 68, 55, and 43 (Found: C, 73.21; H, 10.26. $C_{10}H_{20}O_2$ requires C, 73.43; H, 10.27%).

5-Ethyl-5-methyl-3-methylenetetrahydrofuran-2-one[120] (101g) (86 mg, 61%) as an oil, ν_{max} 1760 s (C=O), 1285 s, 1270 s (C-O), 1095 m, 1085 m, and 940 m (=CH_2) cm^{-1}, δ 0.96 (3H, t, J 7Hz, MeCH_2), 1.36 (3H, s, 5-Me), 1.70 (2H, q, J 7Hz, MeCH_2), 2.60-2.76 (2H, m, 4-CH_2), 5.50 (1H, m, =CH_2), and 6.10 (1H, t, J 3Hz, =CH_2), m/e 140 (M^+), 126, 111 (M^+ - Et·, base), 97, 69, and 68 (Found: C, 68.43; H, 8.83. $C_8H_{12}O_2$ requires C, 68.55; H, 8.62%).

3-Methylene-5-(n-propyl) tetrahydrofuran-2-one[118] (101h) (87 mg, 62%) as an oil, ν_{max} 2965 s, 2940 s, 2880 m, 1760 s (C=O), 1670 m (C=C), 1400 m, 1340 m, 1270 s (C-O), 1255 s, 1155 s, 1115 s (C-O), 1105 s, 1000 s, and 940 m (=CH_2) cm^{-1}, δ 0.70-2.00 (7H, br, ^nPr), 2.40-3.50 (2H, m, 4-CH_2), 4.28-4.80 (1H, m, 5-CH), 5.52 (1H, t, J 2.5 Hz, =CH_2) and 6.12 (1H, t, J 2.5 Hz, =CH_2), m/e 140 (M^+), 111 (M^+ -Et·), 97 (M^+ - ^nPr·, base), 69, and 68 (Found: C, 68.52; H, 8.86. Calc. for $C_8H_{12}O_2$: C, 68.55; H, 8.62%).

5-Ethyl-3-methylenetetrahydrofuran-2-one (101b) (56 mg, 45%) as an oil, ν_{max} 2970 s, 2940 s, 2880 m, 1765 s (C=O), 1670 m (C=C), 1465 m, 1440 m, 1400 m, 1350 s, 1275 s (C-O), 1250 s, 1190 m, 1160 s, 1115 s (C-O), 1090 s, 1000 s, 985 m, 960 s (=CH_2), and 815 m cm^{-1}, δ 1.00 (3H, t, J 7Hz, MeCH_2), 1.70 (2H, dq, J n, 7Hz, MeCH_2), 2.30-3.40 (2H, m, 4-CH_2), 4.50 (1H, ca.

quintet, J 7Hz, 5-CH), 5.60 (1H, t, J 2.5Hz, =CH_2), and 6.10 (1H, t, J 2.5 Hz, =CH_2), m/e 126 ($M^{+\cdot}$), 111 (M^{+}-Me·), 97 (M^{+} - Et·, base), 69, 68, 44, and 40 (Found: C, 66.56; H, 8.10. $C_7H_{10}O_2$ requires C, 66.65; H, 7.99%).

5-(iso-Butyl)-5-methyl-3-methylenetetrahydrofuran-2-one[120] (101e) (129 mg, 66%) as an oil, ν_{max} 2960 m, 2930 m, 1765 s (C=O), 1670 m (C=C), 1470 m, 1430 m, 1382 m, 1370 m, 1285 s (C-O), 1270 m, 1202 m, 1170 m, 1100 m, 1090 m, 1045 m, 940 s (=CH_2), and 812 m cm^{-1}, δ 0.99 (6H, dd, J 6, 1Hz, $CHMe_2$), 1.42 (3H, s, 5-Me), 1.64 (3H, m, CH_2CHMe_2), 2.75 (2H, t, J 2.5 Hz, 4-CH_2), 5.60 (1H, t, J 2.5 Hz, =CH_2), and 6.18 (1H, t, J 2.5 Hz, =CH_2), m/e 168 ($M^{+\cdot}$), 153 (M^{+}-Me·), 111 (M^{+} - ^{iso}Bu·, base), 97, and 58 (Found: C, 71.21; H, 9.74. $C_{10}H_{16}O_2$ requires C, 71.37; H, 9.59%).

5,5-Dimethyl-3-methylenetetrahydrofuran-2-one[119] (101f) (72 mg, 57%) as an oil, ν_{max} 2980 m, 2937 m, 1760 s (C=O), 1670 m (C=C), 1403 m, 1392 m, 1380 m, 1280 s (C-O), 1188 m, 1127 m, 1087 s (C-O), and 942 s (=CH_2) cm^{-1}, δ (CCl_4) 1.40 (6H, s, 5-Me), 2.70 (2H, t, J 2.5 Hz, 4-CH_2), 5.52 (1H, t, J 2.5 Hz, =CH_2), and 6.08 (1H, t, J 2.5 Hz, =CH_2), m/e 126 ($M^{+\cdot}$), 111 (M^{+}-Me·, base), 83, 68, 43, and 40 (Found: C, 66.39; H, 8.07. Calc. for $C_7H_{10}O_2$: C, 66.62; H, 7.99%).

E-*5-(iso-Butyl)-3-ethylidene-5-methyltetrahydrofuran-2-one* (101k) (9 mg, 5%) as an oil, ν_{max} (CCl_4) 2970 m, 2930 m, 1765 s (C=O), 1690 m (C=C), 1290 m, 1275 m, 1230 m (C-O), 1125 m (C-O), 1020 m, and 950 m cm^{-1}, δ (CCl_4) 0.95 (6H, 2 overlapping d, J 6.5 Hz, $CHMe_2$), 1.20-1.70 (3H, br, CH_2CHMe_2), 1.32 (3H, s, 5-Me), 1.76 (3H, dt, J 7, 1Hz, MeC=), 2.44-2.68 (2H, m, 4-CH_2), and 6.40-6.90 (1H, br, HC=), m/e 182 ($M^{+\cdot}$), 167 (M^{+}-Me·), 125 (M^{+}-^{iso}Bu·, base), 111, 97, and 81 (Found: C, 72.35; H, 10.19. $C_{11}H_{18}O_2$ requires, C, 72.49; H, 9.96%).

Z-*5-(iso-Butyl)-3-ethylidene-5-methyltetrahydrofuran-2-one* (101k) (22 mg, 12%) as an oil, ν_{max} (CCl_4) 2960 m, 2930 m, 2880 m, 1760 s (C=O), 1680 m (C=C), 1470 m, 1445 m, 1385 m, 1355 m, 1215 s (C-O), 1115 s (C-O), 1095 m, and 955 m cm^{-1}, δ (CCl_4) 0.96 (6H, 2 overlapping d, J 6.5 Hz, Me_2CH-), 1.20-1.80 (3H, br, Me_2CHCH_2), 1.30 (3H, s, 5-Me), 2.14 (3H, dt, J 7, 2.5Hz, MeC=), 2.50-2.70 (2H, m, 4-CH_2), and 5.90-6.40 (1H, m, HC=), m/e 182 (M^+), 167 (M^+-Me·), 125 (M^+ - ^{iso}Bu·, base), 111, 97, and 83 (Found: C, 72.24; H, 10.29. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.96%).

Z-*5,5-Dimethyl-3-ethylidenetetrahydrofuran-2-one* (101c) (49 mg, 35%) as an oil, ν_{max} 2980,m, 2930 m, 1750 s (C=O), 1680 m (C=C), 1445 m, 1390 m, 1375 m, 1355 m, 1302 s, 1267 m, 1250 s and 1210 s (C-O), 1180 m, 1127 s, 1096 s, 963 m, and 927 m cm^{-1}, δ 1.40 (6H, s, 5-Me), 2.14 (3H, dt, J 7,2.5Hz, MeC=), 2.56-2.80 (2H, m, 4-CH_2), and 5.90-6.50 (1H, m, HC=), m/e 140 (M^+, base), 125 (M^+ - Me·), 95, 84, 82, 55, and 49 (Found: C, 68.38; H, 8.76. $C_8H_{12}O_2$ requires C, 68.55; H, 8.62%).

E-*5,5-Dimethyl-3-ethylidenetetrahydrofuran-2-one* (101c) (3 mg, 2%) as an oil, ν_{max} 2980 m, 2935 m, 1755 s (C=O), 1670 m (C=C), 1445 m, 1390 m, 1377 m, 1274 s (C-O), 1200 s, 1177 m, 1120 m (C-O), 1030 m, 981 m, 923 m, and 714 m cm^{-1}, δ (CCl_4) 1.40 (6H, s, 5-Me), 1.84 (3H, dt, J 7,1.5 Hz, MeC=) 2.50-2.72 (2H, br, 4-CH_2), and 6.40-6.84 (1H, br, HC=), m/e 140 (M^+), 125 (M^+ - Me), 82 (base), 55, 44, and 43 (Found: C, 68.43; H, 8.76. $C_8H_{12}O_2$ requires C, 68.55; H, 8.62%).

Preparation of the α-Methylene-γ-lactone (101f) from the E,Z-hydroxy-sulphonylhydrazone (85)

E,Z-Hydroxy-sulphonylhydrazone (85) (436 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (4.44 mmol) was added, the

yellow solution warmed to -3° over an hour, recooled to -78°, quenched with carbon dioxide gas for 1 min and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (1 g)] afforded a crude residue which was dissolved in dichloromethane (10 ml) and stood at 0° overnight. Chromatography on Kieselgel H (12 g) [eluant light petroleum-diethyl ether (1:0-1:1)] and p.l.c. [three developments with light petroleum:diethyl ether (13:7)] gave the α-methylene-γ-lactone (101f) (102 mg, 74%) identical (t.l.c. and n.m.r.) with an authentic sample.

Preparation of the α-Ethylidene-γ-lactone (101c) from the Hydroxy-sulphonylhydrazone (89)

Mainly Z-hydroxy-sulphonylhydrazone (89) (408 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (4.02 mmol) and sec-butyllithium (1.56 mmol) were added, the solution warmed to -3° over 95 min, recooled to -78°, quenched with carbon dioxide (g) until colourless, and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (1.0 g)], chromatography on Kieselgel H (20 g) (eluant dichloromethane) and p.l.c. [three developments with light petroleum:diethyl ether (3:1)] gave the Z-ethylidene-γ-lactone (101c) (44 mg, 32%) and the E-ethylidene-γ-lactone (101c) (12 mg, 9%) both identical (t.l.c. and n.m.r.) with authentic samples.

Preparation of *2,6-(Dihydroxy)-2,6-dimethylheptan-4-one 2,4,6-Tri-isopropylbenzenesulphonylhydrazone* (102)

Sulphonylhydrazone (82) (366 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.52 mmol) was added, and the golden solution quenched with acetone (1.26 mmol). n-Butyllithium (1.20

mmol) was added and the golden solution quenched with acetone (1.64 mmol). Glacial acetic acid (0.33 g) was added and the solution warmed to 25°. General work up [(A) dichloromethane], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1.0-7:3)] and p.l.c. [three developments with dichloromethane:diethyl ether (9:1)] gave the E,Z-hydroxy-hydrazone (85) (152 mg, 35%) identical (t.l.c. and n.m.r.) with an authentic sample; and the *hydroxy-hydrazone* (102) (153 mg, 31%) m.p. 151-3 (from dichloromethane and diethyl ether), ν_{max} 3300 m (O-H, N-H), 3080 m (O-H, N-H), 1330 m ($-SO_2-N<$), 1168 m and 1158 m ($-SO_2-N<$), 910 m, and 880 m cm^{-1}, δ 1.10-1.50 (30H, m, Me), 2.40 (2H, s, anti-3-CH_2), 2.50 (2H, s, syn-5-CH_2), 2.86 (1H, septet, J 7Hz, p-$CHMe_2$), 3.44 (2H, br, OH), 4.17 (2H, septet, J 7Hz, o-$CHMe_2$), 7.10-7.25 (1H, br, NH), and 7.20 (2H, s, aryl-H), m/e 454 ($M^{+\cdot}$), 438, 381, 332, 267, 251, 233, 204, 189 (base), 161, and 127 (Found: C, 63.36; H, 9.34; N, 6.16. $C_{24}H_{42}N_2O_4S$ requires C, 63.38; H, 9.32; N, 6.16%).

Preparation of *2,6-(Dihydroxy)-6-methyl-1-trideuterio-2-trideuteriomethyl-heptan-4-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (103)

Hydroxy-sulphonylhydrazone (85) (423 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (3.96 mmol) was added, the golden solution warmed to -70° over 20 min and quenched with hexadeuterio-acetone (3.1 mmol). The solution was warmed to -60°, treated with buffer (pH 6.5) and warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-4:1)], p.l.c. [three developments with dichloromethane:diethyl ether (9:1)] and recrystallisation from methanol and water at 25° gave the E,Z-hydroxy-sulphonylhydrazone (85) (340 mg, 80%) identical (t.l.c. and n.m.r.) with an authentic sample; and the *title deuterio-hydroxy-sulphonylhydrazone*

(103) (78 mg, 16%) m.p. 141.5-2.5°, ν_{max} 3300 s, (N-H), 3090 s (O-H), 2230 m (C-^{2}H), 1625 m (C=N), 1602 s (C=C), 1565 m, 1410 s, 1340 s (-SO_2-N<), 1295 m, 1270 m, 1255 m, 1230 m, 1205 m, 1195 m, 1180 m, 1165 and 1155 s (-SO_2-N<), 1105 m, 1065 m, 1050 m, 1040 m, 975 m, 940 m, 930 m, 920 m, 905 s, 890 m, 845 m, 820 m, 765 m, 670 s, and 655 m cm^{-1}, δ 1.12 and 1.35 (6H, 2 s, 6-Me), 1.24 (18H, overlapping d, J 7Hz, $CHMe_2$), 2.37 and 2.48 (4H, 2 s, 3,5-CH_2), 2.92 (1H, septet, J 7Hz, p-$CHMe_2$), 3.25 (1H, br s, OH), 4.25 (2H, septet, J 7Hz, o-$CHMe_2$), and 7.25 (2H, s, aryl-H), m/e 461 ($M^{+\cdot}$ + H), 445 ($M^{+\cdot}$ -Me·), 402 ($M^{+\cdot}$ - C_3H_6O), 396 ($M^{+\cdot}$ - $C_3{}^2H_6O$), 267 (108 d, base), 135, and 129 (Found: C, 62.46; H, 9.33; N, 6.04. $C_{24}H_{36}{}^2H_6N_2O_4S$ requires C, 62.57; N, 6.08%).

Preparation of the Hydroxy-sulphonylhydrazone (102) from the E-Hydroxy-sulphonylhydrazone (85)

E-Hydroxy-sulphonylhydrazone (85) (398 mg) was dissolved in DME (5 ml) and the solution cooled to -76°. n-Butyllithium (5.20 mmol) was added, the solution warmed to -65° over 20 min, quenched with acetone (4.1 mmol), warmed to -60°, treated with glacial acetic acid (0.4 g) and warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-3:1)] and p.l.c. [three developments with dichloromethane:diethyl ether (9:1)] gave the E,Z-hydroxy-sulphonylhydrazone(85) (116 mg, 29%) identical (t.l.c. and n.m.r.) with an authentic sample; and the hydroxy-sulphonylhydrazone (102) (233 mg, 51%) identical (t.l.c. and n.m.r.) with an authentic sample.

An identical sequence applied to the Z-hydroxy-sulphonylhydrazone (85) (400 mg) gave the E,Z-hydroxy-sulphonylhydrazone (85) (173 mg, 43%); and the hydroxy-sulphonylhydrazone (102) (140 mg, 30%) both identical (t.l.c. and n.m.r.) with authentic samples.

Preparation of the α-Methylene-γ-lactone (101f) from the E-hydroxy-sulphonylhydrazone (85)

E-Hydroxy-sulphonylhydrazone (85) (378 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (5.20 mmol) was added, the solution warmed to -3° over 80 min, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (1.0 g)], chromatography on Kieselgel H (14 g) [eluant dichloromethane] and p.l.c. [one development with dichloromethane] gave the α-methylene-γ-lactone (101f) (94 mg, 78%) identical (t.l.c. and n.m.r.) with an authentic sample.

An identical sequence applied to the Z-hydroxy-sulphonylhydrazone (85) (417 mg) gave the α-methylene-γ-lactone (101f) (65 mg, 49%) identical (t.l.c. and n.m.r.) with an authentic sample.

Preparation of 1,2-Epoxydecane

Dec-1-ene (20.0 g) was dissolved in diethyl ether (200 ml). Peracetic acid (0.46 mol, neutralised with sodium acetate) was added dropwise during 20 min, the mixture stirred for 5 d, and extracted with diethyl ether (200 ml). The organic layer was washed with potassium iodide, sodium thiosulphate and water (1:1:8) until the organic phase was non-oxidative, saturated sodium hydrogencarbonate solution and water in sequence. The organic extracts were dried, filtered, and evaporated. Chromatography on Kieselgel H (40 g) [eluant dichloromethane] gave 1,2-epoxydecane (19.85 g, 89%) as an oil, n_D^{25} 1.4261 (lit.,[69] 1.4295 at 20°), ν_{max} 2970 s, 2930 s, 2860 s, 1475 m, 915 m (), 850 m (), and 835 m () cm^{-1}, δ 0.60-1.00 (3H, br, 9-Me), 1.05-2.00 (14H, br, $(CH_2)_7Me$), 2.20-2.40 (1H, m, 2-CH) and 2.45-2.90 (2H, m, 1-CH_2, m/e 156 (M^+).

Preparation of *3-Acetyl-5-(n-octyl) tetrahydrofuran-2-one* (104)

Sodium (0.66 g) was dissolved in ethanol[62], the solution cooled to 0° and ethyl acetoacetate (3.25 g) added. 1,2-Epoxydecane (4.5 g) was added, the solution warmed to 25°, stirred for 5 d, evaporated, and quenched with glacial acetic acid (1.82 g) in ice water (5 g). The excess acid was neutralised with sodium hydrogencarbonate (s). General work up [(B) diethyl ether] and chromatography on Kieselgel H [(i) 35 g, (ii) 30 g] [eluant (i) dichloromethane, (ii) light petroleum-dichloromethane (1:0-0:1)] gave the impure lactone (104) (5.08 g), ca. 75% pure by n.m.r. A sample was purified by p.l.c. [one developemnt with light petroleum:dichloromethane (1:2)] to yield the *lactone* (104) as an oil, ν_{max} 2930 s, 2865 s, 1775 s (O-C=O), 1730 s (C=O), 1470 m, 1367 m, 1235 s, and 1165 s (C-O), δ 0.73-1.05 (3H, br, $\underline{Me}CH_2$), 1.15-2.20 (14H, br, $(\underline{CH}_2)_7$), 2.20-2.30 (2H, m, 4-$\underline{CH}_2$), 2.41 and 2.45 (3H, 2 s, $\underline{Me}C=O$), 3.60-3.90 (1H, m, 3-$\underline{CH}$), and 4.30-4.70 (1H, br, 5-$\underline{CH}$), m/e 240 ($M^{+\cdot}$), 212 ($M^{+\cdot}$-CO), 138, 114, 97, 81, and 55 (base) (Found: C, 69.73; H, 10.19. $C_{14}H_{24}O_3$ requires C, 69.96; H, 10.06%).

Preparation of 5-Hydroxytridecan-2-one (105a)

The impure keto-lactone (104) (4.6 g), concentrated hydrochloric acid (2 ml) and water (11 ml) were heated at 50° for 5 d. Diethyl ether (50 ml) was added and the aqueous phase neutralised and saturated with potassium carbonate. General work up [(B) diethyl ether] and chromatography on Kieselgel H (30 g) [eluant dichloromethane-diethyl ether (1:0-0:1)] gave 5-hydroxytridecan-2-one (105a) (2.06 g, 39% from ethyl acetoacetate) as an oily solid, ν_{max} 3050 m (O-H), 1710 s (C=O), and 1100 s (C-O) cm^{-1}, m/e 214 ($M^{+\cdot}$), 197 ($M^{+\cdot}$ - OH·), 101 ($M^{+\cdot}$ -$^{\wedge}C_8H_{17}$·), 83, and 62. Treatment[63] of the ketone (105a) (105 mg) with 2,4-dinitrophenylhydrazine (103 mg) gave *5-hydroxytridecan-2-one 2,4-dinitrophenylhydrazone* (105b) (168 mg, 87%), m.p. 61.5-3° (from methanol and water at 0°), ν_{max} (CCl_4) 1625 s (C=N), 1600 m

(C=C), 1345 s (C-NO_2), and 1320 m cm^{-1}, δ 0.80-1.06 (3H, br, 12-Me), 1.15-2.00 (16H, br, 4-CH_2, $(CH_2)_7$), 2.10 and 2.17 (3H, 2s, 1-CH_3), 2.65 (2H, ca. t, J 7.5 Hz, 3-CH_2), 3.55-3.90 (1H, br, 5-CH), 7.96-8.50 (3H, m, aryl 5,6-H, HC=N), 9.20 (1H, d, J 2.5 Hz, aryl 3-H), and 10.95 (1H, br, NH), m/e 394 ($M^{+\cdot}$), 377 ($M^{+\cdot}$ - OH), 281 ($M^{+\cdot}$ - $^nC_8H_{17}\cdot$), 196 (base), 83, 71, and 55 (Found: C, 57.72; H, 7.62; N, 14.39. $C_{19}H_{30}N_4O_5$ requires C, 57.85; H, 7.66; N, 14.20%).

Preparation of *3-Methylene-6-(n-octyl) tetrahydropyran-2-one* (107a)

5-Hydroxytridecan-2-one (105a) (214 mg) and 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (298 mg) were dissolved in dry diethyl ether. Activated 4Å molecular sieves (0.5 g) and Amberlite IR-120 (H) resin catalyst were added and the mixture stirred for 30 min. T.l.c. analysis indicated the presence of the assumed hydrazone (106a) (ca. 90%). The solution was filtered, evaporated, the residue was dissolved in toluene (3 x 5 ml) and re-evaporated. The residue was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (4.80 mmol) was added, the yellow solution warmed to -3° over 75 min, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (1.20 g)] gave a crude residue which was dissolved in dichloromethane (10 ml) and stood for 40 min. Chromatography on Kieselgel H (17 g) [eluant light petroleum-diethyl ether (1:0-4:1)] and p.l.c. [six developments with light petroleum:diethyl ether (4:1)] gave the *tetrahydropyran-2-one* (107a) (51 mg, 23%) as an oil, ν_{max} 2960 s, 2928 s, 2858 s, 1726 s (C=O), 1630 m (C=C), 1398 m, 1300 m, 1180 m (C-O), 1165 m (C-O), 1130 m, and 940 m (CH_2=) cm^{-1}, δ 0.70-1.00 (3H, br, $MeCH_2$), 1.05-2.20 (18H, br, $(CH_2)_7$, 5-CH_2), 2.40-2.80 (2H, br, 4-CH_2), 4.04-4.62 (1H, br, 6-CH), 5.40-5.58 (1H, m, CH_2=), and 6.26-6.42 (1H, m, CH_2=), m/e 224 ($M^{+\cdot}$), 179, 111 ($M^{+\cdot}$ - $^nC_8H_{17}\cdot$, base), 83, 55, 43, and 41 (Found: C, 74.82; H, 10.97.

$C_{14}H_{24}O_2$ requires C, 74.95; H, 10.78%).

Preparation of *2,4,6-Tri-iso-propyl-1,α-sultone* (109)

2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (286 mg) in dichloromethane (15 ml) and triethylamine (0.50 g) was stirred for 5 d. Trifluoroacetic acid (1.2 g) was added and after 5 d the mixture was evaporated and chromatographed on Kieselgel H (20 g) to give [eluant petroleum] an oil (2 mg) and [eluant dichloromethane-light petroleum (0:1-4:1)] the *sultone* (109) (77 mg, 28%) m.p. 124-7° (from light petroleum), ν_{max} 1330 s ($-SO_2-O-$), 1190 s ($-SO_2-O-$), 1125 m, 865 m, 825 m, and 800 m cm^{-1}, λ_{max} 266 (ε 680) and 275 nm (670), δ_H 1.33 (12H, t, J 7Hz, $CH\underline{Me}_2$), 1.80 (6H, s, $O-C\underline{Me}_2$), 3.03 (1H, septet, J 7Hz, $o-C\underline{H}Me_2$), 3.60 (1H, septet, J 7Hz, $p-C\underline{H}Me_2$), 7.03 (1H, d, J 1Hz, aryl-H), and 7.34 (1H, d, J 1Hz, aryl-H), δ_C 156.55 (s, 4-C), 145.83 (s, 2-C), 144.84 (s, 6-C), 128.05 (s, 1-C), 125.19 (d, 3-C), 117-02 (d, 5-C), 89.89 (s, 2-C(O-) Me_2), 34.54 (d, $4-\underline{C}HMe_2$), 29.58 (d, $6-\underline{C}HMe_2$), 28.65 [q, $2-C(O-)\underline{Me}_2$], 23.67 (q, $6-CH\underline{Me}_2$), and 23.29 (q, $4-CH\underline{Me}_2$), m/e 282 ($M^{+\cdot}$), 267 [(108d), base], and 175 (Found: 63.81; H, 7.85; S, 11.30; $M^{+\cdot}$, 282.1294. $C_{15}H_{22}O_3S$ requires C, 63.80; H, 7.85; S, 11.35%; $M^{+\cdot}$ 282.1290).

Preparation of 2,4,6-Tri-iso-propylbenzenesulphinic Acid (108a)

Zinc dust (1.34 g) was added during 5 min to a suspension of 2,4,6-tri-iso-propylbenzenesulphonyl chloride[70] (108c) (3.03 g) in boiling water (25 ml). After 5 min the mixture was cooled, the solid filtered off, suspended in water (40 ml), and boiled with sodium carbonate (1.6 g) for 20 min. The suspension was cooled, filtered, and the residue leached with water (2 x 5 ml). The filtrate was washed with dichloromethane (2 x 30 ml), cooled to 0°, and concentrated hydrochloric acid (1.7 ml) in water (50 ml) added. After 30 min the solid was filtered off, and recrystallisation

without warming from aqueous methanol gave 2,4,6-tri-iso-propylbenzenesulphinic acid (108a) (0.89 g, 33%) as white needles, m.p. 84.5-87°(Lit.,[70] 88-90° (lit.,[71] 80-1°), ν_{max} 2500 m br (O-H), 1600 m (C=C), 1570 m, 1075 s, (SO_2H), 1055 s, 1015 s, 940 m, 880 m, 845 m, 820 s, and 654 m cm^{-1}, λ_{max} 273 (ε 1400) and 282 nm (1200), δ 1.10-1.50 (18H, m, $CH\underline{Me}_2$), 2.90 (1H, septet, J 7Hz, p-$C\underline{H}Me_2$), 4.12 (2H, septet, J 7Hz, o-$C\underline{H}Me_2$), 7.10 (2H, s, aryl-H), and 10.00-10.60 (1H, br, O<u>H</u>), m/e 502 (110a), 470 (110b), and 438 (aryl-S-Aryl), 268 ($M^{+\cdot}$), 267 (108d), 251 (108e), 235 (108f, base), 151, 149, and 91. A further recrystallisation gave material with m.p. 87-8° (Found: C, 66.90; H, 9.04. Calc. for $C_{15}H_{24}O_2S$:, C, 67.12; H, 9.01%).

Photolysis of the Sulphinic Acid (108a)

Benzene (10 ml) was deoxygenated with argon for 3 h and 2,4,6-tri-iso-propylbenzenesulphinic acid (108a) (265 mg) and 2,2'-azobis-(2-methylpropionitrile) (340 mg) were added. The solution was deoxygenated for 10 min and photolysed for 3 h. Evaporation and chromatography on Kieselgel H (18g) gave (eluant light petroleum) di-(2,4,6-tri-iso-propylphenyl) disulphide (110b) (14 mg, 6%) m.p. 88-91° (lit.,[73a] 91-2°), ν_{max} (CCl_4) 2965 s, 2930 m, 2872 m, 1600 m (C=C), 1465 m, 1427 m, 1385 m, 1364 m, and 880 m cm^{-1}, δ 1.02 (24H, d, J 7Hz, o-$CH\underline{Me}_2$), 1.33 (12H, d, J 7Hz, p-$CH\underline{Me}_2$), 2.85 (2H, septet, J 7Hz, p-$C\underline{H}Me_2$), 3.58 (4H, septet, J 7Hz, o-$C\underline{H}Me_2$), and 6.90 (4H, s, aryl-H), m/e 470 ($M^{+\cdot}$), 235 [(108f), base], 217, 151, 119, and 117 (Found: C, 76.73; H, 10.01. Calc. for $C_{30}H_{46}S_2$: C, 76.53; H, 9.85%); and [eluant light petroleum-dichloromethane (1:0-0:1)] S-2,4,6-tri-iso-propylphenyl 2,4,6-tri-iso-propylbenzenethiosulphonate (110a) (143 mg, 58%) m.p. 109-111° (from aqueous methanol) (lit.,[73b] 108.5-110°), ν_{max} 1600 m (C=C), 1380 m, 1365 m, 1325 m (-SO_2-), 1144 s (-SO_2-), 880 m, and 650 s cm^{-1}, δ 0.88-1.40 (36H, m, $CH\underline{Me}_2$), 2.90 (2H, 2 overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 3.72 (4H, 2 overlapping septets, o-$C\underline{H}Me_2$), 7.10 and 7.18 (4H, 2s, aryl-H), m/e 502 ($M^{+\cdot}$), 267, 235 [(108f) , base], 234, 233, 151, and

149 (Found: C, 71.58; H, 9.29. Calc. for $C_{30}H_{46}O_2S_2$: C, 71.66; H, 9.22%).

Preparation and Decomposition of 2,4,6-Tri-iso-propylbenzenesulphonyl Iodide (108 g)

Sulphinic acid (108a) (268 mg), sodium hydrogencarbonate (84 mg) and iodine (254 mg) in benzene (5 ml) and water (6 ml) were stirred under nitrogen for 15 min. T.l.c. [light petroleum-dichloromethane (1:1)] indicated a single spot R_f 0.8. The solution was photolysed for 2 h under oxygen until the initial product had completely decomposed. General work up [(B) diethyl ether], chromatography on Kieselgel H (18g) [eluant light petroleum-diethyl ether (1:0-7:3)] and p.l.c. [two developments in light petroleum:diethyl ether (19:1)] gave R_f [0.6, dichloromethane:light petroleum (1:1)] *di-(2,4,6-tri-iso-propylbenzene)sulphonyl sulphone* (110c) (53 mg, 20%) m.p. 117-8° (from aqueous methanol), ν_{max} (CCl_4) 2970 m, 2935 m, 2875 m, 1600 m, 1465 m, 1450 m, 1390 m, 1370 m, 1335 m, 1265 s ($-SO_2-SO_2-$?), 1172 m, 1155 m, 1135 m, and 700 m cm^{-1}, δ 1.30 (36H, 2 overlapping d, J 7Hz, $CH\underline{Me}_2$), 2.94 (2H, septet, J 7Hz, p-$C\underline{H}Me_2$), 4.10 (4H, septet, J 7Hz, o-$C\underline{H}Me_2$), and 7.23 (4H, s, aryl-H), m/e 252, 235, 204, 189 (base), 91, and 64 (Found: C, 67.40; H, 8.80. $C_{30}H_{46}O_4S_2$ requires C, 67.38; H, 8.67%).

Photolysis of the Sulphinic acid (108a) with Triethyl Phosphite

Sulphinic acid (108a) (264 mg), 2,2'-azobis-(2-methylpropionitrile) (340 mg) and triethyl phosphite (0.80 ml) in benzene (10 ml) were photolysed under oxygen for 3.5 h. Chromatography on Kieselgel H (20 g) and repeated p.l.c. [eluant light petroleum-diethyl ether (4:1-3:1)] gave *2,4,6-tri-iso-propylphenyl ethoxy sulphoxide* (108i) (27 mg, 9%) as an oil, ν_{max} 2970 s, 2935 s, 2875 m, 1600 m (C=C), 1465 m, 1390 m, 1130 s ($-SO_2Et$), 1025 s, 885 s, and 730 m cm^{-1}, δ 1.20-1.35 (18H, m, $CH\underline{Me}_2$), 1.40 (3H,

t, J 7Hz, $CH_2\underline{Me}$), 2.94 (1H, septet, J 7Hz, p-$C\underline{H}Me_2$), 3.95-4.45 (4H, m, o-$C\underline{H}Me_2$, $C\underline{H}_2Me$), and 7.20 (2H, s, aryl-H), m/e 296 ($M^{+\cdot}$), 279, 251 (108e), 233 (base), and 149 (Found: C, 68.98; H, 9.59. $C_{17}H_{28}O_2S$ requires C, 68.87; H, 9.52%); the sultone (109) (30 mg, 11%) identical (t.l.c. and n.m.r.) with an authentic sample; and *ethyl 6-(1-hydroxy-1-methylethyl)-2,4-di-iso-propylbenzenesulphonate* (111) (37 mg, 11%) (R_f 0.25, dichloromethane) as an oil, ν_{max} 3525 m (O-H), 2970 s, 2940 s, 2880 m, 1600 m (C=C), 1465 m, 1388 m, 1368 m, 1353 m, 1333 m ($-SO_2-O-$), 1202 m, 1178 s ($-SO_2-O-$), 1002 m, 910 s, 792 m, 778 m, 734 s, 683 m, and 660 m cm^{-1}, δ 1.27 (12H, d, J 8Hz, $CH\underline{Me}_2$), 1.37 (3H, t, J 7Hz, $CH_2\underline{Me}$), 1.77 (6H, s, $OC\underline{Me}_2$), 2.93 (1H, septet, J 8Hz, p-$C\underline{H}Me_2$), 4.10 (1H, septet, J 8Hz, o-$C\underline{H}Me_2$), 4.25 (2H, q, J 7Hz, $C\underline{H}_2Me$), 5.65 (1H, s, O$\underline{H}$), and 7.33 (2H, s, aryl-$\underline{H}$), m/e 313 ($M^{+\cdot}$ - Me·), 310 ($M^{+\cdot}$ - H_2O), 282, 267 (108d, base), and 175 (Found: C, 62.08; H, 8.62. $C_{17}H_{28}O_4S$ requires C, 62.16; H, 8.59%).

Dark Reaction of the Sulphinic Acid (108a) and Triethyl Phosphite

Triethyl phosphite (0.50 g) was added to sulphinic acid (108a) (154 mg) in benzene (5 ml) and the mixture was oxygenated in the dark for 6.5 h. Sulphinic acid (108a) still remained (t.l.c.) thus more triethyl phosphite (0.50 g) was added and the reaction continued for 2 d. Evaporation, chromatography on Kieselgel H (18 g) [eluant diethyl ether] and p.l.c. [two developments in light petroleum-diethyl ether (3:1)] gave the sulphinate (108i) (15 mg, 9%); the sultone (109) (15 mg, 9%); ethyl 2,4,6-tri-iso-propylbenzenesulphonate (108j) (73 mg, 41%) m.p. 59-60° (from petroleum) (lit.[73a] 58-9°), ν_{max} (CCl_4) 2965 m, 2935 m, 2870 m, 1460 m, 1425 m, 1380 m, 1362 m, 1350 m ($-SO_2-O-$), 1333 m, 1193 m, 1180 s ($-SO_2-O-$), 1168 m, 1156 m, 1010 m, 940 m, 912 m, 904 m, 882 m, and 662 m cm^{-1}, δ 1.24 (18H, overlapping d, J 6Hz, $CH\underline{Me}_2$), 1.35 (3H, t, J 7Hz, $\underline{Me}CH_2$), 2.85 (1H, m, p-$C\underline{H}Me_2$), 3.96-4.50 (2H, m, o-$C\underline{H}Me_2$), 4.24 (2H, q, J 7Hz, $C\underline{H}_2Me$), and 7.35

(2H, s, aryl-H), m/e 312 ($M^{+\cdot}$), 283 ($M^{+\cdot}$ - Et·), 251, 218, 202 (base), 187, and 159 (Found: C, 65.14; H, 9.06. Calc.for $C_{17}H_{28}O_3S$: C, 65.35; H, 9.03%); and O,O-*diethyl S-(2,4,6-tri-iso-propylphenyl)thiophosphate* (108k) (27 mg, 13%) as an oil, ν_{max} 2960 s, 2930 m, 2905 m, 2890 m, 2870 m, 1465 m, 1382 m, 1362 m, 1246 m, 1046 s, 1020 s, 962 m, 955 m, and 940 m cm^{-1}, δ 1.24 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.28 (6H, t, J 7Hz, $MeCH_2$), 2.60-3.00 (1H, br, p-$CHMe_2$), 3.75-4.40 (6H, m, CH_2Me, o-$CHMe_2$), and 7.08 (2H, s, aryl-H), m/e 372 ($M^{+\cdot}$), 357 ($M^{+\cdot}$ - Me·), 236, 234, 221, 203 (base), 202, and 149 (Found: C, 61.30; H, 8.98. $C_{19}H_{33}O_3PS$ requires C, 61.26; H, 8.93%).

Preparation of 1,1-Diethoxy-2-phenylthio-ethane[122b,123] (118)

Sodium (1.21 g) was dissolved in ethanol (25 ml) and the solution cooled to 0°. Benzenethiol (5.40 ml) was added dropwise during 5 min. 2-Bromo-1,1-diethoxy-ethane (117) (7.92 ml) was added dropwise during 10 min, the solution warmed to 52° for 70 min, cooled to 25° and filtered. General work up [(B) diethyl ether] and repeated chromatography on Kieselgel H [(a) 30 g, (b) 40 g, (c) 40 g] [eluant light petroleum-dichloromethane (1:0-0:1)] gave the phenylthio-ethane derivative (118) (11.2 g, 97%) as an oil, ν_{max} 2980 s, 2935 m, 2880 m, 1590 m (C=C), 1485 s, 1442 s, 1375 m, 1345 m, 1206 m, 1160 m, 1123 s (C-O), 1090 m, 1040 s (C-O), 1026 m, 1015 m, 1000 m, 740 s (Ph-), and 691 s (Ph-) cm^{-1}, δ 1.16 (6H, t, J 6Hz, $MeCH_2$), 3.10 (2H, d, J 6Hz, SCH_2), 3.64 (4H, dq, J 2, 7Hz, CH_2Me), 4.66 (1H, t, J 6Hz, 1-CH), and 7.08-7.55 (5H, m, aryl-H), m/e 226 ($M^{+\cdot}$), 181 ($M^{+\cdot}$-OEt·), 135, 109 (PhS^+), 103 ($M^{+\cdot}$ - $PhSCH_2$·, base), 75, and 57 (Found: C, 63.52; H, 8.05. Calc. for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.01%).

Preparation of Phenylthio-acetaldehyde (113a)

Acetal (118) (5.35 g), hydrochloric acid (1.5 ml) and water (28.5 ml) were stirred together at 50° for 9 h and cooled to 25°. General work up [(B) diethyl ether] gave the crude aldehyde (113a) (3.2 g, ca. 90% by

n.m.r.). Distillation gave phenylthio-acetaldehyde[122] (113a) (2.69 g, 75%) b.p. 98° at 0.7 mmHg, d_{22} 1.36, ν_{max} 2825 m, 1724 s (C=O), 1588 m (C=C), 1485 s, 1444 s, 1390 m, 1164 m, 1027 m, 742 s (Ph-), and 692 s (Ph-) cm^{-1}, δ 3.60 (2H, d, J 3Hz, $SC\underline{H}_2$), 7.30 (5H, br s, aryl-H), and 9.68 (1H, t, J 3Hz, HCO), m/e 152 ($M^{+\cdot}$, base), 134 ($M^{+\cdot} - H_2O$), 123 ($M^{+\cdot} - CHO\cdot$), 109 (PhS^+), 79, 77 (Ph^+), 65, and 51 (Found: C, 63.24; H, 5.50. Calc. for C_8H_8OS: C, 63.13; H, 5.30%).

A sample of the aldehyde (113a) (110 mg) was reacted[63] with 2,4-dinitrophenylhydrazine (150 mg) to yield phenylthio-ethanal (113a) 2,4-dinitrophenylhydrazone[122a] (175 mg, 73%) m.p. 98.5-110.5°, ν_{max} 3300 s (N-H), 3120 m, 1620 s (C=N), 1595 s (C=C), 1530 s ($C-NO_2$), 1495 m, 1345 s ($C-NO_2$), 1330 s, 1310 s, 1265 s, 1220 m, 1145 m, 1066 m, 1047 m, 835 m, 740 m (Ph-), and 690 m (Ph-) cm^{-1}, δ 3.85 (2H, d, J 6Hz, $SC\underline{H}_2$), 7.20-7.60 (6H, m, Ph-H, HC=N), 7.75 (1H, d, J 9Hz, aryl 6-H), 8.28 (1H, dd, J 3, 9Hz, aryl 5-H), 9.07 (1H, d, J 3Hz, aryl 3-H), and 11.00 (1H, NH), m/e 332 ($M^{+\cdot}$), 298, 223 ($M^{+\cdot} - PhS\cdot$), 196, 123, 110 ($PhSH^+$, base), and 67 (Found: C, 50.46; H, 3.59; N, 16.74. Calc. for $C_{14}H_{12}N_4O_4S$: C, 50.60; H, 3.64; N, 16.86%).

Preparation of *4-Hydroxy-5-phenylthiopentan-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (114a)

Sulphonylhydrazone (82) (360 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (3.12 mmol) was added, the golden solution warmed to -65° over 20 min, quenched with phenylthio-ethanal (113a) (0.30 ml) and the solution warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (13g) [eluant dichloromethane-diethyl ether (1:0-9:1)] and p.l.c. [(i) one development with dichloromethane: diethyl ether (20:1), (ii) four developments with dichloromethane] gave the E,Z-*sulphonylhydrazone* (114a) (124 mg, 24%) as an oily solid, ν_{max} 3480 m br (O-H), 3220 m br (N-H), 3050 m (Ar-H), 2955 s, 2920 s, 2875 s,

1600 m (C=C), 1592 m, 1480 m, 1460 s, 1438 s, 1423 s, 1380 s, 1360 s, 1320 s ($-SO_2-N<$), 1165 and 1150 s ($-SO_2-N<$), 1070 s (C-O), 1038 s, 1030 s, 1023 m, 938 m, 910 m, 880 m, 735 s (Ph-H), 687 s (Ph-H), and 660 s cm^{-1}, δ 1.24 (18H, overlapping d, J 6Hz, $CH\underline{Me}_2$), 1.80 (3H, s, 1-$C\underline{H}_3$), 2.30-2.60 (2H, br, 3-$C\underline{H}_2$), 2.60-3.20 (3H, br, p-$C\underline{H}Me_2$, $SC\underline{H}_2$), 3.70-4.45 (3H, br, o-$C\underline{H}Me_2$ and 4-C<u>H</u>), 7.10-7.60 (5H, br, Ph-<u>H</u>), and 7.16 (2H, s, aryl-<u>H</u>), m/e 490 ($M^{+\cdot}$), 472 ($M^{+\cdot} - H_2O$), 363 $[(M^{+\cdot} - H_2O) - PhS\cdot]$, 251, 204, 189 (base), 95, and 43 (Found: C, 63.65; H, 7.64; N, 5.55. $C_{26}H_{38}N_2O_3S_2$ requires C, 63.64; H, 7.80; N, 5.71%).

Attempted Preparation of 3-Methylene-5-(phenylthiomethyl) tetrahydrofuran-2-one (115a)

Sulphonylhydrazone (82) (338 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.50 mmol) was added, the golden solution warmed to -65° and quenched with the aldehyde (113a) (0.20 ml). The clear solution was recooled to -78° and n-butyllithium (3.12 mmol) added. The orange solution was warmed to -3° over 90 min, the deep red solution recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (1.0 g)] and chromatography on Kieselgel H (17 g)[eluant light petroleum-diethyl ether (1:0-0:1)] gave no detectable methylene lactone (115a).

A similar sequence performed with the thio-hydrazone (114a) (132 mg) and n-butyllithium (1.17 mmol) gave no detectable methylene lactone (115a).

Preparation of 1,1-Diethoxy-2-phenylseleno-ethane (119)

Diphenyl diselenide (6.00 g) was suspended in ethanol (70 ml) at 0°, sodium borohydride (1.60 g) was added slowly over 30 min, the clear solution warmed to 25°, recooled to 0° and the bromo-acetal (117) (5.80 ml) added. The solution was warmed to 58° for 4 h, filtered, and general work

up [(B) dichloromethane] gave the crude acetal (119). Repeated chromatography on Kieselgel H [(i) 35 g, (ii) and (iii) 30 g] [eluant light petroleum-dichloromethane (1:0-0:1)] gave the seleno-acetal[81, 124] (119) (10.0 g, 95%) as a liquid, ν_{max} 2980 s, 2932 s, 2900 s, 2880 s, 1583 m (C=C), 1482 s, 1440 s, 1374 m, 1345 m, 1196 m, 1157 m, 1120 s (C-O), 1056 s (C-O), 1023 s, 1002 s, 981 m, 735 s (Ph-H), and 690 m (Ph-H), δ 1.20 (6H, t, J 7Hz, $\underline{Me}CH_2$), 3.10 (2H, d, J 5.5 Hz, $SeCH_2$), 3.60 (4H, dq, J 2.5, 7Hz, CH_2Me), 4.70 (1H, t, J 5.5Hz, 1-C$\underline{H}$), and 7.14-7.70 (5H, m, aryl-$\underline{H}$), m/e 274/272 ($M^{+\cdot}$), 229/227 ($M^{+\cdot}$ - OEt·), 183/181, 157/155 ($PhSe^{+}$), 103 ($M^{+\cdot}$ - $PhSeCH_2$·, base), and 75 (Found: C, 52.97; H, 6.90. Calc. for $C_{12}H_{18}O_2Se$, C, 52.75; H, 6.64%).

Preparation of Phenylseleno-acetaldehyde (113b)

Seleno-acetal (119) (5.05 g), hydrochloric acid (2.5 ml) and water (47.5 ml) were stirred at 50° for 4½ h and cooled to 25°. General work up [(A) diethyl ether, sodium hydrogencarbonate] and distillation gave phenylseleno-acetaldehyde[81] (113b) (2.92 g, 79%) b.p. 84° at 0·2 mmHg, d_{22} 1.5, ν_{max} 1710 s (C=O), 1580 m (C=C), 1480 m, 1440 m, 1150 m, 1025 m, 740 m and 690 m (Ph-H), and 670 m cm^{-1}, δ 3.60 (2H, d, J 4Hz, $SeCH_2$), 7.40-8.00 (5H, m, Ph-$\underline{H}$), and 9.80 (1H, t, J 4Hz, C$\underline{H}$O), m/e 200/198 ($M^{+\cdot}$, base), 171/169 ($M^{+\cdot}$ - CHO·), 157/155 ($PhSe^{+}$), 91, 77 (Ph^{+}) and 51, (Found: C, 48.13; H, 4.18. Calc. for C_8H_8OSe: C, 48.26; H, 4.05%).

The aldehyde (113b) (180 mg) and 2,4-dinitrophenylhydrazine (198 mg) were reacted[63] to form *phenylseleno-ethanal* (113b) *2,4-dinitrophenylhydrazone* (261 mg, 77%) m.p. 151-2°, ν_{max} 3300 m (N-H), 1620 s (C=N), 1596 s (C=C), 1513 s ($C-NO_2$), 1497 s, 1330 s ($C-NO_2$), 1310 s, 1275 m, 1265 m, 1220 m, and 740 m (Ph-H) cm^{-1}, δ 3.74 (2H, d, J 6Hz, $SeCH_2$), 7.10-7.90 (7H, m, Ph-$\underline{H}$, aryl 6-$\underline{H}$, $\underline{H}$C=N), 8.14 (1H, dd, J 2.5, 10 Hz, aryl 5-$\underline{H}$), 9.16 (1H, d, J 2.5 Hz, aryl 3-$\underline{H}$), and 10.90-11.20 (1H, br, N$\underline{H}$), m/e 380/378 ($M^{+\cdot}$), 314/

312, 266/254, 223 ($M^{+\cdot}$ - PhSe·, base), 157/155 ($PhSe^{+}$), 75, and 55 (Found: C, 44.61; H, 3.15; N, 14.75. $C_{14}H_{12}N_4O_4Se$ requires C, 44.34; H, 3.19; N, 14.77%).

Preparation of *4-Hydroxy-5-phenylselenopentan-2-one 2,4,6-Tri-isopropylbenzenesulphonylhydrazone* (114b)

Sulphonylhydrazone (82) (338 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.52 mmol) was added, the golden solution warmed to -65° over 15 min and recooled to -78°. The selenoaldehyde (113b) (0.25 ml) was added, the solution warmed to -68°, quenched with glacial acetic acid (0.18 ml) and warmed to 25°. General work up [(A) diethyl ether], chromatography on Kieselgel H (18 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] and p.l.c. [two developemnts in dichloromethane:diethyl ether (9:1)] gave the E,Z-*hydroxy-sulphonylhydrazone* (114b) (319 mg, 59%) as an unstable oil, ν_{max} 3490 m br (O-H), 3205 m br (N-H), 3070 and 3058 m (aryl-H), 2960 s, 2930 s, 2890 s, 2870 s, 1600 s (C=C), 1580 m, 1565 m, 1478 s, 1460 s, 1438 s, 1425 s, 1382 s, 1362 s, 1350 m, 1323 s ($-SO_2-N<$), 1300 s, 1256 m, 1216 m, 1194 m, 1170 and 1153 s ($-SO_2-N<$), 1135 s, 1105 s (C-O), 1072 s, 1060 s, 1040 s, 1022 s, 1012 m, 1000 m, 940 s, 932 s, 923 s, 910 s, 882 s, 865 m, 842 m, 735 and 690 s (Ph-H), 668 s, 663 s, and 652 s cm^{-1}, δ 1.28 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.80 and 1.92 (3H, 2s, 1-$C\underline{H}_3$), 2.36-2.68 (2H, br, 3-$C\underline{H}_2$), 2.80-3.30 (4H, br, $\underline{p}$-$C\underline{H}Me_2$, $SeC\underline{H}_2$, $O\underline{H}$), 3.80-4.60 (3H, br, $\underline{o}$-$C\underline{H}Me_2$, 4-$C\underline{H}$), and 7.20-7.80 (8H, m, aryl-$\underline{H}$, $N\underline{H}$), m/e 538/536 ($M^{+\cdot}$, weak), 392/390, 360/358, 314/312, 236, 221, 204, 189 (base), 161 (Found: C, 57.89;, H, 7.33; N, 4.89. $C_{26}H_{38}N_2O_3SSe$ requires C, 58.09; H, 7.12; N, 5.21%).

Attemted preparation of 3-Methylene-5-(phenylselenomethyl)tetrahydrofuran-2-one (115b)

Sulphonylhydrazone (82) (352 mg) was dissolved in DME (5 ml) and the

solution cooled to -78°. n-Butyllithium (2.66 mmol) was added, the golden solution warmed to -65° over 25 min and recooled to -70°. The seleno-aldehyde (113b) (0.25 ml) was added and the clear solution recooled to -78°. n-Butyllithium (1.82 mmol) was added, the golden solution warmed to -3° over 90 min, the red solution recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (0.62 g)], chromatography on Kieselgel H (18g) [eluant light petroleum-diethyl ether (1:0-0:1)] and p.l.c. [two developments in dichloromethane] gave 5-(n-butylselenomethyl)-3-methylenetetrahydrofuran-2-one (115d) (3 mg, ca. 1%) as an oil, ν_{max} ($CHCl_3$) 1765 s (C=O), 1335 m, 1280 m, 1155 m, 1120 m, 995 m, and 945 m (CH_2=) cm^{-1}, δ (weak) 0.80-1.70 (7H, br, ^{n}Pr), 2.50-3.10 (6H, br, CH_2Se, 4-CH_2), 4.50-5.00 (1H, br, 5-CH), 5.70 (1H, ca. t, HC=), and 6.30 (1H, ca. t, HC=), m/e 248/246 ($M^{+\cdot}$) (Found: $M^{+\cdot}$ 248.0300. $C_{10}H_{16}O_2{}^{80}Se$ requires $M^{+\cdot}$ 248.0315) and benzoic acid (21 mg, 17%) m.p. 121-2° (lit.,[64] 122°), identical [i.r., n.m.r. and m/e 122 ($M^{+\cdot}$, base)] with authentic material.

The sequence was repeated with the sulphonylhydrazone (82) (341 mg) except that the solution was warmed to -30° over 1 h and maintained between -30° and -25° for 30 min before recooling to -78° and quenching with carbon dioxide gas. A similar work up gave the selenolactone (115d) (5 mg, ca. 2%), identical (t.l.c., i.r., and n.m.r.) to before; and benzoic acid (21 mg, 17%).

Preparation of *1,1-Diethoxy-2-methylseleno-ethane* (121)

Dimethyl diselenide[83] (120) (4.00 g) was dissolved in ethanol (50 ml) at 0°. Sodium borohydride (1.61 g) was added slowly over 30 min, the clear solution warmed to 25° and recooled to 0°. The bromo-acetal (117) (6.40 ml) was added, the solution warmed to 50° for 3½ h, and t.l.c. analysis indicated incomplete reaction. Further selenium reagent [prepared from dimethyl

diselenide (4.00 g) and sodium borohydride (1.60 g) in ethanol (30 ml) at 0°] was added, the solution cooled to 25° and filtered. General work up [(A) diethyl ether] and repeated chromatography on Kieselgel H [(i) 30 g, (ii) 35 g] [eluant light petroleum-dichloromethane (1:0-0:1)] gave the *seleno-acetal* (121) (7.26 g, 81%) as a liquid, ν_{max} 2980 s, 2930 s, 2900 s, 2880 s, 2830 m, 1448 m, 1425 m, 1410 m, 1392 m, 1375 m, 1346 m, 1202 m, 1160 ms, 1125, 1100 and 1052 s (C-O), 1004 s, and 745 m cm^{-1}, δ 1.22 (6H, t, J 7Hz, $\underline{Me}CH_2$), 2.10 (3H, s, Se$\underline{Me}$), 2.72 (2H, d, J 6Hz, $\underline{CH}_2$ Se), 3.68 (4H, dq, J 2.5, 7Hz, $C\underline{H}_2Me$), and 4.72 (1H, t, J 6Hz, 1-$\underline{CH}$), m/e 212/210 ($M^{+\cdot}$), 167/165 ($M^{+\cdot}$ - EtO·), 139/137, 103 (base), 75, and 48 (Found: C, 39.63; H, 7.66. $C_7H_{16}O_2Se$ requires C, 39.81; H, 7.64%).

Attempted Preparation of Methylseleno-acetaldehyde (113c)

Seleno-acetal (121) (5.90 g), concentrated hydrochloric acid (5 ml), water (95 ml) and THF (50 ml) were stirred together at 40° for 4 d, and the solution cooled to 25°. General work up [(A) dichloromethane, sodium hydrogencarbonate solution] and distillation gave the dimethylseleno-acetaldehyde (122a) (0.55 g, 17%) b.p. 70-2° at 0.45 mmHg, ν_{max} 2925 m, 2820 m, 1695 s (C=O), 1420 m, 1370 m, 1277 m, 1204 m, 1095 m, 1050 m, 1018 m, and 910 m cm^{-1}, δ 2.04 (6H, s, $\underline{Me}$Se), 4.40 (1H, d, J 4Hz, $\underline{H}$CSe), and 9.30 (1H, d, J 4Hz, $\underline{H}$C=O), m/e 232/230/228 ($M^{+\cdot}$, base), 203/201/199 ($M^{+\cdot}$ - CHO·), 175/173/171, 137/135 [$M^{+\cdot}$ - (MeSe·)], 109/107, and 93/91; and the crude seleno-acetaldehyde (113c) isolated from the cold trap.

The diseleno-aldehyde (122a) (133mg) was reacted[63] with 2,4-dinitro-phenylhydrazine (115 mg) to yield *dimethylseleno-acetaldehyde 2,4-dinitro phenylhydrazone* (122b) (174 mg, 73%) m.p. 133-4°, ν_{max} (CCl_4) 1622 s (C=N), 1598 m (C=C), 1508 m ($C-NO_2$), 1432 m, 1340 s and 1327 s ($C-NO_2$), 1309 m, 1276 m, and 1140 m cm^{-1}, δ 2.12 (6H, s, $\underline{Me}$Se), 4.72 (1H, d, J 7Hz, SeC$\underline{H}$), 7.40-8.70 (3H, m, HC=N, aryl 5,6-$\underline{H}$), 9.24 (1H, d, J 3Hz,

aryl 3-H), and 11.35 (1H, br, NH), m/e 412/410/408 (M^+, weak), 395/393/391 (M^+ - OH·), 317/315 (M^+ - MeSe·), 301/299 [M^+ - (MeSeO·?), base], 223, 190, and 95/93 ($MeSe^+$) (Found: C, 29.43; H, 2.78; N, 13.65. $C_{10}H_{12}N_4O_4Se_2$ requires C, 29.28; H, 2.95; N, 13.66%).

The crude aldehyde (113c) was purified by chromatography on Kieselgel H (24 g) [eluant light petroleum-dichloromethane (1:0-0:1)] to yield methylseleno-acetaldehyde (113c) (1.03 g, 27%) as an oil, ν_{max} 2935 m, 2825 m, 2720 m, 1710 s (C=O), 1425 m, 1410 m, 1385 m, 1282 m, 1158 s, 1030 m, 970 m, 910 m, and 833 m cm^{-1}, δ 2.00 (3H, s, MeSe), 3.25 (2H, d, J 4Hz, $SeCH_2$) and 9.60 (1H, t, J 4Hz, HC=O), m/e 138/136 (M^+), 109/107 (M^+-CHO), 95/93 ($MeSe^+$), 83, 57, and 43. A sample of the aldehyde (113c) (70 mg) was reacted[63] with 2,4-dinitrophenylhydrazine (105 mg) to yield *methylseleno-acetaldehyde (113c) 2,4-dinitrophenylhydrazone* (102 mg, 63%) m.p. 134-5°, ν_{max} (CCl_4) 1623 s (C=N), 1598 m (C=C), 1510 m (C-NO_2), 1340 and 1330 m (C-NO_2), 1312 m, and 1140 m cm^{-1}, δ 2.10 (3H, s, MeSe), 3.50 (2H, d, J 7Hz, CH_2Se), 7.50-8.60 (3H, m, HC=N, aryl 5,6-H), 9.24 (1H, d, J 2.5 Hz, aryl 3-H), and 11.30 (1H, br, NH), m/e 318/316 (M^+), 223 (M^+ - MeSe·, base) 196, 176, and 122 (Found: C, 34.10; H, 3.06; N, 17.90. $C_9H_{10}N_4O_4Se$ requires: C, 34.08; H, 3.18; N, 17.67%).

Attempted Preparation of 3-Methylene-5-(methylselenomethyl)tetrahydrofuran-2-one (115c)

Sulphonylhydrazone (82) (340 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. Methyllithium (3.27 mmol) was added, the yellow solution was warmed to -65° over 15 min and recooled to -78°. The seleno-aldehyde (113c) (386 mg) in DME (1 ml) was added, and the solution treated with further methyllithium (3.82 mmol). The solution was warmed to -35° over 70 min, then to -3° over 30 min, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C)

dichloromethane, trifluoroacetic acid (1.10 g)] gave a crude residue. N.m.r. analysis indicated the absence of any significant methylene lactone or selenomethyl compounds.

Reaction of the Dianion (83) with Diphenylketene

Sulphonylhydrazone (82) (335 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.19 mmol) was added, the golden solution warmed to -65° over 20 min and recooled to -78°. Diphenylketene[64] (123) (0.35 ml) was added, the suspension warmed to -66° over 10 min, quenched with glacial acetic acid (0.20 ml) in water (1 ml), and warmed to 25°. General work up [(A) diethyl ether], chromatography on Kieselgel H (20 g) [eluant (i) light petroleum-dichloromethane (1:0-0:1) (ii) dichloromethane-diethyl ether (1:0-0:1)] and p.l.c. [one development with dichloromethane] gave *1,1-diphenyl-2-(diphenylacetoxy) pent-1-ene-4-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone* (126) (181 mg, 25%) m.p. 165-6° (from dichloromethane and diethyl ether), ν_{max} (CCl_4) 3065, and 3035 m, (aryl-H), 2965 s, 2930 m, 2870 m, 1760 s (C=O), 1600 m (C=C), 1497 m, 1465 m, 1457 m, 1447 m, 1430 m, 1385 m, 1366 m, 1333 m, ($-SO_2-N<$), 1260 m, 1195 m, 1168 and 1155 s ($-SO_2-N<$), 1115 s (C-O), 1072 m, 1060 m, 1040 m, 1034 m, 963 m, 940 m, 910 m, 882 m, 696 s (aryl-H), and 660 m, cm^{-1}, δ 1.21 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.55 (3H, s, 5-$C\underline{H}_3$), 2.90 (1H, ca. septet, p-$C\underline{H}Me_2$), 3.30 (2H, s, 3-$C\underline{H}_2$), 4.30 (2H, ca. septet, o-$C\underline{H}Me_2$), 4.94 (1H, s), and 7.00-7.40 (23H, br , aryl-H, NH), m/e 726 (M^+, weak), 236, 234, 221, 189, 167 (base), and 165 (Found: C, 75.97; H, 6.89; N, 3.72. $C_{46}H_{50}N_2O_4S$ requires: C, 76,00; H, 6.93; N, 3.85%).

Reaction of the Dianion of the Sulphonylhydrazone (65) with Trimethylsilylketene

Sulphonylhydrazone (65) (713 mg) was dissolved in DME (5 ml) and the solution was cooled to -78°. sec-Butyllithium (2.26 mmol) was added,

the golden solution warmed to -65° over 30 min and recooled to -78°. Freshly distilled trimethylsilylketene[87] (124) (132 mg) in DME (1 ml) was added during 30 s, the yellow solution warmed to 0° over 150 min, recooled to -10°, quenched with deuterium oxide (0.50 ml) and warmed to 25°. General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) [eluant light petroleum-dichloromethane (1:0-1:1)] gave 5α-cholest-n-ene (n = 2,3) (67) (151 mg, 38%) identical (t.l.c., n.m.r. and mass spectra) [m/e 370 ($M^{+\cdot}$)] with a previous sample and the sulphonylhydrazone (65) (427 mg, 60%) identical (t.l.c., n.m.r., and mass spectra) with the starting material.

Preparation of *5-Endo-hydroxy-5-exo-(2-oxopropyl) bicyclo[2.2.1]hept-2-ene 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (128a)

Sulphonylhydrazone (82) (323 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.75 mmol) was added, the golden solution warmed to -68° over 15 min, and recooled to -78°. Bicyclo[2.2.1] hept-2-en-5-one[88] (0.20 ml) was added, the solution warmed to -65°, quenched with glacial acetic acid (0.25 ml) and warmed to 25°. General work up [(A) diethyl ether] and chromatography on Kieselgel H (17g) [eluant diethyl ether-light petroleum (0:1-1:3)] gave (A) the crude Z-hydrazone (128a) (323 mg) and (B) the crude E-hydrazone (128a) (152 mg). Purification of (B) by p.l.c. [two developments with dichloromethane:diethyl ether (3:1)] and recrystallisation from ethanol and water gave mainly the E-*sulphonylhydrazone* (128a) (72 mg, 17%) m.p. 120-4°, ν_{max} 3550 s (O-H), 3265 s (N-H), 1604 s (C=C), 1335 m ($-SO_2-N<$), 1318 m, 1258 m, 1168 and 1158 s ($-SO_2-N<$), 1147 s, 1125 m, 1108 m, 1085 m, 1075 m, 1065 m, 722 m, 674 m, and 660 m cm^{-1}, δ 1.25 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.30-1.70 (4H, m, 6,7-CH_2), 1.90 (3H, s, 3'-CH_3), 2.45-2.80 (2H, br, 1,4-CH), 2.60 (2H, s, 1'-CH_2), 2.90 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.28 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 5.95-6.20 (1H, m, HC=), 6.30-6.50 (1H, m, HC=),

7.15 (2H, s, aryl-H), and 7.50 (1H, br, NH), m/e 446 ($M^{+\cdot}$), 267, 204, 189 (base), 161, and 66 ($C_5H_6^+$) (Found: C, 67.40; H, 8.74; N, 6.29. $C_{25}H_{38}N_2O_3S$ requires C, 67.23; H, 8.57; N, 6.27%). Double recrystallisation of crude (A) from methanol and water gave mainly the Z-*sulphonylhydrazone* (128a) (165 mg, 39%), δ 1.30 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.30-3.40 (12H, br), 4.25 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 6.10 (1H, br, HC=), 6.30 (1H, br, HC=), and 7.20 (2H, s, aryl-H).

Preparation of *5-exo-(2-Deuterioprop-2-enyl)-5-endo-hydroxybicyclo[2.2.1]hept-2-ene* (130a)

Acetone sulphonylhydrazone (82) (331 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.95 mmol) was added, the yellow solution warmed to -66° over 25 min and recooled to -78°. Bicyclo [2.2.1]hept-2-en-5-one[88] (0.21 ml) was added, the solution was warmed to -66° over 5 min and recooled to -78°. n-Butyllithium (3.90 mmol) was added, the yellow solution warmed to -3° over 130 min, recooled to -10°, quenched with deuterium oxide (0.60 ml) and warmed to 25°. General work up [(B) dichloromethane] and repeated chromatography on Kieselgel H (4 x 25 g) [eluant light petroleum-diethyl ether (1:0-4:1)] gave the *deuterio-olefin* (130a) (104 mg,70%) as an oil, ν_{max} 3450 m (O-H), 3075 (CH_2=), 2970 s, 2878 m, 1618 m (C=C), 1432 m, 1354 m, 1335 s (O-H), 1275 m, 1255 m, 1245 m, 1200 m, 1185 m, 1172 m, 1120 s, 1105 m, 1087 m, 1078 m, 1055 s (C-O), 956 m (CH_2=), 910 s, and 720 s (CH=CH) cm^{-1}, δ 1.50 (2H, br s, 7-CH_2), 1.72 (2H, m, 6-CH_2) 2.50 (2H, br s, 1,4-CH), 2.70-3.00 (2H, m, 1'-CH_2), 5.00-5.30 (2H, m, CH_2=), and 6.10-6.56 (2H, 2m, 2,3-CH), m/e 151 ($M^{+\cdot}$), 109 ($M^{+\cdot}-C_3H_4^2H_1\cdot$, base), 81, 79, and 66 ($C_5H_6^+$), 91% mono-deuteriated (Found: C, 79.37; H, 10.18. $C_{10}H_{13}{}^2H_1O$ requires C, 79.42%).

Preparation of *1-S(R),4-S(R)-Bicyclo[2.2.1]hept-2-ene-5-R(S)-spiro-5,3-methylenetetrahydrofuran-2-one* (131a)

Sulphonylhydrazone (82) (677 mg) was dissolved in DME (8 ml) and the solution cooled to -78°. n-Butyllithium (4.42 mmol) was added, the golden solution warmed to -68° over 25° and recooled to -72°. Bicyclo[2.2.1]hept-2-en-5-one[88] (0.40 ml) was added, the solution stirred for 10 min and recooled to -78°. n-Butyllithium (4.55 mmol) was added, the orange/red solution warmed to -3° over 85 min, recooled to -78°, quenched with carbon dioxide gas, warmed to 25° and evaporated. The residue was extracted with water (100 ml) and dichloromethane (80 ml), the aqueous layer separated, re-extracted with dichloromethane (2 x 60 ml), saturated with sodium chloride(s), filtered, diluted to 122 ml and divided into fraction (A) (64 ml) and fraction (B) (58 ml). Fraction (A) was acidified with glacial acetic acid (0.351 g) and stirred at 25° for 3 d. General work up [(B) dichloromethane, diethyl ether] gave a crude residue. T.l.c. analysis indicated ca. 20% conversion of the intermediate hydroxy-acid to the lactone (131a). The residue was dissolved in dichloromethane (10 ml), acidified with glacial acetic acid (2 drops) and stirred at 25°. Evaporation and chromatography on Kieselgel H (16g) [eluant dichloromethane] and p.l.c. [one development with light petroleum:diethyl ether (1:1)] gave the *bicyclo-spirolactone* (131a) (113 mg, 61%) as an oil, ν_{max} 2970 m, 1765 s (C=O), 1670 m (C=C), 1290 m, 1273 m (C-O), 1215 m, 1165 m, 1138 m, 1124 m, 1093 m, 1028 m, 966 m, 938 m (CH_2=), and 718 m (HC=CH) cm^{-1}, δ_H 1.20-2.00 (4H, m, 6-CH_2, 7-CH_2), 2.70 (1H, s, 1-CH), 2.90 (1H, s, 4-CH), 2.95-3.20 (2H, m, 4'-CH_2), 5.60 (1H, t, J 1Hz, CH_2=), and 6.10-6.50 (3H, m, CH_2=, 2,3-H), δ_C 41.2 (m, 11-C), 42.9 (m, 10-C), 43.2 (d, 9-C), 48.9 (d, 6-C), 52.6 (m, 4-C), 89.7 (s, 5-C), 121.4 (m, CH_2=), 133.3 (d, 8-C), 135.8 (s, 3-C), 138.4 (d, 7-C), and 170.2 (s, 2-C), m/e 176 ($M^{+\cdot}$), 111, 68, 67, 66 ($C_5H_6^+$ base) and 40 (Found: C, 74.85; H, 7.07. $C_{11}H_{12}O_2$ requires C, 74.98; H, 6.86%).

Preparation of *3,5-Dimethylenetetrahydrofuran-2-one* (116)

Spirolactone (131a) (58 mg) was suspended on glass wool and subjected to flash-vacuum pyrolysis under the following conditions: substrate temperature, -78° to 55° over 6 h; furnace temperature, 550°; operating pressure, 10^{-4} mmHg. Extraction of the cold finger with dichloromethane and evaporation at 0° gave the *dimethylene lactone* (116) (30 mg, 83%) as a volatile oil, ν_{max} 1795 s (C=O), 1765 m, 1682 and 1670 s (C=C-O), 1403 m, 1279 s (C-O), 1262 m, 1232 m, 1085 s (C-O), 975 m (CH_2=), 877 m, and 840 m cm^{-1}, λ_{max} 249 nm (ε 1900), δ 3.44-3.68 (2H, m, 4-C$\underline{H}_2$), 4.34 (1H, q, J 2Hz, 5-C=C$\underline{H}_2$), 4.76 (1H, q, J 2Hz, 5-C=C$\underline{H}_2$), 5.68 (1H, t, J 2.5Hz, 3-C=C$\underline{H}_2$), and 6.28 (1H, t, J 3.0 Hz, 3-C=C$\underline{H}_2$), m/e 110 ($M^{+\cdot}$), 68 [$M^{+\cdot}$ - $(C_2H_2O)\cdot$, base], and 40 [$M^{+\cdot}$-$(C_3H_2O_2)\cdot$] only (Found: C, 65.28; H, 5.76; $M^{+\cdot}$, 110.0368. $C_6H_6O_2$ requires C, 65.45; H, 5.49; $M^{+\cdot}$, 110.0368).

Preparation of *1*-S(R),*4*-S(R)-*Bicyclo*[*2.2.1*]*hept-2-ene-5*-R(S)-*spiro-5*-(Z-*3-pentylidene)tetrahydrofuran-2-one* (131b)

Sulphonylhydrazone (244) (417 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.60 mmol) was added, the solution warmed to -66° over 15 min and recooled to -78°. Bicyclo[2.2.1]hept-2-en-5-one[88] (0.20 ml) was added, the solution warmed to -66° over 7 min and recooled to -78°. n-Butyllithium (3.90 mmol) was added, the solution warmed to -3° over 150 min, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, glacial acetic acid (0.51 g)], stirring the residue in dichloromethane (10 ml) for 2 d, chromatography on Kieselgel H (16g) [eluant dichloromethane] and p.l.c. [one development with light petroleum:diethyl ether (3:7)] gave the *alkylmethylene lactone* (131b) (41 mg, 16%) as an oil, ν_{max} 2960 s, 2930 s, 2860 s, 1755 s (C=O), 1675 m (C=C), 1462 m, 1442 m, 1370 m, 1337 m, 1318 m, 1265 m, 1235 m, 1218 s (C-O), 1176 m, 1137 s, 1127 m, 1104 m, 1085 m,

1063 m, 1026 s (C-O), 1008 m, 965 m, and 712 m cm^{-1}, δ 0.80-1.85 (13H, br), 2.30-3.30 (6H, m, allylic-H), and 5.80-6.50 (3H, m, HC=), m/e 246 ($M^{+\cdot}$), 181 ($M^{+\cdot}-C_5H_5^{\cdot}$; base), 180 ($M^{+\cdot} - C_5H_6$), 137, 95, and 66 ($C_5H_6^+$) (Found: C, 77.93; H, 8.98. $C_{16}H_{22}O_2$ requires C, 78.01; H, 9.00%).

Attempted Preparation of the Deuterio-olefin (130b)

Sulphonylhydrazone (244) (405 mg) was dissolved in DME (5 ml) and the solution cooled to -74°. n-Butyllithium (2.60 mmol) was added, the solution warmed to -67° over 13 min and recooled to -70°. Bicyclo[2.2.1]hept-2-en-5-one[88] (0.20 ml) was added, the solution warmed to -66° over 20 min, recooled to -78° and TMEDA (1.0 ml) added. n-Butyllithium (3.90 mmol) was added, the solution was warmed to 0° over 2 h, recooled to -50°, quenched with deuterium oxide (0.50 ml) and warmed to 25°. General work up [(B) dichloromethane] and chromatography on Kieselgel H (16 g) [eluant dichloromethane] gave the crude olefin (130b), m/e 221 ($M^{+\cdot}$), 220, 109 (base), and 65, 70% mono-deuteriated.

Preparation of E,Z-*Hex-5-en-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (142)

Sulphonylhydrazone (82) (1.342 g) was dissolved in DME (14 ml) and the solution cooled to -78°. n-Butyllithium (8.78 mmol) was added, the golden solution warmed to -67° over 25 min and recooled to -78°. Allyl bromide (0.70 ml) was added, the suspension warmed to -65° over 1 h, stirred for 30 min and warmed to -60° over 30 min. Glacial acetic acid (0.66 ml) was added and the solution warmed to 25°. General work up [(A) diethyl ether] and recrystallisation from ethanol and water at 25° gave the *sulphonylhydrazone* (142) (1.405 g, 94%) m.p. 113-5°, ν_{max} 3265 s (N-H), 1605 m (C=C) 1330 s ($-SO_2-N<$), 1305 m, 1262 m, 1170 and 1158 s ($-SO_2-N<$), 1107 m, 938 m, 913 m ($CH=CH_2$), 884 m, and 666 s cm^{-1}, δ 1.28 (18H, overlapping d, J 7Hz,

$CH\underline{Me}_2$), 1.78 and 1.92 (3H, 2s, 1-$C\underline{H}_3$), 2.16-2.32 (4H, br, 3,4-$C\underline{H}_2$), 2.95 (1H, septet, J 7Hz, p-$C\underline{H}Me_2$), 4.30 (2H, septet, J 6.5 Hz, o-$C\underline{H}Me_2$), 4.60-5.80 (3H, m, $C\underline{H}=C\underline{H}_2$), 7.20 (2H, s, aryl-H), and 7.70 (1H, br, NH), E:Z ca. 85:15 by n.m.r., m/e 379 (M^+ + H), 236, 221, 204, 189 (base), 161 and 67 (Found: C, 66.52; H, 9.15; N, 7.42. $C_{21}H_{34}N_2O_2S$ requires C, 66.63; H, 9.05; N, 7.40%).

Preparation of E,Z-*3-(2-Hydroxyprop-2-yl) hex-5-en-2-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (141)

Sulphonylhydrazone (82) (680 mg) was dissolved in DME (7 ml) and the solution cooled to -78°. n-Butyllithium (4.86 mmol) was added, the solution warmed to -68° over 20 min and recooled to -78°. Allyl bromide (0.25 ml) was added, the solution warmed to -65° over 1 h, stirred at -65° for 20 min and recooled to -78°. n-Butyllithium (3.51 mmol) was added, the solution warmed to -68° over 20 min, recooled to -78° and quenched with acetone (0.50 ml). The suspension was warmed to -50°, quenched with glacial acetic acid (0.40 ml) in water (1 ml) and warmed to 25°. General work up [(A) diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] and p.l.c. [two developments with dichloromethane: diethyl ether (9:1)] gave the *hydroxy-sulphonylhydrazone* (141) (772 mg, 88%) m.p. 129-30° (from ethanol and water as mainly the E-isomer), ν_{max} 3530 m (O-H), 3260 m, (N-H), 1605 m (C=C), 1317 m ($-SO_2-N<$), 1300 m, 1167 and 1150 s ($-SO_2-N<$), 1105 m, 1040 m, 940 m, 910 m ($CH_2=$), 900 m, and 667 m cm^{-1}, δ 1.08 and 1.14 (6H, 2s, MeCO), 1.30 (18H, overlapping d, $CH\underline{Me}_2$), 1.80 (3H, s, 1-$C\underline{H}_3$), 2.28 (2H, d, J 4Hz, 4-$C\underline{H}_2$), 2.40 (1H, s, OH), 2.60-3.10 (1H, br, p-$C\underline{H}Me_2$), 3.90-4.60 (3H, br, o-$C\underline{H}Me_2$, 3-CH), 4.60-5.90 (3H, m, $C\underline{H}_2=C\underline{H}$), 7.28 (2H, s, aryl-H), and 7.68 (1H, br, NH), m/e 436 (M^+) 421 (M^+ - Me·), 267, 204, 189 (base), 161, and 111 (Found: C, 66.25; H, 9.37; N, 6.44. $C_{24}H_{40}N_2O_3S$ requires C, 66.02; H, 9.23; N, 6.41%).

Preparation of E-*2-Methylhexa-2,5-dienoic acid* (139)

Sulphonylhydrazone (82) (681 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (5.15 mmol) was added, the golden solution warmed to -66° over 17 min and recooled to -78°. Allyl bromide (0.30 ml) was added, the suspension warmed to -65° over 30 min, stirred for 30 min and recooled to -78°. TMEDA (1.0 ml) and n-butyllithium (4.12 mmol) were added, the golden solution warmed to -3° over 110 min, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (1.50 g)], chromatography on Kieselgel H (16 g) [eluant dichloromethane] and p.l.c. [two developments with dichloromethane] gave the E-*acid* (139) (65 mg, 26%) as an oil, ν_{max} 3500-2400 m br (O-H), 1690 s ($-CO_2H$), 1640 m (C=C), 1420 m, 1285 m (C-O), and 915m(CH_2=CH) cm^{-1}, δ 1.90 (3H, d, J 1Hz, Me), 3.05 (2H, mt, J n, 7Hz, 4-CH_2), 5.00-6.50 (3H, m, CH_2=CH), 7.10 (1H, mt, J n, 7Hz, 3-CH), and 10.50-11.00 (1H, br, OH), m/e 126 ($M^{+\cdot}$), 111 (M^+-Me·), 87, 81 ($M^{+\cdot}$ - CO_2H·, base), 55, and 41 (Found: C, 66.87; H, 8.13. $C_7H_{10}O_2$ requires C, 66.64; H, 7.99%).

Preparation of *2-Hydroxy-2-methyl-octan-7-en-4-one 2,4,6-Tri-iso-propyl-benzenesulphonylhydrazone* (144)

E,Z (85:15)-Sulphonylhydrazone (142) (430 mg) was dissolved in DME (4.5 ml) and TMEDA (0.5 ml) and the solution cooled to -78°. n-Butyllithium (3.38 mmol) was added, the golden solution warmed to -65° over 10 min, quenched with acetone (0.20 ml) and warmed to 25°. General work up [(A) glacial acetic acid (0.30 g), diethyl ether (150 ml)] and chromatography on Kieselgel H (20 g) [eluant (i) light petroleum-dichloromethane (1:0-0:1), (ii) dichloromethane-diethyl ether (1:0-3:1)] gave the *hydroxy-sulphonylhydrazone* (144) (344 mg, 69%) m.p. 102-5° (from ethanol and water at 25° as the Z-isomer), ν_{max} 3480 s (O-H), 3108 m (N-H), 1647 m (C=N), 1605 m

(C=C), 1330 ms ($-SO_2-N<$), 1165 and 1155 s ($-SO_2-N<$), 1133 m, 1104 m, 1060 m, 1039 m, 923 m, 910 s ($CH_2=CH$), 883m, 676 s, and 652 m cm^{-1}; δ 1.28 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.34 (6H, s, 2-Me), 2.20-2.50 (6H, m, 3,5,6-$C\underline{H}_2$), 2.70 (1H, br, O<u>H</u>), 2.95 (1H, septet, J 7Hz, p-$C\underline{H}Me_2$), 4.28 (2H, septet, J 7Hz, o-$C\underline{H}Me_2$), 4.75-5.10 (2H, br, 8-$C\underline{H}_2$), 5.50-6.00 (1H, m, 7-C<u>H</u>), 7.25 (2H, s, aryl-<u>H</u>), and 10.60 (1H, br, N<u>H</u>), m/e 436 ($M^{+\cdot}$), 267, 251, 204, 189 (base), 161, 112, 91, and 59 (Found: C, 66.18; H, 9.38; N, 6.49. $C_{24}H_{40}N_2O_3S$ requires C, 66.02; H, 9.23; N, 6.41%).

Preparation of *6- Iodomethyl -3-methylenetetrahydropyran-2-one* (146)

E,Z(85:15)-Sulphonylhydrazone (142) (1.188 g) was dissolved in DME (10 ml) and TMEDA (1.5 ml) and the solution cooled to -78°. n-Butyllithium (7.34 mmol) was added, the solution was warmed to -3° over 2 h, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) trifluoroacetic acid (1.4 g), dichloromethane] and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-19:1)] gave the slightly impure 2-methylenehex-5-enoic (145) (270 mg, < 68%) as an oil, ν_{max} 3500-2400 br (O-H), 1700 s ($-CO_2H$), 1633 m (C=C), 950 m ($CH_2=C$), and 915 m ($CH_2=CH$) cm^{-1}, δ 2.10-2.60 (4H, m, 3,4-$C\underline{H}_2$), 4.95-5.25 (2H, m, 6-C<u>H</u>), 5.65-6.15 (1H, m, 5-C<u>H</u>), 5.75 (1H, t, J 1Hz, 2-C=C<u>H</u>$_2$), 6.43 (1H, t, J, 1Hz, 2-C=C<u>H</u>$_2$), and 11.60 (1H, br, O<u>H</u>), m/e 126 ($M^{+\cdot}$), 111 ($M^{+\cdot}$ - Me·), 108 ($M^{+\cdot}$ - H_2O), and 81 ($M^{+\cdot}$ - CO_2H·, base). The acid (145) was dissolved in water (20 ml) and dichloromethane (20 ml). Sodium hydrogencarbonate (180 mg) was added and the mixture stirred for 15 min. A solution of iodine (544 mg) in saturated potassium iodide (10 ml) was added dropwise during 30 min and the mixture stirred for 1 h. General work up [(A) sodium thiosulphate solution, dichloromethane] and chromatography on Kieselgel H (21 g) [eluant dichloromethane] gave the *iodolactone* (146) (396 mg, 50%) as an oil, ν_{max} 1728 s (C=O), 1625 m (C=C), 1378 m, 1297 s, 1228 m, 1210 m, 1155 and 1140 s (C-O),

1075 m, 1043 m, 1020 m, 1010 m, 950 m (CH_2=), 933 m, and 804 m cm^{-1}, δ 1.54-2.55 (2H, m, 5-$C\underline{H}_2$), 2.60-3.00 (2H, m, 4-$C\underline{H}_2$), 3.46 (2H, d, $\underline{J}$ 5Hz, $C\underline{H}_2I$), 4.28-4.60 (1H, m, 6-C$\underline{H}$), 5.72 (1H, q, $\underline{J}$ 1.5 Hz, $C\underline{H}_2$=), and 6.47 (1H, q, $\underline{J}$ 1.5 Hz, $C\underline{H}_2$=), m/e 252 ($M^{+\cdot}$), 125 ($M^{+\cdot}$ - I·, base), 111 ($M^{+\cdot}$ - ICH_2·), 97, 83, 55, 43, and 41 (Found: C, 33.51; H, 3.78. $C_7H_9O_2I$ requires C, 33.36; H, 3.60%).

Preparation of *3,6-Dimethylenetetrahydropyran-2-one* (147)

Iodolactone (146) (169 mg) was dissolved in benzene (4 ml). DBU (0.15 ml) was added, the solution heated to 74° for 2.75 h and cooled to 25°. General work up [(B) diethyl ether] and p.l.c. [one development with dichloromethane] gave the *dimethylene lactone* (147) (53 mg, 64%) as an oily solid, ν_{max} 1740 s (C=O), 1660 s (CH=C-O), 1635 m (C=C), 1440 m, 1400 m, 1325 m, 1296 s, 1265 m, 1135 s (C-O), 990 m, 946 (CH_2=), 850 m, and 800 m cm^{-1}, δ 2.62 (4H, br s, 4,5-$C\underline{H}_2$), 4.38 (1H, br s, 6-C=C$\underline{H}_2$), 4.72 (1H, t, $\underline{J}$ 1Hz, 6-C=C$\underline{H}_2$), 5.72 (1H, t, $\underline{J}$ 1Hz, 3-C=C$\underline{H}_2$), and 6.54 (1H, t, $\underline{J}$ 1Hz, 3-C=C$\underline{H}_2$), m/e 124 ($M^{+\cdot}$), 96, 95, 86, 84 (base), and 39 (Found: C, 67.52; H, 6.55. $C_7H_8O_2$ requires C, 67.73; H, 6.49%).

Preparation of *Hept-6-en-3-one 2,4,6-Tri-iso-propylbenzenesulphonylhydrazone* (148a)

Sulphonylhydrazone (86) (971 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (6.55 mmol) was added, the golden red solution warmed to -66° over 20 min and recooled to -78°. Allyl bromide (0.40 ml) was added, the cloudy solution was warmed to -65° over 40 min, stirred for 20 min, quenched with glacial acetic acid (0.50 ml) in water (2 ml) and warmed to 25°. General work up [(A) diethyl ether] and recrystallisation from ethanol and water gave an inseparable mixture of the E,Z-*sulphonylhydrazone* (148a) (major) and E,Z-*3-methylhex-5-ene-2-one 2,4,6-*

tri-iso-propylbenzenesulphonylhydrazone (148b) (minor) (810 mg, 75%) homogeneous on t.l.c., m.p. 78-82°, ν_{max} 3270 m (N-H), 1603 m (C=C), 1328 m ($-SO_2-N<$), 1163 s and 1154 s ($-SO_2-N<$), 1305 m, 942 m, 907 m ($CH_2=CH$), 882 m and 665 s cm^{-1}, δ (148a) 1.05 (3H, ca. t, J 8Hz, 1-CH_3), 1.26 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.95-2.40 (6H, m, 2,4,5-CH_2), 2.95 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.30 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 4.70-5.25 (2H, m, 7-CH_2), 5.40-5.95 (1H, m, 6-CH), and 7.15 (2H, s, aryl-H), m/e 394 (M^+), 267 (108d, base), 189, 161, 55, and 43. Recrystallisation from methanol and water gave m.p. 87-95° (Found: C, 67.36; H, 9.48; N, 7.09. $C_{22}H_{36}N_2O_2S$ requires C, 67.31; H, 9.24; N, 7.13%).

Preparation of *3-Ethylidene-6-iodomethyltetrahydrofuran-2-one* (149a)

A mixture of the sulphonylhydrazones (148a)(major) and (148b) (minor) (693 mg) m.p. 79-82°, was dissolved in DME (6 ml) and the solution was cooled to -78°. n-Butyllithium (5.63 mmol) was added, the brown-red solution warmed to -70° over 45 min, then to -4° over 2 h, recooled to -78°, quenched with carbon dioxide gas and warmed to 25°. General work up [(C) dichloromethane, trifluoroacetic acid (0.70 g)] and chromatography on Kieselgel H (19 g) [eluant dichloromethane-diethyl ether (1:0-19:1)] gave crude 2-ethylidene-hex-5-enoic acid (202 mg), ν_{max} 1690 s (CO_2H), 1645 m (C=C), and 910 s ($CH_2=$) cm^{-1}. Sodium hydrogencarbonate (132 mg) and water (14 ml) were added and the solution stirred for 10 min. Dichloromethane (20 ml) was added and a solution of iodine (367 mg) in saturated potassium iodide (10 ml) added dropwise during 25 min. The solution was stirred for 1 h and then treated with sodium thiosulphate (s) until colourless. General work up [(B) diethyl ether], chromatography on Kieselgel H (18g) [eluant dichloromethane] and p.l.c. (one development with dichloromethane) gave the *iodolactone* (149a) (182 mg, 39%) as an oil, ν_{max} 1720 s (C=O), 1640 s (C=C), 1385 m, 1320 m, 1262 s (C-O), 1232 m, 1200 m, 1150 s (C-O), 1090 m,

1065 m, 1050 m, 965 m, and 726 m cm^{-1}, δ 1.50-1.70 (4H, m, 4,5-$C\underline{H}_2$), 1.83 (3H, dt, J 7, 1Hz, Me), 3.34-3.70 (2H, m, $C\underline{H}_2I$), 4.14-4.47 (1H, m, 6-C<u>H</u>), and 7.06 (1H, qt, J 7, 2Hz, H<u>C</u>=), m/e 266 ($M^{+\cdot}$), 139 ($M^{+\cdot}$ - I·), 125 ($M^{+\cdot}$-CH_2I·, base), 97, and 53 (Found: C, 36.38; H, 4.28. $C_8H_{11}O_2I$ requires C, 36.11; H, 4.17%); and *6-iodomethyl-4-methyl-3-methylenetetrahydropyran-2-one* (149b) (28 mg, 6%) as an oil, ν_{max} 2958 m, 1723 s (C=O), 1618 m (C=C), 1400 m, 1376 m, 1292 m, 1253 s, 1148 s, 1110 m, 1033 m, 950 m (CH_2=), and 800 m cm^{-1}, δ 1.28 (3H, d, J 7Hz, 4-Me), 1.30-3.60 (3H, m, 4-C<u>H</u>, 5-$C\underline{H}_2$), 3.30-3.35 (2H, m, $C\underline{H}_2I$), 4.15-4.75 (1H, m, 6-C<u>H</u>), 5.65-5.85 (1H, m, $C\underline{H}_2$=), and 6.50-6.70 (1H, m, =$C\underline{H}_2$), m/e 266 ($M^{+\cdot}$), 139 ($M^{+\cdot}$ - I·, base), 125 ($M^{+\cdot}$ - CH_2I·), 97, 67, and 53 (Found: C, 36.26; H, 4.37. $C_8H_{11}O_2I$ requires C, 36.11; H, 4.17%).

Preparation of E-*3-Ethylidene-6-methylenetetrahydropyran-2-one* (150)

Methylene lactone (149a) (104 mg) was dissolved in benzene (4 ml) and DBU (0.07 ml); the solution was heated to 80° for 3 h and cooled to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (11 g) [eluant dichloromethane] and p.l.c. [one development with dichloromethane] gave the E-*dimethylene lactone* (150) (38 mg, 71%) as an oil, ν_{max} 1740 s (C=O), 1670 s (C=C-O), 1645 s (C=C), 1440 m, 1326 m, 1315 m, 1277 m, 1250 s, 1174 s, 1158 s, 1140 s (C-O), 1062 m, 1020 m, 968 m, and 736 m cm^{-1}, δ 1.86 (3H, d, J 7Hz, Me), 2.55 (4H, br s, 4,5-$C\underline{H}_2$), 4.37 (1H, br s, $C\underline{H}_2$=), 4.70 (1H, d, J 1.5 Hz, $C\underline{H}_2$=), and 7.10 (1H, qm, J 7, n Hz, 3-C=C<u>H</u>), m/e 138 ($M^{+\cdot}$, base), 96, 95, 68, and 67 (Found: C, 69.58; H, 7.63. $C_8H_{10}O_2$ requires C, 69.54; H, 7.30%).

Attempted preparation of 2-Deuteriohexadec-2-enoic acid (158)

Keto-acid sulphonylhydrazone (152b) (585 mg) was azeotropically dried with toluene (2 x 5 ml), the residue dissolved in DME (5 ml) and cooled to

-78°. n-Butyllithium (4.29 mmol) was added, the golden solution warmed to 25° over 80 min and quenched with deuterium oxide (0.50 ml). General work up [(B) glacial acetic acid (0.5 g), dichloromethane] and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] gave a crude residue (301 mg), ν_{max} 1720 m, 1695 m, 1628 m cm^{-1}. Reaction with 2,4-dinitrophenylhydrazine[63] (198 mg) gave a solid derivative probably eicosan-5,6-dione bis-2,4-dinitrophenylhydrazone (159) (30 mg) m.p. 142-52° (from dichloromethane and methanol), ν_{max} 3320 m (N-H), 1620 s (C=N), 1595 s (C=C), 1500 and 1335 s ($C-NO_2$), 1315 s, 1276 s, 1130 s, and 1094 s, δ 0.75-1.90 (34 H, br, $^nC_3\underline{H}_7$, $^nC_{13}\underline{H}_{27}$), 2.90-3.15 (4H, br, 4,7-$C\underline{H}_2$), 7.95-8.60 (4H, m, aryl 5,6-$\underline{H}$), 9.10-9.30 (2H, m, aryl 3-$\underline{H}$), and 11.60 (2H, N$\underline{H}$), m/e 670 ($M^{+\cdot}$), 473 ($M^{+\cdot}$ - $^nC_{14}H_{29}\cdot$), and 43 (base) (Found: C, 57.72; H, 7.05; N, 16.54. $C_{32}H_{46}N_8O_8$ requires C, 57.30; H, 6.91; N, 16.70%).

Reaction of the Ester Sulphonylhydrazone (152d) with Lithium Di-iso-propylamide

The ester sulphonylhydrazone (152d) (393 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. Lithium di-iso-propylamide (2.60 mmol) in DME (2 ml) was added, the pale yellow solution warmed to -60° over 15 min and recooled to -70°. 1-Bromohexane (0.50 ml) was added, the solution warmed to -60° over 45 min and then to 25° over 40 min. General work up [(B) dichloromethane] and chromatography on Kieselgel H (20 g) [eluant (i) light petroleum-dichloromethane (1:0-0:1), (ii) dichloromethane-diethyl ether (1:0-0:1)] gave the sulphonylhydrazone (152d) (27 mg, 7%), identical (t.l.c. and n.m.r.) with the starting material; and ethyl 2-diazopropionate(?)(161)(35 mg) as a volatile green oil, ν_{max} 2080 m ($C=\overset{+}{N}=\overline{N}$), 1685 ms (C=O), 1325 m, 1310 m, and 1130 m cm^{-1}, δ 1.50 (3H, t, $\underline{J}$ 6.5 Hz, $Me\underline{C}H_2$), 2.25 (3H, s, 3-$C\underline{H}_3$), and 4.40 (2H, q, $\underline{J}$ 6.5 Hz, $MeC\underline{H}_2$), m/e 129

($M^{+\cdot}$ + H), 105, 91, 87 (base), and 43.

Reaction of the Ester Sulphonylhydrazone (152d) with Lithium Di-iso-propylamide and n-Butyllithium in Sequence

The ester sulphonylhydrazone (152d) (397 mg) was dissolved in DME (5 ml) and the solution cooled to -75°. Lithium di-iso-propylamide [prepared from di-iso-propylamine (0.20 ml) and n-butyllithium (1.30 mmol) in DME (2 ml)] was added, and the light yellow solution treated with n-butyllithium (2.86 mmol). The orange solution was warmed to -68° over 15 min, recooled to -78° and treated with 1-bromohexane (0.60 ml). The orange solution was warmed up to -60° over 3 h, quenched with glacial acetic acid (0.32 g) in water (2 ml) and warmed up to 25°. General work up [(B) dichloromethane], chromatography on Kieselgel H (20 g) [eluant dichloromethane] and p.l.c. [one development with dichloromethane:diethyl ether (9:1)] gave *3-(n-butyl)-3-hydroxyheptan - 2-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone* (163) (146 mg, 32%) m.p. 146-8° (from ethanol and water), ν_{max} 3480 m (O-H), 3225 m (N-H), 1602 m (C=C), 1430 m, 1400 m, 1320 m ($-SO_2-N<$), 1305 m, 1268 m, 1170 and 1158 s ($-SO_2-N<$), 1138 m, 1108 m, 1093 m, 1073 m, 1050 s (C-O), 1042 s, 942 m, 918 m, 740 m, and 664 m cm^{-1}, δ 0.50-1.80 (18H, br, ^{n}Bu), 1.28 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 1.76 (3H, s, 1-$C\underline{H}_3$), 2.90 (1H, overlapping septets, J 7Hz, p-$C\underline{H}Me_2$), 3.80 (1H, s, O$\underline{H}$), 4.24 (2H, overlapping septets, J 7Hz, o-$C\underline{H}Me_2$), 7.16 (2H, s, aryl-$\underline{H}$), and 7.90 (1H, s, N$\underline{H}$), m/e 466 ($M^{+\cdot}$), 409 ($M^{+\cdot}$ - ^{n}Bu), 267, 186, 143 (base), 127, and 57 ($^{n}Bu^{+}$) (Found: C, 66.83; H, 9.82; N, 5.89. $C_{26}H_{46}N_2O_3S$ requires C, 66.91; H, 9.93; N, 6.00%).

Reaction of the Ester Sulphonylhydrazone (152d) with Lithium Di-iso-propylamide and t-Butyllithium

Sulphonylhydrazone (152 d) (388 mg) was dissolved in DME (5 ml) and

the solution cooled to -76°. Lithium di-iso-propylamide [prepared from di-iso-propylamine (0.20 ml) and t-butyllithium (1.30 mmol) in DME (2 ml)] was added, the lemon yellow solution stirred for 10 min and t-butyllithium (3.64 mmol) was added. The brown solution was stirred for 5 min, warmed up to -67° over 22 min, recooled to -78°, quenched with allyl bromide (5.90 mmol) and warmed to -70° over 2 h. Glacial acetic acid (0.36 g) in water (2 ml) was added and the solution warmed up to 25°. General work up [(B) dichloromethane] and chromatography on Kieselgel H (18 g) [eluant dichloromethane] gave E,Z-*3-(t-butyl)-4,4- dimethyl -3-hydroxy-pentan-2-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone* (162) (142 mg, 31%) m.p. 209-210° (from methanol and water), ν_{max} 3435 m (O-H), 3238 m (N-H), 1600 m (C=C), 1332 s ($-SO_2-N<$), 1192 m, 1167 and 1155 s ($-SO_2-N<$), 1094 m, 1070 m, 1060 m, 1037 m, 892 m, 882 m, 675 m, and 654 m cm^{-1}, δ 0.88 and 0.95 (18H, 2s, ^tBu), 1.10-1.40 (18H, m, $CHMe_2$), 1.85 and 2.02 (3H, 2s, 1-CH_3), 2.95 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 4.30 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 4.47 (1H, s, OH), 7.15-7.20 (2H, 2s, aryl-H), and 7.75 (1H, br s, NH), m/e 463, 451 (M^+ - Me·), 4.09 (M^+ - ^tBu·, base), 367, 267, 189, and 57 ($^tBu^+$) (Found: C, 66.91; H, 9.83; N, 5.98. $C_{26}H_{46}N_2O_3S$ requires C, 66.91; H, 9.93; N, 6.00%).

Reaction of the Amide Sulphonylhydrazone (152e) with n-Butyllithium

Amide sulphonylhydrazone (152e) (435 mg) was dissolved in DME (10 ml) and the solution cooled to -78°. n-Butyllithium (5.60 mmol) was added, the yellow solution warmed up to 25° over 100 min and quenched with deuterium oxide (0.50 ml). General work up [(B) dichloromethane] and chromatography on Kieselgel H (12 g) [eluant diethyl ether] gave *2-diazoheptanamide* (165) (86 mg, 54%) m.p. 82-4° (from dichloromethane and light petroleum), ν_{max} 3355 s (N-H), 3180 s (N-H), 2080 s ($C=N_2$), 1660 s (C=O), 1590 s (C=O), 1410 s, 1330 m, 1304 m, 1258 m, 1214 m, 1097 m, 726 m, and 663 m cm^{-1},

δ 0.76-1.10 (3H, ca. t, 7-CH_3), 1.20-1.80 (6H, br, 4,5,6-CH_2), 2.30 (2H, ca. t, J 8Hz, 3-CH_2), and 5.70-6.30 (2H, br, NH), m/e 155 ($M^{+\cdot}$, weak), 127 ($M^{+\cdot} - N_2$), 98 ($M^{+\cdot} - {}^{n}Bu\cdot$, base), 59, 44, and 41 (Found: C, 54.35; H, 8.46; N, 26.83. $C_7H_{13}N_3O$ requires C, 54.18; H, 8.44; N, 27.07%).

Attempted Preparation of 3-Hydroxy-N-methyl-2-methylenepent-4-enamide (166)

Amide sulphonylhydrazone (152i) (378 mg) was dissolved in DME (6 ml) and TMEDA (1 ml) and the solution cooled to -78°. n-Butyllithium (4.15 mmol) was added, the solution warmed up to 25° over 100 min, recooled to -78°, quenched with acrolein (0.20 ml) and warmed up to 25°. General work up [(B) dichloromethane, diethyl ether], chromatography on Kieselgel H (20 g) [eluant (i) diethyl ether, (ii) ethyl acetate] and p.l.c. [two developments with diethyl ether] gave the hydroxy-amide (166) (12 mg, 8%), as an oil, ν_{max} 3340 br s (O-H, N-H), 3095 m, 2962 m, 2876 s, 1665 s, 1620 s (C=O), 1555 s 1465 m, 1420 m, 1165 m, 1015 m, 995 m, and 930 m cm^{-1}, m/e 141 ($M^{+\cdot}$), 140, 112, 84 (base), 58, 55, and 41.

Preparation of N-*Cyclohexyl-2-oxohex-5-enamide 2,4,6-Tri-iso-propylbenzene-sulphonylhydrazone* (167)

Amide sulphonylhydrazone (152f) (443 mg) was dissolved in DME (5 ml) and the solution cooled to -76°. Lithium di-iso-propylamide [prepared from di-iso-propylamine (0.40 ml) and n-butyllithium (2.60 mmol) in DME (2 ml)] was added, the solution stirred for 18 min and then treated with n-butyllithium (5.20 mmol). The orange solution was warmed to -69° over 27 min, recooled to -78°, quenched with allyl bromide (0.70 ml) and stirred for 3 h. Glacial acetic acid (0.60 g) in water (2 ml) was added and the solution warmed to 25°. General work up [(B) dichloromethane, diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether

(1:0-9:1)] and recrystallisation of the residue gave the *amide sulphonylhydrazone* (167) (337 mg, 70%) m.p. 153-4° (from methanol and water), ν_{max} 3400 m (N-H), 3170 m (N-H), 1660 s (C=O), 1620 m (C=O), 1605 m (C=C) 1520 s (C=O), 1342 s ($-SO_2-N<$), 1200 m, 1175 and 1160 s ($-SO_2N<$), 1108 m, 1085 m, 1075 m, 1059 m, 1037 m, 910 s (CH_2=CH), 902 m, 886 m, 850 m, 681 s, and 657 m cm^{-1}, δ 1.00-2.10 (10H, br, $(\underline{CH}_2)_5$), 1.30 (18H, overlapping d, J 7Hz, $CH\underline{Me}_2$), 2.05-3.15 (5H, m, 3,4-$\underline{CH}_2$, p-$\underline{CH}Me_2$), 3.40-3.90 (1H, br, HCN), 4.20 (2H, overlapping septets, J 7Hz, o-$\underline{CH}Me_2$), 4.80-6.10 (3H, m, $\underline{CH}_2$=$\underline{CH}$), 6.30-6.70 (1H, br, amide N$\underline{H}$), 7.17 (2H, s, aryl-$\underline{H}$), and 8.00-8.50 (1H, br, N$\underline{H}$), m/e 490 ($M^{+\cdot}$ + H), 251, 233, 204, 189 (base), 161, 112, 83 ($C_6H_{11}^+$), 67, and 55 (Found: C, 66.33; H, 8.97; N, 8.58. $C_{27}H_{43}N_3O_3S$ requires C, 66.22; H, 8.85; N, 8.58%); and the amide sulphonylhydrazone (152f) (106 mg, 24%) identical (t.l.c. and n.m.r.) with the starting material.

Preparation of N-*Cyclohexyl-2-deuterioprop-2-enamide* (168)

Amide sulphonylhydrazone (152f) (467 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. Lithium di-iso-propylamide [prepared from di-iso-propylamine (0.40 ml) and n-butyllithium (2.60 mmol) in DME (2 ml)] was added, the solution warmed up to -68° over 10 min and then recooled to -78°. n-Butyllithium (5.00 mmol) was added, the solution warmed to 0° over 95 min and then stirred for 35 min. Deuterium oxide (0.50 ml) was added, the solution stirred for 5 min and then warmed to 25°. General work up [(B) dichloromethane], chromatography on Kieselgel H (15 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] and p.l.c. [one development with diethyl ether] gave the *deuterio-amide* (168) (86 mg, 54%) m.p. 102-3° (from dichloromethane and light petroleum), ν_{max} 3285 s (N-H), 3075 m, 1640 s (C=O), 1620 s (C=O), 1553 s (C=O), 1315 m, 1282 m, 1258 m, 1097 m, 947 m (CH_2=), and 706 m cm^{-1}, δ 1.00-2.20 (10H, br, $(\underline{CH}_2)_5$),

3.60-4.10 (1H, br, HCN), 5.54 (1H, brs, CH_2=), 6.16 (1H, br s, CH_2=), and 6.60-7.00 (1H, br, NH), m/e 154 ($M^{+\cdot}$), 126 ($M^{+\cdot}$ - CH_2=$CH^2H\cdot$), 111, 97, 73 (base), 57, 56, and 41, ca. 100% mono-deuteriated (Found: C, 69.95; H, 10.18; N, 9.04. $C_9H_{14}{}^2HNO$ requires C, 70.09; N, 9.08%); and the impure starting sulphonylhydrazone (152f) (73 mg), ca. 50% pure by n.m.r. analysis.

Second Preparation of the Deuterio-amide (168)

Amide sulphonylhydrazone (152f) (445 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (4.00 mmol) was added, the orange solution warmed to 25° over 100 min and quenched with deuterium oxide (0.50 ml). A similar work up gave the deuterio-amide (168) (82 mg, 54%) identical (t.l.c., n.m.r., and m/e) with the previous sample; and possibly the sulphonylhydrazone (153 n) (29 mg, 6.5%) m.p. 142-4° (from methanol and water at 0°), ν_{max} (CCl_4) 3420 m (N-H), 2960 s, 2940 s, 2860 m, 1680 s (C=O), 1604 m (C=C), 1505 m, 1467 m, 1455 m, 1430 m, 1388 m, 1368 m, 1340 m (-SO_2-N<), 1260 m, 1170 and 1158 s (-SO_2-N<), 1097 m, 1040 m, 910 s, 883 m, 670 m, and 655 m cm^{-1}, δ 1.00-2.10 (24H, br), 1.24 (36H, overlapping d, J 7Hz, $CHMe_2$), 2.60-3.10 (2H, br, p-$CHMe_2$), 3.50-4.00 (2H, br, HCH), 4.20 (4H, overlapping septets, J 7Hz, o-$CHMe_2$) 6.40-6.80 (2H, br, amide NH), and 7.17 (4H, s, aryl-H), m/e 451, 358, 268, 251, 233 (base), 204, 189, 175, and 161 (Found: C, 63.81; H, 8.85; N, 9.22. Calc. for $C_{48}H_{76}N_6O_6S_2$ C, 64.25; H, 8.53; N, 9.35%).

Third Preparation of the Deuterio-amide (168)

Amide sulphonylhydrazone (152f) (973 g) was dissolved in DME (12 ml) and the solution cooled to -78°. n-Butyllithium (7.02 mmol) was added, the solution warmed to 25° over 2 h, recooled to -78° and quenched with deuterium oxide (0.50 ml). A similar work up as before gave the deuterio-

amide (168) (275 mg, 82%) identical (t.l.c., n.m.r., and mass spectra) with an authentic sample.

Preparation of N-*Cyclohexyl-3-hydroxy-3-methyl-2-methylenebutanamide* (169)

Amide sulphonylhydrazone (152f) (452 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (4.00 mmol) was added, the orange-red solution warmed to 25° over 100 min and quenched with acetone (0.20 ml). General work up [(B) dichloromethane], chromatography on Kieselgel H (19 g) [eluant dichloromethane-diethyl ether (1:0-0:1)] and p.l.c. [one development in diethyl ether] gave the *hydroxy-amide* (169) (126 mg, 59%) as an oil, ν_{max} 3700-3120 br s (O-H), 3070 m (CH_2=), 2980s, 2930 s, 2860 s, 1655 s (C=O), 1608 s (C=C), 1535 s (C=O), 1455 s, 1400 br, 1295 m, 1265 m, 1250 m, 1220 m, 1155 s, 1130 s, (C-O), 975 m, 960 m, 940 m (CH_2=), 893 m, 867 m, 846 m, 808 m, and 745 m cm^{-1}, δ 1.00-2.40 (10H, br, $(\underline{CH}_2)_5$), 1.40 (6H, s, 3-Me), 3.30-4.00 (1H, br, HCN), 4.70 (1H, brs, OH), 5.36 (1H, brs, $\underline{CH}_2$=), 5.52 (1H, brs, $\underline{CH}_2$=), and 6.50-6.90 (1H, br, NH), m/e 211 ($M^{+\cdot}$), 196 ($M^{+\cdot}$ - Me·), 193 ($M^{+\cdot}$ - H_2O),150, 114, 112 (base), 83 ($C_6H_{11}^+$), 67, 56, and 55 (Found: C, 68.12; H, 10.12; N, 6.42. $C_{12}H_{21}NO_2$ requires C, 68.21; H, 10.02; N, 6.63%).

Preparation of N-*Cyclohexyl-3-hydroxy-2-methylenepent-4-enamide* (170)

Amide sulphonylhydrazone (152f) (2.734 g) was dissolved in DME (25 ml) and the solution cooled to -78°. n-Butyllithium (18.76 mmol) was added, the solution warmed to 25° over 100 min, recooled to -78°, quenched with acrolein (0.70 ml) and then warmed to 25°. General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-1:1)] gave the *hydroxy-amide* (170) (1.033 g, 81%) m.p. 87-9° (from diethyl ether and light petroleum), ν_{max} 3500-3150 br (O-H), 3285 s (N-H), 1655 m, 1615 s (C=O), 1550 and 1540 m (C=O), 1095 m, 1045 m,

934 m (CH_2=), and 730 m cm^{-1}, δ 0.90-2.20 (10H, br, ($\underline{CH}_2$)$_5$), 3.40-4.15 (2H, br, $\underline{H}$CN, O$\underline{H}$), 4.90-6.30 (3H, m, $\underline{CH}_2$=C$\underline{H}$), 5.42 (1H, dm, $\underline{J}$ 15, n Hz, 3-C$\underline{H}$), 5.55 (1H, m, 2-C=C$\underline{H}_2$), 5.90 (1H, m, 2-C=C$\underline{H}_2$), and 6.40-6.90 (1H, br, N$\underline{H}$), m/e 209 ($M^{+\cdot}$) 192 ($M^{+\cdot}$ - OH·), 191 ($M^{+\cdot}$ - H_2O), 180 (base), 110, 98, 83 ($C_6H_{11}^+$), and 56 (Found: C, 68.83; H, 9.29; N, 6.56. $C_{12}H_{19}NO_2$ requires C, 68.87; H, 9.15; N, 6.69%).

Preparation of N-*Cyclohexyl-3-hydroxy-2-methylenepropanamide* (171)

Amide sulphonylhydrazone (152f) (1.847 g) was dissolved in DME (20 ml) and the solution cooled to -78°. n-Butyllithium (12.3 mmol) was added, the solution warmed to 25° over 85 min and recooled to 0°. Dry paraformaldehyde (0.50 g) was added and the solution warmed to 25° over 30 min. General work up [(B) dichloromethane, diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-1:1)] and p.l.c. [two developments with diethyl ether] gave the *hydroxy-amide* (171) (446 mg, 59%) m.p. 77-8° (from diethyl ether and light petroleum), ν_{max} 3320 s (O-H), 3295 s (N-H), 1663 s, 1625 s (C=O), 1615 s (C=C), 1548 s (C=O), 1245 m, 1155 m, 1097 m, 1067 m, 1029 m (C-O), 940 m (CH_2=), and 930 m cm^{-1}, δ 1.00-2.10 (10H, br, ($\underline{CH}_2$)$_5$), 3.65-4.20 (2H, br, $\underline{H}$CN, O$\underline{H}$), 4.40 (2H, d, $\underline{J}$ 6Hz, 3-C$\underline{H}_2$), 5.50 (1H, s, C$\underline{H}_2$=), 5.88 (1H, s, C$\underline{H}_2$=), and 6.70-7.15 (1H, br, N$\underline{H}$), m/e 183 ($M^{+\cdot}$), 166 ($M^{+\cdot}$ - OH·), 140, 122, 102 (base), 85, and 56 (Found: C, 65.54; H, 9.37; N, 7.51. $C_{10}H_{17}NO_2$ requires C, 65.54; H, 9.35; N, 7.64%).

Preparation of N-*Cyclohexyl-3-hydroxy-2-methylenepentanamide* (172)

Amide sulphonylhydrazone (152f) (1.434g) was dissolved in DME (15 ml) and the solution cooled to -78°. n-Butyllithium (10.0 mmol) was added, the solution warmed to 25° over 100 min, recooled to -78°, quenched with propanol (0.40 ml) and then warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (19 g) [eluant dichloromethane-diethyl ether

(1:0-7:3)] and precipitation of the residue from light petroleum gave the *hydroxy-amide* (172) (538 mg, 80%) m.p. 98-101° (from dichloromethane and light petroleum), ν_{max} 3460 m (O-H), 3280 s (N-H), 1655 s, 1610 s (C=O), 1540 s (C=O), 1400 m, 1345 m, 1243 m, 1152 m, 1116 m (C-O), 987 m, 973 m, 930 m (CH_2=), and 725 m cm^{-1}, δ 0.90 (3H, ca. t, J 7Hz, 5-CH_3), 1.00-2.10 (12H, br, $(CH_2)_5$, 4-CH_2), 3.30-4.90 (3H, br, 3-CH, HCN, OH), 5.35 (1H, br s, CH_2=), 5.76 (1H, br s, CH_2=), and 6.30-7.10 (1H, br, NH), m/e 211 ($M^{+\cdot}$), 193 ($M^{+\cdot}$ - H_2O), 182 ($M^{+\cdot}$ - Et·), 130, 112 (base), 110, and 56 (Found: C, 68.43; H, 10.03; N, 6.41. $C_{12}H_{21}NO_2$ requires C, 68.21; H, 10.02; N, 6.63%).

Preparation of N-*Cyclohexyl-2-methylene-3,4,5-trihydroxypentanamide 4,5-Acetonide* (173a, 173b)

Amide sulphonylhydrazone (152f) (970 mg) was dissolved in DME (12 ml) and the solution cooled to -78°. n-Butyllithium (6.89 mmol) was added, the solution warmed to 25° over 130 min and recooled to -78°. Freshly distilled 4R-2,2 -dimethyl-4-formyl-1,3-dioxolan [92a] (0.30 ml) was added, the solution stirred for 30 min and warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (18g) [eluant dichloromethane-diethyl ether (1:0-3:2)] and p.l.c. [one development with diethyl ether] gave N-cyclohexylprop-2-enamide (80 mg, 24%), ν_{max} 3280 s (N-H), 1653 s, (C=O), 1618 s (C=O) 1550 m (C=O), 1440 m, 1405 m, 1375 m, 1248 m, 1230 m, 990 m (CH_2=CH), 945 m (CH_2=CH), and 710 m cm^{-1}, δ 1.00-2.10 (10H, br, $(CH_2)_5$), 3.60-4.40 (1H, br, HCN), 5.55-5.70 (1H, 4s, 3-CH_2), 5.80-6.40 (1H, br, NH), and 6.15-6.30 (2H, 3s, 2-CH,3-CH_2), m/e 153 ($M^{+\cdot}$), 110, 72 (base), and 55; *3S,4R-N-cyclohexyl-2-methylene-3,4,5-trihydroxypentanamide 4,5-acetonide* (173a) (280 mg, 46%) m.p. 96-7° (from diethyl ether and light petroleum), $[\alpha]_{589}^{20}$ - 7.0 (C=0.23, dichloromethane), ν_{max} 3400 m (O-H), 3315 s (N-H), 1653 m, 1617 s (C=O), 1545 s (C=O), 1450 m, 1340 m, 1255 m, 1210 m, 1150 m,

1080 m (C=O), 1074 m, 1045 m, 937 m (CH_2=), 848 m, and 684 m cm^{-1}, δ 1.00-2.10 (10H, br, $(CH_2)_5$), 1.35 (3H, s, MeCO), 1.43 (3H, s, MeCO), 3.60-4.40 (6H, br, $CH_2CHCHOH$, HCN), 5.62 (1H, s, CH_2=), 5.82 (1H, s, CH_2=), and 6.25-6.60 (1H, br, NH), m/e 283 ($M^{+\cdot}$) 268 ($M^{+\cdot}$-Me·), 183, 182 ($M^{+\cdot}$ - $C_5H_9O_2\cdot$) 117, 101 ($C_5H_9O_2^+$, base), and 83 ($C_6H_{11}^+$) (Found: C, 63.87; H, 9.07; N, 4.83. $C_{15}H_{25}NO_4$ requires C, 63.58; H, 8.89; N, 4.94%); and *3R,4R-N-cyclohexyl-2-methylene-3,4,5-trihydroxypentanamide 4,5-acetonide* (173b) (87 mg, 14%) m.p. 80-1° (from diethyl ether and light petroleum), $[\alpha]_{589}^{20}$ - 37° (C = 0.225, dichloromethane), ν_{max} 3430 m (O-H), 3360 m (N-H), 1658 m, 1620 s, 1612 s (C=O), 1528 s (C=O), 1450 m, 1372 m, 1258 m, 1240 m, 1152 m, 1120 m (C-O), 1064 m, 1046 m, and 664 m cm^{-1}, δ 1.00-2.10 (10H, br, $(CH_2)_5$), 1.35 (3H, s, MeCO), 1.45 (3H, s, MeCO), 3.40-3.60 (1H, br, OH), 3.70-4.40 (5H, m, CH_2CHCH, HCN), 5.55 (1H, s, CH_2=), 5.95 (1H, s, CH_2=), and 6.70-6.90 (1H, br, NH), m/e 283 ($M^{+\cdot}$), 268 ($M^{+\cdot}$ - Me·), 183, 182 ($M^{+\cdot}$ - $C_5H_9O_2\cdot$), 144, 101 ($C_5H_9O_2^+$, base), 100, and 83 ($C_6H_{11}^+$) (Found: C, 63.84; H, 9.12; N, 4.79. $C_{15}H_{25}NO_4$ requires C, 63.58; H, 8.89; N, 4.94%).

Reaction of the Trianion (154b) with 1-Iodopropane

Amide sulphonylhydrazone (152 f)(448 mg) was dissolved in DME (5 ml) and the solution cooled to -75°. n-Butyllithium (3.50 mmol) was added, the solution warmed to -68° over 20 min and recooled to -75°. 1-Iodopropane (0.20 ml) was added, the suspension stirred to -65° over 165 min, quenched with glacial acetic acid (0.35 g) in water (2 ml) and warmed to 25°. General work up [(B) dichloromethane] and chromatography on Kieselgel H (18 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] gave E,Z-*N-cyclohexyl-2-oxohexanamide 2,4,6-tri-iso-propylbenzenesulphonylhydrazone* (152 l) (184 mg, 38%) m.p. 148-9° (from diethyl ether and light petroleum), ν_{max} (CCl_4) 3420 m (N-H), 3200 m (N-H), 2960 s, 2930 s, 2860 s, 1675 s (C=O), 1600 s, 1515 s, 1505 s (C=O), 1465 s, 1455 s, 1428 s, 1385 s, 1365 s, 1332 s

($-SO_2-N<$), 1246 m, 1192 m, 1165 and 1155 s ($-SO_2-N<$), 1105 s, 1090 s, 1072 m, 1060 m, 1038 m, 940 m, 906 s, 882 m, and 846 m cm^{-1}, δ 0.70-2.00 (17H, $^{n}\underline{Pr}$, $(\underline{CH_2})_5$), 1.28 (18H, overlapping d, J 7Hz, $CH\underline{Me_2}$), 2.30-2.60 (2H, br, 3-$\underline{CH_2}$), 2.88 (1H, overlapping septet, J 7Hz, p-$\underline{CH}Me_2$), 3.30-3.80 (1H, br, HCN), 4.15 (2H, overlapping septets, J 7Hz, o-$\underline{CH}Me_2$), 6.30-6.60 (1H, br, amide NH), 7.20 (2H, s, aryl-H), and 8.50 (1H, br s, NNH), m/e 492 (M^+ + H), 399, 250 (base), 232, 189, 161, 149, and 114 (Found: C, 65.70; H, 9.35; N, 8.47. $C_{27}H_{45}N_3O_3S$ requires C, 65.95; H, 9.22; N, 8.53%); the amide sulphonylhydrazone (152f) (206 mg, 46%), identical (t.l.c. and n.m.r.) with the starting material; and *N-cyclohexyl-3-hydroxy-2-oxopropanamide 2,4,6-tri-iso-propylbenzenesulphenylhydrazone* (152m) (63 mg, 14%) m.p. 134-6° (from diethyl ether and light petroleum), ν_{max} 3360 s (N-H, O-H), 3170 m (N-H), 1645 s (C=O), 1602 m (C=C), 1534 m, 1335 m ($-SO_2-N<$), 1288 m, 1247 m, 1175 and 1160 s ($-SO_2-N<$), 1087 m (C-O), 1070 m, 1032 m, 856 m, 722 m, and 662 m cm^{-1}, δ 1.00-2.00 (10H, br, $(\underline{CH_2})_5$), 1.26 (18H, overlapping d, J 7Hz, $CH\underline{Me_2}$), 2.90 (1H, overlapping septets, J 7Hz, p-$\underline{CH}Me_2$), 3.30-3.80 (1H, br, HCN), 4.10 (2H, overlapping septets, J 6.5 Hz, o-$\underline{CH}Me_2$), 4.72 (2H, s, 3-$\underline{CH_2}$), 6.50-6.80 (1H, br, amide NH), and 7.17 (2H, s, aryl-H) m/e 267, 251 [(108e), base], 233, 204, 189, 169, 149, and 126 (Found: C, 61.97; H, 8.65; N, 8.93. $C_{24}H_{39}N_3O_4S$ requires C, 61.90; H, 8.44; N, 9.02%).

Preparation of 1-Iodotridecane

Tridecan-1-ol (2.00 g) was dissolved in THF (50 ml) and the solution cooled to -78°. n-Butyllithium (12.0 mmol) was added, the solution warmed to 25°, quenched with carbon disulphide (2.0 ml) and then refluxed for 30 min. The solution was cooled to 25° and quenched with methyl iodide (3.0 ml). The solution was then refluxed for 30 min, recooled to 25° and evaporated to 90% volume. Pyrrolidine (4.0 ml) was added, the solution

was stirred for 15 h, evaporated, the residue redissolved in methyl iodide (50 ml) and then refluxed for 46 h. Evaporation and chromatography on Kieselgel H ((i) 30 g, (ii) 25 g) [eluant (i), (ii) light petroleum] gave 1-iodotridecane[121] (2.94 g, 95%) b.p. 116-8° at 0.30 mmHg, ν_{max} 2955 m, 2920 s, 2850 m, 1457 m, and 718 m cm^{-1}, δ 0.70-1.00 (3H, br, 13-C$\underline{H}_3$), 1.10-1.45 (22H, br s, Me(C$\underline{H}_2$)$_{11}$), and 3.16 (2H, t, $\underline{J}$ 7Hz, C$\underline{H}_2$I), m/e 310 ($M^{+\cdot}$) 183 ($M^{+\cdot}$ - I·, base), 127 (I^+), 113, 99, 85, 71, 57, and 55 (Found: C, 50.59; H, 8.98. Calc. for $C_{13}H_{27}I$: C, 50.33; H, 8.77%).

Reaction of the Trianion (154b) with 1-Iodotridecane

Amide sulphonylhydrazone (152f) (444 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (3.40 mmol) was added, the solution warmed to -68° over 15 min and treated with 1-iodotridecane (0.50 ml) in DME (3 ml). The thick suspension was stirred to -65° over 100 min, quenched with glacial acetic acid (0.34 g) in water (2 ml) and then warmed to 25°. General work up [(B) dichloromethane], chromatography on Kieselgel H (17 g) [eluant dichloromethane-diethyl ether (1:0-17:3)] and p.l.c. [one development with dichloromethane:diethyl ether (9:1)] gave the amide sulphonylhydrazone (152f) (291 mg, 66%); and the hydroxy-amide sulphonylhydrazone (152 m) (83 mg, 18%) both identical (t.l.c., and n.m.r.) with authentic samples.

Preparation of E-(N-*Cyclohexyl)-2-deuteriohept-2-enamide* (175)

Amide sulphonylhydrazone (152g) (507 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (4.84 mmol) was added, the solution warmed to -50° over 40 min, to 25° over 110 min, recooled to -70°, quenched with deuterium oxide (0.50 ml) and warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] and p.l.c. [one development with

dichloromethane:diethyl ether (16:1)| gave the E-*deuterio-amide* (175) (130 mg, 62%) m.p. 106-9° (from diethyl ether and light petroleum), ν_{max} 3290 s (N-H), 3075 m, 3020 m, 1654 s, 1620 s (C=O), 1547 s (C=O), 1320 m, 1280 m, 1255 m, 1240 m, 1152 m, 1110 m, 918 m, 892 m, 874 m, 789 m, 720 m, 712 m, 635 m, and 610 m cm^{-1}, δ 0.70-1.10 (3H, br, 7-CH_3), 1.10-3.00 [16H, br, $Me(CH_2)_3$, $(CH_2)_5$], 3.40-4.20 (1H, br, HCN), 5.80-6.40 (1H, br, NH), and 6.75 (1H, br t, J 6Hz, CH=), m/e 210 ($M^{+\cdot}$), 181 ($M^{+\cdot}$ - Et·), 167 ($M^{+\cdot}$ - Pr·), 153 ($M^{+\cdot}$ - ^{n}Bu·), 129 (base), 112, and 56, ca. 100% mono deuteriated (Found: C, 74.46; H, 11.24; N, 6.66. $C_{13}H_{22}{}^{2}HNO$ requires C, 74.24; N, 6.66%).

Preparation of N-*Cycloxyl-2-(2-hydroxyprop-2-yl)hept-2-enamide* (177)

Amide sulphonylhydrazone (152 g) (502 mg) was dissolved in DME (6 ml) and the solution cooled to -78°. n-Butyllithium (6.70 mmol) was added, the solution warmed to 25° over 155 min, recooled to -78°, quenched with acetone (0.40 ml) and warmed to 25°. General work up [(B) diethyl ether], chromatography on Kieselgel H (21 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] and p.l.c. [one development with dichloromethane:diethyl ether (4:1)] gave E-(N-*Cyclohexyl) hept-2-enamide* (178) (80 mg, 38%) m.p. 108-10° (from diethyl ether and light petroleum), ν_{max} 3295 s (N-H), 3075 m, 1665 s, 1620 s (C=O), 1547 s (C=O), 1350 m, 1250 m, 1225 m, 1150 m, 984 s (CH_2=CH), and 675 m cm^{-1}, δ 0.75-2.60 (19H, br, $(CH_2)_5$, ^{n}Bu), 3.50-4.10 (1H, br, HCN), 5.40-6.60 (1H, br, NH), 5.70 (1H, dm, J 15, n Hz, 2-CH), and 6.78 (1H, dt, J 15, 7Hz, 3-CH), m/e 209 ($M^{+\cdot}$) 180 ($M^{+\cdot}$ - Et·), 166 ($M^{+\cdot}$ - ^{n}Pr·), 152 ($M^{+\cdot}$ - ^{n}Bu·), 128 (base), 111, and 55 (Found C, 74.35; H, 11.23; N, 6.67. $C_{13}H_{23}NO$ requires C, 74.59; H, 11.07; N, 6.69%); and the Z-*hydroxy-amide* (177) (56 mg, 21%) m.p. 73-4° (from diethyl ether and light petroleum), ν_{max} 3360 s (O-H), 3290 s (N-H), 3060 m, 1648 s, 1615 s (C=O), 1540 s (C=O), 1355 s, 1332 m, 1292 m, 1262 m, 1247 m, 1190 m, 1168 s (C-O), 1153 m, 1132 m, 1100 m, 1039 m, 958 m, 908 m, 893 m, 873 m, 725 m,

and 692 m cm^{-1}, δ 0.70-1.10 (3H, br, 7-CH_3), 1.00-2.50 (16H, br, Me$(CH_2)_3$, $(CH_2)_5$) 1.50 (6H, s, MeCO), 3.40-4.00 (1H, br, HCN), 4.10 (1H, br s, OH), 5.40-5.90 (1H, br, NH), and 5.63 (1H, t, J 7Hz, HC=), m/e 267 ($M^{+\cdot}$), 252 ($M^{+\cdot}$ - Me·, base), 249 ($M^{+\cdot}$ - H_2O), 206, 168, 153, and 82 (Found: C, 72.05; H, 11.22; N, 5.29. $C_{16}H_{29}NO_2$ requires C, 71.86; H, 10.93; N, 5.24%).

Preparation of N-*Cyclohexyl-2-(1-hydroxyprop-2-enyl)hept-2-enamide* (176)

Amide sulphonylhydrazone (152 g) (512 mg) was dissolved in DME (6 ml) and the solution cooled to -78°. n-Butylithium (6.70 mmol) was added, the solution warmed to 25° over 105 min, recooled to -78°, quenched with acrolein (0.35 ml) and warmed to 25°. General work up [(B) diethyl ether] and chromatography on Kieselgel H (21 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] gave the E,Z-*hydroxy-amide* (176) (136 mg, 51%) as an oil, ν_{max} 3290 br s (O-H, N-H), 3080 m, 2950 s, 2925 s, 2850 s, 1655 s, 1610 s (C=O), 1540 s (C=O), 1460 m, 1448 s, 1420 m, 1347 m, 1323 m, 1255 m, 1240 m, 1115 m (C-O), 1025 m, 987 m, 920 m (CH_2=CH), 705 m, and 610 m cm^{-1}, δ 0.70-2.40 (19H, br, $(CH_2)_5$ ^nBu), 3.30-4.20 (1H, br, HCN), 4.50-4.80 (1H, br, OH), 4.93-6.50 (4H, m, CH_2=CHCH, Z 3-CH), 6.40 (1H, t, J 7Hz, E 3-CH), and 6.55-7.15 (1H, br, NH), m/e 265 ($M^{+\cdot}$), 248 ($M^{+\cdot}$ - OH·), 247 ($M^{+\cdot}$ - H_2O), 234 (base), 128, and 55 (Found: C, 72.12; H, 10.52; N, 5.05. $C_{16}H_{27}NO_2$ requires C, 72.41; H, 10.25; N, 5.28%).

Preparation of Z-(N-*Cyclohexyl)-2-(hexadeuterio-2-hydroxyprop-2-yl)hept-2-enamide* (179)

Amide sulphonylhydrazone (152 g) (507 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (6.70 mmol) was added, the solution warmed to 25° over 2 h, recooled to -65°, quenched with hexadeuterioacetone (0.35 ml), warmed to 25° and evaporated. General work up [(B) diethyl ether], chromatography on Kieselgel H (21 g) [eluant dichloro-

methane-diethyl ether (1:0-9:1)] and p.l.c. [two developments with dichloromethane:diethyl ether (9:1)] gave the E-deuterio-amide (175) (51 mg, 24%) identical (t.l.c., n.m.r., i.r. and mass spectra) with an authentic sample; and the Z-*hydroxy-amide* (179) (104 mg, 38%) m.p. 77-79° (from diethyl ether and light petroleum), ν_{max} 3360 s (O-H), 3280 s (N-H), 3060 m, 2220 m (C-^{2}H), 1645 s, 1610 s (C=O), 1540 s (C=O), 1350 m, 1328 m, 1165 m, 1150 m, 1140 m, 1110 m, 1092 m (C-O), 1047 m, 1015 m, 730 m, 720 m, and 608 m cm^{-1}, δ 0.70-2.50 (19H, br, $(CH_2)_5$, ^nBu), 3.40-4.20 (1H, br, HCN), 4.13 (1H, br s, OH), 5.44-6.00 (1H, br, NH), and 5.64 (1H, t, J 7Hz, HC=), m/e 273 ($M^{+\cdot}$), 253 [$M^{+\cdot}$ — (H_2O or $CD_3\cdot$), base], 212, 156, 89, and 56 (Found: C, 70.48; H, 10.92; N, 5.10. $C_{16}H_{23}{}^2H_6NO_2$ requires C, 70.28; N, 5.12%).

Preparation of 2-(1-Hydroxypropyl)-N-methylhept-2-enamide (181)

Amide sulphonylhydrazone (152j) (882 mg) was suspended in DME (20 ml) and the suspension cooled to -78°. n-Butyllithium (13.4 mmol) was added, the solution warmed to 25° over 2 h, recooled to -78°, quenched with propanal (0.50 ml) and warmed to 25°. General work up [(B) diethyl ether] chromatography on Kieselgel H (18 g) [eluant dichloromethane-diethyl ether (1:0-3:2)] and p.l.c. [three developments with diethyl ether] gave an oil, possibly the E:Z (2:1) -hydroxy-amide (181) (219 mg, 55%), ν_{max} 3320 s (O-H, N-H), 3090 m, 2960 s, 2930 s, 2870 s, 1665 s, 1620 s (C=O), 1550 s (C=O), 1476 m, 1418 m, 1388 m, 1325 m, 1305 m, 1275 m, 1248 m, 1160 m, 1120 m (C-O), 1080 m, 1047 m, 1013 m, and 969 m cm^{-1}, δ 0.75-1.10 (6H, br, $MeCH_2$), 1.10-1.90 (6H, br, 2'-CH_2, 5,6-CH_2), 2.00-2.40 (2H, br, 4-CH_2), 2.80 (3H, 2 overlapping d, J 4.5 Hz, NMe), 4.00 (1H, t, J 7Hz, Z 1'-CH), 4.10-4.40 and 4.80-5.20 (1H, br, OH), 4.55 (1H , t, J 7Hz, E 1'-CH), 5.60 (1H, t, J 8Hz, Z HC=), 6.35 (1H, t, J 8Hz, E HC=), and 6.80-7.10 and 7.40-7.70 (1H, br, NH), m/e 199 ($M^{+\cdot}$, weak), 181 ($M^{+\cdot}$ - H_2O), 170 ($M^{+\cdot}$-Et·,

base), 139, 112, 81 67, and 59 (Found: C, 64.85; H, 10.64; N, 6.55; $M^{+\cdot}$, 199.1573. $C_{11}H_{21}NO_2$ requires C, 66.30; H, 10.62; N, 7.03%; $M^{+\cdot}$, 199.1572).

A sample of the amide (181) (195 mg) was dissolved in THF (10 ml) and the solution cooled to -78°. n-Butyllithium (2.34 mmol) was added, the solution was warmed to 25°, quenched with methyl iodide (3.0 ml) and stirred for 4 d. General work up [(B) diethyl ether], chromatography on Kieselgel H (16 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] and p.l.c. [two developments with diethyl ether] gave E:Z (4:1) N,N-*dimethyl--2-(1-methoxypropyl)hept-2-enamide* (184) (141 mg, 63%) as an oil, ν_{max} 2960 s, 2930 s, 2875 s, 2820 m, 1660 s, 1630 s (C=O), 1498 m, 1460 m, 1393 s, 1268 s, 1130 s, 1108 s, 1084 s (C-O), and 1060 m cm^{-1}, δ 0.80-1.10 (6H, m, $\underline{Me}CH_2$), 1.10-1.55 (4H, m, 6,5,-$C\underline{H}_2$), 1.60-1.90 (2H, m, 2'-$C\underline{H}_2$) 2.15-2.40 (2H, m, 4-$C\underline{H}_2$), 2.95 (6H, br s, $N\underline{Me}_2$), 3.25 (3H, s, $O\underline{Me}$), 3.90 (1H, t, $\underline{J}$ 7Hz, 1'-$C\underline{H}$), 5.45 (1H, tm, $\underline{J}$ 8,n Hz, Z 3-$C\underline{H}$), and 5.50 (1H, t, $\underline{J}$ 8Hz, E 3-CH), m/e 227 ($M^{+\cdot}$), 212 ($M^{+\cdot}$ - Me·), 198 ($M^{+\cdot}$ - Et·), 195 ($M^{+\cdot}$ - MeOH, base), 112, and 88 (Found: C, 69.02; H, 11.42; N, 6.11. $C_{13}H_{25}NO_2$: requires, C, 68.68; H, 11.08; N, 6.16%).

Second Preparation of the Hydroxy-amide (181)

Amide sulphonylhydrazone (152j) (440 mg) was suspended in DME (10 ml) and the suspension cooled to -78°. n-Butyllithium (5.1 mmol) was added, the suspension warmed to 25° over 100 min, recooled to -78°, quenched with propanal (0.20 ml), warmed to 25° and stirred for 16 h. A similar work up as before gave the $\underline{E}$:$\underline{Z}$ (2:1)-hydroxy-amide (181) (128 mg, 64%) identical (t.l.c. and n.m.r.) with the previous sample.

Preparation of 2 (1-Hydroxyprop-2-enyl)-N-methylhept-2-enamide (182)

Amide sulphonylhydrazone (152j) (879 mg) was suspended in DME (24 ml) and the suspension cooled to -78°. n-Butyllithium (13.4 mmol) was added,

the suspension warmed to -30° over 75 min, to 25° over 40 min, recooled to -62°, quenched with acrolein (0.65 ml) and warmed to 25°. General work up [(B) diethyl ether] , chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-1:1)] and p.l.c. [one development with diethyl ether] gave the E,Z-hydroxy-amide (182) (198 mg, 50%) as an oil, R_f 0.35, 0.33 (diethyl ether), ν_{max} 3320 s, (O-H, N-H), 2955 s, 2930 s, 2870 s, 1655 s, 1610 s (C=O), 1548 s (C=O), 1455 m, 1408 m, 1315 m, 1255 m, 1115 m (C-O), 1020 m, 987 m, and 920 m (CH_2=CH) cm^{-1}, δ 0.70-1.10 (3H, br, 7-CH_3), 1.10-1.65 (6H, br, 5,6-CH_2), 1.90-2.50 (2H, br, 4-CH_2), 2.80 (3H, 2 overlapping d, J 5Hz, NMe), 4.60-4.90 (1H, br, OH), 4.90-6.60 (4H, m, CH_2=CHCH), 5.65 (1H, t, J 7Hz, Z 3-CH), 6.40 (1H, t, J 7Hz, E 3-CH) and 6.40-7.55 (1H, br, NH), m/e 197 ($M^{+\cdot}$), 180 ($M^{+\cdot}$ - OH), 168, 166 ($M^{+\cdot}$-Et·, base), 140 ($M^{+\cdot}$ - ^{n}Bu·), 99, and 58 (Found: C, 66.51; H, 9.92; N, 6.65; $M^{+\cdot}$, 197.1412. $C_{11}H_{19}NO_2$ requires C, 66.97; H, 9.71; N, 7.10%; $M^{+\cdot}$, 197.1416).

Preparation of N,N-*Dimethyl-2-(1-methoxyprop-2-enyl)hept-2-enamide* (183)

Amide sulphonylhydrazone (152j) (876 mg) was suspended in DME (20 ml) and the suspension cooled to -78°. n-Butyllithium (13.4 mmol) was added, the suspension was warmed to 25° over 2 h, recooled to -78° and quenched with acrolein (0.60 ml). n-Butyllithium (8.00 mmol) was added, the solution warmed to 25° over 20 min, quenched with methyl iodide (5.0 ml) and stirred for 3 d. General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-4:1)] gave the E:Z (2:1)-*hydroxy-amide* (183) (266 mg, 59%) as an oil, ν_{max} 2960 m, 2930 s, 2870 m, 1635 s (C=O), 1500 m, 1457 m, 1396 m, 1125 m, and 1095 m (C-O) cm^{-1}, δ 0.75-1.05 (3H, br, 7-CH_3), 1.05-1.70 (4H, br, 5,6-CH_2), 1.80-2.50 (2H, br, 4-CH_2), 3.00 (6H, br s, NMe_2), 3.32 (3H, br s, MeO), 4.32 (1H, d, J 8Hz, Z 1'-CH), 4.50 (1H, d, J 8Hz, E 1'-CH), and

5.05-6.20 (4H, m, HC=), m/e 225 ($M^{+\cdot}$), 210 ($M^{+\cdot}$ - Me·), 194 ($M^{+\cdot}$ - MeO·), 180 (base), 121, 72, and 71 (Found: C, 69.19; H, 10.42; N, 5.97. $C_{13}H_{23}NO_2$ requires C, 69.29; H, 10.29; N, 6.22%).

Hydrogenation of the E:Z (2:1)-Hydroxy-amide (183)

E:Z (2:1)-Hydroxy-amide (183) (96 mg) was dissolved in THF (10 ml) and hydrogenated over Adams catalyst (20 mg) for 2.5 h. Hydrogen uptake (7.5 ml) was observed, the solution filtered and evaporated to yield (unoptimised) the E:Z (2:1)-hydroxy-amide (184) (72 mg, 74%) identical (t.l.c. and n.m.r.) with an authentic sample.

Preparation of N-*Methyl* - Z-*2-(pentylidene)-3,4,5-trihydroxypentanamide 4,5-Acetonide* (185a,b)

Amide sulphonylhydrazone (152j) (878 mg) was suspended in DME (20 ml) and the suspension cooled to -78°. n-Butyllithium (13.4 mmol) was added, the suspension was warmed to 25° over 110 min, quenched with 4R-2,2-dimethyl-4-formyl-1,3-dioxolan [92a] (0.40 ml) and stirred for 10 min. General work up [(B) diethyl ether], chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-3:2)] and p.l.c. [three developments with diethyl ether] gave *3S,4R - Methyl — Z-2-(pentylidene)-3,4,5-trihydroxypentanamide 4,5-acetonide* (185a) (116 mg, 21%) m.p. 68-9° (from diethyl ether and petroleum), $[\alpha]_{589}^{20}$ + 17° (C = 0.13, dichloromethane), ν_{max} 3345 s and 3150 m (O-H, N-H), 3080 m, 1655 s, 1620 s (C=O), 1584 m, 1505 s (C=O), 1418 s, 1342 s, 1312 s, 1288 m, 1280 m, 1268 s, 1218 s, 1158 s, 1105 m, 1062 s, 1033 s (C-O), 1002 m, 983 m, 940 m, 854 s, 772 m, 734 m, 720 m, and 677 m cm^{-1}, δ 0.80-1.10 (3H, br, $MeCH_2$), 1.20-1.60 (4H, br, $Me(CH_2)_2$), 1.40 (6H, 2s, MeCO), 2.10-2.40 (2H, m, CH_2C=), 2.90 (3H, d, J 5Hz, NMe), 4.05-4.35 (3H, m, 4-CH, 5-CH_2), 4.40 (1H, br t, J 7Hz, 3-CH), 5.10 (1H, d, J 8Hz, OH), 6.40 (1H, t, J 8Hz, HC=), and 6.60-6.90 (1H, br, NH), m/e

272 (M^{+} + H), 256 (M^{+} - Me·), 171, 170 (M^{+} - $C_5H_9O_2$·, base), 101 ($C_5H_9O_2^{+}$), and 58 (Found: C, 61.71; H, 9.33; N, 5.06. $C_{14}H_{25}NO_4$ requires C, 61.97; H, 9.29; N, 5.16%); and an oil probably containing the isomeric hydroxy-amides (185b) (69 mg, 13%), ν_{max} 3310 s (O-H, N-H), 3095 m, 2980 m, 2960 s, 2930 s, 2870 m, 1670 s, 1625 s (C=O), 1550 s (C=O), 1460 m, 1415 m, 1383 m, 1373 m, 1260 m, 1216 m, 1158 m, and 1068 s cm^{-1}, δ 0.80-1.10 (3H, br, MeCH$_2$) 1.20-1.60 (4H, m, Me(CH$_2$)$_2$), 1.38 (6H, m, MeCO), 2.00-2.45 (2H, br, CH$_2$C=) 2.90 (3H, overlapping d, J 4Hz, NMe), 3.50-4.50 (3H, m, 4-CH, 5-CH$_2$), 4.65-4.75 and 5.75-6.00 (1H, m, 3-CH), 6.00-6.45 and 7.20-7.60 (1H, br, NH), and 6.55, 6.65 and 6.80 (1H, 3t, HC=), m/e 272 (M^{+} + H), 271 (M^{+}·), 256, 171, 170 (M^{+} - $C_5H_9O_2$·, base), 141, 111, and 101 ($C_5H_9O_2^{+}$).

Preparation of N-*Cyclohexyl-3-hydroxy-2-(methoxymethyl)pent-4-enamide* (192)

Hydroxy-amide (170) (134 mg) and powdered potassium hydroxide (152 mg) were suspended in methanol (2 ml) and the solution stirred for 14 d. General work up [(B) acetic acid, diethyl ether] and p.l.c. [one development with diethyl ether] gave the *hydroxy-amide* (192) (111mg, 72%) m.p. 84° (from diethyl ether and light petroleum), ν_{max} 3280 s (N-H), 3090 m, 1630 s (C=O), 1550 s (C=O), 1345 m, 1303 m, 1273 m, 1255 m, 1240 m, 1212 m, 1192 m, 1150 m, 1118 s (C-O), 1058 m, 990 m, 918 m (CH$_2$=CH), 718 m, and 660 m cm^{-1} δ 1.00-2.05 (10H, br, (CH$_2$)$_5$), 2.10-2.60 (1H, br, 2-CH), 3.30 (3H, s, MeO), 3.60 (2H, d, J 6Hz, MeOCH$_2$), 3.60-4.80 (2H, br, HCN, OH), and 4.90-6.60 (5H, m, CH$_2$=CHCH, NH), m/e 241 (M^{+}·), 226 (M^{+} - Me·), 224 (M^{+} - OH·), 184 (M^{+} - C_3H_5O·, base), 154, 104, 72, and 57 (Found: C, 64.65; H, 9.76; N, 5.80. $C_{13}H_{23}NO_3$ requires C, 64.70; H, 9.61; N, 5.81%).

Preparation of (±)-*4,5-trans* E,Z-*5- Iodomethyl -4-methoxy-3-pentylidene-tetrahydrofuran-2-one* (198),(199)

Amide sulphonylhydrazone (152j) (2.143 g) was suspended in DME (40 ml)

and the suspension cooled to -78°. n-Butyllithium (33.5 mmol) was added, the suspension warmed to 25° over 2 h, recooled to -78° and quenched with acrolein (1.0 ml). The solution was stirred for 10 min, quenched with methyl iodide (10.0 ml), warmed to 25° and stirred for 3 d. General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-7:3)] gave the crude methoxy-amide (183). Iodine (1.35 g) was added, the mixture suspended in THF (20 ml) and water (20 ml), stirred for 15 h and saturated with sodium thiosulphate (s). General work up [(B) diethyl ether] , chromatography on Kieselgel H (20 g) [eluant dichloromethane] and p.l.c. [one development with dichloromethane] gave the Z-*iodolactone* (199) (164 mg, 10%) as an oil, ν_{max} (CCl_4) 2960 s, 2925 s, 2860 s, 2825 s, 1775 s (C=O), 1678 s (C=C), 1645 m, 1470 s, 1445 m, 1370 s, 1325 m, 1240 m, 1216 m, 1195 s, 1180 s, 1132 s (C-O), 1116 s, 1082 s, 1000 s, 975 m, 906 m, and 882 m cm^{-1}, δ 0.65-0.95 (3H, br, $\underline{Me}CH_2$), 1.05-1.60 (4H, br, $Me(\underline{CH_2})_2$), 2.50-2.85 (2H, br, $\underline{CH_2}C=$), 3.20 (3H, s, $\underline{MeO}$), 3.20-3.45 (2H, m, $\underline{CH_2}I$), 4.15 (1H, br d, $\underline{J}$ 4.5 Hz, 4-$\underline{CH}$), 4.35-4.60 (1H, m, 5-$\underline{CH}$), and 6.43 (1H, t, $\underline{J}$ 7Hz, $\underline{HC}=$), m/e 324 ($M^{+\cdot}$) 292 ($M^{+\cdot}$ - MeOH), 197 ($M^{+\cdot}$ - I·, base), 165, 154, and 84 (Found: C, 40.97; H, 5.43. $C_{11}H_{17}IO_3$ requires C, 40.76; H, 5.28%); and the E-*iodolactone* (198) (345 mg, 22%) as an oil, ν_{max} 2950 s, 2925 s, 2870 m, 2825 m, 1770 s (C=O), 1680 s (C=C), 1468 m, 1460 m, 1420 m, 1370 m, 1324 m, 1265 m, 1218 m, 1182 s (C-O), 1145 s, 1112 s, 1102 s, 1082 s, 1056 s, 1002 s, 970 m, 912 m, 840 m, and 732 s cm^{-1}, δ 0.70-1.10 (3H, br, $\underline{Me}CH_2$), 1.20-1.75 (4H, br, $Me(\underline{CH_2})_2$), 2.45 (2H, $\underline{ca.}$ q, $\underline{J}$ 8Hz, $\underline{CH_2}C=$), 3.38 (3H, s, $\underline{OMe}$), 3.40-3.60 (2H, m, $\underline{CH_2}I$), 4.50-4.75 (2H, m, 4-$\underline{CH}$, 5-$\underline{CH}$), and 6.88 (1H, t, $\underline{J}$ 8Hz, $\underline{HC}=$), m/e 324 ($M^{+\cdot}$), 292 ($M^{+\cdot}$ - MeOH), 282, 197 ($M^{+\cdot}$ - I·, base), 165, 154, and 84 (Found: C, 41.36; H, 5.46; $M^{+\cdot}$ 324.0223. $C_{11}H_{17}IO_3$ requires C, 40.76; H, 5.28%; M^+, 324.0224).

Attempted Preparation of the Lactones (198,199) via Anhydrous Iodolactonisation

Methoxy-amide (183) (142 mg) and iodine (0.50 g) were dissolved in THF (10 ml) and the solution stirred for 16 h. General work up [(B) sodium thiosulphate, diethyl ether] gave a crude residue, ν_{max} 1770 w, 1630 s (183).

Preparation of N-*Cyclohexyl-3-methoxy*-N-*methyl-2-methylenepent-4-enamide* (200)

Hydroxy-amide (170) (255 mg) was dissolved in THF (6 ml) and the solution cooled to -78°. n-Butyllithium (2.68 mmol) was added, the solution warmed to 25° over 15 min, quenched with methyl iodide (1.0 ml) and stirred for 2 d. Evaporation and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-7:3)] gave the *methoxy-amide* (200) (235 mg, 81%) as an oil, ν_{max} 2940 s, 2865 s, 2835 m, 1620 s (C=O), 1488 m, 1457 s, 1413 s, 1375 m, 1330 m, 1085 s (C-O), 996 m, 925 s (CH_2=CH), and 900 m cm^{-1}, δ 1.00-2.00 (10H, br, $(CH_2)_5$), 2.80 (3H, s, NMe), 3.30 (3H, s, OMe), 4.10-4.55 (1H, br, HCN), and 4.90-6.00 (6H, m, HC=,3-CH), m/e 237 ($M^{+\cdot}$), 222 ($M^{+\cdot}$ - Me·, base), 206 ($M^{+\cdot}$ - MeO·) 162, 140, 124, 112, and 55 (Found: C, 70.58; H, 9.94; N, 5.75. $C_{14}H_{23}NO_2$ requires C, 70.85; H, 9.77; N, 5.90%).

Preparation of *2-(1-Methoxyprop-2-enyl)*-N-*methylhept-2-enamide* (201)

E,Z-Hydroxy-amide (182) (138 mg) and potassium t-butoxide (78 mg) were suspended in dichloromethane (5 ml) and methyl iodide (5 ml). The suspension stirred for 40 min and then evaporated. Purification by p.l.c. [two developments with diethyl ether] gave mainly the E-*methoxy-amide* (201) (81 mg, 55%) as an oil, ν_{max} 3370 s (N-H), 2960 s, 2935 s, 2875 s, 2860 s, 2825 m, 1670 s, 1630 s (C=O), 1540 s (C=O), 1470 m, 1413 m,

1265 m, 1110 m, 1085m(C-O), and 927 m (CH_2=CH) cm^{-1}, δ 0.73-1.10 (3H, br, $MeCH_2$), 1.15-1.60 (4H, br, $Me(CH_2)_2$), 1.93-2.55 (2H, br, CH_2C=), 2.80 (3H, d, J 4.5 Hz, NMe), 3.33 (3H, s, OMe), 4.63-6.26 (4H, m, CH_2=CHCH), 6.70-7.40 (1H, br, NH), and 6.93 (1H, t, J 7.5 Hz, 2-C=CH), m/e 211 ($M^{+\cdot}$), 196 ($M^{+\cdot}$ - Me·), 180 ($M^{+\cdot}$ - OMe·), 179 ($M^{+\cdot}$ - MeOH), 166 (base), 71, and 58 (Found: C, 68.18; H, 10.20; N, 6.70. $C_{12}H_{21}NO_2$ requires C, 68.21; H, 10.02; N, 6.63%).

Preparation of *3-(t-Butyldimethylsilyloxy)*-N-*cyclohexyl*-N-*methyl-2-methyl-enepent-4-enamide* (204)

Hydroxy-amide (170) (62 mg) was dissolved in THF (5 ml) and the solution cooled to -78°. n-Butyllithium (0.80 mmol) was added, the solution warmed to 25°, recooled to -78° and then quenched with t-butylchlorodimethylsilane (103 mg) in THF (5 ml). The solution was warmed to 60° for 30 min, cooled to 25°, quenched with methyl iodide (4.0 ml) and stirred for 3 d. General work up [(B) dichloromethane] and p.l.c. [three developments with dichloromethane:diethyl ether (9:1)] gave the silyl-amide (203) (77 mg, 80%) as an oil, ν_{max} 3330 m (N-H), 1655 s, 1610 s (C=O), and 1528 s (C=O) cm^{-1}, δ 0.07 (3H, s, MeSi), 0.10 (3H, s, MeSi), 0.90 (9H, s, ^tBu), 1.00-2.05 (10H, br, $(CH_2)_5$), 3.50-4.00 (1H, br, HCN), 4.90-6.10 (5H, m, CH_2=CHCH, 2-C=CH), 5.90 (1H, m, 2-C=CH), and 6.50-6.85 (1H, br, NH), m/e 323 ($M^{+\cdot}$), 308 ($M^{+\cdot}$ - Me·), and 266 ($M^{+\cdot}$ - ^tBu·, base), 184, and 75. A sample of the amide (203) (74 mg) was dissolved in THF (5 ml). Sodium hydride (40 mg, excess) was added, the suspension stirred for 10 min, treated with methyl iodide (3 ml) and stirred for 3 d. General work up [(B) dichloromethane] gave the *silyl-amide* (204) (77 mg, 100%) as an oil, ν_{max} 2930 s, 2860 m, 1650 s, 1624 s (C=O), 1450 m, 1408 m, 1367 m, 1326 m, 1257 m, 1072 s (C-O), 1032 m, 1008 m, 992 m, 922 m (CH_2=CH), 870 m, 838 m, and 779 m cm^{-1}, δ 0.07 (6H, s, MeSi), 0.92 (9H, s, ^tBu), 1.00-2.10 (10H, br,

$(CH_2)_5$), 2.80 (3H, s, NMe), 3.30-3.90 (1H, br, HCN), 4.96-6.00 (3H, m, CH_2=CH), 5.00 (1H, s, 2-C=CH), 5.15 (1H, dm, J 16, n Hz, 3-CH), and 5.30 (1H, s, 2-C=CH), m/e 337 ($M^{+\cdot}$), 322 ($M^{+\cdot}$ - Me·), 280 ($M^{+\cdot}$ - ^tBu·, base), 198, 73, and 55 (Found: C, 67.83; H, 10.75; N, 4.34. $C_{19}H_{35}NO_2Si$ requires C, 67.60; H, 10.45; N, 4.15%).

Preparation of *2-[(t-Butyldimethylsilyloxy) prop-2-enyl]-N,N-dimethylhept-2-enamide* (205)

Hydroxy-amide (E:Z ratio high) (182) (567 mg) was dissolved in THF (20 ml) and the solution cooled to -78°. n-Butyllithium (7.0 mmol) was added, the solution warmed to 25° and then recooled to -78°. t-Butylchlorodimethylsilane (1.0 g) in THF (4 ml) was added, the solution was warmed to reflux for 30 min and then evaporated. General work up [(B) diethyl ether] gave a crude residue which was dissolved in THF (20 ml). Sodium hydride (1.5 g, excess) and imidazole (1 crystal) were added, the suspension treated with methyl iodide (15 ml), stirred for 5 d and quenched with water (15 ml). General work up [(B) dichloromethane] and chromatography on Kieselgel H (20 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] gave mainly the E-*silyl-amide* (205) (717 mg, 77%) as an oil, ν_{max} 2960 s, 2930 s, 2860 s, 1630 s (C=O), 1413 m, 1463 m, 1390 s, 1360 m, 1255 m, 1127 m, 1080 s (C-O), 1065 s, 1032 m, 1008 m, 920 m, 870 m, 838 s, and 778 s cm^{-1}, δ 0.05 (6H, s, MeSi), 0.70-1.05 (3H, br, $MeCH_2$), 0.86 (9H, s, ^tBu), 1.10-1.60 (4H, br, $Me(CH_2)_2$), 2.00-2.50 (2H, br, CH_2C=), 3.05 (6H, s, NMe_2), 5.00-6.60 (5H, m, HC=, 3-CH), m/e 325 ($M^{+\cdot}$), 310 ($M^{+\cdot}$ - Me·), 268 ($M^{+\cdot}$ - ^tBu·, base), 180, 102, and 73 (Found: C, 66.60; H, 11.11; N, 4.24. $C_{18}H_{35}NO_2Si$ requires C, 66.40; H, 10.84; N, 4.30%).

Preparation of *(±)-4,5-trans-4-(t-Butyldimethylsilyloxy)-5-iodomethyl-3-pentylidenetetrahydrofuran-2-one* (206)

Silyl-amide (E:Z ratio high) (205) (211 mg) was dissolved in THF (5 ml) and water (4 ml). Iodine (0.50 g) was added and the solution stirred for 20 h. General work up [(B) sodium thiosulphate solution, diethyl ether] and chromatography on Kieselgel H (20 g) [dichloromethane-diethyl ether (1:0-1:1)] gave mainly the E-*iodolactone* (206) (202 mg, 70%) as an oil, ν_{max} 2960 m, 2940 m, 2860 m, 1774 s (C=O), 1685 m (C=C), 1458 m, 1260 m, 1186 m, 1150 m,1118 m (C-O), 1087 m, 1055 m, 1027 m, 994 s, 920 m, 835 s, 780 m and 734 m cm^{-1}, δ 0.10 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.80-1.05 (3H, br, $MeCH_2$), 0.90 (9H, s, ^tBu), 1.10-1.70 (4H, m, $Me(CH_2)_2$), 2.35 (2H, ca. q, J 8Hz, $CH_2C=$), 3.30-3.55 (2H, 3s, CH_2I), 4.40 (1H, m, 5-CH), 4.96 (1H, d, J 4Hz, 4-CH), and 6.70 (1H, tm, J 8, n Hz, HC=), m/e 424 ($M^{+\cdot}$), 423 ($M^{+\cdot}$ - H·), 409 ($M^{+\cdot}$ - Me·), 367 ($M^{+\cdot}$ - ^tBu·), 297 ($M^{+\cdot}$ - I·), 240 (base), 211, and 197 (Found: C, 45.62; H, 7.04; ($M^{+\cdot}$ - H·), 423.0847. $C_{16}H_{29}IO_3Si$ requires C, 45.28; H, 6.89%; ($M^{+\cdot}$ - H·), 423.0854).

Reaction of the Iodolactone (206) with Silver Fluoride

Iodolactone (206) (217 mg) and anhydrous silver fluoride[53] (130 mg) were suspended in pyridine (5 ml) and the mixture was stirred in the dark for 3 d. The suspension was evaporated, dissolved in diethyl ether (50ml), filtered and re-evaporated to yield a crude residue (55 mg). N.m.r. and i.r. analysis indicated the presence of mostly the iodolactone (206) and some de-silylated material, ν_{max} 3600 m cm^{-1}. The residue was redissolved in pyridine (2 ml), silver fluoride (160 mg) added, and the suspension stirred in the dark for 1 week. I.r. analysis indicated that no dimethylene lactone (207) was formed.

Reaction of the Iodolactone (206) with DBU

Iodolactone (206) (45 mg) and DBU (1.6×10^{-5} L) were dissolved in benzene (1 ml) and the solution stood at 25° overnight. Evaporation and

p.l.c. [one development with dichloromethane:diethyl ether (1:1)] gave the uncharacterised product (208) (11 mg)as an oil, ν_{max} (CCl_4) 2970 s, 2960 s, 2880 s, 1790 s (C=O), 1647 s (C=C), 1465 m, 1388 m, 1367 m, 1300 s, 1238 m, 1180 m, 1122 s, 1060 s, 1040 s, 970 s, 928 m, 912 s, 872 m, and 854 m cm^{-1} δ 0.95 (3H, t, J 7Hz, $MeCH_2$), 1.10-1.60 (3H, m), 2.75 (2H, q, J 7Hz), 4.80 (1H, d, J 2.5Hz), 5.10 (1H, d, J 2.5Hz), and 6.00-7.40 (nH, m), m/e 184, 182, 180 (base), 166, 147, 145, 119, 117, 87, 85, 83, and 47. The sample rapidly polymerised at 25°.

Attempted Preparation of the Selenolactone (209)

E,Z-Amide (205) (592 mg) and phenylselenyl chloride[93b] (480 mg) were dissolved in THF (10 ml) and the solution stirred for 5 min. Water (0.50 ml) was added, the solution stirred for 3 d and evaporated. Purification by repeated chromatography on Kiesegel H and repeated p.l.c. gave the impure selenolactone (209) (78 mg, < 9%) as an oil, ν_{max} 2960s, 2940 s, 2870 s, and 1775 s (C=O) cm^{-1}, δ_{max} 0.05 (3H, s), 0.15 (3H, s), 0.85 (9H, s), and 7.20-7.70 (5H, m), m/e 454/452 ($M^{+\cdot}$), 397/395 ($M^{+\cdot}$ - $^{t}Bu\cdot$), 314/312 (base), 275, 171, 157, and 83 (Found: $M^{+\cdot}$, 454.1445. $C_{22}H_{34}O_3SeSi$ requires $M^{+\cdot}$, 454.1442).

Preparation of 1-Cyclohexyl-3-methylene-azetidin-2-one (210a)

Hydroxy-amide (171) (142 mg) was dissolved in THF (10 ml) and the solution was cooled to -78°. n-Butyllithium (1.61 mmol) was added, and the solution warmed to 0°. Toluene-4-sulphonyl chloride (236 mg) was added, the solution stirred overnight at 25° and evaporated. General work up [(B) diethyl ether] and p.l.c. [(i) one development with diethyl ether, (ii) eight developments with dichloromethane] gave the methylene β-lactam[99a] (210a) (77 mg, 60%) as an oil, ν_{max} 2930 s, 2855 s, 1745 s (C=O), 1668 m (C=C), 1628 m, 1530 m, 1467 m, 1452 m, 1390 s, 1364 m,

1350 m, 1318 m, 1259 m, 1223 m, 1110 m, 1088 m, 993 m, 966 m, 918 m (CH_2=), 890 m, 793 m, and 728 m, cm^{-1}, δ 1.00-2.10 (10H, br, (CH_2)$_5$), 3.45-4.05 (1H, br, HCN), 3.80 (2H, d, J 1Hz, 4-CH_2), 5.25 (1H, m , J 1Hz, CH_2=), and 5.85 (1H, m , J 1.5Hz, CH_2=), m/e 165 ($M^{+\cdot}$), 122, 84, 81, and 55 (Found: C, 72.39; H, 9.38; N, 8.34; $M^{+\cdot}$, 165.1152. Calc. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48%; $M^{+\cdot}$, 165.1154).

Preparation of *1-Cyclohexyl-4-ethyl-3-methylene-azetidin-2-one* (210b)

Hydroxy-amide (172) (413 mg) was dissolved in THF (15 ml) and the solution cooled to -78°. n-Butyllithium (4.15 mmol) was added, the solution warmed to 25° over 20 min and recooled to -78°. Toluene-4-sulphonyl chloride (625 mg) in THF (14, 2 ml) was added dropwise during 15 min, the solution warmed to 25°, stirred for 15 h and evaporated. General work up [(B) diethyl ether] and chromatography on Kieselgel H (16 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] gave the *methylene β-lactam* (210b) (258 mg, 68%) as an oil, ν_{max} 2960 m, 2930 s, 2858 m, 1750 s (C=O), 1704 m, 1465 m, 1453 m, 1387 m, 1368 m, 1353 m, 1323 m, 1305 m, 1269 m, 1260 m, 1107 m, 1081 m, and 913 m (CH_2=) cm^{-1}, δ 0.97 (3H, t, J 7Hz, $MeCH_2$), 1.00-2.10 (10H, br, (CH_2)$_5$), 1.75 (2H, q, J 7Hz, $MeCH_2$), 3.30-3.70 (1H, m, HCN), 3.95-4.20 (1H, m, 4-CH), 5.05 (1H, s , CH_2=), and 5.57 (1H, s , H_2C=), m/e 193 ($M^{+\cdot}$), 178 ($M^{+\cdot}$-Me·), 164 ($M^{+\cdot}$ - Et·), 150 (base), 112 and 67, repurified by short path distillation b.p. ca. 100° at 0.2 mmHg (Found: C, 74.16; H, 10.23; N, 7.16. $M^{+\cdot}$, 193.1467. $C_{12}H_{19}NO$ requires C, 74.57; H, 9.91; N, 7.25%; $M^{+\cdot}$ 193.1467).

Preparation of *4S-(2,2-Dimethyl-1,3-dioxolan-4R-yl)-1-cyclohexyl-3-methylene-azetidin-2-one* (210c)

Hydroxy-amide (173a) (237 mg) was dissolved in THF (10 ml) and the solution cooled to -78°. n-Butyllithium (2.01 mmol) was added, the

suspension stirred for 5 min, warmed to 25° and recooled to -78°. Toluene-4-sulphonyl chloride (309 mg) in THF (10, 1 ml) was added dropwise during 15 min, the solution warmed to 25° and stirred for 15 h. General work up [(B) diethyl ether] and chromatography on Kieselgel H (18 g) [eluant dichloromethane-diethyl ether (1:0-9:1)] gave the β-*lactam* (210c) (145 mg, 65%), oil, ν_{max} 3000m, 2940 s, 2865 m, 1760 s (C=O), 1460 m, 1387 m, 1378 m, 1365 m, 1355 m, 1262 m, 1216 m, 1158 m, 1068 s (C-O), and 850 m cm^{-1}, δ 1.10-2.00 (10H, br, $(CH_2)_5$), 1.38 (3H, s, MeCO), 1.47 (3H, s, MeCO), 3.55-3.70 (1H, m, HCN), 3.73-3.82 (1H, dd, J 6,6Hz, CH_2O), 4.04-4.24 (3H, m, NCHCHCH), 5.10 (1H, brs, CH_2=), and 5.68 (1H, t, J 1Hz, CH_2=), m/e 265 ($M^{+\cdot}$), 250 ($M^{+\cdot}$ - Me·) 207, 164 (M^+ - $C_5H_9O_2$·, base), 101 ($C_5H_9O_2^+$), and 83 ($C_6H_{11}^+$), repurified by short path distillation, b.p. ca. 180° at 0.3 mmHg, $[\alpha]_{589}^{22}$ + 36.6° (C = 0.235, dichloromethane) (Found: C, 68.19; H, 8.97; N, 5.32; $M^{+\cdot}$, 265.1679. $C_{15}H_{23}NO_3$ requires C, 67.90; H, 8.74; N, 5.28%; $M^{+\cdot}$, 265.1678).

Attempted Preparation of *4R-(2,2-Dimethyl-1,3-dioxolan-4R-yl)-1-cyclohexyl-3-methylene-azetidin-2-one* (210d)

Hydroxy-amide (173b) (115 mg) was dissolved in THF (10 ml) and the solution cooled to -78°. n-Butyllithium (1.04 mmol) was added, the suspension stirred for 5 min, warmed to 25° and the solution recooled to -78°. Toluene-4-sulphonyl chloride (190 mg) in THF (10, 2 ml) was added during 15 min, the solution warmed to 25° and stirred for 20 h. General work up [(B) diethyl ether] gave the crude tosylate (212) (ca.90%) and the β-lactam (210d) (105 mg) as an inseparable mixture, ν_{max} 1740 m, 1660 s (212), 1625 s, and 1600 s cm^{-1}, δ_{max} 2.45 (3H, s), 5.20 (1H, d, J 6Hz, HCOTs), 5.65 (1H, s), and 5.80 (1H, s). The crude material was dissolved in THF (5 ml), treated with sodium hydride (15 mg) and the suspension stirred for 76 h. General work up [(B) diethyl ether] and p.l.c. [(i) five developments with dichloromethane:diethyl ether (9:1), (ii) three developments with light

petroleum:diethyl ether (1:1)] gave the *methylene β-lactam* (210d) (20 mg, 19%) as an oily solid, m.p. 55-8°, $[\alpha]_{589}^{21}$ -8.3 (C=0.42, dichloromethane) ν_{max} (CCl_4) 2995 m, 2940 s, 2860 m, 1760 s (C=O), 1455 m, 1415 m, 1385 m, 1375 m, 1360 m, 1352 m, 1318 m, 1267 m, 1210 m, 1170 m, 1165 m, 1120 m, 1067 m (C-O), and 924 m cm^{-1}, δ 1.15-2.00 (10H, br, $(CH_2)_5$), 1.35 (3H, s, MeCO), 1.45 (3H, s, MeCO), 3.40-3.55 (1H, m, HCN), 3.80-3.90 (1H, dd, J 6,7-Hz, CH_2O), 4.05-4.12 (1H, dd, J 6,7Hz, CH_2O), 4.30-4.42 (2H, m, NCHCHO) 5.21 (1H, t, J 0.5 Hz, CH_2=), and 5.63 (1H, t, J 0.5Hz, CH_2=), m/e 265 ($M^{+\cdot}$), 250 ($M^{+\cdot}$ - Me·), 164 ($M^{+\cdot}$ - $C_5H_9O_2\cdot$), 108, 101 ($C_5H_9O_2^+$, base), and 83 ($C_6H_{11}^+$) (Found: C, 67.87; H, 8.95; N, 5.32. $C_{15}H_{23}NO_3$ requires C, 67.90; H, 8.74; N, 5.28%).

Preparation of N-*Cyclohexyl-4*R-*5-dihydroxy-2-methylene-3* S *(toluene-4-sulphonyloxy)pentanamide Acetonide* (213)

Hydroxy-amide (173a) (38 mg) was dissolved in THF (5 ml) and the solution cooled to -78°. n-Butyllithium (0.67 mmol) was added, the solution warmed to 25°, treated with toluene-4-sulphonyl chloride (132 mg) stirred for 10 min and quenched with water (5 ml). General work up [(B) diethyl ether] and p.l.c. [one development with diethyl ether] gave the *amide-tosylate* (213) (25 mg, 43%) m.p. 97-8° (from diethyl ether and light petroleum), ν_{max} ($CHCl_3$) 3435 m (N-H), 2930 m, 2860 m, 1670 s (C=O), 1630 s (C=C), 1602 m, 1500 m, 1453 m, 1374 s (SO_2-O), 1355 s, 1170 m, 1150 m (SO_2-O), 1110 s, 1097 s, 1075 s (C-O), 965 m, 942 m, 910 m, and 890 m cm^{-1}, δ 1.00-2.05 (10H, br, $(CH_2)_5$), 1.30 (6H, br s, MeCO), 2.45 (3H, s, p-Me), 3.55-4.15 (3H, m, CH_2O, HCN), 4.40 (1H, q, J 7Hz, 4-CH), 5.25 (1H, d, J 7Hz, 3-CH), 5.35-5.90 (1H, br, NH), 5.55 (1H, ms, CH_2=), 5.66 (1H, ms, CH_2=), 7.25-7.40 and 7.70-7.90 (4H, m, aryl-H), m/e 437 ($M^{+\cdot}$), 422 ($M^{+\cdot}$ - Me·), 182 (base), 101 ($C_5H_9O_2^+$), 91, and 59 (Found: C, 60.37; H, 7.23; N, 3.21. $C_{22}H_{31}NO_6S$ requires C, 60.39; H, 7.14; N, 3.20%).

Attempted Reaction of the β-Lactam (210a) with Benzylamine

β-Lactam (210a) (72 mg) and benzylamine (0.10 ml) were dissolved in THF (10 ml) and the solution stirred for 1 week. Sodium hydride (24 mg) was added, the suspension stirred for 1 week and evaporated. General work up [(B) diethyl ether] gave a crude residue, ν_{max} 1812 w, 1740 s, and 1670 m.

Preparation of N,N-*Di-(toluene-4-sulphonyl) acetophenonehydrazone* (214)

Hydrazone (245) (10.5 g) was dissolved in THF (25 ml), sodium hydride (0.871 g) added, and the mixture stirred for 2 d. Toluene-4-sulphonyl chloride (6.92 g) was added and the mixture stirred for 23 d. General work up [(B) diethyl ether, ethyl acetate] and recrystallisation from ethyl acetate gave the *ditosylhydrazone* (214) (7.93 g, 49%), m.p. 204-6°, ν_{max} 1600 m (C=C), 1560 m, 1360 s (SO_2-N<), 1345 m, 1300 s, 1190s, 1180 s, 1165 s, (-SO_2-N<), 1090 m, 1080 m, 865 s (aryl-H), 810 s, 760 s, 730 s, 690 m, 665 s, and 660 s cm^{-1}, δ 2.40 (6H, s, aryl-Me), 2.58 (3H, s, MeC=N), and 7.00-8.00 (13H, m, aryl-H). Three recrystallisations from ethyl acetate gave m.p. 207-9°, m/e 442 ($M^{+\cdot}$), 155, 139 (base), 104, 91, and 78 (Found: C, 59.76; H, 4.97; N, 6.34; S, 14.85. $C_{22}H_{22}N_2O_4S_2$ requires C, 59.71; H, 5.01; N, 6.33; S, 14.49%).

Reaction of the Hydrazone (214) with n-Butyllithium

Hydrazone (214) (442 mg) was suspended in THF (10 ml) and the suspension cooled to -78°. n-Butyllithium (4.00 mmol) was added, the solution warmed to 25° and stirred for 16 h. General work up [(B) light petroleum] gave as an oil presumably containing the olefin (216) (27 mg), ν_{max} 2960 s, 2920 s, 2870 s, 960 m, 910 m, 730 s, and 700 s, cm^{-1}, δ_{max} 0.60-2.80, 6.30, and 6.80-7.90, m/e 160 ($M^{+\cdot}$ (216), base), 117 ($M^{+\cdot}$ (216) - $^nC_3H_7\cdot$),

104, 84, 77 (Ph^+), 69 and 40.

Preparation of Diphenylacetylene

Hydrazone (217) (480 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.60 mmol) was added, the solution warmed to -70° over 15 min and recooled to -78°. Bromine (0.085 ml) was added, the suspension warmed to -65° over 25 min, then to 25° over 10 min and evaporated. The solid was redissolved in THF (10 ml) and heated to 68° for 6 h without change. Evaporation and chromatography on Kieselgel H (20g) [eluant light petroleum] gave diphenylacetylene (33 mg, 18%) m.p. 62° (lit.,[64] 62.5°), λ_{max} (MeOH) 278 nm, δ 7.05-8.00 (12H, m).

Preparation of 1,3-Diphenylpropyne

Hydrazone (218) (497 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.60 mmol) was added, the red solution warmed to -68° over 27 min and recooled to -78°. Bromine (100 µl) was added, the thick suspension stirred to -67° over 15 min, to 0° over 55 min and stirred for 2 h. Evaporation, chromatography on Kieselgel H [(i) 15 g, (ii) 20 g)] [eluant light petroleum] and p.l.c. [one development with light petroleum] gave 1,3-diphenylpropyne[108] (15 mg, 8%), λ_{max} (EtOH) 251, 240 nm [lit.,[109] 240 (ε 25,200) and 251 nm (22,900)], δ 4.20 (2H, s, Ph-$\underline{CH}_2$), and 7.20-7.40 (10H, m, Ph-$\underline{H}$).

Preparation of 3-β-(t-Butyldimethylsilyloxy) pregn-5-en-20-one (219b)

Pregnenolone (219a) (0.632 g), t-butylchlorodimethylsilane (0.38 g) and imidazole (0.339 g) were suspended in DMF (5 ml) and DME (4 ml). The solution was warmed to 65° over 6 h and then cooled to 25°. General work up [(B) diethyl ether] and recrystallisation from diethyl ether and ethanol

gave the silyl-pregnenolone[125] (219b) (730 mg, 85%), m.p. 161-3° [lit.,[125] 162-4°] ν_{max} 1698 m (C=O), 1354 s, 1242 s, 1190 m, 1167 m, 1150 m, 1126 m, 1104 m, 1062 s (C-O), 1002 m, 885 m, 866 s, 825 s, 805 s, 770 s, and 662 m cm^{-1}, δ 0.08 (6H, s, $SiMe_2$), 0.60-2.60 (20H, br), 0.64 (3H, s, 18-Me), 0.85 and 0.90 (9H, 2s, ^tBu), 1.00 (3H, s, 19-Me), 2.10 (3H, s, MeC=O), 3.10-3.80 (1H, br, HCO), and 5.20-5.45 (1H, br, HC=), m/e 430 ($M^{+\cdot}$), 415 ($M^{+\cdot}$ - Me·), 373 ($M^{+\cdot}$ - ^tBu·, base), 297, 281, 145, 119, and 75 (Found: C, 75.04; H, 10.88. Calc. for $C_{27}H_{46}O_2Si$: C, 75.29; H, 10.76%).

A sample of ketone (219b) (592 mg) and 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (475 mg) were dissolved in dichloromethane (10 ml). Concentrated hydrochloric acid (2 drops) was added, the solution stirred for 3 h and then evaporated. Recrystallisation from ethanol and water gave *3β-(t-butyldimethylsilyloxy)pregn-5-en-20-one 2,4,6-tri-iso-propylbenzenesulphonylhydrazone* (219c) (0.977 g, 100%) m.p. 136-8°, ν_{max} 3240 m (N-H), 1658 m, 1328 s ($-SO_2-N<$), 1250 m, 1160 and 1152 s ($-SO_2-N<$), 1088 s (C-O), 1035 m, 885 m, 878 m, 866 m, 833 m, 772 m, and 663 m cm^{-1}, δ 0.05 (6H, s, SiMe), 0.18 (3H, s, 18-Me), 0.70-2.40 (20H, br), 0.88 (9H, s, ^tBu), 0.94 (3H, s, 19-Me), 1.24 (18H, overlapping d, J 7Hz, $CHMe_2$), 1.72 (3H, s, MeC=N), 2.86 (1H, overlapping septets, J 7Hz, p-$CHMe_2$), 3.20-3.80 (1H, br, HCO), 4.20 (2H, overlapping septets, J 7Hz, o-$CHMe_2$), 5.10-5.40 (1H, br, HC=), 7.15 (2H, s, aryl-H), and 7.20-7.60 (1H, br, NH), m/e 268, 251, 233, 204, 189 (base), 161, 149, 119, 105, 91, and 75 (Found: C, 70.83; H, 10.09; N, 3.91. $C_{42}H_{70}N_2O_3SSi$ requires C, 70.93; H, 9.92; N, 3.94%).

Second Attempted Preparation of 1,3-Diphenylpropyne

Hydrazone (218) (484 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. n-Butyllithium (2.95 mmol) was added, the solution warmed to -67° over 15 min and recooled to -78°. Dimethyl disulphide (2.23 mmol) was added, the solution warmed to -60° over 21 min and then recooled to

-78°. Further n-butyllithium (2.68 mmol) was added and the solution warmed to 25° over 100 min. General work up [(B) diethyl ether] gave no 1,3-diphenylpropyne.

Preparation of 2-Naphthylacetylene (222)

Hydrazone (220) (1.491 g) was dissolved in DME (15 ml) and the solution cooled to -78°. n-Butyllithium (7.40 mmol) was added, the solution warmed to -65° over 15 min, recooled to -78° and quenched with dimethyl disulphide (0.40 ml). The solution was warmed to -50° over 45 min, recooled to -78° and n-butyllithium (6.70 mmol) added. The crimson solution was warmed to 25° over 80 min. General work up [(B) light petroleum] and chromatography on Kieselgel H (20 g) [eluant light petroleum] gave the crude acetylene (222) (447 mg). Purification of a sample (97 mg) by p.l.c. [three developments with petroleum] gave the acetylene (222) (81 mg, 74%) m.p. 34-6° (lit.,[64] 36°), ν_{max} 3280 s (HC=), 1274 m, 950 m, 903 s, 868 s, 855 m, 822 s, 750 m, 740 s, 668 m, and 650 m cm^{-1}, δ 3.05 (1H, s, HC=), 7.40-7.70 (3H, m), 7.70-8.00 (3H, m), and 8.05 (1H, br s, aryl 1-CH), m/e 152 ($M^{+\cdot}$, base).

Preparation of 2-Methyl-4-phenylbut-3-yn-2-ol (224)

Hydrazone (221) (1.00 g) was dissolved in DME (10 ml) and the solution cooled to -78°. n-Butyllithium (5.36 mmol) was added, the solution warmed to -66° over 20 min and recooled to -78°. Dimethyl disulphide (0.30 ml) was added, the solution was warmed to -50° over 50 min and recooled to -78°. n-Butyllithium (5.36 mmol) was added, the solution warmed to 25° over 2 h, recooled to -78° and then treated with further n-butyllithium (4.00 mmol). Acetone (0.50 ml) was added and the solution warmed to 25° over 10 min. General work up [(B) dichloromethane], chromatography on Kieselgel H (20 g) [eluant dichloromethane] and p.l.c. [three developments with dichloromethane] gave the hydroxy-acetylene (224) (187 mg, 47%) m.p. 49° (lit.,[110]

50°), ν_{max} 3600 s (O-H), 1360 s, 1325 s, 1155 s, 1110 s, 955 s, and 900 s cm^{-1}, δ 1.60 (6H, s, Me), 2.20 (1H, br s, OH), and 7.10-7.60 (5H, m, Ph-) m/e 160 ($M^{+\cdot}$), and 145 ($M^{+\cdot}$ - Me·, base).

Preparation of Undec-1-yne (223)

Hydrazone (72) (1.413 g) was dissolved in DME (15 ml) and the solution cooled to -78°. n-Butyllithium (7.70 mmol) was added, the solution was warmed to -69° over 20 min and then recooled to -78°. Dimethyl disulphide (0.40 ml) was added, the solution was warmed to -50° over 45 min and then recooled to -78°. n-Butyllithium (7.00 mmol) was added, the suspension was warmed to 25° over 100 min and evaporated. General work up [(B) light petroleum]and chromatography on Kieselgel H (35 g) [eluant light petroleum] gave slightly impure undec-1-yne (223) (282 mg, <59%), ν_{max} 3280 s (HC=) 2025 m (C=C), and 870 m cm^{-1}, δ 0.70-1.00 (3H, br, $MeCH_2$), 1.10-1.60 (14H, br $(CH_2)_7Me$) , 1.80-2.00 (1H, m, HC≡), and 2.00-2.30 (2H, br, $CH_2C\equiv$). The sample gave a diacetylene-mercury derivative[111] m.p. 78-9°, (lit.,[112] m.p. 79-79.3°).

Reaction of Ribofuranose (228) with 2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b)

2,3,5-Tri-O-benzyl-D-ribofuranose[126] (228) (96 mg), 2,4,6,-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (72 mg) and amberlite IR-120 (H) resin catalyst were stirred in carbon tetrachloride (5 ml) for 1 h. T.l.c. analysis indicated the presence of a hydrazone derivative. The mixture was stirred for 28 d and evaporated. Purification by p.l.c. [two developments with dichloromethane] gave the sultone (109) (20 mg, 30%) identical (t.l.c. and n.m.r.) with the previous sample; and 2,3,5-tri-O-benzyl-D-ribofuranolactone (229) (56 mg, 59%) as an oily solid, $[\alpha]_{589}^{29}$ + 75° (C =

0.09, $CHCl_3$) [lit.,[113] m.p. 54-5°, + 74.8 (C = 3, $CHCl_3$)], ν_{max} 2875 m, 1790 s (C=O), 1695 m, 1500 m, 1458 s, 1368 m, 1210 m, 1180 m, 1150 s, 1100 s (C-O), 1040 s, 1028 s, 735 s (aryl-H), and 698 s (aryl-H) cm^{-1}, δ 3.50-3.64 (2H, br, $OC\underline{H}_2CH$), 3.90-4.90 (9H, br), and 7.16-7.40 (15H, m, aryl-H), m/e 417 (M^+ - H), 341, 327 (M^+ - $PhCH_2$), 253, 205, 181, 107, and 91 ($PhCH_2^+$, base) (Found : C, 74.43; H, 6.45. Calc. for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26%).

Preparation of *3,5-Dimethyl-1-(2,4,6-tri-iso-propylbenzenesulphonyl)-1,2-diazole* (230)

2,4,6-Tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (0.270 g) and pentan-2,4-dione (0.205 g) were dissolved in diethyl ether (10 ml) and the mixture stirred for 1d. General work up [(B) diethyl ether] and chromatography on Kieselgel H (17 g) [eluant dichloromethane] gave the *diazole derivative* (230) (206 mg, 63%) and an oil, ν_{max} (CCl_4) 2960 s, 2940 m, 1602 m (C=C), 1470 s, 1430 s, 1410 m, 1390 s, 1380 s, 1370 s, 1350 s, ($-SO_2-N<$), 1300 s, 1180 s ($-SO_2-N<$), 1125 s, and 670 s cm^{-1}, δ 1.20 (12H, d, J 7Hz, o-$CH\underline{Me}_2$), 1.28 (6H, d, J 7Hz, p-$CH\underline{Me}_2$), 2.15 (3H, s, $\underline{Me}C=C$), 2.55 (3H, s, $\underline{Me}C=N$), 2.91 (1H, septet, J 7Hz, p-$C\underline{H}Me_2$), 4.12 (2H, septet, J 7Hz, o-$C\underline{H}Me_2$), 5.80 (1H, s, $\underline{H}C=C$), and 7.14 (2H, s, aryl-H), m/e 363 (M^+ + H), 319 (M^+ - $^{iso}Pr\cdot$), 263, 176, 119 (base), 103, and 77 (Found: C, 66.23; H, 8.17; N,7.47. $C_{20}H_{30}N_2O_2S$ requires C, 66.26; H, 8.34; N, 7.73%).

Preparation of *1,2-Dihydro-3,6-dimethyl-1-(tri-iso-propylbenzenesulphonyl) pyridazine* (231)

Hexan-2,5-dione (104 mg) and 2,4,6-tri-iso-propylbenzenesulphonylhydrazine[70] (108b) (269 mg) were suspended in diethyl ether and the reaction mixture stirred for 1 d. Evaporation and purification by chromatography on Kieselgel H (20 g) [eluant dichloromethane] gave the *dihydropyridazine*

derivative (231) (253 mg, 75%) m.p. 138-40°, ν_{max} 3200 s (N-H), 1600 m, (C=C), 1325 s ($-SO_2-N<$), 1165 and 1155 s ($-SO_2-N<$), 755 s, 735 m, 660 m, and 640 m cm^{-1}, δ 1.20 (18H, 2 overlapping d, J 6Hz, $CH\underline{Me}_2$), 1.90 (6H, s, $\underline{Me}C=$), 2.90 (1H, septet, J 7Hz, p-$C\underline{H}Me_2$), 3.70 (2H, septet, J 7Hz, o-$C\underline{H}Me_2$), 5.68 (2H, s, $\underline{H}C=$), 7.16 (2H, s, aryl-H), and 7.30 (1H, s, N$\underline{H}$), m/e 376 ($M^{+\cdot}$), 333 ($M^{+\cdot}$ - $^{iso}Pr\cdot$), 282, 267, and 109 ($M^{+\cdot}$ - $ArSO_2\cdot$, base) (Found: C, 66.72; H, 8.60; N, 7.35. $C_{21}H_{32}N_2O_2S$ requires C, 66.98; H, 8.57; N, 7.44%).

Reaction of the Ester Sulphonylhydrazone (232) with Lithium di-iso-propylamide

The ester sulphonylhydrazone (232) (420 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. Lithium di-iso-propylamide [prepared from di-iso-propylamine (0.52 ml) and n-butyllithium (3.74 mmol)] was added, the solution was warmed to -67° over 2 h and quenched with acetone (3.45 mmol). The solution was warmed to -50°, quenched with glacial acetic acid (0.25 ml) and then warmed to 25°. General work up [(B), diethyl ether] and recrystallisation from methanol and water at 0° gave the unreacted ester sulphonylhydrazone (232) (328 mg, 78%) identical (t.l.c. and n.m.r.) with the starting material.

Preparation of *2,4-Di-[bis(methylthio)methylene]-5α-cholestan-3-one* (236)

Sulphonylhydrazone (65) (656 mg) was dissolved in DME (5 ml) and the solution was cooled to -78°. sec-Butyllithium (2.45 mmmol) was added, the solution warmed to -70° over 1 h, to 0° over 40 min and then recooled to -78°. Carbon disulphide (0.15 ml) was added, the solution warmed to 0°, quenched with methyl iodide (0.30 ml) and stirred for 4 h. General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) [eluant light petroleum-diethyl ether (1:0-3:1)] gave 5α-cholest-n-ene (n = 2,3) (67)

(269 mg, 74%) identical (t.l.c., n.m.r. and mass spectra) with a previous sample; and the *tetrathio-ketone* (236) (85 mg, 15%) m.p. 126-7° (from diethyl ether and methanol), ν_{max} (CCl_4), 2950 s, 2930 s, 2875 s, 2850 m, 1650 m, 1495 m, 1470 m, 1445 m, 1432 m, 1384 m, and 1224 m cm^{-1}, λ_{max} 347 (ε 10,400) and 258 nm (4,200), δ 0.66 (3H, s, 18-Me), 0.75-2.00 (33H, br), 0.88 (3H, s, 19-Me), 2.10 and 3.25 (2H, ABq, J 16Hz, 1-CH_2), 2.67 (1H, dd, J 11, 2Hz, 5-CH), 2.30 (3H, s, SMe), 2.36 (6H, s, SMe), and 2.42 (3H, s, SMe), m/e 594 ($M^{+\cdot}$), 579 ($M^{+\cdot}$ - Me, base), 547, 533, 531, and 519 (Found: C: 66.78; H, 9.19; S, 21.33. $C_{33}H_{54}OS_4$ requires C, 66.59; H, 9.15; S, 21.57%).

Second Preparation of the Ketone (236)

Sulphonylhydrazone (65) (694 mg) was dissolved in DME (8 ml) and the solution cooled to -78°. sec-Butyllithium (3.00 mmol) was added, the solution warmed to -70° over 80 min, to -3° over 70 min and recooled to -78°. Carbon disulphide (0.30 ml) was added, the solution warmed to 0°, quenched with methyl iodide (1.40 ml), warmed to 25°, stirred for 90 min and evaporated. General work up [(B) diethyl ether] and chromatography on Kieselgel H (25 g) [eluant light petroleum-diethyl ether (1:0-3:1)] gave 5α-cholest-n-ene(n = 2,3) (67) (81 mg, 21%) identical (t.l.c., n.m.r. and mass spectra) with a previous sample; and a solid probably *3-[methylthio-(thiocarbonyl)thio]-5α-cholest-n-ene (n = 2,3)* (238) (98 mg, 19%) m.p. 105-7° (from dichloromethane and acetonitrile), ν_{max} (CCl_4) 2940 s, 2872 s, 1470 s, 1448 s, 1430 m, 1425 m, 1388 m, 1385 m, 1378 m, 1370 m, 1268 m, 1080 s (C=S), 1056 s (C=S), 960 m, 910 s, and 865 m cm^{-1}, λ_{max} (CH_2Cl_2) 312 (ε 10,900) and 250 nm (4,200), δ 0.68 (3H, s, 18-Me), 0.70-2.00 (nH, br), 1.96-2.42 (nH, br, CH_2C=), 2.69 (3H, s, MeS), and 5.95-6.45 (1H, br, HC=), m/e 492 ($M^{+\cdot}$), 477 ($M^{+\cdot}$ - Me·), 445 ($M^{+\cdot}$ - SMe·), 370 (base), 316, 215, 203, and 81 (Found: C, 70.68; H, 9.88; S, 19.61. $C_{29}H_{48}S_3$ requires C, 70.67; H, 9.82; S, 19.51%); and the ketone (236) (13 mg, 2%), identical (t.l.c.

and n.m.r.) with the previous sample.

Third Preparation of the Ketone (236)

Sulphonylhydrazone (65) (661 mg) was dissolved in DME (7 ml) and the solution cooled to -78°. sec-Butyllithium (2.45 mmol) was added, the solution was warmed to -62° over 70 min, to -16° over 60 min and recooled to -78°. Carbon disulphide (0.15 ml) was added, the solution was warmed to 25°, quenched with methyl iodide (0.40 ml), stirred for 90 min and evaporated. A similar work up gave 5α-cholest-n-ene (n = 2,3) (67) (176 mg, 48%); the trithiocarbonate (238) (120 mg, 25%); and the ketone (236) (49 mg, 8%), all identical (t.l.c. and n.m.r.) with authentic samples.

Reductive Desulphurisation[106] of the Trithiocarbonate (238)

The trithiocarbonate (238) (51 mg) was dissolved in ethanol (50 ml). Nickel chloride hexahydrate (2.38 g) and boric acid (1.0 g) were added, and the suspension cooled to 0°. A solution of sodium borohydride (0.76 g) in water (10 ml) was added, the suspension refluxed for 3 h, cooled to 25°, filtered through celite and evaporated. The residue was extracted with petroleum (3 x 75 ml), the extracts evaporated and chromatography on Kieselgel H (10 g) (eluant petroleum) gave a crude product (36 mg), m/e 372/370. Platinum oxide (50 mg) and THF (10 ml) were added and the sample hydrogenated for 3 d. Filtration and evaporation gave 5α-cholestane (32 mg, 83%) m.p. 78-9.5°, $[\alpha]_{589}^{20}$ + 29° (C = 0.066, $CHCl_3$) [lit.,[64] 80-81.5°, + 30.2° (C = 2, $CHCl_3$)], δ 0.76-2.40 (48H, br) only, m/e 372 (M^+) and 357 (M^+ - Me·).

Attempted Preparation of 2,6-Di-[bis-(methylthio)methylene] cyclohexanone (240)

Hydrazone (239) (395 mg) was dissolved in DME (5 ml) and the solution cooled to -78°. sec-Butyllithium (2.45 mmol) was added, the solution

stirred to -70° over 1 h, warmed to -2° over 75 min and recooled to -78°. Carbon disulphide (0.15 ml) was added, the solution warmed to 0°, quenched with methyl iodide (0.30 ml) and warmed to 25° over 3 h. General work up [(B) diethyl ether] and chromatography on Kieselgel H (20 g) [eluant light petroleum -dichloromethane (1:0-1:1)] gave the impure ketone (240) (25 mg). Purification by p.l.c. [three developments with light petroleum:diethyl ether (3:1)] gave the slightly impure ketone[114] (240) (18 mg, 6%) as an oil, λ_{max} 379 nm (ε 13,000), ν_{max} 1640 m and 1490 s cm^{-1}, δ_{max} 2.42 and 2.47 (12H, 2s, MeS), m/e 306 ($M^{+\cdot}$), and 291 ($M^{+\cdot}$ -Me·, base) (Found: $M^{+\cdot}$ 306.0239. Calc. for $C_{12}H_{18}OS_4$ $M^{+\cdot}$ 306.0241).

Preparation of 4-(t-Butyl)-2,6-di[bis(methylthio)methylene]cyclohexanone (242)

Hydrazone (241) (0.420 g) was dissolved in DME (5 ml) and the solution cooled to -78°. sec-Butyllithium (2.35 mmol) was added, the solution warmed to -65° over 50 min, to -16° over 1 h and recooled to -70°. Carbon disulphide (0.15 ml) was added, the solution warmed to 25°, quenched with methyl iodide (0.30 ml) and stirred for 1 h. General work up [(B) dichloromethane], chromatography on Kieselgel H (20 g) [eluant light petroleum-dichloromethane (1:0-1:1)] and p.l.c. [two developments with light petroleum: diethyl ether (13:3)] gave the tetrathioketone[127] (242) (69 mg, 20%) as an oil, ν_{max} 2955 s, 2920 s, 2865 s, 1614 m (C=O), 1480 s, 1427 s, 1367 m, 1287 m, 1250 s, 1205 m, 1057 m, and 730 m cm^{-1}, λ_{max} (CH_2Cl_2), 380 nm (ε 13,600), δ 0.88 (9H, s, ^tBu), 1.25-1.65 (1H, br, 4-CH), 1.95-2.25 (2H, br), 2.20 (6H, s, SMe), 2.23 (6H, s, SMe), and 2.80-3.10 (2H, br), m/e 362 ($M^{+\cdot}$), 347 ($M^{+\cdot}$ - Me·, base), 315, 272, 257, and 107 (Found: C, 53.00 ; H, 7.11. Calc. for $C_{16}H_{26}OS_4$: C, 53.00; H, 7.23%).

Second Preparation of the Ketone (242)

4-t-Butylcyclohexanone (1.313 g) was dissolved in THF (50 ml).

Potassium t-butoxide (1.997 g) was added and the solution stirred for 3 h. Carbon disulphide (1.05 ml) was added, the solution was stirred for 5 min, quenched with methyl iodide (1.25 ml), stirred for 13 h, and evaporated. The residue was dissolved in diethyl ether (50 ml) and potassium t-butoxide (2.0 g) added. The solution was stirred for 6 h, quenched with carbon disulphide (1.10 ml) and stirred for 5 min. Methyl iodide (1.30 ml) was added, the solution stirred for 3 d and evaporated. A similar work up gave the ketone (242) (34%) identical (t.l.c., i.r. and n.m.r. spectra) with the previous sample.

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Novel Synthesis of α-Methylene-γ-lactones

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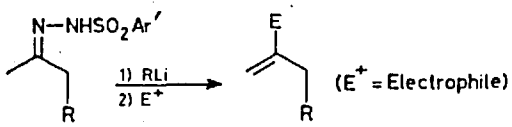
Novel Synthesis of α-Methylene-γ-lactones

By ROBERT M. ADLINGTON and ANTHONY G. M. BARRETT*
(*Department of Chemistry, Imperial College, London* SW7 2AY)

Summary α-Methylene-γ-lactones have been prepared from acetone 2,4,6-tri-isopropylphenylsulphonydrazone, an aliphatic ketone or aldehyde, and carbon dioxide in a 'one pot' good yield reaction.

ON account of the cytotoxicity of numerous sesquiterpene lactones, several syntheses of α-methylene-γ-lactones have been developed. Outstanding total syntheses of vernolepin,[1] vernomenin,[1] *etc.* rely on α-methylenylation of preformed γ-lactones[2] or the oxidation of α-methyl-γ-lactones.[3] Alternative procedures exist,[4] some of which are synthetically less versatile on account of low yields and/or multistage reactions. Herein is described the preparation of α-methylene-γ-lactones from two ketones and carbon dioxide or a β-hydroxyketone and carbon dioxide.

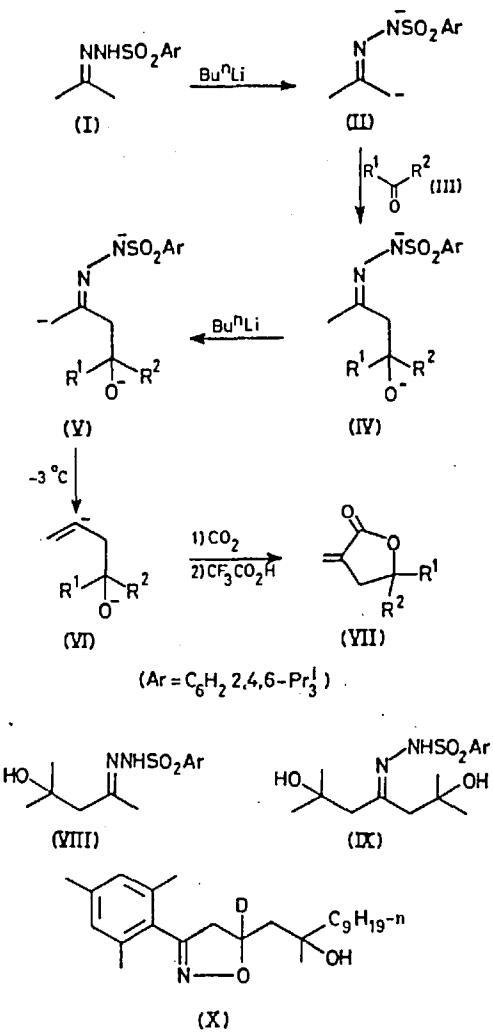
Ketone arylsulphonylhydrazones are useful intermediates in the generation of alkene derivatives by the Shapiro reaction (Scheme 1).[5] The recently described



SCHEME 1

preparation of homoallylic alcohols from ketones[6] prompts us to describe the application of acetone 2,4,6-tri-iso propylphenylsulphonylhydrazone (I) in the preparation of α-methylene-γ-lactones (VII). Typically, n-butyl-lithium (2.2 equiv.), the ketone or aldehyde (III) (1·2 equiv.), and n-butyl-lithium (1·2 equiv.) were added in sequence to acetone 2,4,6-tri-isopropylphenylsulphonylhydrazone (I)† (1 mmol) in 1,2-dimethoxyethane (DME) at −70 °C. After warming to −3 °C and recooling to −70 °C the mixture was quenched with carbon dioxide. Work up, acidification, and chromatography gave the α-methylene-γ-lactones (VII) (Scheme 2), in the following yields: R^1 = Me, R^2 = hexyl, 61; R^1 = Me, R^2 = Bu^i, 66; R^1 = R^2 = Me, 57; R^1 = Me, R^2 = Et, 61; R^1 = H, R^2 = Pr^n, 62; R^1 = H, R^2 = Et, 45; R^1, R^2 = $-(CH_2)_5-$, 40%. Alternatively, the lactone (VII, R^1 = R^2 = Me) (74%) was prepared from hydrazone (VIII),‡ n-butyl-lithium, and carbon dioxide. The yields of the lactones (VII) are good and the reaction is carried out in one vessel, with each step self-indicating [(II) golden, (IV) colourless, (V) orange-yellow, (VI) pale yellow].

Intermediacy of the anion (IV, R^1 = R^2 = Me) has precedent[6] and was consistent with the fact that quenching with water gave the hydrazone (VIII)§ (95%). Addition of acetone and acetic acid in sequence to the trianion (V, R^1 = R^2 = Me) gave the hydrazone (IX) (31%). The stability of the vinyl anion (VI, R^1 = Me, R^2 = nonyl) in DME at −3 °C was confirmed by quenching with D_2O and trapping of the olefin as the isoxazoline (X) with 2,4,6-trimethylbenzonitrile oxide (85%, *ca.* 100% D incorporation). The regioselective third deprotonation, (IV) to (V), has precedent.[6]



SCHEME 2

Since both ketones (or aldehydes) and β-hydroxyketones are readily available versatile units, this reaction should find application in natural product synthesis.

(*Received, 7th September* 1978; *Com.* 981.)

† From acetone and 2,4,6-tri-isopropylphenylsulphonylhydrazine (92%). Structural assignments for all new compounds and all lactones were consistent with spectral data and microanalyses.

‡ Obtained (93%) as a mixture of isomers from 4-hydroxy-4-methylpentan-2-one and 2,4,6-tri-isopropylphenylsulphonylhydrazine.

§ Obtained as a single isomer, most plausibly *syn* (n.m.r.).

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Novel Syntheses of 3-Methylene- and 3,6-Dimethylene-tetrahydropyran-2-one and 3,5-Dimethylenetetrahydrofuran-2-one Derivatives

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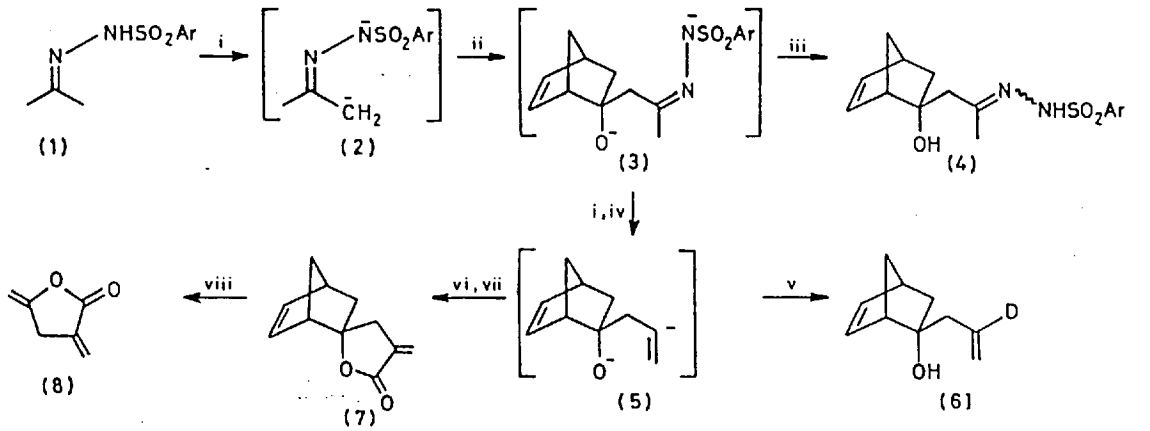
By ROBERT M. ADLINGTON and ANTHONY G. M. BARRETT*
(*Department of Chemistry, Imperial College, London* SW7 2AY)

Summary By modification of the Shapiro reaction, the title compounds were prepared by short convenient syntheses.

RECENTLY, we have described the application of the Shapiro reaction to the synthesis of 3-methylenetetrahydrofuran-2-ones.[1] Derivatives of the 3,5-dimethylenetetrahydrofuran-2-one unit (**8**) occur naturally in the obtusilactones and mahubenolides.[2] Herein we describe a convenient two-step synthesis of (**8**) and syntheses of the related 3-methylene-(**23c**), 3,6-dimethylene-(**21**), and 3-ethylidene-6-methylene-(**24**) tetrahydropyran-2-one derivatives.

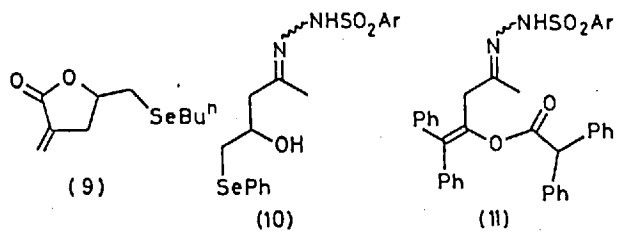
The lactone (**8**) should be available from acetone 2,4,6-tri-isopropylphenylsulphonylhydrazone (**1**) and a keten equivalent. Thus, reaction of the dianion (**2**), obtained from (**1**), with bicyclo[2.2.1]hept-2-en-5-one, n-butyl-lithium, carbon dioxide, and acetic acid in sequence gave the lactone (**7**) [61% from (**1**)]† (Scheme 1). The product was stereochemically homogeneous (^1H and ^{13}C n.m.r. and t.l.c. analy-



SCHEME 1. Reactions i—vi were carried out in 1,2-dimethoxyethane (DME). Ar = 2,4,6-$Pr^i_3C_6H_2$. i, Bu^nLi, −78 °C; ii, bicyclo-[2.2.1]hept-2-en-5-one, −65 °C; iii, HOAc, −65 °C; iv, −3 °C; v, D_2O; vi, CO_2, −78 °C; vii, HOAc, CH_2Cl_2, 20 °C; viii, 550 °C, 10^{-4} mmHg.

† All new compounds were fully characterised by microanalyses and spectral data.

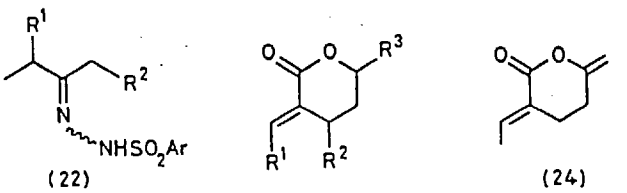
sis) and plausibly resulted from *exo* carbanion attack.[3] The intermediacy of the dianions (3) and (5) followed from, respectively, trapping with acetic acid and D_2O to give the hydrazone (4) [56% from (1)] as a *syn–anti* mixture, and the olefin (6) [70% from (1), 91% D incorporation]. The lactone (7) on flash vacuum pyrolysis at 550 °C and 10^{-4} mmHg gave 3,5-dimethylenetetrahydrofuran-2-one (8) (83%) *via* a retro Diels–Alder[4] reaction.



(9) (10) (11)

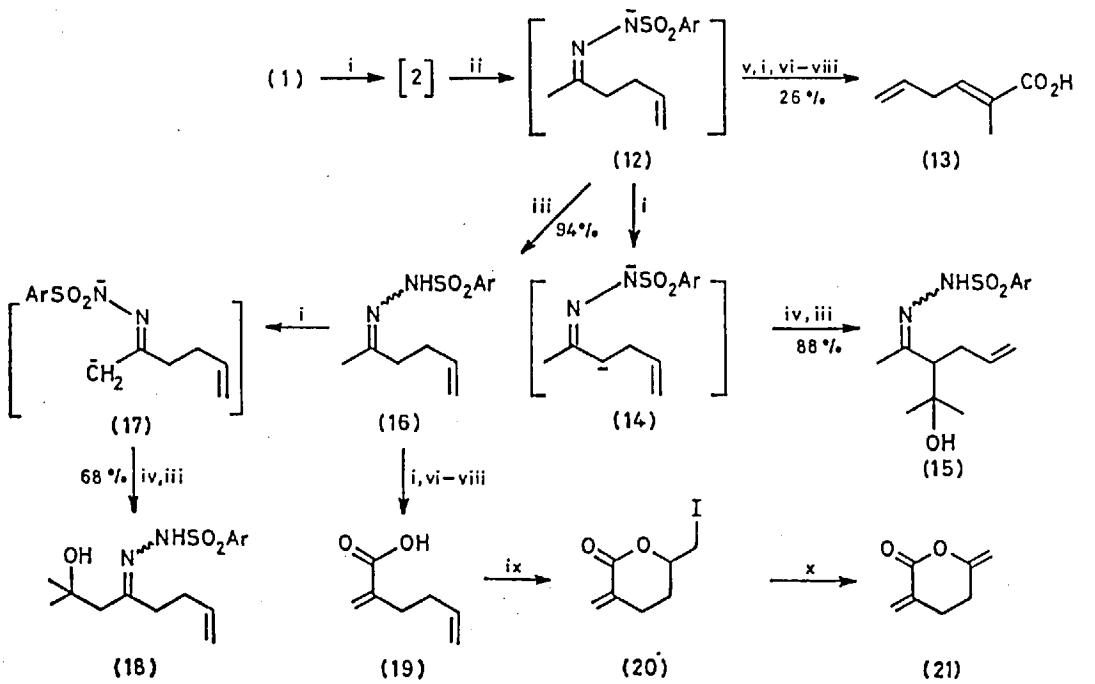
Alternative keten equivalents were examined. Reaction of the hydrazone (1) with phenylselenylacetaldehyde (available *via* 2-bromo-1,1-diethoxyethane and 1,1-diethoxy-2-phenylselenylethane) as in Scheme 1, gave only the lactone (9) (2%) formed *via* the hydrazone (10) (59%) and benzoic acid (17%). The dianion (2) and diphenylketen gave the diacylated product (11) (25%).

The lactone (21) should be available *via* the iodolactonisation of 2-methylenehex-5-enoic acid (19). The allylation of dianion (2) provided an easy route to acid (19) *via* (12) and (16) (Scheme 2). Clearly the regioselectivity of reaction [(15) *vs.* (18) and (13) *vs.* (19)] was controlled by the exclusive formation[5] of the *syn*-dilithio species (14) and (17), and by the predominance of *anti* stereochemistry when the hydrazones were isolated and allowed to equilibrate in solution at room temperature. The anions (14) and (17) did not equilibrate under the reaction conditions. The acid (19) was not fully characterised but was iodolactonised giving (20) [50% overall yield from (16)]. Subsequent reaction with DBU gave the novel 3,6-dimethylenetetrahydropyran-2-one (21) (64%). As in Scheme 2 butanone 2,4,6-tri-isopropylphenylsulphonylhydrazone was allylated giving the hydrazones (22a) (major) and (22b) (minor) (75% yield) which then gave the lactones (23a) (39%) and (23b)



a; R^1 = H, R^2 = $CH_2CH{=}CH_2$
b; R^1 = $CH_2CH{=}CH_2$, R^2 = H

a; R^1 = Me, R^2 = H, R^3 = CH_2I
b; R^1 = H, R^2 = Me, R^3 = CH_2I
c; R^1 = R^2 = H, R^3 = n-C_8H_{17}



Scheme 2. All reactions, except ix and x, were carried out in DME. i, Bu^nLi, −78 °C; ii, $CH_2{=}CHCH_2Br$, −60 °C; iii, HOAc, −78 to −50 °C; iv, Me_2CO, −78 °C; v, $Me_2NCH_2CH_2NMe_2$, −78 °C; vi, −3 °C; vii, CO_2, −78 °C; viii, CF_3CO_2H; ix, CH_2Cl_2, H_2O, $NaHCO_3$, KI_2, 20 °C; x, PhH, 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU), 74 °C.

The hydrazones (15), (16), and (18) were of *syn*-stereochemistry on initial isolation but isomerised at room temperature. At equilibrium the hydrazone (16) was *ca.* 15:85 *syn*:*anti*. In the sequences (16)—(18) and (16)—(21) the *syn* isomer gave rise to minor side products.

(6%). Dehydrohalogenation of (**23a**) gave the dialkylidene lactone (**24**) (71%). Reaction of 5-hydroxytridecan-2-one with 2,4,6-tri-isopropylphenylsulphonylhydrazine, n-butyllithium (−78 to −3 °C), carbon dioxide (−78 °C), and trifluoroacetic acid in sequence gave the lactone (**23c**) (23%).

Clearly, application of the Shapiro reaction provides the most convenient syntheses of the lactones (**8**), (**21**), (**23a—c**), and (**24**) and analogues.

We thank the S.R.C. for support.

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Sultone Formation from 2,4,6-Tri-isopropylbenzenesulphinic Acid

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Sultone Formation from 2,4,6-Tri-isopropylbenzenesulphinic Acid

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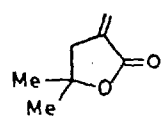
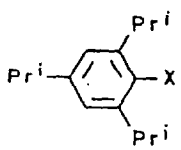
2,4,6-Tri-isopropylbenzenesulphinic acid decomposed in the presence of oxygen giving 2,4,6-tri-isopropyl-1,α-sultone; a mechanism involving arylsulphonyl and peroxyarylsulphonyl radicals and intramolecular hydrogen atom abstraction is suggested.

RECENTLY we have applied the Shapiro reaction in the synthesis of α-methylene-γ-lactones. Typically, reaction of the 2,4,6-tri-isopropylbenzenesulphonyl hydrazone of 2-hydroxy-2-methylpentan-4-one with n-butyl-lithium, carbon dioxide, and trifluoroacetic acid in sequence gave 5,5-dimethyl-3-methylenetetrahydrofuran-2-one (1) (74%).[1] The by-product 2,4,6-tri-isopropylbenzenesulphinic acid (2a) partially decomposed in the presence of acid. Chromatography was required to separate the methylene lactone (1) from a minor aromatic product. Herein is described a study of this unexpected product, the sultone (3).

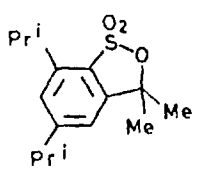


(1)



(2)

a; X = SO_2H
b; X = SO_2NHNH_2
c; X = SO_2Cl
d; X = $SO_2^{\bullet}$
e; X = $SO^{\bullet}$
f; X = $S^{\bullet}$
g; X = SO_2I
h; X = $SO_2^{\bullet}$
i; X = S(=O)—OEt
j; X = SO_3Et
k; X = S(=O)—P(=O)(OEt_2)
l; $SO_2OO^{\bullet}$

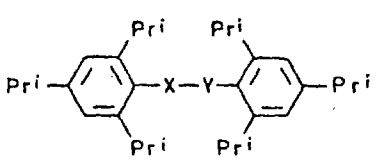


(3)

RESULTS AND DISCUSSION

2,4,6-Tri-isopropylbenzenesulphonylhydrazine (2b) was slowly decomposed by triethylamine. Subsequent acidification gave, after 5 d, the sultone (3) (28%) as a crystalline solid, m.p. 124—127 °C. Both microanalysis and the mass spectrum (M^+ 282.1294) were in excellent agreement with a composition of $C_{15}H_{22}O_3S$. The i.r. spectrum showed the absence of OH and the presence of the $-SO_2-O-$ unit (1 330 and 1 190 cm^{-1}). The ^1H and ^{13}C n.m.r. spectra were most informative. Clearly the molecule possessed only two isopropyl functions [δ_H 1.33 (12 H, 2 overlapping doublets, J 7 Hz), 3.03 (1 H, septet, J 7 Hz), and 3.6 (1 H, septet, J 7 Hz); δ_C 23.29 (q), 23.67 (q), 29.58 (d), and 34.54 (d)], and was unsymmetrical. The low-field methyl resonance [δ_H 1.8 (6 H, s), δ_C 89.89 (s)] indicated an *ortho*-fused isopropyloxysulphonyl function. Thus formulation as sultone (3) was unambiguous. Most probably sultone (3) arose *via* aerial oxidation of the sulphinic acid (2a).

Zinc-dust reduction[2] of 2,4,6-tri-isopropylbenzenesulphonyl chloride (2c) gave the sulphinic acid (2a). Identity and purity were confirmed by microanalysis, homogeneity by t.l.c., spectral characteristics, and by analogy with literature data.[2] The mass spectrum showed ions derived from the thiosulphonate (4a) and disulphide (4b), clearly arising from decomposition in the probe. Of note, ions at *m/e* 267 (2d), 251 (2e), 235 (2f), and 203 ($C_{15}H_{23}^+$) were observed; these were common to many sulphinic acid derivatives in the sequel. With careful exclusion of oxygen, 2,4,6-tri-isopropylbenzenesulphinic acid (2a) [$\lambda_{max.}$ 273 (ε 1 400) and 282 nm (1 200)] was photolysed (≥316 nm)[3] in the presence of 2,2'-azobis-(2-methylpropionitrile) (hereinafter referred to as the initiator) [$\lambda_{max.}$ 345 nm (ε 12)] for 3 h. Chromatography gave the disulphide (4b) (3%) and thiosulphonate (4a) (58%). Assignment of structures followed from microanalyses, spectral data, and comparisons with literature data.[4] Further experiments are tabulated and only selected experiments are described in the Experimental section.



(4)

a; X = S, Y = SO_2
b; X = Y = S
c; X = Y = SO_2

The sulphinic acid (2a) decomposed in the dark under argon without initiator giving the same two products. Clearly under these conditions the well known[5] sulphinic acid disproportionation giving the thiosulphonate (4a) was observed. In the presence of oxygen, initiated photolysis of the sulphinic acid (2a) gave the sultone (3) (34%). In no instance was the sultone (3) detected in anaerobic reactions. Sultone (3) was also formed under oxygen without initiation on photolysis or in the dark.

TABLE

Reactions of 2,4,6-tri-isopropylbenzenesulphinic acid (2a) and *S*-2,4,6-tri-isopropylphenyl 2,4,6-tri-isopropylbenzene thiosulphonate (4a)

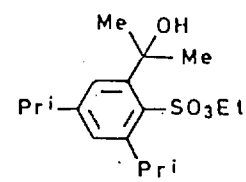
Reaction	Starting material/ mmol	Time	Reaction conditions *	Isolated products
1	0.99	3 h	O_2, initiator (2.1 equiv.), *hν*	sultone (3) 34%
2	0.69	3 h	Ar	thiosulphonate (4a) 53%, disulphide (4b) 7%
3	0.99	3 h	Ar, initiator (2.1 equiv.), *hν*	thiosulphonate (4a) 58%, disulphide (4b) 6%
4	0.60	2 h	O_2, *hν*	sultone (3) 29%
5	0.38	2 h	O_2	sultone (3) 23%
6	0.40	16 h	O_2	sultone (3) 33%
7	1.0	(*a*) 15 min (*b*) 2 h	(*a*) N_2, $NaHCO_3$ (1 equiv.), I_2 (1.06 equiv.) (*b*) O_2, *hν*	sulphonylsulphone (4c) 20%
8	1.0	(*a*) 15 min (*b*) 2 h	(*a*) N_2, $NaHCO_3$ (1 equiv.), I_2 (1.0 equiv.) (*b*) O_2, *hν*	sultone (3) 8%, sulphonylsulphone (4c) 6%
9	0.99	3.5 h	O_2, initiator (2.1 equiv.), $(EtO)_3P$ (4.7 equiv.), *hν*	sultone (3) 11%, hydroxysulphonate (5) 11%, sulphinate (2i) 10%
10	0.52	2 d	O_2, $(EtO)_3P$ (11.7 equiv.)	sulphonate (2j) 41%, phosphate (2k) 13%, sultone (3) 9%, sulphinate (2i) 9%
11	0.076	4.5 h	O_2, initiator (1.5 equiv.), *hν*	sultone (3) 51%, thiosulphonate (4a) 20%
12	0.18	2 d	air, CF_3CO_2H (14 equiv.)	thiosulphonate (4a) 98%
13	0.10	4 h	O_2	thiosulphonate (4a) 100%

* Reactions 1—10 refer to the sulphinic acid (2a) and reactions 11—13 to the thiosulphonate (4a). In reaction 11, the yield of sultone (3) refers to a 1 : 1 stoicheiometry. All reactions were carried out in the dark unless stated to the contrary; photolyses (*hν*) conditions are described in the Experimental section. The reactions were conducted whilst bubbling oxygen (O_2), argon (Ar), nitrogen (N_2), or air through the solutions. Reactions 1—6 and 9—13 were carried out in benzene as solvent; reactions 7 and 8 in water–benzene.

Prolonged reaction in the dark gave the sultone (3) in 33% yield.

Arylsulphonyl iodides are readily homolysed on photolysis giving arylsulphonyl radicals.[6] The sulphinic acid (2a) rapidly reacted with iodine in the presence of sodium hydrogencarbonate. Subsequent photolysis of the presumed arylsulphonyl iodide (2g) under oxygen gave in low but variable yield the sultone (3). A new compound was also isolated, microanalytically pure, and assigned as the disulphone (4c). Clearly the arylsulphonyl radical was unable to abstract hydrogen atoms efficiently *via* an intramolecular pathway.

Sulphinic acid (2a) was decomposed in the presence of triethyl phosphite in order to capture any alkyl hydroperoxide intermediates. Photolysis in the presence of initiator and triethyl phosphite under oxygen gave a mixture of products. Chromatography gave the sultone (3) (11%). A more polar alcohol ($\nu_{max.}$ 3 530 and 3 500—3 150 cm^{-1}) ($C_{17}H_{28}O_4S$) (11%) was also isolated, the n.m.r. spectrum of which showed the presence of two non-equivalent isopropyl functions [δ_H 1.3 (12 H, d, *J* 8 Hz), 2.9 (1 H, septet, *J* 8 Hz), and 4.01 (1 H, septet, *J* 8 Hz)] and one 1-hydroxy-1-methylethyl function [δ_H 1.8 (6 H, s)]. The molecule was most reasonably the ethyl arylsulphonate (5). Fragmentations in the mass spectrometer at 313 (M^+ — Me) and 310 (M^+ — H_2O) were in agreement. A third product (10%) showed properties consistent with the sulphinate (2i) ($\nu_{max.}$ 1 130 cm^{-1} with the absence of an intense band at 1 350—1 300 cm^{-1}, M^+ 296). Reaction of the sulphinic acid (2a) with triethyl phosphite in the dark under oxygen gave the sultone (3) (9%), the sulphinate (2i) (9%), ethyl 2,4,6-tri-isopropylbenzenesulphonate (2j) (41%), and *OO*-diethyl *S*-(2,4,6-tri-isopropylphenyl) thiophosphate (2k) (13%). Both microanalysed satisfactorily, and showed molecular ions in the mass spectra and intact 2,4,6-tri-isopropylphenyl functions in the n.m.r. spectra. Presumably both the sulphinate (2i) and thiophosphate (2k) arose *via* the thiosulphonate (4a) and an Arbusov-like reaction; this has precedent in the literature.[7] Alternatively, ethylation of sulphonate anions would have provided the ethyl arylsulphonates (2j) and (5). The introduction of



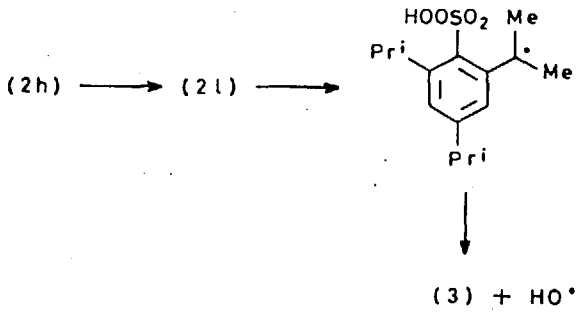
(5)

the hydroxy-function in sulphonate (5) was consistent with interception of a hydroperoxide by triethyl phosphite.

The thiosulphonate (4a) was examined as a precursor of the sultone (3). In the dark under oxygen, or in air in the presence of trifluoroacetic acid the thiosulphonate (4a) was recovered unchanged. However, on photolysis in the presence of initiator and oxygen the sultone (3) (51%) was formed and thiosulphonate (4a) (20%) recovered unchanged.

The conversion of benzenesulphinic acid into benzenesulphonic acid by oxygen has been reported by Horner and Basedow.[8] The reaction was accelerated by photolysis and proposed to proceed by a chain-radical pathway *via* the benzenesulphonyl radical and peroxybenzenesulphonic acid. Intermediacy of the peroxybenzenesulphonic acid was consistent with *in situ* oxidation of dibenzyl disulphide to the sulphoxide. Consistent with these observations and the results in the Table, sultone (3) most probably arose by a radical pathway. In the absence of initiator radical (21) is capable of intramolecular hydrogen-atom abstraction giving the 2-arylpropyl

radical (as in the Scheme). Hydrogen-atom abstraction *via* a 7-membered transition state has precedent.[9]



SCHEME

EXPERIMENTAL

M.p.s were determined on a Kofler hot stage. I.r. spectra were recorded as Nujol mulls (solids) or in carbon tetrachloride solution (oils). U.v. and n.m.r. spectra were recorded as ethanol and deuteriochloroform solutions respectively. All reactions were carried out at room temperature unless stated to the contrary. Organic extracts were dried over sodium sulphate. Solvents were re-distilled; light petroleum refers to the reagent with b.p. 40—60 °C. Both t.l.c. and p.l.c. were carried out on Merck Kieselgel GF_{254}; developing solvents are given in parentheses. Photolyses were carried out using Pyrex apparatus with an externally cooled 125-W high-pressure mercury-arc lamp; a 1-cm 0.1M solution of naphthalene in light petroleum (b.p. 60—80 °C) cut out light below 316 nm.[3]

Preparation of 2,4,6-*Tri-isopropyl*-1,α-*sultone* (3).—2,4,6-Tri-isopropylbenzenesulphonylhydrazine (2b) (286 mg) in dichloromethane (15 ml) and triethylamine (0.50 g) were stirred for 5 d. Trifluoroacetic acid (1.2 g) was added and after 5 d the mixture was evaporated and chromatographed on Kieselgel H (20 g) to give (eluant light petroleum) an oil (2 mg) and [eluant dichloromethane–light petroleum (0 : 1—4 : 1)] the *sultone* (3) (77 mg, 28%), m.p. 124—127 °C (from light petroleum); $\nu_{max.}$ 1 605w (C=C), 1 330s (−SO_2−O), 1 300w, 1 255w, 1 220w, 1 190s (−SO_2−O), 1 155w, 1 125m, 1 105w, 1 090w, 1 050w, 970w, 940w, 905w, 890w, 865m, 840w, 800m, and 760w cm^{-1}; $\lambda_{max.}$ 266 (ε 680) and 275 nm (670); δ_H 1.33 (12 H, t, *J* 7 Hz, $CHMe_2$), 1.80 (6 H, s, O−CMe_2), 3.03 (1 H, septet, *J* 7 Hz, *o*-$CHMe_2$), 3.60 (1 H, septet, *J* 7 Hz, *p*-$CHMe_2$), 7.03 (1 H, d, *J* 1 Hz), and 7.34 (1 H, d, *J* 1 Hz); δ_C 156.55 (s, 4-C), 145.83 (s, 2-C), 144.84 (s, 6-C), 128.05 (s, 1-C), 125.19 (d, 3-C), 117.02 (d, 5-C), 89.89 [s, 2-*C*(O−)Me_2], 34.54 (d, 4-*C*HMe_2), 29.58 (d, 6-*C*HMe_2), 28.65 [q, 2-C(O−)*Me*$_2$], 23.67 (q, 6-CH*Me*$_2$), and 23.29 (q, 4-CH*Me*$_2$); *m/e* 282 (M^+), 267 (100%), and 175 (Found: C, 63.8; H, 7.85; S, 11.3%; M^+, 282.1294. $C_{15}H_{22}SO_3$ requires C, 63.8; H, 7.85%; S, 11.35; *M*, 282.1290).

Preparation of 2,4,6-*Tri-isopropylbenzenesulphinic Acid* (2a).—Zinc dust (1.34 g) was added during 5 min to a suspension of 2,4,6-tri-isopropylbenzenesulphonyl chloride (2c) (3.03 g) in boiling water (25 ml). After 5 min the mixture was cooled, and the solid filtered off, suspended in water (40 ml), and boiled with sodium carbonate (1.6 g) for 20 min. The suspension was cooled, filtered, and the residue leached with water (2 × 5 ml). The filtrate was washed with dichloromethane (2 × 30 ml), cooled to 0 °C, and concentrated hydrochloric acid (1.7 ml) in water (50 ml) added. After 30 min the solid was filtered off, and recrystallised without warming from aqueous methanol to give 2,4,6-tri-isopropylbenzenesulphinic acid (2a) (0.89 g, 33%) as white needles, m.p. 84.5—87 °C (lit.,[2] 80—81 °C); $\nu_{max.}$ 3 050w, 2 500m, br, 1 770w, 1 600m, 1 570m, 1 430m, 1 340w, 1 320w, 1 300w, 1 260w, 1 240w, 1 190w, 1 170w, 1 115w, 1 135w, 1 100w, 1 075s, 1 055s, 1 015s, 940w, 920w, 880m, 845m, 820s, 760w, 720w, 665w, and 655m cm^{-1}; $\lambda_{max.}$ 273 (ε 1 400) and 282 nm (1 200); δ 1.15—1.5 (18 H, m), 2.9 (1 H, septet, *J* 8 Hz), 4.15 (2 H, m), 7.10 (2 H, s), and 10.7 (1 H, br s); *m/e* 502 (aryl-SO_2S-aryl), 470 (aryl-S_2), 438 (aryl-S-aryl), 284, 267, 251, 235, 221, 183, 151, 149, 91, 43, and 41. A further recrystallisation gave material with m.p. 87—88 °C (Found: C, 66.9; H, 9.05. Calc. for $C_{15}H_{24}O_2S$: C, 67.1; H, 9.0%).

Photolysis of 2,4,6-*Tri-isopropylbenzenesulphinic Acid* (2a).—Dry benzene (10 ml) was deoxygenated with argon for 3 h and dry 2,4,6-tri-isopropylbenzenesulphinic acid (2a) (265 mg) and 2,2′-azobis-(2-methylpropionitrile) (340 mg) were added. The solution was deoxygenated for 10 min and photolysed for 3 h. Evaporation and chromatography on Kieselgel H (18 g) gave (eluant light petroleum) di-(2,4,6-tri-isopropylphenyl) disulphide (4b) (14 mg, 6%), m.p. 88—91 °C (lit.,[4a] 91—92 °C); $\nu_{max.}$ (CCl_4) 3 050w, 2 960s, 2 930m, 2 810m, 1 600m, 1 465m, 1 425m, 1 385m, 1 365m, 1 315w, 1 170w, 1 100w, 1 060w, 940w, and 880w cm^{-1}; δ 0.9—1.3 (36 H, 2 d, *J* 7 and 6 Hz), 2.85 (2 H, m), 3.5 (4 H, septet, *J* 6 Hz), and 6.9 (4 H, s); *m/e* 470 (M^+), 235 (100%), 217, 183, 151, 149, 119, 117, 43, and 41 (Found: C, 76.75; H, 10.0. Calc. for $C_{30}H_{46}S_2$: C, 76.55; H, 9.85%) and [eluant dichloromethane–light petroleum (0 : 1—1 : 0)] *S*-2,4,6-tri-isopropylphenyl 2,4,6-tri-isopropylbenzenethiosulphonate (4a) (143 mg, 58%), m.p. 109—111 °C (from aqueous methanol) (lit.,[4b] 108.5—110 °C); $\nu_{max.}$ 3 050w, 2 960s, 2 930m, 2 900m, 2 870m, 1 600w, 1 560w, 1 460m, 1 425m, 1 380m, 1 360m, 1 320m, 1 250w, 1 190w, 1 160m, 1 140s, 1 100w, 1 070w, 1 060w, 1 030w, 940w, 880m, 840w, 790s, 765s, and 650s cm^{-1}; δ 0.8—1.35 (36 H), 2.80 (2 H, m), 3.7 (4 H, m), and 6.8—7.0 (4 H, 2 s); *m/e* 502 (M^+), 470, 438, 303, 236, 235 (100%), 221, 193, 151, 85, 83, 43, and 41 (Found: C, 71.6; H, 9.3. Calc. for $C_{30}H_{46}O_2S_2$: C, 71.65; H, 9.2%).

Preparation and Decomposition of 2,4,6-*Tri-isopropylbenzenesulphonyl Iodide* (2g).—2,4,6-Tri-isopropylbenzenesulphinic acid (2a) (268 mg), sodium hydrogencarbonate (84 mg), and iodine (254 mg) in benzene (5 ml) and water (6 ml) were stirred under nitrogen for 15 min. T.l.c. [light petroleum–dichloromethane (1 : 1)] indicated a single product (R_F 0.8). The solution was photolysed for 2 h under oxygen when the initial product had completely decomposed. The aqueous phase was extracted with diethyl ether (3 × 50 ml) and the combined organic phase was dried, evaporated, chromatographed on Kieselgel H (18 g) [eluant light petroleum—diethyl ether (1 : 0—7 : 3)], and separated by p.l.c. [two developments in diethyl ether–light petroleum (1 : 19)] to give [R_F 0.6, dichloromethane–light petroleum (1 : 1)] *di*-(2,4,6-*tri-isopropylbenzene*)*sulphonyl sulphone* (4c) (53 mg, 20%), m.p. 117—118 °C (from aqueous methanol); $\nu_{max.}$ (CCl_4) 3 050w, 2 970w, 2 930w, 2 880w, 1 600m, 1 550w, 1 465m, 1 450m, 1 430m, 1 390m, 1 375m, 1 370m, 1 335m, 1 265s, 1 170m, 1 155m, 1 135m, 1 125m, 1 105w, 1 070w, 1 060w, 1 020w, 935w, 895w, 885w, and 700m cm^{-1}; δ 1.3 (18 H, 2d, *J* 7 Hz), 2.95 (1 H, septet, *J* 7 Hz), 4.1 (2 H, septet, *J* 7 Hz), and 7.23 (2 H, s); *m/e* 470, 267, 252, 251, 235, 233, 204, 189 (100%), 187, 161, 149, 105, 91, 85, 71, 69, 64, 57, 43, and 41 (Found: C, 67.4; H, 8.8. $C_{30}H_{46}O_4S_2$ requires C, 67.4; H, 8.65%).

Photolysis of 2,4,6-*Tri-isopropylbenzenesulphinic Acid* (2a) *with Triethyl Phosphite*.—2,4,6-Tri-isopropylbenzenesulphinic acid (2a) (264 mg), 2,2′-azobis-(2-methylpropionitrile) (340 mg), and triethyl phosphite (0.80 ml) in dry benzene (10 ml) were photolysed under oxygen for 3.5 h. Chromatography on Kieselgel H (20 g) and repeated p.l.c. [diethyl ether–light petroleum (1 : 3—1 : 4)] gave 2,4,6-*tri-isopropylphenyl ethoxy sulphoxide* (2i) (27 mg, 10%) as an oil; $\nu_{max.}$ 2 970s, 2 930s, 2 880m, 2 250w, 1 715w, 1 600m, 1 570w, 1 460m, 1 430m, 1 390m, 1 370m, 1 345m, 1 325w, 1 265w, 1 245w, 1 200w, 1 175w, 1 160w, 1 130s, 1 105m, 1 075w, 1 065w, 1 020s, 940w, 920w, 885s, 845w, 820w, 805w, 770w, 730m, 700m, 670w, and 650m cm^{-1}; δ 1.2—1.35 (18 H, m), 1.4 (3 H, t, *J* 7 Hz, CH_2Me), 3.9 (1 H, septet, *J* 7 Hz), 3.95—4.45 (4 H, m), and 7.2 (2 H, s); *m/e* 296 (M^+), 279, 267, 251, 233 (100%), 191, 149, 120, 71, 57, 47, 43, and 40 (Found: C, 69.0; H, 9.6. $C_{17}H_{28}O_2S$ requires C, 68.85; H, 9.5%), sultone (3) (30 mg, 11%), and *ethyl* 6-(1-*hydroxy*-1-*methylethyl*)-2,4-*di-isopropylbenzenesulphonate* (5) (37 mg, 11%) (R_F 0.25, dichloromethane) as an oil; $\nu_{max.}$ (film) 3 530m, 3 500—3 150m, br, 3 080w, 3 050w, 2 970s, 2 930s, 2 880 m, 1 710w, 1 600m, 1 570m, 1 510w, 1 470m, 1 430m, 1 420w, 1 390m, 1 370m, 1 355m, 1 335m, 1 260m, 1 200m, 1 180s, 1 155m, 1 125m, 1 100m, 1 070m, 1 010m, 965w, 940w, 910m, 885m, 875w, 840w, 790m, 780m, 755w, 735w, 700w, 685m, and 665m cm^{-1}; δ 1.3 (12 H, d, *J* 8 Hz), 1.4 (3 H, t, *J* Hz, CH_2Me), 1.8 (6 H, s, $OCMe_2$), 2.9 (1 H, septet, *J* 8 Hz), 4.01 (1 H, septet, *J* 8 Hz), 4.27 (2 H, q, *J* 7 Hz, CH_2Me), 5.65 (1 H, s, OH), and 7.3 (2 H, s); *m/e* 313 (M^+ — Me), 310 (M^+ — H_2O), 282, 281, 267 (100%), 249, 203, 175, 161, 156, 145, 129, 115, 105, 97, 91, 71, 69, 59, 55, 43, and 40 (Found: C, 62.1; H, 8.6. $C_{17}H_{28}O_4S$ requires C, 62.15; H, 8.6%).

Dark Reaction of 2,4,6-*Tri-isopropylbenzenesulphinic Acid* (2a) *and Triethyl Phosphite*.—Triethyl phosphite (0.50 g) was added to 2,4,6-tri-isopropylbenzenesulphinic acid (2a) (154 mg) in dry benzene (5 ml) and the mixture was oxygenated in the dark for 6.5 h. Sulphinic acid (2a) still remained (t.l.c.) thus more triethyl phosphite (0.50 g) was added and the reaction continued for 2 d. Evaporation, chromatography on Kieselgel H (18 g) (eluant diethyl ether) and p.l.c. [two developments in diethyl ether–petroleum (1 : 3)] gave the sulphinate (2i) (15 mg, 9%), the sultone (3) (15 mg, 9%), *ethyl* 2,4,6-*tri-isopropylbenzenesulphonate* (2j) (73 mg, 41%), m.p. 59—60 °C (from light petroleum at −30 °C); $\nu_{max.}$ (CCl_4) 2 960m, 2 930m, 2 910w, 2 890w, 2 870m, 1 600m, 1 460m, 1 425m, 1 380m, 1 365m, 1 350m, 1 335m, 1 300w, 1 230w, 1 195m, 1 180s, 1 170m, 1 155m, 1 135w, 1 105w, 1 070w, 1 060w, 1 040w, 1 010w, 940m, 910m, 905m, 880m, 685w, and 660m, cm^{-1}; δ 1.3 (18 H, d, *J* Hz), 1.35 (3 H, d, *J* 7 Hz), 2.85 (1 H, m), 3.9—4.0 (2 H, m), 4.25 (2 H, q, *J* 7 Hz), and 7.35 (2 H, s); *m/e* 312 (M^+), 297, 283, 269, 267, 266, 265, 251, 218, 202, 187, 159, 145, 131, 117, 105, 19, 43, and 41 (Found: C, 65.15; H, 90.5. $C_{17}H_{28}O_3S$ requires C, 65.35; H, 9.05%), and OO-*diethyl* S-(2,4,6-*tri-isopropylphenyl*) *thiophosphate* (2k), 27 mg, 13%) as an oil; $\nu_{max.}$ 3 030w, 2 960s, 2 930m, 2 905m, 2 890m, 2 870m, 1 595w, 1 460m, 1 440w, 1 425w, 1 390m, 1 380m, 1 300m, 1 350w, 1 315w, 1 245m, 1 185w, 1 170w, 1 095w, 1 045s, 1 020s, 965m, 955m, 940m, and 865w cm^{-1}; δ 1.2 (18 H, d, *J* 7Hz), 1.25 (6 H, t, *J* 6 Hz), 2.8 (1 H, m), 3.75—4.4 (6 H, m), and 7.05 (2 H, s); *m/e* 372 (M^+), 357, 355, 341, 339, 329, 281, 264, 236, 234, 203 (100%), 191, 187, 149, 43, and 40 (Found: C, 61.3; H, 9.0. $C_{19}H_{33}O_3PS$ requires C, 61.25; H, 8.95%).

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