ALKENYLIDENECYCLOPROPANES IN SYNTHESIS

BY

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Thesis submitted to the University of Nottingham
for the degree of Doctor of Philosophy, December, 1982.

DECLARATION

I declare that the work presented in this thesis is the result of my own investigations, and where the work of others has been used, this is fully acknowledged. The material embodied in this thesis has not been submitted, nor is currently being submitted, for any other degree.

P.M. Cairns

Directors of Studies: L. Crombie

G. Pattenden

ACKNOWLEDGEMENTS

I would like to express my sincere thanks to my supervisors, Professors L. Crombie and G. Pattenden, for their invaluable help and advice throughout the period of this work.

I am grateful to the technical staff of the Chemistry Department at the University of Nottingham for their assistance and co-operation.

I thank Miss Santosh Mangal for typing the thesis.

Finally, I would like to thank the SERC for a grant and Proprietary Perfumes Limited for financial support (CASE award).

Dedicated to my Parents

C O N T E N T S

Abstract

This thesis reports an investigation into the synthetic potential of alkenylidenecyclopropanes, with particular emphasis on bicyclic and tricyclic systems.

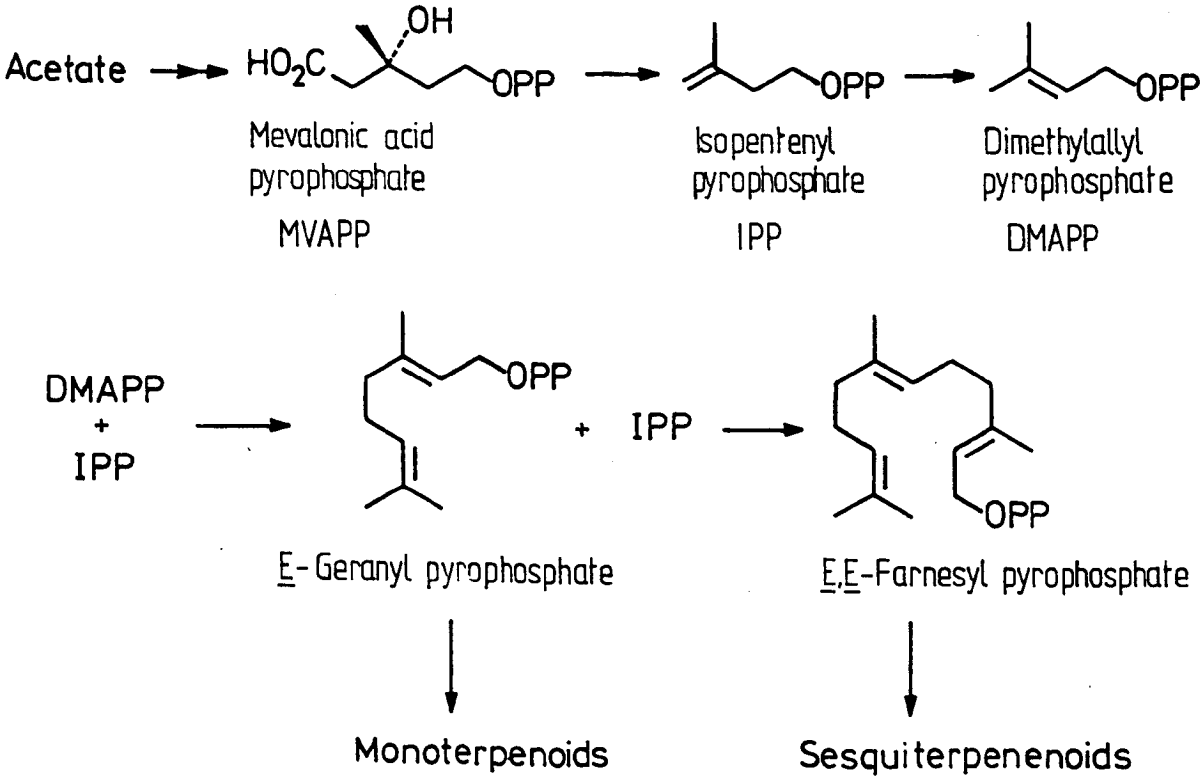
In Chapter 1 alkenylidene carbenes and alkenylidenecyclopropanes are briefly reviewed. The bicyclic alkenylidenecyclopropanes obtained by addition of 2-methyl-1-propenylidenecarbene to cyclopentene, cyclohexene, 1-methylcyclohexene, methylenecyclohexane, dihydrofuran and dihydropyran, and the tricyclic alkenylidenecyclopropanes obtained from α- and β-pinene, were the pivotal molecules of our research. Chapter 2 reports the synthesis of these compounds along with a number of functionalised systems. Also described are unsuccessful attempts to prepare carbene precursors for a projected intramolecular carbene synthesis of the sesquiterpene, bicyclogermacrene. Chapter 3 details the acid catalysed reactions of alkenylidenecyclopropanes. Alkenylidenecyclopropanes having a fused six membered ring gave mainly cyclopropane ring opened acetylenes arising from initial electrophilic attack at the terminal C-5 carbon atom of the allene system. Minor products formally derived by trapping of cyclopropyl cations arising from C-4 attack were also isolated. However, in the case of the alkenylidenecyclopropane obtained from cyclopentene only ring expanded products resulting from initial attack at C-4 were isolated. The C_{15} alkenylidenecyclopropanes obtained from α- and β-pinene gave ring opened monocyclic enynes possessing a menthane type skeleton. Mechanisms are proposed to account for all the products isolated. In contrast to previous studies in this area the same products were obtained on changing from Lewis to protic acid. A new route to 3-substituted γ- and δ-lactones from dihydrofuran and dihydropyran respectively is given. Under Lewis acid catalysed conditions allylidenecyclopropanes gave exclusively the same major products obtained on acid catalysed reaction of the parent alkenylidenecyclopropanes. In Chapter 4 the peracid oxidation of alkenylidenecyclopropanes has been extended to bicyclic systems. The stereochemistry of the resulting ketoesters and derived products are discussed. The dissolving metal reduction of bicyclic and tricyclic alkenylidenecyclopropanes is shown to be regiospecific and stereoselective affording vinylcyclopropanes of predominantly exo stereochemistry. Chapter 5 describes the reaction of alkenylidenecyclopropanes with thiophenol to give regioselectively and stereoselectively endo cyclopropyl enol thioethers. Reductive cleavage gave vinylcyclopropanes; together with

the dissolving metal reduction of the parent alkenylidenecyclopropanes providing a stereoselective route to vinylcyclopropanes from alkenes. A novel synthesis of the seven membered ring monoterpenoid, karahanaenone via Cope rearrangement of a thiodivinylcyclopropane is described.

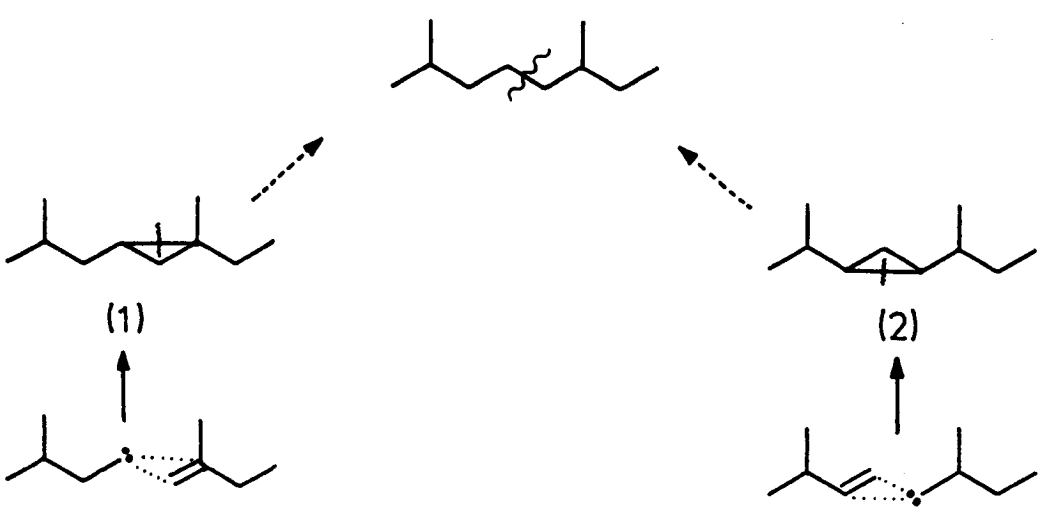
CHAPTER ONE

Introduction

The volatile, odorous substances of many plant constituents are known collectively, as the essential oils. Early studies on the chemical composition of the essential oils led to the discovery of structurally related ten-carbon substances, called monoterpenes. Later work also established the presence of similar fifteen - carbon compounds; the sesquiterpenes. Together, because of their volatility, they are largely responsible for the odour and flavour of essential oils. The early finding that monoterpene hydrocarbons could be formally derived by the head to tail linkage of C_5 isoprene units led to Wallach's formulation of the isoprene rule.[1] However, it soon became apparent that many terpenes did not obey this rule, not being exact multiples of five, or possessing "abnormal" head to head or tail to tail carbon skeletons. To rationalise these findings Ruzicka put forward his "biogenetic isoprene rule", which briefly states that the natural products are derived from isoprenoid precursors by a series of additions, hydride shifts and rearrangements, giving rise to the parent cations of various structural types.[2] Ruzicka's scheme was based largely on mechanistic considerations and did not concern itself with the nature of the biological processes involved. It was only when the discovery of mevalonic acid and its conversion to isopentenyl pyrophosphate - the biological isoprene unit - that an understanding of terpenoid biosynthesis on a molecular level was possible.[3] Scheme 1 shows the enzymatic conversion of mevalonic acid to isopentenyl pyrophosphate, and its subsequent transformation to geranyl and farnesyl pyrophosphate; the first C_{10} and C_{15} compounds respectively.[4]

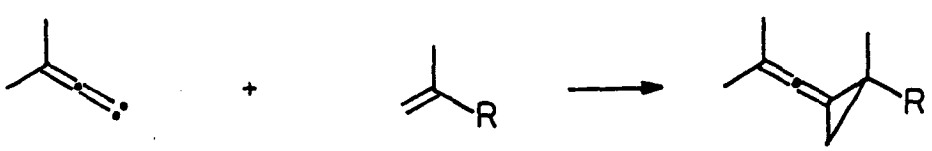


Scheme 1



Scheme 2

Over the years, considerable effort has been expended towards developing methods for the synthesis of monoterpenoids by the head to tail linking of isopentane units.[5,6] Owing to the interest in cyclopropane chemistry within this Department an approach utilising C_{10} cyclopropane intermediates; obtained from the combination of a C_5 carbene and an appropriate C_5 alkene, seemed attractive. Of the nine theoretically possible monocyclic cyclopropane containing carbon skeletons having head to tail union of isopentane units only two, (1) and (2), are available from the addition of a C_5 carbene. Cleavage of these cyclopropane intermediates at the positions shown in Scheme 2 leads to the regular monoterpenoid skeleton. Of the two intermediates, (1) appeared the more attractive since the C_5 carbene was known in the form of dimethylallene carbene (3). Moreover, the products of carbene (3) addition, alkenylidene-cyclopropanes (4), are very reactive species and it was hoped that subsequent reaction would provide scope for various modes of ring opening, leading to regular and abnormal monoterpenoid skeletons.



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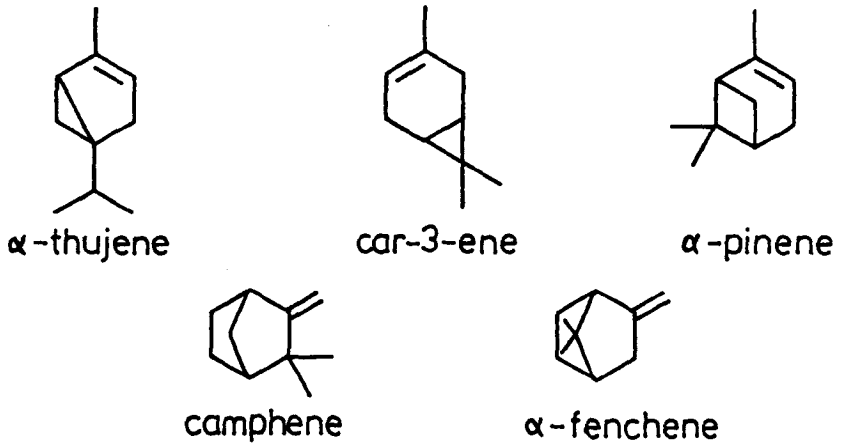
As an added interest, it was also hoped that some of the products obtained from these studies would be of some use in the perfumery and flavour industry. More detailed discussion of Maddocks' work; on the exploitation of C_{10} alkenylidenecyclopropanes in monoterpenoid synthesis, is presented within the relevant chapters.

At the outset of our work, it was our aim to extend these studies to C_{15} alkenylidenecyclopropanes; obtained by the addition of carbene (3) to suitable monoterpenoids. Examination of the known monoterpenoids shows a wide variety of structural types, encompassing ring sizes from three through to seven e.g.



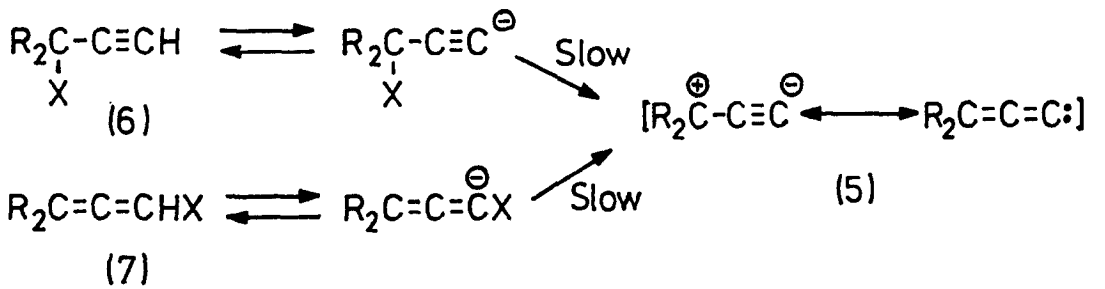
As the vast majority of monoterpenoids are cyclic, in some form or other, and carbene addition would generate at least a bicyclic system, we thought it necessary to firstly examine the chemical reactivity of simpler ring fused bicyclic alkenylidenecyclopropanes.

Before discussing our results, a brief description of the nature and properties of alkenylidene carbenes and alkenylidenecyclopropanes is presented.

1.1 Alkenylidene Carbenes

Alkenylidene carbenes have been comprehensively reviewed by Hartzler.[7] and more recently by Stang.[8] Hennion and Maloney originally proposed carbene (5, R=CH_3) as an intermediate in the alkaline solvolysis of propargylic and allenic halides.[9]

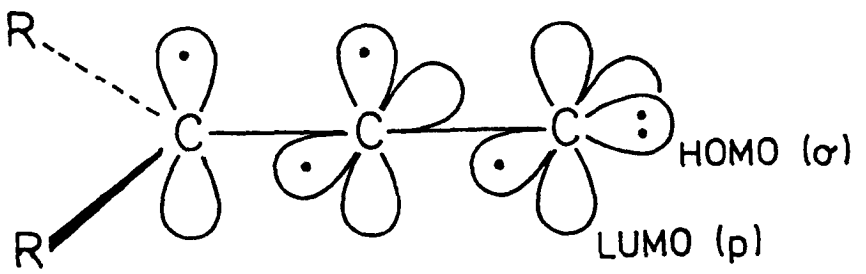
The mechanism now established is that reaction occurs via rapid pre-equilibrium and anion formation followed by a rate determining loss of halide and carbene formation (Scheme 3).[10]



Scheme 3

Alkenylidene carbenes (5) can be generated in aprotic media by the action of base, usually potassium t-butoxide, with acetylenes (6)[11-13] or allenes (7).[14,15] However, the more recently developed phase transfer catalysed (PTC)[16-18] or crown ether[19] procedures generally offer better yields of carbene derived products. 1-Bromoalkynes[20] and dihaloallenes[21] have also served as carbene (5) precursors. The acetylenic route has been extended to vinylalkenylidene carbenes (8) using potassium t-butoxide.[22] The same base has also been used to prepare related allenylidene carbenes (9) from triflate functionalised enynes.[23]

Relative reactivity data for carbenes (5) suggests that there is very little carbene encumberance in the transition state of olefin additon. The similarity of olefin selectivity of alkenylidene carbenes regardless of precursor suggests a free carbene. That dimethyl-, di-t-butyl- and diphenyl-carbene react similarly also shows that there is very little



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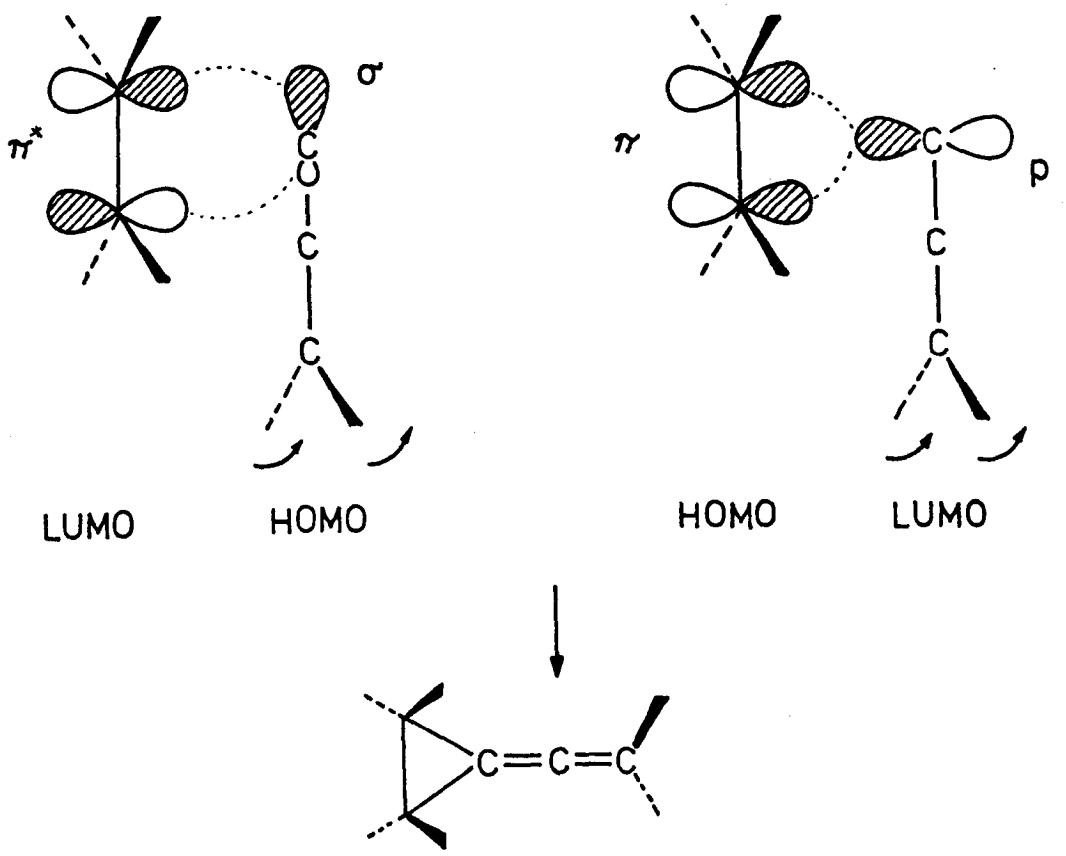
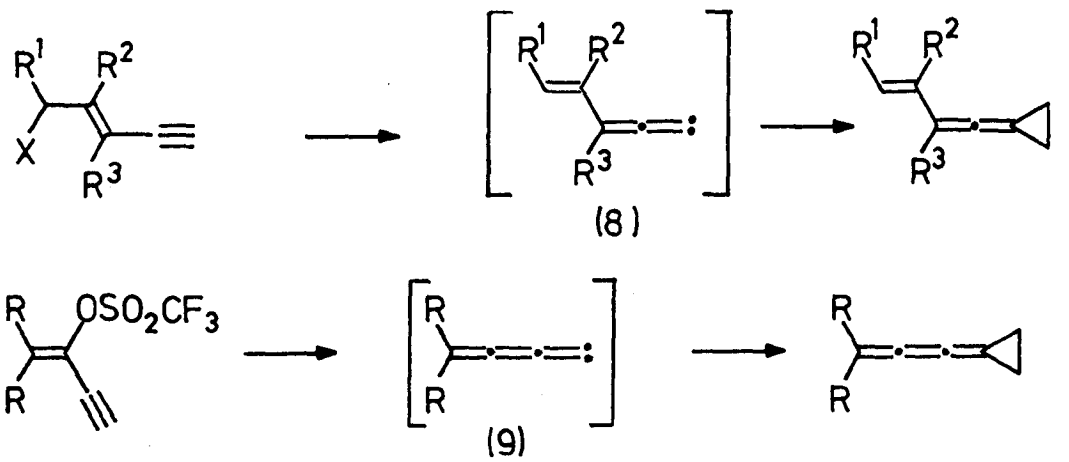


The Non-Linear Approach of an Alkenylidene Carbene to an Olefin

Scheme 4



steric requirement for reaction. This is not unexpected as, unlike alkylidene carbenes, the substituents are perpendicular and one carbon removed from the reactive site at the vacant carbene p orbital.[8] Indeed, it has been pointed out that the steric requirement of (5) should be the lowest of any carbene, in that a nearly "naked" carbon atom is added to the olefin.[24] However, it should be borne in mind that the approach of a carbene is probably non-linear; orbital overlap begins to develop at a stage when the carbene is sideways on to the olefin.[25] In terms of frontier molecular orbital (FMO) theory, addition of singlet carbene (10) to an alkene would involve simultaneous interaction of the vacant carbenic p orbital (LUMO) with the filled alkene π orbital (HOMO), and of the filled carbenic σ orbital (HOMO) with the vacant alkene π^* orbital (LUMO) (Scheme 4). The dominant orbital interaction is determined by both the differential energies of the competitive interactions and by the comparative extent of orbital overlap.[26]

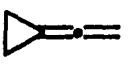
Further reaction, and higher yields, with more substituted

and hence electron rich olefins indicates that alkenylidene carbenes (5) are electrophilic. The stereospecificity of carbene (3) addition to Z- and E-2-butene implies that the carbene is the expected singlet.[24,27] The enhanced stability of (5), over alkylidene carbenes, has been attributed to the overlap of the vacant p-orbital with the π-electrons of the C(2-3) double bond.[24]

Although alkenylidene carbenes have been shown to react with a wide variety of nucleophiles, and to undergo insertion reactions into C-H and Si-H bonds,[8,28] we have been solely concerned with the cyclopropanation reaction with olefins to form alkenylidenecyclopropanes.

1.2 Alkenylidenecyclopropanes

The reactions of alkenylidenecyclopropanes have been very briefly reviewed by Hopf.[29] The parent alkenylidenecyclopropane (11) has been synthesised from methylenecyclopropane by the Doering-Moore-Skattebol method.[30] All other alkenylidenecyclopropanes, including those discussed in our work, have been prepared by the addition of alkenylidene carbenes to alkenes.



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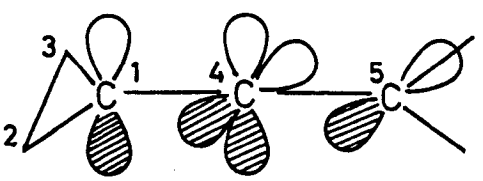
Considerable attention has been focussed on the electronic structure and reactivity of alkenylidenecyclopropanes. However, for the most part, reports in the literature concerning the reactions of alkenylidenecyclopropanes have been directed towards an understanding of their reactivity, rather than from a synthetic point of view. In particular, the pioneering work of D. J. Pasto and his co-workers in this area, has led to a better understanding of the reactivity of these fascinating systems.[31-33] The unique bonding properties of alkenylidenecyclopropanes have, in part, been attributed to the significant interaction between the Walsh orbitals of the cyclopropane ring[34] with the in plane C(4-5) π system of the allene portion of (12).[33]



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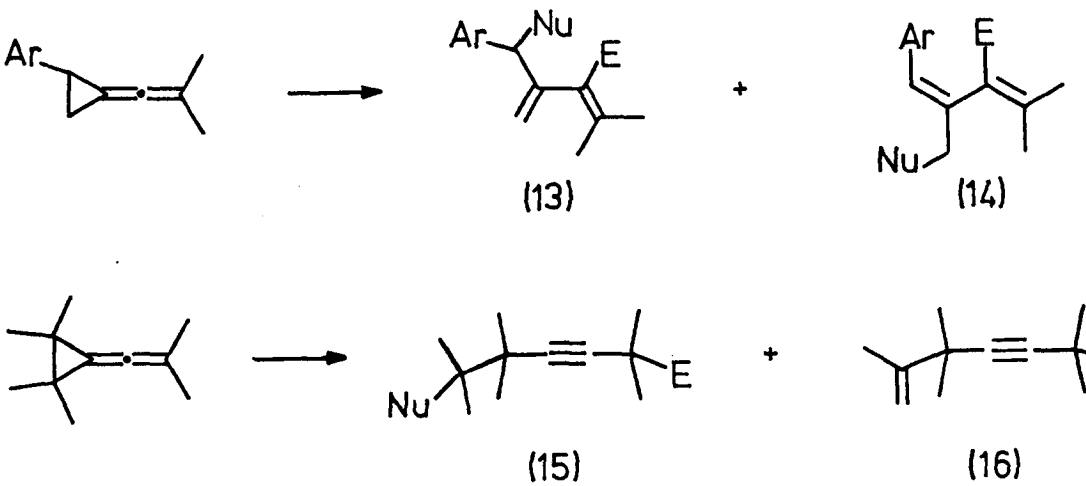
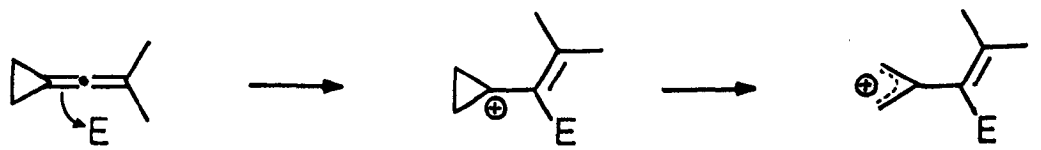
The reaction of alkenylidenecyclopropanes with electrophilic reagents, e.g. chlorosulphonyl isocyanide (CSI), mercuric acetate, benezenesulphonyl chloride and protic acids have been examined in some detail.[35-37] Work has shown that the selectivity of electrophilic attack is greatly dependent on the nature of the substituents attached to the three membered ring and, to some extent, the nature of the electrophilic species. While aryl substituted alkenylidenecyclopropanes react almost exclusively at the p orbital on the central C-4 carbon atom of the C(1-4) double bond to produce ring opened dienes of type (13) and (14),

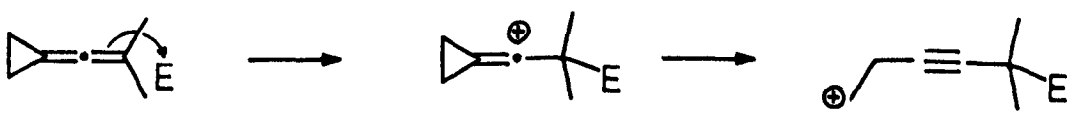
alkyl substituted alkenylidenecyclopropanes react with the same reagents almost exclusively at the terminal C-5 carbon atom to produce acetylenes of general structure (15) and (16).



Electrophilic attack at C-4 results in the formation of a cyclopropyl cation, which derives very little stabilisation from the groups attached to the cyclopropane ring.[35] Disrotatory ring opening gives rise to an allyl cation intermediate.

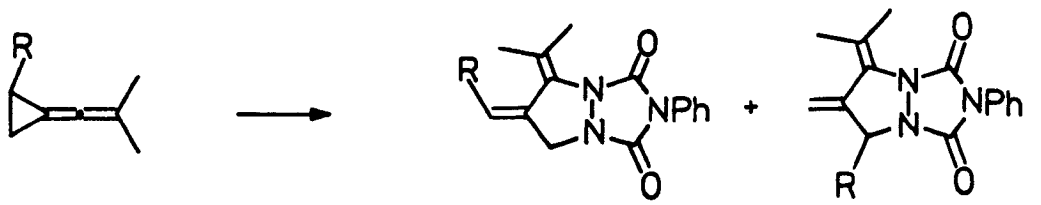


However, the greater stability afforded the allyl cation by aryl, relative to alkyl, groups cannot be a factor until very late in the ring opening process.[35,36] Electrophilic attack at C-5 results in the formation of a vinyl cation which derives extensive stabilisation by interaction of the vacant in plane p orbital on C-4 with the Walsh orbitals of the cyclopropane ring.[35,36]



Alkyl groups interact more strongly with the Walsh orbitals of the ring than do unsaturated groups, hence they should stabilise cation formation at C-4 to a greater degree than at C-1. Unsaturated groups attached to the cyclopropane ring do not lead to stabilisation at either centre.[35,36] Thus, alkyl substituted alkenylidenecyclopropanes should be more reactive towards electrophilic attack at C-5 than unsaturated derivative. However, this does not explain the difference in regioselectivity of electrophilic attack, and arguments based on molecular orbital calculations have been invoked.[36]

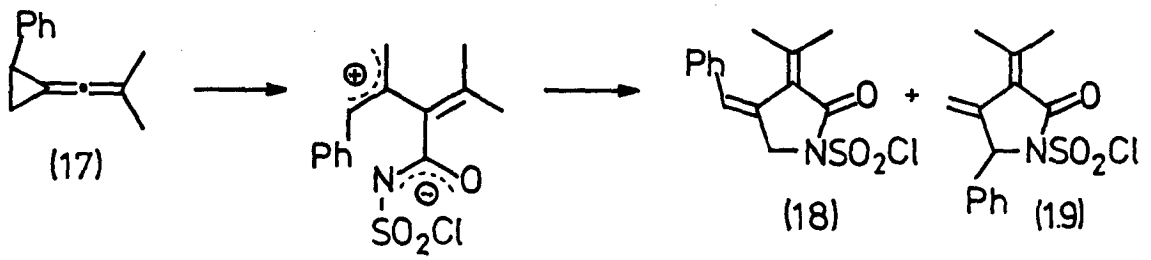
Apart from their reaction with electrophiles, alkenylidene-cyclopropanes take part in many cycloadditon reactions. They undergo facile cycloadditon with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) across the exocyclic C(1-4) double bond regardless of the nature and number of groups attached to the three membered ring.[31,38-41] The reaction has been shown to proceed via a concerted $[(\pi^2+\pi^2+\sigma^2)+\pi^2]$ pathway. Methyl groups attached to the cyclopropane ring increase the reactivity of the alkenylidene-cyclopropane while unsaturated groups decrease it. (Scheme 5).[31]



Scheme 5

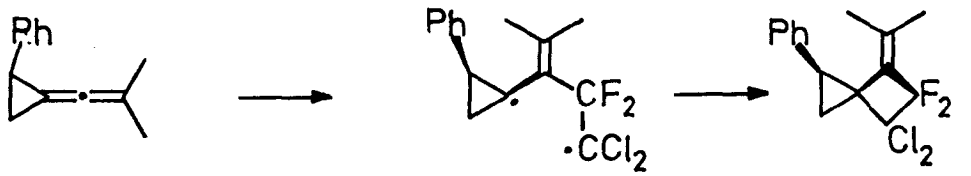
An attempt by Pasto and Whitmer to extend this reaction with maleic anhydride and N-phenylmaleimide, in the hope of obtaining five membered carbocycles met with failure. Instead, the only

products isolated were those arising from: ene reaction of the C(4-5) double bond followed by further [4+2] cycloaddition, [2+2] cycloadditon across the C(1-4) double bond, and [1,3] sigmatropic rearrangement followed by [4+2] cycloaddition.[42] CSI does not exhibit the same slectivity as PTAD; the phenyl substituted alkenylidenecyclopropane (17) undergoes exclusive attack of C-4 across the C(1-4) double bond. The resulting dipolar intermediate then undergoes ring opening and recyclisation to give mixtures of γ-lactams (18) and (19) (Scheme 6).[40,41,43,44] The formation of isomeric γ-lactones has also been reported.[45] Conversely, alkyl



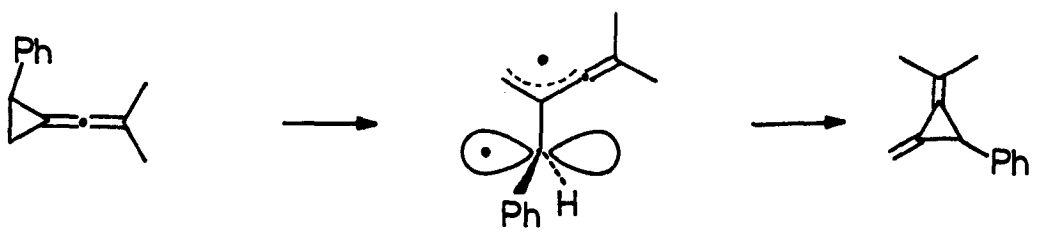
Scheme 6

substituted alkenylidenecyclopropanes undergo attack solely at C-5 across the C(4-5) double bond to give [2+2] cycloadducts. Alkenylidencyclopropanes also react with acetylenic dienophiles to give mixtures of [2+2] cycloadducts arising from addition to both allene double bonds.[46] Diradical intermediates have been proposed in the reaction of 1,1-dichloro-2,2-difluoroethene[47] (Scheme 7) and methylene malonitriles,[48] with aryl and alkyl substituted alkenylidenecyclopropanes to give [2+2] cycloadducts by addition across the exocyclic C(1-4) double bond. In many of these cycloaddition reactions the phenyl substituted alkenylidenecyclopropane (17) reacts exclusively across the C(1-4) double bond on the face opposite the phenyl group.



Scheme 7

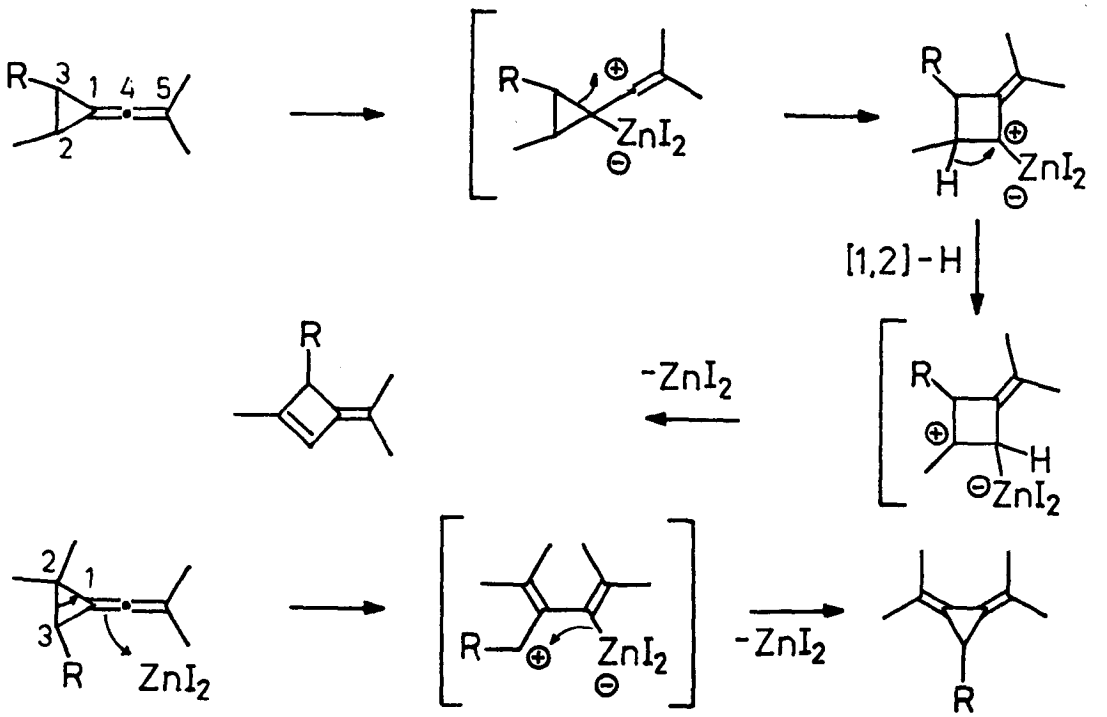
Alkenylidenecyclopropanes are thermally labile and undergo smooth rearrangement to give 1,2-dialkylidenecyclopropanes on heating (Scheme 8).[49] In aryl substituted alkenylidenecyclopropanes the aryl group always remains on the ring and does not migrate to the double bond. Reaction is thought to occur via a perpendicular diradical of type (10). Product formation is rationalised in terms of the most stable diradical intermediates. The importance of the aryl function in affording stability to the benzyl radical portion of diradical (10) is shown by the ease of reaction with aryl substituted alkenylidenecyclopropanes compared to alkyl substituted derivatives.



Scheme 8

The reaction of alkenylidenecyclopropanes with zinc iodide in boiling ether to give quantitative yields of rearrangement products is also most interesting.[50] Whilst 2-methyl- and 2,3-dimethyl- substituted alkenylidenecyclopropanes give isopropylidenecyclobutenes, 2,2-dimethyl- and 2,2,3-trimethyl-substituted ones give only dialkylidenecyclopropones. Formation of the isopropylidenecyclobutenes was accounted for by initial

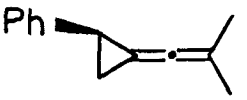
electrophilic attack at the cyclopropyl C-1 carbon atom followed by ring expansion and a [1,2] -H shift, while formation of the dialkylidenecyclopropanes was rationalised by initial C-4 attack, ring opening and recyclisation. Remarkably, it is the carbon atom displaying the lowest degree of substitution, C-3, which undergoes alkyl shift or 1,3-elimination (Scheme 9).



Scheme 9

Studies on the catalytic hydrogenation of alkenylidenecyclopropanes have been carried out using palladium, platinum and Raney nickel catalysts.[51] Reaction with one equivalent of hydrogen gives good yields of cis- or endo-vinylcyclopropanes. However, care must be taken not to use excess hydrogen otherwise stereomutation or complete reduction (with ring opening) results. Chiral alkenylidenecyclopropanes have been produced by the partial asymmetric hydroboration of (17) using (+)-diisopinocampheylborane

to give (-)-(R)-(20).[52] The same authors also report the



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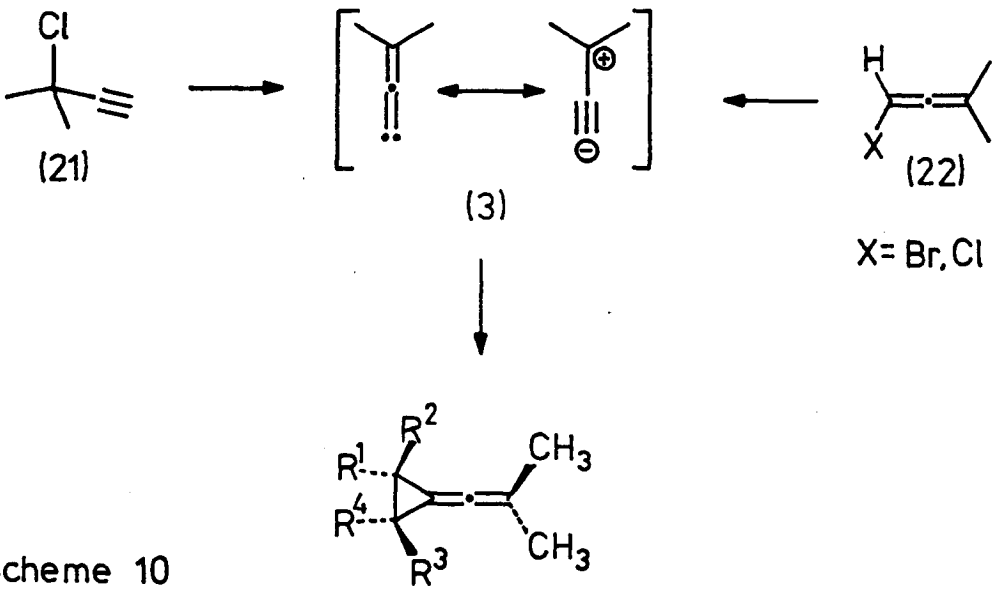
reduction of (17) using excess diimide to give a mixture of cis-vinylcyclopropane and a product with complete reduction of the allene portion[52].

CHAPTER TWO

Synthesis of Alkenylidenecyclopropanes

2.1 Preparation of 2-Methyl-1-propenylidenecyclopropanes

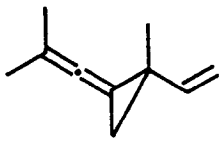
Our work has primarily been concerned with 2-methyl-1-propenylidenecyclopropanes;* easily prepared by addition of 2-methyl-1-propenylidene carbene (3) to alkenes (Scheme 10).[12,14,16-19,24,53,54] The work of Hartzler and others showed that carbene (3) could be produced from chloroyne (21) or holoallene (22, X=Cl) under anhydrous conditions employing potassium t-butoxide. Recently phase transfer catalysed (PTC) methods



Scheme 10

using quaternary ammonium salts, have become available, permitting generation of carbene (3) in aqueous media, and leading to improved yields of many carbene adducts.[55] Interestingly, Patrick has shown that the PTC reaction of 1-bromo-3-methyl-1,2-butadiene (22, X=Br) derived carbene is time dependent for maximum yields whereas potassium t-butoxide exhibited maximum yield after two hours.[16] Good yields of cyclopropane adducts have also been obtained under non-hydrolytic conditions using powdered potassium hydroxide in the presence of crown ethers.[19] The generation of carbene (3)

*Also referred to in the literature as isobutenylidene- and 2-methylvinylidenecyclopropanes



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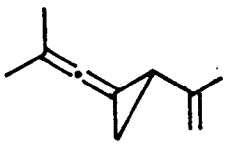

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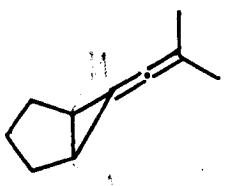

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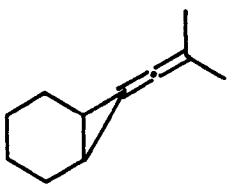

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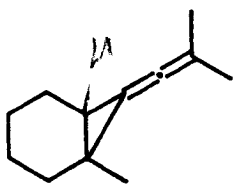

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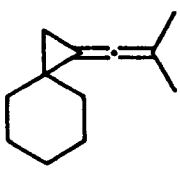

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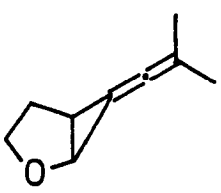

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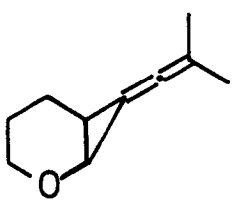

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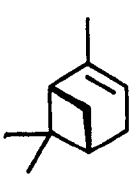

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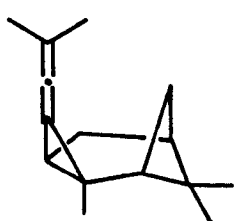

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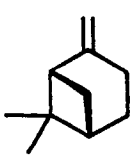

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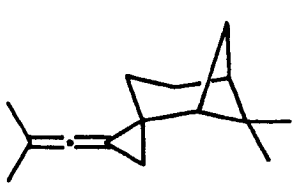
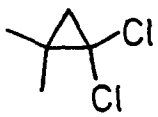


(34)

from dichlorocyclopropane (23) using potassium t-butoxide in hexamethylphosphoramide would appear to be of theoretical interest only.[56]



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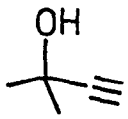
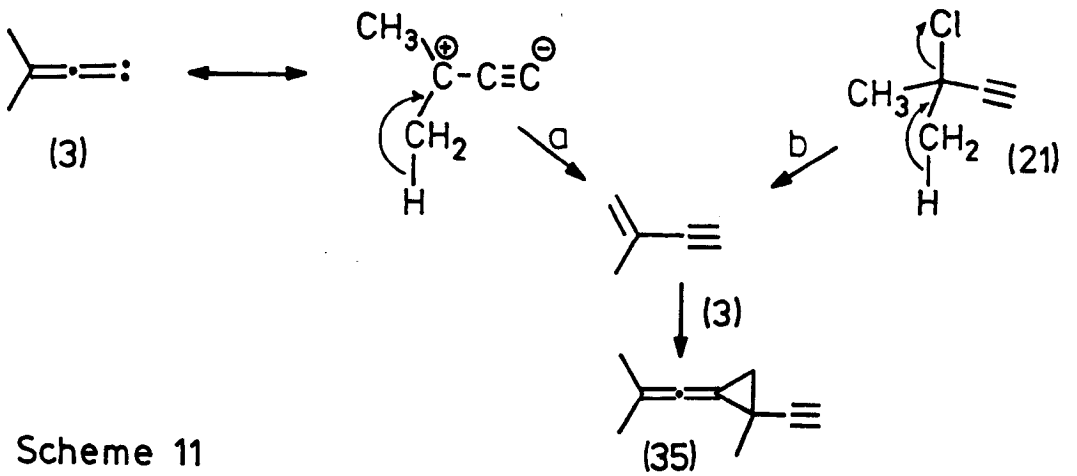


(24)

The operational simplicity of the PTC procedure, and the availability of 3-chloro-3-methyl-1-butyne (21); readily prepared from commercially available 2-methyl-3-butyn-2-ol (24), lend themselves to the viable synthesis of a variety of 2-methyl-1-propenylidenecyclopropanes, and were the method and carbene precursor respectively, used throughout this study. Essentially, the procedure of Sasaki et al.[18] was followed, using 50% aqueous sodium hydroxide as base and Aliquat 336 as the phase transfer catalyst. One to three mole equivalents of the alkene - with respect to the carbene precursor - were used, depending on the availability of the alkene and the ease of separation from the resulting carbene adducts, which were isolated by distillation under reduced pressure.

Yields of alkenylidenecyclopropanes isolated in this manner ranged from 10-67%, the higher yields being obtained from trialkyl-, alkoxy- and phenyl-substituted alkenes. As reported previously, reaction with isoprene occurred regioselectively across the more substituted double bond giving a 9:1 mixture of (25) and (26) by GC. Both trends are in accord with the electrophilic nature of (3). The bicyclic alkenylidenecyclopropanes (27)-(32), and the tricyclic alkenylidenecyclopropanes (33) and (34) were the pivotal molecules of our study. In the

preparation of the lower boiling alkenylidenecyclopropanes the presence of acetylene (35) proved to be a nuisance, codistilling with the required adducts. Fortunately, it could easily be removed by column chromatography generally being the more polar component. Its formation presumably arises by base induced dehydrochlorination of chloroyne (21) to give initially 2-methyl-1-buten-3-yne, which then undergoes cyclopropanation with carbene (3). Another explanation involving a prototropic rearrangement of carbene (3) to give the same enyne has been proposed by Landor et al.[57] who showed that in the absence of any olefinic substrate, reaction of bromoallene (22, X=Br) with potassium t-butoxide gave a 50% yield of acetylene (35) (Scheme 11).

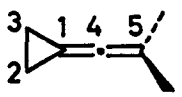


Scheme 11

An attempt to use the liquid-solid two phase method of Makosza et al.[58] employing chloroyne (21), crown ether and cyclohexene, with potassium carbonate as base gave only a trace of the required alkenylidenecyclopropane (28). The higher temperature (140°) used in their preparation of dibromocarbene by this method precludes formation of carbene (3) from chloroyne (21). Efforts to generate carbene (3) from the acetate of (24)

under anhydrous conditions using crown ether surprisingly met with failure.

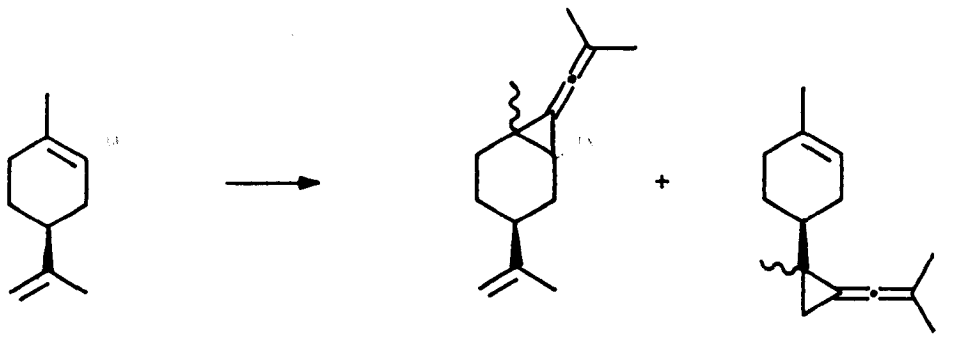
All the alkenylidenecyclopropanes were characterised on the basis of their spectral properties.[59] The IR spectrum is dominated by an intense allenic absorption at 2000-2040cm^{-1}.[60] Interestingly, the bicyclic allenes (27), (28) and (29) show two bands in this region.[60] In the ^{1}H NMR spectrum the geminal methyl protons of the allenyl system occur at δ1.76-1.85. ^{13}C NMR spectroscopy provides a means of clearly recognising the alkenylidenecyclopropane system. In agreement with the ^{13}C NMR



study of Pasto and Borchardt[61] the cyclopropyl C-1 carbon signal appears at δ81-91, the terminal C-5 signal at δ97-100, and the central C-4 signal at much lower field, at δ185-188. The allenyl methyls appear at around δ22.

Addition of carbene (3) to (-)-α-pinene (36) gave the tricyclic alkenylidenecyclopropane (33); $[\alpha]_D^{21}$ -70.9°. Similarly, (-)-β-pinene (37) gave the adduct (34); $[\alpha]_D^{21}$ +106.5°. Although both adducts have been prepared previously,[18,62] presumably using chiral starting materials, these being more generally available, their optical rotations have not been reported. While the stereochemistry of both adducts has not been rigourously proven, carbene addition is expected to occur stereoselectively at the less hindered (methylene bridged) exo-face of the alkene in accord with other carbene additions and reagents.[63] That the adducts isolated were single isomers is substantiated by their homogeneity by TLC and GC, and especially by their ^{13}C NMR spectra which showed no duplication of resonances. Addition of

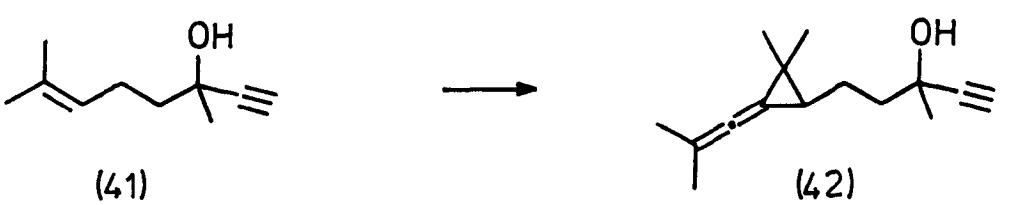
carbene (3) to the diene (+)-limonene (38) occurred regioselectively to afford a 4:1 mixture (by ^{1}H NMR analysis) of inseparable monoadducts (39) and (40); once again demonstrating the electrophilic nature of (3). Under the conditions employed



(38) (39) (40)

for our GC analysis only three peaks could be resolved. Four diastereoisomers are expected from carbene attack at either face of the alkene, and indeed four cyclopropylmethyl singlets are apparent in the ^{1}H NMR spectrum.

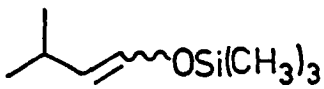
In an effort to extend the cyclopropanation reaction to functionalised systems we have examined the reaction of carbene (3), generated under the usual conditions, with the ethynyl carbinol-containing monoterpenoid dehydrolinalool (41), which proceeded smoothly to afford a 46% yield of the adduct (42).



(41) (42)

The cyclopropanation of trimethylsilyl enol ethers[64] is readily performed in high yield and the resulting cyclopropyl trimethylsilyl ethers are versatile synthetic intermediates. Extension of this route to provide siloxy alkenylidenecyclopropanes seemed

worthwhile, as such compounds should exhibit interesting chemistry. A previous study by Gibbins had shown that under the usual aqueous PTC conditions none of the expected alkenylidenecyclopropanes were obtained.[62] Bearing in mind the known lability of trimethylsilyl enol ethers under hydrolytic conditions we tried using anhydrous conditions[19] employing 18-crown-6 and the silyl enol ether (43), but once again no cyclopropanation occurred. Reaction of (3) with electrophilic olefins is discussed in the next section.



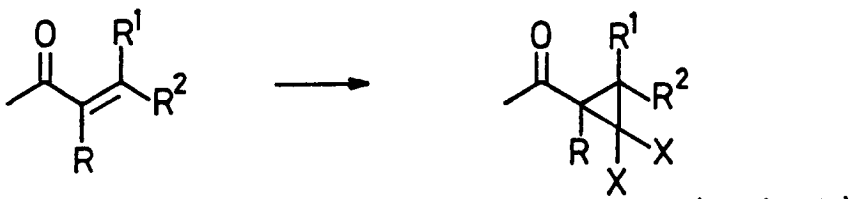
(43)

Most of the alkenylidenecyclopropanes isolated in our work were unstable oils, gradually oxidising and polymerising on exposure to the air. As soon as possible after isolation they were stored under nitrogen or vacuum at 0^{o}. Under these conditions they were stable for several months; if necessary they could be purified by column chromatography and/or distillation under reduced pressure.

2.2 Attempted Preparation of Alkenylidenecyclopropanes from Electrophilic Olefins

Barlett has shown that α-substituted enones react with chloroform or bromoform under aqueous PTC conditions to give good yields of the corresponding acyl cyclopropanes (Scheme 12).[65] Especially noteworthy is the finding that addition to carvone occurs regioselectively across the enone C-C double bond. Makosza

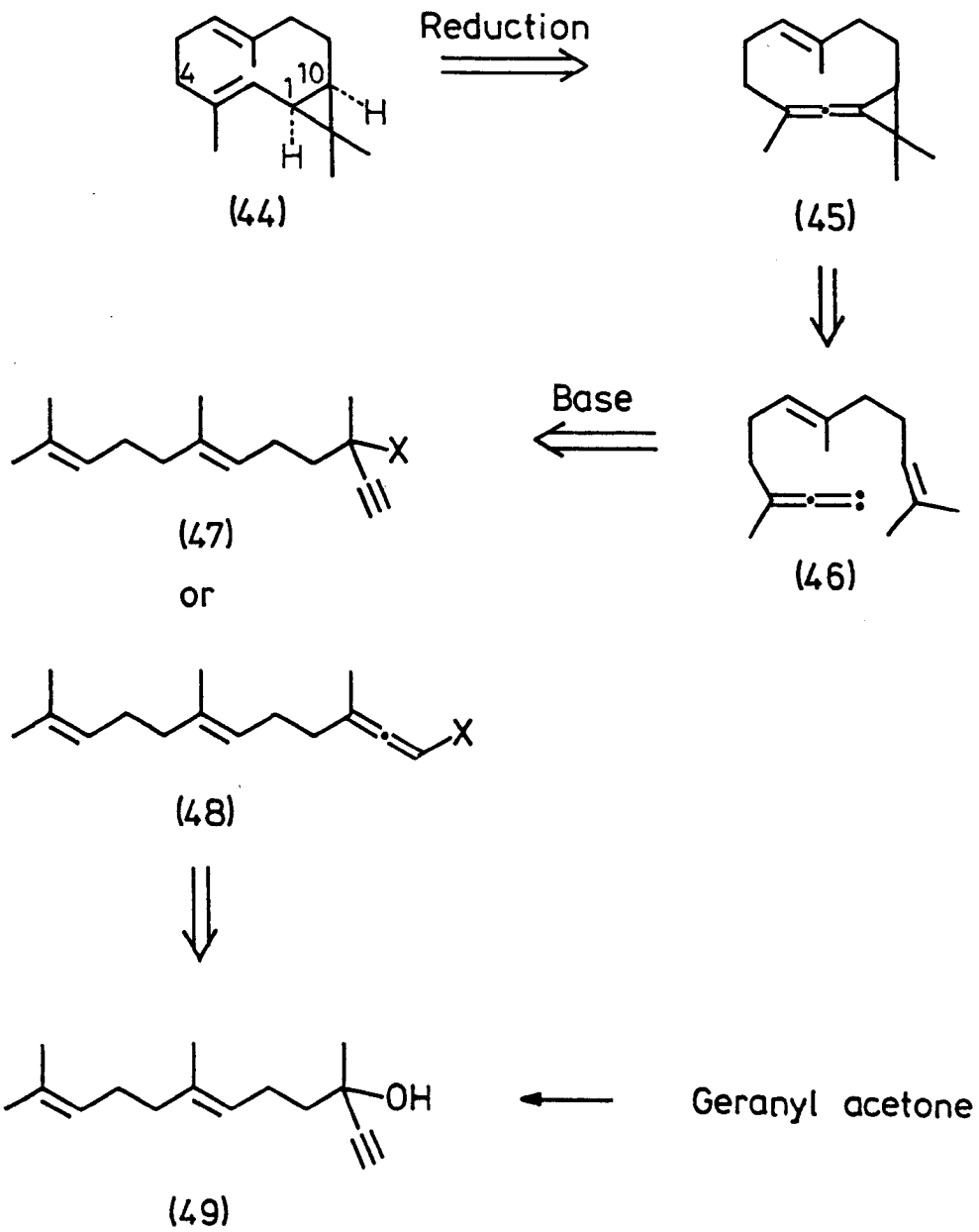
et al. report that under similar PTC conditions chloroform reacts with α,β-unsaturated nitriles, esters and sulphones to give trichloromethyl or dichlorocyclopropyl compounds; resulting from trichloromethyl anion or dichlorocarbene intermediates respectively, depending on the nature of the electron withdrawing group.[66]



Scheme 12 (X = Br, Cl)

If the analogous alkenylidenecyclopropanes could be formed by reaction of electrophilic olefins with carbene (3), then a means of directly preparing functionalised alkenylidenecyclopropanes would become available. The only other reported attempt in this area is that of Raphael et al. who unsuccessfully attempted to prepare dehydrochrysanthemic acid by reaction of (3) with 3-methylcrotonic acid.[18]

Reaction of citral and mesityl oxide with (3) under anhydrous conditions[19] gave only aldol type products. Using the normal aqueous PTC conditions, pulegone and carvone gave complex mixtures of products, but some cyclopropanation had occurred as evidenced from the allenic absorptions in the IR spectrum. Under the same conditions geranyl nitrile reacted cleanly, but unfortunately the products could not be separated from unreacted starting material, precluding assignement of regiochemistry.

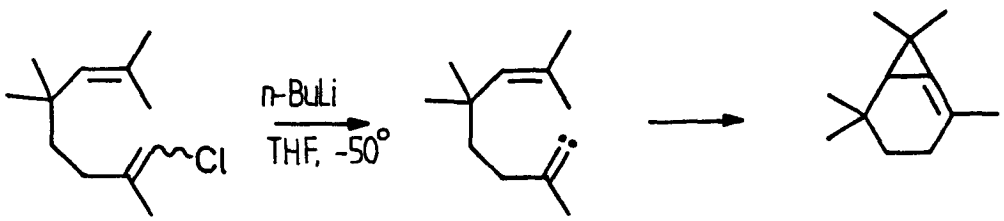


Scheme 13

2.3 Synthetic Approaches to Bicyclogermacrene

Bicyclogermacrene, originally isolated from the cold pressed peel oil of *Citrus junos*[67] and subsequently from many other species,[68] has been shown to have the sesquiterpene structure (44), containing a 1,1-dimethylcyclopropane ring fused to a ten membered ring.[67-70] Our strategy for the synthesis of bicyclogermacrene centres around the intramolecular cyclisation of alkenylidene carbene (46) (Scheme 13). Conversion of E-dehydronerolidol (49) to a suitable carbene precursor (47) or (48), followed by carbene formation and key intramolecular cyclisation to give alkenylidenecyclopropane (45) is envisaged. Stereoselective reduction of the exocyclic allene C(1-2) double bond would then provide (44).

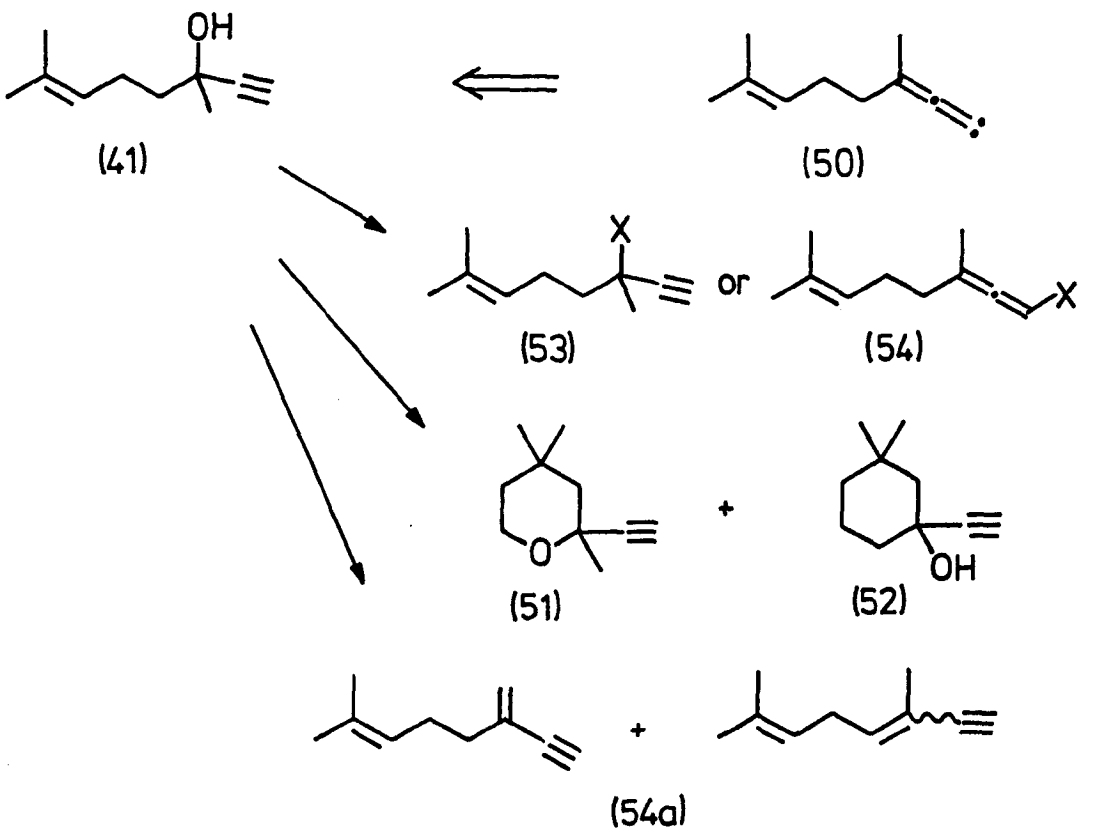
Although intramolecular cyclisations of alkenylidenecarbenes are unknown, Kobrich and co-workers have shown that alkylidene carbenes can undergo such reaction to give moderate yields of bicyclic compounds when the preferential insertion into a C-H bond is unfavourable (Scheme 14).[71]



Scheme 14

Alkenylidene carbenes of type (46) are unknown, so initially we attempted the preparation of suitable precursors. Previous model studies in these laboratories using dehydrolinalool (41), had shown that the required carbene precursors were by no means simple to prepare. Treatment of (41) with triphenylphosph te

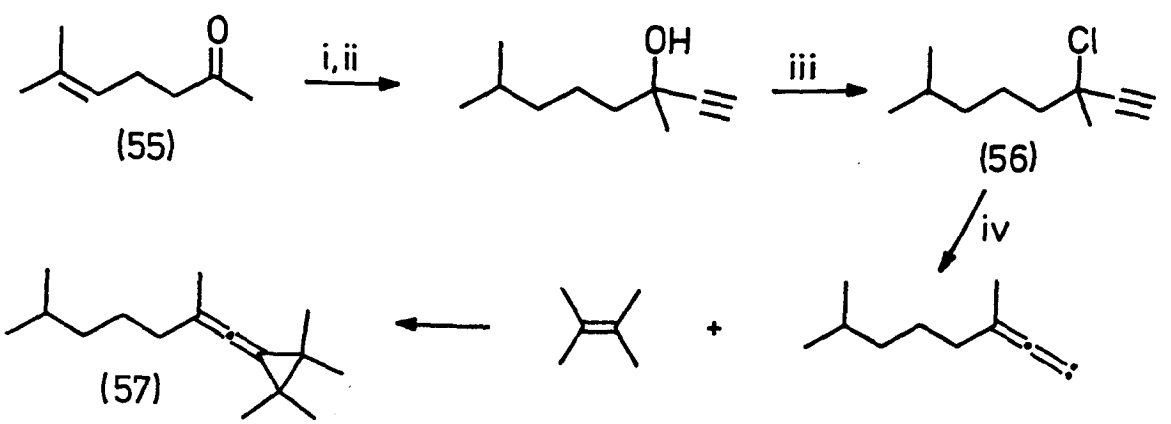
methodide, triphenylphosphite dibromide or thionyl chloride gave tetrahydropyranyl ether (51), or low yields of the presumed halides (53) or (54). The use of concentrated hydrochloric acid gave the cyclic ethynyl carbinol (52) as the major product along with the expected ether (51).[72] In any event no carbenes were generated from the presumed precursors. Similarly, attempts by us to use triphenylphosphine dibromide[73,74] or bromotrimethylsilane[75] resulted in ether (51) formation, while triphenylphosphine-tetrachloromethane[76] resulted in the apparent formation of the required chloride (53, X=Cl) along with the dienynes (54a) as the major products.



Thus, it would appear that the electrophilic nature of all the preceeding halogenating agents results in either ether formation or dehydration-elimination. Another alternative is to use leaving groups other than halides. Various esters of (41)

were prepared (53, X=acetate, benzoate, p-nitrobenzoate) by standard procedures but attempts to generate the carbene (50) under hydrolytic or anhydrous conditions in the presence of styrene as carbene trap gave only the parent alcohol (41). Attempts to prepare the tosylate were unsuccessful; the mesylate is reported to be too unstable to isolate.[74]

In order to see if C_{10} alkenylidene carbenes could be generated at all, we prepared the monoterpenoid propargyl chloride (56) in good yield from 6-methyl-5-hepten-2-one (55). Catalytic hydrogenation of enone (55) followed by ethynylation and chlorination gave the propargyl chloride (56) contaminated with its separable (by column chromatography) allenic isomer. Under the normal aqueous PTC conditions the mixture of chlorides gave, on reaction with 2,3-dimethyl-2-butene a 48% yield of the alkenylidenecyclopropane (57) after chromatography and distillation.



Reagents i, H_2-Pt,EtOAc; ii, NaC≡CH, NH_3; iii, CuCl, $CaCl_2$, HCl; iv, NaOH, PTC

Scheme 15

The product exhibited an intense allene absorption at 2000cm^{-1} in the IR spectrum. In the ^{1}H NMR spectrum the cyclopropyl methyl groups appeared as a singlet at δ 1.23, the allenyl methyl singlet came at δ 1.72. The adduct showed a molecular ion at m/z

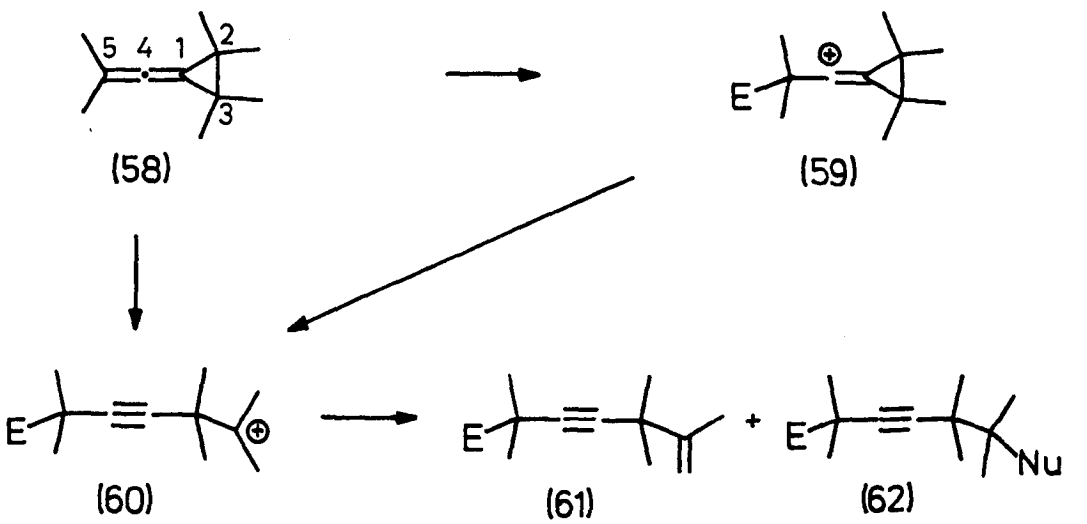
220 analysing correctly for $C_{16}H_{23}$.

Having demonstrated that C_{10} alkenylidene carbenes can be formed, there seems no reason why carbenes of type (46) and (50) should not be formed in a similar manner, providing suitable precursors can be prepared. As attempts to prepare propargyl compounds as carbene precursors were not satisfactory, approaches based on allenic precursors may prove more fruitful.[77]

CHAPTER THREE

Acid Catalysed Reactions of Alkenylidenecyclopropanes and Allylidenecyclopropanes

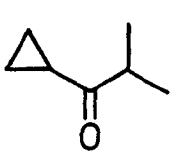
The acid catalysed reactions of alkenylidenecyclopropanes have been investigated by many workers.[35-37,45,78-80] Alkyl substituted derivatives have been shown to give predominantly products arising from initial protonation or electrophilic attack at the terminal C-5 carbon atom of the allene system.[35,37,78,79] For example, the most widely studied system, the tetramethyl substituted derivative (58) reacts almost exclusively with electrophilic reagents to give ring opened products of general structure (61) and (62) (Scheme 16).



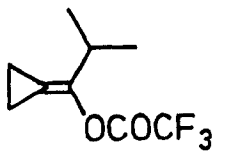
E = Electrophile e.g. H^+, BF_3; Nu = Nucleophile e.g. OR, OCOR

Scheme 16

Ring opening could occur via vinyl cation (59) or via a concerted process to give carbenium ion (60), since the orbital system is perfectly arranged for synchronous fission to (60).[78] However, products (63) and (64) related to cation (59) have also been isolated by Poutsmo and Ibarbia.[37] The same authors also report the formation of minor products, trienes, resulting from initial protonation at the central C-4 carbon atom

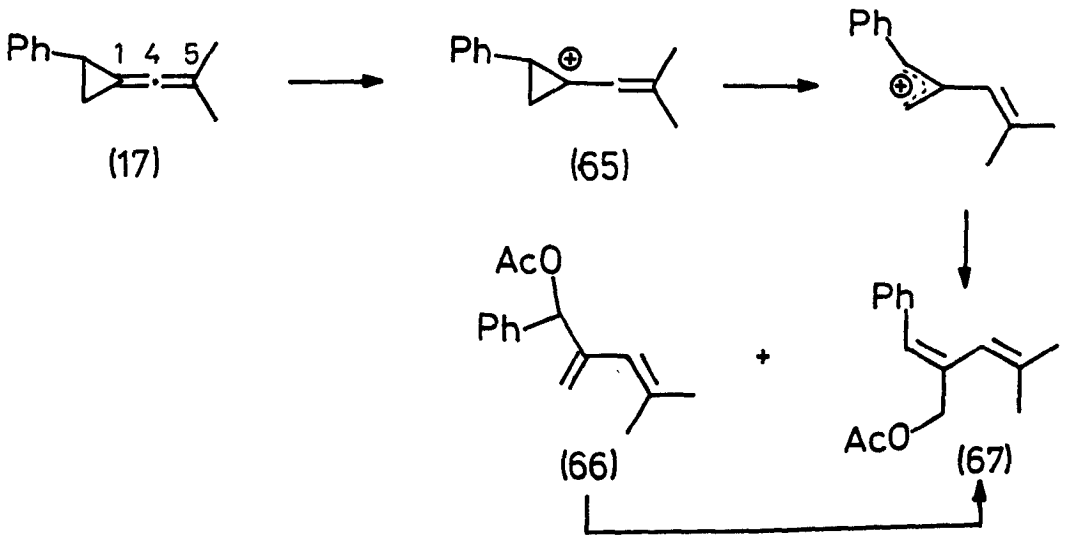


(63)



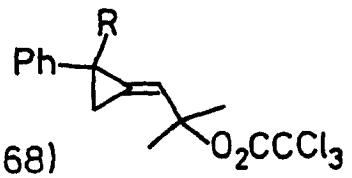
(64)

of the allene system. Phenyl substituted alkenylidenecyclopropanes undergo attack predominantly on the central C-4 carbon atom of the C(1-4) double bond to give ultimatley 1,3-dienes arising from disrotatory ring opening of the intermediate cyclopropyl cation (65).[35,36] Pasto et al. have shown that the kinetic diene (66) is converted into its thermodynamic isomer (67) at higher reaction temperatures.[35]



The differences in reactivity between phenyl and alkyl substituted alkenylidenecyclopropanes is not attributable solely to the stability of the intermediates, or the transition states leading to them, formed in the two different modes of reaction.[36] A fuller discussion of the mechanism of electrophilic attack at alkenylidenecyclopropanes is given in the introduction. As a result of several studies Pasto and Miles concluded that the site of electrophilic attack is dependent on the number and nature of the groups attached to the cyclopropane ring.[35] Additionally,

the picture is complicated by the fact that both electrophile and solvent appear to affect the site of electrophilic attack. For example, reaction of 1-phenyl and 1-methyl-1-phenyl substituted alkenylidenecyclopropanes with trichloroacetic acid in tetrachloromethane gave adducts (68), formed by addition across the C(4-5) double bond; a process not previously observed in electrophilic additions to these systems, in addition to the expected ring opened dienes resulting from C-4 attack. Their formation was attributed to a possible concerted addition due to the less polar solvent used.[36]



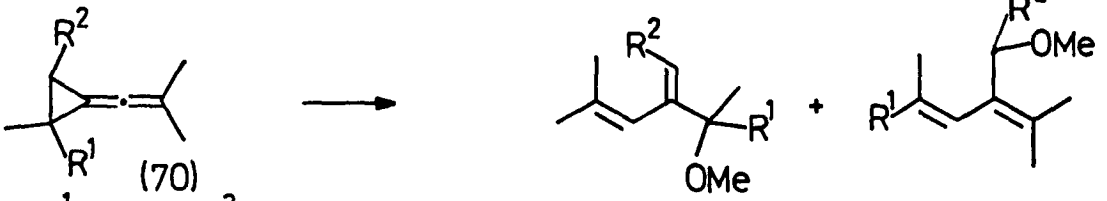
(68) R = H, CH_3

Earlier work in these laboratories had shown that the bicyclic alkenylidenecyclopropane (28) could be hydrated by a catalyst mixture of red mercuric oxide, boron trifluoride etherate and trifluoroaretic acid in methanol to give the bicyclic ketone (69).[81]

(28) (69)

However, attempts by Maddocks to obtain similar carbonyl containing products from a series of C_{10} alkenylidenecyclopropanes by reaction with the same catalyst mixture gave only ring opened acyclic ethers.[72] Somewhat surprisingly, the alkyl substituted derivatives (70) gave only 1,3-dienes (71) and (72) resulting from initial complexation of the Lewis acid at the central C-4 carbon atom, followed by ring opening to give both secondary and

tertiary carbenium ions.

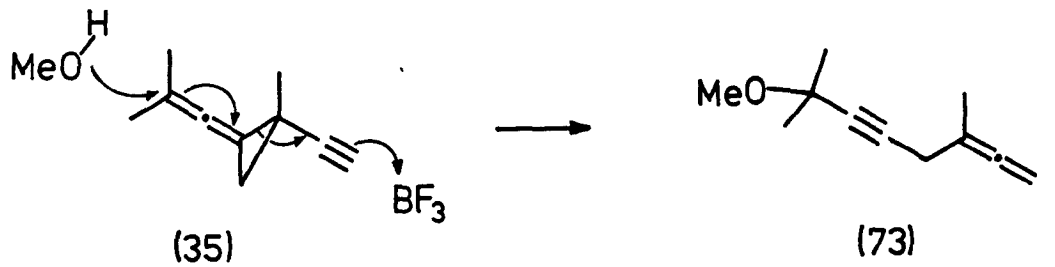


(70)

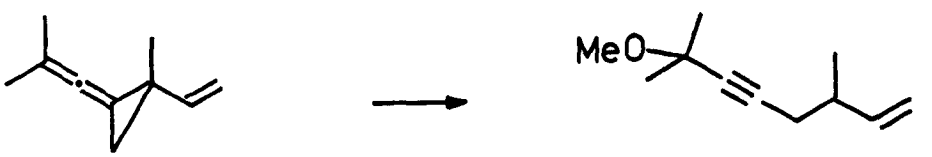
a) R^1 = Et, R^2 = H
b) R^1 = Me, R^2 = Me

(71) (72)

By contrast the ethynyl and vinyl substituted derivatives (35) and (25) gave the acetylenes (73) and (74) respectively, arising from initial co-ordination of the Lewis acid at the non-allenic unsaturation (Scheme 17). That these transformations were likely to be due to Lewis acid catalysed reaction was confirmed, in that treatment of the C_{10} alkenylidenecyclopropanes with boron trifluoride etherate in methanol did indeed give the same products.[62,72]



(35) (73)

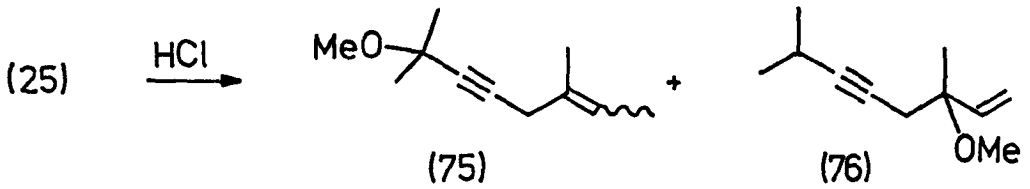


(25) (74)

Scheme 17

Maddocks also studied the reaction of C_{10} alkenylidenecyclopropanes with hydrochloric acid in methanol. While the acetylene (35) gave the same product (73) obtained above, the vinyl derivative (25) gave a 4:1 mixture of acetylenes (75) and (76).

The major product (75) arises from initial co-ordination at the non-allenic site, and (76) from initial C-5 attack.



(75) (76)

Conversely, treatment of the alkyl substituted derivatives gave ring opened acetylenes, resulting from the more stable carbenium ion as the major products, along with 1,3-dienes (71) and (72) isolated earlier. The initial sites of protonation of the alkenylidene-cyclopropanes were established conclusively by deuteration studies using MeOD-DCl.[62,72]

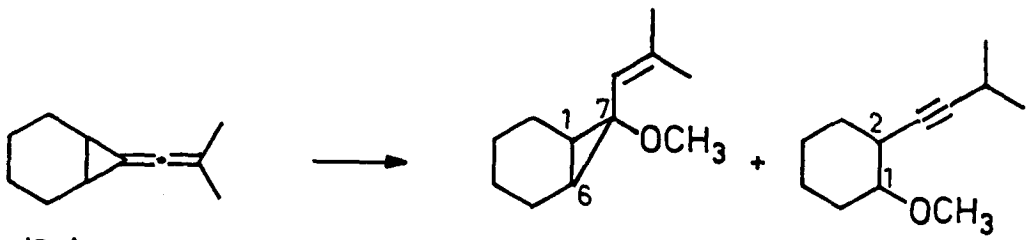
The work just described has been almost entirely concerned with monocyclic alkenylidenecyclopropanes. It was our intention to extend this knowledge to include fused bicyclic and tricyclic alkenylidenecyclopropanes. For the alkenylidenecyclopropanes derived from α- and β-pinene the possibility arises that under the reaction conditions the cyclobutane ring may also participate in skeletal rearrangements. In contrast to the work of Maddocks, we observed no major differences in product formation on chang-ing the acid catalyst from boron trifluoride etherate to hydro-chloric acid. Consequently, the reactions of our alkenylidene-cyclopropanes under these, and other, conditions are discussed together.

3.1 Bicyclic Hydrocarbon Alkenylidenecyclopropanes

We have examined the acid catalysed reactions of a series of bicyclic and tricyclic alkenylidenecyclopropanes using hydrochloric acid and boron trifluoride etherate in methanol.

The use of methanol as reaction solvent is twofold: (a) it allows the carbenium ion centre to be neutralised giving a methyl ether; providing a characteristic marker in the ^{1}H NMR spectrum, and (b) facilitates the isolation of products by chromatography - hydrocarbon products generally being more difficult to separate.

Reaction of the bicyclic alkenylidenecyclopropane (28) with hydrochloric acid in methanol gave a mixture of four products by GC. Column chromatography on alumina gave an inseparable mixture of two unidentified hydrocarbon components (in a 6:1 ratio by GC), vinyl cyclopropane (77) in 21% yield and acetylene (78) in 26% yield.



(28) (77) (78)

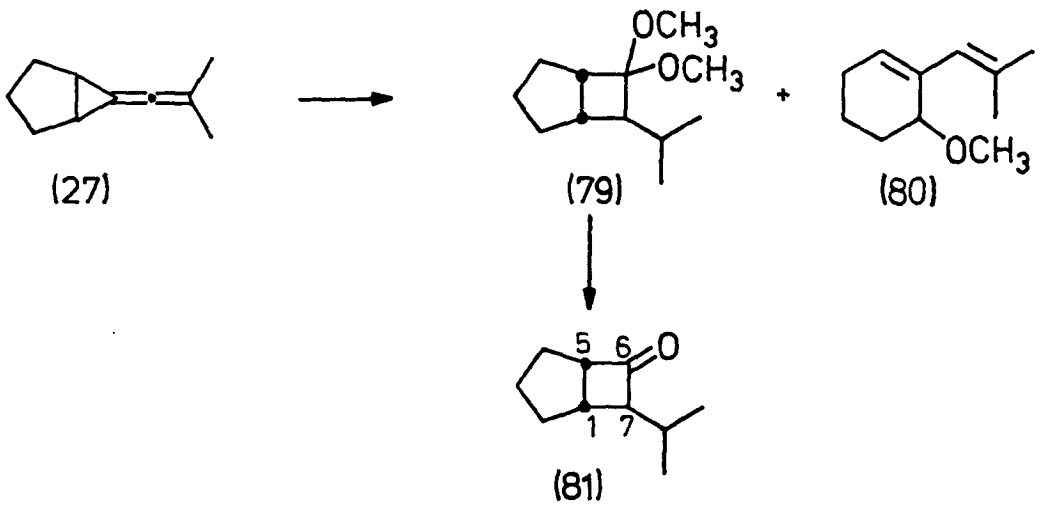
The mass spectrum of the hydrocarbon mixture indicated the presence of a dimer, $C_{24}H_{36}$, but no further characterisation was attempted. Both methoxy components analysed for $C_{12}H_{20}O$ by high resolution mass spectroscopy. The structure of vinyl cyclopropane (77) followed from the olefinic and methyl ether absorptions at 1660(C=C), 2810 (C-H) and 1105 cm^{-1}(C-O) respectively in the IR spectrum. The ^{1}H NMR spectrum displayed a six proton vinyl methyl singlet at δ1.82, a methoxy singlet at δ 3.09 and a vinyl proton singlet at δ5.18. The ^{13}C NMR spectrum showed only nine signals consistent with the symmetrical nature of (77). While the IR spectrum of acetylene (78) was unremarkable, its ^{1}H NMR spectrum contained an isopropyl methyl doublet at δ1.14($\underline{J}$=7Hz), a two proton multiplet at δ 2.46 attributable to the methine protons adjacent to

the acetylene linkage, a multiplet at δ3.10 assigned to the C-1 proton, and a methoxy singlet at δ3.42. The ^{13}C NMR spectrum exhibited eleven signals in accord with the proposed structure; in particular singlets at δ81.3 and 87.3 clearly show the presence of a disubstituted acetylene. Reaction of the same alkenylidenecyclopropane (28) with the Lewis acid boron trifluoride etherate in methanol gave the same two methoxy components (77) and (78) isolated above, in the ratio 1:2 by GC. In addition the reaction was somewhat cleaner, in that no hydrocarbon products were observed. The simplicity of the ^{1}H NMR spectra of the isolated methoxy adducts, together with their homogeneity by TLC and GC suggest that they are single isomers. However, while attack of methanol from the less hindered face of the intermediate cyclopropyl cation to give exo-vinyl cyclopropane (77) might be expected, neutralisation of the secondary carbenium ion leading to (78) would be expected to show little stereoselectivity.

Attempts to alter the initial site of electrophile complexation by the use of rhodium species were uniformly unsuccessful. Reaction of (28) with chlorotris(triphenylphosphine)-rhodium(I) in refluxing methanol gave only recovered starting material, while the use of rhodium(III) chloride trihydrate gave mainly unreacted (28), along with the same two methoxy components (77) and (78) isolated previosuly. Thus, it would appear that the use of rhodium catalysts offer no alternative reaction paths. They also have the disadvantage of making the reactions more difficult to work up.

Turning our attention to alkenylidenecyclopropane (27), reaction with boron trifluoride etherate gave two major products in the ratio 26:64 by GC. Chromatography, initially on silica,

which led to some decomposition, then alumina, gave dimethyl ketal (79) and diene (80) as the major products.



(27) (79) (80) (81)

Isolation of the latter proved difficult due to the presence of a minor component with similar TLC mobility. Ketal (79) had methyl ether and gem-dimethyl abosrptions at 2830, 1150, 1050 and 1380, 1360cm^{-1} respectively in the IR spectrum. The ^{1}H NMR spectrum showed two overlapping isopropyl methyl doublets at δ0.82 and 0.97, a triplet at δ2.62(J=8 Hz) assigned to the cyclobutyl C-7 proton, and a six proton methoxy singlet at δ3.10. The ^{13}C NMR confirmed the bicyclic structure of (79), exhibiting twelve signals; in particular a low field singlet at δ101.5 and quartets at 47.5 and 48.3 confirm the presence of the dimethyl ketal moiety. The mass spectrum had a weak molecular ion at m/z 198 analysisng for $C_{12}H_{22}O_2$, the base peak oocurring at m/z 69. Additional confirmation of this structure comes from the quantitative hydrolysis of (79) using aqueous hydrochloric acid in tetrahydrofuran to give the known bicyclo[3.2.0] heptan-6-one (81).[82] The cyclobutanone (81) had a carbonyl absorption at 1770cm^{-1} (Lit.,[82] 1768cm^{-1}) in the IR spectrum. The ^{1}H NMR spectrum of (81) again displayed two overlapping isopropyl methyl

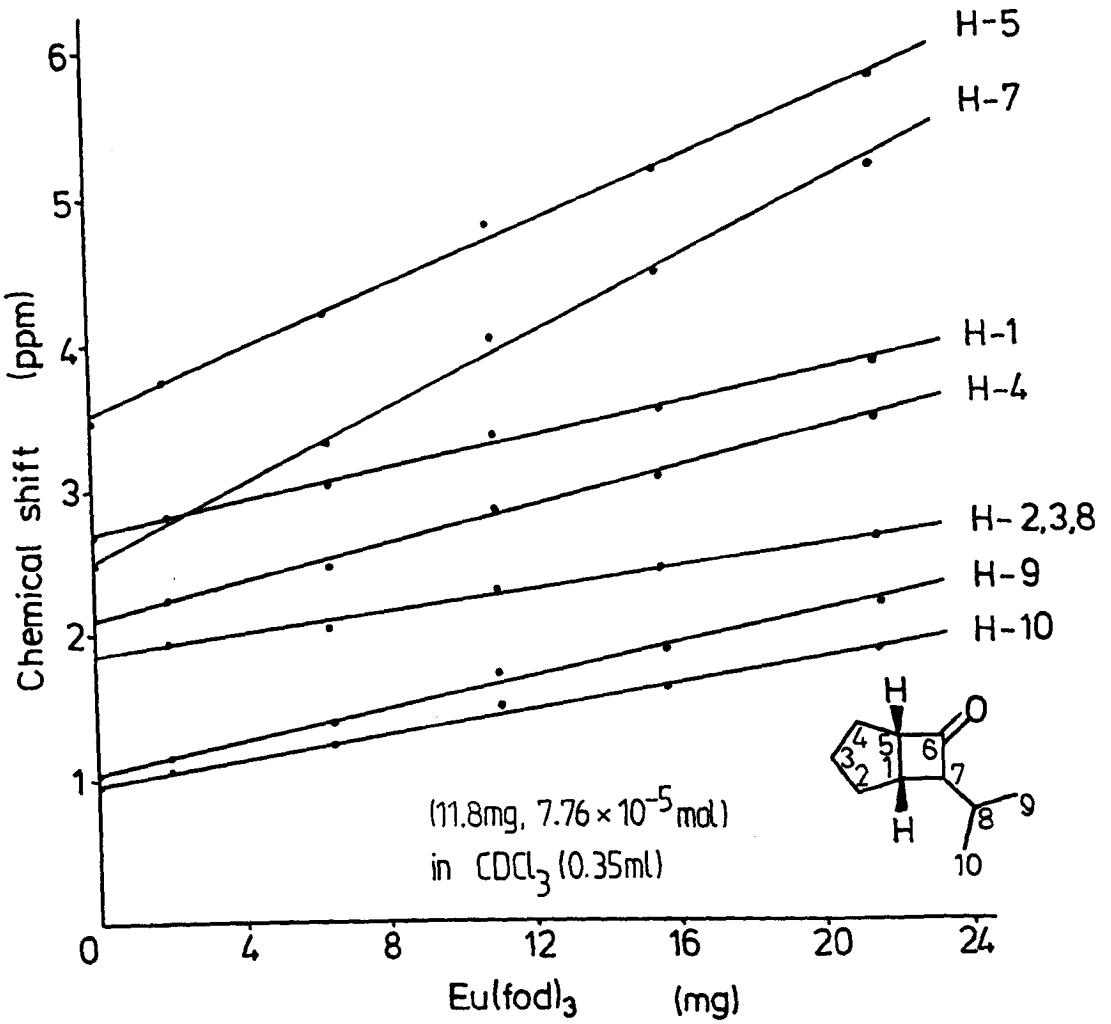


Figure 1

Signal	Eu(fod)$_3$ (mg) 0	2.0	6.5	11.1	15.7	21.6
1	2.67	2.82	3.02	3.37	3.53	3.85
2,3,8	-	1.93	2.04	2.28	2.42	2.64
4	-	2.23	2.45	2.85	3.08	3.46
5	3.45	3.73	4.20	4.82	5.18	5.80
7	2.43	2.82	3.32	4.03	4.48	5.19
9	1.01	1.14	1.38	1.70	1.86	2.19
10	0.95	1.05	1.23	1.50	1.61	1.87

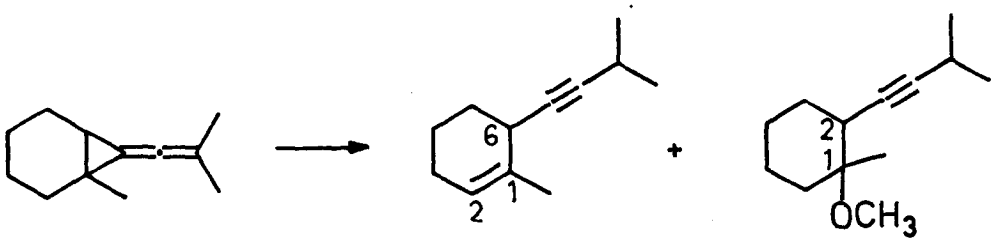
Chemical shifts (ppm) for signals in the ^{1}H NMR spectrum of ketone (81)

doublets at δ0.87 and 0.94, cyclobutyl methine multiplets at δ2.31, 2.55 and 3.50; assigned respectively to the C-7, C-1 and C-5 protons. Some support for these assignments comes from a ^{1}H NMR lanthanide induced shift (LIS) study using $Eu(fod)_3$ (Figure 1). The two protons adjacent to the carbonyl group, at C-7, and C-5 experience the greatest induced shifts. Interestingly, the C-7 proton, which initially occurred at higher field than the C-1 proton experiences the greater shift and hence the lines intersect The mass spectrum of (81) is particularly informative, having a very strong peak at m/z, 84, corresponding to the ketene fragment ion C_5H_8O, resulting from cycloreversion of the cyclobutanone ring. Whether (79) and (81) are formed as a mixture of isomers about C-7 is not known. However, if the intermediate vinylcyclopropane, analogous to (77), is formed as the exo-isomer, cyclopropylcyclobutyl ring expansion[83] would be expected to occur stereospecifically to afford exo-(81). Diene (80) showed a weak diene absorption at 1645 cm^{-1} in the IR spectrum. Further evidence for the 1,3-diene nature of (80) was obtained from the UV spectrum which had a maxima at 233nm; in excellent agreement with the calculated value of 234nm.[84] The ^{1}H NMR spectrum displayed an isopropylidene methyl singlet at δ1.79, a methoxy singlet at δ 3.33 and a two proton olefinic multiplet centred at δ5.64. The ^{13}C NMR spectrum showed eleven signals, four of which occurred in the olefinic region, consistent with the ring expanded diene structure (80). Reaction of (27) with hydrochloric acid in methanol gave the diene (80) as the major product in 74% yield, as a percentage of the volatiles by GC.

As we proposed to examine the acid catalysed reactions of

the C_{15} alkenylidenecyclopropanes (33) and (34) we decided to initially investigate the reactivity of their simpler bicyclic counterparts (29) and (30), as models for the above, in which the additional element of a cyclobutane ring was absent.

Reaction of alkenylidenecyclopropane (29) with boron trifluoride etherate in methanol gave a mixture comprising two major products in the ratio 19:81 by GC. Chromatography on silica gel gave the unstable enyne (82) and methoxyacetylene (83)

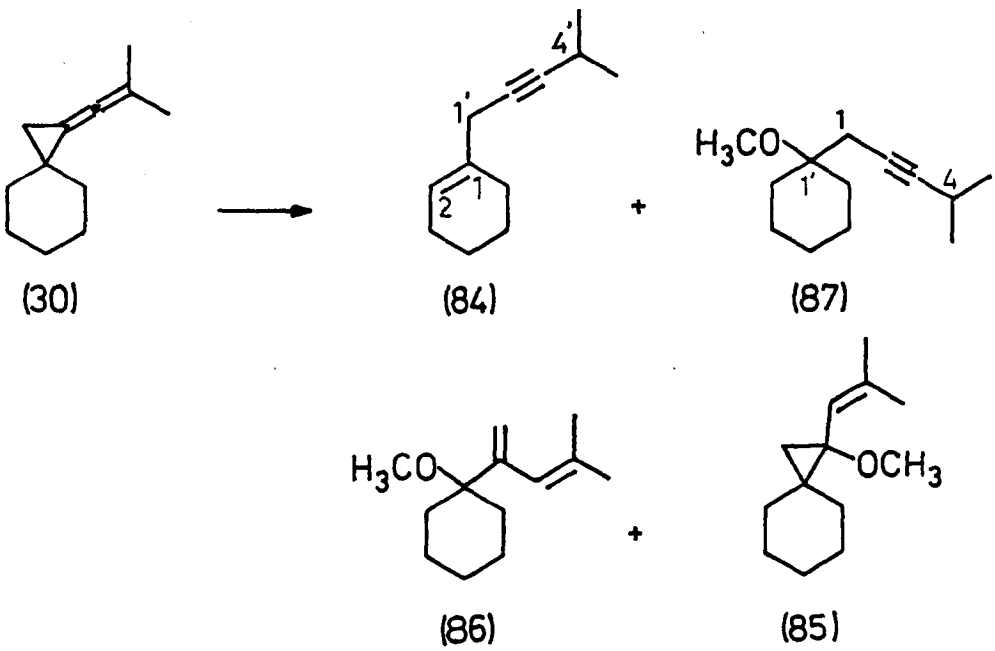


(29) (82) (83)

in 12 and 27% isolated yields respectively. Attempts to isolate another minor methoxy component were unsuccessful. The IR spectrum of (82) indicated the presence of a trisubstituted double bond with an absorption at 805cm^{-1} (out of plane deformation). The ^{1}H NMR spectrum consisted of an isopropyl methyl doublet at δ1.13, a methine multiplet at δ2.48, a vinyl methyl singlet at δ 1.76, a vinyl proton singlet at δ 5.36 and a broad singlet at δ2.82 assigned to the C-6 proton. Methyl ether (83) had an aliphatic methyl singlet at δ1.22 and a methoxy singlet at δ3.17 in its ^{1}H NMR spectrum. Reaction of (29) with hydrochloric acid gave the same two major products (82) and (83) obtained above, in the ratio 42:58 respectively by GC; the change to a "harder" acid resulting in a higher proportion of hydrocarbon product.

Reaction of spiro-alkenylidenecyclopropane (30) with

hydrochloric acid gave a complex mixture of products. However, GC showed that two major components were present in the ratio 37:63. Chromatography on silica gel gave, after elution with hexane, an unidentified mixture of hydrocarbon components and enyne (84) in 22% yield. Further elution with hexane-ether gave a mixture of methoxy components which were rechromatographed on alumina to give, in order of elution: vinylcyclopropane (85) in 1% yield, diene (86) in 3% yield after further purification by PLC and, acetylene (87) in 17% isolated yield as the major product. The low yields are attributable to poor chromatographic separation.



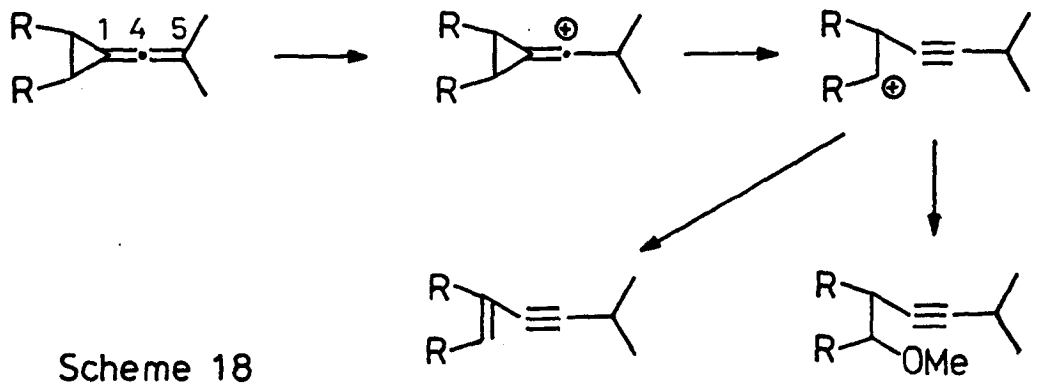
(30) (84) (87) (86) (85)

The IR spectrum of enyne (84) showed a weak acetylene absorption at 2260cm^{-1} and an olefinic absorption at 805cm^{-1} due to a trisubstituted double bond. The ^{1}H NMR spectrum displayed isopropyl signals, a broad vinyl proton singlet at δ 5.64 and a broad two proton singlet at δ 2.77 corresponding to the C-1' methylene protons. Confirmation of the proposed structure was obtained from the ^{13}C NMR spectrum which displayed eleven signals, including

two acetylenic carbon singlets at δ 76.5 and 88.2. Vinylcyclopropane (85) had a weak olefinic absorption of 1655cm^{-1} in the IR spectrum. The ^{1}H NMR spectrum clearly showed that the cyclopropane ring was still intact, displaying an AB quartet at δ 0.27 and 0.57(J=5Hz), also present were vinyl methyl singlets at δ1.72 and 1.77, and methoxy and vinyl proton singlets. Although the molecular ion was not observed in the mass spectrum the M-CH_3 ion was strong and correctly analysed for $C_{12}H_{19}O$. Diene (86) exhibited a UV absorption maxima at 230nm, in good agreement with the calculated value of 229nm.[84] The IR spectrum showed diene absorptions at 1660 and 1625cm^{-1}, and methylene absorptions at 935 and 910cm^{-1}. The ^{1}H NMR consisted of vinyl methyl singlets at δ1.75 and 1.78, a methoxy singlet, methylene signals at δ 4.96 and 5.15, and the vinyl proton signal as a broadened singlet at δ 5.72. Acetylene (87) showed an isopropyl methyl doublet at δ 1.14(J=7Hz), a methylene proton doublet at δ 2.26(J=3Hz) assigned to C-1 (long range coupling to the C-4 proton being observed) and a methoxy singlet. The ^{13}C NMR spectrum showed ten signals consistent with the symmetrical structure of (87).

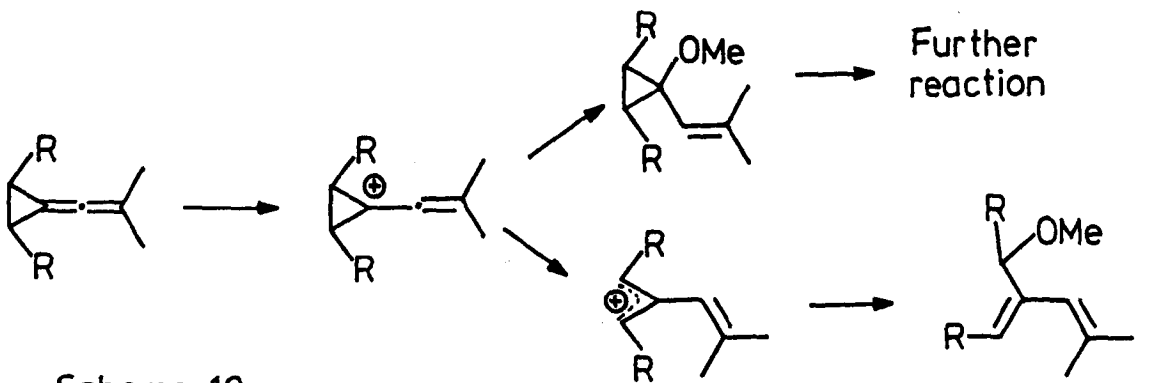
The formation of all the products isolated can be rationalised in terms of two initial modes of electrophilic attack at the allene system. Acetylenes (78), (82), (83), (84) and (87) can be seen to arise from initial attack at the terminal C-5 carbon atom, followed by ring opening and neutralisation of the resulting carbenium ion; by loss of a proton to give an enyne or addition of methanol to give an acetylenic ether (Scheme 18).

Interestingly, only the non conjugated enynes appear to be formed; this may be as a result of anti-elimination of the intermediate vinyl cation.



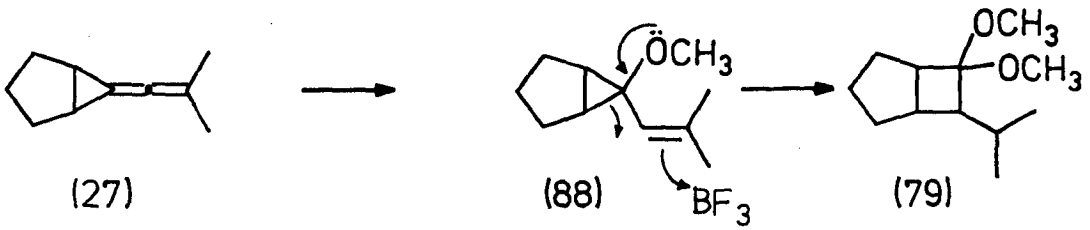
Scheme 18

Vinylcyclopropanes (77) and (85), dienes (80) and (82), and ketal (79) are envisaged as arising via initial electrophilic attack at the central C-4 carbon atom of the allene C(1-4) double bond to give an intermediate cyclopropyl cation, which then undergoes either neutralisation with methanol to give vinylcyclopropanes or cyclopropane ring cleavage to give dienes (Scheme 19).



Scheme 19

In the case of the bicyclo[3.1.0]hexane system (27) reaction occurs to give the ring expanded diene (80). Formation of ketal (79) is rationalised as arising via the intermediacy of vinylcyclopropane (88), analogous to vinylcyclopropane (77) isolated from the higher homologue, which undergoes subsequent acid catalysed ring expansion. Such ring expansions of related 1-siloxy-



(27) (88) (79)

1-vinylcyclopropanes in the preparation of cyclobutanones are well known.[83,85,86] In all of these reactions no products were detected which would have been formed by electrophilic attack on the three membered ring or by addition across the allene C(4-5) double bond. While alkenylidenecyclopropane (28) gave products arising from initial electrophilic attack at both the central C-4 and terminal C-5 carbon atoms of the allene system, (27) undergoes exclusive electrophilic attack at C-4. Presumably, subtle electronic factors control the site of electrophilic attack. Like the phenyl and tetramethyl substituted cases discussed previously stability of the intermediates should not solely be the cause of the differences of reactivity. The formation of vinylcyclopropanes (77) and (85) demonstrate, at least formally, the intermediacy of a cyclopropyl cation. Only rarely have such products been isolated previously,[35,45] normally undergoing ring cleavage to form dienes. The absence of ring expanded product from (28) presumably reflects the greater ring strain inherent in the five membered ring. Even so, the absence of such products is surprising bearing in mind the known reactivity of the bicyclo [4.1.0] heptyl cation. In the case of the methyl substituted bicycle (29) only products arising from initial attack at C-5, followed by ring opening to give a tertiary carbenium ion were isolated, demonstrating the effect of an additional methyl substituent. Whereas, for (30) the major

pathway of electrophilic attack is again via C-5, with minor products arising from initial attack at C-4 also being formed.

Our results show that the use of either boron trifluoride etherate or hydrochloric acid in methanol at ambient temperature results in the same major products. This is in contrast to the results of Maddocks who found that reaction of alkyl substituted C_{10} alkenylidenecyclopropanes gave mainly products arising from initial C-4 attack with boron trifluoride etherate, while the use of hydrochloric acid resulted in products largely arising from C-5 attack.[72] The following observations concerning the use of the two different catalysts are noteworthy. Use of hydrochloric acid resulted in somewhat more complex product mixtures; in particular, the mixture composition contained a higher proportion of hydrocarbon components. Also the use of hydrochloric acid would seem to favour reaction pathways resulting from initial electrophilic attack at the terminal C-5 carbon atom of the allene system. Together, these observations probably reflect the "harder" nature of the mineral acid.

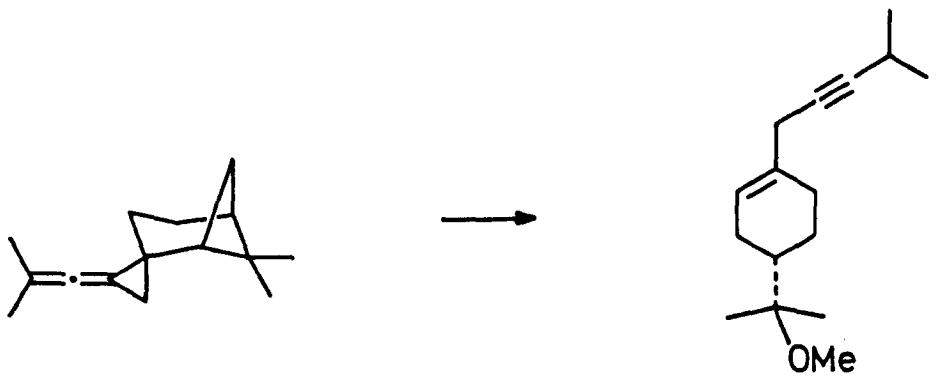
3.2 Tricyclic Hydrocarbon Alkenylidenecyclopropanes

Having investigated the acid catalysed reactions of bicyclic alkenylidenecyclopropanes in some detail we turned our attention to the tricycles (33) and (34), derived from α- and β-pinene respectively. Since we had shown that their bicyclic counterparts (29) and (30) underwent acid catalysed reaction predominantly via the major pathway for alkyl substituted alkenylidenecyclopropanes i.e. by initial electrophilic attack at C-5, we had some grounds for believing that (33) and (34) would react initially in a similar

manner via analogous tertiary carbenium ion intermediates. The effect of the cyclobutane moiety should only influence the course of reaction at a much later stage.

Prior to our work, Gibbins had briefly investigated the reactions of (33) and (34) under various acidic conditions: the use of p-toluenesulphonic acid, hydrochloric acid or boron trifluoride etherate resulted in either recovered starting material or complex mixtures from which no identifiable products could be isolated; and concluded that no single preferred pathway was operating.[62]

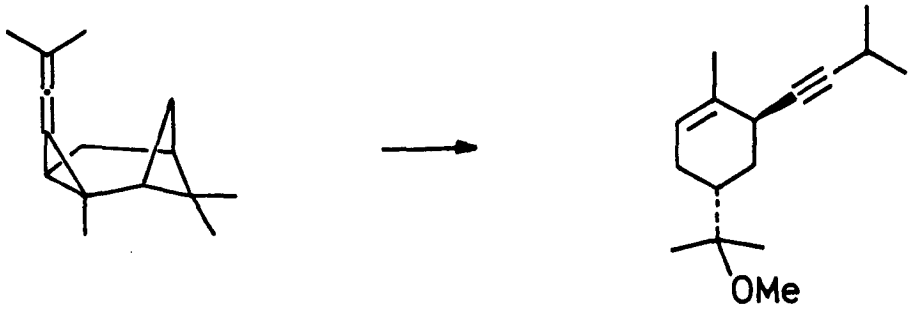
We decided to re-examine this work using boron trifluoride etherate as the acid catalyst in the light of our earlier findings. Reaction of the tricyclic spiro-fused alkenylidene-cyclopropane (34) with boron trifluoride etherate in refluxing methanol gave a complex mixture of at least nine components by TLC. However, GC showed the presence of one major component which was isolated by column chromatography on Kieselgel G and shown to be the sesquiterpenoid enyne (89) containing a methane type skeleton.



(34) (89)

The optically active enyne, $[\alpha]_D^{23}$-66.8°, was assigned structure (89) on the basis of its spectral data. The ^{13}C NMR spectrum exhibited fourteen signals, of which the olefinic and acetylenic signals are easily identifiable (Figure 2). However, the complexity of the high field region of the spectrum precluded a complete assignment. The ^{1}H NMR spectral values are given in Figure 3; note that the methylene protons of the side chain appear as a broadened singlet at δ 2.77. In the mass spectrum the base peak occurred at m/z 73 corresponding to the $C(CH_3)_2OCH_3$ fragment.

Reaction of the tricyclic alkenylidenecyclopropane (33) with boron trifluoride etherate at ambient temperature again proceeded to give a complex mixture of at least eight components by TLC. GC showed that two major components were present in 58% and 14% yields, as a percentage of the volatiles. Column chromatography on silica gel gave two methanol adducts; a triene of undetermined structure and enyne (90) isolated in 34% yield as the major component.



(33) (90)

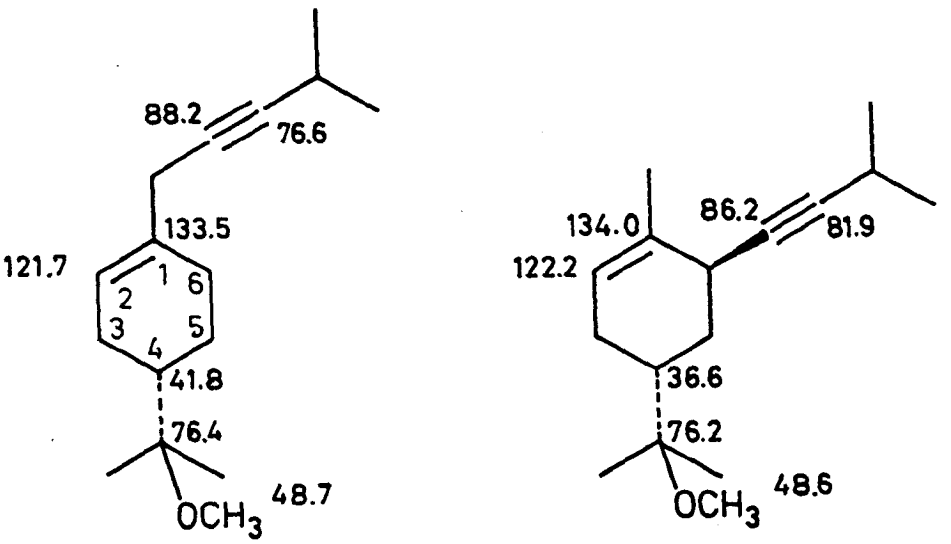


Figure 2 ^{13}C NMR spectral data

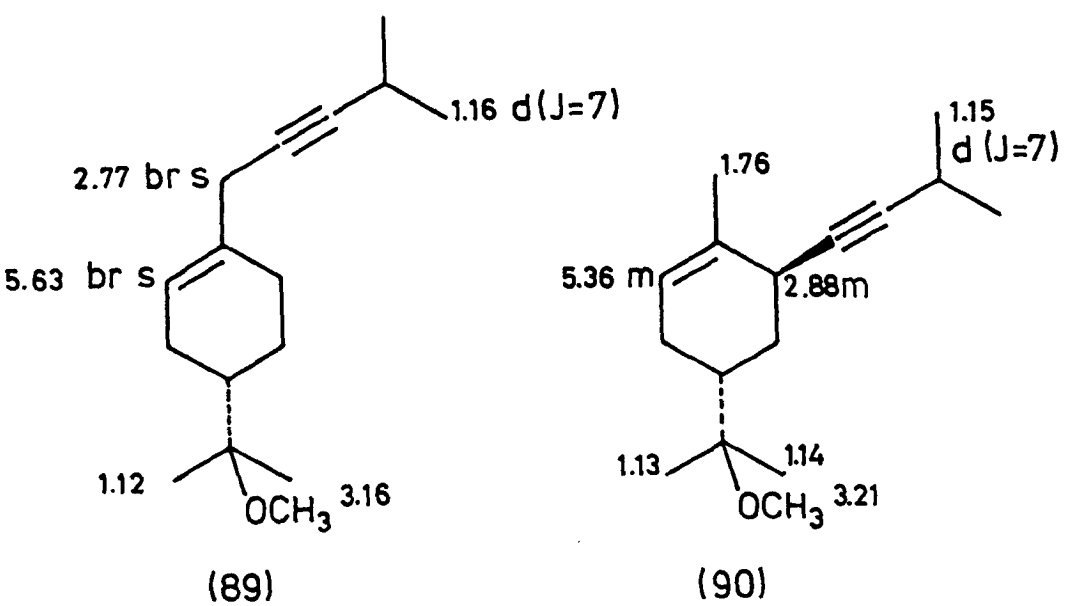
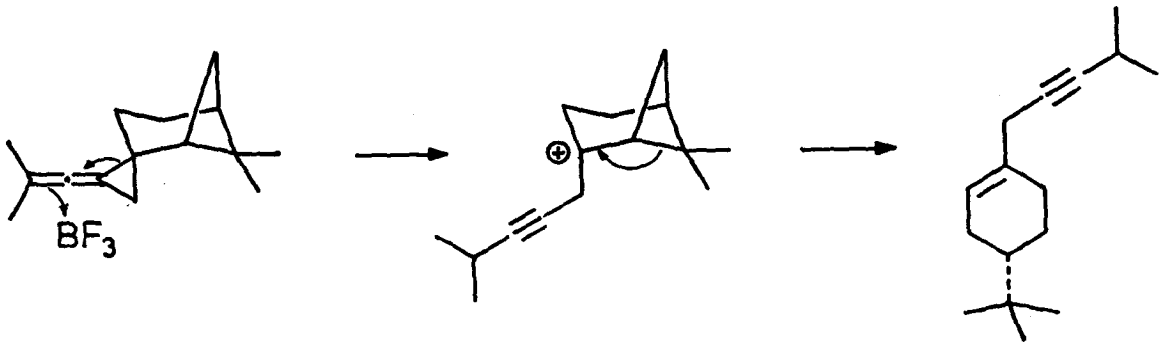


Figure 3 ^{1}H NMR spectral data

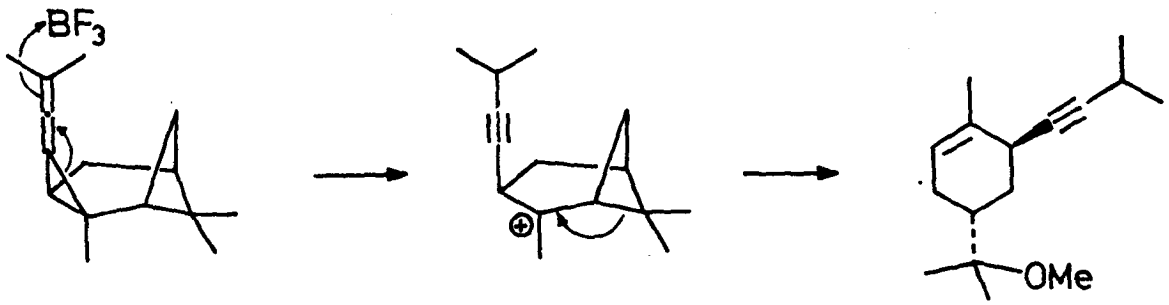
The triene nature of the minor component was apparent from its ^{13}C NMR spectrum which cleanly showed fourteen signals, six of which were present in the olefinic (sp^2) region. The UV spectrum contained a maxima at 248nm ruling out a conjugated triene chromophore. The low optical rotation, $[\alpha]_D^{24}$ +2.5°, of this triene, compared to the other compound isolated, suggests that racemisation or rearrangment may have occurred. The major product enyne (90), had an optical rotation of $[\alpha]_D^{26}$ -188.9° and was assigned the monocyclic structure (90) on the basis of its NMR spectra (Figures 2 and 3). Interestingly (90) shows two non-equivalent methyl groups associated with the ether side chain. Both are seen in the ^1H NMR spectrum and all fifteen signals are observable in the ^{13}C NMR spectrum. The distinctive C-6 methine proton appears as a multiplet at δ2.88 in the ^1H NMR spectrum. A weak molecular ion at m/z 234 analysing correctly for $C_{16}H_{26}O$ was recorded in the mass spectrum.

The formation of the two major products (89) and (90) can indeed be rationalised by the formation of the intermediate tertiary carbenium ions (91) and (92) respectively, resulting from initial electrophilic attack of the Lewis acid at the terminal C-5 carbon atom of the allene system, followed by ring opening in a manner analagous to the formation of (82), (83) and (84), (87); Schemes 20 and 21 respectivley. Some support for this mechanism comes from an independent study on (33), in which the methyl ether (93), formed as a result of direct trapping of (92), was isolated.[87] Three routes involving the rupture, and



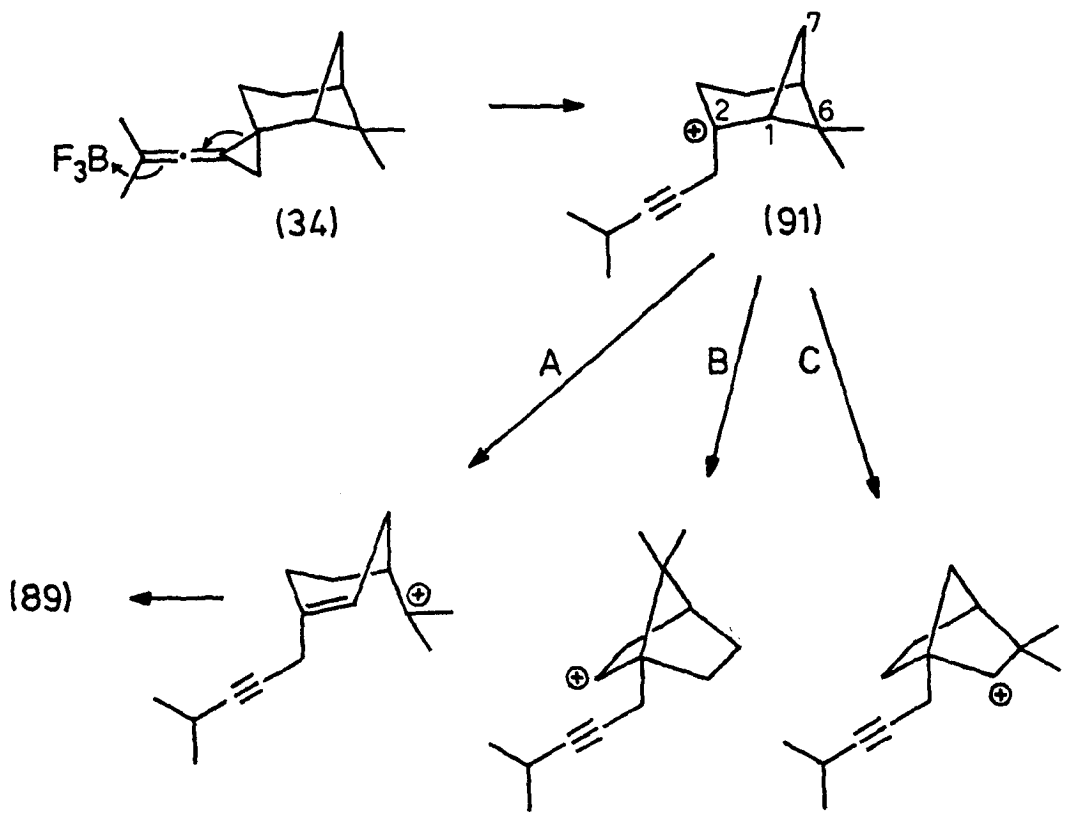
(34) (91) (89)

Scheme 20



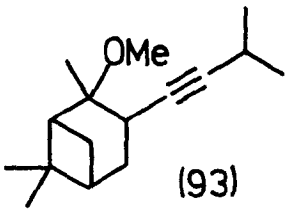
(33) (92) (90)

Scheme 21



(34) (91) (89)

Scheme 22

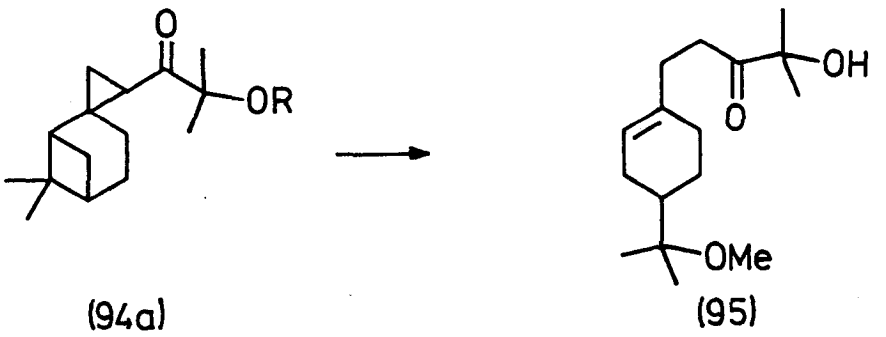


(93)

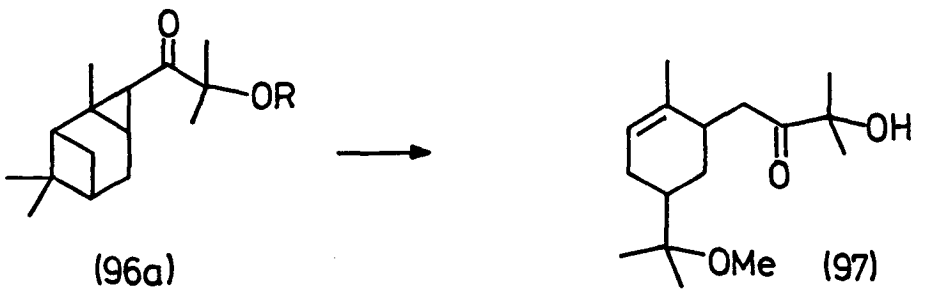
hence relief of ring strain, of the cyclobutane moiety are possible. Considering alkenylidenecyclopropane (34), ring opening by cleavage of the C(1-6) bond giving an olefinic linkage between C-1 and C-2 leads to a monocyclic tertiary carbenium ion containing a menthane type skeleton (Route A). Two other modes of rearrangement are: migration of the bond electrons of the gem -dimethyl bridge, the C(1-6) bond, to give a bicyclic secondary carbenium ion containing the bornyl skeleton (Route B); or, alternatively, migration of the methylene bridge electrons, the C(1-7) bond, would give rise to a secondary carbenium ion containing a fenchyl skeleton (Route C),[88] as outlined in Scheme 22. Similar considerations hold for (33). Both of the major products isolated, (89) and (90), can be seen to arise via Route A; by cleavage of the C(1-6) bond giving a new tertiary carbenium ion, which is then neutralised with methanol.

In conclusion, our results show that the boron trifluoride etherate reaction of alkenylidenecyclopropanes (33) and (34) proceeds in a manner similar to their bicyclic counterparts. The products, (89) and (90) isolated, show that the major pathway is via cyclobutane ring cleavage, rather than Wagner-Meerwein rearrangement, to give tertiary carbenium ions containing a menthane type skeleton. That the major pathway for cations of type (91) and (92) proceeds along Route A, to give menthyl type structures, has also been demonstrated for the tricyclic ketols

(94b) and (96b), which gave the monocyclic products (95) and (97) respectively on treatment with hydrochloric acid in methanol.[62]

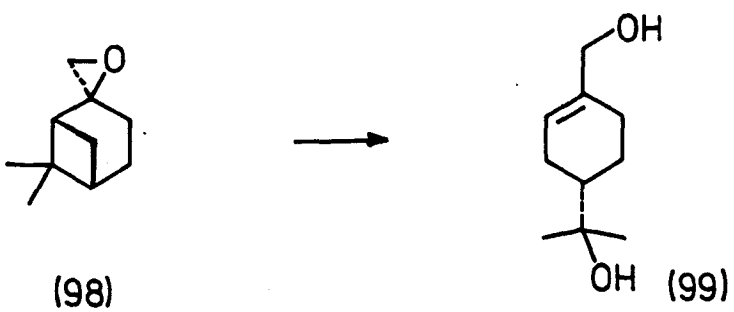


(94a) (95)



(96a) (97)

A further example is provided by the epoxide (98), which gives the diol (99) on reaction with carbon dioxide-water.[89]

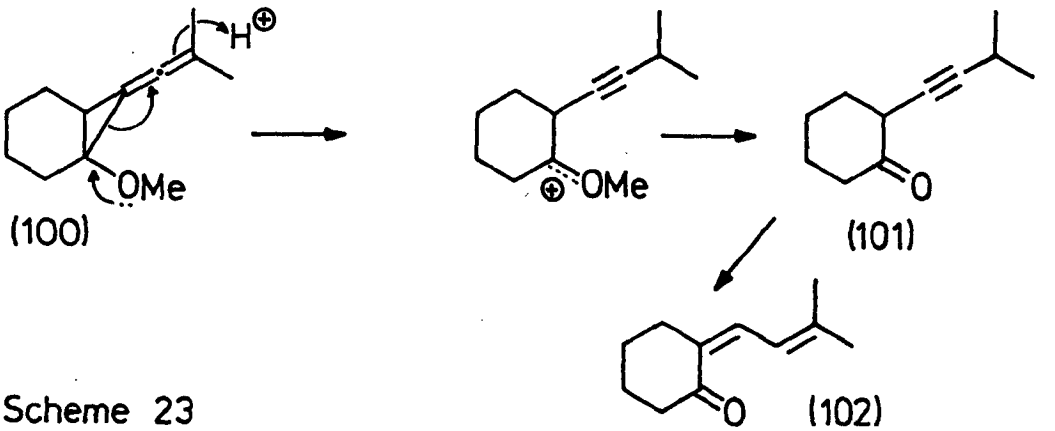


(98) (99)

3.3 α-Oxygenated Alkenylidenecyclopropanes

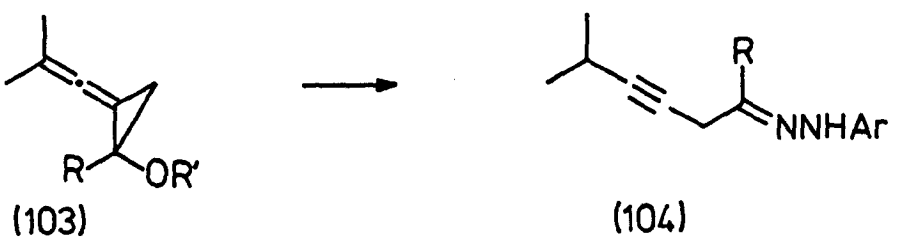
Wenkert et al. reported the isolation of dienone (102) from the acid catalysed hydrolysis of 1-alkoxyalkenylidenecyclopropane (100). Their proposed mechanism assumed an initial methoxy assisted protolysis reminiscent of the major pathway of cleavage of unoxygenated alkenylidenecyclopropanes (see earlier), leading on hydration to the acetylenic ketone (101) and/or its conjugated allenic isomer, followed by acid catalysed double bond

isomerisation (Scheme 23).[90]



Scheme 23

In a related study Maddocks showed that although no aldehyde or ketone products could be obtained by acid catalysed reaction of alkenylidenecyclopropanes (103) and (105), their corresponding 2,4-dinitrophenylhydrazones could be isolated in good yield. Monocyclic 1-alkoxy derivatives (103) gave acetylenic products (104), whereas the bicyclic derivative (105) gave the conjugated dienone derivative (106).



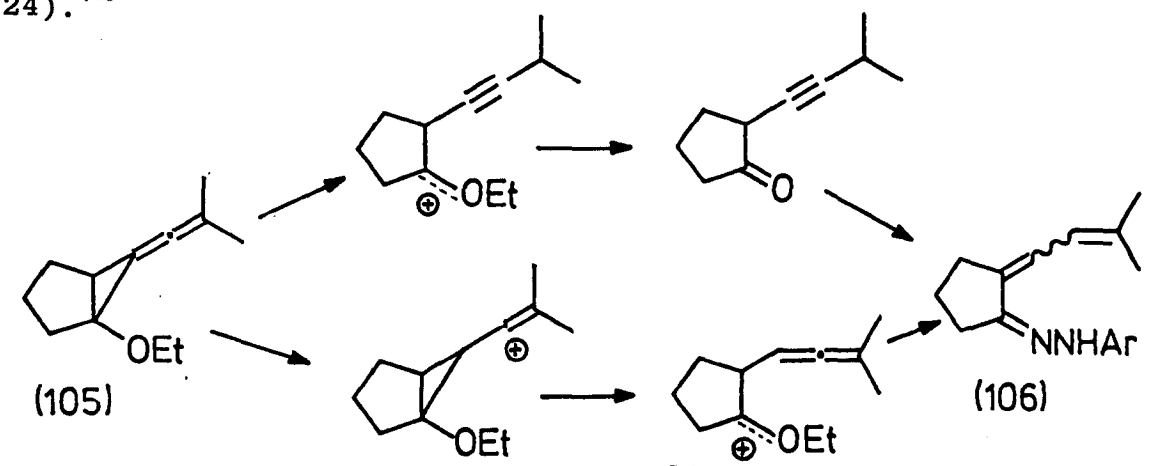
a) R = $CH(CH_3)_2$, R' = C_2H_5

b) R = H, R' = C_4H_9

Ar = 2,4-$(NO_2)_2C_6H_3$-

The formation of the acetylenic products was rationalised in terms of initial protonation of the terminal C-5 carbon atom of the allene system, followed by ring opening. Formation of the dienone (106) was accounted for by either proceeding via an acetylenic intermediate (analagous to that just described) followed by isomerisation, or by initial protonation at the cyclopropyl C-1

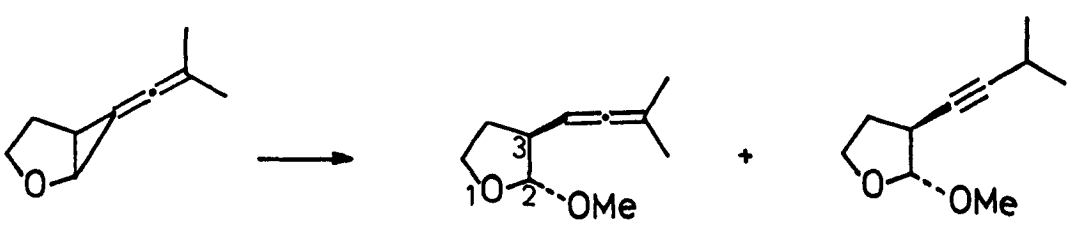
carbon atom of the allene system to give a vinyl cation, followed by ring opening and isomerisation of the resulting allene (Scheme 24).[72]



Scheme 24

As we had some previous experience with the acid catalysed reactions of bicyclic hydrocarbon alkenylidenecyclopropanes, we turned our attention to alkenylidenecyclopropanes containing the oxabicyclic system.

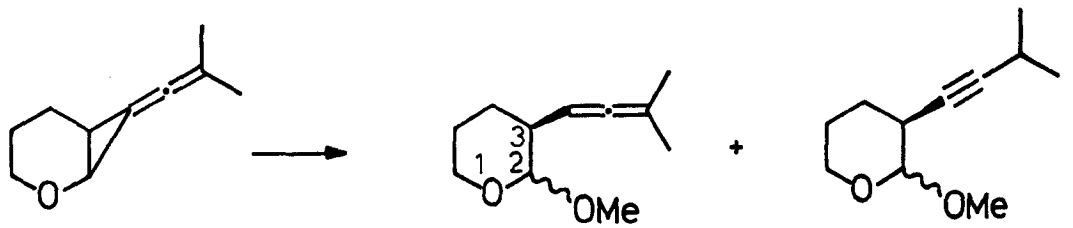
Reaction of alkenylidenecyclopropane (31) with boron trifluoride in methanol proceeded slowly at ambient temperature to afford a 7:2 mixture, by GC, of the cyclic methyl acetals (107) and (108) in 59% yield.



Chromatography on Kieselgel G using hexane-ether gave samples of the individual acetals. The less mobile major product allene

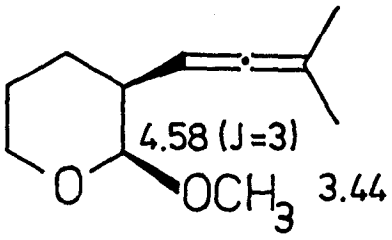
(107) had a weak allene absorption at 1965cm^{-1} in the IR spectrum. The ^{1}H NMR spectrum showed a vinyl methyl doublet at δ1.70(J=3Hz) attributed to the allenic methyls, a methoxy singlet at δ3.33, a vinyl proton multiplet at δ 4.94, the acetal C-2 methine proton occurred as a slightly broadened singlet at δ4.73($w_{\frac{1}{2}}$=3.5Hz). The minor product, acetylene (108) had an isopropyl methyl doublet at δ1.02, a methoxy singlet at δ 3.30, the C-2 acetal proton occurring at δ 4.87($w_{\frac{1}{2}}$=4Hz). Both acetals correctly analysed for methanol adducts, $C_{10}H_{16}O_2$, by high resolution mass spectroscopy. As the two acetals appear to be homogeneous (cf. ^{1}H NMR data of the homologous tetrahydropyran derivates, see below), they are tentatively assigned trans-stereochemistry on the basis of their C-2 proton chemical shifts and coupling constants in the ^{1}H NMR spectrum, compared with those recorded for 3-hydroxy-2-methoxytetrahydrofuran: cis at δ 4.95(J=6.3Hz) and trans at 4.78(unresolved singlet).[92] Isomerisation studies may show if this is really so. Reaction of (31) with hydrochloric acid in methanol gave the same two acetals (107) and (108), isolated previosuly, in the ratio 2:5 by GC. The change to a harder Lewis acid resulting in the formmation of acetylene (108) as the major product.

Similarly, reaction of alkenylidenecyclopropane (32) with boron trifluoride etherate gave a mixture of diastereoisomeric allenic and acetylenic acetals in 74% yield. Although TLC and GC only indicated the presence of three components, all four acetals were clearly apparent on examination of the ^{1}H NMR spectrum of the crude product; the acetal C-2 protons appearing as well separated doublets in the ratio 1:1.5:2:2 corresponding to acetals (109), (110), (111) and (112) respectively. Chromatography gave

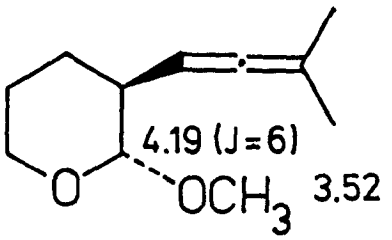


(32) (109) + (112) (110) + (111)

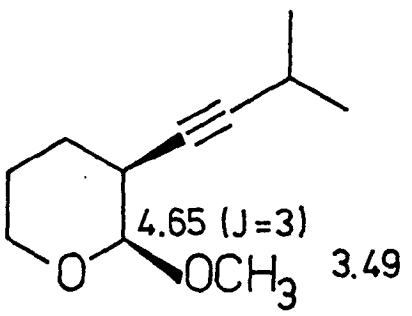
only poor resolution but pure components were isolated, in order of elution: an inseparable (homogeneous on TLC) mixture of cis-allenic acetal (109) and cis-acetylenic acetal (110), trans-acetylenic acetal (111), and trans-allenic acetal (112). All the acetals analysed correctly for methanol adducts, $C_{11}H_{18}O_2$, and had spectral data consistent with their assigned structures. That the component comprising cis-acetals (109) and (110) was a mixture of the two was readily seen from the ^1H NMR spectrum which in addition to isopropyl and vinyl methyl signals showed duplication of the methoxy and acetal C-2 proton signals. Structural confirmation for the allenic, and especially the acetylenic acetals was also obtained from their ^{13}C NMR spectra. The stereochemistry of the acetals was assigned by comparison of the acetal C-2 proton chemical shifts and coupling constants of the cis- and trans-isomers respectively (Figure 4); that of the cis-isomer appearing at lower field and having a smaller coupling constant that that of the corresponding trans-isomer. The magnitude of the coupling constant reflecting the equilibrium between the two chair conformations. Our assignments are in general agreement with the values reported for 3-hydroxy-2-methoxy tetrahydropyrans[92,93] and 2-methoxy-3-methyltetrahydropyrans.[94] Reaction of (32) with hydrochloric acid gave the same mixture of acetals (109), (110), (111) and (112), isolated above, in the ratio 2:1:4.5:1.4 (by ^1H NMR) in 57% yield. Again, as in



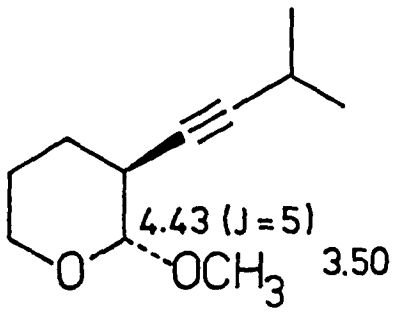
(109)



(112)



(110)



(111)

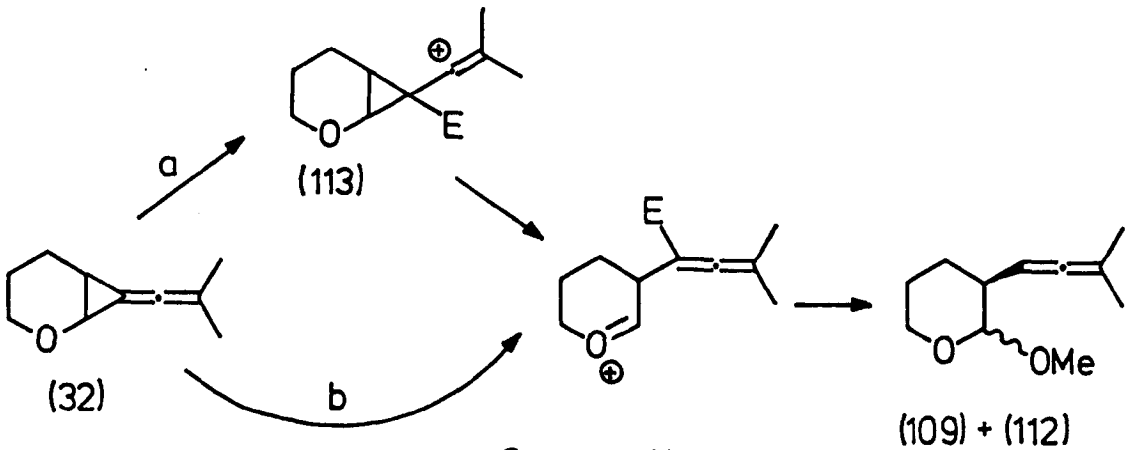
Figure 4 ^{1}H NMR data of C-2 acetal and methoxy protons

the acid catalysed reaction of (31), changing from boron trifluoride etherate to hydrochloric acid brings about the formation of the acetylenic acetals as the major products. For reaction of (32), it would seem that the trans-isomers are the slightly favoured products under both conditions.

Preliminary investigation of the acid catalysed reaction of (32) under aqueous conditions (HCl-THF-H_2O) indicate that the corresponding lactols analogous to the acetals (109) - (112) were formed.

Interestingly, no real differences in reactivity between (31) and (32) are seen. This is in contrast to the behaviour of their carbocyclic analogoues, in which the five membered ring undergoes ring expansion under acid catalysed conditions. The formation of the acetylenic acetals has been discussed earlier. Formation of the allenic acetals - such products have not previously been isolated in electrophilic reactions of alkenyli-

denecyclopropanes - can be rationalised in terms of: (a) initial electrophilic attack at the cyclopropyl C-1 carbon atom of the allene system to give an intermediate vinyl cation, followed by alkoxy assisted ring opening and acetal formation or (b) alkoxy assisted electrophilic attack, again at C-1, but with cleavage of the cyclopropane ring (Scheme 25).



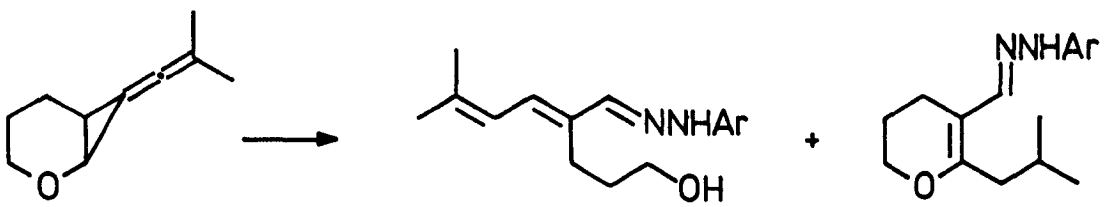
Scheme 25

However, such a process has previously only been observed with bridging electrophiles, e.g. in acetoxymercuration.[35] Returning to path (a), it is difficult to see why such a process should be favoured, as the transition state leading to vinyl cation (113) is afforded no additional stabilisation, in contrast to that formed from initial attack at C-5 (see earlier). Also, products arising from vinyl cations of type (113) have not previously been observed. The formation of the allenic products by isomerisation of their acetylenic isomers can be discounted on the grounds that while acetylenic products have frequently been isolated in the reactions of alkenylidenecyclopropanes with electrophiles, the isomeric allenes have never been observed.

3.3.1 Dinitrophenylhydrazone Formation

We have further investigated the acid catalysed reaction of 1-alkoxyalkenylidenecyclopropanes (31) and (32) with 2,4-dinitrophenylhydrazine in methanol in an attempt to obtain crystalline derivatives of the aldehydes implicated in the formation of the acetals described in the previous section.

Reaction of (32) with 2,4-dinitrophenylhydrazine reagent deposited red needles of the dienal derivative (114). Examination of the filtrate showed the presence of another dinitrophenylhydrazone derivative which was isolated by chromatography and given the dihydropyran structure (115). Both derivatives analysed

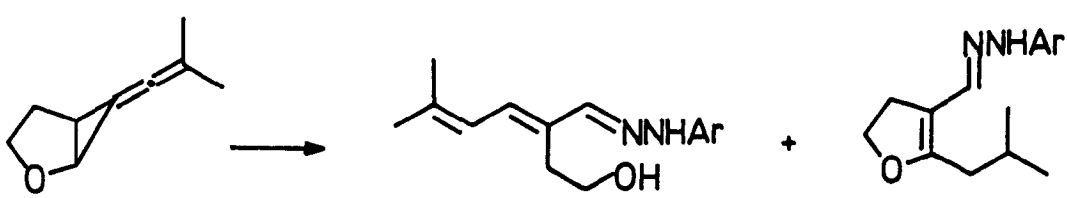


(32) (114) (115)

correctly for $C_{16}H_{20}N_4O_5$. The dienal derivative (114) exhibited no allene abosrptions in the IR spectrum, but a hydroxyl absorption was present at 3350cm^{-1}. The ^{1}H NMR spectra showed vinyl methyl singlets at δ1.88 and δ 1.93, an olefinic AB quartet at δ6.22 and 6.64 (J=12Hz), and the imine proton at δ 7.73. The ^{13}C NMR spectrum confirmed the structure (114); having eleven signals in the olefinic (sp^2) region. The UV spectrum of (114) exhibited a maxima at 404nm consistent with a dinitrophenylhydrazone derivative of an α, β, γ, δ-unsaturated carbonyl compound.[84] The more chromatographically mobile (silica/benzene) derivative (115) showed no hydroxyl absorptions in its

IR spectrum. The ^{1}H NMR displayed an isopropyl methyl doublet at δ 0.99, allylic protons at δ 2.26 and 2.44, and only one olefinic signal; that of the imine proton at δ 8.05. Significantly, the UV maxima of (115) occurred at 402nm, very close to that obtained for (114). The only structure consistent with all the spectral data is that of a 5-formyl-3,4-dihydro-2H-pyran derivative. The similar UV maxima obtained for (115) can be explained by the bathochromic (red) shift due to the oxygen substituent acting as an auxochrome on the parent α,β-conjugated system. The effect of -OMe on an α,β-unsaturated aldehyde at the β position is an additional 30nm,[84] roughly equivalent to another double bond in conjugation.

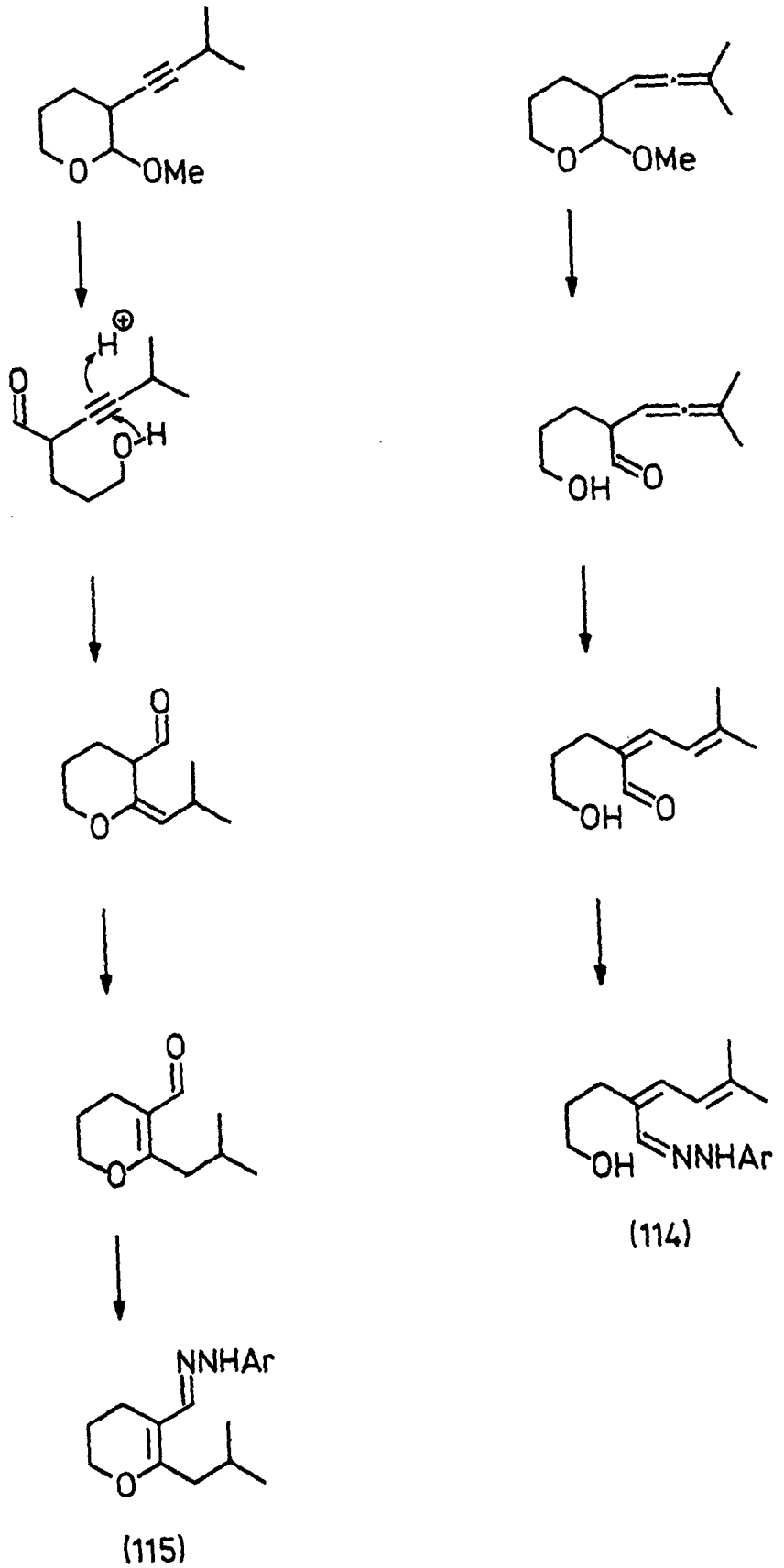
Similarly, under the same conditions alkenylidenecyclopropane (31) gave the homologous dienal (116) and dihydrofuran (117) derivatives. The spectral and analytical data fully



(31) (116) (117)

supported the proposed structures. Once more, no differences in reactivity between (31) and (32) were seen.

The formation of the dinitrophenylhydrazone derivatives can best be rationalised if one accepts the assumption that the reaction proceeds through similar acetal, or their equivalent, intermediates isolated from the acid catalysed reaction in methanol. Considering alkenylidenecyclopropane (32) - similar arguments hold for (31) - formation of the simpler dienal derivative

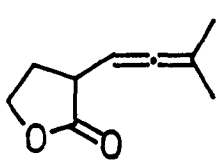


Scheme 26

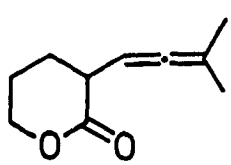
(114) is rationalised by isomerisation of the initially formed allenic acetal to the conjugated dienal. For the cyclic derivative (115), the initial hydroxy aldehyde undergoes acid catalysed ring closure (6-exo-Dig[95]) across the acetylene C-C triple bond to give an alkylidenetetrahydropyran derivative which suffers isomerisation to the α, β-unsaturated aldehyde derivative (Scheme 26). Although dinitrophenylhydrazone formation has been drawn as the last step, it could conceivably occur at any stage. In any event, it would seem that the formation of a conjugated aldehyde is the driving force for the reaction.

3.3.2 Synthesis of Lactones

The trans-allenic acetals (107) and (112) could be converted in one step to the corresponding γ- and δ-lactones (118) and (119) respectively, by oxidation with excess pyridinium chlorochromate in dichloromethane at ambient temperature.



(118)



(119)

Although the conversion did not proceed to completion, the lactones could easily be isolated by chromatography from unreacted acetal. The reaction appears to proceed cleanly, and it is noteworthy that the allene moiety is unaffected. Under the same conditions the γ-lactone is formed in higher yield than the δ-lactone; similar behaviour in the one step oxidation of cyclic acetals has been noted previously.[96] Both lactones exhibited weak allene absorptions at 1965cm^{-1} in the IR spectrum, (118) had a carbonyl

absorption at 1770cm^{-1} (γ-lactone) whereas (119) had one at 1735cm^{-1} (δ-lactone) confirming the allenic lactone structures. Further confirmation comes from the ^{1}H NMR spectra, both lactones showing allenic methyl doublets and vinyl proton signals. As to the mechanism of the oxidation, presumably the slightly acidic nature of the reagent allows reaction to proceed via the intermediate lactol.

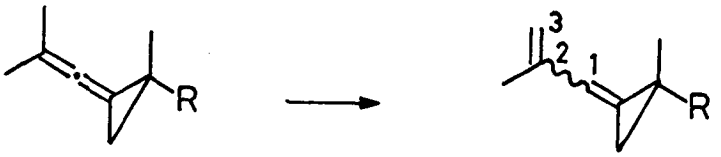
The direct conversion of functionalised cyclic methyl acetals (protected lactols) to lactones has also been accomplished with m-chloroperoxybenzoic acid in the presence of boron trifluoride etherate,[96] and Jones reagent.[97]

The acetylenic acetals would also be expected to form the corresponding lactones. More acidic reagents could be used as the acetylene moiety is known to be stable under such conditions.

The formation of these lactones represents a simple synthesis of 3-substituted γ-and δ-lactones from dihydrofuran and dihydropyran respectively. The lactones (118) and (119) should be easily alkylated, or transformed into unsaturated lactones by a selenylation-elimination sequence.

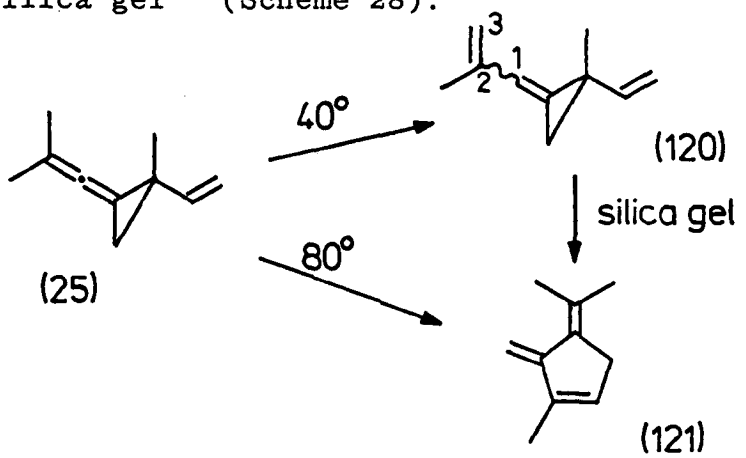
3.4 Allylidenecyclopropanes

Using a method originally employed by Poutsma and Ibarbia,[37] Maddocks et al.[72,80] showed that C_{10} alkenylidene-cyclopropanes could be isomerised at 40° using potassium t-butoxide in dimethylsulphoxide to give mixtures of E- and Z-isomers of the corresponding allenylidenecyclopropanes (Scheme 27).



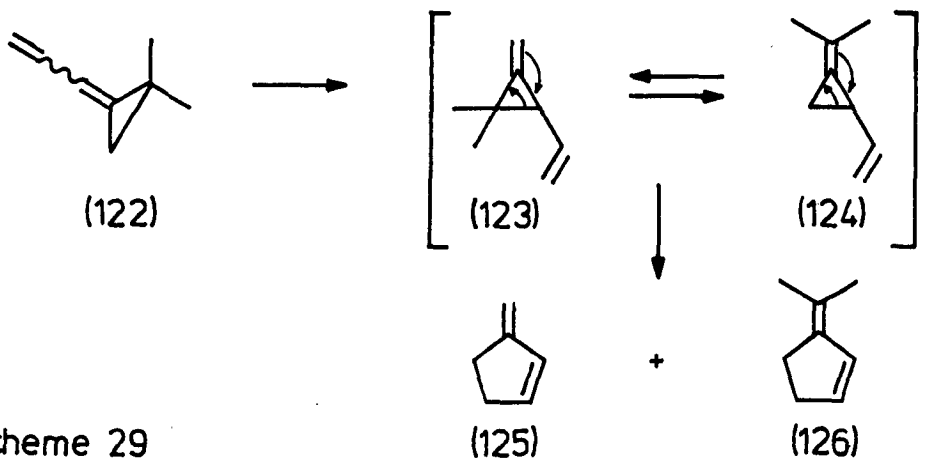
Scheme 27 R = C≡CH, HC=CH$_2$, Et

However, when (25) was isomerised at 80° the bisalkylidenecyclopentene (121) was obtained.[72] Rearrangement of (120) to the iridoid structure (121) could also be achieved by chromatography on silica gel[62] (Scheme 28).



Scheme 28

It seems likely that the formation of (121) at a higher temperature proceeds via the allylidenecyclopropane. Such thermal rearrangements of allylidenecyclopropanes to alkylidenecyclo-

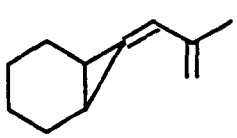


Scheme 29

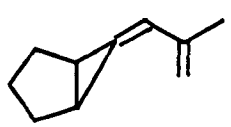
pentenes are well precedented, albeit at higher temperatures.[98] Kende and Riecke showed that an E,Z-mixture of allylidenecyclopropanes (122) gave a mixture of alkylidenecyclopentenes (125) and (128) via the intermediate vinylmethylenecyclopropanes (123) and (124) upon thermal rearrangement (Scheme 29).[98]

3.4.1 Preparation

Using similar conditions to those above, isomerisation of alkenylidenecyclopropane (28) proceeded at ambient temperature to give a good yield of the diene (127), along with some unreacted (28). However, while reaction of 50° gave complete isomerisation, as shown by TLC, the yield of (127) was low. Similarly, isomerisation of (27) at 50° gave the diene (128) in only moderate yield.



(127)

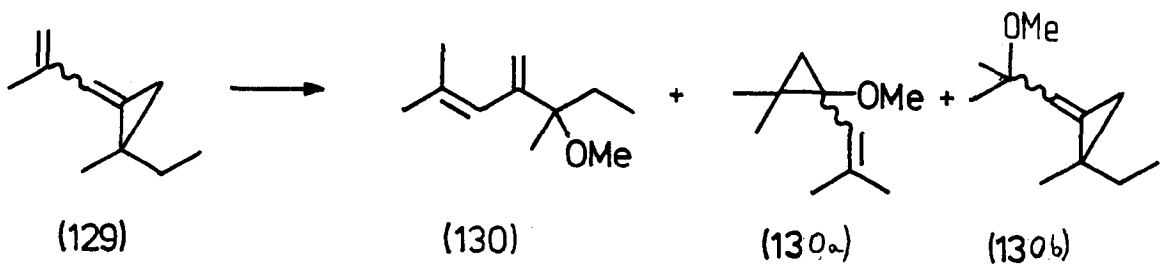


(128)

The spectral data of both dienes is very similar, and in good agreement with previously recorded data for allylidenecyclopropanes.[37,72] The IR spectra show the presence of a terminal methylene group with bands at 3080 and 890cm^{-1}, a conjugated double bond at 1615cm^{-1}, and a weak band at 1770cm^{-1} assigned to the methylenecyclopropane C=C absorption.[99] The ^{1}H NMR spectra show a vinyl methyl singlet at δ2.00, the olefinic methylene and methine protons appearing as broadened singlets at δ4.92 and 6.50 respectively. Both compounds exhibit strong molecular ions in the mass spectrum.

3.4.2 Lewis Acid Catalysed Reactions

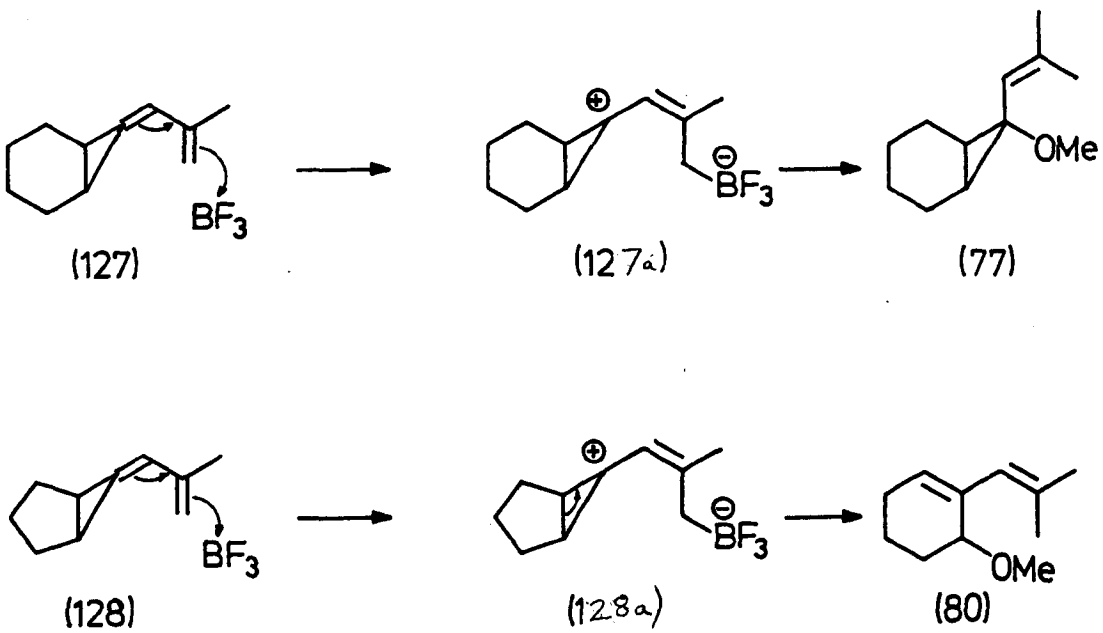
The acid catalysed reactions of allenylidenecyclopropanes (127) and (128) were next investigated. Previous work by Maddocks employing hydrochloric acid in methanol showed that reaction of diene (129) gave the ring opened diene (130) as the major products along with the cyclopropyl adducts (130a) and (130b).



Reaction of (120), containing a vinyl substituent, proceeded similarly to give ring opened diene compounds analagous to (130). Formation of all the products could be rationalised as arising from initial proton attack at the terminal C-3 carbon atom of the diene system.[72]

Since we had shown that acid catalysed reaction of the parent alkenylidenecyclopropanes proceeds more cleanly when employing boron trifluoride etherate as catalyst (see earlier), this reagent was used in preference to a protic acid. Reaction between diene (127) and the Lewis acid in methanol proceeded cleanly to give exo-vinylcyclopropane (77) in 77% yield, identical in all respects to that obtained from acid catalysed reaction of the parent alkenylidenecyclopropane (28) (See section 3.1). Similarly, reaction of (128) gave the ring expanded diene (80), isolated earlier, in 73% yield.

In accord with Maddock's work the formation of both products can be rationalised in terms of initial complexation of the Lewis acid at the terminus of the diene system to give an intermediate cyclopropyl cation. However, while cation (127a) undergoes neutralisation by methanol, in effect 1,4-addition of methanol, cation (128a) suffers ring expansion and subsequent neutralisation (Scheme 30), once again, demonstrating the propensity for ring expansion in systems containing a more strained five membered ring.



(127) (127a) (77)

(128) (128a) (80)

Scheme 30

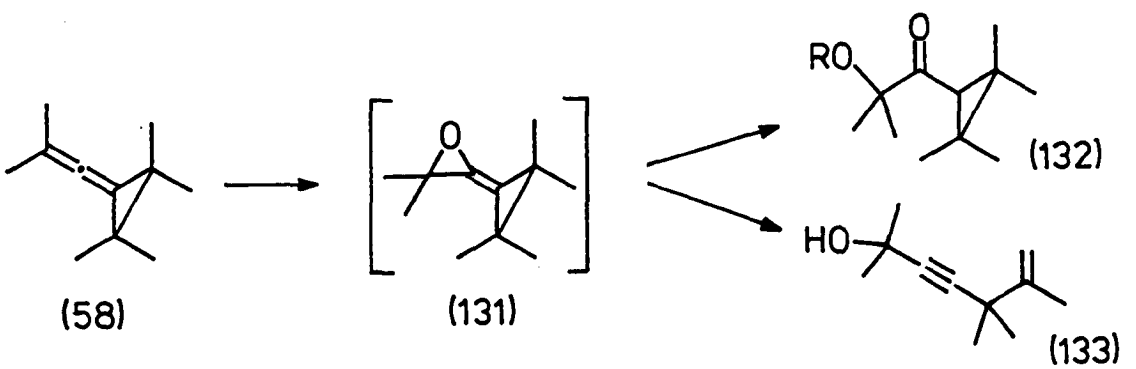
This series of reactions provides an efficient route to vinylcyclopropanes or ring opened dienes, depending on the nature of the substituents attached to the cyclopropane ring.

CHAPTER FOUR

Peracid Oxidations and Dissolving Metal Reductions of Alkenylidenecyclopropanes

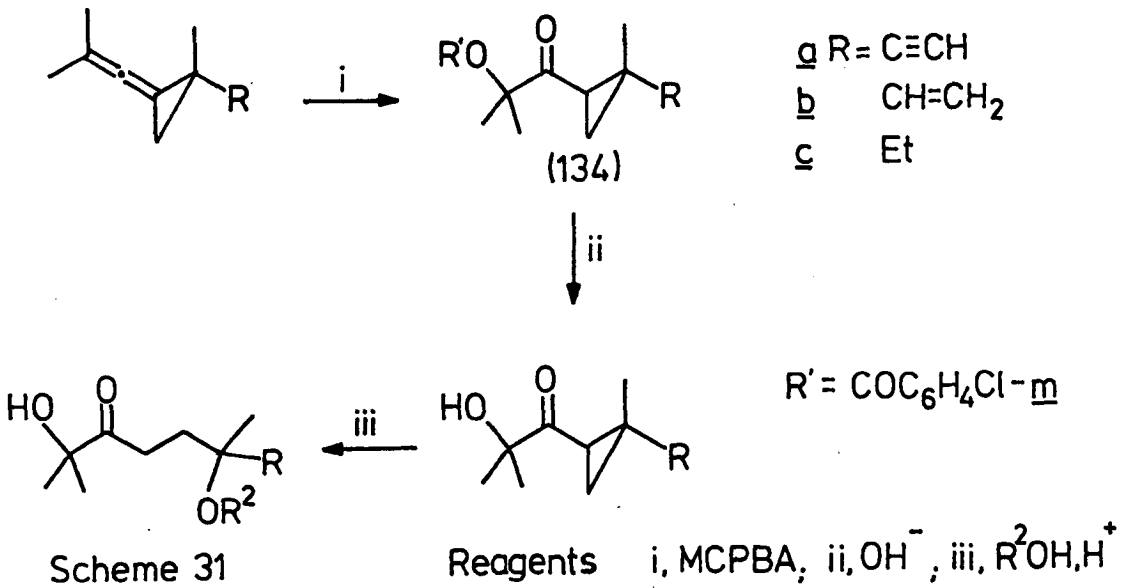
4.1 Peracid Oxidations

Crandall et al. found that the peracid oxidation of alkenylidenecyclopropane (58) using peracetic acid gave keto-ester (132a) along with hydroxy enyne (133) as a minor component.



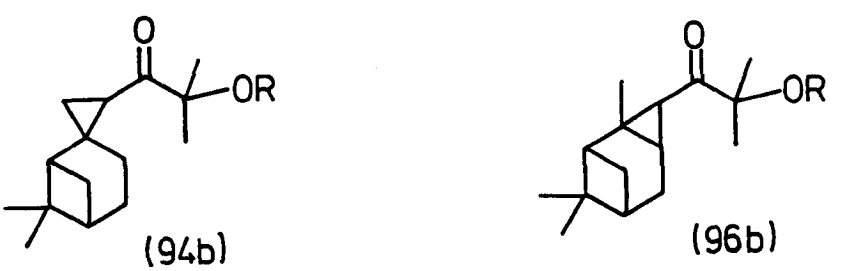
a R = Ac
b R = COC_6H_4Cl-m

Both products were perceived as arising from the intermediate allene oxide[103] (131) by the addition of acetic acid to give (132a) via its enol, or by cyclopropane ring opening of protonated (131) to give (133).[78] Poutsma and Ibarbia using m-chloroperoxy-benzoic acid (MCPBA) only isolated ketoester (132b).[37] Maddocks has shown that MCPBA oxidation of monocyclic C_{10} alkenylidene-cyclopropanes proceeds in a regiospecific manner to give cis- and trans- mixtures of cyclopropyl ketoesters (134). Subsequent hydrolysis and acid catalysed ring opening provides an excellent route to highly oxygenated monoterpenoids (Scheme 31).[72,100] This route has been extended by Gibbins to include C_{15} alkenyli-denecyclopropanes. Both (33) and (34) gave mixtures of the corresponding ketoesters (96b) and (94b) respectively, on treatment with MCPBA. The formation of the endo-isomer of (96b) is somewhat surprising, bearing in mind the severe steric



Scheme 31 Reagents i, MCPBA; ii, OH^-; iii, R^2OH,H^+

crowding between the cyclobutane methylene bridge and the geminal methyls of the ketoester portion.

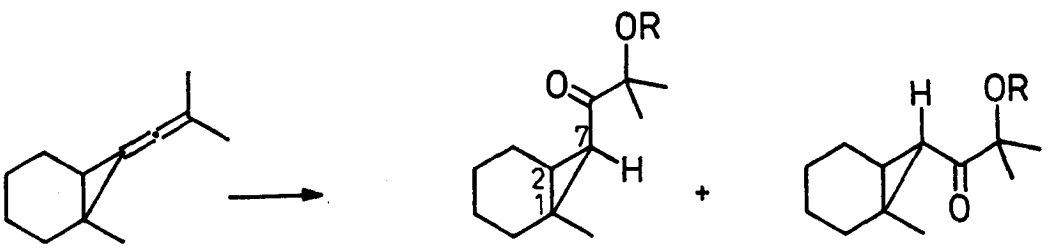


In all of the examples of peracid oxidation of alkenylidenecyclopropanes cited above, the products are formally derived from an intermediate allene oxide, formed by epoxidation of the allene C(4-5) double bond.

We wished to extend this reaction to bicyclic systems in order to examine the effect of a fused ring on the alkenylidenecyclopropane system.

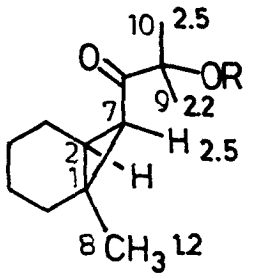
Treatment of alkenylidenecyclopropane (29) with one equivalent of MCPBA gave a separable 1:1 mixture of exo- and endo-ketoesters in 63% yield. The more chromatographically mobile

endo-isomer (135) was isolated as a crystalline solid m.p. 71-72°, while the exo-isomer (136) could only be obtained as a viscous oil.

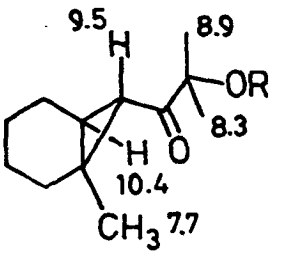


(29) (135) (136)

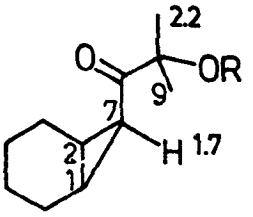
Both analysed correctly for MCPBA adducts, and had ketone and ester carbonyl absorptions in the IR spectrum at 1700 and 1720cm^{-1} respectively. In the ^{1}H NMR spectrum both exhibited a gem-dimethyl singlet at δ 1.61. Only in the case of the exo-isomer was the cyclopropyl C-7 proton sufficiently deshielded to appear as a perturbed doublet at δ 1.91 (J=5Hz). This compares well with the vicinal coupling constant of 4Hz recorded[62] for the analogous exo-isomer of ketoester (96b), sugggesting a trans relationship between the cyclopropyl protons.[102] The stereochemical assignments are based on a comparison of the chemical shifts of the cyclopropyl methyl groups; that of the exo-isomer occurring at lower field (δ 1.13) than for the endo-isomer (δ 1.06), suggesting a syn relationship between the cyclopropyl methyl and carbonyl substituents.[102] Confirmation of these assignments was obtained from LIS studies. Although the C-7 proton of the endo-isomer (135) was still not resolved by the addition of shift reagent, comparison of the magnitudes of the extrapolated shifts for a 1:1 mole ratio of ketoester to shift reagent show that the cyclopropyl methyl protons of the exo-isomer (136)



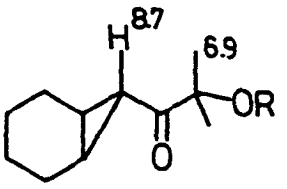
(135)



(136)



(138)



(139)

$Eu(fod)_3$ - Induced Molar Chemical Shift Changes (ppm) for Ketoesters

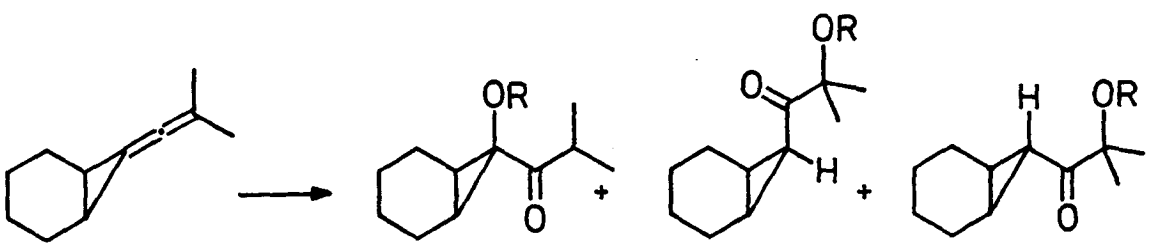
Figure 5

SIGNAL	$Eu(fod)_3$ (mg)					
(135)	0	5.0	10.6	17.9	24.9	39.8
7	-	1.80	1.89	2.02	2.11	2.32
8	1.10	1.17	1.20	1.27	1.31	1.41
9	-	1.80	1.92	2.06	2.16	2.40
10	1.80	1.92	2.04	2.16	2.27	2.48
(136)	0	6.6	12.6	18.3	24.1	36.7
2	-	-	2.91	3.39	3.79	4.66
7	-	-	2.91	3.31	3.64	4.35
8	1.19	1.61	1.88	2.23	2.51	3.08
9	1.67	2.11	2.45	2.79	3.08	3.71
10	1.67	2.17	2.54	2.92	3.24	3.93
(138)	0	2	7	12	17	
1	2.09	2.11	2.18	2.27	2.35	
9	1.71	1.72	1.79	1.89	2.00	
(139)	0	4.7	9.6	15.5	21.5	
1	1.81	2.17	2.48	2.90	3.29	
9	1.70	1.97	2.22	2.55	2.89	

Chemical shifts (ppm) for signals in the ^1H NMR spectrum of ketoesters

experience a shift six times greater than for the endo-isomer (135). All other comparisons, though less dramatic, unequivocally support the assigned structures (Figure 5). Interestingly for (136) it is the C-2 proton which has the greatest induced shift.

Under the same conditions, alkenylidenecyclopropane (28) gave as the major product, in 47% yield, a separable 6:1 mixture of exo- and endo-ketoesters (139) and (138) respectively. Also isolated in 5% yield was the regioisomeric ketoester (137).



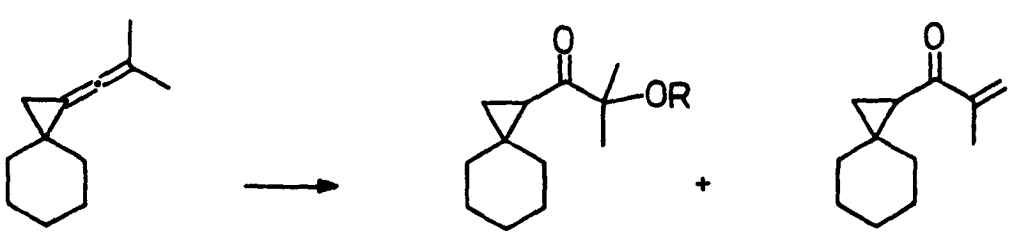
(28) (137) (138) (139)

Chromatography gave in order of elution: ketoester (137) as a crystalline solid m.p. 66-67°, apparently as a single isomer, endo-ketoester (138) also as a crystalline solid m.p. 55-56° and exo-ketoester (139) as a viscous oil. All three ketoesters analysed correctly and had similar IR spectral data to the ketoesters obtained above. The structure of ketoester (137) was readily apparent from its ^{1}H NMR spectrum which contained an isopropyl methyl doublet at δ1.07 and a methine septet at δ2.85 (J=7Hz). The ^{1}H NMR spectra of ketoesters (139) and (138) were very similar having geminal methyl singlets at δ1.63 and 1.64 respectively, in neither case was the cyclopropyl C-7 proton signal sufficiently resolved to enable a stereochemical assignment on the basis of vicinal coupling constants (expected triplets), nor did LIS studies improve matters. However, the assignments were made by a comparison of the induced shifts of

the C-7 and geminal dimethyl protons (Figure 5), that of the exo-isomer again experiencing a much greater shift. Presumably the differences in induced shifts reflect the ability of the shift reagent to complex more effectively with the less sterically crowded exo-isomers.

In both of the peracid oxidations of (28) and (29) material of a more polar nature than the isolated ketoesters was also obtained. IR spectral analysis showed this to contain some hydroxy components, possibly similar to the ring opened enyne (133) isolated by Crandall et al.[78] However, repeated chromatography failed to isolate any pure material.

Reaction of the spiro fused alkenylidenecyclopropane (30) under the usual conditions gave a modest yield of ketoester (140). Also isolated was a minor component in ca. 2% yield, assigned the enone structure (141) on the basis of carbonyl absorptions at 1720 and 1660cm^{-1} in the IR spectrum, and vinyl methyl at δ1.91 and vinyl protons at δ5.70 and 6.01 in the ^{1}H NMR spectrum. Enone (141) presumably arises by elimination of the ester function from (140).

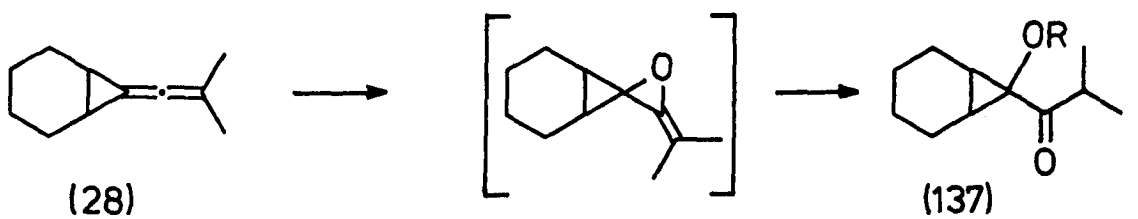


(30) (140) (141)

Reaction of MCPBA with the α-oxygenated alkenylidenecyclopropane (32) only resulted in the formation of complex mixture of products. Whether this is as a result of a different

mode of attack, or further reaction of the products is uncertain.

It is noteworthy that when mixtures of exo- and endo-ketoesters were formed in this study, it is the endo-isomer that is the more chromatographically mobile. Similar TLC mobility was also observed for the exo- and endo-isomers of ketoester (96b). The formation of exo-isomer (139) as the major product of peracid oxidation of (28) is in accord with its expected greater thermodynamic stability relative to the endo-isomer (138). While formation of the major products, the C-2' esters is accounted for by epoxidation across the allene C(4-5) double bond, formation of the regioisomeric C-1 ester (137) can best be rationalised in terms of initial epoxidation across the exocyclic C(1-4) double bond of the allene system to give an intermediate oxaspiropentane, followed by protonation and ring opening (Scheme 32).



(28) (137)

Scheme 32 R = COC_6H_4Cl-m

This is the first time that a product derived from an oxaspiropentane intermediate has been isolated in the peracid oxidation of an alkenylidenecyclopropane. That such products have not been isolated before may be due to unfavourable approach of the peracid to the C(1-4) double bond on steric grounds.

4.1.1 Saponification of Cyclopropyl Ketoesters

Maddocks showed that the ketoesters (134) obtained from C_{10} alkenylidenecyclopropanes could be readily saponified using aqueous sodium hydroxide in methanol. Under the reaction conditions epimerisation of the ketone occurs. For example hydrolysis of either pure cis- or trans-ketoester (134a) gave the same mixture of cis- and trans-ketols.[72] Similarly, saponification of ketoester (94) gave a 3:1 mixture of ketols, while (96) gave only the more thermodynamically stable exo-ketol.[62]

Employing aqueous sodium hydroxide in methanol exo-ketoester (139) gave the expected ketol (142) having strong IR hydroxyl and carbonyl absorptions at 3480 and 1680cm^{-1} respectively. The ^1H NMR spectrum displayed a gem-dimethyl singlet at δ1.45. The TLC and GC homogeneity of ketol (142) suggest it is a single isomer. Also isolated as a minor component was an unidentified ketone, possibly pyran-3-one (143). All attempts to convert ketol (142) to products such as (143), by means of acid catalysed reaction met with failure. In theory, pyran-3-ones such as (143) could be formed by acid catalysed ring opening of cyclopropyl α-ketols, followed by cyclic ether formation (see Scheme 33).

Similarly, hydrolysis of either exo- or endo-ketoester (135) or (136) gave the same ketol, apparently as a single isomer. Spiro fused ketoester (140) also gave the expected ketol along with several other minor components.

Thus, even in such an apparently straightforward transformation as the hydrolysis of an ester, other reactions are also occurring for our systems. Although the ketols obtained from the

bicyclic ketoesters appear to be single isomers, mixtures would be expected on the basis of earlier work.[62,72]

Hydrolysis of the trans-isomer* of ketoester (134a) gave a 1.7:1 mixture of separable trans- and cis-ketols respectively, as previously described by Maddocks.[72] However, we reverse his assignments for the following reasons: (a) Comparison of the chemical shifts of the cyclopropyl methyl groups in the ^{1}H NMR spectrum show that the trans-isomer (our assignment) occurs at lower field (δ1.46) than for the cis-isomer (δ 1.25), suggesting a syn relationship between the cyclopropyl methyl and ketone groups.[102] A similar argument holds for the precursor ketoesters, whose assignments are also reversed. (b) The trans-isomer is the expected major product on thermodynamic grounds. (c) The more chromatographically mobile isomer is generally the cis one.

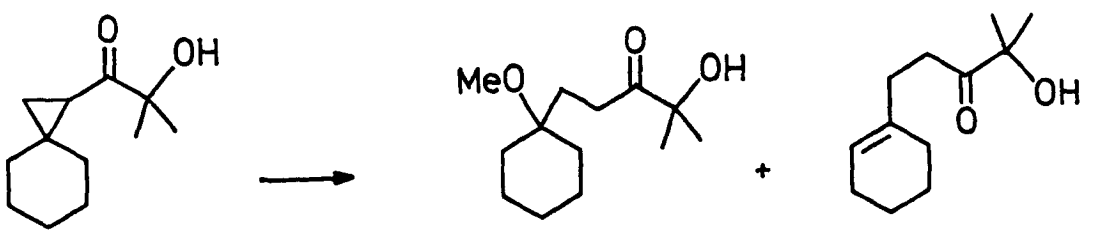
4.1.2 Acid Catalysed Ring Opening of Cyclopropyl Ketols

Studies on the acid catalysed ring opening of cyclopropyl ketones by Walborsky and Plonsker have shown that ring opening occurs via the most stable carbenium ion intermediates.[101] This was found to be the case for the ketols prepared from C_{10} alkenylidenecyclopropanes; reaction with hydrochloric acid in methanol giving highly oxygenated monoterpenoids (Scheme 31).[72,100] Extension of this scheme to the ketols (94a) and (96a) derived from C_{15} alkenylidenecyclopropanes gave the monocyclic compounds

*Prepared by P.J. Maddocks and assigned cis-stereochemistry

(95) and (97) (see Chapter 3.2).

Reaction of ketol (142) with hydrochloric acid in methanol gave a low yield of the expected ring opened product (144), along with an unidentified product having the same TLC mobility as (142). Ketol (144) exhibited strong hydroxyl and carbonyl absorptions at 3460 and 1705cm^{-1} respectively in the IR spectrum. The ^{1}H NMR spectrum displayed geminal methyl singlets at δ1.36 and 1.38, a methoxy singlet at δ3.28, and a two proton multiplet at δ2.87 consistent with methylene protons α to a ketone (Scheme 33). Similarly, the ketol from hydrolysis of ketoester (140) gave the methyl ether (145) as the major product in 52% yield along with the olefin (146) in 5% yield, and an unidentified ketol.

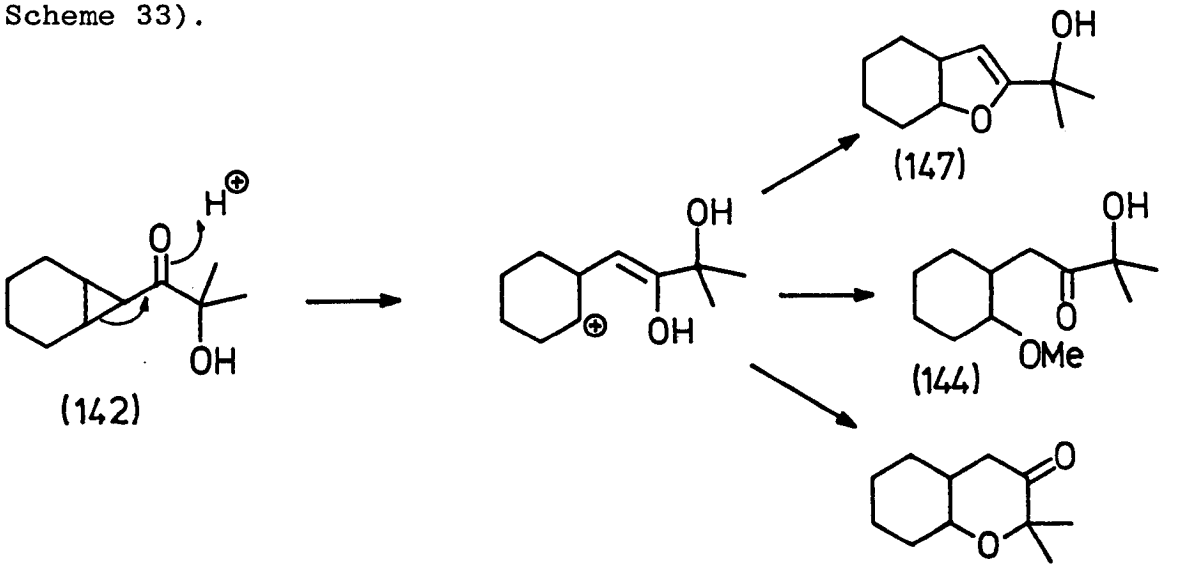


(145) (146)

The major product, ether (145), had similar spectral data to (144), except that the methyl protons α to the ketone occurred as a triplet at δ2.55 in the ^{1}H NMR spectrum.

That some of these acid catalysed reactions of cyclopropyl ketols give mixtures of products is not unexpected. Considering ketol (142) for example, protonation at the carbonyl oxygen atom followed by ring cleavage gives rise to a secondary carbenium ion. As well as the expected neutralisation by addition of a nucleophile (e.g. methanol) or loss of a proton, ring closure to

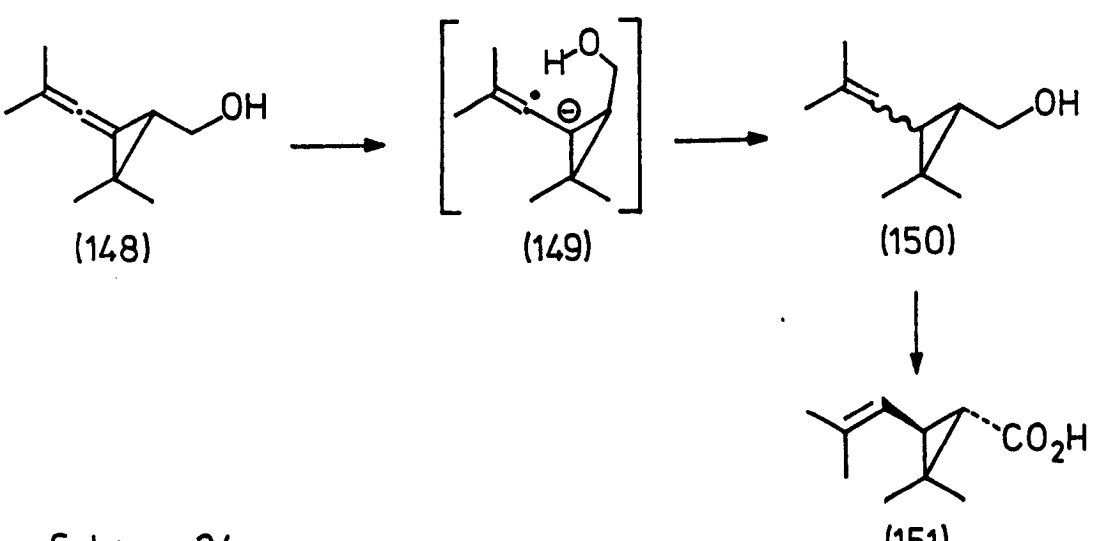
give enol ether (147) or pyran-3-one (143) could also occur (Scheme 33).



Scheme 33

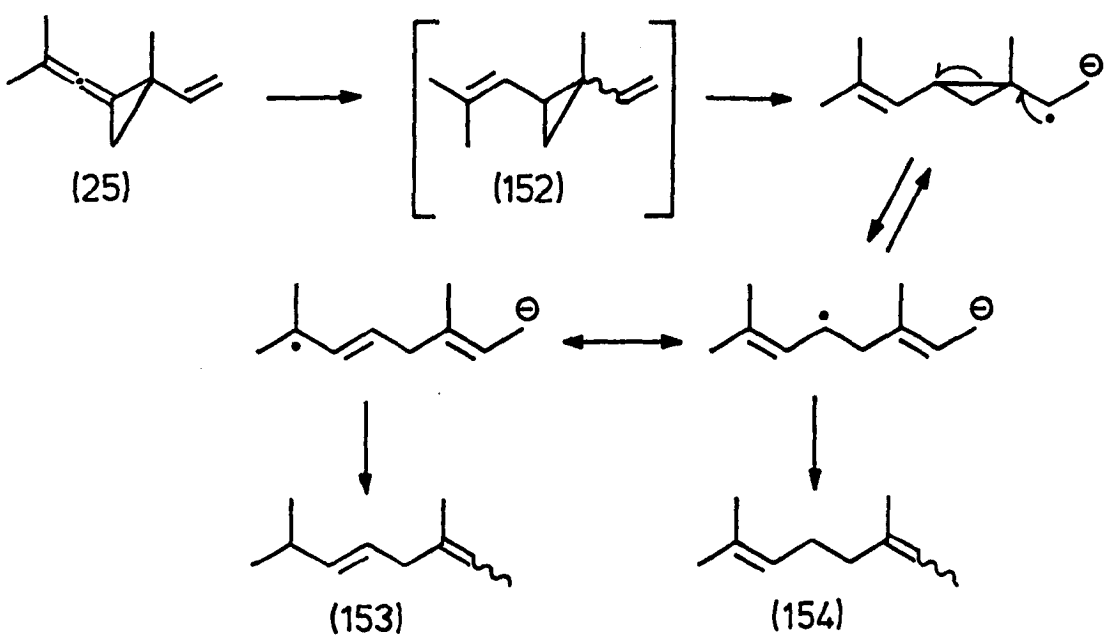
4.2 Dissolving Metal Reductions of Alkenylidenecyclopropanes

The regiospecific reduction of alkenylidenecyclopropanes was first carried out by Raphael *et al*. in the synthesis of *trans*-chrysanthemic acid (151).[13] Treatment of dehydrochrysanthemol (148) with sodium in liquid ammonia gave a 3:1 mixture of *trans*- and *cis*-vinylcyclopropanes (150) (Scheme 34). It was proposed



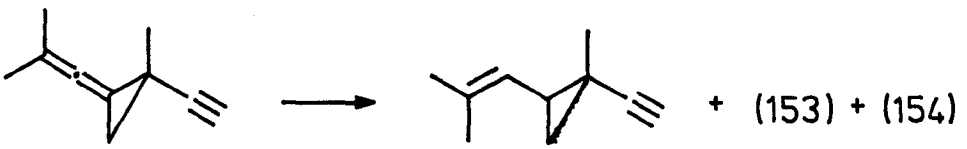
Scheme 34

that the stereoselectivity arose by intramolecular participation of the pendant hydroxy group, conveniently placed to effect proton transfer to the carbanionic centre of radical anion (149). Some support for this rationale came from reduction studies on the protected alcohol, in which no stereoselectivity was observed. Using similar conditions, Maddocks investigated the dissolving metal reduction of a series of hydrocarbon C_{10} alkenylidene-cyclopropanes.[72,100] Those containing only alkyl substituents gave roughly 1:1 mixtures of the corresponding cis and trans-vinylcyclopropanes. The vinyl substituted derivative (25) did not give the expected divinylcyclopropane (152), but instead gave ring opened diene (154) as the major product, along with diene (153), both as a mixture of E- and Z-isomers (Scheme 35)



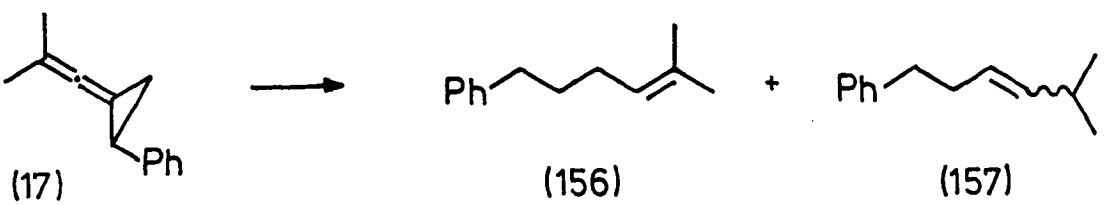
Scheme 35

Acetylene (35) underwent reduction to give mainly the expected vinylcyclopropane (155), apparently as a single isomer,[72] along with dienes (153) and (154).



(35) (155)

The formation of these dienes was rationalised as proceeding via 1,4-addition to the divinylcyclopropane intermediate (152). Further support for these proposals came from independent studies on the reduction of synthetic (152). Similarly, reduction of the phenyl substituted derivate (17) led to a 3:1 mixture of ring opened olefins (156) and (157), presumably, also by way of a vinylcyclopropane intermediate.[51]



(17) (156) (157)

Thus, it would appear that alkenylidenecyclopropanes which have unsaturated substituents attached to the three membered ring undergo further reduction under the reaction conditions.

Maddocks also demonstrated that the C_{10} vinylcyclopropanes obtained above underwent acid catalysed reaction in a similar manner to that of the parent alkenylidenecyclopropanes. For vinylcyclopropanes containing no other unsaturation, protonation occurred at the terminus of the vinyl group to afford an intermediate cyclopropyl cation.[72,100]

In an effort to examine the stereochemical consequences of the sodium-ammonia reduction we turned our attention to bicyclic and tricyclic alkenylidenecyclopropanes. Reduction of alkenylidenecyclopropanes (27)-(29) and (33) gave good yields of

the corresponding vinylcyclopropanes, as mixtures of exo- and endo-isomers (Table 1). That the yields of the bicyclic vinylcyclopropanes are not higher is probably due to their volatility. In agreement with previous work, the reduction appears to be regiospecific, occurring solely across the exocyclic C(1-4) double bond of the allene system. No ring opened or methylenecyclopropane type products were detected. The structures of the vinylcyclopropanes rest mainly on their ^{1}H NMR spectral data (IR and MS data were unremarkable) which contained isopropylidene methyl signals at δ1.68-1.75, and vinyl proton signals corresponding to the exo- and endo-isomers (Table 1). The relative proportions of exo- and endo-isomers were conveniently assessed by comparison of the intensities of the vinyl protons associated with each; that of the exo-isomer appearing as a broad doublet at higher field. The relative deshielding of the endo-isomer presumably occurs because of steric interaction with the fused ring protons. These observations are in agreement with those made for the vinylcyclopropanes discussed in Raphael et al.'s work.

Concerning the mechanism of the dissolving metal reduction. Devaprabhakara and Gardner have shown that sodium-ammonia reduction of substituted allenes affords olefins by selective reduction of the more hindered double bond.[104] The experimental evidence suggests that the dissolving metal reduction of substituted allenes occurs by alternate electron transfer and protonation, and not by a consecutive two electron transfer to proceed via a dianion as was originally thought.[105] Electrochemical[106] and theoretical studies[107] suggest that protonation of the initially formed radical anion occurs rapidly at the central

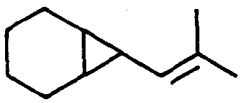
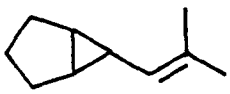
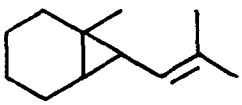
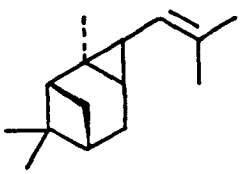
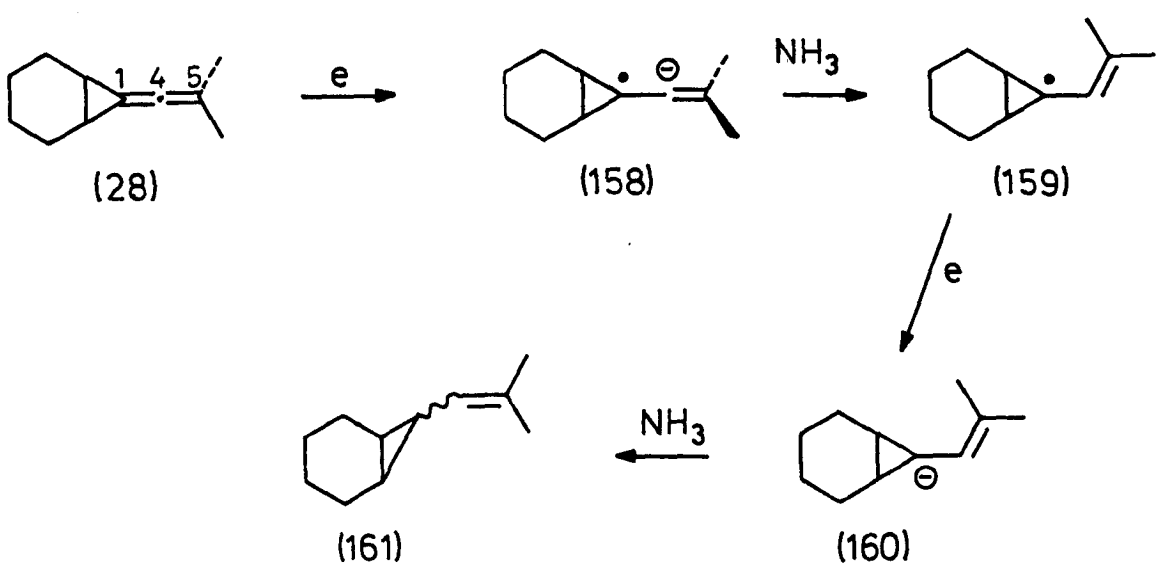
Alkenylidene-cyclopropane	Vinyl-cyclopropane	Yield %	exo/endo ratio	Vinyl proton Chemical shift (δ)
(28)		82	5:1	4.58 (J 8) exo 5.00 endo
(27)		73	6:1	4.55 (J 8) exo 4.90 endo
(29)		66	1:1	4.87 (J 8) exo 5.00 (J 7) endo
(33)		88	9:1	4.81 (J 7) exo 5.39 endo

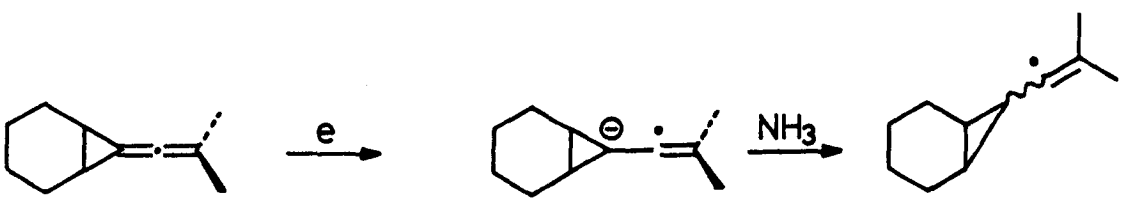
Table 1 Vinylcyclopropanes obtained by sodium-ammonia reduction of alkenylidenecyclopropanes



(28) (158) (159) (160) (161)

Scheme 36

carbon atom to give a coplanar allyl radical. Applying such a scheme to the metal-ammonia reduction of alkenylidenecyclopropanes, for example to the bicycle (28) leads to electron attack at the central C-4 carbon atom, across the C(1-4) double bond of the allene system to give radical anion (158) which then undergoes rapid protonation at C-4 to give cyclopropyl radical (159) containing a coplanar allyl radical portion. A second electron transfer to (159) provides cyclopropyl carbanion (160) which undergoes rehybridisation to afford a thermodynamic mixture of exo- and endo-cyclopropyl carbanions, followed by protonation to give the observed mixture of vinylcyclopropanes (161) (Scheme 36). Protonation of a carbanion such as (160), in which the vinylcyclopropane portion is coplanar, would be expected to occur selectively from the least hindered side, producing mainly the endo-isomer, and this is found not to be the case. Reaction could of course proceed via the alternative radical anion (162) cf. (149) invoked by Raphael et al.[13] to explain their stereochemical results. However, with such an intermediate, the stereochemistry would be decided in the first protonation step. Moreover the resulting vinyl radical (163) would receive little stabilisation compared to (159).



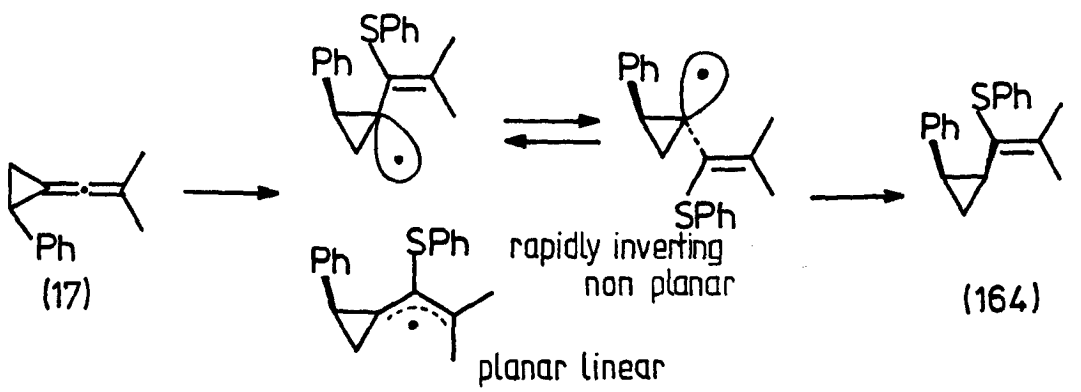
(28) (162) (163)

In any event, our mechanistic rationale goes some way in explaining the exo-stereoselectivity of the reduction.

CHAPTER FIVE

Reaction of Alkenylidenecyclopropanes with Thiophenol and Some Product Transformations

Pasto and Miles have shown that phenyl and methyl substituted alkenylidenecyclopropanes undergo a free radical chain addition reaction with thiophenol to give regio- and stereoselectively cis-enol thioethers.[108] Attack by the thiophenoxy radical was shown to occur regiospecifically at the central C-4 carbon atom of the allene system for both phenyl and methyl substituted cyclopropanes. They proposed that the stereochemistry of the adducts is determined in the hydrogen atom abstraction step. Whatever the structure of the intermediate radical - whether a rapidly inverting pair of nonplanar radicals or a planar linear radical - approach to the radical must occur preferentially at the least hindered side, opposite the bulky phenyl group in the case of (17) to produce cis-enol thioether (164) (Scheme 37).



Scheme 37

Such a route to enol thioethers (or vinyl sulphides) provides an entry into functionalised systems, as in principle the enol thioethers can be hydrolysed to give ketones[109] or regiospecifically generated α-bromoketones.[110]

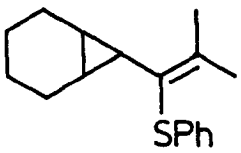
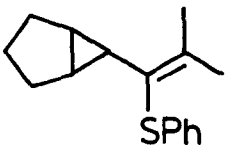
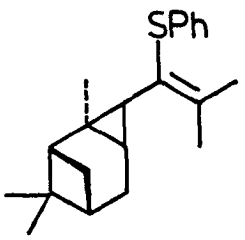
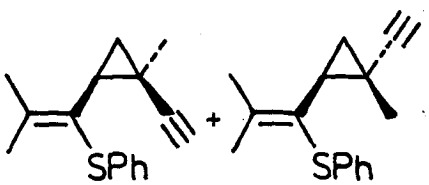
Alkenylidene-cyclopropane	Enol thioether		Yield %	endo/exo ratio
(28)		(165)	80	9 : 1
(27)		(166)	79	4 : 1
(33)		(167)	66	-
(35)		(169) (168)	46	3 : 1 cis/trans

Table 2 Cyclopropyl enol thioethers

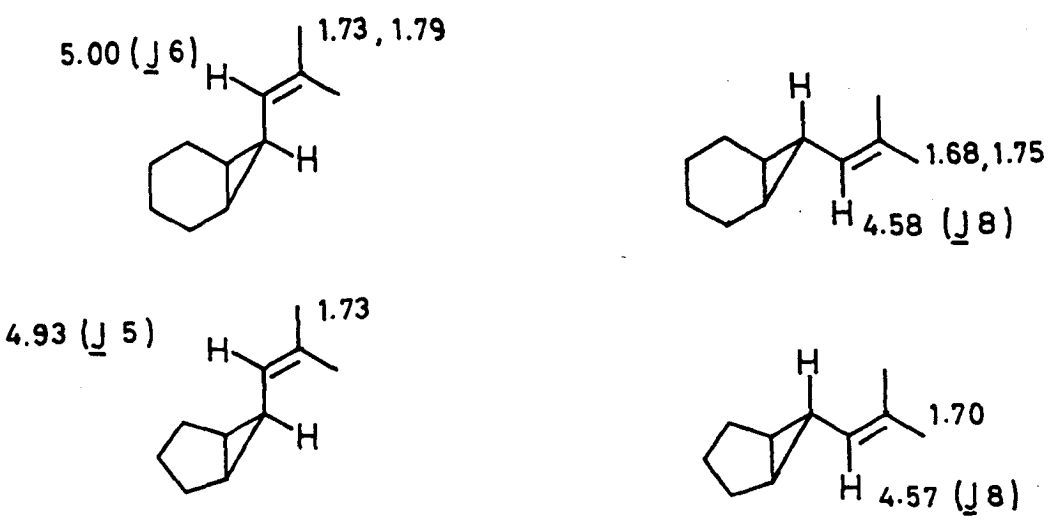


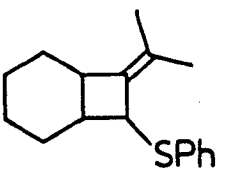
Figure 6 ^{1}H NMR data (vinyl and methyl signals) of Vinyl-cyclopropanes obtained by Desulphurisation of Cyclopropyl enol thioethers

5.1 Preparation of Cyclopropyl Enol Thioethers

Our studies with bicyclic, tricyclic and functionalised alkenylidenecyclopropanes have shown, in agreement with Pasto and Miles' results that reaction with thiophenol in benzene at ambient temperature gives good to excellent yields of the corresponding cyclopropyl enol thioethers (Table 2). The structure of the thiophenol adducts follows from their strong parent molecular ions in the mass spectrum, and from their ^{1}H NMR spectra which show isopropylidene methyl signals at δ1.93-2.11, phenyl protons and importantly no signals in the olefinic region (δ 4.5-7.0). Enol thioethers (165) and (166) were isolated as inseparable mixtures of exo- and endo-isomers. Reaction of thiophenol with the ethynyl derivative (35) also proceeded in a regioselective manner, producing the separable adducts (169) and (168) in a 3:1 ratio. No products resulting from thiol addition to the acetylene C-C triple bond were detected. Chromatography on silica gel gave pure (168) and (169) along with unreacted (35). The stereochemistry of (168) and (169) is assigned on the basis of their ^{1}H NMR spectra. The major, less mobile isomer (169) is assigned cis-stereochemistry as its cyclopropyl methyl group occurs at lower field δ1.34, than for the trans-isomer (168) at δ1.14; the thiophenyl group exerting a shielding effect[102,108] on the synfacial cyclopropyl methyl group of the trans-isomer.

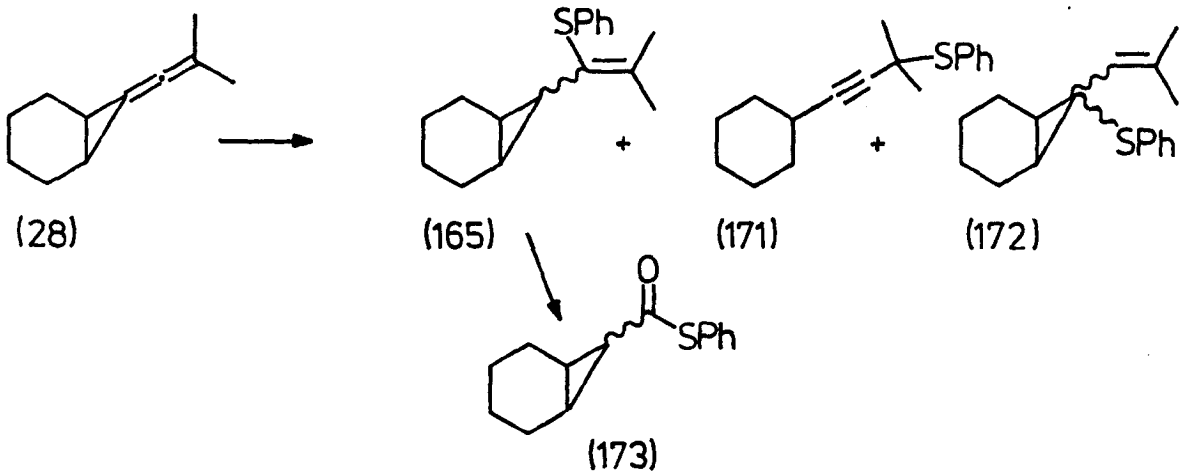
Prior to our study, Gompper and Lach proposed bicyclo-

[4.2.0]octane (170) as the product of thiophenol addition to alkenlidenecyclopropane (28).[48]



(170)

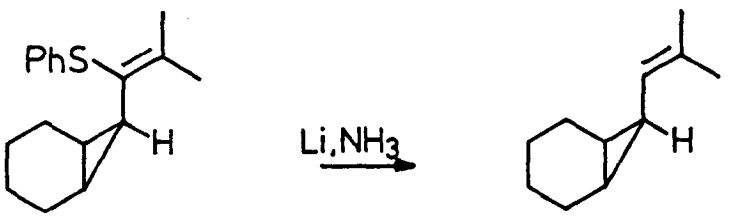
We very carefully examined the reaction of (28) with thiophenol and found that, in addition to enol thioether (165) two other minor components were formed. These were isolated by preparative layer chromatography in ca. 1% yields and given the structures (171) and (172). No evidence for the formation of (170) was obtained. Both (171) and (172) correctly analysed for thiophenol adducts by high resolution mass spectroscopy. Acetylene (171) displayed a weak IR acetylene absorption at 2240cm^{-1}, while the ^{1}H NMR spectrum contained an aliphatic methyl singlet at δ1.51. Interestingly, the phenyl protons appeared as two distinct multiplets, in contrast to those of the other thiophenol adducts isolated, which showed a single narrow multiplet. Vinylcyclopropane (172) had isopropylidene methyls at δ1.75 and a vinyl proton singlet at δ5.35 in the ^{1}H NMR spectrum. Further proof of the structure of (165) comes from desulphurization (see below) and ozonisation studies. Low temperature ozonisation of (165) gave the expected thioester (173) with a carbonyl absorption at 1710cm^{-1} in the IR spectrum (compared to a cyclobutanone at ca. 1770cm^{-1}), along with an unidentified alcohol as the major product.



(28) (165) (171) (172) (173)

5.1.1 Reductive Cleavage

Reductive cleavage of enol thioethers (165) and (166) with lithium in liquid ammonia[111] proceeded smoothly to give mixtures of exo- and endo-isomers of the corresponding vinylcyclopropanes. Comparison of their ^{1}H NMR spectra with those of the vinylcyclopropanes obtained from dissolving metal reduction of the parent alkenylidenecyclopropanes (see Chapter 4.2) clearly showed that the endo-isomers were the major products of thiophenol addition to (27) and (28). Vinylcyclopropane (174) obtained by desulphurisation of (165) and consisting primarily of the endo-isomer, showed closely similar spectral data to that of the authentic endo-vinylcyclopropane obtained by catalytic semi-hydrogenation of (28).[51] The exo/endo ratios were easily determined by integration of the well separated olefinic signals. The vinyl proton of the endo-isomers occurring as broad doublets, at lower field and with a smaller $^{3}J_{HH}$ coupling constant than the exo-isomers (Figure 6, compare with Table 1). Attempted desulphurization using nickel boride[112] was unsuccessful.



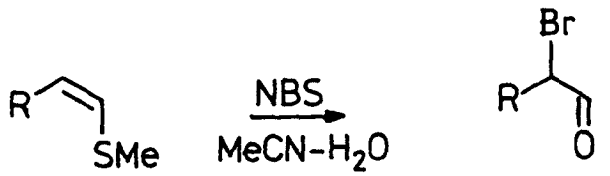
(165) (174)

Together with the dissolving metal reduction of alkenylidenecyclopropanes, this thiol addition-desulphurisation sequence provides a stereoselective route to vinylcyclopropanes from alkenes. While dissolving metal reduction of alkenylidenecyclopropanes gives mainly exo-isomers, thiol addition followed by desulphurisation leads predominantly to the endo-isomers. Similar stereoselectivity would be expected with other alkenylidenecyclopropanes. Although we have not tried any experiments, it may be possible to alkylate the intermediate vinyl anions formed on reductive cleavage of the enol thioethers.

5.1.2 Attempted Preparation of Cyclopropyl Ketones

In an effort to uncover the latent ketone functionality of the cyclopropyl enol thioethers various hydrolysis procedures were investigated. Unfortunately, all attempts to convert enol thioether (165) into the corresponding cyclopropyl ketone met with failure. Mercuric chloride in wet acetonitrile[113] gave recovered (165), even after three days at reflux. Reaction with titanium tetrachloride in acetonitrile,[114] or with hydrochloric acid, gave some ketone (IR: 1705cm^{-1}) containing material as part of complex mixture of products, along with unreacted (165). Seebach and co-workers have shown that methyl enol thioethers can be converted

into α-bromoaldehydes using N-bromosuccinimide (Scheme 38).[110]



Scheme 38

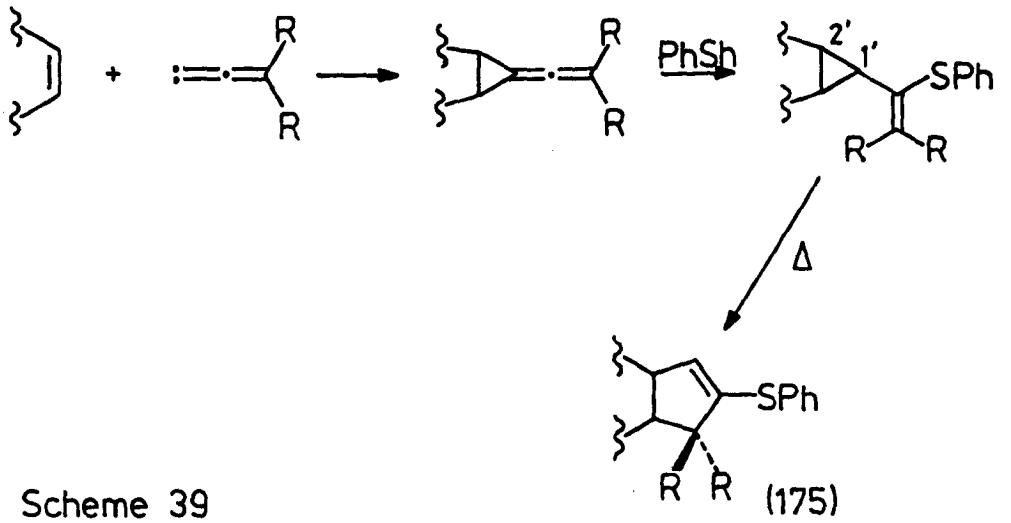
Attempting a similar transformation of (165) resulted in a complex mixture of products.

In conclusion, it would seem that hydrolysis of cyclopropyl enol thioethers does not proceed in a straightforward manner. On consideration, this is not unexpected. If hydrolysis of the enol thioether part proceeds in the normal way[115] the intermediate cyclopropylmethyl cation that is formed can undergo further reaction. Nevertheless, with judicious choice of reagent it may be possible to effect hydrolysis without ring cleavage or rearrangement.

5.1.3 Attempted Vinylcyclopropane-Cyclopentene Rearrangement

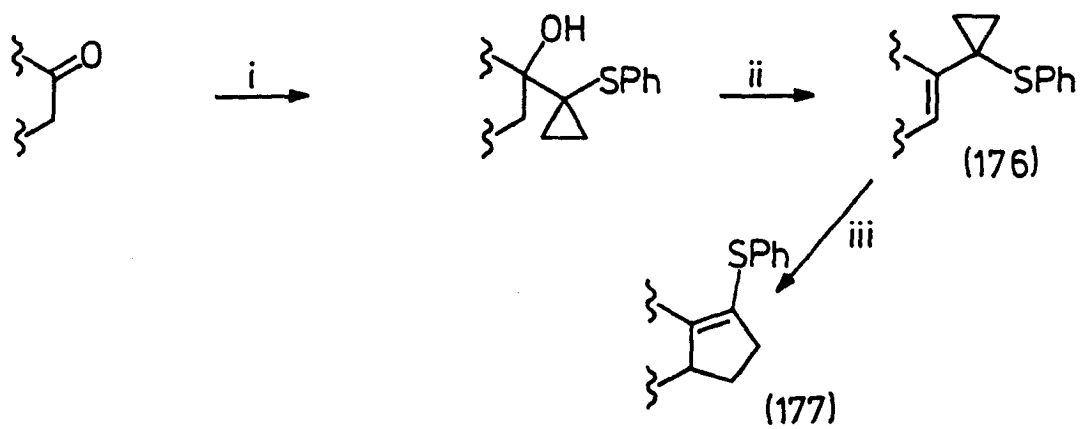
In principle, cyclopropyl enol thioethers are cyclopentene precursors, as on thermolysis they might be expected to undergo vinylcyclopropane-cyclopentene rearrangement to afford new enol thioethers of type (175). If such an objective could be achieved it would provide a new method of cyclopentane annulation starting from an alkene (Scheme 39) and employing inexpensive materials.

In a related method starting from ketones, Trost and Keeley have shown that 1-phenylthio-1-vinylcyclopropanes (176)



Scheme 39

undergo stereocontrolled thermolysis to give cyclopentenes (177) in excellent yield (Scheme 40).[116]



Reagents i,  ; ii. $SOCl_2$-py; iii, 350°, hot tube

Scheme 40

The use of functionalised vinylcyclopropanes in this rearrangement provides a powerful method of cyclopentane annulation[117-119] and has found use in natural product synthesis.[120]

Due to the lack of time only a few brief experiments were carried out. Attempted pyrolysis of enol thioether (166) at 140° gave only recovered starting material. Reaction of (166), if any, would probably only occur at higher temperatures as the reported vinylcyclopropane-cyclopentene rearrangments have

required very high temperatures, frequently in the range 500 -600°. Rearrangement of (176), for example, was carried out at 300°in a flow reactor. Very recent work, however, would suggest that vinylcyclopropanes of type (166) are not suitable candidates for vinylcyclopropane-cyclopentene rearrangmeent, being more likely to undergo homo[1,5] hydrogen shifts for the following reasons. (a) Cyclopropanes bearing syn vinyl and CH groups are subject to homo[1,5]sigmatropic hydrogen migration; activation energies for the latter are significantly lower than that required for normal vinylcyclopropane rearrangment. (b) While heteroatoms in the 1' or 2' postions (see Scheme 39) facilitate the rearrangement, a heteroatom on the vinyl substituent would appear to hamper it. (c) Vinylcyclopropanes having a cis-vinyl substituent show a natural reluctance to rearrangment.[121] Unfortunately, vinylcyclopropanes of type (166) fulfill all these negative criteria, and the possibility of cyclopentene formation would seem remote, especially as they are of predominantly endo-stereochemistry. Obviously, only further work in this area will show if these predictions are borne out in practice.

5.2 Synthesis of Karahanaenone

Karahanaenone, an odoriferous constituent of Japanese hop[122] and Cypress oil (Cupressus sempervirens),[123] belongs to a small group of naturally occuring seven membered ring mono-terpenes, the best known of which is eucarvone.[124] Karahanaenone was originally isolated by Naya and Kotake and shown to have structure (178),[122] which can be considered as the anti-Markownikoff cyclisation product of geranyl pyrophosphate.

The development of our findings on the addition of thiophenol to alkenylidenecyclopropanes has led to a novel and simple synthesis of karahanaenone.

The addition of thiophenol to alkenylidenecyclopropane (25) produced from isoprene and dimethylallene carbene, led to a 2:1 mixture of cis- and trans-isomers of the enol thioethers (179) and (180) in ca. 25% yield. Although the trans-isomer (180) could be separated by chromatography on silica gel using hexane, the cis-isomer (179) instead underwent spontaneous Cope rearrangmeent, in situ at room temperature, leading to 1,4-cycloheptadiene (181). No products arising from thiol addition to the minor alkenylidenecyclopropane (26) were detected. The more chromatographically mobile trans-isomer (180) was readily identified by the olefinic absorpitons at 1680 and 895cm^{-1} in the IR spectrum. Its ^{1}H NMR spectrum consisted of isopropylidene methyl singlets at δ1.88 and 2.07, and a cyclopropyl methyl singlet at δ1.04 in addition to an olefinic ABX system. The cycloheptadiene structure of (181) was apparent from its ^{1}H NMR spectrum which displayed a six proton gem-dimethyl singlet at δ1.14, a vinyl methyl singlet at δ1.78, olefinic methine triplets at δ5.40 and 6.01, and significantly two allylic methylene doublets at δ2.23 and 2.81. The alternative regioisomer resulting from thiol addition to (26) would be expected to exhibit a singlet and a doublet of doublets for the allylic methylene signals. Both adducts had strong molecular ions in the mass spectrum, correctly analysing for $C_{16}H_{20}S$.

Hydrolysis of the vinyl sulphide moiety of (181) using

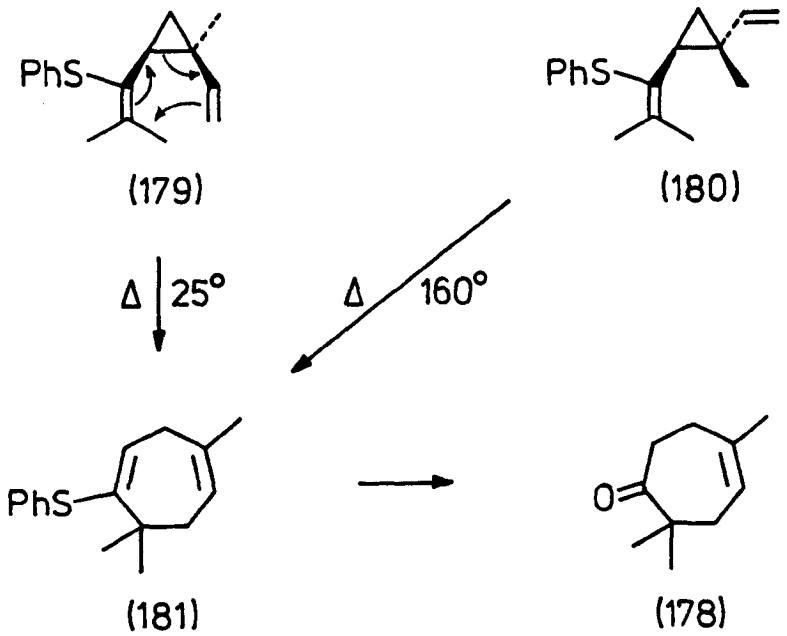
	Natural Karahanaenone[122]	Our Synthetic Karahanaenone
IR:	1695(C=O), 1640(C=C), 1375, 1355(CMe_2)	(film): 2970, 2930, 2855, 1705(ketone) 1465, 1450, 1380, 1065
^{1}H NMR(CCl_4):	1.05(6H, s, Me_2), 1.70(3H, slightly split signals, C=CMe), 2.05-2.40(4H, m, $CH_2C{=}CCH_2$), 2.60-2.85(2H, m, CH_2CO),	($CDCl_3$): 1.09(6H, s), 1.66(3H, s), 2.25(4H, m, allyl CH_2x2), 2.71(2H, br t, CH_2CO), 5.43(1H, br t, C=CH)
MS:	152(M), 109(M-43), 95, 81, 67, 41(base)	152(98, m), 137(24, M-CH_3), 109(59), 95(100, M-C_4H_9), 81(92), 68(73), 67(98), 41(98)

The following data of synthetic karahanaenone prepared by Demole and Enggist is also given for comparison.[125]

IR: 1700(C=O). - ^{1}H NMR(60MHz, CCl_4): 1.05(6H, s), 1.70(3H, s), 2.0-2.5(4H, m), 2.5-2.8(2H, m), 5.47(1H, deformed t).

Note: the omission of the olefinic proton from the ^{1}H NMR data of Naya and Kotake.[122]

Semicarbazone (pyridine method[139]): colourless prisms (EtOH-H_2O) m.p. 164-168°. (Lit.[125], 160-165°).

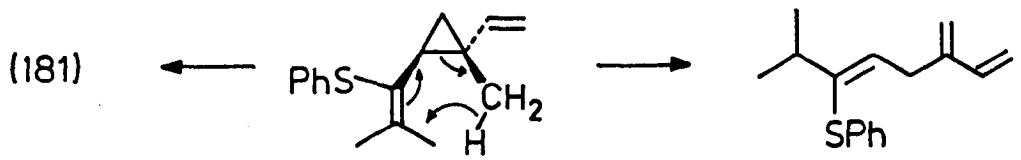


mercuric chloride in refluxing wet acetonitrile,[113] followed by chromatography on silica gel, then led to karahanaenone (178), a pleasant smelling oil in 45% yield, showing spectral data closely similar to those reported for the natural product. Spectral data of natural and synthetic karahanaenone are given opposite.

According to the literature a one pot conversion of both cis- and trans-divinylcyclopropanes to cycloheptadienes is possible if the thermolysis is conducted at a high enough temperature, presumably by thermal epimerisation of the trans- to the cis-isomer.[126-129]

Preliminary experiments showed that the trans-divinylcyclopropane (180) could indeed be converted to cycloheptadiene (181), by thermolysis at 160°. However, along with the formation of (181), a by-product was obtained in ca. 20% yield by ^{1}H NMR analysis. This is thought to be triene (182) arising from a homo[1,5] sigmatropic hydrogen shift involving the cyclo-

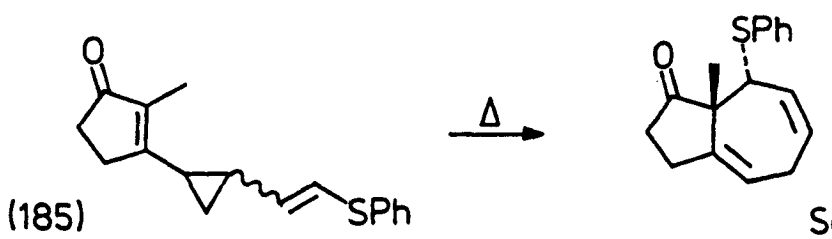
propyl methyl group (Scheme 41).



(180) (182)

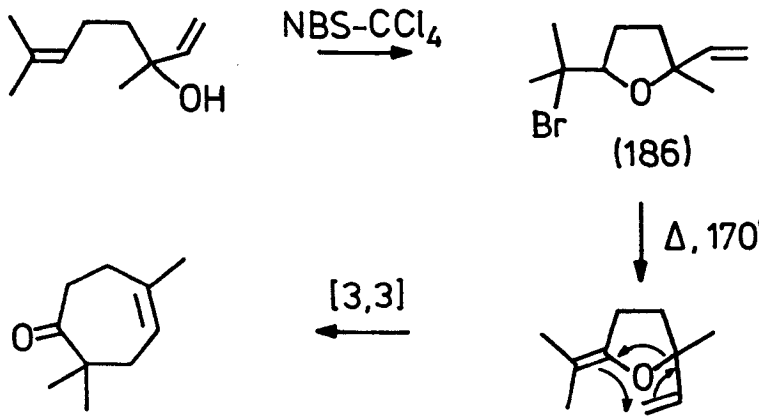
Scheme 41

Similar problems have been encountered by other workers on thermolysis of trans-divinylcyclopropanes containing synfacial cyclopropyl methyl groups.[127,129] However, Wender and co-workers in their work on pseudoguaiane synthesis overcame this problem by photoepimerisation (irradiation > 290nm) followed by, or simultaneously with, thermolysis.[127] Such a solution may be applicable in our case. It should be mentioned, however, that in a similar approach to karahanaenone using siloxydivinylcyclopropanes (see later), Wender and Filosa experienced no difficulty in conversion of their cis- and trans-mixture (183) at 165-175° to cycloheptadiene (184).[126] To our knowledge, the only other example in the literature of Cope rearrangment of thiodivinylcyclopropanes is that of Marino and Kaneko in which 2'-phenylthiodivinylcyclopropanes of type (185) were used (Scheme 42).[130]

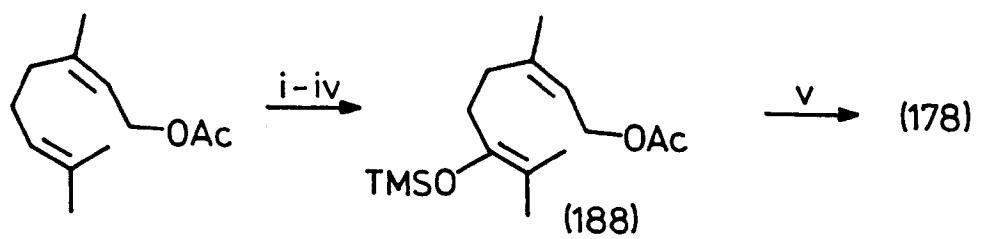


(185) Scheme 42

While overall yields are not high, conditions have not been optimised. Our route provides karahanaenone in a simple and straightforward manner without recourse to organometallic reagents.

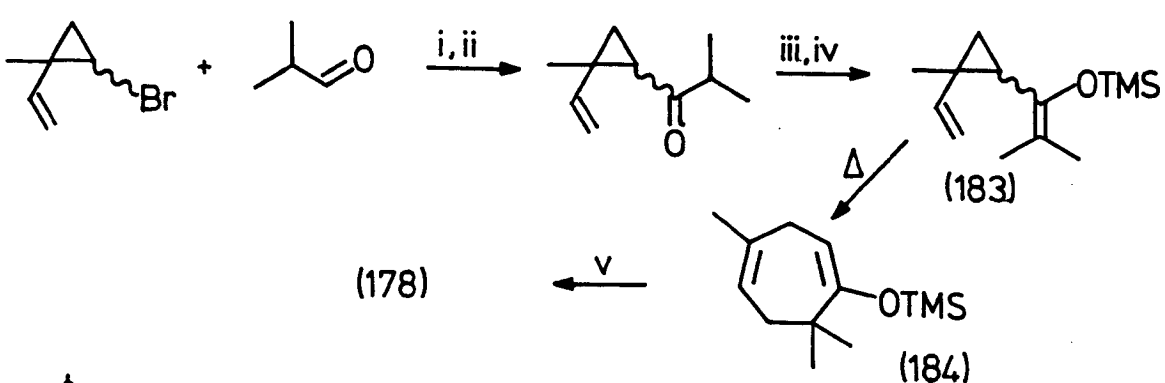


Scheme 43



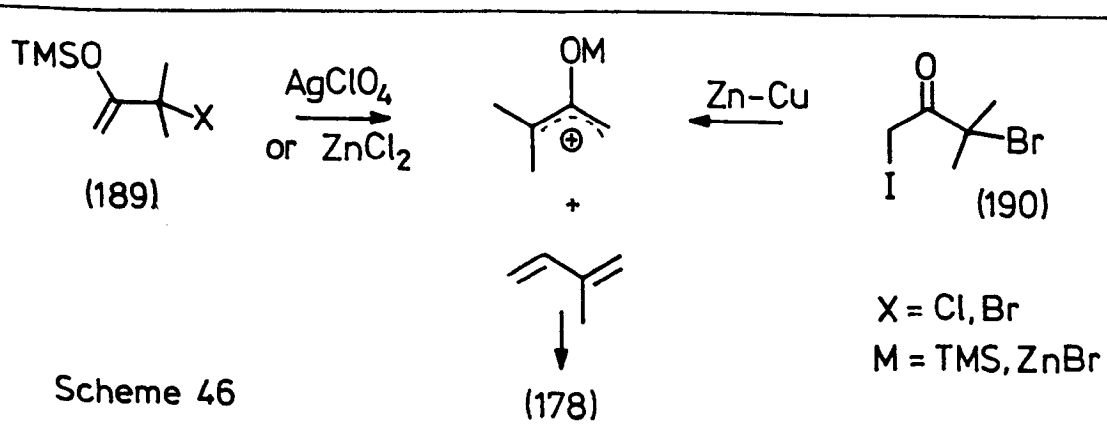
i, MCPBA, ii, HBr; iii, Me_2S-NCS; iv, Zn-TMSCl; v, $MeAl(OCOCF_3)_2$

Scheme 44



i, Bu^tLi; ii, PCC; iii, LDA; iv, TMSCl; v, Bu^nLi; vi, H_2O

Scheme 45



Scheme 46

Only recently has the thermal (Cope) rearrangement of 1,2-divinylcyclopropanes been applied to the synthesis of natural products[126,127,131,132] containing seven membered rings,[124] and our strategy may provide a new route, especially if the second vinyl group (to complete formation of a divinylcyclopropane) could be introduced after the thiol addition.

Karahanaenone has previously been synthesised by several routes.

(a) Thermal Cope rearrangement of furan (187), formed *in situ* from bromide (186) (Scheme 43).[125]

(b) Biomimetic type cyclisation using Lewis acid promoted anti-Markownikoff cyclisation of silyl enol ether (188) (Scheme 44).[133]

(c) Thermal Cope rearrangment of siloxydivinylcyclopropane (183) followed by desilylation of cycloheptadiene (184) (Scheme 45).[120]

(d) Reaction of oxyallyl species[134] - prepared from siloxyallyl halides (189)[135,136] or α,α'-dihaloketones (190)[137]- with isoprene (Scheme 46).

(e) Lewis acid catalysed rearrangement of terpinolene 4,8-oxide.[138]

However the last two routes give mixtures of products.

EXPERIMENTAL SECTION

Instrumentation

Melting points (m.p.) were recorded using open capillaries on a Buchi 510 or Gallenkamp capillary melting point apparatus and are uncorrected. Boiling points (b.p.) are uncorrected. Electronic absorption spectra (UV) were recorded using a Pye-Unicam SP800 spectrometer, λ_{max} in nm(ε). Infrared spectra (IR) were recorded using Perkin-Elmer 710B or Pye-Unicam SP200 spectrometers; calibrated with the 2951, 1602 and 907cm^{-1} absorptions of polystyrene film, λ_{max} in cm^{-1} (w=weak absorption). ^{1}H NMR spectra were recorded at 100 MHz using a Joel MH100 spectrometer. ^{13}C NMR spectra were obtained at 25.15 or 62.90 MHz using a Joel JNM-PS-100 or Bruker WM 250 PFT spectrometer respectively. NMR spectra were recorded in dueterochloroform solution (unless otherwise stated), internal standard tetramethylsilane (δ=Oppm); abbreviations: s=singlet, d=doublet, t=triplet, q=quartet, m-multiplet, br-broad; J-spin-spin coupling constant (Hz), $w_{\frac{1}{2}}$=half-width(Hz). Mass spectra (MS) were obtained on an AEI MS902 instrument; electron energy 70eV, signals are given in m/z (rel.%). Optical rotations were obtained on an Optical Activity AA-10 Automatic Digital Polarimeter employing polarimeter cells of dimensions: 2.5mm x1.0dm (volume ca. 0.5ml). Gas chromatography (GC) was performed on a Pye 104 machine equipped with a flame ionization detector; analyses were conducted isothermally at a nitrogen flow rate of 40ml/min unless otherwise stated. Column 1: 10% Carbowax 20M on Chromosorb W (60-80 mesh), 5'x¼"; Column 2: 10% Apiezon L on Chromosorb W(80-100mesh), 5'x¼" glass; Column 3: 3% SE 30 on Diatomite CQ(100-120mesh), 5'x¼" stainless steel. Retention time in min (ratio of peak areas - by triangulation).

Reagents

Hydrocarbon solvents were dried over sodium wire. Ether and THF were distilled from lithium aluminium hydride prior to use. DMSO and t-butanol were dried by distillation from calcium hydride prior to use. Chlorinated solvents were dried by distillation from P_2O_5. Methanol was dried by distillation from magnesium methoxide and stored over molecular sieves (3A). Pyridine and triethylamine were dried over potassium hydroxide pellets and distilled before use. Acetylene was purified by passage through concentrated sulphuric acid. Commercial liquid ammonia was used without further purification. Boron trifluoride etherate was purified by distillation from calcium hydride under reduced pressure. DCC was purified by distillation (b.p. 85-95°/ 0.05 Torr). Potassium t-butoxide was prepared[139] from potassium and t-butanol, and resublimed before use. 3,5-Dinitrobenzoyl chloride was purified by recrystallisation from petrol (b.p. 80-100°). 4-Toluenesulphonyl chloride was purified before use.[139] $Eu(fod)_3$ was dried over P_2O_5 *in vacuo* (0.01 Torr/12h) prior to use.

Materials

Cyclopentene[140] and methylenecyclohexane[141] were prepared by standard procedures. 1-Methylcyclohexene was prepared by addition of methylmagnesium iodide to cyclohexanone, followed by orthophosphoric acid catalysed dehydration.[142] All olefinic substrates were distilled before use. (-)-α-Pinene; $[\alpha]_D^{20}$ -40 $\pm$ 5° and (-)-β-pinene; $[\alpha]_D^{20}$ -20.5$\pm$2° were obtained from Fluka. (+)-Limonene; $[\alpha]_D^{20}$ +107.5° (MeOH, c 2.0) was obtained from Hopkins and Williams. Aliquat 336 is mainly tricapryl-

-methylammonium chloride (mixture of C_8-C_{10}; predominantly C_8).

Short column chromatography[143] was carried out on Fluka Kieselgel G or Merck Aluminium Oxide G (Type 60/E). Conventional and dry column chromatography[144] was carried out on Woelm silica gel (TSC) or Woelm neutral alumina. Analytical TLC was carried out on Fluka Kieselgel G, Kieselgel HF_{254} (or a 1:1 mixture of the two) and Merck Aluminium Oxide G (Type 60/E) of 0.3mm thickness. Preparative layer chromatography (PLC) was carried out on 20x20cm plates coated with Fluka Kieselgel HF_{254} (0.8mm thickness); pre-run with acetone before use. Compounds were removed by extraction with ether.

General Details

Organic solutions were dried over anhydrous magnesium sulphate unless stated otherwise. Evaporation refers to solvent removal at water aspirator pressure, employing a Buchi Rotavapor with a bath temperature at 20-25° (RT) unless stated otherwise. All solvents for chromatography were distilled before use. Hexane and pentane refer to the n-alkanes. Petrol refers to light petroleum (b.p. 40-60°). Ether refers to diethyl ether. Viscous oils were evaporated under reduced pressure (10^{-2} Torr) to constant weight. TLC plates were visualised by examination under UV light (λ =254nm) and iodine vapour; compounds not containing carbon double or triple bonds were visualised by spraying with concentrated sulphuric-concentrated nitric acid (95:5) followed by heating. R_f values refer to those obtained from Kieselgel coated TLC plates.

Alkenylidenecyclopropanes and their reaction products were stored under nitrogen or vacuum at 0^{o}. Under these conditions the former are reasonably stable; purification was readily achieved by chromatography and/or distillation prior to use if needed. However, on distillation, the initially colourless alkenylidenecyclopropanes (from chromatography) often became slightly discoloured.

2-Methyl-1-buten-3-yne.- A solution of 2-methyl-3-butyn-2-ol (50g, 0.595mol) and 89% orthophosphoric acid (13ml) was stirred and heated (oil bath) until distillation commenced. The distillated b.p. 32-45° was collected (bath temperature: 80-120°) and dried over potassium carbonate. Distillation (10cm Vigreux column) gave the enyne (20g, 51%), b.p. 32.5-34.5°. (Lit.,[145] 32°). - IR(film): 3295(C≡CH), 1610(C=C), 905. - ^{1}H NMR: 1.90(3H, s, CH_3), 2.86(1H, C≡CH), 5.30(1H, m, C=CH), 5.38(1H, br s, C=CH).

E,Z-3-Methyl-1-trimethylsiloxy-1-butene (43). - By the method of House et al.,[146] to a solution of dry drimethylformamide (20ml) and dry triethylamine (13.6g, 0.135mmol) was added freshly distilled chlorotrimethylsilane (4.0g, 46.5mmol) and 3-methyl-butanal (4.0g, 46.5mmol). The mixture was stirred and heated under reflux for 24h. Cooled, diluted with pentane (40ml), washed with aqueous sodium bicarbonate (x3), then rapidly in succession with portions of 1.5M hydrochloric acid and aqueous sodium bicarbonate. The pentane solution was dried (Na_2SO_4) and concentrated at atmospheric pressure (10cm Vigreux column). Fractionation of the residue (8cm Vigreux column) gave a mixture of Z- and E-trimethylsilyl enol ethers (43) as a colourless mobile oil (3.61g, 49%), b.p. 133-136°. (Lit.,[147] 134-136°). - GC (Column 3, 60°): 2.1 and 2.9, ratio 1.3:1, respectively Z/E). - IR(film): 1660(C=C). - ^{1}H NMR: 0.19(9H, s, $SiMe_3$), 0.94 and 0.96 (6H, both d, J8, $CHMe_2$), 2.20 and 2.77(1H, both m, respectively[147] E, Z, $CHMe_2$), 4.32 and 4.93(1H, both dd, J8,7 and 12,8, respectivley Z and E, HC=CHOSiMe$_3$), 6.0 and 6.16(1H, both d, J7 and 12, respectively Z and E HC=CHOSiMe$_3$).

3-Chloro-3-methyl-butyne (21). - 2-Methyl-3-butyn-2-ol(336g, 4mol) was added dropwise over 1.5h to a stirred mixture of calcium chloride (444g, 4mol) and concentrated hydrochloric acid (1.78l) at 0^{o} (ice-water). The mixture was allowed to warm to room temperature (RT) with stirring over 2h. The upper green organic layer was separated of, shaken with anhydrous potassium carbonate (green colour removed) and dried over fresh potassium carbonate until HCl could not be detected . Failure to ensure that no HCl remained resulted in poor yields with the distillate fuming in moist air. Fractionation (30cm Dufton column) gave pure chloroyne (21), as a colourless mobile oil (191.7g, 47%), b.p. 75-77^{o}. (Lit.[148], 75.5-75.6^{o}) - $\underline{N}_{D}^{19}$ 1.4203. (Lit.[148], $\underline{N}_{D}^{25}$ 1.4145). - IR(film): 3295(C≡CH), 2130(C≡C), 785. - ^{1}H NMR: 1.91(6H, s, Me_2), 2.68(1H, s, C≡CH). The chloroyne could be stored under nitrogen at 0^{o} without apparent decomposition.

2-Acetoxy-2-methyl-3-butyne. - By the method of Saucy et al.[149] a solution of 2-methyl-3-butyn-2-ol (20g, 0.238mol), acetic anhydride (27g, 0.256mol) and orthophosphoric acid (0.2g) was stirred at 50-60^{o} for 1h, then 16h at RT, poured onto ice (200g) and extracted with petrol (3x40ml). The organic extracts were combined, washed with water (x5) and dried (Na_2SO_4).

Removal of solvent at atmospheric pressure (10cm Vigreux column) and fractionation at the residue (10cm Vigreux column) under reduced pressure gave the acetate as a colourless mobile oil (18.47g, 62%), b.p. 72-73°/85 Torr. (Lit.[149], 75-76°/100 Torr). - $\underline{N}_D^{22}$ 1.4178. (Lit.[149], $\underline{N}_D^{21}$ 1.4164). - IR(film): 3290, 2130, 1735(ester), 1250, 1140 - ^{1}H NMR: 1.70(6H, s, Me_2), 2.04(3H, s, $OCOCH_3$), 2.56(1H, s, C≡CH).

General Procedure for the Synthesis of Alkenylidene - Cyclopropanes. - A method adapted from that of Sasaki et al.[18] was used. To a mechanically stirred and cooled (ice-water) mixture of sodium hydroxide solution (50% w/w, 100g), benzene (10ml), Aliquat 336(1.6g, ca. 4mmol*), and an appropriate olefin (0.1-0.3mol) under nitrogen, was added a solution of freshly distilled 3-chloro-3-methly-1-butyne (10.3g, 0.1mol) in benzene (20ml) over 2h. After the addition was complete the mixture was stirred for a further 15-24h at RT, diluted with brine (300ml), the phases separated, and the aqueous phase extracted with ether or petrol (3x50ml). The combined organic extracts were washed with brine (x3), dried (Na_2SO_4) and evaporated to afford crude adduct, which was purified by distillation under reduced pressure.

Use of pentane or toluene as cosolvent gave comparable yields of adducts. With the exception of cyclopropane (58) all the cyclopropanes prepared by this procedure were isolated as colourless or slightly discoloured mobile oils.

1,1,2,2-Tetramethyl-3-(2-methyl-1-propenylidene)cyclopropane (58). - By the general procedure, 2,3-dimethyl-2-butene afforded

* Based on $C_{25}H_{54}ClN$

the cyclopropane (58), as long colourless needles (67%), m.p. 55-57°(Lit.[12], 48.6-49.3°). - b.p. 63-65°/24 Torr. (Lit.[12], 80°/55 Torr). - IR($CHCl_3$): 2020(allene). ^1H NMR: 1.25(12H, s, cyclopropyl Mex4), 1.76(6H, s, allene Me_2).

[2-(2-Methyl-1-propenylidene)cyclopropyl]benzene (17). - Styrene afforded the cyclopropane (17) (54%), b.p. 54-56°/0.1 Torr. (Lit.[12], 78-80°/0.5 Torr). - N_D^{19} 1.5751. (Lit.[12], N_D^{25} 1.5717-1.5722). - GC(Column 1, 150°): 9.7. - IR(film): 2030(allene), 1600, 965, 760. - ^1H NMR: 1.51 and 1.99(2H, m, AB of cyclopropyl ABX, respectively cis- and trans-H), 1.83(6H, s, allene Me_2), 2.86(1H, dd, J9, 5 CH Ph), 7.29(5H, m, phenyl H). - ^{13}C NMR (25.15MHz): 17.1(t, C-3), 21.0(q, C-3'), 21.3(q, C-3'), 23.5(d, C-1), 81.7(s, C-2), 99.4(s, C-2'), 125.9(d, C-2"), 126.3(d, C-4"), 128.2(d, C-3"), 141.5(s, C-1"), 187.2(s, C-1').

1-Ethenyl-1-methyl-2-(2-methyl-1-propenylidene)cyclopropane (25) and 1-(1-Methylethenyl-2-(2-methyl-1-propenylidene)-cyclopropane (26). - Isoprene afforded the cyclopropanes (25) and (26) (31%), b.p. 60-62°/13 Torr. (Lit.,[18] 68-72°/22 Torr). - N_D^{20} 1.5068(Lit.[18], N_D^{24} 1.5074). - GC(Column 1, 100°): 8.7 and 18.5, ratio 9:1. - IR(film): 2040, 1630, 995, 900. - ^1H NMR: 1.38(3H, s, cyclopropyl Me), 1.55(2H, s, CH_2), 1.80(6H, s, allene Me_2), 4.78-5.16(2H, m, AB of ABX, $CH=CH_2$+ other minor isomer), 5.73(1H, dd, J18, 8, X of ABX, $CH=CH_2$).

1,1-Dimethyl-2-(3-hydroxy-3-methyl-4-pentynyl)-3-(2-methyl-1-propenylidene)cyclopropane (42). - Dehydrolinalool afforded the cyclopropane (42) (46%), b.p. 114°/2 Torr. - $\underline{N}^{24}_{D}$ 1.4998. - GC(Column 1, 160°): 11.1. - IR(film): 3370 br(OH), 3300(C≡CH), 2970, 2920, 2860, 2120w(C≡C), 2000 (allene), 1450, 1370, 1265, 1120, 1090, 915. - ^{1}H NMR: 1.21 and 1.23(6H, both s, cyclopropyl Me_2), 1.48(3H, s, CH_3), 1.74(6H, s, allene Me_2), 2.38(1H, br s, OH, removed on D_2O exchange) 2.41(1H, s, C≡CH), 0.8-2.0(5H, m, $(CH_2)_2CH$). - MS: 218(2, M), 213(14, M, CH_3), 121(35), 119(83), 91(100), 77(46),. (Found: $\underline{M}^{+}$, 218.1682. $C_{15}H_{22}O$ requires $\underline{M}$ 218.1671).

1-Ethynyl-1-methyl-2-(2-methyl-1-propenylidene)cyclopropane (35). - 2-methyl-1-buten-3-yne afforded the cyclopropane (35) (18%), b.p. 56-58°/17 Torr. (Lit.[31], 55-56.5°/18 Torr). $\underline{N}^{14}_{D}$ 1.5133. - GC(Column 1, 150°): 3.7. - IR(film): 3295, 2115, 2025. - ^{1}H NMR: 1.48(3H, s, CH_3), 1.81 and 1.85(6H, both s, allene Me_2), 1.52 and 1.89(2H, ABq, $\underline{J}$7, cyclopropyl CH_2), 2.02(1H, s, C≡CH). Preparation using the anhydrous crown ether - catalysed method gave a 28% yield of (35).

6-(2-Methyl-1-propenylidene)bicyclo[3.1.0.]hexane (27). - Cyclopentene afforded the cyclopropane (27) (27%), b.p. 76-80°/9 Torr. (Lit.[17], 140-145°/105 Torr). - GC(Column 1, 110°) 4.4. - IR(film): 2025(allene), 1995(allene). - ^{1}H NMR: 0.71-2.12(8H, m, $(CH_2)_2$ +cyclopropyl Hx2), 1.77(6H, s, allene Me_2).

7-(2-Methyl-1-propenylidene)bicyclo[4.1.0]heptane (28). - Cyclohexene afforded the cyclopropane (28) (10%), b.p. 92-96°/19Torr. (Lit.[12], 84-87°/15 Torr). - $\underline{N}^{16}_{D}$ 1.5217. (Lit.[12], $\underline{N}^{25}_{D}$ 1.5215-1.5218. - GC(Column 1, 120°): 4.6. - IR(film): 2040(allene), 1995(allene). - ^{1}H NMR: 1.0-2.1 (10H, m, $(CH_2)_4$ +cyclopropyl Hx2), 1.76 and 1.78(6H, both allene Me_2).

1-Methyl-7-(2-methyl-1-propenylidene)bicyclo[4.1.0] heptane (29). - 1-Methylcyclohexene afforded the cyclopropane (29) (46%), b.p. 92-94°/17 Torr. (Lit.[51], 84°/21 Torr). - $\underline{N}^{22}_{D}$ 1.5117. (Lit[51], $\underline{N}^{21}_{D}$ 1.5100). - GC(Column 1, 100°): 10.0. - IR(film): 2030 (allene), 2000 (allene), - ^{1}H NMR: 1.24(3H, s, cyclopropyl Me), 1.79(6H, s, allene Me_2), 0.8-2.0(9H, m, $(CH_2)_4$ + cyclopropyl H).

1-Methyl-7-(2-methyl-1-propenylidene)spiro[2.5]octane (30). - Methylenecyclohexane afforded the cyclopropane (30) (23%), b.p. 89-90°/16Torr. - $\underline{N}^{20}_{D}$ 1.5116. - GC(Column 1, 100°): 7.2. - IR (film): 3040, 2920, 2850, 2040 (allene), 1450, 1370, 1360, 1350, 1095, 1010, 920, 725. - ^{1}H NMR: 1.26(2H, s, cyclopropyl CH_2), 1.51(10H, br s, $(CH_2)_5$, 1.78(6H, s, allene Me_2). - MS: 162(27, M), 147(14, M-CH_3), 91(38), 80(100, C_6H_8), 79(43). (Found: $\underline{M}^{+}$, 162.1414. $C_{12}H_{18}$ requires $\underline{M}$, 162.1408).

(-)-(1R, 2S)-Trimethyl-3-(2-methyl-1-propenylidene)-tricyclo[4.1.1.$O^{2,4}$]octane (33). -(-) 1- α-Pinene afforded the cyclopropane (33) (26%), b.p. 52-54°/0.03 Torr. (Lit.[18], 62-65°/2.0 Torr). $\underline{N}^{22}_{D}$ 1.5210 (Lit.[18], $\underline{N}^{25}_{D}$ 1.5236). - $[\alpha]^{21}_{D}$ - 70.9° ($CHCl_3$, C 2.0). - GC(Column 2, 200°): 4.5; (Column 1, 130°): 7.1. - IR(film): 2020, 1445, 1375, 1365. - ^{1}H NMR: 1.03(3H, s, cyclopropyl Me), 1.26 and 1.29 (6H, both s, cyclobutane Me_2), 1.77 and 1.79/6H, both s, allene Me_2), 1.35-2.42

(7H, m, other H). - ^{13}C NMR(25.15 MHz): 21.1, 21.4, 23.3, 23.6, 27.1, 29.1, 30.1, 39.3(s, C-8), 41.5(d, C-6), 44.8(d, C-1), 91.9(s, C-3), 97.2(s, C-2'), 185.3(s, C-1').

(+)-(1R,2S)-6,6-Dimethyl-2'-(2-methyl-1-propenylidene)spiro-bicyclo[3.1.1]heptane-2,1'-cyclopropane (34). - (-)-β-Pinene afforded the cyclopropane (34) (36%), b.p. 53-57°/0.13 Torr (Lit.,[18] 55-57°/0.2 Torr). - $\underline{N}_D^{18}$ 1.5237. (Lit.,[18] $\underline{N}_D^{24}$ 1.5247). - $[\alpha]_D^{21}$ +106.5°($CHCl_3$, C2.0). - GC(Column 1, 130°, 60ml/min): 6.3. - IR(film): 2020. - ^1H NMR: 1.00(3H, s, exo-Me), 1.22(3H, s, endo-Me), 1.24-2.42(8H, m, $(CH_2)_2$+cyclobutane Hx4), 1.37(2H, d, J2.5, cyclopropyl CH_2), 1.74 and 1.78(6H, both s, allene Me_2). - ^{13}C NMR (24.14MHz): 21.5, 22.8, 24.0, 25.7, 26.4, 27.0, 28.8(s, C-2), 40.5(d, C-5), 41.1(s, C-6), 50.1(d, C-1), 84.9(s, C-2'), 97.4(s, C-5'), 185.7(s, C-4').

1-Methyl-4-(1-methylethenyl)-7-(2-methyl-1-propenylidene)bicyclo 4.1.0 heptane (39) and 1-methyl-4-[1-methyl-2-(2-methyl-1-propenylidene)cycloprop-1-yl]cyclohexene (40). - (+)-Limonene afforded the cyclopropanes (39) and (40) (57%), b.p. 54.5-59.5°/0.03 Torr. - $\underline{N}_D^{21}$ 1.5105-1.146. - GC(Column 1, 140°): 6.3, 6.7 and 9.7, ratio 53:28:19; the last peak appears to consist of two components. - IR(film):2970, 2920, 2850, 2010(allene), 1640(C=C), 1440, 1370, 890, - ^1H NMR: 1.06, 1.08, 1.12 and 1.16(3H, each s, cyclopropyl CH_3), 1.67(6H, s, allene Me_2), 4.56(m, $C=CH_2$), 5.24(br s, C=CH), 0.9-2.1(8H, m, other H). - MS:: 202(4, M), 187(4, CH_3), 44(100), 41(80). (Found: $\underline{M}^+$, 202. 1740.$C_{15}H_{22}$ requires M, 202.1721).

6-(2-Methyl-1-propenylidene)-2-oxabicyclo[3.1.0]hexane (31). - 2,3-Dihydrofuran afforded the cyclopropane (31)(51%), b.p. 96-97°/22 Torr. - n_D^{21} 1.5269. - GC(Column 1, 120°): 8.8. - IR(film): 2975, 2935, 2010 (allene), 1450, 1430, 1075(C-O), 960, 855. - ^{1}H NMR: 1.42-2.40(3H, m, CH_2+ cyclopropyl H), 1.78(6H, s, allene Me_2), 3.29-3.66 and 3.84-4.09 (each 1H, m, OCH_2), 4.33(1H, d, J 6, OCH). - MS: 136(72, M), 121(38, M-CH_3), 91(100, M-C_3H_7), 79(74), 77(85). (Found: M^+, 136.0902. $C_9H_{12}O$ requires M, 136.0888).

7-(2-methyl-1-propenylidene)-2-oxabicyclo[4.1.0] hexane (32). - 2,3-Dihydropyran afforded the cyclopropane (32) (33%), b.p. 93-94°/16 Torr (Lit.[19], 65-66°/11 Torr). - n_D^{19} 1.5283 (Lit.[19], n_D^{19} 1.5312). - GC(Column 1, 130°): 7.9. - IR(film): 2010, 1435, 1090, 765.- ^{1}H NMR: 1.78 and 1.82(6H, both s, allene Me_2), 1.12-2.20(5H, M, $(CH_2)_2CH$), 3.25-3.76(2H, m, OCH_2), 4.05(1H, d, J 7, OCH). -^{13}C NMR(25.15 MH_z): 18.9(d, C-6), 20.6(t, C-5), 21.1(q, C-3'), 22.1(t, C-4), 53.8(d, C-1), 64.0(t, C-3), 81.8(s, C-7), 97.8(C-2'), 187.6(s, C-1').

Attempted Generation of Alkenylidenecyclopropanes using a Liquid - Solid Two Phase System. - Using a method adapted from Makosza et al.[58], to a mechanically stirred mixture of cyclohexene (12.3g, 0.15mol), powdered anhydrous potassium carbonate (16.56g, 0.12mol) and dicyclohexyl 18-crown-6 (0.37g, 1.0mmol) under N_2 was added chloroyne (21)(10.25g, 0.1mol). The resulting mixture was heated to 70° for 19h, cooled and diluted with water (100ml). The phases were separated and the aqueous portion extracted with ether (3 x 20ml) and dried. Evaporation gave an orange oil (0.6g) which was

chromatographed on silica gel (40g, 1.8 x 28cm) using hexane to give alkenylidenecyclopropane (28)(0.2g, 1.4%), having identical (IR and ^{1}H NMR) spectral data to that obtained previously using the aqueous PTC method.

Reaction of 3-Methyl-1-trimethylsiloxy-1-butene (43) with Dimethylallene Carbene. - Using the crown ether catalysed conditions of Sasaki et al.[19], to a stirred slurry of enol ether (43) (2.19g, 13.9mmol), powdered potassium hydroxide (2.2g, 44mmol), 18-crown-6(0.15g, 0.57mmol) and dry petrol (5ml) at 0° under N_2 was added dropwise a solution of chloroyne (21) (1.42g, 13.9mmol) in dry petrol (15ml) over 1Ih After stirring for 17h, at RT the reaction mixture was diluted with petrol (15ml) and filtered through a Kieselguhr pad with generous ether washings. Evaporation of the filtrate gave a brown viscous oil (2.22g), shown by IR and ^{1}H NMR to consist mainly of unreacted enol ether. No vinyl methyl or aldehyde proton signals were observable in the crude product.

Attempted Reaction of Dimethylallene Carbene with Electrophilic Olefins

A Anhydrous Conditions

By the method of Sasaki et al.[19], to a stirred mixture of citral (2.22g, 14.6mmol), powdered potassium hydroxide (2.5g, 44.6 mmol), dicyclohexyl-18-crown-6 (0.25g, 0.67mmol) and dry petrol (4ml) at 0° under N_2 was added dropwise over 2h chloroyne (21) (1.5g, 14.6mmol) in dry petrol (3ml). After stirring for a further 15h at RT the resulting oily residue was filtered through alumina with generous ether wastings. Evaporation of

the filtrate gave a residue which was taken up in ether and insoluble material filtered off. Evaporation gave a viscous orange oil shown by TLC (silica./benzene and chloroform) to be a complex mixture ($\geqslant 9$ components). IR and ^{1}H NMR spectra suggest that mainly aldol type products had resulted.

B Hydrolytic Conditions:

Under the normal aqueous PTC conditions and employing one mole equivalent of olefinic substrate, the following results were obtained:- Mesityl oxide reacted mainly to give aldol type products as suggested by IR and ^{1}H NMR analysis. (+)-Pulegone did give some allenic material as evidenced from the IR spectrum, however TLC showed a complex mixture of products. The reaction with (-)-carvone gave two major products as shown by GC(Column 1, 170°): 12.5, 19.5 in addition to unreacted starting material. The IR spectrum showed a weak allene absorption at 2020cm^{-1} along with carbonyls at 1705 and 1670cm^{-1} while ^{1}H NMR analysis of the methyl signals suggested that some addition to the enone double bond had occurred. Attempts to obtain pure material by distillation met with failure. Reaction with geranyl nitrile (E,Z-mixture) gave two products as shown by GC(Column 1, 150°): 20.4, 22.2 (1:1.8). However, these could not be separated by chromatography on Kieselgel G using petrol-ether (96:4 - 9:1). The IR spectrum of the mixture showed a strong allene absorption, the complexity of the olefinic region in the ^{1}H NMR spectrum, precluded any conclusions concerning the regioselectivity of addition.

3,7-Dimethyl-6-octen-1-yn-3-ol (Dehydrolinalool)(41). - Acetone - free acetylene was passed through a stirred suspension of sodium amide- prepared from sodium (79g, 3.43 gatom) and ferric nitrate (0.2g) - in liquid ammonia (2l) until a uniform black colouration, of sodium acetylide,[150] had formed (ca. 4h). 6-Methyl-5-hepten-2-one (214g, 1.7mol) in dry ether (300ml) was added over 1.5h with the continued passage of a slow stream of acetylene. After the addition was complete the acetylene flow was stopped and the reaction mixture was stirred for a further 4h. Solid ammonium chloride (195g, 3.64mmol) was cautiously added and the ammonia was allowed to evaporate overnight with continued stirring. The residue was diluted with water (300ml), the phases separated, and the aqueous phase extracted with ether (4x100ml). The organic extracts were combined, washed with brine (xl), dried (K_2CO_3) and evaporated to leave an orange oil (238g). GC(Column 1, 110°) indicated that some ketone was still present. An attempt to remove unreacted ketone by shaking an ethereal solution of the crude reaction product overnight with an equal volume of saturated sodium bisulphite met with little success. Distillation under reduced pressure (15cm Vigreux column) gave the ethynyl carbinol (41) (178g, 69%) as a pungent colourless mobile oil, b.p. 92-95°/21 Torr. (Lit.[151], 81-82°/Torr). $\underline{N}^{22}_D$ 1.4612-1.4622. (Lit.[151], $\underline{N}^{20}_D$ 1.4634). - GC(Column 1, 160°): 3.8- IR(film): 3360 br(OH), 3295(C≡CH), 2120(C≡C). - ^{1}H NMR 1.49(3H, s, CH_3), 1.64(3H, s, C=CMe-Z), 1.69(3H, s, C=CMe-E), 0.71-2.42(4H, m, CH_2CH_2), 2.45(1H, s, C≡CH), 2.94(1H, s, OH, removed on D_2O exchange, 5.12(1H, m, C=CH). - ^{13}C NMR(25.15MHz): 17.7(q, C-8-Z), 23.6(t, C-5), 25.6(q, C-8-E), 29.8(q, CH_3),

43.3(t, C-4), 68.1(s, C-2), 71.3(d, C-1), 87.7(s, C-3), 123.7(d, C-6), 132.2(s, C-7). Preparation using 1.1 mole equivalents of lithium acetylide[150] gave a similar yield.

3-Acetoxy-3,7-dimethyl-6-octen-1-yne. - By the method of Hofle et al.[152], a mixture of dehydrolinalool (41) (1.52g, 10mmol), triethylamine (1.52g, 15mmol), acetic anhydride (1.64g, 15mmol), and 4-dimethylaminopyridine (DMAP) (80mg, 0.66mmol) was stirred for 18h at RT. The resulting solution was partioned between ether (20ml) and 2M hydrochloric acid (20ml). The organic phase was washed with saturated sodium carbonate (2x20ml), dried and evaporated to leave a yellow oil (1.90g). Chromatography on silica gel (70g, 2.5x27cm), eluting with benzene gave the acetate[149] (1.79g, 92%) as a pungent colourless mobile oil, IR (film): 3280, 2140w, 1730(ester), 1225. - ^{1}H NMR: 1.62(3H, s, C=CMe-Z), 1.68(6H, s, Me+C=CMe - E), 2.01(3H, s, COMe), 1.4-2.3(4H, M, CH_2CH_2), 2.53(1H, s, C≡CH), 5.06(1H, m, C=CH), MS:134(41), 119(93), 105(100), 91(63), 77(76), 41(65).

Reaction using excess acetic anhydride in pyridine[153] at RT gave only a poor (23%) yield of the acetate. The best procedure appears to be that of Saucy et al.,[149] employing phosphoric acid as catalyst.

3-Benzoyl-3,7-dimethyl-6-octen-1-yne. - By the method of Steglich and Neises,[154] to a stirred solution of benzoic acid (1.22g, 10mmol) in dry dichloromethane (10ml) was added dehydrolinalool (41) (1.52g, 10mmol) and DMAP (60mg, 0.49mmol). The resulting solution was cooled to 0°and dicyclohexylcarbodiimide (DCC) was added in one portion. The reaction mixture was then stirred at 0°for 5 min and 24h at RT. Precipitated urea was

filtered off and the filtrate evaporated to leave an oil containing a little precipitated urea. The residue was taken up in dichloromethane and filtered free of urea, this procedure was repeated until the residue was obtained free from solid. Chromatography on Kieselgel G(100g, 3 x 21cm), eluting with benzene gave a colourless oil (1.44g). Distillation gave the benzoate (1.22g, 48%) as a colourless viscous oil, b.p. 95-100° (oven)/0.02 Torr. - N_D^{13} 1.5171. - IR(film): 3290, 3050, 2970, 2920, 2850, 2140w, 1715(ester), 1450, 1375, 1370, 1275, 1100, 1065, 710. - ^{1}H NMR: 1.63(3H, s, C=CMe-Z), 1.69(3H, s, C=CMe-E), 1.84(3H, s, Me), 1.87-2.52 (4H, m, CH_2CH_2), 2.60(1H, s, C≡CH), 5.13(1H, m, C=CH), 7.42(3H, m, H-3'-5'), 8.02(2H, m, H-2',6'). - MS: M+ not observed, 152(7), 91(45), 69(31), 43(100). (Found:C, 79.37; H, 8.23%. $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.86%).

3-(4-Nitrobenzoyl)-3,7-dimethyl-6-octen-1-yne. - A solution of dehydrolinalool (41) (1.52g, 10mmol), triethylamine (1.1g, 11mmol), 4-nitrobenzoyl chloride (1.86g, 10mmol) and DMAP (0.1g, 0.82mmol) in dry dichloromethane (25ml) was stirred for 3 days at RT. The resulting dark red-brown solution which contained fine needles (presumably triethylamine hydrochloride) was diluted with water. The phases were separated and the organic phase was washed with 2M hydrochloric acid (x2), saturated sodium bicarbonate (x1), dried and evaporated to give a red-tinged solid. Dry column chromatography on silica gel (120g, 3.5x25cm) using dichloromethane gave an off-white solid (2.9g). Recrystallisation from ether-petrol after treatment with Norit gave the 4-nitrobenzoate (2.30g, 76%) as white irregular prisms, m.p. 77-78°. - IR(KBr): 3280, 2980, 2920, 2860, 2140w, 1715 (ester),

1605, 1530, 1445, 1350, 1290, 1115, 1110, 1080, 880, 850, 715, 690. - ^{1}H NMR: 1.64(3H, s, C=CMe-Z), 1.68(3H, s, C=CMe-E) 1.86(3H, s, Me), 1.2-2.4(4H, m, CH_2CH_2, 2.66(1H, s, C≡CH),5.16 (1H, m, C=CH), 8.08-8.34(4H, m, aryl H). - ^{13}C NMR (25.15 MHz): 17.6(q, C-8-Z), 23.2(t, C-5), 25.7(q, C-8-E), 26.4(q, Me), 21.5(t, C-4), 74.6(s), 76.7(s), 83.1(C-1), 123.2(d), 123.5(d), 130.6(d), 132.3(s), 136.3(s), 150.5(s), 162.6(s, C=O). - MS: 301(9, M), 150(98), 119(100), 69(53), 41(96). (Found: C, 67.70; H, 6.39; N, 4.62%; M^+, 301.1330. $C_{17}H_{19}NO_4$ requires C, 67.76; H, 6.36; N, 4.65; M, 301.1314).

Reaction using the DMAP-DCC coupling method[154] in DMF at 60° only gave poor yield (31%) of the ester.

Attempted Preparation of 3,Bromo-3,7-dimethyl-6-octen-1-yne. -

A Triphenylphosphine dibromide method:

By the method of Machinek and Luttke,[73] to a stirred suspension of triphenylphosphine dibromide; prepared in situ from triphenylphosphine (1.73g, 16.6mmol) and bromine (1.05g, 6.6ml), in dry acetonitrile (9ml) at RT under N_2 was added a solution of the alcohol (41) (1.0g, 6.6mmol) in dry acetonitrile (4ml), dropwise over 15 min. The reaction mixture was stirred for 3h at RT (TLC indicated very little reaction) and at 55° for 24h. On cooling precipitated solid was filtered off and thoroughly washed with ether. Evaporation of the filtrate gave a yellow oil (0.79g), shown by ^{1}H NMR and IR analysis to consist mainly of tetrahydropyranyl ether (51).

B Bromotrimethylsilane method:

By the method of Jung and Hatfield,[75] alcohol (41) (15mg, 0.1mmol) was added to a solution of bromotrimethylsilane (31mg, 0.2mmol) in deuterochloroform (0.35ml) in a NMR tube imparting a pink colouration which rapidly darkened to purple. After ten minutes ^{1}H NMR analysis showed only the formation of tetrahydropyranyl ether (51).

Attempted Preparation of 3-Chloro-3,7-dimethyl-6-octen-1-yne. - By the method of Lee and Nolan.[76] - To a solution of triphenylphosphine (1.73g, 6.6mmol) in dry tetrachloromethane (15ml) was added the alcohol (41) (1.0g, 6.6mmol). The resulting solution was heated to reflux for 19h under N_2. On cooling precipitated solids were filtered off and washed with ether. Evaporation of the filtrate gave a residue which was taken up in ether and filtered to remove residual solid. This process was further repeated to leave an oil. TLC (hexane and chloroform) showed apart from starting material (alcohol) two higher R_f components. Dry column chromatography on silica gel (2x25cm) using hexane gave a pale yellow mobile oil (0.55g). IR examination showed olefinic, acetylenic and weak allenic absorptions but no C-Cl absorptions. ^{1}H NMR analysis indicated the presence of acetylenic, vinyl methyl and olefinic protons. GC showed a mixture of five components GC(Column 1, 90°): 5.8, 6.9, 9.8, 20.1, 22.5 (34:30:15:17.4).

Attempted Preparation of Tosylate of Alcohol (41). - A solution of the alcohol (41), (1.52g, 10mmol), tosyl chloride (1.91g, 10mmol) and DMAP (40mg, 0.33mmol) in dry pyridine (25ml) was stirred for ten days, poured into brine (100ml) and extracted

with ether (3x20ml). The combined organic extracts were washed with 2M sulphuric acid (x1), saturated sodium bicarbonate (x2), water (x1), dried and evaporated to leave an orange oil (1.81g). TLC, ^{1}H NMR, and IR analysis of this oil showed it be mainly unreacted alcohol (41).

Attempted Generation of C_{10}-Alkenylidene Carbenes from Dehydrolinalool Esters

A Anhydrous Conditions:

To a stirred slurry of potassium t-butoxide (0.7g, 6.25mmol) and styrene (2.0g, 19.2mmol) in dry THF (30ml) at 0° under N_2 was added dehydrolinalool acetate (0.8g, 4.12mmol) in dry THF (5ml). After 1.5h the resulting brown mixture was poured into water (100ml) and extracted with ether (4x15ml). The organic extracts were combined, dried and evaporated to leave an orange oil (1.37g) which was chromatographed on silica gel (3x25cm) using petrol then chloroform to give dehydrolinalool (41) (0.33g, 52%) as the only isolable product.

B Aqueous Conditions:

Using the normal aqueous PTC conditions, acetate (53, X=OAc) (1.0g, 5.15mmol) was added to a mixture of styrene (1.6g, 15.4mmol), Aliquat 336 (0.14g, 0.35mmol) and aqueous sodium hydroxide (50% w/w, 50g) at 0°. After stirring at RT for 24h, the usual work up gave a brown oil (1.3g). Excess styrene was removed under reduced pressure on the Rotavapor at 50°, and the residue chromatographed on silica gel (80g, 3x22cm) using petrol-ether (9:1 - 4:1) to give recovered styrene (0.32g) and

and dehydrolinalool (0.59g, 76%).

6-Methyl-2-heptanone (55). - A solution of 6-methyl-5-hepten-2-one (20.3g, 0.16mol) in ethyl acetate (80ml) was hydrogenated over platinum dioxide hydrate (Adam's catalyst) (0.15g) at atmospheric pressure and RT until hydrogen uptake ceased. The catalyst was filtered off using Kieselguhr and the filtrate evaporated and distilled to afford the ketone (55) (15.42g, 75%) as a colourless mobile oil, b.p. 66.5-67°/14 Torr. (Lit.[155], 61-62°/16Torr). - $\underline{N}_D^{23}$ 1.4115. (Lit.[155], $\underline{N}_D^{25}$ 1.4114). - GC(Column 1, 160°):1.2. - IR(film): 1715(ketone). - ^{1}H NMR: 0.86(6H, d, J7, $CHMe_2$), 0.96-1.72(5H, m, $(CH_2)_2CH$), 2.09 (3H, s, COMe), 2.36(2H, t, J7, $COCH_2$).

3,7-Dimethyloctan-1-yn-3-ol. - Using a similar procedure to that used for ethynyl carbinol (41), a solution of 6-methyl-2-heptenone (15.25g, 0.119mol) in dry ether (40ml) was added over 1h to a solution of sodium acetylide (prepared from sodium - 3.3g, 0.143gatom) in liquid ammonia (250ml). The reaction mixture was stirred for a further 2h then worked up as before to give an almost colourless oil (17.06g). Distillation under reduced pressure afforded the ethynyl carbinol (12.87g, 70%), as a pungent colourless mobile oil, b.p. 91-92°/23 Torr. (Lit.[155], 83°/10 Torr). - $\underline{N}_D^{22}$ 1.4382 (Lit.[155], $\underline{N}_D^{25}$ 1.4384). - GC(Column 1, 160°): 2.6, (Column 3, 140°): 7.3. - IR (film): 3400 br (OH), 3300 (C≡CH). - ^{1}H NMR: 0.89 (6H, d, J7, $CHMe_2$), 1.03-1.79(7H, m, $(CH_2)_3CH$), 1.47(3H, s, Me), 2.40(1H,s, C≡CH), 2.72(1H, s, OH, removed on D_2O exchange).

3-Chloro-3,7-dimethyl-1-octyne(56). - By the method of Hennion and Boiselle,[157] to a stirred mixture of calcium chloride (3.24g, 32.7mmol), copper bronze powder (50mg) and concentrated hydrochloric acid (40ml, 0.33mol) at 0^{o} was added 3,7-dimethyloctan-1-yn-3-ol (12.58g, 81.7mmol) dropwise over 0.5h After stirring for a further 2h at 0^{o} the upper organic layer was separated off, washed with concentrated hydrochloric acid (2x20ml), water (3x20ml) and dried (K_2CO_3). Distillation under reduced pressure from a small amount of fresh potassium carbonate gave the chloroyne (56) contaminated with a small amount of chloroallene (9.06g, 64%) as a colourless mobile oil, b.p. $80-93^{o}$/20 Torr. - N_D^{21} 1.4418-1.4438. Chromatography on Kieselgel G (160g) eluting with petrol, gave in order of elution: chloroallene (56a)(0.57g, 4%), mixed fractions (2.35g, 17%) and chloroyne (56) (3.65g, 26%). Attempted GC(Column 3, 150^{o}) analysis led to decomposition. 1-Chloro-3,7-dimethyl-1,2-octadiene (56a) an unstable colourless mobile oil had:- TLC (hexane): R_f 0.64. - IR(film): 2950, 2925, 2870, 1955 (allene), 1465, 1385, 1210, 780, 740, 720. - ^{1}H NMR: 0.90(6H, d, J7, $CHMe_2$), 1.03-1.72(5H, M, $(CH_2)_2CH$), 1.79(3H, d, J2, allene Me), 2.04(2H, t, J7, CH_2-C=C=C), 5.93(1H, m, C=C=CH). - MS: 136 (6), 89(10), 69(23), 43(88), 41(100), 39(43), M^+ not observed.

3-Chloro-3,7-dimethyl-1-octyne (56). - A colourless mobile oil had:- TLC (hexane): R_f 0.49. - IR (film): 3300, 2950, 2900, 2865, 2130w, 1465, 1440, 1380, 1365, 1135, 780. - ^{1}H NMR: 0.90(6H, d, J7, $CHMe_2$), 1.24(2H, t, J7, CH_2), 0.39-2.0 (5H, m, $(CH_2)_2CH$), 1.84(3H, s, Me), 2.61(1H, s, C≡CH). - MS: 149(9), 44(21), 32(> 100), M^+ not observed.

1.1.2.2-Tetramethyl-3-(2,6-dimethyl-1-heptenylidene)cyclopropane (57). - Using the general procedure for the preparation of alkenylidenecyclopropanes, 3-chloro-3,7-dimethyl-1-octyne (56) (1.73g), 10mmol) containing some chloroallene and 2,3-dimethyl-2-butene (2.53g, 30mmol) gave after work-up an orange mobile oil (2.21g). Dry column chromatography on silica gel (3.5x26cm) using pentane gave a colourless mobile oil (1.54g) which was distilled under reduced pressure to give the cyclopropane (57) (1.05g, 48%) as a colourless mobile oil, b.p. 80-90°(oven)/0.4 Torr. - GC (Column 1, 150°): 2.1. - IR(film): 2975, 2950, 2920, 2865, 2000 (allene), 1465, 1440, 1380, 1370, 1105, 920. - ^{1}H NMR: 0.87(6H, d, J7, $CHMe_2$), 1.23(12H, s, cyclopropyl Mex4), 1.72(3H, s, allene Me), 0.99-1.82(5H, m, $(CH_2)_2CH$), 1.92(2H, t, J7, $C=CCH_2$). - MS: 220(14, M), 205(5, M $-CH_3$), 136(91, M-C_6H_{12}), 121(58), 43(67), 41(100). (Found: M^+, 220.2203. $C_{16}H_{28}$ requires M, 220.2191).

Acid Catalysed Reaction of 7-(2-Methyl-1-Methyl-1-propenylidene)-bicyclo [4.1.0]heptane in Methanol. - Concentrated hydrochloric acid (0.7ml) was added to a stirred solution of the cyclopropane (28) (1.0g, 6.76mmol) in dry methanol (10ml). TLC (silica/hexane) showed the reaction to be essentially complete after six days. The reaction mixture was poured into brine (30ml) and extracted with ether (3x15ml). The combined ethereal extract were washed with saturated $NaHCO_3$ (x1), water (x1), dried and evaporated to give an orange oil (1.07g). GC(Column 1, 130°) showed four major components in the ratio 34:34:19.7, as a percentage of the volatiles. Chromatography on Alumina G (95g, 3x18cm) using hexane (100ml) followed by hexane-ether (98:2-40:60) gave in order of elution: - a mixture of hydrocarbon components (297mg), vinylcyclopropane (77) (260mg, 21%) and acetylene (78) (315mg, 26%). Repeated chromatography of the hydrocarbon fractions on silica using hexane gave a colourless mobile oil (140mg), homogeneous by TLC. However, GC(Column 1, 130°): 4.1, 5.8(1:6) showed two peaks. This mixture of hydrocarbon components had IR(film): 2940, 2850, 1765, 1450, 1005, 865, 840. - ^{1}H NMR: 1.19(d, J7, $CHMe_2$), 1.0-2.0(m, CH_2CH), 2.72(septet, J7, $CHMe_2$). - MS: 324(1), 309(10), 163(100). (Found: M^+, 325.2822. $C_{24}H_{36}$ requires M, 324.2817).

7-Methoxy-7(2-methyl-1-propenyl)bicyclo[4.1.0]heptane (77). - a colourless camphoraceous mobile oil had: TLC (benzene): R_f 0.45. - GC(Column 1, 100°): 7.4. - IR(film): 3000, 2970, 2930, 2855, 2810 (OMe), 1660(C=C), 1460, 1445, 1380, 1210, 1105 (C-O), 1010, 850. - ^{1}H NMR: 0.8-1.8(10H, m, $(CH_2)_4$ +cyclopropyl Hx2), 1.82(16H, s, $C=CMe_2$), 3.09(3H, s, OMe), 5.18(1H, s, C=CH).

- ^{13}C NMR (62.90MHz): 19.5(t, C-2*), 19.7(q, C-3'), 19.8(d, C-1), 21.6(t, C-3*), 25.4(C-3'), 53.6(q, OCH_3), 63.8(s, C-7), 117.6(d, C-1'), 141.9(s, C-2'). - MS: 180(47, M), 165 (100, M $-CH_3$), 133(20), 83(52), 55(64), 41(65). (Found: $\underline{M}^+$, 180.1506. $C_{12}H_{20}O$ requires $\underline{M}$, 180.1514).

1-Methoxy-2-(3-methyl-1-butynyl)cyclohexane (78), a colourless mobile oil had:- TLC (benzene): R_f: 0.39. - GC(Column 1, 100°): 9.7. - IR(film): 2940, 2870, 2830, 1450, 1365, 1320, 1185, 1145, 1125, 1100, 945. - ^1H NMR: 1.14(6H, d, J7, $CH\underline{Me}_2$), 1.1-2.1(8H, m, $(CH_2)_4$), 2.46(2H, m, $C\underline{H}C{\equiv}CC\underline{H}$), 3.10(1H, m, $C\underline{H}OMe$), 3.42 (3H, s, OMe). - ^{13}C NMR: 20.6(d, C-3'), 23.0(t), 23.5(q, C-4'), 23.7(t), 29.3(t), 30.3(t), 34.4(d, C-2), 57.1(q, OCH_3), 81.3(s, C-2'), 81.6(d, C-1), 87.3(s, C-1').- MS: 180(41, M), 165(41, M-CH_3), 137(100, M-C_3H_7), 105(85), 91(59), 41(96). (Found: $\underline{M}^+$ 180.1509. $C_{12}H_{20}O$ requires $\underline{M}$, 180.1514).

Reaction of 7-(2-Methyl-1-propenylidene)bicyclo[4.1.0] heptane (28) with $Et_2O.BF_3$ in Methanol. - Boron trifluoride etherate (0.4ml, 3.24mmol) was added to a stirred solution of the cyclopropane (28) (2.0g, 13.5mmol) in dry methanol (20ml). After 12 days the reaction mixture was poured into brine (80ml) and extracted with ether (3x30ml). The combined organic extracts were washed with saturated $NaHCO_3$ (x1), water (x1), dried and evaporated to give a pale yellow oil (2.53g). TLC (silica/benzene) showed the presence of two major methoxy components. Chromatography on silica gel using benzene gave recovered cyclopropane (28) (0.18g,

*Assignments interchangeable

9%) as shown by IR, ^{1}H NMR, TLC and GC. Subsequent fractions gave a mixture of methoxy components, shown by GC(Column 1, 100°) to be in the ratio 36:64. Chromatography on Alumina G (90g, 3x17cm) using hexane-ether (99:1) gave in order of elution:- vinylcyclopropane (77) (204mg, 8%) and acetylene (78) (672mg, 28%) identical (IR, ^{1}H NMR, TLC, GC) to those obtained from the acid catalysed reaction. Mixed fractions (379mg, 16%).

Reaction of 7-(2-Methyl-1-propenylidene)bicyclo[4.1.0]-heptane (28) with Wilkson's Catalyst [$Rh(PPh_2)_3Cl$] in Methanol. - Chlorotris(triphenylphosphine)rhodium (I) (0.02g, 0.02mmol) was added to a solution of the cyclopropane (28) (2.0g, 13.5mmol) in dry methanol (40ml), and the mixture heated to reflux, whereupon the catalyst dissolved imparting a brown colouration. After 18h at reflux GC(Column 2, 120°) showed very little reaction, so more catalyst (0.18g, 0.19mmol) was added. After a total of 64h at reflux the reaction mixture was cooled. Solid material (yellow crystals) was filtered off, the filtrate diluted with brine (150ml) and extracted with ether (4x30ml). The combined ethereal extracts were washed with dilute $NaHCO_3$ (x1), water (x2), dried and evaporated to leave a brown oil (1.9g), shown to be identical (IR, ^{1}H NMR, GC and TLC) with the starting cyclopropane (28).

Reaction of 7-(2-Methyl-1-propenylidene)bicyclo[4.1.0]heptane (28) with $RhCl_2.3H_3O$ in Methanol. - Rhodium trichloride trihydrate (0.02g, 0.076mmol) was added to a solution of the cyclopropane (28) (2.0g, 1.5mmol) in dry methanol (40ml) and the mixture heated to reflux causing the catalyst to dissolve giving an

orange colouration. After 35h at reflux the reaction mixture was cooled, poured into brine (150ml) and extracted with ether (4x30ml). The combined organic extracts were washed with dilute $NaHCO_3$ (x1), water (x1), dried and evaporated to leave a brown oil (2.56g). Chromatography on silica gel using benzene gave recovered cyclopropane (28) (1.25g, 63%) as a pale yellow mobile oil. Subsequent fractions gave a mixture of the two methoxy components (77) and (78), isolated previously, as a pale yellow-orange oil (0.66g, 27%), as shown by IR, ^1H NMR, and GC.

Reaction of 6-(2-Methyl-1-propenylidene)bicyclo[3.1.0]hexane (27) with $Et_2O.BF_3$ in Methanol. - Using the general procedure, cyclopropane (27) (1.0g, 7.46mmol) gave after ten days a brown oil (1.15g). TLC (silica/benzene) showed five components. GC (Column 2, 150°) showed two major components in the ratio 63:22, GC(Column 1, 100°) also showed two components, ratio 26:64 (as a percentage of the volatiles) - the order of elution being reversed on changing columns. Preliminary separation of the components was effected by chromatography on silica gel (25g, 2x19cm) using petrol (200ml) then petrol-ether (9:1) (300ml) to give high R_f (0.28g) and low R_f material (0.71g) respectively. Chromatography of the higher R_f material on silica gel (which led to some hydrolysis), then alumina, using hexane gave ketal (79) (0.18g, 12%). Chromatography of the lower R_f material on Alumina G(80g, 3x13cm) using hexane- ether (99:1 - 95:5) gave diene (80) (0.10g, 8%); separation from slightly higher R_f material proved troublesome.

6,6-Dimethoxy-7-(1-methylethyl)bicyclo[3.2.0]heptane (79), a colourless mobile oil, had: - TLC(benzene): R_f 0.43. - GC(Column 1, 120°): 4.1. - IR(film): 2950, 2870, 2830, 1460, 1440, 1380, 1360, 1220, 1150, 1050, 1035, 980, 920. - ^1H NMR: 0.82 and 0.97 (6H, both d, J7, $CH\underline{Me}_2$), 1.06-2.1(9H, M), 2.62(1H, t, J8, H-7), 3.10(6H, s, OMex2). - ^{13}C NMR(62.90MHz): 19.8(q, C-2'), 23.2(q, C-2'), 25.7(t), 26.7(t), 28.8(d, C-1'), 32.7(t), 36.8(d), 43.9(d), 47.5(q, OCH_3), 48.3(q, OCH_3), 56.1(d), 101.5(s, C-6). - MS: 198 (0.6, M), 166(24, M-CH_3OH), 151(73), 115(45), 84(51), 69(100, C_5H_9), 41(86). (Found: M^+, 198.1637. $C_{12}H_{22}O_2$ requires M, 198.1620).

6-Methoxy-1-(2-methyl-1-propenyl)cyclohexene (80), a colourless mobile oil had: - TLC(benzene): R_f 0.26. - GC(Column 1, 120°): 5.8. - UV(hexane): 233(11,100). - IR(film): 2970, 2930, 2860, 2820, 1645w, 1450, 1190, 1095, 1075, 950, 925. - ^{1}H NMR: 1.0-2.4(6H, m, $(CH_2)_3$), 1.79(6H, s, $C{=}CMe_2$), 3.33(3H, s, OMe), 3.61 (1H, m, CHOMe), 5.64(2H, m, HC=Cx2). - ^{13}C NMR(62.90MHz): 17.8(t), 19.6(q, C-3'), 25.7(t), 26.8, 26.9, 56.3(q, OMe), 77.2(d, C-6), 125.7(d), 129.0(d), 133.6(s), 135.7(s). - MS: 166(0.3, M), 134(37, M-CH_3OH), 119(43), 106(31), 91(100), 41(39). (Found: M^+, 166. 1333.$C_{11}H_{18}O$ requires M, 166,1357).

Acid Catalysed Reaction of 6-(2-Methyl-1-propenylidene)bicyclo-[3.1.0]hexane (27) in Methanol. - Using the general procedure, cyclopropane (27), (0.20g, 1.49mmol) gave after eight days a brown oil (0.24g), TLC(silica/benzene) showed the presence of five components. GC(Column 1, 100°) showed one major component (74%) of the volatiles); examination of the ^{1}H NMR and IR spectra of the crude product showed this to be the diene (80) isolated previously in the $Et_2O.BF_3$ catalysed reaction. The ^{1}H NMR spectrum also showed traces of ketal (79) and ketone (81).

7-(1-Methylethyl)bicyclo[3.2.0]heptan-6-one (81).[82] - To a stirred solution of the ketal (79) (50mg, 0.25mmol) in tetrahydrofuran-water (3:1 v/v) (2.5ml) was added 1M hydrochloric acid (0.15ml). After 4.5h, (TLC indicated that hydrolysis was complete within 1h), the resulting solution was quenched with saturated $NaHCO_3$ (10ml) and extracted with ether (3x5ml). The combined organic extracts were washed with brine (x1), dried (Na_2SO_4) and evaporated to yield essentially pure ketone. Chromatography on silica gel using petrol-ether (95:5) gave the ketone (81)

(39mg, 100%), as a colourless strongly camphoraceous mobile oil, TLC (benzene): R_f 0.28. - GC(Column 1, 120°): 3.7. - IR(film) 2950, 2870, 1770 (ketone), 1470, 1370, 1100, 1020, 810. - ^{1}H NMR: 0.87 and 0.94 (6H, both d, J 7, $CH\underline{Me}_2$), 1.03-2.12(7H, m), 2.31 and 2.55 (each 1H, each m, H-1 and 7), 3.50(1H, m, H-5). MS: 152(24, M), 84(82, C_5H_8O), 69(100, C_5H_9), 67(40), 41(46). (Found: $\underline{M}^+$, 152.1191. Calc. for $C_{10}H_{16}O$, 152.1201). The results of a ^{1}H NMR LIS study are recorded, in Chapter Three.

Reaction of 1-Methyl-7-(2-methyl-1-propenylidene)bicyclo-[4.1.0]heptane (29) with $Et_2O.BF_3$ in Methanol. - Using the general procedure, cyclopropane (29) (1.0g, 6.17mmol) gave after five days an orange oil (1.05g). TLC (silica/hexane and benzene) showed the presence of at least six components. GC(Column 1, 110°), (Column 2, 150°) showed two major components in the ratio 19:81 (Column 2). Initial separation was effected by chromatography on silica gel (25g, 2x18cm), initially using petrol to give hydrocarbon components (0.25g), followed by petrol-ether (9:1) to give methoxy components (0.63g). The hydrocarbon fractions were rechromatographed on Kieselgel G using pentane to give unreacted cyclopropane (29) (57mg, 6%) followed by enyne (82) (116mg, 12%). Chromatography of the methoxy components on Alumina G (90g, 3x15cm) using hexane-ether (99:1) gave acetylene (83) (299mg, 27%) and mixed fractions (268mg). Attempts to isolate other minor methoxy components by chromatography on Kieselgel G using hexane-ether were unsuccessful.

1-Methyl-6-(3-methyl-1-butynyl)cyclohexene (82), an unstable colourless mobile oil, had: - GC(Column 1, 110°): 4.9. - IR(film): 2970, 2920, 2860, 1450, 1390, 1325, 900, 805. - ^{1}H NMR: 1.13(6H, d, J7, $CH\underline{Me}_2$),1.3-2.1(6H, m, $(CH_2)_3$), 1.76(3H, br s, C=CMe), 2.48 (1H, m, $CH\underline{Me}_2$), 2.82(1H,br s, C=C$\underline{H}$ C≡C), 5.36(1H, m, C=CH). - MS: 162(24, M), 147(22, M-CH_3), 105(68), 91(100). Found: $\underline{M}^+$, 162.1420. $C_{12}H_{18}$requires $\underline{M}$, 162.1408).

1-Methoxy-1-methyl-2-(3-methyl-1-butynyl)cyclohexane (83), a colourless mobile oil, had: - GC(Column 1, 110°):9.1. -IR(film): 2970, 2925, 2880, 2820, 1460, 1440, 1365, 1320, 1180, 1170, 1130, 1110, 1085. - ^{1}H NMR: 1.15(6H, d, J7, $CH\underline{Me}_2$), 1.22(3H, s, C(OMe) $\underline{Me}$), 1.25-1.94(8H, m, $(CH_2)_4$),2.50(2H, m, CHC≡CCH), 3.17(3H, s, OMe). -MS: 194(14, M), 179(100, M-CH_3), 105(85), 85(56), 77(64), 55(63), 41(69). (Found: $\underline{M}^+$, 194.1688. $C_{13}H_{22}O$ requres $\underline{M}$, 194.1671).

Acid Catalysed Reaction of 1-Methyl-7-(2-methyl-1-propenylidene) bicyclo[4.1.0]heptane (29) in Methanol. - Using the general procedure, cyclopropane (29) (1.0g, 6.17mmol) gave after six days a yellow oil (1.14g). Examination of the crude product mixture (^{1}H NMR, IR, TLC and GC) showed that the composition was very similar to that obtained from the $Et_2O.BF_3$ catalysed reaction. TLC showed a few more components and GC(Column 2, 150°) showed that the two major components (82) and (83), isolated in the previous reaction, were present in the ratio 42:58.

Acid Catalysed Reaction of 1-(2-Methyl-1-propenylidene)spiro-[2.5]octane (30) in Methanol. - Using the general procedure, cyclopropane (30) (1.0g, 6.17mmol) gave after seven days an orange oil (1.09g). TLC (silica/hexane and benzene) showed at least eight components. GC (Column 1, 105°) showed ten components with two major components in the ratio 37:63(25 and 43% of the volatiles respectively). Chromatography on Kieselgel G (80g, 3x23cm) using hexane gave a mixture of hydrocarbon components (181mg) and enyne (84) (217mg, 22%). Further elution using hexane-ether (98:2 - 80:20) gave a mixture of methoxy components (708mg) which were rechromatographed on Alumina G (50g, 2x23cm) using hexane-ether (99:1) to give in order of elution: - vinylcyclopropane (85) (10mg, 1%), diene (86) - further purified by PLC (hexane-ether (98:2), two elutions); being the only band visible under UV light, λ = 254nm - (34mg, 3%) and acetylene (87) (200mg, 17%)

1-(4-Methyl-2-pentynyl)cyclohexene (84), a colourless mobile oil had: - GC(Column 1, 120°): 7.0. - IR(film): 2950, 2800, 2260w (acetylene), 1470, 1450, 1430, 1390, 1370, 1325, 1135, 930, 805. - ^{1}H NMR: 1.16(6H, d, J7, $CH\underline{Me}_2$), 1.59 and 1.97 (each 4H, each br s, $(CH_2)_2$ and allylic CH_2x2 respectively), 2.55(1H, m, $CH\underline{Me}_2$), 2.77 (2H, br s, $CH_2C{\equiv}C$); 5.64(1H, br s, C=CH). - ^{13}C NMR: 20.8, 22.6, 23.0, 23.5, 25.3(t), 27.43(t), 28.4(t), 76.5(s, C-3'), 88.2(s, C-2'), 121.9(d, C-2), 133.5(s, C-1). - MS: 162(51, M), 147(M-CH_3), 105(31), 81(74), 28(100). (Found: $\underline{M}^+$, 162.1419. $C_{12}H_{18}$ requires $\underline{M}$, 162.1408).

1-Methoxy-1-(2-methyl-1-propenyl)spiro[2.5]octane (85), a colourless mobile oil, had: - TLC (benzene): R_f 0.57. - GC(Column 1, 120°): 5.4. - IR(film): 2935, 2860, 1655w(C=C), 1450, 1380, 1225, 1205, 1180, 1130, 1070, 1050, 1030. - ^{1}H NMR: 0.28 and 0.57 (each 1H, ABq J 5, cyclopropyl CH_2), 1.72 and 1.77(6H, both s, $C=CMe_2$), 0.9-1.7(10H, m, $(CH_2)_5$), 3.15(3H, s, OMe), 5.19(1H, br s, C=CH). - MS: 194(M^+, not observed), 179(3, M-CH_3), 81(21), 71(28), 69(74), 57(100), 55(61), 43(100), 41(77). (Found: M^+-CH_3, 179.1439. $C_{12}H_{19}O$ requires M, 179.1436).

2-(1-Methoxycyclohexyl)-4-methyl-1,3-pentadiene (86), a slightly discoloured mobile oil, had: - TLC(benzene): R_f 0.50. - GC(Column 1, 120°): 9.8. - UV(hexane): 230(6, 500). - IR(film): 2940, 2870, 1660, 1625, 1450, 1145, 1080, 1050, 935, 910($C=CH_2$). - ^{1}H NMR: 1.75 and 1.78(6H, both s, $C=CCMe_2$), 0.9-1.9(10H, m, $(CH_2)_5$), 3.16(3H, s, OMe), 4.96(1H, br s, C=CHH), 5.15(1H, d, J2, C=CHH), 5.72(1H, br s, C=CH). - MS: 194(2, M), 113(100, M-C_6H_9) 32(24). (Found: M^+, 194.1683. $C_{13}H_{22}O$ requires M, 194.1671).

1-Methoxy-1-(4-methyl-2-pentynyl)cyclohexane (87), a colourless, mobile oil, had:- TLC(benzene): R_f 0.41 - GC(Column 1, 120°): 11.7. - IR(film): 2950, 2880, 1465, 1445, 1365, 1200, 1145, 1080, 930. - ^{1}H NMR: 1.14(6H, d, J7, $CHMe_2$), 1.2-1.8(10H, m, $(CH_2)_5$, 2.26(2H, d, J3, $CH_2C\equiv C$), 2.49(1H, m, $CHMe_2$), 3.17(3H, s, OMe). - ^{13}C NMR: 20.8(d, C-4'), 21.9(t), 23.5(q, C-5'), 25.9(t), 28.1(t), 33.1(t), 48.6(q, OCH_3) 74.8(s), 75.6(s), 88.2(s). - MS: 194(0.7, M), 113 (100, M-C_6H_9), 81(17, C_6H_9), 55(14), 41(29). (Found: M^+, 194.1670. $C_{13}H_{22}O$ requires M, 194.1671).

Reaction of 6,6-Dimethyl-2'-(2-methyl-1-propenylidene)spiro-bicyclo[3.1.1]heptane-2,1'-cyclopropane (34) with $Et_2O.BF_3$ in Methanol. - Using the general procedure, cyclopropane (34) (1.2g, 5.94mmol) gave after one day at RT and reflux for 4h a yellow oil (1.30g). TLC(silica/hexane and benzene) showed a very complex mixture consisting of at least nine components. GC(Column 1, 150°, 60ml/min) showed one major component and a complex mixture of presumed hydrocarbons. Chromatography on Kieselgel G(70g, 3x20cm) using hexane-ether (95:5) gave a methoxy component which was further purified by PLC to give (-)-(4S)-(1-Methoxy-1-methylethyl)-1-(4-methyl-2-pentynyl)cyclohexene (89) as a slightly discoloured unstable mobile oil (168mg, 12%). $[\alpha]_D^{23}$-66.8°($CHCl_3$, c 1.48). - GC(Column 1, 150°, 60ml/min); 16.4-IR(film): 2980, 2940, 2880, 2830, 1470, 1385, 1370, 1325, 1185, 1145, 1080. - ^1H NMR: 1.12(6H, s, $C(OMe)\underline{Me}_2$), 1.16(6H, d, J7, $CH\underline{Me}_2$), 1.3-2.2(7H, m, $(\underline{CH}_2)_3$+CH), 2.50(1H, m, $CH\underline{Me}_2$), 2.77(2H, br s, $C\underline{H}_2C{\equiv}C$), 3.16(3H, s, OMe), 5.63(1H, br s, C=CH). - ^{13}C NMR, 20.6, 21.9, 22.4, 23.5, 23.9, 26.8(t), 29.3(t), 41.8(d, C-4), 48.7(q, OCH_3), 76.4(s, $\underline{C}OMe$), 76.6(s, C-3'), 88.2(s, C-2'), 121.7(d, C-2), 133.5(s, C-1). - MS: 234(0.2, M), 202(20, M-CH_3OH), 73(100, $C(CH_3)_2OCH_3$), Found: $\underline{M}^+$, 234.2008. $C_{16}H_{26}O$ requires $\underline{M}$ 234.1984).

Reaction of 2,7,7-Trimethyl-2-(2-methyl-1-propenylidene)tricyclo[4.1.1.$O^{2,4}$] octane (33) with $Et_2O.BF_3$ in Methanol. - Using the general procedure, cyclopropane (33) (1.0g, 4.95mmol) gave after ten days a brown oil (1.1g). TLC(silica/pentane and benzene) showed a complex mixture of at least eight products. GC(Column 1, 130°) showed two major components in the ratio 81:19(58 and 14% of the volatiles respectively). Initial separation of

hydrocarbon and methoxy components was achieved by chromatography on silica gel (2.5x20cm) using hexane followed by hexane-ether (1:1) to give hydrocarbon components (145mg) and methoxy components (831mg). The methoxy components were rechromatographed on Alumina G(120g, 3.5x25cm) using hexane-ether (99:1) to give an unidentified triene (115mg, 10%) and enyne (90) (396mg, 34%) as the two major products.

Unidentified triene, a colourless mobile oil, had: - $[\alpha]_D^{24}$ + 2.5°($CHCl_3$, c 0.56). - TLC(Benzene): R_f 0.29. - GC (Column 1, 160°): 8.6. - UV(hexane): 223(14,800), 248(6,400), IR(film): 2970, 2920, 2830, 1640, 1465, 1440, 1380, 1360, 1180, 1145, 1080. - ^{1}H NMR: 1.12(6H, s, Me_2), 1.0-1.3(1H, m, CH), 1.73 (6H, s, C=CMe_2), 1.78(3H, s, C=CMe), 1.6-2.1(4H, m, allylic CH_2x2), 3.15(3H, s, OMe), 5.62-5.91(3H, m, C=CHx3). - ^{13}C NMR(62.90MHz): 19.1, 21.1, 23.1(q), 26.1, 27.6, 27.7, 48.6(q, OCH_3), 58.3, 125.0(d), 127.7(d), 130.1(d), 134.3(s), 138.4(s), 141.2(s). MS: 234(0.8, M), 202(2, M-CH_3OH), 73(100, $C(CH_3)_2OCH_3$). (Found: M^+, 234.1979. $C_{16}H_{26}O$ requires M, 234.1984).

(-)-(4R, 6R)-4-(1-Methoxy-1-methylethyl)-1-methyl-6-(3-methyl-1-butynyl)-cyclohexene (90), a colourless mobile oil, had: - $[\alpha]_D^{26}$ -188.9°($CHCl_3$, c 1.6). - TLC(Benzene): R_f 0.24. - GC(Column 1, 160°): 6.1. - IR(film): 2965, 2930, 2830, 1445, 1380, 1360, 1320, 1155, 1075. - ^{1}H NMR: 1.13 and 1.14(6H, both s, C(Me_2)OMe), 1.15(6H, d, J7, CHMe_2), 0.7-1.5(3H, m, CH_2CH), 1.7-2.3(2H,m, CH_2C=C), 1.76(3H, s, C=CMe), 2.51(1H, m, CHMe$_2$), 2.88(1H, m, C≡CCH), 3.21(3H, s, OMe), 5.36(1H, m, C=CH). - ^{13}C NMR(62.90MHz): 20.6(d), 22.1, 22.6, 22.7, 23.5, 27.1(t), 30.6(q), 32.6(d), 36.6(d), 48.6(q, OCH_3), 76.2(s, C-4), 81.9(s, C-2'), 86.2(s, C-1'),

122.2(d, C-2), 134.0(s, C-1). - MS: 234(0.1, M), 202(11),M-CH_3OH), 159(28), 73(100,C_4H_9O).. (Found: $\underline{M}^+$, 234.1995. $C_{16}H_{26}O$ requires $\underline{M}$, 234.1984).

Acid Catalysed Reaction of 2,7,7-Trimethyl-3-(2-methyl-1-propenylidene)tricyclo[4.1.1.$0^{2,4}$]octane (33) in Methanol. - Using the general procedure, cyclopropane (33)(1.0g, 4.95mmol) gave after ten days a brown oil (1.09g). TLC(silica/pentane and benzene) showed a similar, if more complex, mixture composition to that obtained in the $Et_2O.BF_3$ catalysed reaction; in particular more hydrocarbon components were present. GC(Column 1, 130°) showed a very complex mixture consisting of a high proportion of hydrocarbons, and one major methoxy component (37% of the volatiles) corresponding (by examination of the ^1H NMR, TLC and GC of the crude product) to the enyne (90), isolated previously from the $Et_2O.BF_3$ catalysed reaction.

Reaction of 7-(2-Methyl-1-propenylidene)-2-oxabicyclo[4.1.0]-heptane (32) with $Et_2O.BF_3$ in Methanol. - Using the general procedure, cyclopropane (32) (1.0g, 6.67mmol) gave after 13 days a brown oil (1.16g). TLC(silica/dichloromethane) showed apart from a trace of starting material three poorly resolved spots. GC(Column 1, 100°) showed three product peaks at 14.7, 16.4 and 19.0 min in the ratio 41:31:26(as a % of the volatiles). GC (Column 2, 150°) shwoed four components, but the last eluted component was coincident with unreacted cyclopropane (32). Examination of the ^1H NMR spectrum of the crude product mixture showed that the acetals (109), (110), (111), and (112) were present in the ratio 1:1.5:2:2 respectively. Chromatography on

Kieselgel G(90g, 3x25cm) using dichloromethane gave poor resolution, but the following pure fractions were obtained in order of elution: - a mixture of cis-allenic acetal (109) and cis-acetylenic acetal (110) (69mg), trans-acetylenic acetal (111) (57mg), and trans-allenic acetal (123) (114mg). The total yield of methoxy components was 0.83g (74%). GC(Column 1) showed that the methoxy components were eluted in the same order in which they were separated by column chromatography. Attempted resolution of the acetals on Alumina G using hexane-ether (95:5) gave even poorer results.

cis-Tetrahydro-2-methoxy-3-(3-methyl-1-butynyl)pyran (110) and cis-Tetrahydro-2-methoxy-3-(3-methyl-1-,2-butadienyl)pyran (109), a colourless mobile oil, had:- TLC(CH_2CL_2): R_f 0.47. - GC(Column 1, 130°): 4.8.- IR(film): 2920, 1975w(allene), 1450, 1215, 1175,1130 1115, 1080, 1035, 1030, 980, 910, 890. - ^1H NMR: Acetylene signals at 1.16(d, J6, $CHMe_2$), 3.49(s, OMe), 4.65(d, J3, OCHOMe). Allene signals at 1.72(d, J3, allene Me_2), 3.44(s, OMe), 4.58(d, J3, OCHOMe), 4.98(m, HC=C=C). Also 0.2-2.7(m, CH_2+CH), 3.0-4.0(m, OCH_2). ^{13}C NMR: 20.6(q), 23.4(d), 24.7, 25.4, 33.6(d), 41.3(d), 54.9(q, OCH_3), 55.2(q, OCH_3), 59.2(t, C-6), 59.4(t, C-6), 78.8(s, C=C), 89.8(d, allene C-1'), 95.1(s, allene C-3'), 99.5(d, C-2), 100.8(d, C-2), 201.9(s, allene C-2'). - MS: 182(13, M), 107(35), 79(100). (Found: M^+, 182.1301.$C_{11}H_{18}O_2$ requires M, 182.1307).

trans-Tetrahydro-2-methoxy-3-(3-methyl-1-butynyl)pyran (111), a colourless mobile oil, had:- TLC(CH_2Cl_2): R_f0.40. - GC(Column 1, 130°): 5.2. - IR(film): 2960, 2860, 1450, 1320, 1205, 1180, 1130, 1100, 1075, 1050, 1020, 970, 880. - ^1H NMR: 1.18(6H, d, J7,

$CHMe_2$), 1.3-2.2(4H, m, CH_2CH_2), 2.4-2.8(2H, m, HCC=CCH), 3.50 (3H, s, OMe), 3.5-4.05(2H, m, OCH_2), 4.43(1H, d, J5, OCHOMe). - ^{13}C NMR: 20.6, 22.9, 23.5(t), 26.4(t), 32.8, 55.3(q, OCH_3), 62.3(t, C-6), 79.1(s, C≡C), 87.7(s, C≡C), 102.2(d, C-2).- MS: 182(1.5, M), 107(57), 79(100). (Found: M^+, 182.1296 $C_{11}H_{18}O_2$ requires M, 182.1307).

trans - Tetrahydro-2-methoxy-3-(3-methyl-1,2-butadienyl)pyran (112), a colourless mobile oil, had:- TLC(CH_2Cl_2): R_f 0.33.- GC(Column 1, 130°): 5.9. - IR(film): 2920, 2850, 1975w(allene), 1445, 1365, 1220, 1200, 1180, 1130, 1075, 1045, 1035, 960. ^1H NMR: 1.74 (6H, d, J3, allene Me_2), 1.1-2.28(5H, m, $(CH_2)_2CH$), 3.52(3H, s, OMe), 3.2-4.12(2H, m, OCH_2), 4.19(1H, d, J6, OCHOMe), 5.17(1H, m, C=C=CH).- ^{13}C NMR: 20.6(q, C-4'), 23.9(t), 26.6(t), 39.8(d, C-3), 55.6(q, OCH_3), 63.9(t, C-6), 89.5(d, C-1'), 96.2(s, C-3'), 105.0(d, C-2), 202.1(s, C-2'). MS: - 182(18, M), 107(19), 79(100), 41(22). (Found: M^+, 182.1299. $C_{11}H_{18}O_2$ requires M, 182.1307).

Acid Catalysed Reaction of 7-(2-Methyl-1-propenylidene)-2-oxabicyclo[4.1.0]heptane (32) in Methanol. - Using the general procedure, cyclopropane (32) (1.0g, 6.67mmol) gave after three days an orange oil (1.19g). TLC, GC, ^1H NMR and IR showed this to consist of the same mixture of acetals as obtained in the $Et_2O.BF_3$ catalysed reaction. GC(Column 1, 100°) showed four major components in the ratio 35:43:11:11 (as a % of the volatiles); the first three corresponding to those of the GC of the latter reaction. Examination of the ^1H NMR spectrum of the crude product mixture showed that the acetals (109), (110), (111) and (112) were present in the ratio 2:1:4.5:1.4 respectively.

Chromatography on Kieselgel G using dichloromethane gave a mixture of all four acetals (0.69g, 57%).

Reaction of 6-(2-Methyl-1-propenylidene)-2-oxabicyclo[3.1.0]hexane (31) with $Et_2O.BF_3$ in Methanol. - Using the general procedure, cyclopropane (31) (1.0g, 7.35mmol) gave after 15 days a yellow oil (1.11g). TLC(silica/benzene) showed apart from unreacted starting material, two overlapping product spots. GC(Column 1, 120°) showed two poorly resolved components in the ratio 19:69 (as a % of the volatiles), GC(Column 2, 140°) gave good separation of products but cyclopropane (31) was coincident with one of the product peaks. Chromatography on Kieselgel G(80g, 3x23cm) using hexane-ether (98:2-95:5) - monitoring the fractions by TLC and GC - gave in order of eluction: - unreacted cyclopropane (31) (91mg, 9%), acetylenic acetal (108) (133mg, 11%), mixed acetal fractions (90mg, 7%) and allenic acetal (107)(487mg, 39%).

trans - Tetrahydro-2-methoxy-3-(3-methyl-1-butynyl)furan (108), a colourless mobile oil, had: - TLC(hexane-ether 9:1): R_f 0.27. - GC(Column 1, 120°):5.9. - IR(film): 2970, 2930, 2830, 1465 1450, 1360, 1320, 1190, 1105, 1040, 935. - ^1H NMR: 1.02(6H, d, J7, $CHMe_2$), 1.58-2.64(3H, m, CH_2+ $CHMe_2$), 2.90(1H, m, CH), 3.30(3H, s, OMe), 3.89 and 3.95(2H, overlapping t, J7, OCH_2), 4.87(1H, s, $w_{\frac{1}{2}}$=4Hz, OCHOMe). - MS: 168(2,M), 136(17, M-CH_3OH), 93(100), 91(73), 77(82). (Found:M^+,168.1133. $C_{10}H_{16}O_2$ requires M, 168.1150).

trans - Tetrahydro-2-methoxy-3-(3-methyl-1,2-butadienyl)furan (107), a colourless mobile oil, had:- TLC(hexane-ether 9:1): R_f 0.21. - GC(Column 1, 120°): 6.1. - IR (film): 2970, 2930, 2900, 2830, 1965w

allene), 1450, 1360, 1190, 1105, 1040, 945. - ^{1}H NMR: 1.70 (6H, d, J3, allene Me_2), 1.6-2.36(2H, m, CH_2), 2.68(1H,m, C-3 H), 3.33(3H, s, OMe), 3.89(2H, t, J7, OCH_2), 4.73(1H, s, $w_{\frac{1}{2}}$=3.5Hz. OCHOMe), 4.94(1H, m, HC=C=C). - MS: 168(23, M), 136(37, M-CH_3OH), 93(100), 91(69), 77(69). (Found: M^+, 168.1153. $C_{10}H_{16}O_2$ requires M, 168.1150).

Acid Catalysed Reaction of 6-(2-Methyl-1-propenylidene)-2-oxabicyclo[3.1.0]hexane (31) in Methanol. - Using the general procedure, cyclopropane (31) (0.2g, 1.47mmol) gave after seven days a brown oil (0.2 g). TLC, GC, ^{1}H NMR and IR showed this to consist mainly of the same mixture of acetals as isolated from the $Et_2O.BF_3$ catalysed reaction. GC(Column 2, 140°) showed two major peaks in the ratio 51:23 (as a % of the volatiles); the major product being the acetylene (108).

Acid Catalysed Reaction of 7-(2-Methyl-1-propenylidene)-2-oxabicyclo[4.1.0]heptane (32) in Aqueous Tetrahydrofuran. - A solution of the cyclopropane (32) (1.0g, 6.67mmol) in THF-water (7:1, 40ml) and concentrated hydrochloric acid (1.0ml) was refluxed for 4h. On cooling the resulting orange solution was evaporated and the residue partitioned between ether (30ml) and brine (30ml). The aqueous phase was further extracted with ether (2x20ml). The combined organic extracts were washed with water (x2), dried and evaporated to leave a mobile red oil (1.03g). TLC(silica/benzene and ethyl acetate) examination showed the presence of four major products. IR showed strong hydroxyl absorptions and only a trace of starting material. ^{1}H NMR analysis indicated isopropyl methyl, vinyl methyl and weak aldehyde signals. The ^{1}H NMR data suggests that the products exist primarily in the cyclic lactol form.

Reaction of 7-(2-Methyl-1-propenylidene)-2-oxabicyclo[4.1.0]-heptane (32) with 2,4-Dinitrophenylhydrazine Reagent. - To a stirred freshly prepared solution of the reagent[142] (prepared from 2,4-dinitrophenylhydrazine 1.5g, 7.58mmol) was added a solution of the cyclopropane (32) (1.0g, 6.67mmol) in methanol (5ml). On mixing the colour of the solution deepened but there was no immediate precipitation. After 14h the copious red-brown precipitate was filtered off, washed with methanol-water (4:1) and dried to leave a red-brown solid (0.49g). Recrystallisation from ethanol afforded the hydroxydienal derivative (114) (0.29g, 13%) as a fibrous mass of long red hair-like needles. The filtrate and mother liquors from the above recrystallisation were evaporated to give a red solid (0.99g). TLC (silica/benzene) examination showed, in addition to (114), the presence of a higher R_f 2,4-dinitrophenylhydrazine (DNP) adduct. Dry column chromatography on silica (3.5x25cm) using benzene gave a red solid (0.51g). Recrystallisation from ethyl acetate-ethanol afforded the dihydropyran derivative (115) (0.45g, 19%) as a fibrous mass of burgundy hair-like needles. Further elution with acetone gave more (114) (0.38g). Recrystallisation from ethanol afforded purple prisms (0.22g). m.p. 188-189°, with identical ^{1}H NMR, IR and UV spectra to those obtained for the DNP derivative that crystallised from the original reaction solution. Although the m.p. of this material is lower, it would appear that it is just another crystalline form of the same compound.

4-Formyl-7-methyl-4,6-octadien-1-ol, (2,4-dinitrophenyl)-hydrazone (114), m.p. 196-197°. - UV(EtOH): 268.5(15,300),

310(14,900), 404(32,100).- - IR(Kbr): 3350br, 3250(NH), 2930, 1620, 1595, 1515, 1420, 1335, 1315, 1270, 1130. - ^{1}H NMR ($CDCl_3$): 1.6-2.3(2H, m, CH_2), 1.88 and 1.93(6H, both s, $C=CMe_2$), 2.67(2H, t, J7, $C=CCH_2$), 3.67(2H, m, resolved to t, J7 on D_2O exchange, CH_2OH), 6.22 and 6.64(2H, both d, J12, ABq, C=CHHC=C), 7.73(1H, S, N=CH), 7.82(1H, d, J10, H-6'), 8.23(1H, dd, J10, 3, H-5'), 9.13(1H, d, J3, H-3'), 11.19(1H, s, NH, not removed on D_2O exchange). - ^{1}H NMR (d^6-DMSO): 1.57(2H, m, CH_2), 1.84 and 1.88(6H, both s, $C=CMe_2$), 2.28(2H, m, $C=CCH_2$), 3.39(2H, m, OCH_2OH), 4.36(1H, t, J6, CH_2OH), 6.19 and 6.55(2H, ABq, J12, C=CHHC=C), 7.76(1H, d, J10, H-6'), 8.10(1H, s, N=CH), 8.19(1H, dd, J10,3,H- 5'), 8.70(1H, d, J3, H-3'), 11.25(1H, s, NH). - ^{13}C NMR:20.1, 23.4, 28.1, 33.7, 62.4, 118.0, 122.7, 124.4, 130.5, 131.2, 136.3, 136. 7, 138.2, 143.5, 145.8, 155.7. The sample was too insoluble to obtain an off resonance decoupled spectrum. - MS: 348(14, M), 334(14), 333(100, M-CH_3), 152(5), 133(10), 91(10), 77(10), 41(16). (Found: C, 54.95; H, 5.56; N, 16.11%; M^+, 348.1458. $C_{16}H_{20}N_4O_5$ requires C, 55.17; H, 5.79; N, 16.08%; m, 348.1434).

3,5-Dihydro-5-formly-6-(2-methylpropyl)-2H-pyran,(2,4-dinitrophenyl)hydrozone (115), m.p. 196-197°. - UV (EtOH): 225(13, 800), 262(16,000), 301(10, 600), 402(26, 600). - IR(KBr): 3260, 2950, 1615, 1590, 1515, 1330, 1305, 1265, 1125, 1085, 1065. - ^{1}H NMR: 0.99(6H, d, J7, $CHMe_2$), 1.77-2.17(3H, m, CH_2 +CH), 2.26(2H, d, J7, CH_2CH), 2.44(2H, t, J7, $C=CCH_2$), 4.10(2H, t, J5, OCH_2) 7.85(1H, d, J10, H-6'), 8.05(1H, s, N=CH), 8.24(1H, dd, J10, 3, H-5'), 9.07(1H, d, J3, H-3'), 11.06(1H br s, NH). - MS: 348(90, M), 291(15), 151(100, $C_{10}H_{15}O$), 123(36), 43(51), 41(65). (Found:C, 54.94; H, 5.87; N, 16.12%; M^+,

348.1455. $C_{16}H_{20}N_4O_5$ requires C, 55.17; H, 5.79; N, 16.08%; M, 348.1434.

Reaction of 6-(2-Methyl-1-propenylidene)-2-oxabicyclo[3.1.0] hexane (31) with 2,4-Dinitrophenylhydrazine Reagent. - Using an identical procedure to that used for cyclopropane (32), cyclopropane (31) (1.0g, 7.35mmol) gave after 24h a heavy read precipitate, which was filtered off, washed with water, cold ethanol, and dried to give a deep red solid (0.92g). However repeated recrystallisation from various solvents (ethanol, ethyl acetate, ethanol-ethyl acetate, methanol or chloroform-methanol) failed to remove a higher R_f impurity even though well formed crystals were produced. Purification was achieved by dry column chromatography on silica gel (3.5x25cm) using chloroform then ethyl acetate to give a red solid, which on recrystallisation from ethyl acetate-ethanol gave the hydroxydienal derivative (116) (0.26g, 11%) as red needles. The original filtrate was evaporated and chromatographed (dry column) on silica gel (3.5x25cm) using chloroform to yield a red solid (0.49g). Recrystallisation from ethyl acetate-ethanol afforded the dihydrofuran derivative (117) (0.27g, 11%) as a mass of red-brown fibrous needles.

3-Formyl-6-methyl-3,5-heptadien-1-ol,(2,4-dinitrophenyl) hydrazone (116), m.p. 197-199°. - UV(EtOH): 268(22,300), 309(21, 500), 404(37,600). - IR(KBr): 3400br, 3270, 1610, 1595, 1500, 1325, 1305, 1265, 1135. - ^{1}H NMR: 1.71(1H, m, OH, removed on D_2O exchange), 1.94 and 1.98 (6H, both s, $C{=}CMe_2$), 2.92(2H, t, J7, $C{=}CCH_2$), 3.85(2H, t, J7, OCH_2), 6.33 and 6.77(2H, ABq, J 12, C=CHHC=C), 7.83(1H, s, N=CH), 7.87(1H, d, J10, H-6'), 8.28(1H,

d, J10, H-5'), 9.08(1H, d, J3, H-3'), 11.21(1H, br s, NH). - MS: 376(0.4, acetate impurity?), 334(35, M), 319(100, M-CH_3), 108(69), 107(65), 77(71), 41(76). (Found: C, 53.48; H, 5.55; N, 16.20%; M^+, 334.1263. $C_{15}H_{18}N_4O_5$ requires C, 53.89; H, 5.43; N, 16.76%; M, 334.1277).

2,3-Dihydro-4-formyl-5-(2-methylpropyl)furan, (2,4-dinitrophenyl) hydrazone (117), m.p. 218-219°. - UV(EtOH): 264(13,600), 303(10, 000), 406(27,700). - IR(KBr): 3270(NH), 1615, 1585, 1500, 1420, 1325, 1245, 1195, 1140, 1125, 1000. - ^{1}H NMR: 0.97(6H, d, J7, $CHMe_2$), 1.98(1H, m, CH), 2.26(2H, d, J7, CH_2CH), 2.98(2H, t, J9, CH_2CH_2O), 4.50(2H, t, J9, OCH_2), 7.82(1H, d, J10, H-6'), 7.97(1H, s, N=CH), 8.23(1H, dd, J10, 3, H-5'), 9.07(1H, d, J3, H-3'), 11.12(1H, br s,NH). - MS: 334(76, M), 171(31), 137(100), 106(86). (Found: C, 53.80; H, 5.44; N, 16.64%; M^+, 334.1279. $C_{15}H_{18}N_4O_5$ requires C,53.89; H, 5.43; N, 16.76%; M, 334.1277).

Dihydro-3-(3-methyl-1,2-butadienyl)-2(3H)-furanone (118). - A solution of the trans-allenic acetal (107) (254mg, 1.51mmol) in dry dichloromethane (3ml) was added to a stirred suspension of pyridinium chlorochromate (1.63g, 7.56mmol) in dry dichloromethane (10ml). The mixture was stirred for 39h under N_2. Ether (10ml) was added, and after stirring for ten minutes the supernatant solution was removed. The brown residue was washed with ether and the combined organic extracts were filtered through Florisil (2x7cm). Evaporation of the filtrate gave an oil (190mg) which was chromatographed on Kieselgel G(20g) (2x14cm) using petrol-ether (9:1 - 4:1) to give in order of elution:- unreacted allene (107) (88mg, 35%) - as shown by TLC, IR and ^{1}H NMR - and lactone (118) (81mg, 35%) as a colourless mobile oil:- GC(Column 1, 160°): 7.9. - IR(film): 2980,

2915, 1965w(allene), 1770(γ-lactone), 1450, 1370, 1215, 1160, 1030. - ^{1}H NMR: 1.71(6H, d, J3, allene Me_2), 1.97-2.56(2H, m, CH_2), 3.10(1H, m, CHCO), 4.21(2H, t, J7, CH_2O), 5.14(1H, m, C=C=CH). - MS: 152(7, m), 124(100, M-C_2H_4), 82(35), 77(37), 39(37). (Found: M^+, 152.0813. $C_9H_{12}O_2$ requires M, 152.0837).

Tetrahydro-3-(3-methyl-1,2-butadienyl)-2H-pyran-2-one (119). - Using an identical procedure to that used for the lactone (118), the trans-allenic acetal (112) (60mg, 0.33mmol) gave after two days an oil (59mg) which was chromatographed on silica gel (1x21cm) using petrol-ether (9:1 - 4:1) to give in order of eluction:- unreacted allene (112) (46mg, 77%) - as shown by TLC, IR and ^{1}H NMR - and lactone (119) (8mg, 15%) as a colourless mobile oil:- IR(film): 2930, 1965w(allene), 1735(δ-lactone), 1155, 1090. - ^{1}H NMR: 1.17-2.34(4H, m, CH_2CH_2), 1.72(6H, d, J3, allene Me_2), 3.20(1H, m, C=CCH), 4.32(2H, m, OCH_2), 5.34(1H, m, C=C=CH). - MS: 166(41, M), 151(100, M-CH_3), 79(85), 77(63), 41(81), 39(96). (Found: M^+, 166.1009, $C_{10}H_{14}O_2$ requires M, 166.0994).

7-(2-Methyl-1-propenylidene)bicyclo[4.1.0]heptane (127).[51] By the method of Poutsma and Ibarbia,[37] cyclopropane (28) (0.83g, 5.61mmol) in dry DMSO (2ml) was added to a stirred solution of potassium t-butoxide (1.3g, 11.6mmol) in dry DMSO (20ml) under N_2. After 19h the dark brown reaction mixture was poured into water (140ml) and extracted with dichloromethane (4x30ml). The combined organic extracts were evaporated, and the residue taken up in pentane (40ml), washed with water (x3), dried and evaporated to leave an orange oil (0.72g). Chromatography on Kieselgel G(60g, 3x17cm) using pentane gave,

in order of elution:- diene (127) (0.51g, 61%) and unreacted allene (28) (50mg, 6%) - as shown by TLC IR, and ^{1}H NMR. Diene[51] (127), an unstable colourless mobile oil, had:- GC(Column 1, 110°): 7.5. - IR(film): 3080, 2970, 2940, 2850, 1770w, 1615, 1445, 1370, 1355, 890, 875. - ^{1}H NMR: 1.05-2.15(10H, m, $(CH_2)_4$+ cyclopropyl Hx2), 2.00(3H, s, C=CMe), 4.92(2H, br s, $C=CH_2$), 6.50(1H,br s, C=CH). - MS: 148(27, M), 133(61, M-CH_3), 119(86, M-C_2H_5), 105(94), 91(100, M-C_4H_9), 79(67), 77(43), 41(55), 39(51). (Found: $\underline{M}^+$, 148.1269. Calc. for $C_{11}H_{16}$, 148.1251). Reaction of (28) at 50°±5°gave complete isomerisation as shown by TLC, but recovery of diene (127) was low (40% isolated yield).

6-(2-Methyl-2-propenylidene)bicyclo[3.1.0]hexane (128). - Using a similar procedure to that used for the preparation of diene (127), cyclopropane (27) (1.01g, 7.54mmol) gave after 15h at 60°± 5° an orange oil (0.32g). Chromatography on silica gel (35g, 2x25cm) using petrol gave diene (128) 131mg, 13%) as an unstable colourless mobile oil, having:- IR(film): 3080, 2950, 2860, 1765m, 1615, 1450, 1375, 1295, 1090, 985, 925, 910, 890, 855, 805. - ^{1}H NMR: 0.72-2.61(8H, m, $(CH_2)_3$ + cyclopropyl Hx2), 1.96(3H, s, C=CMe), 4.90(2H, br s, $C=CH_2$), 6.48(1H, br s, C=CH). - MS: 134(58, M), 119(58, M-CH_3), 91(100, M-C_3H_7). (Found: $\underline{M}^+$, 134.1099. $C_{10}H_{14}$ requires $\underline{M}$, 134.1096).

Reaction of 7-(2-Methyl-2-propenylidene)bicyclo[4.1.0]heptane (127) with $Et_2O.BF_3$ in Methanol. - To a stirred solution of the diene (127) (206mg, 1.39mmol) in dry methanol (7ml) under N_2 was added boron trifluoride etherate (0.05ml, 0.41mmol).

After 22h the mixture was poured into brine (30ml) and extracted with ether (3 x 10ml). The combined ethereal extracts were washed with water (x1), dried and evaporated to leave a yellow oil (240mg). TLC (silica/pentane and benzene) and GC(Column 1, 100°) indicated a single product. Chromatography on silica gel using (25g, 2x17cm) using petrol-ether (97:3) gave vinylcyclopropane (77) (194mg, 77%) as a colourless camphoraceous mobile oil, having identical, TLC, GC, IR, ^{1}H NMR to the product obrained from the parent alkenylidenecyclopropane.

Reaction of 6-(2-Methyl-2-propenylidene)bicyclo[3.1.0]hexane (128) with $Et_2O.BF_3$ in Methanol. Using a similar procedure to that used for diene (127), diene (128) (92mg, 0.69mmol) and boron trifluoride etherate (0.03ml, 0.24mmol) gave after 22h an orange oil (106mg). TLC(silica/benzene) and GC (Column 2, 150°) showed one major product. Chromatography on silica gel (1x20cm) using petrol then petrol-ether (95:5) gave ring expanded diene (80) (83mg, 73%) as a colourless comphoraceous mobile oil, having identical TLC, GC, IR and ^{1}H NMR to the product obtained earlier.

Reaction of 7-(2-Methyl-1-propenylidene)bicyclo[4.1.0]heptane (28) with m-Chloroperoxybenzoic Acid (MCPBA). To a stirred solution of the cyclopropane (28) (1.0g, 6.76mmol) in dry dichloromethane (10ml) containing suspended carbonate (1.1g, 10.4mmol) at 0° was added a solution of MCPBA (1.38g, 6.8mmol) based on 85% assay) in dry dichloromethane(25ml) dropwise over 0.5h . After the addition was complete the reaction was allowed to warm to RT and stirred for three days (TLC indicated that reaction was

complete after one day), washed with freshly prepared sodium sulphite solution (x1), saturated $NaHCO_3$ solution (x2), brine (x1), water (x1), dried and evaporated to give a pale yellow viscous oil (1.75g). TLC(silica/hexane-ether) showed two major components and several minor ones. Chromatography on Kieselgel G(85g, 3x23cm) using hexane-ether (95:5) gave in order of elution: unreacted cyclopropane (28)(88mg, 9%), ketoester (137) (112mg, 5%), endo-ketoester (138) (159mg, 7%) and exo-ketoester (139) (866mg, 40%). Further elution with hexane-ether (9:1-3:2) gave a pale yellow viscous oil (200mg). Attempts to isolate other products from this material were unsuccessful. Reaction of (28) without the use sodium carbonate gave comparable yields and mixture composition.

1-(3-Chlorobenzoyl)-2-methyl-1-(bicyclo[4.1.0]hept-7-yl)-1-propane (137), colourless prisms, m.p. 66-67° (pentane, 0°). - TLC(hexane-ether 9:1): R_f 0.50. - IR(Kbr): 2980, 2900, 1720 (ester), 1700(ketone), 1295, 1250, 1190, 1115, 775. - ^1H NMR: 1.07(6H, d, J7, $CHMe_2$), 1.0-2.0(10H, m, $(CH_2)_4$+cyclopropyl CHx2), 2.85(1H, sept. J7, $CHMe_2$), 7.45 and 7.89(4H, both m, aryl H). - MS: 320(2, M), 141(27), 139(100), 71(38), 43(35, C_3H_7). (Found C, 67.64; H; 6.46; Cl, 10.87% M^+, 320.1202. $C_{18}H_{21}ClO_3$ requires C, 67.39; H, 6.60; Cl, 11.05%; M, 320.1179).

endo-2-(3-Chlorobenzoyl)-2-methyl-1-(bicyclo[4.1.0]hept-7-yl)-1-propanone (138), colourless prisms m.p. 55-56° (MeOH). - TLC (hexane-ether 9:1): R_f 0.45. - IR(KBr): 2950, 1715, 1700, 1290, 1265, 1150, 1120, 755. - ^1H NMR: 0.94-2.0(11H, m, $(CH_2)_4$+cyclopropyl Hx3), 1.63(6H, s, Me_2), 7.39 and 7.92(4H, both m, aryl H). -

MS: 320(0.05, M), 156(23), 139(60), 131(46), 123(100). (Found: C, 67.39; H, 7.02; Cl, 10.27%; $\underline{M}^+$ 320.1183. $C_{18}H_{21}ClO_3$ requires C, 67.39; H, 6.60; Cl, 11.05% $\underline{M}$, 320.1179).

exo-2-(3-Chlorobenzoyl)-2-methyl-1-(bicyclo[4.1.0]hept-7-yl-1-propanone (139), colourless viscous oil. - TLC(hexane-ether (9:1): R_f 0.27. - IR(film), 2950, 2870, 1720, 1700, 1300, 1270, 1150, 1145, 1100, 1075, 750. - ^{1}H NMR: 0.8-2.0(11H, m, $(CH_2)_4$+ cyclopropyl Hx3), 1.64(6H, s, Me_2), 7.41 and 7.99(4H, both m, aryl H). - MS: 320(0.07, m), 139(31), 123(100, $C_8H_{11}O$), 95(18). (Found $\underline{M}^+$, 320. 1174. $C_{18}H_{21}ClO_3$ requires $\underline{M}$, 320.1179).

Reaction of 1-Methyl-7-(2-methyl-1-propenylidene)bicyclo-[4.1.0]heptane (29) with MCPBA. - Using an identical procedure to that used for cyclopropane (28), cyclopropane (29) (1.0g, 6.17mmol) gave after two days a pale yellow viscous oil (1.84g). Chromatography on Kieselgel G(80g, 3x23cm) using hexane, then hexane-ether (97:3-3:2) gave, in order of elution:- unreacted allene (29) (20mg, 2%), endo-ketoester (135) (644mg, 31%), exo-ketoester(136) 651mg, 32%) and a yellow viscous oil (131mg) - show to be a mixture of products by TLC.

endo-2-(3-Chlorobenzoyl)-2-methyl-1-(-methyl-bicyclo[4.1.0]hept-7-yl)-1-propanone (135), colourless prisms m.p. 71-72°(pentane, 0°). - TLC (Benzene): R_f0.49. - IR(Kbr): 2950, 1715 (ester), 1700(ketone), 1420, 1285, 1265, 1145, 1115, 1060, 755. - ^{1}H NMR: 0.9-2.0(10H, m, $(CH_2)_4$+cyclopropyl Hx2), 1.06(3H, s, cyclopropyl Me), 1.61(6H, s, Me_2), 7.38 and 7.92(4H, both as, aryl H). -

^{13}C NMR: 18.0, 20.9, 21.2, 23.0, 24.0, 24.9, 29.4, 30.1, 32.0, 85.6(s, C-2'), 127.8, 129.7, 132.1, 133.0, 134.5, 163.9(s, ester C=O), 206.2(s, C-1'). MS: 334(0.4, M), 137(68), 94(100), 41(157). (Found: C, 68.45; H, 6.98; Cl, 10.18%; $\underline{M}^+$, 334.1437. $C_{19}H_{23}ClO_3$ requires C, 68.15; H, 6.92; Cl, 10.59% $\underline{M}$, 334.1336).

exo-2-(3-Chlorobenzoyl)-2-methyl-1-(1-methyl-bicyclo[4.1.0]hept-7-yl)-1-propanone (136), a colourless viscous oil, had:- TLC (benzene): R_f 0.37. - IR(film): 2950, 2870, 1720(ester), 1700(ketone), 1260, 1200, 1145, 1125, 1085, 750. - ^1H NMR: 0.9-2.0(9H, m, $(CH_2)_4$ + cyclopropane H), 1.13(3H, s, cyclopropyl Me), 1.61(6H, s, Me_2), 1.91(1H, d, J5, CHCO), 7.39 and 7.93(4H, both m, aryl H). - ^{13}C NMR: 20.9, 21.1, 22.9, 23.3, 24.0, 30.3, 32.0, 32.7, 33.0, 33.7, 85.2(s, C-2'), 127.7, 129.5, 129.8, 132.0, 133.0, 134.5, 163.8(s, ester), 206.0(ketone). - MS: 334(0.3, M), 139(35), 137(100, $C_9H_{13}O$), 67(26), 41(45). (Found: $\underline{M}^+$, 334.1351. $C_{19}H_{23}ClO_3$ requires $\underline{M}$, 334.1336).

Reaction of 1-(2-Methyl-1-propenylidene)spiro[2.5]octane (30) with MCPBA. - Using the general procedure, cyclopropane (30) (1.0g, 6.17mmol) gave after 17.5h a yellow viscous oil (1.41g). TLC (silica, hexane-ether 9:1) showed one major component and at least nine minor ones. Chromatography on Kieselgel G (60g, 3x16cm) using petrol-ether (95:5 - 1:1) gave in order of elution: enone (141) (24mg, 2%); after further purification by PLC, ketoester (140) (806mg, 39%), and a yellow glass (302mg). TLC showed the latter to be a complex mixture of components.

2-Methyl-1-(spiro[2.5]oct-1-yl)-2-propen-1-one (141) was obtained ightly impure, as a pungent almost colourless mobile oil, having:- TLC(hexane-ether 9:1): R_f 0.55. - IR(film): 2920, 2850, 1720, 1660, 1630, 1450, 1400, 1260, 1125, 1075, - ^{1}H NMR: 0.78 (1H, dd, J8, 4, trans H-2'), 1.91(3H, s, C=CMe), 0.96-2.01(11H, m, $(CH_2)_5$+cis H-2'), 2.20(1H, dd, J8,6, H-1'), 5.70 and 6.01 (2H, both s, $C=CH_2$). - MS: 178(0.8, m), 44(100). (Found: M^+, 178.1383. $C_{12}H_{18}O$ requires m, 178.1358).

2-(3-Chlorobenzoyl)-2-methyl-1-(spiro[2,5]oct-1-yl)-1-propanone (140), a colourless viscous oil, had:- TLC(hexane-ether 9:1): R_f 0.46. - IR(film): 2945, 2925, 2850, 1720, 1700, 1295, 1260, 1145, 1125, 1070, 745. - ^{1}H NMR: 0.87(1H, dd, J8,4,,trans H-2'), 0.93-1.81(11H, m, $(CH_2)_5$+cis H-2'), 1.68(6H, s, Me_2), 1.91(1H, dd, J8, 6, H-1'), 7.02-8.26(4H, m, aryl H). - MS 334(0.9, m), 178(61), 139(96), 137(62), 55(100). (Found: M^+, 334.1327. $C_{19}H_{23}ClO_3$ requires M, 334.1336).

Reaction of 7-(2-Methyl-1-propenylidene)-2-oxabicyclo[4.1.0]-heptane (32) with MCPBA. - Using the general procedure, cyclopropane(32) (1.0g, 6.67mmol) gave after three days a yellow viscous oil (1.87g). TLC(silica/benzene and hexane-ether 4:1) showed at least eight components, including unreacted allene (32). Repeated chromatography on silica gel failed to isolate any pure products.

Hydrolysis of exo-2-(3-Chlorobenzoyl)-2-methyl-1-bicyclo[4.1.0]-hept-7-yl)-1-propanone (139). - To a stirred solution of ketoester (139) (0.5g, 1.56mmol) in methanol (10ml) was added

aqueous sodium hydroxide (50% w/v, 10ml) resulting in the immediate formation of a precipitate which quickly dissolved to give a clear solution. The progress of the reaction was monitored by TLC(silica/hexane-ether 4:1). After 4.5h the reaction mixture was poured into brine (80ml), and extracted with ether (4x20ml). The combined organic extracts were washed with water (x1) dried and evaporated to leave an almost colourless oil (256mg). Chromatography on Kieselgel G (30g, 2x24cm) using hexane-ether (4:1 - 3:2)gave, in order of elution: an unidentified carbonyl component (9mg) and the expected ketol (142) (233mg, 82%). The carbonyl component had:- TLC(hexane-ether 4:1): R_f 0.39. - IR(film): 1740, no OH absorptions.

2-Hydroxy-2-methyl-1-(bicyclo[4.1.0]hept-7-yl)-1-propanone (142) a colourless mobile oil, had:- TLC(hexane-ether 4:1): R_f 0.18. - GC(Column 1, 160°): 7.6. - IR(film): 3480(OH), 2940, 2870, 1680 (ketone), 1455, 1315, 1160, 1100, 1075, 975, 780. - ^{1}H NMR: 0.98-2.16(11H, m, $(CH_2)_4$+cyclopropyl Hx3), 1.45(6H, s, Me_2), 4.01(1H, s, OH, removed on D_2O exchange). - MS: 182(0.5, M), 124(39), 123(29), 95(17), 59(100). (Found: $\underline{M}^+$, 182.1311. $C_{11}H_{18}O_2$ requires $\underline{M}$, 182.1307).

Hydrolysis of exo-2-(3-Chlorobenzoyl)-2-methyl-1-(1-methyl-bicyclo[4.1.0]hept-7-yl)-1-propanone (136). - Using a similar procedure to that of ketoester (139), but employing 33% (w/w) sodium hydroxide solution, ketoester (136) (0.5g, 1.49mmol) gave after 2.5h an almost colourless oil (256mg). Chromatography on silica gel (60g, 2x36cm) using hexane-acetone (95:5 - 3:2) gave in order of elution:- unreacted ketoester (136) (8mg, 2%) and ketol (136a) (236mg, 81%).

2-Hydroxy-2-methyl-1-(1-methylbicyclo[4.1.0]hept-7-yl)-1-propanone (136a), a slightly discoloured mobile oil, had:- TLC (hexane-ether): R_f 0.25. - IR(film): 3520(OH), 2980, 2900, 1685 (ketone), 1460, 1420, 1390, 1370, 1200, 1165, 1095, 965. - ^{1}H NMR: 1.09(3H, s, cyclopropyl Me), 1.33 and 1.42(6H, both s, Me_2), 0.85-2.03(10H, m, $(CH_2)_4$+cyclopropyl Hx2), 3.99(1H, s, OH, removed on D_2O exchange). - MS: 196(15, M), 137(31, M-C_3H_7O), 59(47, C_3H_7O), 41(21), 32(100). (Found: M^+, 196.1483. $C_{12}H_{20}O_2$ requires M, 196.1463). Qualitatively hydrolysis of the corresponding endo-ketoester (135) occured at a slower rate as evidenced by TLC.

Hydrolysis of 2-(3-Chlorobenzoyl)-2-methyl-1-(spiro[2,5]oct-1-yl)-1-propane (140). Using the general procedure (sodium hydroxide solution, 33% w/w), ketoester (140) (0.51g, 1.52mmol) gave after 17h an oil (233mg). TLC (silica/hexane-ether 4:1) showed one major component and three minor ones. Chromatography on silica gel (7g, 0.8x29cm) using petrol-ether (95:5 - 4:1) gave the ketol (140a) 193mg, 65%).

2-Hydroxy-2-methyl-1-(spiro[2.5]oct-1-yl)-1-propanone (140a), a colourless mobile oil, had:- GC(Column 1, 160°): 9.2. - IR(film): 3460 br, 2970, 2925, 2845, 1680, 1440, 1355, 1160, 1070, 965. - ^{1}H NMR: 0.96(1H, dd, J8,4, trans H-2'), 1.08-1.66 (11H, m, $(CH_2)_5$ + cyclopropyl cis H-2'), 1.47(6H, s, Me_2), 1.92(1H, dd, J8,6, H-1'), 3.97(1H,br s, OH). - MS: 196(11, M), 178(15, M-H_2O), 138(36), 67(40), 59(100, C_3H_7O). (Found: M^+, 196.1451. $C_{12}H_{20}O_2$ requires M, 196.1463).

Hydrolysis of trans-2-(3-Chlorobenzoyl)-2-methyl-1-(1-ethynyl-1-methylcyclopropyl)-1-propanone (134a) (prepared by P J Maddocks). - Using the general procedure, ketoester (134a) (220mg, 0.72mmol) gave after 3h a semi-solid residue (143mg). PLC using hexane-ether (4:1) on four plates gave cis-2-Hydroxy-2-methyl-1-(2-methyl-2-ethynylcyclopropyl)-1-propanone (37mg, 31%) as white needles m.p. 56-57° (Lit.[72], 55-56°). - TLC (hexane-ether 3:2): R_f 0.41. - GC(Column 1, 140°):7.1. - IR(KBr): 3460, 3230, 1680, 1150. - ^{1}H NMR: 1.25(3H, s, cyclopropyl Me), 1.45 and 1.46(6H, both s, Me_2), 1.29-1.60(2H, m, cyclopropyl CH_2), 1.99 (1H, s, C≡CH), 2.51(1H, dd, J8,7, H-2'), 3.81(1H, s, OH). Also isolated was trans-2-Hydroxy-2-methyl-1-(2-methyl-2-ethynyl-cyclopropyl)-1-propanone[72] (63mg, 53%), as a colourless mobile oil, with:- TLC(hexane-ether 3:2): R_f 0.26. - GC(Column 1, 140°): 13.0. - IR(film): 3460, 3280, 2130, 1700, 1090. - ^{1}H NMR: 1.14 (1H, dd, J8,5, trans - H-3'), 1.46 and 1.47(9H, both s, cyclopropyl Me+Me_2), 1.78(1H, dd, J7,5 cis H-3'), 2.00(1H, s, C=CH), 2.26(1H, dd, J8,7, H-2'), 3.87(1H, s, OH).

Acid Catalysed Reaction of 2-Hydroxy-2-methyl-1-bicyclo[4.1.0]-hept-7-yl)-1-propanone (142) in methanol. - A solution of ketol (142) (100mg, 0.55mmol) in methanol (5ml) was stirred with concentrated hydrochloric acid (0.3ml). After seven days the reaction was quenched with saturated $NaHCO_3$ (20ml) and ether extracted (3x10ml). The combined ethereal extracts were washed with water (x1), dried and evaporated to give an oil (113mg). PTLC (hexone-ether 3:2) on three plates gave, in order of elution:- an unidentified slightly discoloured mobile oil (91mg); having an identical R_f value to the starting ketol,

and the expected product, 3-hydroxy-3-methyl-1-(2-methoxy cyclohexyl)-2-butanone (144) (17mg, 15%), a colourless mobile oil had:- TLC(hexane-ether 3:2): R_f 0.18. - IR(film): 3460br, 2970, 2930, 2860, 2820, 1705 (ketone), 1460, 1450, 1360, 1190, 1100, 1045, 970. - ^{1}H NMR: 1.36 and 1.38(6H, both s, Me_2), 1.0-2.5(10H, m, $(CH_2)_4$+CHx2), 2.87(2H, m, $COCH_2$), 3.28(3H, s, OMe), 3.89(1H, s, OH). - MS: 214(0.1, M), 96(75), 81(88), 59(100, C_3H_7O), 43(96). (Found: M^+, 214.1582. $C_{12}H_{22}O_3$ requires M, 214.1569).

Acid Catalysed Reaction of 2-Hydroxy-2-methyl-1-(spiro[2.5]oct-1-yl)-1-propanone (140a) in Methanol. - Using an identical procedure to that for ketol (142), ketol (140a) (85mg, 0.43mmol) gave after 12 days a semi-solid residue (106mg). TLC (silica/petrol-ether 3:2) showed four components. Chromatography on Kieselgel G (20g, 2x15cm) using petrol-ether (4:1 - 3:2) gave in order of elution:- unreacted ketol (140a) (22mg, 26%), slightly impure unsaturated ketol (146) (4mg, ca 5%), unidentified ketol (7mg) and the expected ether (145) (51mg, 52%).

2-Hydroxy-2-methyl-5-(1-cyclohexenyl)-3-pentanone (146), a colourless mobile oil, had:- TLC (petrol-ether 3:2): R_f 0.36. - IR(film): 3400br (OH), 1705(ketone). - ^{1}H NMR: 1.41(6H, s, Me_2), 1.13-1.84(4H, m, $(CH_2)_2$), 1.97(4H, m, allyl CH_2x2), 2.28(2H, m, CH_2CH_2CO), 2.64(2H, t, J7, CH_2CO), 3.78(1H, s, OH), 5.42(1H, br s, C=CH), impurity at ca. 1.0.

Unidentified ketol, had:- TLC (petrol-ether 3:2): R_f 0.29. - IR (film): 3460br, 2930, 2850, 1705, 1440. - ^{1}H NMR: 1.42(6H, s, Me_2), 1.0-2.0(m), 2.06(2H, t, J7), 2.68(2H, t, J7, CH_2CO), 3.68 (1H, s, OH).

2-Hydroxy-2-methyl-5-(1-methoxycyclohexyl)-3-pentanone (145), a colourless mobile oil, had:- TLC (petrol-ether 3:2): R_f 0.19.- IR(film): 3450 br, 2970, 2930, 2850, 1705, 1460, 1360, 1080, 965. - ^{1}H NMR: 1.40(6H, s, Me_2), 1.03-1.85(12H, m, $(CH_2)_5$ + CH_2), 2.55(2H, t, J7, CH_2CO), 3.07(3H, s, OMe), 3.82(1H, br s, OH). - MS: 228(0.1, M), 153(10), 113(100), 55(90). (Found: M^+, 228.1738.$C_{13}H_{24}O_3$ requires M, 228.1725).

Acid Catalysed Reaction of 2-Hydroxy-2-methyl-1-(2-methyl-2-ethynylcyclopropyl)-1-propanone. - Using the general procedure a mixture of isomeric ketols (67mg, 0.40mmol) obtained from hydrolysis of ketoester (134a) was refluxed for 44h (TLC showed no reaction after eight days at RT) to leave a brown semi-solid (63mg). TLC showed a complex mixture of products. However, it appears that the major products of reaction are coincident with the starting material by TLC, as ^{1}H NMR examination of the reaction mixture showed the absence of starting material. Thus, the progress of this reaction is best followed by GC or ^{1}H NMR analysis.

exo, endo-2,7,7-Trimethyl-3-(2-methyl-1-propenyl)-tricyclo-[4.1.1.$0^{2,4}$]octane (33a). - By the metnod of Raphael et al.[13], to a stirred solution of sodium (0.23g, 10mmol) in liquid ammonia (40ml) was added a solution of cyclopropane (33) (1.0g, 4.95mmol) in dry ether (10ml), dropwise over 15 min. After a further 2h, solid ammonium chloride (1.5g, 28mmol) was cautiously added and the ammonia allowed to evaporate (or removed under N_2 on a warm water bath). Water (10ml) was added to the residue and the resulting mixture was extracted with ether (4x10ml). The combined organic extracts were washed with brine (x1), dried

and evaporated to leave an oil (0.92g). Chromatography on silica gel(35g, 2x26cm) using petrol gave vinylcyclopropane (33a) (887mg, 88%) as a colourless mobile oil, having:- TLC(pentane) R_f 0.74, two just discernable spots. - GC(Column 1, 110°) showed two peaks in the ratio: - 12:88. - IR(film): 2990, 2920, 2860, 1450, 1380, 1365, 980. - ^{1}H NMR: 0.62(1H, m, cyclopropyl H), 1.08-1.28(2H, m), 1.06(6H, s, Me_2), 1.28(3H, s, Me), 1.37-2.27(5H, m), 1.74(6H, s, $C{=}CMe_2$), 4.81 and 5.39 (1H, br d, J7 and m respectively, C=CH; higher field signal is the major isomer - exo?), - MS: 204(5, M), 161(4, M-C_3H_7), 95(100), 69(67). (Found: M^+, 204.1888. $C_{15}H_{24}$ requires M, 204.1878).

exo, endo-7-(2-Methyl-1-propenyl)bicyclo[4.1.0]heptane (161).[51]- Using an identical procedure to that used for the reduction of cyclopropane (33), cyclopropane (28) (0.9g, 6.08mmol) gave a mixture of exo- and endo- vinylcyclopropanes (161) as a colourless mobile oil (0.75g, 82%), having:- TLC(pentane): R_f 0.66 and 0.70 (minor component). - GC(Column 1, 80°): 15.3, (Column 2, 150°): 10.9, 11.4 overlapping peaks. - IR(film): 3020, 2970, 2940, 2850, 1455, 1390, 1150, 870, 780. - ^{1}H NMR: 0.64-2.04(11H, m, $(CH_2)_4$+cyclopropyl Hx3), 1.68 and 1.75(6H, both s, $C{=}CMe_2$), 4.58 and 6.00(1H, br d, J8 and in respectively, C=CH, ratio by integration 5:1 respectively). - ^{13}C NMR(62.90MHz): 18.3, 19.4, 21.6, 22.5, 23.6, 25.5, 129.0(d), 129.4(s), minor signals (endo-isomer?) at 12.5(d), 17.4, 18.6, 25.7, 120.1(d).

exo, endo-6(2-Methyl-1-propenyl)bicyclo[3.1.0]hexane (27a). - Using the general procedure, cyclopropane (27) (1.0g, 7.46mmol) gave a mixture of exo- and endo- vinylcyclopropanes (27a) (0.74g, 73%) as a colourless mobile oil, having TLC(hexane):

R_f 0.47 and 0.53 (minor component). - GC(Column 1, 75°): 7.7, 9.1(13.87). - IR(film): 3015, 2950, 2920, 2850, 1445, 1370, 1145, 1170, 860, 845. - ^{1}H NMR: 0.76-2.08(9H, m, $(CH_2)_3$+cyclopropyl Hx3), 1.70(6H, br s, $C{=}CMe_2$), 4.55 and 4.90(1H, br d, J8 and m respectively, C=CH, ratio by integration 6:1 respectively). - MS: 136(65, M), 121(41), 95(45), 93(100), M-C_3H_7), 79(71), 67(67), 41(71). (Found: M$^+$, 136.1257. $C_{10}H_{16}$ requires M, 136.1252).

exo, endo-1-Methyl-7-(2-methyl-1-propenyl)bicyclo-[4.1.0]heptane (29a). - Using the general procedure, cyclopropane (29) (1.0g, 6.17mmol) gave a mixture of exo- and endo- vinylcyclopropanes (29a) (663mg, 66%) as a colourless mobile oil, having:- TLC(pentane): R_f 0.78. - GC(Column 1, 80°): 10.3, 11.6(46:54). - IR(Film): 2935, 2860, 1450, 1380, 1135, 1070, 845. - ^{1}H NMR: 0.57(1H, m, cyclopropyl H-6), 1.03 and 1.10(3H, both s, cyclopropyl Me), 1.71(6H, s, $C{=}CMe_2$), 0.66-2.24(9H, m, $(CH_2)_4$+CH), 4.87 and 5.00(1H, both br d, J8 and 7 respectively, C=CH, integration ratio ca. 1:1 MS: 164(0.4, M), 149(0.4, M-CH_3), 43(76, C_3H_7), 32(100). (Found: M$^+$, 164.1580. $C_{12}H_{20}$ requires M, 164.1565).

Reaction of 7-(2-Methyl-1-propenylidene)bicyclo[4.1.0]heptane (28) with Thiophenol. - By the method of Pasto and Miles,[108] a solution of cyclopropane (28) (1.0g, 6.76mmol) and thiophenol (0.74g, 6.73mmol) in benzene (20ml) was stirred at RT open to the atmosphere. The progress of the reaction was monitored by ^{1}H NMR analysis; by the following the disappearance of the thiophenol SH signal at δ 3.39. After 4h the resulting pale yellow solution was washed with 2M sodium hydroxide solution (x2), brine (x1), water (x1), dried and evaporated to leave a pale yellow mobile

oil (1.72g). TLC (silica/pentane and benzene) indicated one major, and several minor components. Chromatography on Kieselgel G (65g, 3x20cm) using pentane, gave in order of elution:- enol thioether (165) (1.4g, 80.5%), vinylcyclopropane (172) (30mg) and acetylene (171) (17mg). The two minor components were further purified by PLC to give pure (172) (23mg, 1.3%) and (171) (15mg, 0.8%).

exo, endo-7-(2-Methyl-1-(phenylthio)-1-propenyl)bicyclo[4.1.0]-heptane (165), a colourless mobile oil, had:- b.p. 100-105° (oven) /0.1 Torr. - TLC(pentane): R_f 0.49. - UV(EtOH): 255(10, 400). 272(7, 700), - IR(film): 3070, 3000, 2930, 2855, 1580, 1475, 1455, 1440, 1025, 740, 690. - ^{1}H NMR: 0.84-1.96(11H, m, $(CH_2)_4$+ cyclo -propyl Hx3), 1.99(6H, s, C=CMe_2), 6.95-7.33(5H, m, phenyl H). - ^{13}C NMR: 0.0(d), 14.9(d), 20.6(t), 22.2(t), 22.5, 23.1, 23.5, 123.7(s), 124.6(d), 127.4(d), 128.5(d), 138.3(s), 145.3(s). - MS: 258(100, M), 181(23), 133(40), 41(63). (Found: C, 78.96; H, 8.61%; M^+, 258.1460. $C_{17}H_{22}S$ requires C, 79.01; H, 8.58%; M, 258.1442).

7-(Phenylthio)-7-(2-methyl-1-propenyl)bicyclo[4.1.0]heptane (172) a colourless mobile oil, had TLC (pentane): R_f 0.29. - IR(film): 2935, 2850, 1580, 1475, 1440, 1375, 1090, 1025, 735, 690. - ^{1}H NMR: 0.94-2.08(10H, m, $(CH_2)_4$+ cyclopropyl Hx2) 1.75(6H, s, C=CMe_2), 5.35(1H, s, C=CH), 6.95-7.45(5H, m, phenyl H). - MS: 258(51, M), 243(24, M-CH_3), 181(63), 149(M-SC_6H_5), 105(75), 91(100), 81(81), 79(69), 77(69), 55(51). (Found: M^+, 258.1458. $C_{17}H_{22}S$ requires M, 258.1442).

1-Cyclohexyl-3-methyl-3-(phenylthio)-1-butyne (171) an almost colourless mobile oil, had:- TLC(pentane): R_f 0.18.- IR(film): 2965, 2925, 2850, 2240w(C≡C), 1445, 1435, 1360, 1130, 750, 690. - ^{1}H NMR: 1.06-1.86(10H, m, $(CH_2)_5$), 1.51(6H, s, Me_2), 2.29(1H, m, C≡CCH), 7.16-7.36(3H, m, phenyl H-3,5), 7.52-7.68(2H, m, phenyl H-2,6). - MS: 258(20, M), 243(8, M-CH_3), 181(46), 149(86, M-SC_6H_5), 110(89, C_6H_5SH), 107(79), 93(100), 91(98), 79(74), 41(99). (Found: $\underline{M}^+$, 258.1460. $C_{17}H_{22}S$ requires $\underline{M}$, 258.1442).

Reaction of 6-(2-Methyl-1-propenylidene)bicyclo[3.1.0]hexane (27) with Thiophenol - Using an identical procedure to that used for cyclopropane (28), cyclopropane (27) (1.0g, 7.46mmol) gave after 3h a pale yellow oil. Chromatography on Kieselgel G (70g, 3x20cm) using petrol gave an oil which was distilled under reduced pressure gave exo, endo-6-(2-Methyl-1-(phenylthio) -1-propenyl)bicyclo [3.1.0] hexane (166) (1.43g, 79%) as a colourless mobile oil, b.p. 95-100°(oven)/0.04 Torr. - GC(Column 2, 80ml/min, 220°): 14.5, 15.5(15:85). - IR(film): 3015, 2950, 2855, 1580, 1475, 1440, 1025, 740, 690. - ^{1}H NMR: 0.82-2.4(9H, m, $(CH_2)_3$ + cyclopropyl Hx3), 1.93 and 1.97(6H, both d, J3, C=CMe_2), 6.88-7.28(5H, m, phenyl H). - 244(100, M), 134(56, M-C_6H_5SH), 91(42), 67(51). (Found: $\underline{M}^+$, 244.1280. $C_{16}H_{20}S$ requires $\underline{M}$, 244.1286).

Reaction of 2,7,7,-Trimethyl-3-(2-methyl-1-propenylidene)-tricyclo[4.1.1.$O^{2,4}$]octane (33) with Thiophenol. - Using the general procedure, cyclopropane (33) (1.0g, 4.95mmol) gave after 3.5h a pale yellow oil (1.57g). Chromatography on Kieselgel G(80g, 3x23cm) using petrol gave 3-(2-Methyl-1-(phenylthio)-propenyl)2,7,7,-trimethyltricyclo[4.1.1.$O^{2,4}$]-octane (167) (1.014g, 66%) as a colourless viscous oil, having:- IR(film): 3070, 2975, 2955, 2910, 2860, 1580, 1470, 1440, 1380, 1360, 1025, 740, 690. - ^{1}H NMR: 0.99(3H, s, cyclopropyl Me), 1.24(6H, s, Me_2), 1.95 and 1.98(6H, both s, C=CMe_2), 0.57-2.55(8H, m), 6.89-7.39(5H, m, phenyl H). - MS: 312(42, M), 159(166), 119(51), 110(74, C_6H_5SH), 93(53), 91(64), 69(100). (Found: $\underline{M}^+$, 312.1924. $C_{21}H_{28}S$ requires $\underline{M}$, 312.1912). Further elution with ether gave a yellow viscous oil (278mg), shown by TLC to be a mixture of products.

Reaction of 1-Ethynyl-1-methyl-2-(2-methyl-1-propenylidene)-cyclopropane (35) with Thiophenol. - Using the general procedure, cyclopropane (35) (1.0g, 7.58mmol) gave after 4h a yellow oil(1.79g). TLC(silica/pentane and benzene) showed two major components, unreacted cyclopropane (35) and at least eight minor components. ^{1}H NMR examination of the crude reaction mixture showed no vinyl proton resonances in the olefinic region (δ4.5-6.5). Chromatography on Kieselgel G(80g, 3x23cm)

using pentane, gave in order of elution:- slightly impure unreacted cyclopropane (35) (167mg, ca. 17%) - as shown by IR and ^{1}H NMR, trans-enol thioether (168) (189mg, 10%), mixed fractions (59mg, 3%) and cis-enol thioether (169) (608mg, 33%). Elution with ether gave a brown oil (342mg) shown by TLC to be a mixture of components. The isomeric cyclopropyl enol thioethers were further purified by PLC (multiple elution using hexane).

trans-1-Ethynyl-1-methyl-2-(2-methyl-1-(phenylthio)-1-propenyl)-cyclopropane (168), a slightly discoloured mobile oil, had:- TLC (hexane-benzene 4:1): R_f 0.59. - IR(film): 3310, 2970, 2930, 2110, 1580, 1475, 1435, 1070, 1025, 735, 685. - ^{1}H NMR: 1.14(3H, s, cyclopropyl Me), 0.78 - 1.32(3H, m, cyclopropyl CH_2CH), 1.84(1H, s, C≡CH), 2.06 and 2.12(6H, both s, C=CMe_2), 7.18(5H, m, phenyl H).- ^{13}C NMR(62.90MHz): 14.6(s, C-1), 18.7(q), 22.1(q), 23.8(t, C-3), 31.4(d, C-2), 63.4(d, C-2'), 91.0(s, C-1'), 122.2(s), 125.2(d), 127.9(d), 128.7(d), 137.3(s), 146.8(s). - MS: 242(64, M), 227(6, M-CH_3), 133(48, M-C_6H_5S), 117(100), 91(50). (Found: $\underline{M}^+$, 242.1144. $C_{16}H_{18}S$ requires $\underline{M}$, 242.1129).

cis-1-Ethynyl -1-methyl-2-(2-methyl-1-(phenylthio)-1-propenyl)-cyclopropane (169), a slightly discoloured mobile oil, had: - TLC(hexane-benzene 4:1): R_f 0.49. - IR(film): 3310, 2960, 2925, 2120, 1580, 1475, 1435, 1070, 1025, 740, 690. - ^{1}H NMR: 0.70(1H, dd, J8,5, cyclopropyl C$\underline{H}$H), 1.34(3H, s, cyclopropyl Me), 1.08-1.84 (2H, m, cyclopropyl Hx2), 1.89(1H, s, C≡CH), 2.03 and 2.11(6H, both s, C=CMe_2), 7.20(5H, m, phenyl H). - ^{13}C NMR(62.90MHz): 16.4(s, C-1), 22.1(q), 23.9(q and t, CH_3 and C-3 respectively), 24.8(q), 31.7(d, C-2), 66.9(d, C-2'), 87.2(s, C-1'), 122.9(s),

124.4(d), 124.8(d), 128.6(d), 137.9(d), 146.8(s). - MS: 242(29, M), 227(7, M-CH_3), 133(34, M-C_6H_5S), 117(100), 91(40). (Found: $\underline{M}^+$, 242.1137. $C_{16}H_{18}S$ requires $\underline{M}$, 242.1129).

Attempted ^1H NMR LIS studies of enol thioethers (168) and (169) using Eu(fod)$_3$ gave no induced shifts.

Ozonolysis of Enol Thioether (165). - A solution of enol thioether (165) (194mg, 0.75mmol) in 1:1 dichloromethane-pyridine (5ml) was cooled to -78° and treated with a slight excess of ozone. The reaction mixture was allowed to warm to RT, diluted with ether (50ml) and washed with 1M HCl (x4), water (x1), dried and evaporated to leave a pale yellow viscous oil (176mg). ^1H NMR examination of the crude reaction product showed the absence of thioether (165). TLC(silica/benzene) showed the presence of three products. Chromatography on silica gel (9g, 1x35cm) using hexane gave diphenyldisulphide (4mg); further elution using hexane-ether (95:5 - 4:1) gave in order of elution: - thioester (173) (52mg, 30%) and an unidentified alcohol (75mg, 36% based on $C_{17}H_{22}OS$).

Diphenyldisulphide, a white crystalline solid with a strong thiol odour, had:- m.p. 57-59°(Lit.[158], 61.5°). - TLC (hexane): R_f 0.38. - MS: 218(100, M), 110(24), 109(57). (Found: $\underline{M}^+$, 218.0229. Calc. for $C_{12}H_{10}S_2$, 218.0224).

Thioester (173), a colourless mobile oil, had:- TLC(benzene): R_f 0.59. - IR(film): 2960, 2880, 1710(C=O), 1450, 1405, 1095, 1040, 985, 940, 885, 780, 745, 690. - ^1H NMR: 1.0 - 2.2(11H, m, $(CH_2)_4$+cyclopropyl Hx3), 7.40(5H, s, phenyl H). - MS: 232(0.7, M), 123(100, M-C_6H_5S), 95(30), 81(38). (Found: $\underline{M}^+$, 232.0947. $C_{14}H_{16}OS$ requires $\underline{M}$, 232.0922).

Unidentified Alcohol, a pale yellow mobile oil, had:- TLC (benzene): R_f 0.14. - IR (film): 3480br (OH), 2950, 2870, 1585, 1485, 1450, 1365, 1335, 1170, 1135, 935, 740, 690. - ^{1}H NMR: 0.18-1.9(10H, m), 1.47 and 1.48(6H, s, Me_2), 2.54(1H, s, OH, removed on D_2O exchange), 7.51(5H, m, phenyl H). - ^{13}C NMR: 13.2(d), 18.5(d), 21.0(t), 21.1(t), 21.5(t), 23.4(t), 29.0(q), 29.7(q), 74.6(s), 77.2, 77.3, 125.7(d), 128.7, 129.1, 130.7, 137.3, 140.0. - MS: 274(7, M), 256(4, M-H_2O), 165(100, M-C_6H_5S), 43(69). (Found: $\underline{M}^+$, 274.1408. $C_{17}H_{22}OS$ requires $\underline{M}$, 274.1391).

Reductive Cleavage of 7-(2-Methyl-1-phenylthio-1-propenyl)-bicyclo[4.1.0]heptane (165). - Using a method adapted from Truce and Breiter,[111] a solution of enol thioether (165) (0.20g, 0.78mmol) in dry petrol (8ml) was added dropwise over ten minutes, to a stirred solution of lithium (33mg, 4.76mgatom, 6equiv.) in liquid ammonia (30ml). The mixture was stirred for a further 15 min, quenched by the addition of solid ammonium chloride (0.40g, 7.5mmol) and the ammonia allowed to evaporate. The residue was diluted with water (10ml) and extracted with petrol (3 x 10ml). The combined organic extracts were washed with 2M sodium hydroxide (x1; to remove thiophenol), water (x2), dried and evaporated to leave an oil (90mg). TLC (silica/hexane) showed two poorly resolved components and a trace of unreacted enol thioether (165). Chromatography on silica gel (1x20cm) using petrol gave a mixture of exo and endo-vinylcyclopropane (161) (69mg, 59%), as a colourless mobile oil, consisting of predominantly the endo-isomer. The mixture of (161), had:- TLC

(hexane): R_f 0.43 and 0.52, exo- and endo-isomers respectively.- GC(Column 1, 90°) showed one peak; identical on coinjection with the mixture of vinylcyclopropanes obtained from sodium-liquid ammonia reduction of the parent alkenylidenecyclopropane (28). - IR(film): 3020, 2935, 2870, 1450, 1380,1165, 1130, 840, 770. - ^{1}H NMR: 0.6-2.4(11H, m, $(CH_2)_4$+cyclopropyl Hx3), 1.73 and 1.79 (6H, both s, $C=CMe_2$), 4.58 and 5.00(1H, both br d, J8 and 6 respectively, C=CH, integration ca. 1:9 respectively exo/endo).

Reductive Cleavage of 6-(2-Methyl-1-phenylthio-1-propenyl)-bicyclo[3.1.0]hexane (166). - Using an identical procedure to that for enol thioether (165), enol thioether (166) (0.20g, 0.82mmol) gave an oil (90mg). TLC indicated a trace of starting material (166). Chromatography (as before) gave a mixture of exo- and endo - vinylcycloprane (27a) 53mg, 48%), as a colourless mobile oil, TLC(hexane): R_f 0.47 and 0.55; exo- and endo-isomers respectivley. - IR(film) 3020, 2955, 2920, 2855, 1450, 1375, 1095, 840, 810. - ^{1}H NMR: 0.74-2.16(9H, m, $(CH_2)_3$+cyclopropyl H), 1.73(6H, s, C=CMe), 4.57 and 4.93(1H, both br d, J8 and 5 respectively, C=CH, integration ca 1:4 respectivley exo/endo).

Reductive Cleavage of 3-(2-Methyl-1-phenylthio-1-propenyl-2,7,7-trimethyl[4.1.1.$O^{2,4}$]octane (167). - Using the general procedure, enol thioether (167) (0.25g, 0.80mmol) gave an oil (0.15g). Chromatography on Kieselgel G (20g, 2x14cm) using hexane gave a mixture of hydrocarbon components (134mg). ^{1}H NMR examination of this mixture suggests it is largely composed of the expected endo-vinylcyclopropane. However, TLC and GC(Column 1, 120°) show it to consist of at least three components. This suggests that either enol thioether (167) is impure, or

that the reductive cleavage reaction is not clean.

Attempted Desulphurization of Enol Thioether (165). - By the method of Barton et al.[112], a solution of sodium borohydride (140mg, 3.7mmol). in water (12ml) was added dropwise to a stirred solution of enol thioether (165) (104mg, 0.403mmol) and nickel (II) chloride. $6H_2O$ (1.03g, 4.33mmol) in ethanol (120ml) under N_2, producing an immediate black precipitate of nickel boride. After the addition was complete the reaction mixture was heated to reflux for 1.25h. On cooling, the precipitate was removed by filtration through Celite, washing well with water then petrol. The filtrate was poured into brine (200ml) and extracted with petrol (3x50ml). The combined organic extracts were washed with water, dried and evaporated. The resulting residue was taken up in petrol, filtered, and the filtrate evaporated to leave a pale yellow oil (106mg), shown by TLC, IR and ^1H NMR to be essentially unreacted (165).

Attempted Hydrolysis of Enol Thioether (165). -

A Mercuric Chloride:

By the method of Corey and Shulman,[113] a solution of mercuric chloride (630mg, 2.32mmol) in acetonitrite-water (3:1, 5ml) was added to a stirred solution of enol thioether (165) (300mg, 1.16mmol) in acetonitrite-water (3:1, 8ml). The resulting solution was heated to reflux under N_2 for three days. Precipitated solid was removed by filtration through Kieselguhr, with generous ether washings. The filtrate was washed with saturated sodium bicarbonate (2x), brine (x2), dried and evaporated to leave an oil containing some solid This material was

taken up in ether, filtered, and evaporated to give an oil (280mg); shown by TLC(silica/hexane and benzene) to consist of unreacted (165) and traces of more polar material. Chromatography on alumina (2x10cm) using hexane gave recovered enol thioether (165) (203mg, 68%), as shown by TLC, IR and ^{1}H NMR.

B Titanium Tetrachloride:

By the method of Mukaiyama *et al.*[114], to a stirred solution of enol thioether (165) (234mg, 0.91mmol) in dry acetonitrite (7ml) under N_2 was added titanium (IV) chloride (0.2ml, 1.82mmol) causing an immediate brown colouration. The reaction mixture was stirred for 20min, then water (three drops, *ca.* 3.6mmol) was added (colour of solution lightened). After stirring for a further 21h, the reaction mixture was poured into brine (20ml), and extracted with ether (3x10ml). The combined organic extracts were washed with 2M sodium hydroxide (x2), water (x1), dried and evaporated to leave an orange oil (214mg). TLC (silica/pentane and benzene) showed a complex mixture, consisting of at least eight components, including unreacted (165). ^{1}H NMR showed vinyl and aliphatic methyl signals, traces of vinyl proton resonances and phenyl proton signals. The IR spectrum indicated that some carbonyl containing material had been produced; ketone absorption at 1705cm^{-1}.

C Hydrochloric Acid:

A solution of enol thioether (165) (149mg, 0.58mmol) and concentrated hydrochloric acid (0.5ml) in methanol (10ml) was refluxed for 41h (no reaction occurred at RT).

Cooled, poured into brine (30ml), and extracted with ether (4x40ml). The combined organic extracts were washed with saturated sodium bicarbonate (xl), water (xl), dried and evaporated to leave an oil (130mg). TLC (silica/hexane and benzene) showed at least six components including unreacted (165). ^{1}H NMR at the crude product showed strong isopropyl signals, weak vinyl protons, phenyl protons, and one strong methoxy signal. IR again showed a strong carbonyl absorption at 1705cm^{-1}.

D N-Bromosuccinimide:

By the method of Seebach et al.[110], a solution of enol thioether (165) (55mg, 0.21mmol) in acetonitrite (2ml) was added dropwise to a stirred solution of N-bromosuccinimide (170mg, 0.96mmol) in acetonitrite-water (4:1, 4ml) producing a transient orange colouration. After the addition was complete the reaction mixture was stirred for 15min, poured into saturated sodium sulphite solution (30ml; yellow colour removed) and extracted with ether (2xl0ml). The combined organic extracts were washed with dilute sodium bicarbonate (xl), brine (xl), dried and evaporated to leave a pale yellow viscous oil (55mg). TLC(silica/benzene and ether) showed a very complex mixture of products, with no trace of (165). IR of the crude product showed some carbonyl and hydroxyl absorptions. ^{1}H NMR displayed very complex high field signals, and strong vinyl methyl signals. No vinyl proton, and only a trace of phenyl proton signals were apparent.

Attempted Thermolysis of 6-(2-Methyl-1-(phenylthio)-1-propenyl)-bicyclo[3.1.0]hexane (166). - A solution of enol thioether (166) (30.6mg, 0.125mmol, 0.96M) in benzene (0.13ml) contained in a Pierce "Reacti-Vial" was heated at 140° for 1h, using a Pierce "Reacti-Therm" heating module. Evaporation of solvent gave a colourless oil (32mg); shown by TLC and ^{1}H NMR to be unreacted (166).

Reaction of 1-Ethenyl-1-methyl-2-(2-methyl-1-propenylidene) cyclopropane (25) and 1-(1-Methylethenyl)-2-(2-methyl-1-propenylidene)cyclopropane (26) with Thiopennol. - Using the general procedure, the mixture of cyclopropanes (25) and (26) (1.0g, 7.46mmol) gaver after 4h a pale yellow mobile oil (1.64g). TLC(silica/pentane) showed, apart from unreacted starting material, two poorly resolved major components. Chromatography on Kieselgel G (70g, 3x20cm) using hexane, gave in order of elution:- recovered cyclopropanes (25) and (26) (61mg, 3%), trans-vinylcyclopropane (180)(107mg, 6%), mixed fractions (133mg, 7%) and cycloheptadiene (181) (102mg, 6%). Further elution with ether gave a yellow mobile oil (543mg); shown by TLC(silica/benzene) to be a complex mixture of products. In another experiment, cyclopropanes (25) and (26) (2.04g) gave after 5h, a mixture of thiophenol adducts (180) and (181) 935mg, 22%); present in the ratio ca. 1:2, by ^{1}H NMR analysis. No adducts arising from thiophenol addition to the minor cyclopropane (26) were isolated. TLC indicates that separation of the two major adducts might be better effected on Alumina G using hexane.

trans-1-Ethenyl-1-methyl-2-(2-methyl-1-(phenylthio)-1-propenyl)-cyclopropane (180), a colourless mobile oil, had:- TLC(hexane): R_f 0.32 - IR(film): 2910, 1630, 1580, 1475, 1440, 895, 740, 685. - ^{1}H NMR: 0.68-1.15(2H, m, cyclopropyl CH_2), 1.04(3H, s, cyclopropyl Me), 1.54-1.86(1H, m, cyclopropyl CH), 1.88 and 2.07(6H, both s, C=CMe_2), 4.75-5.03(2H, m, AB system, HC=$C\underline{H}_2$, 5.47(1H, dd, J14,9, X of ABX, $\underline{H}C$=CH_2), 7.1(5H, m, phenyl). - MS 244(57, M), 188(73), 135(147), 119(100), 91(77). (Found: $\underline{M}^+$, 244.1305. $C_{16}H_{20}S$ requires $\underline{M}$, 244.1285).

5-(Phenylthio)-2,6,6-trimethyl-1,4-cycloheptadiene (181), a pale yellow mobile oil, had:- TLC(hexane): R_f0.19. - IR(film): 2970, 2930, 2850, 1580, 1475, 1430, 1375, 1355, 1020, 735, 685. - ^{1}H NMR: 1.14(6H, s, Me_2), 1.78(3H, s, C=CMe), 2.23(2H, d, J7, $C\underline{H}_2$C=CMe), 2.81(2H, d, J6, $C\underline{H}_2$C=CSPh), 5.40(1H, br t, J7, $\underline{H}C$=CMe), 6.01(1H, t, J6, $\underline{H}C$=CSPh), 7.04-7.42(5H, m, phenyl H). - MS: 244(39, M), 188(100), 135(37, M-C_6H_5S), 119(87), 91(74). (Found: $\underline{M}^+$, 244.1298. $C_{16}H_{20}S$ requires $\underline{M}$, 244.1285).

2,5,5-Trimethyl-4-cyclohepten-1-one (Karahanaenone) (178). - By the method of Corey and Shulman,[113] a solution of mercuric chloride (231mg, 0.841mmol) in acetonitrite-water (4:1, 3ml) was added to a stirred solution of cycloheptadiene (181) (104mg, 0.426mmol) in acetonitrile-water (4:1, 6ml). The resulting solution was heated to reflux under N_2 for 14h. On cooling, precipitated solid was removed by filtration through Kieselguhr, with generous ether washings. The filtrate was washed with saturated sodium bicarbonate (x2), brine (x1), dried and evaporated to leave an oil containing some solid. This was taken

up in petrol, solid material filtered off, and the filtrate evaporated to give a pale yellow oil (58mg). TLC(silica/benzene) showed, that apart from the expected ketone, a few higher R_f impurities were present. Chromatography on silica gel (1x24cm) using hexane then hexane-ether (95:5) afforded karahanaenone (178) (29mg, 45%), as a pleasant smelling colourless mobile oil, having:- TLC(hexane-ether 9:1): R_f 0.31. Spectral data of our synthetic karahanaenone are given in Chapter Five, in comparison with the natural product.

Thermolysis of trans-1-Ethenyl-1-methyl-2-(2-methyl-1-(phenylthio)-1-propenyl)cyclopropane (180). - A solution of trans-vinyl-cyclopropane (180) (10.8mg, 0.044mmol, 0.59M) in benzene (75 µl) contained in a Pierce "Reacti-Vial" was heated, using a Pierce "Reacti-Therm" heating module, at 120° for 2h, then at 160° for a further 3h. Evaporation of solvent gave a pale yellow mobile oil (10mg). TLC(silica/hexane) showed one major component corresponding to cycloheptadiene (181). Examination of the ^{1}H NMR spectrum of the crude product showed that cycloheptadiene (181) was indeed the major product (ca. 70%) along with a trace of (180). Additionally, signals at δ3.50(d, J7) and 1.24(d, J7), suggest the formation of some 1,5-H rearranged product (ca. 20%); possibly triene (182).

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