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STUDIES IN CYCLOPROPENE CHEMISTRY

THESIS

Submitted to the

UNIVERSITY OF WALES

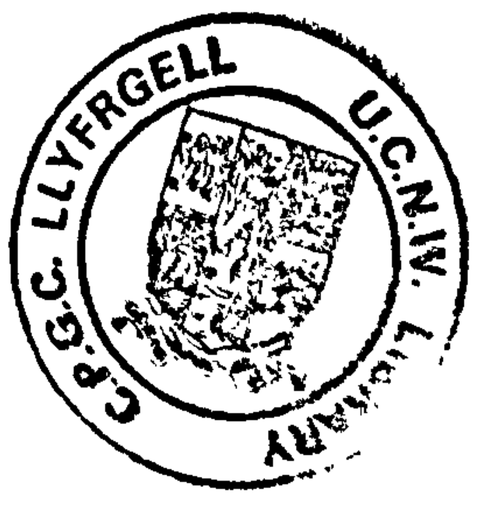
for the degree of

DOCTOR OF PHILOSOPHY

by

Ahmad R. Al-Dulayymi,

B. S c. (Baghdad) 1986



To my mother, father, brothers and sisters for their constant love, support and encouragement throughout my education

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Ahmad Al-Dulayymi

TABLE OF CONTENTS

Page No.

Dedication.

Acknowledgment.

Abstract. i

Publications. v

Abbreviations. vi

CHAPTER ONE: INTRODUCTION.

1.1 Carbenes. 1

1.2 Generation of dihalocarbenes. 4

1.3 Cyclopropenes. 7

1.3.1 Structure of the cyclopropene ring. 8

1.3.2 Synthesis of cyclopropenes. 9

1.3.2.1 Base induced elimination and intramolecular trapping of carbenes. 9

1.3.2.2 Carbene addition to an alkyne. 12

1.3.2.3 1,2-Elimination in cyclopropenes. 14

1.3.2.3.1 Dehydrohalogenation of monohalocyclopropanes. 14

1.3.2.3.2 Dehydrohalogenation of 1,1-dihalocyclopropanes. 15

1.3.2.3.3 1,2-Dehalogenation. 18

1.3.2.3.4 Dehalosilylation. 20

1.4 Chemistry of cyclopropene. 22

1.4.1 Electrophilic addition. 21

1.4.2 Reaction with nucleophiles. 25

1.4.3 The ene- reaction. 29

1.4.4 Cycloaddition. 31

CHAPTER TWO: RING OPENING OF CYCLOPROPENES

2.0 Introduction. 38

2.1 Aims of the project. 45

2.2 Results and discussion. 47

2.2.1 Preparation of tri- and tetrahalocyclopropanes. 47

2.2.2 Reaction of tri- and tetrahalocyclopropanes with methyllithium. 52

2.3 Conclusion. 70

CHAPTER THREE: PREPARATION OF 1-BROMO-2-ALKYLCYCLO-PROPENES USING DIALKYL PHSPHITE AND A TRIALKYL AMINE OR SODIUM HYDRIDE.

3.1 Introduction. 71

3.2 Aims of the project. 75

3.3 Results and discussion. 76

3.3.1 Reaction of trihalocyclopropanes with dialkyl phosphite and trialkylamine or sodium hydride. 76

3.3.2 Elimination of halogen from 1,2-dihalo or 1,1,2,2-tetrahalo-cyclopropanes. 82

3.4 Conclusion. 85

CHAPTER FOUR: FOUR CARBON CYCLOPROPANE AND CYCLOPROPENE SYNTHETIC INTERMEDIATES.

4.1	Introduction.	86
4.2	Aims of the project.	90
4.3	Results and discussion.	92
4.3.1	Preparation of required tri-bromocyclopropane ester.	92
4.3.2	Conversion of the ester into other groups.	93
4.3.3	Reaction of tribromocyclopropanes with methyllithium.	95
4.3.4	Dimerization of the cyclopropene alcohol.	99
4.3.5	Synthetic approaches to polycyclopropanes.	104
4.3.6	Reaction of the vinyl tribromo ester with methyllithium.	109
4.3.7	Reaction of Diels-Alder adducts of 1-bromo-2-bromomethyl cyclopropene and furans with butyllithium.	111
4.3.8	Reaction of Diels-Alder adducts of 1-bromo-2-bromoethyl cyclopropene and furans with butyllithium.	121
4.4	Conclusion.	124

CHAPTER FIVE: 2-VINYL-1,2,2-TRIHALOCYCLOPROPANES: VALUABLE FIVE CARBON CYCLOPROPANE AND CYCLOPROPENE INTERMEDIATES.

5.1	Introduction.	125
5.2	Aims of the project.	129
5.3	Results and discussion.	129
5.3.1	Preparation of vinyl trihalocyclopropanes.	129
5.3.2	Reaction of vinyl trihalocyclopropane with methyllithium.	134

5.4 Conclusion. 154

CHAPTER SIX: ADDITION OF DIAZOMETHANE TO 1-BROMO AND 1,2-DIBROMOCYCLOPROPENES.

6.1 Introduction. 156

6.2 Aims of the project. 161

6.3 Results and discussion. 162

6.3.1 Reaction of 1,2-dibromocyclopropene with diazoalkanes. 162

6.3.2 Reaction of 1-bromo-2-alkylcyclopropenes with diazomethane. 168

6.4 Conclusion. 177

CHAPTER SEVEN: EXPERIMENTAL

7.1 General Experimental Details. 178

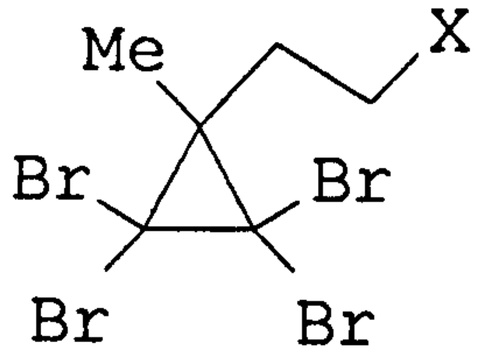
7.2 Experiments. 179

8. REFERENCES. 249

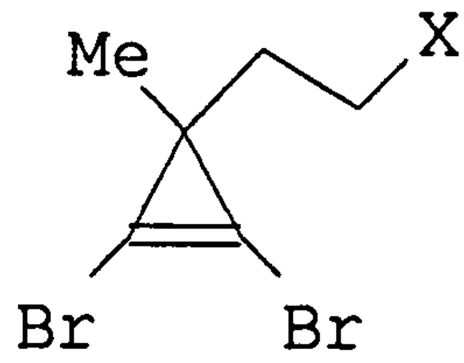
9. APPENDIX I.

ABSTRACT

1,2-Dehalogenation of the 1,1,2,2-tetrabromocyclopropanes (A, X = OMe, Br) by reaction with one mol. equiv. of methyllithium at -78 °C, leads to 1,2-dibromocyclopropenes (B, X = OMe, Br).

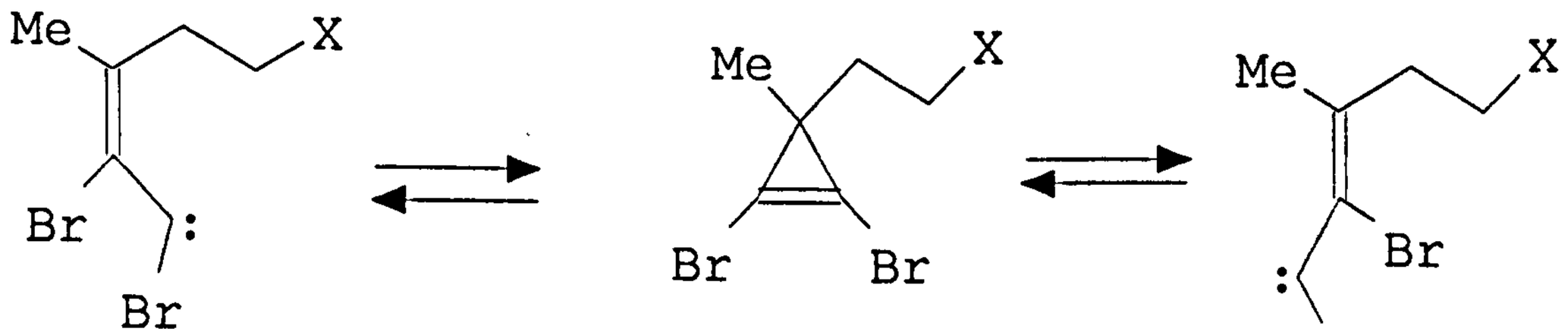


(A)



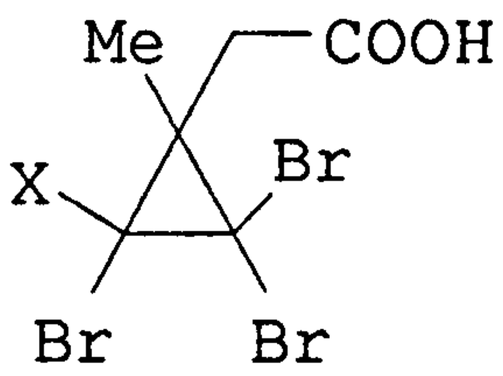
(B)

The cyclopropenes (B, X = OMe, Br) undergo ring-opening at ambient temperature to produce two stereoisomeric carbenes (C) and (D).



(C) (B) (D)

The tri- and tetrabromocyclopropane acids (E, X = Br, H) react with HgO/Br_2 giving unexpectedly (F, X = Br, H), which on dehydrohalogenation using a bulky base such as DBU give (G, X = Br).



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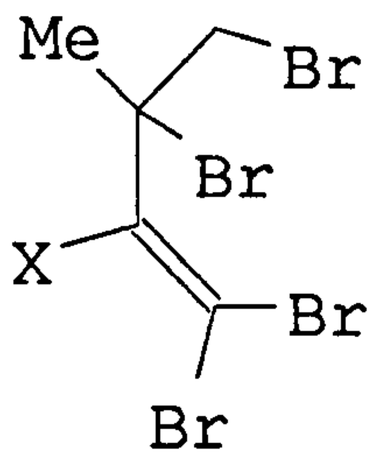

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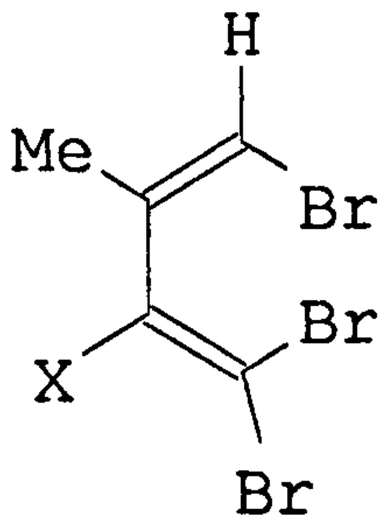
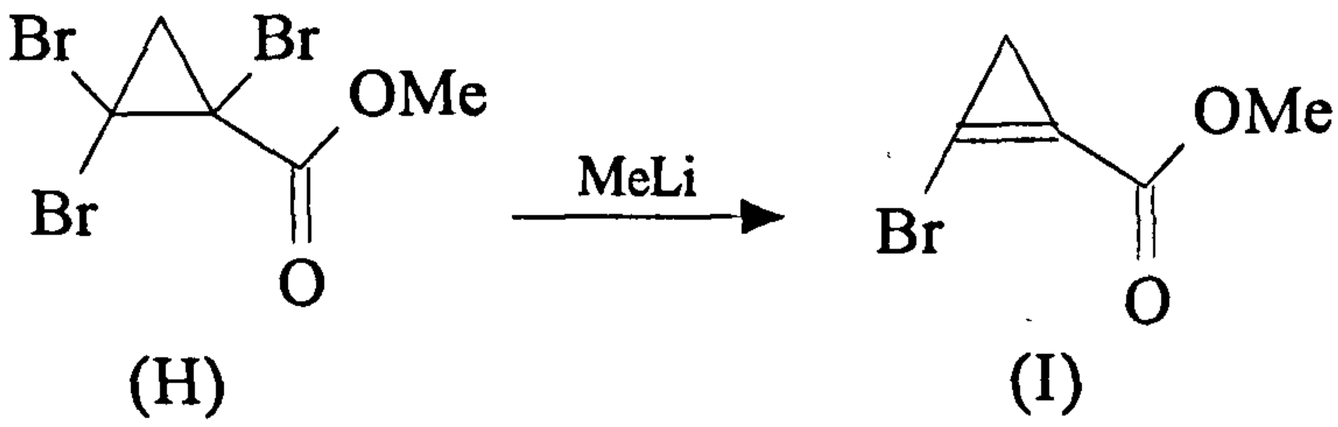


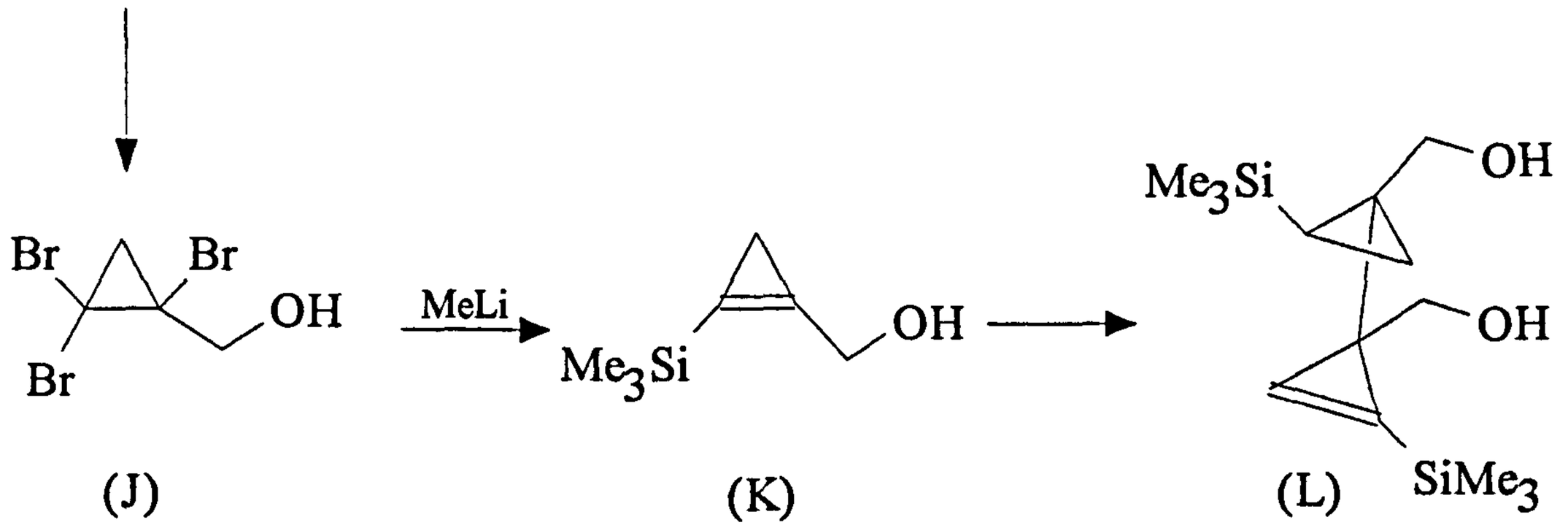
(G)

The reaction of 1,1,2-trihalocyclopropanes with dialkyl phosphite in presence of a base such as Et_3N or sodium hydride leads to a high yield of the corresponding 1-halocyclopropene via a 1,2-dehalogenation. Moreover, 1,1,2,2-tetrahalocyclopropanes react with dialkyl phosphite and base leading to an allenic carbene, which in the presence of an electron rich alkene is trapped to give the allenic cyclopropane.

The trihalocyclopropane ester (H) is readily available by dibromocyclopropanation of methyl α-bromoacrylate. The reaction of (H) with methyllithium at low temperature provides a simple route to methyl 2-bromocyclopropene carboxylate (I). Modification of the ester group followed by reaction with methyllithium leads to a series of related four-carbon cyclopropenes, e.g. the cyclopropene alcohol (K). The cyclopropene (K) was found to undergo an ene-type reaction to a dimer (L). The stereochemistry of the product was determined by X-Ray crystallography.

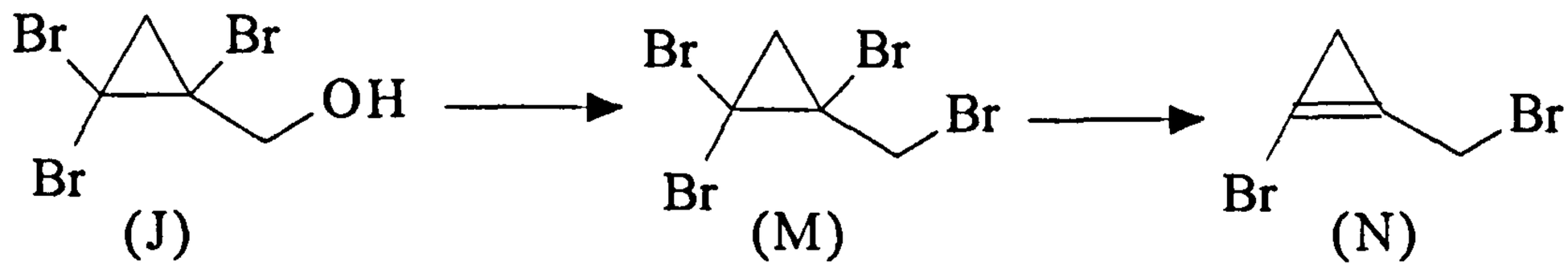


(H) (I)

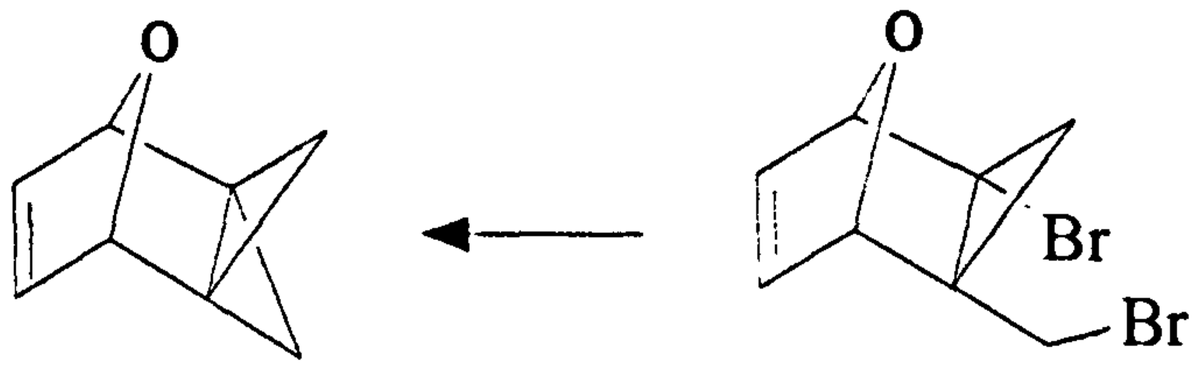


(J) (K) (L)

The cyclopropane alcohol (J) was converted into the tetrabromocyclopropane (M), which reacted with one mol. equiv. of methylithium to give (N). (N) was trapped by a [4+2]-cycloaddition with furan (O). The cycloadduct (O) were found to react with butyllithium to give the propellane (P).

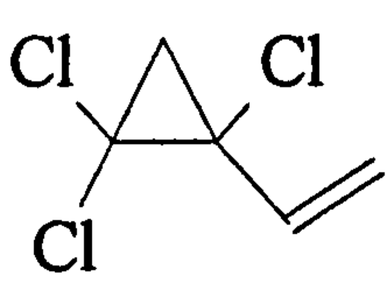


(J) (M) (N) (O)



(P)

Dihalocyclopropanation of chloroprene and 2,3-dichlorobutadiene with dibromo-carbene or dichloro carbene leads to trihalocyclopropanes (Q), (R), (S) and (T).



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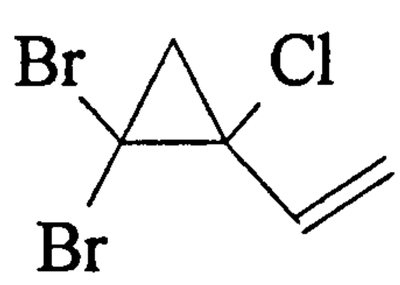

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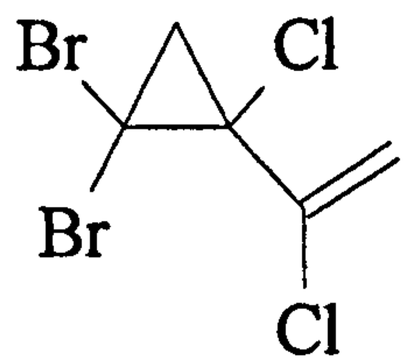

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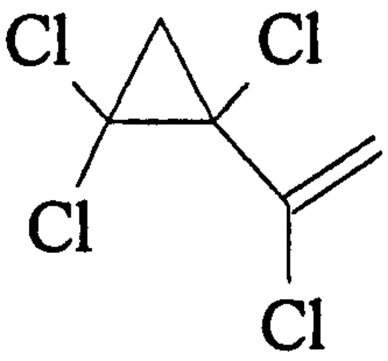
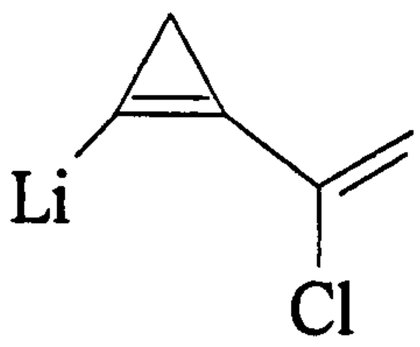


(T)

Reaction of these cyclopropanes with one or two mol. equiv. of methyllithium provides a practical route to a series of related five carbon cyclopropenes. These cyclopropenes are readily trapped in a Diels-Alder reaction. The trapping of 1-lithio-2-(1-chlorovinyl)cyclopropene (U) with methyl chloroformate leads to a very unusual cyclononadienyne (V), the structure of which was again confirmed by X- Ray crystallography.



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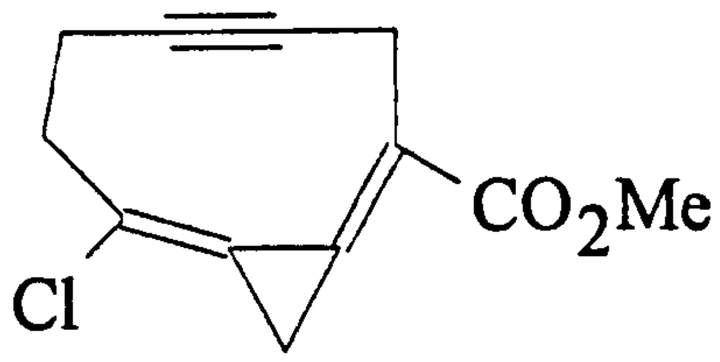
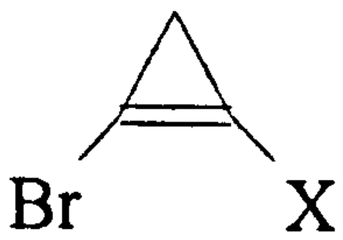
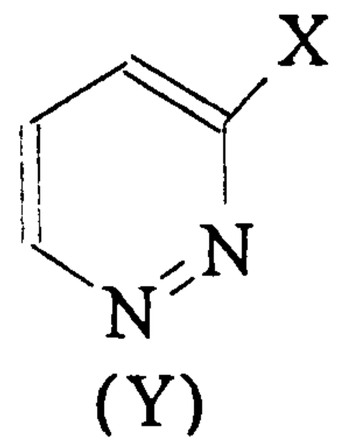


(V)

The reaction of a diazoalkene with 1,2-dihalo- or 1-halo-2-alkylcyclopropene (W, X = Br, R) gave 3-bromo or 3-alkylpyridazines (Y, X = Br, R) respectively.



(W)



(Y)

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Ahmad R. Al-Dulayymi and Mark S. Baird, *J. Chem. Soc., Perkin Trans. 1*, 1994, 1547.

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Ahmad R. Al-Dulayymi, M. S. Baird, J. R. Al-Dulayymi and L. Rajaram, *Tetrahedron.*, 1995, **51**, 8371.

3- 1,2,2-Tribromocyclopropanecarboxylic Acid and Derivatives-Valuable Intermediates for Four Carbon Cyclopropane and Cyclopropene Synthons.

Ahmad R. Al-Dulayymi, M. S. Baird, J. R. Al-Dulayymi, M. E. Gerrard, G. Koza, S. D. Harkins and E. Roberts, *Tetrahedron.*, 1996, **52**, 3409.

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Ahmad R. Al-Dulayymi and Mark S. Baird, *Tetrahedron.*, 1996, **52**, 10955.

5- A Strained Cyclononadienyne.

Ahmad R. Al-Dulayymi, M. S. Baird and W. Clegg, *Acta Crystallographica*, 1996, **C52**, 3219.

6- An Efficient Route to Oxygen Bridged [4.1.1] Propellanes.

Ahmad R. Al-Dulayymi and Mark S. Baird, (paper in preparation).

7- Simple Four and Five Carbon Cyclopropane and Cyclopropene Synthetic Intermediats.

Ahmad R. Al-Dulayymi, M. S. Baird, J. R. Al-Dulayymi and G. Koza, (in press).

ABBREVIATIONS

aq	aqueous
b.p	boiling point
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DPIBF	diphenylisobenzofuran
DEP	diethyl phosphite
DIBAL-H	diisobutylaluminium hydride
DMF	dimethylformamide
DMSO	dimethylsulphoxide
equiv.	equivalent
g	gram(s)
h	hour(s)
ir	infra red
m.p	melting point
ppm	parts per million
PTC	phase transfer catalyst
PCC	pyridinium chlorochromate
PPTSA	pyridinium *p*-toluenesulfonate
TEBA	triethyl benzyl ammonium chloride
tlc	thin layer chromatography

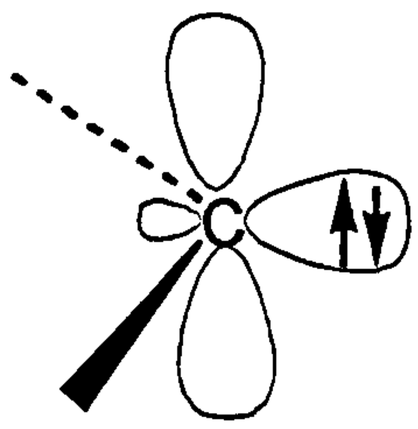
Chapter 1

Introduction

1.0. INTRODUCTION

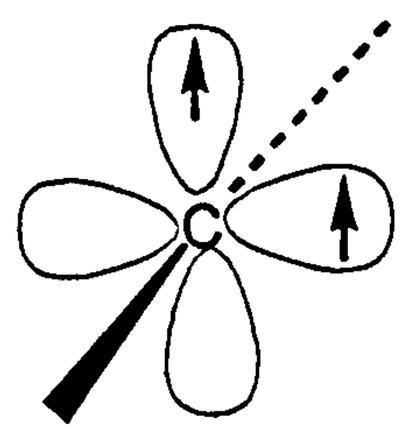
1.1. CARBENES

Carbenes are short lived, neutral intermediates, in which the carbon atom has two electrons distributed between two non-bonding orbitals.[1] If the two electrons are spin paired, then the carbene is a singlet, and if the two electrons are spin parallel then the carbene is a triplet. A singlet carbene is believed to have a bent sp^2 hybrid structure (**1**) with an empty p-orbital. However the triplet carbene has a linear sp hybrid structure (**2**) with one electron in each orbital.



(1)

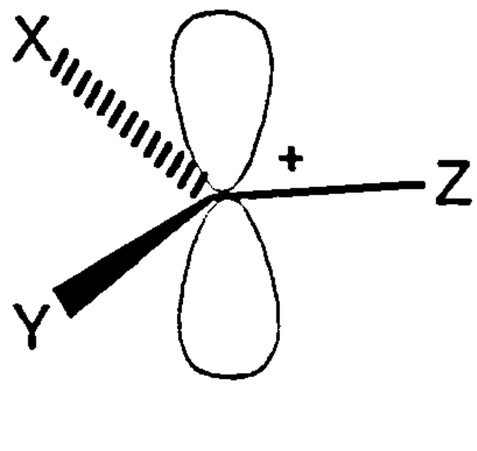
Singlet



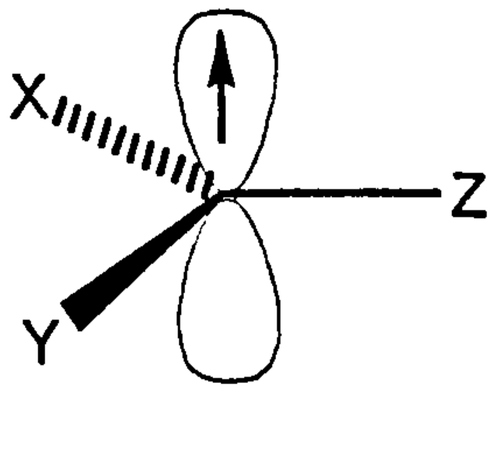
(2)

Triplet

A carbene in the singlet state is reminiscent of a carbenium ion (**3**), whilst the linear triplet carbene resembles a free radical (**4**).



(3)

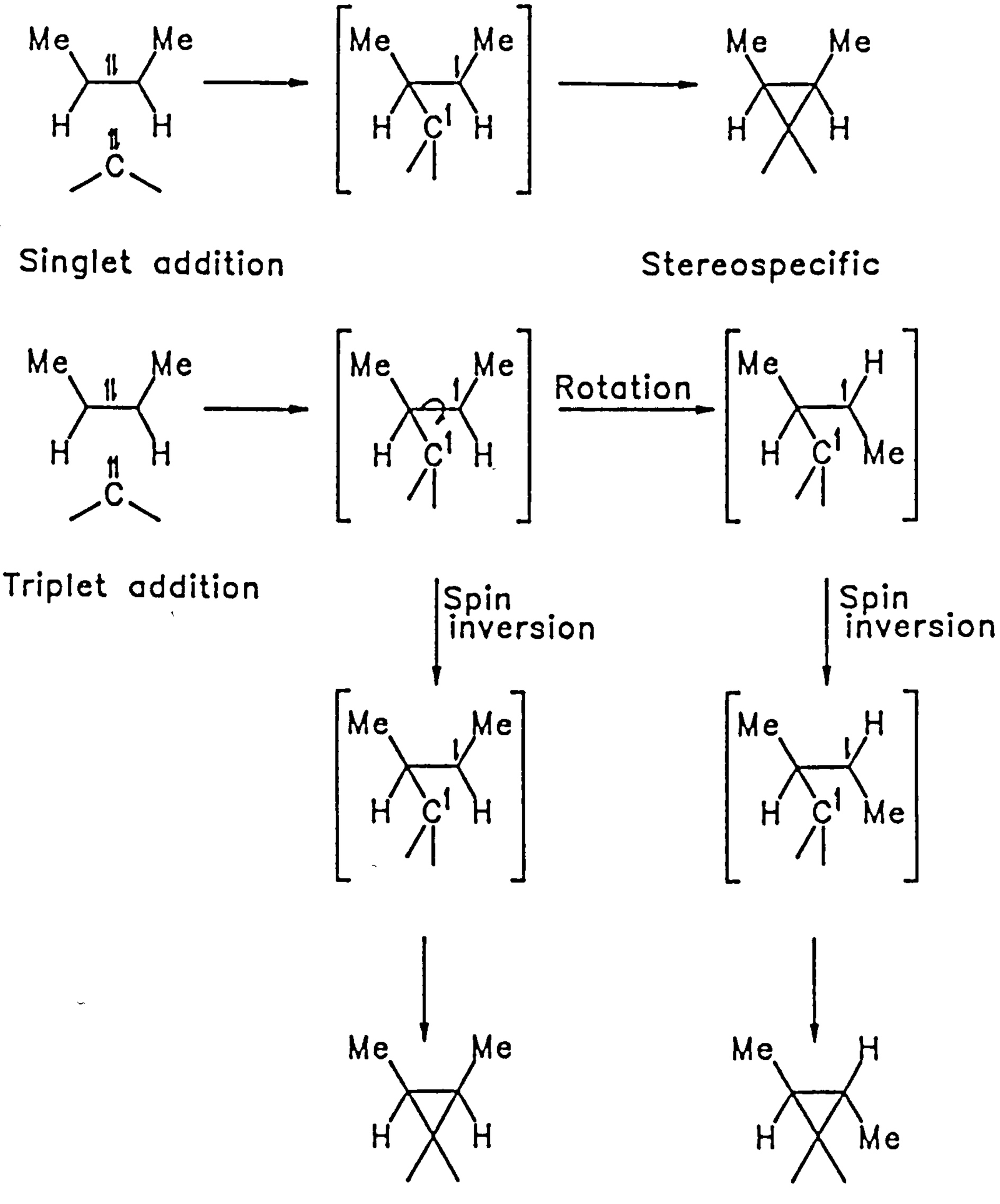


(4)

One important difference between the behaviour of singlet carbenes and that of triplet carbenes is the stereochemistry of their additions to alkenes. This was investigated by Skell, who found that the mechanism of additon of the carbene depends on the spin.[2] The singlet addition is stereospecific and reaction with a *cis*-alkene will always give only a *cis*-isomer. The triplet addition is non-stereospecific, and with a *cis* alkene can give two isomers because it forms a triplet state 1,3-diradical intermediate which must invert the spin of one electron by a collisional process before ring closure is possible (**Figure 1**). The intermediate may exist sufficiently long to enable rotation about the C-C bond to occur and hence the addition is non-stereospecific.

Figure 1

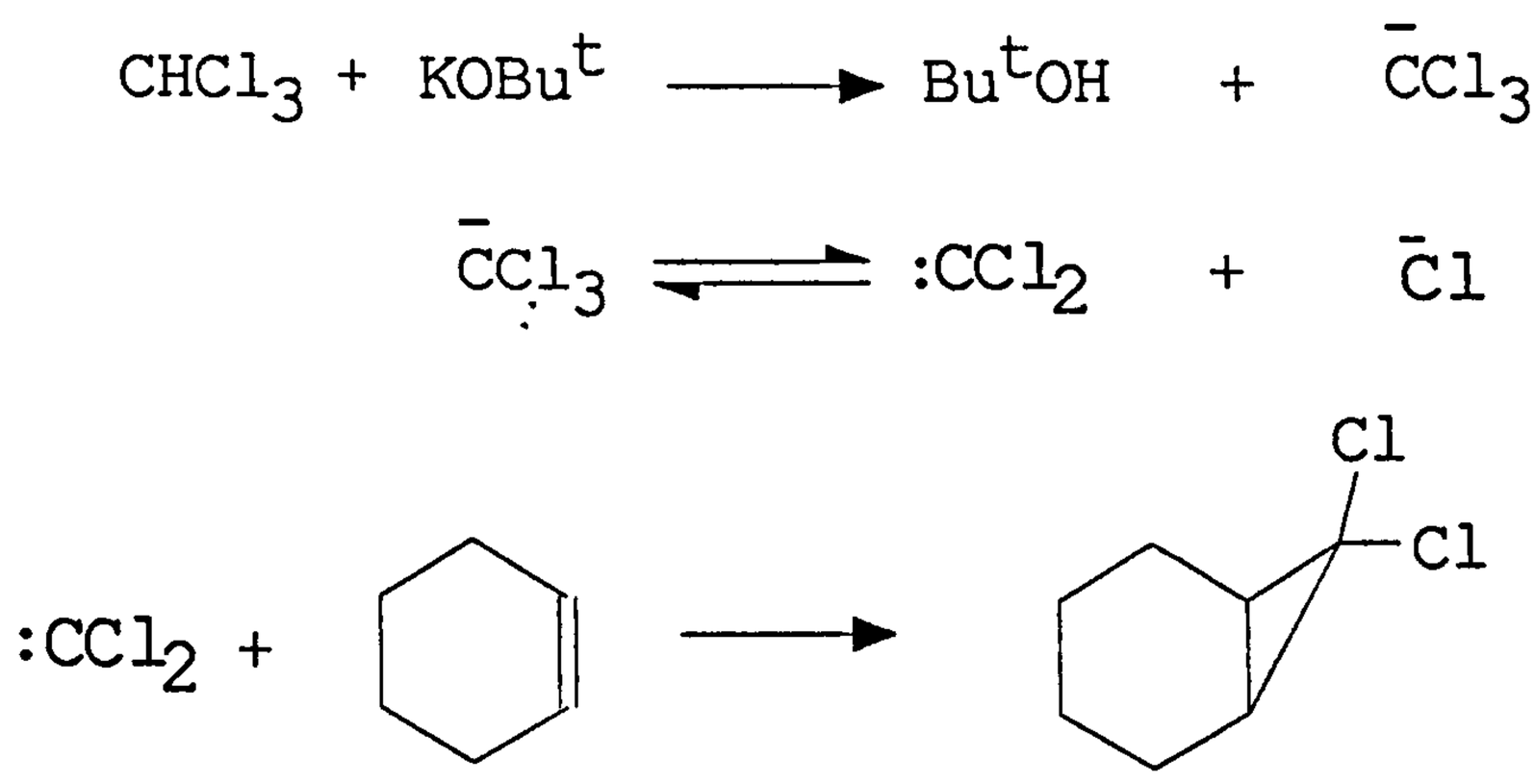
Skell 's hypothesis.[2a,2b]



Non-Stereospecific

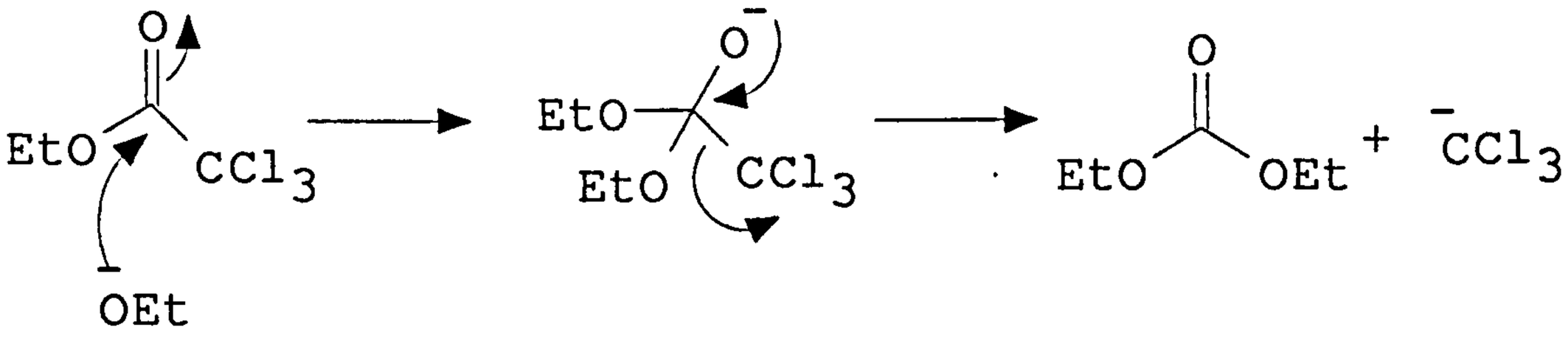
1.2. GENERATION OF DIHALOCARBENES

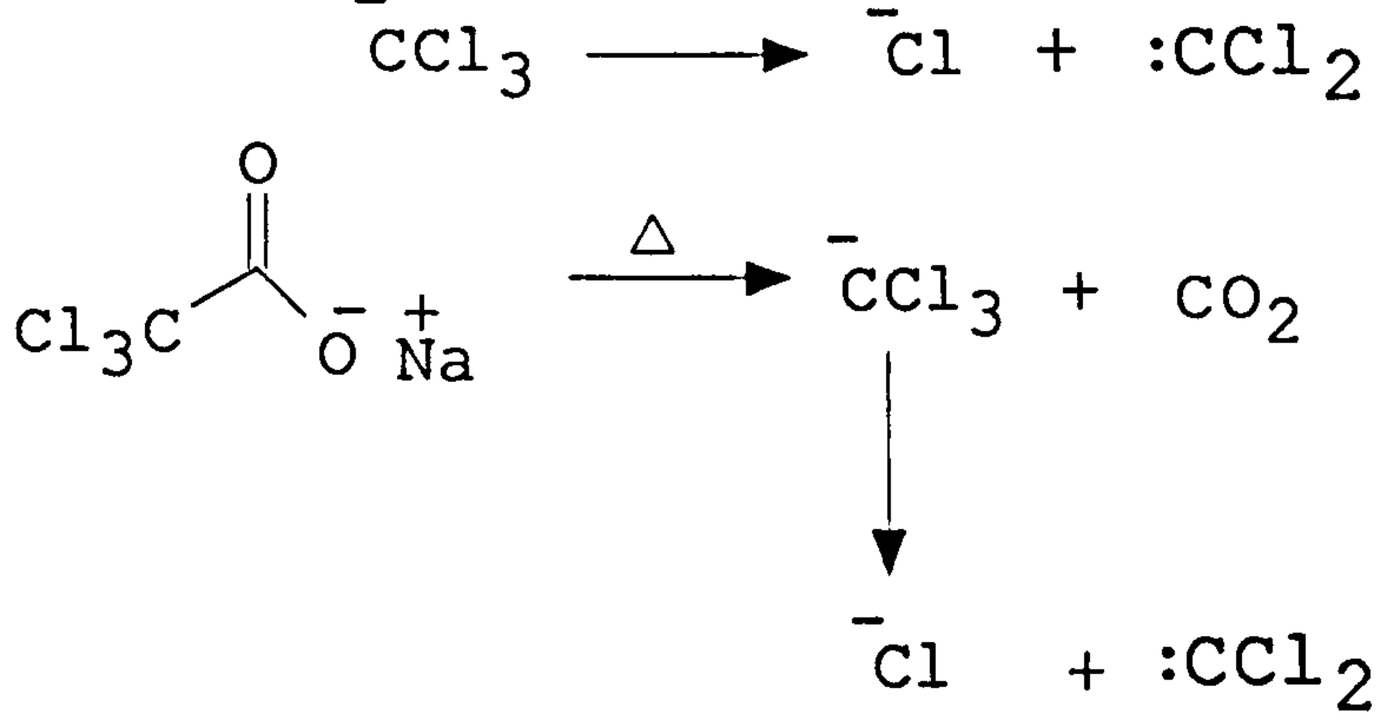
In 1954, Doering and Hoffman obtained the first dichlorocyclopropanes by treating chloroform with potassium t-butoxide in the presence of an alkene such as cyclohexene.[3] The strong base deprotonates the chloroform to give the trichloromethylanion followed by loss of a chloride anion to give a neutral dichlorocarbene, which in turn adds to the alkene.



A major disadvantage of this method, however, is the formation of the alcohol which can react with the carbene.

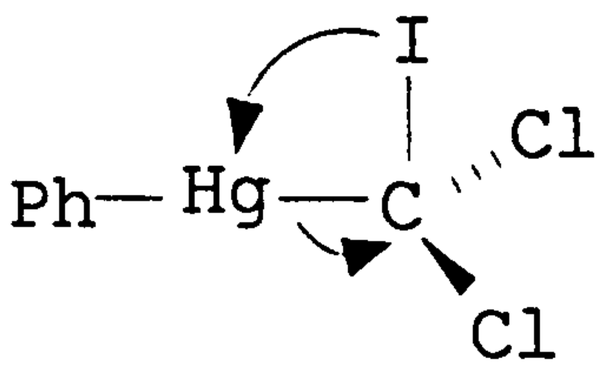
It was later found that dichlorocarbene could be prepared by treatment of ethyl trichloroacetate with sodium ethoxide and by thermal decomposition of sodium trichloroacetate, which gave good routes to dichlorocarbenes which are free from alcohol formation.[4,5]





Thermolysis of a trihalomethyl phenylmercury, introduced by Seyferth, is a good method of generating dihalocarbenes under mild, neutral conditions (e.g refluxing benzene), and is applicable to base sensitive substrates. The compound liberates dihalocarbene without a formation of an intermediate trihalomethylanion.[6] The problems associated with this method, however, are the high cost and the toxic nature of the reagents.

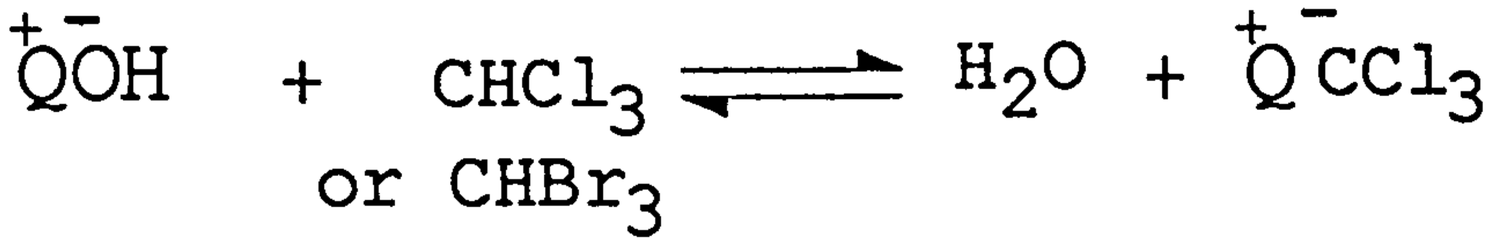
The most reactive such reagent is considered to be Ph Hg CCl_2I.[7] The increased reactivity is due to the weaker C-I bond compared to the carbon-chlorine and carbon-bromine bonds and subsequent ease of nucleophilic attack at mercury by iodine.



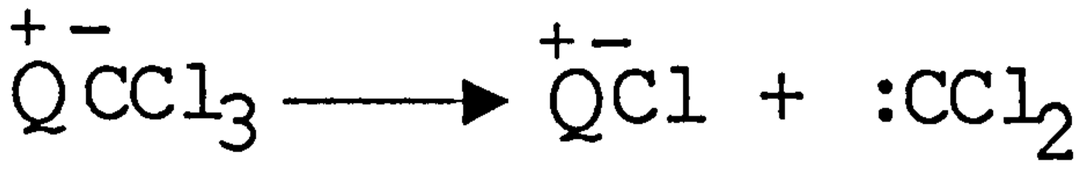
In 1969, Makosza provided a simple route for generating dihalocarbenes which does not requires anhydrous conditions.[18] This employs a two phase system in which the haloform is treated with 50 % aqueous sodium hydroxide in the presence of a phase transfer catalyst - a quaternary ammonium salt ($Q^+ X^-$), usually triethylbenzylammonium chloride (TEBA), cetyl trimethylammonium chloride (cetrimide) or tetrabutylammonium chloride. The reaction is formulated as occurring at the phase boundary and may be described by the following steps.

(A) Exchange of halogen for hydroxide anion in aqueous medium

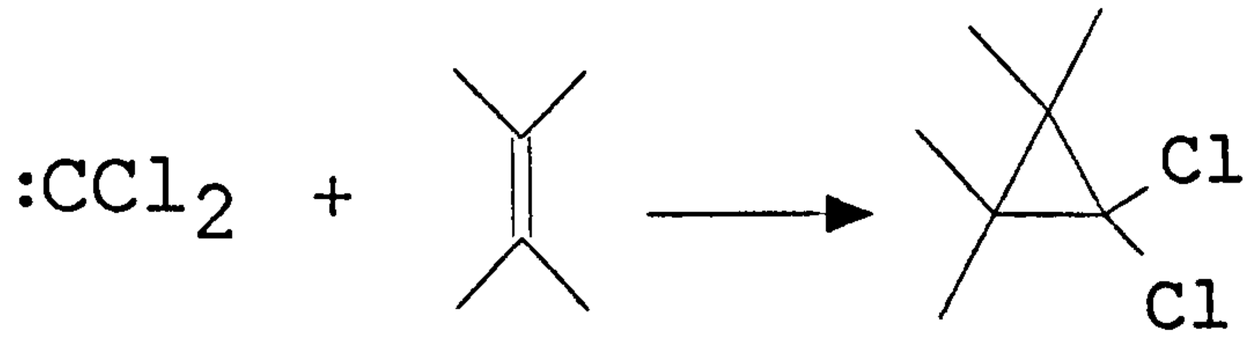
(B) Deprotonation of haloform at the interface



(C) Dissociation of trihalomethylanion in organic medium

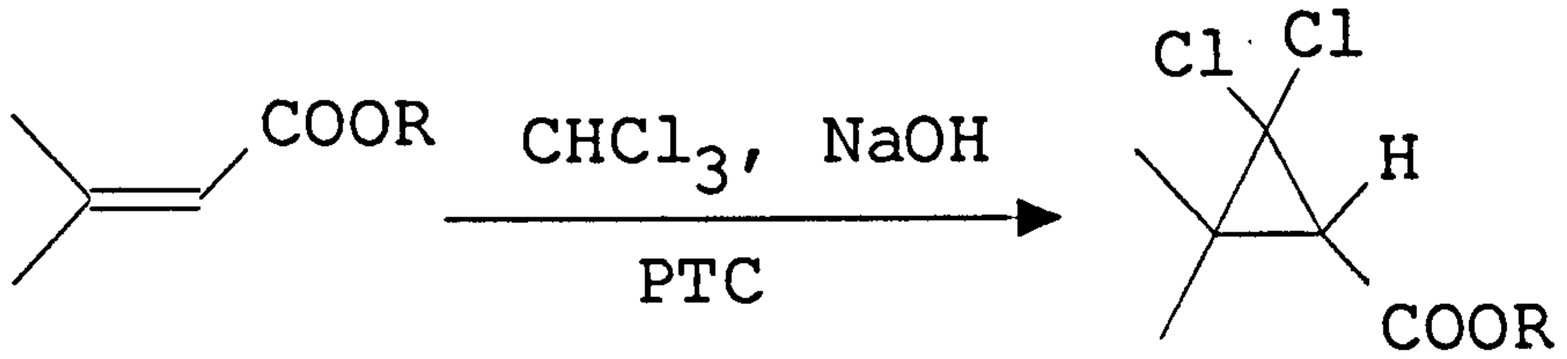


(D) Addition of dihalocarbene to the alkene in organic medium

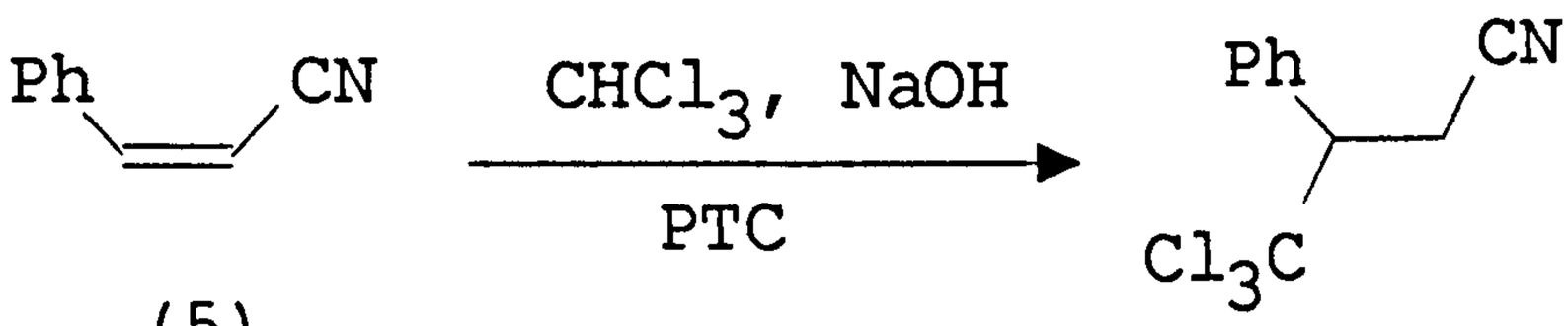


The carbenes generated by this method were found to be particularly reactive, $:CBr_2$ more so than $:CCl_2$. This may be attributed to the reversible generation of a large excess of carbene at the site of reaction.[8]

As stated above, the dichloro- or dibromocarbene of the Makosza process is in equilibrium with trihalomethylanion. Depending upon whether electron rich or electron poor olefins are present, either the electrophile :CCl_2, or the nucleophile $^-CCl_3$, or in some cases both are captured.[9]



In the presence of electron deficient alkenes such as (**5**) the trihalomethyl anion is trapped in a Michael type addition to give the trihalomethyl-compound.[9]

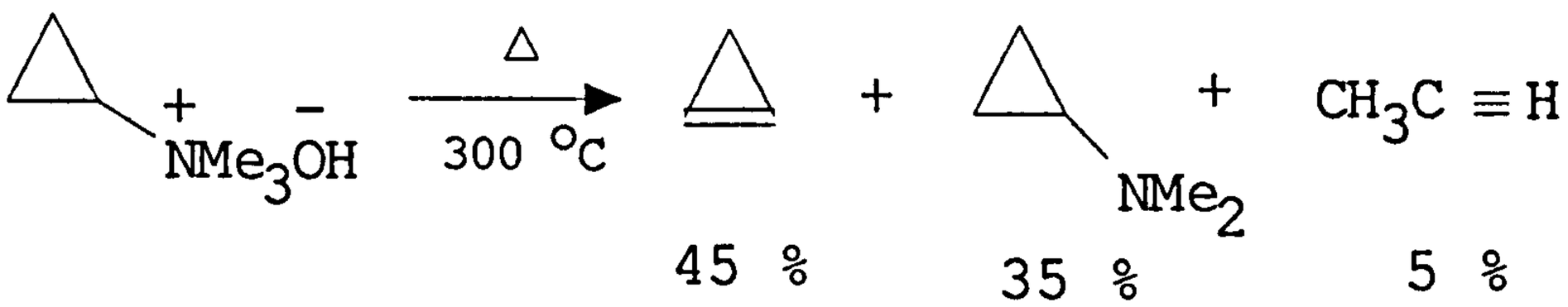


(5)

The advantage of the phase transfer process is that it utilises inexpensive reagents and a simple procedure. It is perhaps the most important source of dihalogenocarbenes.

1.3. CYCLOPROPENES

Although cyclopropane was obtained as early as 1884 by Freundler,[10] the first preparation of cyclopropene was claimed in 1922 by Demyanov and Doyarenko, who pyrolysed trimethylcyclopropyl ammonium hydroxide on platinized clay at approximately 300 °C to afford cyclopropene in 45 % yield, via Hoffman elimination.[11]



Despite these early begining, the chemistry of cyclopropene and its derivatives received little attention until the middle 1950' s and has grown rapidly in recent years due to the presence of cyclopropenes in natural fatty acids and the developments of synthetic routes based on cyclopropenes. The development of the chemistry provided new and more facile routes to these compounds.

1.3.1. STRUCTURE OF THE CYCLOPROPENE RING

Attention was pointed towards cyclopropene and its derivatives because of their highly strained structure. Whereas the ring strain of cyclopropane is 118 KJ mol^{-1},[12] that of cyclopropene is 228 KJ mol^{-1}.[13] This additional strain energy is believed to be localised in the σ-framework, with increased angular strain at all three carbon atoms contributing significantly; the $C_1C_2C_3$ angle is 51 ° and the $C_1C_3C_2$ angle is 64.5 ° corresponding to a bond angle in cyclopropane of 78.8 °.[14] The highly strained nature of cyclopropene results in a deviation of the hybridisation of the alkene carbons from the sp^2 hybridisation characteristic of open chain and large ring alkenes. Analysis of structural data of a variety of cyclopropene derivatives has led to the conclusion that the vinylic carbon atoms of cyclopropene use $sp^{1.19}$ hybrid orbitals in bonding to substituents and $sp^{2.68}$ hybrids to the σ-framework.[14] The short carbon-carbon double bond length (129.6 pm) and the high vibrational frequency in the infra-red, 1641 cm^{-1}, would suggest that the π-bond is strong,

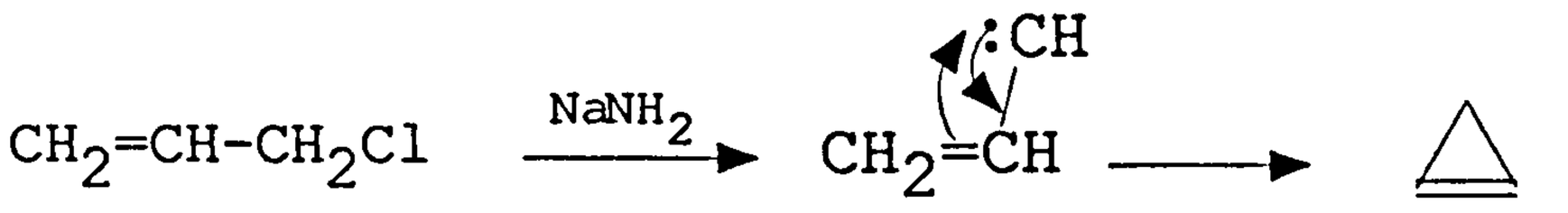
though the high reactivity as a dienophile in a [4+2] cycloaddition contradicts this.[14,15] Calculations have shown that σ-donating, π-withdrawing and most π-donating substituents stabilize cyclopropene, which is common with other strained molecules. This is supported by the shifting of the infra-red stretching vibration to 1740 cm^{-1} when the vinylic hydrogen was replaced by the methyl group and a further 145 $cm^{-1}$to 1885 cm^{-1} when both hydrogens are replaced by methyl group.

The nuclear magnetic resonance spectrum reflects the unusual bonding in the ring; thus the vinylic protons resonate at 7.01 ppm, approximately 1 ppm to lower field than other cycloalkenes.[15] This deshielding reflects the enhanced s character in the C-H bond and the magnetic anisotropy of the ring bond. The methylene protons resonate at δ 0.92 ppm, shielded by the existence of a ring current from the σ-framework electrons within the molecule. In the ^{13}C spectrum, the vinylic carbons resonate at δ 108.7, a lower chemical shift than for an open chain alkene signal, while the C_3 carbon resonates at 2.3 ppm.

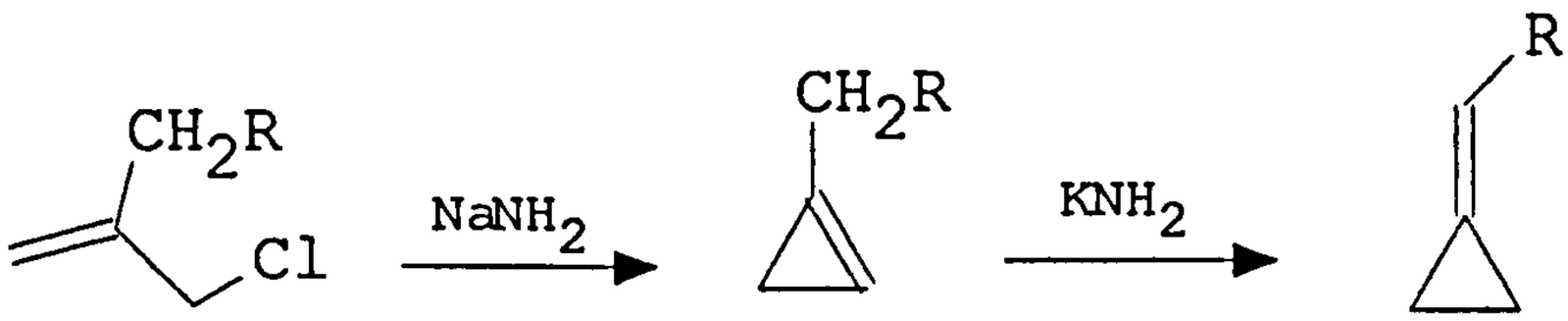
1.3.2. SYNTHESIS OF CYCLOPROPENES

1.3.2.1. BASE INDUCED 1,1-ELIMINATION AND INTRAMOLECULAR TRAPPING OF CARBENES

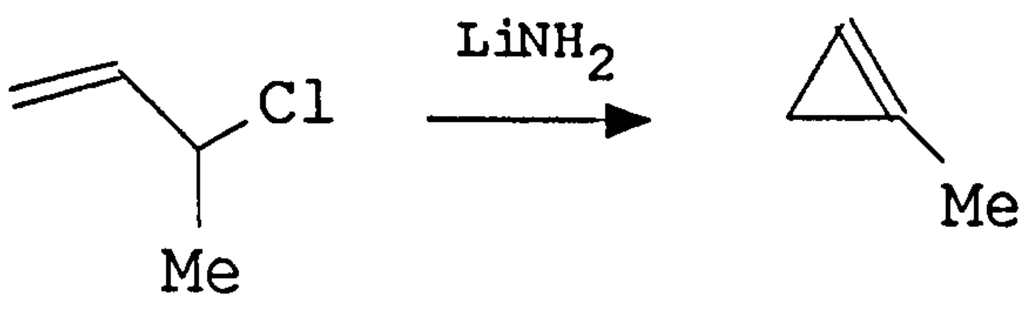
The rearrangment of a vinylcarbene to cyclopropene is well known and provides a method for the synthesis of compounds whose substituents range from simple to complex. Base induced dehydrohalogenation of an allylic chloride gives simple cyclopropenes as well as cyclopropene itself.[16,17,18]



63 %

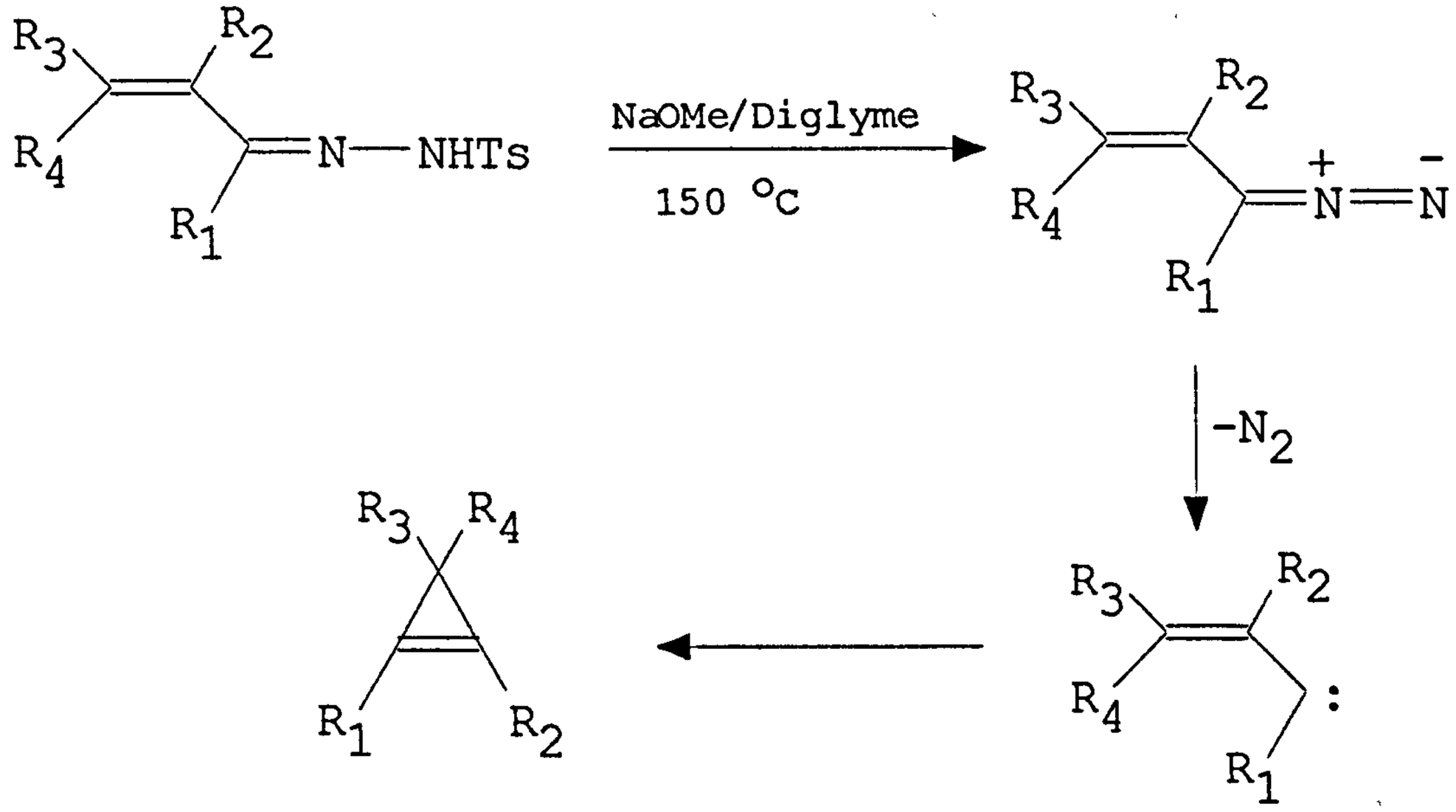


R = H, Me



With substituted allylic chlorides, the strong base can react further with the cyclopropene to give a methylenecyclopropane; however lithium amide appears to be the base of choice for cyclopropene formation. The position of the alkyl substituent in the product indicates that cyclisation occurs with rearrangment of the double bond, arising by 1,1-elimination of hydrogen chloride and formal formation and cyclisation of a vinylcarbene.

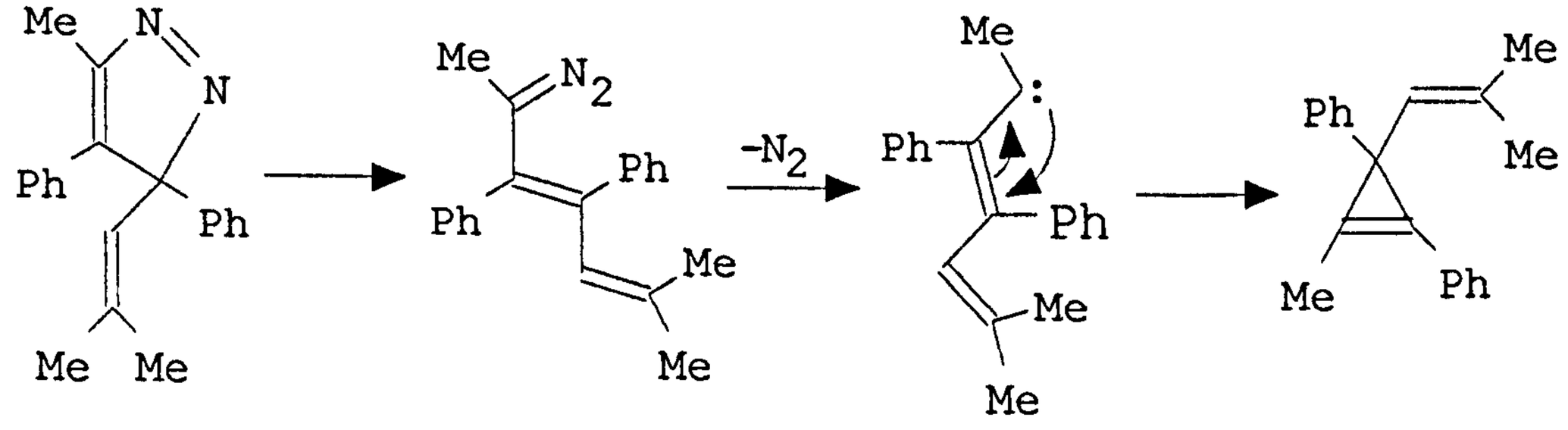
Vinylcarbenes are also available by the loss of nitrogen from a diazoalkene. Base induced pyrolysis of tosylhydrazones of α, β-unsaturated aldehydes or ketones leads to the elimination of nitrogen to give the alkenylcarbene followed by cyclization to the desired cyclopropene:[19]



R_1, R_2 = H or alkyl

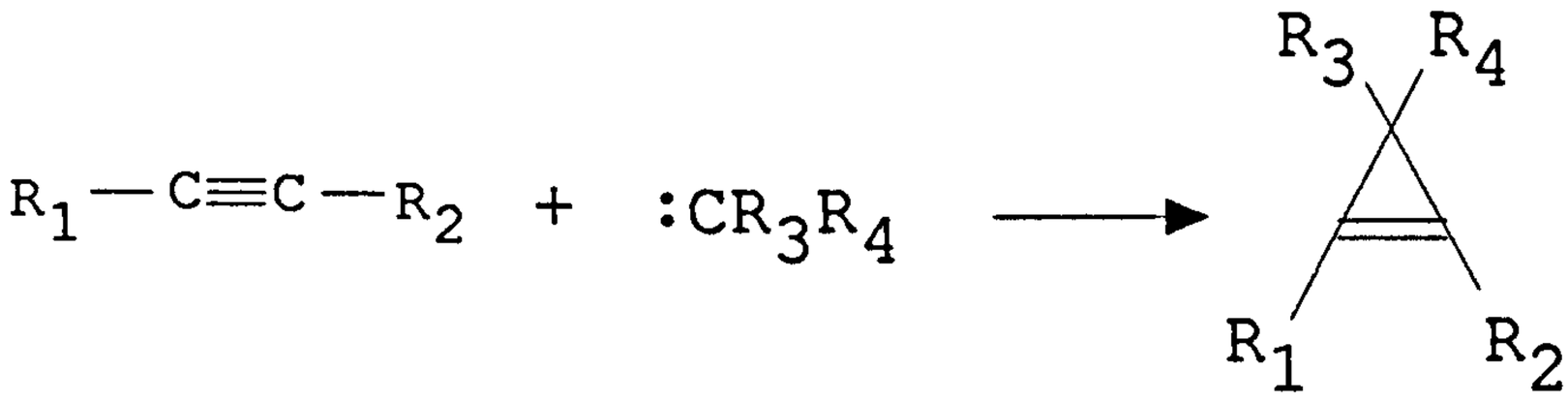
R_3, R_4 = alkyl

The decomposition of 3H-pyrazoles is the most common source of α, β-unsaturated carbenes. On photolysis or pyrolysis these compounds undergo ring cleavage to an α-diazoalkene, which loses nitrogen to form the vinyl carbene followed by cyclisation to form the cyclopropene.[20]



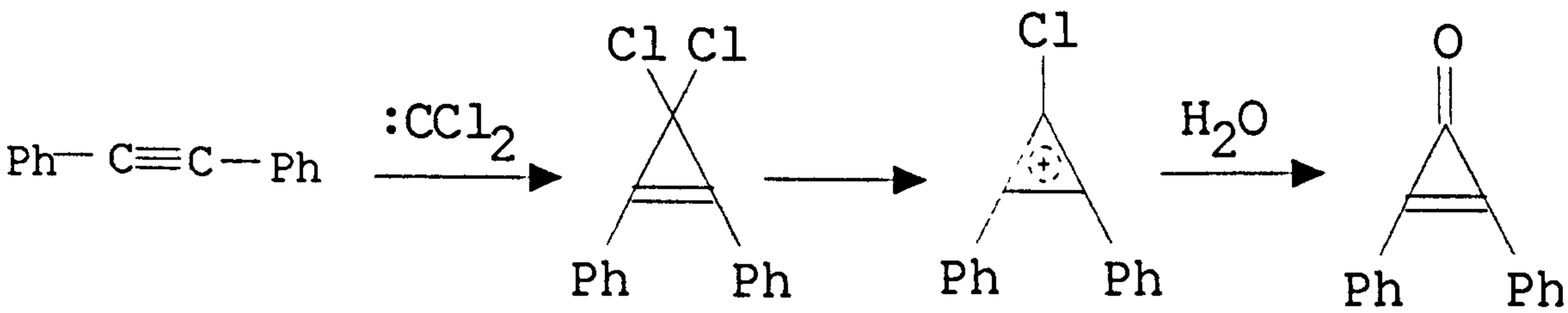
1.3.2.2. CARBENE ADDITION TO AN ALKYNE

The addition of a carbene to the a carbon-carbon triple bond of an alkyne provides a good and versatile route to a range of cyclopropenes.

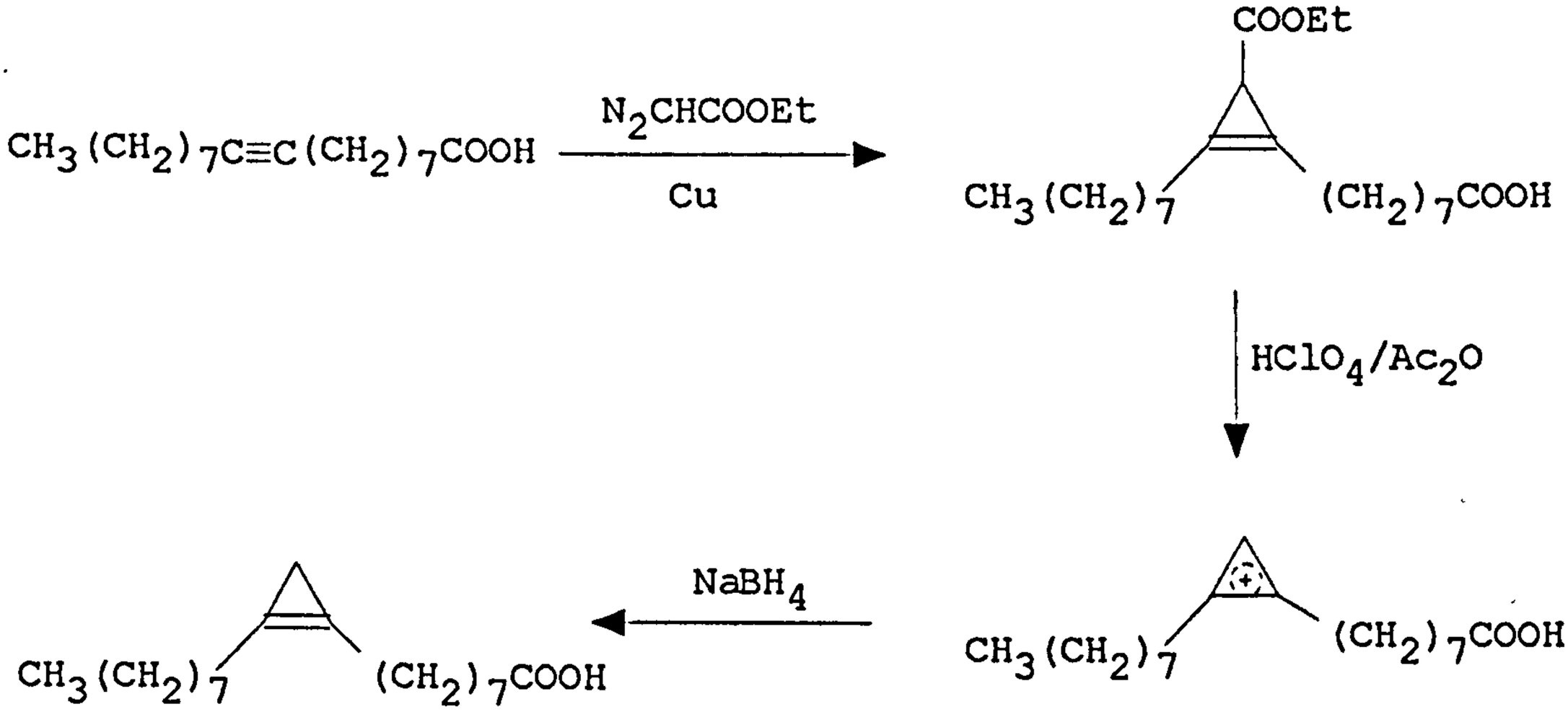


The cyclopropene ring is constructed in a single step by the formation of two σ-bonds, but the concertedness or otherwise of the reaction is dependent upon the multiplicity of the carbene. In general this method is limited by the availability of the divalent carbon species. It is not suitable for the preparation of cyclopropenes bearing an alkyl group at the C_3 position due to the instabilty of the alkylcarbene which rearranges rapidly to an alkene . The second restriction is the requirement for an internal alkyne because with the terminal alkyne insertion of the carbene into the C-H bond competes with addition.

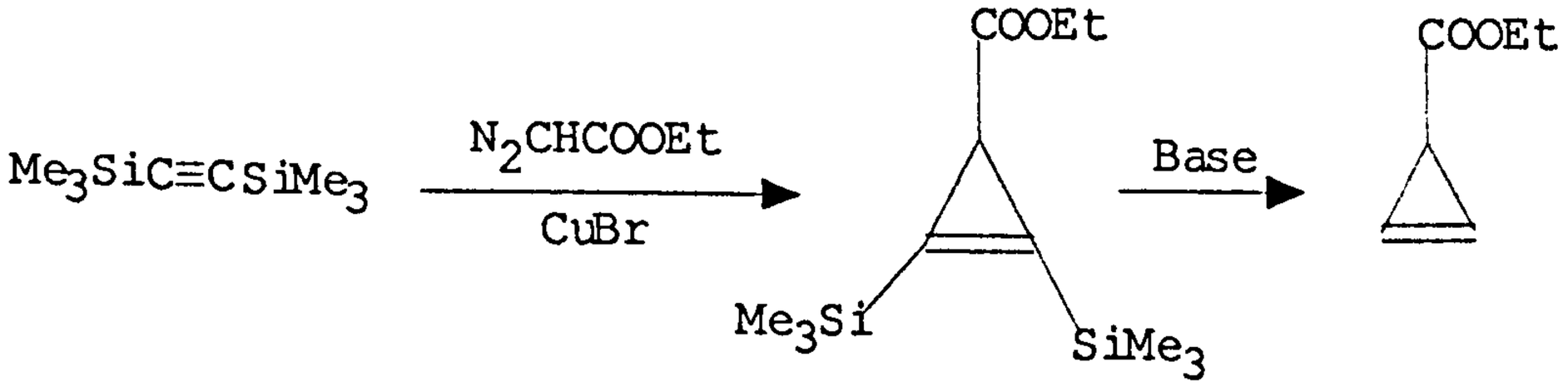
As mentioned previously, halocarbenes are readily generated by a variety of methods and provide a general route to 3,3-dihalocyclopropenes,[21] but the weak bond between the carbon and halogen in the resulting cyclopropene leads to the formation of the cyclopropenium cation, which may in turn be trapped by a nucleophile, such as water, leading to the cyclopropenone.



In other case cyclopropenes have been obtained by direct reaction of an alkyne with a diazo-compound in the presence of a suitable catalyst. Typical of these is the reaction of ethyl diazoacetate with alkynes in the presence of copper, which is reported to lead to about 40 -50 % conversion to cyclopropene per equivalent of diazocompound. This has been applied to the synthesis of the important naturally occurring cyclopropene, sterculic acid.[22]



The use of labile silicon based protecting groups to prevent C-H insertion provides a route to terminal alkyne addition products, releasing the cyclopropene after carbene addition by removal of the silyl-groups either by base or fluoride ion. The protecting group must be a trialkylsilyl derivative to prevent insertion of the carbene into a Si-H bond.[23]

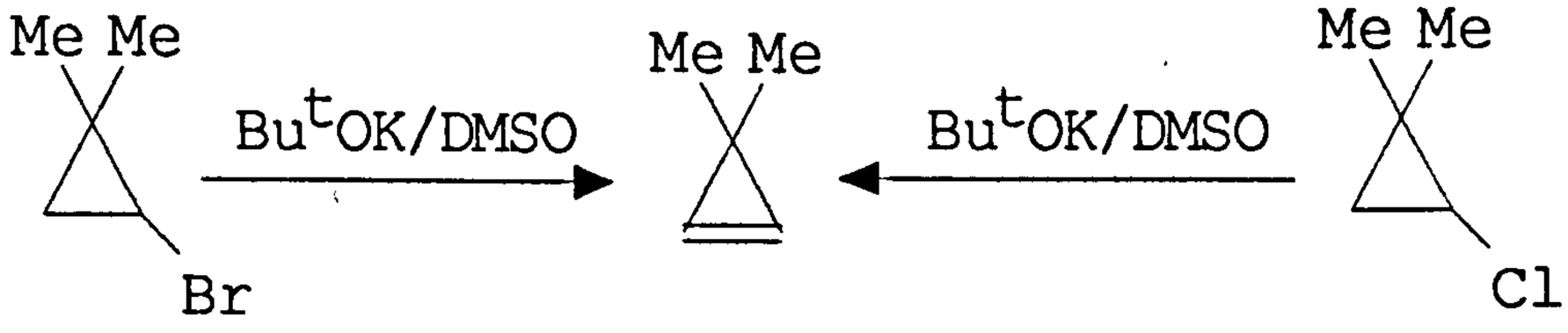


1.3.2.3. 1,2-ELIMINATION IN CYCLOPROPANES

The first synthesis of cyclopropene was by an elimination from a cyclopropane[16] and this still remains the most widely used method of preparation.

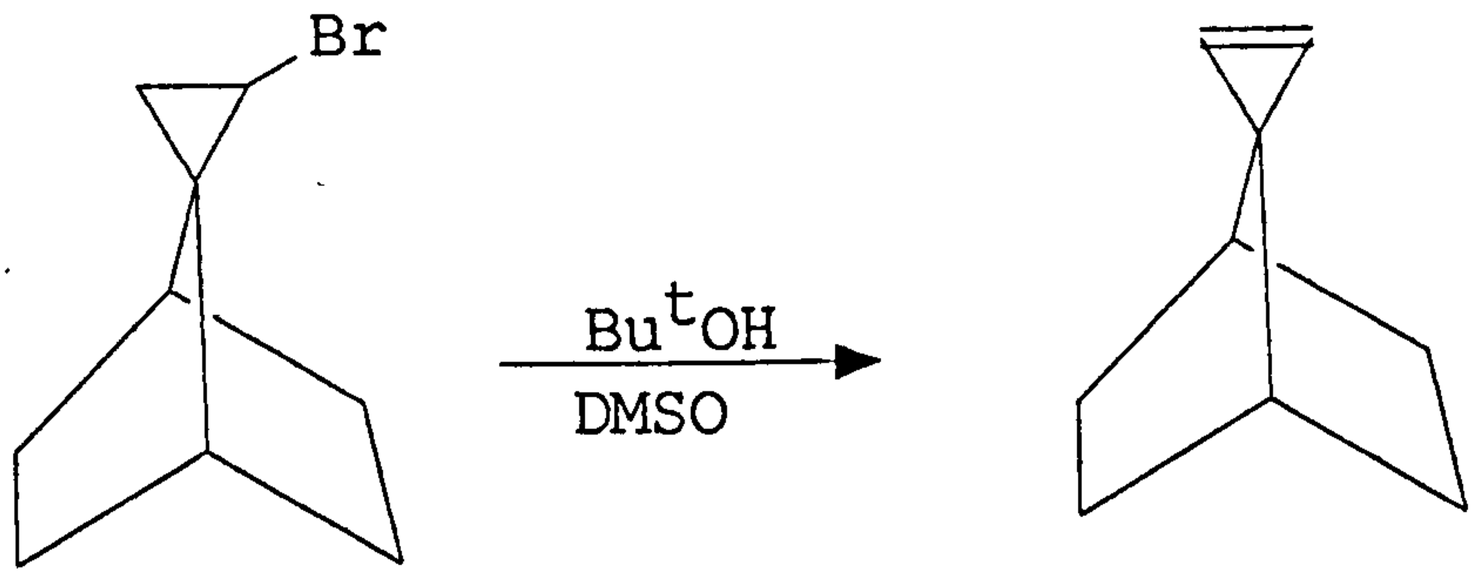
1.3.2.3.1. DEHYDROHALOGENATION OF MONOHALOCYCLOPROPANES

The dehydrohalogenation of a monobromo- or monochlorocyclopropane provides one of the simplest routes to a range of cyclopropenes. For 3,3-disubstituted cyclopropanes carrying alkyl or aryl groups, the reaction is normally achieved using potassium t-butoxide or potassium hydroxide in DMSO. Treatment of 1-bromo-3,3-dimethylcyclopropane with potassium t-butoxide in DMSO gave 3,3-dimethylcyclopropene (**6**) in high yield.[24,25]

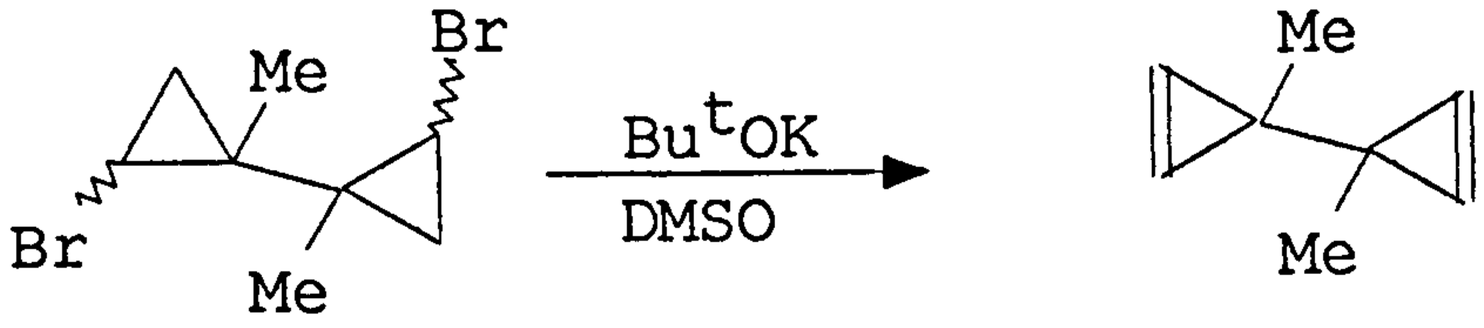


(6)

This method has also been applied to the preparation of spiro-fused cyclopropenes or dicyclopropenes, e.g, treatment of (**7**) and (**8**) with potassium t-butoxide in DMSO gave (**9**)[26] and (**10**)[27] respectively.

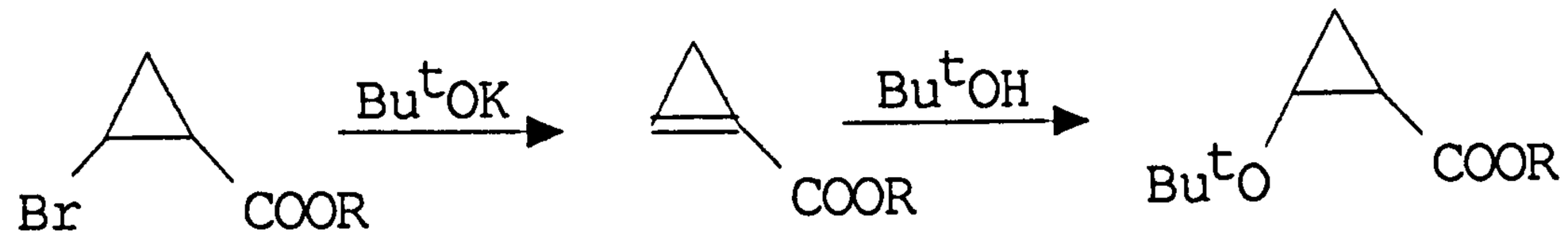


(7) (9)



(8) (10)

However, on dehydrobromination of (**11**) with potassium t-butoxide, the product isolated was (**13**); the desired cyclopropene carboxylate (**12**) was apparently the initial product, but this underwent a rapid addition of t-butoxide.[28]

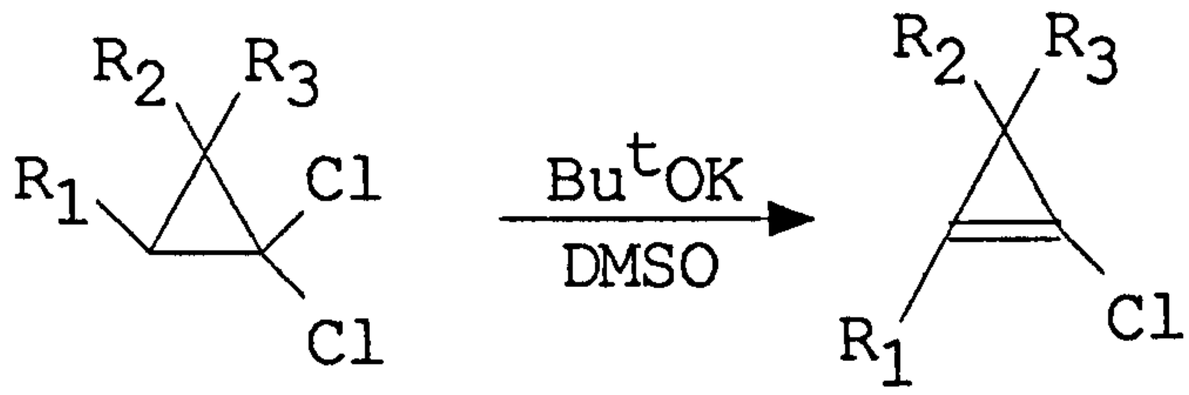


(11) (12) (13)

1.3.2.3.2. DEHYDROHALOGENATION OF 1,1-DIHALO-CYCLOPROPANES

Because 1,1-dihalocyclopropanes are so readily available by carbene addition to alkenes, their dehydrohalogenation to 1-halocyclopropenes provides, in principle, one of the most attractive routes to functionalised cyclopropenes. However, most early studies of the

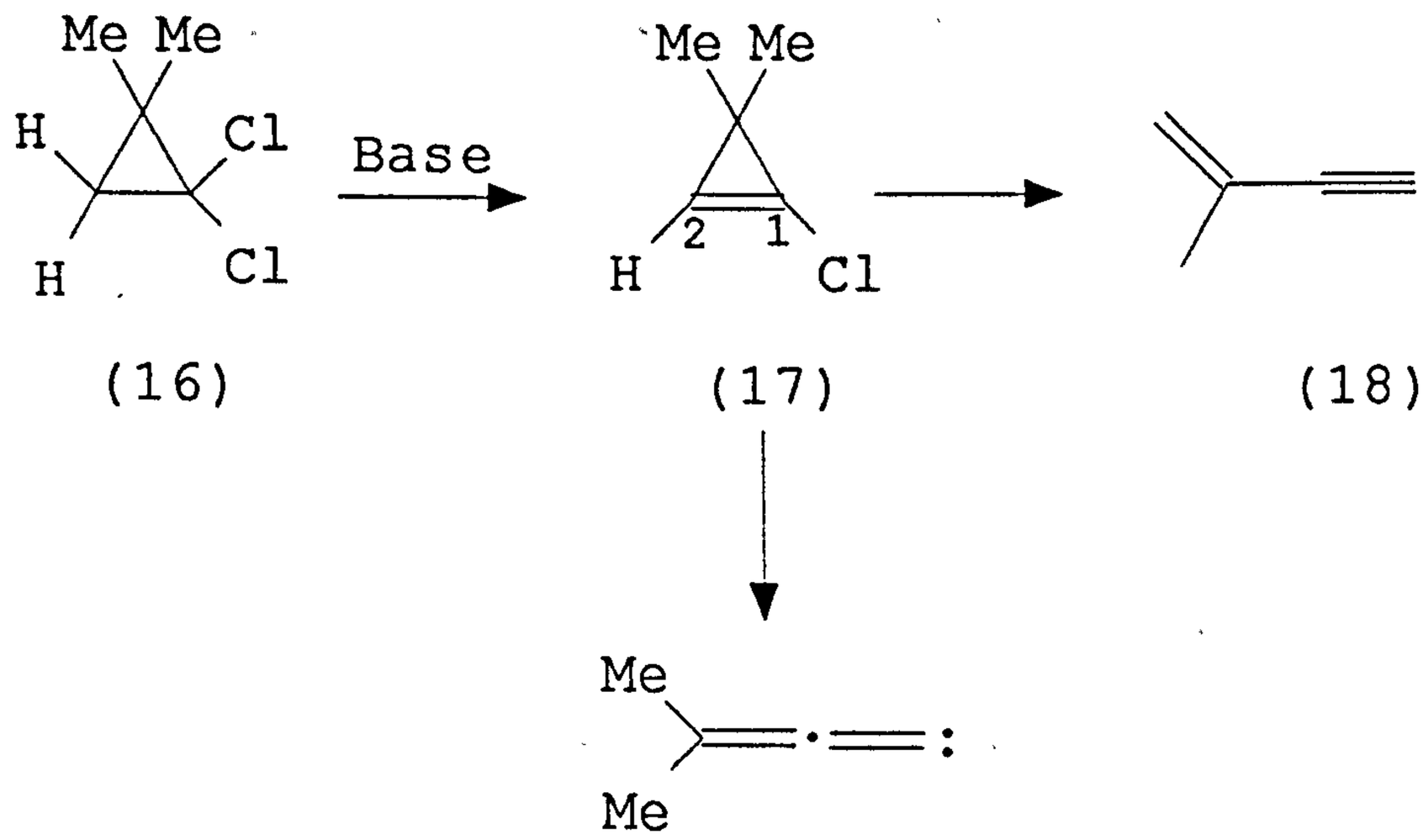
reaction did not lead to the cyclopropenes themselves, but to products of their further reaction. The dehydrohalogenation of cyclopropanes **(14)** bearing three alkyl or aryl substituents does lead to cyclopropenes **(15)**.[29,30]



(14) (15)

R_1 = Ph R_2 = H or alkyl

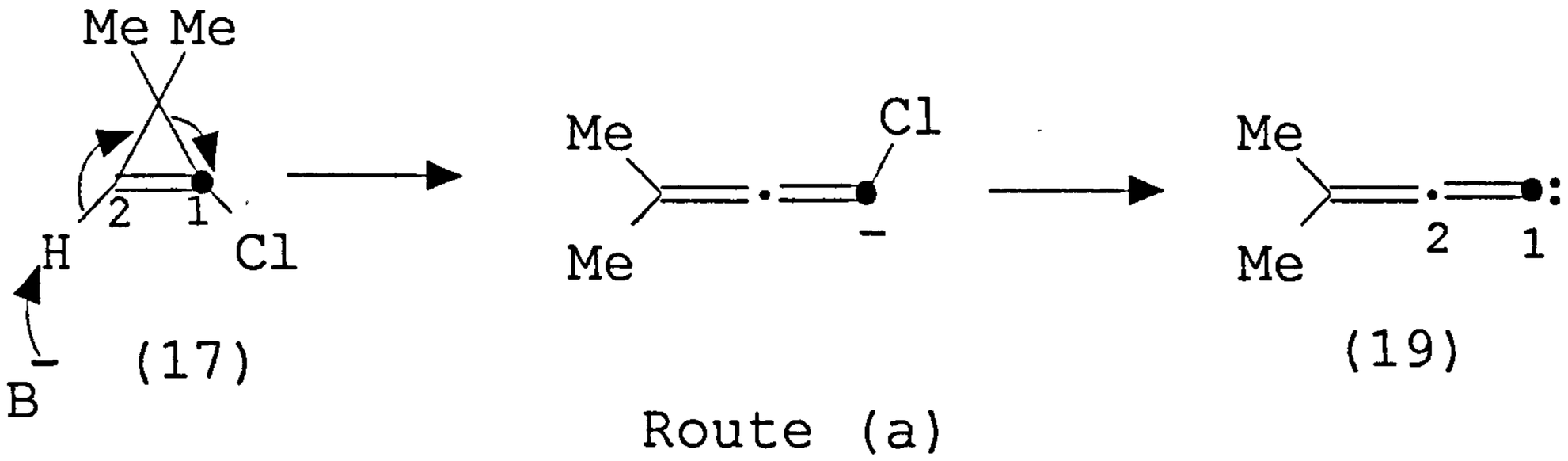
In other cases, ring-opening may be observed; treatment of dimethyl derivitive **(16)** with base might be expected to produce the chlorocyclopropene **(17)**; however, in practice two eliminations occur to produce **(18)** and the carbene **(19)**, which can be trapped by an added alkene. Both products may be derived from **(17)** by a 1,4- or a formal 1,2-elimination respectively.[31]



(16) (17) (18)

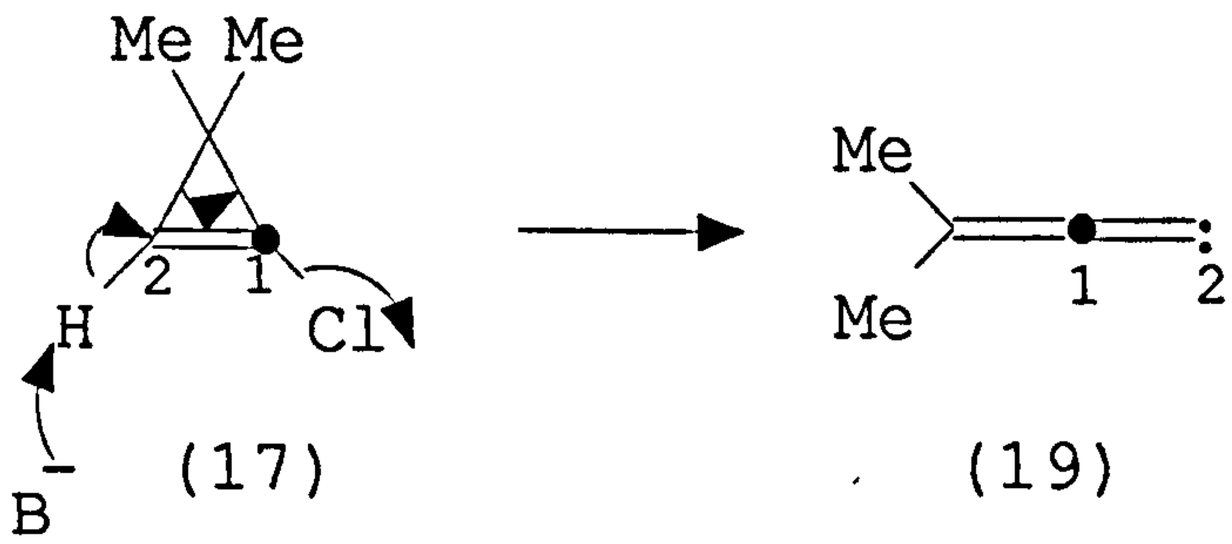
(19)

For the formal 1,2-elimination, labelling studies have suggested two possible pathways .[31,32] When the isolated cyclopropane **(16)** was labelled at C_1 of the carbene and treated with butoxide ion, the carbene **(19)** was formed with the label exclusively at C_1 suggesting rearrangment by route (a).



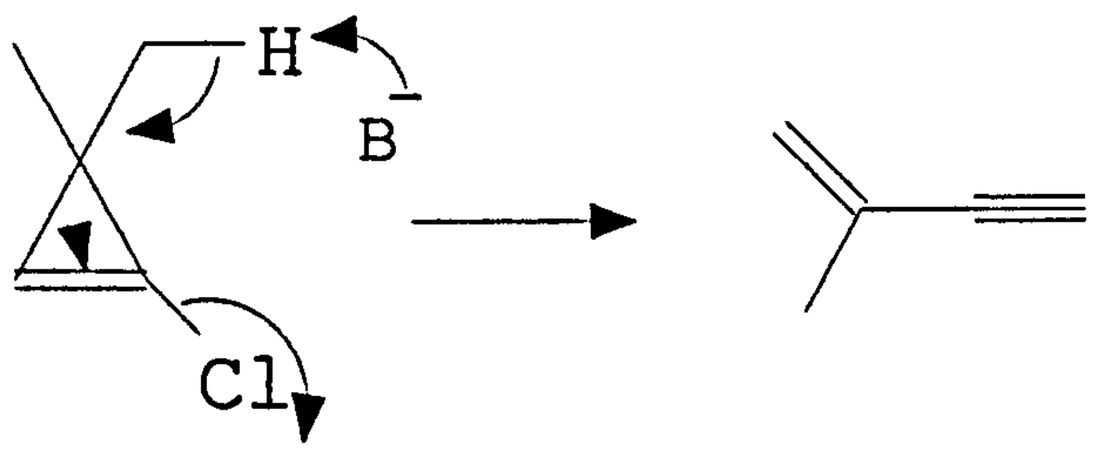
Route (a)

However, when the labelled cyclopropene **(17)** was treated with methylithium the label was found exclusively at C_2 of the carbene, route (b).



Route (b)

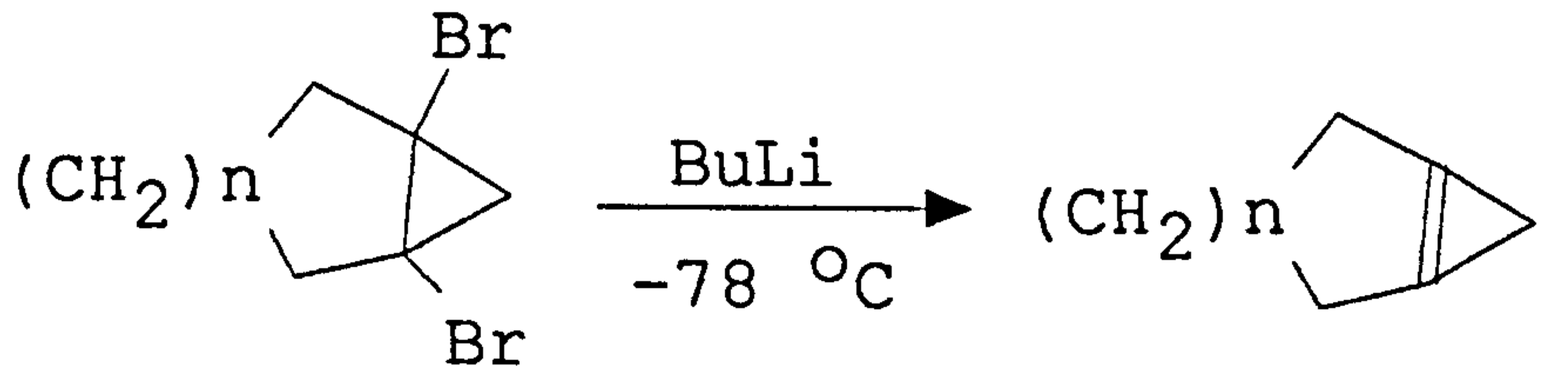
These results suggest that either the reaction of **(17)** with butoxide follows a completely different course to that with methyllithium, or that **(17)** is not involved in the reaction of **(16)** with base. The mechanism proposed for the 1,4-elimination is shown below.



(17) (18)

1.3.2.3.3. 1,2-DEHALOGENATION

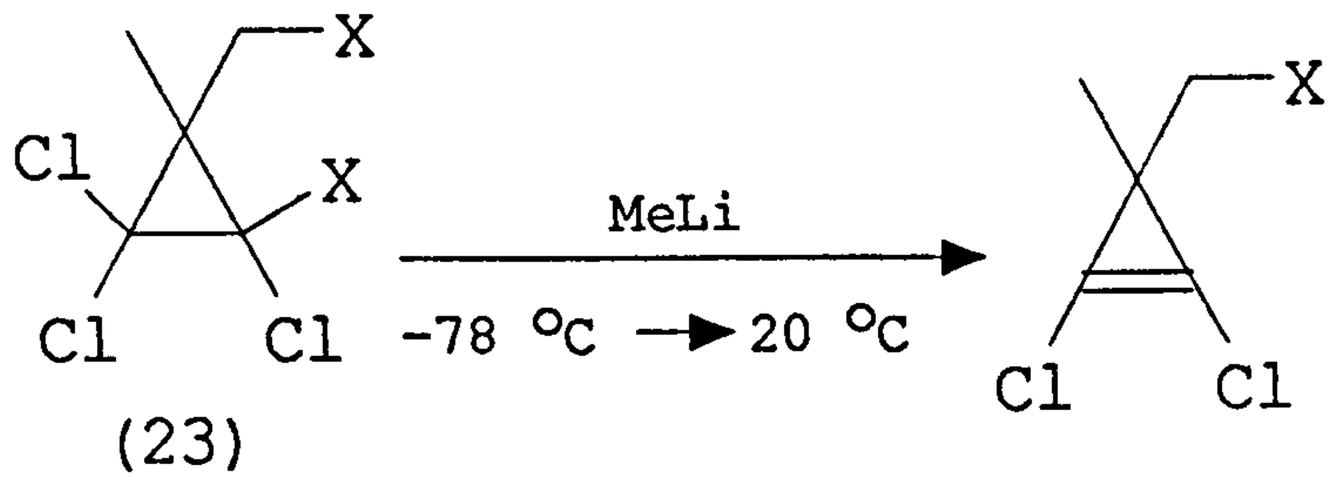
The 1,2-dehalogenation of cyclopropanes is one of the easiest routes to cyclopropenes. The 1,2-dihalocyclopropanes themselves can be prepared from the corresponding dicarboxylic acids by the Hunsdiecker reaction, but otherwise are not widely reported, though they can be obtained by reduction of tri- or tetrahalocyclopropanes. Reaction of the dibromides **(20)** with one equivalent of butyllithium in ether at -78 °C gave the cyclopropene **(21)**.[33]



(20) (21)

In general, it is simple to dehalogenate 1,1,2-trihalocyclopropanes or 1,1,2,2-tetrahalocyclopropanes as these are readily available by dihalocarbene addition to halogenated alkenes. The 1,2-dehalogenation of tri- or tetrahalocyclopropanes by an alkyllithium provides a method for the preparation of functionalised cyclopropenes in good to excellent yields. Thus treatment of **(22)** and **(23)** with one equivalent of methyllithium in

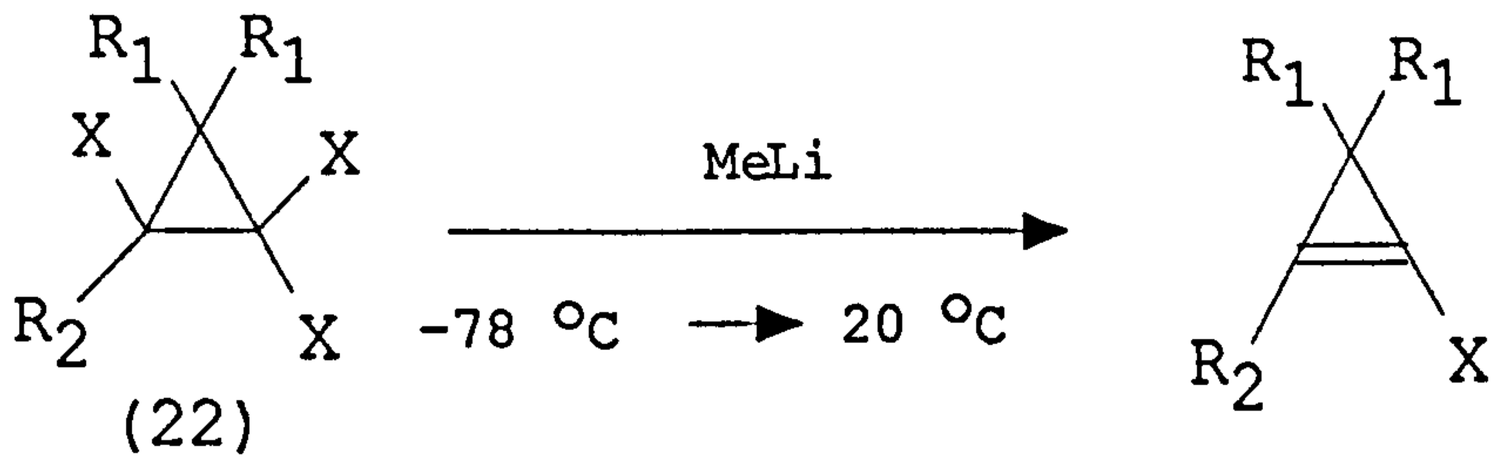
ether at -78 °C afforded 1-halo- and 1,2-dihalocyclopropenes respectively.



(23)

X = Cl, Br

Y = H, Cl, OMe, Ph



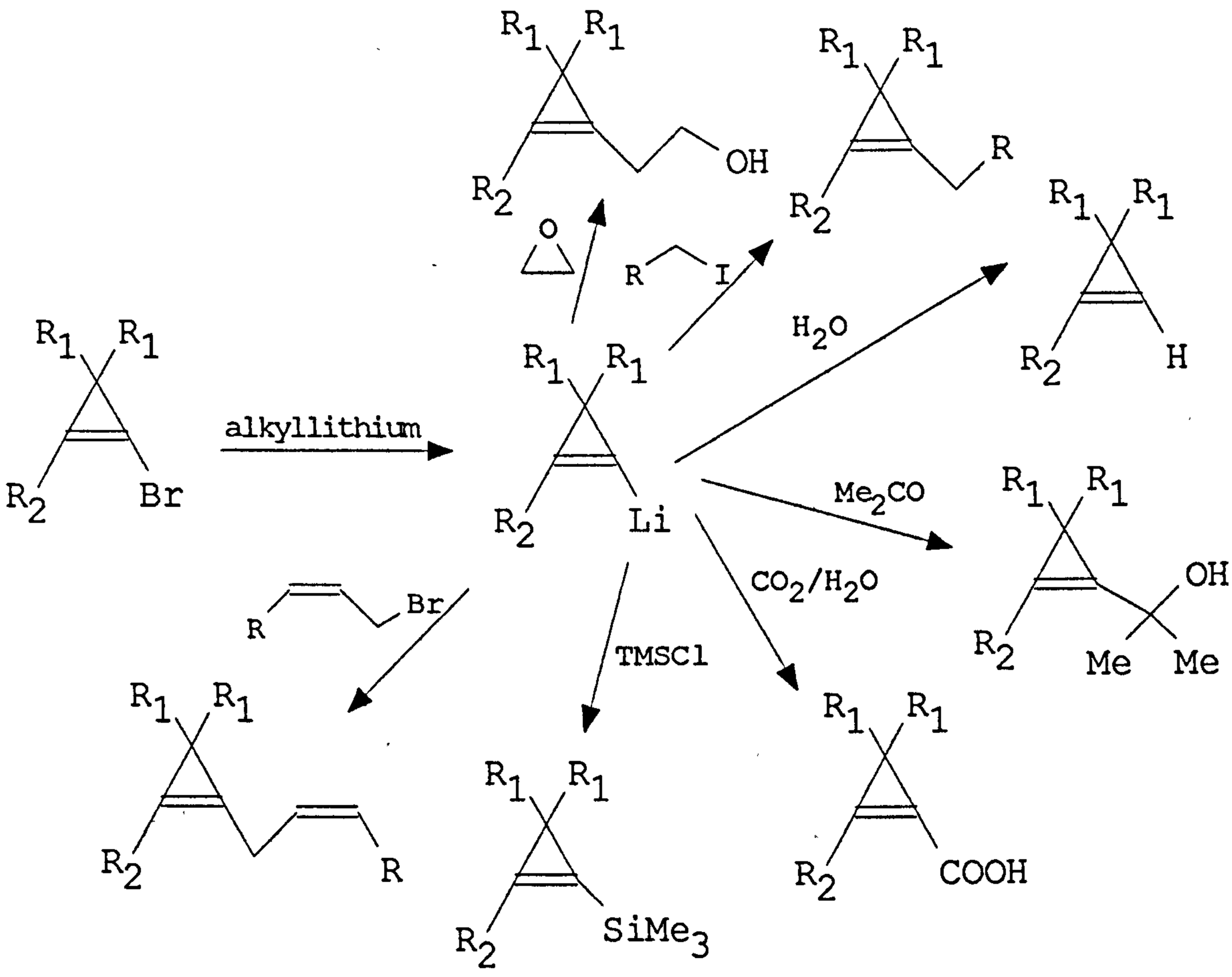
(22)

X = Cl, Br

R_1 = H, alkyl group

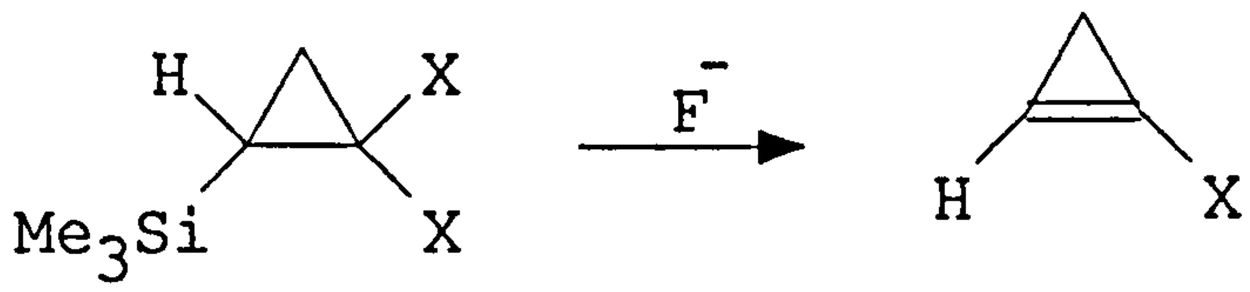
R_2 = alkyl group

The presence of the additional halogen has the added advantage of making the initial lithium halogen exchange more facile. When the halocyclopropene generated from a tribromocyclopropane is treated with a further equivalent of alkyllithium, a second lithium halogen exchange occurs with the formation of a lithiocyclopropene.This may be trapped by a series of electrophiles giving a 'one-pot route' to an extensive range of substituted cyclopropenes.[34 - 40]



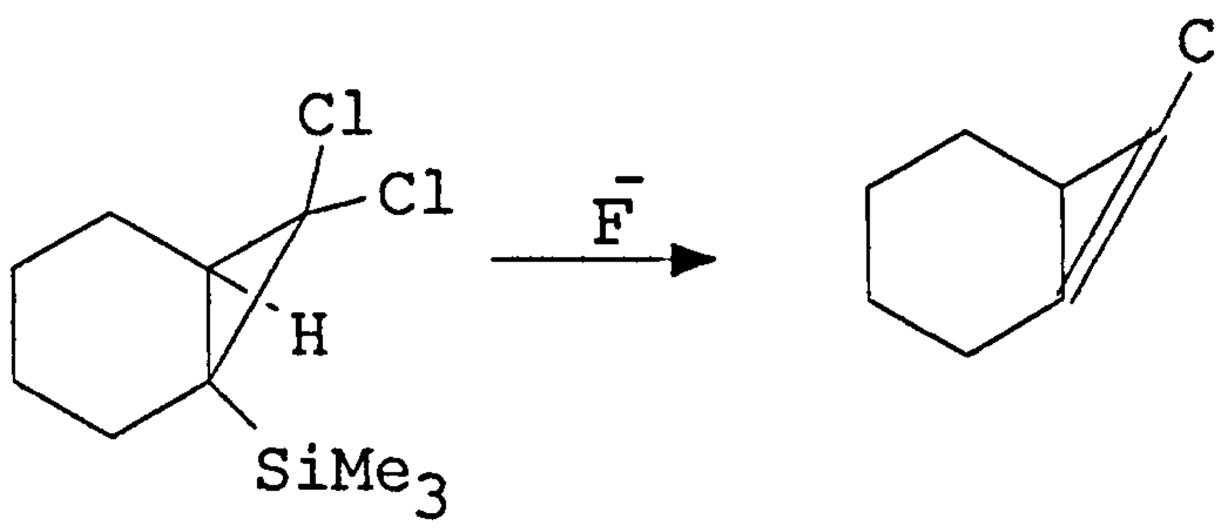
1.3.2.3.4. DEHALOSILYLATION

A recent development in 1,2-elimination is fluoride ion induced elimination of trimethylsilylhalide to form a cyclopropene without further rearrangment. Thus treatment of **(24)** with caesium fluoride leads to 1-chloro- or 1-bromocyclopropenes in a good yield, while **(25)** is converted into the highly strained cyclopropene **(26)**, which can be trapped as a Diels-Alder adduct with furan.[41]



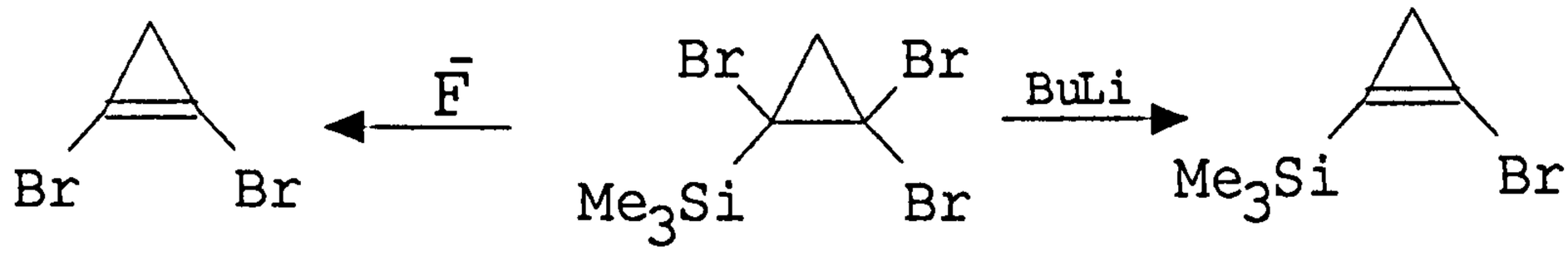
(24)

X = Cl, Br



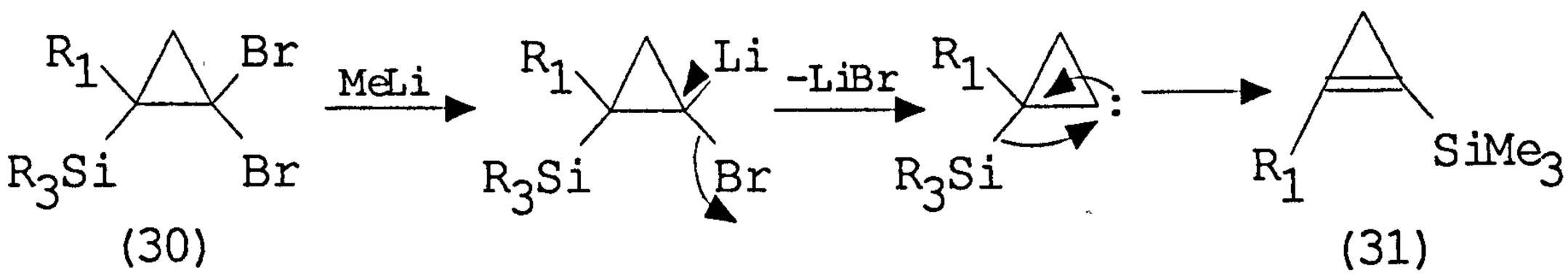
(25) (26)

Reaction of the tribromide **(27)** with tetrabutylammonium fluoride provides a convenient route to **(28)**, while treatment with butyllithium leads to **(29)**.[42]



(28) (27) (29)

Recently Baird and co-workers,[43] found that when the cyclopropanes **(30)** were allowed to react with one mol. equivalent of methyllithium at -90 to -50 °C, the cyclopropenes **(31)** were obtained in good yield. The products **(31)** can be explained by lithium halogen exchange followed by 1,1-elimination to give a carbene intermediate (carbenoid) followed by a 1,2-shift of the silyl group.



(30) (31)

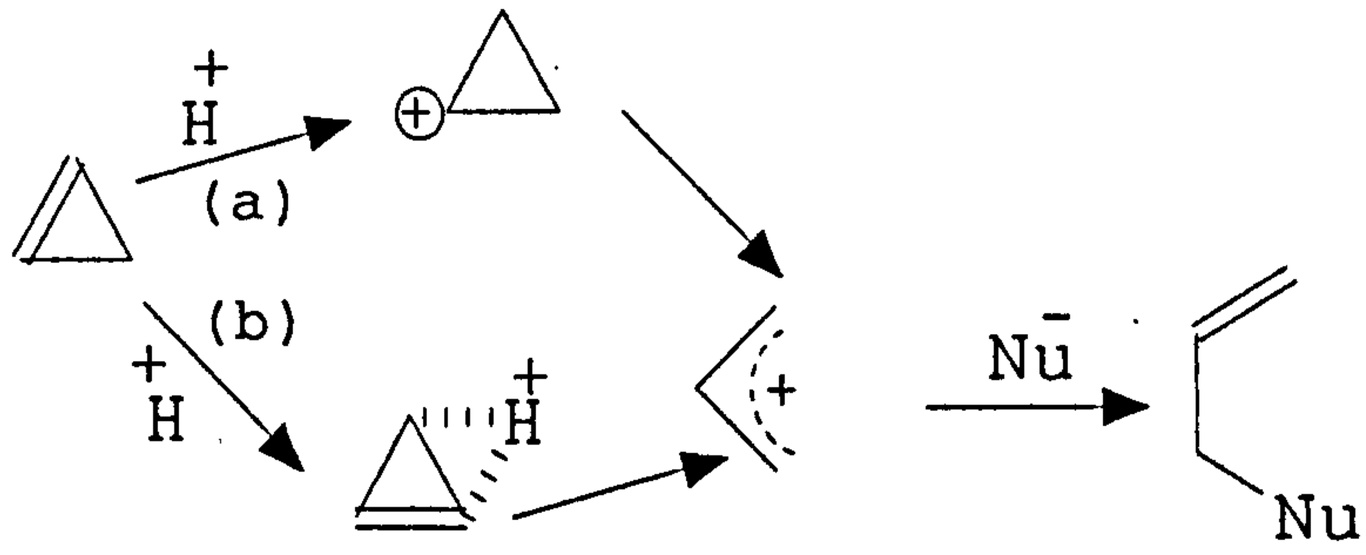
R_1 = octyl, methyl, butyl

1.4. CHEMISTRY OF CYCLOPROPENE

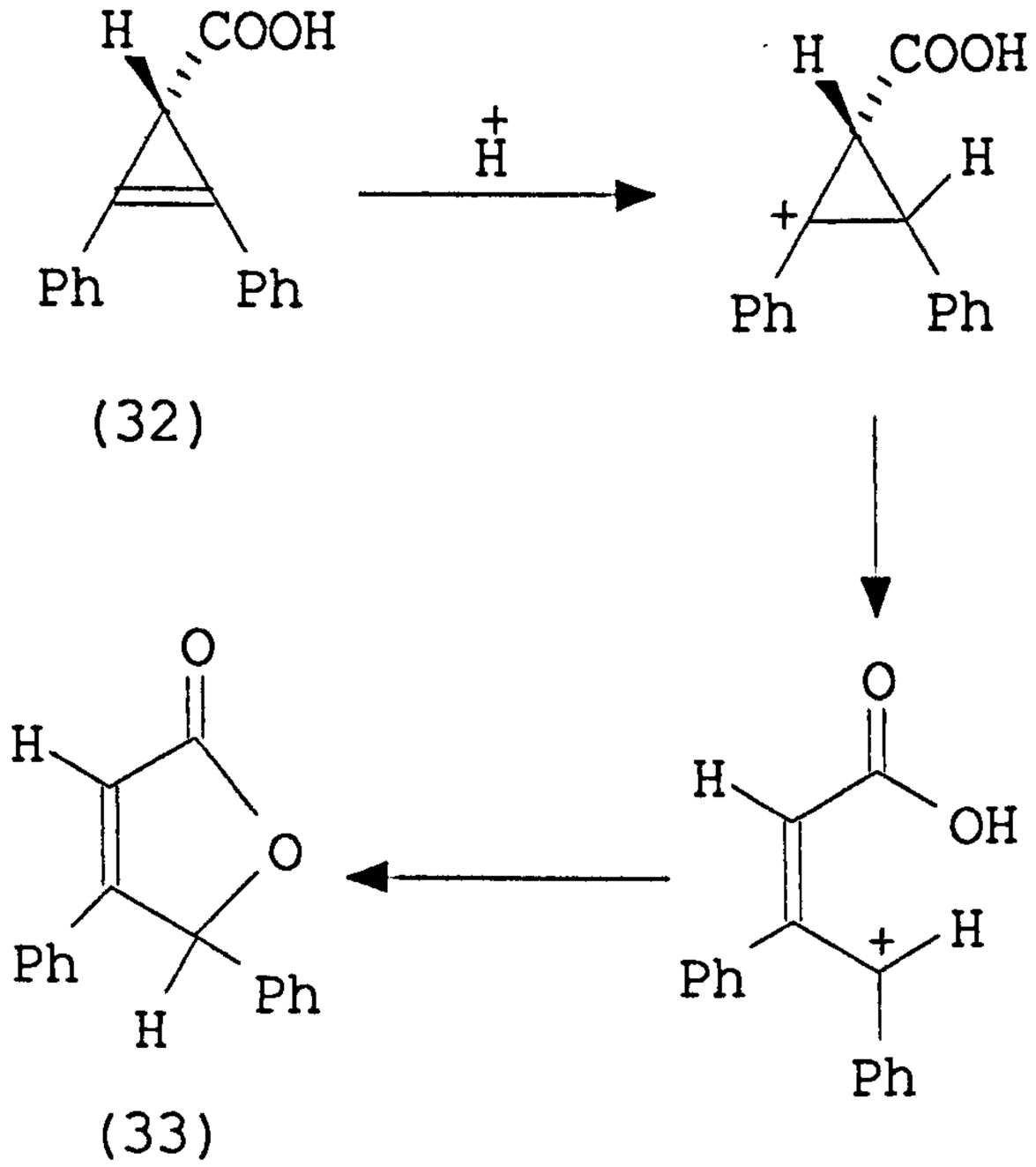
Due to the unusual bonding, compounds containing a cyclopropene ring are among the most reactive cycloalkenes. The short bond length of the cyclopropene double bond infers it must have a very strong π-component. Nevertheless, addition reactions at the double bond are known to occur very readily and are usually highly exothermic,[44] since the cyclopropene loses strain energy of about 27 kcal/mol through saturation of the π-bond to give less strained cyclopropanes. These reaction are electrophilic addition, catalytic hydrogenation, Diels- Alder reactions, 1,3-dipolar addition, dimerization, and nucleophilic addition.

1.4.1. ELECTROPHILIC ADDITION

The addition of an electrophile to the cyclopropene double bond formally leads to a cyclopropyl cation; this may be expected to undergo ring-opening to an allyl ion unless it is rapidly trapped by a nucleophile (path a). In some cases electrophilic attack may occur at one of the σ-bonds leading directly to an allylic cation (path b). The final products of reaction are derived from nucleophilic capture of the allyl cation.



The polymerization of naturally occuring sterculic acid in the presence of a proton source has been known for over 40 years and proceeds via acid catalysed opening of the cyclopropene ring.[44] The rearrangment of cyclopropene (**32**) to lactone (**33**) is reported to proceed via acid catalysed protonation of the π-bond to give the cyclopropyl cation followed by ring opening to give the allylic cation; this in turn reacts intramolecularly to give the final product (**33**).[44]

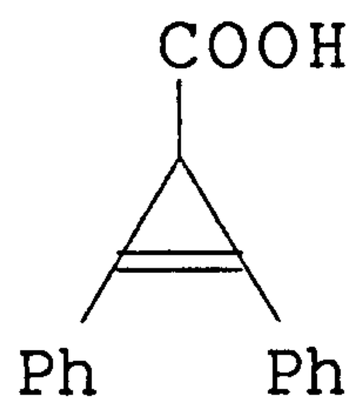


(32)

(33)

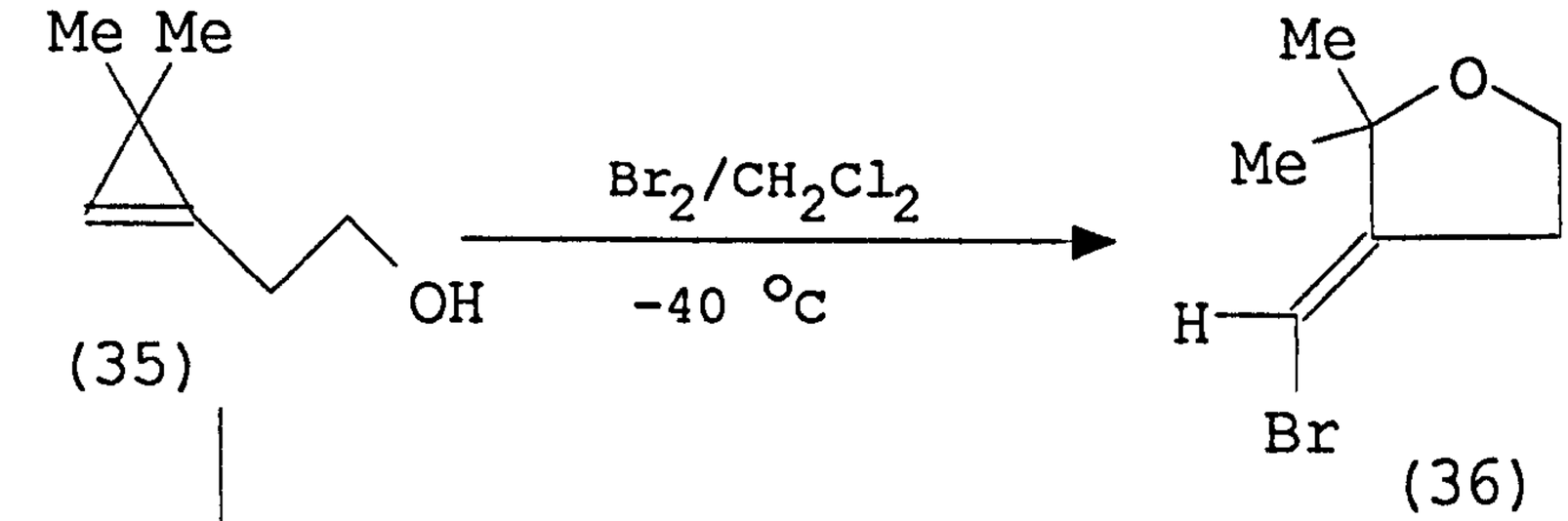
Addition of halogens to cyclopropenes often occurs without ring opening to give 1,2-dihalocyclopropanes in high yields. The stereochemistry of the addition of chlorine to (**34**)

in CCl_4 is 71 % *cis*;[46] however, the addition of bromine in $CHCl_3$ and acetic acid gave the *trans*-adduct.[47]



(3 4)

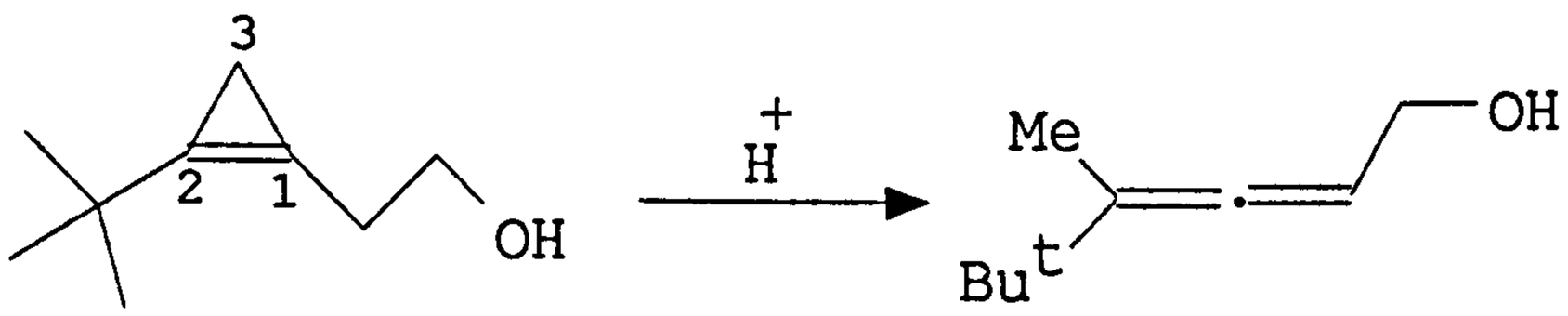
Baird and Al-Dulayymi[40] found that, when the cyclopropene alcohol (**35**) was allowed to react with bromine in dichloromethane at -40 °C or with a catalytic amount of p.toluene sulfonic acid in benzene at room temperature it produced the methylene furans (**36**) and (**37**) respectively. The bromide (**36**) was obtained as a single diastereoisomer.



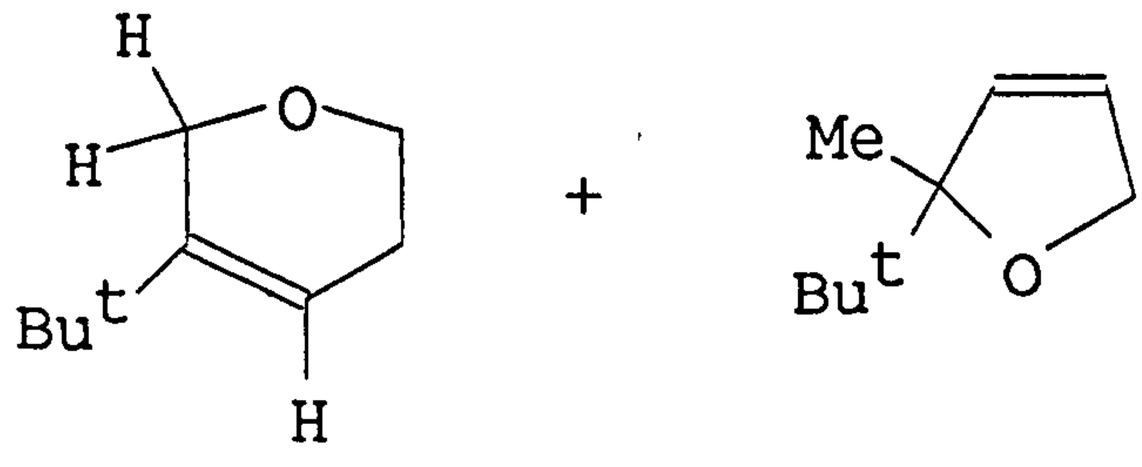
The regioselectivity of the addition of Br_2 to the cyclopropene may in principle be explained by addition of Br^+ to the less substituted and of the π-bond to give cation (**38**) followed by

cyclopropyl-allyl ring-opening with rotation of the bromine outwards to give (**39**), followed by trapping of the allyl cation intramolecularly by the hydroxyl group. However, the reaction with acid required several hours at room temperature to reach completion and is apparently much slower than bromination. In agreement with this, one molecular equivalent of HBr is generated during the bromination but no product from addition of H^+ is isolated. This suggests that in view of the known greater reactivity of π-bonds to Br^+, it is possible that the H^+ prefers to react with cyclopropene by σ-attack and the bromine by π- attack.

Reaction of the cyclopropene alcohol (**40**) with p.toluene sulfonic acid in benzene led to three products:[40]

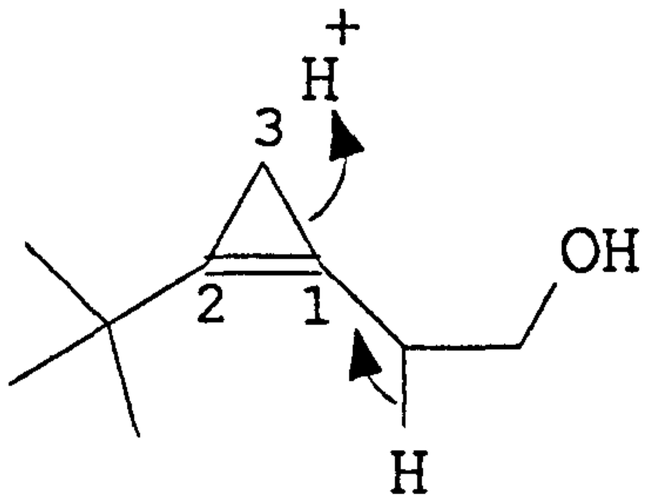


(40) (41)



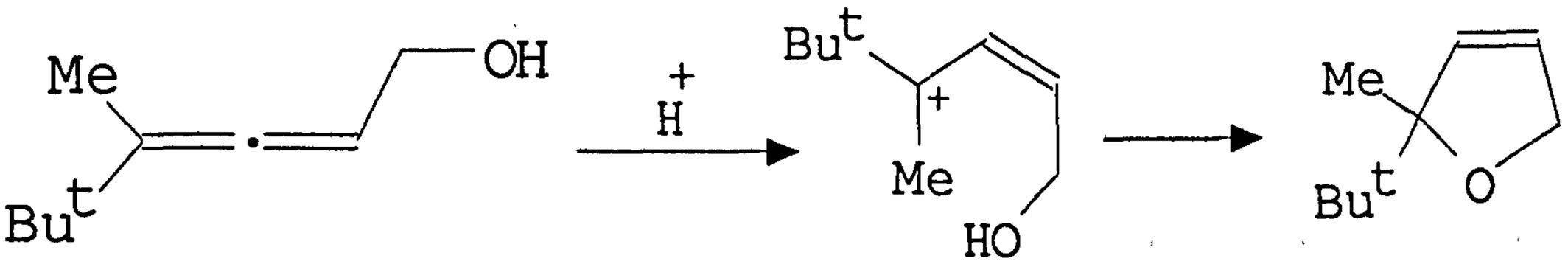
(42) (43)

The major product was the allene (**41**) which may arise by protonation of (**40**) at the methylene end of the 1,3-σ-bond with subsequent or concurrent elimination of a proton from the allylic methylene group as in (**44**).



(44)

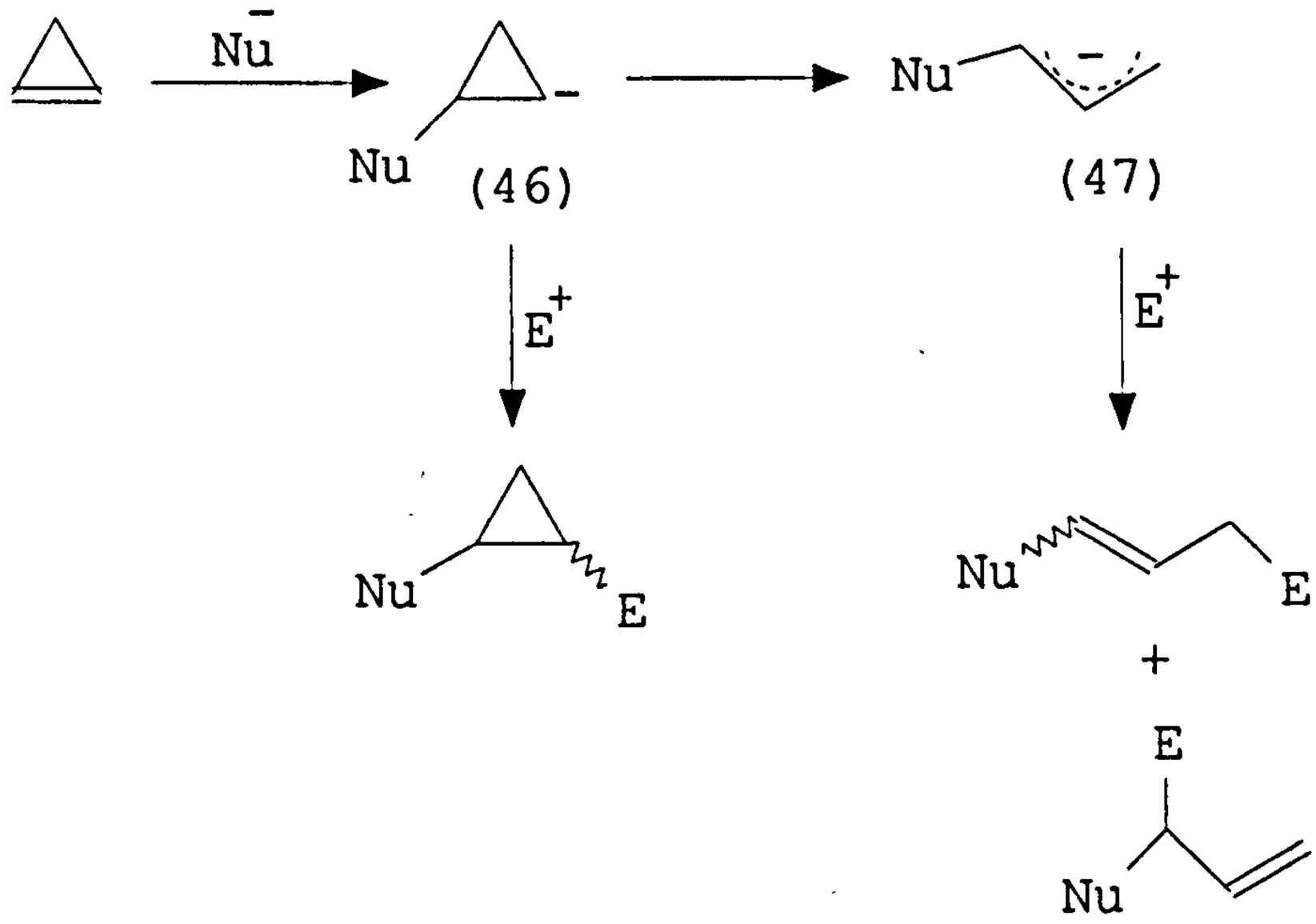
The dihydrofuran **(43)** may arise by acid induced reaction of **(41)** to give more stable cation **(45)** followed by intramolecular reaction with the hydroxyl group.



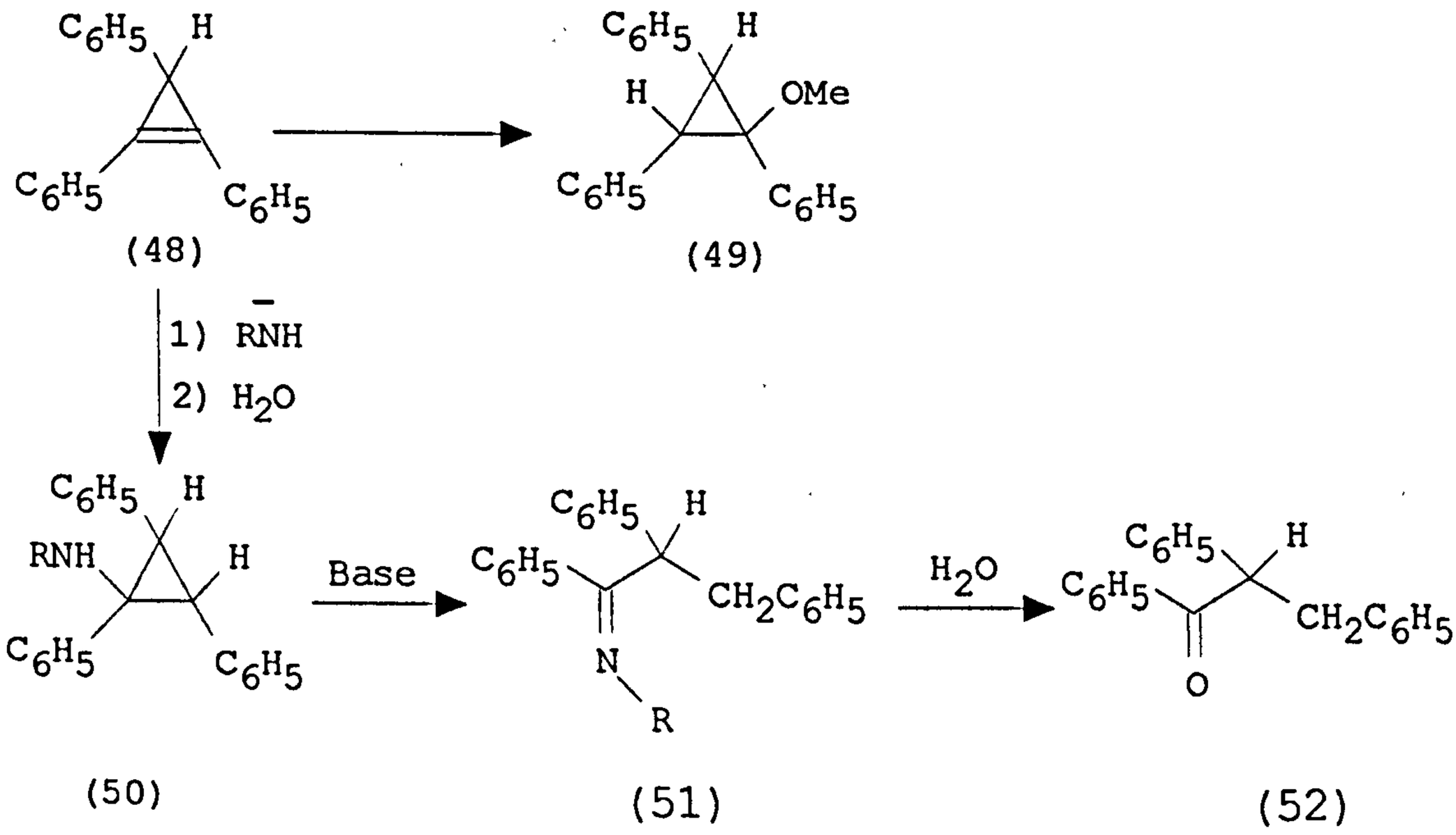
(41) (45) (43)

1.4.2. REACTION WITH NUCLEOPHILES

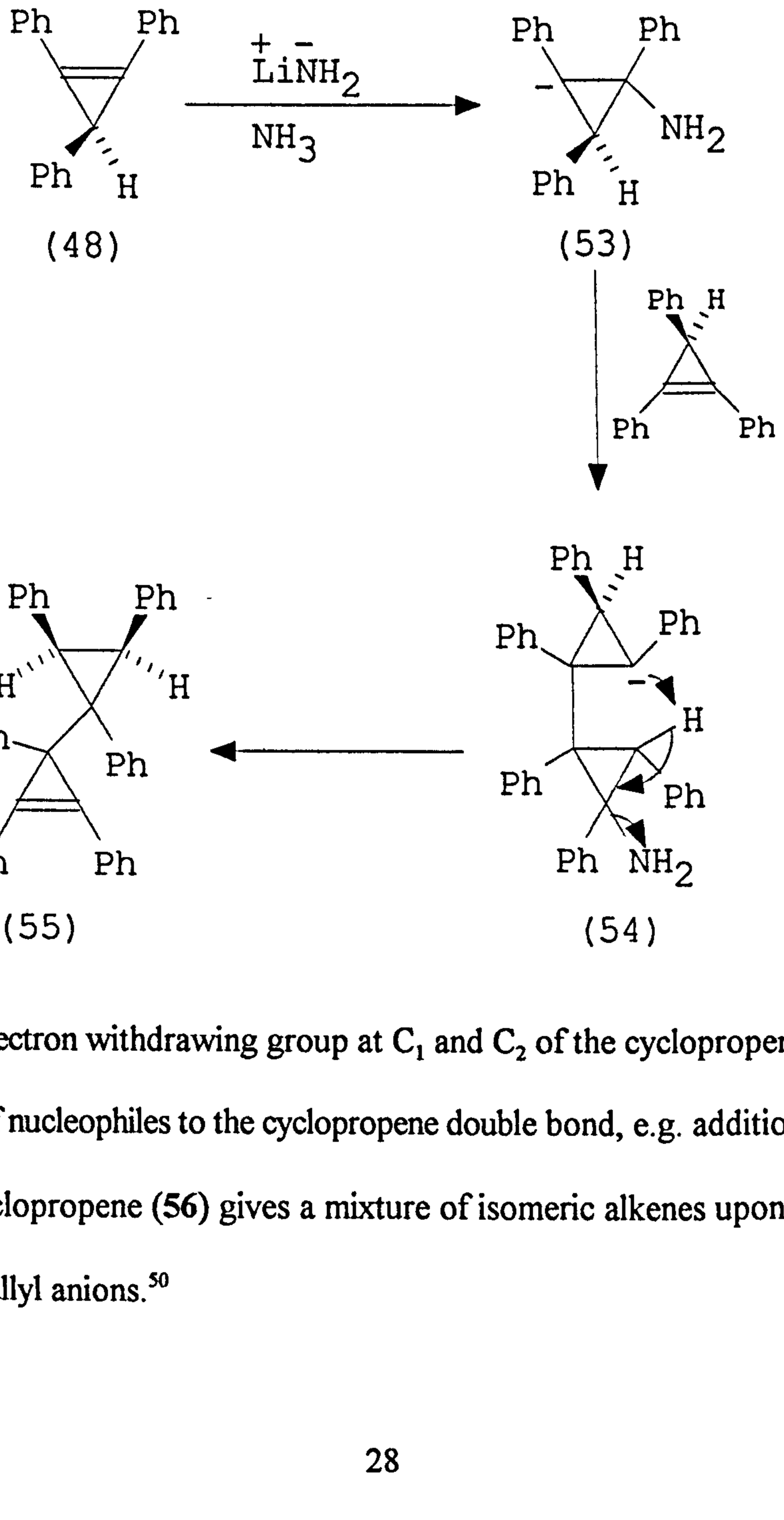
The addition of a nucleophile to cyclopropenes leads to cyclopropyl anions **(46)** which may trapped by electrophiles (E^+) or may undergo ring opening to give an allyl anion **(47)** which is then trapped by an electrophile.[48] The presence of an electron withdrawing group on the cyclopropene ring could stabilize the carbanion intermediate.[48]



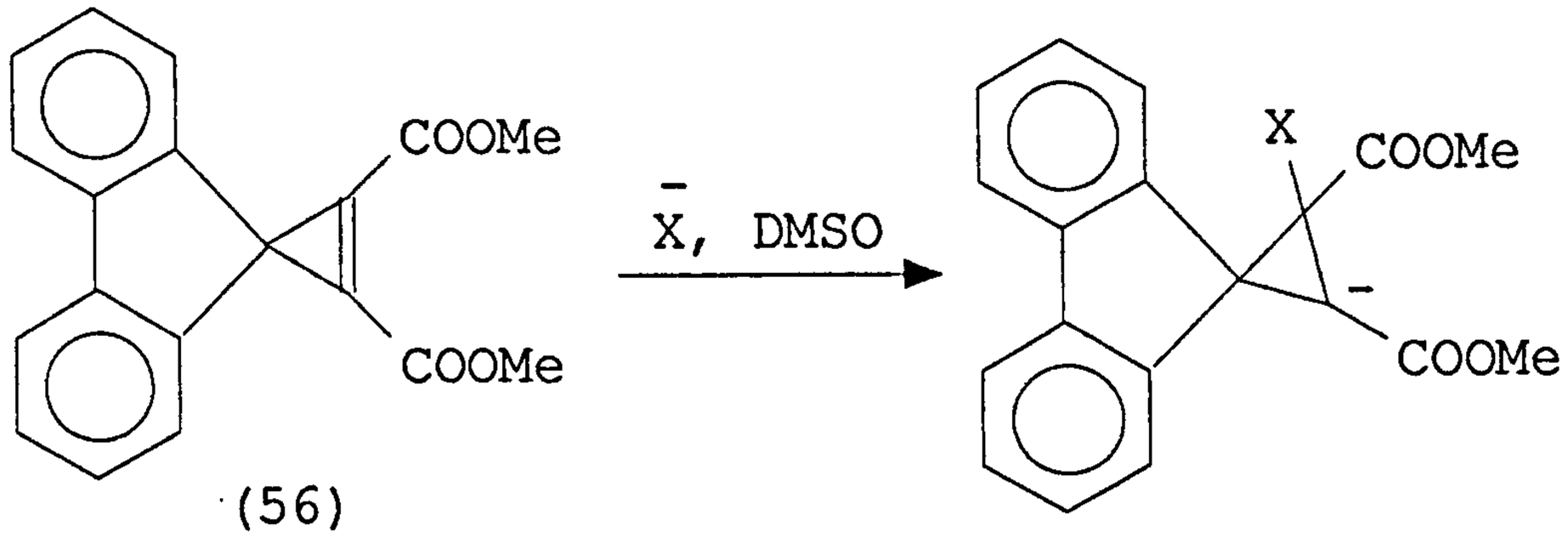
The triphenylcyclopropene (**48**) underwent nucleophilic addition readily,[49] and when sodium methoxide was added in DMSO, the cyclopropane (**49**) was obtained, while with sodium p-toluidide or with lithium propylamide in propylamine, the product after hydrolysis was (**52**). This may arise by addition of the nucleophile to give (**50**) followed by rearrangment and ring-opening to give the imine (**51**), facilated by delocalisation of the lone pair on nitrogen. The imine (**51**) undergoes hydrolysis during the work up.



Addition of lithium amide to cyclopropene (**48**) followed a different course to that above. When lithium amide was allowed to react with the cyclopropene (**48**) in liquid ammonia, the dimer (**55**) was formed in good yield. This suggests that the anion (**53**) was formed via addition of lithium amide, which reacts with another molecule of cyclopropene to give the anion dimer (**54**). This must abstract a proton intramolecularly, followed by elimination of amide ion. The mechanism of this reaction is confirmed by deuterium labelling studies.[49]



Introduction of electron withdrawing group at C_1 and C_2 of the cyclopropene increases the rate of addition of nucleophiles to the cyclopropene double bond, e.g. addition of methoxide or cyanide to cyclopropene (**56**) gives a mixture of isomeric alkenes upon methylation or protonation via allyl anions.[50]



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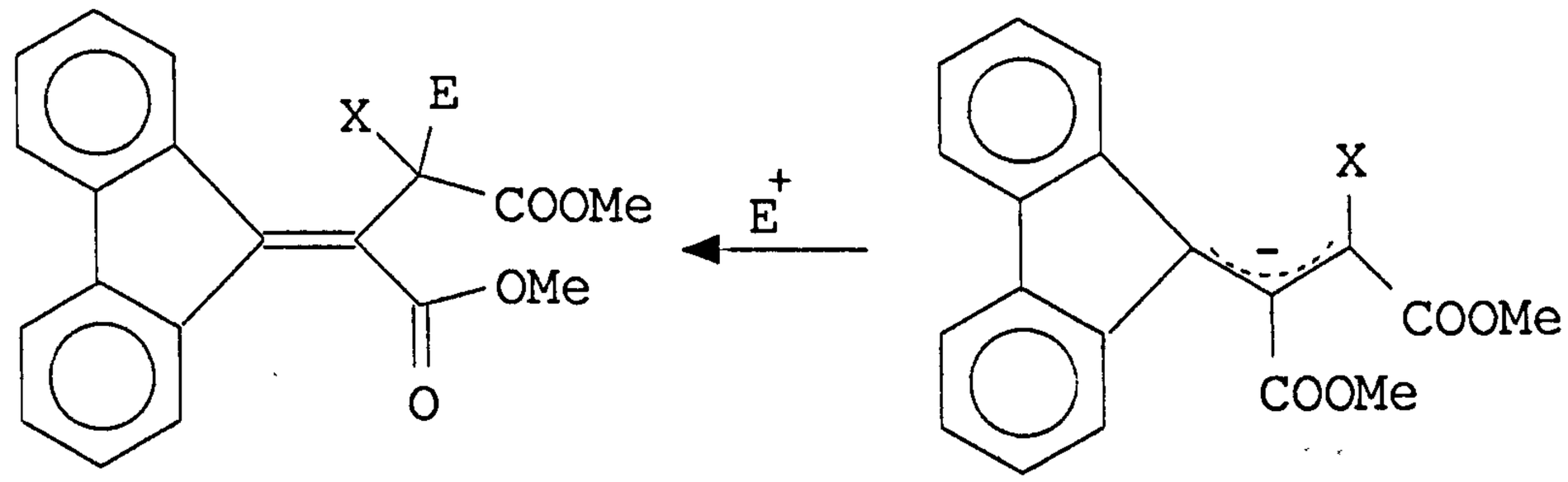

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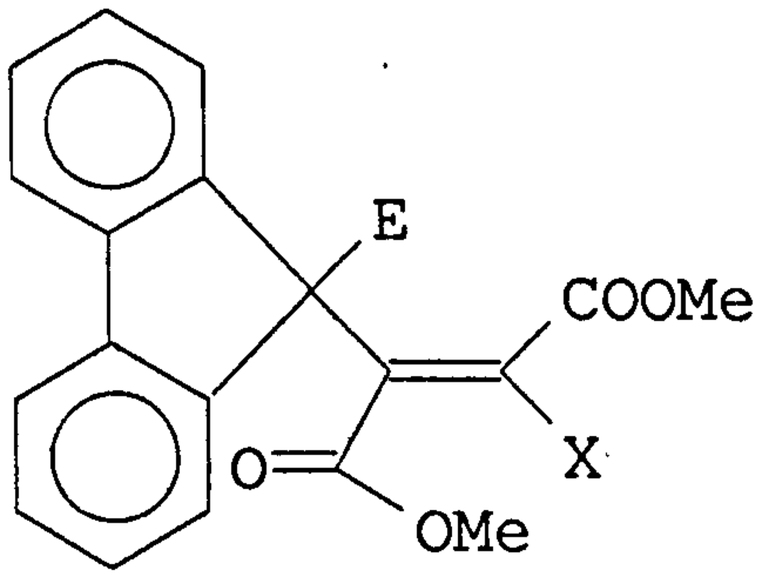
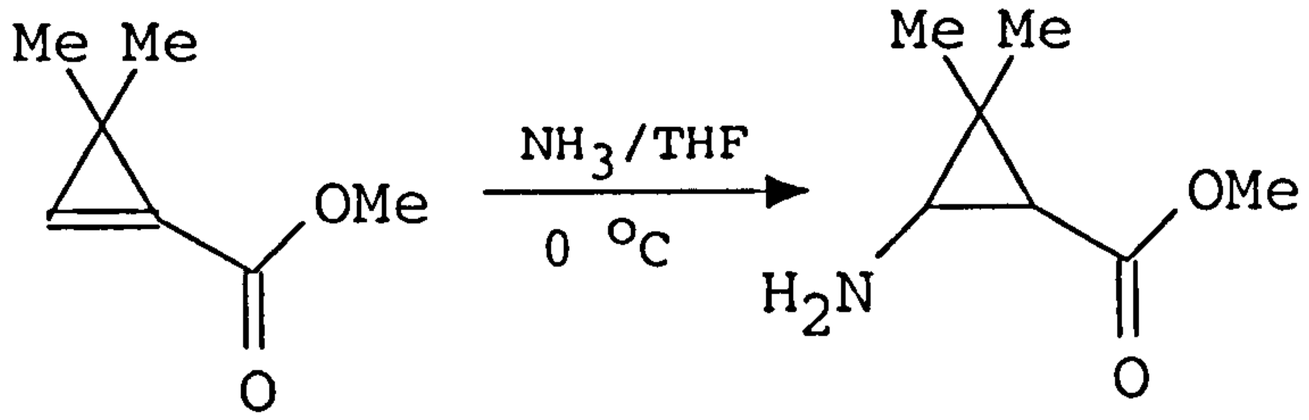
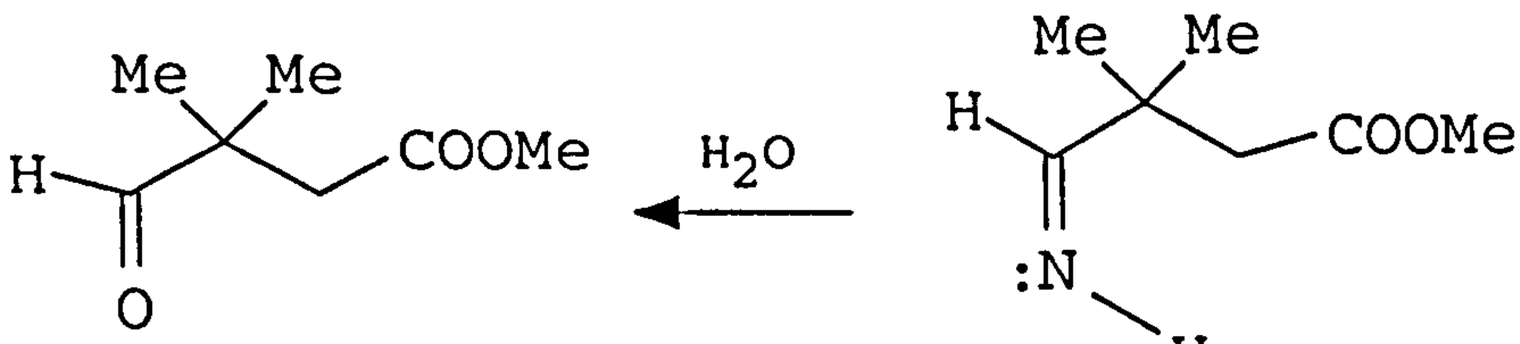


The reaction of ammonia with the cyclopropene ester (**57**) has been reported to give (**59**) in high yield.[51]



(57) (58)

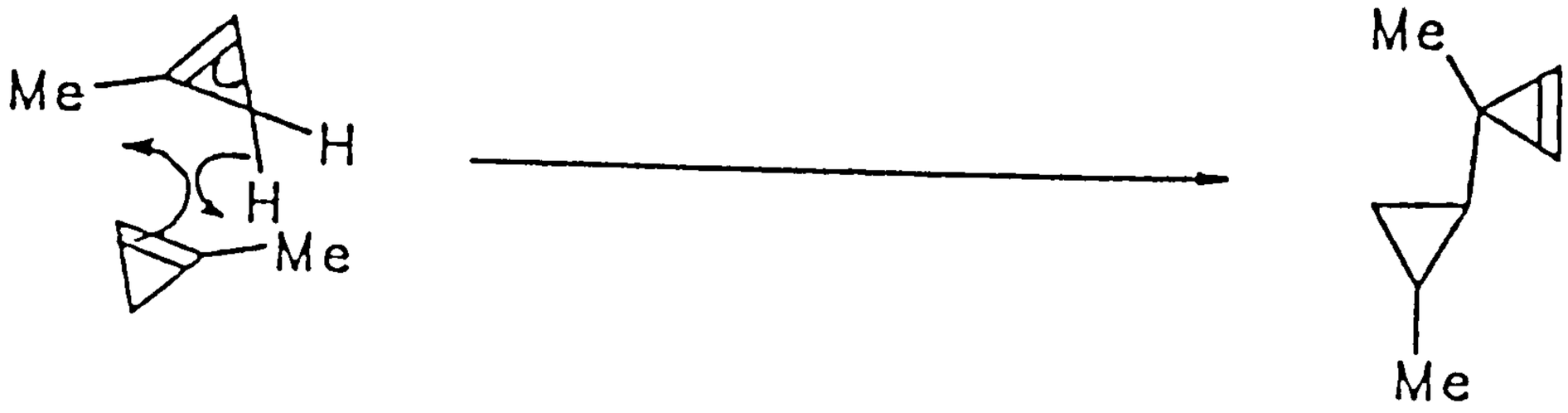


(59)

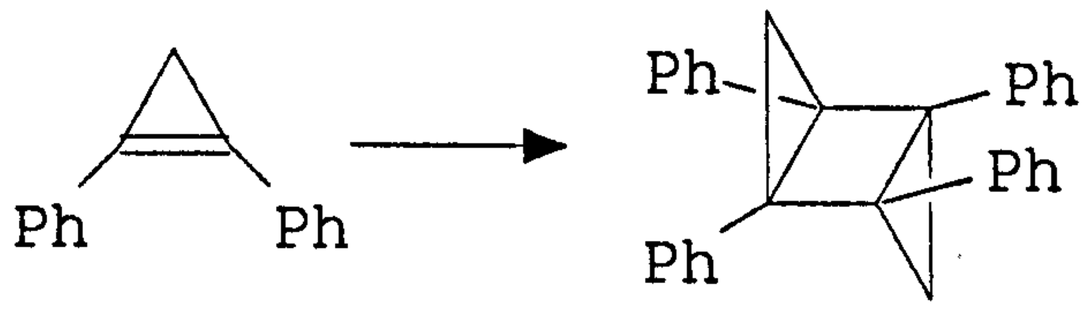
The aldehyde (**59**) arises via the cyclopropane (**58**) which undergoes a rapid rearrangment facilitated by the delocalization of the lone pair on the nitrogen atom, causing ring opening. The resulting imine is then hydrolysed by water.

1.4.3. THE ENE-REACTION

Cyclopropenes having a hydrogen at C_3 often undergo a particularly facile dimerisation by an ene-type reaction. Thus cyclopropene itself has long been known to undergo dimerisation to cyclopropenyl-cyclopropane on standing at -25 °C; the dimer is converted into oligomers at longer reaction time.[52]



When there is no hydrogen at C_3 the cyclopropenes can be more stable, although their ring opening by thermolysis or photolysis has been widly reported. In other cases, these reactions may compete with the ene- reaction. Thus photolysis of 1,2-diphenylcyclopropene produced one product **(60)**, while **(61)** gave a mixture of two dimers **(62)** and **(63)** in ratio 6:4.[53]



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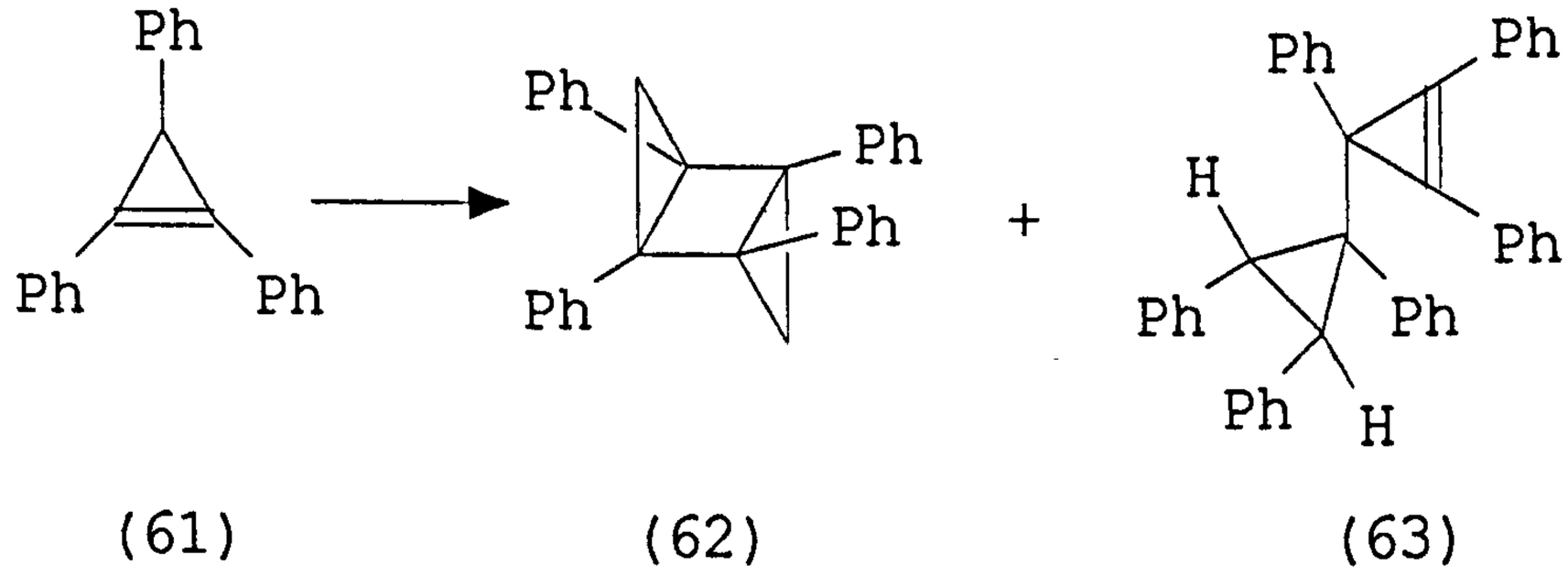
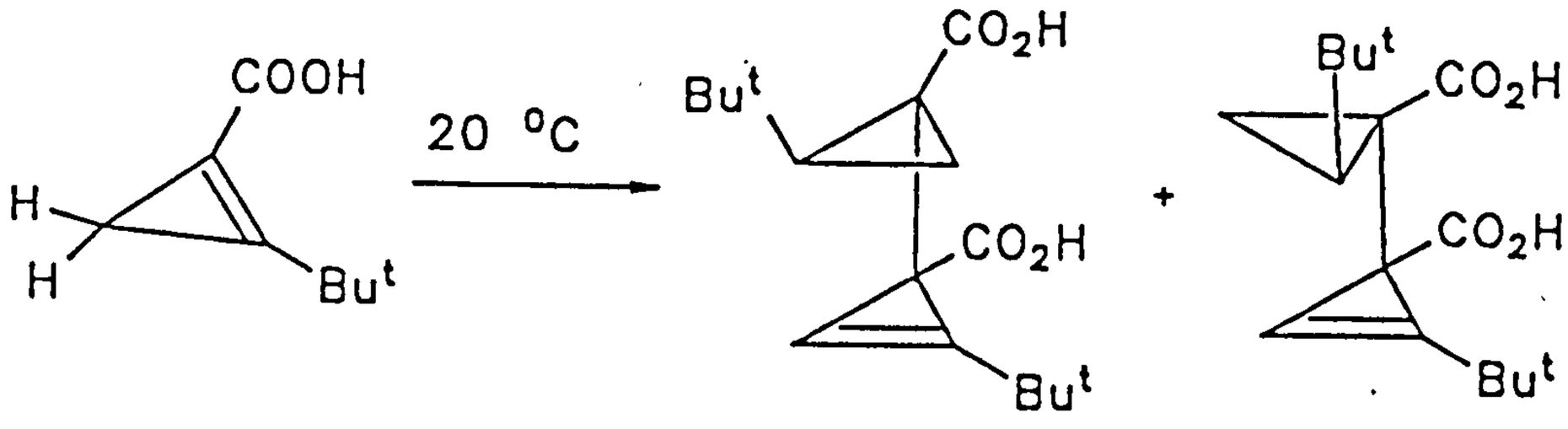
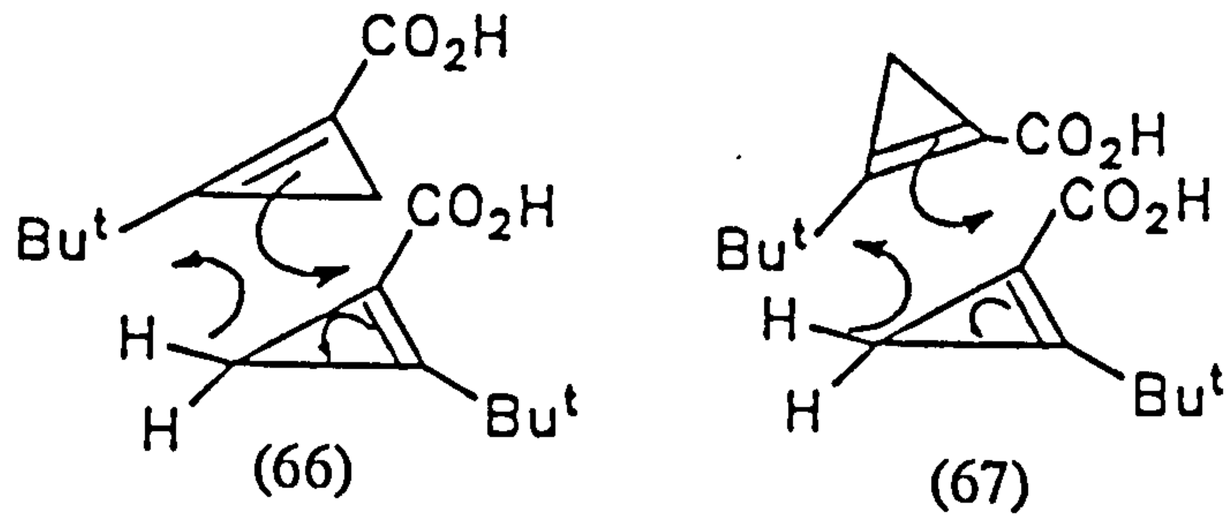


(61) (62) (63)

When the cyclopropene acid **(64)** was allowed to stand as a neat liquid at room temperature, a mixture of two products **(65)** and **(66)** was obtained in ratio 3:2 respectively. The major product was derived via the ene-reaction as in **(66)**, while the minor product goes through **(67)**.[54]



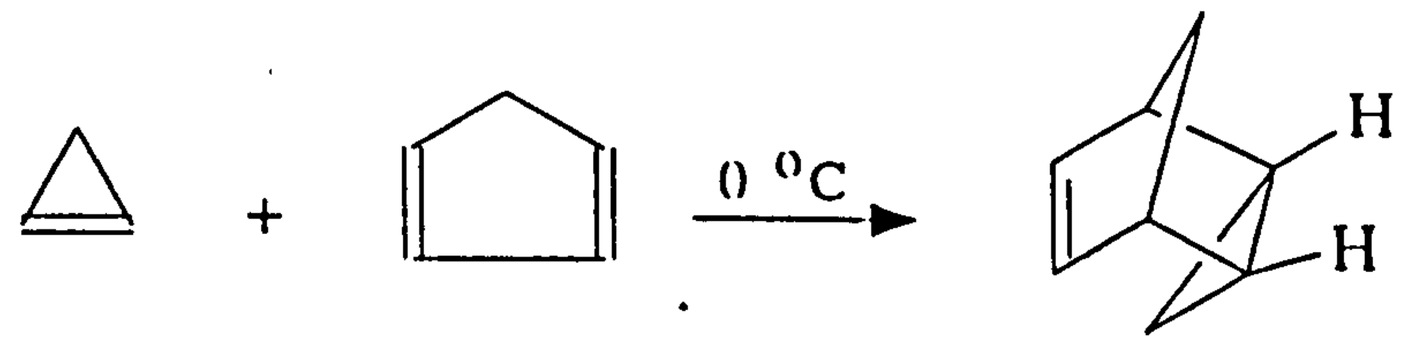
(64) (65) (66)

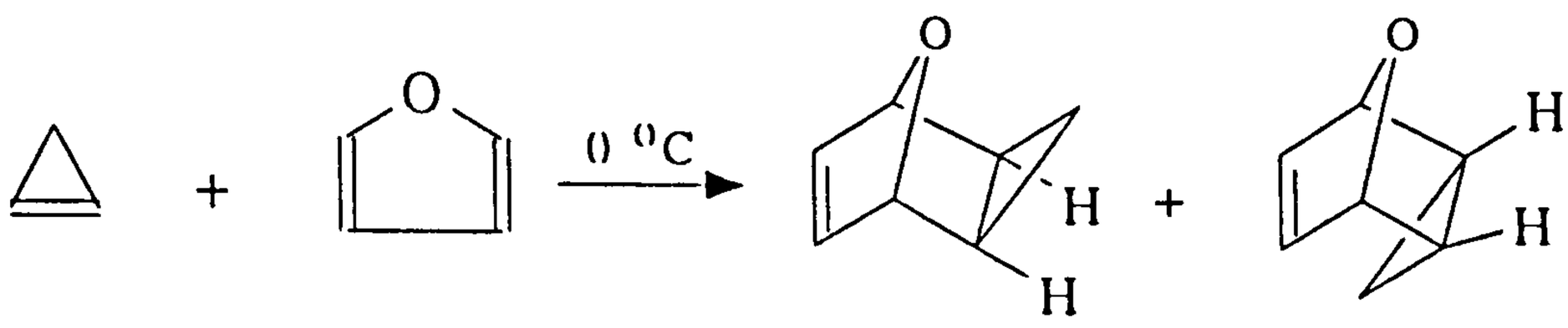


(66) (67)

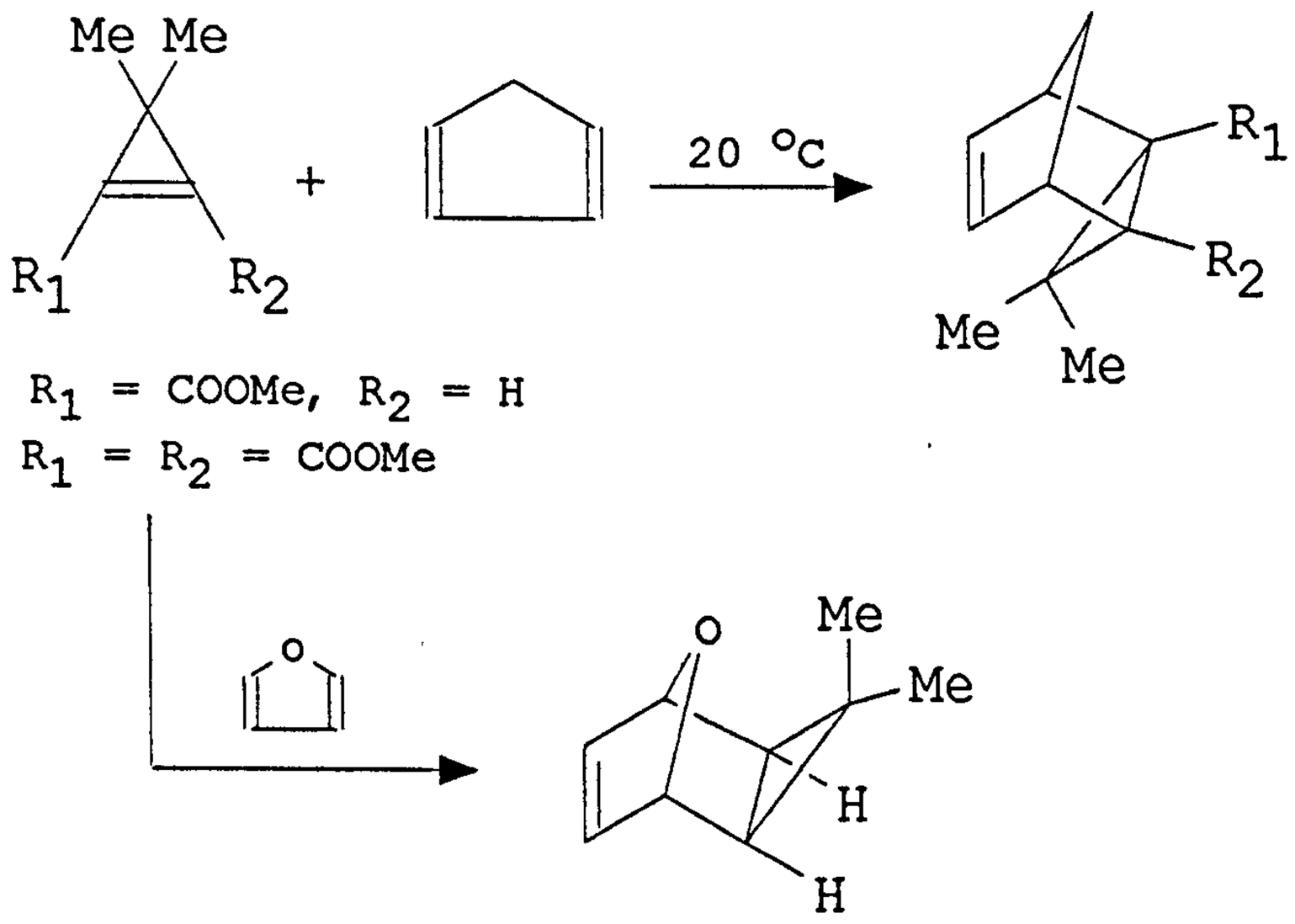
1.4.4. CYCLOADDITION

In general, cyclopropenes are good dienophiles, although their inherent thermal instability can lead to side reactions, and the presence of substituents at C_3 causes some steric retardation. Cyclopropene itself cycloadds to a range of dienes including forming an endo-adduct with cyclopentadiene; in contrast a 1:1 mixture of *exo*-and *endo*-adducts is formed with furan.[55,56]

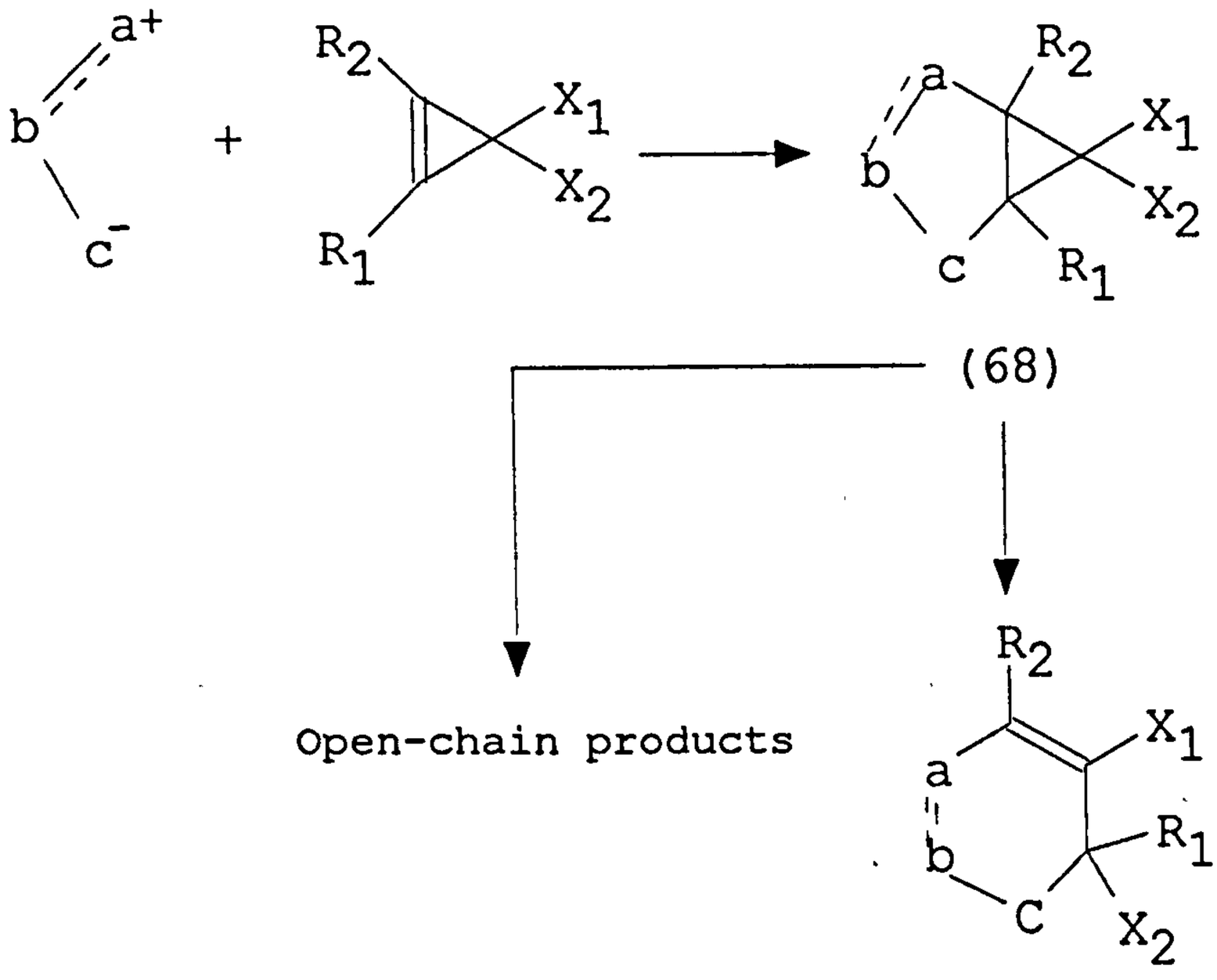




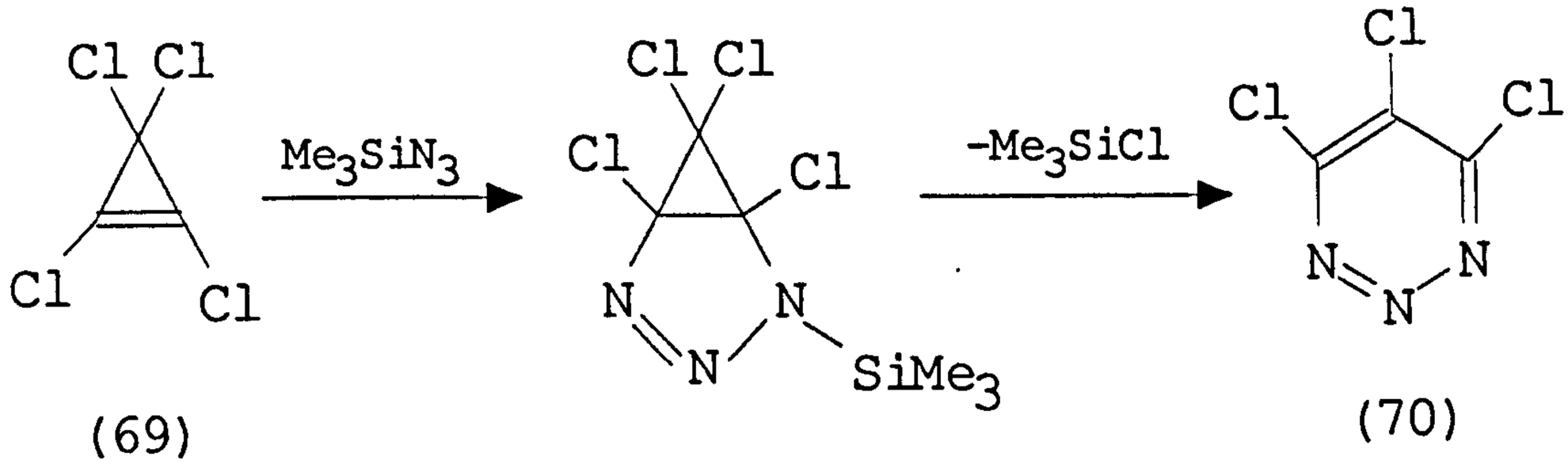
However, 3,3-dimethylcyclopropene does not add to cyclopentadiene even at 100 °C,[57] the deactivation resulting from steric hindrance due to the C_3-methyl groups. Cyclopropenes substituted with electron withdrawing groups at C_1 and C_2, e.g. esters and cyano groups, follow the same steric course of cycloaddition as non-electrophilic cyclopropenes, i.e cyclopentadiene produces *endo* and furan produces predominantly *exo*- adducts.[58]



The cyclopropene π-bond acts as a dipolarophile for a wide range of a 1,3-dipoles.[59] The initial [2+3] adduct (**68**) (a, b and c represent substituted atoms of C, N and/ or O) can expand to a six membered heterocycle, particularly when the cyclopropane contains a good leaving group at C_3 e.g. (X_2 = Cl). Less frequently ring fission in (**68**) gives an open-chain product.

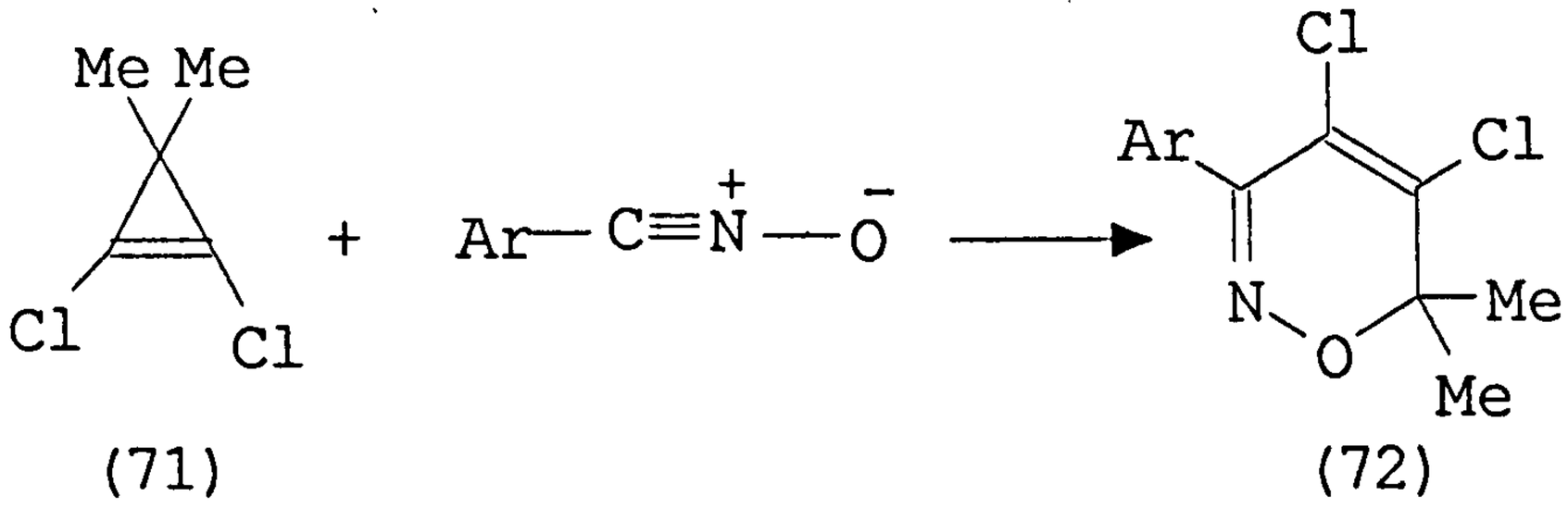


When the cyclopropene (**69**) was allowed to react with trimethylsilyl azide, the final product was (**70**); this may arise by addition and subsequent loss of trimethylsilyl chloride.[60]



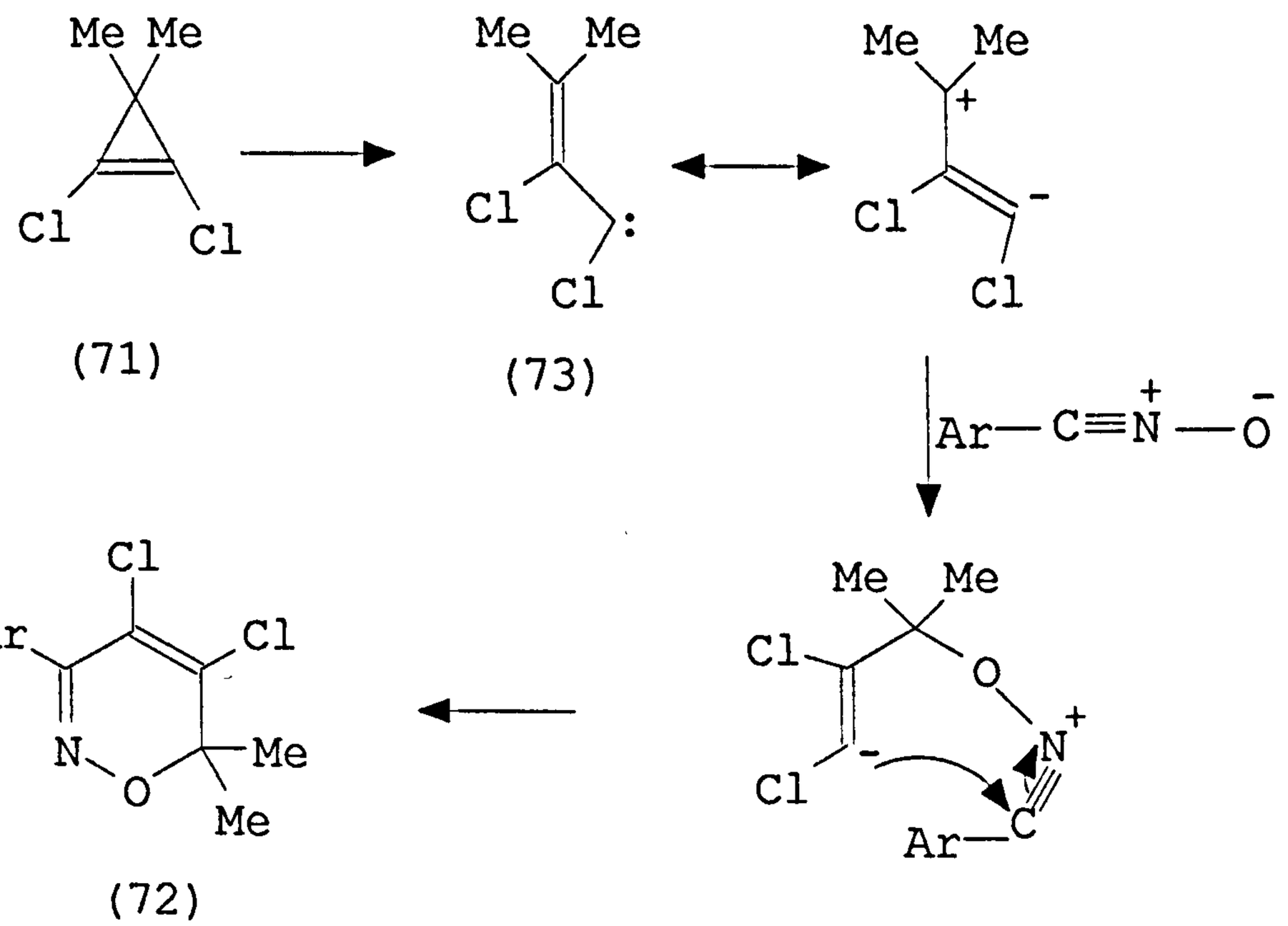
(69) (70)

However, when the cyclopropene (**71**) was treated with a nitrile oxide for 18 h at 20 °C in diethylether it gave the oxazine (**72**) (65 %).[61]



(71) (72)

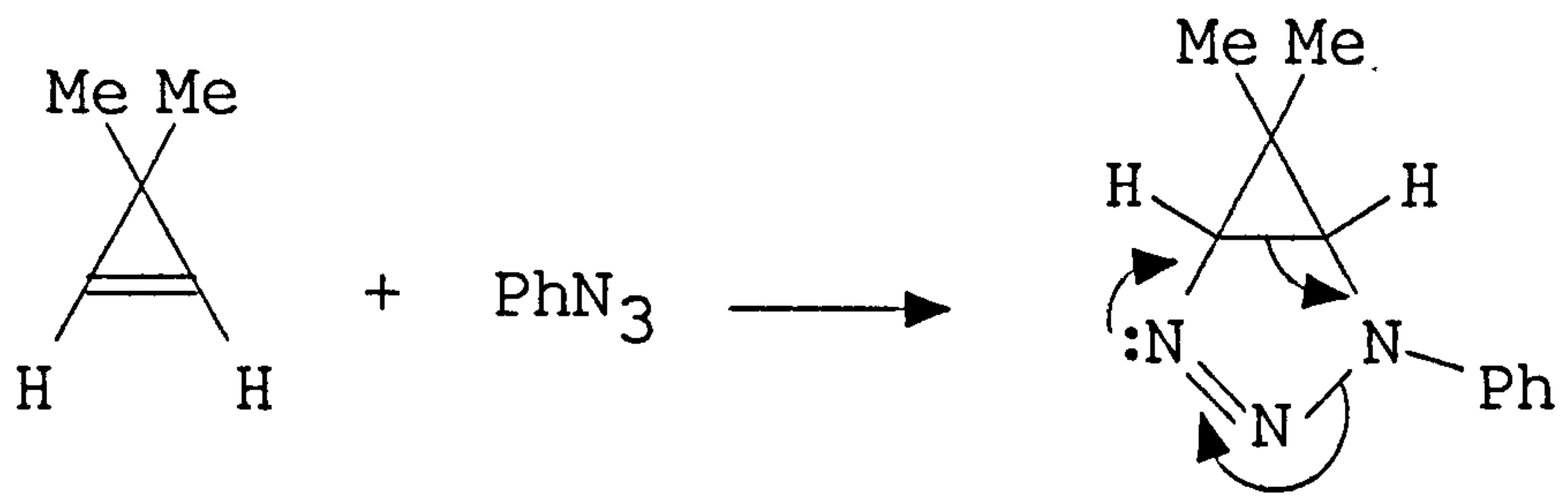
It is known that the cyclopropene (**71**) undergoes ring-opening at ambient temperature to produce vinylcarbene (**73**), which could be trapped by alkenes.[36] The formation of oxazines (**72**) could formally occur by addition of the singlet vinylcarbene (**73**), which may be regarded as an allyl cation adjacent to an anion on C_1, to the nitrile oxide.



(72)

The reaction of 3,3-dimethylcyclopropene (**6**) with phenylazide gave a 2:1 adduct (**75**), apparently derived from initial [2+3]cycloaddition to give (**74**), rearrangment to the diazo-

derivative, and a 1,3-dipolar addition to a second molecule of cyclopropene to give (75).[62]



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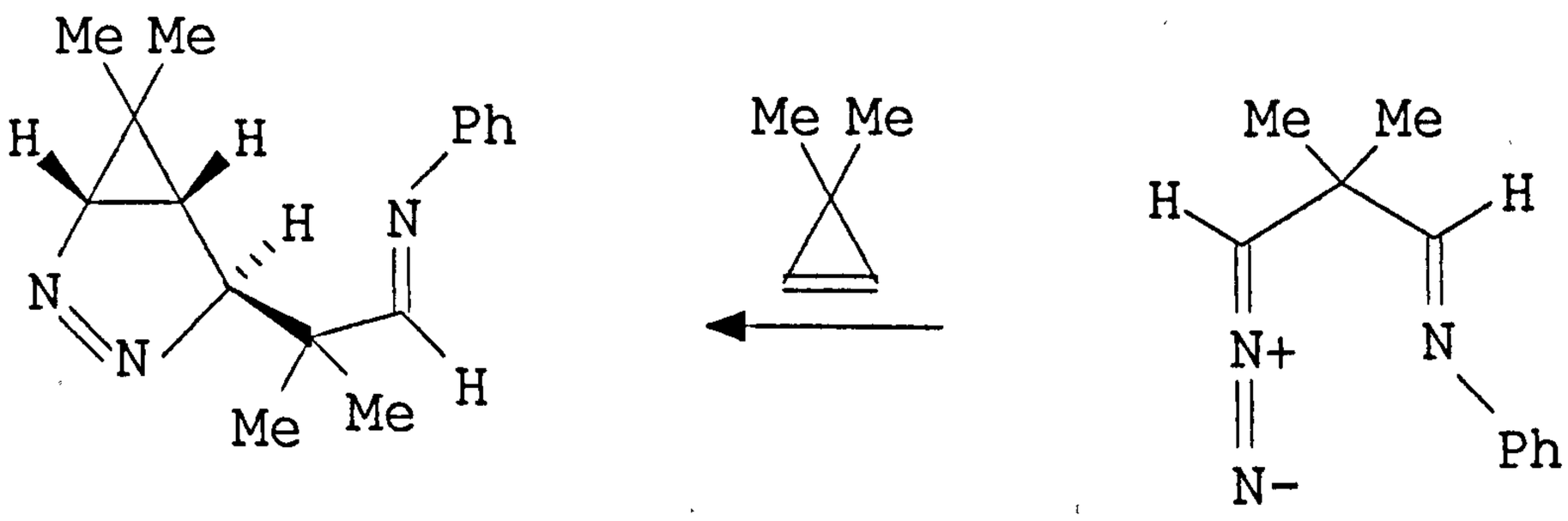


(75)

DISCUSSION

The result of this thesis are divided into five chapters, 2 - 6. This page summarises the results for each chapter:

a) **Chapter 2:**

This chapter describes the stereochemistry of ring opening of 3-(2-bromoethyl)-3-methyl-1,2-dibromocyclopropene at 0 - 20 °C to a vinyl-carbene.

b) **Chapter 3:**

This chapter describes a simple method for the preparation of 1-halo-2-alkylcyclopropenes from a 1,1,2-trihalocyclopropane using a dialkyl phosphite and either a trialkylamine or sodium hydride.

c) **Chapter 4:**

This chapter describes the preparation of four carbon cyclopropene building blocks, starting with methyl 1,1,2-tribromocyclopropane carboxylate.

d) **Chapter 5:**

In this chapter the addition of dihalocarbenes to chloroprene and 2,3-dichlorobutadiene was investigated in order to prepare the bis adducts. In practice these were obtained only in low yield. However, the mono adducts provided a simple route to five carbon vinylcyclopropenes.

e) **Chapter 6:**

This chapter describes the addition of diazoalkenes to 1,2-dibromocyclopropenes and reactions of the products.

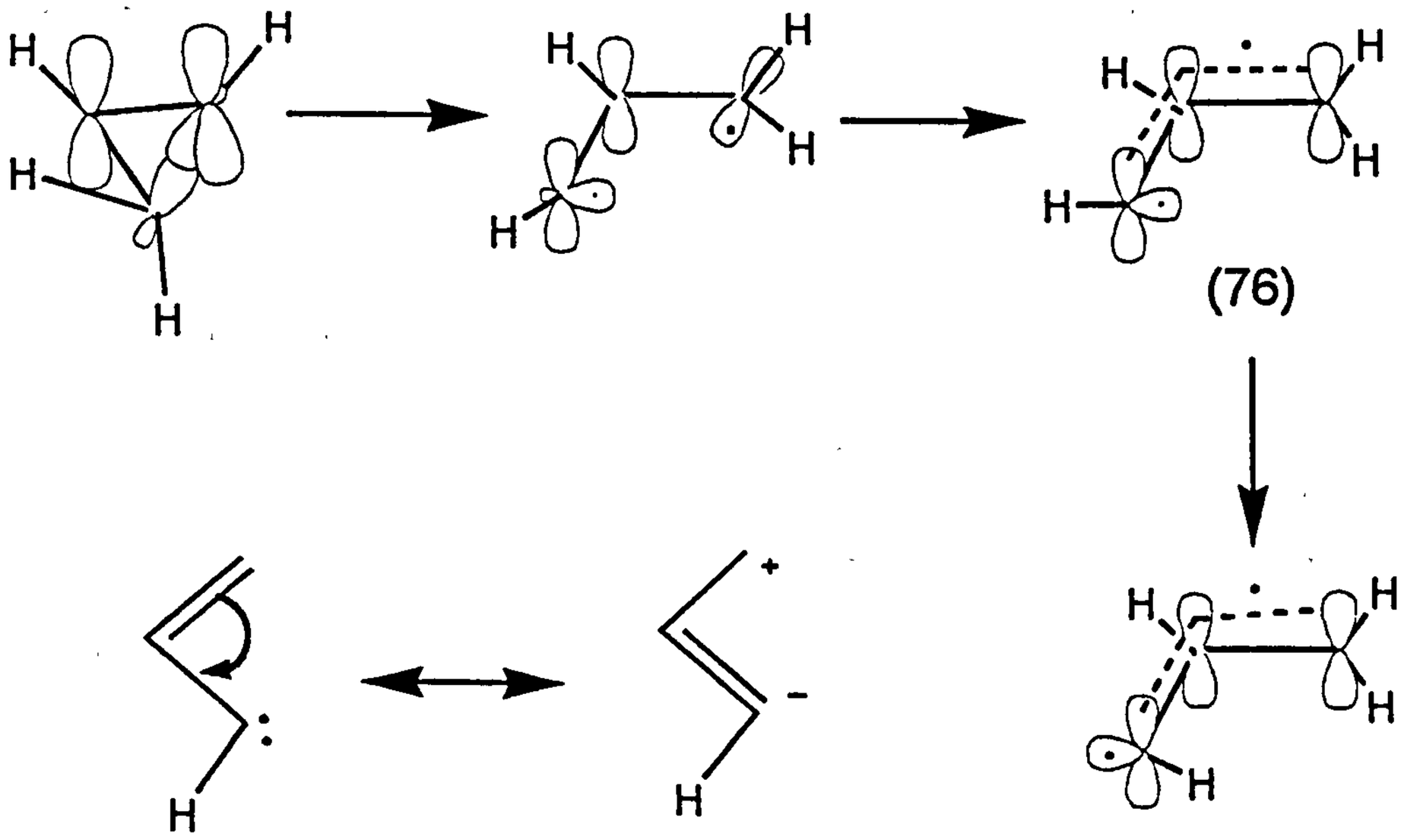
Chapter 2

Ring opening of cyclopropenes

2.0. INTRODUCTION

Cyclopropenes, as the most highly strained compounds among cyclo-olefins, are at present the object of many investigations. Interest in cyclopropene chemistry has grown rapidly in recent years because of the development of many synthetic procedures using cyclopropenes and the discovery of natural products incorporating the cyclopropene ring.

Vinylcarbenes have frequently been proposed as intermediates in the thermal and photochemical reactions of cyclopropenes, because of the relief of ring strain, combined with possible resonance stabilization of the corresponding ring-opened species.[63] The thermal ring-opening of cyclopropenes may be explained in terms of cleavage of one σ-bond and monorotation about the second σ-bond to produce the allylic system (**76**). The electron distribution and multiplicity of the ground state carbene will depend on substituents, but the singlet species may be expected to show some characteristics of a dipolar form (**78**).



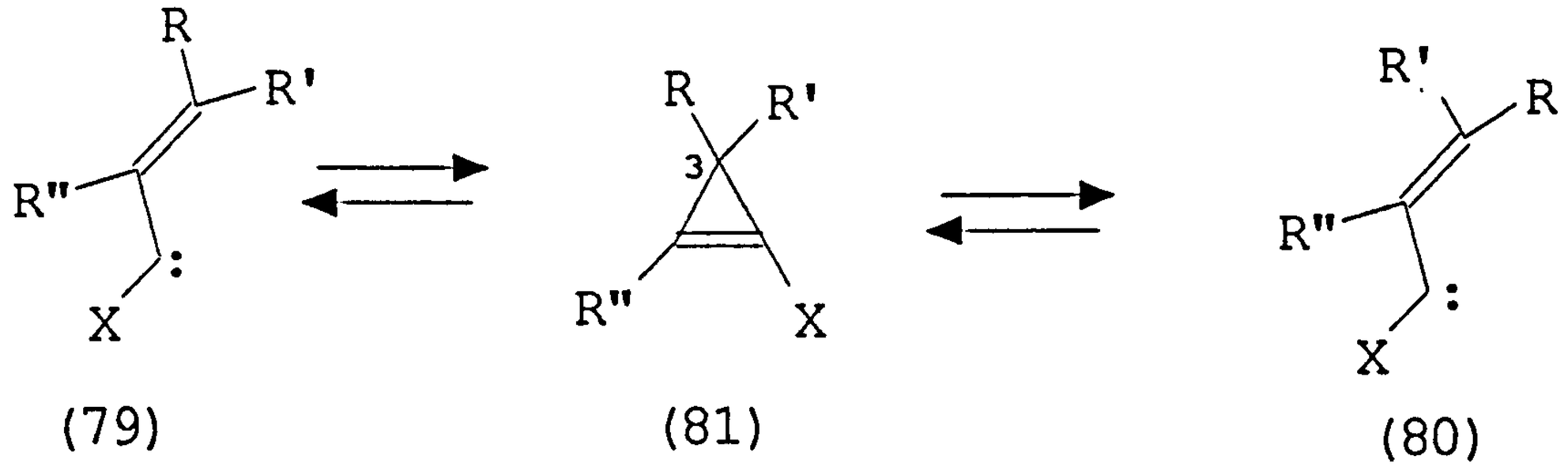
(76)

(78)

(77)

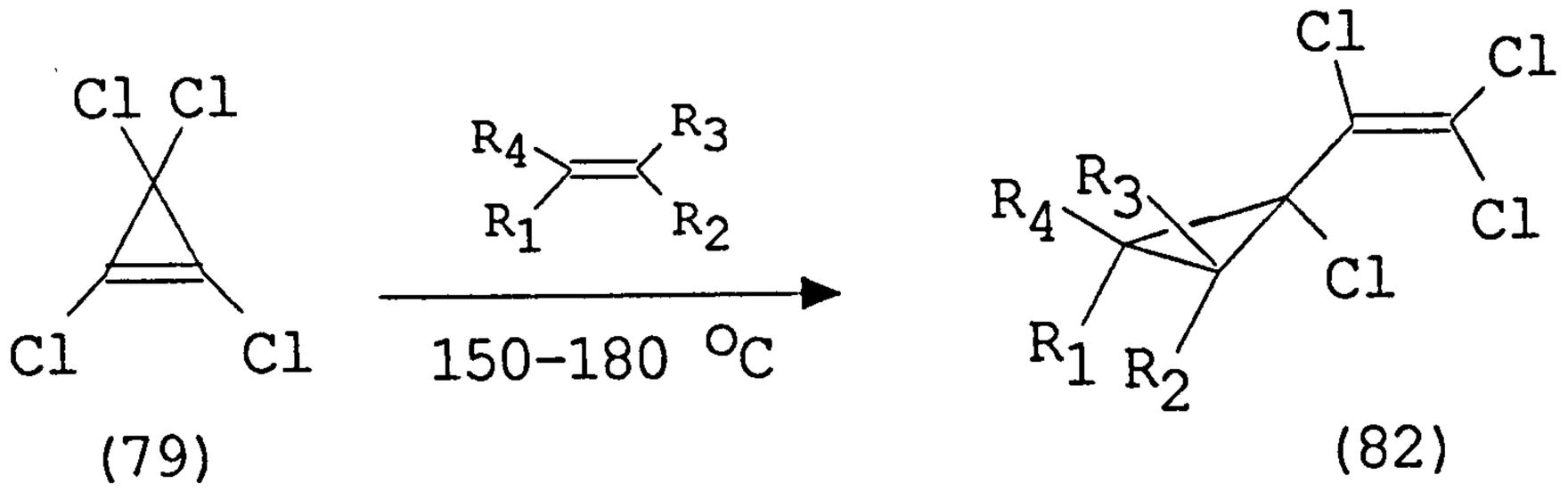
The species (**76**) may also interconvert with (**77**), either by rotation or inversion at

C_1.[45] The ring-opening of cyclopropene (**81**) to a vinylcarbene, which in several cases is reported to be reversible, involves a formal monorotation at C-3 leading to either *E*- or *Z*-isomers (**79**) and (**80**) about the double bond, which may be trapped by inter- and intramolecular processes.[45]



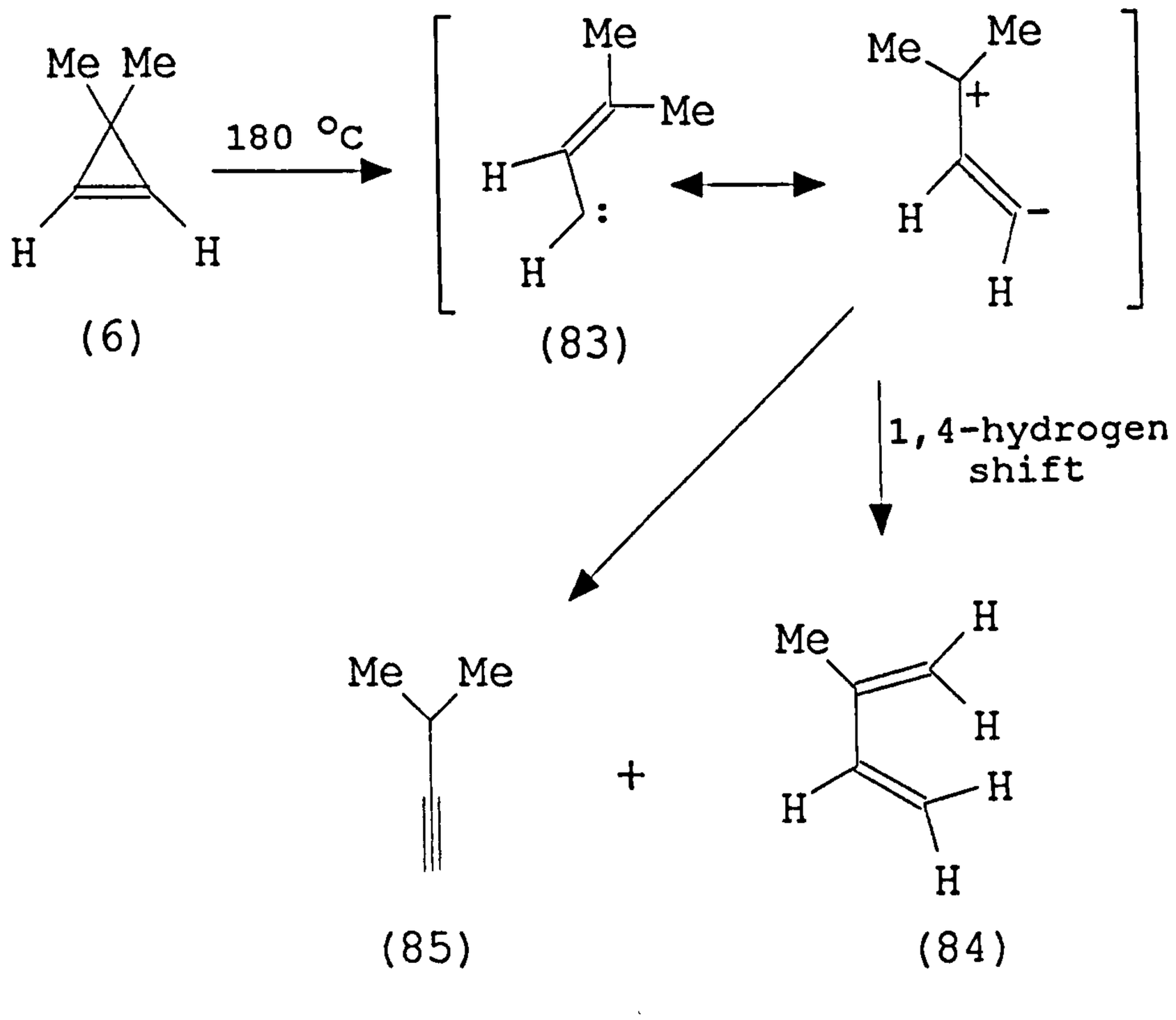
(79) (81) (80)

There are several example of intramolecular trapping of the carbene by a 3-substituent which require these centres to be *Z*- related; this may arise by stereocontrolled ring-opening or could be the result of a reversible process and selective trapping of one carbene stereoisomer. In some cases, steric effects apparently play a controlling role; thus, while photolysis of (**81**, X = R" = R = Ph, R' = CH_2OH) leads to a furan derived by trapping of the *E*- isomer (**79**) by the hydroxyl group, compound (**81**, X = R" = R = Ph, R' = CH(Me)OH) leads to an indene by trapping of the *Z*- isomer of the corresponding carbene (**80**) by the phenyl group.[64] The thermal reaction often requires relatively high temperature, e.g. the tetrachlorocyclopropene (**69**) undergoes ring opening to the corresponding carbene at 150-180 °C, and in the presence of alkenes this leads to the cyclopropanes (**82**).[65]



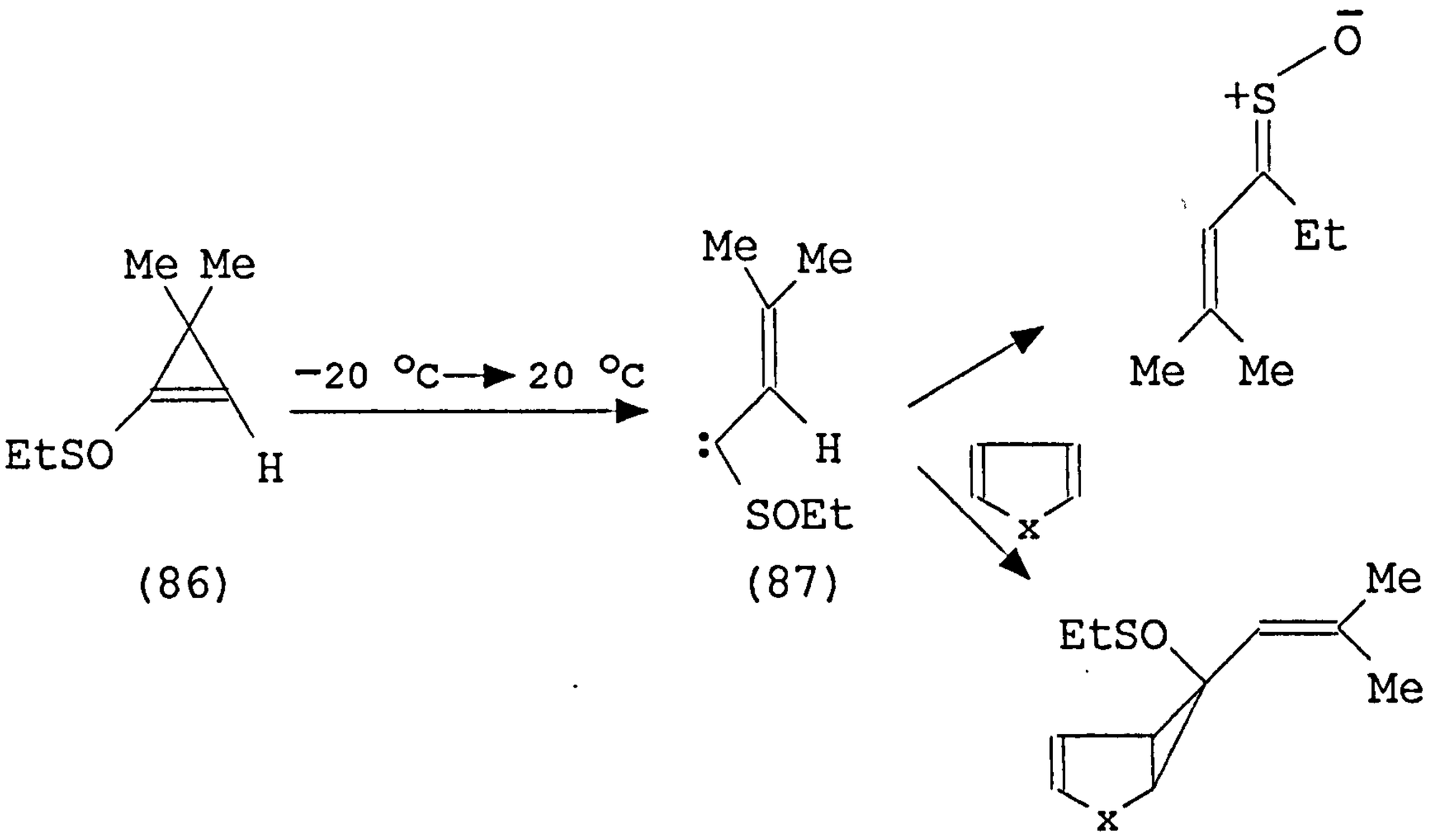
(79) (82)

Moreover, the cyclopropene (**6**) undergoes ring opening at 180 °C to the carbene (**83**), which reacts intramolecularly to give the diene (**84**) and alkyne (**85**) apparently through a 1,4 or 1,2 hydrogen shift respectively.[66]



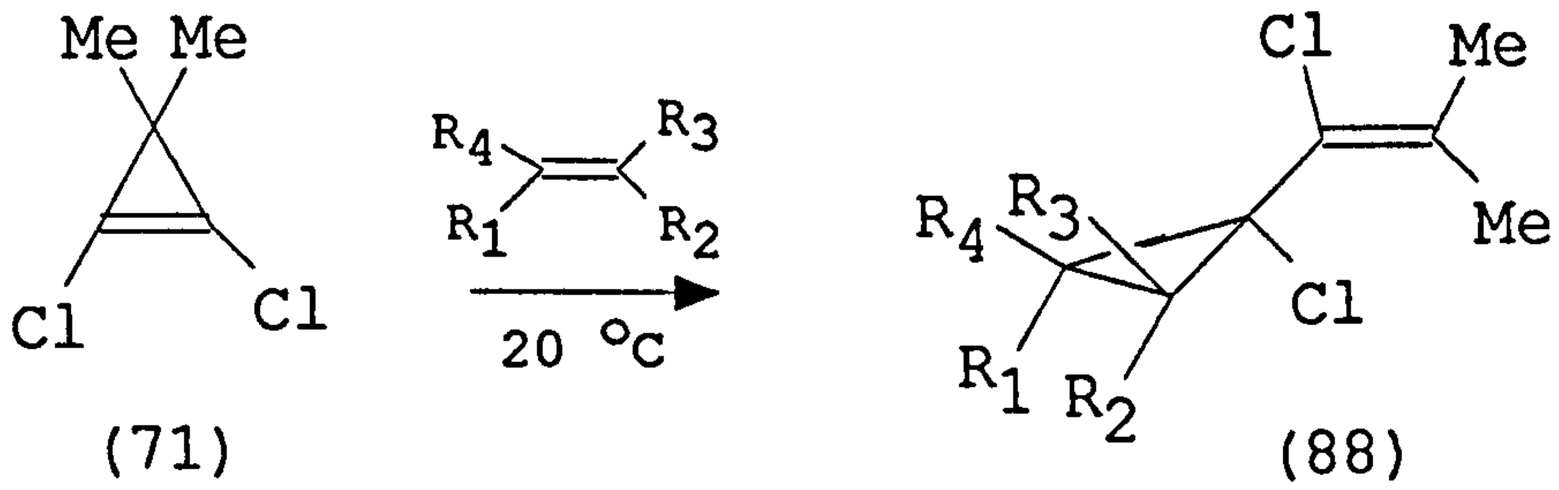
(6) (83) (85) (84)

However, the ring-opening of cyclopropenes to carbenes can occur even at or below ambient temperature; thus, the cyclopropene (**86**) is reported to undergo ring opening at -20 °C, and the resulting carbene (**87**) is readily trapped by alkenes.[67]

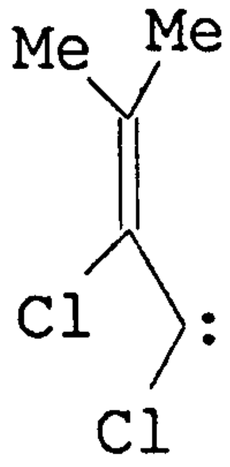


(86) (87)

Moreover, when the cyclopropene (**71**) was treated with a range of alkyl substituted alkenes in ether at 20 °C for 1-2 h, the cyclopropanes (**88**) were obtained.[36]

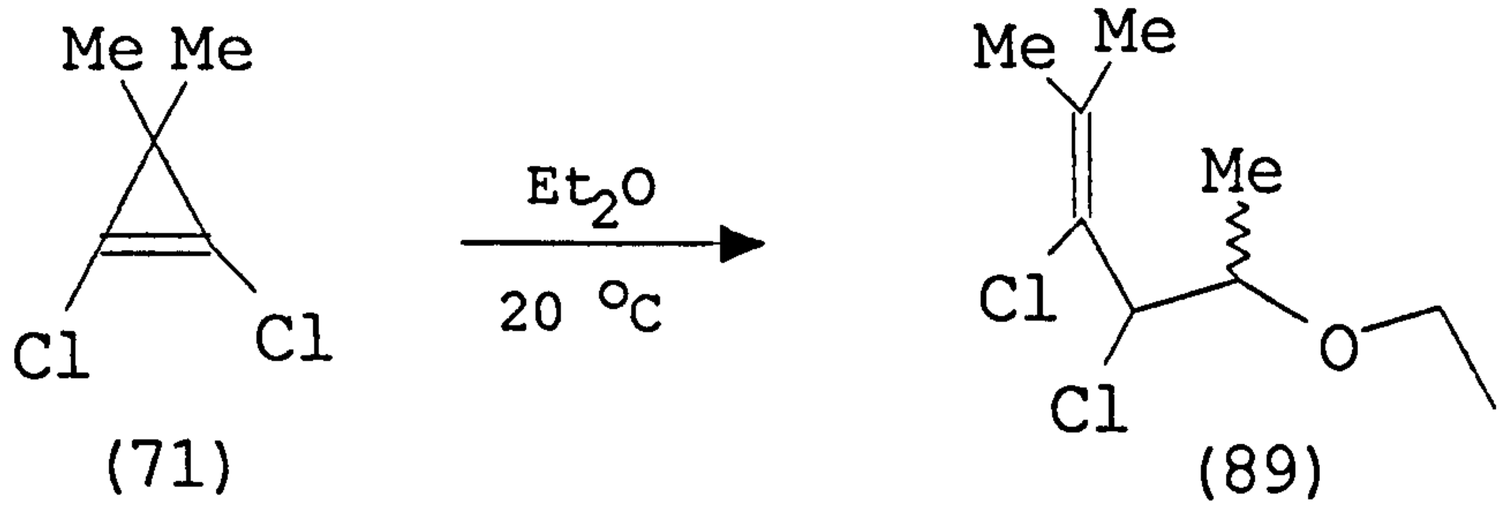


(71) (88)



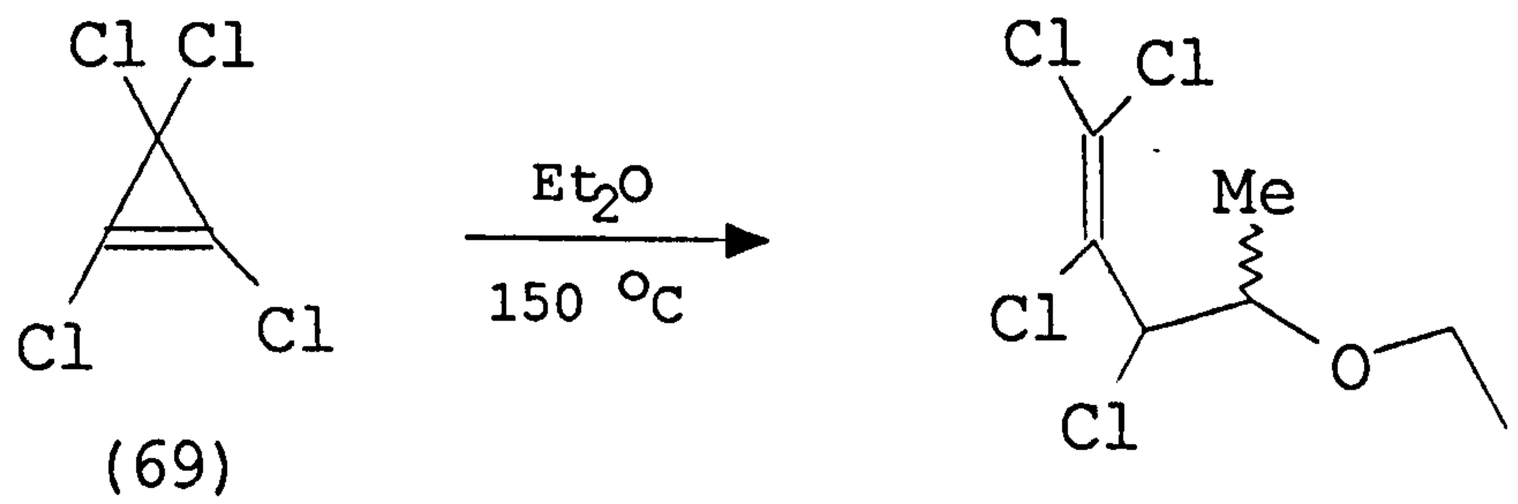
(73)

These are apparently derived by addition of the singlet carbene (**73**) to the double bond, as (*Z*)-and (*E*)-but-2-enes each reacted with retention of the alkene stereochemistry. In principle compounds (**88**) could also arise by either [2+2]-cycloaddition of (**71**) to the alkene or [3+2]-addition of the carbene to the alkene, in each case followed by rearrangment. However, when the alkenes were omitted, (**71**) underwent a slower reaction with the solvent, ether, giving (**89**) in 18 h at 20 °C.[36b]



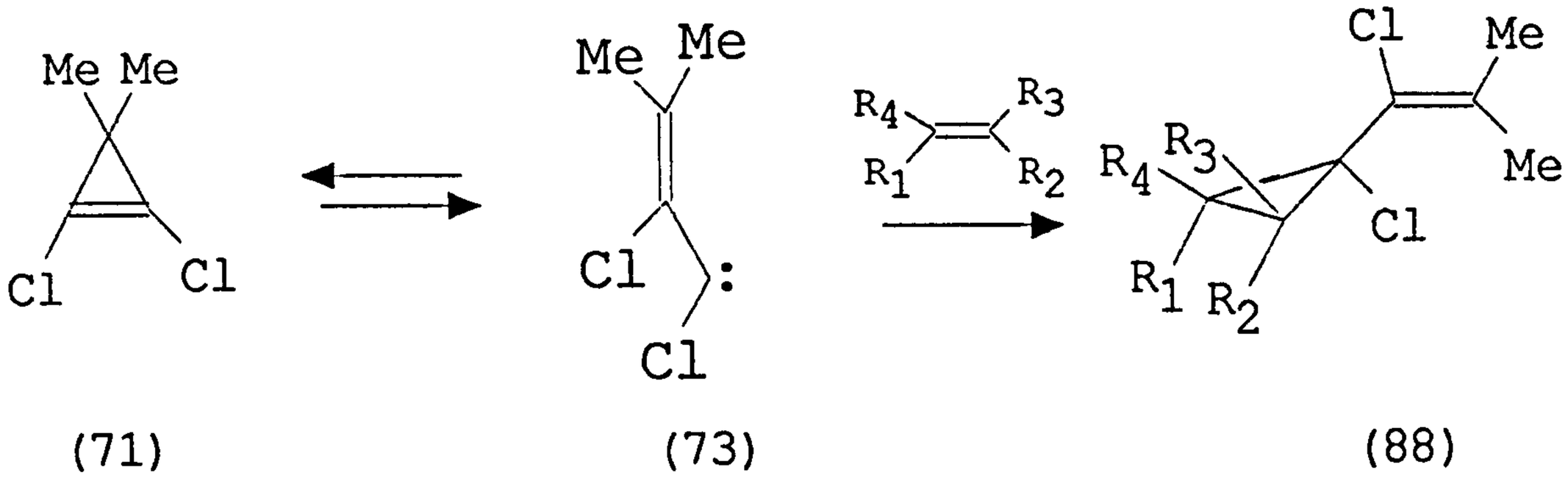
(71) (89)

This last product is typical of formal carbene insertion adjacent to oxygen in ethers and would be very difficult to explain by another process. A similar reaction has been observed for tetrachlorocyclopropene (**69**) at 150 °C.[68]



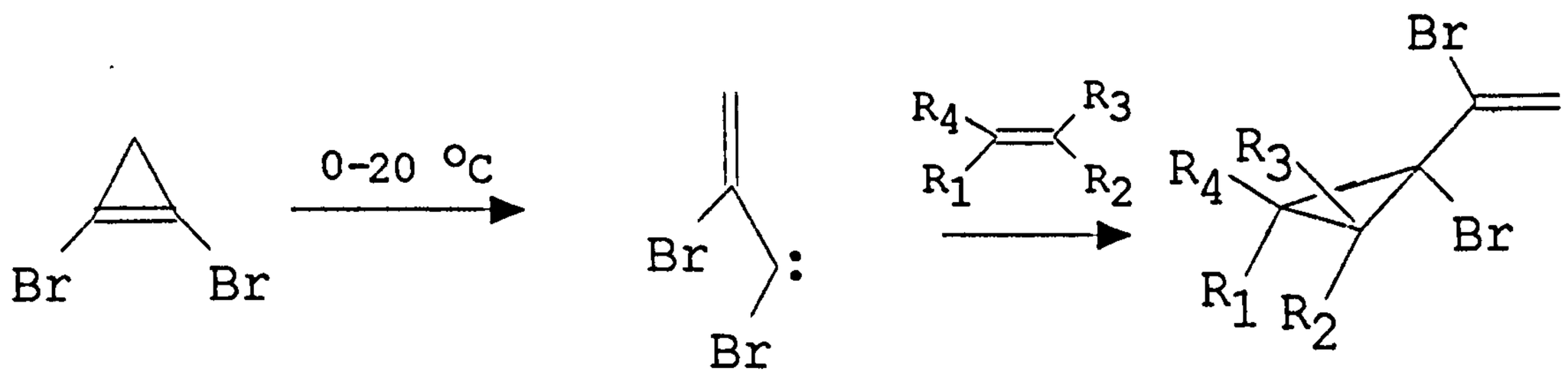
(69)

The fact that the cyclopropene (**71**) reacts more rapidly when an alkene is added suggests that the cyclopropene and the carbene are in equilibirum and the latter is only consumed rapidly in the presence of an alkene.



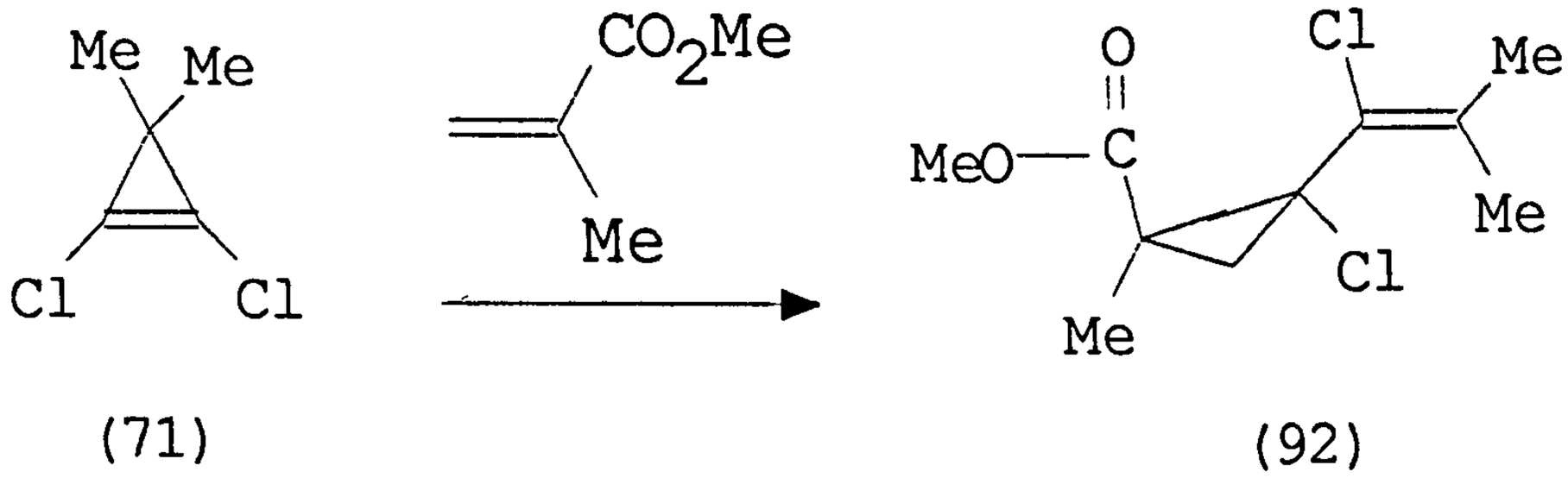
(71) (73) (88)

Recently, the parent dibromocyclopropene (**28**) was also found to undergo ring-opening to the carbene (**90**) which could be trapped by an alkene to give the vinyl-cyclopropane (**91**).[69]

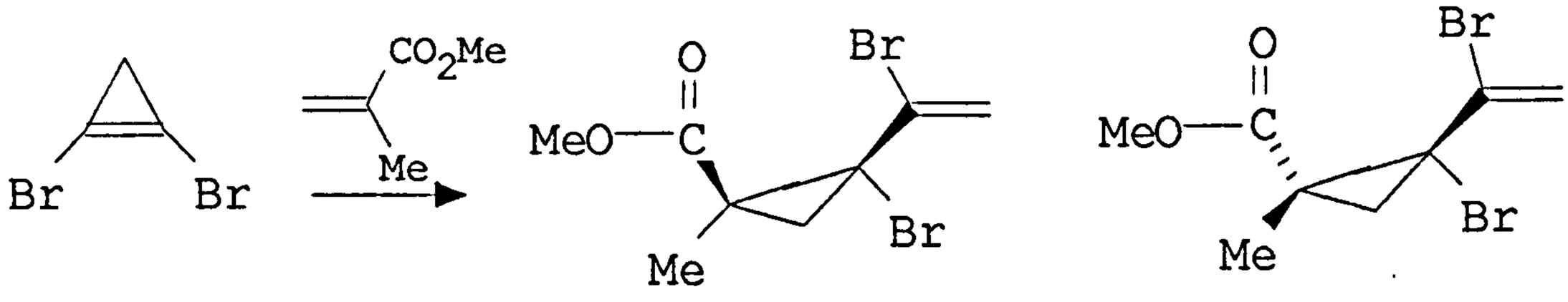


(28) (90) (91)

The carbene (**73**) could be trapped by electron poor alkenes such as methyl methacrylate to give (**92**) with the ester and alkyl group *cis* to each other,[36b] while (**90**) gave two isomers (**93**) and (**94**) in ratio 5:1,[69] with ester and vinyl group *cis* to each other in the major isomer.

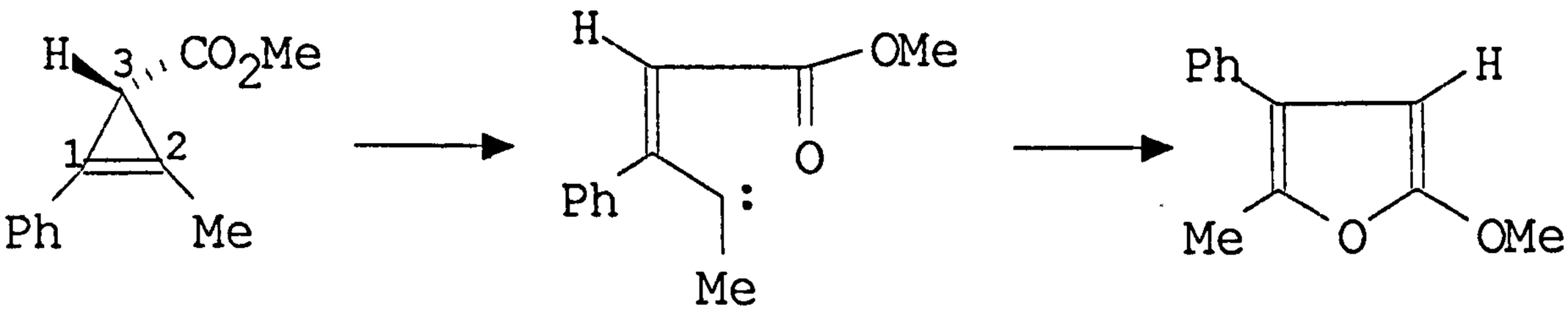


(71) (92)



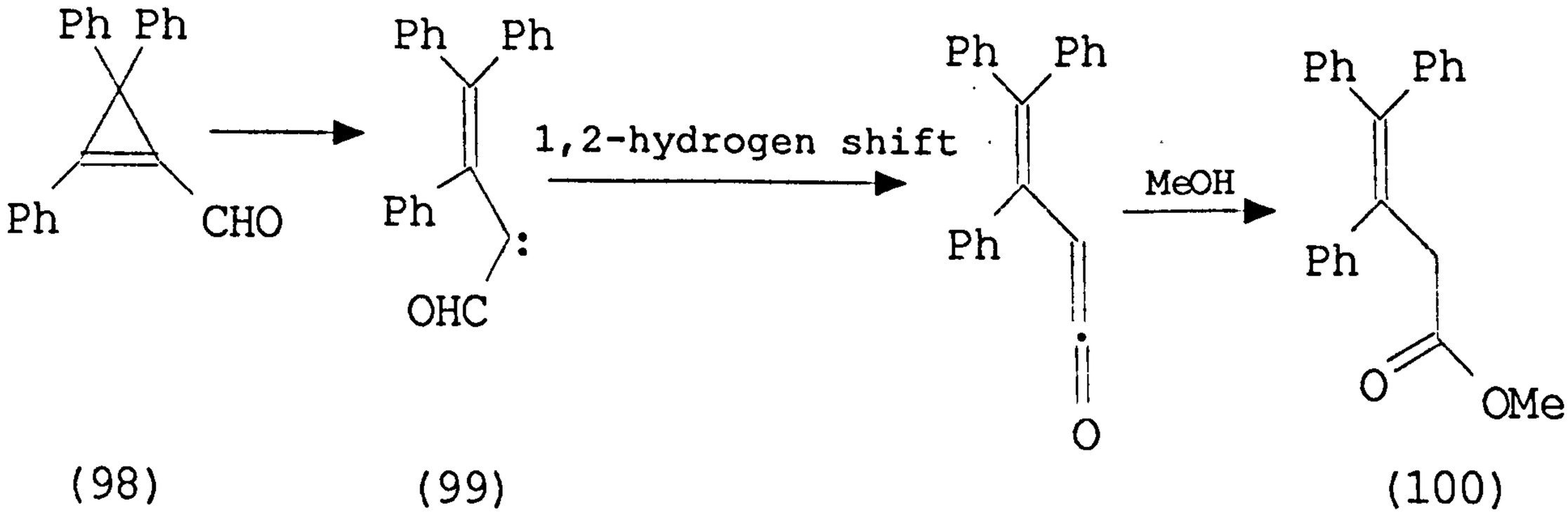
(28) 5 : 1 (93) (94)

Vinylcarbenes can also be trapped by intramolecular reactions; for example, the optically active cyclopropene (**95**) undergoes a facile ring-opening via C_2-C_3 cleavage to give the vinylcarbene (**96**) rather than the regioisomer which may be derived via C_1-C_3 ring opening. The former carbene reacts intramoleculary with the carbonyl group giving the furan (**97**).[70]



(95) (96) (97)

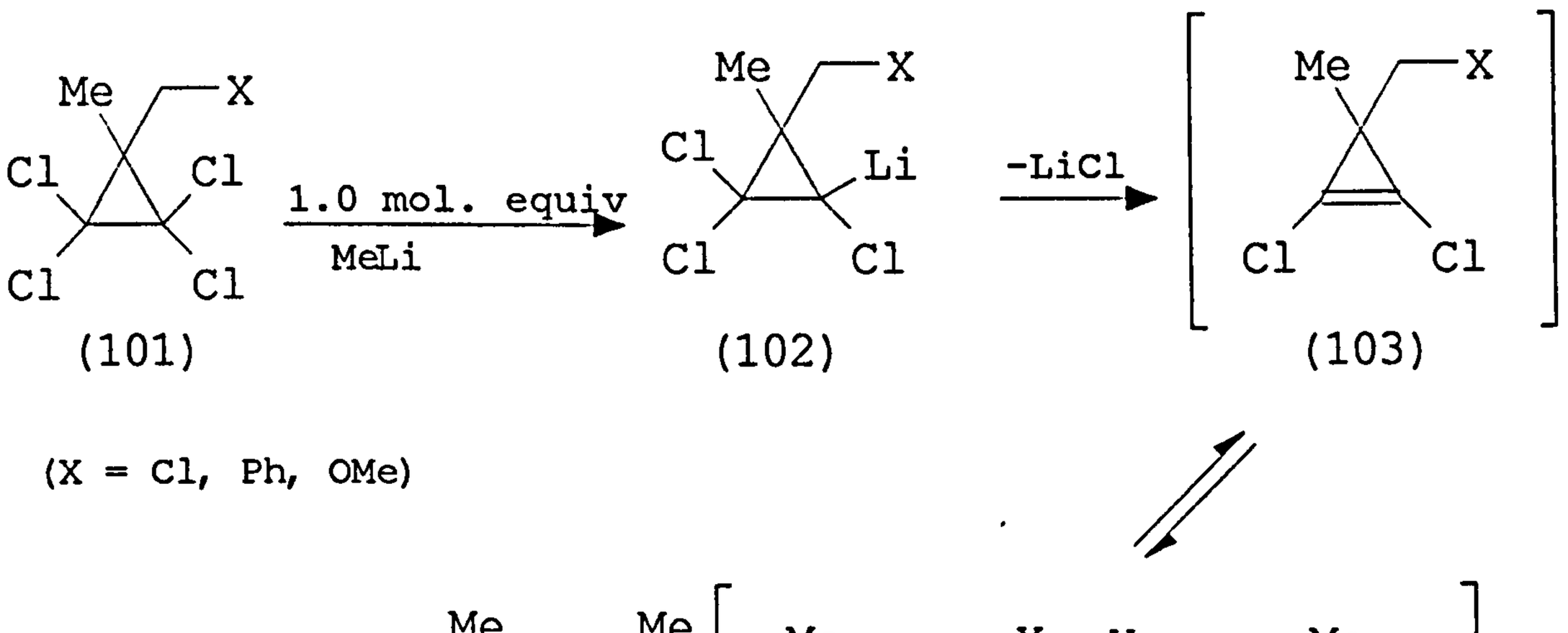
The photolysis of (**98**) in methanol also leads to the ring opening of the cyclopropene to the carbene (**99**), which undergoes a 1,2-hydrogen shift giving the corresponding ketene. This is in turn can be trapped by methanol to produce the β,γ-unsaturated ester (**100**).[71]



(98) (99) (100)

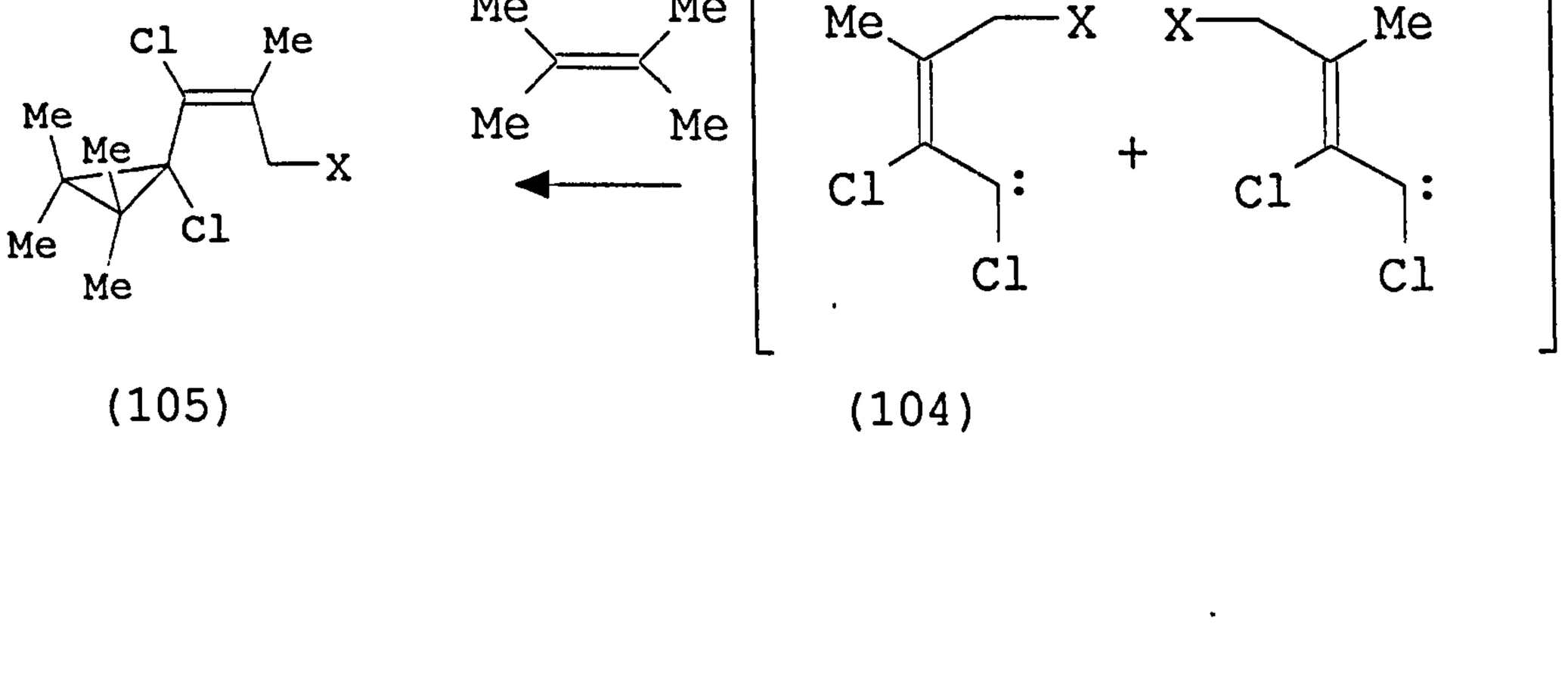
2.1. AIMS OF THE PROJECT

It is known that the reaction of tetrachlorocyclopropanes (**101**) with one equivalent of methyllithium at 0 °C in the presence of an alkene leads to mainly one stereoisomer of the cyclopropanes (**105**) derived from carbenes (**104**).[34, 35, 72]



(101) (102) (103)

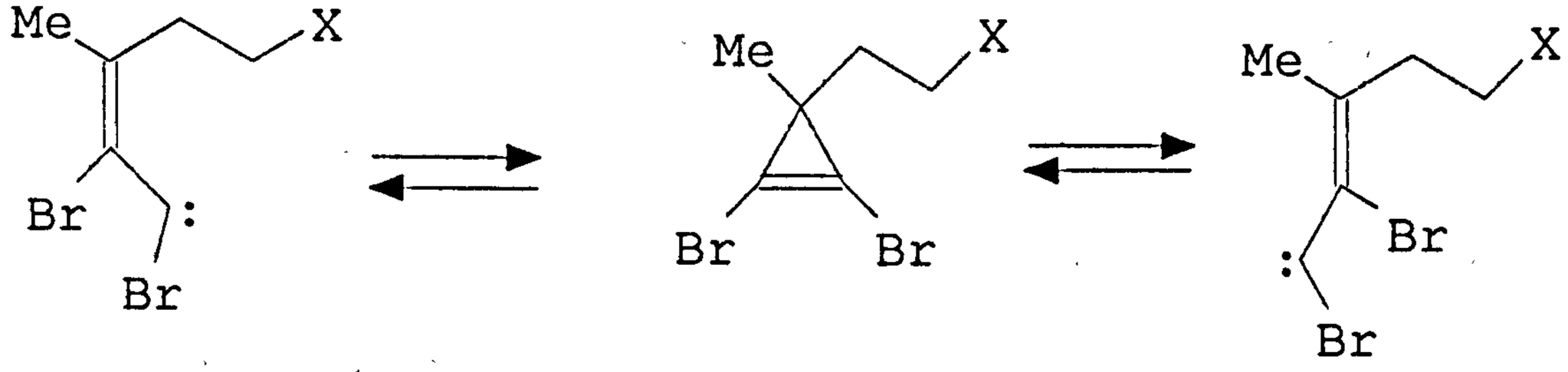
(X = Cl, Ph, OMe)



(105) (104)

These may arise by lithium-chlorine exchange to give (**102**), followed by or concurrent with 1,2-elimination to give (**103**), which undergoes ring-opening at 0-20 °C to the carbene (**104**), which is in turn trapped by alkene to give the adduct (**105**).

It was therefore of particular interest to find out if cyclopropenes such as (**107**) undergo ring-opening to give the carbene (**106**) rather than (**108**), and if it is possible to trap these inter- or intramolecularly.



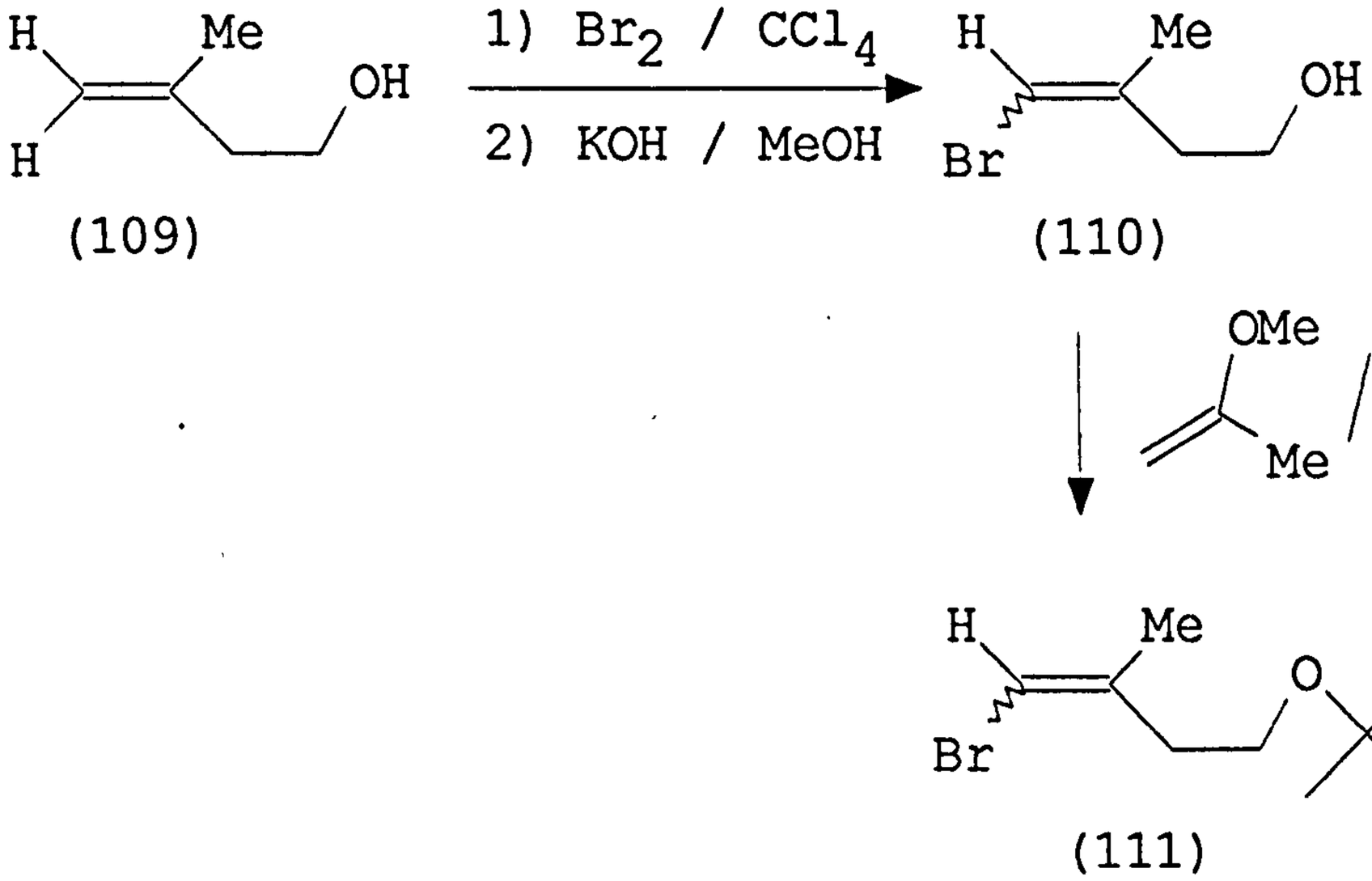
(106) (107) (108)

X = halogen, OH, OMe

2.2. RESULTS AND DISCUSSION

2.2.1. PREPARATION OF TRI- AND TETRAHALOCYCLOPROPANES

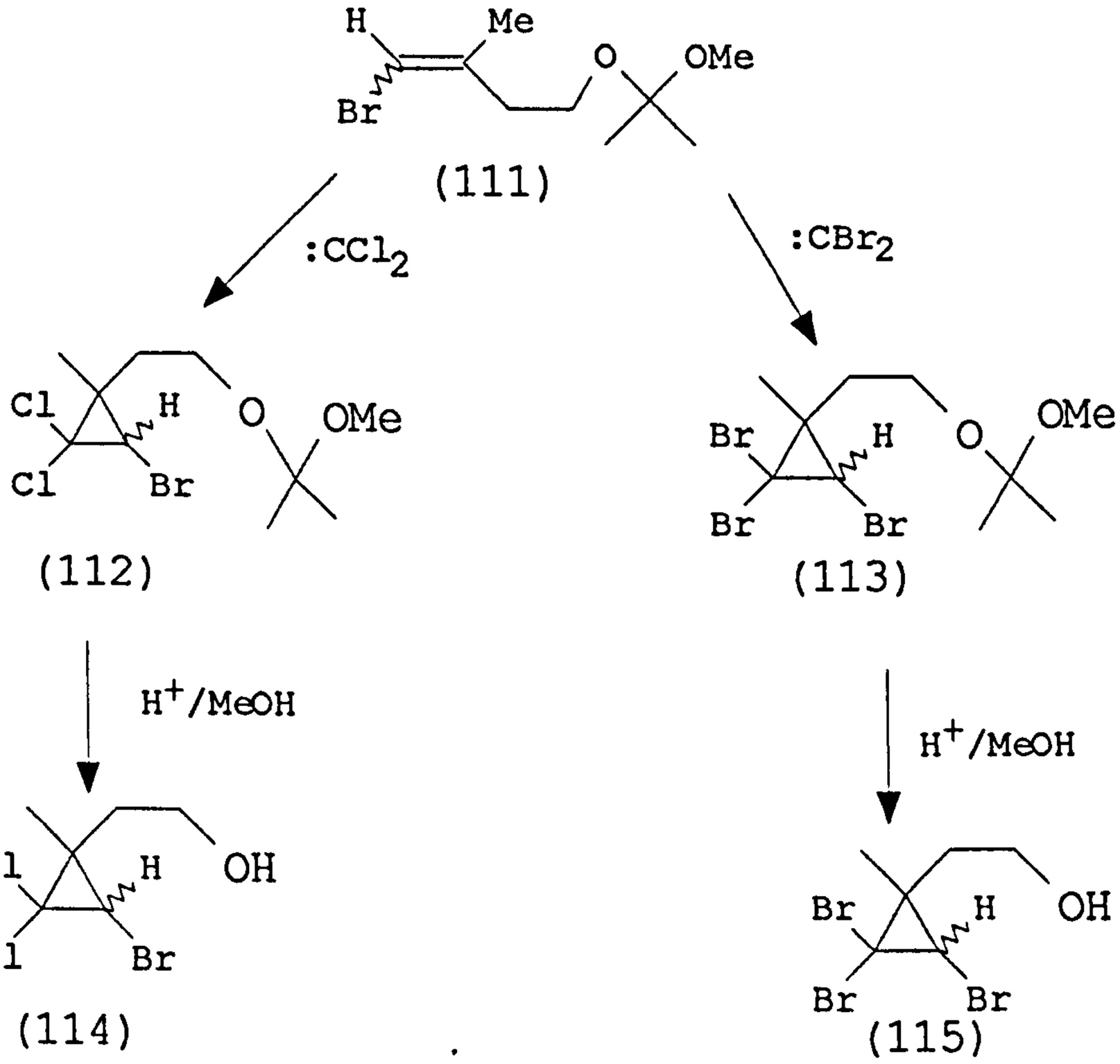
Reaction of the alcohol **(109)**, which is commercially available, with bromine followed by dehydrohalogenation provides a convenient large scale route to the *E/Z*-bromoalkene **(110)**.[73] The *E/Z* mixture was protected with 2-methoxypropene in the presence of a catalytic amount of PPTSA to give **(111)** (91%) as an *E/Z* mixture in ratio 4:1.



The mixture gave one spot by TLC. The ^{1}H n.m.r of the major isomer showed a singlet integrating to six hydrogens at δ 1.28 assigned to the two methyls in the protecting group; a singlet at δ 3.1 integrating to three hydrogens was for the methoxy group while a narrow doublet for the olefinic methyl appeared at δ 1.78 with a coupling constant of 1.2 Hz. The vinylic proton appeared as a broad quartet with a coupling constant of 1.2 Hz. The olefinic methylene group showed a double triplet at δ 2.3 with coupling constants of 0.9 and 6.8 Hz,

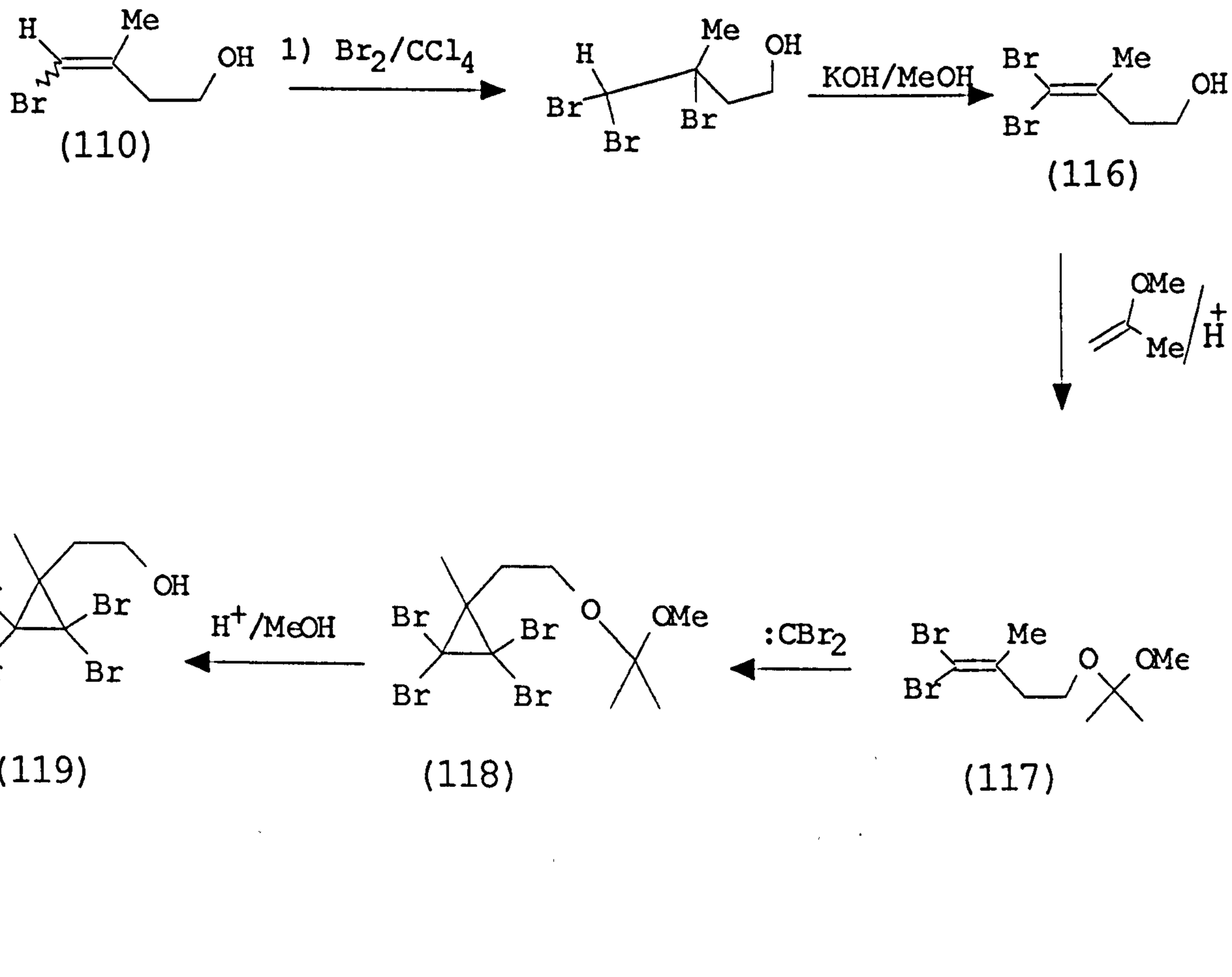
while the methylene next to the oxygen appeared as a triplet at δ 3.41 with coupling constant 6.8 Hz. The minor isomer showed a broad singlet at δ 5.89 for the vinylic proton and a singlet at δ 3.15 for the methoxy group together with a triplet at δ 2.4 for the olefinic methylene, while the protecting methyls resonated at δ 1.29 and the remaining signals were obscured by those for the major isomer.

The trihalocyclopropanes **(112)** and **(113)** were obtained in good yield, by the reaction of **(111)** with $:CCl_2$ or $:CBr_2$ respectively, generated under PTC from an excess of chloroform or bromoform and 50% sodium hydroxide with a catalytic amount of cetrimide. Deprotection to the alcohol by PTSA in aqueous methanol for 20 min gave **(114)** in 73 % and **(115)** in 57 % yield (from **111**).



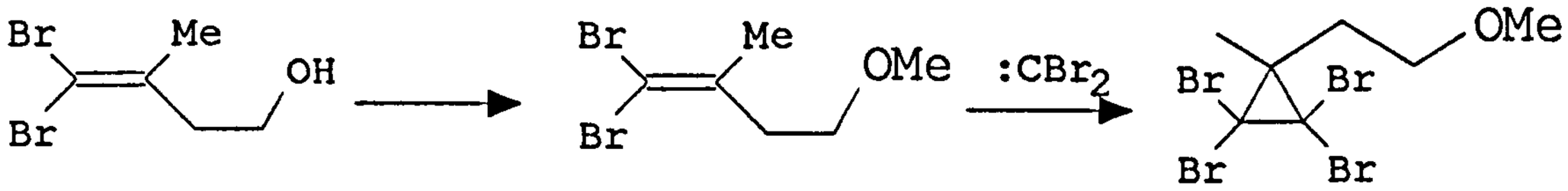
The product (**114**) showed the correct measured mass for $C_6H_9OBrCl_2$, and the ^1H n.m.r spectrum showed a mixture of two isomers in the ratio 4.5:1; these could not be separated by column chromatography. The major isomer showed a multiplet for two hydrogens next to the hydroxy group at δ 3.8, with a singlet at δ 3.4 for the cyclopropyl proton and a double triplet at δ 1.98 integrating to two protons with coupling constants of 3.5 and 7.0 Hz, together with a singlet for the methyl group at δ 1.34. The ^{13}C n.m.r spectrum contained six signals including one at δ 59.7 for the methylene next to the hydroxy group and a signal at δ 41 corresponding to the CCl_2 group.[74] The ^1H n.m.r spectrum for (**115**) was very similar to that for (**114**) and also showed two isomers in the ratio 4:1.

Reaction of the mixture *E/Z* (**110**) with bromine, followed by dehydrohalogenation provided the dibromoalkene (**116**) in 42 % yield.[75] Protection of the alcohol (**116**) with 2-methoxypropene in the presence of a catalytic amount of PPTSA gave (**117**) in 93% yield.

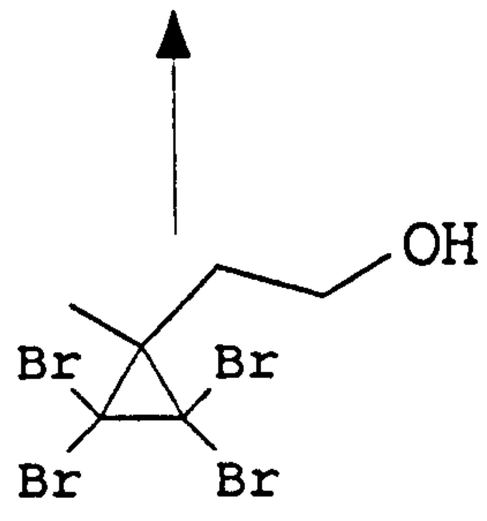


Similar addition of $:CBr_2$, generated under PTC from an excess of bromoform, 50 % aqueous sodium hydroxide, and cetrimide to **(117)** gave the protected tetrabromocyclopropane **(118)**. Deprotection with PTSA in methanol generated the tetra-bromocyclopropane alcohol **(119)** in 56 % yield as a crystalline solid.The product showed a correct C,H analysis for the formula $C_6H_8OBr_4$, while the ^1H n.m.r spectrum showed two triplets resonating at δ 3.8 and 2.1 (J = 7 Hz each), a broad singlet at δ 1.8 integrating for one proton, and a singlet at δ 1.5 for the methyl group. The ^{13}C spectrum showed the expected six signals including one at δ 60, assigned to the methylene next to the hydroxyl group, and the CBr_2 group at δ 41.

The methyl ether **(120)** was conveniently prepared by a phase transfer catalysed alkylation of the alcohol **(116)** with dimethyl sulphate using a procedure described by Merz 's.[76]



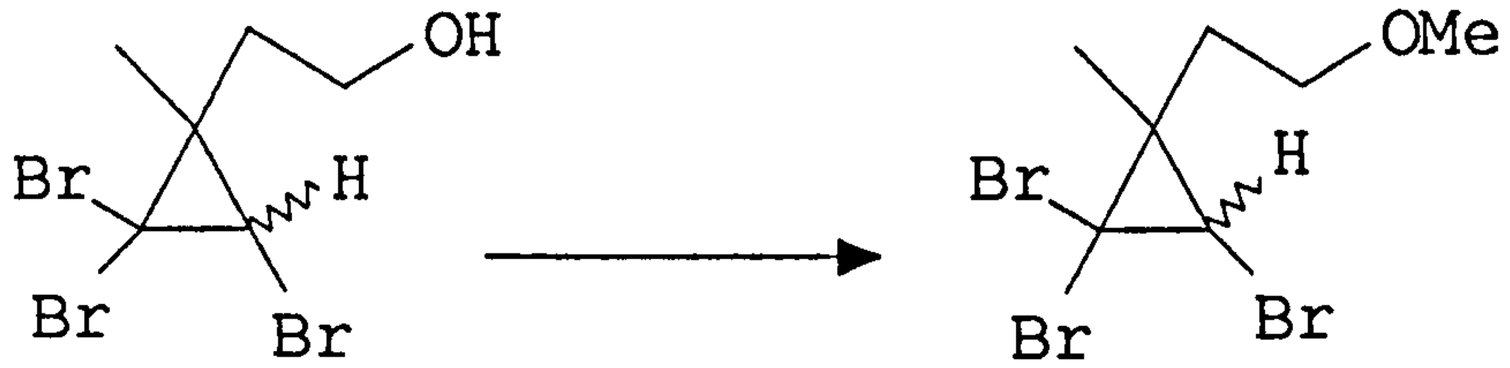
(116) (120) (121)



(119)

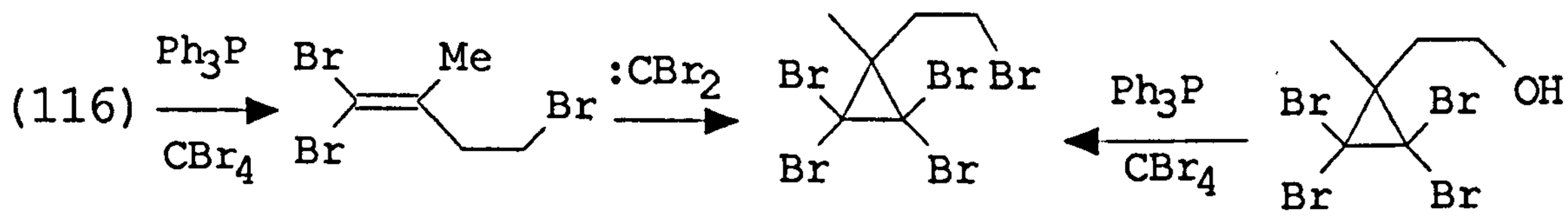
The tetrabromocyclopropane **(121)** was obtained either by dihalocyclopropanation of **(120)** under phase transfer conditions (41%) or by direct conversion of the hydroxy group of cyclopropane alcohol **(119)** to methoxy in 82 % yield by using Merz 's procedure.[76] The ^1H

n.m.r spectrum for **(121)** showed two triplets at δ 3.5 and 2.0 with coupling constant 6.9 Hz together with two singlets at δ 3.3 and 1.5 for the methoxy and methyl groups respectively. The tribromocyclopropane methyl ether **(122)** was also obtained in 74 % yield, from the reaction of **(115)** using Merz's procedure.[76]



(115) (122)

Treatment of the alcohol **(119)** with triphenylphosphine and carbon tetrabromide, gave directly the pentabromocyclopropane **(123)** in 72 % as a crystalline solid, which could also be obtained by dihalocyclopropanation of the tribromide **(124)** under phase transfer conditions in 50 % yield. The tribromide **(124)** was generated from the reaction of alcohol **(116)** with triphenylphosphine and carbon tetrabromide in 66 % yield.



(124) (123) (119)

The ^{1}H n.m.r spectrum for **(123)** showed two complex multiplets at δ 3.5 and 2.36 for methylenes next to halogen and the cyclopropane respectively, and a singlet at δ 1.52 for the methyl group **(see Figure 2)** . The ^{13}C n.m.r showed the expected five signals .

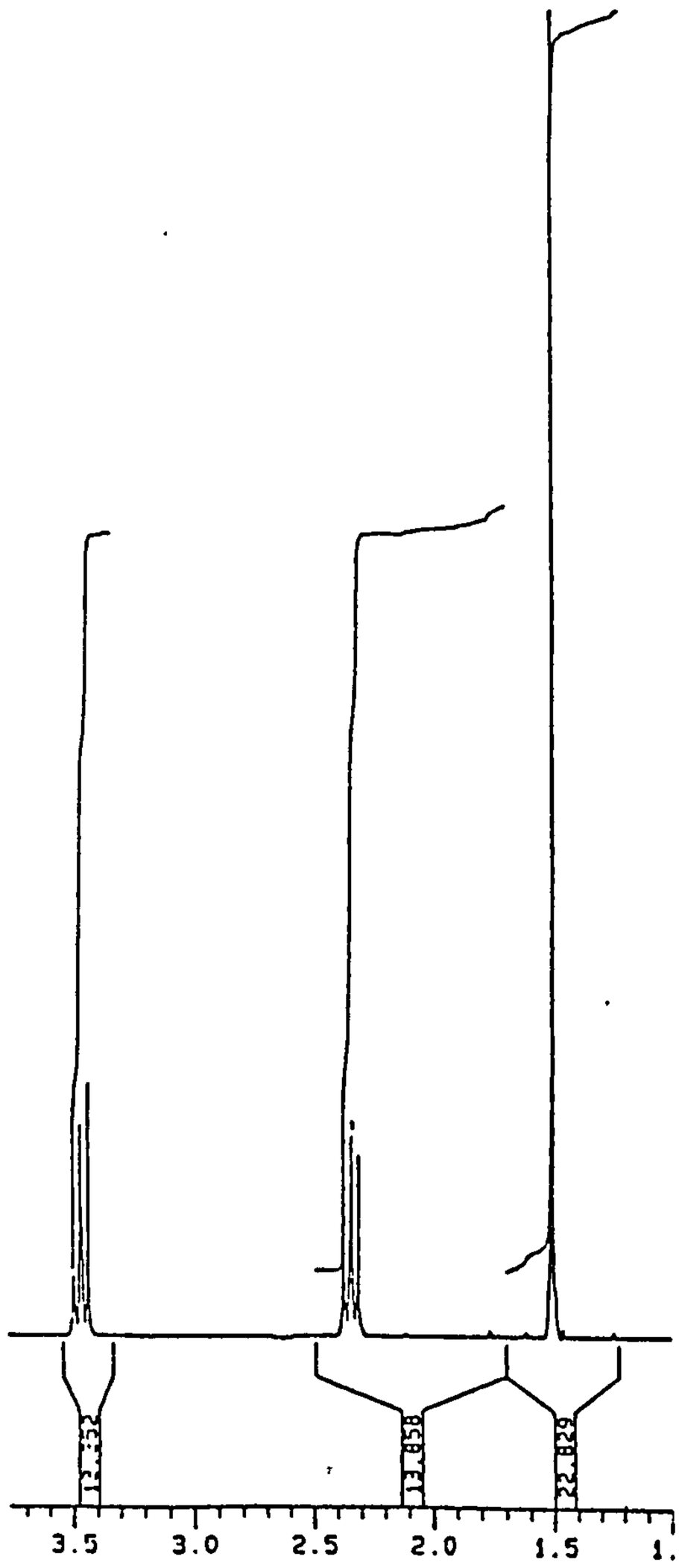


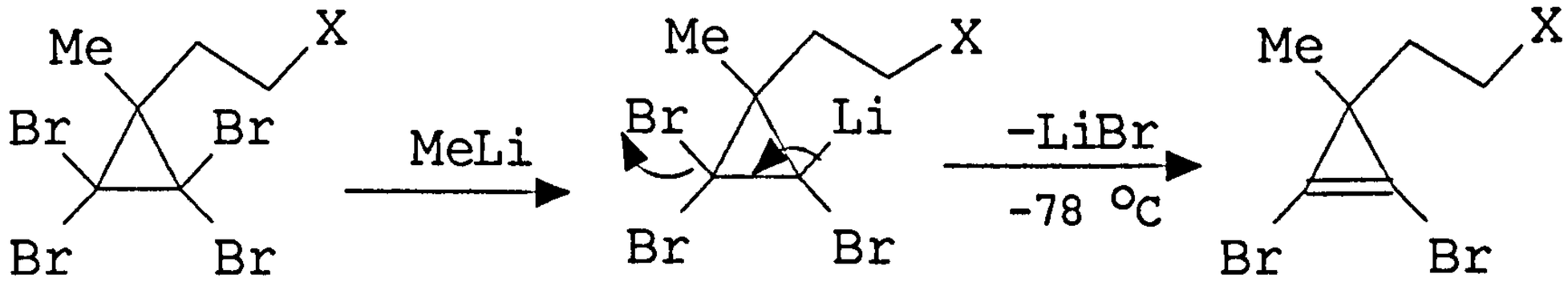
Figure 2. ^{1}H NMR spectrum of (123)

2.2.2. REACTION OF TRI-AND TETRAHALOCYCLO-PROPANES WITH METHYLLITHIUM

Treatment of the tetrabromocyclopropanes (**125**, X = Br, OMe) with one mol. equiv. of methyllithium at -78 °C, followed by quenching with water at -50 °C, led to 1,2-dibromocyclopropenes (**126**, X = Br, OMe) in 84 and 80 % yield respectively; the solvent was removed by rotary evaporation at 0 °C under water vacuum. The ^{1}H n.m.r spectrum for

(**126**, X = OMe) showed two triplets at δ 3.2 and 1.86 with a coupling constant of 6.4 Hz and two singlets resonating at δ 3.23 and 1.22 for the methoxy and methyl groups respectively. The ^{13}C spectrum for (**126**, X = OMe) showed six signals including the cyclopropene signals in the olefinic region at δ 108.5. The i.r spectrum showed a cyclopropene band at 1736 cm^{-1}.

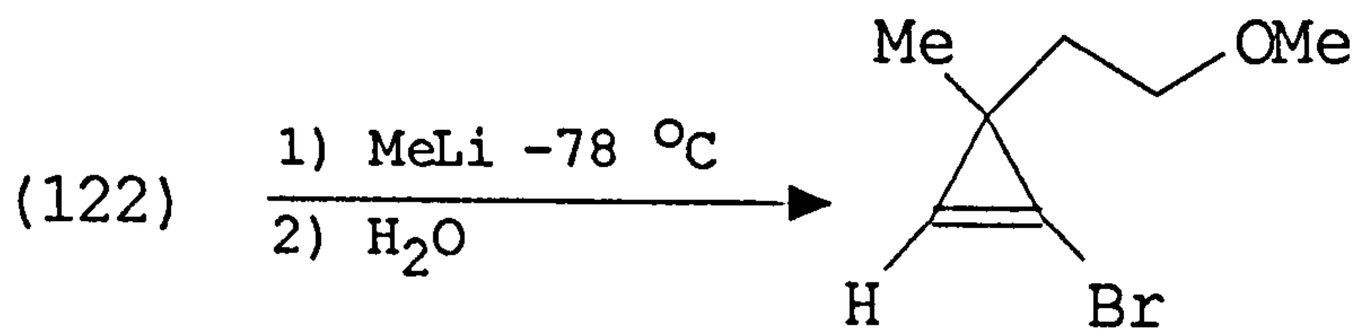
These products may arise by lithium-bromine exchange at one of the gem-dibromides followed by a 1,2-elimination of lithium bromide.



(125, X = Br, OMe) (126)

If the cyclopropenes (**126**, X = Br, OMe) were allowed to stand in chloroform at room temperature, a complex product was obtained in each case over a period of 3-5 h.

Similarly the cyclopropene (**127**) was isolated in 92 % yield, from the reaction of (**122**) with one mol.equiv of methyl lithium at -78 °C.

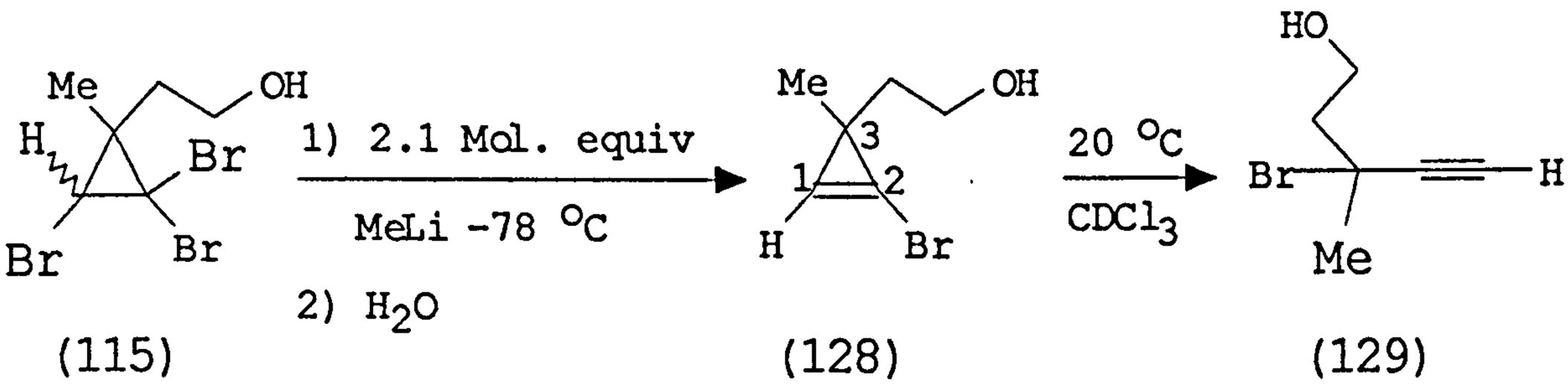


(127)

The ^{1}H n.m.r spectrum showed a low field singlet at δ 7.3 for the cyclopropene proton, two triplets at δ 3.18 and 1.76 with coupling constant 6.5 Hz, together with two singlets for methoxy and methyl groups, while seven peaks were observed in the ^{13}C n.m.r spectrum including two signals at δ 118.7 and 113.2 for the alkenes carbons.

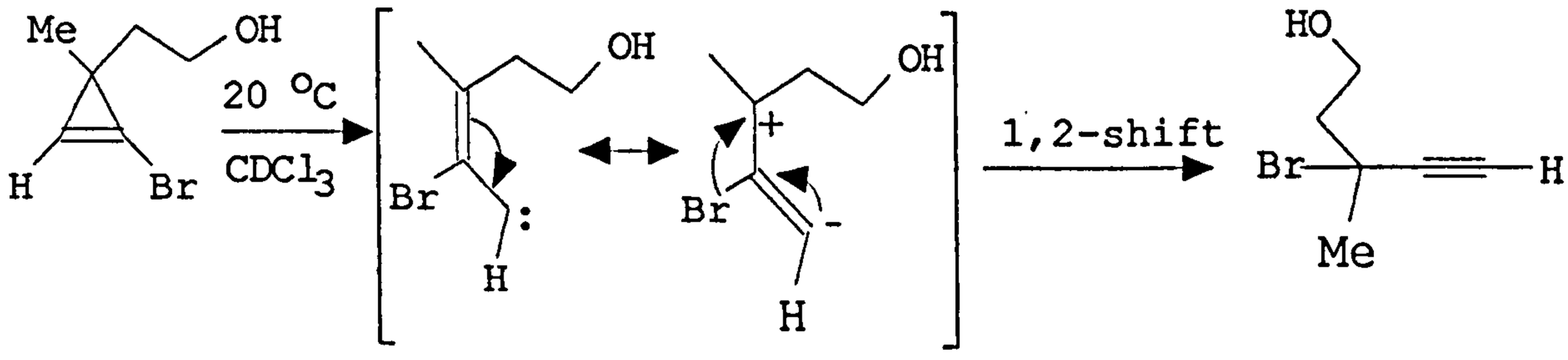
Moreover, on reaction of (**115**) with 2.1 mol. equiv. of methyllithium at -78 °C followed by quenching with water at -5 °C, the cyclopropene (**128**) was isolated in 76 % yield. The ^{1}H n.m.r spectrum was very similar to that for (**127**).

When the cyclopropene (**128**) was allowed to stand in $CDCl_3$ at 20 °C while monitoring the reaction mixture by n.m.r spectroscopy, a complete rearrangment was seen to have occurred over a period of 24 h to produce the bromoalkyne (**129**) in 83 % yield.



(115) (128) (129)

This compound apparently arises by cleavage of the C_2-C_3 cyclopropene single bond giving the vinyl carbene (**130**), followed by 1,2-shift of the bromide from the canonical struture (**131**), although the carbene could not be trapped by addition of an added alkene.

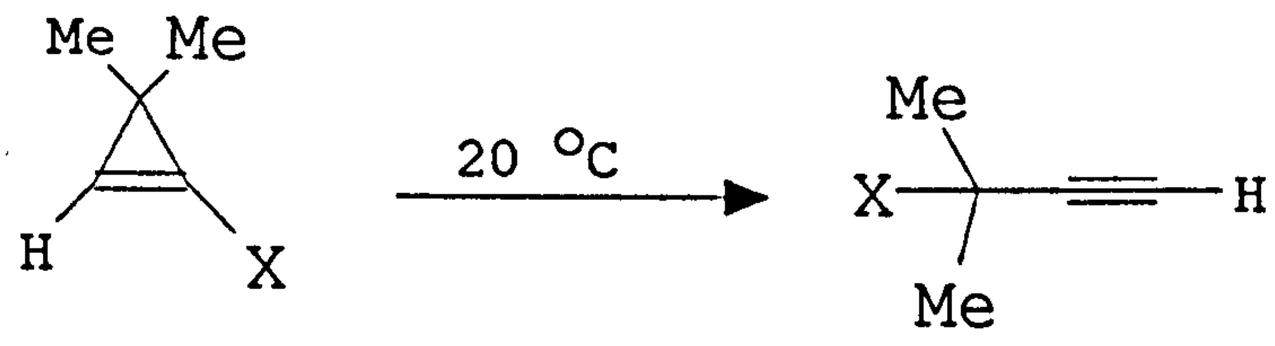


(128) (130) (131) (129)

The i.r spectrum of (**129**) contained a sharp band at 2112 cm^{-1} assigned to the alkyne, while the ^{1}H n.m.r spectrum showed a singlet at δ 2.8 integrating to one proton assigned to the acetylenic hydrogen, a double triplet for methylene group next to the hydroxyl group with coupling constants of 1.7 and 6.7 Hz, together with a multiplet at δ 2.3 integrating for two

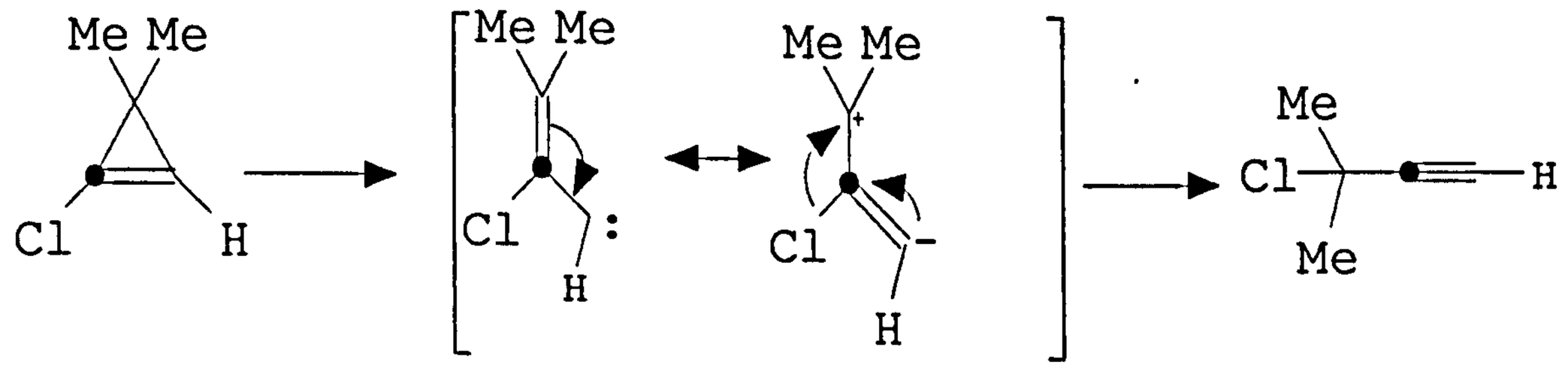
protons and a singlet for the methyl group. The ^{13}C showed six signals including two in the acetylenic region at δ 86 and 74.8 ppm.

It is known that the cyclopropenes (**132**, X = Cl, Br) have also been found to be unstable at ambient temperature, rearranging readily as the neat liquid or in solution, giving the halogenated alkyne (**133**, X = Cl, Br).[77]



(132, X = Cl, Br) (133, X = Cl, Br)

The product also apparently arose through cleavage bond of the C_2-C_3 cyclopropene single bond giving the vinylcarbene (**134**) followed by migration of the chloride anion from the canonical structure (**135**) resulting in the formation of (**133**); labelling study indicated that C_1 of the cyclopropene became C_2 of the alkyne.[77]

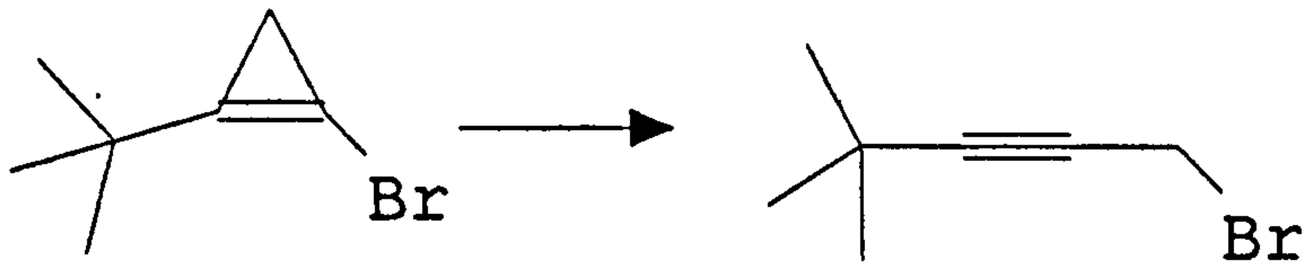


(132, X = Cl, Br) (134) (135) (133, X = Cl, Br)

• = ^{12}C

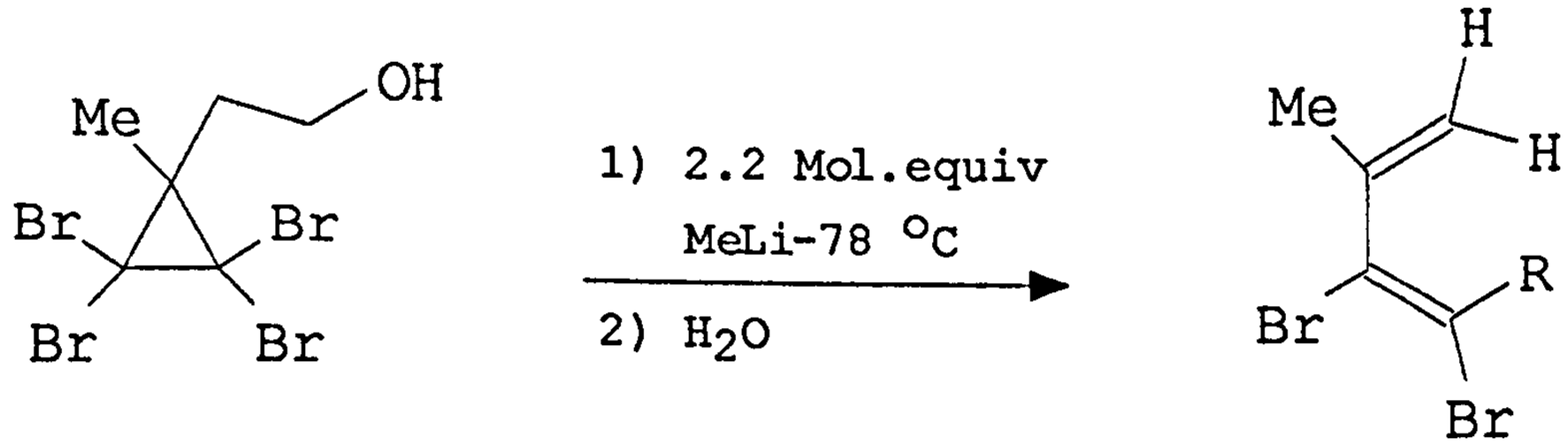
The bromide (**136**) undergoes a similar rearrangment. The reaction occurs more slowly with distilled than with crude cyclopropene; this may be caused by the presence of traces of lithium

bromide in the solution and indeed addition of this increased the reaction rate. This suggests that intermolecular rather than intramolecular halide transfer is important.[78]



(136)

In contrast, when tetrabromocyclopropane (**119**) was treated with 2.2 mol. equiv. of methyllithium at -78 °C, followed by quenching with water at that temperature, no cyclopropene was isolated, and instead the dibromodiene (**137**, R = H) was obtained in 38 % yield.

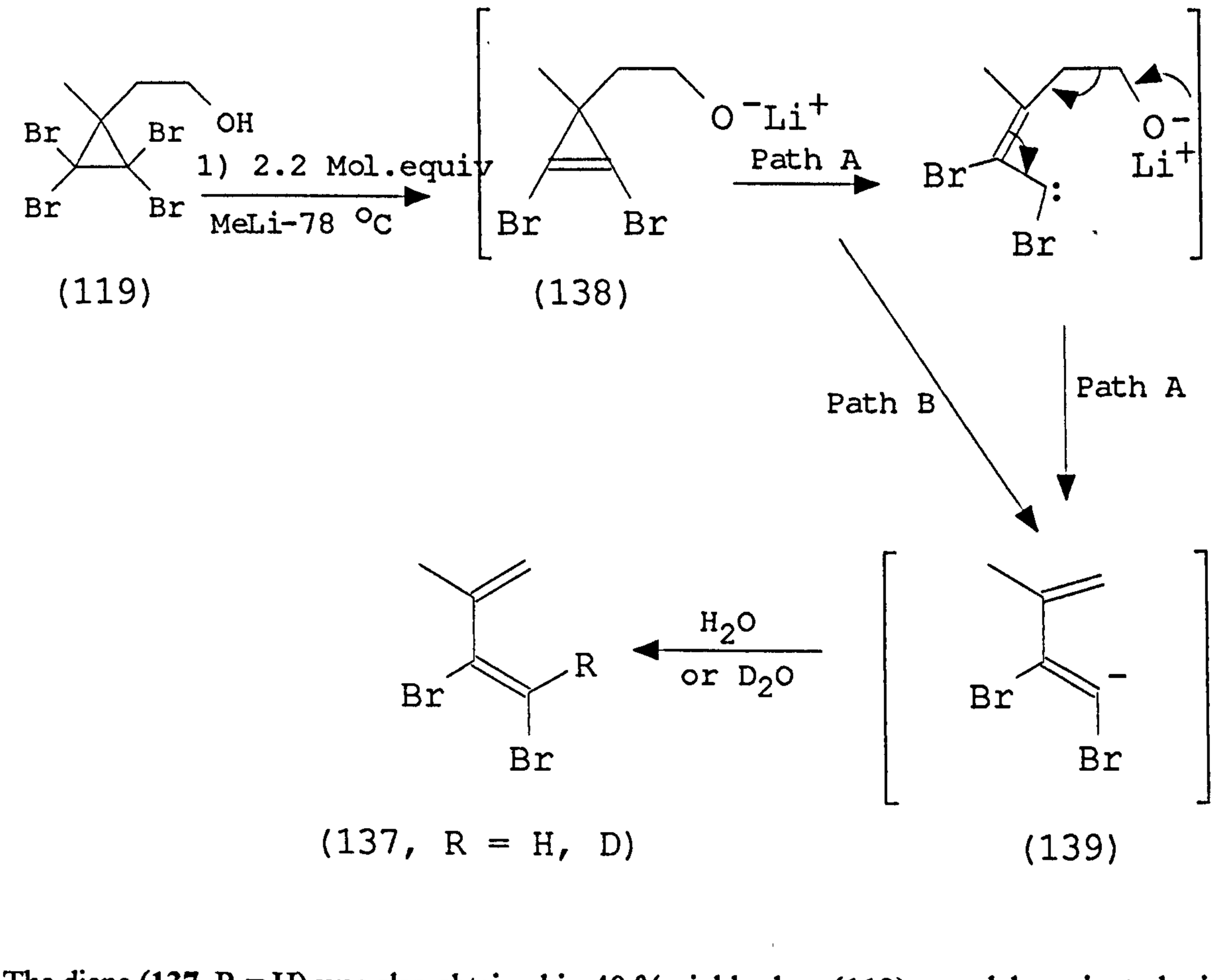


(119) (137, R = H, D)

The ^{1}H n.m.r spectrum for the diene (**137**, R = H) showed a singlet at δ 6.9 integrating for one proton, two broad singlets at δ 5.5 and 5.2 for the protons of the methylene group and a singlet for the olefinic methyl at δ 2.0. The ^{13}C spectrum contained the expected five signals, including four in the alkene region at δ 140, 132, 120 and 109.7.[79] The data was identical to that for an authentic sample.[80] If the reaction was worked up by addition of D_2O, the product was the deuterated diene (**137**, R = D) with an incorporation of *ca.* 75 %. The anion (**139**) could not, however, be trapped by addition of carbon dioxide or trimethylsilyl

chloride. The reason for the formation of (**137**, R = H, D) is not yet clear, but it seemed to be likely that the two equivalents of methyllithium are required to remove the alcoholic hydrogen and eliminate one equivalent of bromine leading to (**138**). Ring opening of this could lead to stabilized vinylic anion (path A) to give (**139**). Alternatively losing the formaldehyde molecule might be concerted with ring opening (path B) to give (**139**).

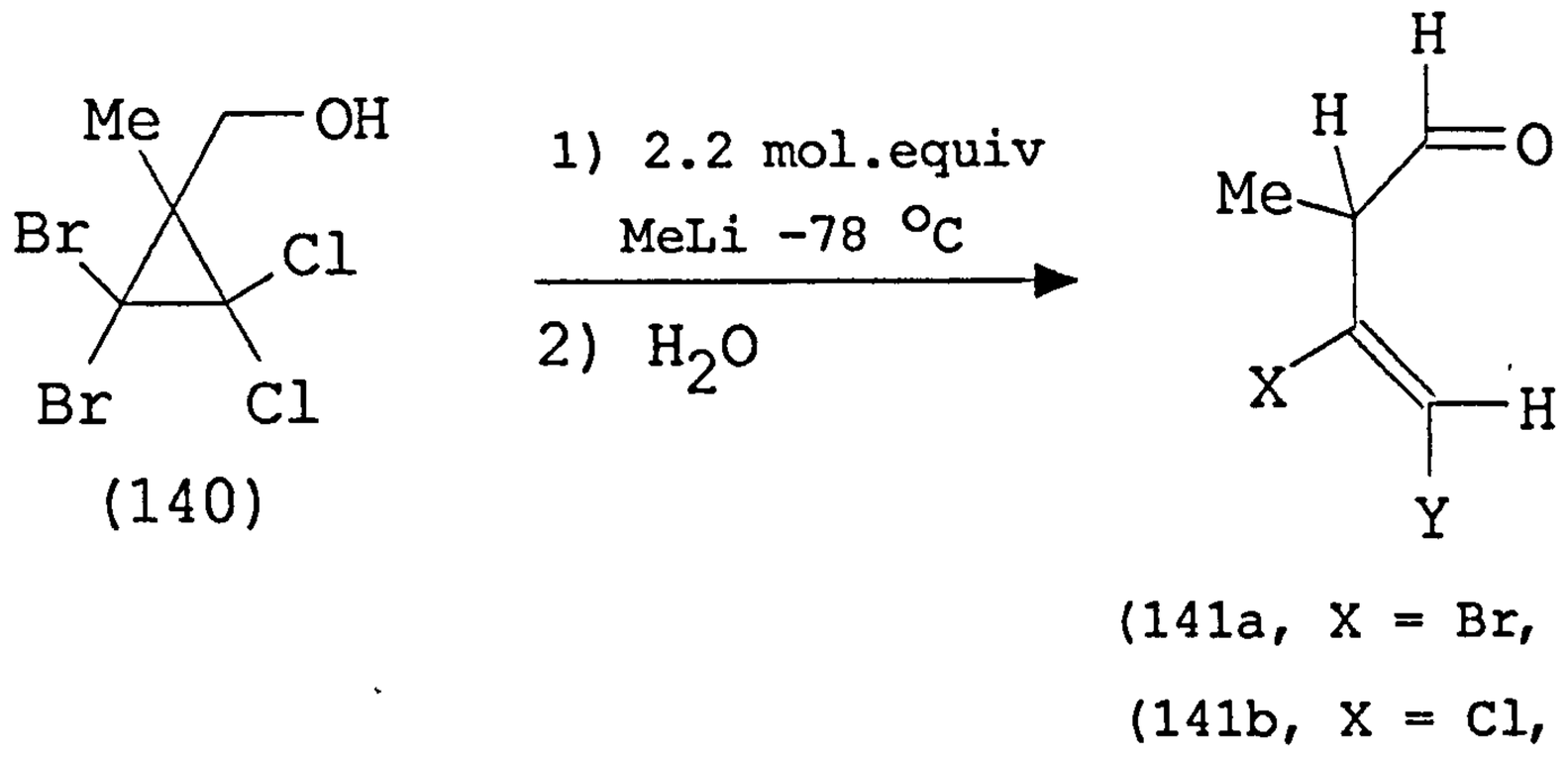
In either case it is suprising that the anion (**139**) did not eliminate bromide to give an alkyne rather than remaining in solution to be protonated.



The diene (**137**, R = H) was also obtained in 40 % yield when (**119**) was debrominated with diethyl phosphite and triethylamine.[79]

Recently, Baird and J. R. Al-Dulayymi found that, when the cyclopropane (**140**) was allowed to react with 2.2 mol. equiv. of methyllithium at -78 °C, immediate work up at 0-20 °C led to the bromochloro-aldehyde (**141**) in a reaction involving an anion promoted hydride

shift.[81]

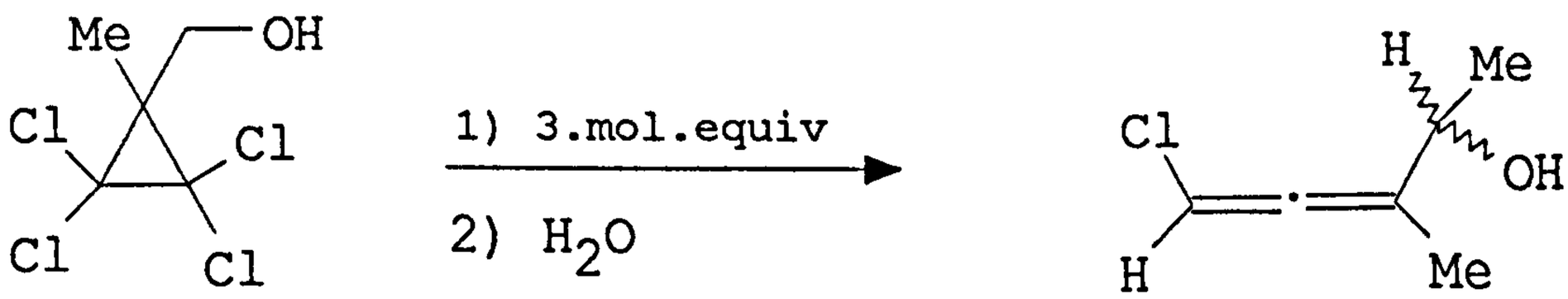


(140)

(141a, X = Br, Y = Cl)

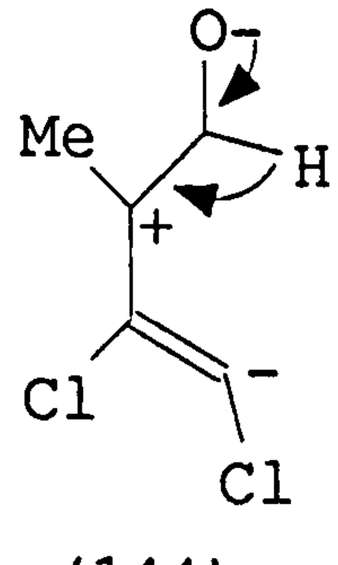
(141b, X = Cl, Y = Br)

Moreover, treatment of the alcohol (**142**) with three mol. equivalents of methyllithium led directly to the allene (**143**) as a mixture of diastereoisomers; no intermediate cyclopropene was isolated.[81] The rearrangment may also involve an anion-promoted hydride shift related to the above fragmentation.



(142)

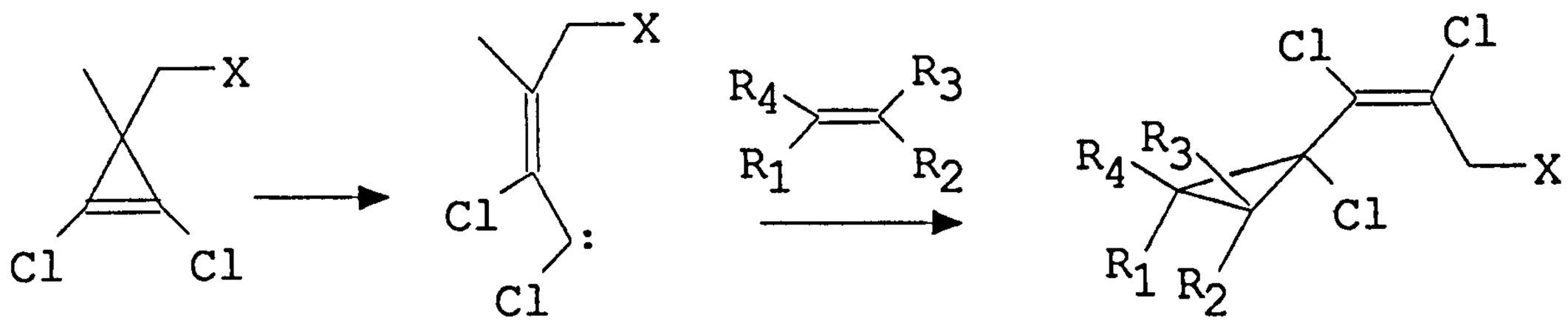
(143)



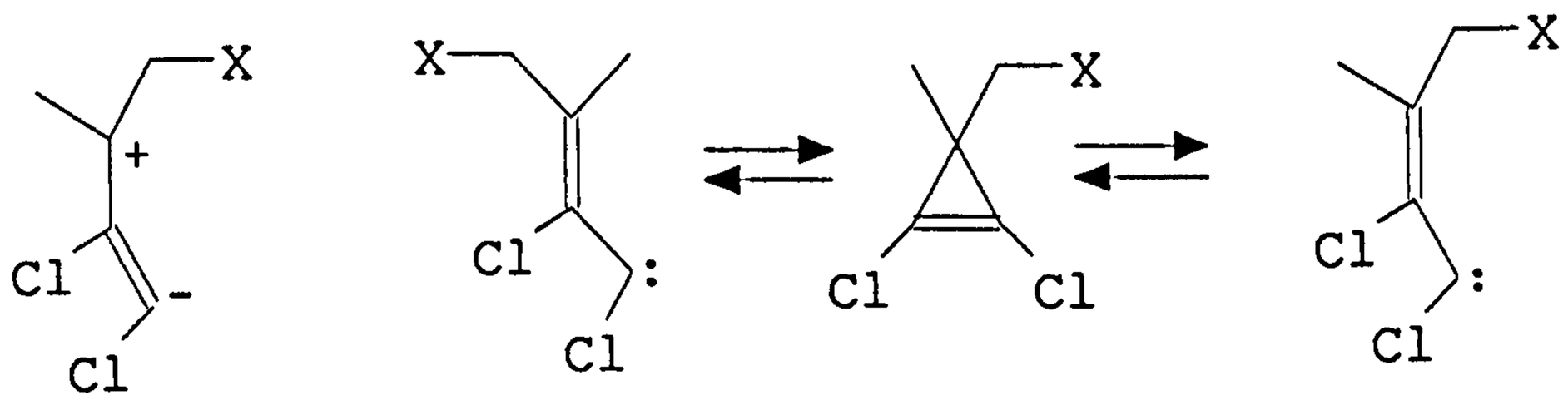
(144)

The ring opening of the dichlorides (**103**, X = Cl, OMe, Ph, $OC(Me_2)OMe$) has been shown to lead to the trapping of single steroisomers of the vinylcarbenes (**104**) by added

alkenes.[34,35,72] It seems unlikely that only one carbene would be trapped by alkenes if both were present in an equilibrium.



(103, X = Cl, OMe, Ph, O(Me)$_2$OMe) (105)

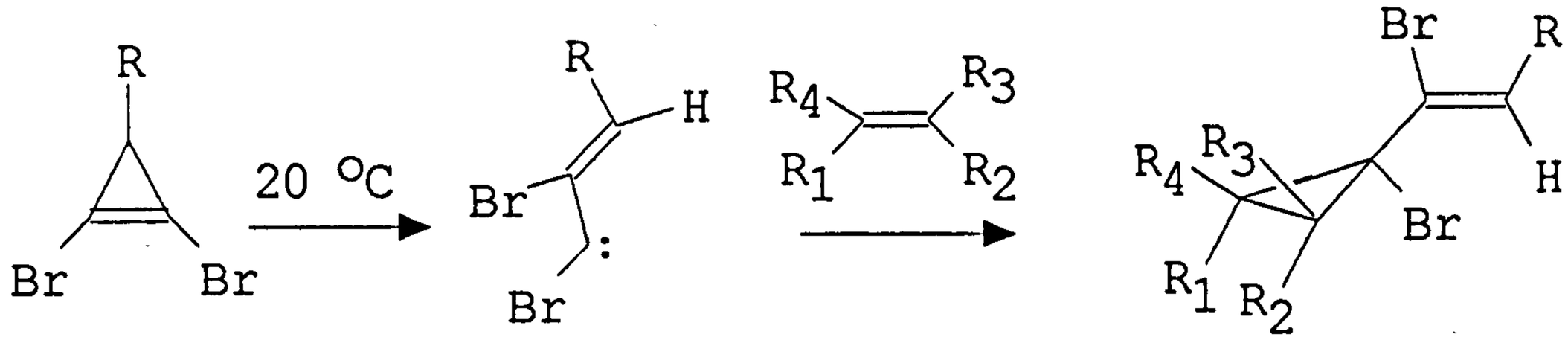


(146) (145) (103) (104)

The origin of this stereocontrol has been explained in terms of an interaction between the developing carbene centre and an antibonding orbital of the C-X bond. [82]

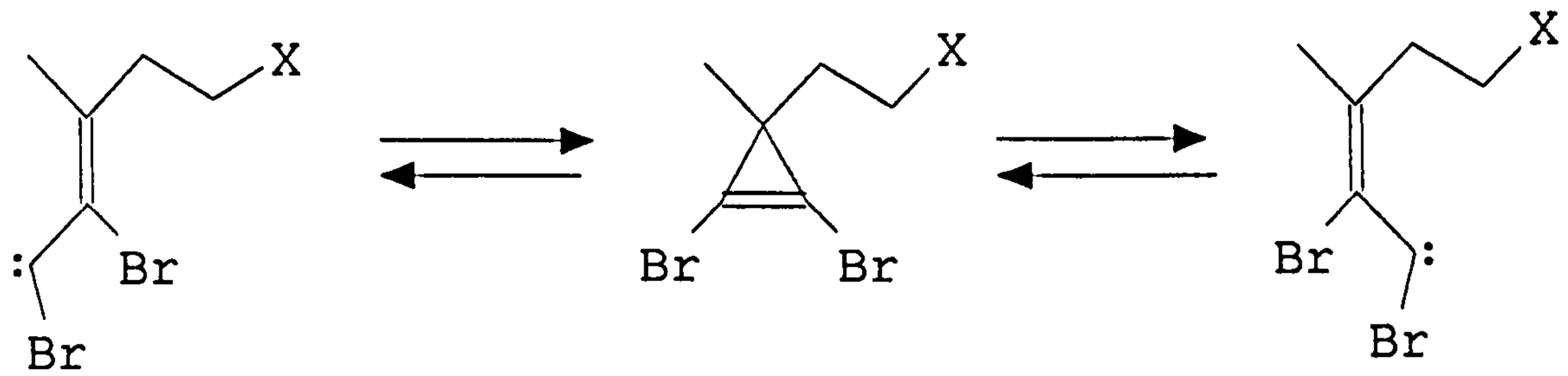
In the case of the cyclopropene (**103**, X = Ar), the rate of the reaction with 2,3-dimethylbut-2-ene increased in the presence of electron releasing group in the para- position of the benzene ring.[83] This may result from stabilization of the dipolar form of the carbene (**146**).

The mono-alkyl 1,2-dibromocyclopropenes (**147**) also undergo ring-opening at room temperature to the carbenes (**148**) which are trapped by alkenes. In these cases the alkyl subsitutent are *trans* to the carbene centre[84] and the selectivity can be explained in steric terms .[82]



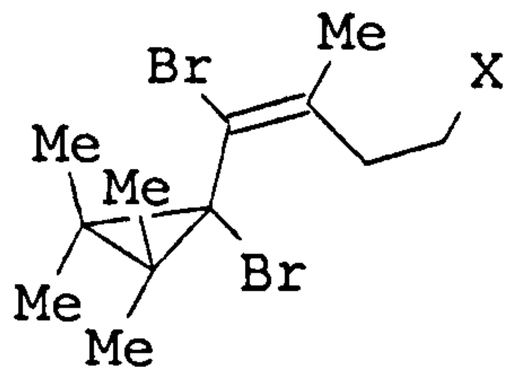
(147) (148)

It was of interest therefore to determine whether the ring opening of cyclopropenes (**106**, X = OMe, Br) would be controlled by the presence of the more distant X-group and lead to a preferred stereoisomer of the carbenes (**107**) or (**108**).

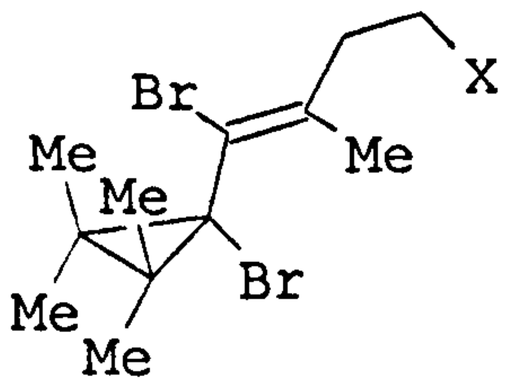


(108, X = OMe, Br) (106, X = OMe, Br) (107, X = OMe, Br)

When the cyclopropene (**106**, X = Br) was allowed to undergo ring opening in ether solution at 20 °C in the presence of 2,3-dimethylbut-2-ene for 3 hr complete reaction occurred and resulted in the formation of two isomers of vinylcyclopropanes (**149**, X = Br) and (**150**, X = Br) in ratio 2:1. It was uncertain which was the major isomer.



(149, X = OMe, Br)



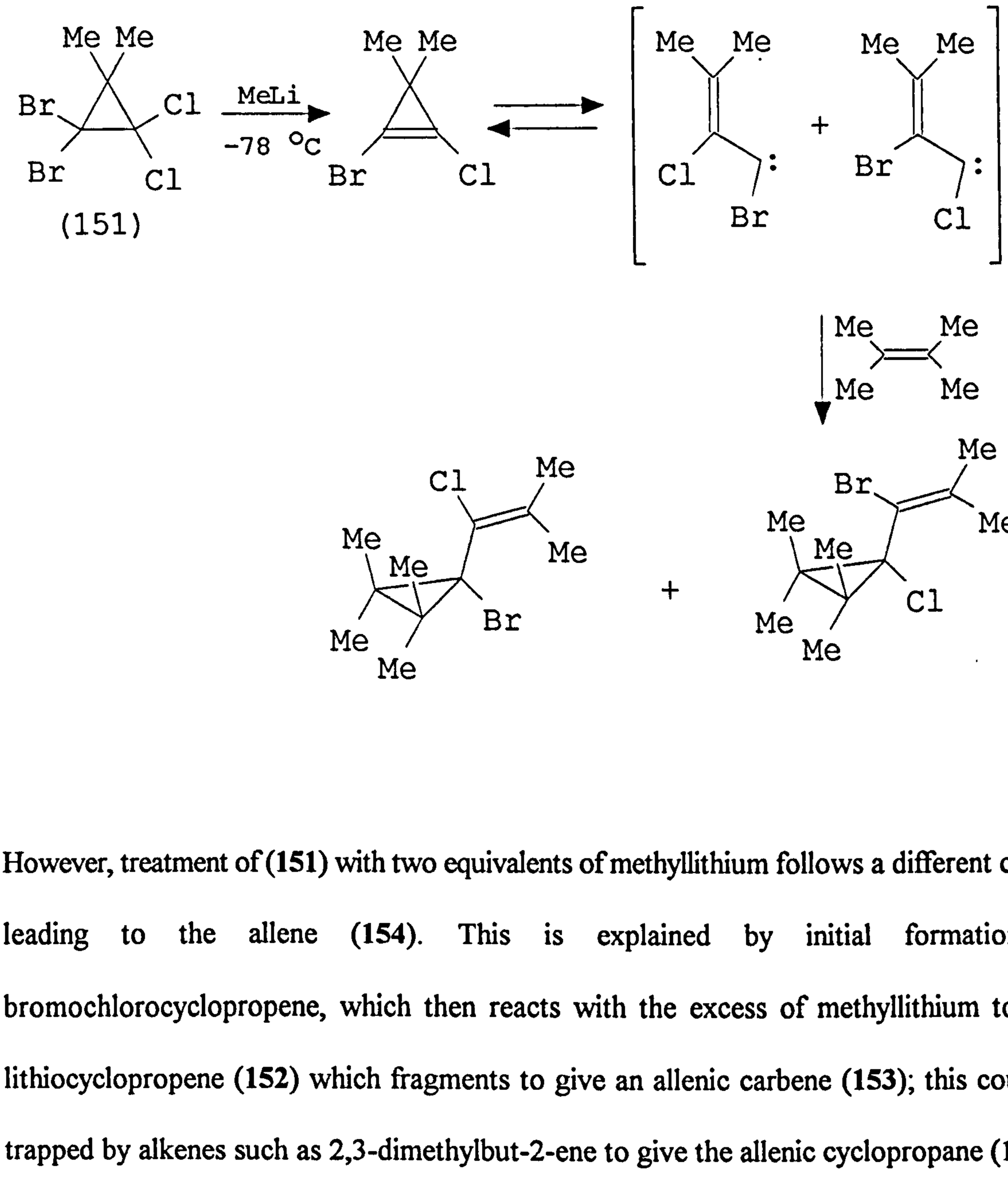
(150, X = OMe, Br)

The two isomers were separated by column chromatography on silica eluting with petroleum ether. The major isomer showed four methyl singlets at δ 1.13, 1.19, 1.25 and 1.38, (the four ring methyl group are not equivalent because the preferred conformation of such vinyl cyclopropanes has the alkene on C_3 twisted so that it is almost parallel to the C_1-C_2 bond and rotation is slow on the n.m.r time scale),[84a] a multiplet at δ 3.55 for the methylene next to the bromine, a doublet of doublets of doublets with coupling constants 11.3, 5.8 and 1.8 Hz at δ 2.95, and a double triplet with coupling constant of 5.8 and 11.3 Hz, at δ 2.6 for the diastereotopic protons of the methylene group adjacent the double bond, together with a singlet at δ 1.9 for olefinic methyl. The ^{13}C spectrum contained twelve signals including two in the alkene region. The minor isomer showed very a similar ^1H n.m.r spectrum to that for major isomer.

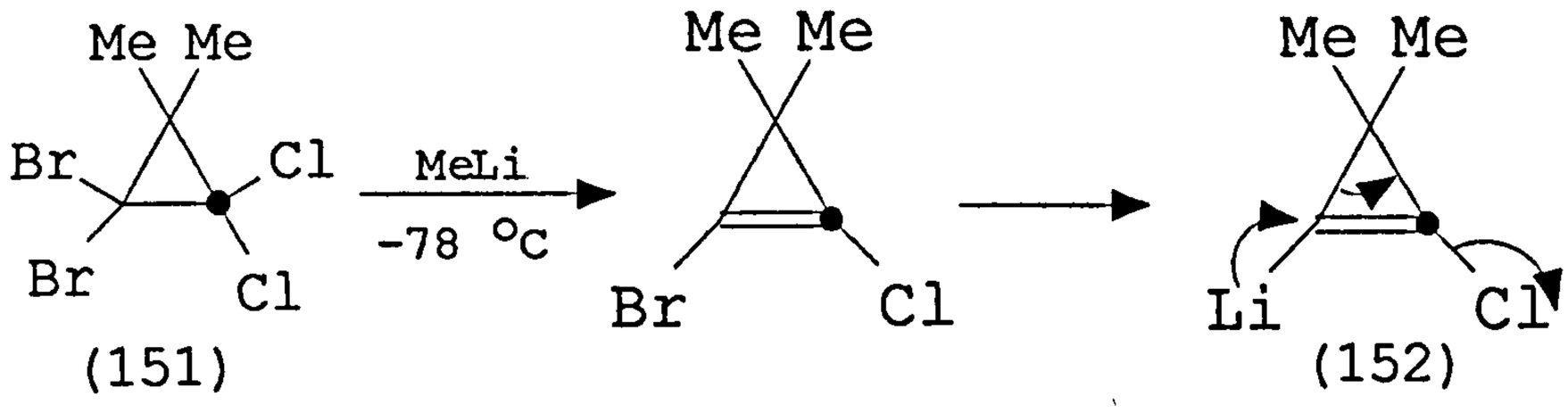
In the same way (**106**, X = OMe) reacted with 2,3-dimethylbut-2-ene to give a mixture of two isomers of vinyl cyclopropanes (**149**, X = OMe) and (**150**, X= OMe) in ratio 4:3. The ^1H n.m.r spectrum of the major isomer showed five methyl signals including the olefinic methyl, again in keeping with a preferred twisted conformation, and rotation about the exocyclic carbon-carbon bond which is slow on the n.m.r time scale.[84a]

The products may be explained in terms of ring-opening of the cyclopropene (**106**, X = Br) to the two isomeric vinylcarbenes (**107**) and (**108**) and trapping of these by the alkene. There was little stereocontrol in the ring opening of the cyclopropene.

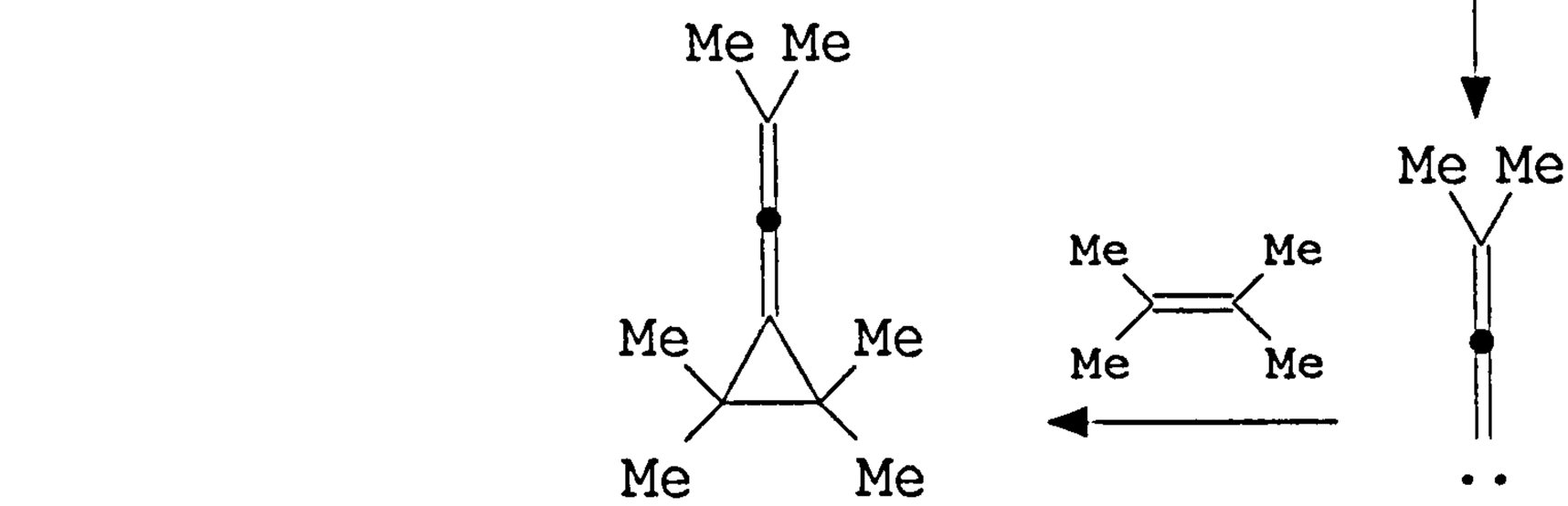
It is known that the reaction of 1,1-dibromo-2,2-dichlorocyclopropane (**151**) with one mol. equiv. of methyllithium at -78 °C leads to 1-bromo-2-chlorocyclopropene which undergoes ring opening to the isomeric vinylcarbenes which are trapped by alkenes such 2,3-dimethylbut-2-ene to give a mixture of cyclopropanes.[85]



However, treatment of (**151**) with two equivalents of methyllithium follows a different course leading to the allene (**154**). This is explained by initial formation of bromochlorocyclopropene, which then reacts with the excess of methyllithium to give lithiocyclopropene (**152**) which fragments to give an allenic carbene (**153**); this could be trapped by alkenes such as 2,3-dimethylbut-2-ene to give the allenic cyclopropane (**154**).[85] The mechanism of the formation of the allenic carbene has been examined by labelling studies, which show that C_2 of the cyclopropene becomes C_2 of the allene (**154**), consistent with lithium-bromine exchange followed by elimination as in the mechanism shown in (**152**).[85]



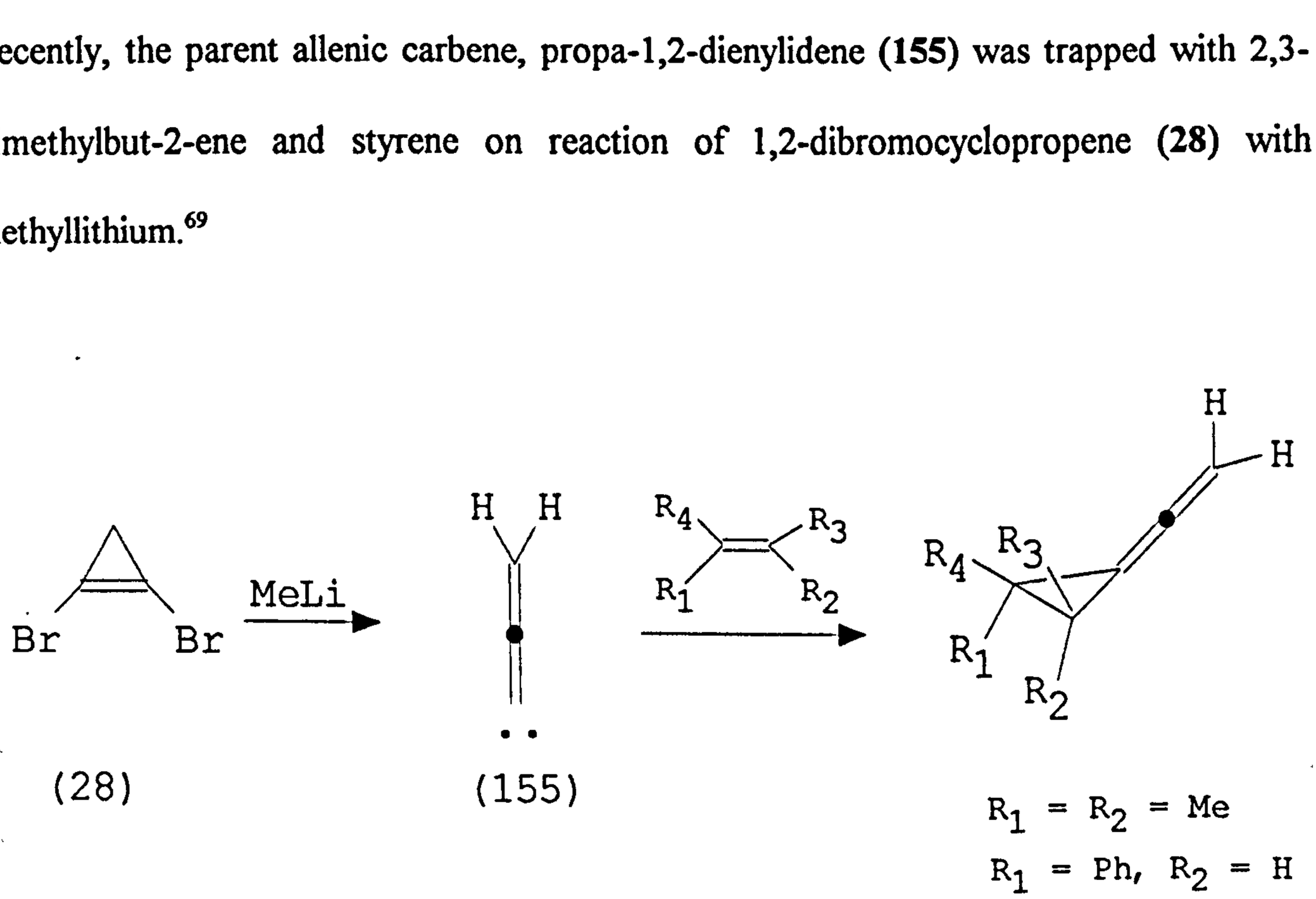
(151) (152)



• = ^{12}C

(154) (153)

Recently, the parent allenic carbene, propa-1,2-dienylidene (**155**) was trapped with 2,3-dimethylbut-2-ene and styrene on reaction of 1,2-dibromocyclopropene (**28**) with methyllithium.[69]

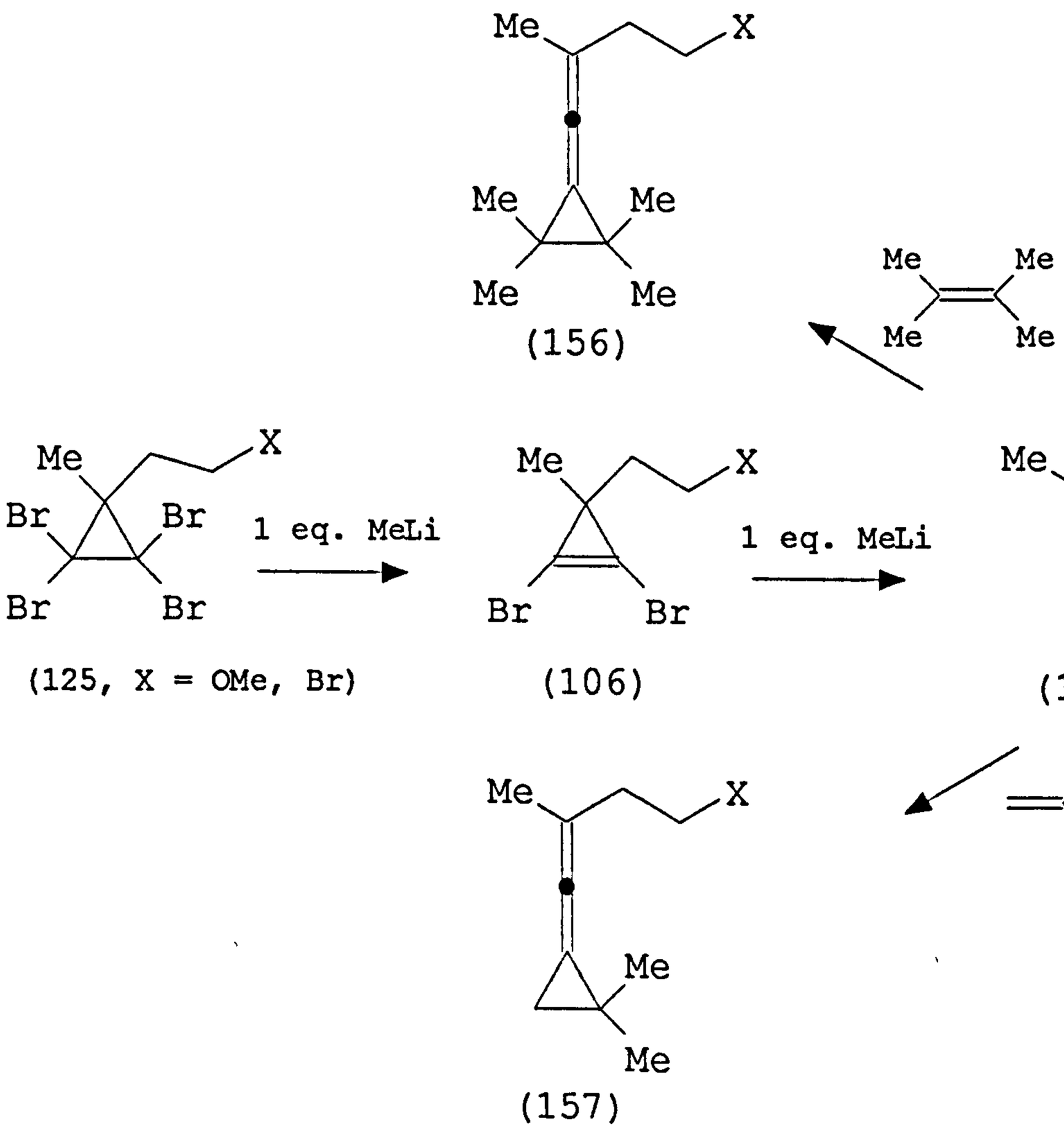


(28) (155)

$R_1 = R_2 = Me$

$R_1 = Ph,\ R_2 = H$

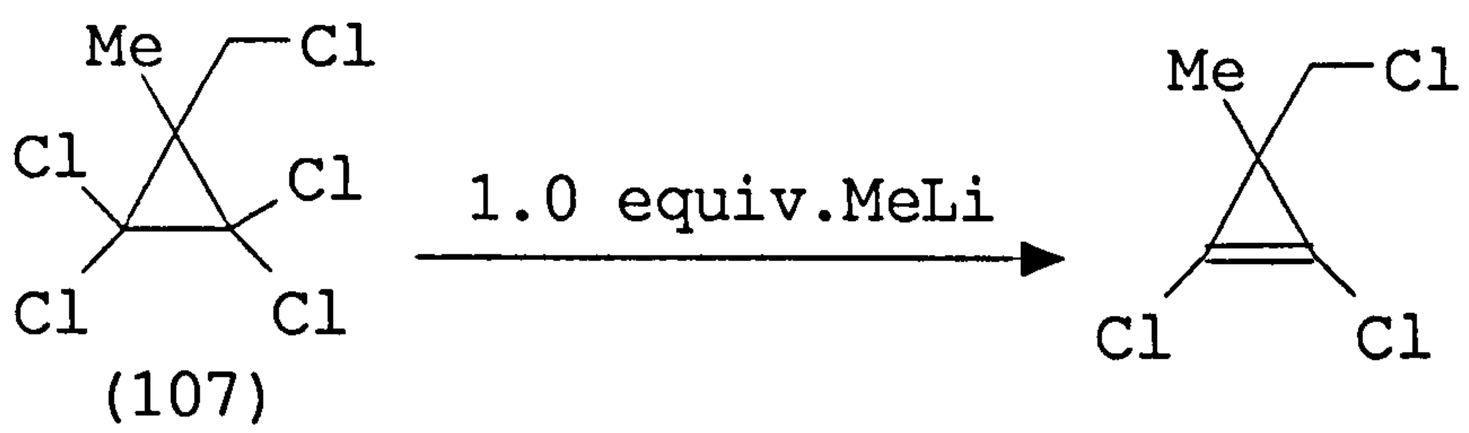
Treatment of (**125**, X = OMe, Br) with two mol. equiv. of methyllithium at -78 °C in the presence of 2,3-dimethylbut-2-ene or isobutene, followed by quenching with water gave in each case the allene (**156**) and (**157**) respectively. This occurs by lithium-bromine exchange followed by loss of lithium bromide to produce the cyclopropenes (**106**), which react with the excess of methyllithium to give the allenic carbenes (**158**) which add to the alkenes.



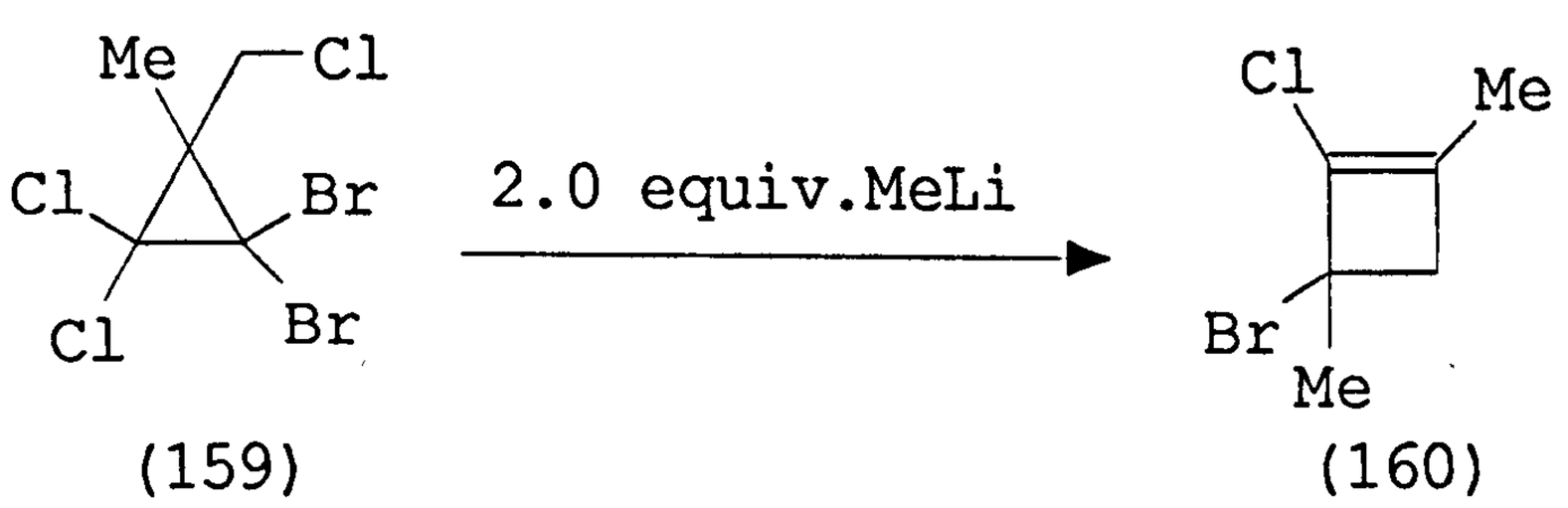
The cyclopropane (**156**, X = Br) showed the characteristic C=C=C stretching absorption at 2003 cm^{-1} in the i.r and the ^1H n.m.r spectrum showed two triplets with coupling constant of 7.4 Hz at δ 3.4 and 2.5, together with a singlet for olefinic methyl and a singlet for the

cyclopropane methyl groups; the ^{13}C n.m.r spectrum showed ten signals, including two in the olefinic region and a characteristic allenic carbon singlet at δ182.6.

It is known that the reaction of pentachlorocyclopropane (**107**) with one equivalent of methyllithium at 0 °C leads to a 1,2-dichlorocyclopropene through 1,2-elimination.[35] However, treatment of (**159**) with two equivalents of methyllithium at -78 °C gave the cyclobutene (**160**) via 1,3-elimination.[86]

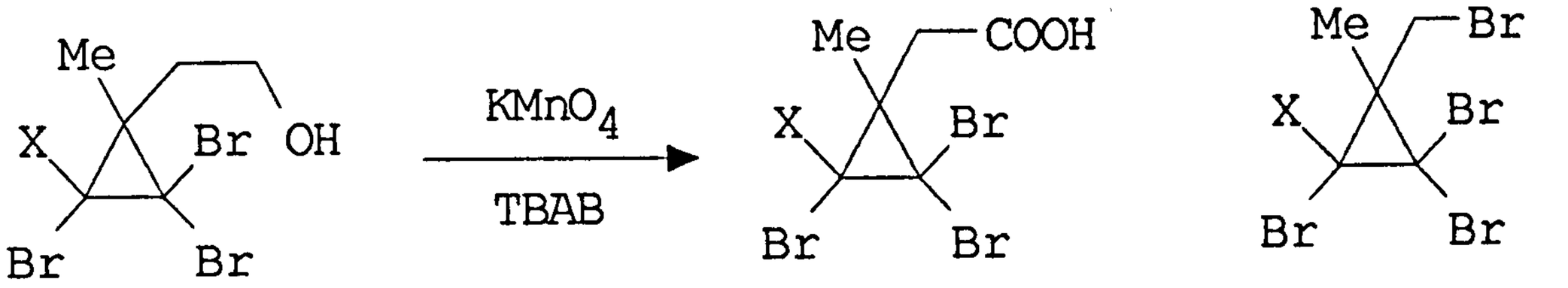


(107)



(159) (160)

In order to compare the reactivity of (**107**) and (**159**) with that of the corresponding penta- or tetrabromocyclopropanes (**161**, X = H, Br) in reaction with methyllithium, the preparation of (**161**) was examined. The cyclopropanes (**151**, X = H) and (**119**, X = Br) were oxidised to (**162**, X = H) and (**163**, X = Br) in 60 and 87 % yield respectively using potassium permanganeat under PTC.[87]



(115, X = H)

(119, X = Br)

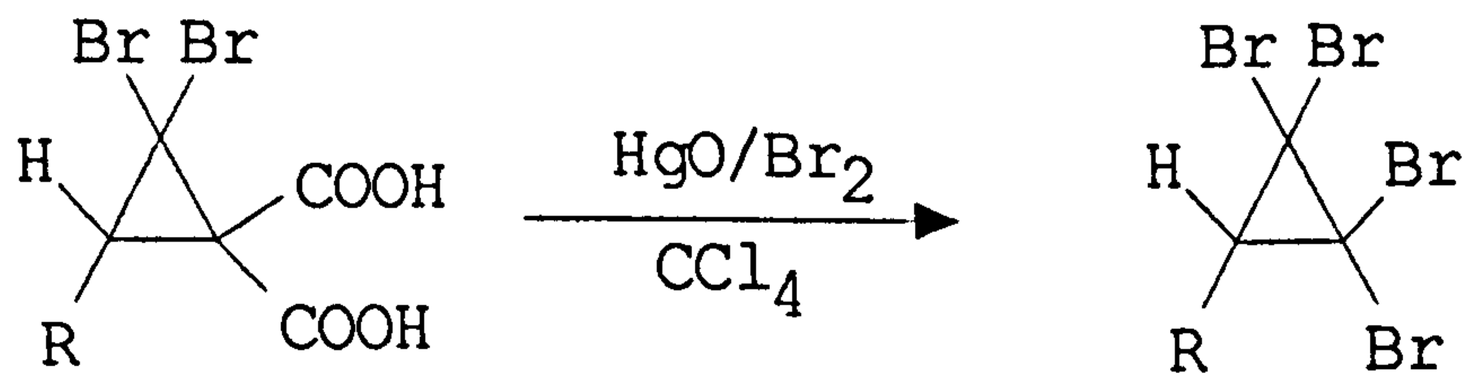
(162, X = H)

(163, X = Br)

(161, X = H, Br)

The i.r spectrum of (**163,** X = Br) contained a very broad band at 3021 cm^{-1} assigned to the O-H stretching of the carboxyl group and a sharp band at 1708 cm^{-1} for carbonyl group. The ^{1}H n.m.r spectrum showed only two singlets at δ 1.7 (3H) and δ 3.0 (2H) in ratio 3:2, while the ^{13}C nmr showed the expected six signals including one in the carbonyl region at δ 176, together with five signals in the saturated region at δ 47, 43, 37, 23, and 20.

The conversion of a carboxylic acid into a halide with one less carbon known historically as the Hunsdiecker Reaction,[88] involves converting the carboxylic group into the anhydrous silver salt which is later treated with bromine in an inert solvent like carbon tetrachloride.[88] This reaction has the practical disadvantage that the silver salt must be relatively pure and must be scrupulously dry in order to obtain a good yield. A modification of this procedure,[89] treatment of a slurry of excess red mercuric oxide in a refluxing solution of an aliphatic carboxylic acid in CCl_4 with one equivalent of bromine in the dark, also leads to the corresponding alkyl bromide. In this way, treatment of dicarboxylic acid (**164**) with HgO and Br_2 in CCl_4 gave in excellent yield the tetrabromocyclopropanes (**165**).[84a]

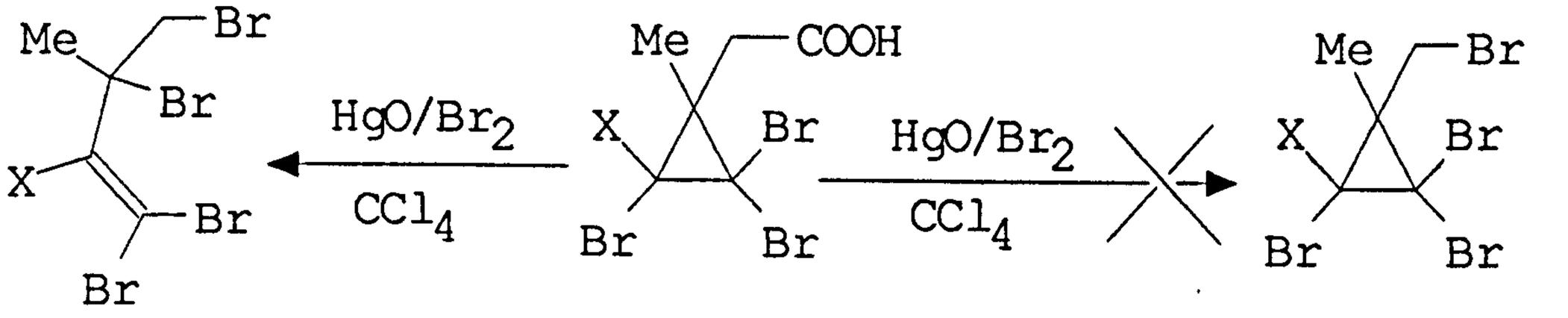


(164)

(165)

R = Me, butyl, isopropyl

It was anticipated that a Hunsdiecker reaction on the acids (**163**, X = Br) and (**162**, X = H) with red mercuric oxide and bromine in carbon tetrachloride would lead to (**161**, X = Br, H). Instead it led to the pentabromide (**166**, X = Br) and tetrabromide (**166**, X = H) respectively.

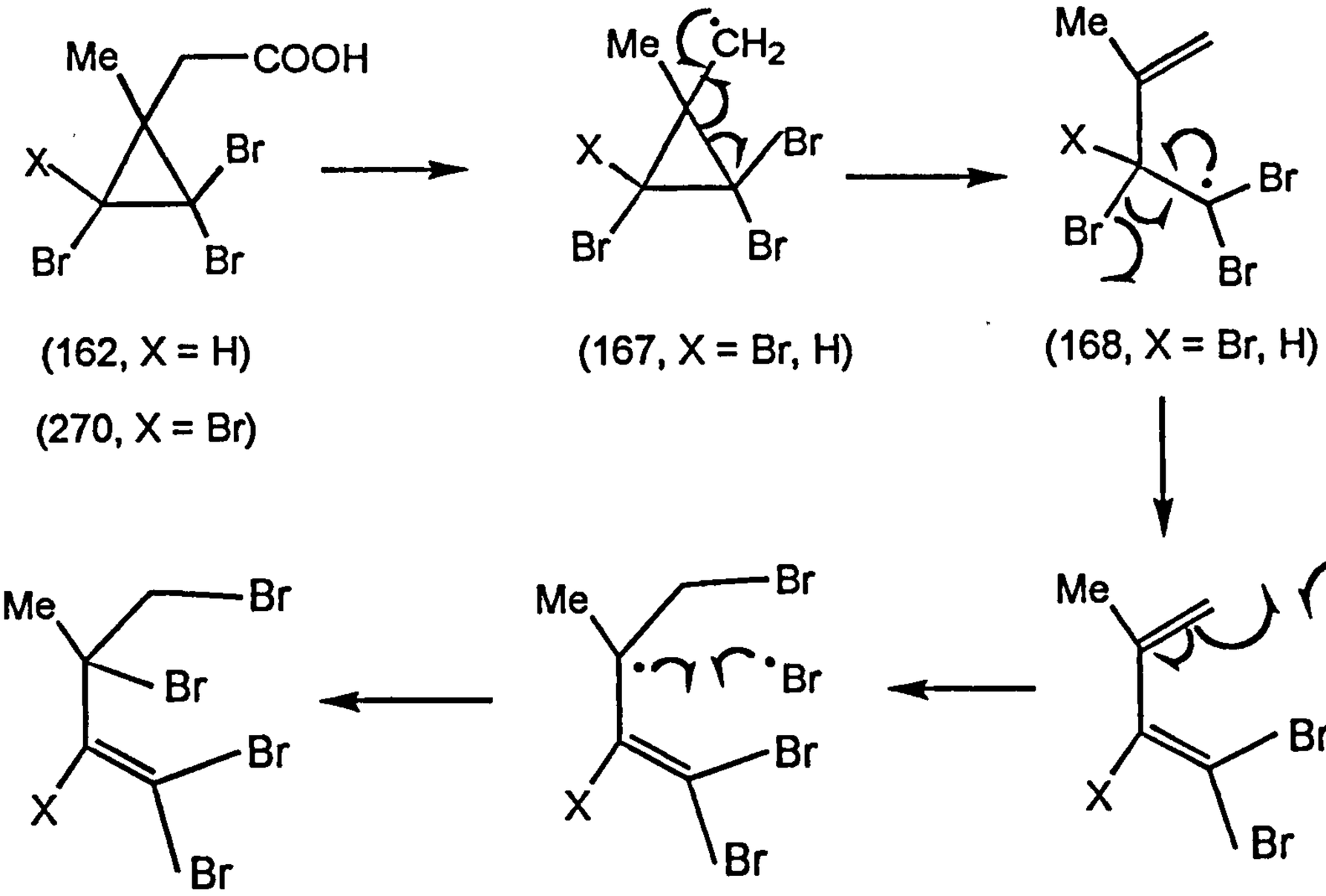


(166, X = Br, H) (162, X = H) (161, X = Br, H)

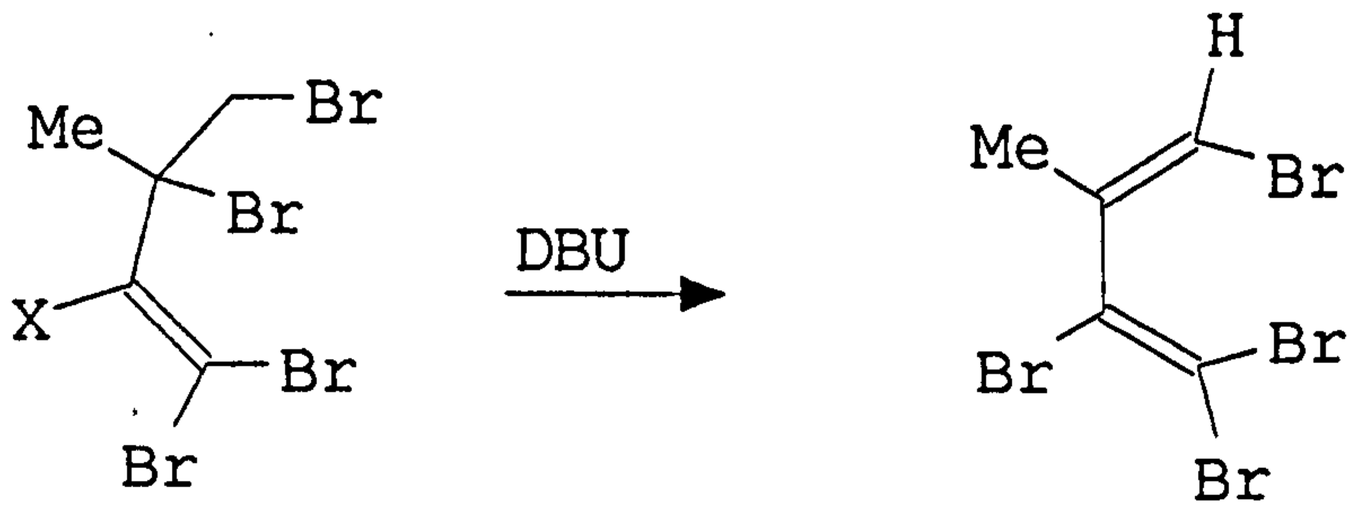
(163, X = Br, H)

The ^{1}H n.m.r spectrum of (**166**, X = Br) showed a doublet of quartets at δ 4.87 with coupling constants of 1.1 and 10.3 Hz, which integrated to one hydrogen, a doublet at δ 3.7 (1H) with coupling constant 10.3 Hz and a doublet at δ 2.4 (3H). The ^{13}C nmr spectrum contained five signals including two in the olefinic region.

The products (**166**, X = Br, H) may be derived by generation of the corresponding cyclopropyl methyl radical (**167**, X = Br, H) by decarboxylation, and fragmentation of this to (**168**, X = Br, H)[90], loss of a bromine atom from (**168**, X = Br, H) to give (**169**, X = Br, H), followed by the addition of a bromine radical to the disubstituted alkene.



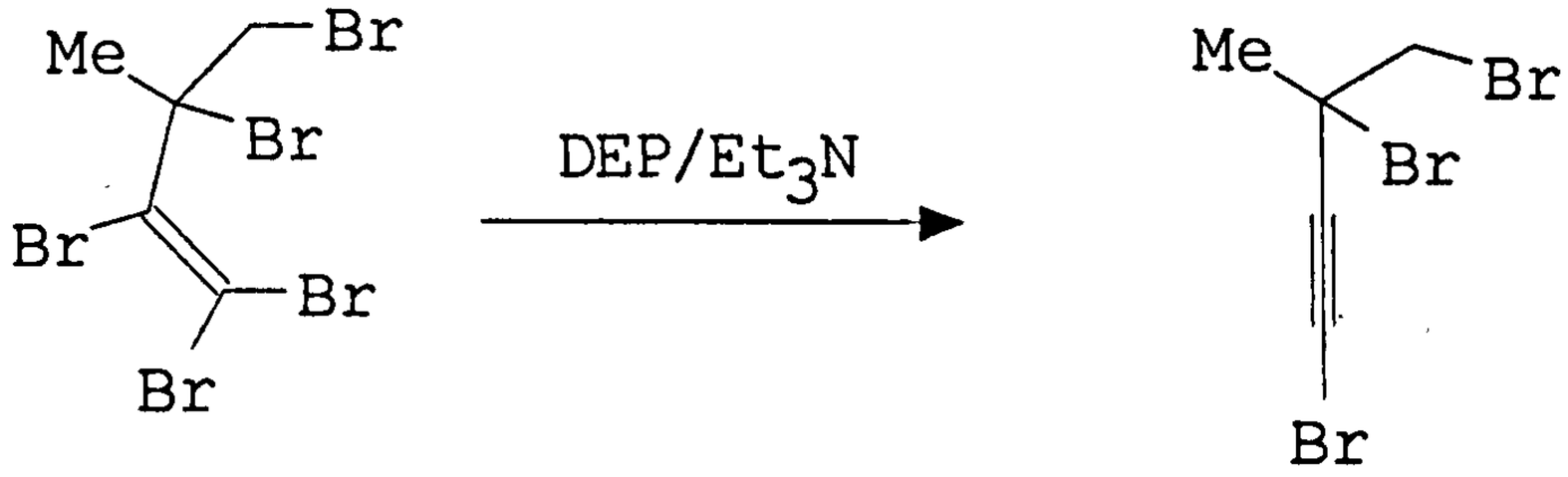
Compound (**166**) was dehydrobrominated with diazabicyclo[5.4.0]undec-7-ene (DBU) in dry benzene at room temperature for 5 min, when the tetrabromodiene (**170**) was obtained in 90 % yield.



(166) (170)

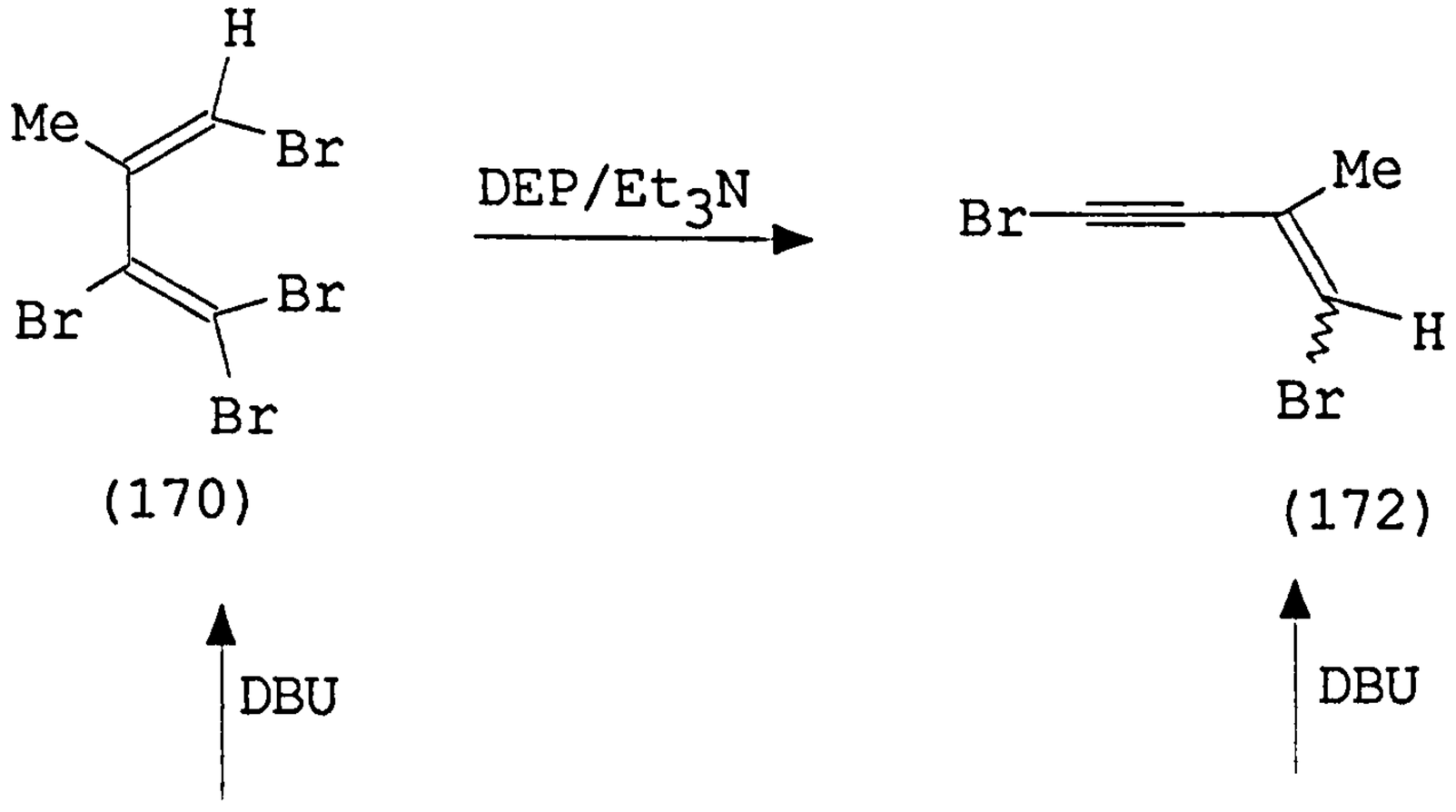
The diene (**170**) may arise by the abstraction of a proton from the methylene group, which is more acidic than the methyl group. The ^{1}H n.m.r spectrum showed a quartet at δ 6.4 with coupling constant of 1.1 Hz and a doublet for the methyl group at δ 1.9, while the ^{13}C nmr spectrum contained the expected five signals including four in the olefienic region at δ 139.8, 124.7, 119.2 and 112.5.

Debromination of **(166, X = Br)** by reaction with diethylphosphite and triethylamine at 5 °C for 30 min gave **(171)** in 38 %,[91] as a colourless oil. The ^{1}H n.m.r showed an AB pattern at δ 4.0 and 3.8 with a coupling constant of 10.1 Hz and a singlet for the methyl at δ 2.1. The ^{13}C spectrum contained 5 signals including two in the acetylenic region at δ 93 and 79.



(166) (171)

The compound **(172)** was prepared in two ways, either from **(171)** with DBU or from **(170)** with diethylphosphite and triethylamine.



(170) (172)

(166) (171)

2.3. CONCLUSION

1,2-Dibromo-3,3-dialkylcyclopropenes in which one 3- substituent is a 2-substituted ethyl group have been obtained by 1,2-debromination of 1,1,2,2-tetrabromocyclopropanes by reaction with one mol. equiv. of methyllithium. They ring-open at ambient temperature, and in the presence of an electron rich alkene, two stereoisomers of vinylcyclopropanes are formed by apparent addition of intermediate vinylcarbenes. However, reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxylethyl) cyclopropane with two mol. equiv. of methyllithium leads to a 1,3-substituted butadiene by formal elimination of a formaldehyde molecule. Oxidation of tri- or tetrahalocyclopropane alcohols with potassium permanganate leads to the corresponding cyclopropanecarboxylic acid, which, on bromination using a modified Hunsdiecker procedure, does not lead to the tetra- or pentahalocyclopropane, but instead to ring-opening of the cyclopropane.

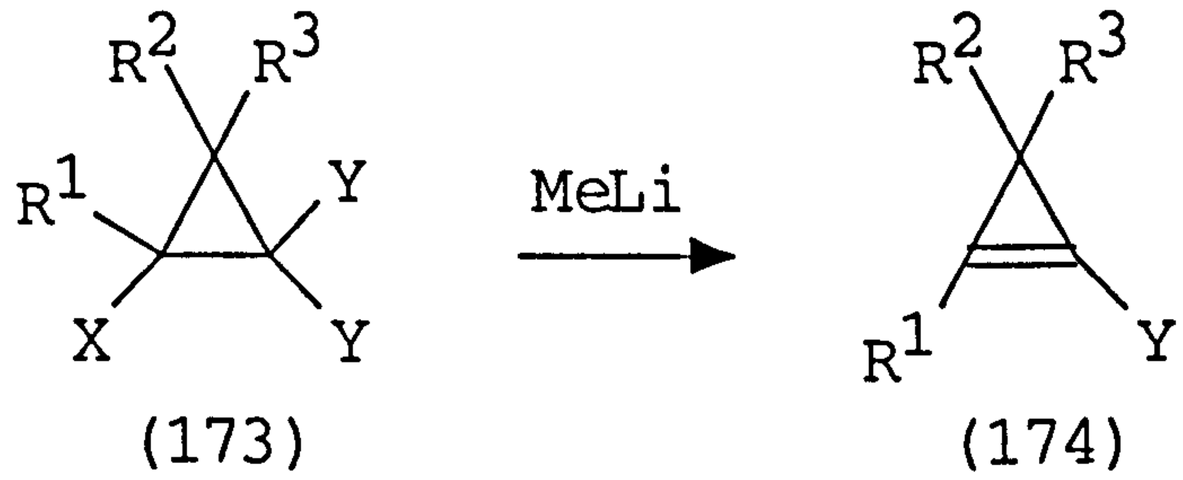
Chapter 3

Preparation of 1-Bromo-2-alkyl-Cyclopropenes Using Dialkyl Phosphite and Trialkylamine or Sodium Hydride

3.0. PREPARATION OF 1-BROMO-2-ALKYL CYCLO-PROPENES USING DIALKYL PHOSPHITE AND A TRIALKYLAMINE OR SODIUM HYDRIDE

3.1. INTRODUCTION

It has been established for many years that the reaction of methyllithium with 1,1,2-trihalocyclopropanes (**173**) leads to efficient 1,2-dehalogenation to generate 1-halocyclopropenes (**174**) which, in some cases, react further with a second equivalent of methyllithium, to afford a 1-lithiocyclopropene which can be trapped by an electrophile.[35,36,92]



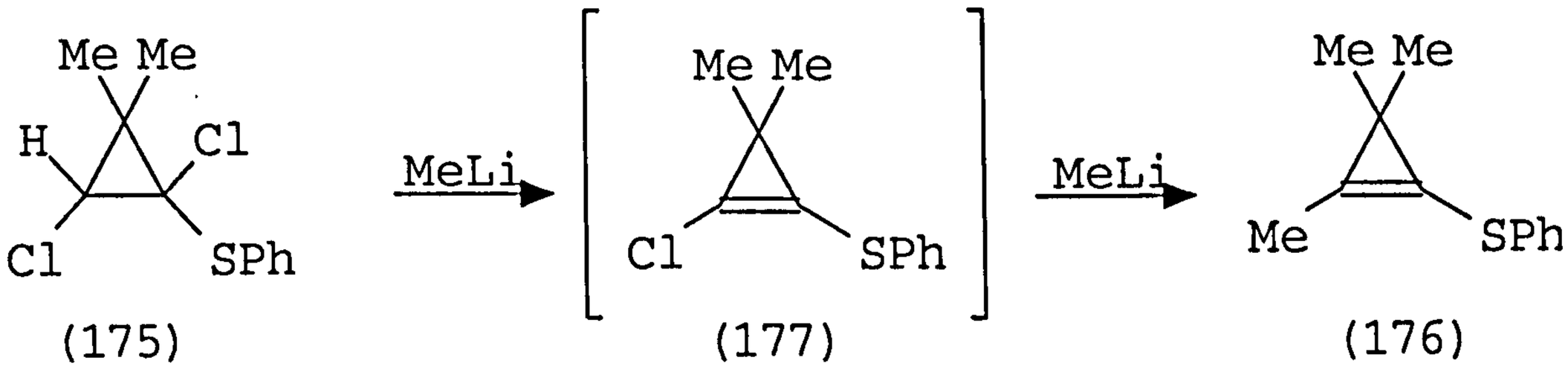
(173) (174)

X, Y = Halogen

The reactions appear to be initiated by lithium-halogen exchange followed by 1,2-elimination of lithium bromide. The rates of exchange follow the order Br >H > Cl. Thus, the elimination occurs at -90 °C when Y = Br and at 0-20 °C for trichlorides, X = Y = Cl. When either X or Y of (**173**) is bromine the reaction is successful when R^1 is either alkyl, hydrogen or trimethylsilyl.[48] However, for (**173**) (X = Y = Cl) success is achieved only when R^1 is alkyl, and if R^1 is hydrogen an alternative dehydrohalogenation occurs and gives a 1,2-dichlorocyclopropene.

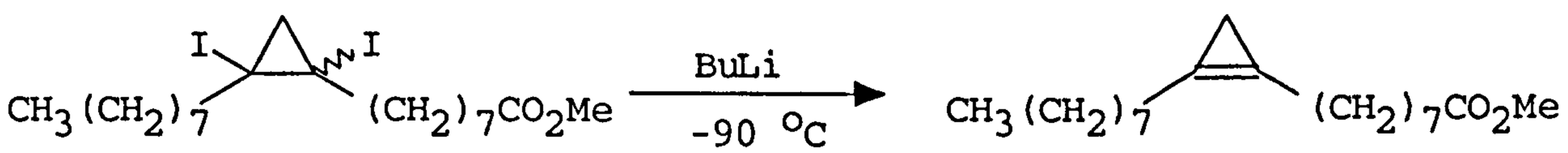
In general, these eliminations proceed cleanly with one mol. equivalent of methyl

lithium. However, treatment of compound (**175**) with one equivalent of methyl lithium at 20 °C afforded a mixture, showing one product as well as the starting material. Addition of another equivalent of methyl lithium gave the product, (**176**) in high yield.[51] Apparently, the intermediate (**177**) which is derived by the loss of hydrogen chloride was unstable to the reaction conditions and underwent a rapid addition-elimination reaction with methyllithium across the cyclopropene double bond.[51]

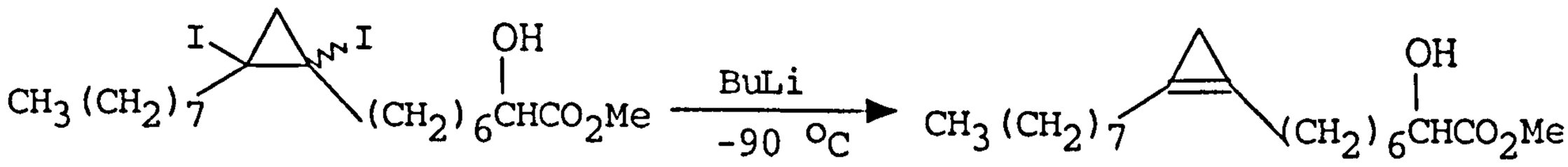


(175) (177) (176)

A similar 1,2-dehalogenation of 1,2-diiodocyclopropanes, induced by sodium hydroxide,[93] gives a low yield. However, recently Baird and Grehan found that the dehalogenation of diiodocyclopropane fatty acids (**178**) and (**179**) is successful using BuLi at -90 °C to generate the cyclopropenes (**180**) and (**181**) in 90 % yield, with no reaction at the ester group under these conditions.[94]

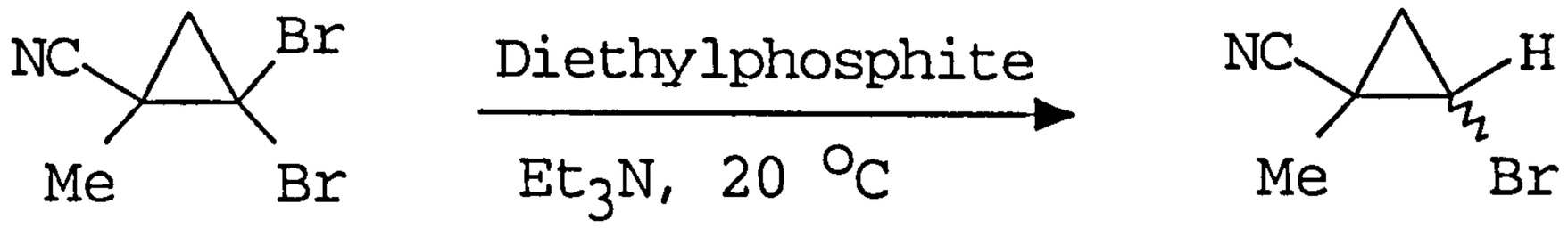


(178) (180)

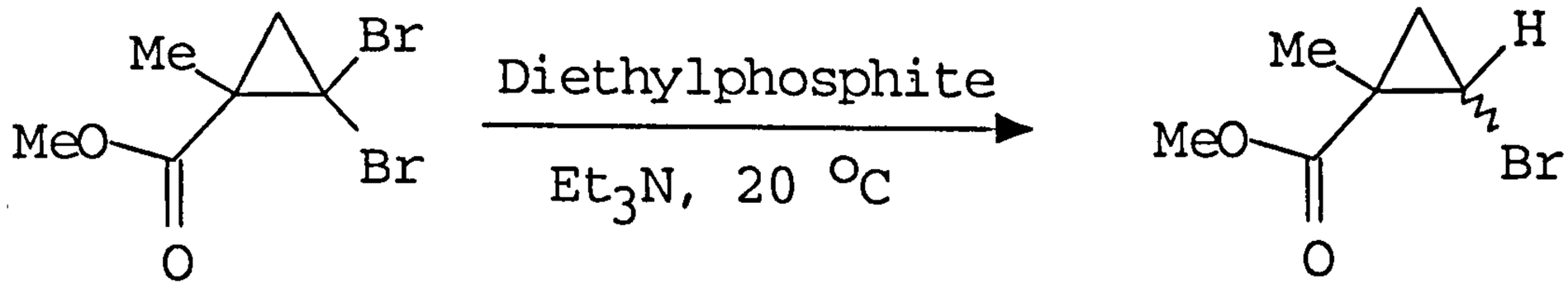


(179) (181)

It is known that the combination of diethyl phosphite and triethylamine efficiently reduces alkyl and aryl substituted 1,1-dibromocyclopropanes to 1-bromocyclopropanes. Gem-dibromo-cyclopropanes (**182**) and (**183**), having an electron withdrawing group were debrominated even at room temperature to produce the corresponding mono-bromocyclopropanes (**184**) and (**185**) in 88 % and 86 % yield respectively, without reaction at the functional groups.[95]

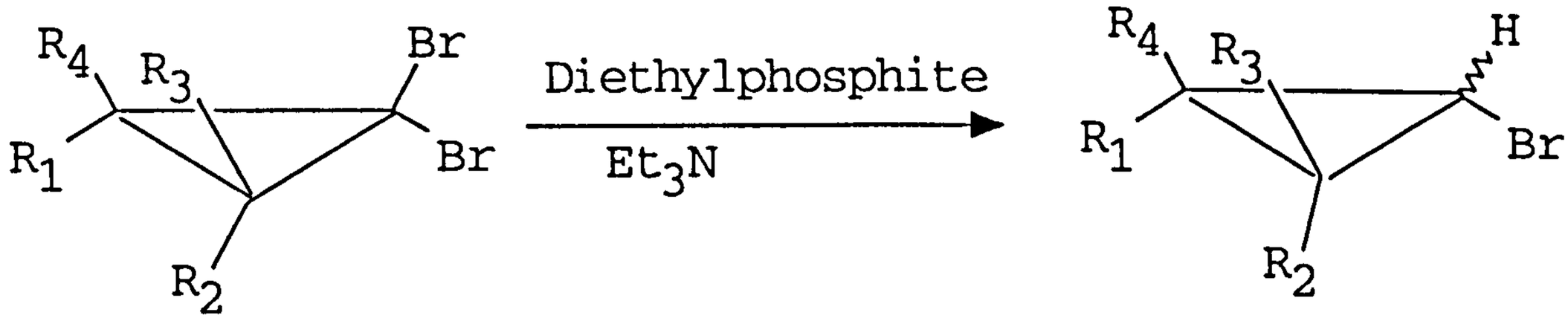


(182) (184)



(183) (185)

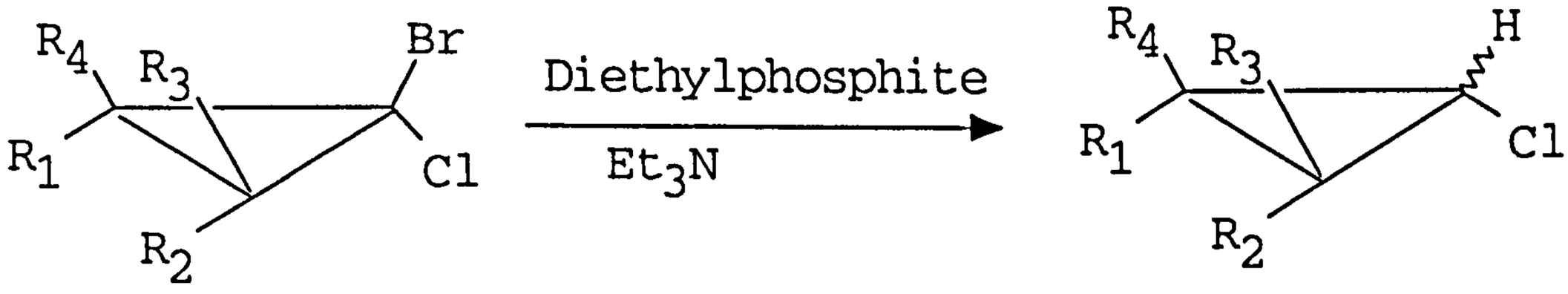
Treatment of a range of other gem-dibromocyclopropanes (**186**) with diethylphosphite in the presence of triethylamine at 90 °C gave the monobromocyclopropanes (**187**) in a good yield, with the deposition of $Et_3N.HBr$. No further reduction of the monobromide was observed.[95]



(186) (187)

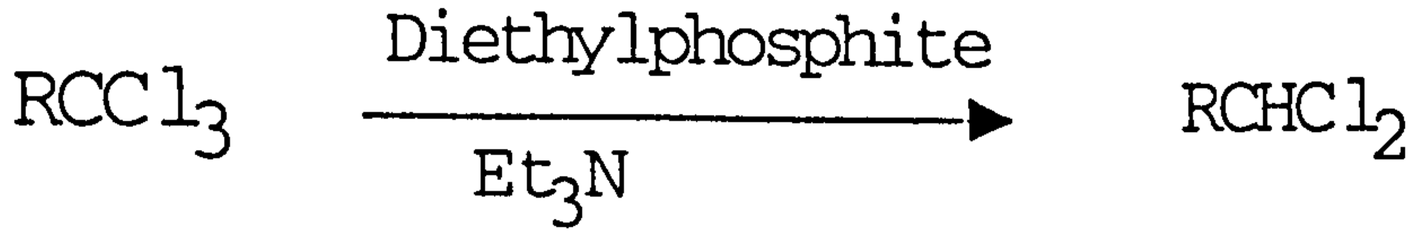
Moreover, gem-dibromoalkenes are also reduced to bromoalkenes using the same reagent at room temperature; for example, β, β-dibromostyrene reacted with two mol. equivalents of diethylphosphite and triethylamine at room temperature for 4 h to give β-bromostyrene in 96 % yield.[95]

The reduction could be extended to the conversion of gem-bromochlorocyclopropanes into monochlorocyclopropanes. Treatment of (188) with diethylphosphite and triethylamine gave mainly the corresponding chlorocyclopropanes (189) without formation of bromocyclopropane.[96]



(188) (189)

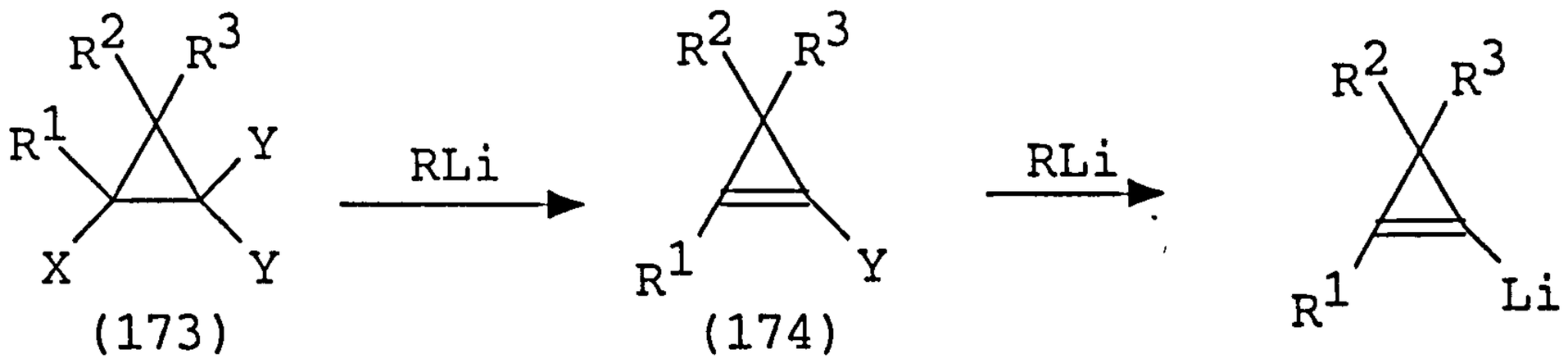
One of the chlorine atoms of trichloromethane derivatives was, however, reduced to yield the corresponding dichloromethane, which was inert under the reaction conditions.[96]



These results are considered to indicate that only an activated halogen atom is reactive towards reduction.[96]

3.2. AIMS OF THE PROJECT

It is known that the reaction of 1,1,2-trihalo- **(173)** or 1,1,2,2-tetrahalo-cyclopropanes **(190)** with an alkyllithium, provides a valuable entry to 1-halocyclopropanes which in the former case often undergo lithium-halogen exchange to produce synthetically valuable 1-lithio cyclopropenes, while in the latter case they undergo further elimination and rearrangement to an allenic carbene.[36,77,97,98]



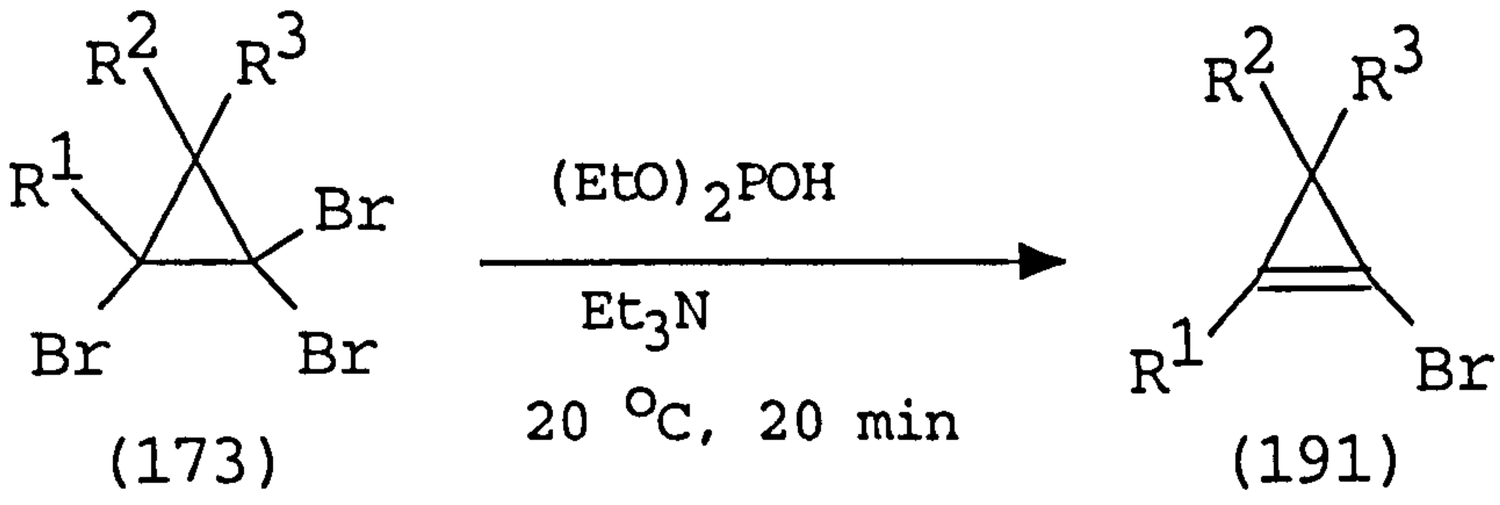
X = Y = Br
X = Cl, Y = Br
X = Br, Y = Cl
X = Y = Cl

Sometimes it was difficult to control the addition of exactly one equivalent of methyl lithium and the initially formed halocyclopropenes reacted further. It was of interest therefore to provide an efficient route to 1-halocyclopropenes from trihalocyclopropanes which did not suffer from the problem of further reactions.

3.3. RESULTS AND DISCUSSION

3..3.1. REACTION OF TRIHALOCYCLOPROPANES WITH DIALKYLPHOSPHITE AND TRIALKYLAMINE OR SODIUM HYDRIDE

Treatment of the tribromide (**173**) (R^1 = octyl, $R^2 = R^3 = H$) with diethyl phosphite and triethylamine at 20 °C for 20 min led to 1-bromo-2-octylcyclopropene (**191**) in 95% yield.[91]

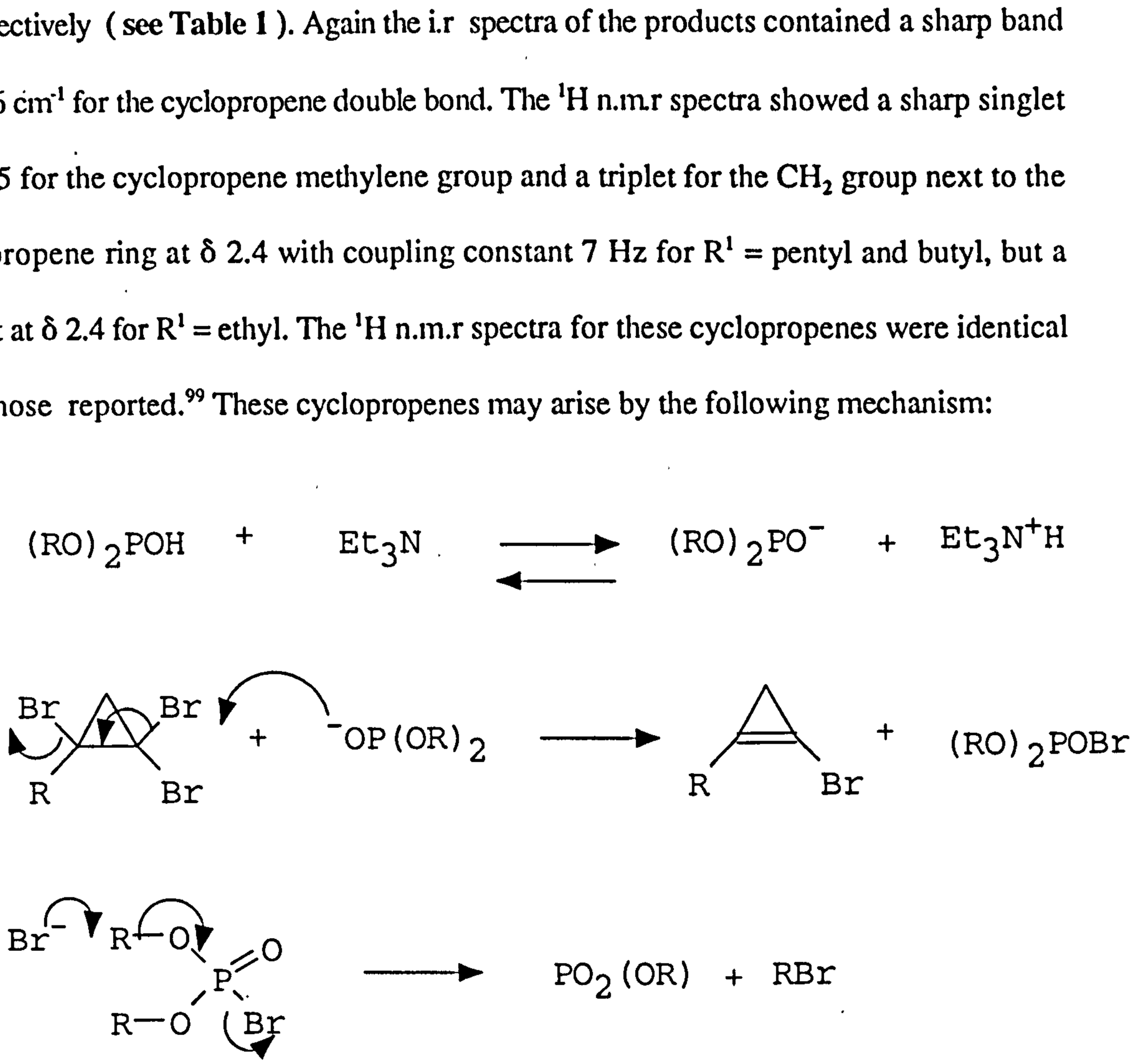


(173) (191)

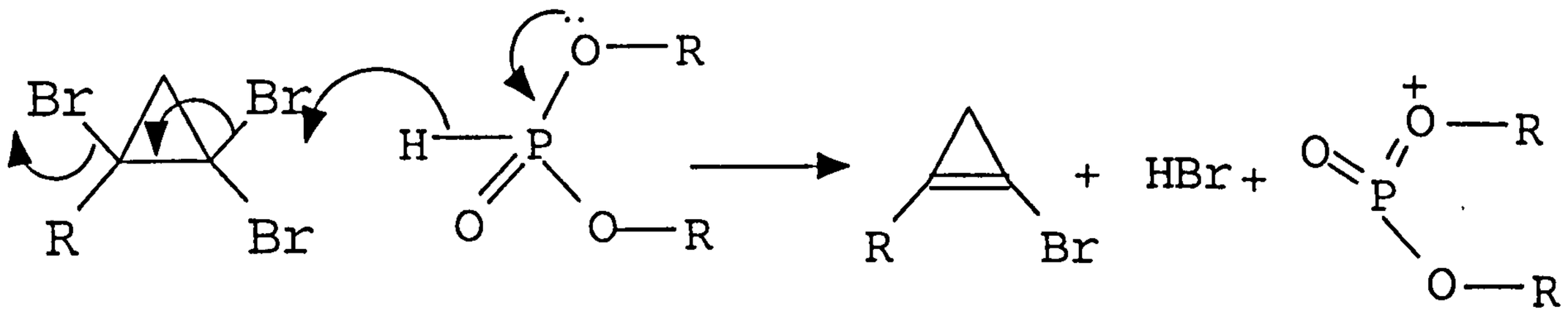
The ^1H n.m.r spectrum of (**191**) showed a sharp singlet at δ 1.4 for the cyclopropene methylene group and a triplet for the CH_2 group next to the cyclopropene at δ 2.39 with coupling constant 7 Hz. The i.r spectrum showed a sharp band for the cyclopropene double bond at about 1836 cm^{-1}. The ^1H n.m.r spectrum was identical with that reported.[39] The relatively low temperature at which this elimination occurred is in line with the reduction of 1,1-dibromocyclopropanes by diethyl phosphite and triethylamine, which occurred at room temperature when an electron withdrawing group was present on C_2.[95]

Using this same method, the lower homologues (**191**) (R^1 = pentyl, butyl and ethyl, $R^2 = R^3$

= H) were obtained in 93, 69, and 63 % yield respectively at 20 °C for 20 min, 1 h, and 1 hr respectively (see **Table 1**). Again the i.r spectra of the products contained a sharp band at 1836 cm^{-1} for the cyclopropene double bond. The ^1H n.m.r spectra showed a sharp singlet at δ 1.5 for the cyclopropene methylene group and a triplet for the CH_2 group next to the cyclopropene ring at δ 2.4 with coupling constant 7 Hz for R^1 = pentyl and butyl, but a quartet at δ 2.4 for R^1 = ethyl. The ^1H n.m.r spectra for these cyclopropenes were identical with those reported.[99] These cyclopropenes may arise by the following mechanism:

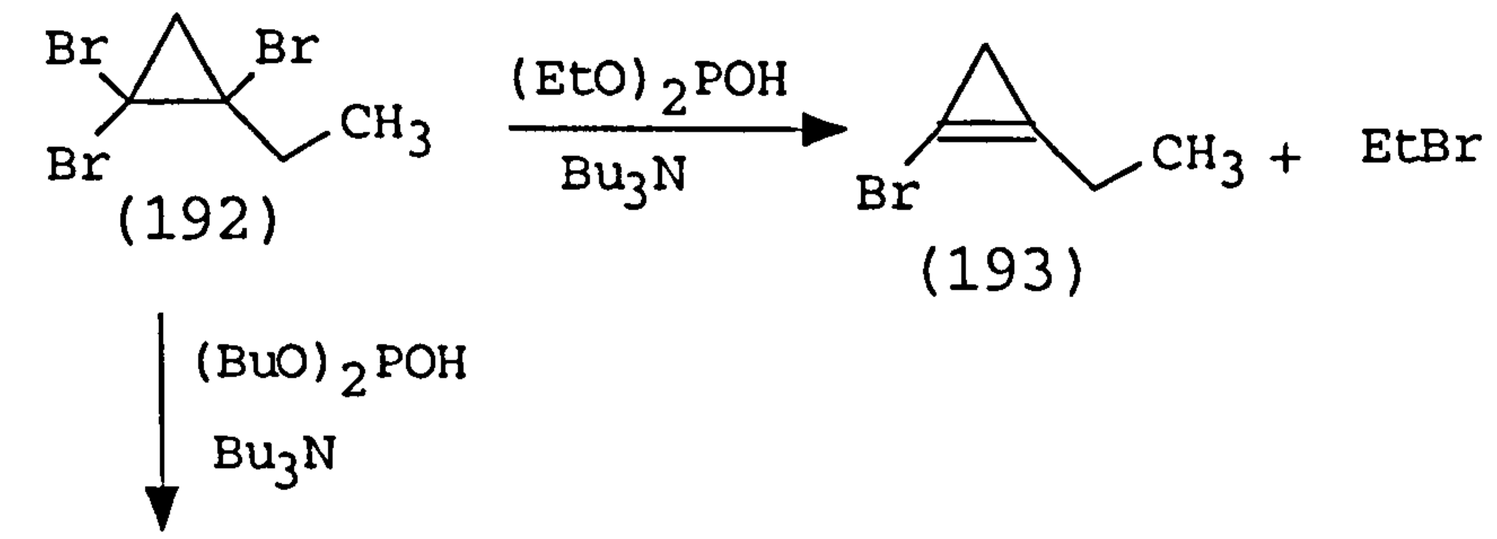


The first step is to react the base with alkylphosphite to generate the dialkyl phosphoxide anion, which reacts with one of the gem-dibromocyclopropane bromine atoms to give a cyclopropyl anion, followed by or concurrent with 1,2-elimination to give the cyclopropene, or it may arise in another way as shown below:



The absence of triethylamine apparently reduced the yield, so triethylamine must play a significant part in the reaction.[95] It was reported that dialkylphosphite reacts with carbon tetrachloride in the presence of triethylamine to give dialkyl chlorophosphite and chloroform, and the intermediate $(RO)_2PO^-$ was supported.[100]

To support the mechanism further, when the cyclopropane (**192**) was reacted with either diethylphosphite or dibutylyphosphite and tributylamine and the product was distilled into a cold trap, it gave the cyclopropene (**193**) together with ethyl bromide or butyl bromide respectively, derived from the dialkylphosphite. The structures of these products were confirmed by GC-MS and NMR.

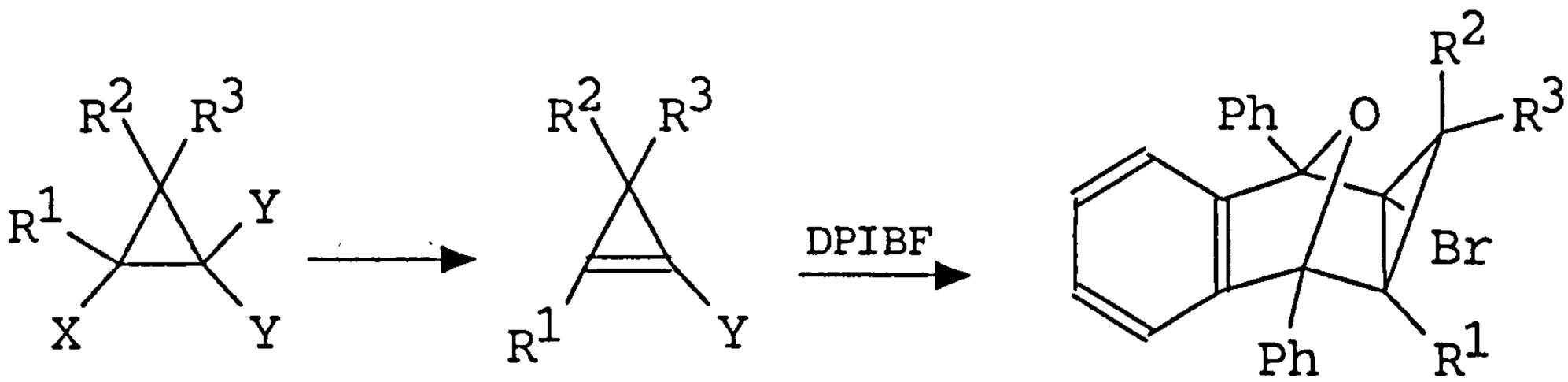


The cyclopropene (**191**) (R^1 = octyl, $R^2 = R^3 = H$)) was also obtained in high yield (84 %) when replacing the triethylamine with dimethylaminopyridine, tripropylamine or

dibutylamine after 4 h, 30 min and 30 min respectively. The dimethylaminopyridine required more time to complete the reaction probably because it is a more sterically hindered base. However, the use of tributylamine instead of triethylamine in the reaction required 20 h at room temperature and the cyclopropene was a mixture with *cis* and *trans*-1,2-dibromo-1-octylcyclopropanes. The same cyclopropenes (**191**, R^1 = pentyl, butyl, ethyl, $R^2 = R^3 = H$) were obtained, when the tribromocyclopropanes were treated either with dioctyl phosphite and triethylamine or with either diethyl or dioctylphosphite and sodium hydride (See Table 1).

The cyclopropene (**191**, R^1 = pentyl, $R^2 = R^3 = H$) was also obtained from (173) in 73 % yield when replacing the diethylphosphite with dioctylphosphite, although it was accompanied by a small amount of *cis* and *trans*-1,2-dibromo-1-pentylcyclopropane. When this reaction was repeated using dioctylphosphite and tripropylamine for 20 h at room temperature a mixture of the cyclopropene and dibromides was obtained in ratio ca. 2:1.

Although the yield decreased as the size of the alkyl group on the cyclopropane was reduced, the cyclopropenes could be distilled into a cold trap accompanied by a low boiling alkyl phosphite and tri-ethylamine. Therefore, it was possible with low boiling point cyclopropenes to avoid work up, by treating the tribromocyclopropanes (**173**) with dioctylphosphite and sodium hydride *in vacuo* (1 mm Hg) and continuously distilling the products into a cold trap (**See Table 1**). However, the yields were rather low. It was, however, possible to carry out the elimination in the presence of a diene such as diphenylisobenzofuran and to trap the derived cyclopropenes *in situ*. In this way, treatment of (**173**, X = Y = Br) with dioctylphosphite and sodium hydride in the presence of DPIBF gave [4 + 2]-cycloadducts in a moderate yield.



(194a) $R^1 = Br, R^2 = R^3 = H$

(194b) $R^1 = Me, R^2 = R^3 = H$

(194c) $R^1 = R^2 = Me, R^3 = H$

(194d) $R^1 = Br, R^2 = H, R^3 = Me$

(194e) $R^1 = H, R^2 = R^3 = Me$

(194f) $R^1 = COOMe, R^2 = R^3 = H$

(194g) $R^1 = Ethyl, R^2 = R^3 = H$

The compound **(194f)** gave a correct micro analysis and its ^{1}H.n.m.r spectrum contained two doublets at δ 3.0 and 2.7 with a coupling constant of 6.1 Hz, and a singlet at δ 3.6 for the methoxy group, together with a complex multiplet for the phenyl group. The stereochemistry was assigned by analogy with related adducts of 3,3-unsubstituted cyclopropenes with DPIBF.[101] Moreover, the ^{1}H n.m.r. spectrum of the adduct **(194b)** showed the expected two doublets at δ 2.8 and 1.5 with coupling constant of 6 Hz, for the methylene group of cyclopropane, one doublet being at low field due to the deshielding by the bridging oxygen atom and phenyl groups. The stereochemistry again was assigned by analogy with related adducts, supported by the large chemical shift difference between the cyclopropane hydrogens.[101]

Table (1)

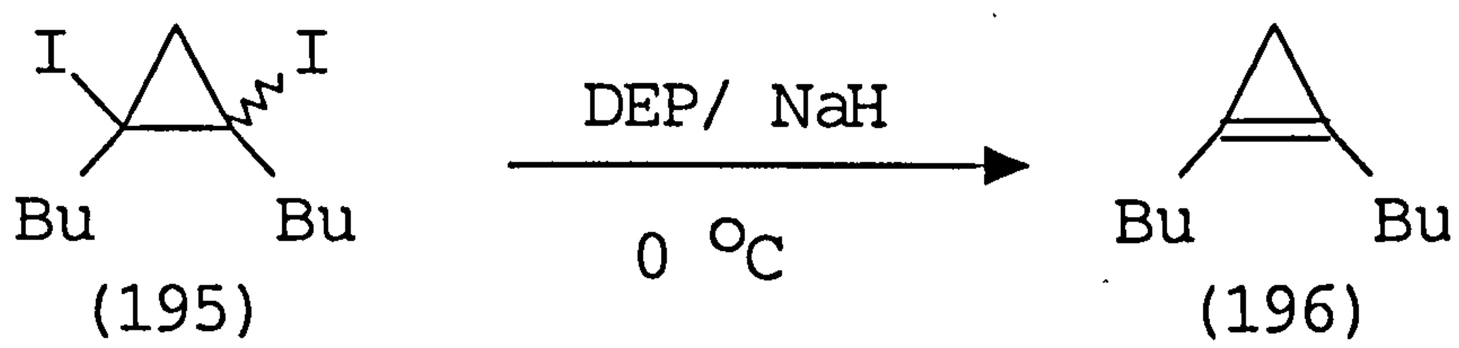
1,2-Debromination of 1,1,2-Tribromocyclopropanes to Cyclopropenes (174) by a Dialkylphosphite and Base

Cyclopropane (173)			Phosphite	Base	Conditions temp (°C) time	Cyclopropene (%) (174)
R^1	R^2	R^3				
Oct	H	H	diethyl	Et_3N	20, 20 m	95
"	"	"	"	NaH	0- 20, 5 m	96
"	"	"	dioctyl	NaH	"	96
Pen	"	"	diethyl	Et_3N	20, 20 m	93
"	"	"	"	NaH	0- 20, 5 m	64
"	"	"	dioctyl	NaH	0- 20, 5 m	90
"	"	"	"	Et_3N	20, 1 h	73
Bu	"	"	diethyl	Et_3N	20, 1 h	69
Et	"	"	"	Et_3N	20, 1 h	63
"	"	"	dioctyl	NaH	20, 30 m	52
Me	"	"	diethyl, THF	NaH*	0, 18 h	80
Me	Me	"	diethy	NaH*	0, 18 h	69
CO_2Me	H	"	diethyl, THF	NaH*	0, 18 h	50
Br	"	"	diethyl	Et_3N*	20, 18 h	76
Br	Me	"	diethyl, THF	NaH*	0, 18 h	36
Et	H	"	diethyl	NaH*	0, 18 h	81
H	Me	Me	"	NaH*	0, 18 h	46

* Trapped as (4 + 2) cycloadduct in the presence of DPIBF.

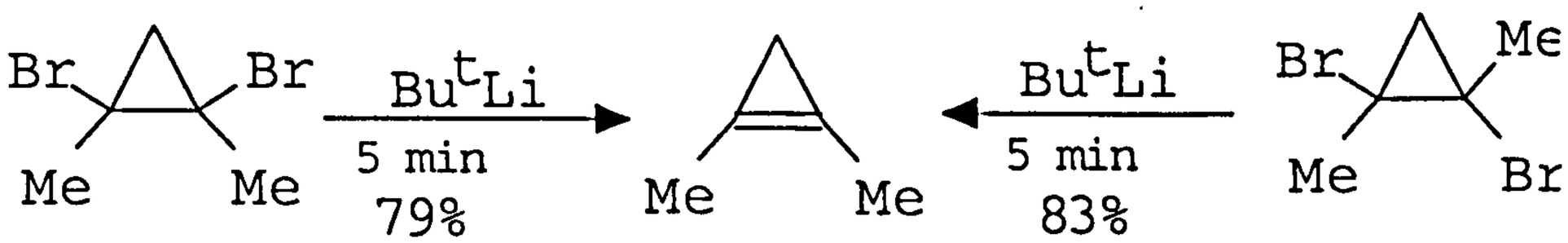
3.3.2. ELIMINATION OF HALOGEN FROM 1,2-DIHALO OR 1,1,2,2-TETRAHALOCYCLOPROPANES

The isomeric *cis* and *trans*-1,2-dibutyl-1,2-diiodocyclopropanes (**195**) both reacted rapidly with diethylphosphite and sodium hydride at 0 °C to form 1,2-dibutylcyclopropene (**196**) in 84 % yield in each case. The ^{1}H n.m.r spectrum for (**196**) was identical to that of an authentic sample.[94] Both diiodides are also known to undergo elimination on reaction with butyllithium.[94]



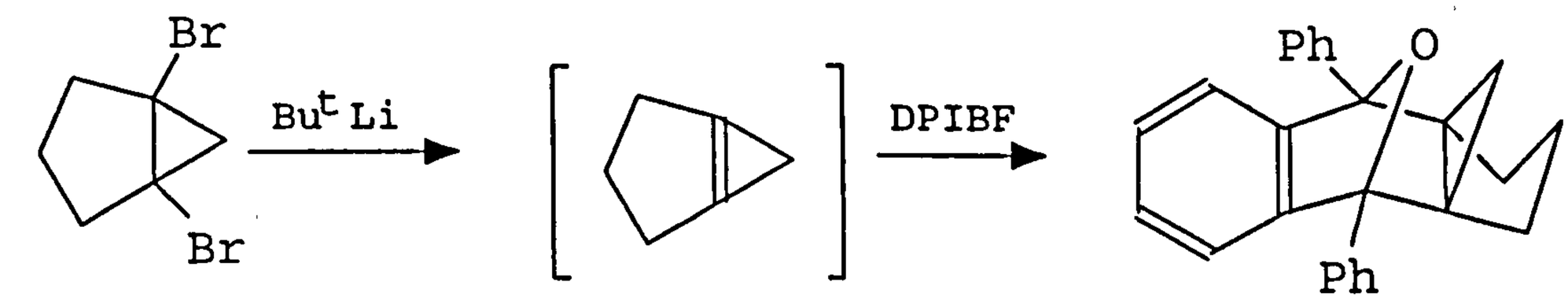
(195) (196)

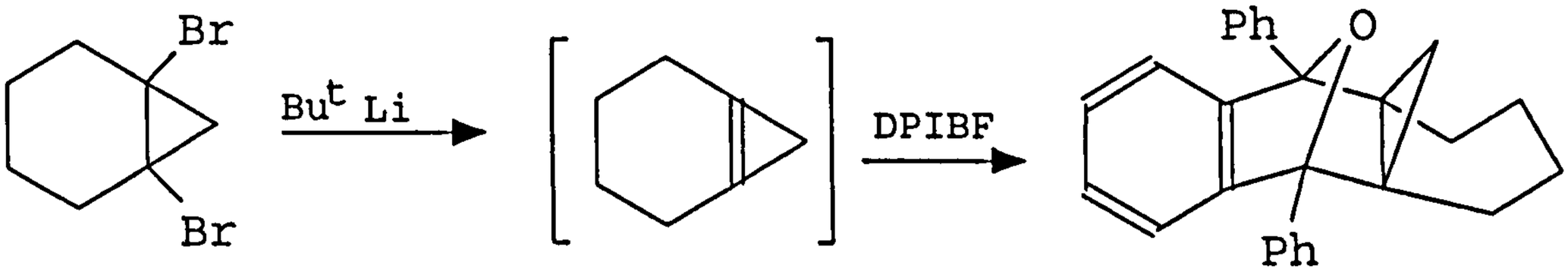
It is known that the reaction of either *cis* or *trans*-1,2-dibromo-1,2-dimethylcyclopropane with t-butyllithium leads to 1,2-dimethycyclopropene at low temperature.[33,102]



Although it is not possible to judge from the available evidence whether *trans* or *cis*-elimination occurs at a higher rate, application of this method to a range of 1,2-dibromocyclopropanes fused to other ring systems at C_1 and C_2 leads to a highly strained short lived cyclopropenes, which are trapped by [4 + 2]-cycloaddition to DPIBF when the reactions were carried out in the presence of the trapping agent. The use of methyl lithium

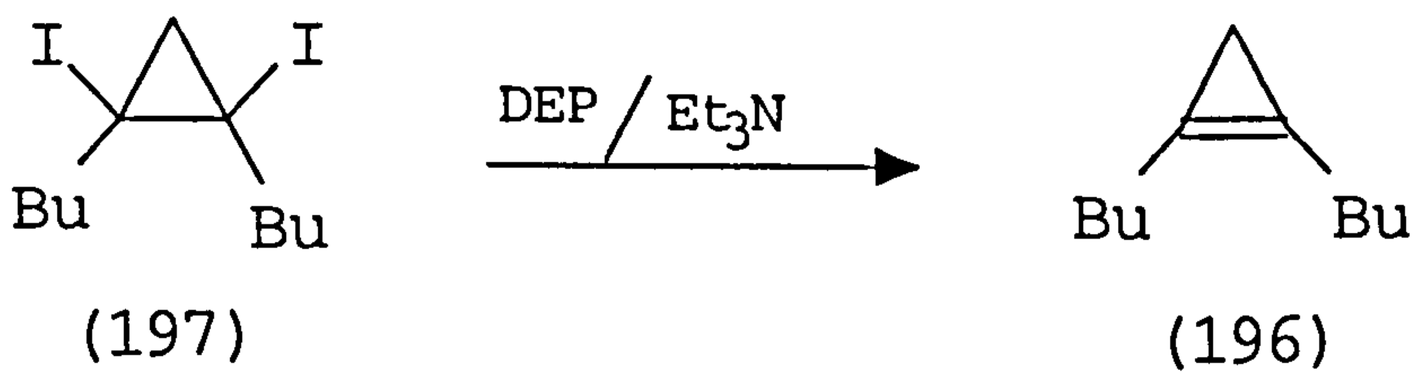
in place of t-butyllithium led to sluggish reactions and to the formation of products which apparently included tetramers.[103]





The corresponding diiodides also reacted with methyl lithium in solution at - 78 °C to give complex products apparently derived by further reaction of the initially formed cyclopropenes.[103]

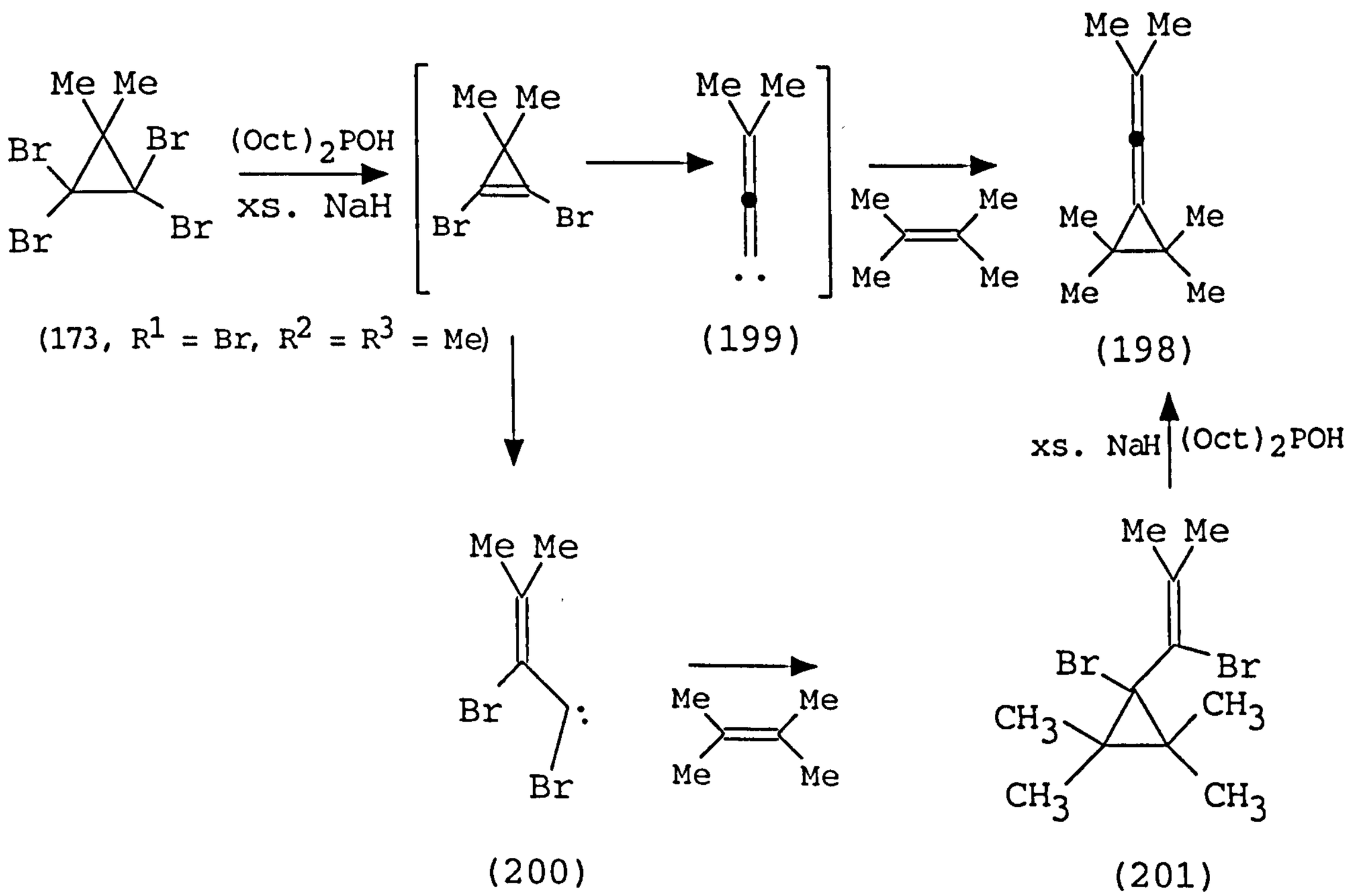
However, reaction of the *cis*-diiodide (**197**) with diethylphosphite and triethylamine was complete in 20 h, to give 1,2-dibutylcyclopropene (**196**) in 95 % yield.[91]



(197) (196)

When the same reaction was repeated on *trans*-diiodide with diethylphosphite and triethylamine after 22 h, the 1,2-dibutylcyclopropene was obtained in 22 % yield, accompained by a large amount of starting material.[91]

Reaction of the dimethyl tetrabromocyclopropane (**173**, $R^1 = Br$, $R^2 = R^3 = Me$) with an excess of dioctylphosphite and sodium hydride in the presence of diphenylisobenzofuran gave no product of trapping of the cyclopropene, but a similar reaction in the presence of 2,3-dimethylbut-2-ene gave the allene (**198**, $R^2 = R^3 = Me$) in 39% yield. This may arise by 1,2-debromination of the cyclopropene to give the allenic carbene (**199**) and the trapping of this carbene by the alkene, or by ring-opening of the intermediate cyclopropene to vinyl carbene (**200**),[85] trapping of this by the alkene and then debromination of the resultant bromo-1-(1-bromovinyl)cyclopropane (**201**) by an excess of the reagent to give the allene (**198**).



These result have been published.[91]

3.4. CONCLUSION

Reaction of a 1,1,2-trihalocyclopropane with a dialkylphosphite in the presence of base gave a high yield of the corresponding 1-halocyclopropene via a 1,2-dehalogenation. Using a bulky and weak base such as dimethyaminopyridine, the reaction required more time, while with tributylamine, the cyclopropene was obtained as a mixture with *cis* and *trans* 1,2-dibromocyclopropanes. With volatile cyclopropenes, trapping of the derived cyclopropene with diphenylisobenzofuran also gave a good yield. The reaction with dialkylphosphite and base provides a cheap and efficient method for the preparation of halocyclopropenes without further reaction, which can be a problem when an alkyllithium is used.

1,1,2,2-Tetrahalocyclopropanes reacted with dialkylphosphite and base leading to an allenic carbene, which in the presence of electron rich alkene gave the allenic cyclopropane.

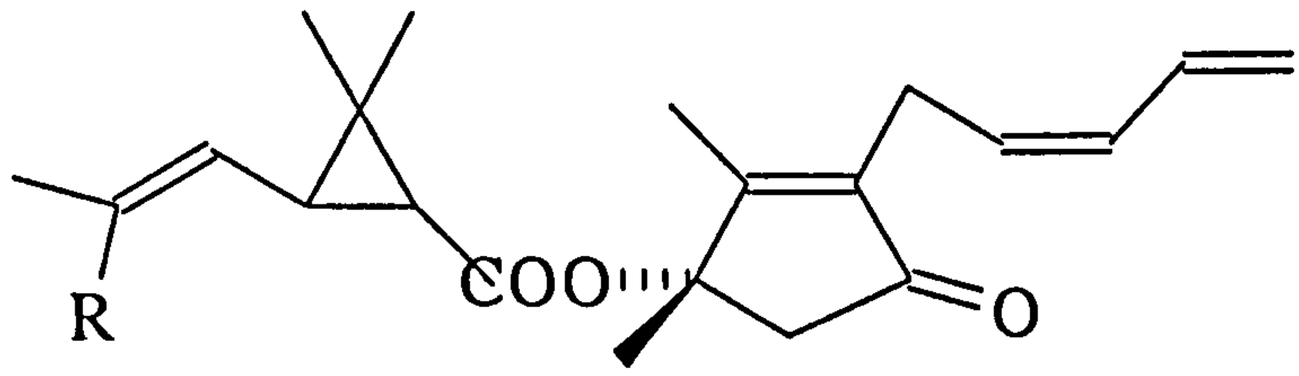
Chapter 4

Four Carbon Cyclopropane and Cyclopropene Synthetic Intermediates

4.1. INTRODUCTION

The chemistry of the cyclopropyl group has been of great general interest for almost a century, because cyclopropane containing compounds have very specialised biological activities and this has encouraged commercial interest from many fields.

Pyrethroid insecticides are such an example. These have evolved in a classical sequence; activity was observed in a natural extract, compounds responsible were isolated and identified, then increasingly active analogues were synthesised. In 1924, Staudinger and Ruzicka discovered that the active constituents of the chrysanthemum species, *Chrysanthemum Cinerariaefolium* are pyrethrin I (**202**) and pyrethrin II (**203**); these are esters of functionalised cyclopropane carboxylic acids.[104]



(202, R = Me)

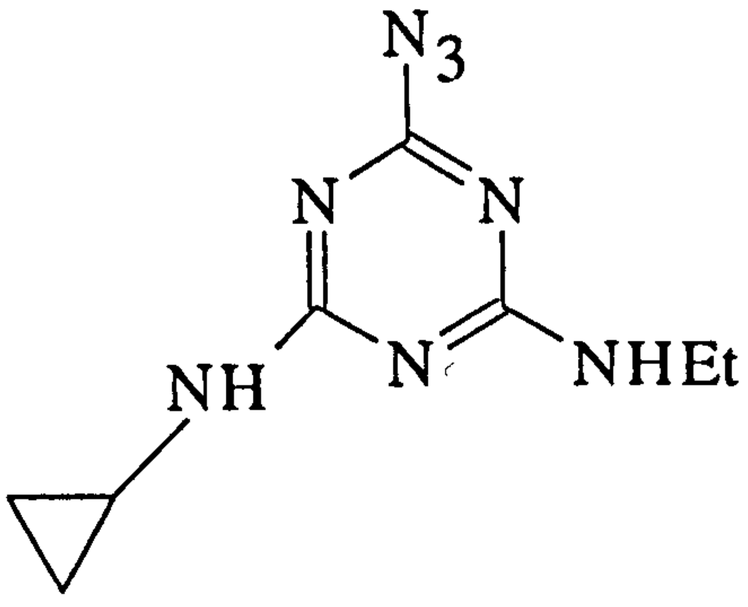
(203, R = COOMe)

The first synthetic analogues of the natural chrysanthemic acid esters were prepared by Staudinger.[105] Subsequently some synthetic compounds from this group proved to be superior to the natural substances in their action, but due to their limited photostability their use remained restricted to the hygiene sector. At the beginning of seventies, the situation changed, when a research team at the National Research and Development Corporation,[106] led by M. Elliott, reported new analogues of the active constituents of pyethrum, which out-

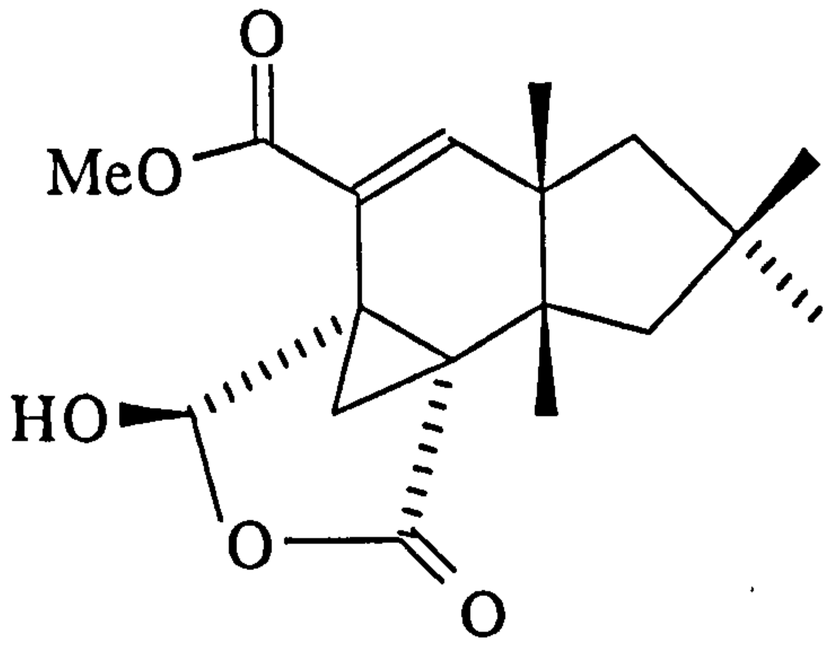
performed the previously known chrysanthemates due to their enormously increased activity and photostability. Thus began a worldwide development which ended in a new class of compounds whose economic significance has matched that of long established insecticides, e.g. carbamates and esters of phosphoric acid.

The activity of cyclopropane containing compounds is by no means restricted to insecticide activity; indeed, biologially active compounds may be subdivided in many ways, e.g. stuctural framework, substitution or activity.

Ciprofloyacin (**204**), is an aminotriazine derivative, manufactured by Bayer pharmaceuticals; it is highly active against gram positive and gram negative bacteria, particularly the latter. Due to its considerable activity, its use is restricted whenever possible to the treatment of infections caused by organisms resistant to standard drugs.



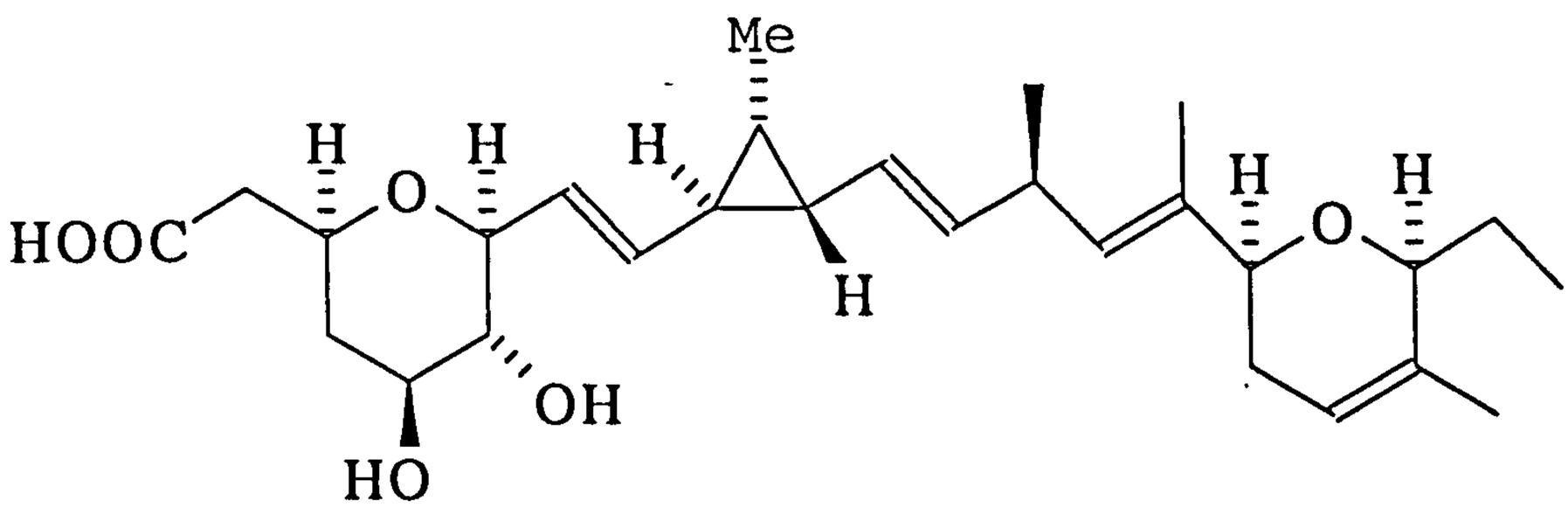
(204)



(205)

Marasmic acid (**205**) was isolated from the basidiomycete *Marasmium conigenus* (mold) and possesses potent antibacterial activity against *Staphylococcus aureus* and E. Coli, although no mechanism of action has been establised.[107]

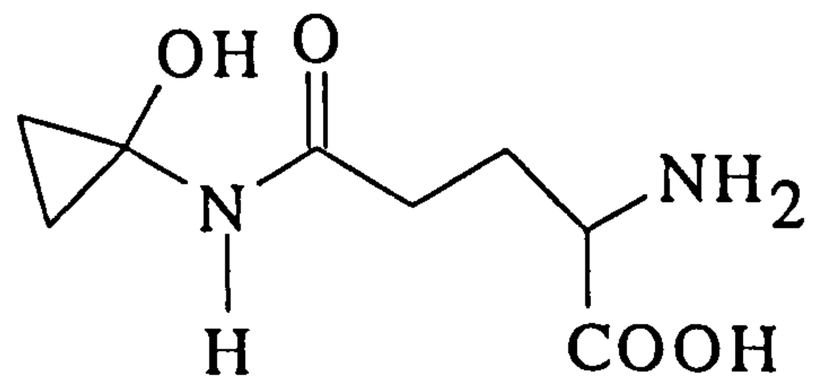
Ambruticin (**206**) is present in the fermentation medium of *polyangium cellulosum var. Rulvum* and is highly active against systemic pathogenic fungi.[108,109]



(206)

Moreover, there have been many cyclopropane containing compounds whose activity could be exploited with a view to drug manufacture.

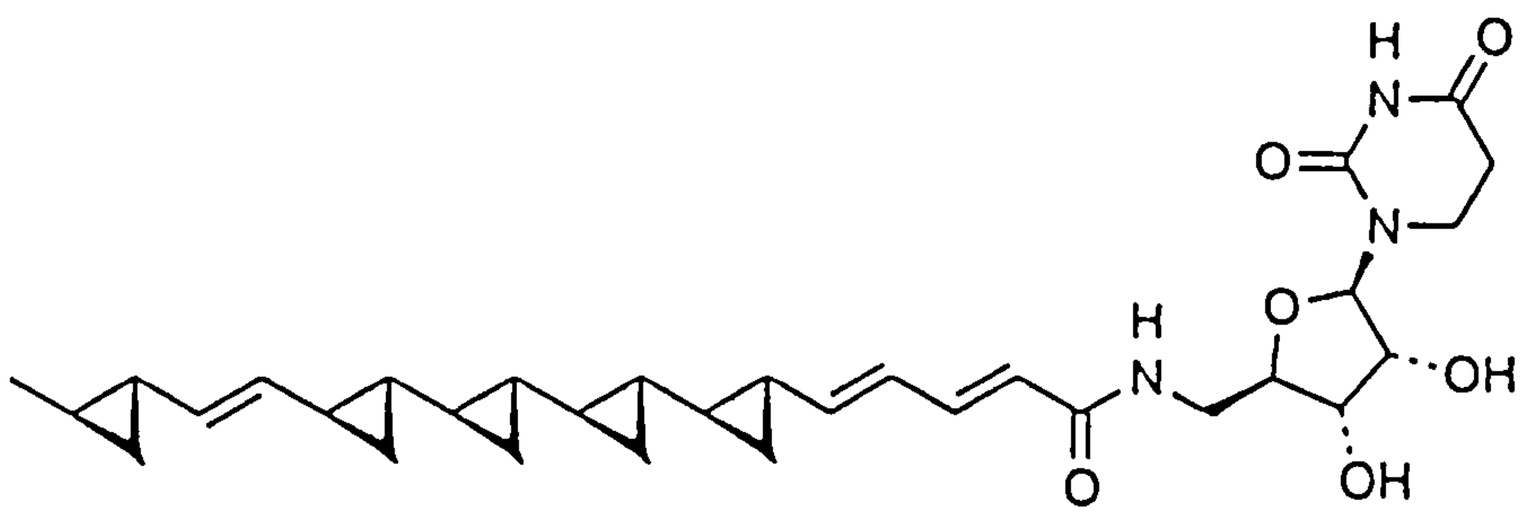
One such compound is Coprine (**207**), a product of the common ink cap mushrooom. Coprine was found to be a potent inhibitor for aldehyde dehydrogenase, and its ability to inhibit the liver enzyme suggests a use for the treatment of alcoholism.[110] Coprine is highly toxic therefore it was limited in its scope.



(207)

Recently a natural product was isolated from the fermentation broth of *streptoverticillium fervens* which shows remarkable selective activity toward filamentous fungi such as *aspergillus niger* but is essentially inactive against nonfilamentous fungi such as *candida*

albicans and gram-positive and negative bacteria.[111] FR-900848 (208) is a fatty acid nucleoside which possesses an unprecendented five cyclopropanes on a single fatty acid backbone, four of which are located on consecutive two carbon fragments.



(208)

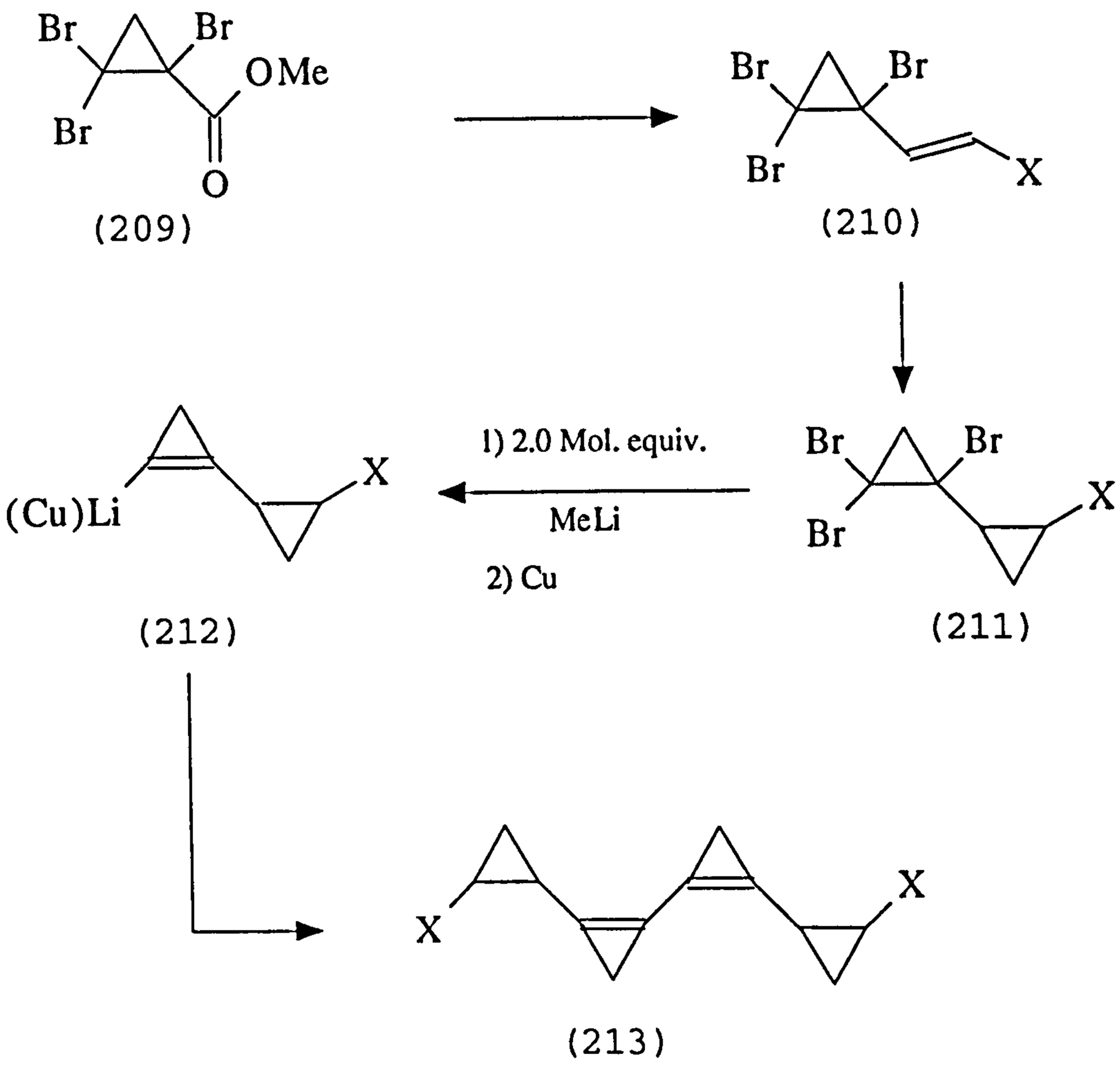
The combination of the unusual structure and the selective biological activity make (208) and its analogues attractive synthetic targets.

Many synthetic approaches to poly-cyclopropanes have been described recently. However, all these efforts have been directed towards the preparation of polycyclopropanes which possess the *trans-syn-trans* and *trans-anti-trans* stereochemical relationship.[112]

4.2. AIMS OF THE PROJECT

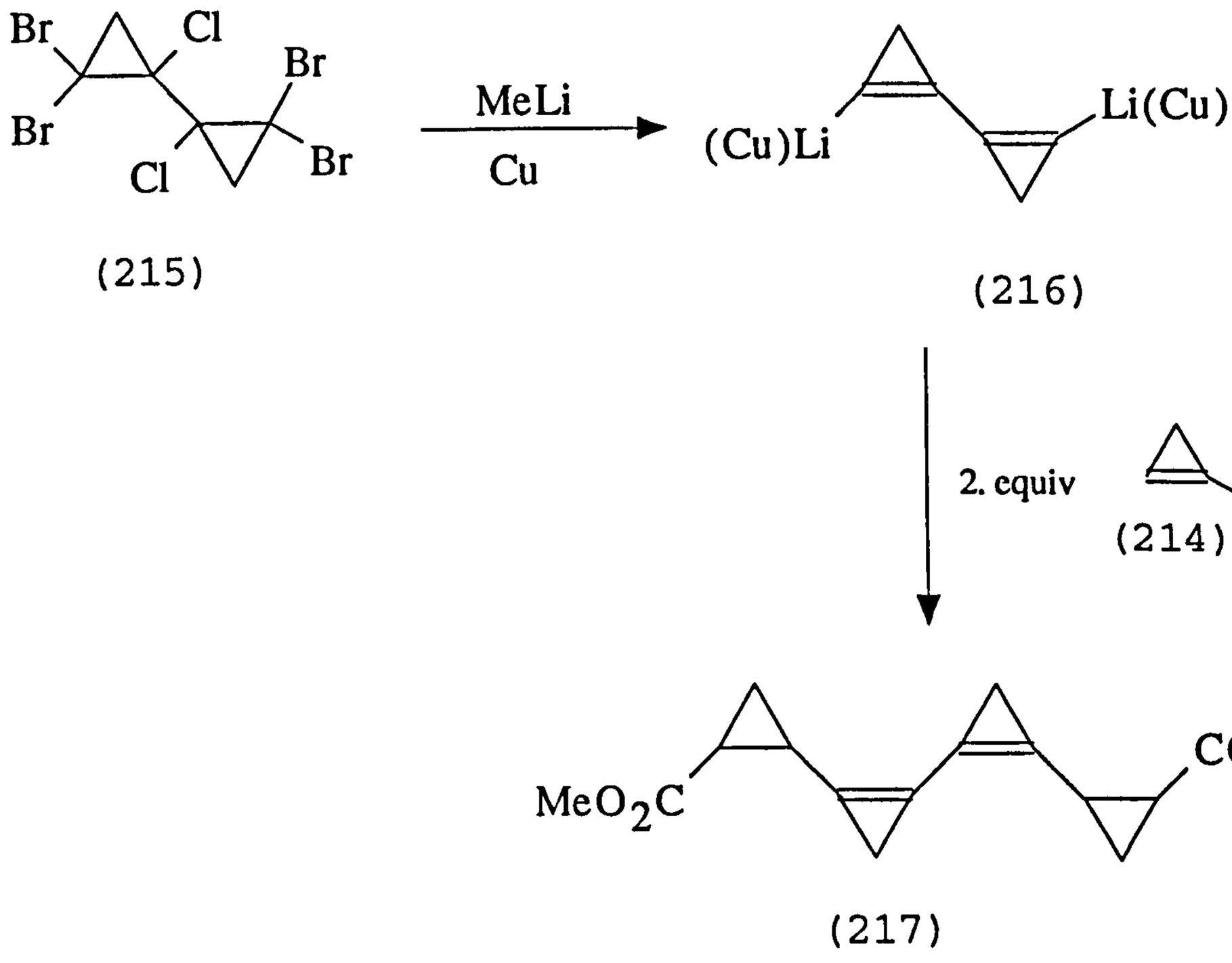
The aim of this project was to prepare *cis*-polycyclopropanes by:

a) Using trihalocyclopropane ester (**209**), which could be easily converted into the vinyl cyclopropane (**210**), followed by cyclopropanation to give (**211**), which should react with methyllithium in the presence of a metal such as copper to give (**213**) through the intermediate (**212**).



X = group capable of conversion into ester

b) Using a bis-hexahalocyclopropane such as (**215**) which again should react with methylithium to give (**216**), followed by coupling with (**214**) to give (**217**).



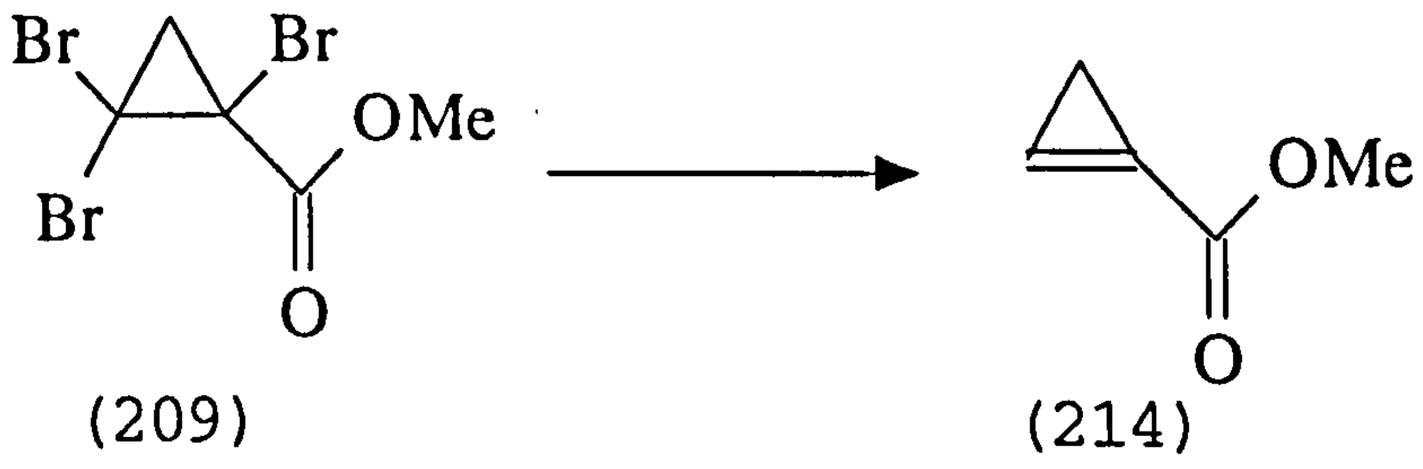
(215)

(216)

(214)

(217)

Compound (**214**) might also be obtained from (**209**) using chemistry described earlier:



(209)

(214)

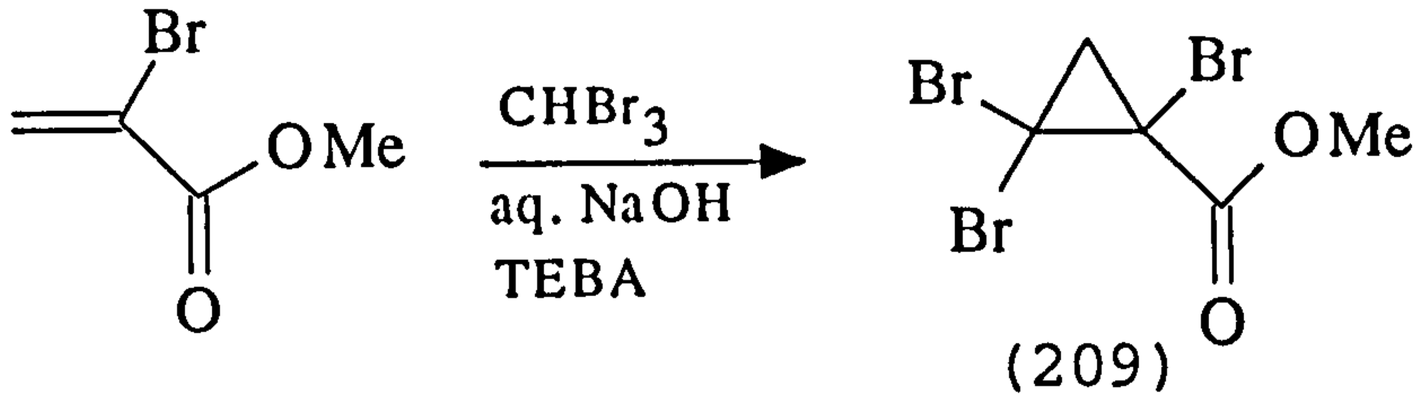
Compounds of type (215) were expected to be available by dihalocyclopropanation of 2-chlorobutadiene or 2,3-dichlorobutadiene.

This and the next chapter discuss the results of some of these experiments. Although in the event, it was not possible to prepare polycyclopropanes in this way, a range of interesting reactions was discovered.

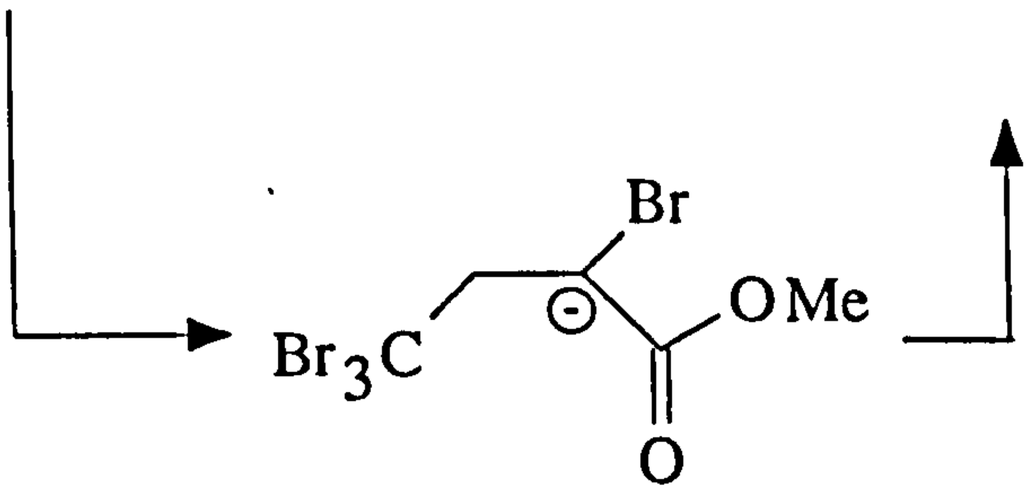
4.3. RESULTS AND DISCUSSION

4.3.1. PREPARATION OF THE REQUIRED TRI-BROMOCYCL-OPROPANE ESTER

Reaction of methyl α-bromoacrylate with aqueous sodium hydroxide and bromoform under phase transfer conditions in the presence of benzyltriethyl ammonium chloride (TEBA) leads to the tribromoester (**209**) in 56 % yield,[113,114] in a reaction which may be conveniently carried out on a large laboratory scale.

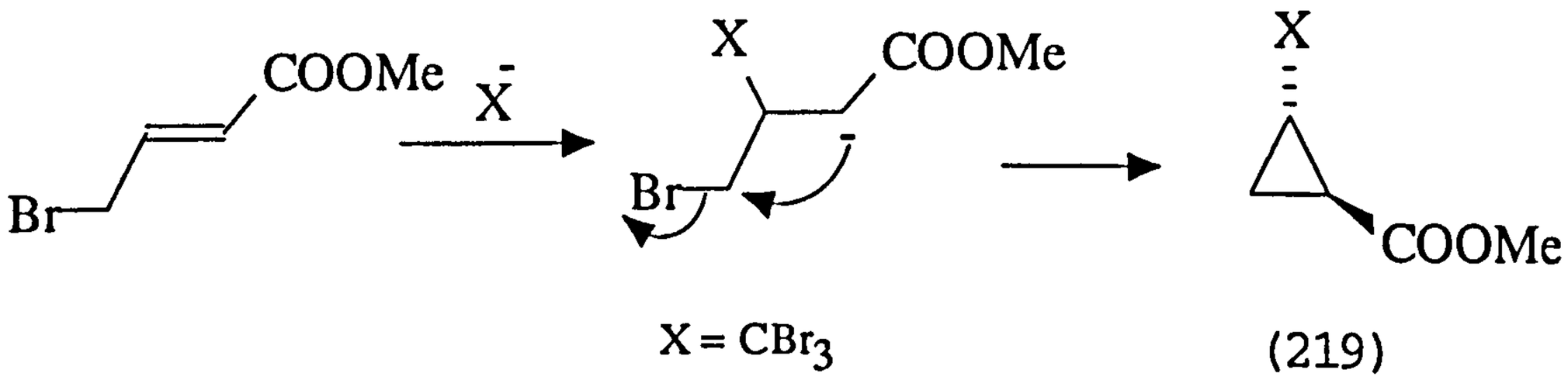


(209)



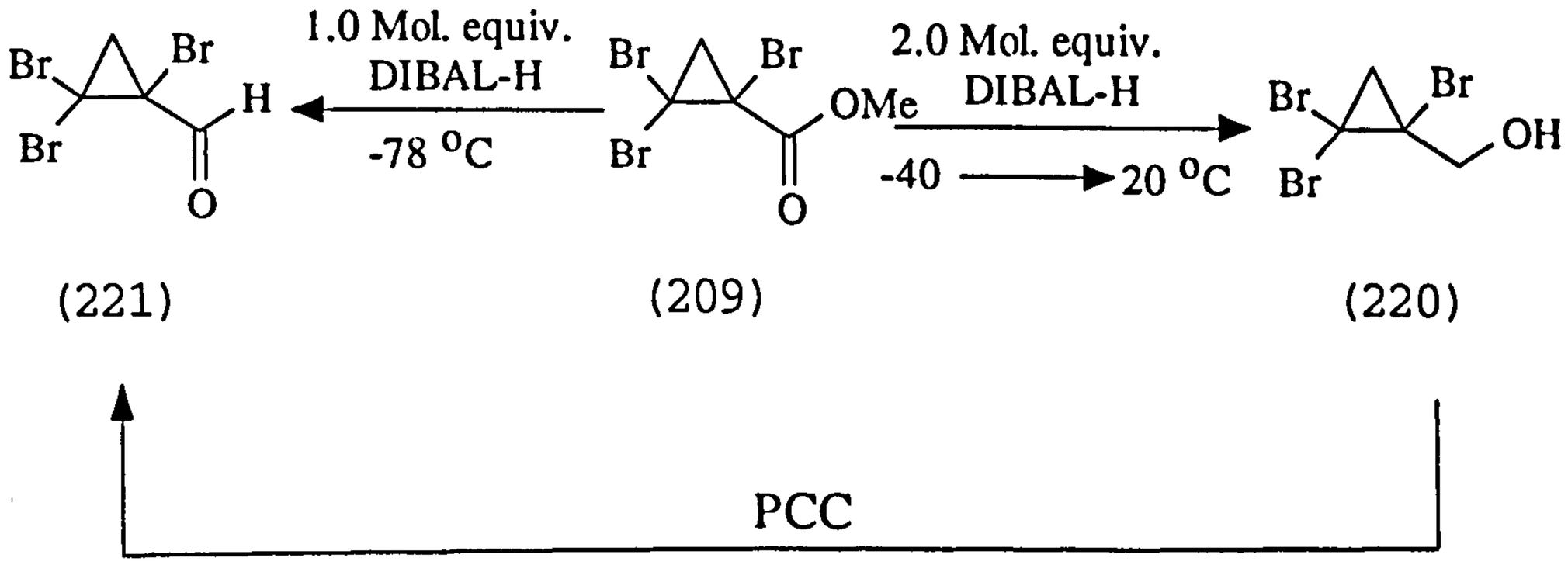
(218)

The formation of (**209**) arises by Michael - type addition of the tribromomethyl anion to the electron poor alkene to give (**218**) followed by subsequent cyclization, rather than by carbene addition. This mechanism was supported when, if methyl γ-bromocrotonate was treated with bromoform and sodium hydroxide in the presence of TEBA, a single product (**219**) was isolated.[113]



4.3.2. CONVERSION OF THE ESTER INTO OTHER GROUPS

The ester (**209**) could be reduced to the corresponding alcohol (**220**) by reaction with diisobutylaluminum hydride at -40 to 20 °C and to the aldehyde (**221**) at -78 °C in 78 and 70 % yield respectively. No replacement of bromine by hydrogen was observed in either of these reactions. The aldehyde (**221**) could also be obtained in 85 % yield by oxidation of the alcohol (**220**) with pyridinumchlorochromate (PCC).

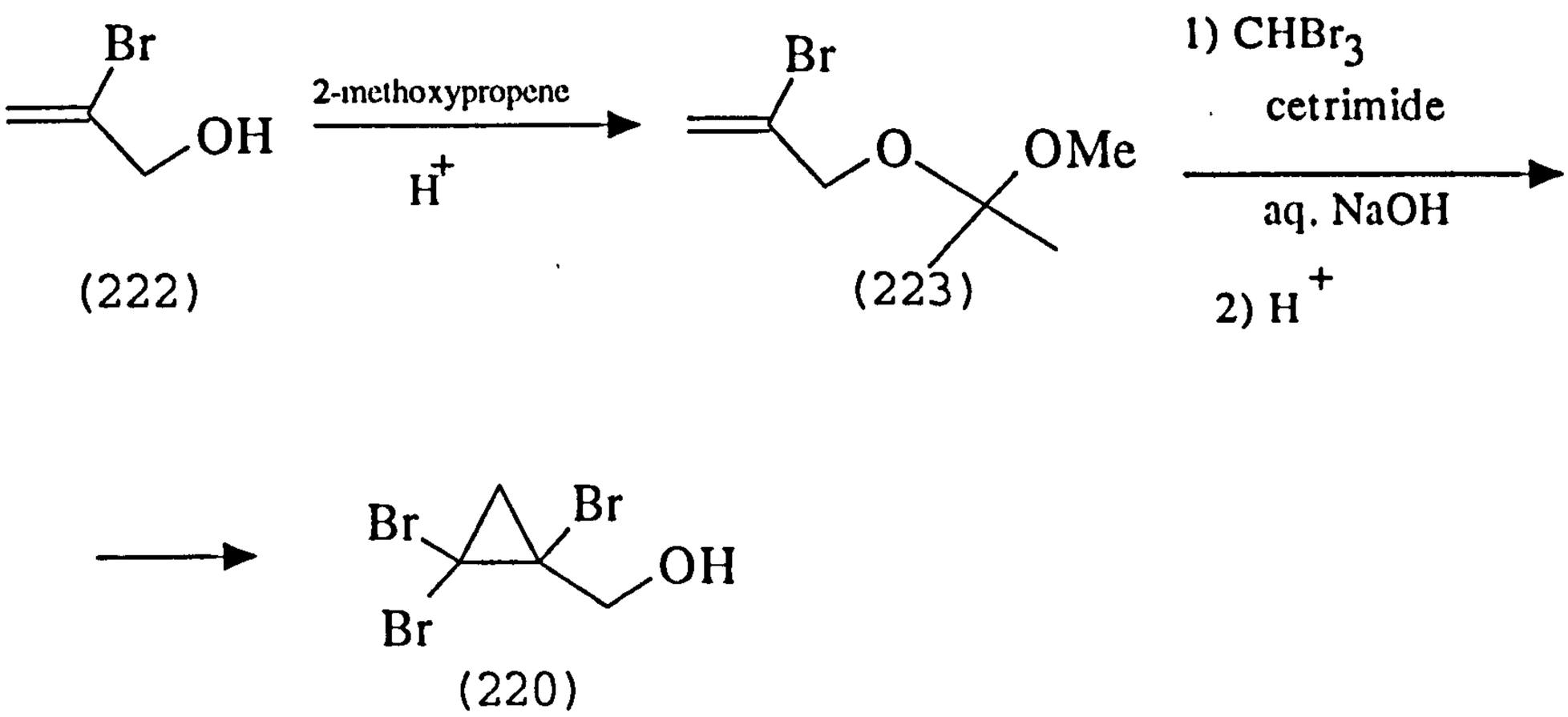


The ^{1}H n.m.r spectrum of (**220**) showed a one proton doublet of doublets (J 7.7, 13.0 Hz) at δ 4.1, caused by one of the protons of the methylene group adjacent to the hydroxyl group; the other proton was apparent at δ 4.0, also as a doublet of doublets (J 6.3, 13.0 Hz).

This is because the chiral centre makes the methylene group diastereotopic. In addition, two doublets were seen at δ 2.0 and δ 1.9 for the methylene group of the cyclopropane with a coupling constant 9.4 Hz, together with a doublet of doublets for the hydroxy group at δ 2.5. After shaking with D_2O, the spectrum showed only four doublets at δ 4.1, 4.0, 2.09 and 2.01, while the ^{13}C spectrum showed the expected four signals including the quaternary CBr_2 carbon at δ 35.71.

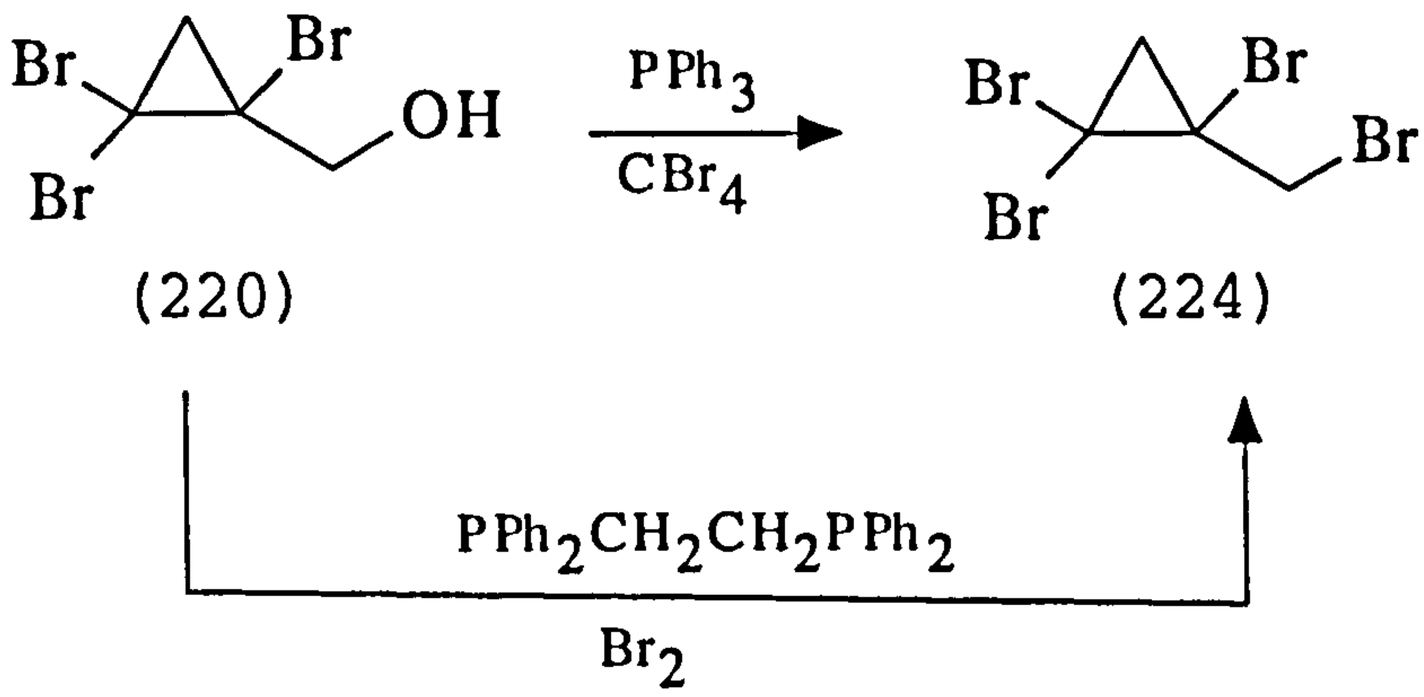
The ^1H n.m.r spectrum of (**221**) showed a singlet for the aldehyde proton and two doublets for methylene group at δ 2.8 and 2.0 with coupling constant 9.4 Hz. One of the protons was shifted downfield by 0.8 ppm possibly due to deshielding by the carbonyl group. The ^{13}C spectrum of (**221**) showed four signals including the carbonyl group at δ 189.5.

The alcohol (**228**) could also be prepared by another method from (**222**), albeit in low yield, by protecting the alcohol with 2-methoxypropene in the presence of acid to give (**223**) followed by dihalocyclopropanation under phase transfer conditions and deprotection to give (**220**) in 25 % yield, for the three steps from (**222**).[114]



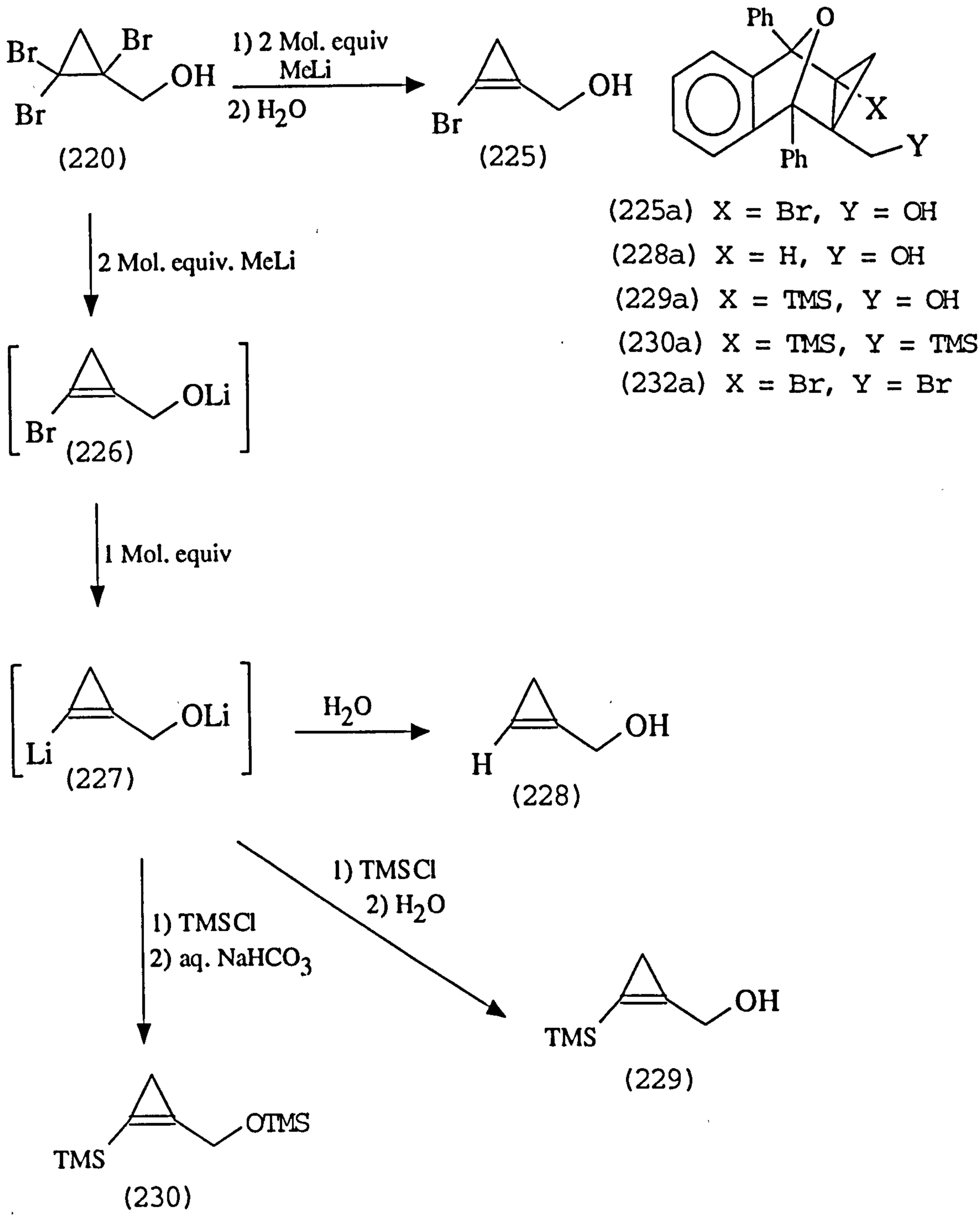
(222) (223) (220)

Alcohol (220) could be brominated by reaction with carbon tetrabromide and triphenyl phosphine to give (224) in 61 % yield. However it was difficult to separate the cyclopropane from the triphenylphosphine and therefore in an alternative approach, the bromide (224) was also obtained in 90 % yield by using bromine and 1,2-bis(diphenylphosphino)ethane.



4.3.3. REACTION OF TRIBROMOCYCLOPROPANES WITH METHYLLITHIUM

Reaction of the alcohol (220) with two mol. equivalents of methyllithium at -78 °C followed by quenching with water to give the cyclopropene (225) which was trapped as (225a) by reaction with diphenylisobenzofuran. The ^1H n.m.r showed two doublets at δ 2.8 and 1.84 (J = 6.8 Hz) for the cyclopropane protons; the difference in the chemical shift is due to one the protons being close to the oxygen of the furan ring and is typical for cyclopropene adducts in which the derived cyclopropane is *cis*- to the ether bridge.[42]



(225a) X = Br, Y = OH

(228a) X = H, Y = OH

(229a) X = TMS, Y = OH

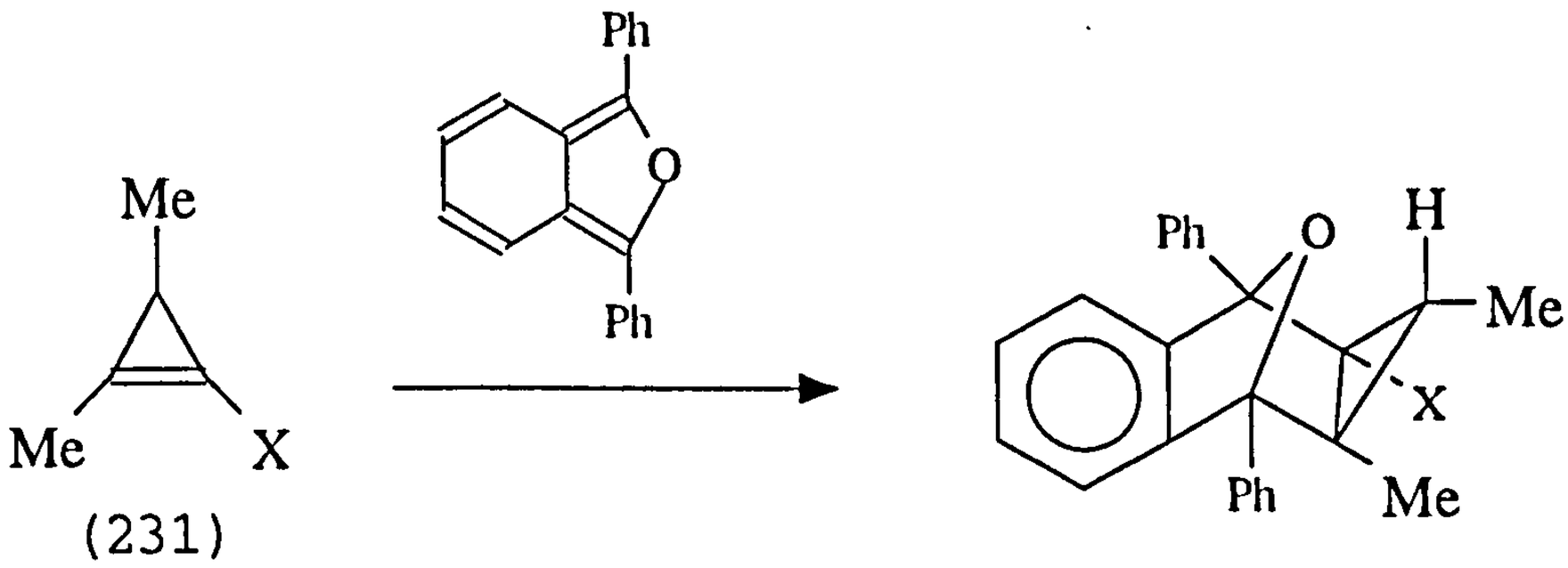
(230a) X = TMS, Y = TMS

(232a) X = Br, Y = Br

Reaction of (**220**) with 3 mol. equivalent of methyllithium at -78 to 20 °C followed by trapping with water led to the cyclopropene (**228**) which was again trapped by addition of DPIBF to give (**228a**); presumably (**228**) is derived by initial formation of (**226**) followed by lithium-halogen exchange to give (**227**), which is quenched by water. The cyclopropene

(228) is rather less stable than (225), and had completely decomposed after standing for 18 h at room temperature in $CDCl_3$, leading to a complex mixture.

Quenching of (227) with trimethylsilylchloride and then water led to the silane (229), which showed three singlets at δ 4.68 (2H) for the methylene next to the hydroxyl group, at 0.9 (2H) for the methylene group of the cyclopropene and at 0.16 (9H) for the silyl group. In contrast, working up the reaction with sat. aq. sodium bicarbonate led to the silylether (230) (76 %). The cyclopropenes (229) and (230) could be trapped by [4+2]-cycloaddition to diphenylisobenzofuran leading to a single product in each case, (229a) (89 %) and (230a) (54 %) respectively. The stereochemistry of the adducts was again assigned by analogy with related adducts of 3,3-unsubstituted cyclopropenes with DPIBF and supported by the large chemical shift difference between the cyclopropane hydrogens in each case (1.17 and 0.86 ppm respectively).[101] Moreover, Baird and Fitton found that, when the cyclopropene (231) was allowed to undergo[4+2]-cycloaddition with DPIBF, a single stereoisomer was obtained, and the stereochemistry was proved by X-ray crystallography.[115]



(231)

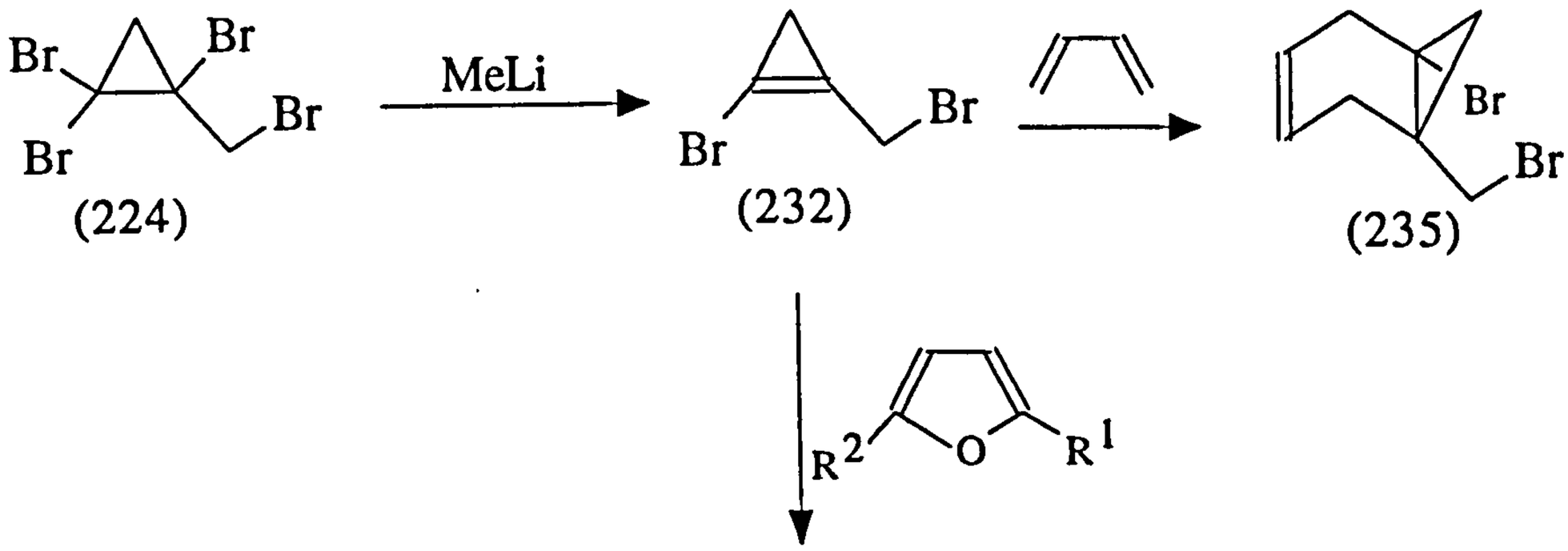
X = H, Br

Reaction of (224) with one mol. equivalent of methyllithium at -78 °C led to the cyclopropene (232) in 64 % yield by *endo*cyclic 1,2-debromination rather than *exo*cyclic

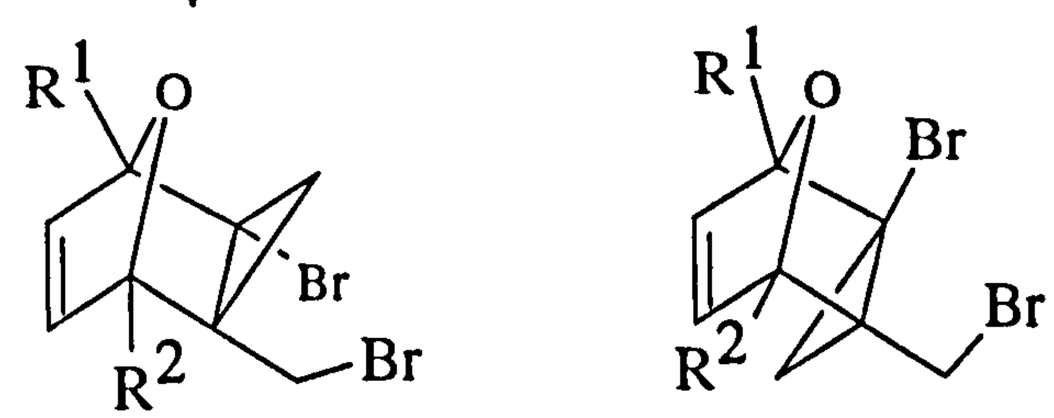
elimination to the corresponding methylene cyclopropane, or 1,3-dehalogenation on reaction with methyllithium.[103]

The ^{1}H n.m.r spectrum (**232**) showed two singlets each integrating for two protons which resonated at δ 4.2 and 1.6, while the ^{13}C spectrum contained the expected four signals at δ 113, 97.6, 21.54 and 18.7, and the i.r. spectrum showed the characteristic cyclopropene band at 1828 cm^{-1}. The cyclopropene (**232**) was trapped by DPIBF as (**232a**) (70 %) and with furan leading to a major isomer characterised as the *exo*-adduct (**233a**) and a minor isomer (**234a**). The ^{1}H n.m.r spectrum of the major isomer included an AB pattern for the cyclopropane hydrogens centred at δ 2.46 and 1.37, while for the minor isomer these appeared at δ 1.85 and 1.65. The stereochemistry of the major isomer was confirmed by the large difference in the chemical shift of the cyclopropane protons (1.1 ppm).

Reaction of (**232**) with 2-methylfuran gave also two regioisomeric adducts (**233b**) and (**233c**) in ratio (2.2:1). The ^{1}H n.m.r spectrum of the major isomer included an AB pattern for the cyclopropane hydrogens resonating at δ 2.4 and 1.2, while for the minor isomer (*exo* adduct) these appeared at δ 2.4 and 1.3. In both cases, the chemical shift different between the hydrogens was large, indicating that both were *exo*-isomers - the difference for an *endo*-isomer, e.g. (**234a**) being small. It was uncertain which was the major isomer, because it was very difficult to separate them by chromatography, the mixture giving one spot by TLC. 2,5-Dimethylfuran gave one isomer characterised as the *exo*-adduct (**233d**), the ^{1}H n.m.r spectrum of which showed two doublets in the alkene region with coupling constant 5.4 Hz and two AB patterns for the CH_2 next to bromine and the cyclopropane protons (at δ 2.4 and 1.2 with coupling constant 6.2 Hz), together with two singlets for the methyl-groups. The cyclopropene (**232**) could also be trapped by 1,3-butadiene leading to (**235**).



(224) (232) (235)



(233a) $R^1 = R^2 = H$ (234a) $R^1 = R^2 = H$

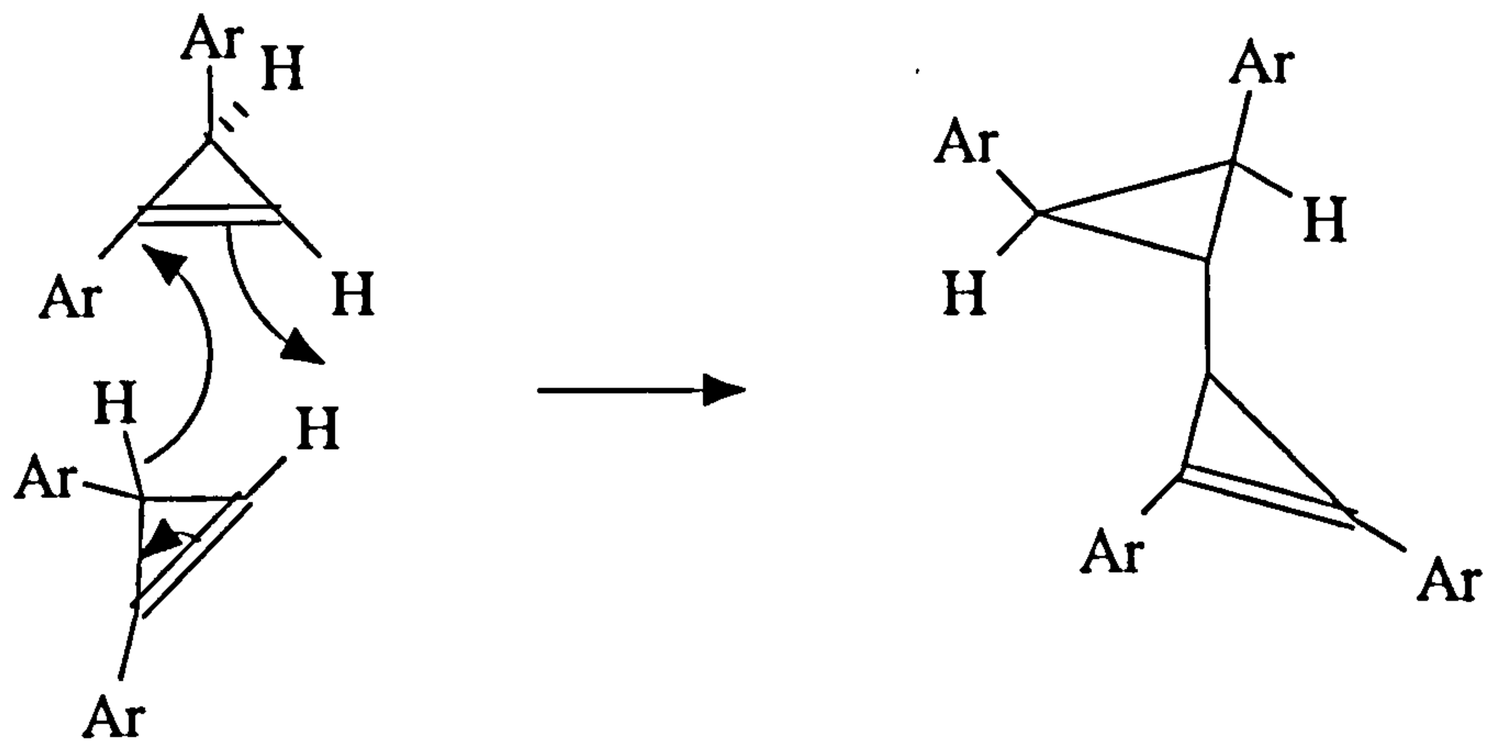
(233b) $R^1 = Me, R^2 = H$

(233c) $R^1 = H, R^2 = Me$

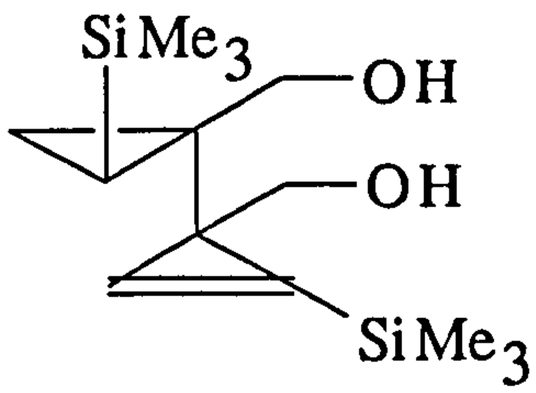
(233d) $R^1 = R^2 = Me$

4.3.4. DIMERIZATION OF THE CYCLOPROPENE ALCOHOL

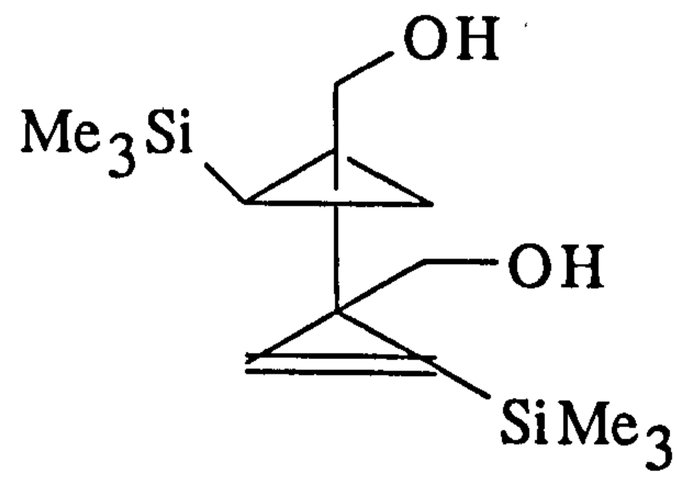
As mentioned previosly, cyclopropenes bearing a hydrogen at C-3 often undergo a ready dimerisation through an ene-type reaction. The dimerisation of 1,3-diaryl cyclopropenes was reported to be highly regioselective and accelerated by electron releasing groups on the benzene rings; the existence of *exo* or *endo* transition states could not, in this case be established with certainly because both would lead to the same product.[116]



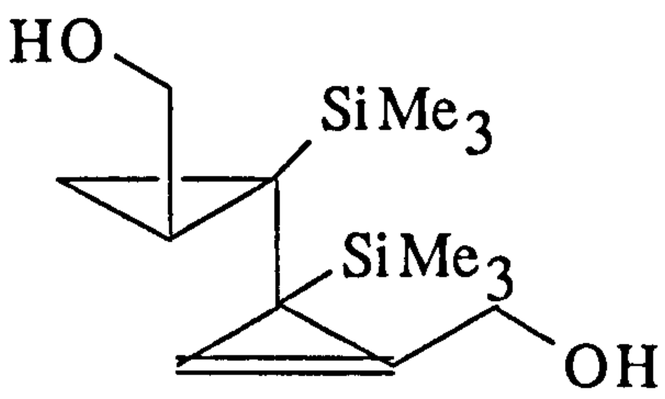
When the cyclopropene alcohol (**229**) was allowed to stand in chloroform at room temperature it slowly dimerized, leading to a crystalline product in 63 % yield. This gave a correct CH analysis for a dimer, and the proton spectrum included an olefinic signal at δ 7.7 integrating to one proton, a one proton doublet at δ 3.45 with coupling constant 10.6 Hz and a multiplet integrating for three protons at δ 3.3-3.4. In addition, three, one hydrogen doublets appeared at δ 0.5, 0.4 and -0.53 with characteristic coupling constants for the cyclopropane protons of a 1,1,2-trisubstituted cyclopropane (J 10.1, 7.8 and 3.7 Hz) together with two singlets for trimethylsilyl groups. The ^{13}C n.m.r spectrum showed eleven signals including two in the alkene region. On the basis of these data, the compound was provisionally characterised as an ene-dimer. In fact, because the cyclopropene (**229**) has two different groups on the double bond, the ene-type dimerisation of this monomer could lead to eight possible structures arising through the *exo*-and *endo*- transition state conformations (each as pairs of enantiomers):



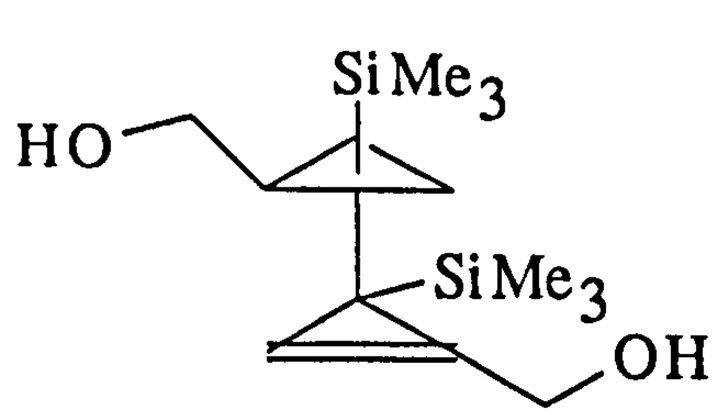
(236a)



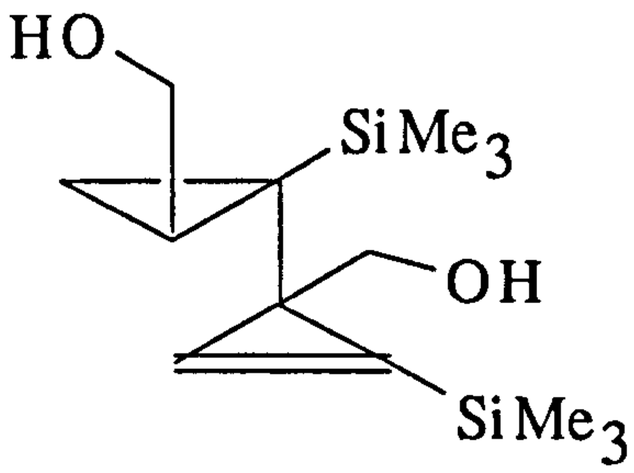
(236b)



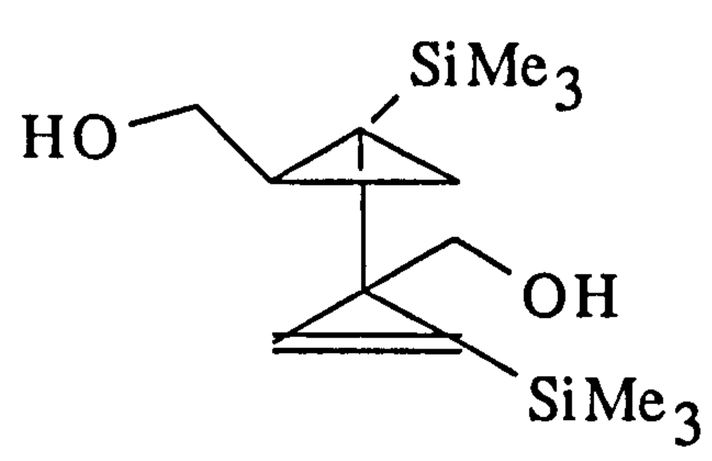
(237a)



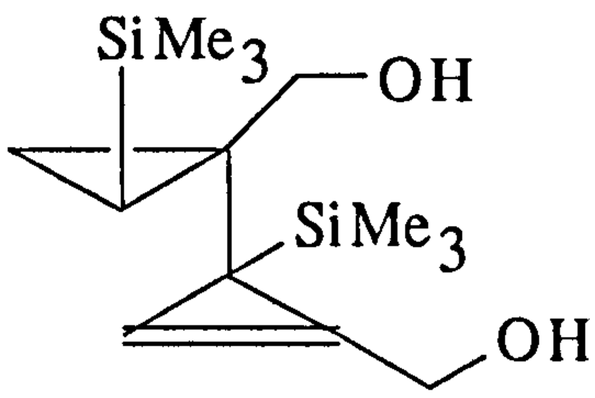
(237b)



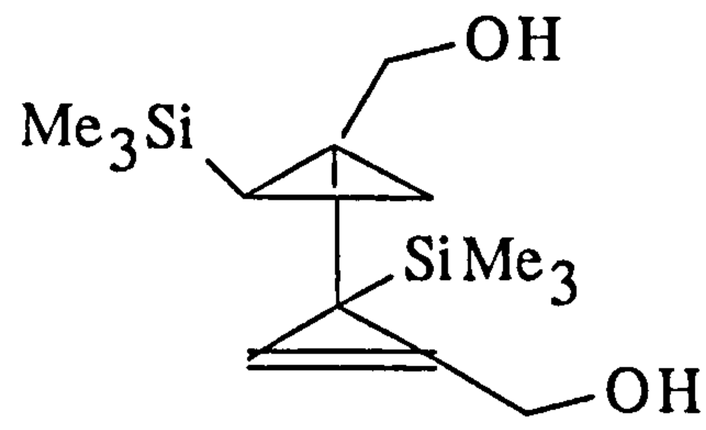
(238a)



(238b)

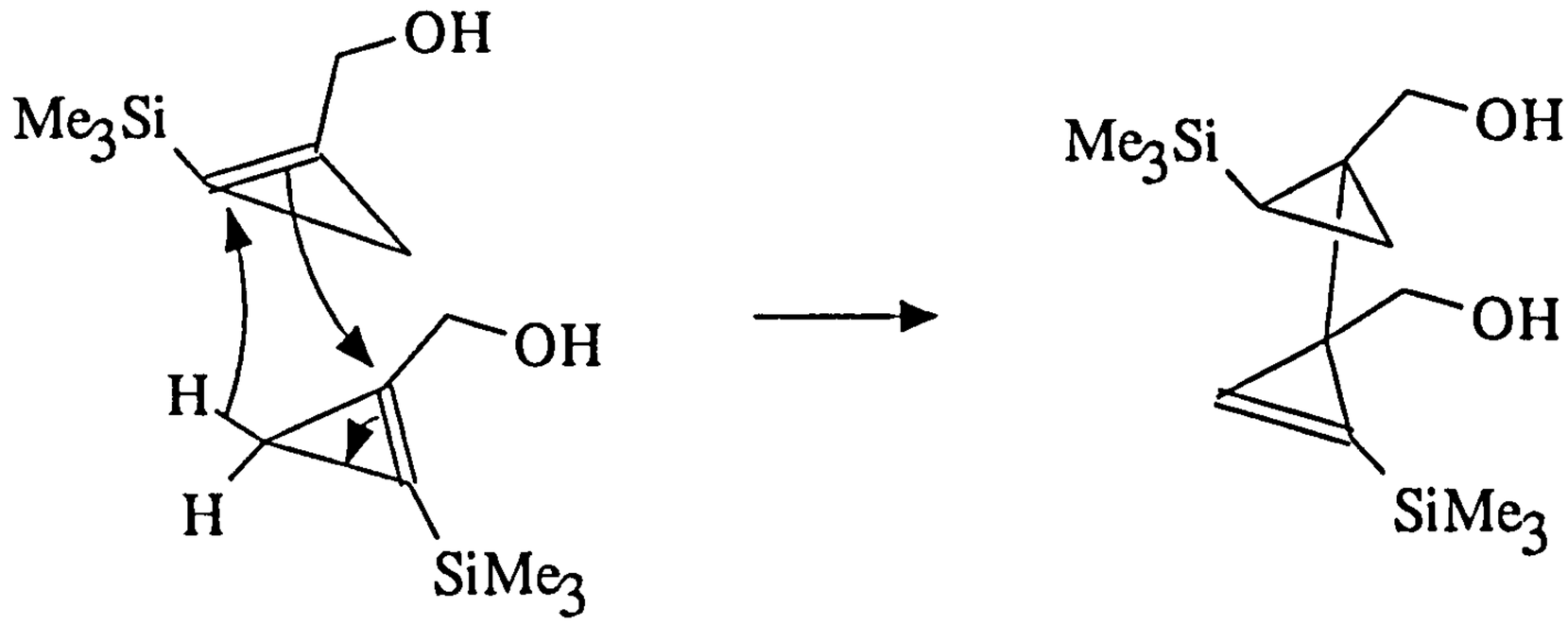


(239a)



(239b)

However, the sterochemistry and the regiochemistry of the product was confirmed by an X-ray crystallography study to be that in (236b) (**Figure 3**) produced from the *endo* - conformation which is normally the less sterically favoured transition state in an ene-type reaction.[117]



(229) (236b)

The regiochemistry of this dimer places both hydroxymethyl group on the carbon-carbon bond which forms, and keeps the large trimethylsilyl group in the less hindered positions- typical of these reaction which are often controlled by steric effects.

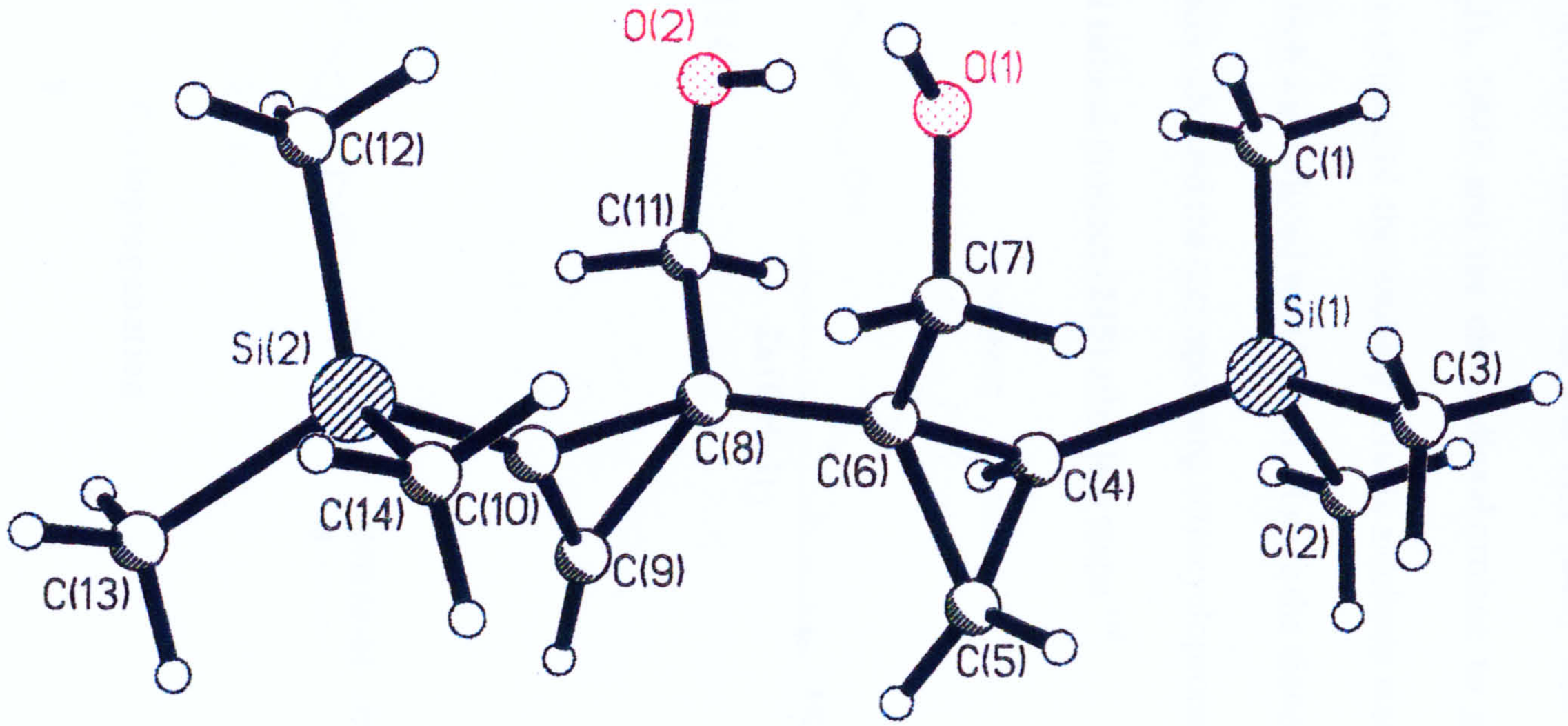
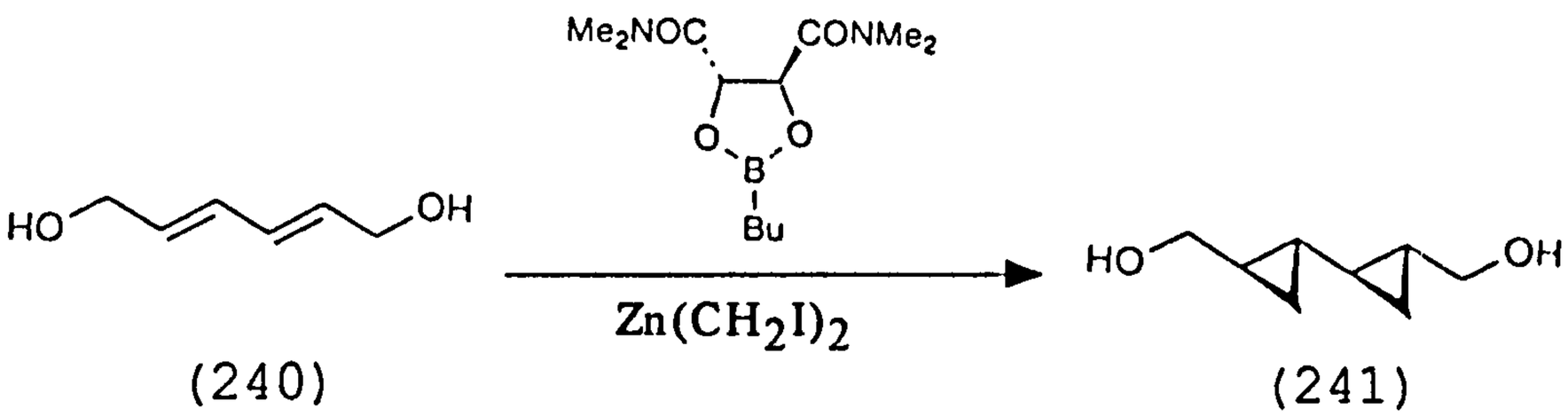


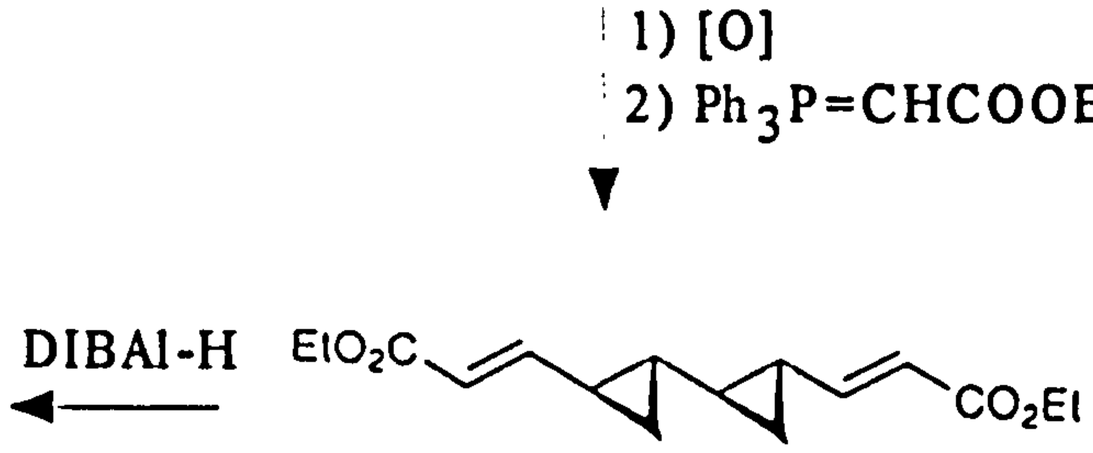
Figure 3. Crystal structure of the dimer (236b)

4.3.5. SYNTHETIC APPROACHES TO POLYCYCLOPROPANE NATURAL PRODUCTS

It was recently reported that the diol (**240**) was cyclopropanated using preformed $Zn(CH_2I)_2$, DMF and the chiral dioxaborolane to give (**241**) in excellent yield. After oxidation of the diol the resulting volatile aldehyde was directly converted in to the diester (**242**) which was reduced with DIBAL-H gave the dienediol (**243**). Double cyclopropanation of the diene afforded the corresponding tetracyclopropane dimethanol (**244**) which leads to the final natural product (**245**) after few steps.[118]



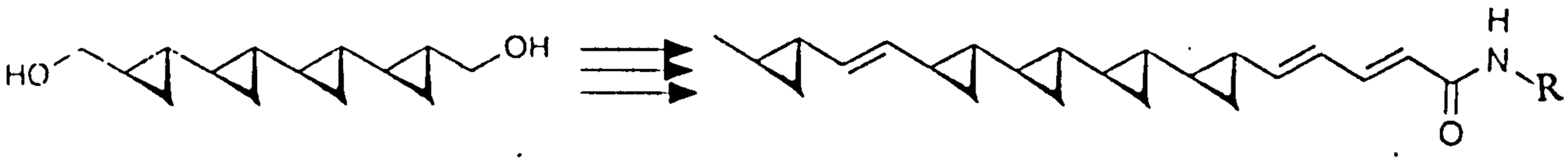
(240) (241)



(242)

(243)

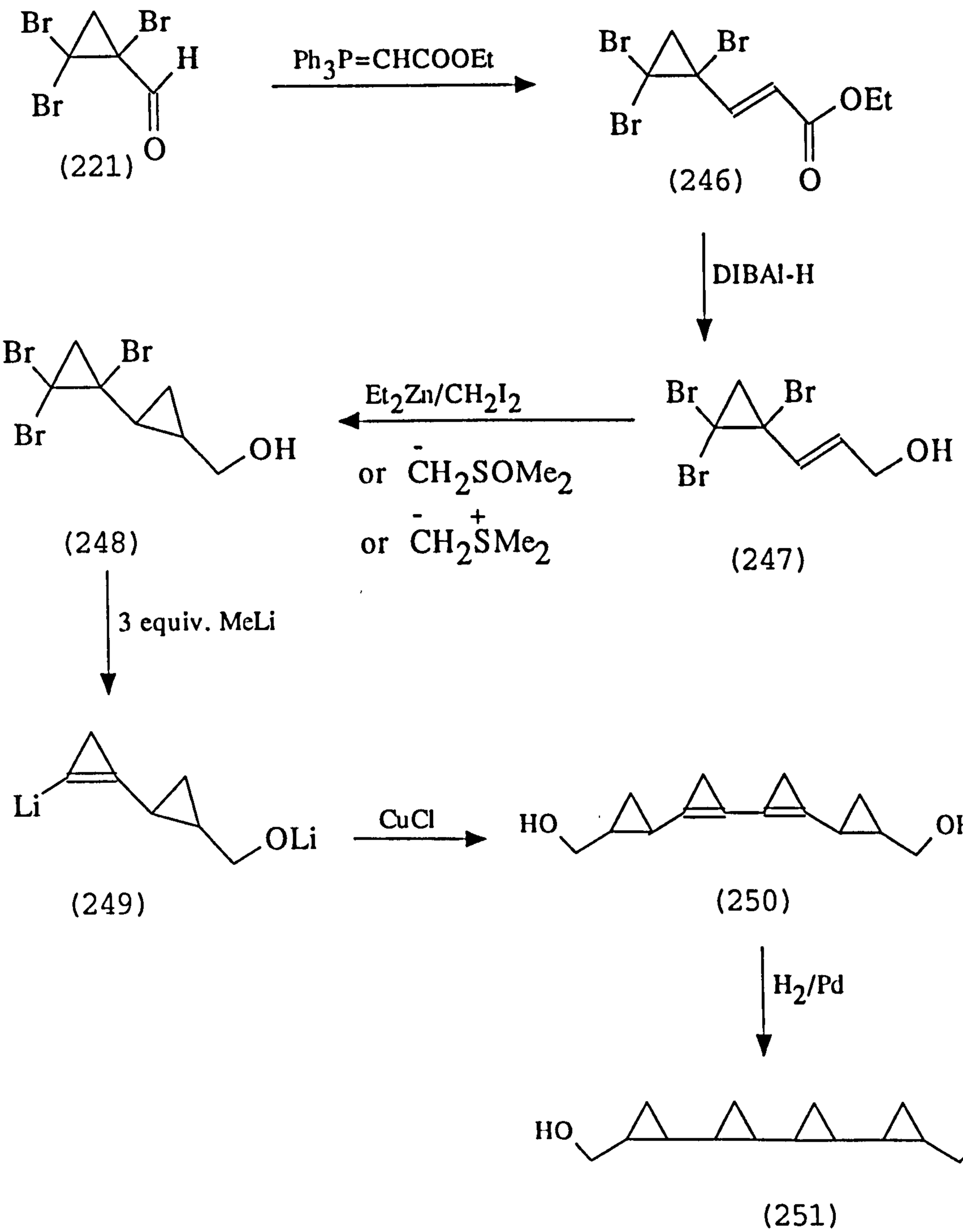
Cyclopropanation



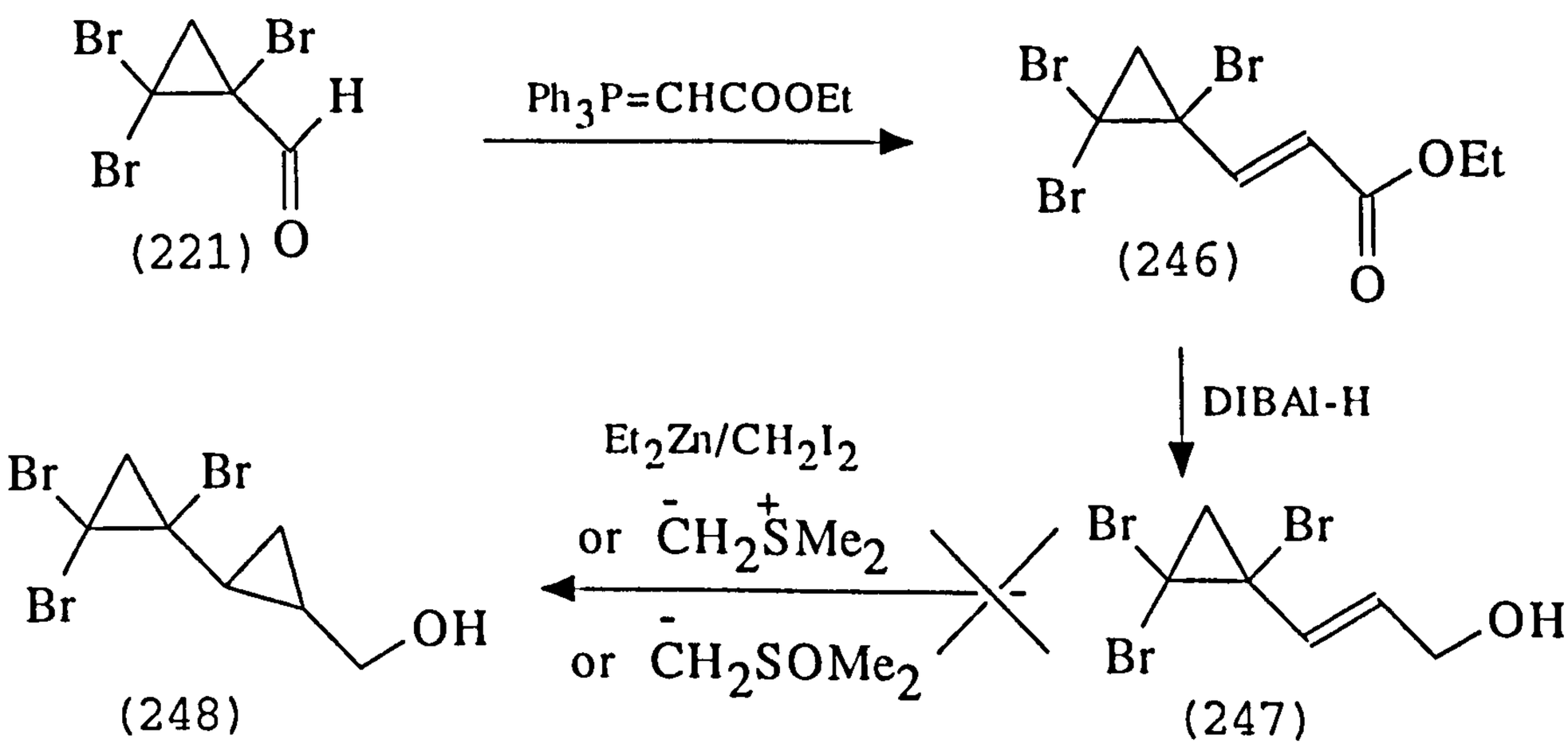
(244) (245)

Interest of the current project was to use the aldehyde (**221**), which could be prepared on large scale as a cheap material to prepare polycyclopropanes such as the natural product (**245**).The scheme for the attempted synthesis of such polycyclopropanes is outlined in (**Figure 4**).

Figure 4



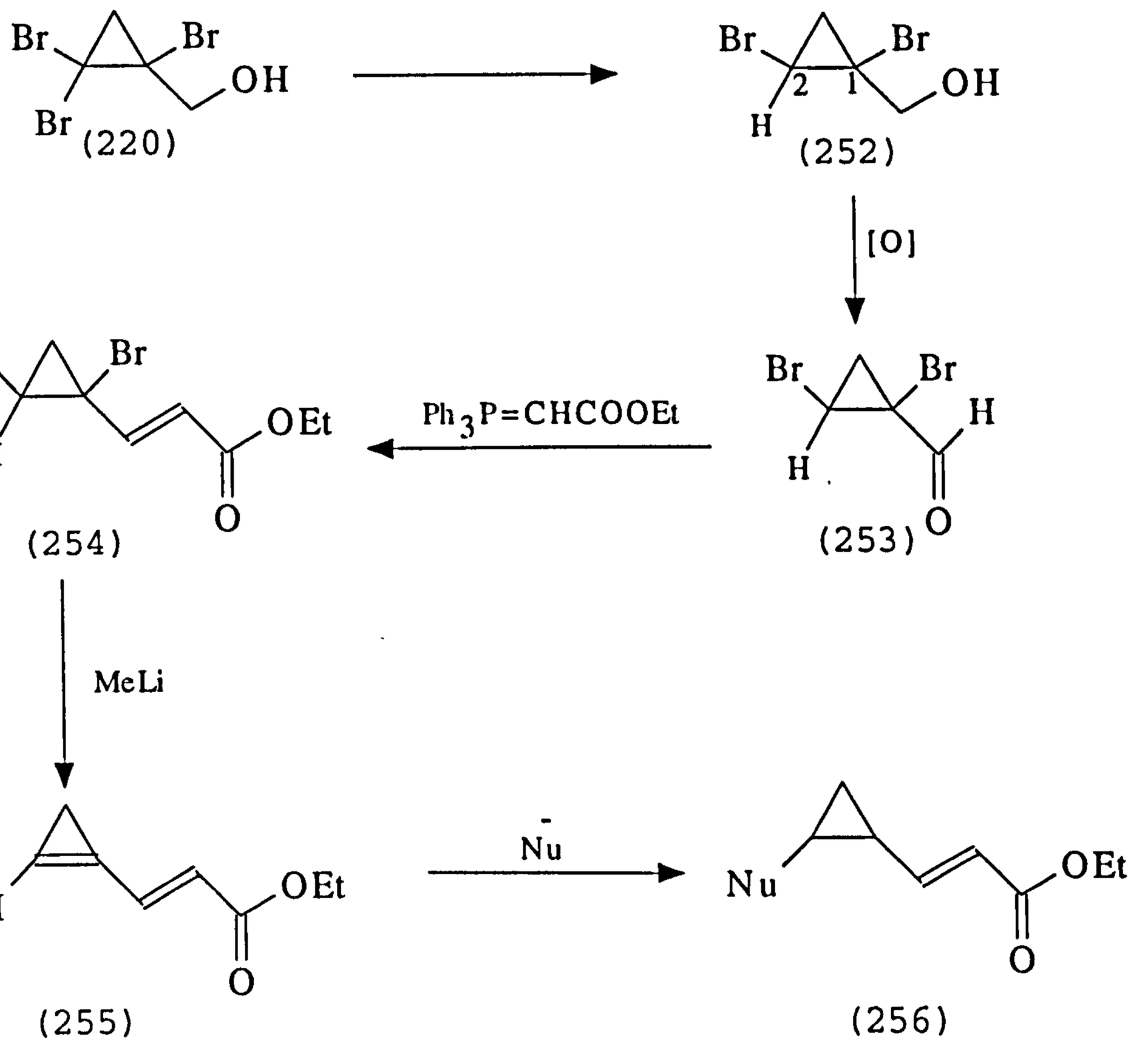
The aldehyde (**221**) was therefore treated with 1.2 equiv. of carboethoxymethylene triphenyl phosphorane producing the α,β-unsaturated ester (**246**) in 91 % yield. The ^{1}H n.m.r spectrum of this showed two doublets in the olefinic region with a coupling constant of 15.0 Hz integrating for two protons, together with a pair of heavily tented doublets at δ 2.3 and 2.2 with a geminal coupling constant of 9.4 Hz for the ring methylene protons, characteristic of the methylene group of a tetrasubstituted cyclopropane. The Wittig product was cleanly converted into the alcohol (**247**) in 91 % yield using DIBAL-H as the reducing agent. In the ^{1}H n.m.r spectrum this showed the methylene group adjacent to the hydroxy group as two doublets at δ 4.28 and 4.21 with a coupling constant of 14.1 Hz, together with a broad singlet at δ 2.5 for the hydroxyl group. The ^{13}C spectrum included two resonances at δ 135 and δ 130 from the double bond with the methylene carbon next to the hydroxyl group appearing at δ 62.0 together with cyclopropane carbons which resonated at δ 41.6, 37 and 32.5. The next step required was to cyclopropanate the double bond using diethylzinc and methylene iodide,[119] or dimethyloxosulfonium methylide [$(CH_3)_2SOCH_2$] or dimethylsulfonium methylide [$(CH_3)_2SCH_2$].[120] However this proved not to be possible, probably due to the steric effect by bromine atoms which affects the reactivity of double



bond.

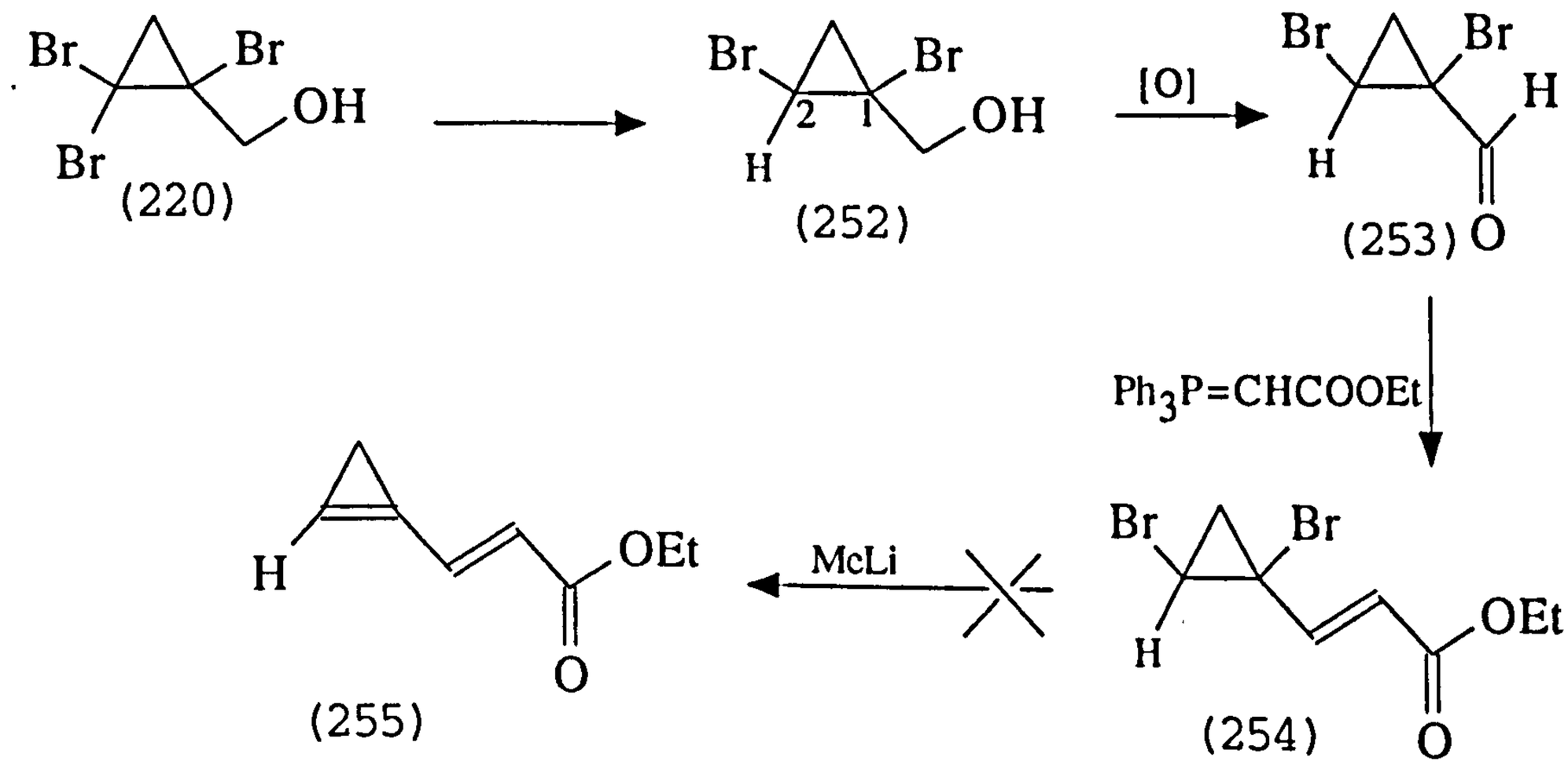
It was therefore proposed to synthesise (**256**) to try reduce the steric effect, by first preparing the cyclopropene (**255**) which is conjugated to the ester group and may be a good acceptor for nucleophilic attack (**Figure 5**).

Figure 5



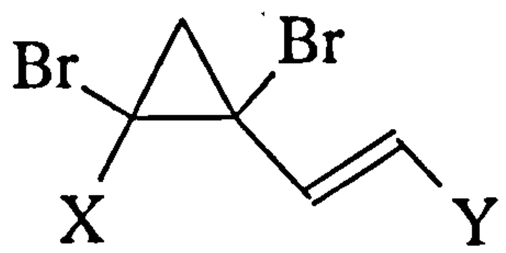
The tribromo-alcohol (**220**) was reduced to a single isomer of the dibromocyclopropane alcohol (**252**) with tributyltinhydride in 10 % yield; when tributyltinhydride was replaced by

hydrogen and palladium in the presence of sodium carbonate the same dibromide (**252**) was obtained in 31 % yield. It is not clear at this point which diastereoisomer was obtained but on the basis of the downfield shift of this hydrogen by 0.4 ppm on oxidation (see below) it is provisionally characterised as the stereoisomer shown. The ^1H n.m.r spectrum of (**252**) showed two doublets (J 12.3 Hz) at δ 3.8 and δ 3.7 for the diastereotopic protons of the methylene group adjacent to the hydroxyl group, and two doublets of doublets at δ 3.0 (J 5.8, 8.1 Hz) and δ 1.3 (J 6.6, 8.1 Hz) integrating for one proton each, the low field for the first proton (C_2-H) being due to deshielding by the bromine atom. In addition there was a broad triplet with coupling constant of 8.1 Hz integrating to one proton. Oxidation of the alcohol (**252**) with PCC gave the corresponding aldehyde (**253**) in 83 % yield, coupling of the aldehyde with carboethoxymethylene triphenylphosphorane then producing the α,β-unsaturated ester (**254**). Reaction of (**254**) with one mol. equiv. of methyllithium failed to generate the cyclopropene (**255**) by dehalogenation, or its trapping product if the reaction was carried out in the presence of DPIBF. This was probably due to the fact that vigorous conditions are required for the dehalogenation of a 1,2-dibromo and therefore competing reaction occurs at the ester group.

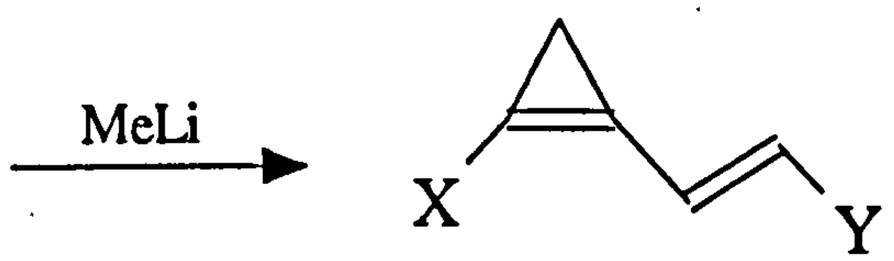


4.3.6. REACTION OF THE VINYL TRIBROMO-ESTER WITH METHYLLITHIUM

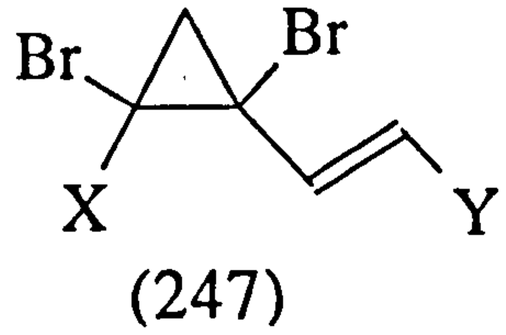
Although the dibromo-ester (**254**) could not be debrominated above, the α,β-unsaturated tribromo ester (**246**) was debrominated with one equivalent of methyllithium at -78 °C, to give bromocyclopropene (**257**) in 87 % yield without attack at ester the group. In the infrared spectrum, the characteristic stretch for the disubstituted cyclopropene double-bond were observed at *ca.* 1794 cm^{-1}, shifted from the more usual position of 1870 cm^{-1} due to the conjugation to the double bond and the ester. The ^{1}H m.n.r spectrum of the compound showed a sharp two proton singlet at ca. δ 1.7 for the cyclopropene methylene group. Two doublets at δ 7.4 and 6.0 ppm integrated for two olefinic protons, the first shifted to low field by 1.4 ppm due to the deshielding effect of the cyclopropene and ester group. In addition there was a quartet and a triplet for the ethyl group. The ^{13}C spectrum showed the expected eight signals including the cyclopropene double bond which resonated at δ 112.7 and 105.4 ppm. The cyclopropene (**257**) decomposed to a complex mixture in $CDCl_3$ at ambient temperature; *ca.* 50 % remained after 18 h. The cyclopropene was trapped with DPIBF by [4+2]-cycloaddition to give one isomer (**260**), which showed two characteristic doublets resonated at δ 3.0 and 2.1 ppm with coupling constant 6.4 Hz for the two protons attached to the cyclopropyl ring, as well as two doublets for the alkene protons together with a quartet and triplet for ethyl group and a complex multiplet in the aromatic region for the protons on the phenyl rings. The stereochemistry of the adduct was assigned by analogy with related adducts of 3,3-unsubsituted cyclopropenes with DPIBF and supported by the large chemical shift difference between the cyclopropane hydrogens (0.9 ppm).[101]



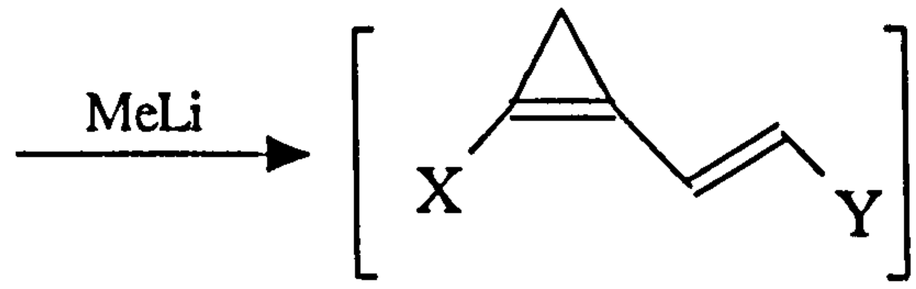
(246)



(257) X = Br, Y = COOEt

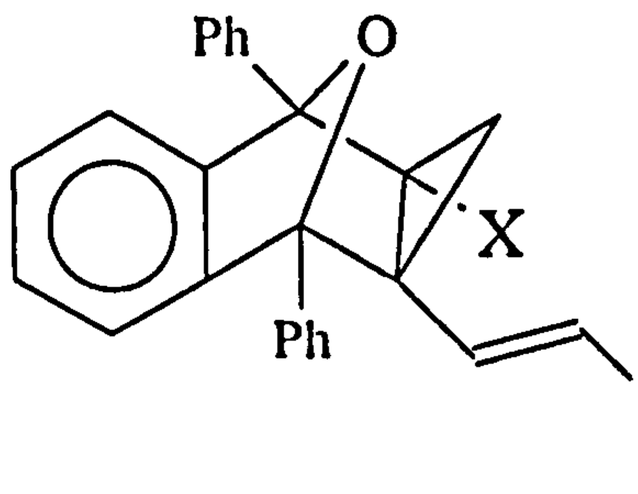


(247)



(258) X = Br, Y = CH_2OH

(259) X = H, Y = CH_2OH



(260) X = Br, Y = COOEt

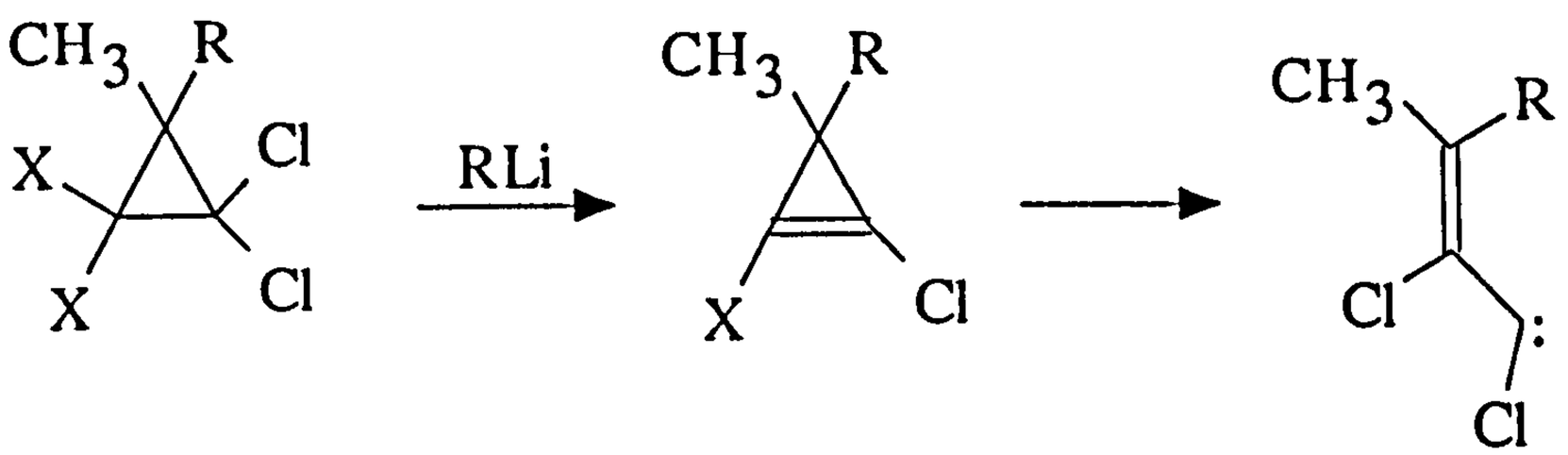
(261) X = Br, Y = CH_2OH

(262) X = H, Y = CH_2OH

In the same way, reaction of (247) with two or three mol. equiv. of methyllithium at -78 °C gave the cyclopropenes (258) and (259) respectively. Compounds (258) and (259) could be trapped by [4+2]-cyclodddition to DPIBF leading to a single product in each case, (261) (80 %) and (262) (40 %) respectively. Again the stereochemistry was assigned as *exo*, supported by the large chemical shift difference between the cyclopropane hydrogens in each case.[101]

4.3.7. REACTION OF DIELS-ALDER ADDUCTS OF 1-BROMO-2-BROMOMETHYL CYCLOPROPENE AND FURANS WITH BUTYLLITHIUM

Although dehydrohalogenation and dehalosilylation of monohalocyclopropanes are the methods most used to produce strained cyclopropenes,[45] a 1,2-elimination of two halogens in di-and tetrahalocyclopropanes also provides a good synthetic path to cyclopropenes and 1,2-dihalocyclopropenes.[34,35]



X = Cl, R = Me, CH_2Cl, CH_2OMe, CH_2Ph

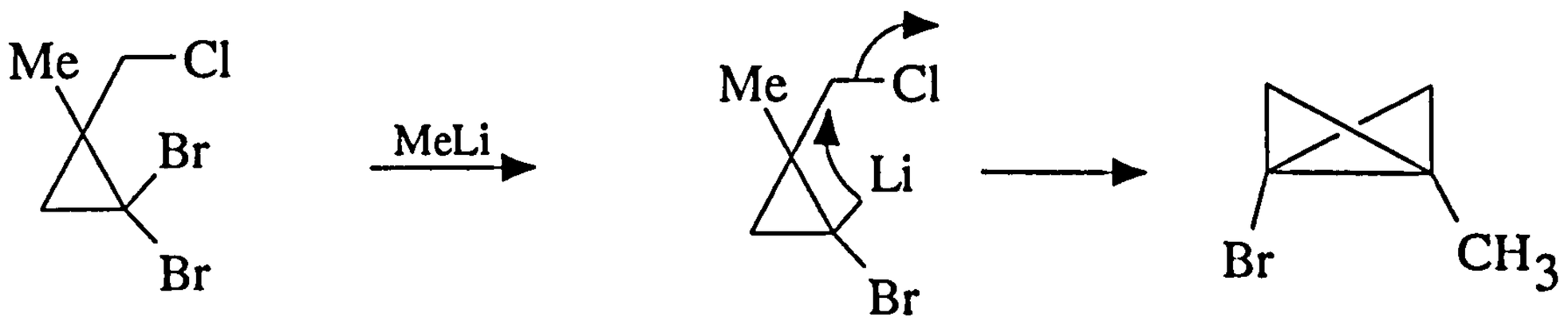
X = Br, R = CH_3

The ring opening of these 1,2-dihalocyclopropenes occurs at room temperature or less to give vinyl- carbenes which can be trapped by intra- or intermolecular processes.

1,1-Dehalogenation, or α-elimination of geminal dihalocyclopropanes is also a very important reaction which generates the carbenoids cyclopropylidenes, which undergo rearrangment to allenes or can be trapped by intramolecular reaction.[45]

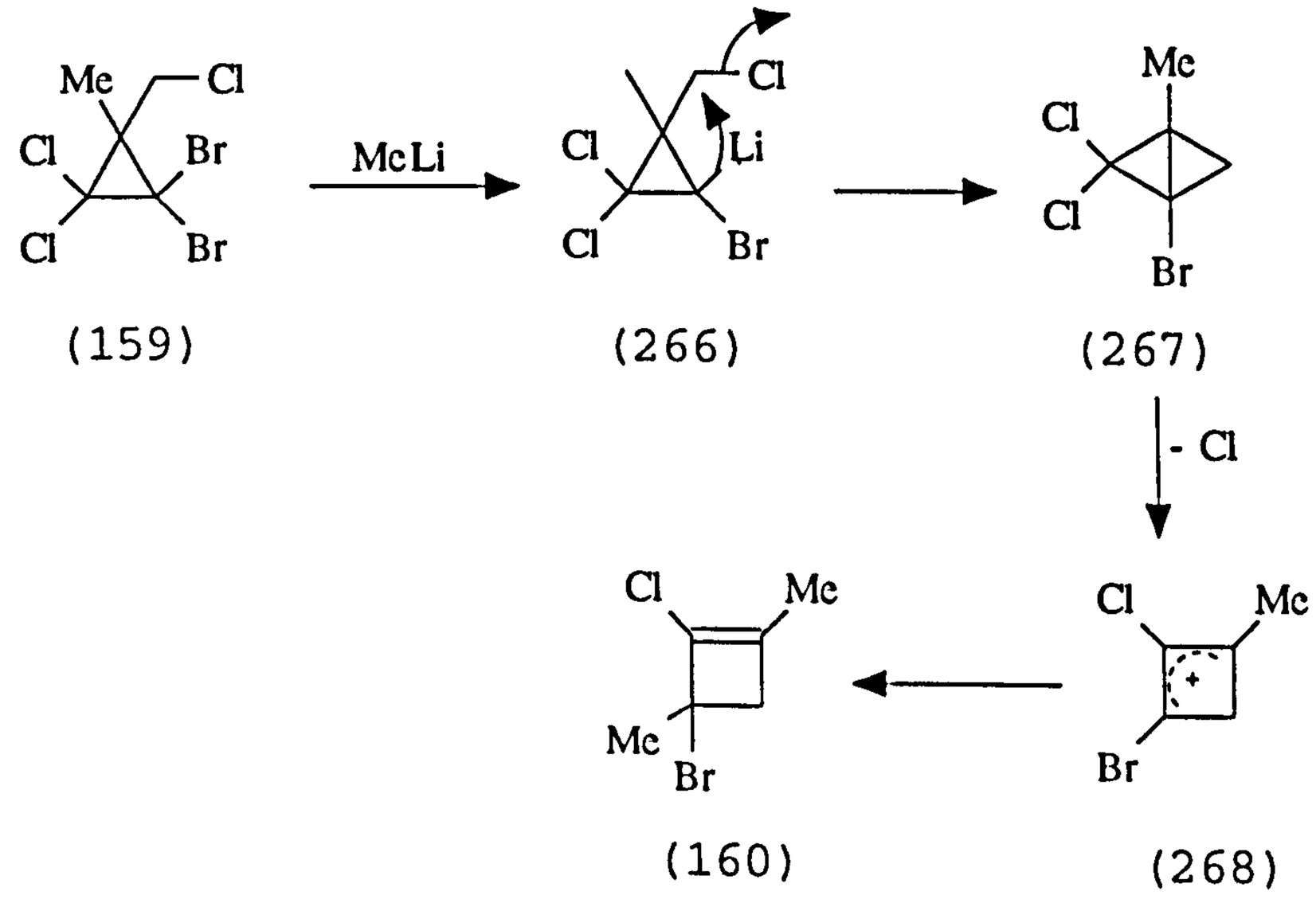
Aside from 1,1-and 1,2-eliminations, a few examples of 1,3-elimination have been reported. All types of 1,n-elimination reactions involve the same mechanistic sequence. In the first step, a halogen metal exchange takes place followed by a 1,n-elimination (n = 1, 2, 3 etc) step. It was reported some years ago that the reaction of 1,1-dibromo-2-chloromethyl-2-

methylcyclopropane (**263**) with methyllithium leads to the formation of bicyclo[1.1.0]butane (**265**) as a major product.[121] The bicyclobutane is obtained by lithium-halogen exchange to give (**264**) followed by intramolecular displacement of chlorine through 1,3-elimination.



(263) (264) (265)

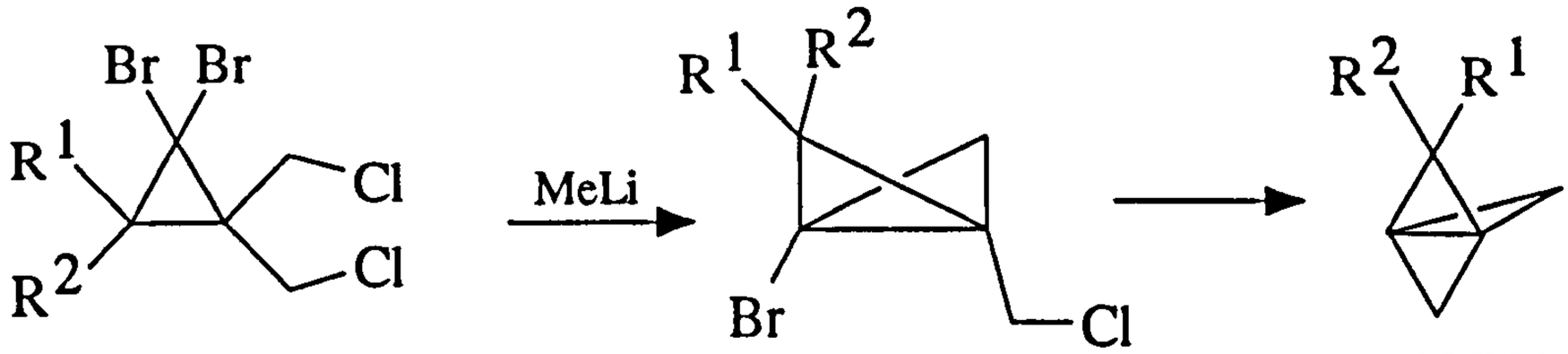
Moreover, Baird and Al-Dulayymi found that, when the pentahalocyclopropane (**159**) was reacted with two mol. equiv. of methyllithium a cyclobutene (**160**) was obtained[86] which is again most reasonably explained in terms of an initial lithium-halogen exchange to give the intermediate (**266**) followed by intramolecular displacement of chloride through 1,3-elimination to give the bicyclo[1.1.0]butane (**267**); ready loss of chloride ion to produce (**268**), and regioselective trapping by excess methyllithium could then lead to the cyclobutene (**160**).



(159) (266) (267)

(160) (268)

These reactions have been widely used in the preparation of highly strained propellanes by bridging of the bicyclobutane 1,3-position. Recently Szeimies and co-workers[122] found that when the cyclopropane (**269**) were treated with two mol. equivalents of methyllithium the propellanes (**270**) were isolated through the bicyclo[1.1.0]butane, in a one pot reaction.

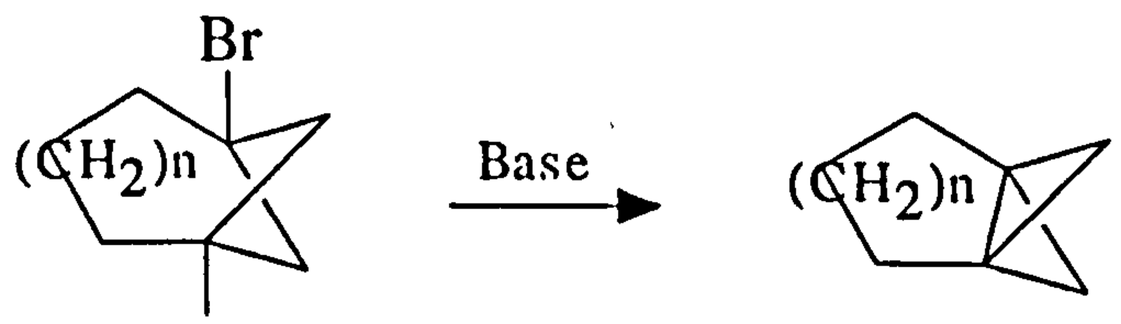


(269) (270)

$R^1 = H, R^2 = H$

$R^1 = H, R^2 = C_2H_5, C_3H_7$

The parent [2.1.1] and [3.1.1] propellanes (**271**, n = 0, 1, 2) have been generated by dehalogenation of the corresponding 1,4-dihalobicyclo[2.1.1]hexane and 1,5-dihalobicyclo[3.1.1]heptane respectively.[123,124] Although the former compound is detectable in a nitrogen matrix at low temperature, and the latter can be detected even at somewhat higher temperature, neither compound is long-lived at ambient temperature.



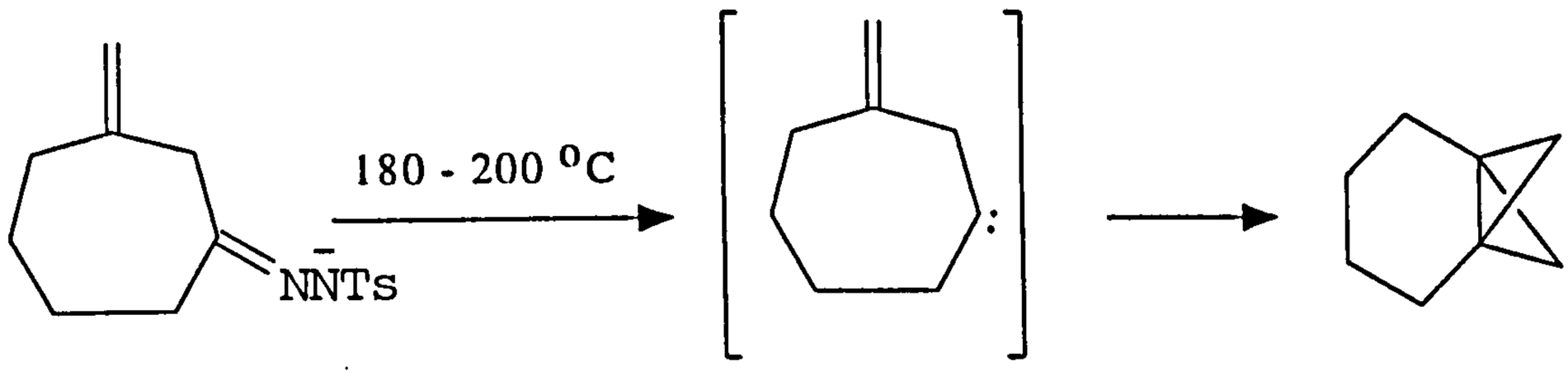
Br

(271)

n = 0, 1, 2

The corresponding [4.1.1] propellane (**271**, n = 2) has been also obtained by intramolecular

addition of a carbene to an alkene and is stable enough to detect at ambient temperature. [125] Thus pyrolysis at 180 to 200 °C of the dry sodium salt of tosylhydrazone derivatives (**272**) caused an evolution of nitrogen to give the carbene (**273**) which was trapped by the double bond to give the propellane (**271**, n = 2) as a mixture with 3-methylenecycloheptene (**274**) and 4-methylenecycloheptene (**275**).



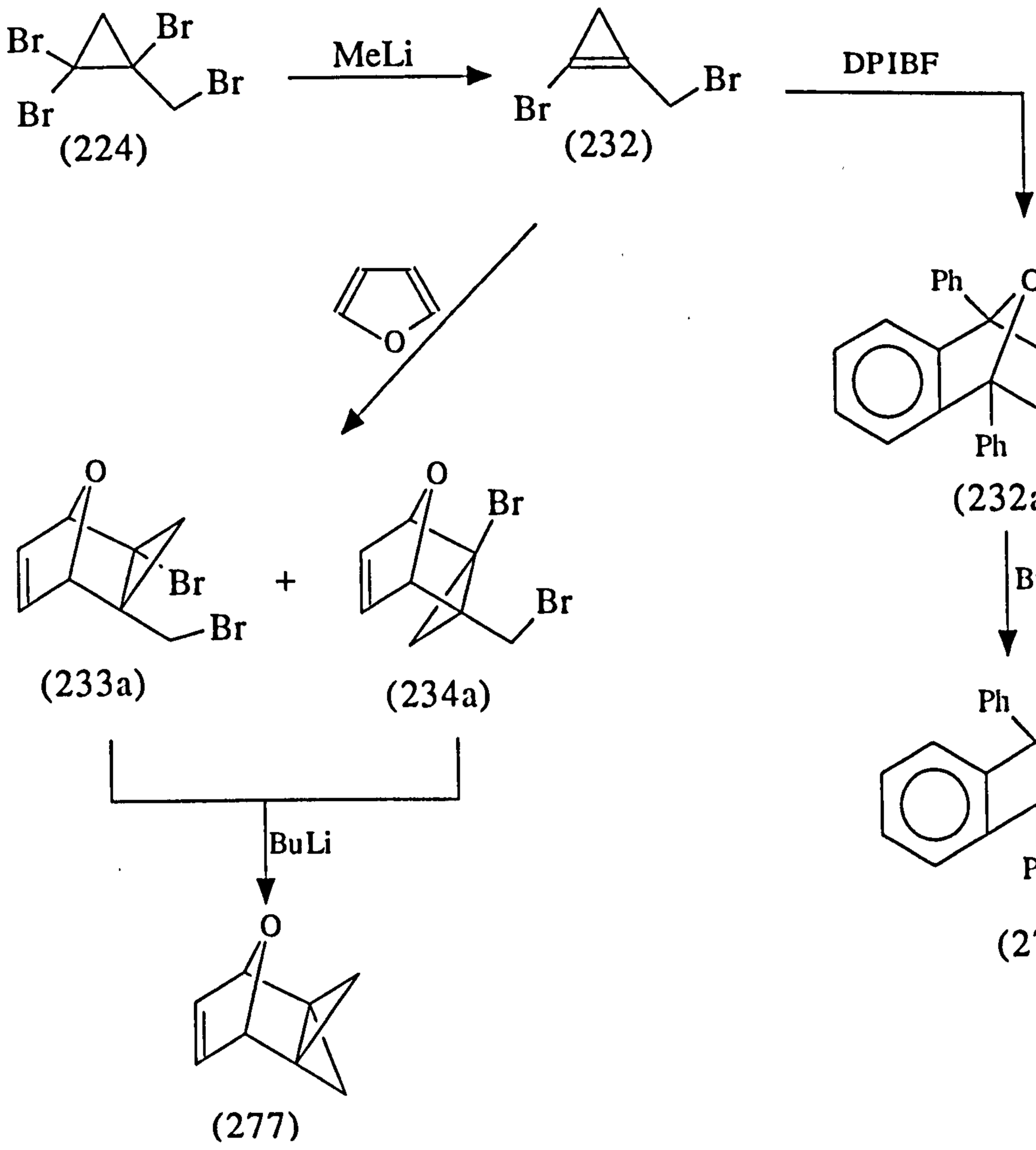
(272) (273) (271)

(275) (274)

Although there are now many examples of related tricyclics in which the methylene carbons of the cyclobutane ring are bridged by a third ring, other examples of propellanes with the cyclobutane methylene positions unsubstituted are relatively uncommon.

As mentioned previously, the reaction of 1,1,2-tribromo-2-bromomethylcyclopropane (**224**) with one mole. equiv. of methyllithium led to 1-bromo-2-bromomethylcyclopropene (**232**), which was be trapped in good yield by reaction with dienes, e.g. as the adducts (**232a**) and (**233a**), (**234a**). Although these adducts appear to be unreactive towards methylithium, they

do react with one mol. equiv. of butyllithium in hexane at -78 to 0 °C.



When the adduct (**232a**) was treated with 1.1 mol. equiv. of butyllithium at -78 °C, and then the reaction was allowed to reach 0 °C before quenching with water at -40 °C, the product was 2,5-diphenyl-3,4-benzo-2,5-epoxy tricyclo[4.1.1.$0^{1,6}$]octane (**276**) in 76 % yield. This showed an accurate mass for $C_{24}H_{18}$, while the ^1H n.m.r spectrum included four discrete bicyclobutane hydrogens, two doublets of doublets at δ 3.5 (J 7.5, 2.9 Hz) and 1.8 (J 7.5, 4 Hz) and two narrow doublets at δ 2.0 (J 4.0 Hz) and 1.86 (J 2.9 Hz). The proton at δ 3.5

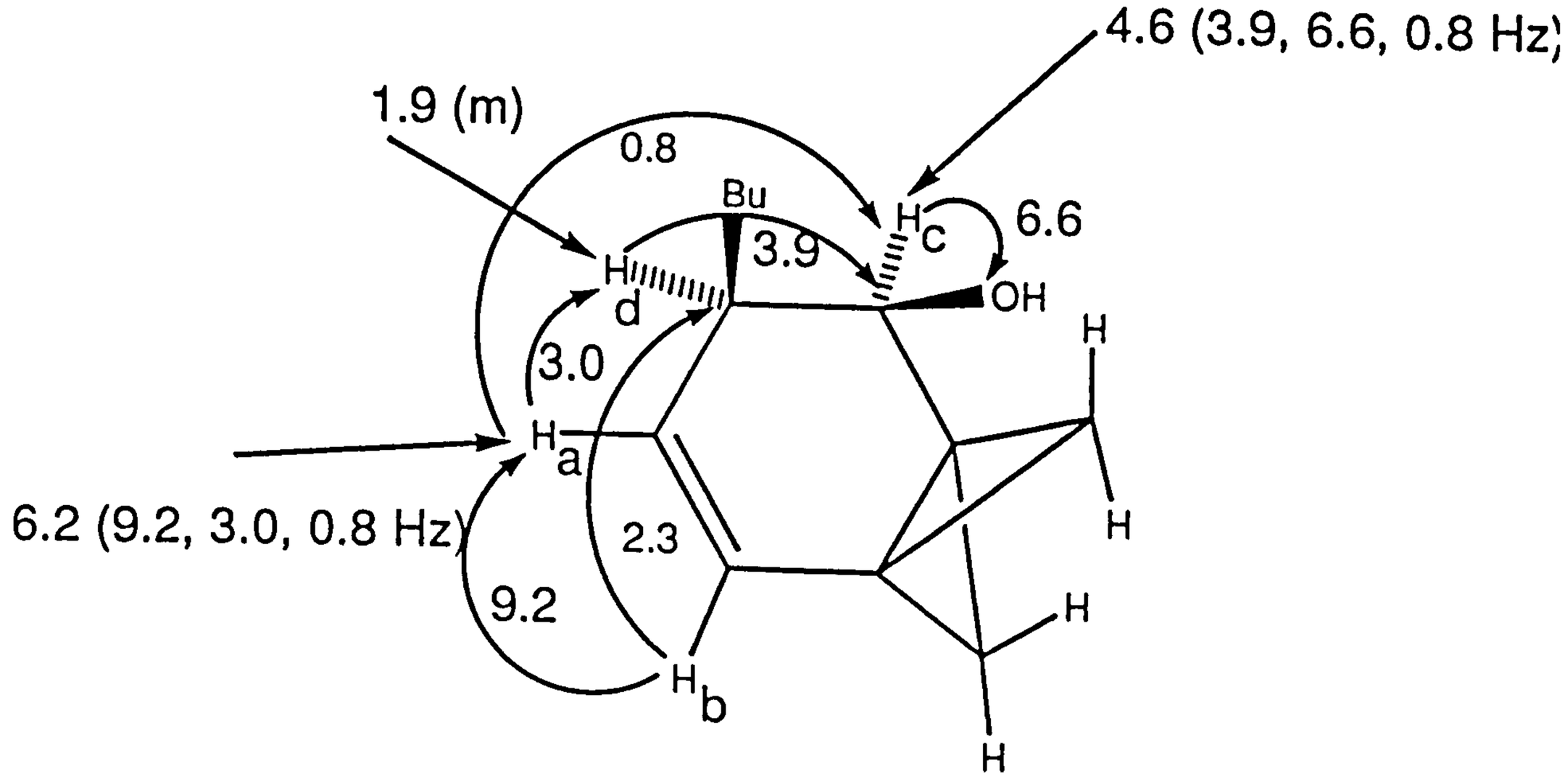
appeared downfield compared to the others probably due to deshielding by the ether group. Compound (**276**) was stable to reaction with a second mol. equivalent butyllithium.

The mixture of adducts (**233a**) and (**234a**) underwent similar elimination, leading to (**277**), on treatment with one mol. eqiuv. of butyllithium. The ^{1}H n.m.r spectrum of (**277**) showed a broad singlet at δ 6.1 for the vinylic protons, while the bridghead protons appeared as a broad singlet at δ 4.8 ppm. The bicyclobutane hydrogens showed two doublets of doublets with coupling constants of 7.7, 3.7 and 2.7 Hz, at δ 3.2 and 2.7 together with two doublets at δ 1.8 and 1.6 with coupling constant 3.7 and 2.7 Hz respectively. Moreover, in this case when the reaction was repeated with two mole. equiv. of butyllithium at -78 °C under nitrogen, and the reaction was allowed to reach 10 °C before quenching with water at -40 °C, an alcohol (**278**) was isolated as a thick yellow oil in 94 % yield.

(233a) (234a) (279) (278)

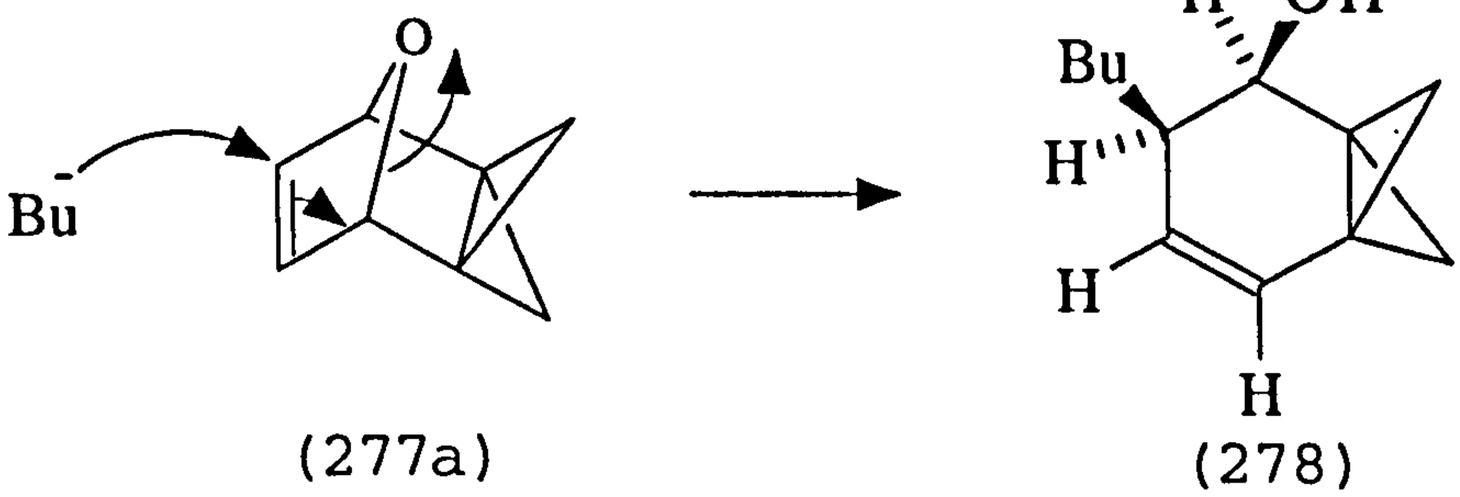
The product gave a correct mass measurment for $C_{12}H_{18}O$ and its i.r spectrum displayed a broad band at 3428 cm^{-1} assigned to the hydroxyl group, while the ^{13}C n.m.r spectrum showed twelve signals including two in the alkene region resonating at δ 131.67 and 126.24 and one signal at δ 66.12 due to the carbon next to the hydroxyl group. The ^{13}C DEPT spectrum showed five CH_2 signals at δ 41.28, 39.86, 31.9, 31.2 and 27.05 together with four signals for CH carbons and two quaternary signals. The ^1H n.m.r spectrum included a doublet of doublets of doublets at δ 6.2 with coupling constants of 9.2, 3.0, and 0.8 Hz, integrating for one proton (H_a) (**Figure 6**). A double of doublets with coupling constants of 9.2, 2.3 Hz resonated at δ 5.5 (H_b), with a doublet of doublets of doublets at δ 4.6 with coupling constant 3.9, 6.6, 0.8 Hz which reduced to a broad doublet (J 3.8 Hz) on shaking with D_2O (H_c). Two of the bicyclobutane hydrogens resonated at δ 2.0 and 1.8 and appeared as doublets of doublets with coupling constants of 1.6, 6.8 and 2.3, 6.8 Hz respectively. The third and fourth protons were obscured by the butyl group. A multiplet resonated at δ 1.9 integrating for one proton (H_d) see (**Figure 6**).

Figure 6

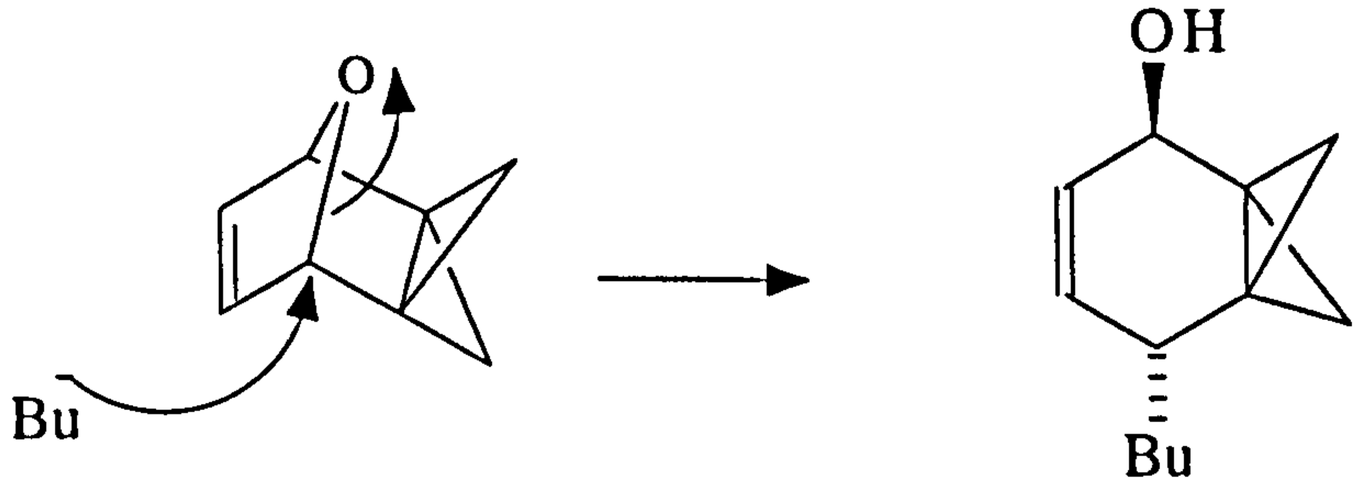


Irradiation of the signal at δ 1.98 reduced those at 6.2, 5.5 and 4.6 to doublets or broad doublets. The stereochemistry of the product was not absolutely clear on the basis of the 3.9 Hz coupling between H_c and H_d, but this is more consistent with a *cis*-relationship. Moreover, on the basis of the data it was not possible to exclude completely an alternative structure (**279**). It was therefore interesting to establish the structure completely by X-ray crystallography; unfortunately it was very difficult to prepare a crystalline derivative. Attempted oxidation of the product with PCC gave a complicated mixture, and converstion of the alcohol to an ester group using 3,5-dinitrobenzoyl chloride was very slow, leading to ring opening of the bicyclobutane. Reaction with bromine also was unsuccessful.

A reasonable explanation of the formation of the product may involve attack of the butyl anion at the double bond (**277a**) with opening of the furan ring to give (**278**) or by attacking at the bridge carbon (**277b**) and ring opening of the furan ring leading to (**279**).

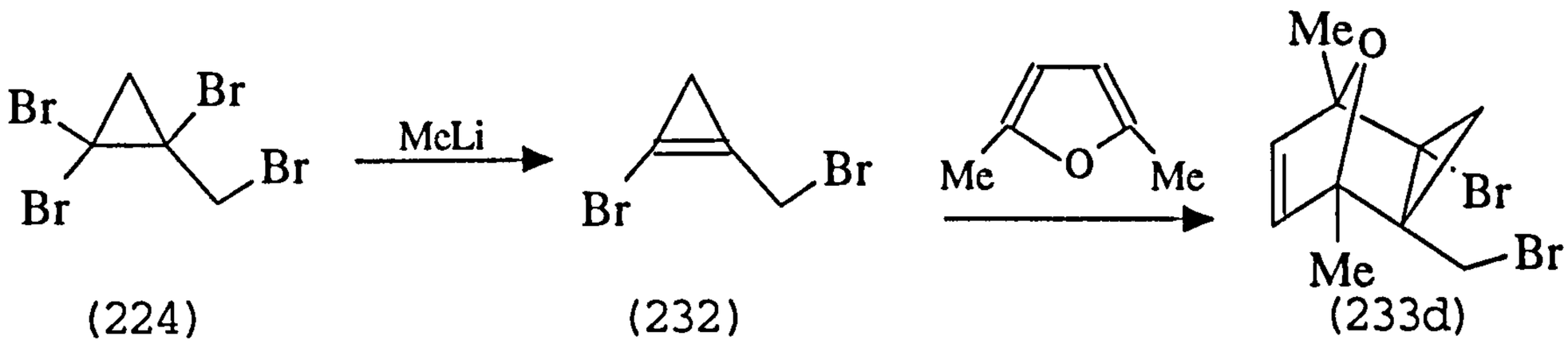


(277a) (278)

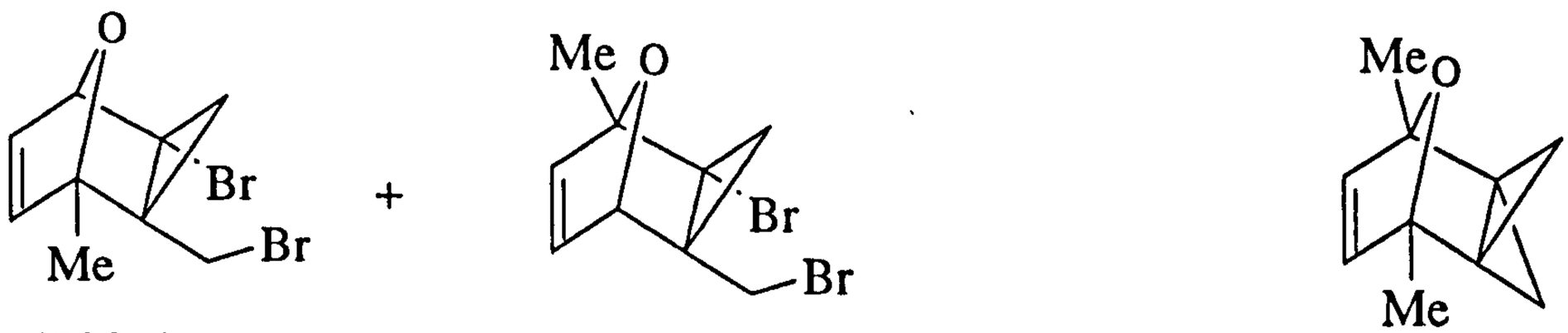


(277b) (279)

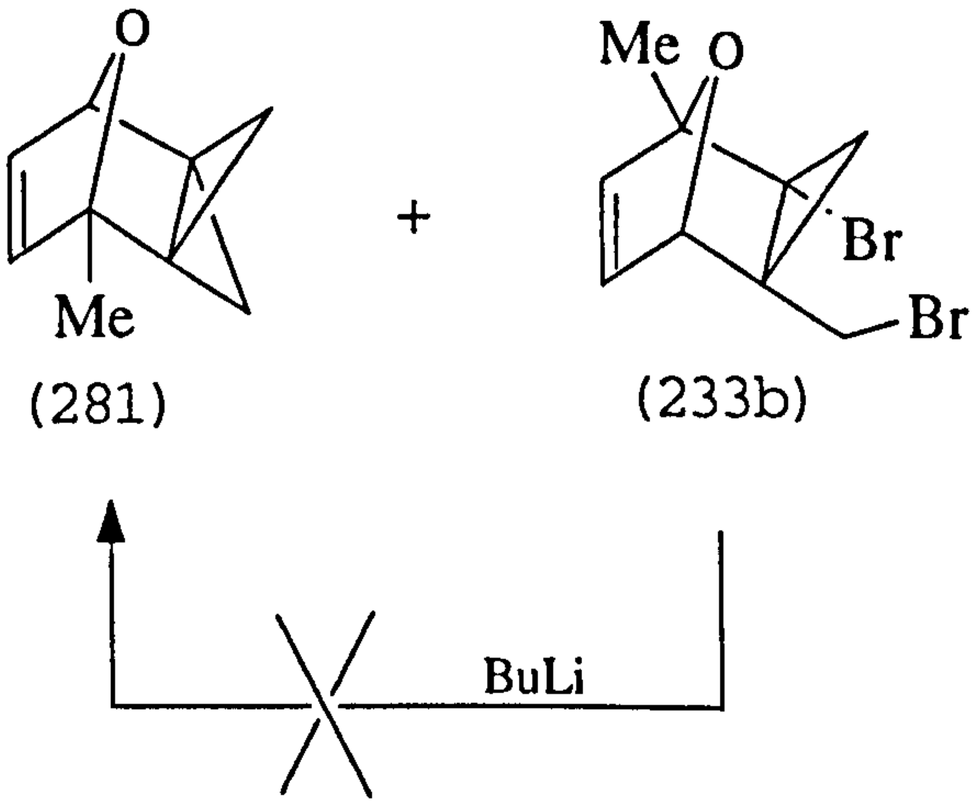
In order to establish the structure, the cyclopropene (**232**) was trapped by [4+2]-cycloaddition with 2,5-dimethylfuran leading to a single product (**233d**); this proved to be unreactive with butyllithium and did not give (**280**), probably due to the steric effect of methyl groups. Therefore the cyclopropene (**232**) was also trapped with 2-methylfuran to give an *ca.* 2.2:1 mixture of the regioisomeric adduct (**233b**) and (**233c**).



(224) (232) (233d)

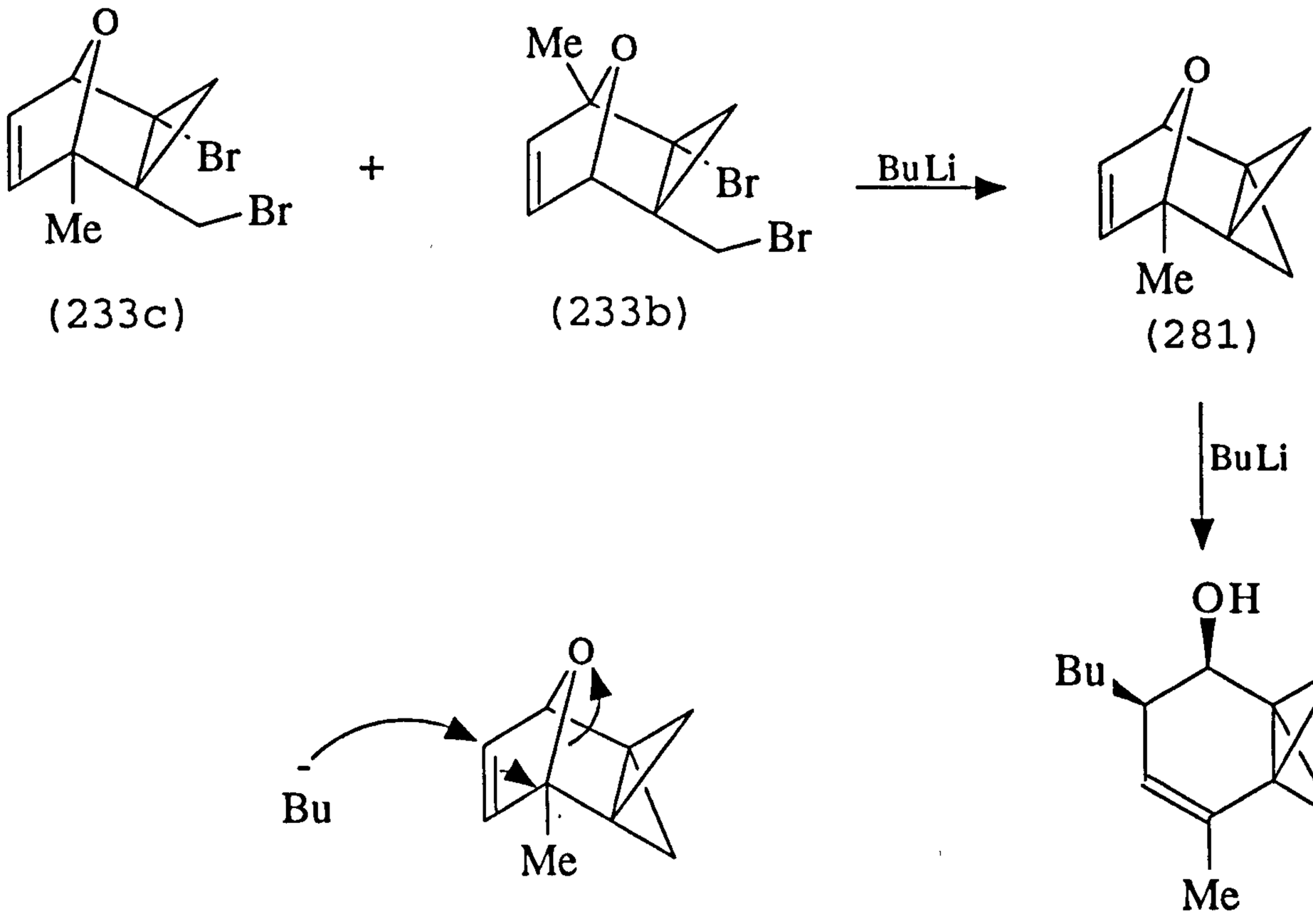


(233c) (233b) (280)



(281) (233b)

Treatment of the mixture with one mol. equiv. of butyllithium at -78 °C to 0 °C, then quenching with water at -40 °C, followed by flash distillation of the product gave (**281**), resulting from the reaction of the minor isomer probably (**233c**), with butyllithium. The major isomer (**233b**) remained unreacted under these conditions. The product (**281**) showed a doublet of doublets for one of the vinylic protons at δ 6.1 with coupling constants of 1.6 and 5.4 Hz. The second vinylic proton appeared as a doublet (J 5.4 Hz) at δ 6.0, the bridge proton as a doublet (J 1.6 Hz), while the bicyclobutane hydrogens appeared at the same chemical shifts as in (**277**), together with methyl group at δ 1.5. When the recovered starting material, which was only the major isomer, was treated with one mol. equiv. of butyllithium, no reaction occurred and only starting material was isolated. However, when the mixture of (**233b**) and (**233c**) was treated with two mol. equiv. of butyllithium at -78 to 10 °C, the alcohol (**282**) was then isolated. These reactions involve lithium-bromine exchange followed by or concerted with 1,3-elimination, to produce the propellane (**281**), which reacts further with butyllithium acting as nucleophile by attacking as in (**283**) leading to (**282**) and this could be clearly distinguished from the product of possible attack at the other positions, since it showed just one alkene hydrogen (a broad singlet) in its ^{1}H n.m.r spectrum.



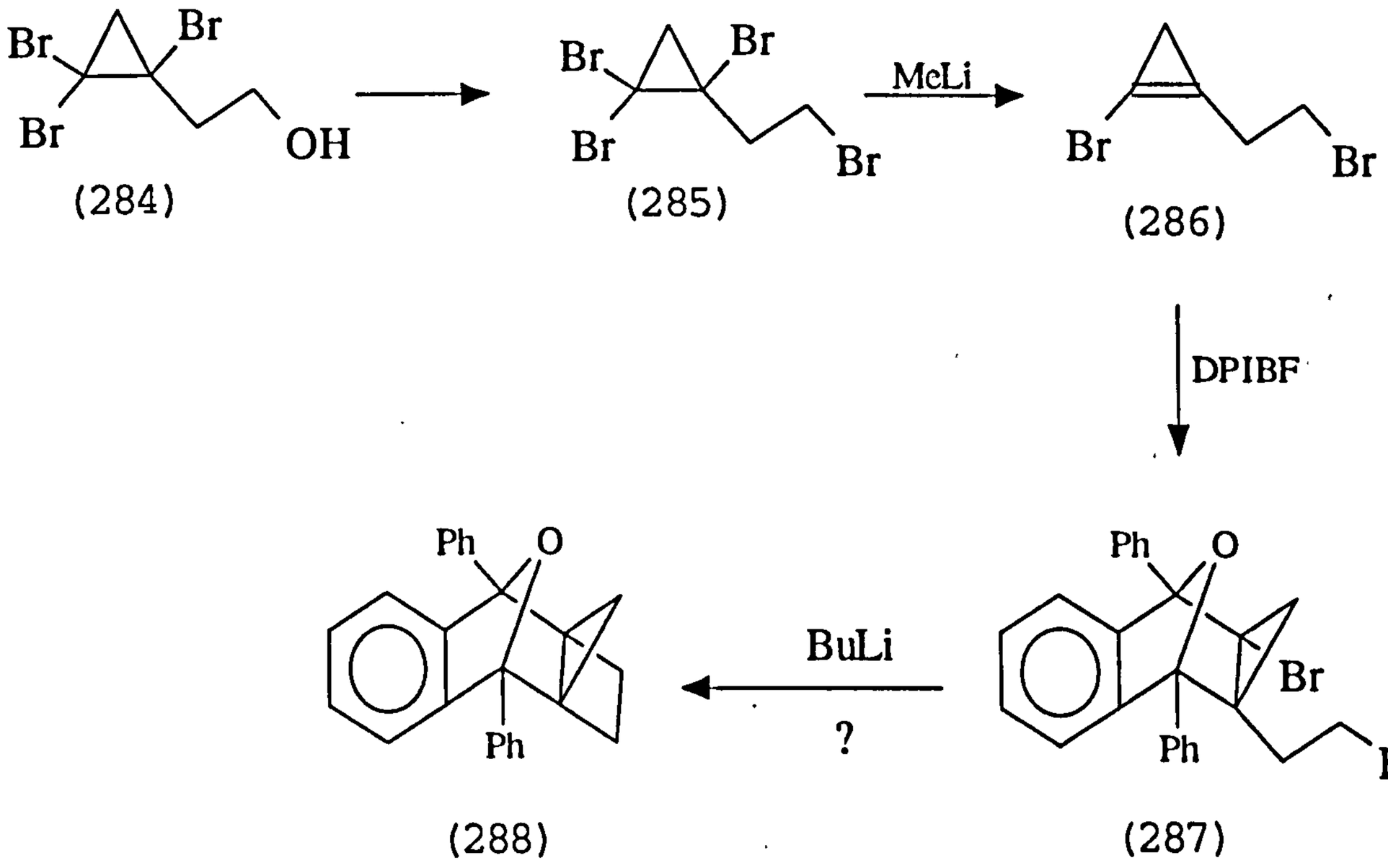
(233c) (233b) (281)

(283) (282)

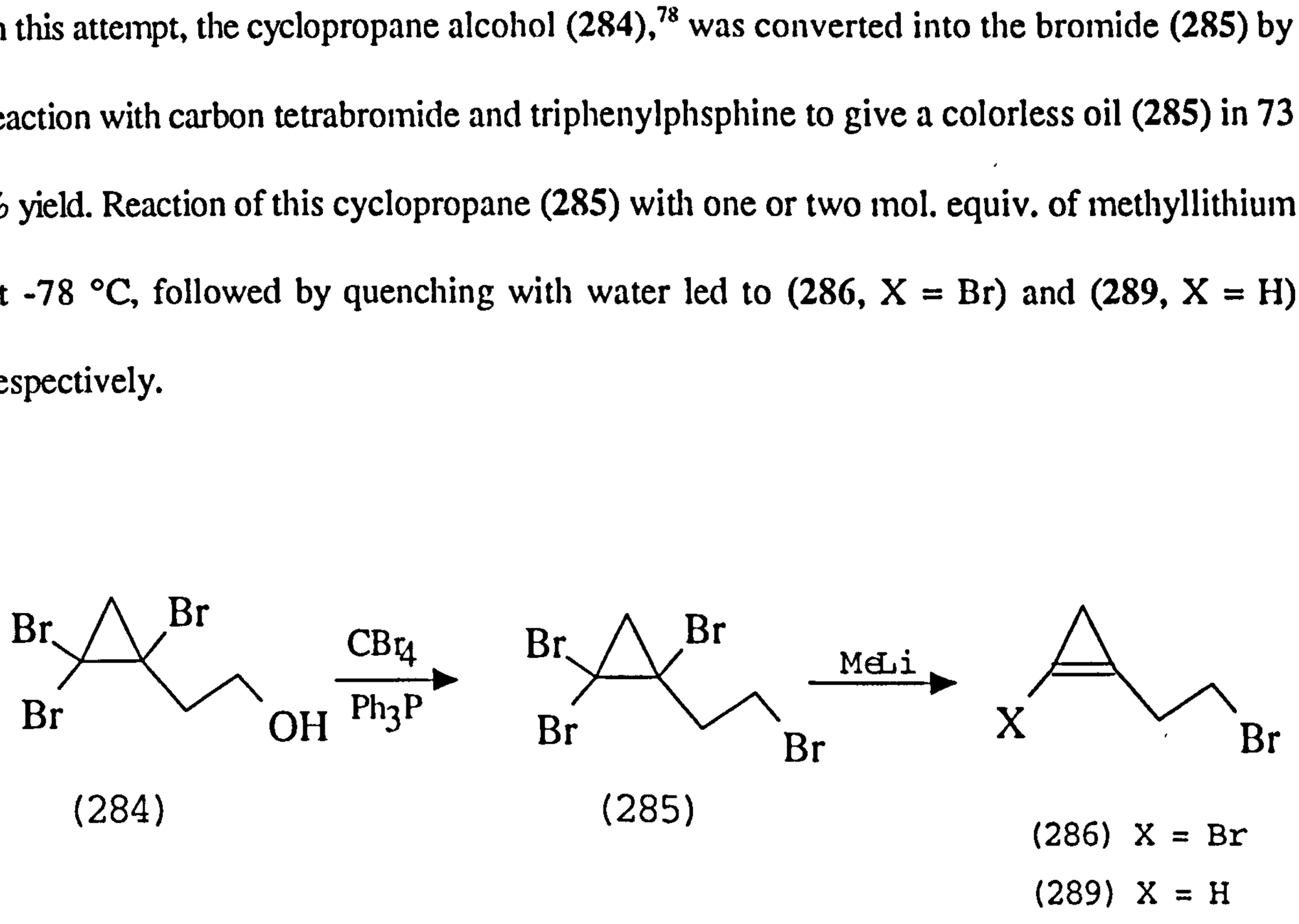
4.3.8. REACTION OF DIELS-ALDER ADDUCTS OF 1-BROMO-2-BROMOETHYLCYCLOPROPENE AND FURANS WITH BUTYLLITHIUM

In order to extend this reaction to investigate if 1,4-elimination is possible and to prepare compounds such as (n.2.1)propellanes (288) via the formation and debromination of adducts such as (287), the homologous cyclopropene (286) was prepared (**Figure 7**).

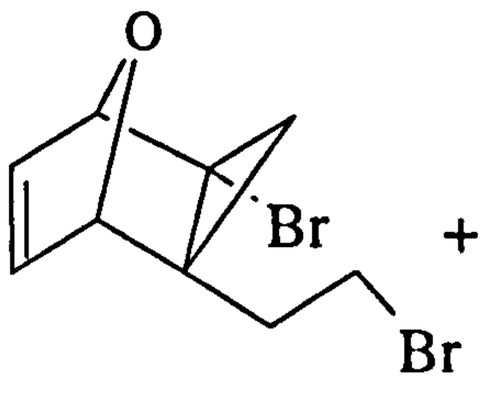
Figure 7



In this attempt, the cyclopropane alcohol (**284**),[78] was converted into the bromide (**285**) by reaction with carbon tetrabromide and triphenylphsphine to give a colorless oil (**285**) in 73 % yield. Reaction of this cyclopropane (**285**) with one or two mol. equiv. of methyllithium at -78 °C, followed by quenching with water led to (**286**, X = Br) and (**289**, X = H) respectively.

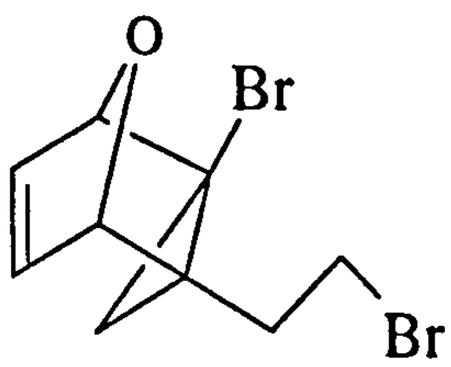


The cyclopropene (**286**) showed two triplets at δ 3.5 and 3.0 with a coupling constant of 7.0 Hz, together with a singlet for the methylene of the cyclopropene. The ^{13}C spectrum showed the expected five signals, while the i.r spectrum showed a very sharp peak at 1838 cm^{-1} for the cyclopropene ring. The ^{1}H n.m.r spectrum of (**289**) was identical to that of (**286**) apart from a broad singlet at δ 6.6 for the vinylic proton. Compounds (**286**) and (**289**) could be trapped by [4+2]-cycloaddition to DPIBF leading to a single product in each case (**290**) (77 %) and (**291**) (70 %) respectively. The stereochemistry of the adducts was assigned by analogy with related adducts of 3,3-unsubstituted cyclopropenes with DPIBF and supported by the large chemical shift difference between the cyclopropane hydrogens in each case (1.1 and 0.4 ppm respectively).[101] Compound (**286**) was also trapped by [4+2]-cycloaddition to furan leading to major isomer characterised as (**292**) (38 %) and a minor isomer (**293**) (11.5 %). In the ^{1}H n.m.r spectrum of (**292**) the cyclopropane hydrogens appeared at δ 2.2 and 1.1, while those of the minor isomer appeared at δ1.7 and 1.4.

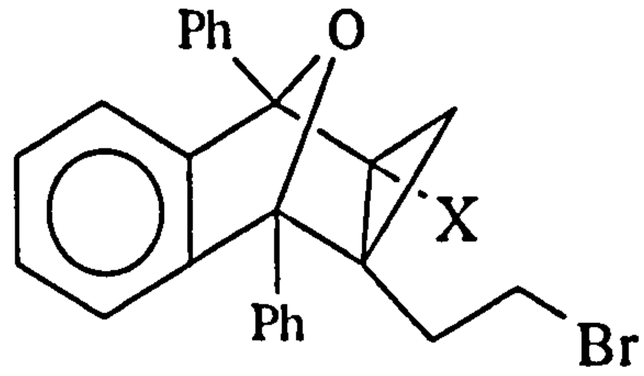


(292)

+



(293)

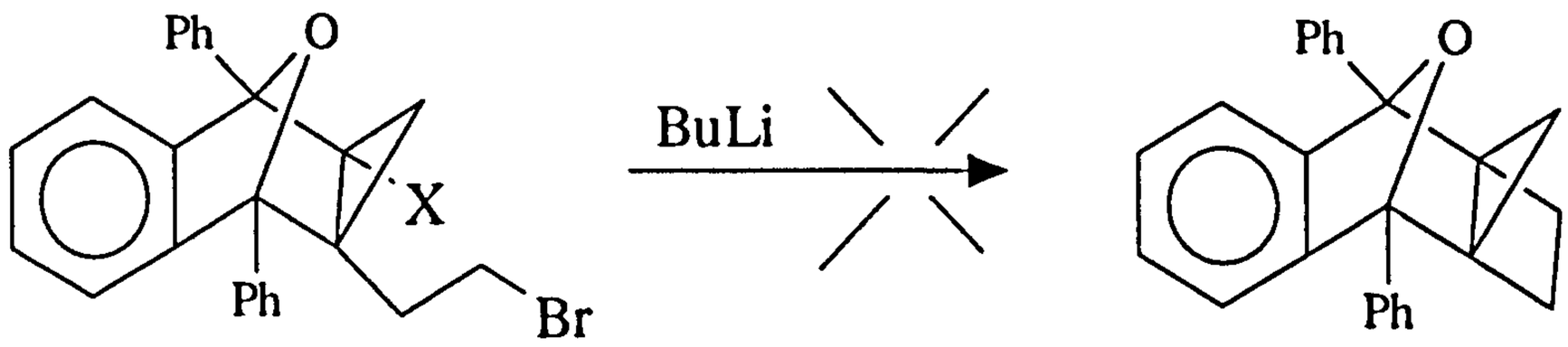


(290) X = Br

(291) X = H

3.5 : 1

Attempted reaction of the adduct (**290**, X = Br) with butyllithium at -78 to 20 °C gave only starting material.



(290, X = Br)

(288)

4.4. CONCLUSION

Reduction of methyl 1,2,2-tribromocyclopropanecarboxylate with di-isobutyl aluminium hydride led to 1,2,2-tri-bromocyclopropane-2-methanol or 1,2,2-tribromocyclopropanecarboxaldehyde depending on the reaction conditions. 1,2,2-Tribromocyclopropane-2-methanol reacted with two or three mol. equiv. of methyllithium leading to cyclopropenes, which could be trapped by [4+2]-cycloaddition. 2-Trimethylsilyl-1-(hydroxymethyl)cyclopropene underwent an ene-type reaction to give a single major dimer. The 1,2,2-tribromocyclopropanecarboxaldehyde reacted with a stabilised Wittig reagent to give an α,β-unsaturated ester cyclopropane. Reaction of α,β-unsaturated ester cyclopropane with one mol. equiv. of methyllithium led to a 1-halocyclopropene with out affecting the ester group. However, reacting with two mol. equiv. of methllithium failed to generate the cyclopropene and instead gave a complex mixture. All attempts to cyclopropanate this failed even after reducing the ester group to an alcohol. The cycloadduct of 1-bromo-2-bromomethylcyclopropane and furans reacted with one mol. equiv. of butyllithium to give [4.1.1] propellanes.

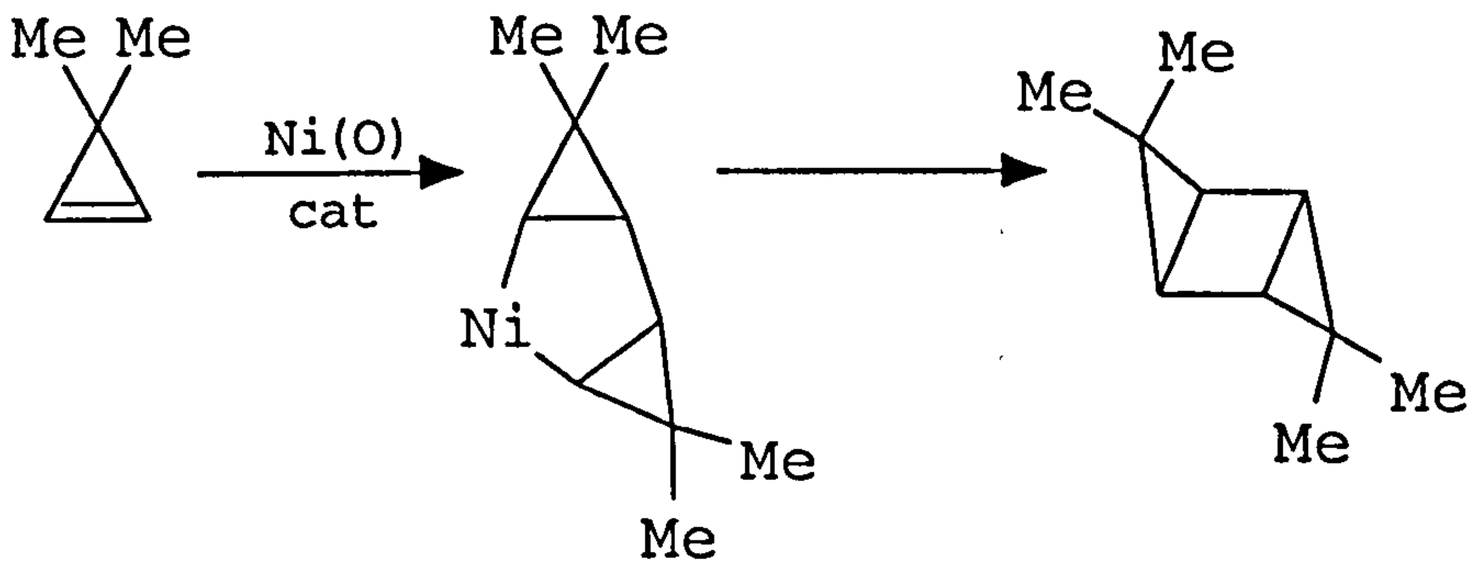
Chapter 5

2-Vinyl-1,1,2-trihalocyclopropanes: Valuable Five Carbon Cyclopropane and Cyclopropene Intermediates

5.0. 2-VINYL-1,1,2-TRIHALOCYCLOPROPANES: VALUABLE FIVE CARBON CYCLOPROPANE AND CYCLOPROPENE INTERMEDIATES

5.1. INTRODUCTION

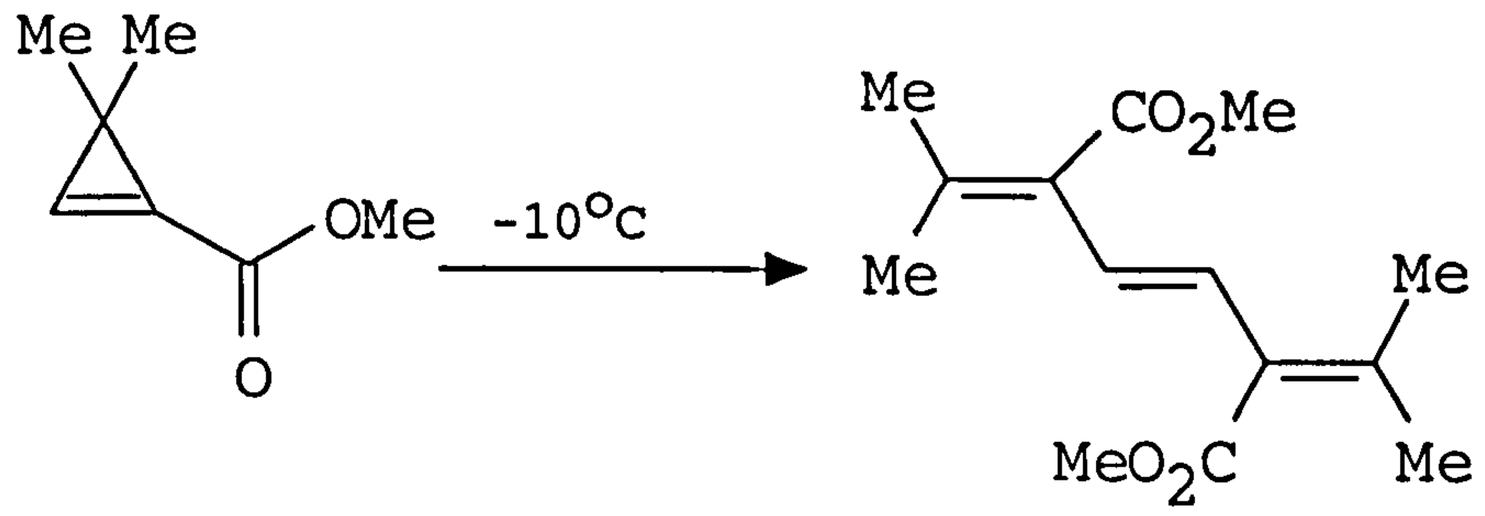
Although cyclopropenes have been known for many years, the number of simple derivatives that have been characterised is not great. The absence of substituents at the methylene position of the cyclopropene generally renders the compound unstable and requires that such molecules be handled at temperatures below ambient.[48] The high strain energy (54 Kcal/mole) of cyclopropenes, results in many unusual reactions such as [2+2]- and [4+2]-cycloaddition that indicate that the molecule is a highly reactive monoene. Cycloaddition across the cyclopropene double bond reduces the strain by 25 Kcal/mole.[48] The thermodynamic and kinetic stability is significantly affected by the position and the number of their substituents.[12] For example, 3,3-diphenylcyclopropene was reported to be relatively stable,[126] while 1,2-diphenylcyclopropene with two hydrogens at the C_3 position is reactive both in ionic reactions such as nucleophilic addition or in non-ionic reactions such as the ene-reaction.[127] Moreover, although 1,3-diphenylcyclopropene was found to be stable in solution at low temperature, it undergoes a facile dimerisation at ambient temperature by the ene-reaction.[116] As mentioned above, cyclopropenes having a hydrogen at the 3-position undergo dimerisation, while those with no such hydrogen substituents are often very stable.[116] However, in the presence of a metal such as Ni(O) in a catalytic amount, 3,3-dimethylcyclopropene (**6**) underwent cyclodimerisation to (**295**).[128]



(6) (294) (295)

The reaction is believed to proceed through a complex (**294**) which could be separated from the reaction of (**6**) with 2,2′-bipyridyl(cyclo-octa-1,5-diene)nickel at 250 °C as a stable crystalline compound.[129] This intermediate reacts with an activated olefin, e.g. maleic anhydride to give (**295**).

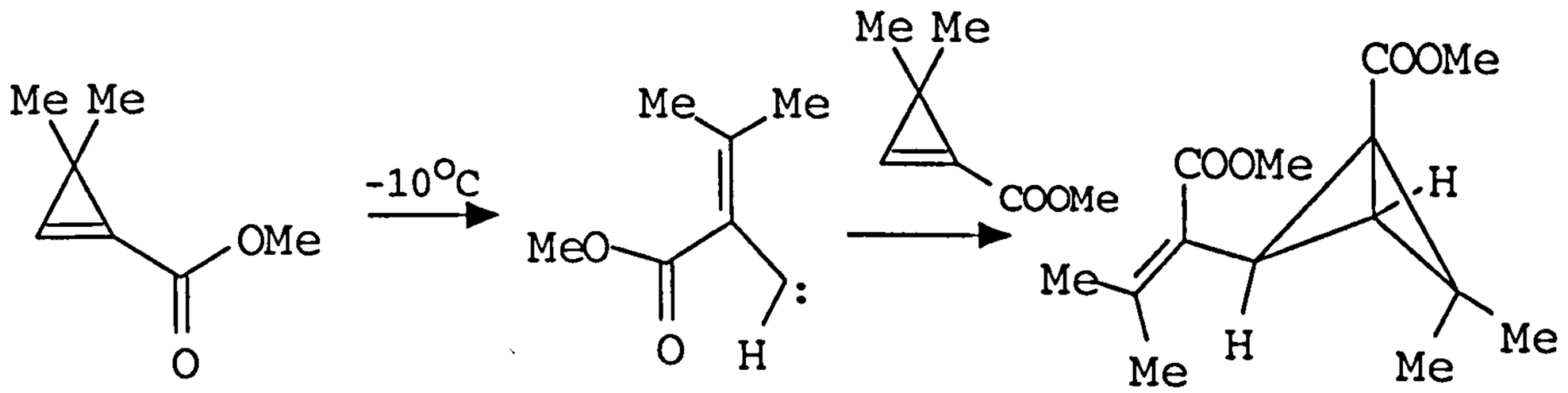
However, Baird and Hussain found that the cyclopropene ester (**57**) was stable in ether solution at -20 °C for three months, but that a neat liquid sample deposited colourless crystals of (**296**) on standing at -10 °C for several days.[130]



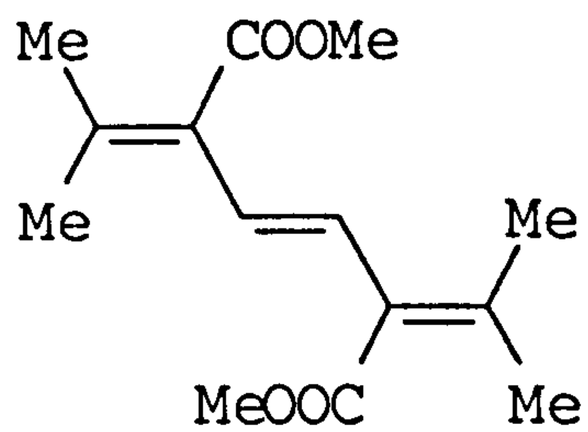
(57) (296)

The formation of (**296**) probably arises by an initial ring-opening of the cyclopropene (**57**) to the carbene (**297**) which could be trapped by unreacted starting material to give the bicyclobutane (**298**) which undergoes rearrangement to give (**296**). However, the carbene could not be trapped by added alkenes. The precise factors affecting the rate of cyclopropene ring opening have not been fully established, although the presence of an

electron withdrawing substituent at C_1 and or C_2 and of a pair of alkyl substituents at C_3 does appear to lead to carbene formation at ambient temperature or below.[36b]

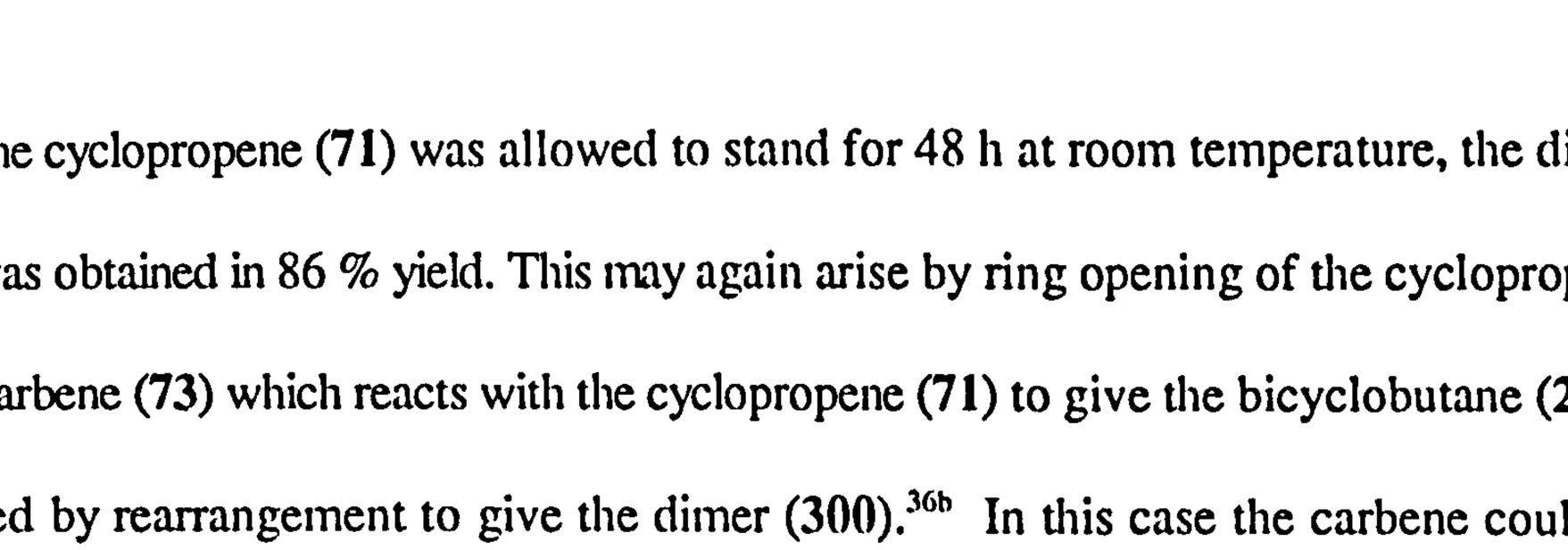


(57) (297) (298)

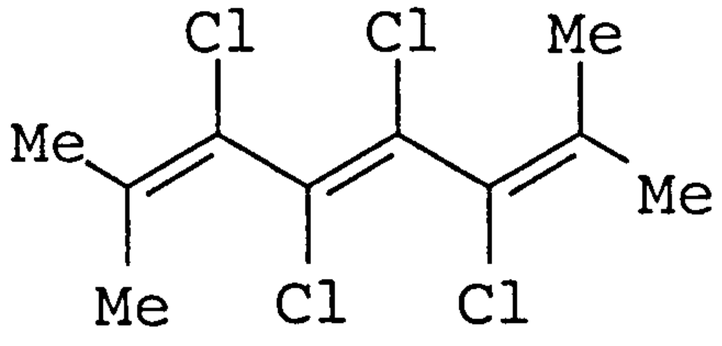


(296)

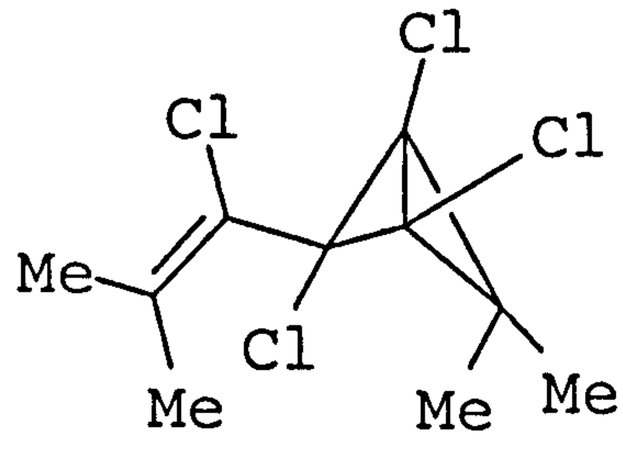
When the cyclopropene (**71**) was allowed to stand for 48 h at room temperature, the dimer (**300**) was obtained in 86 % yield. This may again arise by ring opening of the cyclopropene to the carbene (**73**) which reacts with the cyclopropene (**71**) to give the bicyclobutane (**299**), followed by rearrangement to give the dimer (**300**).[36b] In this case the carbene could be trapped by added alkenes, though (**299**) was not detected.



(71) (73)

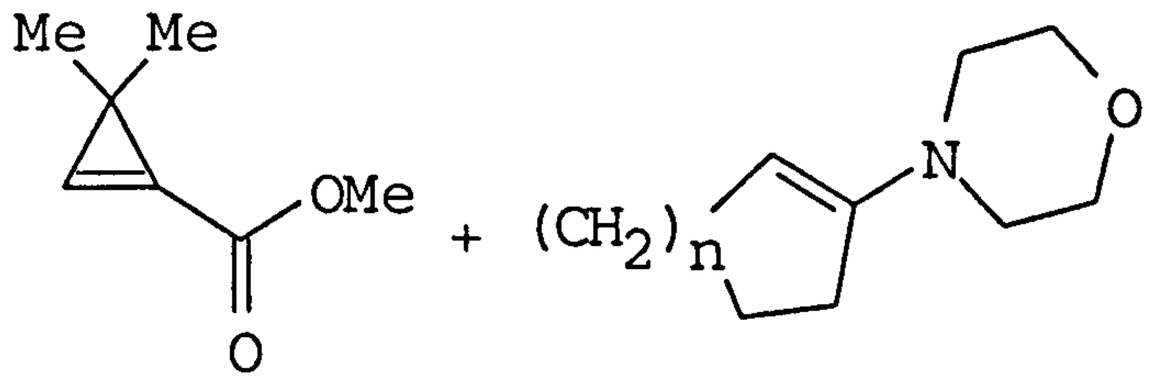


(300)

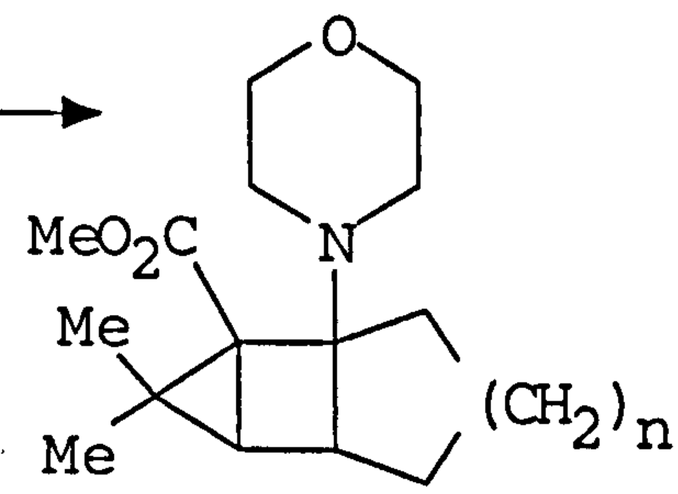


(299)

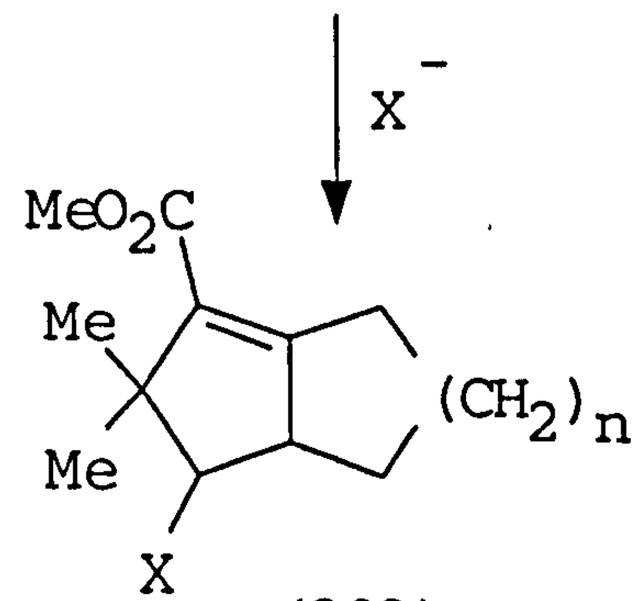
The cyclopropene ester (**57**) also undergoes [2+2]-cycloaddition to enamines to give (**301**) followed by ring opening of the derived bicyclopentane to give (**302**). This provides the basis of an elegant route to a number of natural products containing bicyclo[3.3.0]octane and [4.3.0]nonane skeletons, such as hirsutene and silphinene.[131]



(57)



(301)



(302)

5.2. AIMS OF THE PROJECT

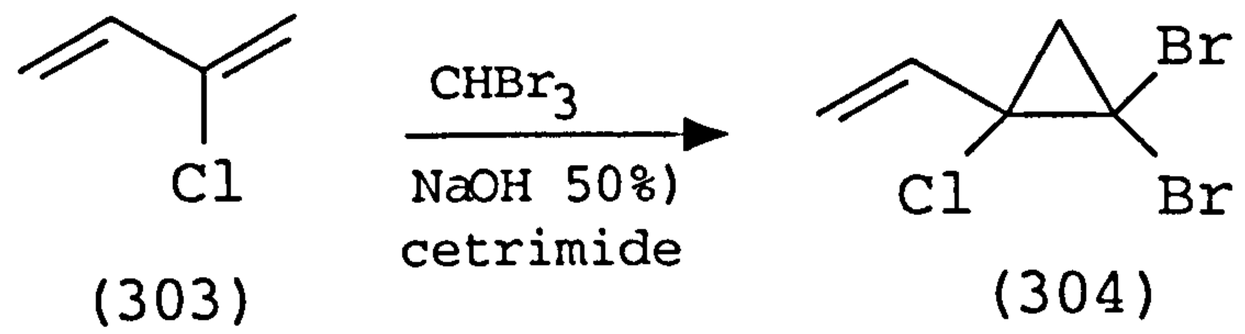
The original aim in this chapter was to synthesise the polyhalodicyclopropanes as described on page 90 and 91. This was to be achieved by adding two mol. equiv. of dihalocarbenes to chloroprene and 2,3-dichlorobutadiene; as described below, in the event the preparation was not achieved in an efficient way. However, in studying these reactions routes were developed to a wide range of vinylcyclopropenes and the chemistry of these were examined.

5.3. RESULTS AND DISCUSSION

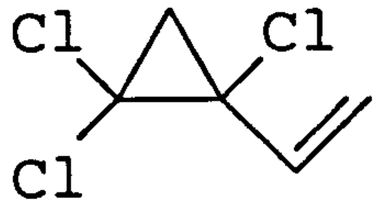
5.3.1. PREPARATION OF VINYLTRIHALOCYCLO-PROPANES

A range of vinyltrihalocyclopropanes were prepared for this work, following known procedures. However, a number of new compounds of this type were also prepared and these will be described below.

The cyclopropane (**304**) was prepared under phase transfer conditions by treatment of chloroprene (**303**) (2-chloro-1,3-butadiene) in 50 % xylene with an excess of bromoform cetrimide as a phase transfer catalyst and aqueous sodium hydroxide (50 %), maintaining the temperature of the reaction below 20 °C. The reaction mixture was stirred vigorously for 8 h until consumption of the starting material had occurred.



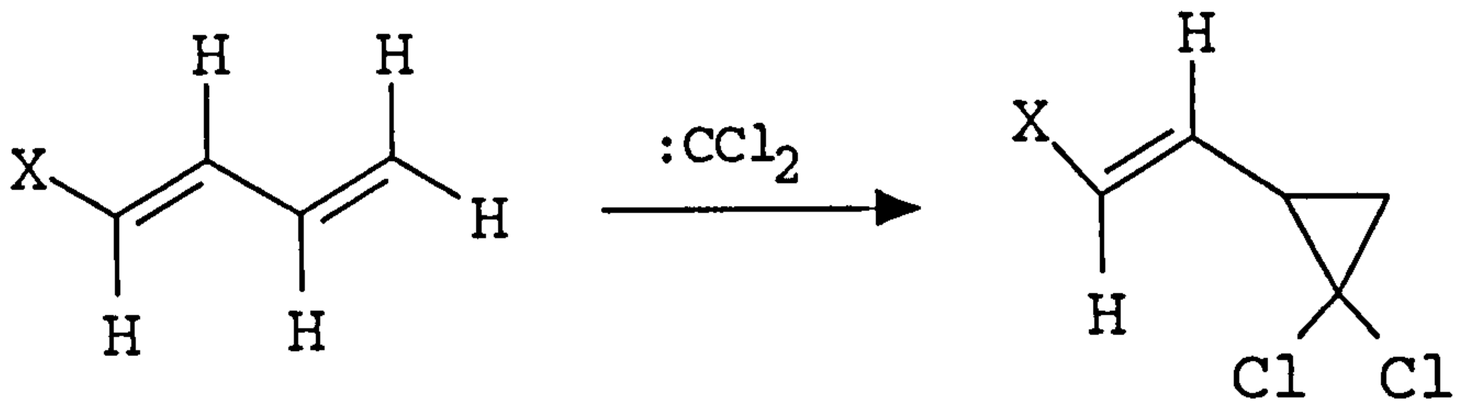
(303) (304)



(305)

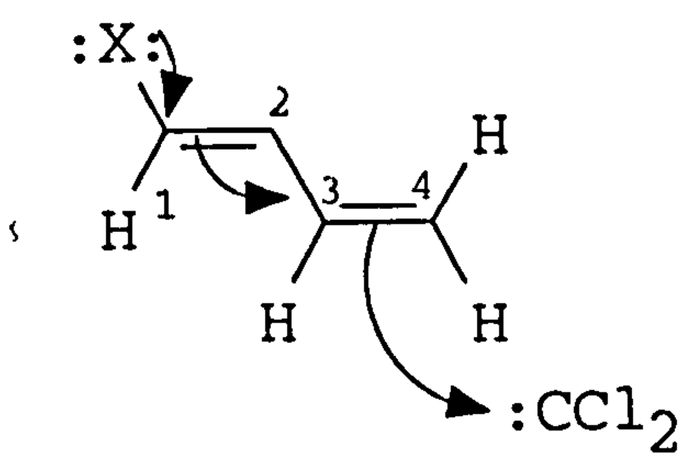
The product (304) arose by addition of dibromocarbene predominantly at the halogen substituted bond. This is contrary to the result predicted on the basis that halogen substituted alkenes are less reactive to $:CX_2$ than non-halogenated ones, but is the same result as that observed for the addition of $:CCl_2$.[132,133] The product (304) showed the correct measured mass for $C_5H_5Br_2Cl$ and the ^1H n.m.r spectrum contained one double doublet at δ 6.00 with coupling constant of 10.2 and 16.5 Hz, and two doublets at δ 5.6 and 5.4 with coupling constants 16.5 and 10.2 Hz respectively, together with an AB pattern for the methylene group of the cyclopropane. The ^{13}C spectrum showed five signals including two in the olefinic region.

Similarly, the cyclopropane (305) was obtained by the addition of $:CCl_2$ generated under phase transfer conditions.[11,12] However, the addition of $:CCl_2$ to dienes of type (306) leads selectively to reaction at the less substituted double bond to give (307).[134]

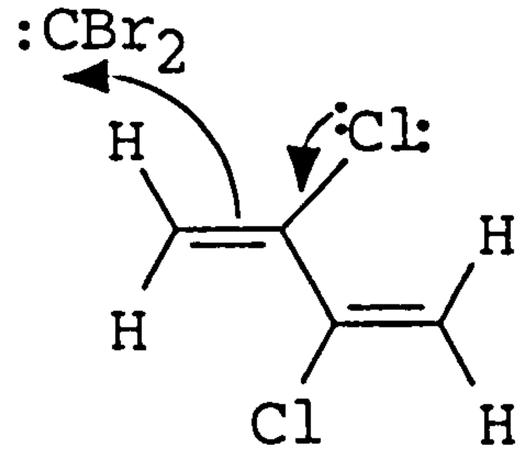


(306, X = halogen) (307)

The terminal halogen on the diene (306) exerts a mesomeric electron releasing effect experienced by both double bonds. The inductive effect acts in the opposite direction, and falls off rapidly through the carbon skeleton; hence this effect is experienced more by the C_1-C_2 bond. The overall result is that the C_3-C_4 bond is the more nucleophilic of the two olefinic bonds and it is here that :CCl_2 addition is observed. In the case of chloroprene (303), the mesomeric effect of the halogen is only transmitted to the 1,2-bond. The smaller inductive effect at the 3,4-bond, added to a significient steric effect of the halogen at C_2, is not great enough to offset this positive mesomeric effect, and dichloro-and dibromo-carbenes therefore add at the 1,2-bond to give the adducts (304).



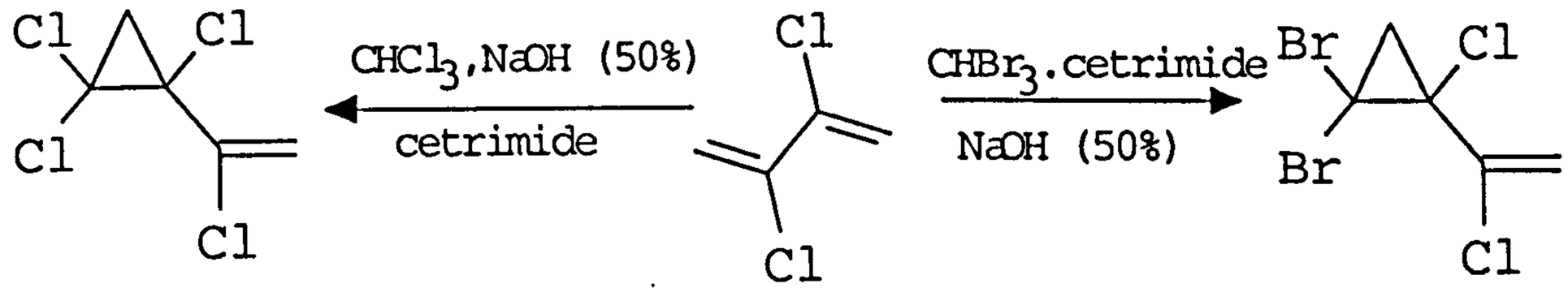
(306)



(303)

Similarly, addition of dibromocarbene or dichlorocarbene generated under phase transfer conditions from an excess of bromoform or chloroform, aqueous sodium hydroxide and cetrimide to 2,3-dichlorobuta-1,3-diene in xylene led to (308) and (309) respectively. This reaction had to be carried out by careful addition of sodium hydroxide, otherwise an

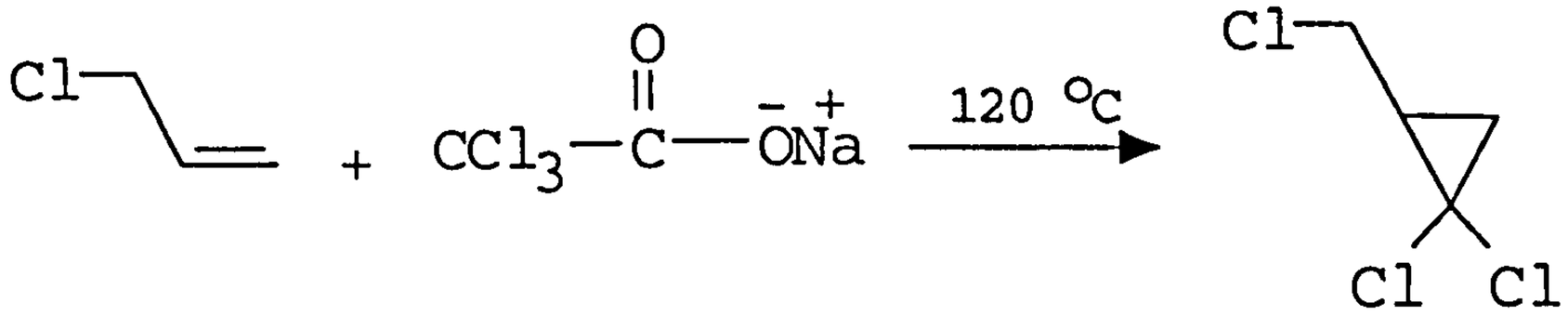
exothermic reaction accompanied by refluxing occurred and the elevated temperature and strong base led to decomposition of the cyclopropane obtained.



(309) (308)

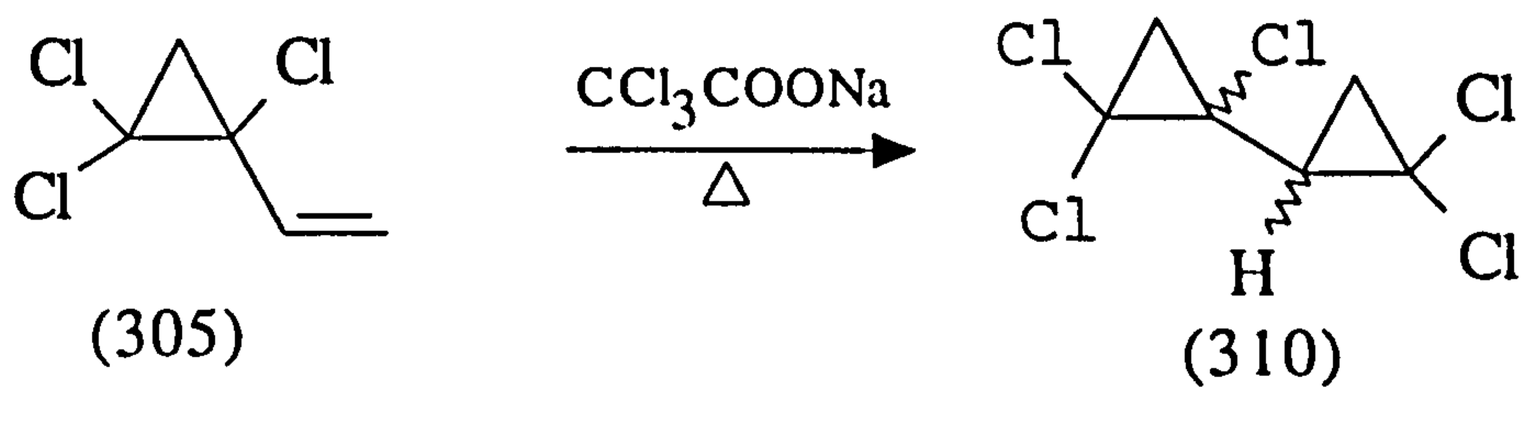
The products (**308**) and (**309**) showed the correct measured masses and the ^{1}H n.m.r spectrum for each cyclopropane showed two doublets in the olefinic region with a coupling constant of 2.2 Hz, together with an AB pattern for the methylene group of the cyclopropane with geminal coupling constant about 9.3 Hz. The ^{13}C spectra showed the expected five signals including two in the alkene region. Although the yields of these reactions were low, ~30 %, the ready availability of the starting materials made it possible to obtain large quantities of the cyclopropanes.

However, one of the primary aims of the project was to obtain bis-dihalocarbene adducts of chloroprene and 2,3-dichlorobutadienes. Addition of dibromocarbene or dichlorocarbene generated under phase conditions to the second double bond in compounds (**304**), (**305**) and (**316**) failed and gave complex products, maybe due to the base sensitivity of the cyclopropanes. It is known that the thermal decomposition of sodium trichloroacetate in an aprotic solvent in the presence of an olefin leads to dihalogenocyclopropanes in good yield,[135] while in protic solvents it leads to the formation of chloroform and carbon dioxide.[136] This method has a special advantage in the preparation of carbene adducts from base-sensitive acceptors.



The disadvantage, apart from the acid sensitivity of the intermediate anion, is the reaction of :CCl_2 and trichloroacetate ion leading to the formation of CO, CO_2 and CCl_4.

Addition of dichlorocarbene generated by thermal decomposition of sodium trichloroacetate to compounds (304), (305), (308) and (309) was therefore attempted. On refluxing (305) with sodium trichloroacetate in dimethoxyethane, the bis-adduct (310) was slowly formed over a period of several hours. Attempts to accelerate the rate of the reaction by increasing the temperature of reflux from 85 °C to 120 °C or by changing the solvent to toluene were then made. In refluxing toluene, sodium trichloroacetate did not decompose and no dichlorocarbene addition took place. Addition of a catalytic amount of 18-crown-6-ether did cause the thermal decomposition of sodium trichloroacetate to dichlorocarbene to occur and the bis-adduct (310) was formed in 9.4 % yield as a mixture of diastereoisomers in a ratio of 1:1.

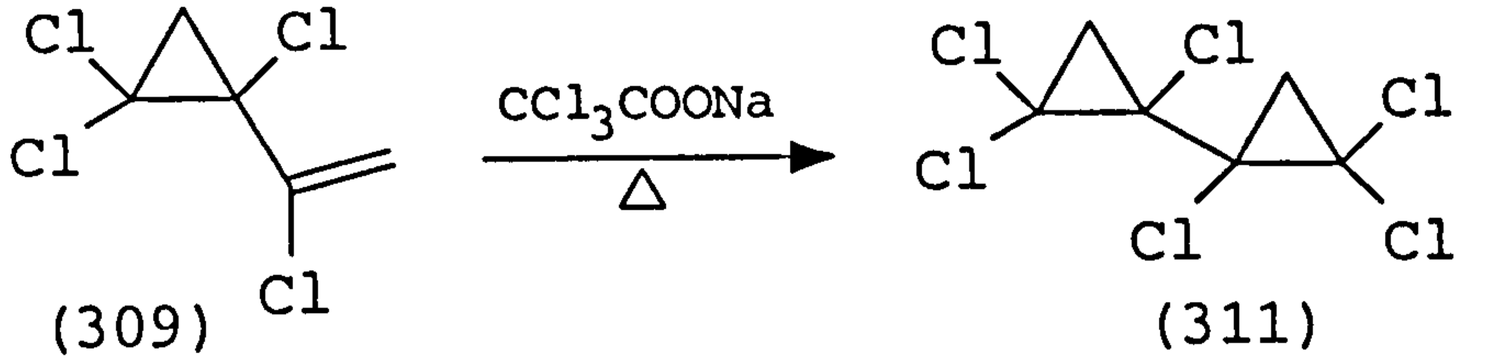


(305) (310)

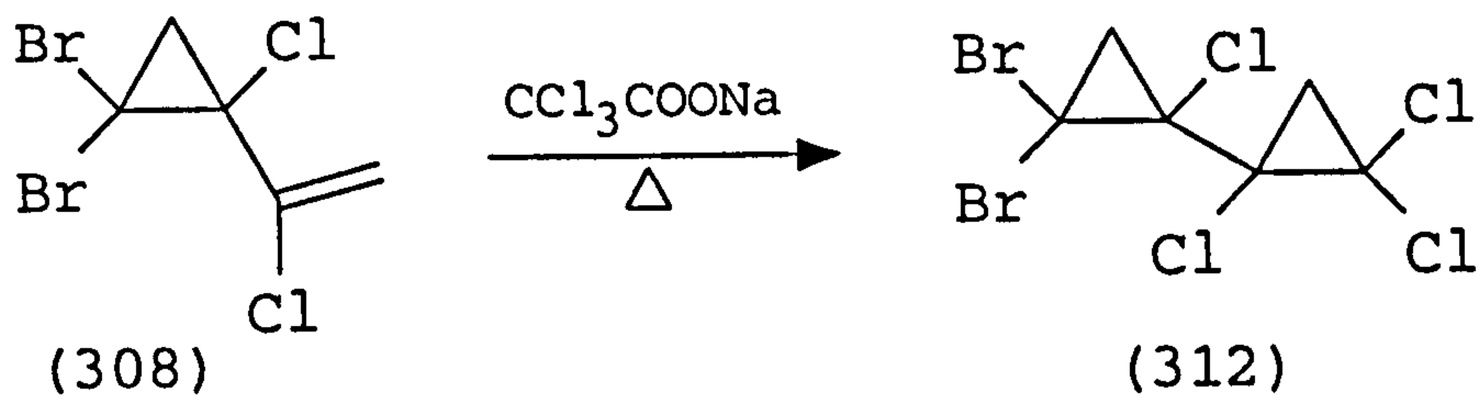
Compound (310) gave the correct measured mass for $C_6H_5Cl_5$.

Similarly, the bis-adduct (311) was obtained in 20 % yield using the same procedure. The ^1H n.m.r spectrum of (311) showed only one AB pattern at 2.1 and 1.9 ppm for the methylene group of the cyclopropane with a coupling constant of 10.0 Hz, while the

^{13}C spectrum contained only three signals at δ 62, 55.5 and 36.6 ppm. This suggests that only one diastereomer of (**311**) was obtained, though it was not clear which. Moreover, thermal addition of dichlorocarbene to (308) occurred very slowly but ultimately yielded the bis-adduct (**312**) (8.3 %).



(309) (311)



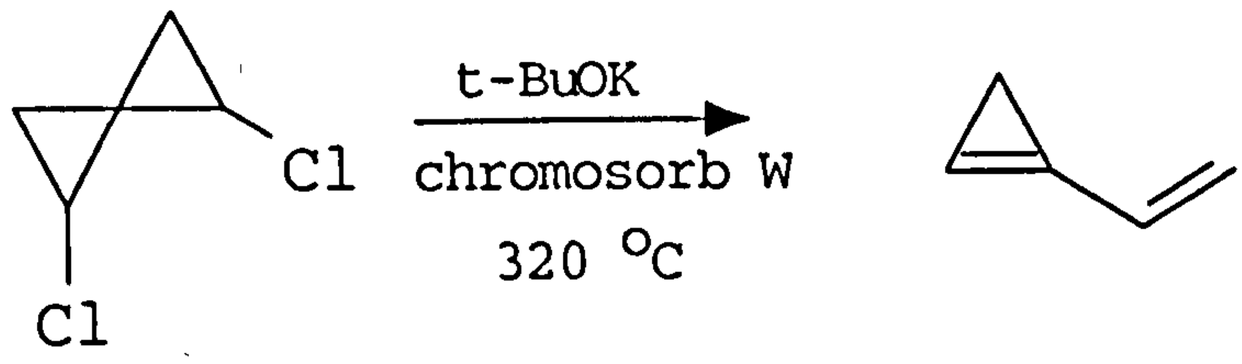
(308) (312)

Compound (**312**) showed an accurate mass for the formula $C_6H_4Cl_4Br_2$. The ^1H n.m.r spectrum showed two AB patterns for the two methylene groups of the cyclopropanes at δ 2.2, 2.1 and 2.0, 1.9 with coupling constants of 10.2 and 10 Hz.

5.3.2. REACTION OF VINYLTRIHALOCYCLO-PROPANES WITH METHYLLITHIUM

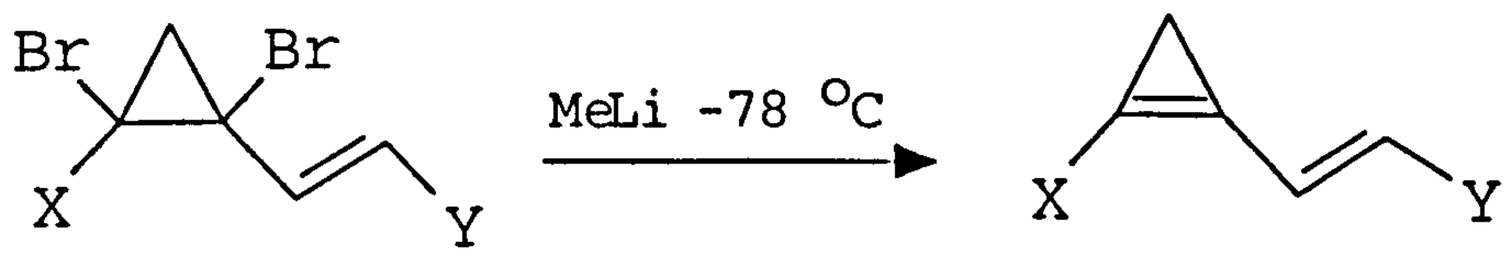
It has been established for many years that the reaction of methyllithium with 1,1-dibromocyclopropane leads to either a cyclopropylidene or a related 1-bromocyclopropyl lithium, depending on the temperature of the reaction and the nature of the substituents

attached to the cyclopropyl ring.[137] Often the cyclopropylidene can undergo rapid and efficient rearrangement to form the allene; alternatively, the carbene may undergo reactions such as addition to carbon-carbon bonds, insertion into C-H single bonds, formation of ylides or rearrangement.[137] Trapping of the bromocyclopropyl lithium with a range of electrophiles has also been accomplished. In contrast, reaction of a 1,1,2-trihalo- or 1,1,2,2-tetrahalocyclopropane with one equivalent of methyllithium gave 1-halo- or 1,2-dihalocyclopropenes respectively, via a 1,2-dehalogenation.[17] Surprisingly, despite a considerable expansion in the chemistry of cyclopropenes, and particularly in their application in synthesis, there are very few reports of 1-vinylcyclopropenes.[77] The parent compound (**314**) has been obtained by a gas-phase dehydrochlorination of 1-chloro-2-vinylcyclopropane or the dichloride (**313**) by using reagents adsorbed on an inert surface.[138]



(313) (314)

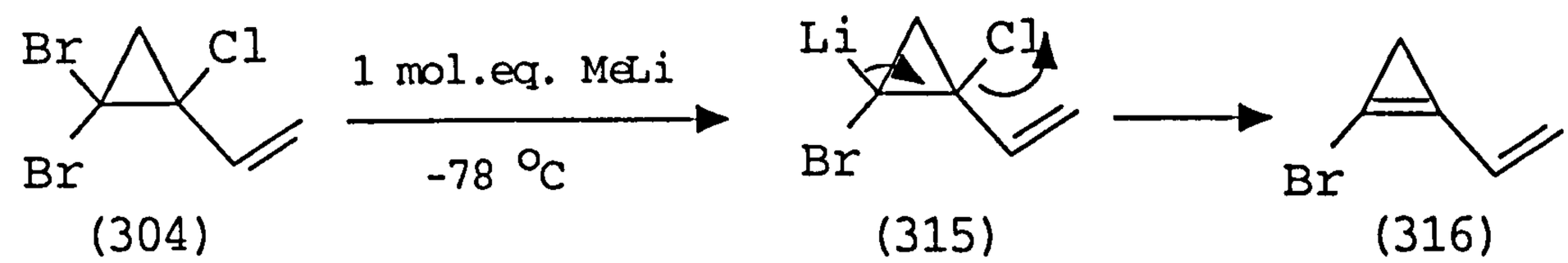
As mentioned previously, the cyclopropene (**257**) which prepared by dehalogenation of tribromides (**246**) with methyllithium, are rather more stable than (**314**), decomposing over a period of about 18 h at 20 °C.[114]



(246) (257, X = Br, Y = COOEt)

In view of the ready availabilty of vinyl trihalocyclopropanes, the preparation of vinylcyclopropenes was examined.

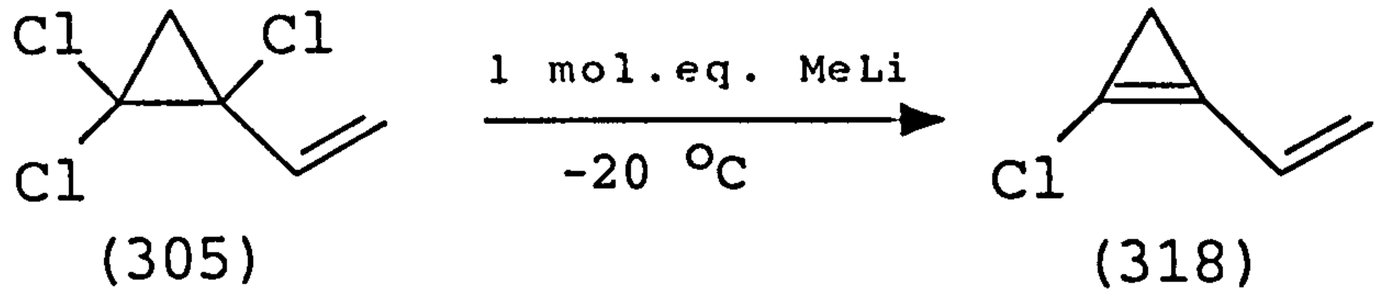
The reaction of dibromides (**304**) and (**308**) with 1 mol. equiv. of methyllithium at -78 °C and quenching with water at that temperature led to 1-bromocyclopropenes (**316**) and (**317**) respectively. These may have arisen by lithium-bromide exchange to give, e.g., (**315**) followed by or concurrent with 1,2-elimination to give (**316**) or (**317**).[77]



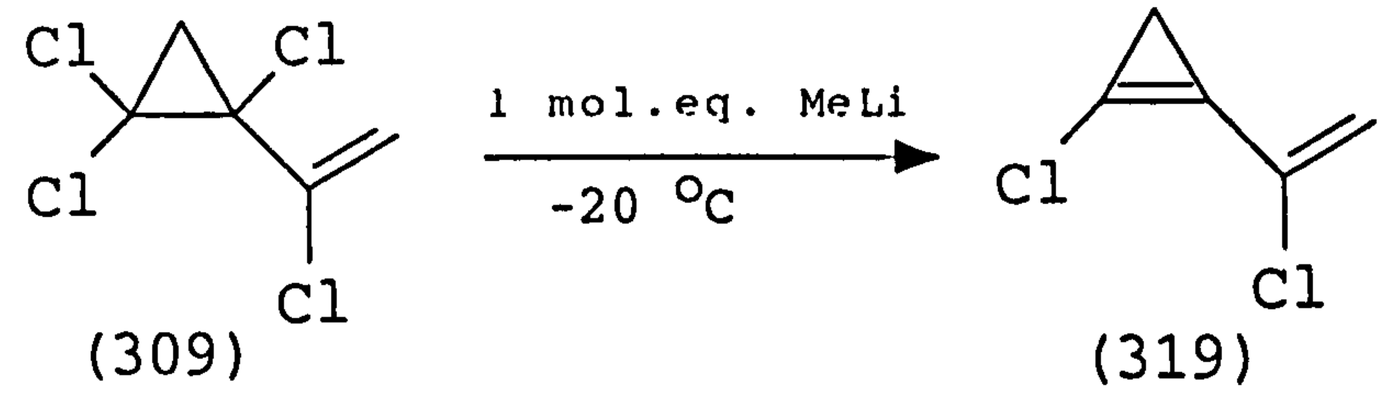
In each case, the cyclopropene could be characterised on the basis of a singlet at δ 1.6 and 1.9 respectively for the cyclopropene methylene group in their ^{1}H n.m.r spectra. The methylene group in (**317**) resonated downfield by 0.3 ppm from that in (**316**) due to the deshielding effect of the halogen atom on the double bond. The ^{13}C nmr spectra each showed five signals including four in the olefinic region and one in the saturated region resonating at δ 15.8 and 19.9 respectively. The cyclopropene (**316**) decomposed on standing in $CDCl_3$ at room temperature; after 0.5 h some decomposition could be seen by ^{1}H nmr, and after two days no starting material remained and a very complex spectrum was observed. When (**316**) was allowed to stand in ether or benzene, a similar complex mixture was obtained. Compound (**317**) was rather more stable and after standing for 18 h at 20 °C

in $CDCl_3$ about 50 % remained; after two days a complex mixture had been produced but the signal for (**317**) could still be seen in the ^1H n.m.r spectrum.

In the same way, reaction of (**305**) and (**309**) with 1 mol. equivalent of methyllithium at -20 °C for 20 min gave cyclopropenes (**318**) and (**319**) respectively.



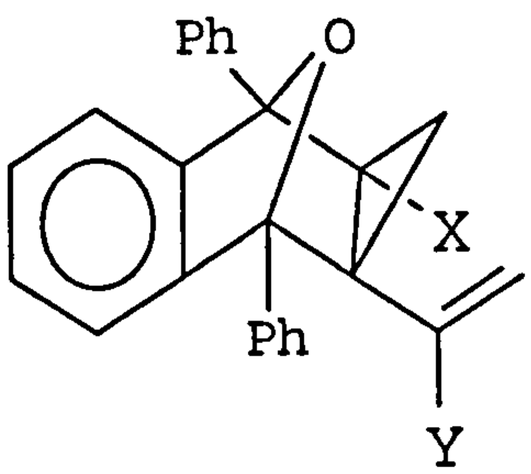
(305) (318)



(309) (319)

The cyclopropene (**318**) was very volatile and it was not possible to separate it completely from the solvent, ether. The ^1H n.m.r spectrum showed a vinyl pattern in the alkene region and a singlet at δ 1.65 corresponding to the cyclopropene methylene group, while the ^{13}C n.m.r spectrum showed four signals in the olefinic region and one at δ 15.08. This compound decomposed relatively quickly in $CDCl_3$ at 20 °C and, even after one hour, complex new signals were observed in the ^1H spectrum. Compound (**319**) was rather more stable and even after one day at 20 °C in $CDCl_3$ about 25 % remained.

Compounds (**316**) and (**317**) could be trapped by [4+2]-cycloaddition to diphenylisobenzofuran, leading to a single product in each case (**320a**) and (**320b**).



(320a) X = Br, Y = H

(320b) X = Br, Y = Cl

(320c) X = Cl, Y = H

(320d) X = Cl, Y = Cl

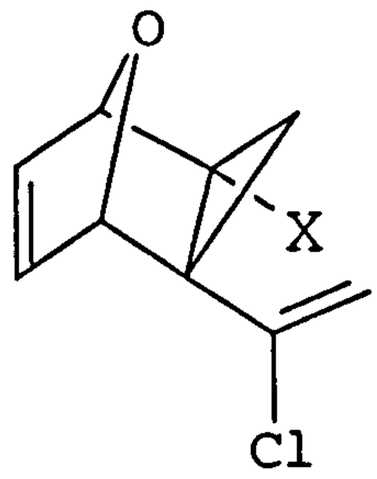
(320e) X = H, Y = H

(320f) X = TMS, Y = H

(320g) X = H, Y = Cl

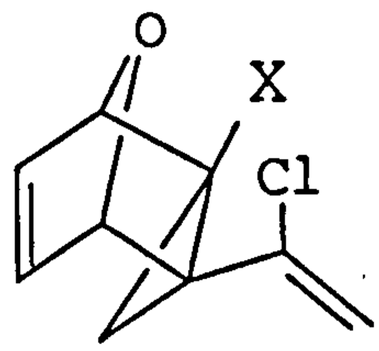
(320h) X = D, Y = Cl

(320i) X = TMS, Y = Cl



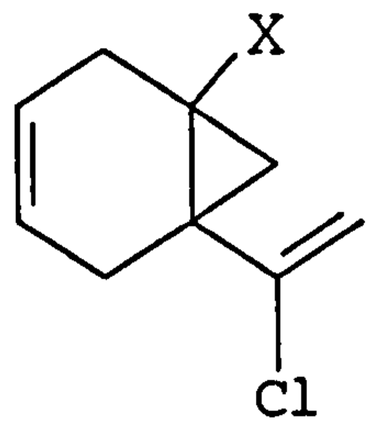
(321a) X = Br

(321b) X = Cl



(322a) X = Br

(322b) X = Cl



(323a) X = Br

(323b) X = Cl

(323c) X = TMS

The compounds **(320a)** and **(320b)** each showed a correct microanalysis and their ^{1}H n.m.r spectra contained two doublets at δ 2.9, 2.1 for **(320a)** and δ 3.0, 2.0 for **(320b)** each with coupling constants of 6.3 Hz. The low field of one doublet in each case can only arise by deshielding of the cyclopropane proton by the bridging oxygen atom,[42] and the stereochemistry of the adducts was assigned by analogy with related adducts of 3,3-unsubstituted cyclopropene with DPIBF, supported by the large chemical shift difference between the cyclopropane hydrogens in each case (0.8 and 1 ppm respectively).[101] Compound **(317)** was also trapped by [4+2]-cycloaddition to furan leading to a major isomer characterised at **(321a)** and a minor isomer **(322a)** (ratio 3.5:1). The two isomers were separated by column chromatography on silica eluting with petroleum ether and ether

(5:1). The major isomer (**321a**) showed the correct measured mass for C_9H_8OBrCl and its ^1H nmr spectrum contained two double doublets at δ 6.8 and 6.7 with coupling constant 1.5 and 5.6 Hz, and three doublets at δ 5.4, 5.3 and 4.9 together with AB pattern for the cyclopropane hydrogens at δ 2.5 and 1.6 with a coupling constant of 6 Hz. The stereochemistry was again supported by the large chemical shift difference between the cyclopropane hydrogen (0.9 ppm), while the ^1H n.m.r spectrum of the minor isomer (**322a**) showed two doublets of the cyclopropane protons resonating at δ 1.99 and 1.92 ppm.

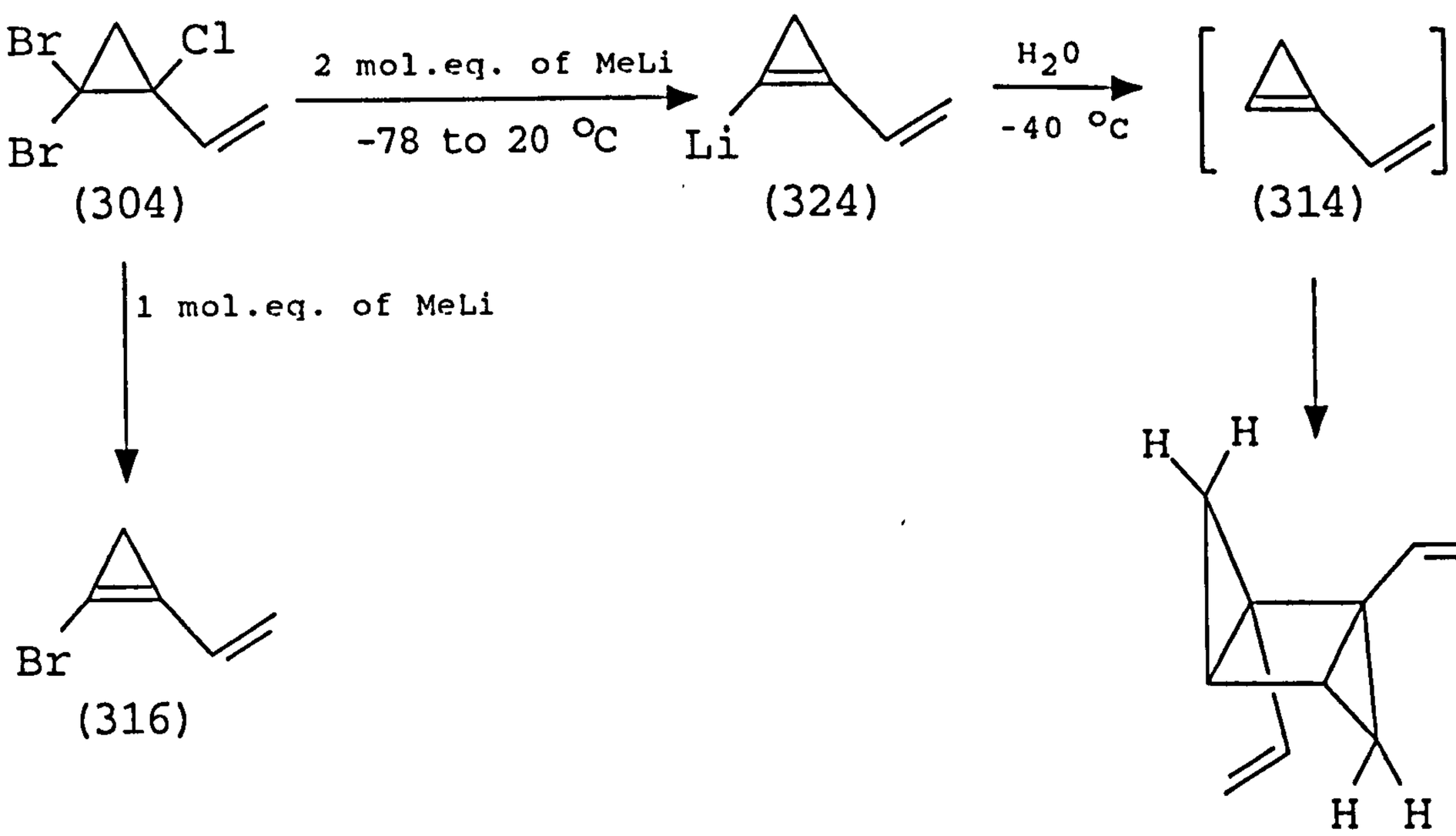
Moreover, the cyclopropene (**317**) could be trapped with 1,3-butadiene, leading to (**323a**). Adduct (**323a**) showed the expected AB pattern for its cyclopropane hydrogens at δ 1.5 and 1.6, and four single hydrogen signals in the alkene region, two singlets and two complex multiplets. The signals for the methylene groups in the six membered ring were unusual, three hydrogens appearing as a complex multiplet at δ 2.9-3.1 and one as a complex doublet at δ 2.3.

Attempted reaction of the cyclopropene (**316**) with furan led only to complex products, presumably either because decomposition competed with cycloaddition or the product was unstable.

Similarly, the cyclopropenes (**318**) and (**319**) were trapped in moderate yield by addition to DPIBF to give adducts (**320c**) and (**320d**), with ^1H n.m.r spectra very similar to those from (**316**) and (**317**). Compound (**319**) was also trapped by the addition to furan and butadiene giving (**321b**) and (**322b**) in ratio *ca.* 5:1 and (**323b**) respectively. On chromatography of the mixture of (**321b**) and (**322b**), only (**321b**) was obtained pure.

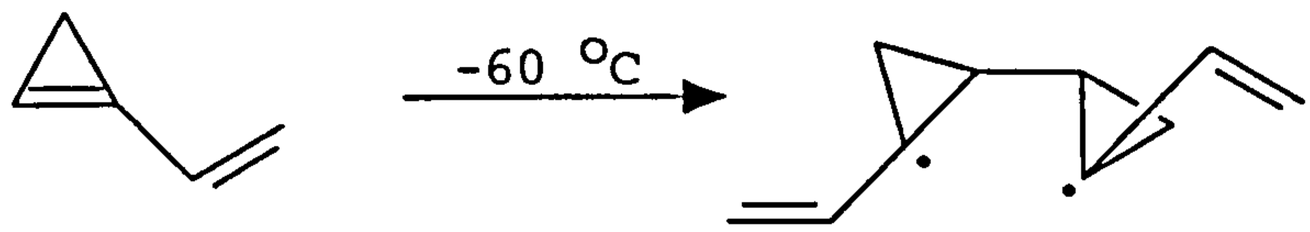
Reaction of (**304**) with two mol. equiv. of methyllithium at -78 °C under nitrogen, and then allowing the reaction to reach room temperature for five minutes, followed directly by removal of the solvent at -40 °C and 1 mm Hg gave the lithiocyclopropene (**324**) as a

white solid. This was quenched with water under vacuum and the volatiles produced condensed into a trap cooled in liquid nitrogen, to give (325) in 40 % yield.[138]

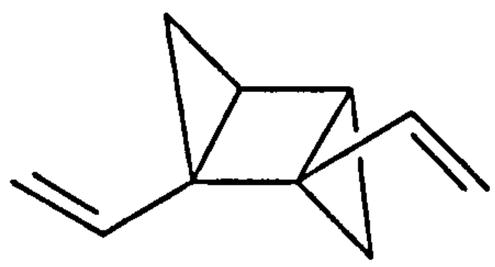


The ^{1}H n.m.r spectrum of the distillate showed three double doublets for the vinyl group at δ 5.5, 5.1 and 4.9 with coupling constants of 17.2, 10.4 and 2.0 Hz, together with two double doublets for the methylene groups of the cyclopropanes at δ 1.6 and 1.5, and a multiplet for ring junction hydrogens. The data were identical to those reported.[138] The ^{13}C spectrum showed five signals including two in the olefinic region. The dimer (325) may arise by lithium-halogen exchange on (304) followed by 1,2-elimination of lithium bromide to give (316) which reacts with the second equivalent of methyllithium to give (324). This reacted with the water to give (314), which was flash distilled into the cooled reciever, where it underwent a thermal [2+2]-cyclodimerisation. The mechanism of [2+2]-cycloaddition of vinylcyclopropenes has not been clearly determined, but may in this case involve a biradical (326), which is stabilised by the vinyl group, followed by simple collapse of (326) with

carbon-carbon bond formation to give (**325**). The driving force for the dimerisation is mostly due to loss of strain in (**314**).

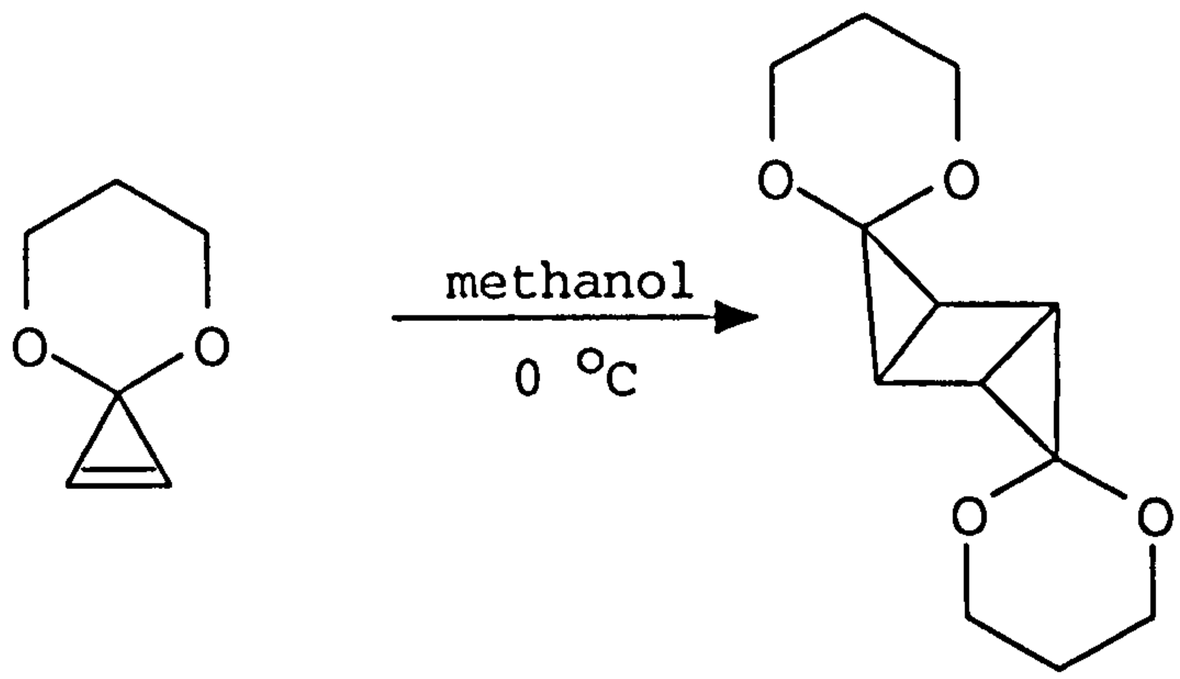


(314) (326)



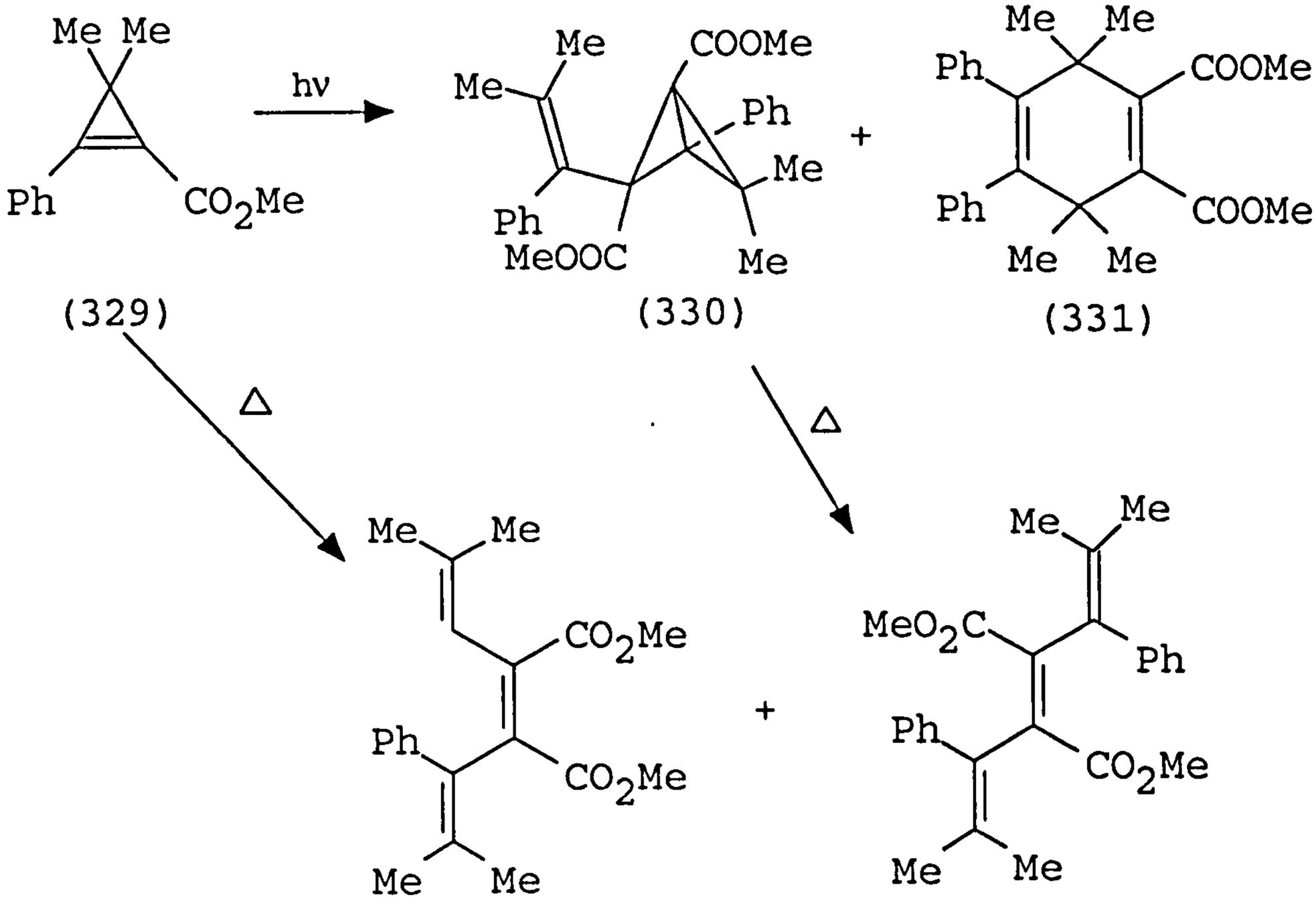
(325)

As discussed before, cyclopropenes having a hydrogen atom at C_3 often undergo a rapid dimerisation by an ene-type reaction involving the transfer of the hydrogen to the double bond of another molecule with concurrent C-C bond formation between them.[139] [2+2]-Cycloaddition is an alternative mode of dimer formation, and may occur under thermal, metal catalysed or photochemical conditions; it is particularly common when the ene-reaction is slow or when it is blocked by 3,3-disubstitution. Thus, when the cyclopropene (**327**) was allowed to stand at 0 °C in methanol, a quantitative yield of (**328**) was obtained by [2+2]-dimerisation.[140]

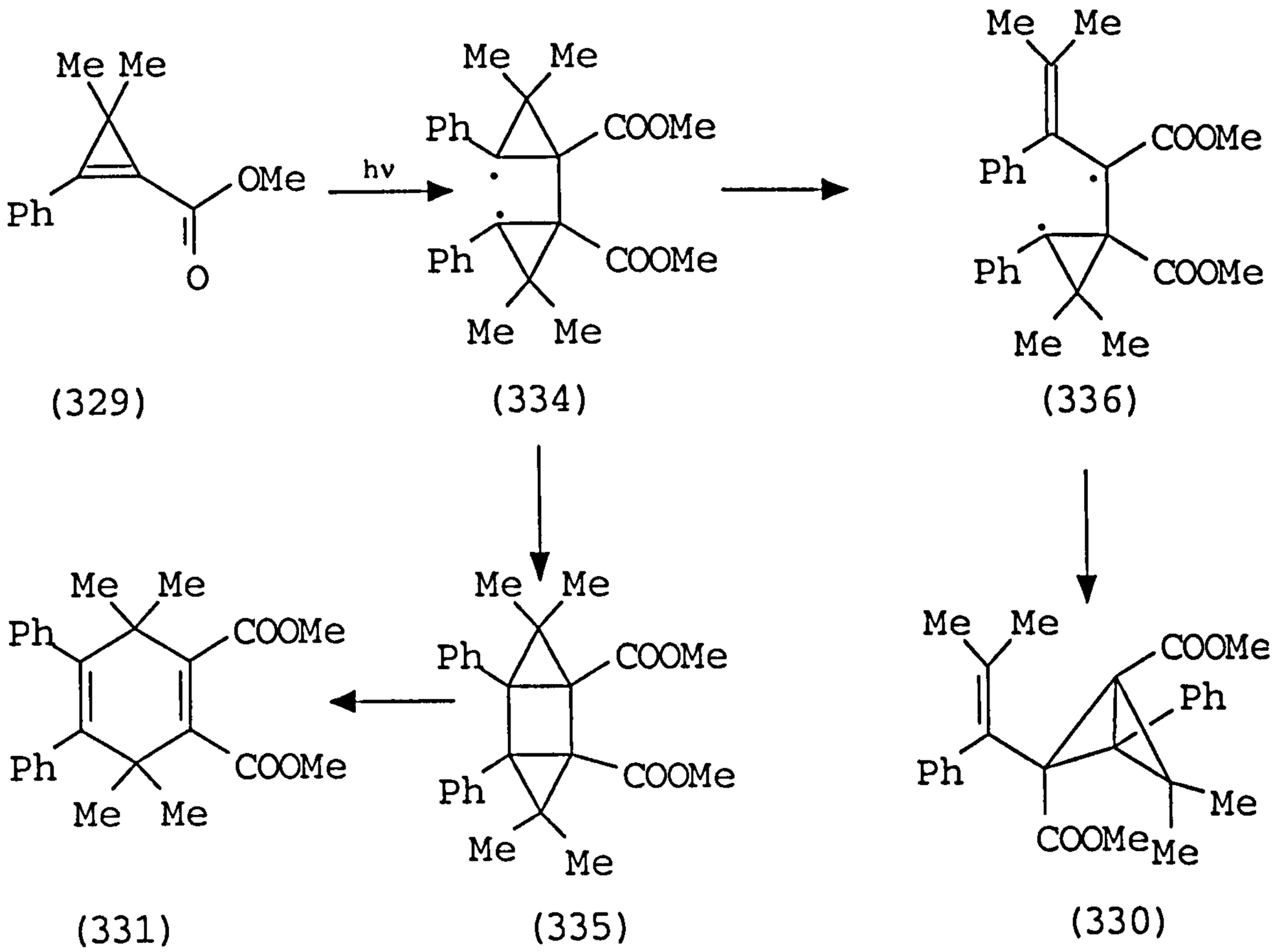


(327) (328)

In other cases thermal reaction of cyclopropenes leads to ring opening, but the [2+2]-cycloaddition can be brought about by photolysis or by the presence of a metal salt. Padwa and Kennedy[141] showed that irradiation of (**329**) in benzene gave a mixture of two dimers (**330**) and (**331**) in ratio *ca.* 5:1, while heating (**329**) at 175 °C for 72 h, resulted in the formation of two new dimers (**332**) and (**333**) in ratio *ca.* 1:1; the latter dimers were also formed by thermolysis of the bicyclobutane (**330**).



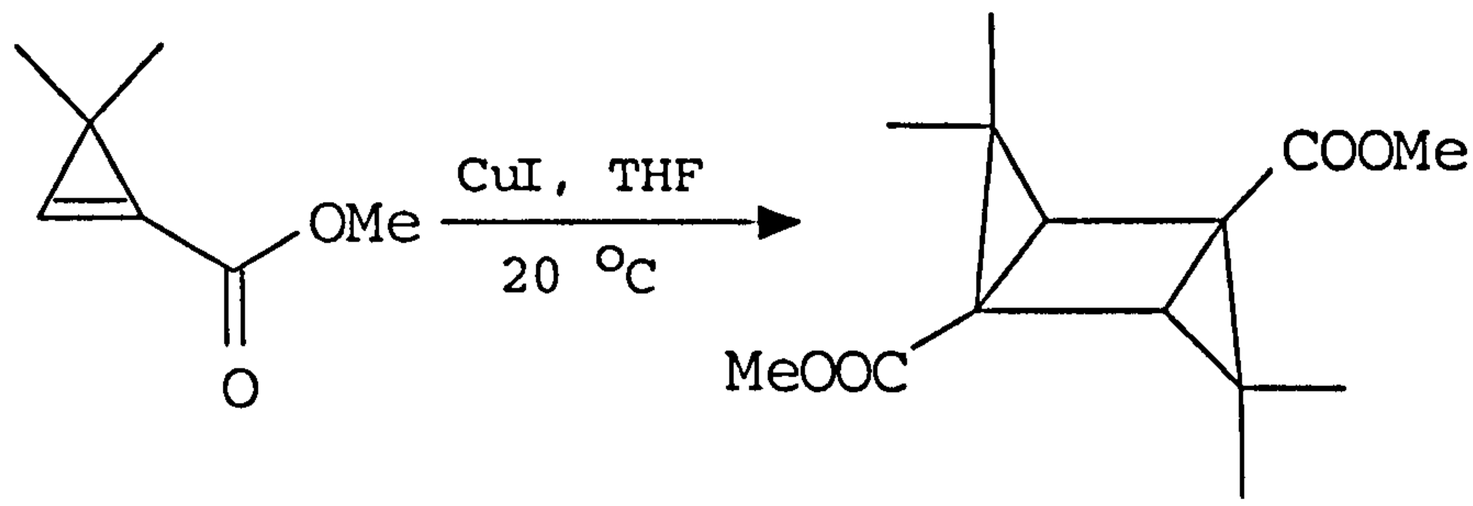
The formation of these compound may involve of a stepwise process. Generation of the diradical (**334**) and collapse of this with carbon-carbon bond formation furnishes the tricyclohexane (**335**),which rearranges to (**331**). In addition, the diradical (**334**) can undergo ring opening to give (**336**) which subsequently cyclises to give the bicyclobutane (**330**). Moreover, the formation of (**332**) and (**333**) by heating of (**329**) may also proceed via the intermediate biradical (**336**).



(329) (334) (336)

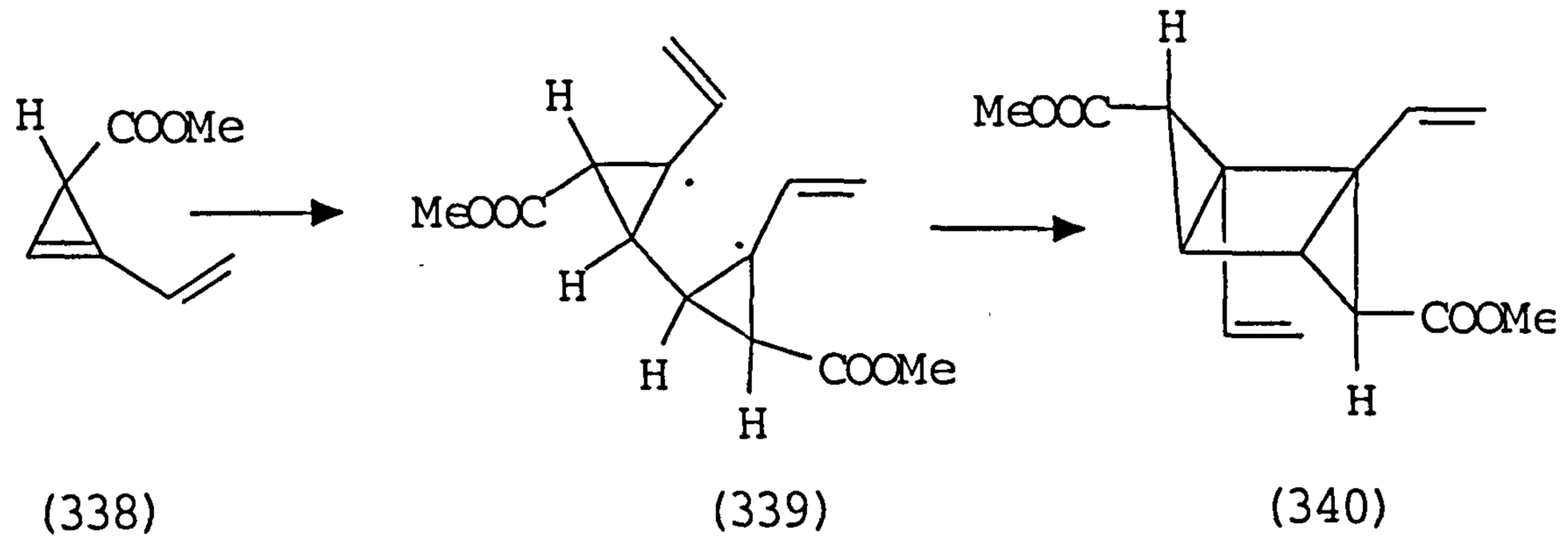
(331) (335) (330)

Baird and Hussain found that, when the cyclopropene (**57**) was allowed to stand in tetrahydrofuran in the presence of copper(I) halide, a dimer (**337**) was obtained in good yield via [2+2]-cycloaddition.[130]



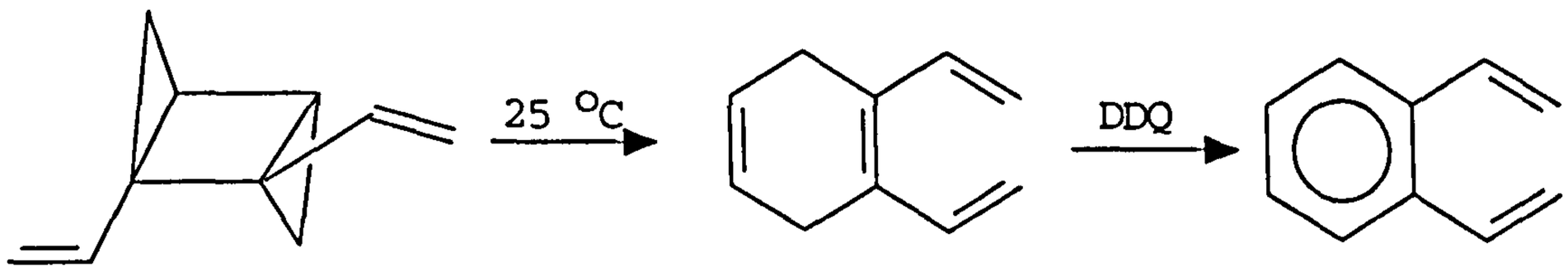
(57) (337)

Recently, Nefedov[142] and co-workers found that vinylcyclopropene (**338**) underwent similar thermal [2+2]-cycloaddition to give (**340**) via the diradical (**339**).



(338) (339) (340)

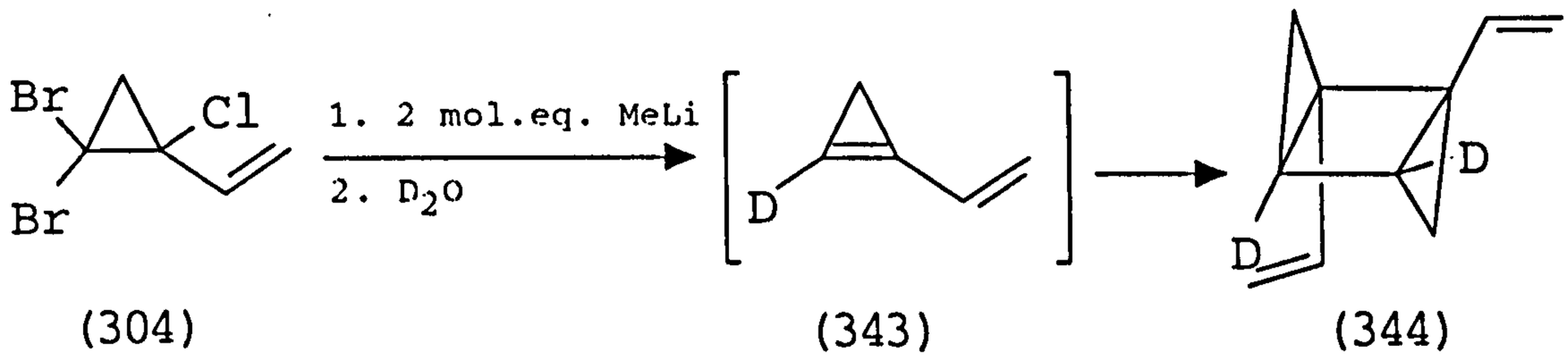
When (**325**) was allowed to stand in $CDCl_3$ at room temperature for 4 weeks, it rearranged slowly to (**341**) in 50 % yield. The ^1H n.m.r spectrum of (**341**) showed three double doublets for the vinyl group at δ 7.1, 5.2 and 5.1 with coupling constant 17.2, 11.0 and 1.1 Hz, a singlet integrating for one proton at δ 5.8, together with a broad singlet at δ 2.9 for the bis-allylic protons. These data are in agreement with those reported.[138] The structure (**341**) was further supported by converting it into 1,2-divinylbenzene, (**342**) by reaction with DDQ for 0.5 h at room temperature.[138]



(325) (341) (342)

If (**304**) was treated with two mol. equivalents of methyllithium in the presence of DPIBF at -78 to -20 °C, followed by quenching with water, a single [4+2]-cycloadduct (**320e**) was

obtained in a moderate yield. The stereochemistry of this compound was assigned by analogy with other related adducts.[101] Moreover, when (**304**) was treated as above with 2 mol. equivalents of methyllithium followed by evaporation of the solvent at low temperature and then the solid was quenched with D_2O, the 2-deuteriovinylcyclopropene (**343**) was obtained.



(304) (343) (344)

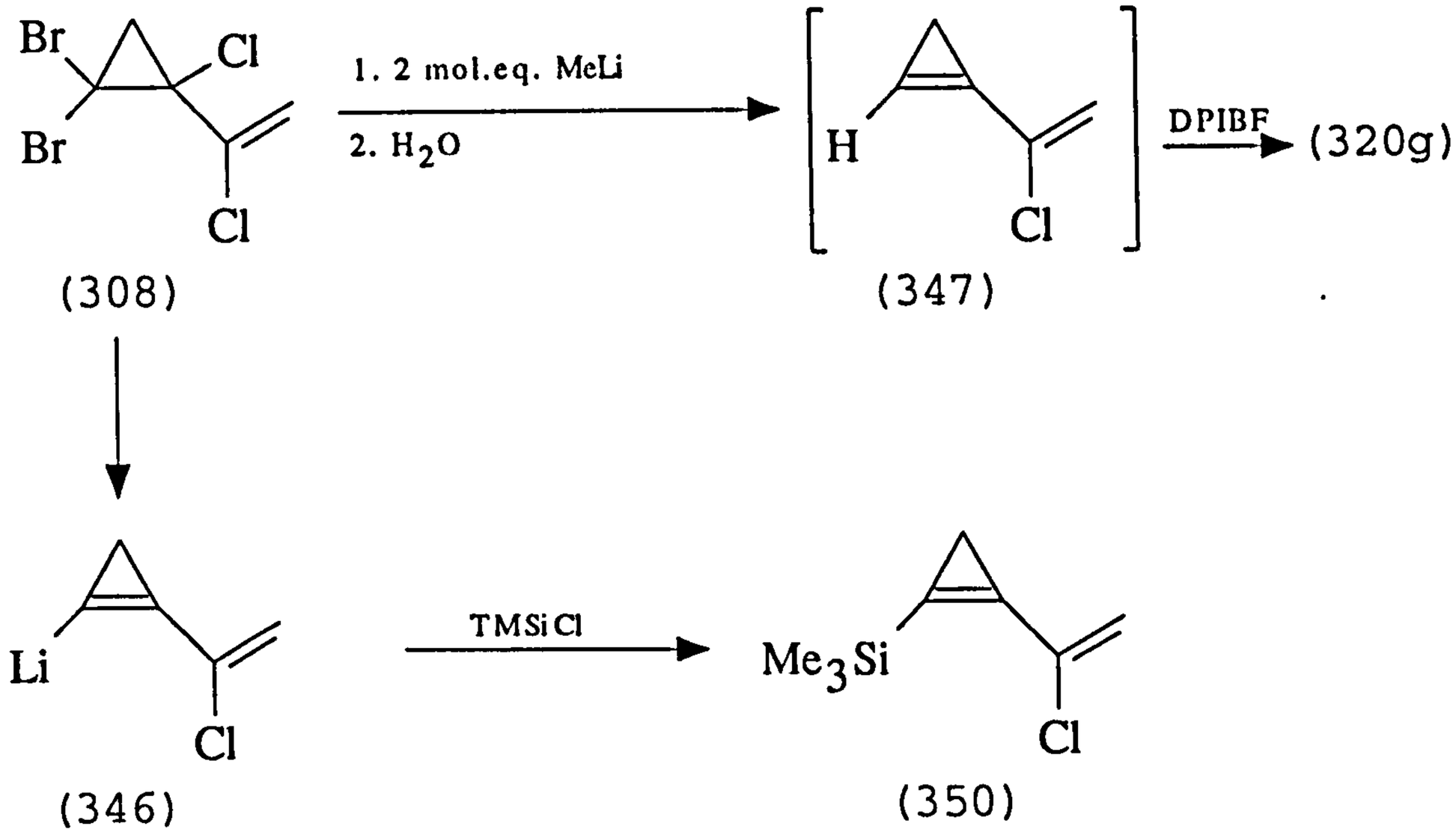
(345)

The product was again distilled as it formed and collected at low temperature. On warming to room temperature, ^1H n.m.r in $CDCl_3$ showed the presence of the [2+2]-cycloadduct (**344**). The spectrum of this was very similar to that for (**325**) except that only two signals were present in the high field region, an AB pattern at δ 1.5 and 1.5 (J 4.1 Hz). Compound (**344**) again rearranged over a period of weeks, to give (**345**), the ^1H nmr spectrum of which was identical to that of (**341**) apart from the lack of the broad singlet for the ring alkene hydrogen at δ 5.85. Deuterium incorporation was apparently >95 % complete by nmr.

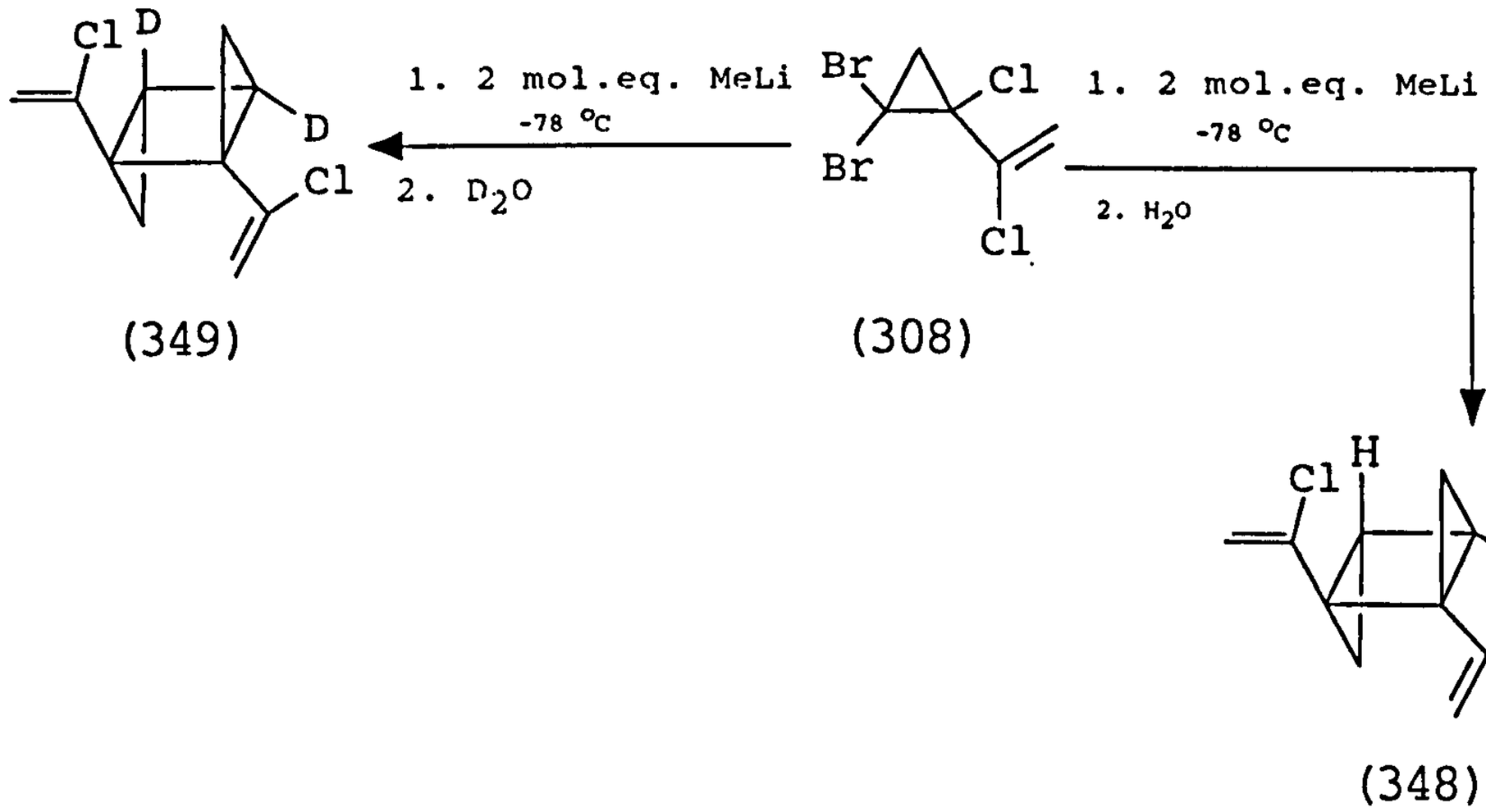
Quenching of (**324**) with trimethylsilylchloride followed by warming to room temperature gave a complex mixture. However, if the lithiocyclopropene (**324**) was

quenched with TMSCl at -78 °C and then treated at that temperature with DPIBF the adduct (**320f**) was obtained in moderate yield. This was characterised on the basis of its ^{1}H·nmr spectrum which included signals for the vinyl and silyl groups and an AB pattern for the cyclopropane at δ 2.5 and 1.8 (J 4.7 Hz).

Reaction of (**308**) with two mol. equivalents of methyllithium at -78 °C followed by warming to room temperature for 5 min and then quenching with water at -78 °C followed by addition of DPIBF led to (**320g**) together with *ca.* 25 % of a stereoisomer. Both reactions occurred via the formation and quenching of the lithiocyclopropene (**346**).



Moreover, when (**308**) was treated with two mol. equivalents of methyllithium at -78 °C and the reaction was allowed to reach room temperature and quenched with water or deuterium oxide at -78 °C, followed by work up at room temperature the [2+2]-cycloadducts (**348**) and (**349**) respectively were obtained both in 50 % yield.

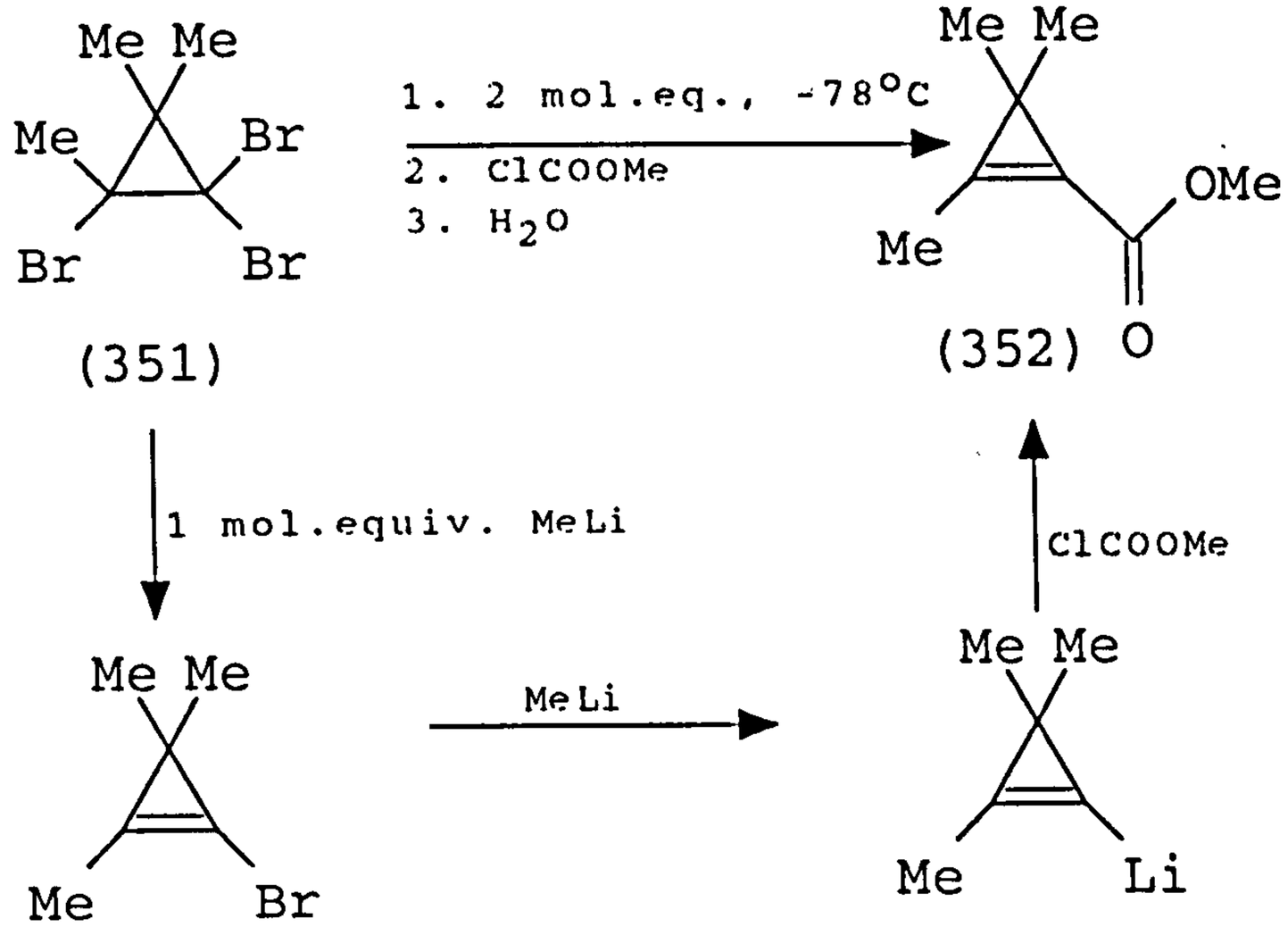


(349) (308) (348)

The dimer (**348**) gave a correct mass measurement for $C_{10}H_{10}Cl_2$, while the ^1H n.m.r was very similar to that of (**325**); the spectrum showed two narrow doublets in the alkene region with a coupling constant of 1.4 Hz and an ABC pattern at δ 1.6 - 2, and the ^{13}C spectrum showed two signals in the olefinic region and three signals in the saturated region. The dimer (**348**) remained unchanged after a week in $CDCl_3$ at 20 °C, maybe due to the presence of the halogen group on the double bond which prevents the rearrangement. The product (**349**) showed complete dideuteriation by ^1H n.m.r, a clean pair of doublets being observed in the cyclopropane region. Addition of DPIBF at low temperature after quenching with D_2O, followed by warming to room temperature led to (**320h**), again in a 5:1 ratio of stereoisomers.

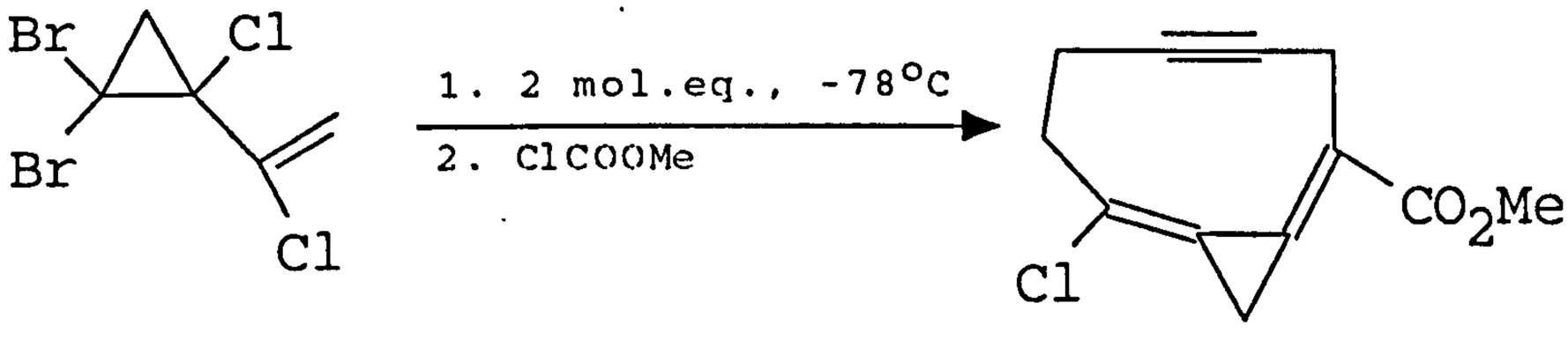
Quenching of (**346**) with TMSiCl led to the cyclopropene (**350**) in 60 %, which was stable for several days at 20 °C, and showed four singlets in its ^1H nmr spectrum at δ 0.1 (9H), 1.2 (2H), 5.7 (1H) and 5.8 (1H). Trapping with DPIBF lead to a single cycloadduct (**320i**) which showed large chemical shift difference between the cyclopropane hydrogens (δ 2.7 and 1.7) in agreement with an *exo*-stereochemistry.[101]

It is known that on reaction of 1,1,3-tribromo-2,2,3-trimethylcyclopropane (**351**) with two equivalents of methyllithium at -78 °C followed by addition of an electrophile such as methylchloroformate, (**352**) was obtained in a good yield.[77]



The formation of (**352**) as mentioned above, involves 1,2-elimination of lithium bromide to produce the bromocyclopropene (**353**) which in turn reacts further with methyllithium via a lithium-bromine exchange to give a lithiocyclopropene (**354**). This reacts with methyl chloroformate giving the desired product. It was expected that (**346**) would react with $ClCO_2Me$ in the same way.

However, reaction of (**308**) wih two mol. equivalents of methyllithium at -78 °C to 20 °C followed by addition of methyl chloroformate at -50 °C and stirring overnight at room temperature, gave a crystalline solid characterised as (**355**), in moderate yield.

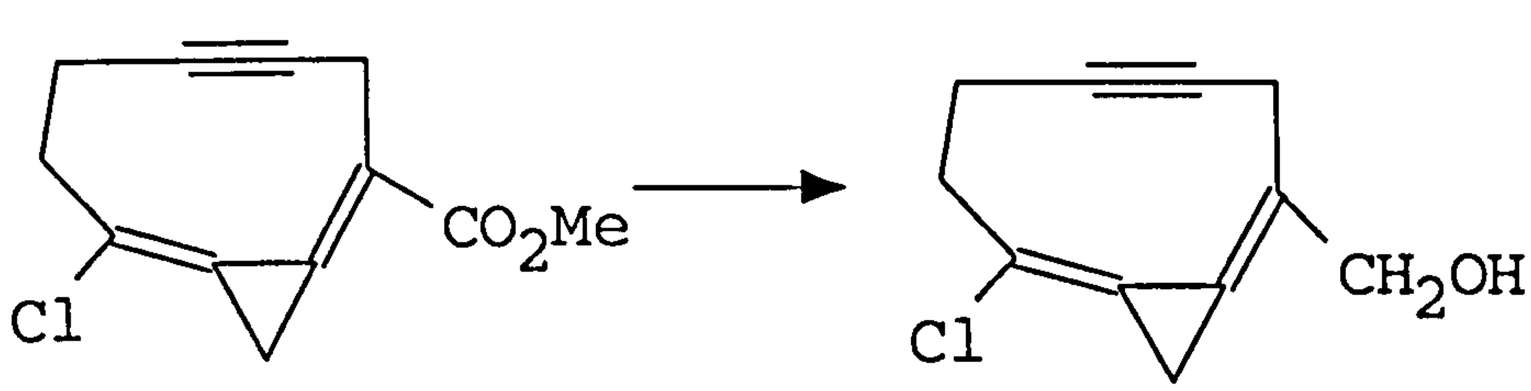


(308) (355)

Compound (**355**) showed an accurate C, H micro analysis for the formula $C_{12}H_{11}O_2Cl$, and the IR spectrum displayed a single carbonyl bond at 1700 cm^{-1} for the unsaturated ester. The ^{13}C nmr spectrum showed the expected signals, including four quaternary alkene signals and two quaternary alkyne signals as well as four methylene groups. In the fully proton coupled spectrum, three of the methylene carbons showed $^1J_{CH}$ values of *ca.* 130 Hz, but the fourth one, that at highest field, showed a value of 167 Hz and is assigned to the cyclopropane carbon. All of the alkene and alkyne carbons appeared as narrow multiplets, suggesting long range coupling to at least two methylene groups. In the ^1H nmr spectrum there was a methyl ester signal together with four complex multiplets at δ 3.2, 2.9, 2.4 and 1.9. The signal at δ 3.2 could be analysed as a pentuplet (J 2.1 Hz); the one at δ 1.9 was also a pentuplet (J 2.1 Hz). The signals at δ 2.9 and 2.4 were much more complex. Irradiation at δ 2.4 caused the signal at δ 3.2 to be decoupled to a triplet but did not change the one at δ 1.9; it did decouple the signal at δ 2.9 to a broad singlet with smaller satellite lines. Irradiation at δ 2.9 had an identical effect on the signal at δ 2.4, but in this case decoupled the one at δ 1.9 to a triplet and left that at δ 3.2 unchanged. Irradiation at δ 3.2 decoupled the signal at δ 1.9 to a triplet, sharpened the signal at δ 2.4 removing some small couplings and did affect that at δ 2.9. Irradiation at δ 1.9 decoupled the signal at δ 3.2 to a triplet, sharpened the signal at δ 2.9 and left that at δ 2.4 unchanged. It appears therefore that the signals at δ 2.4 and 2.9 are best explained in terms of a $-CH_2-CH_2-$group with long-range coupling of one of the

methylenes (that at 2.9) to the CH_2 at δ 1.9 and of the other (at 2.4) to the CH_2 at 3.2; the signal at δ 1.9 and 3.2 also showed long-range coupling to each other.

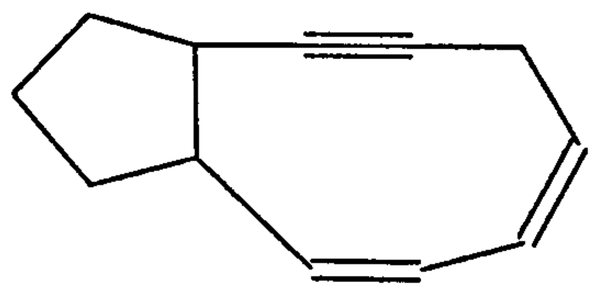
Reduction of (355) with diisobutylaluminium hydride at -50 °C to room temperature in dichloromethane gave (356) in 92 % as a white solid.



(355) (356)

The ^1H n.m.r spectrum was a quite similar to that for (355) except for the disappearance of the methyl signal at δ 3.8 and the appearance of a broad singlet at δ 4.2 integrating to two hydrogens for the methylene adjacent to the alcohol. This rules out the presence of a CH_2-COOMe group. The ^{13}C spectrum showed the expected signals, including four in the olefinic region at δ 126, 125, 117 and 115.41, two signals in the alkyne region and one signal at δ 65.70 for the CH_2-OH group, together with four signals in the saturated region. The structure of the product (355) was confirmed by an X-ray crystallographic study **(Figure 8)**.

The cyclononyne (355) is a most unusual product; a substructure search of Chemical Abstracts revealed only one other example of a cyclonona-1,3-dien-6-yne (357).[143]



(357)

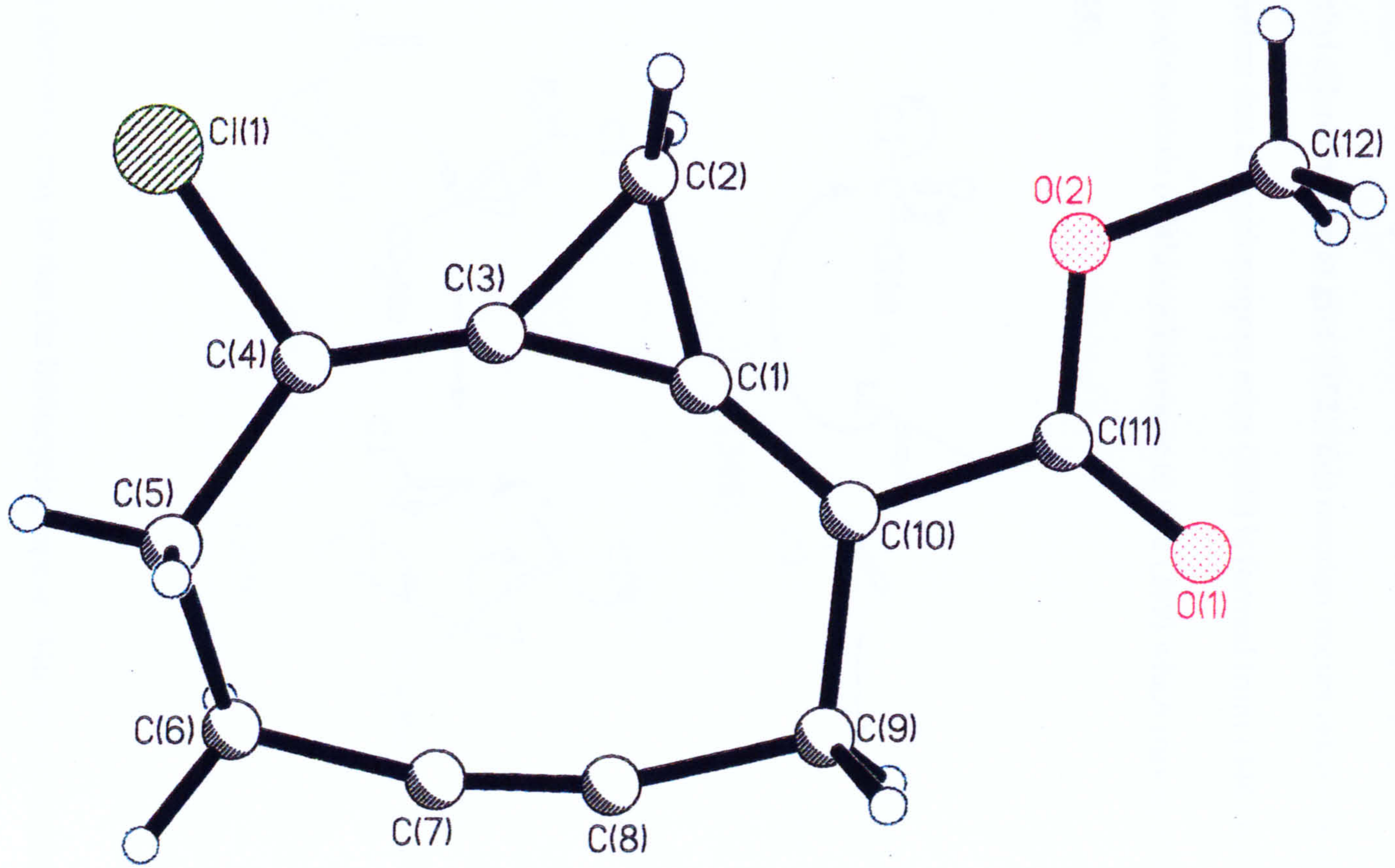
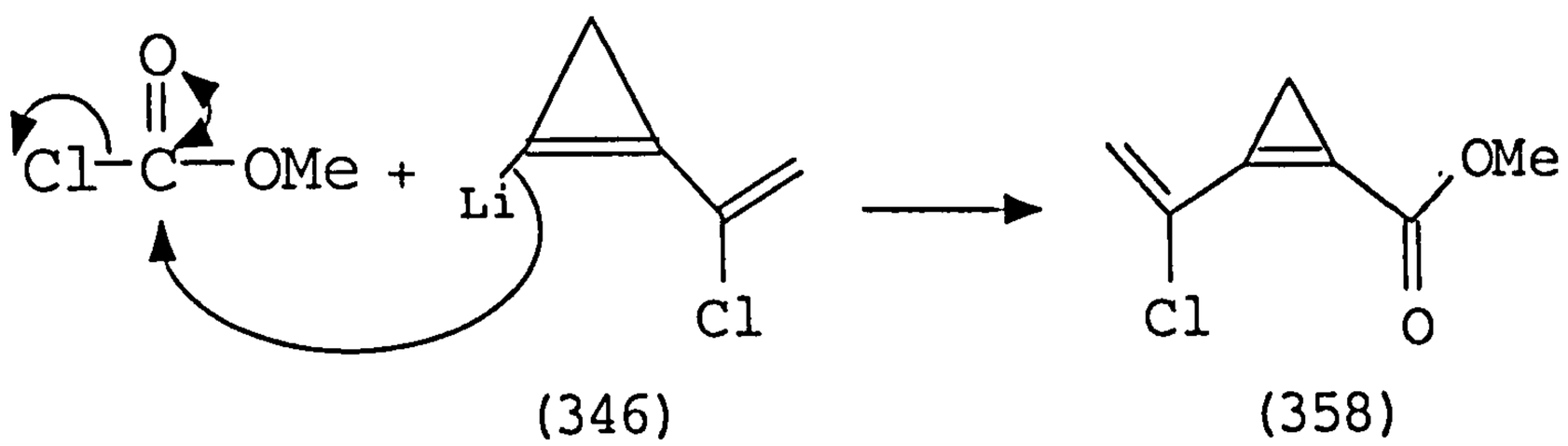
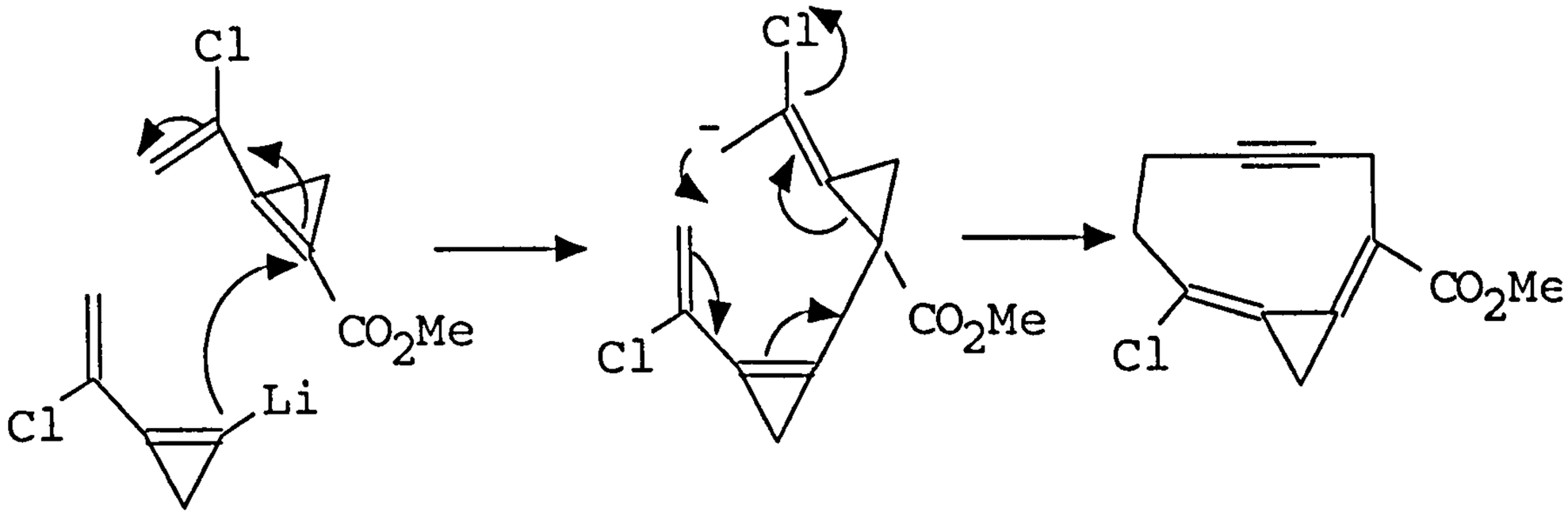


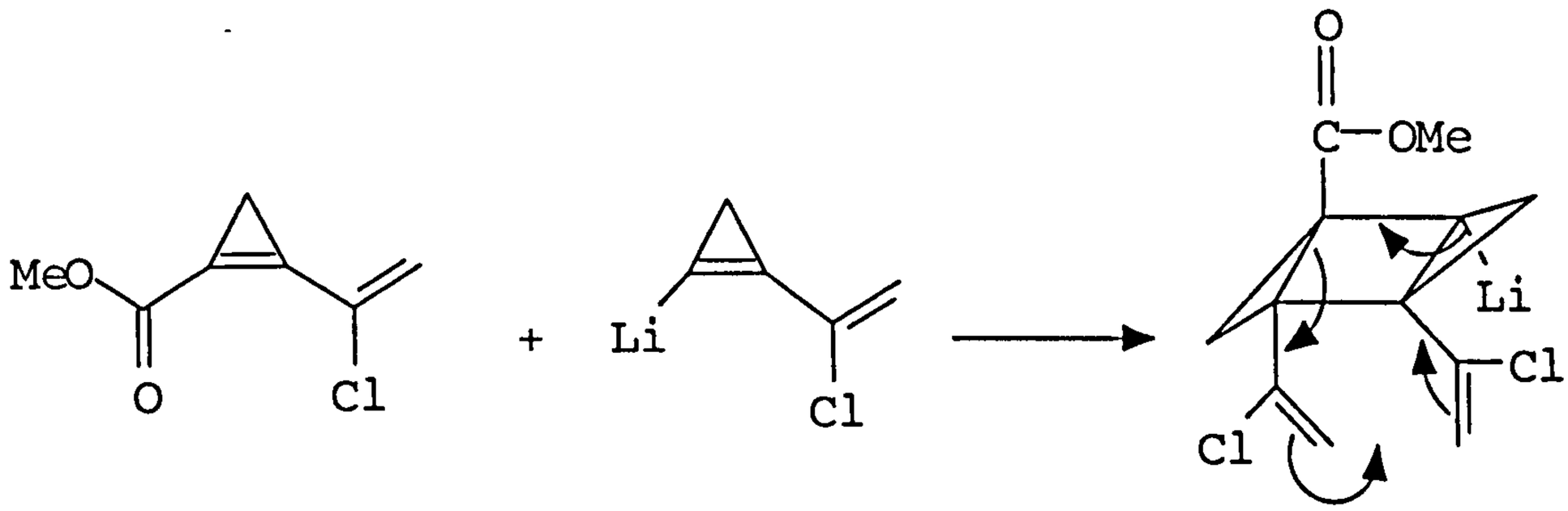
Figure 8. Crystal structure of the compound (355)

It appears that the product (**355**) resulted from two molecules of lithiocyclopropene (**246**) and one of methyl chloroformate, with the elimination of two molecules of lithium chloride. The results above (p. 149) showed that the lithiocyclopropene (**354**) can be trapped by methyl chloroformate to give (**352**); this reaction occurs relatively slowly and it is possible therefore that the cyclopropene ester (**358**) is formed from (**346**) but rapidly trapped by the second molecule of lithiocyclopropene to give (**359**) which may cyclise as shown to produce (**355**).

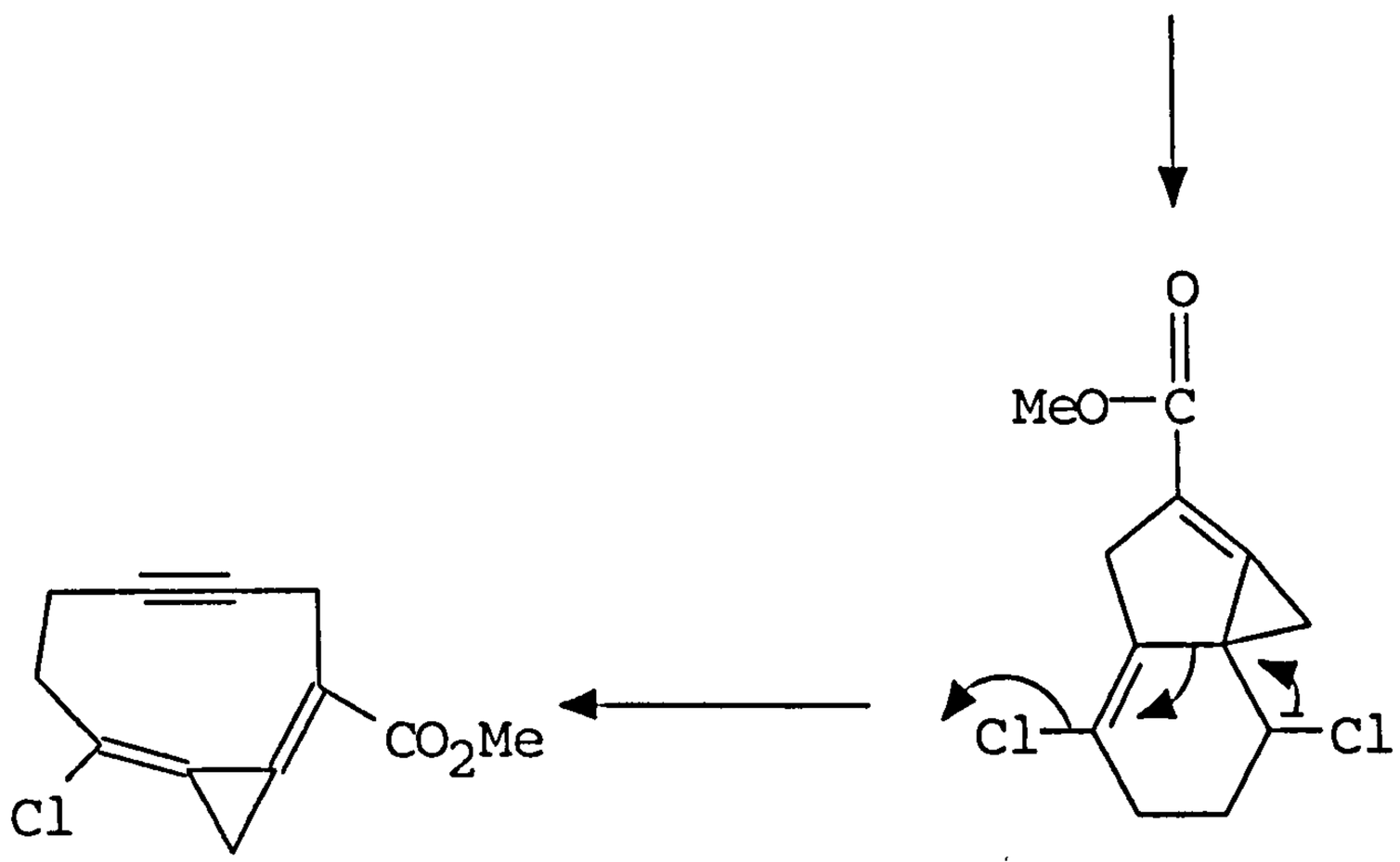




An alternative may be that the lithiocyclopropene (**346**) reacts with the ester (**358**) through [2+2]-cycloadduct to give (**360**), which undergoes cyclisation and rearrangement to the final product.



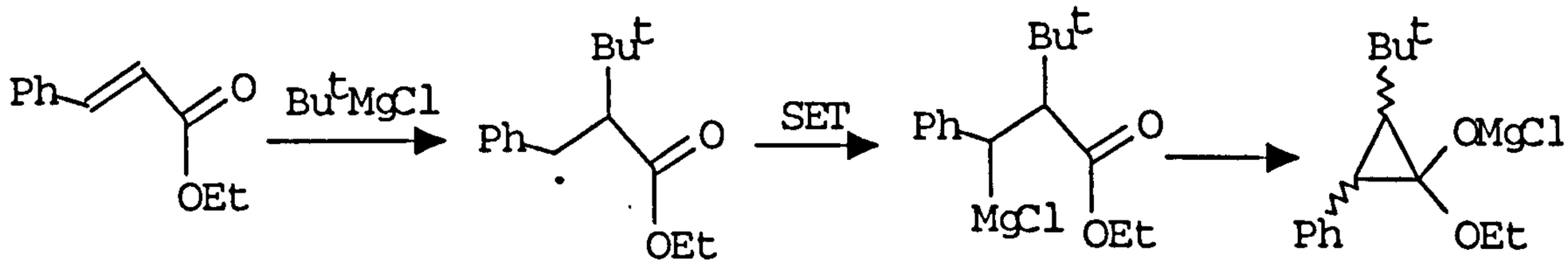
(358) (346) (360)



(355)

However, there is no direct evidence for this mechanism, and it must be said that the regiochemistry of the first addition is unusual ! However, the relief of strain is going from a cyclopropene to an exocyclic allylic ion may overcome the directing effect of the ester. It should be noted that this mechanism also requires the allylic anion to be formed in a geometry suitable for cyclisation; further experiments are required to establish the mechanism more clearly. However, it is perhaps significant that the addition of t-butylmagnesium chloride to ethyl cinnamate also leads to a product derived by addition of a t-butyl group to the α-carbon of the α, β-unsaturated ester. This reaction has been

explained in terms of the addition of a t-butyl radical to produce (**361**) followed by single electron transfer to give the corresponding anion, and then cyclisation to (**362**).[144]



(361) (362)

5.4. CONCLUSION

The addition of dihalocarbenes to 2-chloro- or 2,3-dichlorobutadiene to form trihalocyclopropanes which react with one or two molecular equivalents of methyllithium provides a practical route to 1-halo-2-vinylcyclopropenes and vinylcyclopropenes respectively. These are readily trapped in Diels-Alder reactions. Moreover, vinylcyclopropenes undergo a [2+2]-cycloaddition to release the strain of the cyclopropene. However, the reaction of 1-lithio-2-vinylcyclopropene with methyl chloroformate gave an unusual product containing a cyclononadienyne unit. Addition of dihalocarbene, generated under phase transfer or anhydrous conditions, to vinyltrihalocyclopropanes led to a very low yield of the coresponding bicyclopropane.

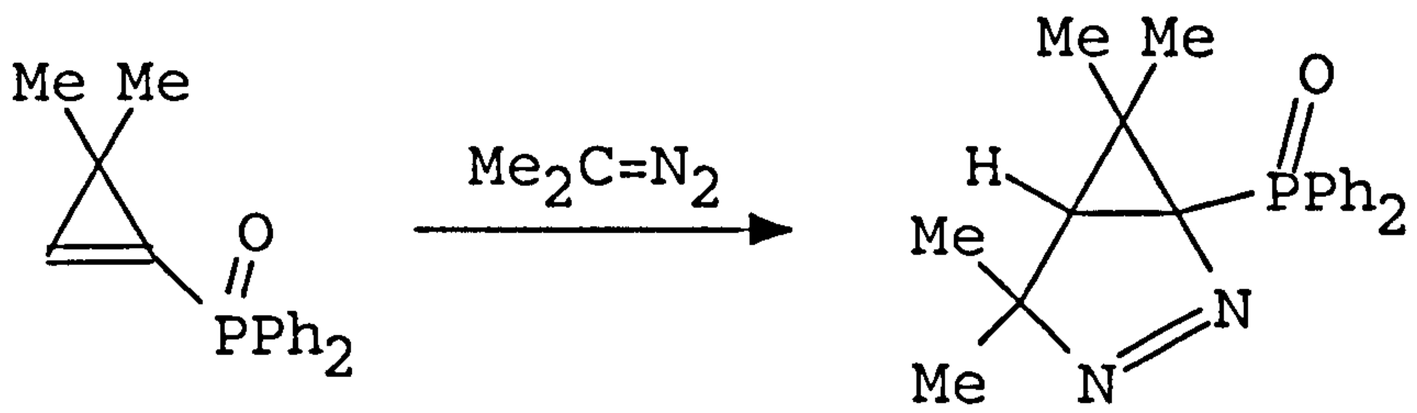
Chapter 6

Addition of diazomethane to 1-bromo- and 1,2-dibromocyclopropenes

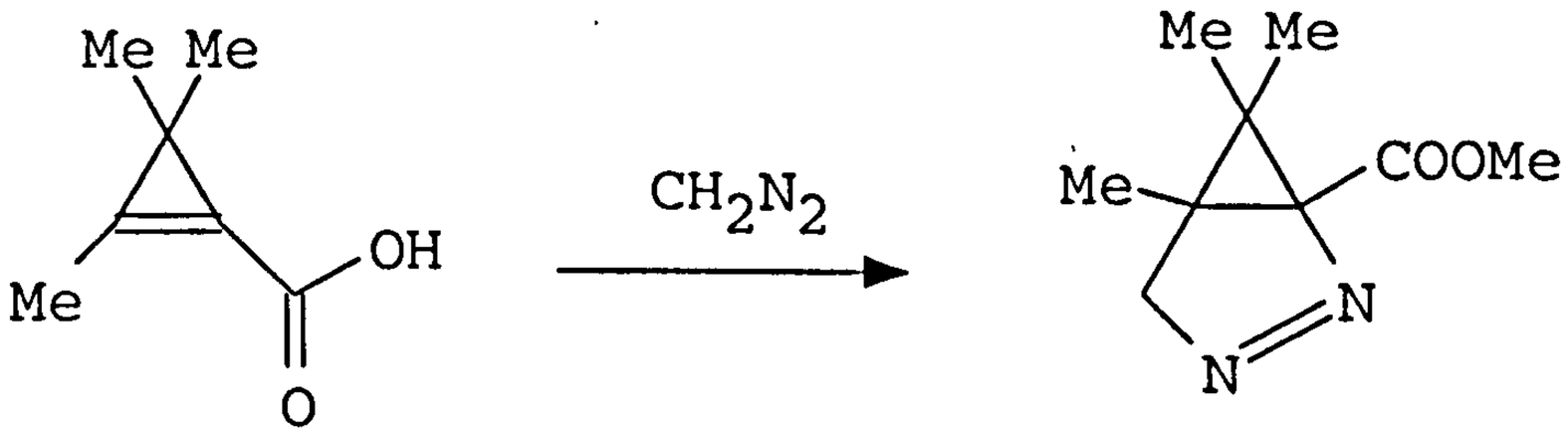
6.0. ADDITION OF DIAZOMETHANE TO 1-BROMO- AND 1,2-DIBROMOCYCLOPROPENES

6.1. INTRODUCTION

Diazoalkanes are known to undergo 1,3-dipolar cycloaddition to a number of cyclopropenes under very mild conditions leading initially to pyrazolines. However, these are in some cases very sensitive to base or acid and rearrange to pyridazines.[145] The reaction can show high regioselectivity, e.g., treatment of (**363**) with diazopropane leads only to the pyrazole (**364**).[146] Moreover, when the cyclopropene (**365**) was treated with an excess of diazomethane only one regioisomer (**366**) was obtained, in 92 % yield.[146]

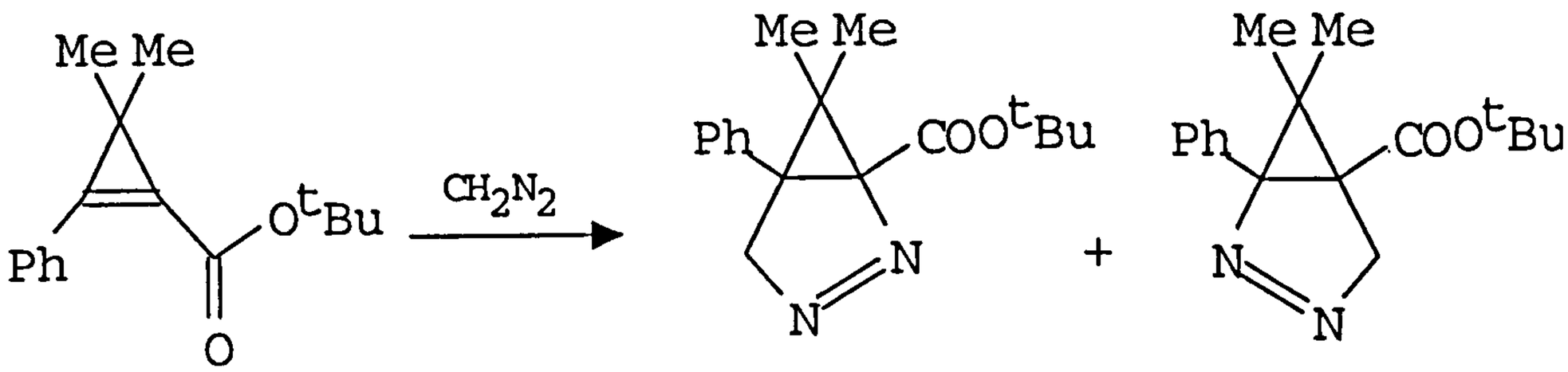


(363) (364)



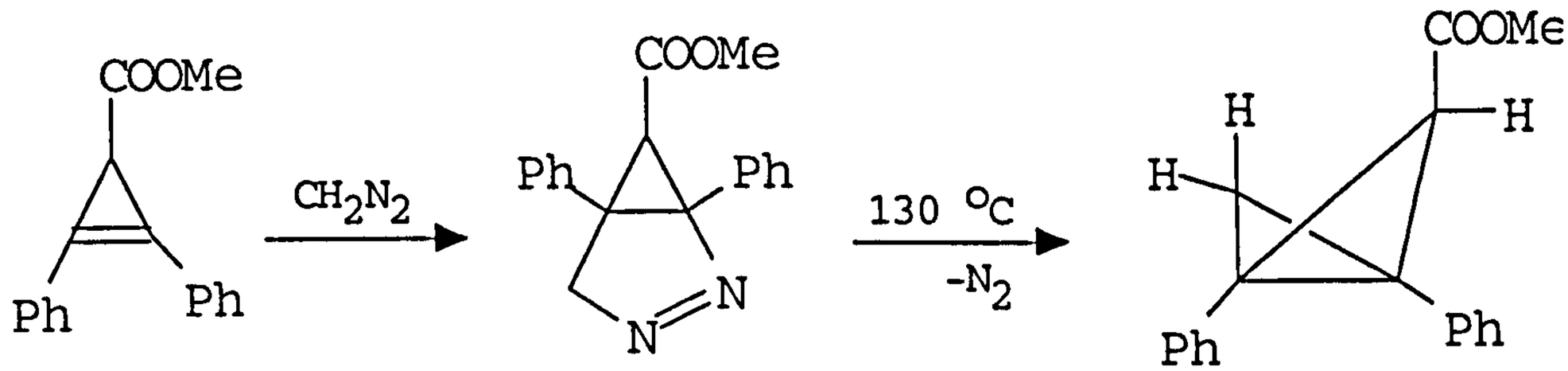
(365) (366)

In other cases, less selectivity is observed, and reaction of the cyclopropene (**367**) with diazomethane gave two isomers in ratio *ca.* 1:1.[147,148]



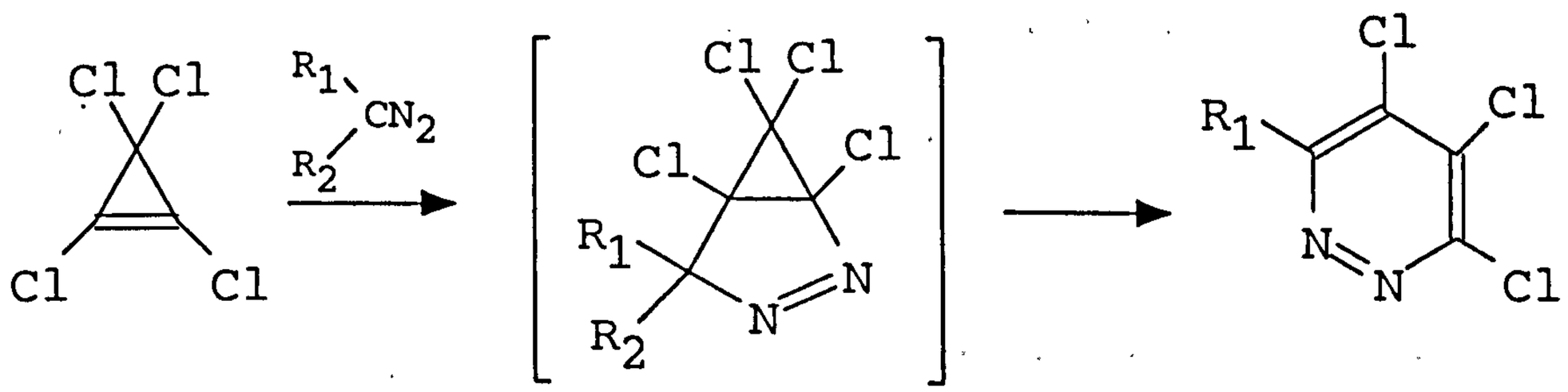
(367)

Moreover, reaction of (**368**) with diazomethane gave the pyrazole (**369**) (80 %) of unspecified stereochemistry, which rearranged to (**370**) upon heating at 130 °C, after losing nitrogen.[149]



(368) (369) (370)

It has been reported that the reactivity of cyclopropenes towards diazoalkanes, depends on the substituents on the cyclopropene in the reactivity order, cyclopropene > 1-methylcyclopropene > 3,3-dimethylcyclopropene > 1,3,3-trimethylcyclopropene, and has been explained in terms of steric effects.[62] Furthermore, the stability of product pyrazolines has also been reported to be affected by substituents.[62] Although some could be isolated as stable compounds, a number of other examples could not be identified and rearranged rapidly under the reaction conditions. Thus the reaction of the tetrachlorocyclopropene (**69**) with alkyl diazomethane leads directly to the pyridazines (**372**) without isolation of the intermediate (**371**).[150]

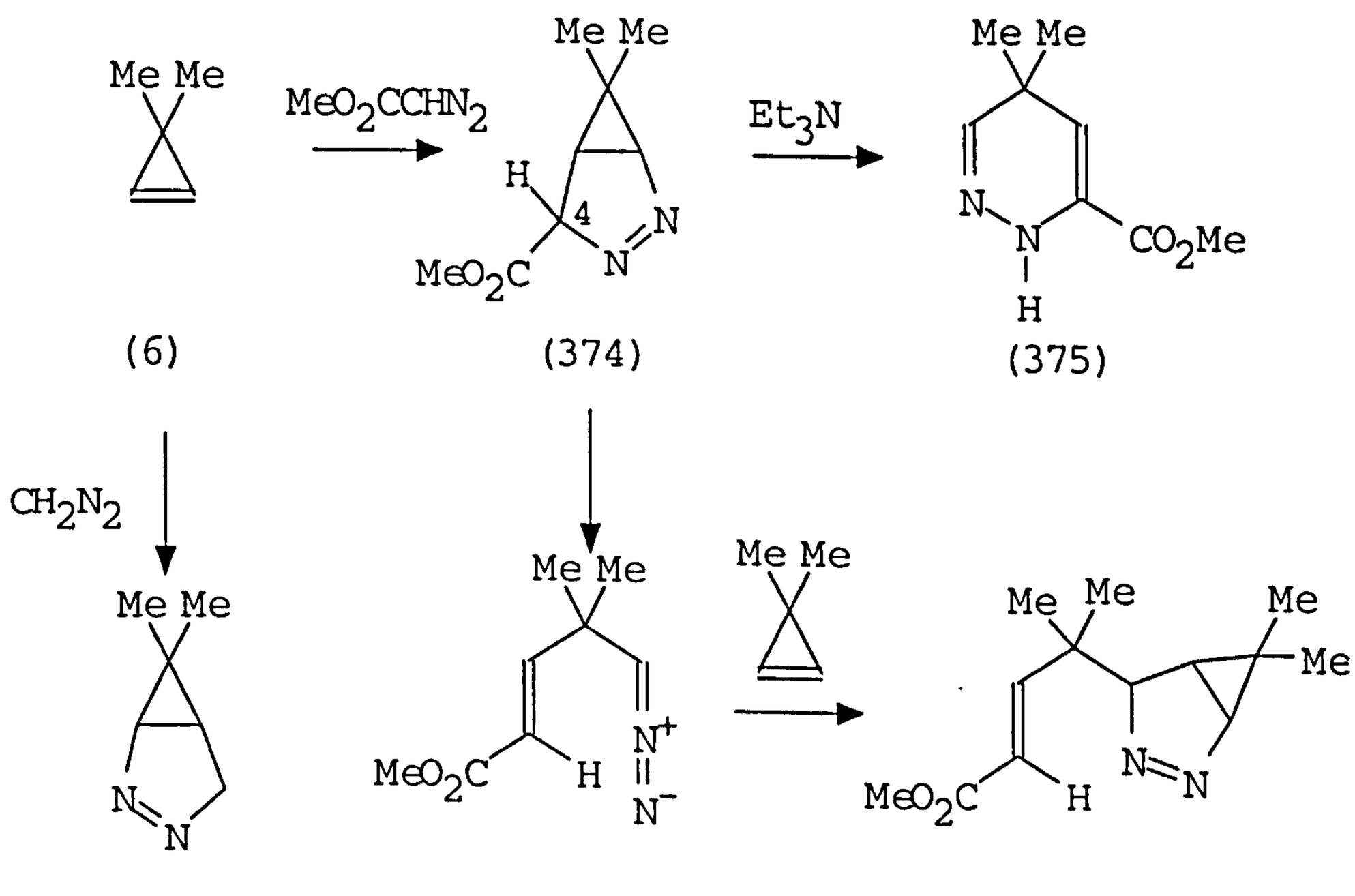


(69) (371) (372)

R_1 = H, Me, COOEt

R_2 = H

Moreover, reaction of 3,3-dimethylcyclopropene (**6**) with diazomethane led to pyrazoline (**373**) as a stable compound, while with methyl diazoacetate, it gave a mixture of two products (**375**) and (**376**) originating from the initial adduct (**374**).[62]

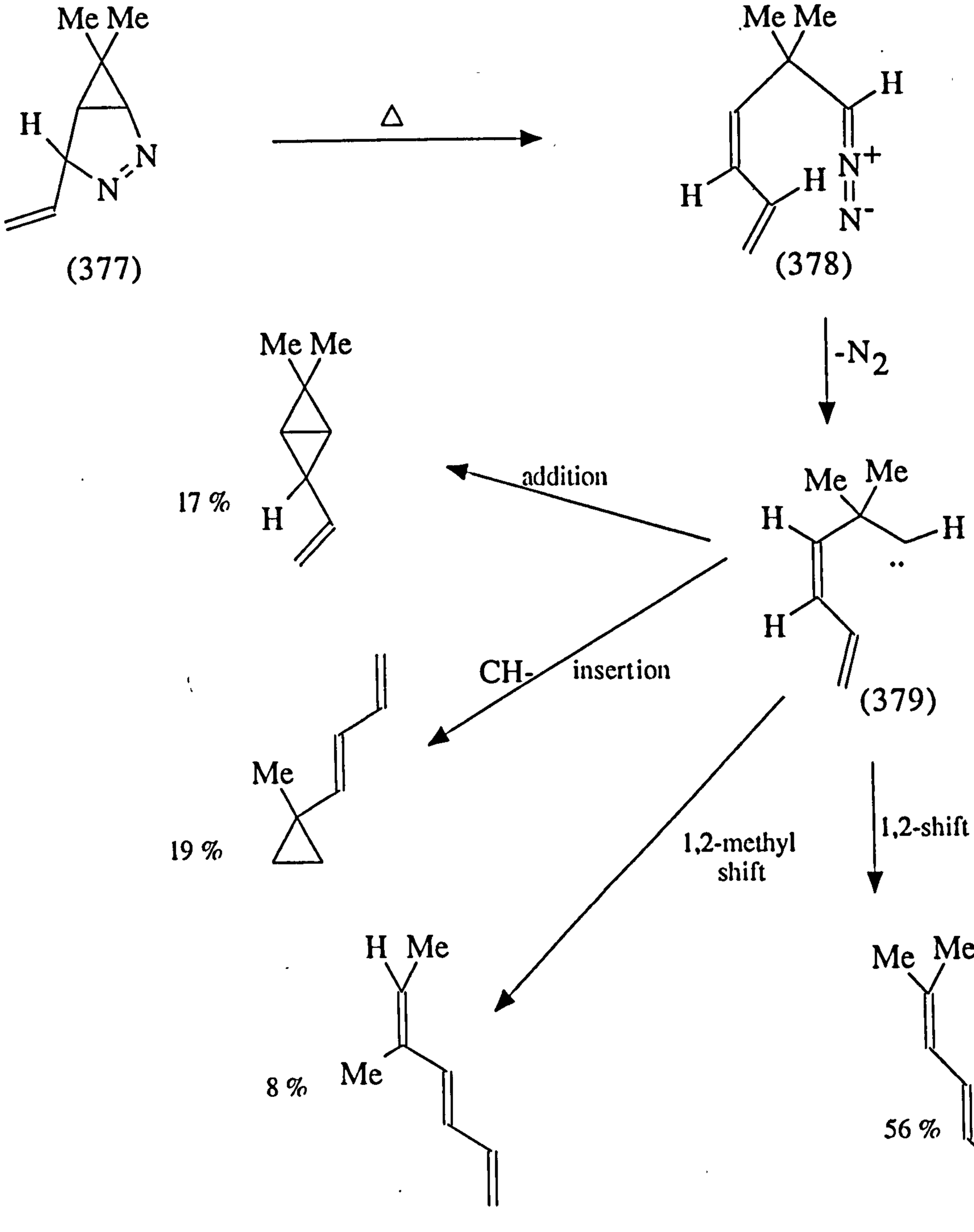


(6) (374) (375)

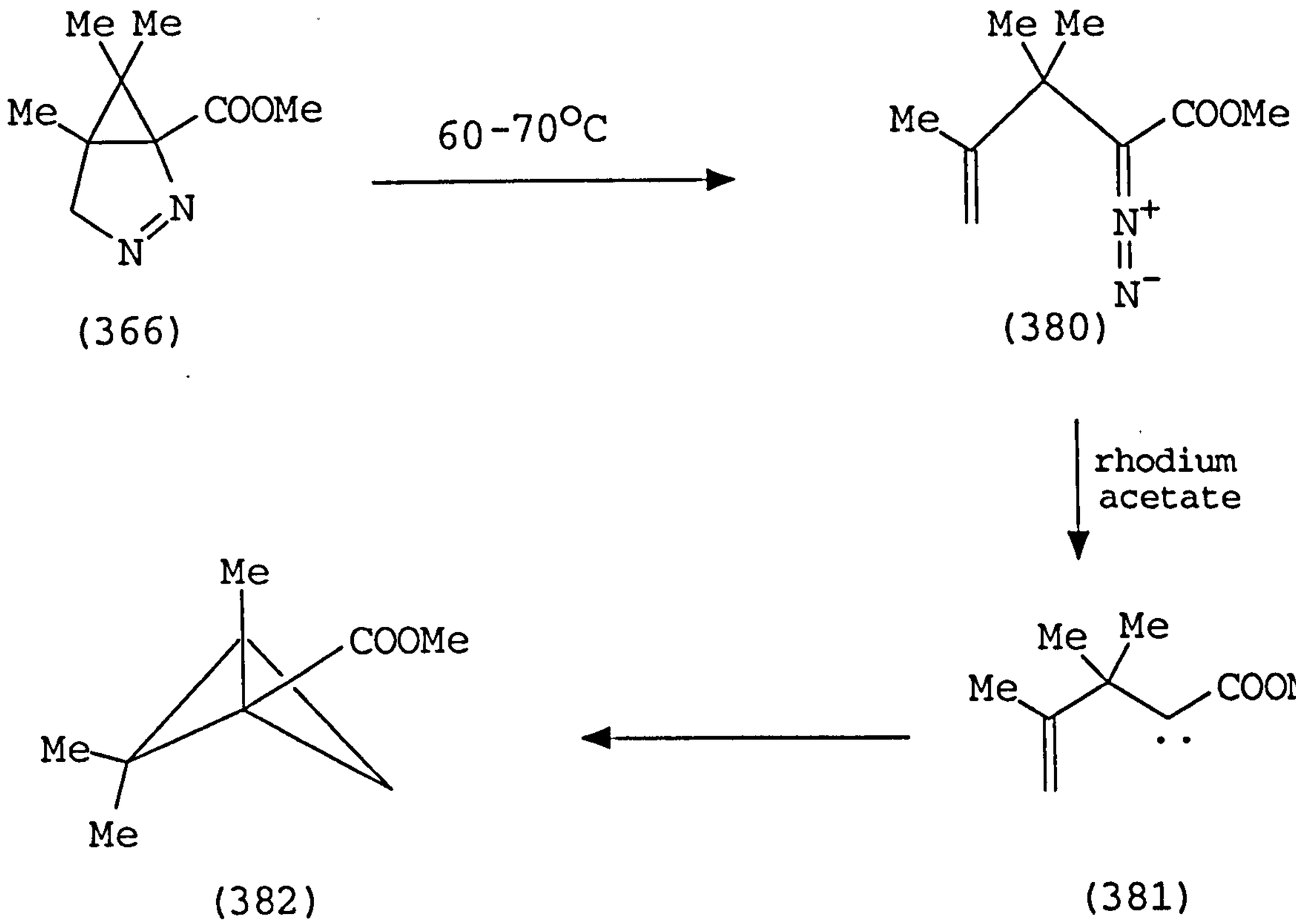
(373) (376)

The instability of the adduct (**374**) was explained by the presence of the electron withdrawing group at C_4, facilitating its rearrangment to the diazo-derivative. This in turn underwent a 1,3-dipolar addition with a second molecule of cyclopropene to give (**376**). The formation of dihydropyridazine (**375**) was again explained by the presence of the electron withdrawing group at C_4 in (**374**), and it also seems possible that the excess of diazoacetate ester may act as a basic catalyst in the rearrangment of (**374**) to (**375**). This is supported by the exclusive formation of (**375**), when the reaction was run in the presence of triethylamine.[62]

The thermal decomposition of a number of pyrazolines was also reported. In some cases, thermolysis leads to the clean formation of bicyclo [1.1.0]butanes;[146] in other cases, complex products are obtained which are consistent with rearrangment of the pyrazoline to a diazo-compound. Thus the pyrolysis of (**377**) gave a mixture of four components. The products may arise by decomposition of the pyrazoline to the diazo-derivatives (**378**), and this could eliminate a nitrogen to produce the carbene (**379**) which in turn can undergo various intramolecular reactions.[151]



In contrast, Baird and Hussain[146] found that, when the pyrazoline (**366**) was heated at 60 - 70 °C for 48 h, a smooth rearrangment occurred to produce the diazocompound (**380**), which after treatment with rhodium acetate gave the carbeniod (**381**) which underwent a relatively clean addition to the alkene bond give (**382**) in preference to alternative carbenic reactions such as a 1,2-alkyl or alkenyl shift.



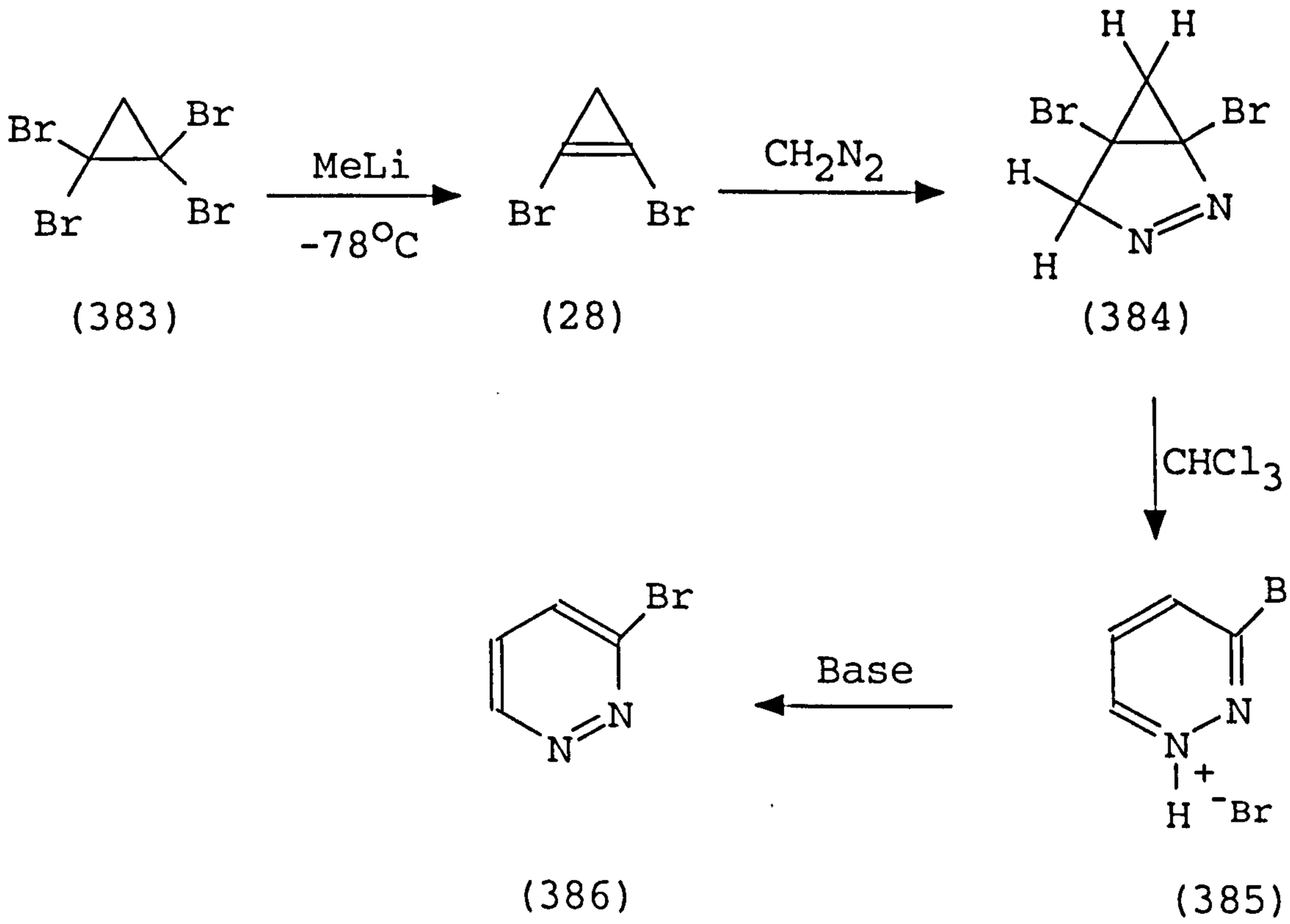
6.2. AIMS OF THE PROJECT

As mentioned previously, the addition of diazomethane to a range of stable cyclopropenes, e.g. tetrachlorocyclopropene or 3,3-dimethylcyclopropene leads to pyridazines and pyrazolines respectively. It was of interest to investigate the addition of diazoalkanes to 1-halo-and 1,2-dihalocyclopropenes.

6.3. RESULTS AND DISCUSSION

6.3.1. REACTION OF 1,2-DIBROMOCYCLOPROPENE WITH DIAZOALKANES

Cyclopropene (**28**) was prepared by treatment of the tetrabromocyclopropane (**383**) with one equivalent of methylithium at -78 °C, followed by quenching with water at this temperature; the ether layer was treated with an excess of diazomethane at 0 °C. A rapid reaction occurred leading to the pyrazoline (**384**) in 85 % yield, after evaporation of the solvent and excess of diazomethane at 0 °C.



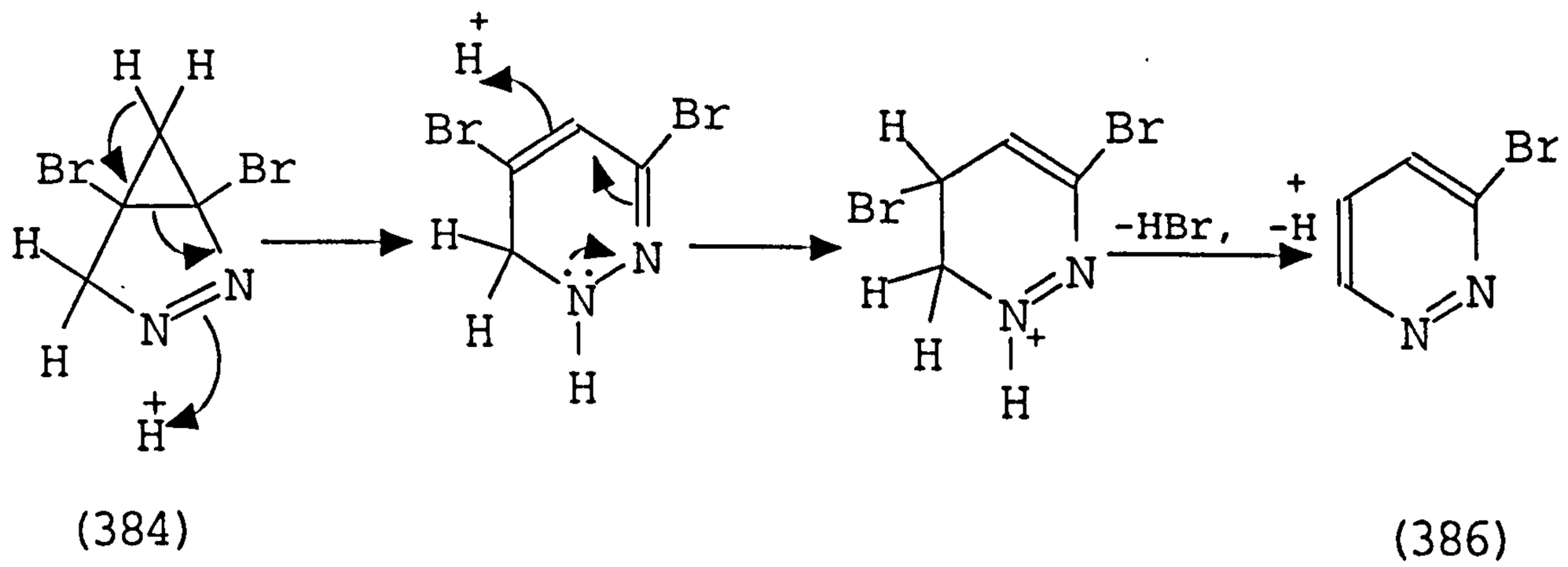
(383) (28) (384) (385) (386)

The lack of rearrangment of (**384**) was indicated by the absence of an olefinic signal in the ^{1}H n.m.r and the presence of the geminal hydrogens next to nitrogen with a coupling

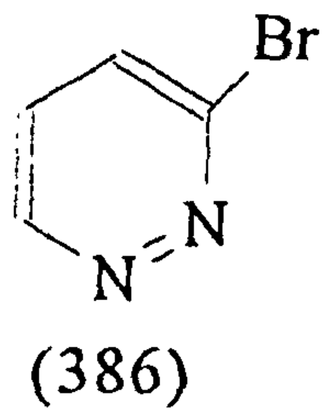
constant of 19.8 Hz, while the methylene of the cyclopropane appeared as two doublets at δ 2.0 and 1.2 with a coupling constant of 7.7 Hz (**Figure 9**). The ^{13}C spectrum showed the expected four signals. The pyrazoline (**384**) was relatively stable at 0-5 °C as a neat liquid. However, when the compound was allowed to stand in chloroform for one hour, it completly rearranged to a brown solid identified as (**385**) in 82 % yield.

The product (**385**) showed the correct C,H,N analysis and the ^1H n.m.r spectrum in D_2O showed a double doublet at δ 9.1 with coupling constants of 1.4 and 4.9 Hz, integrating to one proton, together with two doublets of doublets at δ 8.1 and 7.7 with coupling constants of 1.4, 8.7 and 4.9, 8.7 Hz respectively (**Figure 10**), while the ^{13}C spectrum gave four signals in the aromatic region. Treatment of the salt (**385**) with conc. sodium hydroxide solution at room temperature for 5 min, then extraction with diethylether, gave the free pyridazine (**386**) in 67 % yield. The ^1H n.m.r spectrum of this showed the expected three doublets of doublets at δ 9.1, 7.7 and 7.3[152] (see **Figure 11**).

The mechanism for the formation of pyridazine (**386**) is not certain, However, the reaction may involve the protonation at one of the nitrogens followed by or concurrent with ring opening of the cyclopropane as shown below.

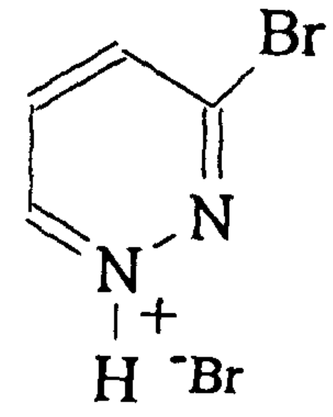


(384) (386)



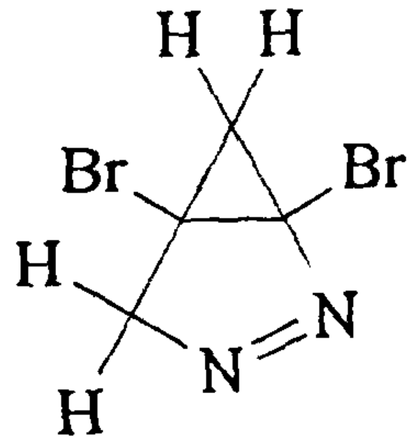
(386)

Figure 11.



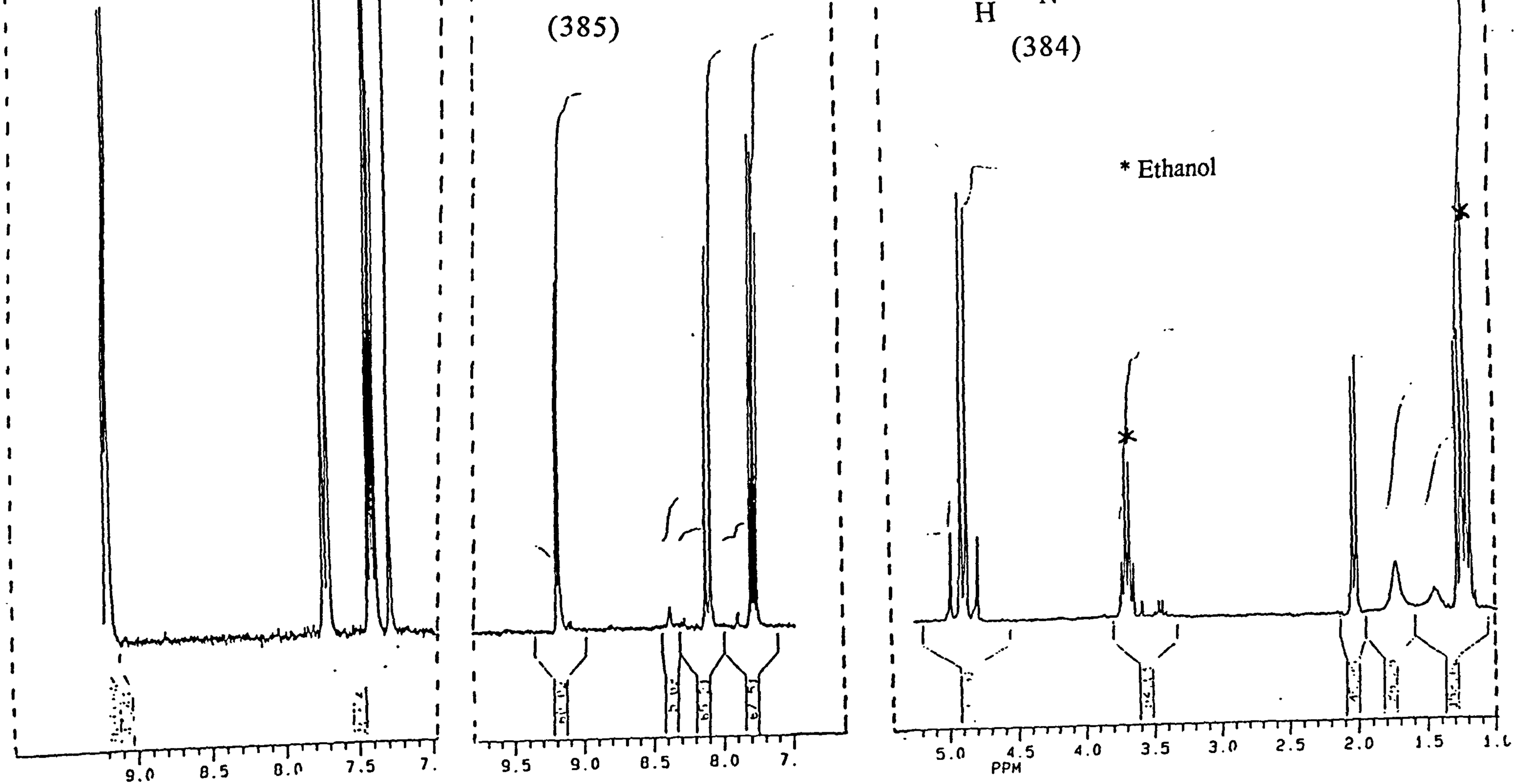
(385)

Figure 10.

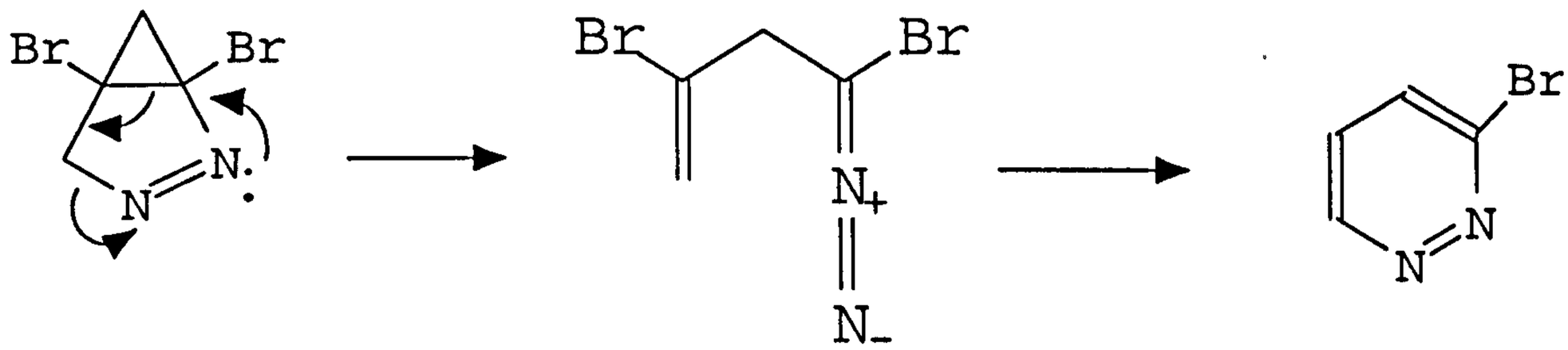


(384)

Figure 9.

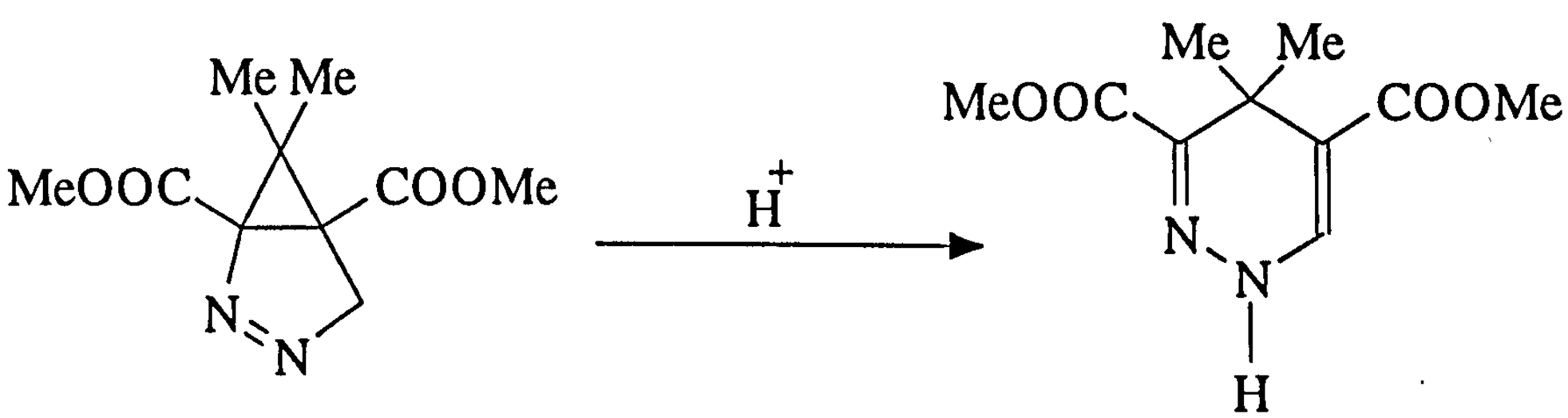


Another, mechanism could be by decomposition of the pyrazoline (**384**) to the diazo-compound (**387**), followed by cyclization and loss of HBr to give the pyridazine (**386**), However there was no evidence for the formation of the diazocompound by ^{1}H n.m.r or i.r.

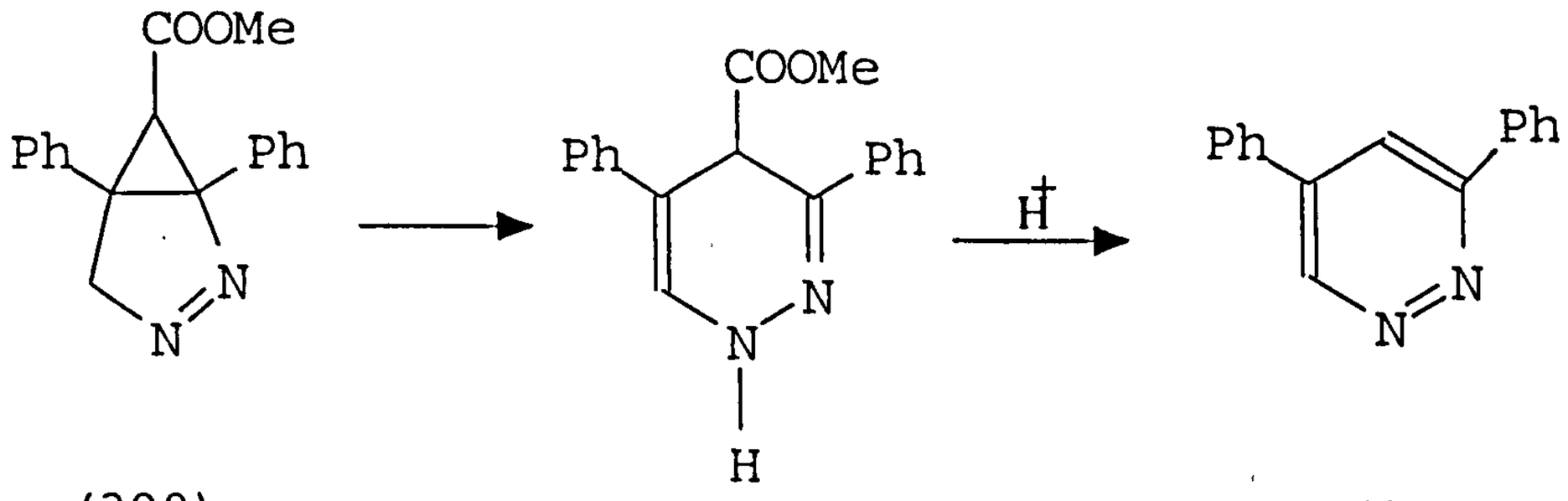


(384) (387) (386)

It has been reported that the cycloadduct (**388**) underwent acid catalysed rearrangment to the dihydro-pyridazine (**389**).[153] Similarly, the cycloadduct (**390**) is converted by alkali or acid into 3,5-diphenyl-pyridazine (**391**).[149,154]



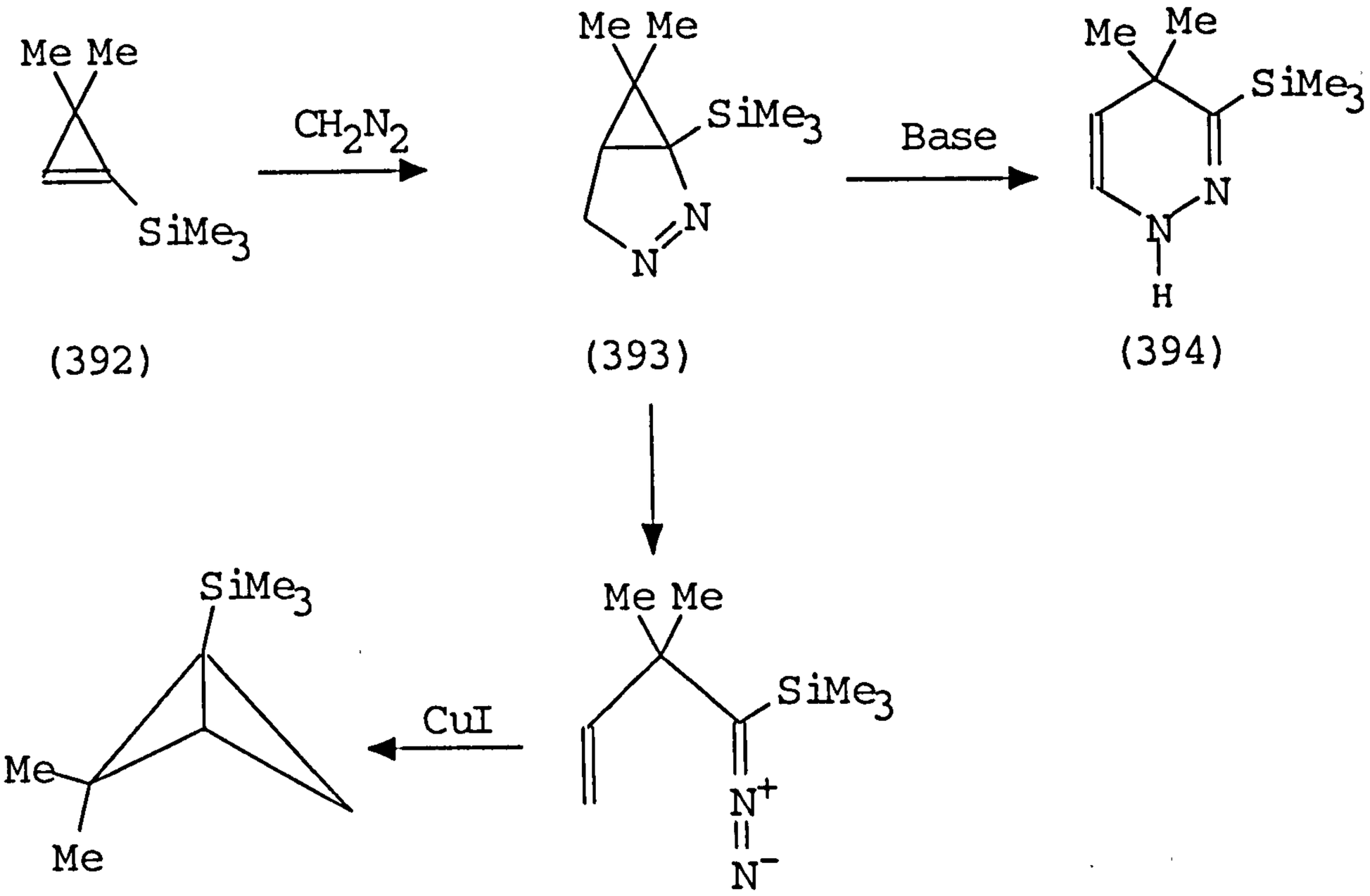
(388) (389)



(390) (391)

Addition of diazoalkanes to nonhalogenated cyclopropenes follow a different course, e.g.

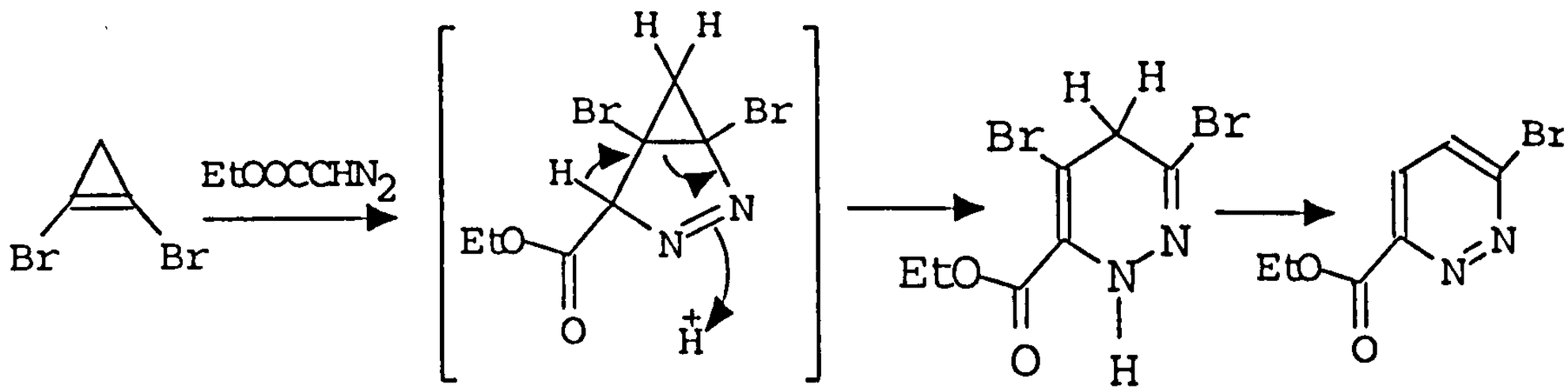
addition of diazomethane to the silane (**392**) gave the pyrazoline (**393**) in a good yield, which was completly rearranged with base to the dihydropyridazine (**394**). In the absence of base the pyrazoline (**393**) was relatively stable and underwent an alternative rearrangment to the diazosilane (**395**) by refluxing with benzene for one hour. On treatment of the diazosilane (**395**) with cuprous iodide, the bicyclobutane (**396**) was obtained.[146]



(392) (393) (394)

(396) (395)

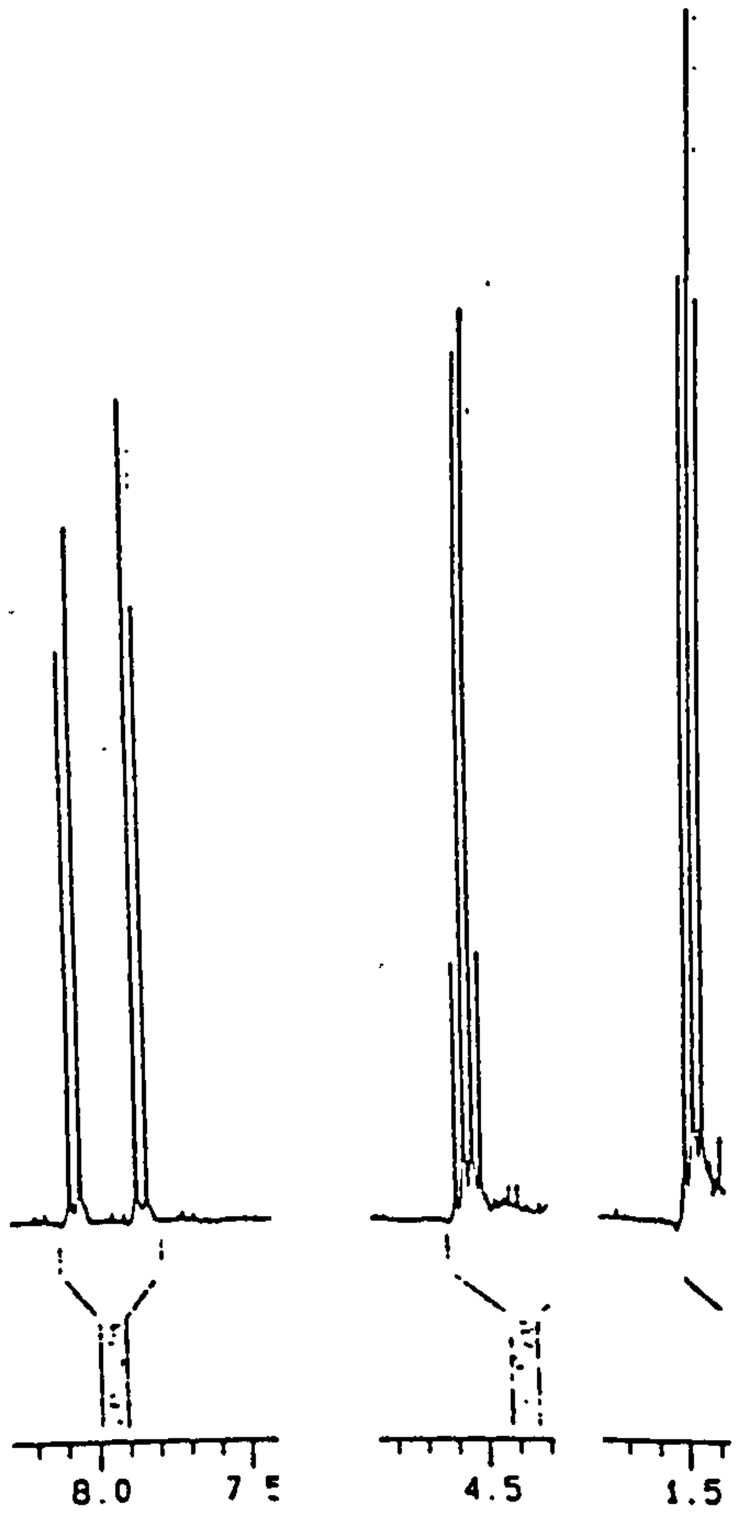
The reaction of 1,2-dibromocyclopropene (**28**) with ethyl diazoacetate in ether solution was slow compared to that with diazomethane. When t.l.c showed no starting material was left after 36 h, the solvent was evaporated to leave behind a semi-solid, which solidified after several hours at room temperature. The solid was treated with petroleum ether and filtered. The solvent was removed and the residue was treated with chloroform, followed by treatment with a saturated solution of sodium bicarbonate. The aqueous layer was extracted with diethylether to give the free pyridazine (**399**) in 52 % yield.



(28) (397) (398) (399)

The product (399) was suggested by the observation of correct C,H,N analysis and the ^{1}H n.m.r spectrum which showed two doublets in the phenyl region at δ 8.0 and 7.0 with coupling constant 8.8 Hz, together with a quartet and triplet for the ethyl group, while the ^{13}C spectrum showed the expected seven signals including the conjugated carbonyl which resonated at δ 163.45 and four carbons in the aromatic regions. The mechanism for the formation of (399) may be involve an initial 1,3-dipolar addition to give the unstable pyrazoline (397) which undergoes a rapid rearrangment to (398) followed by aromatization, rearrangement and loss of HBr to give (399) (see **Figure 12**).

Figure 12. ^{1}H NMR spectrum of (399)

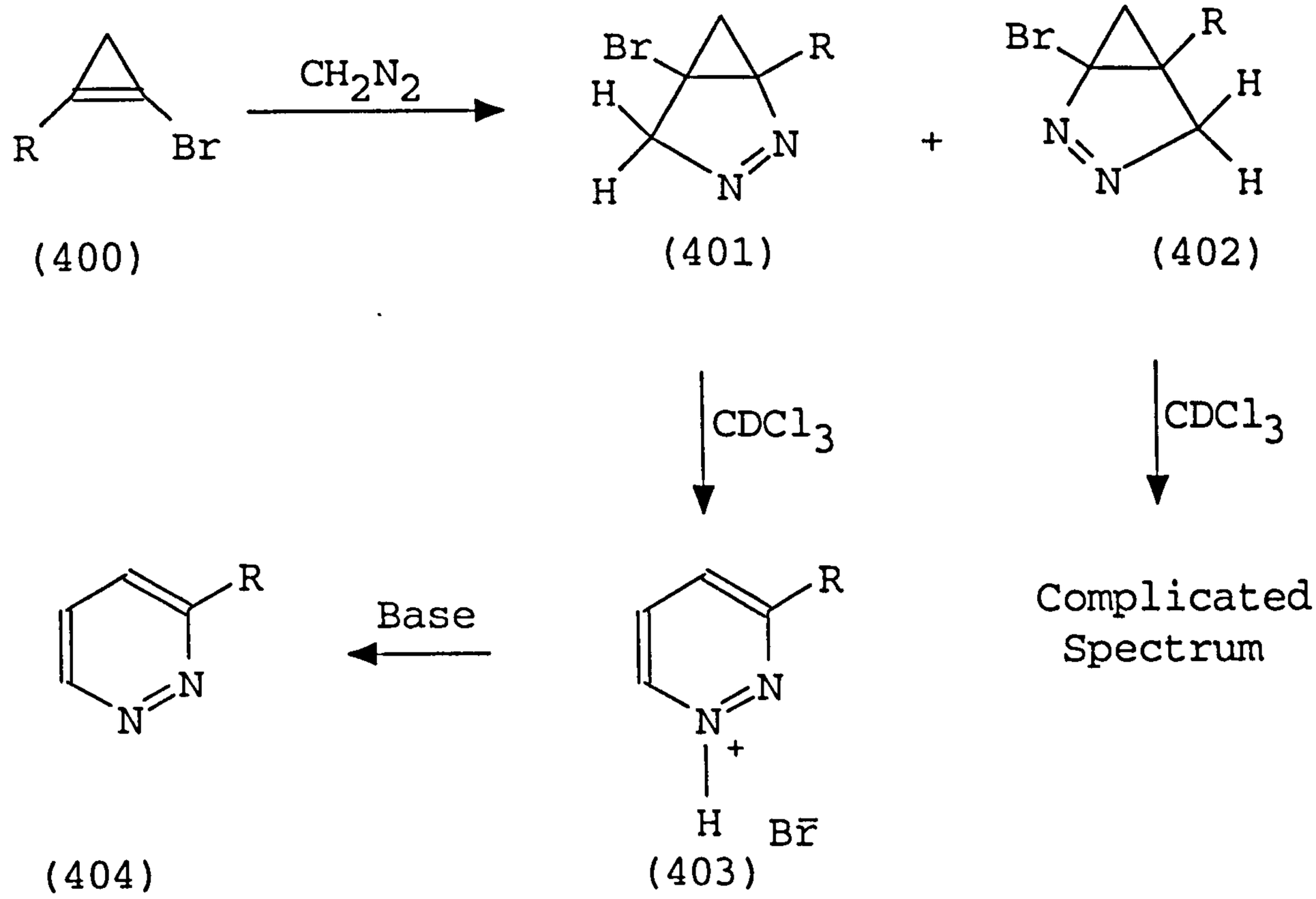


6.3.2. REACTION OF 1-BROMO-2-ALKYLCYCLOPROPENES WITH DIAZOMETHANE

The reaction of a 1-bromo-2-alkylcyclopropenes (**400**, R = octyl, pentyl, butyl, t-butyl, ethyl) with an excess of diazomethane was found to be less selective, leading to a mixture of two regioisomers, which appeared as two spots on t.l.c. The mixture was separated by column chromatography on silica eluting with petroleum ether and ether in ratio 5 : 0.5. In the case of the octyl derivative, the ^1H n.m.r spectrum of the first isomer (**401**, R = octyl) showed an AB pattern for the methylene group with a coupling constants 19.4 Hz, and two double double doublets for the -CH_2- next to the ring at δ 2.3 and 1.8, with a coupling constant of 5.3, 10.4, 14.5 and 5.3, 10.3, 15.8 Hz respectively, two doublets for the methylene of the cyclopropane with a coupling constant of 6.4 Hz, a multiplet at δ 1.5 integrating to two protons and a broad singlet at δ 1.2 integrating for ten protons, together with a triplet for the methyl group. The minor isomer (**402**) showed a very similar spectrum to that for major isomer apart from the cyclopropane methylene group which appeared at a higher field by 0.3 ppm due to the shielding of the alkyl group.

When the minor isomer (**402**, R = octyl) was allowed to stand in $CDCl_3$ for 24 h at room temperature, no starting material was left and a complicated spectrum was obtained. When the major isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature, a complete rearrangment was observed, which gave, after evaporation of the solvent, a brown solid identified as 3-octylpyridazine hydrobromide (**403**, R = octyl) in a moderate yield. The structure of (**403**, R = octyl) was based on the C,H,N analysis and proton n.m.r. When compound (**403**, R = octyl) was treated with a saturated solution of sodium bicarbonate and the aqueous layer extracted with ether, it gave, after evaporation of the solvent, the

free pyridazine (**404**, R = octyl). This gave one peak by g.l.c., while the ^{1}H n.m.r spectrum contained three double doublets in the aromatic region and the ^{13}C spectrum gave the expect twelve signals including four in the aromatic and alkene region for (**404**, R = octyl) **(see Table 2).**



R = Octyl, pentyl, butyl, t-butyl, ethyl

The mechanism for the formation of pyridazines (**404**) is not yet clear, but initially involves the formation of 1,3-dipolar cycloadducts (**401**) and (**402**), one of which undergoes complete rearrangment to the salt (**403**) under slightly acidic conditions followed by treatment with base to give the free pyridazine (**404**). The formation of 3-alkyl pyridazine rather than 4-alkyl pyridazine was proved by comparisom of the N.M.R data of known compounds 3-methyl pyridazine[155] and 4-methyl pyridazine[156] as shown in **Tables 2** and **3** respectively.

Chemical shifts for pyridazines

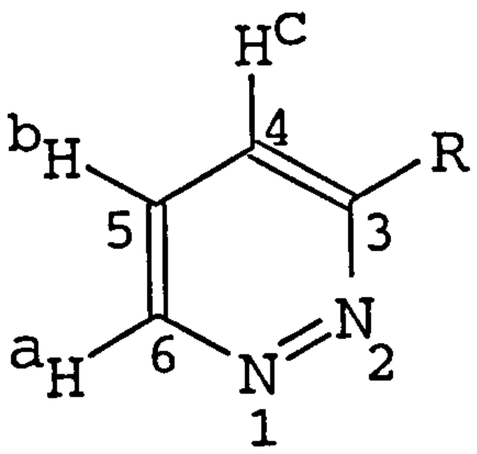
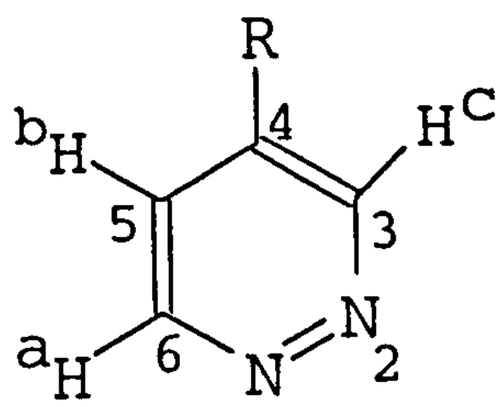


Table (2)

R	No.	Carbon shifts				Proton shifts	
		3	4	5	6	b/c	a
Me^{155}		160.2	126.9	126.4	149.4	7.3	9.0
C_2H_5	404	164.9	126.5	125.7	149.5	7.3	9.0
^tBu	404	170.33	126.2	123.0	149.2	7.5	9.0
Butyl	404	164.0	126.3	126.12	149.5	7.31	9.0
Pentyl	404	164.0	126.34	126.2	150.9	7.33	9.0
Octyl	404	163.2	126.3	126.12	149..5	7.33	9.0

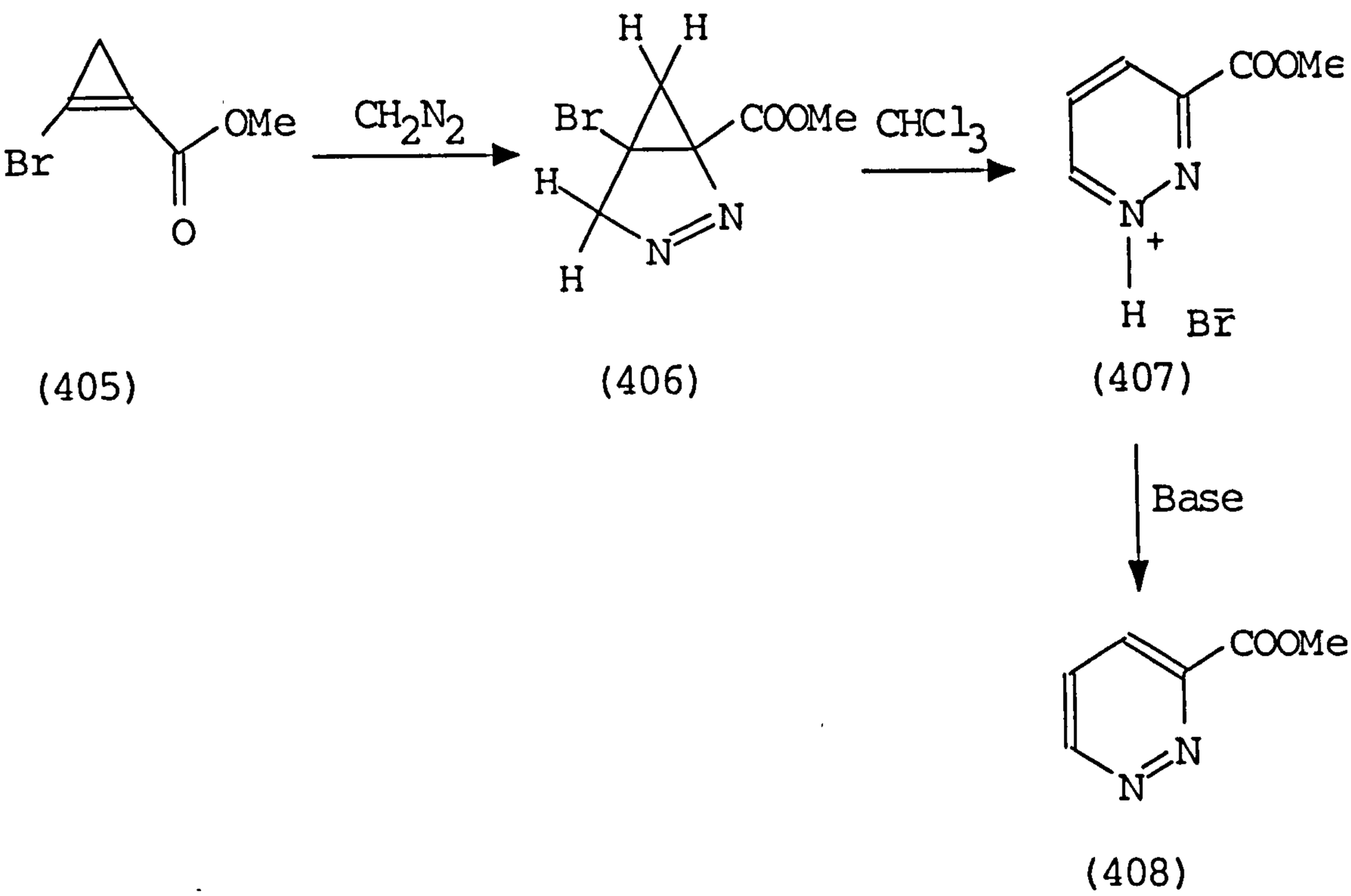
Table (3)



1

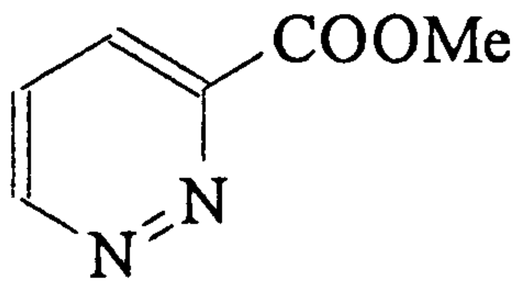
R	Carbon shifts				Proton shifts		
	3	4	5	6	b	c	a
Me^{156}	153.13	137.73	126.76	150.67	7.28	9.04	9.00

Addition of an excess of diazomethane in ether solution to methyl 1-bromo-cyclopropenecaboxylate (**405**) at -50 °C, followed by stirring at room temperature for two hours, gave the pyrazoline (**406**), which rearranged rapidly in chloroform or benzene to a brown solid (**407**) in 56 % yield. The ^{1}H n.m.r spectrum in D_2O showed three double doublets in the aromatic region resonating at δ 9.4, 8.5 and 8.7 with coupling constants of 1.6, 5.2 and 8.6 Hz, together with a singlet at δ 4.0 for the methyl group (**Figure 13**), while the ^{13}C spectrum showed the expected six signals. Treatment of the methyl 3-pyridazine hydrobromide (**407**) with base for 10 min , followed by extraction with ether, gave the free pyridazine (**408**) in 45 % yield.



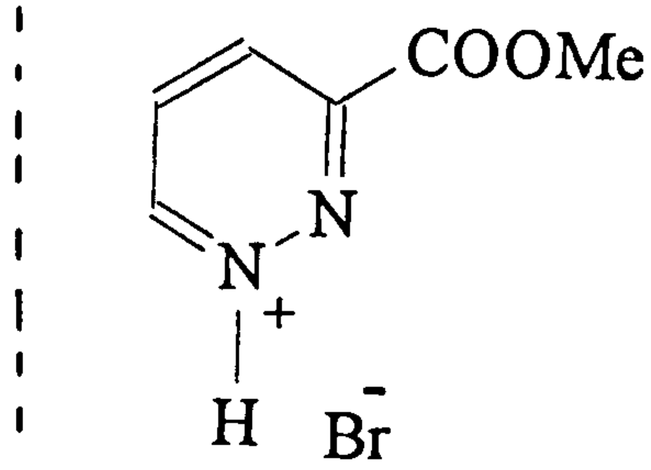
(405) (406) (407) (408)

Compound (**408**) gave the correct measured mass for the formula $C_6H_6O_2N_2$, while the ^{1}H n.m.r spectrum showed three double doublets in the aromatic region together with a singlet resonating at δ 4.1.[157] (**see Figure 14**)



(408)

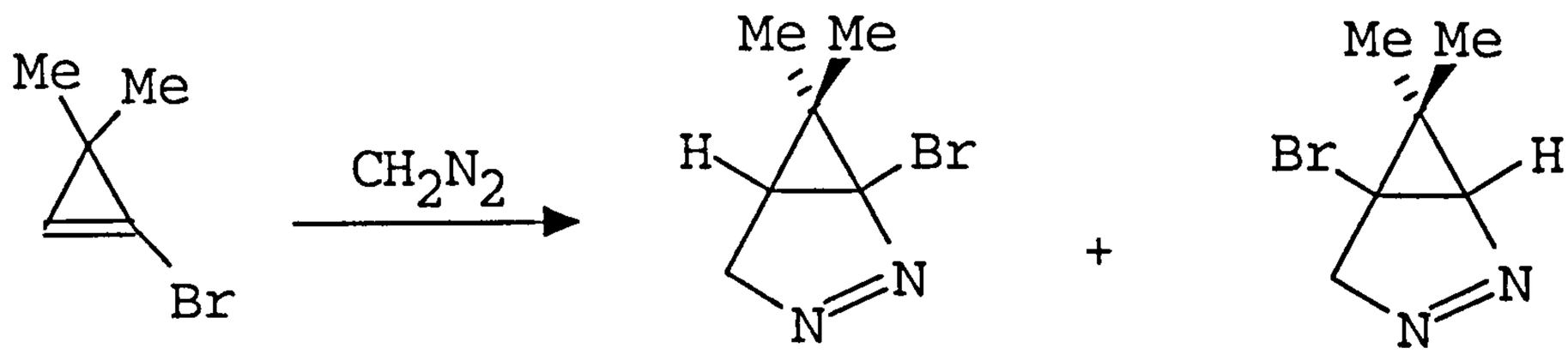
Figure 14.



(407)

Figure 13.

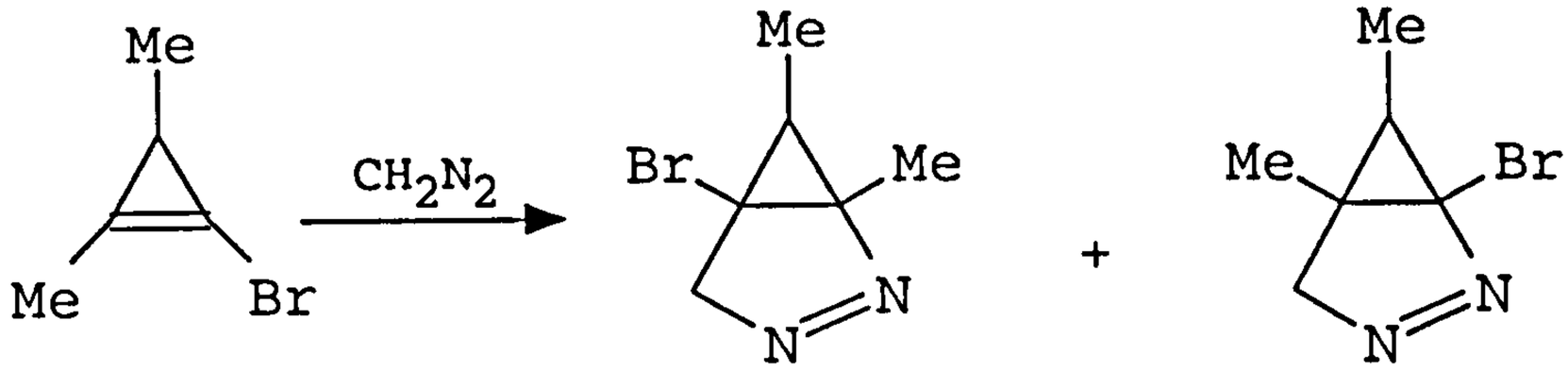
As mentioned previously, the addition of diazomethane to 3,3-dimethylcyclopropene led to a stable pyrazoline. However, the presence of halogen at C_1 of the cyclopropene gave a pyrazoline which showed less stability. Addition of diazomethane to 1-bromo-3,3-dimethylcyclopropene (**409**) in ether solution at 0 °C, showed low selectivity and produced a mixture of two isomers (**410**) and (**411**) in ratio 2.2:1, which were separated by a rapid coloumn chromatography on silica eluting with petrol and ether in ratio (5:0.5).



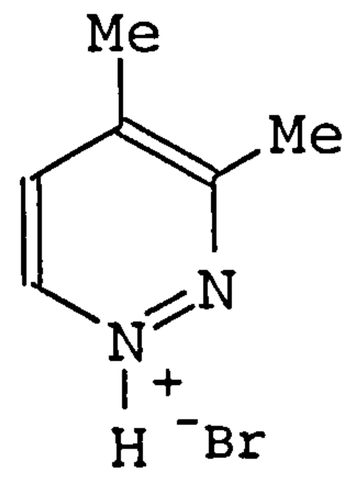
(409) (410) (411)

The ^1H n.m.r spectrum of the pyrazoline (**411**) showed a doublet at δ 4.7 with geminal coupling (19.9 Hz), a doublet for the proton of the cyclopropane ring with long range coupling (2.5 Hz), and a double doublet at δ 4.5 with coupling constant (19.9 and 2.5 Hz). The methyl groups appeared as two singlets, one of them deshielded by the N=N group and resonating at δ 1.6, while the other methyl appeared at a higher field (δ 0.6 ppm). The second isomer (**410**) showed three double doublets for the ring hydrogens and two singlets for the methyl group. When the two isomers were allowed to stand in $CDCl_3$ a complicated mixture was obtained and no pyridazine could be separated.

Moreover, reaction of diazomethane with 1-bromo-2,3-dimethylcyclopropene (**412**) in ether solution at 0 °C to 20 °C for 2 h, led after work up and column chromatography, to the two pyrazolines (**413**) and (**414**) in ratio 1:1.



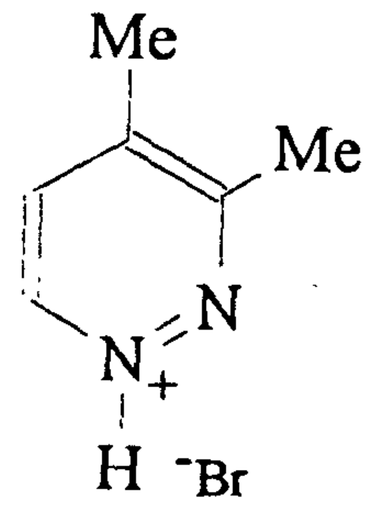
(412) (413) (414)



(415)

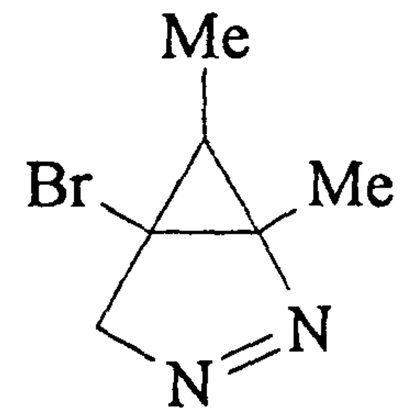
The first isomer (**413**) showed an AB pattern for the methylene group with a coupling constant of 19.9 Hz and one singlet for the methyl group at δ 1.7 together with a doublet at δ 1.1 integrating to three protons and a quartet at δ 0.5 for the cyclopropane proton, (see **Figure 15**). When this isomer was allowed to stand in $CDCl_3$ for 10 h, no starting material was left and 3,4-dimethylpyridazine hydrobromide (**415**) was obtained. Compound (**415**) showed two doublets in the aromatic region with coupling constant of 5.3 Hz, and two singlets at δ 3.0 and 2.6 for the methyl groups (see **Figure 16**). However, the second isomer (**414**), which showed the same coupling pattern as (**413**), but different chemical shifts, decomposed to a complicated mixture when allowed to stand in $CDCl_3$.

Addition of a diazoalkane to a cyclopropene fused to a second ring was also investigated. When diazomethane was allowed to react with the unstable 1-bromobicyclo-[5.1.0]oct-8-ene (**416**) at 0 °C in ether solution , and then the reaction was allowed to reach



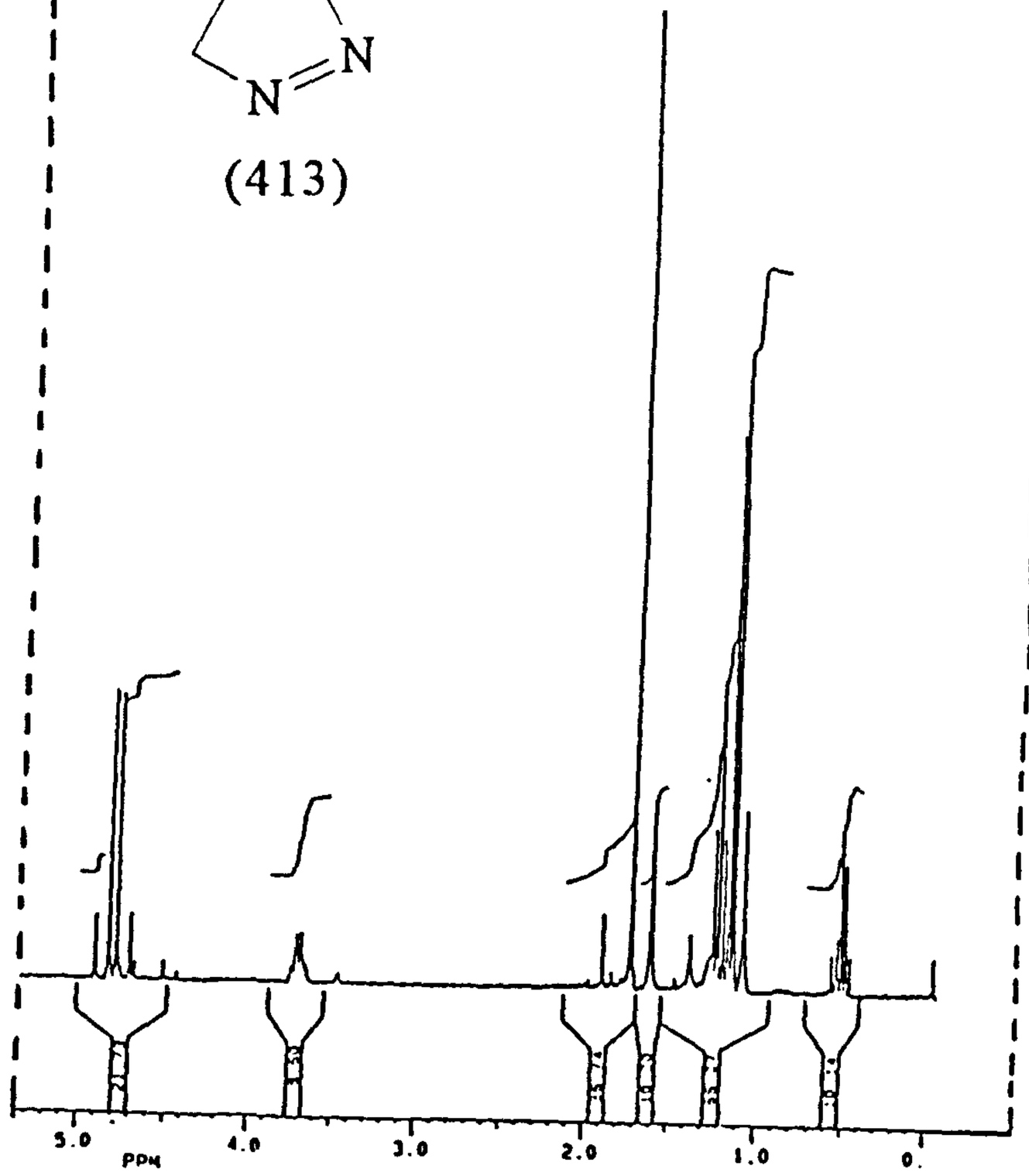
(415)

Figure 16.

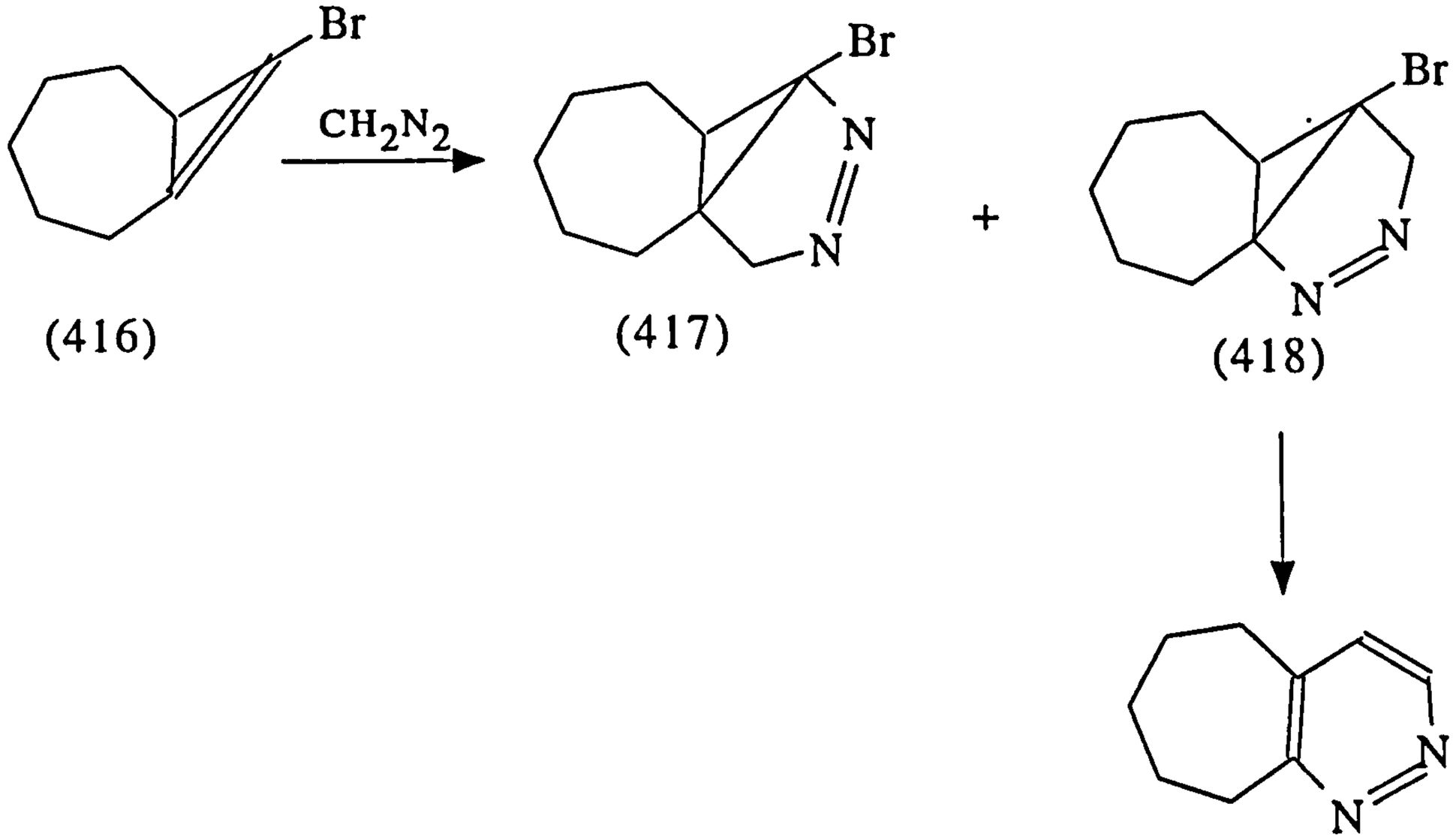


(413)

Figure 15.



room temperature for 2 h, t.l.c showed no starting material was left. The crude product was a mixture of two components (**417**) and (**418**) in ratio 1:1. Chromatography on silica eluting with petrol and ether (5:2) and few drops of triethylamine gave a brown solid (**419**) in 35 % yield.



(416) (417) (418)

(419)

The pyridazine (**419**) gave the correct measured mass for $C_9H_{12}N_2$, while the ^1H n.m.r spectrum showed two doublets in the aromatic region with a coupling constant of 5.3 Hz, two multiplets integrating to four protons at δ 3.5 and 3.1, together with another multiplet at δ 1.8 for (6 H). The ^{13}C spectrum showed the expected nine signals including four in the aromatic region and five signals in the saturated region.

The mechanism of the formation of (**419**) is again uncertain, but may involve first 1,3-dipolar cycloaddition to give a mixture of pyrazolines (**417**) and (**418**) , which are unstable and decompose in the presence of triethylamine, in the case of (**418**) to give (**419**).

6.4. CONCLUSIONS

The addition of diazoalkene to 1,2-dibromocyclopropene led to the 3-bromopyridazines through an intermediate pyrazoline. Moreover, with a 1-bromo-2-alkylcyclopropene, two isomers of pyrazoline were obtained in ratio 1:1, which were separated by chromatography. One of them was converted in sligltly acidic solution in to the free pyridazine.

Chapter 7

Experimental

7.1. GENERAL EXPERIMENTAL DETAILS:

Organic solution were dried using magnesium sulphate, and solvents were removed at 14 mm Hg. Dichloromethane was distilled over calcium hydride. Diethyl ether and tetrahydrofuran were distilled over sodium wire; methanol and ethanol were purified and dried by distillation from magnesium turnings containing iodine. Petrol was either of boiling point 40-60 or 60-80 °C. Both were purified by distillation.

Melting Point were determined using a Gallenkamp Melting Point Apparatus and are uncorrected.

Infra-red spectra were obtained as KBr discs (solids) or as liquid films on a Perkin-Elmer 1600 FTIR.

The purity of compounds was assessed by either gas liquid chromatography or by thin layer chromatography. Gas liquid chromatography was conducted using a Perkin-Elmer Model F17 F.I.D. on a capillary column (30 m x 0.32 mm id Phase, DB5) with nitrogen as carrier gas.

Thin layer chromatography was performed using Aldrich silica plates coated with silica gel 60 (F245). Column chromatography was conducted with Merck 7736 silica gel under medium pressure. Proton NMR spectra were recorded using a Brucker AC250 at 250 MHz and 62.5 MHz for carbon unless otherwise stated. Both proton and carbon NMR were calibrated using tetramethylsilane (TMS) as an internal reference.

Mass measurements reported refer to ^{79}Br and ^{35}Cl isotopes unless stated and were obtained from the Swansea Mass Spectrometry Service. Microanalyses were performed with a Carlo-Erba Instrumentazione model 1106 CHN analyser.

7.2. EXPERIMENTS

Preparation of 3,4-dibromo-3-methyl-butan-1-ol

3-Methyl-3-buten-1-ol (40 g) in dry CCl_4 (140 ml) was cooled in ice and stirred during addition of a solution of bromine (80 g) in CCl_4 (200 ml) until a permanent pale yellow colour resulted. The solvent was removed at 14 mm Hg to give 3,4-dibromo-3-methylbutan-1-ol (100 g, 89 %) which showed an identical ^1H nmr spectrum to an authentic sample.[73]

Preparation of *cis* and *trans*-4-bromo-3-methylbut-3-en-1-ol (110)

A solution of KOH in methanol (101 ml, 5M, 25% excess) was added gradually to the above dibromide (100 g, 0.4 mol) with cooling and stirring. After 5 h at room temperature the solvent was removed at 14 mm Hg; diethyl ether (500 ml) was added and the products were neutralized with a few drops of glacial acetic acid. The mixture was dried, filtered and the filter residue was washed with ether. The solvents were removed at 14 mm Hg and 60 °C. The residue was flash distilled at 0.1 mm Hg and 56-58 °C to give a colourless oil consisting of *E*/*Z*-4-bromo-3-methylbut-3-en-1-ol (**110**) (37 g, 55 %), which showed an identical ^1H nmr spectrum to an authentic sample.[73]

Preparation of 3,4,4-tri-bromo-3-methylbutan-1-ol

A solution of bromine (62.3 g, 0.38 mol) in dichloromethane (200 ml) was added to a stirred solution of *E*/*Z*-4-bromo-3-methylbut-3-en-1-ol (58.4 g, 0.35 mol) in dichloromethane (500 ml) at -20 °C. The solution was allowed to stand at room temperature for 24 h, then the solvent was removed under reduced pressure to give 3,4,4-tribromo-3-

methylbutan-1-ol (98 g, 84.5%) which showed υ_{max}: 3290 br s, 1379 m, 1049 s, 669 m cm^{-1}; δ_H: 1.8 (1H, s), 2.01 (3H, s), 2.26-2.54 (2H, m), 3.89-4.10 (2H, complex multiplet), 6.03 (1H, s); δ_C: 28.8, 43.7, 55.0, 60.6, 69.6; m/z 322/324/326/328, 243/245/247, 225/227/229, 213/215/217, 163/165, 145/147, 133/135.

Preparation of 4,4-dibromo-3-methylbut-3-en-1-ol (116)

A 5M solution of potassium hydroxide in methanol (75 ml) was added to a rapidly stirred solution of 3,4,4-tribromo-3-methylbutan-1-ol (98 g, 0.30 ml) at 0 °C. The reaction mixture was stirred at room temperature for 5 h, then diethyl ether (500 ml) was added and the products were neutralized with a few drops of glacial acetic acid, and worked up as before. The residue was columned on silica eluting with petrol and ether (5:2) to give *4,4-dibromo-3-methylbut-3-en-1-ol* (**116**) (31 g, 42 %) (Found: M^+ 241.8952. $C_5H_8Br_2O$ requires M, 241.8942) which showed υ_{max}: 3354, 1439, 1049, 819 cm^{-1}; δ_H: 1.8 (1H, br s), 1.95 (3H, s), 2.6 (2H, t, J 6 Hz), 3.8 (2H, t, J 6 Hz); δ_C: 22, 41, 60, 86.8, 129; m/z 242/244/246 , 163/165, 145/147, 131/133.

Preparation of 1,1-dibromo-4-methoxy-2-methylbut-1-ene (120)

A mixture of 4,4-dibromo-3-methylbut-3-en-1-ol (112 g, 0.049 mol) and tetra-n-butylammonium iodide (0.18 g, 0.49 mmol) in dichloromethane (20 ml) was equilibrated by vigorous stirring for 30 min with 50% aqueous sodium hydroxide solution (5.9 g, 0.14 mol) in water (5.9 ml). Dimethyl sulphate (6.9 ml, 0.07 mol) was added dropwise with cooling then the mixture was stirred at room temperature for 18 h. Concentrated aqueous ammonia (12 ml) was added and the mixture was stirred for 30 min, and then poured into water (100 ml). After extracting with dichloromethane (3 x 50 ml), the organic layers were washed with

water (50 ml), dried and concentrated under reduced pressure. The residue was columned on silica eluting with petrol and ether (5:1) to give 1,1-dibromo-4-methoxy-2-methylbut-1-ene (**120**) (9.45 g, 74 %) which showed δ_H: 1.93 (3H, s), 2.56 (2H, t, J 7 Hz), 3.33 (3H, s), 3.49 (2H, t, J 7 Hz); δ_C: 139.3, 86.4, 69.9, 58.6, 38, 23; υ_{max}: 2826, 1116, 822 cm^{-1}.

Preparation of 1,1-dibromo-2-methylbut-1-en-4-yl 2-methoxyprop-2-yl ether (117)

2-Methoxypropene (36.8 g, 48.9 mol) was added to a stirred solution of 4,4-dibromo-3-methylbut-3-en-1-ol (25 g, 0.1 mol) in ether (50 ml) at 0 °C. An exothermic reaction commenced on addition of pyridinum p-toluenesulphonic acid (0.05 eq). The reaction was stirred for 0.25 h at room temperature, after which TLC showed no starting material was left . The reaction was quenched with a saturated aq. sodium bicarbonate and the aqueous layer was extracted with ether (2 x 50 ml), the organic layers were dried and the solvent was removed at 14 mm Hg to give 1,1-dibromo-2-methylbut-1-en-4-yl 2-methoxyprop-2-yl ether (**117**) (30 g, 93 %).

Preparation of 3-(2-hydroxyethyl)-3-methyl-1,1,2,2-tetrabromocyclopropane (119)

A mixture of bromoform (13.8 ml), cetrimide (2.5 g) and few drops of triethylamine in dichloromethane (50 ml) was stirred for *ca.* 10 min, after which 1,1-dibromo-2-methylbut-1-ene-4-yl 2-methoxyprop-2-yl-ether (25 g) was added. Whilst being rapidly stirred, sodium hydroxide (40 g) in water (40 ml) was added slowly and the temperature was maintained below 30 °C. The reaction mixture was stirred at room temperature for 48 h, and then poured into water (20 ml) and extracted with dichloromethane (3 x 100 ml). The solvent was removed at 14 mm Hg and petrol (300 ml) was added to the residue and stirred for 15 min. Cetrimide separated out and was filtered off. The filtrate was dried and

evaporated at 14 mm Hg to give the protected cyclopropane alcohol. The crude product was stirred with aqueous methanol in the presence of p-toluenesulphonic acid for 0.25 h, then the clear solution was decanted and concentrated. The residue was washed with water and extracted with ether (3 x 100 ml), the organic layer was dried and the solvent was removed at 14 mm Hg to give a crude solid product (15 g, 70.3%), which was columned on silica eluting with petrol and ether (1:1) to give *3-(2-hydroxyethyl)-3-methyl-1,1,2,2-tetrabromocyclopropane* (**119**) (12 g, 56 %), m.p. 72-74°C (Found: C 17.42, H 1.84; $C_6H_8OBr_4$ requires C 17.33, H 1.93) which showed δ_H: 1.5 (3H, s), 2.1 (2H, t, J 7.0 Hz), 1.8 (br, s), 3.8 (2H, t, J 7.0 Hz); δ_C: 60.0, 48.98, 40.83, 37.8, 22.6; υ_{max}: 3600, 1449, 1288, 1267, 832.0 cm^{-1}.

Preparation of E/Z-1-bromo-2-methylbut-1-en-4-yl 2-methoxyprop-2-yl ether (111)

2-Methoxypropene (17.6 g, 23.4 ml) was added to a stirred solution of *E/Z*-4-bromo-3-methylbut-3-en-1-ol (8.1 g, 0.04 mol) in ether (50 ml) at 0 °C. An exothermic reaction occurred on addition of pyridinium p-toluene sulphonic acid (0.24 g, 0.98 mmol). The reaction was stirred for 0.25 h at room temperature, after which TLC showed no starting material, and then worked up as above to give *E/Z*-1-bromo-2-methylbut-1-en-4-yl-2-methoxyprop-2-yl ether (**111**) in ratio 4:1 (10.5 g, 91 %), which showed δ_H (major isomer): 5.9 (1H, q, J 1.2 Hz), 3.4 (2H, t, 6.8 Hz), 3.1 (3H, s), 2.3 (2H, dt, J 0.9, 6.8 Hz), 1.78 (3H, d, J 1.2 Hz), 1.28 (6H, s); (minor isomer) 5.89 (1H, br, s), 3.15 (3H, s), 2.4 (2H, t, J 7.16 Hz), 1.29 (6H, s). The remaining signals were obscured by those for the major isomer.

Preparation of 3-(2-hydroxyethyl)-3-methyl-1,1,2-tribromocyclopropane (115)

A mixture of bromoform (14.8 ml), cetrimide (2.5 g) and a few drops of triethylamine

in dichloromethane (50 ml) was stirred for ca. 10 min, after which *E/Z*-1-bromomethylbut-1-ene-4-yl-2-methoxyprop-2-yl ether (20 g) was added. While the mixture was rapidly stirred, sodium hydroxide (50 g) in water (50 ml) was added slowly and the temperature was maintained below 30 °C. After stirring at room temperature for 48 h, work up and deprotection as above gave *3-(2-hydroxyethyl)-3-methyl-1,1,2-tribromocyclopropane* (**115**) as a mixture of two isomers in ratio 4:1 (16.2 g, 57 %) (Found M^+: 333.8203. $C_6H_9OBr_3$ requires 333.8203) which showed δ_H (major isomer): 3.85 (2H, m), 3.55 (1H, s), 2.02 (2H, dt, J 3.85, 7.0 Hz), 1.82 (1H, broad, s), 1.36 (3H, s); δ_C 59.77, 42.38, 42.03, 41.01, 38.15, 20.21); (minor isomer) 3.4 (1H, s), 1.9 (2H, m), 1.49 (3H, s) (the remaining signals were obscured by those for the major isomer); δ_C: 59.51, 42.13, 41.153, 31.812, 31.44, 22.79; υ_{max}: 3354, 1449, 1050, 794, 692 cm^{-1}.

<u>Preparation of 3-(2-hydroxyethyl)-3-methyl-1,1-dichloro-2-bromocyclopropane (114)</u>

A mixture of chloroform (100 ml), cetrimide (2 g) and a few drops of triethylamine in dichloromethane (20 ml) was stirred for ca. 10 min, after which *E/Z*-1-bromomethylbut-1-ene-4-yl-2-methoxyprop-2-yl ether (20 g, 0.084 mol) was added. While the mixture was rapidly stirred, sodium hydroxide (33.8 g, 0.84 mol) in water (33 ml) was added slowly and the temperature was maintained below 30 °C. The reaction mixture was stirred at room temperature for 48 h; work up as above gave (**114**) as a mixture of two isomers in ratio 4.5:1 (73 %) (Found M^+: 245.9214. $C_6H_9OBrCl_2$ requires 245.9214), which showed δ_H (major isomer): 3.8 (2H, m), 3.4 (1H, s), 2.4 (1H, br.s), 1.98 (2H, dt, J 3.5, 7.0 Hz), 1.34 (3H, s); δ_C: 59.7, 40.92, 40.57, 38.78, 32.16, 18.7; δ_H (minor isomer): 3.3 (1H, s), 1.4 (3H, s) (the remaining signals were obscured by the major isomer); δ_C: 59.37, 36.16, 31.47, 20.65; υ_{max}: 3343, 2887, 1079, 862, 716; z/e 211/213/215 (M^+-Cl), 201/203/205 (M^+-C_2H

$_5$O), 167/169 (M^+-Br).

Preparation of 1,1,2,2-tetrabromo-3-methyl-3-(2-methoxyethyl)cyclopropane (121)

(a) Sodium hydroxide (15 g, 0.36 mol) in water (15 ml) was added carefully to a rapidly stirred solution of 1,1-dibromo-4-methoxy-2-methylbut-1-ene (9.45 g, 0.03 mol) in dichloromethane (50 ml), bromoform (0.07 mol, 6.4 ml) and cetrimide (2 g) at room temperature. The mixture was stirred rapidly for 48 h at room temperature. Dichloromethane (300 ml) was then added followed by brine (300 ml) and the product was extracted with further dichloromethane. The combined organic layers were dried and the solvent was removed at 14 mm Hg. The residue was stirred with petrol (250 ml) for 15 min and filtered. The filtrate was dried and the solvent was removed at 14 mm Hg to give brown oil, which was columned on silica eluting with petrol and ether (5:1) to give *1,1,2,2-tetrabromo-3-methyl-3-(2-methoxyethyl)cyclopropane* (**121**) (6.5 g, 41 %) (Found: M^+ 425.7465. $C_7H_{10}OBr_4$ requires 425.7465) which showed δ_H: 1.5 (3H, s), 2.0 (2H, t, J 6.9 Hz), 3.3 (3H, s), 3.5 (2H, t, J 6.9 Hz); δ_C: 69.5, 53.9, 49.05, 38.19, 22.96, 20.35); υ_{max}: 2925.8, 1449.1, 1383.4, 1115.8, 760.5 cm^{-1}.

(b) A mixture of 3-hydroxyethyl-3-methyl-1,1,2,2-tetrabromocyclopropane (2 g, 4.8 mmol) and tetra-n-butylammonium iodide (0.05 g, 0.14 mmol) in dichloromethane (20 ml) was equilibrated by vigorous stirring for 30 min with 50% aqueous sodium hydroxide solution (0.6 g, 0.014 mol) in water (0.6 ml). Dimethyl sulphate (0.68 ml, 7.2 mmol) was added dropwise with cooling, then the mixture was stirred for 18 h. Concentrated aqueous ammonia (2 ml) was added and the mixture was stirred for 30 min then poured into water (100 ml). After extracting with dichloromethane (3 x 50 ml) the organic layers were washed with water (50 ml), dried and concentrated under reduced pressure to give 1,1,2,2-

tetrabromo-3-methyl-3-(2-methoxyethyl)cyclopropane (**121**) (1.7 g, 82 %), identical to that in (a).

Preparation of 1,1,3-tribromo-3-methyl-3-(2-methoxyethyl)cyclopropane (122)

The above procedure in (b) was repeated using 3-(2-hydroxyethyl)-3-methyl-1,1,2-tribromocyclopropane to give *1,1,2-tribromo-3-methyl-3-(2-methoxyethyl)-cyclopropane* (**122**) (0.77 g, 74 %) (Found: M^+ 347.8360. $C_7H_{11}OBr_3$ requires 347.8360); δ_H showed two isomers in ratio 4.2:1 (major isomer): 3.56 (2H, m), 3.53 (1H, s), 3.34 (3H, s), 2.0 (2H, dt, J 4.3, 7.0 Hz), 1.4 (3H, s); δc: 70.0, 60.0, 42.6, 38.6, 35.7, 32.28, 20.33; (minor isomer): 3.3 (3H, s), 1.9 (2H, dt, J 3.5, 6.8 Hz), 1.47 (3H, s) (the remaining signals were obscured by those for the major isomer); δ_C: 69.59, 42.7, 31.93, 23.33; υ_{max}: 2925, 1451, 692 cm^{-1}; m/z: 269/271/273 (M^+ - Br), 189/191 (M^+ - Br_2).

Preparation of 1,1,4-tribromo-2-methylbut-1-ene (124)

(d) Triphenylphosphine (15.03 g, 0.05 mol) was added to a rapidly stirred solution of 4,4-dibromo-3-methylbut-3-en-1-ol (10.76 g, 0.04 mol) and carbon tetrabromide (10.01 g, 0.5 mol) in dry ether (50 ml). The reaction mixture was stirred vigorously for 18 hr. TLC showed no starting material was left. The reaction mixture was poured into petrol (200 ml), and the precipitate was filtered off on a sinter. The solvent was evaporated and the residue was columned on silica eluting with petrol to give 1,1,4-tribromo-2-methylbut-1-ene (**124**) (8.95 g, 66 %) which showed δ_H: 1.9 (3H, s), 2.8 (2H, t, J 7.4 Hz), 3.4 (2H, t J 7.4 Hz); δ_C: 22.9, 27.9, 46.9, 88.5, 138.9; υ_{max}: 1600, 1270, 1217, 819 cm^{-1}.

Preparation of 1,1,2,2-tetrabromo-3-methyl-3-(2-bromoethyl)cyclopropane (123)

(e) Reaction of 1,1,4-tribromo-2-methylbut-1-ene with bromoform and base as above in (a) under phase transfer conditions gave *1,1,2,2-tetrabromo-3-methyl-3-(2-bromoethyl)cyclopropane* (**123**) (38 %), m.p. 74-76 °C (Found: C 14.92, H 1.24; $C_6H_7Br_5$ requires C 15.05, H 1.47) δ_H: 3.5 (2H, complex), 2.36 (2H, complex), 1.52 (3H, s); δ_C: 47.8, 41.6, 38.8, 27, 22.2; υ_{max}: 760 cm^{-1}.

(f) The procedure in (d) was repeated using 3-hydroxyethyl-3-methyl-1,1.2,2-tetrabromocyclopropane to give (**123**) yield (72 %), which was identical by ^1H nmr to the product in (e).

<u>Oxidation of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxyethyl)cyclopropane</u>

Potassium permanganate (15.1 g, 0.09 mol) in water (100 ml) was stirred rapidly at 0 °C for 10 min. Tetrabutylammonium bromide (0.5 g) and a solution of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxyethyl)cyclopropane (4 g, 9.6 x 10^{-3} mol) in benzene (20 ml) were added and the reaction mixture was stirred rapidly for 16 h. The reaction was treated carefully at 0 °C with saturated aq. sodium metabisulphite until the brown colouration was discharged, acidified to pH 1 with dil sulphuric acid (10%) and then extracted with ether (3 x 100 ml). The organic layers were dried and the solvent was removed at 14 mm Hg to give a solid (4 g, 97 %), which was crystallised from petrol and ether to give 2-(*1,1,2,2-tetrabromo-3-methylcycloprop-3-yl)ethanoic acid* (**163**), m.p. 140-142 °C (Found: C 17.21, H 1.38. $C_6H_6O_2Br_4$ requires C 17.21, H 1.4) δ_H: 1.7 (3H, s), 3.0 (2H, s); δ_C: 156.29, 47.2, 43.1, 36.7, 23.3, 20.29; υ_{max}: 3021 (v. br), 1708, 1410, 1229, 760 cm^{-1}.

<u>Oxidation of 1,1,2-tribromo-3-methyl-3-(2-hydroxyethyl)cyclopropane</u>

Oxidation as above gave *(1,1,2-tribromo-3-methylcycloprop-3-yl) ethanoic acid*

(**162**) (1.9 g, 60 %), m.p. 104-106 °C (Found: C 20.68, H 1.93. $C_6H_7O_2Br_3$ requires: C 20.51, H 1.99) δ_H: 3.64 (1H, s), 2.9 (1H, d, J 17 Hz), 2.8 (1H, d, J 17 Hz), 1.49 (3H, s); δ_C: 175.8, 43, 41.2, 40.5, 30.6, 20.4; υ_{max}: 2933 (v.br), 1705, 1412, 1268, 1229, 908, 820 cm^{-1}.

Reaction of (1,1,2,2-tetrabromo-3-methylcycloprop-3-yl) ethanoic acid with red mercuric oxide and bromine

Bromine (0.2 g, 1.28 mmol) in carbon tetrachloride (5 ml) was added dropwise to a stirred suspension of the acid (0.5 g, 1.16 mmol) and red mercuric oxide (0.27 g, 1.2 mmol) in carbon tetrachloride (15 ml) at 85 °C. The mixture was refluxed for 3 h, stirred at room temperature for 12 h, treated with petrol (20 ml), stirred for 5 min and filtered through flash silica. The filtrate was evaporated at 14 mm Hg and the residue was columned on silica eluting with petrol to give *1,1,2,3,4-pentabromo-3-methyl-1-butene* (**166**) (0.35 g, 65 %) as an oil which showed δ_H: 4.87 (1H, dq, J 1.1, 10.3 Hz), 3.70 (1H, d, J 10.3 Hz), 2.44 (3H, d, J 1.1 Hz); δ_C: 129.11, 93.33, 61.59, 42.32, 40.65; υ_{max}: 1523, 1443, 1228, 1080, 1036, 855, 778, 700 cm^{-1}; z/e: 380/382/384/386/388/ (M^+ - Br), 301/303/305/307 (M^+ - Br_2), 222/224/226 (M^+ - Br_3), 143/145 (M^+ - Br_4).

Reaction of (1,1,2-tribromo-3-methylcycloprop-3-yl)ethanoic acid with red mercuric oxide and bromine

Reaction as above adding bromine (0.25 g, 1.5 mmol) in carbon tetrachloride (5 ml) to a stirred suspension of the above acid (0.5 g, 1.4 mmol) and red mercuric oxide (0.34 g, 1.5 mmol) in carbon tetrachloride (15 ml), gave *1,1,3,4-tetrabromo-3-methyl-1-butene* (**166**) (0.15 g, 27 %) as an oil which showed δ_H: 6.8 (1H, s), 4.3 (1H, d, J 10.1 Hz), 3.78

(1H, d, J 10.1 Hz), 2.1 (3H, s); δ_C: 138.84, 95.31, 59.27, 41.92, 30.46; υ_{max}: 1602, 1037, 864, 816, 775 cm^{-1}; z/e: 302/304/306/308 (M^+ - Br), 223/225/227 (M^+ - Br_2), 143/145 (M^+ - Br_3), 63/65 (M^+ - Br_4).

Reaction of 1,1,2,3,4-Pentabromo-3-methylbut-1-ene with diethylphosphite and triethylamine

Triethylamine (0.02 ml, 0.215 mmol) was added to a stirred solution of 1,1,2,3,4-pentabromo-3-methylbut-1-ene (0.1 g, 0.21 mol) and diethylphosphite (0.1 ml, 0.86 mmol) at 5 °C. The mixture was allowed to reach 20 °C, stirred for 30 min, and then columned directly on silica, eluting with petrol to give a colourless oil, *1,3,4-tribromo-3-methyl-1-butyne* (**171**) (0.025 g, 38 %) which showed δ_H: 4.01 (1H, d, J 10.1 Hz), 3.8 (1H, d, J 10.1 Hz), 2.12 (3H, s); δ_C: 93.31, 79.7, 42.0, 36.64, 32.1; υ_{max}: 2205, 1037 cm^{-1}; z/e: 302/304/306/308 (M^+), 223/225/227 (M^+ - Br), 144/146 (M^+ - Br_2), 63/65 (M^+ - Br_3).

Reaction of 1,1,2,3,4-pentabromo-3-methylbut-1-ene with 1,8-Diazabicyclo[5.4.0]-undec-7-ene (DBU)

1.8-Diazabicyclo[5.4.0]undec-7-ene (0.4 ml, 2.6 mmol) was stirred for 30 min with 1,1,2,3,4-pentabromo-3-methyl-1-butene (0.5 g, 1.07 mmol) in dry benzene (5 ml) at 20 °C. After 5 min a precipitate had formed. After addition 5% HCl (10 ml) and ether (15 ml), and extraction of the aqueous layer with ether (2 x 10 ml), the combined ether layers were washed with water (10 ml), and dried, and the solvent removed at 14 mm Hg to give an oil which was one spot by TLC. This was further purified by chromatography on silica eluting with petrol to give *1,1,2,4-tetrabromo-3-methylbuta-1,3-diene* (**170**) (0.37 g, 90 %) as an oil which showed δ_H: 6.4 (1H, q, J 1.2 Hz), 1.9 (3H, d, J 1.24 Hz); δ_C: 139.83, 124.69,

119.19, 112.54, 17.95; υ_{max}: 1611, 1280 cm^{-1}; m/z: 380/382/384/386/388 (M^+), 301/303/305/307 (M^+-Br), 223/225/227 ($M^+ - Br_2$), 143/145 ($M^+ - Br_3$).

Reaction of 1,1,2,4-tetrabromo-3-methylbuta-1,3-diene with diethylphosphite and triethylamine

(a) Triethylamine (0.06 ml, 0.46 mmol) was added dropwise to a stirred solution of the above diene (0.15 g, 0.39 mmol) and diethyl phosphite (0.2 ml, 1.5 mmol) at room temperature. A precipitate was formed and the reaction was stirred for 1 h, and then columned directly on silica, eluting with petroleum and ether (b.p. 40-60 °C) to give *E & Z-1,4-dibromo-2-methyl-but-1-en-3-yne* as an oil (**172**). The first isomer (30 mg, 34 %) showed δ_H: 6.6 (1H, q, J 1.3 Hz), 1.9 (3H, d, J 1.3 Hz); υ_{max}: 2197, 1588, 1012 cm^{-1}. The second isomer (34 %) showed δ_H: 6.2 (1H, q, J 1.5 Hz), 1.98 (3H, d, J 1.5 Hz); δ_C: 140.39, 123.47, 1097.35, 90.3, 20; υ_{max}: 2200, 1622, 1437 cm^{-1}; z/e: 222/224/226 (M^+), 143/145 (M^+ - Br), 63/65 ($M^+ - Br_2$).

Reaction of 1,3,4-tribromo-3-methyl-1-butyne with 1,8-diazabicyclo[5.4.0]undec-7-ene

(b) The previous procedure was repeated on 1,3,4-tribromo-3-methyl-1-butyne to give *E* & *Z*-1,4-dibromo-2-methyl-but-1-en-3-yne (**172**) (40 %), which was identical by ^1H nmr to the product in (a).

Preparation of 1-bromo-3-methyl-3-(2-hydroxyethyl)cyclopropene (128)

Methyllithium (6.2 ml, 9.3 mmol) was added to a stirred solution of 1,1,2-tribromo-3-methyl-3-(2-hydroxyethyl)cyclopropane (1.5 g, 4.45 mmol) in dry ether (15 ml) at -78 °C under nitrogen. The reaction mixture was stirred until the temperature increased to -50 °C.

It was then quenched with water (5 ml) at -50 °C, and the ether layer was decanted from the ice. The ice was extracted with cold ether (3 x 15 ml). Evaporation of ether at 0 °C and 14 mm Hg gave *1-bromo-3-methyl-3-(2-hydroxyethyl)cyclopropene* (**128**) (0.6 g, 76 %) which showed δ_H: 7.4 (1H, s), 3.56 (2H, m), 3.0 (1H, br, s), 1.8 (2H, t, J 6.8 Hz), 1.2 (3H, s); δ_C: 119, 113.6, 59.86, 40.58, 31.1, 25.6; υ_{max}: 3298, 1954, 1050 cm^{-1}.

Rearrangement of 1-bromo-3-methyl-3-(2-hydroxyethyl)cyclopropene to 3-bromo-5-hydroxy-3-methyl-1-pentyne

The cyclopropene was allowed to stand for 24 h in solution in $CDCl_3$, when complete reaction had occurred; the solvent was removed and the residue was columned on silica eluting with petroleum ether (5:2) to give *3-bromo-3-methylpent-4-yn-1-ol* (**129**) (84 %) which showed δ_H: 3.97 (2H, dt, J 1.7, 6.7 Hz), 2.8 (1H, s), 2.5 (1H, br, s), 2.3 (2H, m), 2.1 (3H, s); δ_C: 86.01, 74.87, 60.92, 50.0, 48.75, 35.06; υ_{max}: 3292, 2112 cm^{-1}; z/e: M^+ (177), 96 ($M^+ - Br_2$).

Preparation of 1-bromo-3-methyl-3-(2-methoxyethyl)cyclopropene (127)

Methyllithium (1.2 ml, 1.8 mmol) was added to a stirred solution of 1,1,2-tribromo-3-(2-methoxyethyl)cyclopropane (0.5 g, 1.4 mmol) in dry ether (15 ml) at -78 °C under nitrogen. The mixture was stirred until the temperature increased to -50 °C. Work up as above gave *1-bromo-3-methyl-3-(2-methoxyethyl)cyclopropane* (**127**) (0.25 g, 92 %) which showed δ_H: 7.3 (1H, s), 3.2 (3H, s), 3.18 (2H, t, J 6.5 Hz), 1.76 (2H, dt, J 2.4, 6.5 Hz), 1.1 (3H, s); δ_C: 118.67, 113.16, 69.85, 58.57, 37.56, 31.30, 25.79; υ_{max}: 1118, 944, 701 cm^{-1}.

Preparation of 1,2-dibromo-3-methyl-3-(2-bromoethyl)cyclopropene (126)

Methyllithium (0.62 ml, 0.93 mmol) was added to a stirred solution of 1,1,2,2-tetrabromo-3-(2-bromoethyl)cyclopropane (0.3 g, 0.62 mmol) in dry ether (15 ml) at -78 °C under nitrogen . The mixture was stirred for 5 min before quenching with water at this temperature; work-up as above gave *1,2-dibromo-3-methyl-3-(2-bromoethyl)cyclopropene* (**126**) (0.16 g, 84 %) as an oil which showed δ_H: 3.2 (2H, t, J 7.3 Hz), 2.1 (2H, t, J 7.3 Hz), 1.19 (3H, s); δ_C: 128.9, 109.98, 42.56, 41.29, 29.74, 23.73; υ_{max}: 1777, 1446, 1248, 844 cm^{-1}.

<u>Preparation of 1,2-dibromo-3-methyl-3-(2-methoxyethyl)cyclopropene (126)</u>

Methyllithium (1.55 ml, 2.32 mmol) was added to a stirred solution of 1,1,2,2-tetrabromo-3-(2-methoxyethyl)cyclopropane (1.0 g, 2.31 mmol) in dry ether (15 ml) at -78 °C under nitrogen. Work-up as above gave *1,2-dibromo-3-methyl-3-(2-methoxyethyl)cyclopropene* (**126**) (0.5 g, 80 %) as an oil which showed δ_H: 3.23 (3H, s), 3.21 (2H, t, J 6.4 Hz), 1.86 (2H, t, J 6.4 Hz), 1.22 (3H, s); δ_C: 108.57, 68.35, 57.57, 40.23, 35.86, 23.08; υ_{max}: 1736, 1448, 1118, 738 cm^{-1}.

<u>Reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-methoxyethyl)cyclopropane with methyllithium and 2,3-dimethylbut-2-ene</u>

Methyllithium (0.85 ml, 1.3 mmol) was added to a stirred solution of 1,1,2,2-tetrabromo-3-methyl-3-(2-methoxyethyl)cyclopropane (0.5 g, 1.16 mmol) and 2,3-dimethylbut-2-ene in dry ether (10 ml) under nitrogen at -78 °C. The reaction mixture was stirred for 3 hr at room temperature, and then quenched with water (5 ml) and the ether layer dried and the solvent was removed at 14 mm Hg to give a brown oil, which was columned on silica eluting with petrol and ether (5:1) to give a mixture of two isomers of

4-(1-bromo-2,2,3,3-tetramethylcyclopropyl)-4-bromo-3-methylbut-3-en-1-yl methyl ether (**149, 150**) in ratio 4:3 (62.5 %) (Found: M^+ 352.0037. $C_{13}H_{22}OBr_2$ requires 352.0037) which showed δ_H: 3.54-3.31 (4H, m), 3.3 (3H, s), 3.26 (3H, s), 2.69-2.5 (2H, m), 2.47-2.2 (2H, m), 1.78 (3H, s), 1.74 (3H, s), 1.27 (3H, s), 1.25 (3H, s), 1.16 (6H, s), 1.1 (6H, s), 1.04 (6H, s); δ_C: 139.7, 139.23, 125.8, 125.2, 69.68, 69.53, 58.46, 58.31, 38.37, 35.81, 31.56, 31.39, 22.83, 22.62, 22.16, 21.41, 21.15, 20.45, 19.33, 10.04; υ_{max}: 2921, 2825 , 1622, 1377, 1114, 856 cm^{-1}.

The reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-bromoethyl)cyclopropane with methyllithium (1.1 mol. equiv.) in the presence of 2,3-dimethylbut-2-ene

Reaction as above gave a mixture of two isomers of *3-bromo-3-(1,4-dibromo-2-methylbut-1-en-1-yl)-1,1,2,2-tetramethylcyclopropane* (**149, 150**) (60 %), which was separated by chromatography on silica eluting with petroleum ether. The first isomer (Found: M^+ 399.9037; $C_{12}H_{19}Br_3$ requires 399.904) showed δ_H: 3.6-3.45 (2H, m), 2.95 (1H, ddd, J 5.8, 11.3, 1.8 Hz), 2.6 (1H, dt, J 4.8, 11.3 Hz), 1.9 (3H, s), 1.38 (3H, s), 1.25 (3H, s), 1.19 (3H, s), 1.13 (3H, s); δ_C: 138.90, 127.20, 59.,17, 41.62, 39.66, 36.73, 31.18, 27.74, 22.76, 22.37, 20.56, 20.27; m/z: 316/318/320/322 (M^+ - Br), 237/239/241 (M^+ - Br_2), 158/160 (M^+ - Br_3); υ_{max}: 2358, 1448, 1114 cm^{-1}.

The second isomer showed δ_H: 3.6-3.45 (2H, m), 2.9-3.1 (1H, m), 2.7 (1H, m), 1.85 (3H, s), 1.34 (3H, s), 1.24 (3H, s), 1.2 (3H, s), 1.17 (3H,s); δ_C: 139.13, 126.98, 41.29, 39.66, 31.74, 29.28, 28.00, 22.75, 22.25, 21.10, 20.49, 19.3.

Reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxyethyl)cyclopropane with methyllithium

(a) Methyllithium (1.6 ml, 2.52 mmol) was added slowly to a stirred solution of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxyethyl)cyclopropane (0.5 g, 1.2 mmol) in dry ether (10 ml) under nitrogen at -78 °C. Stirring was continued for 3 min before the reaction was quenched with water (3 ml) at -78 °C. The aqueous layer was extracted with ether (5 x 10 ml) and the extracts were dried and the solvent evaporated carefully at 5 °C and 14 mm Hg to give a brown oil; chromatography on silica eluting with petrol gave Z-1,2-dibromo-3-methyl-1,3-butadiene (**137**) as a colourless oil (0.11 g, 38 %) which showed δ_H: 6.9 (1H, s), 5.5 (1H, br, s), 5.2 (1H, br,s), 2.01 (3H, d, J 0.76 Hz); δ_C: 140.06, 133.16, 119.91, 109.76, 20.61, identical to an authentic sample.[80]

(b) The above reaction was repeated and quenched with D_2O, to give Z-1,2-dibromo-1-deuterio-3-methyl-1,3-butadiene (**137**) (40 %) which was identical by ^1H NMR to the product from (a) except that the signal at δ 6.9 was reduced in size to about 20% of one proton. The mass spectrum of the product showed *ca.* 75% incorporation of one D.

Reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxyethyl)cyclopropane with diethylphosphite and triethylamine

Triethylamine (0.14 g, 1.4 mmol) was added to a stirred solution of 1,1,2,2-tetrabromo-3-methyl-3-(2-hydroxyethyl)cyclopropane (0.3 g, 0.72 mmol) and diethylphosphite (0.4 g, 2.8 mmol) under argon at room temperature. The reaction was stirred at 90 °C for 4.5 h, then cooled to room temperature and diluted with ether (15 ml), filtered and the solvent evaporated carefully at 0-5 °C and 14 mm Hg. The residue was columned on silica eluting with petrol to give Z-1,2-dibromo-3-methyl-1,3-butadiene (**137**) (0.065 g, 40 %), identical to that obtained above.

Reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-bromoethyl)cyclopropane with methyllithium (2.3 mol. equiv)

(a) In the presence of 2,3-dimethylbut-2-ene: Methyllithium (1.6 ml, 2.4 mmol) was added over 3 min to a stirred solution of the above cyclopropane (0.5 g, 1.04 mmol) in dry ether (10 ml) in the presence of 2,3-dimethylbut-2-ene (1.24 ml, 10 mmol) under nitrogen at -78 °C. The reaction was allowed to reach room temperature and after 2 h was quenched with water (5 ml). The aqueous layer was extracted with ether (2 x 10 ml) and the combined organic layers were washed with water (5 ml), dried, and the solvent was removed at 14 mm Hg. The residue was columned on silica eluting with petrol to give a colourless oil *(2-methyl-4-bromobut-1-enylidene)-2,2,3,3-tetramethylcyclopropane* (**156**) (0.14 g, 55 %) (Found: M^+ 242.066. $C_{12}H_{19}Br$ requires 242.067) which showed δ_H: 3.4 (2H, t, J 7.4 Hz), 2.5 (2H, t, J 7.4 Hz), 1.7 (3H, s), 1.2 (12H, s); δ_C: 182.6, 99.1, 98.6, 37.0, 30.73, 26.85, 21.4, 21.3, 21.26, 20.22; υ_{max}: 2003 cm^{-1}; m/z: 242/244 (M^+), 227/229 (M^+-CH_3), 133/135 (M^+-C_2H_5Br).

(b) In the presence of 2-methylpropene (isobutene): Methyllithium (2.14 ml, 3.2 mmol) was added to a stirred solution of 1,1,2,2-tetrabromo-3-methyl-3-(2-bromoethyl)cyclopropane (0.67 g, 1.39 mmol) in dry ether (10 ml) in the presence of 2-methylpropene (5 ml) under nitrogen at -78 °C. The reaction mixture was allowed to reach room temperature and stirred overnight, and worked up by quenching with water (5 ml) at -30 °C. The aqueous layer was extracted with ether (3 x 10 ml) and the combined organic layers were dried and the solvent was removed at 14 mm Hg. The residue was columned on silica eluting with petrol to give *(2-methyl-4-bromobut-1-enylidene)-2,2- dimethylcyclopropane* (**157**) (0.21 g, 70 %) (Found: M^+ 214.0356. $C_{10}H_{15}Br$ requires 214.03571) which showed δ_H: 3.4 (2H, t, J 7.4 Hz), 2.5 (2H, t, J 7.4 Hz), 1.7 (3H, s), 1.3 (2H, s), 1.2 (6H, s); δ_C: 184.9, 99.6,

90.02, 37.8, 30.61, 24.57, 24.43, 21.9, 21.44, 19.93; υ_{max}: 2009, 1115 cm^{-1}.

Reaction of 1,1,2,2-tetrabromo-3-methyl-3-(2-methoxyethyl)cyclopropane with methyllithium

(i) In the presence of 2,3-dimethylbut-2-ene: Reaction as above in (a) gave: (*2-methyl-4-methoxybut-1-enylidene)-2,2,3,3-tetramethylcyclopropane* (**156**) (49 %) (Found: M^+ 194.167. $C_{13}H_{22}O$ requires 194.167) which showed δ_H: 3.4 (2H, t, J 6.9 Hz), 3.2 (3H, s), 2.2 (2H, t, J 6.9 Hz), 1.73 (3H, s), 1.2 (12H, s); δ_C: 182.6, 98.18, 97.61, 71.32, 58.45, 34.37, 27.37, 21.3, 20.59; υ_{max}: 2004.2 cm^{-1}; m/z: 194 (M^+), 179 (M^+-CH_3), 162 (M^+-OCH_3), 149 (M^+-CH_2OCH_3).

(ii) In the presence of 2-methylpropene (isobutene): Reaction as above in (b) gave: *(2-methyl-4-methoxybut-1-enylidene)-2,2-dimethylcyclopropane* (**157**) (75 %) (Found: M^+ 166.13573. $C_{11}H_{18}O$ requires 166.13573); δ_H: 3.4 (2H, t, J 7.0 Hz), 3.3 (3H, s), 2.3 (2H, t, J 7 Hz), 1.8 (3H, s), 1.34 (1H, d, J 6.6 Hz), 1.3 (1H, d, J 6.6 Hz), 1.2 (6H, s); δ_C: 184.8, 98.9, 88.9, 71.17, 58.52, 34.47, 24.55, 24.45, 21.72, 21.03, 20.30; υ_{max}: 2012, 1119 cm^{-1}.

General procedure for the reaction of 1,1,2-tribromo-2-alkylcyclopropanes with diethylphosphite and triethylamine

(a) **1-Bromo-2-octylcyclopropene** : Triethylamine (0.35 ml, 2.5 mmol) was added to a stirred solution of 1,1,2-tribromo-2-octylcyclopropane (0.5 g, 1.27 mmol) and diethylphosphite (0.65 ml, 5.11 mmol) at 5 °C under nitrogen. The reaction mixture was allowed to reach room temperature and stirred at that temperature for 20 min, when TLC showed no starting material. The reaction was diluted with ether, the solid filtered off, and the solvent evaporated to give a brown oil which was columned on silica eluting with

petroleum ether (b.p. 40-60 °C) to give 1-bromo-2-octylcyclopropene (**174**) (0.28 g, 95 %) which showed δ_H: 2.39 (2H, t, J 7 Hz), 1.5 (2H, pent, J 7 Hz), 1.4 (2H, s), 1.2 (10H, br, s), 0.86 (3H, t, J 7 Hz); υ_{max}: 1836 cm^{-1}, which showed an identical ^1H nmr spectrum to an authentic sample.[39,99]

(b) <u>1-Bromo-2-pentylcyclopropene (174)</u>: This was prepared from 1,1,2-tribromo-2-pentylcyclopropane as above (93 %), and showed δ_H: 2.4 (2H, t, J 7 Hz), 1.59 (2H, pent, J 7 Hz), 1.5 (2H, s), 1.3 (4H, m), 0.9 (3H, t, J 6.9 Hz); υ_{max}: 1836 cm^{-1}. It was identical by ^1H nmr to an authentic sample.[99]

(c) <u>1-Bromo-2-butylcyclopropene (174)</u>: This was prepared from 1,1,2,-tribromo-2-butylcyclopropane as above but with a reaction time of 1 h (69 %), and showed δ_H: 2.4 (2H, t, J 7 Hz), 1.55 (2H, pent, J 7 Hz), 1.5 (2H, s), 1.38 (2H, sextet, J 7 Hz), 0.9 (3H, t, J 7 Hz); υ_{max}: 1836 cm^{-1}. It was identical by ^1H nmr to an authentic sample.[99]

(d) <u>1-bromo-2-ethylcyclopropene (174)</u>: This was prepared from 1,1,2-tribromo-2-ethylcyclopropane as above but with a reaction time of 1 h (63 %), and showed δ_H: 2.4 (2H, q, J 7.2 Hz), 1.5 (2H, s), 1.17 (3H, t, J 7.2 Hz); δ_C: 118.94, 91.18, 19.06, 17.04, 10.72; υ_{max}: 1838 cm^{-1}. It was identical by ^1H nmr to an authentic sample.[99]

<u>Reaction of 1,1,2-tribromo-2-alkylcyclopropanes with a dialkyl phosphite and sodium hydride</u>.

(a) Sodium hydride (0.012 g, 10.51 mmol) was added to a stirred solution of 1,1,2-tribromo-2-octylcyclopropane (0.2 g, 0.51 mmol) and diethyl phosphite (0.26 ml, 2.0 mmol) at 0 - 5 °C and stirred at that temperature for 20 min, when TLC showed no starting material. The product was columned directly on silica, eluting with petroleum ether (b.p. 40-60 °C) to give 1-bromo-2-octylcyclopropene (**174**) (0.114 g, 96 %), which identical by ^1H

nmr to an authentic sample.[99]

(b) In the same way the reaction of 1,1,2-tribromo-2-pentylcyclopropane with diethyl phosphite and sodium hydride, and work up as above gave 1-bromo-2-pentylcyclopropene (**174**) (64 %), which identical by ^{1}H nmr to an authentic sample.[99]

(c) The reaction was repeated as in (b) except that dioctyl phosphite (0.43 ml, 2.0 mmol) was used instead of diethyl phosphite. This gave 1-bromo-2-octylcyclopropene (**174**) (96 %), which was again identical by ^{1}H nmr to an authentic sample.[99]

(d) Reaction of 1,1,2-tribromo-2-pentylcyclopropane as in (c) using an excess of sodium hydride gave 1-bromo-2-pentylcyclopropene (90 %), which was identical by ^{1}H nmr to an authentic sample.[99]

(e) Reaction of 1,1,2-tribromo-2-ethylcyclopropane using the same procedure as in (c) gave 1-bromo-2-ethylcyclopropene (**174**) (52 %) (flash distilled at 0.1 mm Hg), which was identical by ^{1}H nmr to an authentic sample.[99]

<u>Reaction of *Z* or *E*-1,2-diiodo-1,2-dibutylcyclopropanes with diethylphosphite and sodium hydride.</u>

Sodium hydride (0.01 g, 0.24 mmol) was added to a stirred solution of either *Z* or *E*-1,2-di-iodo-1,2-dibutylcyclopropane (0.05 g, 0.12 mmol) and diethylphosphite at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 20 min, when TLC showed no starting material. The product was columned directly on silica eluting with petroleum ether (b.p. 40-60 °C) to give 1,2-dibutylcyclopropene (**196**) (0.026 g, 84 % from either isomer) which showed an identical ^{1}Hnmr spectrum to an authentic sample.[94]

<u>Reaction of *Z* or *E*-1,2-di-iodo-1,2-dibutylcyclopropanes with diethylphosphite and</u>

triethylamine.

(a) Triethylamine (0.06 ml, 0.49 mmol) was added dropwise to a stirred solution of Z-1,2-di-iodo-1,2-dibutylcyclopropane (0.05 g, 0.12 mmol) and diethylphosphite (0.127 ml, 0.99 mmol) at 0 °C. The reaction mixture was allowed to reach room temperature and stirred for 20 hr, when TLC showed no starting material. The product was columned directly on silica eluting with petroleum ether (b.p. 40-60 °C) to give 1,2-dibutylcyclopropene (**196**) (0.018 g, 95 %) which was identical ^{1}H nmr to an authentic sample.[94]

(b) The above reaction was repeated using *E*-1,2-di-iodo-1,2-dibutylcyclopropane, which gave after 20 h 1,2-dibutylcyclopropene (**196**) (22 %) and recovered starting material (0.023 g, 46 %).

Reaction of 1,1,2-tribromo-2,3-dimethylcyclopropane with diethyl phosphite and sodium hydride in the presence of 1,3-diphenylisobenzofuran

Sodium hydride (0.06 g, 2.6 mmol) was added to a stirred solution of the cyclopropane (0.2 g, 0.65 mmol) and diethylphosphite (0.67 ml, 5.2 mmol) at 0 °C, in the presence of 1,3-diphenylisobenzofuran (0.15 g, 0.58 mmol). The reaction was stirred at room temperature for 18 h, followed by quenching with water (5 ml) and ether (10 ml). The aqueous layer was washed with ether (2 x 5 ml), the combined organic layers were dried, and the solvent was evaporated at 14 mm Hg. The residue was columned on silica eluting with petroleum ether and ether (5:2) to give 4-bromo-2,3-dimethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane (**194**) (0.19 g, 69%) which showed δ_H: 7.2-7.8 (14H, complex), 2.7 (1H, q, J 6.7 Hz), 1.3 (3H, d, J 6.7 Hz), 1.01 (3H, s), which showed an identical ^{1}H nmr spectrum to an authentic sample.[115]

2,4-Dibromo-3-methyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane

In the same way reaction of 1,1,2,2-tetrabromo-3-methylcyclopropane with diethyl phosphite and sodum hydride in the presence of DPIBF as above gave *2,4-dibromo-3-methyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**194**) (36 %), m.p. 160-162 °C (Found: C 59.31, H 3.92; $C_{24}H_{18}OBr_2$ requires C 59.7, H 3.76) showed δ_H: 7.2-7.8 (14H, complex), 3.01 (1H, q, J 6.6 Hz), 1.5 (3H, d, J 6.6 Hz); δ_C: 146.85, 133.128, 129.33, 129.19, 128.58, 126.92, 122.68, 91.37, 54.46, 31.77, 16.07.

4-Bromo-3,3-dimethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane

Reaction of 1,1-dibromo-2-chloro-3,3-dimethylcyclopropane with diethylphosphite and sodium hydride in the presence of DPIBF as above gave *4-bromo-3,3-dimethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**194**) (46 %), m.p. 138-140 °C (Found: C 72.05, H 5.22; $C_{25}H_{21}OBr$ requires: C 71.95, H 5.07) showed δ_H: 7.2-7.8 (14H, complex), 1.7 (1H, s), 1.5 (6H, s); δ_C: 149.9, 149.88, 136, 133.5, 130.12, 129, 128.64, 128.46, 128.36, 127.9, 126.56, 125.91, 122.62, 119.29, 93.46, 89.47, 56.61, 44.4, 40.71, 30.2, 20.28, 18.86; υ_{max}: 1600, 1301, 1056, 978 cm^{-1}.

2-Bromo-4-ethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane

Reaction of 1,1,2-tribromo-2-ethylcyclopropane with diethylphosphite and sodium hydride in the presence of DPIBF as above gave *2-bromo-4-ethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**194**) (81 %), m.p. 154-156 °C, (Found: C 71.42, H 5.56; $C_{25}H_{21}OBr$ requires: C 71.95, H 5.07) showed δ_H: 7.2-7.8 (14H, complex), 2.8 (1H, d, J 6.2 Hz), 1.8 (1H, m), 1.7 (1H, d, J 6.2 Hz), 1.3 (1H, m), 0.9 (3H, t, J 7.6 Hz); δ_C: 148.2, 147.4, 134.6, 133.8, 129.34, 129.02, 128.96, 128.79, 128.50, 128.41, 126.35, 126.26,

122.86, 121.91, 90.52, 50.90, 37.95, 27.39, 21.06, 12.69; υ_{max}: 1600, 1301, 1056, 978 cm^{-1}.

4-Bromo-2-methyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane

Reaction of 1,1,2-tribromo-2-methylcyclopropane with diethylphosphite and sodium hydride in the presence of DPIBF gave 4-bromo-2-methyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane (**194**) (80 %), m.p. 118-120 °C (Found: C 71.31, H 5.13; $C_{24}H_{19}OBr$ requires: C 71.47, H 4.75) showed δ_H: 7.2-7.8 (14H, complex, 2.8 (1H, d, J 6.0 Hz), 1.5 (1H, d, J 6.0 Hz), which showed an identical ^1H nmr spectrum to an authentic sample.[158]

Methyl 2-bromo-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octan-4-carboxylate

Reaction of methyl 1,2,2-tribromo-1-cyclopropanecarboxylate with diethylphosphite and sodium hydride in the presence of DPIBF gave *methyl 2-bromo-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octan-4-carboxylate* (**194**) (50 %), m.p. 63-65 °C (Found: C 67.17, H 4.55; $C_{25}H_{19}O_3Br$ requires: C 67.10, H 4.28) showed δ_H: 7.2-7.8 (14H, complex), 3.6 (3H, s), 3.0 (1H, d, J 6.0 Hz), 2.7 (1H, d, J 6.0 Hz); δ_C: 168.62, 148.56, 147.4, 134.21, 132.9, 129.24, 129.12, 129.00, 128.55, 128.51, 128.3, 126.64, 126.3, 123.55, 122.41, 91.08, 89.20, 52.08, 51.16, 42.78, 30.12; υ_{max}: 1724, 1326, 980 cm^{-1}.

Treatment of 1,1,2,2-tetrabromocyclopropane with diethylphosphite and triethylamine in the presence of 1,3-diphenylisobenzofuran

Triethylamine (0.15 ml, 1.11 mmol) was added to a stirred solution of the cyclopropane (0.2 g, 0.55 mmol) and diethylphosphite (0.28 ml, 2.23 mmol) at 0-5 °C, in the presence of 1,3-diphenylisobenzofuran (0.13 g, 0.502 mmol). The reaction was allowed

to reach room temperature and stirred for 18 h. The reaction product was columned directly on silica, eluting with petroleum ether (b.p. 40-60 °C) and ether (5:2) to give 2,4-dibromo-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane (**194**) (0.22 g, 76 %), which showed δ_H: 7.2-7.8 (1H, complex), 3.2 (1H, d, J 7.2 Hz), 2.1 (1H, d, J 3.0 Hz) m.p. 148-150 °C, lit. m.p 148-148.5 °C. The ^{1}H nmr spectrum was identical to an authentic sample.[42]

Reaction of 1,1,2,2-tetrabromo-3,3-dimethylcyclopropane with dioctylphosphite and sodium hydride in presence of 2,3-dimethylbut-2-ene

Sodium hydride (0.04 g, 2.07 mmol) was added to a stirred solution of cyclopropane (0.2 g, 0.518 mmol) in dry ether (3 ml) and dioctylphosphite in the presence of 2,3-dimethylbut-2-ene (0.3 ml, 2.5 mmol) at 0 °C. The reaction was stirred at room temperature for 3 h before quenching with water (2 ml), and the aqueous layer was extracted with ether (2 x 5 ml). The combined ether layers were dried, the solvent was evaporated, and the residue was columned on silica eluting petroleum ether (40-60 °C) to give a white solid, *1-(2-methylprop-1-enylidene)-2,2,3,3-tetramethylcyclopropane* (**198**) (0.03 g, 39 %) which showed δ_H: 1.7 (6H, s), 1.2 (12H, s), identical to the ^{1}Hnmr spectrum of an authentic sample.[85]

Preparation of 1,2,2-tribromocyclopropanecarboxylate (209)

Methyl acrylate (43.05 g, 0.5 mol) and dichloromethane (90 ml) were stirred at 5 °C and bromine (87.0 g, 0.55 mol) in dichloromethane (70 ml) was added dropwise over 2.5 h at 5 - 10 °C. The mixture was allowed to stand at 20 °C overnight, and then the excess of bromine was destroyed by shaking with sodium thiosulphate solution (100 ml). The organic phase was separated and the aqueous phase re-extracted with dichloromethane (2 x 20 ml). The combined organic layers were washed with sat.aq. sodium chloride (100 ml), dried and filtered to give a clear colourless solution of methyl 2,3-dibromopropionate. This was cooled to 5 °C in an ice water bath and triethylamine (60.0 g, 0.59 mol) in dichloromethane (90 ml) was added dropwise over 80 m with stirring at 5 - 10 °C. Triethylamine hydrobromide soon separated as a white solid. The mixture was stirred at ambient for 1 h. Saturated aq.sodium chloride (150 ml) and 2N sulphuric acid (150 ml) were then added and the phases separated. The aqueous phase was re-extracted with dichloromethane (20 ml). The combined organic phases were washed with 0.2N sulphuric acid (150 ml), and then brine (200 ml) and then dried. Removal of the solvent from a small portion of the solution gave methyl 2-bromoacrylate.

Dichloromethane (140 ml) and triethyl benzyl ammonium chloride (TEBA) (7 g) were stirred rapidly in an ice-bath and a solution of sodium hydroxide (160 g, 4.0 mol) in water (160 ml) was added followed by bromoform (129 g), maintaining the temperature at 10 - 15 °C. The dichloromethane solution of methyl 2-bromoacrylate was added over 30 m at such a rate that the temperature was maintained at 10 - 15 °C. The mixture was then allowed to reach a maximum of 24 °C. After 3 h, further bromoform (28.9 g) was added. When the reaction was complete by GLC (*ca* 5.5 - 6 h), an ice-cold, half saturated solution of sodium chloride (1 L) was added at below 30 °C. The lower dichloromethane layer was

separated and the aqueous phase was re-extracted with dichloromethane (2 x 50 ml). The combined organic phases were washed with half saturated sodium chloride solution (500 ml). The aqueous phase re-extracted with dichloromethane (2 x 50 ml). The combined organic phases were dried and evaporated to leave an almost black residue. To this was added petroleum (b.p. 40 - 60, 450 ml) and the mixture was vigorously shaken for 5 m, when some black solid separated. The mixture was filtered through a bed of magnesium sulphate to give a pale yellow solution. Evaporation gave a reddish oil which was vacuum distilled. The fraction boiling at 65 - 90 °C at 0.2 mm Hg (86 g) was *methyl 1,2,2-tribromocyclopropanecarboxylate* (**209**), an additional fraction at 90 - 110 °C (8.2 g) contained a small amount of high boiling impurity (total yield 56 % based on methyl acrylate), (found M^+ : 333.7820 $C_5H_5Br_3O_2$ requires: 333.7840) showed δ_H 3.9 (3 H, s), 2.77 (1 H, d, J 9.6 Hz), 2.00 (1 H, d, J 9.6 Hz); δ_C 165.7, 54.0, 38.1, 26.4, 36.1; ν_{max} 2960, 1740, 1435, 1300. (This procedure is as developed by Mr. E. Roberts)

Reaction of methyl 1,2,2-tribromocyclopropanecarboxylate with di-isobutyl aluminium hydride

(i) Di-isobutyl aluminium hydride (23.73 mmol, 23.7 ml, 1M solution in hexane) was added to a stirred solution of methyl tribromocyclopropanecarboxylate (4 g, 11.86 mmol) in dry dichloromethane (25 ml) at -40 °C under nitrogen. The mixture was allowed to reach room temperature and stirred for 30 min, when TLC. showed no starting material, and then quenched with sat.aq. ammonium chloride (15 ml) at -40 °C, followed by hydrochloric acid (4%, 10 ml). The cooling was removed, and the mixture stirred for 30 min. The product was extracted with dichloromethane (3 x 10 ml), and the combined organic layers were dried and evaporated to give a white solid, *1,2,2-tribromocyclopropane-2-methanol* (**220**)

(2.8 g, 78 %), m.p. 86-88 °C (Found: C 15.67, H 1.99; $C_4H_5OBr_3$ requires C 15.56, H 1.63); δ_H: 4.1 (1 H, dd, J 7.7, 13.0 Hz), 4.0 (1 H, dd, J 6.3, 13.0 Hz), 2.5 (1 H, dd, J 6.6, 7.4 Hz), 2.0 (1 H, d, J 9.4 Hz), 1.9 (1 H, d, J 9.4 Hz); after shaking with D_2O the ^1H nmr showed δ_H: 4.1 (1 H, d, J 13.0 Hz), 4.0 (1 H, d, J 13.0 Hz), 2.09 (1 H, d, J 9.5 Hz), 2.01(1H, d, J 9.5 Hz); δ_C: 70.45, 46.07, 35.71, 29.57.

(ii) Di-isobutyl aluminium hydride (2.96 ml, 2.96 mmol, 1M solution in hexene) was added to a stirred solution of methyl tribromocyclopropanecarboxylate (1 g, 2.9 mmol) in dry methylene chloride (15 ml) under nitrogen at -78 °C. The mixture was stirred for 1 h at -78 °C followed by quenching at -78 °C with sat.aq. ammonium chloride (5 ml). Hydrochloric acid (4%, 10 ml) was added, the cooling bath removed, and the mixture stirred for 30 min. The product was extracted, dried and evaporated to give a yellow oil, 1,2,2-tribromocyclopropanecarboxaldehyde (**221**) (0.63 g, 70 %), identical by ^1H nmr spectrum to that below (p. 209).

<u>1,1,2-Bromocyclopropene-1-methanol diphenylisobenzofuran adduct</u>

1,1,2-Tribromocyclopropane-2-methanol (0.2 g, 0.65 mmol, 1 mol.eq.) and diphenylisobenzofuran (0.17 g, 0.65 mmol, 1 mol.eq.) were dissolved in dry ether (10 ml) and stirred under argon at -78 °C. MeLi (0.86 ml, 1.13 mmol, 2 mol.eq.) was added and the reaction warmed to room temperature and stirred for 2 h. The reaction was quenched at -40 °C by the addition of water (2 ml), and the aqueous layer was separated and extracted with ether (3 x 10 ml). The combined organic extracts were dried and evaporated to give *4-bromo-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane-2-methanol* (**225a**) as a yellow solid (150 mg, 55 %) (Found: 403.053. $C_{24}H_{19}{}^{81}BrO$ requires (M - OH): 403.0522) which showed δ_H 7.8 - 7.9 (4 H, m), 7.4 - 7.5 (7 H, m), 7.3 - 7.35 (3 H,

m), 3.95 (1 H, d, J 12.1 Hz), 3.8 (1 H, d, J 12.1 Hz), 2.8 (1 H, d, J 6.8 Hz), 1.84 (1 H, d, J 6.8 Hz), 1.6 (1 H, s); δ_C 156.4, 129.3, 128..1, 121.7, 89, 62.6, 50, 39.5, 27, 20.3.

2-Bromocyclopropene-1-methanol (225)

The above experiment was repeated with out the addition of DPIBF to give *2-bromocyclopropene-1-methanol* (**225**) (84 %) (Found M^+: 147.9524. Calculated for C_4H_5BrO: 147.9524) which showed δ_H 4.62 (2 H, s), 2.65 (1 H, s), 1.7 (2 H, s); δ_C 83.68, 64.99, 50.98, 14.25.

Cyclopropene-1-methanol diphenylisobenzofuran adduct

1,1,2-Tribromocyclopropane-2-methanol (0.55 g, 1.79 mmol, 1 mol.eq.) was stirred in dry ether (10 ml) under argon at -78 °C. MeLi (3.6 ml, 5.37 mmol, 3 mol.eq.) was added and the reaction warmed to room temperature for 5 m. The reaction was re-cooled to -78 °C when water (5 ml) was added, warmed to room temperature for 30 m, and cooled to below 0 °C to decant the ether layer from the frozen aqueous layer. The water layer was washed with ether (3 x 10 ml) and the combined organic layers were added to DPIBF (0.43 g, 1.59 mmol, 0.89 mol.eq.), stirred for 30 m and then evaporated to give a solid (0.58 g, 96 %); chromatography eluting with ether and petrol (1 : 2) gave *1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane-2-methanol* (**228a**) as a white solid (Found M^+: 340.1463. Caculated for $C_{24}H_{20}O_2$: 340.1463) which showed δ_H 7.6 - 7.8 (4 H, m), 7.3 - 7.6 (5 H, m), 7.0 - 7.3 (5 H, m), 3.83 (1 H, d, J 12 Hz), 3.61 (1 H, d, J 12 Hz), 2.15 (1 H, dd, J 5.2, 3.6 Hz), 1.75 (1 H, dd, J 6.8, 3.6 Hz), 1.4 (1 H, dd, J 6.8, 5.2 Hz), 1.1 (1 H, s, OH); δ_C 14 x aromatics at 151.26 - 119.76, plus 89.66, 88.11, 62.48, 37.51, 18.76.

Cyclopropene-1-methanol (228)

The procedure above was repeated without the addition of DPIBF to yield *cyclopropene-1-methanol* (228) (73 %) as a volatile oil which readily decomposed and showed δ_H 6.7 (1 H, pen, J 1.8 Hz), 4.5 (2 H, T, J 1.8 Hz), 2.5 (1 H, s), 1.0 (2 H, t, J 1.8 Hz); ν_{max} 3382, 1772 cm^{-1}.

1-Trimethylsilyl-2-(trimethysilyloxymethyl)cyclopropene

(i) 1,1,2-Tribromocyclopropane-2-methanol (0.61g, 1.97 mmol, 1 eq) was stirred in dry ether (15 ml) under argon and cooled to -78 ^{0}C. MeLi (3.9 ml, 5.92 mmol, 3 eq) was added and the reaction warmed to room temperature. Trimethylsilylchloride (4 mol.eq.) was added and the reaction stirred for 1 h. Diphenylisobenzofuran (0.38g, 1.41 mmol, 0.7 eq) dissolved in a minimum of dry ether was added and the mixture stirred for 18 h. The reaction was quenched at -40 ^{0}C by the addition of sat.aq. sodium bicarbonate (5 ml), the aqueous layer was separated and extracted with ether (3 x 20 ml). The combined organic extracts were dried and evaporated to give an oil which was subjected to chromatography eluting with ether : petrol (1:2) to give the *2-trimethylsilyl-4-(trimethysilyloxymethyl)-1,5-diphenyl-6,7-benzo-8-oxa-tricyclo[3.2.1.0^{2,4}]octane* (230a) (89 %) as a yellow solid (Found: 485.2332 (MH^+). Calculated for $C_{30}H_{36}Si_2O_2$: 485.2332) which showed δ_H: 7.91 - 7.83 (5 H, m), 7.51 - 7.42 (5 H, m), 7.34 - 7.31 (4 H, m), 3.94 (1 H, d, J 11.1 Hz), 3.59 (1 H, d, J 11.1), 2.57 (1 H, d, J 4.3 Hz), 1.71 (1 H, d, J 4.3 Hz), 0.09 (9 H, s), -0.23 (9 H, s); δ_C: 91.8, 89.5, 62.1, 42.9, 25.45, 23.55, 0.58, -0.57 (plus complex aromatics); ν_{max}: 2955, 1664, 1250 cm^{-1}.

(ii) The procedure in (i) was repeated without the addition of diphenylisobenzofuran to give *1-trimethylsilyl-2-(trimethysilyloxymethyl)cyclopropene* (230) (78 %) which

showed δ_H: 4.71 (2 H, s), 0.92 (2 H, s), 0.19 (9 H, s), 0.16 (9 H, s); δ_C: 133.55, 107.76, 60.55, 7.35, -0.50, -1.45; ν_{max}: 2960, 1806, 1250, 842 cm^{-1}.

2-Trimethylsilyl-1-(hydroxymethyl)cyclopropene

(i) Methyllithium (1.37 ml, 1.92 m.mol) was added to stirred solution of *1,1,2-tribromo-2-((1-methoxy-1-methyl)ethoxymethyl)cyclopropane* (prepared as above) (0.35 g, 0.91 m.mol) in dry ether at -80 ^{0}C. The mixture was allowed to reach room temperature for 5 min and then cooled to -70 ^{0}C and quenched with trimethylsilylchloride (0.28 ml, 2.3 mmol) followed by diphenylisobenzofuran (0.2 g, 0.82 m.mol). The mixture was allowed to reach room temperature and stirred for 18 h. Water (3 ml) was added at -40 ^{0}C and the aq. layer was extracted with ether (3 x 10 ml). The combined ether layers were dried and evaporated to give a yellow solid which was treated with p-toluenesulphonic acid (10 mg) in methanol (5 ml) for 5 min and then extracted with ether, washed with sat.aq. sodium bicarbonate, dried and evaporated. Chromatography eluting with petrol and ether (1:1) gave *4-trimethylsilyl-2-(hydroxymethyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.0.^{2,4}]octane* (**229a**) (0.2 g, 54 %) (Found M+ H^+: 413.1937 $C_{27}H_{28}O_2Si$ + H^+ requires 413.1936); which showed δ_H: 7 - 7.8 (14 H, m), 3.8 (1 H, d, J 12.4 Hz), 3.66 (1 H, J 12.4 Hz), 2.54 (1 H, d, J 4.6 Hz), 1.47 (1 H, d, J 4.6 Hz), -0.3 (9 H, s); δ_C: 91.5, 88.7, 62.4, 43.8, 27.4, 24.0, -0.41 (plus complex aromatics); ν_{max}: 3482, 1660, 1279 cm^{-1}.

(ii) The above reaction was repeated without the addition of diphenylisobenzofuran; the mixture after the addition of TMSCl was allowed to reach room temperature and stirred for 1 h, then cooled to -40 ^{0}C and quenched with water (3 ml). The aqueous layer was extracted with ether (2 x 10 ml) and the combined organic layers were dried and evaporated to give a yellow oil, *1-trimethylsilyl-2-(hydroxymethyl)cyclopropene* (**229**) (76 %) which

showed δ_H: 4.68 (2 H, s), 0.9 (2 H, s), 0.16 (9 H, s); ν_{max}: 3334, 841 cm^{-1}.

(iii) The 1-trimethylsilyl-2-(hydroxymethyl)cyclopropene above was allowed to stand in $CDCl_3$ for 48 h when a dimer was obtained in (63 %) (**236b**). The dimer was recrystalised from petroleum ether (b.p. 40-60 °C) and ether to give colourless needles, m.p 82 -84 °C, (Found: C 59.32, H 9.97; $C_{14}H_{28}SiO_2$ requires C 59.12, H 9.93) which showed δ_H: 7.7 (1H, s), 3.45 (1 H, d, J 10.6 Hz), 3.3 - 3.4 (m, 3 H), 0.5 (1H, dd, J 3.7, 10.1 Hz), 0.4 (1H, dd, J 3.7, 7.8 Hz), -0.01 (9H, s), -0.53 (dd, J 7.8, 10.1 Hz); δ_C: 128.54, 127.5, 72.4, 67, 34.46, 33.8, 20.30, 16.30, 12.2, -0.44, -0.81; ν_{max}: 3521, 1675.5, 1246.5 cm^{-1}.

Crystal data. $C_{14}H_{28}O_2Si_2$, M_r = 284.54, orthorhombic, a = 21.310 (3), b = 6.7544 (9), c = 24.613 (3) Å, β = 90°, V = 3542.7 $Å^3$, Z = 8, D_x = 1.067 g cm^{-3}, $\lambda(MoK_\alpha)$ = 0.71073 Å, μ = 0.195 mm^{-1}, F(000) = 1248, T = 160 K. (This result shown in Appendix p. 259)

Reduction of (1,2,2-tribromocyclopropyl)methanol with hydrogen

(1,2,2-Tribromocyclopropyl)methanol (1.0 g, 3.2 mmol) in ethanol (5 ml) was added to a flask containing 5 % palladium on carbon (0.3 g) and sodium carbonate (0.3 g) in ethanol (15 ml) under ahydrogen atmosphere. The mixture was stirred for two days, when g.l.c. showed no starting material was left. The mixture was diluted with ether (25 ml) and the catalyst was removed by filtration. The organic layer was washed with water (15 ml) then dried. The solvent was removed at 14 mm/Hg to give the crude product which was purified by column chromatography on silica eluting with petroleum ether/ether (5:2) and gave *(1,2-dibromocyclopropyl)methanol* (**252**) (0.22 g, 31 %), which showed δ_H: 3.8 (1H, d, J 12.3 Hz), 3.7 (1H, d, J 12.3 Hz), 3.0 (1H, dd, J 5.8, 8.1 Hz), 2.2 (OH, br, s), 1.7 (1H, t, J 8.1 Hz), 1.3 (1H, dd, J 6.6, 8.1 Hz); δ_C: 67.92, 40.63, 22.36, 16.23; ν_{max} 3376 cm^{-1}; m/e: 230 (M^+).

Oxidation of (1,2,2-tribromocyclopropyl)methanol with PCC

(a) (1,2,2-Tribromocyclopropyl)methanol (7 g, 22.0 mmol) was added at room temperature to a stirred solution of pyridinium chlorochromate (9.76 g, 45.0 mmol) in dichloromethane (80 ml). A black colour appeared after 10 m. The reaction was stirred for 1 h, then refluxed for 1 h. The reaction was cooled, diluted with ether (150 ml), and filtered through a bed of silica. The solvent was evaporated to give a yellow oil, *1,2,2-tribromocyclopropanecarboxaldehyde* (**221**) (5.92 g, 85 %) which showed δ_H: 9.4 (1H, s), 2.8 (1H, d, J 9.4 Hz), 2.0 (1H, d, J 9.4 Hz); δ_C: 189.44, 45.80, 34.77, 26.20; ν_{max}: 1722, 1411 cm^{-1}; m/e: 307 (M^+), 225/227/229 (M^+-Br), 145/147 (M^+-Br_2), 67 (M^+-Br_3).

(b) The above oxidation was repeated using (1,2-dibromocyclopropyl)methanol, in place of the tribromide giving *1,2-dibromocyclopropanecarboxaldehyde* (**253**) (0.2 g, 83 %) which showed δ_H: 9.6 (1H, s), 3.4 (1H, dd, J 6.7, 8.8 Hz), 2.3 (1H, dd, J 7.2, 8.8 Hz), 1.6 (1H, t, J 7.1 Hz); δ_C: 196.13, 42.26, 28.45, 20.26; ν_{max}: 1711, 1286 cm^{-1}; m/e: 227 (M^+), 147/149 (M^+-Br).

Ethyl 3-(1,2,2-tribromocycloprop-1-enyl)prop-E-2-en-1-oate

(a) To a stirred solution of 1,2,2-tribromocyclopropane carboxaldehyde (2.5 g, 8.1 mmol) in toluene (20 ml), carboethoxymethylene triphenylphosphorane (4.25 g, 12.21 mmol) was added at room temperature. The mixture was refluxed for 3.5 h, then the solvent was evaporated to give a thick oil which was treated with petroleum (b.p. 40 - 60 °C). The precipitate was filtered off; evaporation of the solvent gave a brown oil which was purified by column chromatography eluting with petroleum ether/ether (5:2) to give *ethyl 3-(1,2,2-tribromocycloprop-1-yl)prop-E-2-en-1-oate* (**246**) (2.8 g, 91 %) (Found M + NH_4^+: 393.8482. Calculated for $C_8H_9{}^{79}Br^{81}BrO_2$+$NH_4^+$: 393.8481) which showed δ_H: 6.9

(1H, d, J 15.0 Hz), 6.2 (1H, d, J 15.0 Hz), 4.2 (2H, q, J 7.1 Hz), 2.3 (1H, d, J 9.4 Hz), 2.2 (1H, d, J 9.4 Hz), 1.3 (3H, t, 7.1 Hz); δ_C: 165.34, 145.41, 126.13, 60.98, 40.09, 38.47, 31.21, 14.20; ν_{max}: 1719, 1649 cm^{-1}; m/e 337 (M^+), 305, 304 (M^+-$C_3H_5O_2$), 224 (305-Br).

(b) The above reaction was repeated using 1,2-dibromocyclopropane carboxaldehyde, in place of 1,2,2-tribromocyclopropanecarboxaldehyde to give *ethyl 3-(1,2-dibromocycloprop-1-yl)prop-E-2-ene-1-oate* (254) (two isomers in ratio 6:1). The major isomer showed δ_H: 6.5 (1H, d, J 14.9 Hz), 6.1 (1H, d, J 14.9 Hz), 4.2 (2H, q, J 7.1 Hz), 3.1 (1H, dd, J 6.4, 8.8 Hz), 1.9 (1H, t, J 8.1 Hz), 1.6 (1H, dd, J 6.4, 8.0 Hz), 1.2 (3H, t, J 7.1 Hz); δ_C: 165.71, 147.32, 123.42, 60.80, 36.04, 28.28, 28.06, 14.20; ν_{max}: 1718, 1648 cm^{-1}. The minor isomer was lost on the column.

Ethyl 3-(2-bromocyclopropenyl)prop-E-2-en-oate

(a) Methyl lithium (0.4 ml, 1.3M, 0.53 mmol) was added to a stirred solution of ethyl 3-(1,2,2-tribromocycloprop-1-yl)prop-E-2-en-1-oate (0.2 g, 0.53 mmol) in dry ether (5 ml) at -78 °C under nitrogen . The reaction was allowed to reach -40 °C, cooled again to -70 °C and quenched with water (3 ml), and the ether layer was then decanted from the ice, which was extracted with cold ether (2 x 10 ml). Evaporation of the ether at 0 °C gave *ethyl 3-(2-bromocyclopropenyl)prop-E-2-en-oate* (257) (0.1 g, 87 %) which showed δ_H: 7.4 (1H, d, J 15.4 Hz), 6.0 (1H, d, J 15.4 Hz), 4.2 (2H, q, 7.2 Hz), 1.7 (2H, s), 1.3 (3H, t, J 7.2 Hz); δ_C: 166.3, 127.9, 126.2, 112.67, 105.4, 60.8, 16.4, 14.3; ν_{max}: 1794, 1712, 1614 cm^{-1}. This decomposed slowly in deuterochloroform at ambient temperature to give a complex mixture; ca. 50 % remained after 18 h.

(b) Diphenylisobenzofuran (0.11 g, 0.41 mmol) was added to a stirred solution of ethyl 3-(2-bromocyclopropenyl)prop-2-en-oate in ether (5 ml) at room temperature. The

reaction was stirred for 6 h, then the solvent was removed at 14 mm Hg to give a yellow solid which was purified by column chromatography on silica eluting with petroleum ether and ether (5:2), which gave *ethyl 4-bromo-2-(3-prop-E-2-enoyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.0^{2,4}]octane* (**260**) (0.15 g, 68 %), m.p. 58-60 °C (Found: C 69.07, H 4.80; $C_{28}H_{23}O_3Br$ requires C 69.00, H 4.76); δ_H: 7.8-7.2 (14H, m), 6.8 (1H, d, J 15.7 Hz), 5.8 (1H, d, J 15.8 Hz), 4.1 (2H, q, 7.1 Hz), 3.0 (1H, d, J 6.4 Hz), 2.1 (1H, d, J 6.4 Hz), 1.2 (3H, t, J 7.2 Hz); δ_C: 165.8, 147.68, 147.38, 144.24, 133.81, 133.04, 130.36, 129.82, 129.33, 129.28, 129.08, 128.81, 128.68, 128.55, 128.32, 127.08, 126.80, 123.70, 122.83, 122.04, 90.78, 89.93, 60.52, 52.84, 40.74, 29.70, 14.20; ν_{max}: 1717, 1648 cm^{-1}.

(c) The above reaction was repeated using ethyl 3-(1,2,2-tribromocycloprop-2-yl)prop-*E*-2-en-1-oate in place of ethyl 3-(1,2-dibromocycloprop-2-yl)prop-*E*-2-en-1-oate, in the presence of 1,3-diphenylisobenzofuran.The ^{1}H nmr in $CDCl_3$ of the product was very complicated.

<u>Reaction of ethyl 3-(1,2,2-tribromocycloprop-1-yl)prop-*E*-2-en-1-oate with methyllithium</u>

Methyllithium (0.37 ml, 1.5M, 0.37 ml, 2.0 mol.eq.) was added to a stirred solution of ethyl 3-(1,2,2-tribromocycloprop-1-ayl)prop-*E*-2-en-1-oate (0.1 g, 0.26 mmol) in dry ether (7 ml) at -78 °C under nitrogen. The reaction was allowed to reach room temperature and stirred for 5 min at that temperature, then cooled again to -70 °C and quenched with water (2 ml), and the ether layer was decanted from the ice. Evaporation of the ether at 0 °C and 14 mm Hg gave an oil. The ^{1}H nmr in $CDCl_3$ of the product showed a complicated spectrum.

Reaction of ethyl 3-(1,2,2-tribromocycloprop-1-yl)prop-*E*-2-en-1-oate with dimethylsulphoxide and sodium hydride.

Sodium hydride (0.09 g, 3.9 mmol) was added to a stirred solution of trimethylsulfoxonium iodide (0.67 g, 3.4 mmol) in dry dimethylsulfoxide (10 ml) under nitrogen at room temperature. The reaction was stirred for 0.5 hr to form a milky solution, cooled to 0 °C, then ethyl 3-(1,2,2-tribromocycloprop-1-yl)prop-*E*-2-en-1-oate (1.0 g, 2.96 mmol) in dimethylsulfoxide (10 ml) was added to give a dark colour. The mixture was stirred for 30 min at room temperature, and then quenched carefully with a saturated solution of ammonium chloride and the product extracted with dichloromethane (2 x 20 ml). The combined organic layers were dried and the solvent was removed *in vacuo* to give the starting material.

Reaction of ethyl 3-(1,2,2-tribromocycloprop-1-yl)prop-*E*-2-en-1-oate with DIBAL

To a stirred solution of ethyl-3-(1,2,2-tribromocyclopropyl)prop-*E*-2-en-1-oate (0.5 g, 1.32 mmol) in dry dichloromethane (20 ml) was added a solution of 1.0M DIBAL in hexane (2.65 ml) at -40 °C. The mixture was allowed to reach room temperature and stirred for 30 m, when TLC. in petroleum ether/ether (5:2) showed no starting material. The mixture was treated with a sat.aq. ammonium chloride (20 ml) at -40 °C. Hydrochloric acid (4 %, 40 ml) was added, the cooling bath removed, and the mixture stirred for 30 min. The mixture was extracted with dichloromethane (4 x 15 ml), and the extracts were dried and evaporated to give a yellow oil. Column chromatography eluting with petroleum ether and ether (5:2) gave *3-(1,2,2-tribromocyclopropyl)-E-2-propen-1-ol* (**247**) (0.4 g, 91 %) which showed δ_H: 6.0 (1H, d, J 15.0 Hz), 5.9 (1H, d, J 15.0 Hz), 4.28 (1H, d, J 14.1 Hz), 4.21 (1H, d, J 14.1 Hz), 2.2 (1H, d, J 9.3 Hz), 2.15 (OH, br, s), 2.10 (2H, d, J 9.3 Hz); δ_C:

135.02, 130.32, 62.16, 41.61, 37.07, 32.46; ν_{max}: 3347.3, 1661.4 cm^{-1}; m/e: 305 (M^+), 303 (M^+-CH_2OH), 222/224/226 (303-Br), 143/145 (224-Br).

4-Bromo-2-(3-hydroxyprop-*E*-1-en-1-yl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane

(i) Methyllithium (1.82 ml, 2.19 mmol, 2.1 mol. equiv.) was added dropwise to a stirred solution of 3-(1,2,2-tribromocyclopropyl)-*E*-2-propen-1-ol (0.35 g, 1.04 mmol) in dry ether (10 ml) in the presence of 1,3-diphenylisobenzofuran (0.25 g, 0.94 mmol) under nitrogen at -78 °C. The reaction mixture was allowed to reach room temperature and stirred for 4 h, then worked up by quenching with water (3 ml) at -20 °C. The product was extracted with ether (3 x 10 ml), dried and evaporated to give a yellow solid. This was purified by column chromatography eluting with petroleum ether and ether (5:2) to give a white solid, *4-bromo-2-(3-hydroxyprop-E-1-en-1-yl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**261**) (0.37 g, 80 %), m.p. 74-76 °C (Found: C 70.39, H 4.72; $C_{26}H_{21}O_2Br$ requires C 70.26, H 4.75); δ_H: 7.9-7.2 (14 H, m), 5.8 (1 H, dt, 5.5, 15.5 Hz), 5.5 (1 H, d, J 15.5 Hz), 4.1 (1 H, d, J 1.0 Hz), 4.0 (1 H, d, J 1.0 Hz), 2.9 (1 H, d, J 6.3 Hz), 2.0 (1 H, d, J 6.3 Hz); δ_C: 147.92, 134.48, 134.0, 133.48, 129.86, 129.21, 129.0, 128.87, 128.52, 127.04, 126.71, 126.62, 122.80, 121.82, 90.60, 89.88, 63.20, 51.61, 40.20, 27.72; ν_{max}: 3421, 1665 cm^1.

(ii) Methyllithium (0.84 ml, 0.92 mmol, 3.1 mol. equiv.) was added to a stirred solution of 3-(1,2,2-tribromocyclopropyl)-2-propen-1-ol (0.1 g, 0.29 mmol) in dry ether at -78 °C. The solution was allowed to reach room temperature and stirred for 5 min before cooling to -60 °C and quenching with water (2 ml). The ether layer was decanted from the ice and added to 1,3-diphenylisobenzofuran (0.07 g, 0.26 mmol). The ether solution was

stirred for 3 h at room temperature then the solvent was removed at 14 mm Hg to give a yellow solid, which was purified by column chromatography eluting with petroleum ether and ether (5:2) to give a yellow solid, *2-(3-hydroxyprop-E-1-en-1-yl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.0^{2,4}]octane* (**262**) (0.04 g, 40 %), m.p. 58 - 60 °C (Found: C 85.42, H 5.83; $C_{26}H_{22}O_2$ requires C 85.22, H 6.05); δ_H: 7.7-7.0 (14H, m), 5.69 (1H, d, J 15.3 Hz), 5.62 (1H, dd, J 4.5, 15.5 Hz), 4.0 (2H, d, 4.5 Hz), 2.2 (1H, dd, J 3.7, 4.9 Hz), 1.7 (1H, dd, J 3.7, 6.8 Hz), 1.6 (1H, dd, J 4.9, 6.8 Hz); δ_C: 150.97, 148.84, 136.28, 135.23, 130.28, 129.56, 129.24, 128.75, 128.50, 128.40, 127.87, 126.37, 125.92, 121.52, 119.60, 90.19, 88.24, 63.45, 36.94, 35.74, 19.80; ν_{max}: 3394, 1663 cm^{-1}.

Reaction of 3-(1,2,2-tribromocyclopropyl)-2-propen-1-ol with diethylzinc and methylene iodide.

Methylene iodide (0.89 mmol, 0.074 ml) was added dropwise to a stirred solution of 3-(1,2,2-tribromocyclopropyl)-2-propen-1-ol (0.2 g, 0.59 mmol) in dry dichloroethane (10 ml) at -20 °C with diethyl zinc (0.08 ml, 0.59 mmol) under nitrogen. The mixture was allowed to reach room temperature and stirred for 24 hr. The reaction mixture was cooled and poured slowly into aqueous HCl (1%, 15 ml) with stirring. The organic layer was washed with water and dil. $NaHCO_3$ solution, then dried and the solvent was removed at 14 mm Hg to give abrown oil, the ^{1}H nmr spectrum of which showed only starting material.

1-Bromoethyl-1,2,2-tribromocyclopropane (285)

1,1,2-Tribromocyclopropane-2-ethanol (3.0 g, 97 mmol) was dissolved in dry ether (60 ml) and stirred at 0 °C under argon. Carbon tetrabromide (4.8 g, 14.6 mmol) and triphenylphosphine (3.8 g, 14.6 mmol) were added and reaction warmed to room

temperature and stirred for 2 h. TLC in petrolum ether then showed no starting material was left. The resulting precipitate was filtered and the filter was washed with ether (3 x 15 ml). The combined organic layers were reduced under vacuum to give a crude oil which was subjected to column chromatography on silica gel eluting with petroleum (b.p. 40-60 °C). *1-Bromoethyl-1,2,2-tribromocyclopropane* (285) was obtained as a colorless oil (2.7 g, 73 %) (Found M^+: 381.69999. $C_5H_6Br_4$ requires 381.7202) which showed δ_H: 3.6 (2H, m), 2.5 (2H, m), 1.9 (2H, s); δc: 44.13, 43.65, 38.02, 31.25, 29.39; ν_{max}: 2967, 1439, 1215.5, cm^{-1}.

1-Bromo-2-bromoethylcyclopropene (286)

Methyl lithium (1.51ml, 2.27 mmol, 1.1 mol.eq) was added to a stirred solution of 1-bromoethyl-1,2,2-tribromocyclopropane (0.8 g, 2.07 mmol) in dry ether (10 ml) under nitrogen at -78 °C. The mixture was allowed to reach 0 °C, before cooling again to -40 °C and quenching with water (2 ml). After extraction with ether (3 x 10 ml), the combined ether layers were dried and the solvent was removed at 14 mm Hg to give *1-bromo-2-(2-bromoethyl)cyclopropene* (286) (0.4 g, 87 %) (Found M^+: 223.8836 $C_5H_6Br_2$ requires 223.8836); δ_H: 3.5 (2H, t, J 7.0 Hz), 3.0 (2H, t, J 7.0 Hz), 1.5 (2H, s); δ_C: 115.37, 94.87, 29.29, 27.88, 17.02; ν_{max}: 2882, 1838, 1268 cm^{-1} .

1-Bromo-2-bromoethylcyclopropene diphenylisobenzofuran adduct

1-Bromoethyl-1,2,2-tribromocyclopropane (0.5 g, 1.29 mmol) and diphenyl-isobenzofuran (0.38 g, 1.92 mmol) were dissolved in dry ether (15 ml) and stirred under nitrogen. The mixture was cooled to -78 °C and MeLi (0.94 ml, 1.42 mmol, 1.1 mol.equiv.)

was added. The reaction was allowed to reach room temperature and stirred overnight. After quenching with water (2 ml) at -40 °C and extracting with ether (3 x 15 ml), the combined ether layers were dried and the solvent was removed at 14 mm Hg to give a yellow oil, *4-bromo-2-bromoethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* **(290)** (0.48 g, 77 %) (Found M^+: 493.9881 $C_{25}H_{20}Br_2O$ requires 493.9880); δ_H: 8.0-7.0 (14H, m), 3.3 (2H, m), 2.9 (1H, d, J 6.6 Hz), 2.2 (1H, ddd, J 6.3, 9.5, 15.4 Hz), 1.9 (1H, ddd, J 6.3, 9.4, 15.5 Hz), 1.8 (1H, d , J 6.6 Hz); δ_C: 90.53, 89.88, 49.68, 36.95, 32.68, 30.41, 28.35 (plus complex aromatics); ν_{max}: 1660, 1447, 1295 cm^{-1}.

2-Bromo-4-bromoethyl-8-oxatricyclo [3.2.1.$0^{2,4}$] oct-6-ene

An excess of furan was added to a stirred solution of 1-bromo-2-bromoethylcyclopropene (0.2 g, 0.88 mmol) in ether (7 ml) at room temperature. The reaction was stirred at that temperature for 5 days, then the solvent was removed at 14 mm Hg to give yellow oil, *2-bromo-4-bromoethyl-8-oxatricyclo-[3.2.1.$0^{2,4}$]oct-6-ene* **(292, 293)** (0.18 g), which showed two isomers in ratio 3.5 : 1. Column chromatography on silica eluting with 5:2 petroleum ether and diethyl ether gave the major isomer (0.1 g, 38 %) (Found M + H^+: 292.9177 $C_9H_{10}Br_2O$ + H^+ requires 292.9176) which showed δ_H: 6.69 (1H, dd, J 1.6, 5.7 Hz), 6.62 (1H, dd, H 1.5, 5.7 Hz), 4.87 (1H, d, J 1.4 Hz), 4.81 (1H, d, J 1.5 Hz), 3.5 (2H, m), 2.2 (1H, dd, J 1.14, 6.3 Hz), 2.0 (2H, m), 1.1 (1H, d, J 6.2 Hz); δc 139.83, 138.38, 81.35, 79.49, 46.62, 34.90, 33.68, 31.55, 28.91; ν_{max}: 2998, 1618, 1296 cm^{-1}. The minor isomer (0.03 g, 11.5 %) showed δ_H: 6.3 (1H, dd, J 1.7, 5.6 Hz), 6.2 (1H, dd, J 1.7, 5.8 Hz), 5.01 (1H, t, J 1.8 Hz), 4.9 (1H, t, J 1.8 Hz), 3.5 (2H, dt, J 1.5, 7.6 Hz), 2.4 (1H, m), 2.2 (2H, m), 1.7 (1H, d, J 6.8 Hz), 1.4 (1H, d, J 6.8 Hz); δ_C: 134.08, 132.79,

88.58, 83.66, 45.59, 39.78, 35.28, 32.05, 31.25.

2-(2-Bromoethyl)cyclopropene diphenylisobenzofuran adduct

Methyl lithium (1.45 ml, 2.17 mmol, 2.1 mol.equiv.) was added to a stirred solution of 2-bromoethyl-1,2,2-tribromocyclopropane (0.4 g, 1.03 mmol) in dry ether (10 ml) under nitrogen at -78 °C. The solution was allowed to reach room temperature and stirred for 5 min before cooling to -60 °C and quenching with water (2 ml). The ether layer was decanted from the ice and added to 1,3-diphenylisobenzofuran (0.25 g, 0.93 mmol). After 18 h the solvent was removed at 14 mm Hg to give a thick yellow oil (0.3 g, 70 %), *2-(2-bromoethyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**291**) (Found M + H^+: 417.0854 $C_{25}H_{21}BrO + H^+$ requires 417.0853); δ_H: 8.0-7.0 (14H, m), 2.9 (2H, m), 2.3 (1H, ddd, J 6.0, 9.6 15.0 Hz), 2.2 (1H, dd, J 3.7, 5.4 Hz), 1.9 (1H, ddd, J 6.1, 10.0, 15.0 Hz), 1.7 (1H, dd, J 3.6, 6.9 Hz), 1.3 (1H, dd, J 5.4, 6.9 Hz); δ_C: 90.50, 88.28, 34.72, 32.62, 30.23, 30.20, 19.34 (plus complex aromatics); ν_{max}: 1663, 1442, 1096 cm^{-1}.

2-(2-Bromoethyl)cyclopropene

The experimental procedure was repeated as for the previous reaction without the addition of diphenylisobenzofuran to give *2-(2-bromoethyl)cyclopropene* (**289**) (0.08 g, 47 %) which showed δ_H: 6.6 (1H, b, s), 3.5 (2H, t, J 6.8 Hz), 3.0 (2H, t, J 6.8 Hz), 0.9 (2H, d, J 1.6 Hz).

Preparation of 1-bromomethyl-1,2,2-tribromocyclopropane (224)

Bromine (0.32 g, 2.0 mmol, 0.1 ml) was added dropwise to a stirred solution of 1,2-

bis(diphenylphosphono)ethane (0.4 g, 1.0 mmol) in dry dichloromethane (10 ml) under nitrogen at 0 °C. The reaction was stirred at that temperature for 15 min, then 1,1,2-tribromocyclopropane-2-methanol (0.5 g, 1.6 mmol) in dry dichloromethane (3 ml) was added. The mixture was allowed to reach room temperature and stirred for 2 h, when TLC showed no starting material. Diethyl ether (30 ml) was added to form a precipitate and the products were filtered through a bed of silica. The solvent was evaporated to give a white solid, 1-bromomethyl-1,2,2-tribromocyclopropane (224) (90 %), which showed an identical ^{1}Hnmr spectrum to an authentic sample.[114]

<u>Preparation of 1-bromo-2-bromomethylcyclopropene (232)</u>

Methyllithium (1.47 ml, 2.06 mmol) was added dropwise to a stirred solution of 1-bromomethyl-1,2,2-tribromocyclopropane (0.7 g, 1.8 mmol) in dry ether (10 ml) under argon at -78 °C. The reaction was allowed to reach 0 °C before quenching with water (3 ml) at -50 °C. The aqueous layer was extracted with ether (3 x 10 ml) and the combined oganic extracts were dried and evaporated at 14 mm Hg to give *1-bromo-2-bromomethylcyclopropene* (232) (0.25 g, 64 %) which showed δ_H: 4.2 (2H, s), 1.6 (2H, s); δ_C: 113.09, 97.60, 21.54, 18.68; ν_{max}: 2959, 1828 cm^{-1}.

<u>1-Bromo-2-bromomethylcyclopropene diphenylisobenzofuran adduct</u>

(i) 1-Bromomethyl-1,2,2-tribromocyclopropane (0.5 g, 1.34 mol) and DPIBF (0.36 g, 1.34 mol) in dry ether (15 ml) were stirred at -78 °C under argon; MeLi (0.9 ml, 1.35 mol) was added. The reaction was warmed to room temperature when a significant decolourisation was observed. After 10 m the reaction was quenched at -40 °C with water

(2 ml). The aqueous layer was extracted with ether (2 x 15 ml) and the combined organic extracts dried and evaporated to give *4-bromo-2-bromomethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (232a) as a white solid (0.45 g, 70 %) (Found M - Br : 401.0541. Caculated for $C_{24}H_{18}Br_2O$: 401.0542) which showed δ_H 7.8 (4 H, m), 7.3 (3 H, m), 3.66 (1 H, d, J 11.9 Hz), 3.44 (1 H, d J 11.9 Hz), 3.11 (1 H, d, J 6.6 Hz), 2.03 (1 H, d, J 6.6 Hz).

(ii) 1-Bromomethyl-1,2,2-tribromocyclopropane (.10 g, 2.69 mmol) and furan (0.18 g, 2.69 mmol) were stirred in dry ether under argon and cooled to -78 °C. MeLi (1.8 ml, 2.69 mmol) was added and the reaction warmed to room temperature for 18 h and then quenched at -40 °C by the addition of water (5 ml). The aqueous layer was extracted with ether (3 x 10 ml). The combined organic extracts were dried and evaporated to give two isomers of *2-bromo-4-bromomethyl-8-oxatricyclo[3.2.1.$0^{2,4}$]oct-6-ene* (233a, 234a)as an oil (0.6 g, 79 %) in ratio 4.5:1 (Found M^+: 277.8947. Calculated $C_8H_8Br_2O$: 277.8943) which showed (major isomer) δ_H: 6.75 (1 H, dd, J 5.7, 1.5 Hz), 6.70 (1 H, dd, J 5.7, 1.5 Hz), 4.95 (1 H, d, J 1.5 Hz), 4.80 (1 H, d, J 1.5 Hz), 3.5 (1 H, dd, J 11.1, 1.37 Hz), 3.4 (1 H, d, J 11.1 Hz), 2.45 (1 H, d, J 6.47 Hz), 1.34 (1 H, d, J 6.47 Hz); (minor isomer) δ_H: 6.35 (1 H, dd, J 1.7, 5.7 Hz), 6.3 (1 H, dd, J 1.6, 5.7 Hz), 4.0 (1 H, dd, J 1.4, 10.7 Hz), 3.6 (1 H, d, J 10.7 Hz), 1.8 (1 H, dd, J 1.4, 7.0 Hz), 1.6 (1 H, d, J 7.0 Hz). The remaining signals were obscured by those of the major isomer; δ_C 140.51, 138.48, 82.29, 79.56, 49.19, 35.71, 31.29, 13.83.

(iii) Methyllithium (4.0 ml, 5.6 mmol) was added dropwise to a stirred solution of 1-bromomethyl-1,2,2-tribromocyclopropane (1.9 g, 5.1 mmol) in dry ether (20 ml) under argon at -78 °C. The reaction was allowed to reach 0 °C before quenching with water (4

ml) at -50 °C. The aqueous layer was extracted with ether (3 x 15 ml) and the combined organic layers were dried and filtered off. An excess of 2,5-dimethylfuran was added to the filtrate and stirred overnight. Work up by evaporation of the solvent gave a yellow oil, which on chromatography eluting with petrol and ether (5:1) gave a colourless oil, *2-bromo-3-bromomethyl-4,7-dimethyl-8-oxatricyclo[3.2.1.0.^{2,4}]oct-6-ene* **(233d)** (1.2 g, 75 %) which showed δ_H: 6.5 (1H, d, J 5.4 Hz), 6.4 (1H, d, J 5.4 Hz), 3.5 (1H, d, J 11.6 Hz), 3.4 (1H, d, J 11.6 Hz), 2.4 (1H, d, J 6.2 Hz), 1,58 (3H, s), 1.56 (3H, s), 1.2 (1H, d, J 6.2 Hz); δ_C: 143.58, 142.22, 88.01, 87.07, 57.94, 41.12, 35.26, 31.24, 16.32, 14.74; ν_{max}: 2977, 1567 cm^{-1}; m/e 227/229 (M^+ - Br), 147 (M^+ - Br_2).

(iv) The above procedure was repeated using an excess of 2-methylfuran to give two isomers *2-bromo-3-bromomethyl-7-methyl-8-oxatricyclo[3.2.1.0.^{2,4}]octane* **(233b, 233c)** (50 %) in ratio 2.2:1 which showed (major isomer) δ_H: 6.64 (1H,dd, J 1.6, 5.6 Hz), 6.4 (1H, d, J 5.6 Hz), 4.73 (1H, d, J 1.6 Hz), 3.4 (1H, d, J 11.0 Hz), 3.3 (1H, d, J 11.0 Hz), 2.3 (1H, d, J 6.3 Hz), 1.58 (3H, s), 1.2 (1H, d, J 6.3 Hz); (minor isomer) δ_H: 6.7 (1H, dd, J 1.6, 5.6 Hz), 6.5 (1H, d, J 5.6 Hz), 4.76 (1H, d, J 1.6 Hz), 1.59 (3H, s). The remaining signals were obscured by those of the major isomer; δ_C: 143.45, 141.95, 140.74, 138.75, 89.38, 87.54, 81.25, 79.23, 53.99, 53.20, 40.05, 38.48, 35.88, 35.11, 31.26, 16.14, 14.62 ;ν_{max}: 2929, 1560.5 cm^{-1}; m/e: 277/279/281 (M^+ - CH_3), 213/215 (M^+ - Br).

(v) Methyl lithium (2.95 ml, 4.43 mmol) was added to a stirred solution of 1-bromomethyl-1,2,2-tribromocyclopropane (1.5 g, 4.03 mmol) in dry ether (15 ml) under nitrogen at -78 °C. The mixture was allowed to reach 0 °C, before cooling again to -60 °C and quenching with water (3 ml). The ether layer was decanted from the ice, the ice was washed with ether (3 x 10 ml), and an excess of 1,3-butadiene was added to the combined

ether layers. The mixture was allowed to reach room temperature and stirred for 18 h. Work up by evaporation of the solvent at 14 mm Hg gave *6-bromo-1-bromomethylbicyclo[4.1.0]hept-3-ene* (235) (0.6 g, 60 %) (Found M^+: 263.899. $C_8H_{10}Br_2$ requires: 263.914) which showed δ_H: 5.4 (2H, m), 3.8 (1H, d, J 10.3 Hz), 3.6 (1H, d, J 10.3 Hz), 2.8 (2H, m), 2.5 (2H, m), 1.4 (1H, d, J 6.2 Hz), 1.0 (1H,, d, J 6.2 Hz); δ_C: 124.33, 123.98, 44.22, 42.77, 37.0, 28.70, 26,69, 23.65; ν_{max}: 2924, 1661, 1431 cm^{-1}.

Reaction of 4-bromo-2-bromomethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo-[3.2.1.0 ^{2,4}]octane with butyl lithium.

Butyl lithium (0.42 ml, 0.59 mmol, 1.1 mol.eq) was added to a stirred solution of 4-bromo-2-bromomethyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.0 ^{2,4}]octane (0.26 g, 0.53 mmol) in dry ether (7 ml) under nitrogen at -78 °C. The mixture was allowed to reach 0 °C before cooling to -40 °C and quenching with water (2 ml). After extraction with ether (3 x 10 ml), the combined ether layers were dried and the solvent was removed at 14 mmHg to give a thick yellow oil, *2,5-diphenyl-3,4-benzo-2,5-epoxy[4.1.1.0^{1,6}]octane* (276) (0.13 g, 76 %) (Found M^+: 322.1358. $C_{24}H_{18}O$ requires 322.1357); δ_H: 7.8-7.0 (14H, m), 3.5 (1H, dd, J 2.9, 7.5 Hz), 2.0 (1H, d, J 4.0 Hz), 1.86 (1H, d, J 2.9 Hz), 1.8 (1H, dd, J 4.0, 7.5 Hz); δ_C: 146.79, 136.97, 128.84, 128.6, 128.4, 128.23, 128.0, 127.0, 126.8, 125.0, 124.7, 120.37, 120.0, 92.84, 62.05, 49.5, 26.4; ν_{max}: 2925, 1662, 1447, 1297cm^{-1}.

Rraction of 2-bromo-3-bromomethyl-8-oxatricyclo [3.2.1.0.^{2,4}] oct-6-ene with butyl lithium

(a) Butyl lithium (2.8 ml, 3.92 mmol, 1.1 mol.equiv.) was added to a stirred solution

of 2-bromo-3-bromomethyl-8-oxatricyclo[3.2.1.0.^{2,4}]oct-6-ene in dry ether (10 ml) under nitrogen at -78 °C. The mixture was allowed to reach 10 °C, before quenching with water (3 ml) at -40 °C. The solvent was removed at 14 mm Hg, and the product was distilled at 0.1 mm Hg into a cold receiver to give a colorless oil, *2,5-epoxytricyclo[4.1.1.0^{1,6}]oct-4-ene* (**277**) which showed δ_H: 6.1 (2H, br, s), 4.8 (2H, br, s), 3.2 (1H, dd, J 2.7, 7.7 Hz), 2.7 (1H,dd, J 3.7, 7.7 Hz), 1.8 (1H, d, J 3.7 Hz), 1.6 (1H, d, J 2.7 Hz); δ_C: 132.78, 80.7, 61.84, 52.62, 31.89, 29.28; ν_{max}: 2956, 1660, 1465 cm^{-1}.

<u>Reaction of 2-bromo-3-bromomethyl-8-oxatricyclo [3.2.1.0.^{2,4}] oct-6-ene with butyl lithium.</u>

Butyl lithium (36.8 ml, 0.04 mol, 2.1 mol.equiv.) was added dropwise to a stirred solution of 2-bromo-3-bromomethyl-8-oxatricyclo [3.2.1.0^{2,4}] oct-6-ene (5.5 g, 0.01 mol) in dry ether (40 ml) under nitrogen at -78 °C. The solution was allowed to reach 10 °C, before quenching with water (5 ml) at -40 °C. The product was further extracted with ether (3 x 20 ml), and the combined organic layers were dried and the solvent was removed at 14 mm gH to give yellow thick oil, *2-hydroxy-3-butyltricyclo[4.1.1.0^{1,6}]oct-4-ene* (**278**) (3.2 g, 94 %) (Found M$^+$: 178.1358. $C_{12}H_{18}O$ requires 178.1357) which showed δ_H: 6.2 (1H, ddd, J 0.8, 3.0, 9.2 Hz), 5.5 (1H, dd, J 2.3, 9.2 Hz), 4.6 (1H, ddd, J 0.8, 3.9, 6.6 Hz), 2.0 (1H, dd, J 1.6, 6.8 Hz), 1.9 (1H, m), 1.8 (1H, dd, J 2.3, 6.8 Hz), 1.6-1.3 (8H, m), 1.2 (OH, br), 0.92 (3H, t, J 7.0 Hz); δ_C: 131.67, 126.24, 66.12, 41.25, 39.83, 37.84, 31.16, 29.98, 22.81, 14.0, 12.0, 1.89; ν_{max}: 3428, 2928, 1610, 1465 cm^{-1}; m/e: M$^+$ (177.9), 120.9 (M$^+$ -C_4H_9). After shaking with D_2O the signal at δ 4.6 changed to a doublet with coupling constant 3.8 Hz.

Reaction of 2-bromo-3-bromomethyl-7-methyl-8-oxatricyclo[3.2.1.$0^{2,4}$]oct-6-ene with butyllithium

(a) Butyllithium (2.38 ml, 2.14 mmol, 1.1 mol. equiv.) was added to a stirred solution of 2-bromo-3-bromomethyl-7-methyl-8-oxatricyclo[3.2.1.$0^{2,4}$]oct-6-ene (0.7 g,) in dry ether (10 ml) under nitrogen at -78 °C. The mixture was allowed to reach 10 °C, when GLC analysis showed a considerable reduction in the peak of the minor isomer without any effect on the major isomer. The products were quenched with water (3 ml) at -40 °C, the aqueous layer was extracted with ether (3 x 10 ml), and the solvent was removed at 5 °C and 14 mm Hg. The product was distilled at 0.1 mm Hg to give, *2-bromo-2,5-epoxytricyclo[4.1.1.$0^{1,6}$]oct-4-ene* (**281**) which showed δ_H: 6.1 (1H, dd, J 1.6, 5.4 Hz), 6.0 (1H, d, J 5.4 Hz), 4.7 (1H, d, J 1.6 Hz), 3.3 (1H, dd, J 2.6, 7.6 Hz), 2.7 (1H, dd, J 3.7, 7.6 Hz), 1.8 (1H, d, J 3.7 Hz), 1.68 (1H, d, J 2.7 Hz), 1.5 (3H, s). The residue was starting material (major isomer).

(b) The procedure above was repeated using 2.1 mol.equiv. of butyllithium to give *2-hydroxy-3-butyl-5-methyltricyclo[4.1.1.$0^{1,6}$]oct-4-ene* (**282**) (85 %) which showed δ_H: 5.2 (1H, br, s), 4.5 (1H, dd, J 3.6, 6.8 Hz), 2.1 (1H, m), 2.0 (3H, m), 1.9 (1H, dd, J 2.2, 6.7 Hz), 1.8 - 0.9 (13H, m) (after shaking with D_2O the signal at δ 4.5 changed to a doublet with coupling constant 3.6 Hz)

Preparation of 1,1-dihalo-2-chloro-2-(vinyl)cyclopropanes (308)

(i) Sodium hydroxide (32.7 g) in water (33.0 ml) was added to a rapidly stirred solution of 2,3-dichloro-1,3-butadiene (10 g, in 50% xylene), cetrimide (2 g), and bromoform (31.0 g, 10.7 ml) in dichloromethane (20 ml) maintaining the temperature of the reaction below 20 °C. The reaction was stirred for 8 h, and then worked up by dilution with brine solution and extracted with dichloromethane (3 x 100 ml). The organic layer was dried and the solvent was evaporated at 14 mm Hg and 0.5 mm Hg to give a brown oil. This was treated with petrol and the solid was filtered off. Evaporation of the solvent at 14 and then 0.5 mmHg gave *1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane* (308) (7.5 g, 31 %) which showed δ_H: 5.59 (1 H, d, J 2.2 Hz), 5.56 (1 H, d, J 2.2 Hz), 2.4 (1 H, d, J 9.3 Hz), 2.2 (1 H, d, J 9.3 Hz); δ_C: 139.66, 118.80, 53.43, 37.69, 30.15; υ_{max}: 1630 cm^{-1}.

(ii) The above procedure was repeated using chloroprene in xylene for the preparation of *1,1-dibromo-2-chloro-2-vinylcyclopropane* (304) (Found M^+: 257.8447. $C_5H_5Br_2Cl$ requires: 257.8446) (28 %) which showed δ_H: 6.0 (1 H, dd, J 10.2, 16.5 Hz), 5.6 (1 H, d, J 16.5 Hz), 5.4 (1 H, d, J 10.2 Hz), 2.27 (1 H, d, J 9.2 Hz), 2.18 (1 H, d, J 9.2 Hz); δ_C: 135.70, 119.54, 50.85, 36.90, 32.86; υ_{max}: 1634 cm^{-1}.

(iii) The above procedure was repeated using chloroform in place of bromoform for preparation of *1,1,2-trichloro-2-(1-chlorovinyl)cyclopropane* (309) (29 %) (Found M^+-H: 202.8989. $C_5H_4Cl_4$-H requires: 202.8988) which showed δ_H: 5.63 (1 H, d, J 2.2 Hz), 5.61 (1 H, d, J 2.2 Hz), 2.3 (1 H, d, J 9.1 Hz), 2.1 (1 H, d, J 9.1 Hz); δ_C: 138.46, 118.94, 62.49, 53.79, 35.54; υ_{max}: 1632 cm^{-1}.

(iv) The above procedure was repeated for preparation of *1,1,2-trichloro-2-vinylcyclopropane* (305) (28 %) (Found M^+- H: 168.9379. $C_5H_5Cl_3$ - H requires: 168.9378)

which showed δ_H: 6.0 (1 H, dd, J 10.2, 16.5 Hz), 5.6 (1 H, d, J 16.5 Hz), 5.4 (1 H, d, J 10.2 Hz), 2.1 (1 H, d, J 9.0 Hz), 2.0 (1 H, d, J 9.0 Hz); δ_C: 134.08, 119.58, 63.92, 51.63, 35.03; υ_{max}: 1634 cm^{-1}.

Reaction of 1,1-dihalo-2-chloro-2-(vinyl)cyclopropanes with 1 mol.equiv. of methyllithium

Methyllithium (2.26 ml, 3.4 mmol, 1.5M) was added over 1 min. to a stirred solution of 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane (1 g, 3.4 mmol) in dry ether (15 ml) at -78 °C under nitrogen. The mixture was stirred for 5 min at that temperature before being quenched with water (2 ml), and the ether layer was decanted from the ice. The ice was extracted with cool ether (3 x 10 ml). Evaporation of ether at 0 °C and 14 mm Hg gave a brown oil, *2-bromo-1-(1-chlorovinyl)cyclopropene* (**317**) (0.45 g, 75 %), which showed δ_H: 5.7 (1 H, br.s), 5.6 (1 H, br.s), 1.9 (2 H, s); δ_C: 130.0, 120.0, 118.74, 98.7, 19.9; υ_{max}: 1763, 1629 cm^{-1}. When the solution of the cyclopropene was allowed to stand in deuteriochloroform at 20 °C, a complex mixture was obtained after 2 days.

2-Bromo-1-vinylcyclopropene (**316**) was prepared as above by reaction of 1,1-dibromo-2-chloro-2-vinylcyclopropane with methyllithium (66 %) δ_H: 6.5 (1 H, dd, J 10.2, 17.0 Hz), 5.6 (1 H, dd, J 1.8, 10.2 Hz), 5.5 (1 H, dd, J 1.8, 17.0 Hz), 1.6 (2 H, s); δ_C (-20 °C): 123.58, 121.88, 115.42, 95.50, 15.80; υ_{max}: 1803, 1638 cm^{-1}. It decomposed in $CDCl_3$ at room temperature; after 2 days no starting material remained.

2-Chloro-1-vinylcyclopropene (**318**) was prepared using the above procedure by the reaction of 1,1,2-trichloro-2-vinylcyclopropane with methyllithium but distilled at 0 °C

and 14 mmHg and could not be completely separated from ether (68 % estimated) (δ_H: 6.5 (1 H, dd, J 10.2, 17.0 Hz), 5.6 (1 H, m), 5.5 (1 H, m), 1.6 (2 H, s); δ_C (-20 °C): 126.7, 123.30, 121.50, 109.3, 15.08, this compound decomposed relatively quickly in $CDCl_3$ at room temperature.

1-Chloro-2-(1-chlorovinyl)cyclopropene (**319**) was prepared using the above procedure by the reaction of 1,1,2-trichloro-2-(1-chlorovinyl)cyclopropane with methyllithium (63 %); it showed δ_H: 5.68 (1 H, d, J 0.7 Hz), 5.57 (1 H, d, J 0.7 Hz), 1.8 (2 H, s); δ_C: 125.89, 119.99, 116.21, 112.11, 19.29; υ_{max}: 1771, 1631 cm^{-1}. After standing for 1 day at 20 °C in $CDCl_3$, a complex mixture had been produced.

<u>Reaction of 1,1-dibromo-2-chloro-2-vinylcyclopropane with methyllithium in the presence of diphenylisobenzofuran</u>

(i) The above procedure was repeated using 1 mol. equiv. of methyllithium at -78 °C to *give 4-bromo-2-vinyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**320a**) (46 %), m.p. 112-114 °C (Found: C 72.27, H 4.40; $C_{25}H_{19}OBr$ requires C 72.29, H 4.61); δ_H: 7.9-7.3 (14 H, m), 5.7 (1 H, dd, J 10.6, 17.0 Hz), 5.3 (1 H, dd, J 1.3, 10.6 Hz), 5.2 (1 H, dd, J 1.3, 17.0 Hz), 2.9 (1 H, d, J 6.3 Hz), 2.1 (1 H, d, J 6.3 Hz); δ_C: 148.09, 147.97, 134.71, 133.65, 133.49, 129.29, 129.22, 129.0, 128.86, 128.58, 128.50, 127.93, 126.72, 126.66, 122.82, 121.79, 119.21, 90.68, 89.87, 51.39, 41.57, 27.14; ν_{max}: 1636 cm^{-1}.

(ii) The above procedure was repeated using 2 mol.equiv. of methyllithium at -78 to 20 °C, followed by quenching with H_2O at -78 °C, then DPIBF was added to give *2-vinyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**320e**) (68 %), m.p. 94 - 98 °C (Found: C 89.43, H 5.81; $C_{25}H_{20}O$ requires C 89.25, H 5.99); δ_H: 7.9-7.0 (14 H, m), 5.8

(1 H, dd, J 10.5, 17.1 Hz), 5.1 (1 H, dd, J 1.4, 17.1 Hz), 5.0 (1 H, dd, J 1.4, 10.5 Hz), 2.2 (1 H, br.t, J 3.5 Hz), 1.76 (1 H, dd, J 3.5, 6.8 Hz), 1.69 (1 H, dd, J 4.6, 6.8 Hz); δ_C: 151.0, 149.0, 140.1, 137.25, 136.4, 135.45, 133.0, 130.4, 129.9, 129.7, 129.2, 128.45, 128.4, 127.9, 126.7, 125.9, 121.5, 119.5, 114.9, 90.15, 88.2, 38.2, 35.9, 19.3; υ_{max}: 1661, 1602 cm^{-1}.

(iii) The above procedure was repeated using 2 mol. equiv. of methyllithium at -78 to 20 °C, followed by quenching with trimethylsilylchloride (1.9 ml, 0.015 mol) at -78 °C followed by addition of diphenylisobenzofuran (0.83 g, 3.0 mmol) after 5 min at the same temperature to give *4-trimethylsilyl-2-vinyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (320f) (47 %), m.p. 125-127 °C (Found: C 82.11, H 6.72; $C_{28}H_{28}OSi$ requires C 82.30, H 6.90) which showed δ_H: 7.7-7.2 (14 H, m), 5.8 (1 H, dd, J 10.4, 17.2 Hz), 5.2 (1 H, dd, J 1.4, 17.2 Hz), 5.1 (1 H, dd, J 1.4, 10.4 Hz), 2.5 (1 H, d, J 4.7 Hz), 1.8 (1 H, d, J 4.7 Hz), -0.3 (9 H, s); δ_C: 150.03, 149.15, 140.10, 137.77, 136.02, 135.69, 135.46, 133.05, 129.90, 129.32, 128.71, 128.39, 128.22, 127.47, 126.98, 121.89, 121.17, 114.67, 91.90, 89.56, 44.17, 30.82, 23.03, 0.56; υ_{max}: 1662 cm^{-1}.

<u>Reaction of 2,2-dibromo-1-chloro-1-(1-chlorovinyl)cyclopropane with 1.1 mol.equiv. of methyllithium in the presence of dienes</u>

(i) **1,3-diphenylisobenzofuran**: Methyllithium (1.36 ml, 1.49 mmol, 1.1 mol. equiv.) was added dropwise to a stirred solution of 2,2-dibromo-1-chloro-1-(1-chlorovinyl)cyclopropane (0.4 g, 1.36 mmol) in dry ether (10 ml) in the presence of 1,3-diphenylisobenzofuran (0.3 g, 1.2 mmol) under nitrogen at -78 °C. The reaction mixture was allowed to reach room temperature and stirred for 18 h, then worked up by quenching

with water (2 ml) at -30 °C. The mixture was extracted with ether (3 x 15 ml), the combined ether layers were dried and the solvent was removed at 14 mm Hg to give a brown solid. The product was purified by column chromatography on silica eluting with petrol and ether (5:2) to give a white solid, *4-bromo-2-(1-chlorovinyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**320b**) (0.3 g, 49 %), m.p. 128-130 °C (Found: C 66.84, H 4.27; $C_{25}H_{18}OBrCl$ requires C 66.76, H 4.03) which showed δ_H: 7.8-7.1 (14 H, m), 5.5 (1 H, d, J 1.5 Hz), 4.4 (1 H, d, J 1.5 Hz), 3.0 (1 H, d, J 6.2 Hz), 2.0 (1 H, d, J 6.2 Hz); δ_C: 147.40, 147.33, 136.52, 134.07, 133.17, 129.25, 129.19, 128.67, 128.50, 128.34, 127.38, 126.72, 126.30, 122.97, 122.82, 120.83, 90.42, 90.0, 51.69, 45.36, 30.54; υ_{max}: 1626, 1447 cm^{-1}.

(ii) **Furan:** The above procedure was repeated using furan (10 mol.equiv.) in place of 1,3-diphenylisobenzofuran. *2-Bromo-4-(1-chlorovinyl)-8-oxabicyclo[3.2.1.$0^{2,4}$]oct-6-ene* (**321a, 322a**) was obtained as a 3.5:1 mixture of two isomers; chromatography on silica eluting with 5:1 petrol and ether gave the major isomer (0.13 g, 40 %) (Found M + NH_4^+ : 263.9791. $C_9H_8OBrCl+NH_4$ requires: 263.9790) which showed δ_H: 6.8 (1 H, dd, J 1.5, 5.6 Hz), 6.7 (1 H, dd, J 1.5, 5.6 Hz), 5.4 (1 H, d, J 1.6 Hz), 5.3 (1 H, d, J 1.6 Hz), 4.9 (1 H, d, J 1.5 Hz), 4.8 (1 H, d, J 1.5 Hz), 2.5 (1 H, d, J 6.0 Hz), 1.6 (1 H, d, J 6.0 Hz); δ_C: 139.8, 138.7, 116.6, 82.5, 79.85, 41.5, 30.8, 29.7, 20.3; υ_{max}: 1625 cm^{-1}.

The minor isomer (0.08 g, 24 %) showed δ_H: 6.4 (1 H, dd, J 1.7, 5.7 Hz), 6.3 (1 H, dd, J 1.7, 5.7 Hz), 5.5 (1 H, d, J 1.5 Hz), 5.4 (1 H, d, J 1.5 Hz), 5.0 (2 H, m), 1.99 (1 H, d, J 6.8 Hz), 1.92 (1 H, d, J 6.8 Hz); δ_C: 134.5, 134.2, 116.3, 88.3, 84.4, 45.7, 40.3.

(iii) **1,3-Butadiene:** The above procedure was repeated using 1,3-butadiene (10 mol. equiv.) in place of 1,3-diphenylisobenzofuran. *6-Bromo-1-(1-chlorovinyl)-*

bicyclo[4.1.0]hept-3-ene (**323a**) was obtained (57 %) (Found M^+: 231.9564. $C_9H_{10}BrCl$ requires: 231.9564) which showed δ_H: 5.6 (1 H, m), 5.46 (1 H, m), 5.42 (1 H, d, J 1.4 Hz), 5.3 (1 H, d, J 1.4 Hz), 2.9 (3 H, m), 2.3 (1 H, m), 1.6 (1 H, d, J 6.3 Hz), 1.4 (1 H, d, J 6.3 Hz); δ_C: 145.27, 124.11, 123.68, 115.07, 38.68, 36.08, 34.18, 29.17, 23.12; υ_{max}: 1640, 1429 cm^{-1}.

<u>Reaction of 1,1,2-trichloro-2-vinylcyclopropane with methyllithium in the presence of 1,3-diphenylisobenzofuran</u>

The above procedure was repeated using 1 mol.equiv. of methyllithium at 0 °C to give *4-chloro-2-vinyl-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**320c**) (38 %), m.p. 114-116 °C (Found: C 81.23, H 5.33; $C_{25}H_{19}OCl$ requires C 80.96, H 5.16); δ_H: 7.8-7.3 (14 H, m), 5.6 (1 H, dd, J 10.7, 17.0 Hz), 5.2 (1 H, dd, J 1.1, 10.7 Hz), 5.1 (1 H, dd, J 1.1, 17.0 Hz), 2.7 (1 H, d, J 6.3 Hz), 1.9 (1 H, d, J 6.3 Hz); δ_C: 148.1, 147.7, 134.7, 133.6, 132.2, 128.9, 128.8, 128.6, 128.5, 127.5, 126.0, 122.9, 121.8, 119.1, 90.1, 90.0, 59.3, 41.8, 22.6; υ_{max}: 1637 cm^{-1}.

<u>Reaction of 1,1,2-trichloro-2-(1-chlorovinyl)cyclopropane with methyllithium</u>

(i) In the presence of 1,3-diphenylisobenzofuran: Methyllithium (3.7 ml, 3.77 mmol) was added to a stirred solution of 1,1,2-trichloro-2-(1-chlorovinyl)cyclopropane (0.7 g, 3.43 mmol) in dry ether (10 ml) in the presence of 1,3-diphenylisobenzofuran (0.8 g, 3.0 mmol) under nitrogen at 0 °C. The mixture was allowed to reach room temperature and stirred for 6 h, then quenched with water (2 ml) at -20 °C; the product was extracted with ether (2 x 10 ml), the combined ether layers were dried and the solvent was removed at 14 mm Hg

to give a solid, which on recrystallization from petrol and dichloromethane (5:0.5) gave a yellow solid, *4-chloro-2-(1-chlorovinyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (320d) (0.6 g, 43 %), m.p. 142-144 °C (Found: C 74.08, H 4.47; $C_{25}H_{18}OCl_2$ requires C 74.36, H 4.20); δ_H: 7.9-7.2 (14 H, m), 5.4 (1 H, d, J 1.5 Hz), 4.3 (1 H, d, J 1.5 Hz), 2.9 (1 H, d, J 6.2 Hz), 1.9 (1 H, d, J 6.2 Hz); δ_C: 147.33, 135.60, 134.14, 133.17, 129.23, 128.88, 128.76, 128.58, 128.40, 127.51, 126.85, 126.41, 122.88, 122.83, 120.97, 90.37, 89.96, 60.57, 45.51, 29.44; υ_{max}: 1626 cm^{-1}.

(ii) **In the presence of furan.** The above procedure was repeated using furan (10 mol. equiv.) in place of 1,3-diphenylisobenzofuran to give two isomers in ratio 4.5:1. After chromatography, one isomer, *4-Chloro-2-(1-chlorovinyl)-8-oxabicyclo-[3.2.1.$0^{2,4}$]oct-6-ene* (**321b, 322b**) (40 %) (Found M^++H: 203.0030. $C_9H_9OCl_2$ requires: 203.0030) was isolated, which showed δ_H: 6.8 (1 H, dd, J 1.5, 5.7 Hz), 6.7 (1 H, dd, J 1.5, 5.7 Hz), 5.4 (1 H, d, J 1.6 Hz), 5.3 (1 H, d, J 1.6 Hz), 4.88 (1 H, d, J 1.5 Hz), 4.85 (1 H, d, J 1.5 Hz), 2.5 (1 H, d, 56.0 Hz), 1.6 (1 H, d, J 6.0 Hz); δ_C : 140.04, 138.29, 116.37, 81.65, 80.38, 55.56, 36.30, 29.75; υ_{max}: 1626 cm^{-1}.

(iii) **In the presence of 1,3-butadiene.** The above procedure was repeated using 1,3-butadiene (10 mol. equiv.) in place of 1,3-diphenylisobenzofuran. *1-(1-Chlorovinyl)-6-chlorobicyclo(4.1.0)hept-3-ene* (**323b**), was obtained (54 %) (Found M^+: 188.0160. $C_9H_{10}Cl_2$ requires: 188.0159) which showed δ_H: 5.5 (2 H, m), 5.4 (1 H, d, J 1.4 Hz), 5.3 (1 H, d, J 1.4 Hz), 2.8 (3 H, m), 2.3 (1 H, m), 1.5 (1 H, d, J 6.1 Hz), 1.3 (1 H, d, J 6.1 Hz); δ_C: 144.0, 136.55, 124.02, 123.39, 115.25, 47.02, 37.88, 34.18, 29.59, 22.30; υ_{max}: 1644 cm^{-1}.

Dimerization of 1-vinylcyclopropene

(i) Methyllithium (10.25 ml, 15.3 mmol) was added to a stirred solution of 2,2-dibromo-1-chloro-1-vinylcyclopropane (2 g, 7.6 mmol) in dry ether (20 ml) under nitrogen at -78 °C. The reaction was allowed to reach room temperature, then cooled to -40 °C, and the ether was removed under high vacuum to give solid 1-lithio-2-vinylcyclopropane which was quenched with water at -40 °C, followed by distillation at 0.1 mm Hg in to a cold reciever to give the dimer 1,2-divinyltricyclo[3.1.0.0^{2,4}]hexane (**325**) (0.4 g, 40 %), which showed δ_H: 5.5 (1 H, dd, J 10.4, 17.2 Hz), 5.1 (1 H, dd, J 2.0, 17.2 Hz), 4.9 (1 H, dd, J 2.0, 10.4 Hz), 1.6 (1 H, dd, J 1.7, 4.0 Hz), 1.5 (1 H, dd, J 1.7, 4.0 Hz), 1.3 (1 H, m); δ_C: 136.68, 112.69, 32.33, 30.51, 25.66; υ_{max}: 1628 cm^{-1}. The data corresponded to those reported.[138]

The dimer rearranged to 1,2-divinylcyclohexa-1,4-diene (**341**) (0.2 g, 50 %) after 4 weeks at 20 °C in $CDCl_3$; the product showed δ_H: 7.1 (1 H, dd, J 11.0, 17.2 Hz), 5.8 (1 H, s), 5.2 (1 H, dd, J 1.1, 17.2 Hz), 5.1 (1 H, dd, J 1.1, 11.0 Hz), 2.9 (2 H, s); δ_C: 133.03, 123.23, 113.33, 29.70, 26.72; υ_{max}: 1664 cm^{-1}, in agreement with the data reported for an authentic sample.[138] Reaction of the cyclohexadiene (0.1 g, 0.75 mmol) with DDQ (0.17 g, 0.75 mmol) for 0.5 h at 20 °C in $CDCl_3$, followed by filtering through silica, washing with petrol (10 ml) and evaporation of the solvent at 14 mmHg gave o-divinylbenzene (**342**) (0.06 g, 61 %).

(ii) The procedure in (i) was repeated but quenching with D_2O instead of H_2O to give 4,5-dideuterio-1,2-divinyltricyclo[3.1.0.0^{2,4}]hexane (**344**) (40%); δ_H: 5.5 (1 H, dd, J 10.4, 17.2 Hz), 5.2 (1 H, dd, 2.0, 17.2 Hz), 4.9 (1 H, dd, J 2.0, 10.4 Hz), 1.5 (1 H, d, J 4.1 Hz), 1.2 (1 H, d, J 4.1 Hz); δ_C: 136.69, 112.70, 31.57, 30.41, 20.28; υ_{max}: 1627 cm^{-1}. This

rearranged over 4 weeks at at 20 °C in $CDCl_3$ to give 4,5-dideuterio-1,2-divinylcyclohexa-1,4-diene (**345**) (50 %) which showed δ_H: 7.0 (1 H, dd, J 11.0, 17.2 Hz), 5.1 (1 H, dd, J 1.0, 17.2 Hz), 5.0 (1 H, dd, J 1.0, 11.0 Hz), 2.8 (2 H, s); δ_C: 133.02, 113.35, 31.91, 29.68, 26.56; υ_{max}: 1636 cm^{-1}.

Reaction of 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane with 2.1 mol.equiv. of methyllithium in the presence of 1,3-diphenylisobenzofuran

(i) Methyllithium (2.59 ml, 2.85 mmol) was added with stirring to 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane (0.4 g, 1.36 mmol) in dry ether (10 ml) at -78 °C. The mixture was allowed to reach room temperature before cooling to -78 °C, and quenching with water (2 ml). The ether layer was decanted from the ice. The ice was washed with cool ether (2 x 10 ml), and 1,3-diphenylisobenzofuran (0.3 g, 1.2 mmol) was added at -70 °C to the combined ether layers. These were allowed to reach room temperature, stirred for 18 h, and evaporated to give a yellow solid, the NMR spectrum of which showed two isomers in ratio 4:1. Recrystallization from petrol and ether (5:1) gave one isomer of *2-(1-chlorovinyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**320g**) (0.2 g, 40 %), m.p. 132 - 134 °C (Found: C 81.23, H 5.46; $C_{25}H_{19}OCl$ requires: C 80.96, H 5.16) which showed δ_H: 7.8-7.1 (14 H, m), 5.2 (1 H, d, J 1.7 Hz), 4.8 (1 H, d, J 1.7 Hz), 2.4 (1 H, dd, J 4.2, 5.0 Hz), 2.2 (1 H, dd, J 4.2, 7.0 Hz), 1.9 (1 H, dd, J 5.0, 7.0 Hz); δ_C: 150.80, 147.63, 140.04, 137.21, 135.91, 134.23, 129.73, 128.64, 128.46, 127.85, 126.33, 125.83, 123.02, 121.34, 116.18, 112.08, 90.24, 88.01, 41.65, 34.75, 20.51; υ_{max}: 1661 cm^{-1}.

(ii) The above procedure was repeated and the reaction was quenched with D_2O instead

of H_2O. *4-Deuterio-2-(1-chlorovinyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo-[3.2.1.0^{2,4}]octane* (**320h**) was obtained (66 %); the crude product showed two isomers in ratio 4.3:1 by ^1H nmr; recrystallisation from petrol and ether gave one isomer, m.p. 138 - 140 °C (Found: C 80.82, H 4.63; $C_{25}H_{18}OClD$ requires C 80.96, H 4.90); δ_H: 7.8-7.1 (14 H, m), 5.2 (1 H, d, J 1.7 Hz), 4.9 (1 H, d, J 1.7 Hz), 2.4 (1 H, d, J 5.1 Hz), 2.0 (1 H, d, J 5.1 Hz); δ_C: 150.79, 147.65, 140.05, 137.22, 135.03, 134.25, 133.04, 130.41, 129.31, 129.0, 128.63, 128.51, 128.38, 127.83, 126.52, 125.82, 122.63, 119.75, 116.16, 112.06, 90.24, 87.94, 41.57, 29.73, 21.12; υ_{max}: 1664 cm^{-1}.

<u>Dimerization of 1-(1-Chlorovinyl)cyclopropene</u>

(i) A solution of 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane (1 g, 3.4 mmol) in dry ether (15 ml) was treated with methyllithium (8.07 ml, 2.1 mol. equiv.) at -78 °C under nitrogen. The reaction mixture was allowed to reach room temperature, then cooled again to -70 °C and quenched with water (2 ml). After extraction with ether (3 x 15 ml), the combined ether layers were dried and the solvent was removed at 14 mm Hg to give *1,2-bis(1-chlorovinyl)tricyclo[3.1.0.0^{2,4}]hexane* (**348**) (0.3 g, 50 %) (Found M$^+$: 200.0160. $C_{10}H_{10}Cl_2$ requires: 200.0159) which showed δ_H: 5.4 (1 H, d, J 1.4 Hz), 5.2 (1 H, d, J 1.4 Hz), 1.9 (1 H, dd, J 2.2, 4.2 Hz), 1.7 (1 H, m), 1.6 (1 H, dd, J 2.2, 4.6 Hz); δ_C: 139.31, 111.99, 34.13, 29.42, 25.57; υ_{max}: 1621 cm^{-1}.

Generation of the cyclopropene in the presence of an excess of furan gave only the above dimer.

(ii) The above procedure was repeated and the reaction was quenched with D_2O instead of H_2O to give *4,5-dideuterio-1,2-bis(1-chlorovinyl)tricyclo[3.1.0.0^{2,4}]hexane* (**349**) (44.5

%) (Found M^+: 202.0285. $C_{10}H_8D_2Cl_2$ requires: 202.0285) which showed δ_H: 5.4 (1 H, d, J 1.4 Hz), 5.2 (1 H, d, J 1.4 Hz), 1.7 (1 H, d, J 4.7 Hz), 1.6 (1 H, d, J 4.7 Hz); δ_C: 139.31, 112.0, 34.0, 29.68, 29.80; υ_{max}: 1621 cm^{-1}.

Preparation of 1-trimethylsilyl-2-(1-chlorovinyl)cyclopropene (350)

(i) Methyllithium (6.49 ml, 7.1 mmol) was added to a stirred solution of 2,2-dibromo-1-chloro-1-(1-chlorovinyl)cyclopropane (1 g, 3.4 mmol) in dry ether (10 ml) at -78 °C under nitrogen. The mixture was allowed to reach room temperature, then cooled to -50 °C and quenched with trimethylsilyl chloride (0.8 ml, 6.8 mmol). The reaction was allowed to reach room temperature and stirred for 30 min before quenching with water (3 ml) at -40 °C, then the water layer was extracted with ether (3 x 10 ml). The combined ether layers were dried and the solvent was removed at 5 °C and 14 mm Hg to give an oil, *1-trimethylsilyl-2-(1-chlorovinyl)cyclopropene* (350) (0.35 g, 60 %), which showed δ_H: 5.8 (1 H, s), 5.72 (1 H, s), 1.2 (2 H, s), 0.09 (9 H, s); δ_C: 132.77, 129.51, 119.82, 29.68, 11.01, -1.39; υ_{max}: 2957, 1781, 1589, 1250 cm^{-1}.

(ii) ***in situ* Trapping with DPIBF:** Methyllithium (6.49 ml, 7.1 mmol) was added to a stirred solution of 2,2-dibromo-1-chloro-1-(1-chlorovinyl)cyclopropane (1 g, 3.4 mmol) in dry ether (15 ml) at -78 °C. The solution was allowed to reach room temperature before cooling to -50 °C and quenching with trimethylsilyl chloride (10.8 ml, 6.8 mmol). The mixture was stirred for 10 min at that temperature before adding 1,3-diphenylisobenzofuran (0.8 g, 3.06 mmol), then allowed to reach room temperature and stirred for 18 h, quenched with water (3 ml) at -40 °C and extracted with ether (3 x 15 ml). The combined ether layers were dried, and the solvent was removed at 14 mm Hg to give a brown solid.

Chromatography on silica eluting with petrol and ether (5:2) gave *4-trimethylsilyl-2-(1-chlorovinyl)-1,5-diphenyl-6,7-benzo-8-oxatricyclo[3.2.1.$0^{2,4}$]octane* (**320i**) (0.5 g, 33 %), m.p. 138 - 142 °C (Found: C 76.11, H 6.28; $C_{28}H_{27}OClSi$ requires C 75.91, H 6.14); δ_H: 8.1-7.2 (14 H, m), 5.4 (1 H, d, J 1.1 Hz), 5.1 (1 H, d, J 1.1 Hz), 2.7 (1 H, d, J 4.6 Hz), 1.7 (1 H, d, J 4.6 Hz), 0.2 (9 H, s); δ_C: 149.86, 148.64, 143.83, 140.80, 137.28, 136.0, 135.1, 133.0, 131.74, 130.44, 129.03, 128.72, 128.42, 128.32, 126.98, 125.80, 123.36, 122.25, 121.90, 120.26, 119.38, 91.17, 89.09, 48.90, 33.17, 29.82, 2.136; υ_{max}: 1660 cm^{-1}.

(iii) **Trapping with 1,3-butadiene:** The above procedure was repeated using 1,3-butadiene (10 mol. equiv.) in place of 1,3-diphenylisobenzofuran. 1-(1-Chlorovinyl)-6-trimethylsilylbicyclo[4.1.0]hept-3-ene (**323c**) was obtained (43 %) which showed δ_H: 5.5 (2 H, m), 5.21 (1 H, d, J 0.8 Hz), 5.17 (1 H, d, J 0.8 Hz), 2.7 (1 H, m), 2.2 (3 H, m), 1.0 (1 H, d, J 3.8 Hz), 0.8 (1 H, d, J 3.8 Hz), 0.04 (9 H, s); δ_C: 147.88, 123.17, 123.27, 113.44, 34.02, 29.39, 26.23, 17.39,m -1.30; υ_{max}: 1632 cm^{-1}.

(iv) **Trapping with furan:** The above procedure was repeated using furan (10 mol. equiv.) in place of 1,3-diphenylisobenzofuran; no adduct was obtained, but instead a complicated mixture was isolated.

<u>Reaction of 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane with methyllithium in the presence of methyl chloroformate</u>

Methyllithium (4.5 ml, 5.0 mmol, 1.1M) was added to a stirred solution of 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane (0.7 g, 2.3 mmol) in dry ether (10 ml) at -78 °C under nitrogen. The reaction was allowed to reach room temperature for 10 min, then cooled to -50 °C, and added to methyl chloroformate (1.87 ml) in ether (10 ml),

maintaining the temperature below -30 °C. After overnight at room temperature, the reaction was cooled to -30 °C and quenched with water, then the aqueous layer was extracted with ether (3 x 10 ml). The combined ether layers were dried over $MgSO_4$, and the solvent was removed at 14 mm Hg to give a brown solid. Chromatography on silica eluting with petrol/ether (5:1) gave *methyl 8-chlorobicyclo[7.1.0]deca-1,8-dien-4-yn-2-carboxylate* (355) (0.3 g, 57 %), m.p. 104 - 106 °C (Found: C 64.46, H 4.85; $C_{12}H_{11}O_2Cl$ requires C 64.72, H 4.97); δ_H: 3.8 (3 H, s), 3.2 (2 H, m), 2.9 (2 H, m), 2.4 (2 H, m), 1.9 (2 H, p, J 2.0 Hz); δ_C: 167.0, 132.86, 131.72, 117.05, 114.88, 87.39, 83.40, 52.0, 38.45, 22.47, 17.40, 14.49; υ_{max}: 1765, 1700 cm^{-1}.

Crystal data. $C_{12}H_{11}ClO_2$, Mr = 222.66, monoclinic, a = 14.8887 (10), b = 20.4239 (13), c = 7.1847 (5) Å, β = 100.743 (2)°, V = 2146.5 $Å^3$, Z = 8, D_x = 1.378 g cm^{-3}, λ(MoK_α) = 0.71073 Å, μ = 0.331 mm^{-1}, F(000) = 928, T = 160 K. (This result shown in Appendix p. 264)

8-Chlorobicyclo[7.1.0]deca-1,8-dien-4-yn-2-methanol (356)

Diisobutylaluminium hydride (1.35 ml, 1.35 mmol, 1 M in hexane) was added to a stirred solution of methyl 8-chlorobicyclo[7.1.0]deca-1,8-dien-4-yn-2-carboxylate (0.15 g, 0.67 mmol) in dry methylene chloride (10 ml) at -40 °C under nitrogen. The mixture was allowed to reach room temperature and stirred for 30 min, when tlc showed no starting material, and then quenched with sat.aq. ammonium chloride (3 ml) at -40 °C. Hydrochloric acid (4%, 5 ml) was added, the cooling bath removed, and the mixture was stirred for 30 m and then extracted with methylene chloride (2 x 10 ml). The extracts were dried and the solvent evaporated at 14 mm Hg to give a yellow solid. Chromatography on

silica eluting with 5:2 petrol and ether gave a white solid, *8-chlorobicyclo[7.1.0]deca-1,8-dien-4-yn-2-methanol* (356) (0.12 g, 92 %), m.p. 92 - 94 °C (Found: C, 67.69; H, 5.42; $C_{11}H_{11}OCl$ requires: C, 67.87; H, 5.69) which showed δ_H: 4.2 (2 H, br, s), 3.0 (2 H, br.s), 2.8 (2 H, t, J 6.0 Hz), 2.4 (2 H, m), 1.6 (1 H, br.s), 1.5 (2 H, br, s); δ_C: 126.32, 125.83, 117.70, 115.41, 87.66, 83.54, 65.70, 37.99, 23.32, 17.64, 10.49; υ_{max}: 3331, 1628 cm^{-1}.

<u>Reaction of 1,1,2-trichloro-2-vinylcyclopropane with sodium trichloroacetate.</u>

A 100 ml round bottomed flask fitted for reflux and heated in an oil bath was charged with 1,1,2-trichloro-2-vinylcyclopropane (98.6 g, 0.05 mol) in 1,2-dimethoxyethane (50 ml). The contents of the flask were stirred magnetically whilst under reflux, and portions of sodium trichloroacetate (5 g) were added at 15 min intervals for 1 h (25 g, in total). Carbon dioxide was evolved and the mixture turned a light brown colour. After refluxing for a further hour, GLC analysis showed the presence of the two isomeric bis-adducts, but also considerable amounts of the starting material. Sodium trichloroacetate (25 g) was added as before in 5 g portions, and the mixture refluxed for a total of 4 h. GLC analysis showed a considerable reduction in the peak of 1,2,2-trichloro-1-vinylcyclopropane and an increase in the peaks for the bis-adducts. After cooling, the solid was filtered off, washed with 1,2-dimethoxyethane (50 ml). The filtrate was concentrated and treated with petroleum ether (150 ml) (b.p. 40-60 °C) . A black tar separated; the petroleum ether was decanted off, washed with saturated brine (100 ml), dried and the solvent was removed at 14 mm Hg to give a dark oil (11.08 g). This was distilled at 0.1 mm Hg to give the starting material (5.34 g); the residue was columed on silica eluting with petrol to give a pale yellow liquid which contained two isomer of *1,1,2, 2', 2'-pentachloro-bicyclopropane* (310) in ratio 1:1 (1.2 g, 9.4 %) (Found M^+ : 251.8833.

$C_6H_5Cl_5$ requires 251.8833) showed δ_H: 2.1 (1H, dd, J 7.9, 11.3 Hz), 1.9 (1H, dd, J 7.8, 10.6 Hz), 1.7 (1H, d, J 9.6 Hz), 1.5 (2H, m), 1.3 (2H, m), 1.1 (1H, dd, J 8.2, 10.6 Hz), 0.9 (1H, d, J 9.8 Hz), 0.6 (1H, t, J 7.9 Hz); δ_C: 63.88, 61.70, 60.0, 58.43, 51.0, 49.86, 35.87, 35.54, 33.95, 33.81, 28.65, 28.0; ν_{max}: 3o93, 1429, 1115 cm^{-1} .

Reaction of 1,1,2-trichloro-2-(1-chlorovinyl)cyclopropane with sodium trichloroacetate

(a) Sodium trichloroacetate was added at approximately 10 min intervals (6 g, portions) over a period of 1 h to 1,1,2-trichloro-2-(1-chlorocinyl)cyclopropane (4.2 g, 0.021 mol) in toluene (80 ml) and 18-crown-6 ether (0.2 g). The mixture was stirred magnetically and heated to reflux in an oil bath. Carbon dioxide was evolved throughout the addition. Refluxing was continued for 90 min. The mixture was cooled, diluted with petroleum ether (80 ml) (b.p. 40-60 °C) and filtered through a celite bed. GLC showed the product and a small amount of starting material. The solvent was removed at 14 mm Hg. The starting material was removed at 0.1 mmHg, and the residue was chromatographed on silica eluting with petrol to give a brown oil (4.1 g). N.M.R analysis showed some toluene with starting material and the bis-adduct. This was further purified by distillation at 60 °C and 0.1 mm Hg to give *1,1,2,1',2',2'-hexachlorobicyclopropane* **(311)** (1.2 g, 20 %) which showed δ_H: 2.1 (1H, d, J 10.0 Hz), 1.9 (1H, d, J 10.0 Hz); δ_C: 62.07, 55.5, 36.62; ν_{max}: 3091, 1419, 1260 cm^{-1}.

(b) The above procedure was repeated on 1,1-dibromo-2-chloro-2-(1-chlorovinyl)cyclopropane for the preparation of *1,1-dibromo-2,1',2',2'-tetrachlorobicyclopropane* **(312)** yield (8.3 %) (Found M^+ : 373.7434. $C_6H_4Br_2Cl_4$ requires 373.7433) showed δ_H: 2.2 (1H, d, J 10.2 Hz), 2.1 (1H, d, J 10.0 Hz), 2.0 (1H, d, J 10.2

Hz), 1.9 (1H, d, J 10.0 Hz); ν_{max}: 2926, 1574, 1424 cm^{-1}.

Reaction of 1-bromo-2-alkylcyclopropenes with diazomethane

General Procedure: An excess of diazomethane in ether (7 ml) was added to a stirred solution of a 1-bromo-2-alkylcyclopropene in ether at 0 °C (which was prepared by the addition of methyllithium (1.02 ml, 1.2 eq) to a stirred solution of 1,1,2-tribromo-2-alkylcyclopropane (0.5 g, 1.2 mmol) in dry ether (10 ml) under nitrogen atmosphere at -78 °C).[99] The reaction mixture was allowed to reach -30 °C before being quenched with water (2 ml). The ether layer was separated and the aqueous layer was extracted with ether (2 x 10 ml), then the ether layers were combined. The reaction was allowed to reach room temperature and stirred for 24 h, when TLC showed no starting material was left; the excess of diazomethane and ether were removed at 0 °C and 14 mm Hg to give a yellow oil.

(a) 1-Bromo-2-octylcyclopropene

Reaction as above gave two components in ratio 1:1, *5-bromo-1-octyl-2,3-diazabicyclo[3.1.0]hex-2-ene and 1-bromo-5-octyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**401, 402**),which were separated by rapid column chromatography on silica gel eluting with petroleum ether (5:0.5). The first isomer (0.27 g, 39 %) showed δ_H: 4.7 (1H, d, J 19.4 H z), 4.6 (1H, d, J 19.4 Hz), 2.3 (1H, ddd, J 5.3, 10.4, 14.5 Hz), 1.8 (1H, ddd, J 5.3, 10.4, 15.8 Hz), 1.5 (2H, m), 1.4 (1H, d, J 6.4 Hz), 1.2 (10H, br, s), 0.3 (3H, t, J 6.8 Hz), 0.6 (1H, d, J 6.4 Hz). The second isomer (0.2 g, 29 %) showed δ_H: 4.5 (1H, d, J 19.3 Hz), 4.3 (1H, d, J 19.3 Hz), 2.3 (1H, ddd, J 4.0, 9.3, 14.3 Hz), 1.8 (1H, ddd, J 4.0, 9.3, 14.8 Hz), 1.5-0.7 (16H, m, including a doublet at 1.4 with coupling constant 6.0 Hz), 0.6 (1H,

d, J 6.0 Hz), When this isomer was allowed to stand in $CDCl_3$ for 24 h at room temperture decomposition led to a complicated ^1H nmr spectrum.

When the first isomer was allowed to stand in $CDCl_3$ for 24 h at room temperture it decomposed completely to give to a brown solid; after evaporation of the solvent *(3-octylpyridazine hydrobromide* (**403**) (0.26 g, 38 %) was obtained (Found: C 52.92, H 8.01, N 10.14. $C_{12}H_{21}N_2Br$ requires C 52.75, H 7.75, N 10.25) which showed δ_H: 9.5 (1H, d, J 5.0 Hz), 8.6 (1H, dd, J 5.0, 8.5 Hz), 8.3 (1H, dd, J 1.2, 8.5 Hz), 3.2 (2H, t, J 7.8 H z), 1.7 (2H, pent, J 7.8 Hz), 1.1 (10H, br, s), 0.7 (3H, t, J 7.0 Hz); δ_C: 156.29, 149.15, 136.38, 136.28, 33.61, 31.65, 29.07, 28.97, 22.51, 14.0; ν_{max}: 1622 cm^{-1}.

The hydrobromide above was treated with a saturated solution of sodium bicarbonate (2 ml) and extracted with ether (2 x 10 ml), dried and the solvent was evaporated to give *3-octylpyridazine* (**404**) (0.14 g, 78 %) (Found M^+: 192.1626. $C_{12}H_{20}N_2$ requires: 192.1626) which gave a single peak on GLC and showed δ_H: 9.0 (1H, dd, J 1.8, 4.6 Hz), 7.35 (1H, dd, J 4.6, 8.4 Hz), 7.29 (1H, dd, J 1.8, 8.4 Hz), 2.94 (2H, complex), 1.74 (2H, pent, J 7.5 Hz), 1.23 (10H, br, s), 0.81 (3H, t, J 7.0 Hz); δ_C: 163.2, 149.47, 126.27, 126.12, 36.4, 32.0, 29.6, 29.3, 29.2, 29.1, 22.6, 14.0; υ_{max}: 2249, 1586, 1463, 1437, 909, 732 cm^{-1}.

(b) **1-Bromo-2-pentylcyclopropene**

Reaction as above gave two components in ratio 1:1, *5-bromo-1-pentyl-2,3-diazabicyclo[3.1.0]hex-2-ene and 1-bromo-5-pentyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**401, 402**) , which showed δ_H (for the mixture): 4.7 (1H, d, J 19.4 Hz), 4.6 (1H, d, J 19.4 Hz), 4.5 (1H, d, J19.4 Hz), 4.3 (1H, d, J 19.4 Hz), 2.4 (2H, m), 1.9 (2H, m), 1.6-1.2 (12H, m), 0.9 (6H, m), 0.62 (1H, d, J 6.1 Hz), 0.58 (1H, d, J 6.1 Hz). These were subjected to rapid column chromotography on silica eluting with petroleum ether and ether (5:2). The

first component isolated was *3-pentylpyridazine hydrobromide* (403) (0.35 g, 35 %) (Found: C 46.73, H 6.37, N 12.11; $C_9H_{15}BrN_2$ requires: C 46.77, H 6.54, N 12.12) which showed δ_H: 9.6 (1H, dd, J 1.38, 5.0 Hz), 8.7 (1H, dd, J 5.0, 8.6 Hz), 8.4 (1H, dd, J 1.3, 8.6 Hz), 3.3 (2H, t, J 7.6 Hz), 1.8 (2H, pent, J 7.5 Hz), 1.3 (4H, br , s), 0.8 (3H, t, J 7.0 Hz); δ_C: 165.36, 150.0, 136.45, 136.37, 33.67, 31.03, 28.53, 22.15, 13.78; ν_{max}: 3415, 1618 cm^{-1}. The second isomer gave a very complicated ^1H nmr spectrum.

The hydrobromide above was treated with a saturated solution of sodium bicarbonate (2 ml) and extracted with ether (2 x 10 ml), dried and the solvent was evaporated to give *3-pentylpyridazine* (404) (0.1 g, 83 %) (Found M^+: 150.1157; $C_9H_{14}N_2$ requires: 150.1157). It gave a single peak on GLC and showed δ_H: 9.0 (1H, dd, J 1.85, 4.7 Hz), 7.37 (1H, dd, J 4.7, 8.45 Hz), 7.3 (1H, dd, J 1.85, 8.5 Hz), 2.94 (2H, complex), 1.74 (2H, p, J 7.5 Hz), 1.32 (4H, br, s), 0.86 (3H, t, J 7 Hz); δ_C: 164.04, 150.92, 126.34, 126.18, 36.28, 31.34, 29.76, 22.36, 13.88; υ_{max}: 2233, 1597, 1456, 912, 732 cm^{-1}; m/e: 121 (M^+-C_2H_5), 107 (M^+-N_2CH_3).

(c) <u>1-Bromo-2-ethylcyclopropene</u>

Reaction as above gave two components in ratio 1:1, *5-bromo-1-ethyl-2,3-diazabicyclo[3.1.0]hex-2-ene and 1-bromo-5-ethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (401, 402), which were subjected to rapid column chromatography on silica eluting with petrolum ether and ether (5:2). The first isomer (0.3 g, 49 %) showed δ_H: 4.8 (1H, d, J 19.4 Hz), 4.7 (1H, d, J 19.4 Hz), 2.4 (1H ,dq, J 7.5,14.9 Hz), 1.9 (1H, dq, J 7.4, 14.9 Hz), 1.4 (1H, d, J 6.4 Hz), 1.2 (3H, t, J 7.4 Hz), 0.6 (1H, d, J 6.4 Hz). The second isomer (0.26 g, 42 %) showed δ_H: 4.5 (1H, d, J 19.4 Hz), 4.3 (1H, d, J 19.4 Hz), 1.6 (2H, q, J 7.5 Hz), 1.4 (1H, d, J 6.1 Hz), 1.0 (3H, t, J 7.5 Hz), 0.6 (1H, d, J 6.1 Hz).

When this isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature,

decomposition led to a complicated spectrum. When the first isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature, the compound was completely changed to a brown solid. After evaporation of the solvent *3-ethylpyridazine hydrobromide* (403) (0.28 g, 46 %) was obtained (Found: C 37.95, H 5.17, N 15.02. $C_6H_9BrN_2$ requires: C38.12, H4.80, N14.82) which showed δ_H: 9.6 (1H d, J 4.65 Hz), 8.5 (1H, dd, J 5.1, 8.5 Hz), 8.3 (1H, d, J 8.5 Hz), 3.4 (2H, q, J 7.4 Hz), 1.48 (3H, t, J 7.6 Hz); δ_C: 164.91, 149.50, 126.50, 125.75, 29.47, 13.60); ν_{max}: 3420, 1621 cm^{-1}.

The hydrobromide above was treated with a saturated solution of sodium bicarbonate (2 ml) and extracted with ether (2 x 10 ml), the combined ether layers were dried and the solvent was evaporated to give *3-ethylpyridazine* (404) (0.09 g, 69 %) (Found M^+: 108.0687. $C_6H_8N_2$ requires: 108.0687) which gave a single peak on GLC and showed δ_H: 8.95 (1H, dd, J 2.0, 4.6 Hz), 7.33 (1H, dd, J 4.6, 8.4 Hz), 7.27 (1H, dd, 51.85, 8.36 Hz), 2.9 (2H, q, J 7.6 Hz), 1.28 (3H, t, J 7.6 Hz); δ_C: 164.91, 149.50, 126.49, 125.75, 29.47, 13.6; υ_{max}: 2235, 1670, 1598, 911 cm^{-1}.

(d) <u>1-Bromo-2-butylcyclopropene</u>.

Reaction as above gave two components in ratio 1:1, *5-bromo-1-butyl-2,3-diazabicyclo[3.1.0]hex-2-ene and 1-bromo-5-butyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (401, 402), which were separated by rapid column chromatography on silica eluting with petroleum ether and ether (5:2). The first isomer (39 %) which showed δ_{II}: 4.8 (1H, d, J 19.55 Hz), 4.7 (1H, d, J 19.6 Hz), 2.3 (1H, ddd, J 5.2, 10.4, 14.5 Hz), 1.8 (1H, ddd, J 5.3, 10.2, 15.5 Hz), 1.6 (2H, m), 1.4 (1H, d, J 6.4 Hz), 1.3 (2H, m), 0.92 (3H, t, J 7.2 Hz), 0.6 (1H, d, J 6.4 Hz). The second isomer (0.4 g, 31 %) showed δ_{II}: 4.5 (1H, d, J 19.3 Hz), 4.4 (1H, d, J 19.3 Hz), 1.6 (2H, m), 1.4 (1H, d, J 6.0 Hz), 1.3 (4H, br, m), 0.8 (3H, t, J 7.0 Hz), 0.6 (1H, d, J 6.0 Hz); when this isomer was allowed to stand in $CDCl_3$ for 24 h at

room temperature complete decomposition occurred to give a mixture showing a complicated spectrum.

When the first isomer was allowed to stand in $CHCl_3$ for 24 h at room temperature, the compound was completely changed and gave a brown solid, *3-butylpyridazine hydrobromide* (**403**) (0.45 g, 35 %) (Found: C 44.26, H 5.81, N 12,78. $C_8H_{13}BrN_2$ requires: C 44.26, H6.04, N 12.90) which showed δ_H: 9.6 (1H, dd, J 3.8, 50 Hz), 8.7 (1H, dd, J 5.0, 8.6 Hz), 8.4 (1H, dd, J 1.35, 8.6 Hz), 3.3 (2H, t, J 7.6 Hz), 1.8 (2H, pent, J 7.2 Hz), 1.4 (4H, m), 0.9 (3H, t, J 7.2 Hz); δ_C: 165.35, 149.11, 136.12, 136.07, 33.26, 30.98, 22.16, 20.30, 13.61.

The hydrobromide above was treated with a saturated solution of sodium bicarbonate (2 ml), and extracted with ether (2 x 5 ml), dried, and evaporated to give *3-butylpyridazine* (**404**) (0.23 g, 82 %) (Found M^+: 136.1000, $C_8H_{12}N_2$ requires: 136.1000) which gave a single peak on GLC and showed δ_H: 9.0 (1H, dd, J 1.87, 4.63 Hz), 7.35 (1H, dd, J 4.7, 8.44 Hz), 7.28 (1H, dd, J 1.88, 8.4 Hz), 2.94 (2H, complex), 1.72 (2H, pent, J 7.3 Hz), 1.2 (2H, m), 0.9 (3H, t, J 7.2 Hz); δ_C: 164.06, 149.47, 126.27, 126.12, 36.05, 31.70, 22.31, 13.78; υ_{max}: 2235, 1670, 1599 cm^{-1}.

(e) <u>1-Bromo-2-t-butylcyclopropene</u>

Reaction as above gave two components in ratio 1:1, *5-bromo-1-t-butyl-2,3-diazobicyclo[3.1.0]hex-2-ene* and *1-bromo-5-t-butyl-2,3-diazobicyclo[3.1.0]hex-2-ene* (**401, 402**), which were separated by rapid column chromatography on silica eluting with petrolum ether and ether (5:1). The first isomer (0.05 g, 42 %) showed δ_H: 4.86 (1H, d, J 19.5 Hz), 4.7 (1H, d J 19.5 Hz), 1.8 (1H, d, J 6.5 Hz), 1.3 (9H, s), 0.47 (1H, d, J 6.5 Hz). The second isomer (0.03 g, 25 %) decomposed very fast and gave a very complicated ^1H nmr spectrum.

When the first isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature, the compound was completely changed to a brown solid. Evaporation of the solvent to gave *3-t-butylpyridazine hydrobromide* (**403**) (0.035 g, 29.4 %) (Found: C 44.62, H 6.37, N 12.27 $C_8H_{13}BrN_2$ requires: C44.35, H 6.04, N 12.93); δ_H: 9.9 (1H, d, J 4.6 Hz), 8.7 (1H, dd, J 4.6, 8.5 Hz), 8.5 (1H, d, J 8.4 Hz), 1.5 (9H, s); δ_C: 173.72, 145.80, 134.93, 134.3, 38.08, 29.48; ν_{max}: 1608 cm^{-1}

The hydrobromide above was treated with a saturated solution of sodium bicarbonate (2 ml), and extracted with ether (2 x 5), dried and evaporated to give *3-t-butylpyridazine* (**404**) (0.01 g, 55.5 %) (Found: M^+ 136.1001, $C_8H_{12}N_2$ requires 136.1000), which gave a single peak on GLC. δ_H: 9.0 (1H, dd, J 1.7, 4.7 Hz), 7.4 (1H, dd, J 1.7, 8.7 Hz), 7.3 (1H, dd, J 4.7, 8.6 Hz), 1.4 (9H, s); δ_C: 170.33, 149.18, 126.16, 122.97, 36.98, 29.93; ν_{max}: 1636.4 cm^{-1} .

<u>Reactions of 1,2-dibromocyclopropene</u>

(1) **With diazomethane:** An excess of diazomethane in ether (20 ml) was added to a stirred solution of 1,2-dibromocyclopropene at 0 °C (which was prepared by the addition of methyllithium (8.7 mmol, 5.86 ml) to a stirred solution of 1,1,2,2-tetrabromocyclopropane (3.0 g, 8.3 mmol) in dry ether (40 ml) at -78 °C.[42,69] The reaction was stirred for 5 min at this temperature before quenching with water (2 ml). The ether layer was decanted from the ice. The ice was washed with ether (2 x 20 ml), then the ether layers were combined. The reaction was allowed to reach room temperature and stirred for 2 h, when TLC showed no starting material was left. The solvent and diazomethane were removed at 0 °C and 14 mm Hg to give a yellow oil, *1,5-dibromo-2,3-diazabicyclo[3.1.0]hex-2-ene* (**384**) (1.7 g, 85 %) which showed δ_H: 4.8 (1H, d, J 19.8

Hz), 4.8 (1H, d, J 19.7 Hz), 2.0 (1H, d, J 7.7 Hz); δ_C: 85.81, 75.04, 34.06, 31.9.

When the compound above was allowed to stand in $CHCl_3$ at room temperature for 1 h, a brown solid was formed identified as *3-bromopyridazine hydrobromide* (385) (1.64 g, 82 %) (Found: C 20.22, H 1.76, N 11.48. $C_4H_4Br_2N_2$ requires: C 20.03, H 1.68, N 11.68) which showed δ_H: 9.1 (1H, dd, J 1.4, 4.9 Hz), 8.1 (1H, dd, J 1.4, 8.7 Hz), 7.7 (1H, dd, J 4.9, 8.7 Hz); δ_C: 150.35, 148.52, 135.42, 131.4.

When 3-bromopyridazine hydrobromide (1.4 g) was treated with sodium hydroxide solution (2 g) in water (2 ml) for 5 min, then extracted with ether (5 x 10 ml), and the combined ether layers were dried, evaporation of the solvent gave yellow crystals of *3-bromopyridazine* (**386**) (0.62 g, 67 %), m.p. 80-82 °C (decomposition) (Found: C 30.07, H 1.61, N 17.31. $C_4H_3N_2Br$ requires C 30.21, H 1.90, N 17.62) which showed δ_H: 9.1 (1H, dd, J 1.2, 4.7 Hz), 7.7 (1H, dd, J 1.3, 8.5 Hz), 7.3 (1H, dd, 4.7, 8.6 Hz); δ_C: 150.6, 148.64, 131.68, 128.32; υ_{max}: 1556, 1369, 1124, 806 cm^{-1}.

(2) **With ethyldiazoacetate:** Ethyldiazoacetate (0.9 ml, 8.5 mmol) was added to a stirred ether solution of 1,2-dibromocyclopropene at 0 °C. The reaction was allowed to reach room temperature and stirred for 38 h. When TLC showed no starting material was left, the solvent was removed at 14 mm Hg to give a yellow oil (1.88 g) which became semi-solid on standing at room temperature for 24 h; this was treated with petroleum ether and the solid was filtered off (0.9 g). The solvent was removed from the filtrate and the residue left standing for 2 h before treating again with petroleum ether. Solid separated out and was again filtered off (0.5 g). The combined solids were treated with $CHCl_3$ and sodium bicarbonate solution to give a brown solid, *ethyl 3-bromo-6-pyridazine carboxylate* (**399**) (1.9 g, 51%), which was recrystallized from petrol and ether to give white crystals (m.p. 143-145 °C) (Found: N 12.3, C 36.76, H 3.14; $C_7H_7N_2O_2Br$

requires: N 12.12, C 36.4, H 3.1) which showed δ_H: 8.0 (1H, d, J 8.77 Hz), 7.8 (1H, d, J 8.8 Hz), 4.5 (2H, q, J 7.1 Hz), 1.4 (3H, t, J 7.1 Hz); δ_C: 163.45, 151.067, 150.94, 132.113, 129.2, 62.9, 14.2; υ_{max}: 1727, 1548, 788 cm^{-1}.

<u>Reaction of 1-bromo-3,3-dimethylcyclopropene with diazomethane</u>

An excess of diazomethane in ether (10 ml) was added to a stirred solution of 1-bromo-3,3-dimethylcyclopropene in ether (20 ml) at 0 °C. The mixture was allowed to reach room temperature and stirred for 3 h. When TLC showed no starting material was left, the solvent and excess of diazomethane were removed at 0 °C and 14 mm Hg to give a yellow oil which was a mixture of two isomers in ratio 2.2 : 1, *1-bromo-6,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene, and 5-bromo- 6,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene* (**410, 411**). These were separated by rapid column chromatography on silica eluting with petroleum ether and ether (5;2). The first isomer (0.35 g, 24 %) showed δ_H: 4.7 (1H, d, J 19.9 Hz), 4.6 (1H, d, J 2.5 Hz), 4.5 (1H, dd, J 2.5, 19.9 Hz), 1.4 (3H, s), 0.6 (3H, s). When this isomer was allowed to stand in $CDCl_3$ for 24 h at room temperature decomposition to a complex product occurred. The second isomer (0.42 g, 29 %) showed δ_H: 4.7 (1H, dd, J 6.2, 19.8 Hz), 4.1 (1H, dd, J 1.3, 19.8 Hz), 1.6 (1H, dd, J 1.3, 6.2 Hz), 1.4 (3H, s), 0.6 (3H, s); δc: 86.38, 76,34, 33.31, 27.70, 24.67, 12.30; ν_{max}: 1608 cm^{-1}; when this isomer was allowed to stand in $CDCl_3$ for 4 days at room temperature decomposition occurred to a mixture which showed a complicated spectrum.

<u>Reaction of 1-bromo-2,3-dimethylcyclopropene</u>

An excess of diazomethane in ether (10 ml) was added to a stirred solution of 1-bromo-2,3-dimethylcyclopropene in ether (20 ml) at 0 °C. The mixture was allowed to

reach room temperature and stirred for 2 h when TLC showed no starting material was left; the solvent and excess of diazomethane were removed at 0° C and 14 mm Hg to give a mixture of two isomers in ratio 1:1, *1-bromo-5,6-dimethyl-2,3-diazabicyclo[3.1.0]hex-2-ene and 5-bromo-1,6-dimethyl-2,3- diazabicyclo[3.1.0]hex-2-ene* (**413, 414**), which were separated by rapid column chromatography on silica eluting with petrolum ether and ether (5:2). The first isomer (0.1 g, 33 %) showed δ_H: 4.8 (1H, d, J 19.3 Hz), 4.7 (1H, d, J 19.3 Hz), 1.7 (3H, s), 1.1 (3H, d, J 6.3 Hz), 0.5 (1H, q, J 6.3 Hz). When this isomer was allowed to stand in $CDCl_3$ at room temperature for 10 h the compound was completely changed to give *3,4-dimethylpyridazine hydrobromide* (**415**) (0.07 g, 23 %) which showed δ_H: 9.4 (1H, d, J 5.3 Hz), 8.2 (1H, d, J 5.3 Hz), 3.0 (3H, s), 2.6 (3H, s); δc: 147.6, 134.09, 38.13, 31.21, 19.42, 18.7; ν_{max}: 1626 cm^{-1}.

The second isomer (0.06 g, 20 %) which showed δ_H: 4.4 (1H, d, J 19.6 Hz), 4.2 (1H, d, J 19.6 Hz), 1.85 (3H, s), 0.85 (1H, q, J 6.4 Hz), 0.6 (3H, d, J 6.4 Hz), decomposed rapidly in $CDCl_3$ but led to a complicated ^1H nmr spectrum.

Reaction of methyl 1-bromo-2-cyclopropene carboxylate with diazomethane

An excess of diazomethane in ether (7 ml) was added to a stirred solution of methyl 1-bromo-2-cyclopropenecarboxylate in ether (15 ml) at -50 °C. The mixture was allowed to reach room temperature for two hours, then the solvent was removed at 0 °C and 14 mm Hg to give a brown oil which decomposed very quickly in benzene or chloroform, to give a brown solid, *methyl 3-pyridazinecarboxylate hydrobromide* (**407**) (0.4 g, 56 %) which showed δ_H (D_2O): 9.4 (1H, dd, J 1.6, 5.2 Hz), 8.5 (1H, dd, J 1.6, 8.6 Hz), 8.2 (1H, dd, J 5.2, 8.6 Hz), 4.0 (3H, s); δ_C: 163.78, 152.28, 151.5, 132.35, 132.1, 53.91.

Methyl 3-pyridazinecarboxylate hydrobromide (0.5 g) was treated with a saturated solution of sodium bicarbonate (2 ml) for 10 min, then extracted with ether (5 x 10 ml), the combined ether layers were dried and evaporated to give a brown solid, *methyl 3-pyridazinecarboxylate* (408) (0.2 g, 45%) (m.p. 130-132 °C) (Found M^+: 138.0429, $C_6H_6O_2N_2$ requires 138.0429) which showed δ_H: 9.4 (1H, dd, J 1.7, 5.0 Hz), 8.24 (1H, dd, J 1.7, 8.4 Hz), 7.7 (1H, dd, J 5.0, 8.4 Hz), 4.1 (3H, s); δ_C: 156.35, 153.1, 151.6, 127.6, 127.0, 53.4; υ_{max}: 1718, 1447, 767 cm^{-1}.

Reactions of 8-bromobicyclo[5.1.0]oct-1-(8)-ene with diazomethane

An excess of diazomethane in ether (10 ml) was added to a stirred solution of 8-bromobicyclo[5.1.0]oct-1(8)-ene[98] in ether (20 ml) at 0 °C. The reaction was allowed to reach temperature and stirred for 2 h, when TLC showed no starting material remained. The solvent and excess of diazomethane were evaporated to give a crude product as a mixture of two components in ratio 1:1 (**417, 418**) which showed δ_H: 4.8 (1H, d, J 19.3 Hz), 4.7 (1H, d, J 19.3 Hz), 4.5 (1H, d, J 19.2 Hz), 4.4 (1H, d, J 19.2 Hz), 2.6 - 1.0 (20H, m), 0.5 (2H, m), which was columned on silica eluting with petrol and ether (5:2) and few drops of triethylamine to give a brown solid, *8,9-diazabicyclo[5.4.0]undeca-7,9,11-triene* (**419**) (0.28 g, 35 %) (m.p. 195-197 °C) (Found M^+: 148.1000, $C_9H_{12}N_2$ requires 148.1000) showed δ_H: 9.4 (1H, d, J 5.3 Hz), 8.3 (1H, d, J 5.3 Hz), 3.56 (2H, m), 3.16 (2H, m), 1.8 (6H, m); δ_C: 166.7, 154.0, 148.3, 133.84, 35.14, 34.0, 31.34, 26.3, 25.4; υ_{max}: 1583, 1534, 1449, 962, 714 cm^{-1}. The second compound decomposed to a complicated mixture on the column.

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APPENDIX I

Table 1. Crystal data, structure solution and refinement for (236b).

Identification code	(236b).
Chemical formula	$C_{14}H_{28}O_2Si_2$
Formula weight	284.54
Temperature	160(2) K
Radiation and wavelength	MoKα, 0.71073 Å
Crystal system, space group	orthorhombic, Pbca
Unit cell dimensions	a = 21.310(3) Å α = 90°
	b = 6.7544(9) Å β = 90°
	c = 24.613(3) Å γ = 90°
Volume	3542.7(8) $Å^3$
Z	8
Density (calculated)	1.067 g/cm^3
Absorption coefficient μ	0.195 mm^{-1}
F(000)	1248
Reflections for cell refinement	8643 (θ range 2.52 to 27.89°)
Crystal colour	colourless
Crystal size	0.60 × 0.34 × 0.24 mm
Data collection method	Siemens SMART CCD diffractometer, ω rotation with narrow frames
θ range for data collection	1.65 to 28.57°
Index ranges	$-28 \leq h \leq 28$, $-8 \leq k \leq 8$, $-14 \leq \ell \leq 31$
Reflections collected	20693
Independent reflections	4219 (R_{int} = 0.0479)
Reflections with I>2σ(I)	3218
Absorption correction	none
Structure solution	direct methods
Refinement method	full-matrix least-squares on F^2
Weighting parameters a, b	0.0413, 1.2428
Data / restraints / parameters	4216 / 0 / 172
Goodness-of-fit on F^2	1.094
Final R indices [I>2σ(I)]	R1 = 0.0406, wR2 = 0.0890
R indices (all data)	R1 = 0.0629, wR2 = 0.1025
Extinction coefficient	0.0004(3)
Largest and mean shift/esd	-0.001 and 0.000
Largest diff. peak and hole	0.310 and -0.238 $eÅ^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacemen parameters ($Å^2$ x 10^3) for (236b). U(eq) is defined as one third of the trace o the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
Si(1)	1217.9(2)	4662.2(7)	4319.8(2)	31.27(13)
Si(2)	1330.3(2)	4361.8(7)	1402.5(2)	27.92(12)
O(1)	257.2(5)	4470(2)	3054.9(5)	34.0(3)
O(2)	551.3(5)	8036(2)	2683.9(6)	39.2(3)
C(1)	489.7(11)	6179(4)	4359.5(9)	60.4(6)
C(2)	1791.2(12)	5505(4)	4841.4(8)	64.2(7)
C(3)	1036.0(11)	2008(3)	4452.9(9)	53.6(6)
C(4)	1610.6(7)	5075(2)	3655.0(6)	25.6(3)
C(5)	1948.8(7)	3476(2)	3328.4(7)	30.3(4)
C(6)	1393.1(7)	4520(2)	3082.8(6)	22.1(3)
C(7)	811.1(7)	3280(2)	3011.9(6)	26.0(3)
C(8)	1520.9(7)	6036(2)	2641.1(6)	23.3(3)
C(9)	2122.1(7)	5945(2)	2331.1(7)	29.5(4)
C(10)	1642.0(8)	5294(2)	2056.0(6)	28.1(3)
C(11)	1218.9(7)	8044(2)	2717.2(7)	27.4(3)
C(12)	569.1(10)	5584(3)	1261.3(9)	51.8(5)
C(13)	1931.5(10)	4963(3)	881.0(8)	50.1(5)
C(14)	1219.2(9)	1631(3)	1430.5(7)	39.0(4)

Table 3. Bond lengths (Å) and angles (°) for (236b).

Si(1)-C(4)	1.859(2)	Si(1)-C(2)	1.861(2)
Si(1)-C(1)	1.862(2)	Si(1)-C(3)	1.863(2)
Si(2)-C(10)	1.851(2)	Si(2)-C(12)	1.853(2)
Si(2)-C(13)	1.858(2)	Si(2)-C(14)	1.861(2)
O(1)-C(7)	1.432(2)	O(2)-C(11)	1.425(2)
C(4)-C(5)	1.527(2)	C(4)-C(6)	1.529(2)
C(5)-C(6)	1.505(2)	C(6)-C(7)	1.507(2)
C(6)-C(8)	1.518(2)	C(8)-C(9)	1.493(2)
C(8)-C(11)	1.513(2)	C(8)-C(10)	1.547(2)
C(9)-C(10)	1.303(2)		
C(4)-Si(1)-C(2)	105.41(9)	C(4)-Si(1)-C(1)	109.81(8)
C(2)-Si(1)-C(1)	110.04(12)	C(4)-Si(1)-C(3)	113.12(9)
C(2)-Si(1)-C(3)	108.04(11)	C(1)-Si(1)-C(3)	110.29(11)
C(10)-Si(2)-C(12)	109.01(8)	C(10)-Si(2)-C(13)	106.17(8)
C(12)-Si(2)-C(13)	112.12(11)	C(10)-Si(2)-C(14)	110.52(8)
C(12)-Si(2)-C(14)	109.71(10)	C(13)-Si(2)-C(14)	109.27(9)
C(5)-C(4)-C(6)	59.00(10)	C(5)-C(4)-Si(1)	124.75(12)
C(6)-C(4)-Si(1)	129.60(11)	C(6)-C(5)-C(4)	60.58(10)
C(5)-C(6)-C(7)	115.72(13)	C(5)-C(6)-C(8)	117.54(13)
C(7)-C(6)-C(8)	116.08(12)	C(5)-C(6)-C(4)	60.42(10)
C(7)-C(6)-C(4)	119.50(13)	C(8)-C(6)-C(4)	116.10(12)
O(1)-C(7)-C(6)	111.00(12)	C(9)-C(8)-C(11)	117.74(13)
C(9)-C(8)-C(6)	119.49(13)	C(11)-C(8)-C(6)	116.09(13)
C(9)-C(8)-C(10)	50.75(10)	C(11)-C(8)-C(10)	118.48(13)
C(6)-C(8)-C(10)	118.56(13)	C(10)-C(9)-C(8)	66.78(11)
C(9)-C(10)-C(8)	62.48(11)	C(9)-C(10)-Si(2)	148.00(13)
C(8)-C(10)-Si(2)	149.28(12)	O(2)-C(11)-C(8)	114.45(13)

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for (236b).

The anisotropic displacement factor exponent takes the form:

$-2\pi^2(h^2a^{*2}U_{11} + \ldots + 2hka^*b^*U_{12})$.

	U(11)	U(22)	U(33)	U(23)	U(13)	U(12)
Si(1)	33.0(3)	35.5(3)	25.3(2)	3.5(2)	-2.5(2)	-4.6(2)
Si(2)	28.0(2)	31.3(2)	24.5(2)	-1.1(2)	-0.4(2)	-1.1(2)
O(1)	18.9(5)	33.4(6)	49.5(7)	-6.8(6)	-3.4(5)	-1.7(5)
O(2)	24.5(6)	31.0(6)	62.1(8)	4.7(6)	-7.1(6)	5.8(5)
C(1)	56.4(14)	72(2)	52.9(13)	8.9(11)	22.3(10)	18.1(12)
C(2)	76(2)	86(2)	30.9(10)	-0.7(11)	-11.4(10)	-29.7(14)
C(3)	68.3(14)	47.6(12)	44.8(11)	16.0(9)	-6.0(10)	-15.0(10)
C(4)	21.9(7)	27.9(8)	27.0(8)	0.4(6)	-3.8(6)	-1.6(6)
C(5)	24.2(8)	31.9(8)	34.7(9)	1.3(7)	-2.7(7)	6.6(7)
C(6)	18.8(7)	22.0(7)	25.6(7)	-1.3(6)	-1.9(5)	2.4(6)
C(7)	25.6(8)	22.4(7)	30.0(8)	-1.9(6)	-1.1(6)	-0.9(6)
C(8)	20.5(7)	24.9(8)	24.5(7)	-1.7(6)	-1.7(6)	-0.4(6)
C(9)	23.2(8)	33.5(9)	31.8(8)	-0.7(7)	2.8(6)	-2.3(6)
C(10)	28.1(8)	29.8(8)	26.2(8)	0.4(6)	2.6(6)	-0.8(6)
C(11)	24.5(8)	25.0(8)	32.7(8)	1.6(6)	-4.1(6)	0.3(6)
C(12)	46.6(12)	52.3(12)	56.3(13)	-12.8(10)	-18.4(10)	14.1(10)
C(13)	56.0(12)	62.8(13)	31.5(10)	0.1(9)	8.2(9)	-18.8(10)
C(14)	44.9(11)	35.9(9)	36.2(9)	-2.9(8)	0.8(8)	-3.4(8)

Table 5. Hydrogen atom coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for (236b).

	x	y	z	U
H(1)	-18(3)	4037(17)	2841(6)	41
H(2)	412.6(7)	6969(13)	2811(7)	47
H(1A)	333(4)	6177(20)	4734(2)	91
H(1B)	171(3)	5617(14)	4118(5)	91
H(1C)	583(2)	7540(7)	4248(6)	91
H(2A)	1606(3)	5362(24)	5203.7(9)	96
H(2B)	1897(6)	6898(8)	4777(4)	96
H(2C)	2173(3)	4699(17)	4818(5)	96
H(3A)	889(7)	1855(4)	4828(2)	80
H(3B)	1415(2)	1211(4)	4399(6)	80
H(3C)	708(5)	1562(7)	4202(4)	80
H(4)	1851.5(7)	6345(2)	3653.6(6)	31
H(5A)	2369.6(7)	3795(2)	3182.2(7)	36
H(5B)	1892.7(7)	2083(2)	3443.2(7)	36
H(7A)	821.0(7)	2630(2)	2651.5(6)	31
H(7B)	801.8(7)	2233(2)	3293.0(6)	31
H(9)	2560.9(7)	6194(2)	2333.0(7)	35
H(11A)	1343.2(7)	8572(2)	3076.7(7)	33
H(11B)	1385.2(7)	8957(2)	2437.2(7)	33
H(12A)	419(4)	5185(18)	901(3)	78
H(12B)	624(2)	7024(3)	1271(6)	78
H(12C)	262(2)	5189(18)	1537(4)	78
H(13A)	1962(5)	6403(3)	840(4)	75
H(13B)	1811(4)	4370(18)	533(2)	75
H(13C)	2339(2)	4434(19)	995(3)	75
H(14A)	1092(6)	1146(4)	1072(2)	59
H(14B)	893(4)	1311(3)	1697(4)	59
H(14C)	1614(2)	998(3)	1538(5)	59

Table 1. Crystal data, structure solution and refinement for (355).

Identification code	(355).
Chemical formula	$C_{12}H_{11}ClO_2$
Formula weight	222.66
Temperature	160(2) K
Radiation and wavelength	MoKα, 0.71073 Å
Crystal system, space group	monoclinic, $P2_1/c$
Unit cell dimensions	a = 14.8887(10) Å α = 90°
	b = 20.4239(13) Å β = 100.743(2)°
	c = 7.1847(5) Å γ = 90°
Volume	2146.5(2) $Å^3$
Z	8
Density (calculated)	1.378 g/cm^3
Absorption coefficient μ	0.331 mm^{-1}
F(000)	928
Reflections for cell refinement	6551 (θ range 2.78 to 28.31°)
Crystal colour	colourless
Crystal size	0.40 × 0.40 × 0.02 mm
Data collection method	Siemens SMART CCD diffractometer, ω rotation with narrow frames
θ range for data collection	1.39 to 28.55°
Index ranges	$-19 \leq h \leq 19$, $-27 \leq k \leq 26$, $-9 \leq \ell \leq 6$
Intensity decay of standards	0%
Reflections collected	13439
Independent reflections	4994 (R_{int} = 0.0369)
Reflections with I>2σ(I)	3362
Absorption correction	none
Structure solution	direct methods
Refinement method	full-matrix least-squares on F^2
Weighting parameters a, b	0.0484, 0.5796
Data / restraints / parameters	4994 / 0 / 274
Goodness-of-fit on F^2	1.020
Final R indices [I>2σ(I)]	R1 = 0.0454, wR2 = 0.0999
R indices (all data)	R1 = 0.0824, wR2 = 0.1133
Extinction coefficient	0.0010(4)
Largest and mean shift/esd	0.001 and 0.000
Largest diff. peak and hole	0.501 and -0.274 $eÅ^{-3}$

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Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacemen parameters ($Å^2$ x 10^3) for (355). U(eq) is defined as one third of the trace o: the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C(1)	4109.1(13)	7203.1(9)	2310(3)	23.1(4)
C(2)	3169.1(14)	6946.5(9)	2244(3)	28.2(5)
C(3)	3981.3(13)	6509.3(9)	2323(3)	23.5(4)
C(4)	4245.6(14)	5890.4(9)	2594(3)	25.2(4)
C(5)	5175.0(14)	5575.0(10)	3038(3)	30.2(5)
C(6)	5842.1(15)	5778.6(11)	1765(3)	33.9(5)
C(7)	5972.3(14)	6488.4(11)	1856(3)	31.0(5)
C(8)	5921.5(14)	7066.5(11)	1991(3)	29.7(5)
C(9)	5611.1(14)	7741.6(10)	2103(3)	29.2(5)
C(10)	4613.3(14)	7738.9(9)	2264(3)	24.4(4)
C(11)	4203.9(15)	8403.7(10)	2342(3)	28.1(5)
C(12)	2895.1(17)	9019.3(10)	2562(3)	40.0(6)
O(1)	4635.6(11)	8900.9(7)	2308(2)	38.4(4)
O(2)	3318.5(10)	8386.5(7)	2463(2)	33.6(4)
Cl(1)	3352.6(4)	5324.9(2)	2622.9(8)	36.76(16)
C(13)	808.1(13)	2802.2(9)	7971(3)	22.9(4)
C(14)	1751.3(14)	3045.0(10)	8670(3)	30.0(5)
C(15)	950.7(13)	3491.6(9)	8110(3)	23.3(4)
C(16)	701.8(14)	4113.7(10)	8154(3)	26.4(4)
C(17)	-221.7(16)	4432.3(10)	7890(3)	36.2(5)
C(18)	-898.8(16)	4242.2(11)	6133(3)	38.9(6)
C(19)	-1037.7(15)	3528.8(11)	6077(3)	32.8(5)
C(20)	-995.6(14)	2949.0(11)	6210(3)	27.9(5)
C(21)	-695.7(14)	2270.9(10)	6565(3)	27.9(5)
C(22)	302.2(14)	2267.5(9)	7505(3)	23.5(4)
C(23)	709.7(16)	1605.5(10)	7886(3)	28.4(5)
C(24)	2046(2)	995.0(11)	9005(4)	48.4(7)
O(3)	275.0(12)	1105.6(7)	7563(2)	39.6(4)
O(4)	1604.2(11)	1623.8(7)	8624(2)	36.9(4)
Cl(2)	1606.9(4)	4668.6(3)	8882.8(8)	36.96(16)

Table 3. Bond lengths (Å) and angles (°) for (355).

C(1)-C(10)	1.331(3)	C(1)-C(3)	1.430(3)
C(1)-C(2)	1.487(3)	C(2)-C(3)	1.496(3)
C(3)-C(4)	1.327(3)	C(4)-C(5)	1.506(3)
C(4)-Cl(1)	1.764(2)	C(5)-C(6)	1.528(3)
C(6)-C(7)	1.462(3)	C(7)-C(8)	1.188(3)
C(8)-C(9)	1.461(3)	C(9)-C(10)	1.512(3)
C(10)-C(11)	1.494(3)	C(11)-O(1)	1.204(2)
C(11)-O(2)	1.337(3)	C(12)-O(2)	1.446(2)
C(13)-C(22)	1.333(3)	C(13)-C(15)	1.425(3)
C(13)-C(14)	1.486(3)	C(14)-C(15)	1.495(3)
C(15)-C(16)	1.326(3)	C(16)-C(17)	1.501(3)
C(16)-Cl(2)	1.764(2)	C(17)-C(18)	1.512(3)
C(18)-C(19)	1.471(3)	C(19)-C(20)	1.189(3)
C(20)-C(21)	1.463(3)	C(21)-C(22)	1.513(3)
C(22)-C(23)	1.486(3)	C(23)-O(3)	1.208(2)
C(23)-O(4)	1.339(3)	C(24)-O(4)	1.446(2)
C(10)-C(1)-C(3)	153.03(19)	C(10)-C(1)-C(2)	145.18(19)
C(3)-C(1)-C(2)	61.66(13)	C(1)-C(2)-C(3)	57.29(13)
C(4)-C(3)-C(1)	155.3(2)	C(4)-C(3)-C(2)	142.13(19)
C(1)-C(3)-C(2)	61.04(13)	C(3)-C(4)-C(5)	132.38(18)
C(3)-C(4)-Cl(1)	114.95(16)	C(5)-C(4)-Cl(1)	112.48(14)
C(4)-C(5)-C(6)	115.54(17)	C(7)-C(6)-C(5)	109.80(17)
C(8)-C(7)-C(6)	168.2(2)	C(7)-C(8)-C(9)	165.4(2)
C(8)-C(9)-C(10)	109.04(17)	C(1)-C(10)-C(11)	120.70(19)
C(1)-C(10)-C(9)	124.89(18)	C(11)-C(10)-C(9)	114.41(17)
O(1)-C(11)-O(2)	124.03(19)	O(1)-C(11)-C(10)	122.9(2)
O(2)-C(11)-C(10)	113.12(17)	C(11)-O(2)-C(12)	115.08(17)
C(22)-C(13)-C(15)	153.7(2)	C(22)-C(13)-C(14)	144.32(19)
C(15)-C(13)-C(14)	61.79(13)	C(13)-C(14)-C(15)	57.10(13)
C(16)-C(15)-C(13)	155.5(2)	C(16)-C(15)-C(14)	142.25(19)
C(13)-C(15)-C(14)	61.11(13)	C(15)-C(16)-C(17)	131.77(19)
C(15)-C(16)-Cl(2)	114.93(16)	C(17)-C(16)-Cl(2)	112.95(14)
C(16)-C(17)-C(18)	116.51(18)	C(19)-C(18)-C(17)	110.20(19)
C(20)-C(19)-C(18)	168.4(2)	C(19)-C(20)-C(21)	165.2(2)
C(20)-C(21)-C(22)	108.94(16)	C(13)-C(22)-C(23)	120.44(19)
C(13)-C(22)-C(21)	124.75(18)	C(23)-C(22)-C(21)	114.81(17)
O(3)-C(23)-O(4)	123.9(2)	O(3)-C(23)-C(22)	123.2(2)
O(4)-C(23)-C(22)	112.91(18)	C(23)-O(4)-C(24)	115.73(18)

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for (355).

The anisotropic displacement factor exponent takes the form:

$-2\pi^2(h^2a^{*2}U_{11} + \ldots + 2hka^*b^*U_{12})$.

	U(11)	U(22)	U(33)	U(23)	U(13)	U(12)
C(1)	26.6(11)	20.6(10)	22.7(10)	-0.6(8)	6.0(8)	1.2(8)
C(2)	27.1(11)	23.4(11)	34.7(12)	-0.6(9)	7.0(9)	-0.5(8)
C(3)	25.1(11)	20.5(10)	25.4(11)	-1.5(8)	6.0(8)	-2.0(8)
C(4)	28.7(11)	18.5(10)	28.6(11)	-0.7(8)	6.3(9)	-4.5(8)
C(5)	35.2(13)	19.6(10)	34.6(12)	1.5(9)	3.7(10)	4.0(9)
C(6)	31.9(12)	31.2(12)	38.8(13)	-2.6(10)	6.9(10)	9.4(9)
C(7)	22.9(11)	37.8(13)	33.6(12)	2.0(10)	8.6(9)	2.0(9)
C(8)	22.3(11)	38.2(13)	30.3(12)	1.1(9)	9.2(9)	-3.3(9)
C(9)	32.8(12)	27.6(11)	27.6(11)	0.2(9)	6.8(9)	-7.3(9)
C(10)	33.3(12)	19.7(10)	19.8(10)	-0.1(8)	4.3(8)	-1.8(8)
C(11)	42.7(13)	19.5(10)	20.2(10)	0.2(8)	1.2(9)	-2.5(9)
C(12)	51.0(16)	21.9(11)	43.8(14)	-4.4(10)	0.1(11)	13.6(10)
O(1)	54.3(11)	18.0(7)	41.3(10)	2.5(7)	4.8(8)	-7.0(7)
O(2)	40.7(10)	17.8(7)	42.1(9)	-3.3(6)	6.9(7)	5.7(6)
Cl(1)	40.3(3)	22.4(3)	47.6(4)	2.7(2)	8.3(3)	-9.7(2)
C(13)	25.3(11)	20.9(10)	23.5(11)	0.1(8)	7.0(8)	1.4(8)
C(14)	25.0(11)	23.7(11)	40.9(13)	-0.5(9)	4.8(9)	-0.1(8)
C(15)	23.8(11)	19.3(10)	26.9(11)	-0.6(8)	4.6(8)	-2.7(8)
C(16)	29.7(12)	20.9(10)	29.0(11)	-1.8(8)	6.6(9)	-4.7(8)
C(17)	40.6(14)	20.8(11)	46.3(14)	-3.3(10)	6.1(11)	5.3(9)
C(18)	39.0(14)	29.1(12)	46.1(15)	-1.4(10)	1.4(11)	9.4(10)
C(19)	24.9(12)	35.6(13)	36.0(13)	-6.4(10)	0.7(9)	1.4(9)
C(20)	19.8(11)	36.5(12)	26.7(11)	-4.2(9)	2.7(8)	-4.0(9)
C(21)	33.8(12)	24.7(11)	26.2(11)	-3.2(8)	8.6(9)	-8.8(9)
C(22)	32.8(12)	19.0(10)	20.5(10)	0.5(8)	9.3(8)	-1.9(8)
C(23)	45.2(14)	20.2(10)	21.7(11)	-0.5(8)	11.2(9)	-0.8(9)
C(24)	69.4(19)	27.5(13)	46.4(16)	3.9(11)	5.7(13)	22.4(12)
O(3)	61.3(11)	17.7(7)	42.0(10)	-2.8(7)	15.5(8)	-5.8(7)
O(4)	45.1(10)	20.1(7)	43.0(10)	2.9(7)	1.7(8)	8.9(7)
Cl(2)	40.0(3)	23.0(3)	48.1(4)	-6.9(2)	8.8(3)	-11.2(2)

Table 5. Hydrogen atom coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for (355).

	x	y	z	U
H(2A)	2729	6978	1032	34
H(2B)	2899	6987	3398	34
H(5A)	5095	5094	2949	36
H(5B)	5454	5679	4366	36
H(6A)	6436	5556	2184	41
H(6B)	5599	5645	443	41
H(9A)	5692	7986	955	35
H(9B)	5977	7961	3221	35
H(12A)	3202	9251	3698	60
H(12B)	2248	8960	2621	60
H(12C)	2948	9275	1434	60
H(14A)	2199	3011	7813	36
H(14B)	2010	2997	10035	36
H(17A)	-134	4913	7872	43
H(17B)	-496	4329	9009	43
H(18A)	-1489	4465	6132	47
H(18B)	-667	4384	4991	47
H(21A)	-778	2027	5354	33
H(21B)	-1067	2055	7397	33
H(24A)	2704	1060	9445	73
H(24B)	1946	732	7843	73
H(24C)	1789	767	9985	73