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Dissertation for the degree Doctor Scientiarum

A study of ring-opening reactions of some di- and trihalogenated cyclopropanes

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I would like to thank my supervisor Professor Leiv K. Sydnes for encouragement, fruitful discussions and valuable input, through my four years as a research fellow at the Department of Chemistry, University of Bergen.

I wish to express my sincerest thanks to Professor Doctor Udo H. Brinker for giving me the opportunity to do research in beautiful historical surroundings at the Department of Chemistry, University of Vienna. The stay in his carbene group was both professionally and socially very rewarding.

Thanks to all the friends and colleagues at the Department of Chemistry and elsewhere at the University of Bergen, and especially the research fellows in Professor Sydnes' group.

I am grateful for all the support from the technical staff at the Department of Chemistry with various instruments, software and problems. Special thanks to Ann Margot Whyatt and Dag Ekeberg for recording all the mass spectra.

Last, but not least, I want to offer my heartfelt gratitude and appreciation to my wife Felicia for her love and patience through the last years, and to my family for their love and support.

Foreword

The work which is presented was carried out under the supervision of Professor Leiv K. Sydnes at the Department of Chemistry, University of Bergen (UoB) between 2001 and 2005. Three months, during the summer of 2005, were spent under the supervision of Professor Doctor Udo H. Brinker at the Department of Chemistry, University of Vienna.

The first nine months as a research fellow was spent on a completely different project than the one presented in this dissertation. The project was a study of a new marine toxin and was carried out in collaboration with the Department of Biology and the Section of Anatomy and Cell Biology, UoB. Incubation of extracts from a new alga induced apoptosis in different cell types. A quest for the active component was initiated, but difficulties with growth of the alga and isolation of the toxin caused a change of project.

The dissertation is divided into five main chapters: At first, a short introduction of halogenated cyclopropanes is given. Secondly, the results of the studies are discussed in three main chapters, covering three specific subjects. Finally, the experimental results are gathered in the last chapter. A fold-out page with an overview of most of the compounds with numbering is attached to the back cover of the thesis.

Recordings of mass spectra were performed by Ann Margot Whyatt at the Department of Chemistry, UoB. Spectra for some compounds were not recorded due to problems with the instrument and limited stability of the products. When the stability of the compounds so permitted mass spectral analyses were done by Dag Ekeberg at the Norwegian University of Life Sciences at Ås.

Abstract

Ring-opening reactions of halogenated cyclopropanes under different conditions were studied. The studies can be divided into three groups:

1) The base-induced ring opening of 2-alkyl-1,1,2-tribromocyclopropanes, with sodium hydroxide and ethanol under phase-transfer conditions with TEBA as the catalyst, gave mixtures of acetylenic diethyl acetals and acetylenic diethyl ketals. The formation of acetal and ketal was sensitive to the steric bulk of the alkyl substituent; thus, when the steric crowding increased acetal formation dominated, and when 1,1,2-tribromo-2-*tert*-butylcyclopropane was ring opened the acetal 1,1-diethoxy-4,4-dimethylpent-2-yne was formed as the only product.

2) Metal-halogen exchange in 2-substituted 1,1,2-tribromocyclopropanes, promoted by addition of methyllithium at -78 ºC, provides the corresponding 1-bromocyclopropenes through a 1,2-debromination. Due to limited stability some of the 1-bromocyclopropenes undergo ring-opening reactions involving rearrangement to give complex product mixtures with brominated acetylenes and allenes as the major products. However, when the 1-bromocyclopropenes were reacted with different cyclic dienes [4+2]-cycloadduct formation was achieved. Cycloaddition with 1,3-diphenylisobenzofuran (DPIBF) gave the corresponding *exo* cycloadducts, in most cases in excellent yield, whereas cyclopentadiene afforded *endo* cycloadducts only, but in moderate yield. In most reactions with furan no cycloadduct was formed, but three 1-bromocyclopropene derivatives with an aromatic side chain were exceptions to this rule and furnished mixtures of *exo* and *endo* cycloadducts in moderate yields.

3) Thermal ring opening of 1,1-dihalo-2-R-2-halomethylcyclopropanes in hot quinoline gave unpredicted halogenated 1,3-butadienes arisen from a formal elimination of Br_2 and/or BrCl, which has not yet been described in the literature. A more common reaction pathway would be elimination of HX or nucleophilic substitution of the expelled halide ion, but no products whatsoever originating from these routes were observed. Thermal ring opening in the gas phase gave slightly higher yields of halogenated 1,3-butadienes, and in addition ring-opening products formed by elimination of HX were observed.

Abbreviations

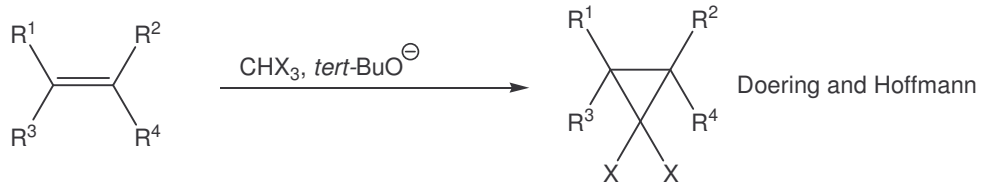
^{13}C	Carbon-13 nucleus
^{1}H	Hydrogen-1 nucleus
AIBN	*α*,*α*'-Azobisisobutyronitrile
ATR	Attenuated total reflection
BTH	Tributylstannane (tributyltin hydride)
Cetrimide	Hexadecyltrimethylammonium chloride
COSY	Correlation spectroscopy
DEPT	Distortionless enhancement by polarisation transfer
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethylsulfoxide
FID	Flame ionisation detection (GC chromatograph)
FID	Free induction decay (NMR spectroscopy)
FT	Fourier-transformation
FTIR	Fourier-transform infrared
FVP	Flash vacuum pyrolysis
GC	Gas chromatography
GC-MS	Gas chromatography-Mass spectroscopy
HCl	Hydrochloric acid
HMBC	Heteronuclear multiple bond correlation
HOMO	Highest occupied molecular orbital
HPLC	High performance liquid chromatography
HSQC	Heteronuclear single quantum coherence
IR	Infrared
LAH	Lithium aluminium hydride
Lit.	Literature
LUMO	Lowest unoccupied molecular orbital
MS	Mass spectroscopy
Mp.	Melting point
NMR	Nuclear magnetic resonance
NOESY	Nuclear Overhauser enhancement spectroscopy
PTAD	*N*-Phenyl-1,2,4-triazoline-3,5-dione
Ppm	Parts per million
PTC	Phase-transfer conditions/catalysis
R_f	Retention factor
Rt	Room temperature
SEFT	Spin-echo fourier transform
SOI	Secondary orbital interactions
TEBA	Triethylbenzylammonium chloride
THF	Tetrahydrofuran
TIC	Total ion chromatogram (GC-MS)
TLC	Thin-layer chromatography
TMS	Tetramethylsilane

Contents

1 Introduction

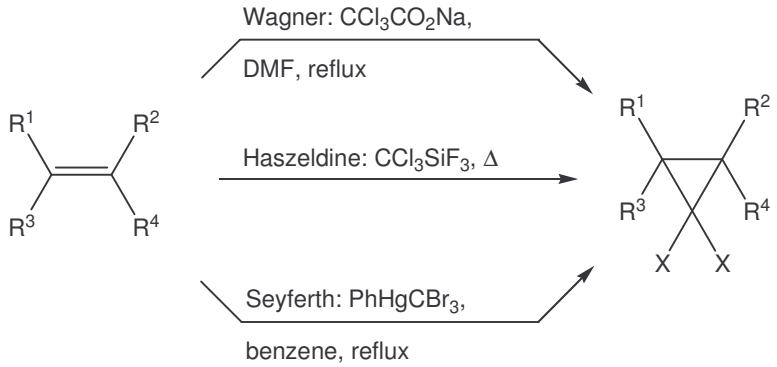
1.1 Synthesis of halogenated cyclopropanes

gem-Dihalocyclopropanes have been readily available through dihalocarbene addition to appropriate alkenes ever since the classical paper of Doering and Hoffmann was published in 1954.[1] In this procedure the dihalocarbene is generated from haloform by α-elimination promoted by *tert*-butoxide under strictly non-aqueous conditions (Scheme 1.1).



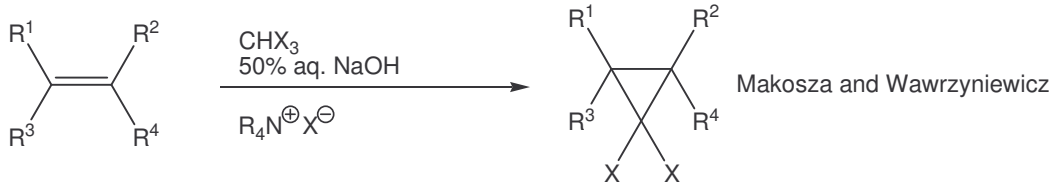
Scheme 1.1

Later, a variety of other methods have been developed for the preparation of such compounds,[2-7] but, irrespective of the method employed the products are formed by addition of a divalent carbon intermediate to a double bond. In many procedures the cyclopropanation takes place under basic conditions, but the methods of Wagner,[2] Haszeldine,[8] and Seyferth[4] involve essentially neutral conditions (Scheme 1.2).



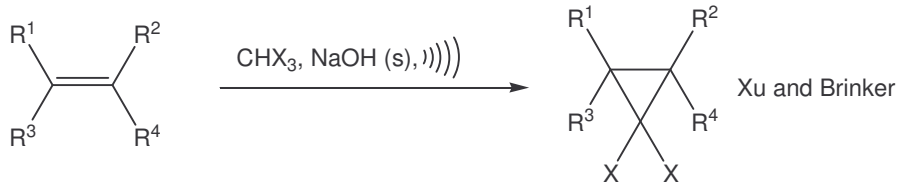
Scheme 1.2

Furthermore, non-aqueous conditions are a necessity in every method except one, namely the Makosza procedure where the cyclopropanation takes place under phase-transfer conditions (PTC) by vigorously stirring a mixture of haloform, olefin, and an excess of 50% aqueous sodium hydroxide in the presence of catalytic amounts of a tetraalkylammonium salt (Scheme 1.3).[9] This method made *gem*-dihalocyclopropanes conveniently available on a large scale.



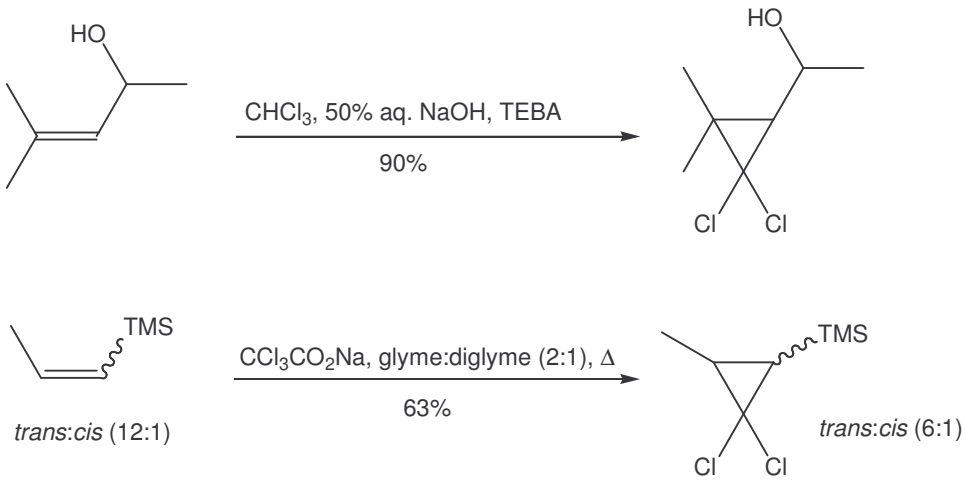
Scheme 1.3

Finally, in most cases it is necessary to stir, especially in the Makosza procedure where vigorous mechanical stirring is essential for achieving high yields. But in the recent Xu-Brinker procedure, cyclopropanation is accomplished without any stirring at all by utilising ultrasound irradiation to generate the dihalocarbene (Scheme 1.4).[10]



Scheme 1.4

With the use of the procedures mentioned above dihalocarbene has successfully been added to alkenes with many different functional groups in close proximity to the double bond (Scheme 1.5). Some examples are olefinic alcohols,[11-13] ethers,[14,15] nitriles,[16] halides,[17,18] ketones,[19,20] carboxylic groups and silyl ethers.[19,21-23]

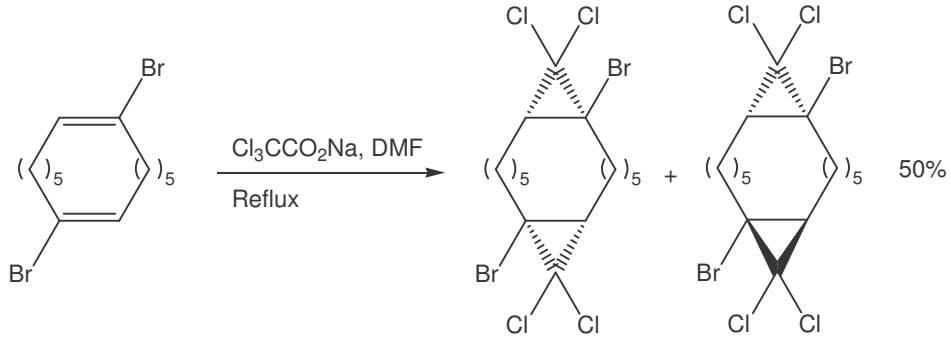


Scheme 1.5

Since the thesis concerns the study of 1,1,2-trihalocyclopropanes, the addition of dihalocarbene to vinyl halides is of particular interest. Despite the lowered reactivity reported

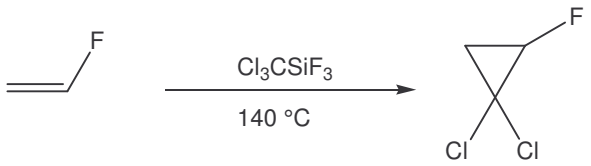
for dihalocarbene towards these electron-poor alkenes,[24] the Makosza procedure has precedence in the literature using primarily TEBA,[9,25,26] Cetrimide,[27-29] or tetrabutylammonium bromide[30] as the phase-transfer catalyst.

Other methods can also be used in the synthesis of 1,1,2-trihalocyclopropanes. Gleiter *et al.* preferred the non-basic Wagner procedure, generating the dichlorocarbene from sodium 2,2,2-trichloroacetate by reflux in DMF,[2] in the preparation of *syn*- and *anti*-dibromotetrachlorotricyclohexadecane from 1,8-dibromocyclotetradecadiene (Scheme 1.6).[31]



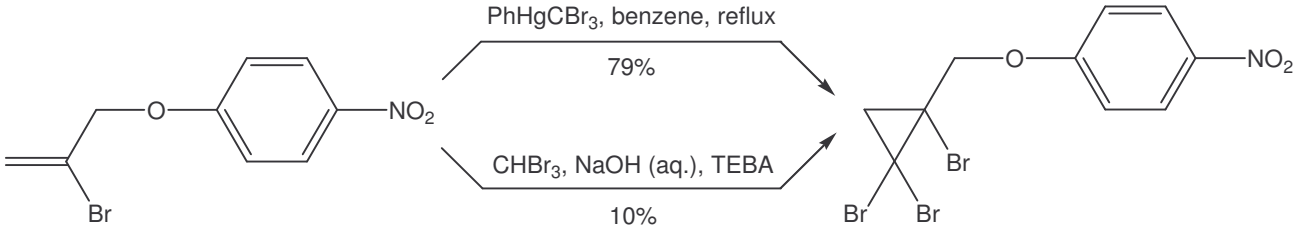
Scheme 1.6

The Haszeldine procedure[8] gave almost quantitative yields of 1,1-dichloro-2-fluorocyclopropane, when dichlorocarbene produced by thermolysis of trichloromethyltrifluorosilane was reacted with fluoroethene (Scheme 1.7).[32] However, the high temperature required makes the method somewhat unattractive, because thermal decomposition of the cyclopropanes may occur.



Scheme 1.7

When cyclopropanation under Makosza conditions gives unsatisfactory results, the Seyferth procedure[4] for generating dihalocarbene may be a good alternative. Thus, 1,1,2-tribromo-2-(4-nitrophenoxy)methylcyclopropane was obtained in only 10% under PTC, whereas thermal decomposition of phenyl(tribromomethyl)mercury in the presence of 2-bromo-3-(4-nitrophenoxy)propene gave high yield of the trihalide (Scheme 1.8).[26]

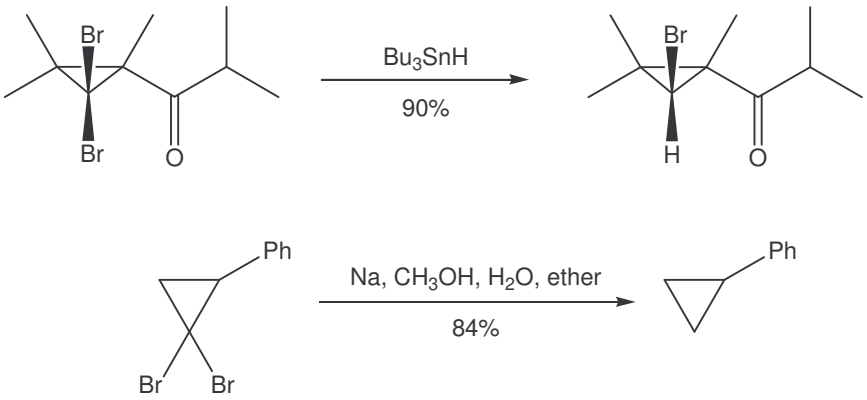


Scheme 1.8

1.2 Transformations involving *gem*-dihalocyclopropanes

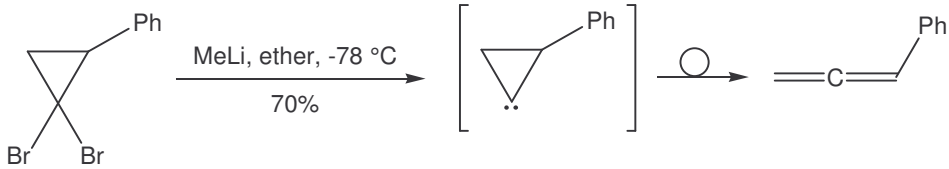
gem-Dihalocyclopropanes may undergo numerous transformations when treated with appropriate reagents.[33] These transformations may proceed with the conservation of the cyclopropane ring or with a simultaneous ring opening.

Reductive dehalogenation are most often accomplished with tributyltin hydride,[34,35] lithium aluminium hydride,[36] sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al®),[37] or alkali metals (Scheme 1.9).[38]



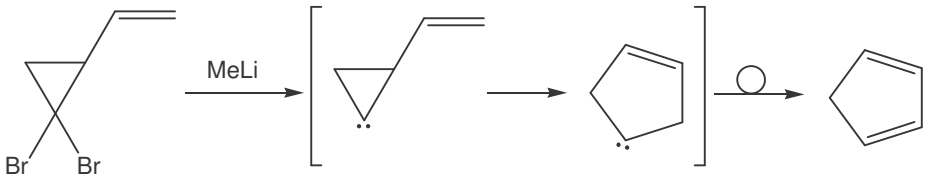
Scheme 1.9

When treated with alkyllithium reagents some *gem*-dihalocyclopropanes undergo metal-halogen exchange and form intermediate cyclopropylidenes, which can rearrange to the corresponding allene (Scheme 1.10).[39]



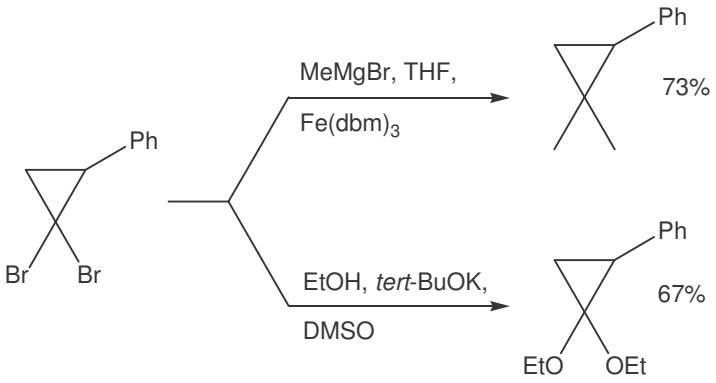
Scheme 1.10

The rearrangement of these cyclopropylidenes depends significantly on the substituents. Thus, when a double bond is directly connected to the cyclopropane ring a Skattebøl rearrangement to the corresponding cyclopentadiene may take place (Scheme 1.11).[40]



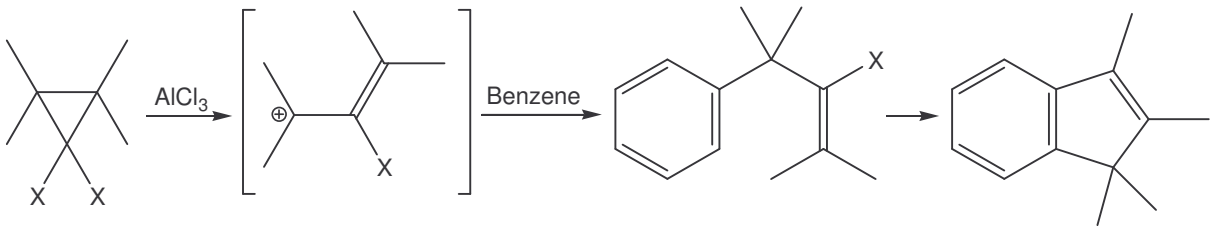
Scheme 1.11

Nucleophilic substitution of both bromo substituents has been achieved in 1,1-dibromo-2-phenylcyclopropane with a Grignard reagent and ethanol under basic conditions (Scheme 1.12).[41,42]



Scheme 1.12

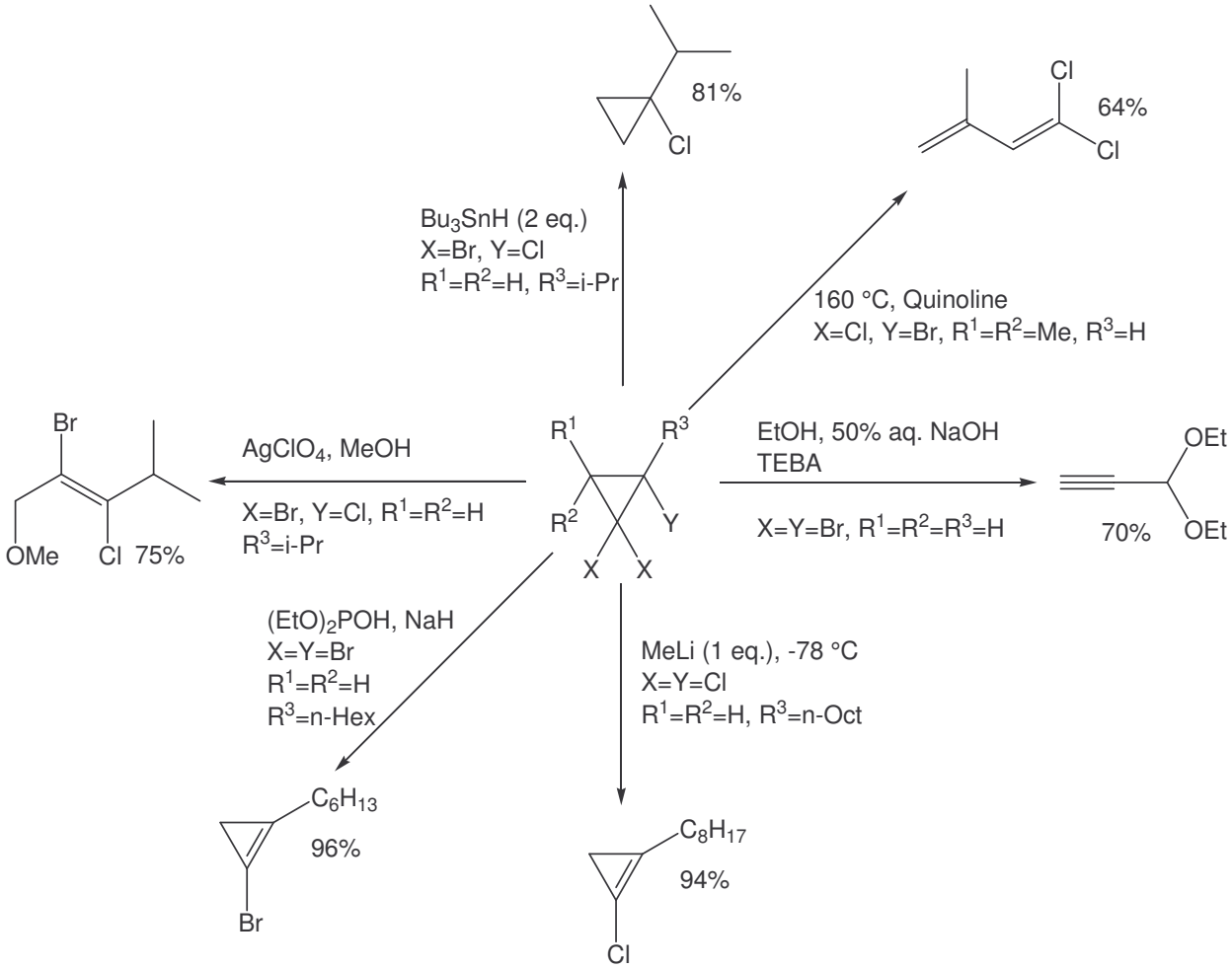
In the presence of Lewis acids *gem*-dihalocyclopropanes may undergo ring opening to the haloallyl cation, which in the presence of aromatic solvents reacts in an electrophilic aromatic substitution as outlined in Scheme 1.13. When benzene is used as solvent the final products are substituted indenes.[43]



Scheme 1.13

1.3 Reactions of 1,1,2-trihalocyclopropanes

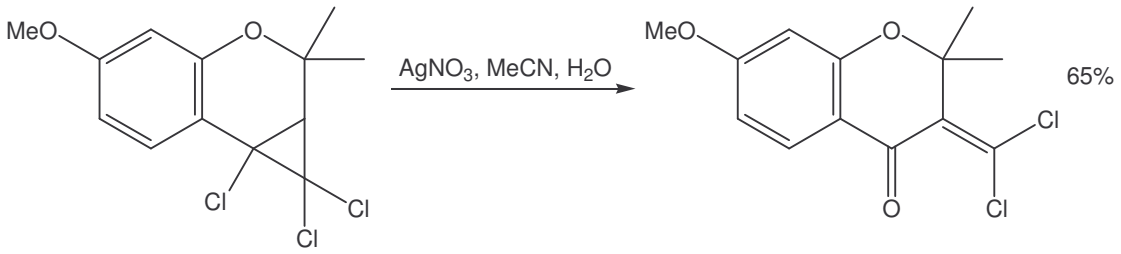
As previously described the chemistry of *gem*-dihalocyclopropanes have been extensively studied, and their usefulness as synthetic intermediates are well established.[33] But 1,1,2-trihalocyclopropanes have attracted much less attention as synthetic synthons, despite the fact that these compounds may undergo a range of valuable transformations.



Scheme 1.14

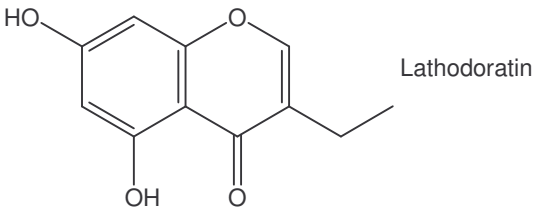
As outlined in Scheme 1.14 the transformations include reductions,[44] 1,2-dehalogenations,[45] different metal-halogen exchanges,[46,47] and several ring-opening reactions which may be induced by heat,[48] bases,[17] or silver salts.[49,50]

Many of these reactions have been used in the preparation of natural products. Silver-assisted ring opening of 1,1,2-trihalocyclopropanes proceeds via the allylic carbocation and has been used in the syntheses of substituted chromanones,[51,52] which are related to a family of phytoalexins with anti-fungal activity (Scheme 1.15).[53]

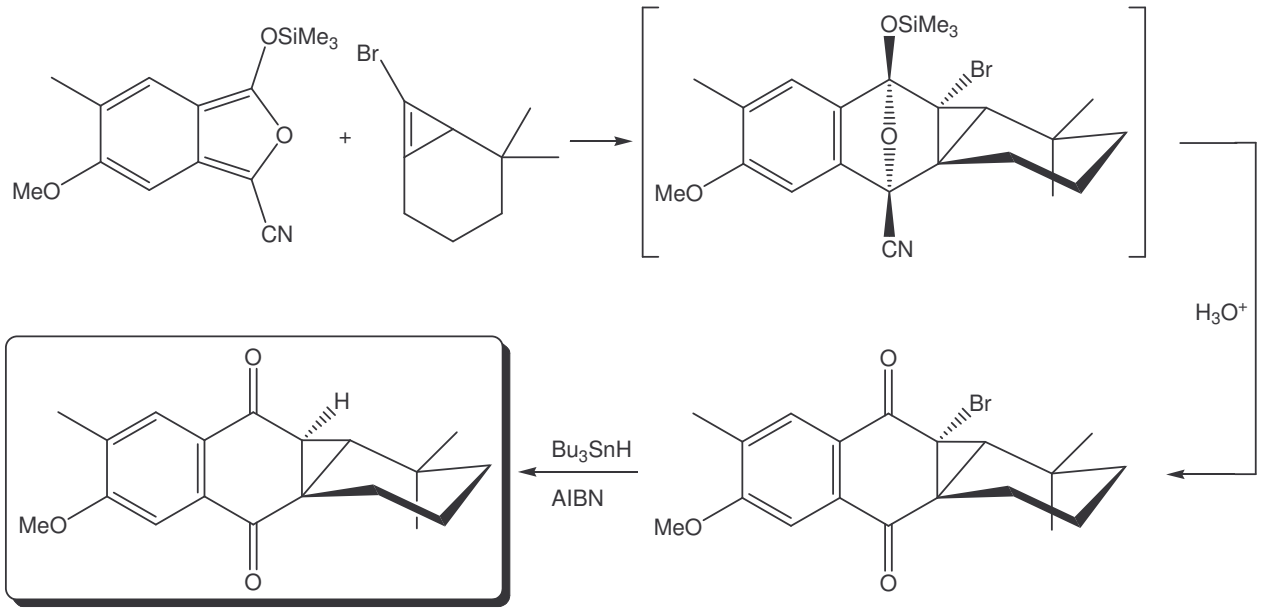


Scheme 1.15

Phytoalexins produced in plants act as toxins toward attacking organism and the sweet pea (*Lathyrus odoratus*) releases lathodoratin as part of the induced resistance (Scheme 1.16).



Scheme 1.16

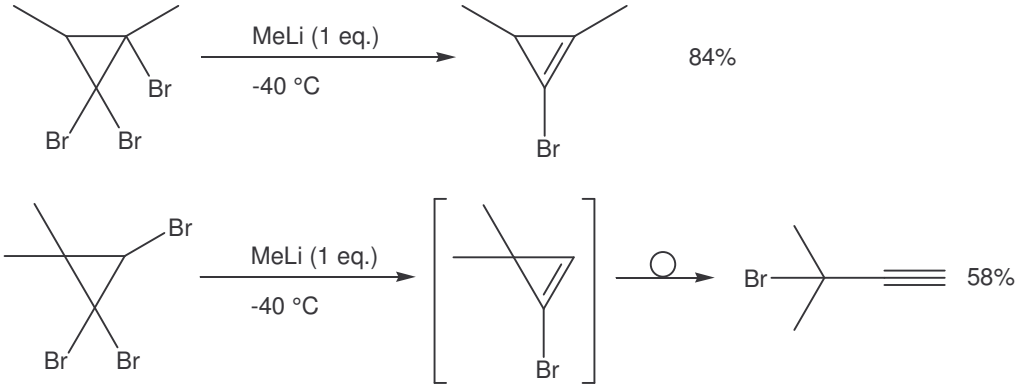


Scheme 1.17

Substituted 1-bromocyclopropenes have been used as dienophiles in Diels-Alder reactions, and an important application of this reaction was found in the total synthesis of favelanone isolated from the Brazilian plant favela (*Cnidoscolus phyllacanthus*),[54] where the

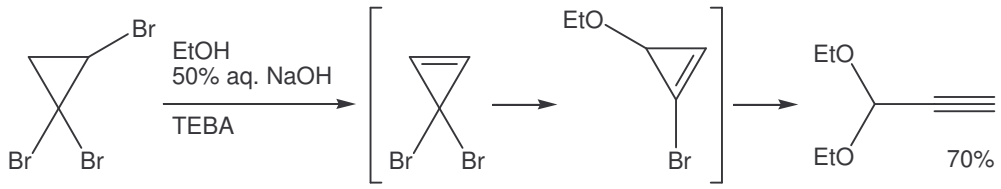
[4+2]-cycloaddition between a bicyclic cyclopropene and a cyclic diene is a key step (Scheme 1.17).[55]

1,1,2-Trihalocyclopropanes are excellent starting materials for the syntheses of 1-halocyclopropenes. The transformation is carried out by treating the trihalides with an alkyllithium reagent, which leads to a 1,2-dehalogenation via a metal-halogen exchange. The course of this reaction depends primarily on the substituents on the cyclopropane ring. Thus, when 1,1,2-tribromo-2,3-dimethylcyclopropane was treated with one equivalent methyl-lithium at -40 ºC only 1-bromo-2,3-dimethylcycloprop-1-ene was obtained,[56] while 1,1,2-tribromo-3,3-dimethylcyclopropane was converted to 3-bromo-3-methylbut-1-yne under the same conditions (Scheme 1.18).[47]



Scheme 1.18

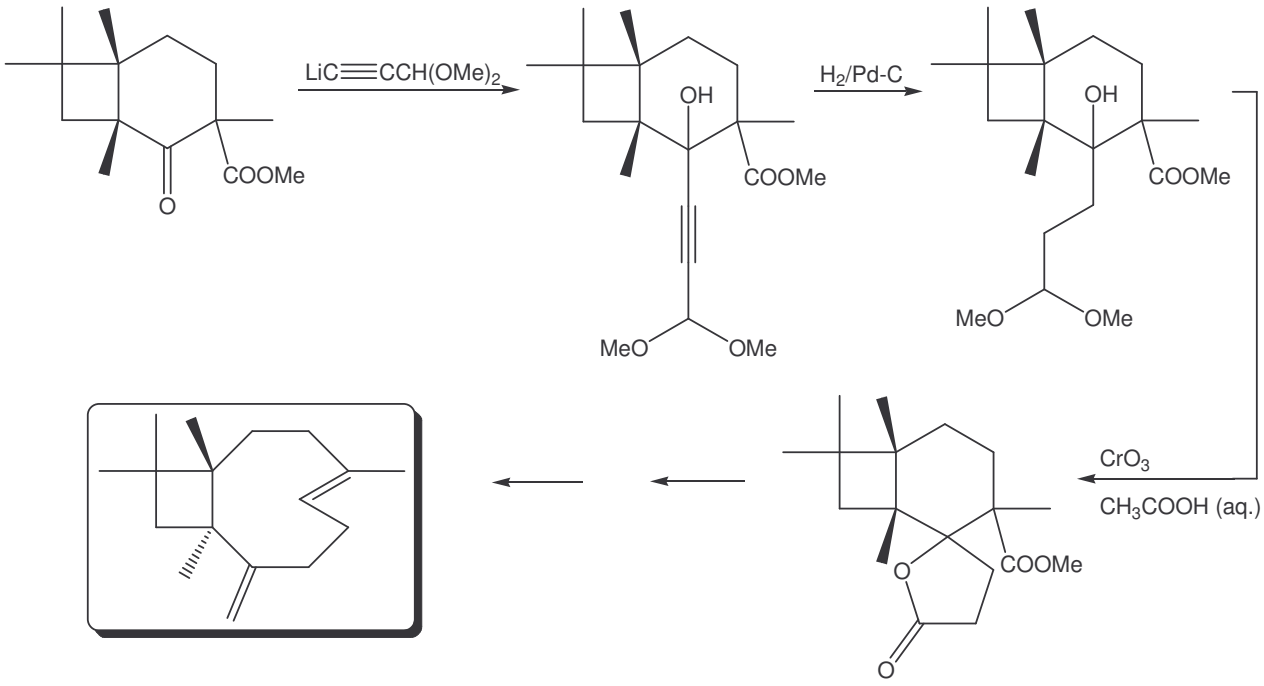
Sydnes and co-workers have recently shown that 1,1,2-trihalocyclopropanes containing at least one cyclopropyl hydrogen atom are capable of forming acetylene derivatives.[57] When treated with ethanol under basic PTC conditions 1,1,2-tribromocyclopropane underwent β-elimination and two consecutive nucleophilic attacks of ethanol, causing a ring opening of the cyclopropane and isolation of 70% of 3,3-diethoxyprop-1-yne (Scheme 1.19).[17]



Scheme 1.19

This acetylenic diethyl acetal is a highly functionalised molecule and can undergo many potential transformations: Deprotonation of the terminal triple bond and subsequent treatment of the acetylide with different aldehydes or ketones will lead to chain elongation and formation of propargylic alcohols. The triple bond may be partly hydrogenated to the corresponding alkene or completely to the alkane. The aldehyde can be deprotected and further oxidised to the carboxylic acid or reduced to the propargylic alcohol.

A complete application of the functionalities in a similar acetylenic acetal can be seen in Corey's total synthesis of the sesquiterpene *d*,*l*-caryophyllene (Scheme 1.20).[58]



Scheme 1.20

1.4 Purpose of the study

As the brief introduction illustrates many important transformations of halogenated cyclopropanes involve ring-opening reactions. The course of some of these reactions has appeared to be sensitive to the substituents attached to the ring. It was therefore decided to study the substituents' influence on the reactivity and outcome of three different ring-opening reactions, *viz.* ethoxide-induced ring opening, methyllithium-induced ring opening, and thermal ring opening of trihalogenated cyclopropanes:

1) Ring opening of 2-alkyl-1,1,2-tribromocyclopropanes with ethanol, 50% aqueous sodium hydroxide and TEBA furnishes mixtures of the acetylenic diethyl acetal and acetylenic diethyl

ketal.[57] The ring opening is believed to occur through the initial formation of 1-alkyl-3,3-dibromocyclopropene, which is attacked by ethanol at C-1 or C-2 to give the ketal or acetal respectively. Hence, the course of the reaction supposedly depends on the nature of the substituent attached to C-2; and the hydrogen-bonding ability of this substituent has been proved to affect the ratio of acetal and ketal.[26] It was therefore decided to examine the ring opening of trihalides containing alkyl substituents with different steric bulk, to see how the acetal/ketal distribution is influenced by steric interactions.

2) Treatment of 1,1,2-tribromocyclopropanes with methyllithium at -78 ºC results in 1,2-debromination and formation of the corresponding 1-bromocyclopropenes, which in a couple of cases have suffered ring opening to yield brominated acetylenes in good yields.[47] As reported in this thesis it appeared that most of the 2-substituted 1,1,2-tribromocyclopropanes gave complex mixtures with brominated acetylenes and allenes as the major products. It was therefore decided to refocus and study the trapping of the intermediate 1-bromocyclopropenes with different cyclic conjugated dienes. By doing so it was possible to examine the reactivity of the cyclopropenes as dienophiles in these [4+2]-cycloadditions, with a special emphasis on stereochemical aspects.

3) Thermal ring opening of halogenated cyclopropanes are known to proceed by a disrotatory cyclopropyl-allyl rearrangement. The expelled counter-anion can either function as a base or a nucleophile. Hence, elimination of a proton in the intermediate haloallyl cation produces substituted 1,3-dienes, while substitution gives the allylic halide. A variety of substituted cyclopropanes with one or two halogen atoms attached to the ring have been studied,[48,59-61] but few compounds with halogens connected to both the ring and a ring substituent have been investigated. It was therefore decided to examine the thermal ring opening of 1,1-dihalo-2-R-2-halomethylcyclopropanes. In order to study the effect of the temperature on the product distribution ring opening was performed in both hot quinoline and the gas phase.

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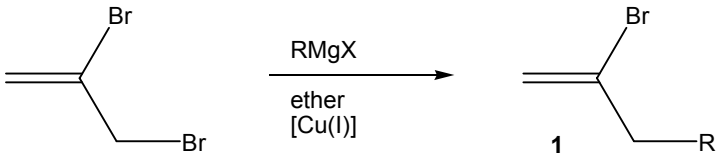
2 Base-induced ring opening of trihalogenated cyclopropanes

2.1 Synthesis of 2-bromo-1-alkenes

2-Bromo-1-alkenes (**1**) were used as starting materials for the synthesis of 2-alkyl-1,1,2-tribromocyclopropanes (**2**) used in the study of base-induced ring-opening reactions under PTC. In most cases **1** was prepared from 2,3-dibromopropene, which suffered nucleophilic substitution when treated with the appropriate Grignard reagents (Scheme 2.1). The Grignard reagents were synthesised from an alkyl bromide or an alkyl chloride, dried magnesium turnings, and a few crystals of iodine in ether under nitrogen atmosphere. The halides were added slowly to the ethereal solution, maintaining a gentle reflux, to avoid high concentrations of alkyl halides which may lead to the formation of unwanted by-products.[1,2]



Scheme 2.1

The yields of **1** were moderate, ranging from 42 to 61% due to the formation of fair amounts of Wurtz-coupling products (Table 2.1). However, since the Wurtz-coupling products were easily removed by fractional distillation the method was efficient for our purpose.

Table 2.1 Preparation of **1** from 2,3-dibromopropene with Grignard reagents.

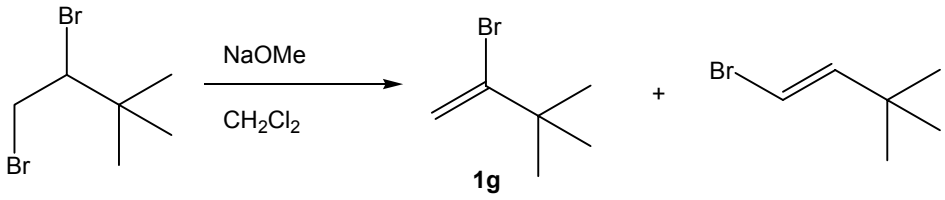
Entry	R		Isolated yields (%)	
			Product	Wurtz-coupling product
1	Ethyl	**1a**	46	0
2	Butyl	**1b**	53	0[a]
3	Heptyl	**1c**	42	23
4	Benzyl	**1d**	61	21
5	Cyclohexyl	**1e**	56[b]	8[c]
6	*i*-Propyl	**1f**	46	0

[a] Traces of octane was seen in the ^{1}H NMR spectrum of the crude product.
[b] Obtained with CuCN as a catalyst.
[c] Determined by GC analysis.

Lespieau and Bourguel achieved a 64% yield of 2-bromo-3-cyclohexylprop-1-ene (**1e**), which we never reproduced, in the synthesis between cyclohexylmagnesium bromide and 2,3-dibromopropene.[3] It was therefore decided to perform some of the Grignard reactions in the

presence of copper(I) cyanide, a salt which is known to catalyze such reactions.[4,5] Significant improvements in the yields were observed in one case only, *viz.* the preparation of **1e** which was formed in 56% with a catalytic amount of copper(I) cyanide and only 23% in the absence of the catalyst.

2-Bromo-3,3-dimethylbut-1-ene (**1g**), on the other hand, was prepared from 3,3-dimethylbut-1-ene as outlined in Scheme 2.2, following a procedure by Miller and McGarvey.[6] A structural isomer, (*E*)-1-bromo-3,3-dimethylbut-1-ene, was formed concomitantly (the isomeric ratio was 76:24, with **1g** being the major isomer) and appeared to be so difficult to remove without significant loss of the desired product that the following cyclopropanation was carried out with the mixture (*vide infra*).



Scheme 2.2

The two vinylic protons in **1g** appear as two doublets at 5.38 ppm and 5.59 ppm, coupled to each other with a *geminal* coupling constant ($^2J_{H,H}$) of 2.1 Hz in the ^{1}H NMR spectrum of the mixture (Figure 2.1).

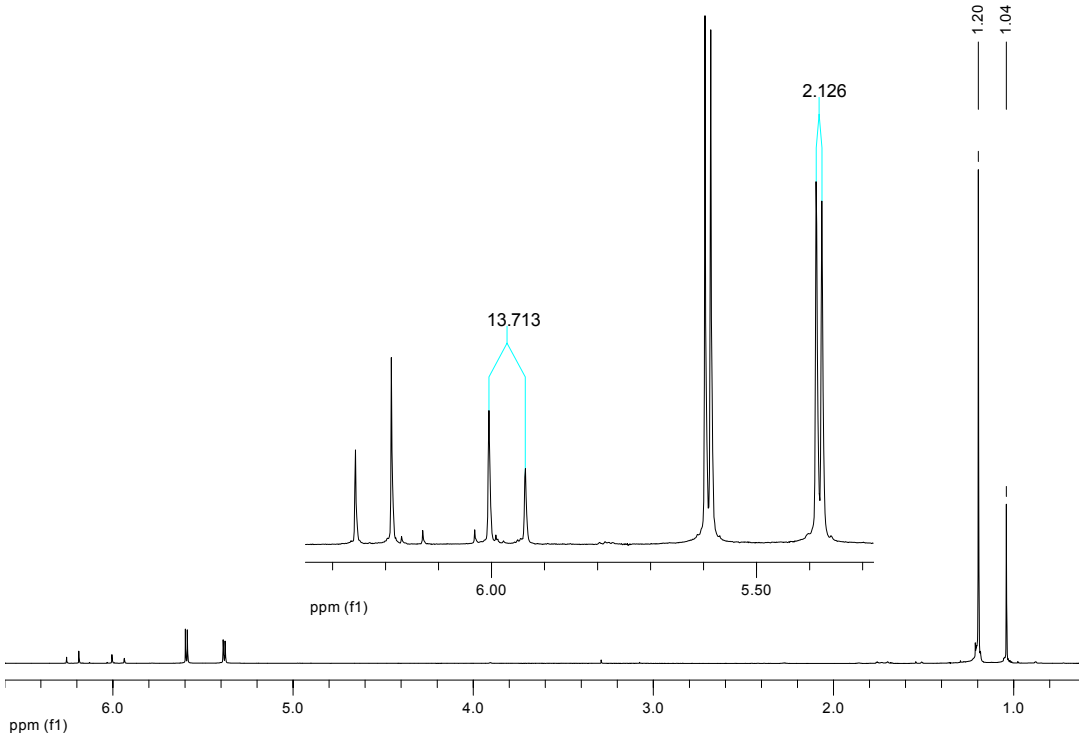


Figure 2.1 ^{1}H NMR spectrum of the mixture of 2-bromo-3,3-dimethylbut-1-ene (**1g**) and (*E*)-1-bromo-3,3-dimethylbut-1-ene.

Geminal coupling constants are known to be strongly dependent upon the angle of interaction of the two nuclei involved (Figure 2.2). When the angle increases to above 110° the magnitude of the coupling constant drops below 10 Hz. In the sp^2-hybridised carbon of **1g** the H-C-H angle is close to 120° and the *geminal* coupling constant is at a minimum.

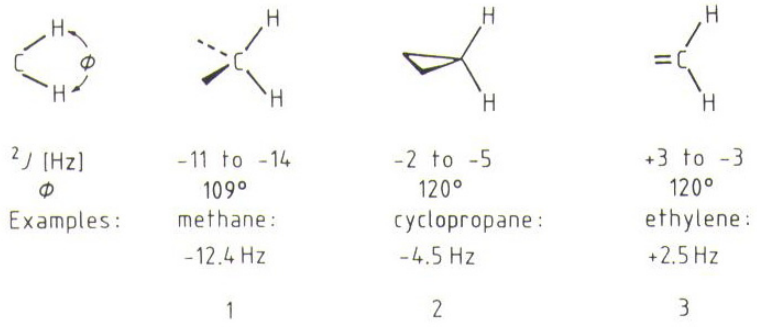


Figure 2.2 The magnitude of the *geminal* coupling constant depends on the H-C-H angle (Φ).

In alkenes the *vicinal* coupling constant ($^3J_{H,H}$) between *cis* proton pairs is smaller than the corresponding constant between *trans* proton pairs. Both types of couplings are greatly affected by substituents, and become smaller as the electronegativities of the substituents increase (Figure 2.3, Table 2.2).[7]

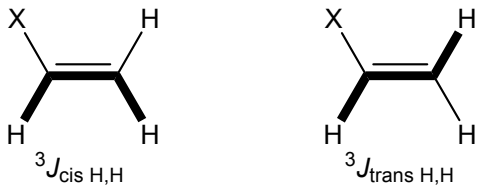


Figure 2.3 Illustration of the possible *vicinal* coupling constant ($^3J_{H,H}$) in alkenes.

Table 2.2 *Vicinal* coupling constants in monosubstituted ethylenes.[7]

Entry	X	$^3J_{cis\ H,H}$ (Hz)	$^3J_{trans\ H,H}$ (Hz)	E_x[a]
1	Li	19.3	23.9	1.0
2	H	11.6	19.1	2.2
3	Cl	7.3	14.6	3.0
4	OMe	7.1	15.2	3.5
5	F	4.7	12.8	4.0

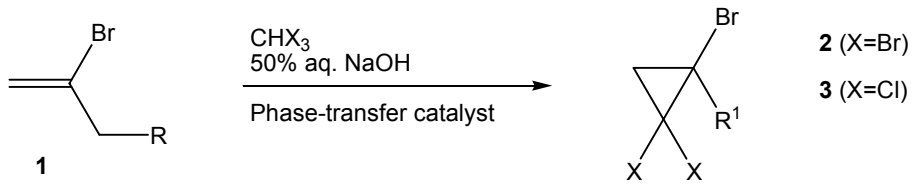
[a] Electronegativities according to Pauling.

The two vinylic protons in (*E*)-1-bromo-3,3-dimethylbut-1-ene give rise to two doublets at 5.97 ppm and 6.22 ppm coupled with a *vicinal* coupling constant of 13.7 Hz (Figure 2.1).

These protons have a *trans* relationship, so the observed magnitude of the *vicinal* coupling constant is in accordance with the literature (Table 2.2; entry 3).

2.2 Synthesis of 2-alkyl-1,1,2-trihalocyclopropanes

As briefly mentioned before, the 2-bromoalkenes (**1**) were converted to the corresponding 1,1,2-trihalocyclopropanes (**2** and **3**) under PTC, with either triethylbenzylammonium chloride (TEBA) or hexadecyltrimethylammonium chloride (Cetrimide) as a catalyst (Scheme 2.3). The best yields were obtained when no solvent as used and the ratio of **1**, NaOH and haloform was 1:3:8 respectively. The haloform was easily recycled by distillation.



Scheme 2.3

Generally, the yields were fair to good, but the steric influence seemed to be slightly more important with dibromocarbene addition than with dichlorocarbene addition to the double bond.[8] This may perhaps be attributed to the slightly smaller atomic radius of the chlorine atom compared to the bromine atom. Thus, in the former addition the yield decreased somewhat when the steric bulk of the alkyl group increased, from 77% to 60% when R^1 changed from propyl to *tert*-butyl and afforded **2a** and **2g** respectively (Table 2.3).

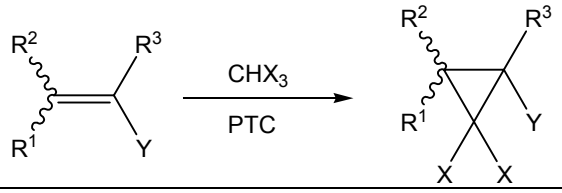
Table 2.3 Preparation of 2-alkyl-1,1,2-trihalocyclopropanes from **1** under PTC.

Entry	R^1	Product	Yields (%)	
			2	**3**
1	Propyl	**a**	77	55
2	Pentyl	**b**	70	
3	Octyl	**c**	72	
4	2-Phenylethyl	**d**	77	
5	Cyclohexylmethyl	**e**	68	59
6	Isobutyl	**f**	69	
7	*tert*-Butyl	**g**	60	58

The yields of cyclopropanes **2** were higher than those of the corresponding cyclopropanes **3**, probably due to a higher reactivity of dibromocarbene than the dichlorocarbene towards electron-poor alkenes. This could be connected to the more electrophilic character of the

dichlorocarbene as opposed to the dibromo analogue.[9-11] Sydnes and co-workers observed the same reactivity difference in the syntheses of 1,1,2-trihalocyclopropanes from different halogenated olefins (Table 2.4).[12,13]

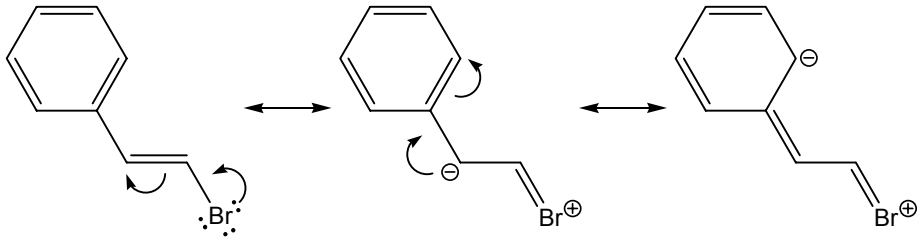
Table 2.4 Preparation of 1,1,2-trihalocyclopropanes by Sydnes and co-workers.[12,13]



					Yields (%)		
Entry	R^1	R^2	R^3	Y	X=	Br	Cl
1	H	H	H	Br		58	42
2	H	H	Me	Br		50	50
3	H	H	Me	Cl		69	43
4	H	Me	H	Br		46	35
5	H	Me	H	Cl		48	41
6	H	Me	Me	Br		65	69
7	H	Me	Me	Cl		59	64

Addition of dibromocarbene to the double bond gave higher yields of 1,1,2-trihalocyclopropanes in all cases apart from the more substituted and less polarised alkenes (Table 2.4; entries 6 and 7).

It is also noteworthy that when the isomeric mixture containing **1g** and (*E*)-1-bromo-3,3-dimethylbut-1-ene was reacted under standard PTC, only the former alkene appeared to react and furnished the corresponding cyclopropane, 1,1,2-tribromo-2-(*tert*-butyl)cyclopropane (**2g**), in rather good yield based on the amount of **1g**. Consequently, these isomers exhibit the same reactivity difference as 1-bromo-1-phenylethene and 1-bromo-2-phenylethene under the same reaction conditions,[12] a pattern which conceivably is intimately connected to the electron distribution in the molecule. An alleged mesomeric effect from the bromine atom in 1-bromo-2-phenylethene would lead to a delocalisation of the halogen lone-pair electrons, and the negative charge could be redistributed by resonance in the phenyl ring (Scheme 2.4).



Scheme 2.4

In a chart, which was made from GC and ^{1}H NMR data, showing the formation of **2g** on the expense of **1g** (Chart 2.1), one clearly sees that the conversion of **1g** declines after approximately 25 hours, while the amount of (*E*)-1-bromo-3,3-dimethylbut-1-ene in the reaction mixture is fairly stable throughout the entire reaction.

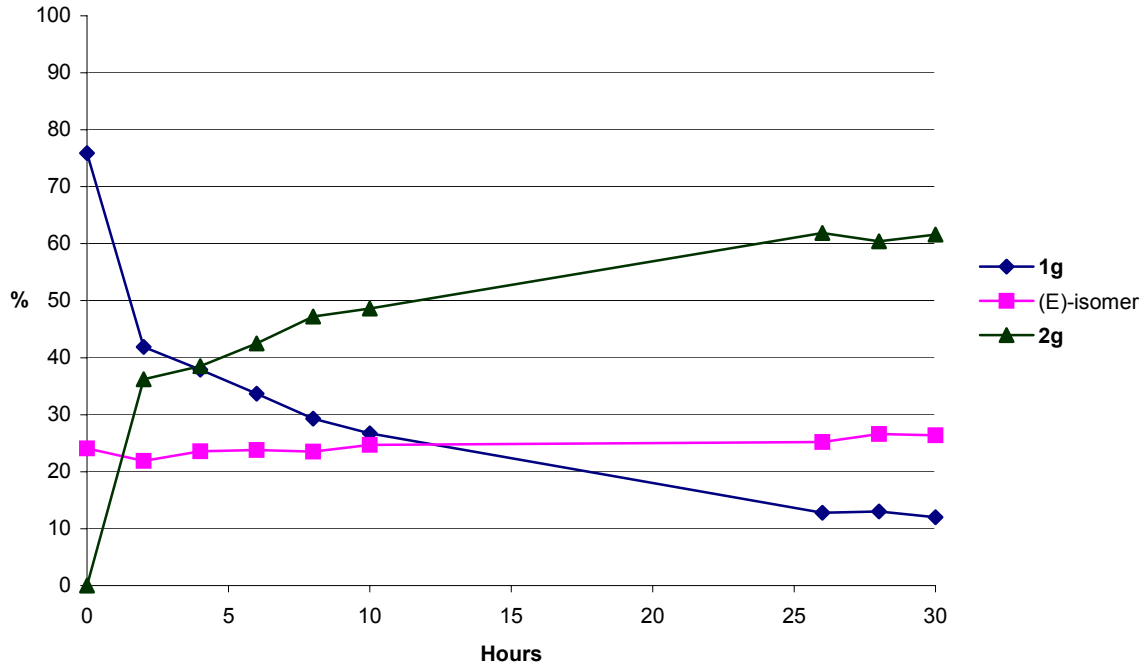


Chart 2.1 Study of the formation of cyclopropane **2g** from the isomeric mixture of **1g** and (*E*)-1-bromo-3,3-dimethylbut-1-ene.

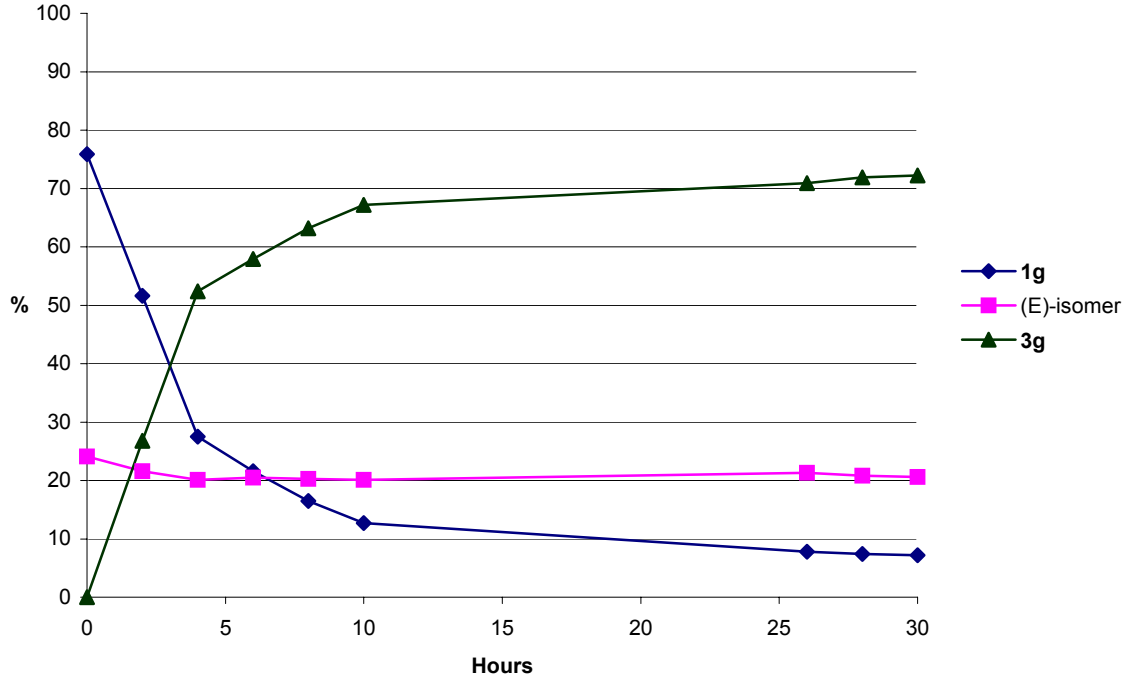


Chart 2.2 Study of the formation of cyclopropane **3g** from the isomeric mixture of **1g** and (*E*)-1-bromo-3,3-dimethylbut-1-ene.

A similar chart was produced with data from the synthesis of **3g** by dichlorocarbene addition to **2g** (Chart 2.2). It is obvious that the addition of dichlorocarbene follows the same trend as the previous addition, leaving the (*E*)-isomer unreacted. However, the conversion of **1g** seems to be slightly faster with dichlorocarbene addition than with dibromocarbene addition to the double bond,[8] giving a high outcome of **3g** already after approximately 10 hours.

The structures of the 2-alkyl-1,1,2-trihalocyclopropanes were elucidated on the basis of their spectroscopic and spectrometric properties, which were as expected. An example is the ^{13}C NMR and IR spectra of 1,1,2-tribromo-2-pentylcyclopropane (**2b**) which can be seen in Figure 2.4, 2.5 and 2.6. Signals from all the carbon atoms in **2b** were found in the aliphatic region between 45.7 and 13.9 ppm in the ^{13}C NMR spectrum (Figure 2.4). The two quaternary carbon atoms could be assigned to the signals at 45.7 and 33.1 ppm, since those signals were absent in the DEPT-135 spectrum of the molecule (Figure 2.5). In the IR spectrum of **2b** strong bands due to C-Br absorption could be seen around 680 cm^{-1},[14] while the weak absorption at 3076 cm^{-1} might be due to vibrations in the cyclopropyl protons (Figure 2.6).[15]

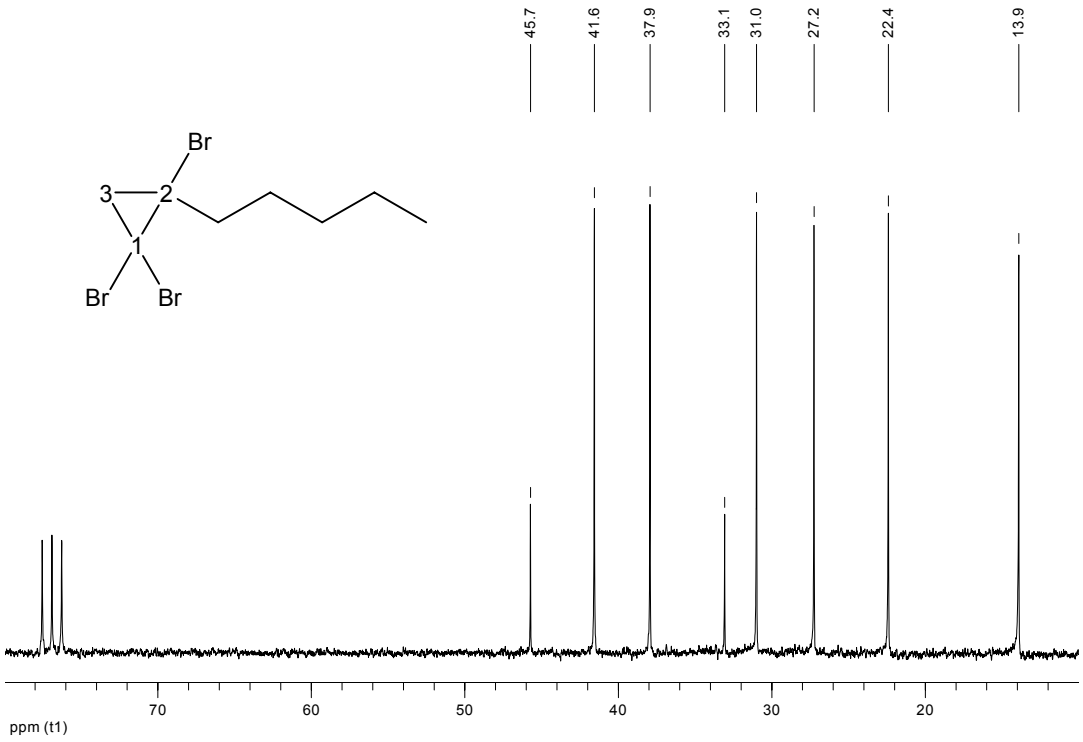


Figure 2.4 ^{13}C NMR spectrum of 1,1,2-tribromo-2-pentylcyclopropane (**2b**).

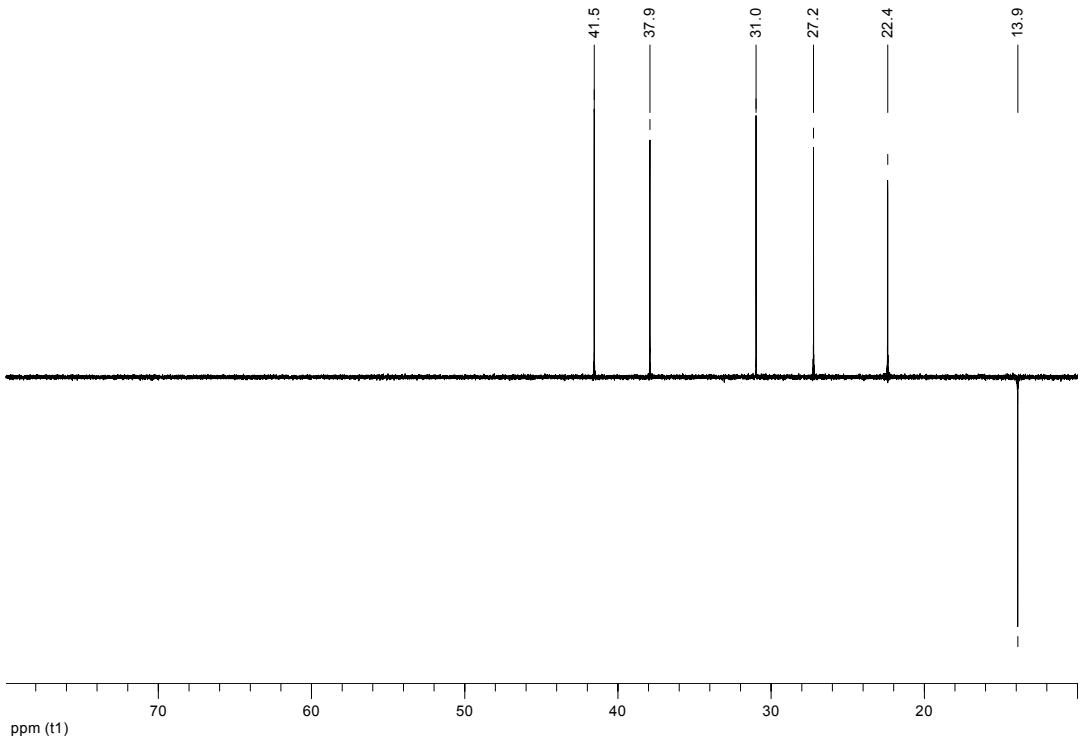


Figure 2.5 DEPT-135 spectrum of 1,1,2-tribromo-2-pentylcyclopropane (**2b**), where the methylene carbons are phased in the positive direction.

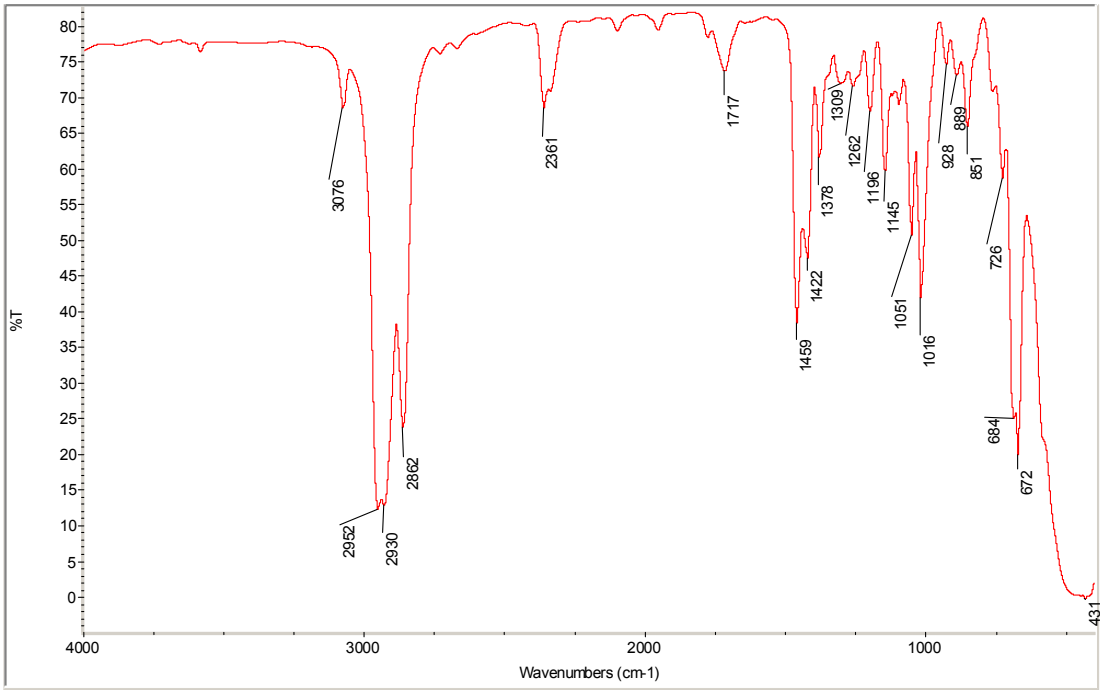


Figure 2.6 IR spectrum of 1,1,2-tribromo-2-pentylcyclopropane (**2b**).

However, a remark about the ^{1}H NMR spectra of **2d** and **2f** is also appropriate, because both compounds exhibit long-range coupling between one of the cyclopropyl protons and one of the protons in the methylene group next to the ring (Figure 2.7).

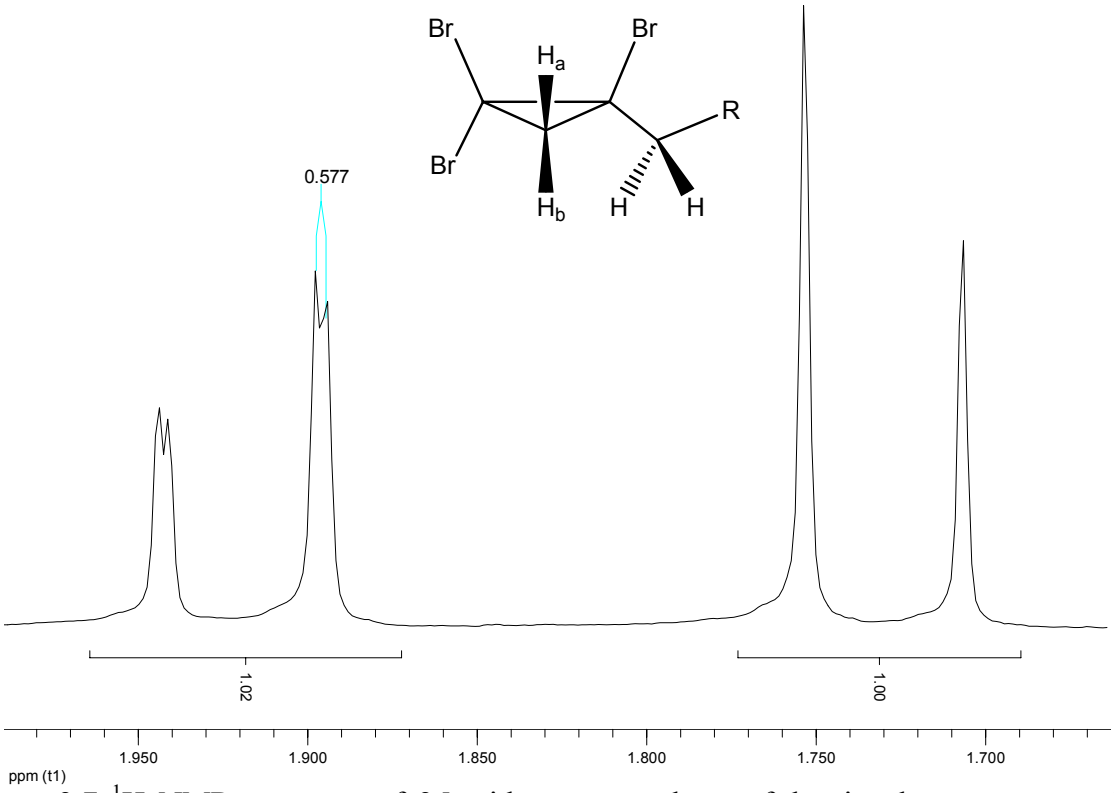


Figure 2.7 ^{1}H NMR spectrum of **2d** with an unusual out-of-the-ring long-range coupling ($^{4}J_{H,H}$=0.6 Hz). The doublet at 1.73 ppm can be assigned to H_b, while the double doublet at 1.92 ppm is the signal from H_a.

Both coupling constants are small, 0.6 Hz in **2d** to 1.0 Hz in **2f**, but their values are similar to those displayed by a large number of 2,2-disubstituted 1,1-dihalocyclopropanes.[16,17] For both **2d** and **2f** the cyclopropyl proton involved in long-range coupling appears at a lower field than the other cyclopropyl proton; this clearly indicates that it is the proton *cis* to two bromo atoms that is engaged in the $^{4}J_{H,H}$ coupling (Figure 2.7).[17] Because electrostatic interaction between a proton and a bromine atom should lead to a decrease in the magnetic shielding of the proton nucleus.

Most likely the long-range coupling is present in **2c**, **2e** and **3e** also, although over-lapping of proton signals in the aliphatic region made the interpretation dubious. However, an AB system of a double doublet and a doublet can be seen in the range between 1.70-2.00 ppm in the ^{1}H NMR spectra of all of these compounds. The long-range coupling constants in **2e** and **3e** were both 1.0 Hz, while the coupling constant in **2c** was found to be 0.7 Hz by using Lorentz-to-Gaussian apodisation (Figure 2.8).

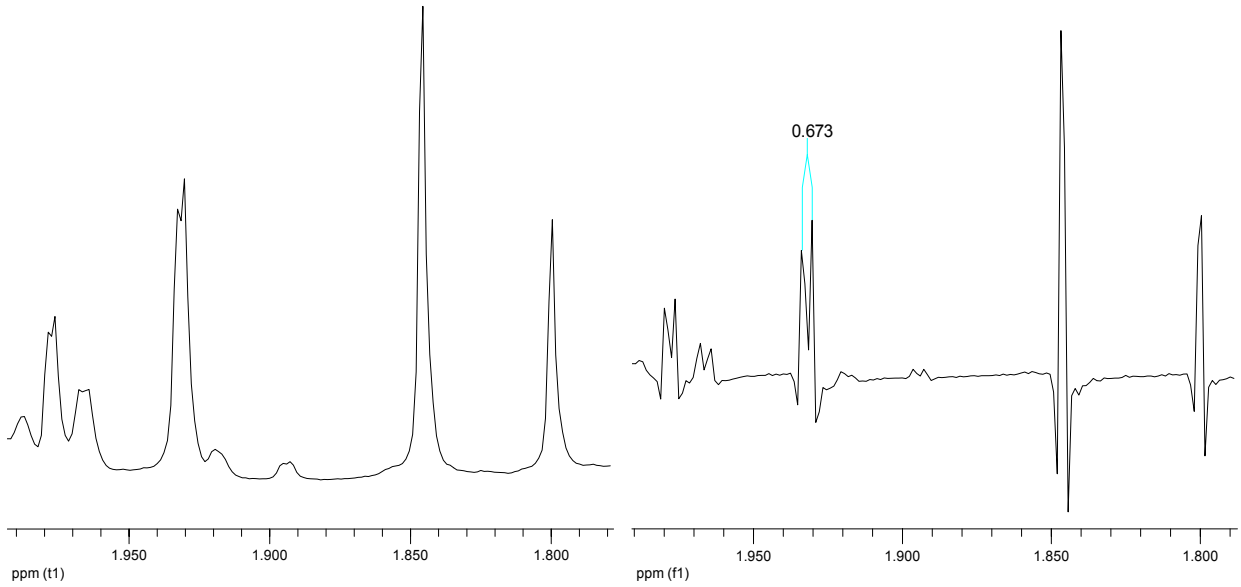


Figure 2.8 ^{1}H NMR spectrum of **2c** with an unusual out-of-the-ring long-range coupling ($^{4}J_{H,H}$=0.7 Hz), processed without window functions on the left and with Lorentz-to-Gaussian apodisation on the right hand side.

The structure elucidation of the cyclopropanes (**2**) was furthermore simplified by performing some 2D NMR experiments. In the HMBC spectrum correlations between proton and carbon nuclei via $^{1}J_{C,H}$ couplings (optimised for 150 Hz) is suppressed in order to obtain information on long-range C,H correlations (optimised for 8 Hz) in molecules. It is known that due to heavy-atom effect a carbon atom attached to two bromine atoms is shifted to a higher field in the ^{13}C NMR spectrum compared to a carbon atom attached to only one bromine atom,[18,19] and indeed in the HMBC spectrum of **2d** it is clear that the carbon shift at 45.0 ppm belongs to C-2, while the shift at 32.6 ppm can be attributed to C-1 (Figure 2.9). An obvious starting point for solving this HMBC spectrum is in the upper left corner where some aromatic protons are correlated with a methylene carbon. This must be a $^{3}J_{C,H}$ coupling between the *ortho*-protons and C-2´ at 33.8 ppm. Furthermore, it is clear that C-2´ is coupled to the protons attached to C-1´ at 2.16-2.47 ppm, while the carbon signal at 32.6 ppm seems to correlate with both the protons attached to C-1´ and C-3 by respectively $^{3}J_{C,H}$ and $^{2}J_{C,H}$ couplings (Figure 2.9).

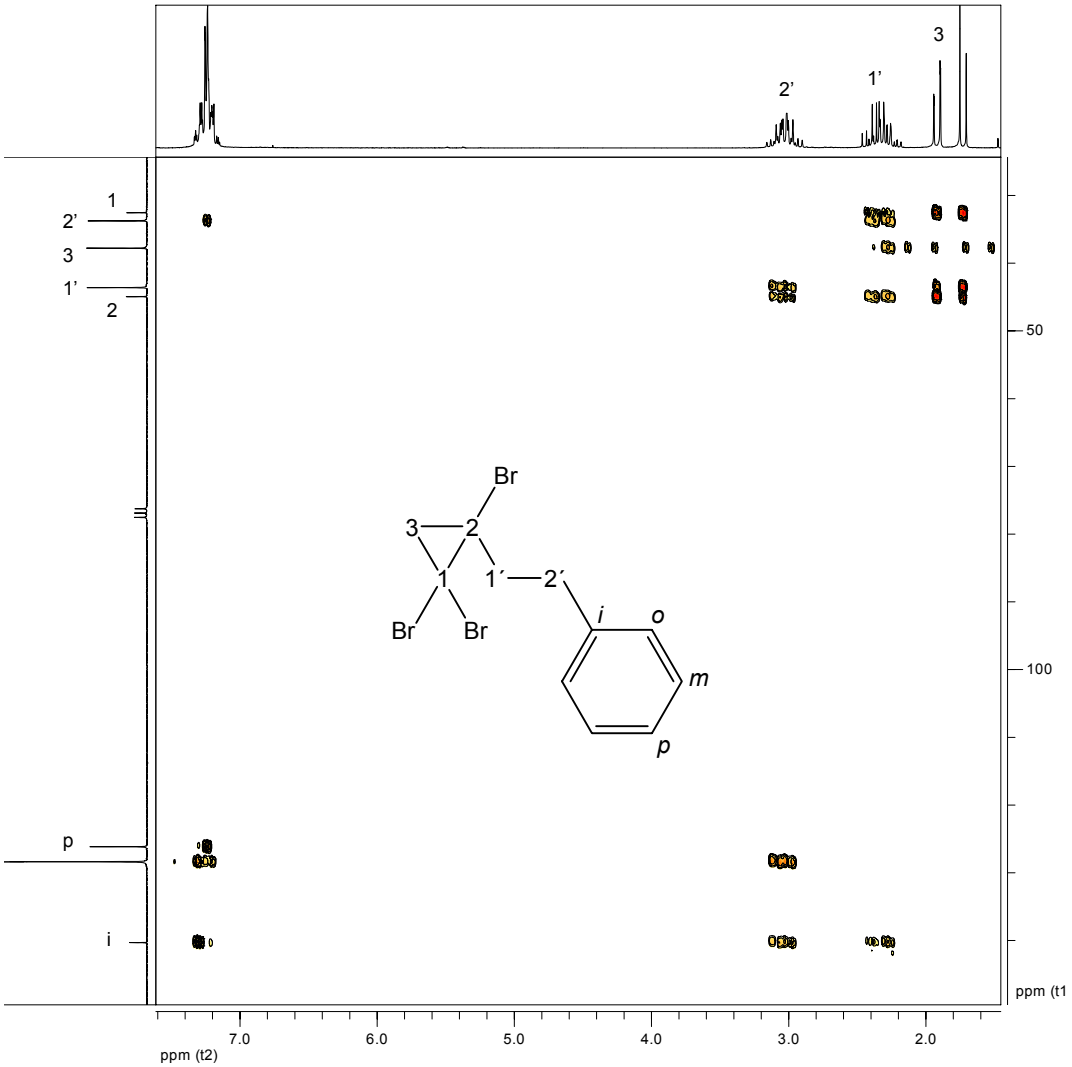
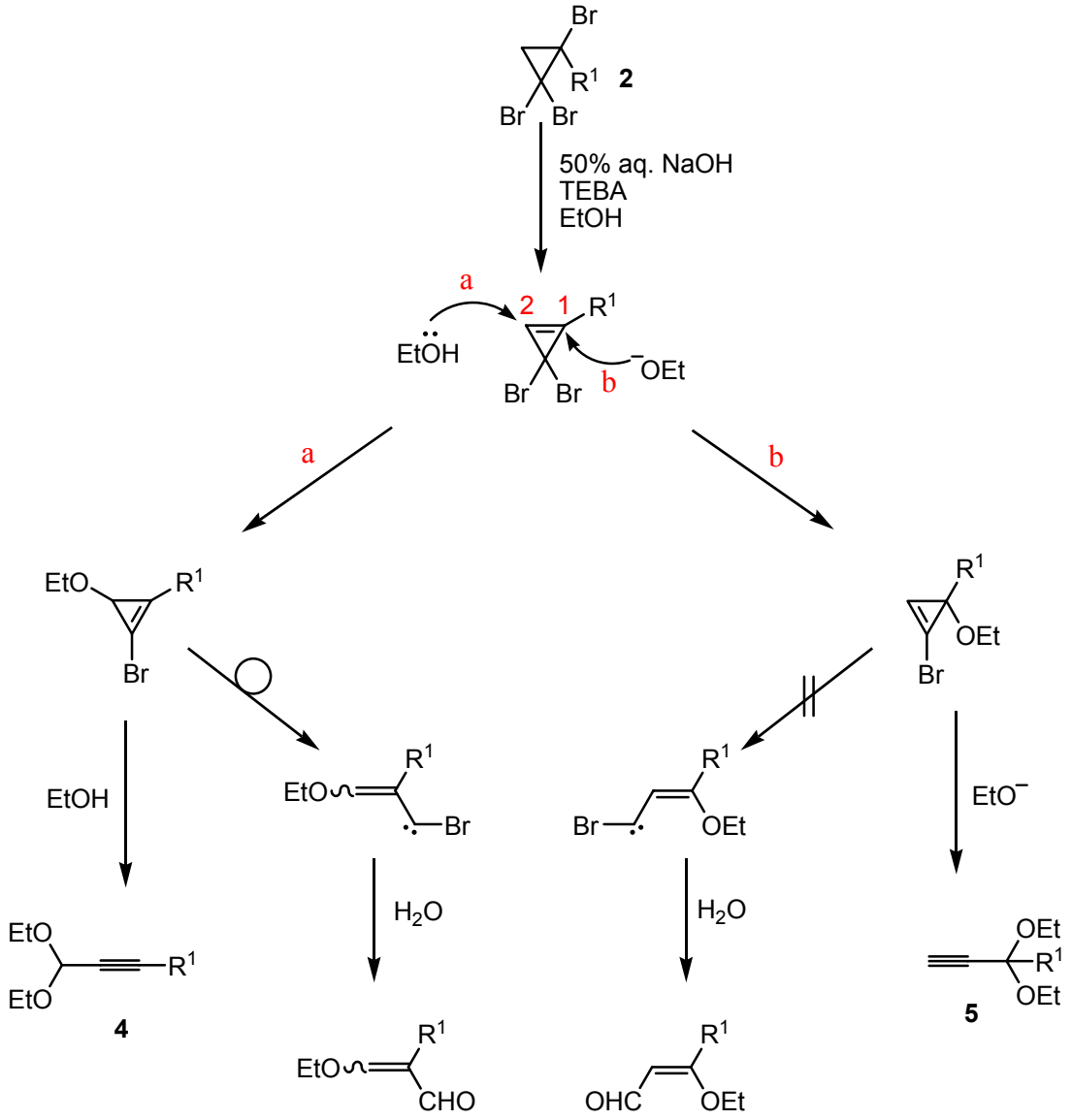


Figure 2.9 HMBC spectrum of **2d** with some key features outlined.

2.3 Ring opening of 2-alkyl-1,1,2-tribromocyclopropanes

It is known that when 2-substituted 1,1,2-trihalocyclopropanes (**2**) are exposed to 50% sodium hydroxide in the presence of ethanol, dichloromethane, and a small amount of a phase-transfer catalyst (TEBA), the trihalides undergo ring opening and are converted to the corresponding acetylenic diethyl acetals (**4**) and ketals (**5**).[12,13,20-22] Mechanistic studies showed that the ring-opening reaction is a multistep process involving dehydrohalogenation, formal substitution of halogen atoms by ethoxy groups, and finally ring opening. Furthermore, it appeared that the acetals and ketals were formed via a common intermediate, the corresponding 1-substituted 3,3-dibromocyclopropene, which is consumed by nucleophilic attack of ethoxide and ethanol at C-1 and C-2, respectively (Scheme 2.5). A possible by-product is an *α,β*-unsaturated aldehyde, which is formed by insertion reaction[23] on a vinylidene originating from an intermediate cyclopropene.[12]



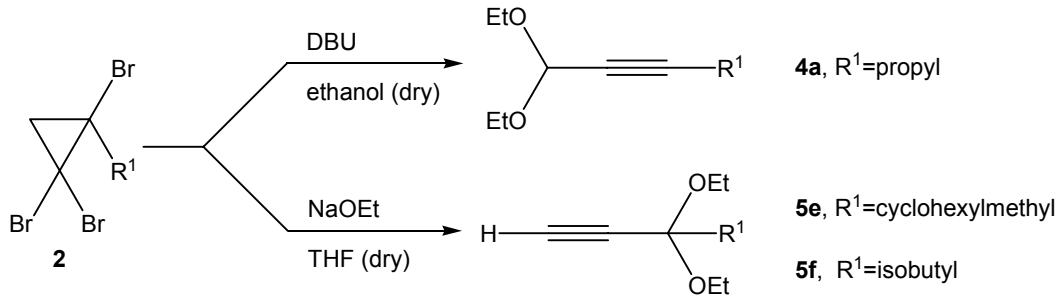
Scheme 2.5

From the nature of this reaction it was reasonable to believe that the regioselectivity of the nucleophilic attack, and thus the acetal/ketal ratio, would be sensitive to the steric bulk of the substituent R^1. It was therefore decided to examine reactions of selected 1,1,2-trihalocyclopropane derivatives containing R^1 with different steric bulk, to see to what extent the acetal/ketal distribution is influenced by steric interactions.

Indeed, when 2-alkyl-1,1,2-tribromocyclopropanes (**2**) were reacted with 50% aqueous sodium hydroxide in the presence of ethanol and a small amount of TEBA, the substrates suffered ring opening and gave in general a mixture of the acetylenic diethyl acetal (**4**) and the corresponding acetylenic ketal (**5**) (Scheme 2.5).

In most cases the combined yield of **4** and **5** was moderate; in the best case, which involved 1,1,2-tribromo-2-octylcyclopropane (**2c**) as starting material, only 60% yield was

obtained. Another important feature is how difficult it was to separate the acetal from the corresponding ketal. In most cases separation was not achieved without a significant drop in yield for both compounds, and in three cases the loss was so significant that 1,1-diethoxyhex-2-yne (**4a**), 3,3-diethoxy-4-cyclohexylbut-1-yne (**5e**), and 3,3-diethoxy-5-methylhex-1-yne (**5f**) could not be properly analyzed spectroscopically and spectrometrically. The formation and structures of **4a**, **5e** and **5f** were therefore substantiated by independent synthesis (Scheme 2.6; Table 2.5).



Scheme 2.6

Table 2.5 Alternative syntheses of acetals (**4**) and ketals (**5**).

Entry	R^1		Yields (%)
1	Propyl	**4a**	46
2	Cyclohexylmethyl	**5e**	46
3	Isobutyl	**5f**	57

The only mixture that allowed straightforward separation of the ketal and the acetal, was that of 1,1-diethoxy-5-phenylpent-2-yne (**4d**) and 3,3-diethoxy-5-phenylpent-1-yne (**5d**) obtained from **2d**; pure samples of both **4d** and **5d** were obtained fairly easily without a considerable loss of material.

The acetal proton in **4d** appeared as a downfield triplet at 5.24 ppm in the ^{1}H NMR spectrum (Figure 2.10), due to a magnetic deshielding of the proton nucleus caused by the inductive effect from the two ethoxy groups. The acetylenic proton in **5d** appeared as an upfield singlet at 2.58 ppm (Figure 2.11), due to an increased shielding caused by the diamagnetic anisotropy from the triple bond.

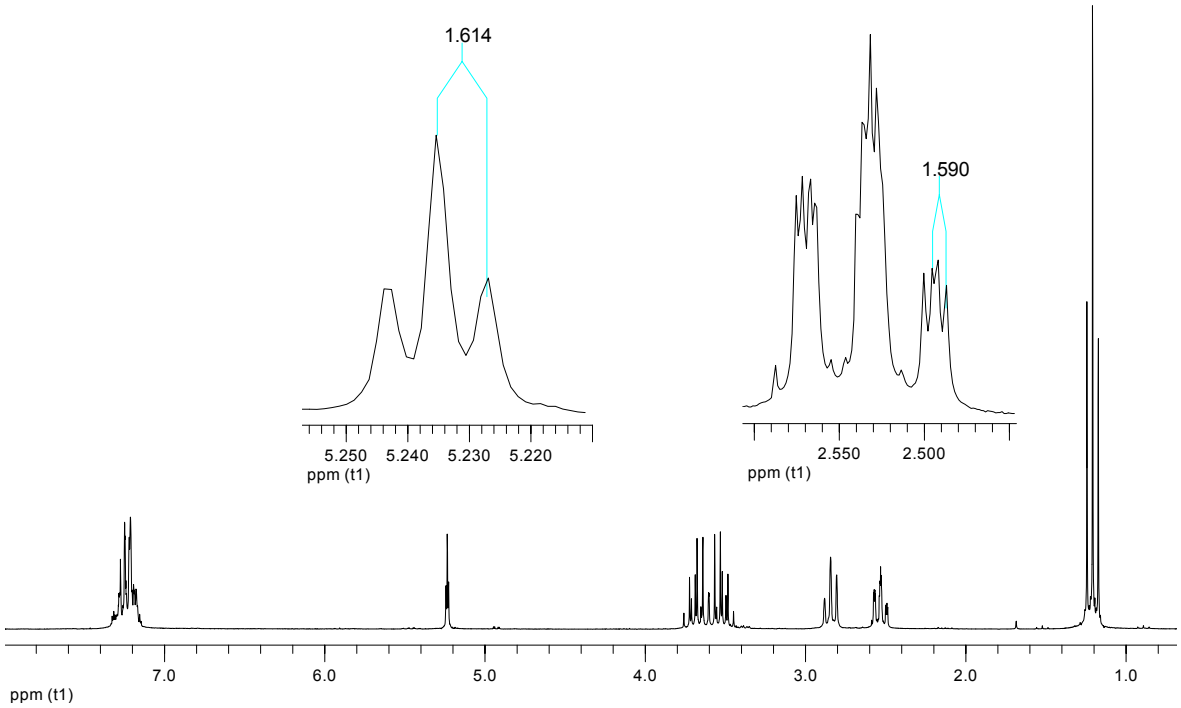


Figure 2.10 ^{1}H NMR spectrum of pure 1,1-diethoxy-5-phenylpent-2-yne (**4d**) with an expansion of the triplet ($^{5}J_{H,H}$=1.6 Hz) of the acetal proton at 5.24 ppm.

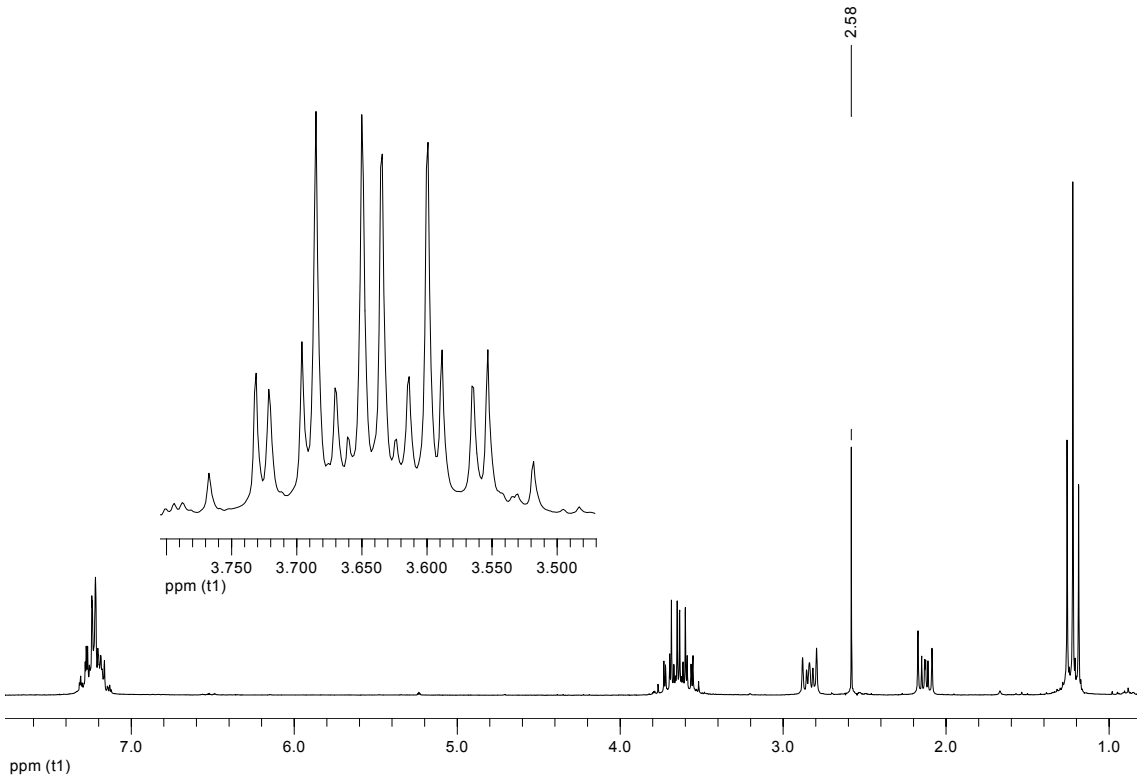


Figure 2.11 ^{1}H NMR spectrum of pure 3,3-diethoxy-5-phenylpent-1-yne (**5d**) with the characteristic singlet of the acetylenic proton at 2.58 ppm.

The IR spectrum of the **4d** contained one characteristic stretch at approximately 2240 cm^{-1} due to the triple bond (Figure 2.12), while the IR spectrum of the **5d** also contained, in

addition to a triple bond stretch at 2112 cm^{-1}, a stretch at 3287 cm^{-1} due to the terminal proton at the triple bond (Figure 2.13).

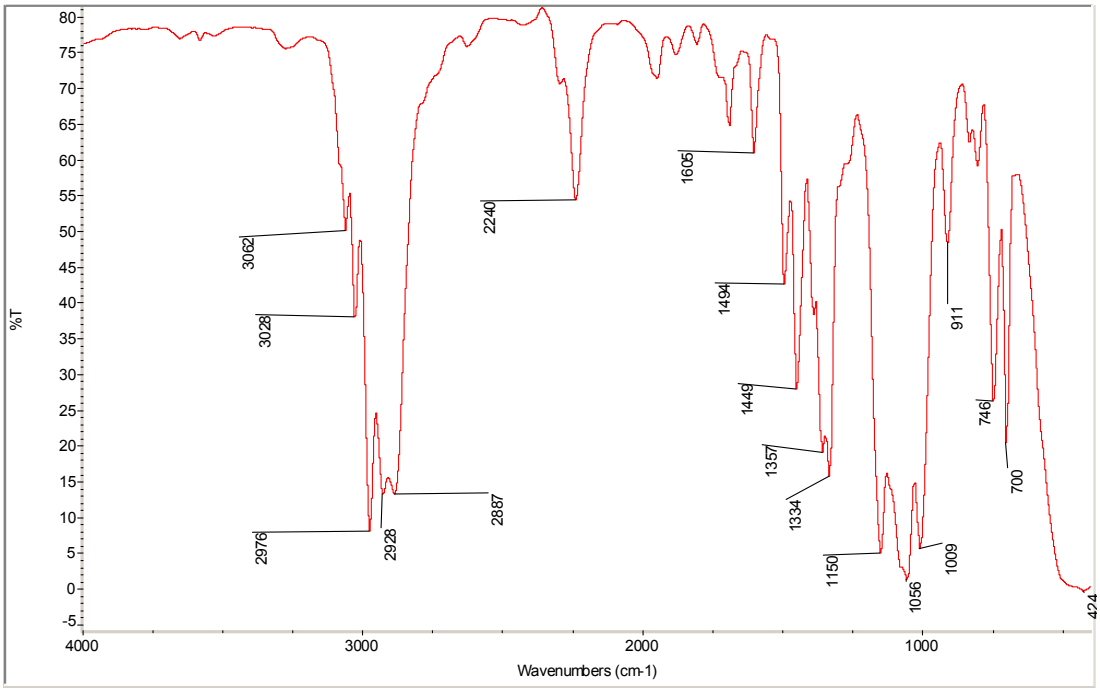


Figure 2.12 IR spectrum of the acetal 1,1-diethoxy-5-phenylpent-2-yne (**4d**) with the characteristic triple-bond stretch at 2240 cm^{-1}.

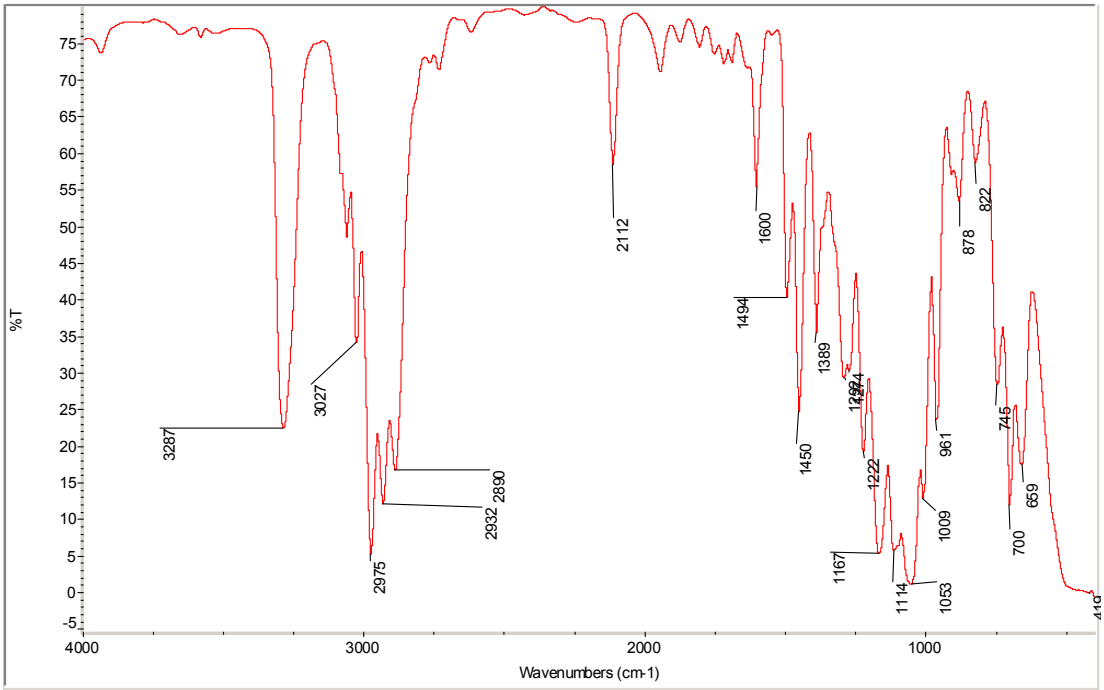


Figure 2.13 IR spectrum of the ketal 3,3-diethoxy-5-phenylpent-1-yne (**5d**) with two characteristic stretches at 2112 and 3287 cm^{-1}.

In the experiments where the acetal and ketal were not completely separated from one another, the acetal/ketal ratio was easily calculated from ^{1}H NMR data (supplemented by GC

data) because of the distinct feature of the acetal proton (**4**) and the acetylenic proton (**5**). The acetylenic proton in **5** appeared as a sharp singlet between 2.52 ppm in 3,3-diethoxyhex-1-yne (**5a**) and 2.58 ppm in 3,3-diethoxy-5-phenylpent-1-yne (**5d**), while the acetal proton in **4** always gave rise to a triplet at between 5.17 ppm in 1,1-diethoxyhex-2-yne (**4a**) and 5.27 ppm in 1,1-diethoxy-4-cyclohexylbut-2-yne (**4e**), apart from in 1,1-diethoxy-4,4-dimethylpent-2-yne (**4g**) where only a singlet was found at 5.26 ppm (Table 2.6).

Table 2.6 Spectral data of acetylenic diethyl acetals (**4**).

Entry	R^1		Acetal δ_H (ppm)	Magnitude of $^5J_{H,H}$ (Hz)
1	Propyl	**a**	5.17	1.6
2	Pentyl	**b**	5.24	1.6
3	Octyl	**c**	5.26	1.6
4	2-Phenylethyl	**d**	5.24	1.6
5	Cyclohexylmethyl	**e**	5.27	1.7
6	Isobutyl	**f**	5.27	1.7
7	*tert*-Butyl	**g**	5.26[a]	—

[a] Appears as a singlet in the ^{1}H NMR spectrum.

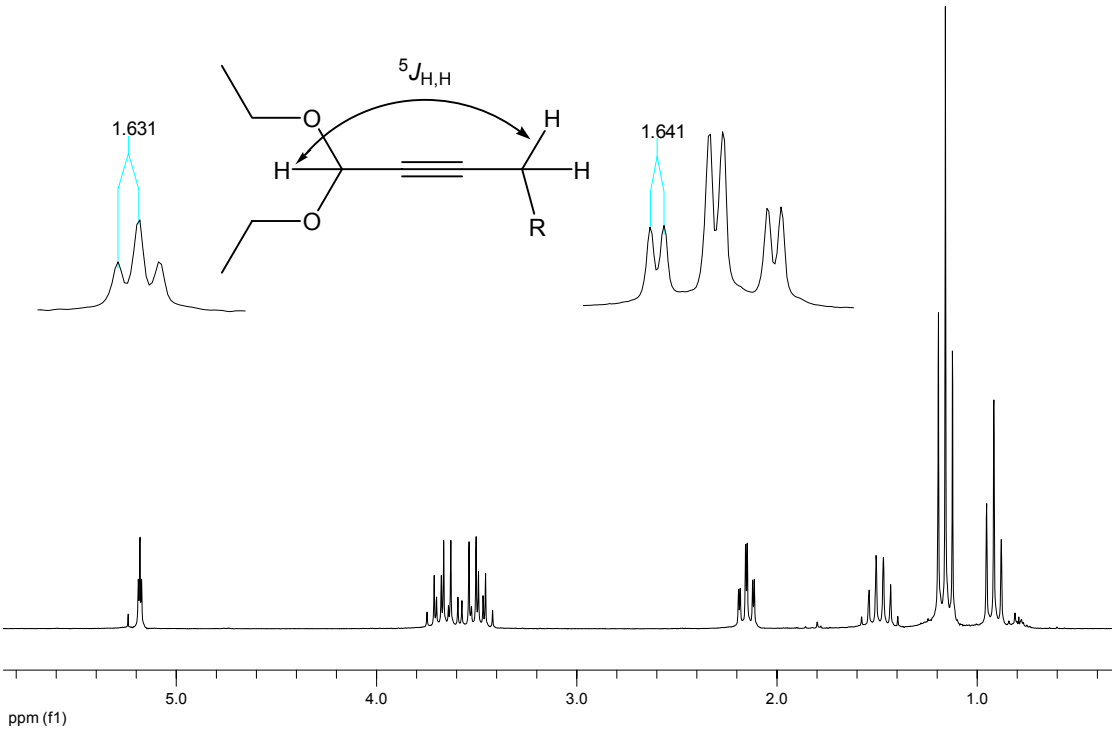


Figure 2.14 ^{1}H NMR spectrum of **4a** with an expansion of the acetal proton triplet at 5.17 ppm and the methylene group which it couples to at 2.14 ppm.

The fact that the acetal proton in **4g** appears as a singlet in the ^{1}H NMR spectrum and the coupling pattern in the spectrum of **4a** (Figure 2.14), prove that the acetal proton in **4** does

not couple through oxygen in the ethoxy groups ($^4J_{H,H}$), but through the triple bond to the methylene group in the alkyl chain instead. This long-range coupling ($^5J_{H,H}$) was in the magnitude of 1.6-1.7 Hz in **4a**-**4f** (Table 2.6).

In some ring-opening experiments (**2a**, **2b** and **2f**) signals attributed to an *α*,*β*-unsaturated aldehyde (see Scheme 2.5) could be seen in the ^{1}H and ^{13}C NMR spectra of the crude products. The two singlets at approximately 9.1 and 6.9 ppm could be assigned to the aldehyde and the vinylic proton (Figure 2.15), while the carbon atoms attached to these protons resonated at around 190 and 170 ppm.

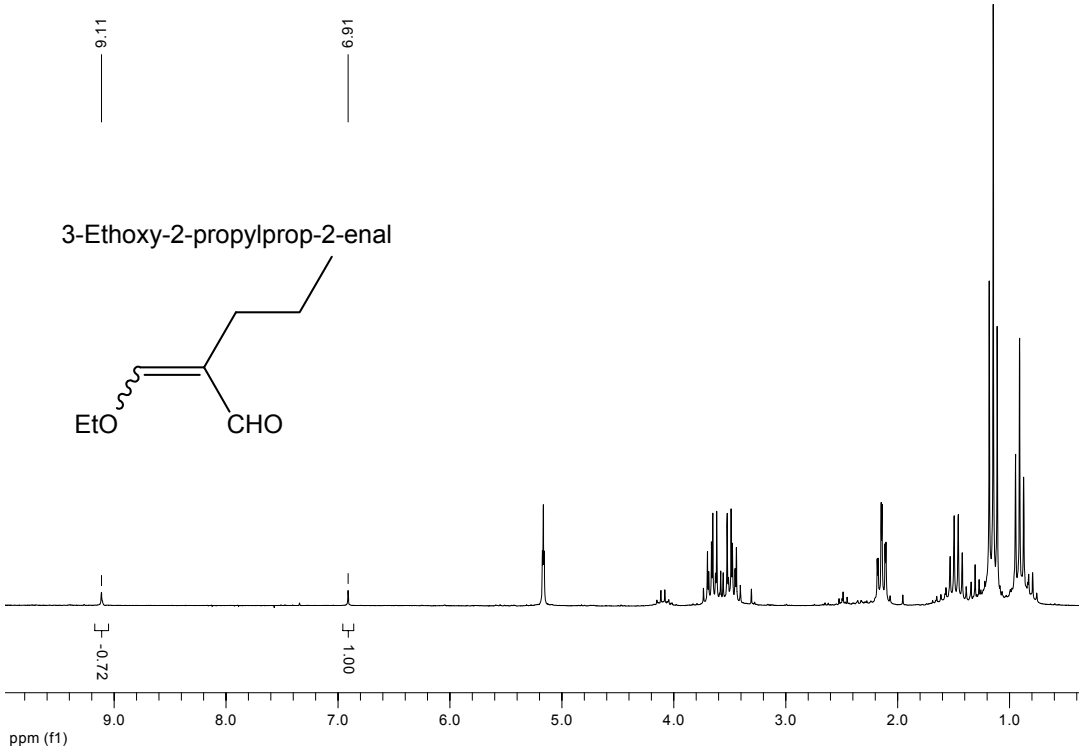
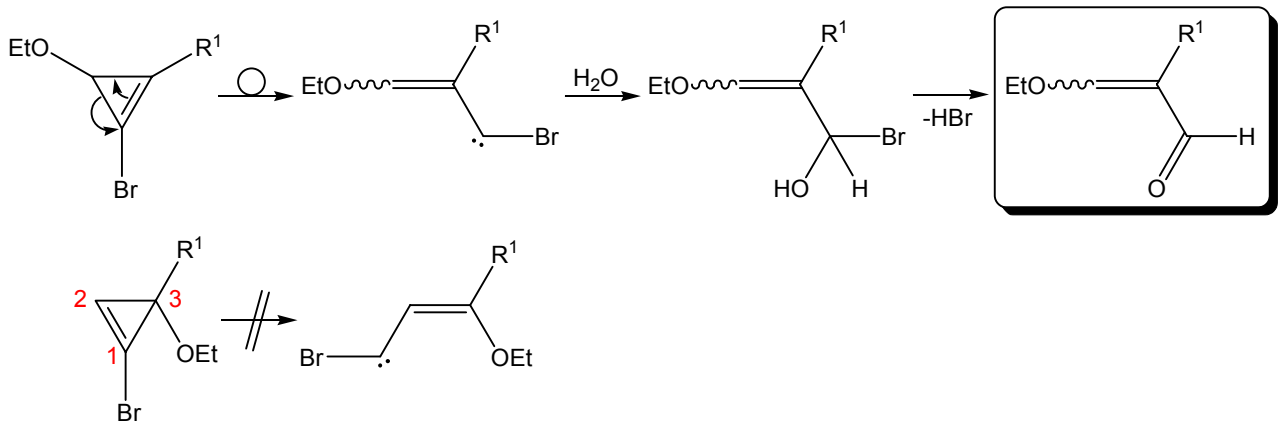


Figure 2.15 ^{1}H NMR spectrum of the crude product after the ring opening of **2a**, showing the singlets at 9.11 and 6.91 ppm which probably belong to the *α*,*β*-unsaturated aldehyde.

However, efforts on isolating these *α*,*β*-unsaturated aldehydes by flash chromatography failed. Although, the fact that the vinylic proton resonates as a singlet at a low field proves that the *α*,*β*-unsaturated aldehydes are the 2-substituted instead of the corresponding 3-substituted 3-ethoxyprop-2-enal analogues, which could have been formed from a different cyclopropene-vinylcarbene rearrangement as envisaged in Scheme 2.7.

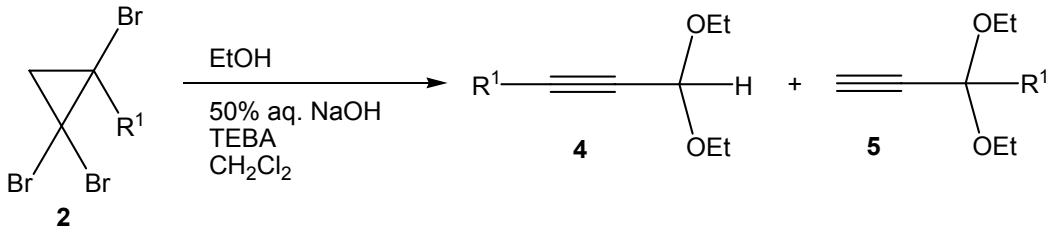


Scheme 2.7

The vinylic proton in 3-alkyl-3-ethoxyprop-2-enal should, based on calculations, resonate at a higher field and a possible *vicinal* coupling between this proton and the carbonylic proton should be seen in the ^{1}H NMR spectrum. The exclusive formation of 2-substituted 3-ethoxyprop-2-enal derivatives in the cyclopropene-vinylcarbene rearrangement is supported in studies done by Müller and Pautex,[24] who found the intermediate 1,3,3-substituted cyclopropenes to be reluctant towards rearrangement.

In order to try to improve the reaction and increase the yield of **4** and/or **5**, the ring opening was carried out under different conditions by changing reactant concentrations, the excess of sodium hydroxide and ethanol, and reaction temperature. These experiments did not significantly improve the total yield of the products, but based on data from GC and ^{1}H NMR analyses of the crude product mixtures, it became evident that the acetal/ketal ratio (**4**/**5**) was somewhat sensitive to the conditions prevailing during the reaction. It was therefore important to carry out the ring opening of **2** under identical conditions so that it would be possible to detect the steric influence of R^{1} on the course of the reaction.

After some consideration it was decided to run the reaction in the same amount of dichloromethane (15 mL) containing the same amount of TEBA (0.2 g), to have the same initial concentrations of **2** (5 mmol), EtOH (20 mmol), and NaOH (40 mmol), and to cool the reaction mixtures in the same fashion during the reaction (0 °C) (Scheme 2.8).



Scheme 2.8

When the experiments were performed according to this protocol, it appeared that the **4**/**5** ratio increased as the steric crowding of R^1 increased (Table 2.7). The smallest alkyl groups, propyl and pentyl, gave a ratio of 1.2, which is slightly above the 1.0 ratio observed by Sydnes and Bakstad when R^1=Me.[12] The ratio increases to 3.5 when R^1=i-Bu, and ring opening of 1,1,2-tribromo-2-(*tert*-butyl)cyclopropane (**2g**) afforded acetal only; no signals were detected which could be ascribed to the presence of the corresponding ketal. It is therefore clear that attack of the carbon atom attached to R^1, *viz*. C-1, in the 3,3-dibromocyclopropene formed as intermediate during the reaction (Scheme 2.5), is hampered when the steric bulk of R^1 becomes significant and completely prevented when R^1=*t*-Bu.

Table 2.7 Combined isolated yield of acetal (**4**) and ketal (**5**) and the acetal/ketal ratio (**4**/**5**) in the ring opening of 1,1,2-tribromocyclopropanes (**2**).

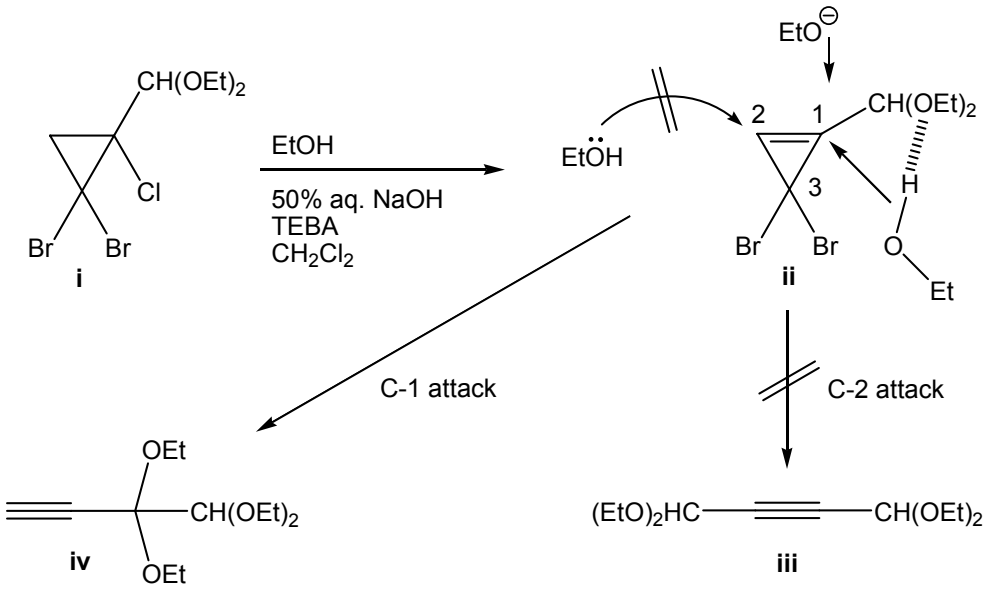
Entry	R^1	Cyclopropane	**4**/**5**[a]	Isolated yield (%)[b]
1	Propyl	**2a**	1.2	55
2	Pentyl	**2b**	1.2	43
3	Octyl	**2c**	1.4	60
4	2-Phenylethyl	**2d**	1.5	54
5	Cyclohexylmethyl	**2e**	1.8	57
6	Isobutyl	**2f**	3.5	36
7	*tert*-Butyl	**2g**	>80	37

[a] The ratios are based on GC and ^{1}H NMR analyses. Some of the numbers differ somewhat from data published earlier;[22] this is due to different conditions during the reaction.

[b] Combined yield of **4** and **5** except for **2g**, which gave no **5g**, only **4g**.

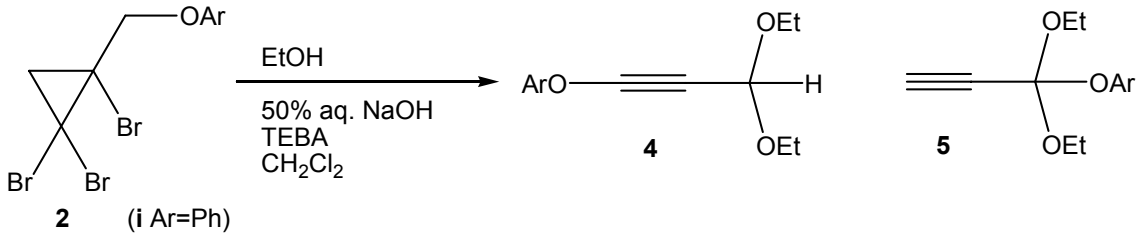
The observation that R^1 renders attack of C-1 and makes ketal formation more difficult when the steric influence of R^1 increases, suggests that from a steric point of view, acetal predominance should be the rule when R^1 is sterically demanding. On this basis it is expected that when 1,1-dibromo-2-chloro-2-diethoxymethylcyclopropane (**i**) is exposed to the reaction conditions used to trigger ring opening of **2**, formation of 3,3-dibromo-1-diethoxymethylcyclopropene (**ii**) would occur, followed by predominant attack of C-2 and generation of 1,1,4,4-tetraethoxybut-2-yne (**iii**). However, syntheses conducted by Sydnes and co-workers

yielded 3,3,4,4-tetraethoxybut-1-yne (**iv**) exclusively (Scheme 2.9).[22,25,26] Exclusive formation of **iv** requires regiospecific attack of **ii** at C-1, and this is conceivably achieved because the steric repulsion between ethanol molecules and the diethoxymethyl moiety is more then compensated by attractive forces due to hydrogen bonding between the same entities.



Scheme 2.9

When the ring-opening of 1,1,2-tribromo-2-phenoxymethylcyclopropane (**2i**), which is previously performed by Bakstad and co-workers,[21] were repeated the result was consistent with the theory of hydrogen bonding between ethanol and an oxygen-carrying substituent. The cyclopropane suffered ring opening and afforded 61% of a mixture of acetal (**4i**) and ketal (**5i**) of which 53% was **5i**, giving a ketal/acetal ratio of 6.6 (Scheme 2.10).



Scheme 2.10

Bakstad *et al.* performed ring-opening of a series of 2-aryloxymethyl-1,1,2-tribromo-cyclopropanes (**2**) and achieved total yields of better than 80%.[21] The acetylenic diethyl ketals (**4**) predominated significantly and was in some cases almost the exclusive product (Table 2.8).

Table 2.8 Ring opening of 2-aryloxymethyl-1,1,2-tribromocyclopropanes (**2**), performed by Bakstad *et al.*[21]

Entry	**2** (Ar)	**5**/**4**	Total yield of **4** and **5** (%)
1	Phenyl	18	95
2	4-Methylphenyl	7	83
3	4-Methoxyphenyl	8	89
4	4-Chlorophenyl	40	82
5	4-Nitrophenyl	2.5	—

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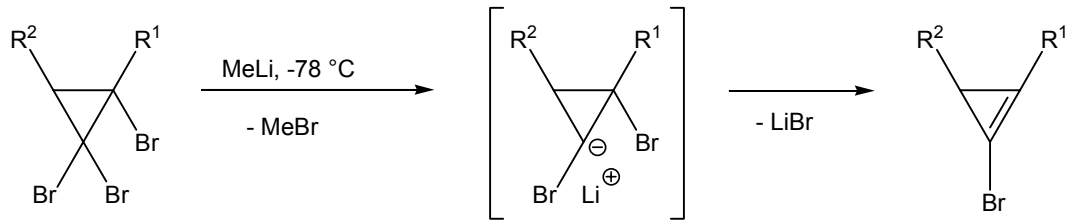
3 Synthesis and trapping of substituted 1-bromocyclopropenes

When substituted 1,1,2-tribromocyclopropanes **2** were treated with methyllithium, based on a procedure published by Baird and co-workers,[1] formation of 1-bromocyclopropenes (**6**) was achieved by 1,2-dehalogenation (Scheme 3.1).



2 **6**

Scheme 3.1

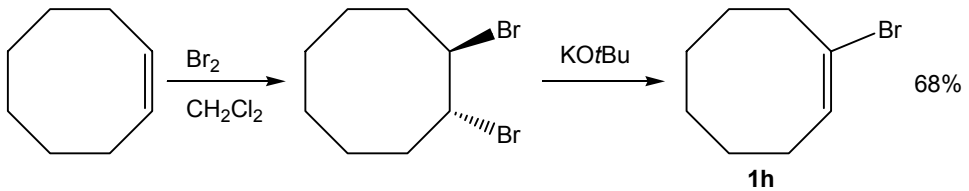
Based on the willingness of 1-halocyclopropenes to undergo Diels-Alder reactions and the fact that **6** appears to be easily available from readily accessible **2**, we decided to study the reactivity of selected 2-substituted 1-bromocyclopropenes as dienophiles toward some conjugated dienes, with special emphasis on stereochemical aspects.

The 2-alkyl-1,1,2-tribromocyclopropanes (**2a**-**2g**) described in Chapter 2.2 were used as precursors for **6**, together with 2-substituted 1,1,2-tribromocyclopropanes (**2h**-**2l**) which were prepared in analogous syntheses (*vide infra*).

3.1 Synthesis of bromoalkenes

The bromoalkenes (**1**) used as starting material for 2-substituted 1,1,2-tribromocyclopropanes (**2**) were prepared from different alkenes.

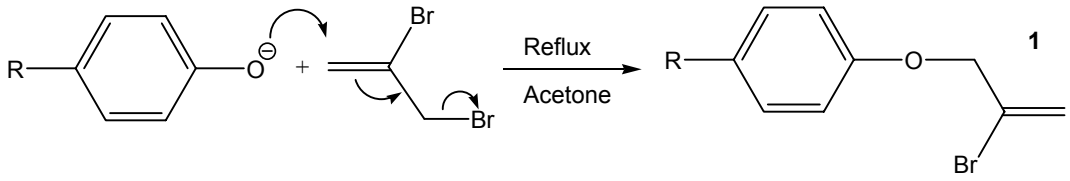
1-Bromocyclooctene (**1h**) was synthesised from cyclooctene in a two-step synthesis via *trans*-1,2-dibromocyclooctene. Bromine adds to cyclooctene in a *trans* fashion, and when the crude product reacted with potassium *tert*-butoxide **1h** was produced through *syn* elimination in 68% total yield (Scheme 3.2).



1h

Scheme 3.2

In addition three aryl 2-bromoprop-2-enyl ethers (**1i-1k**) were prepared from 2,3-dibromopropene, in a base-catalyzed S_N2' reaction with phenols (Scheme 3.3).[2] Allylic halides react faster with nucleophiles than alkyl halides, because of the rearrangement of the π-system when HBr is eliminated.[3]



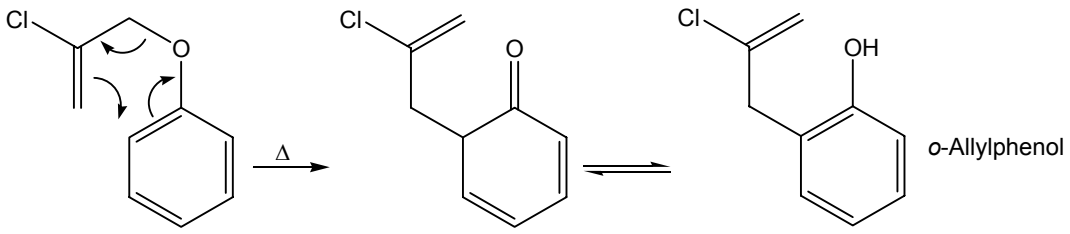
Scheme 3.3

Table 3.1 Syntheses of allyl aryl ethers (**1**) from 2,3-dibromopropene.

Entry	R		Yield (%)
1	H	**1i**	77
2	Me	**1j**	79
3	Br	**1k**	73[a]

[a] 4-Hydroxy-4-methylpentan-2-one was isolated.

The yields were good and no by-products, like for example *o*- or *p*-allylphenols produced in possible [3,3]-sigmatropic Claisen rearrangements of the allyl aryl ethers, were observed (Table 3.1). Although, Anderson and co-workers isolated 2-(2-chloroallyl)phenol in a thermal *ortho*-Claisen rearrangement of 2-chloro-3-phenoxypropene (Scheme 3.4).[4] The unstable ketonic form of *o*-allylphenol is produced as an intermediate in the rearrangement, which spontaneously tautomerises to the stable phenolic form.[5] When the *ortho*-positions are substituted, rearomatisation cannot take place before the allyl group undergoes a Cope rearrangement to the *para*-position.

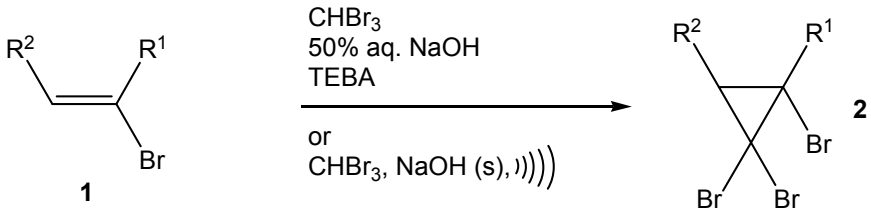


Scheme 3.4

The Claisen rearrangement of allyl aryl ethers is strongly acid catalyzed,[6] so the formation of *o*- or *p*-allyl phenols in base-catalyzed condensations of 2,3-dibromopropene with phenols is probably suppressed.

3.2 Synthesis of substituted 1,1,2-tribromocyclopropanes

Substituted 1,1,2-tribromocyclopropanes (**2**) were synthesised by dibromocarbene addition to corresponding bromoalkenes (**1**) under PTC,[7] like the previous preparation of 2-alkyl-1,1,2-trihalocyclopropanes in Chapter 2.2, or by employing finely ground NaOH and ultrasound irradiation in accordance with the Xu-Brinker procedure (Scheme 3.5).[8]



Scheme 3.5

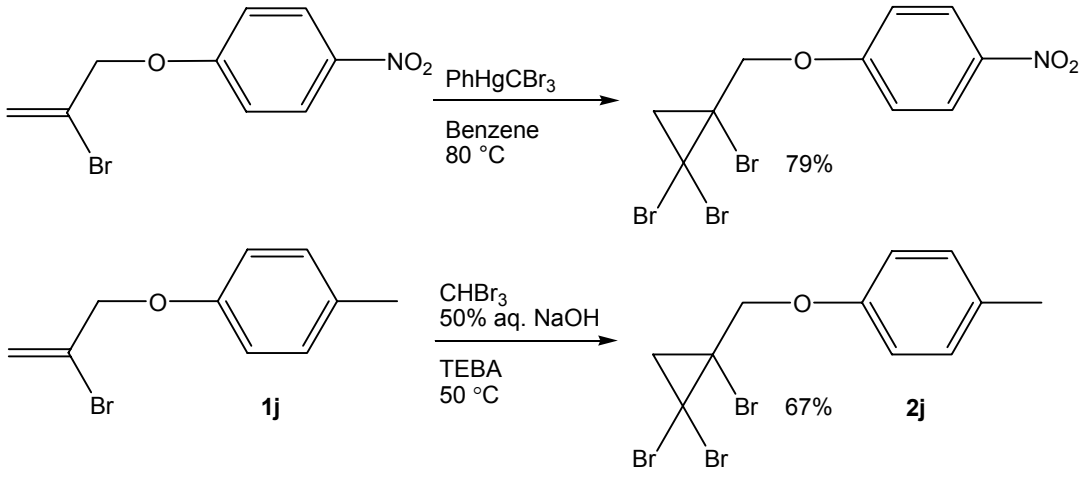
Table 3.2 Syntheses of substituted 1,1,2-tribromocyclopropanes (**2**) under PTC.

Entry	R^1	R^2		Yield (%)
1	—$CH_2CH_2CH_2CH_2CH_2CH_2$—		**2h**	72
2	CH_2OPh	H	**2i**	28
3	CH_2OPh-Me	H	**2j**	23
4	CH_2OPh-Br	H	**2k**	25
5	Ph	H	**2l**	57[a]

[a] Synthesised with the Xu-Brinker ultrasonication method.[8] When utilising the Makosza method Sydnes and Bakstad obtained 38%.[9]

The yields were acceptable, with the exceptions of aryloxymethylcyclopropanes **2i-2k** which were formed in only 28-23% (Table 3.2). The low yields are probably due to the intrinsic alkene reactivity and the conditions prevailing during the cyclopropanation, instead of by-product formation, since considerable amounts of **1** were recovered. Decrease in the electron density in alkenes makes them less reactive towards dihalocarbene addition and this becomes especially apparent in vinyl halides.[10,11] The inductive electron-withdrawing effect from the aryloxy groups in **1i-1k** probably leads to a further decrease in the electron density in the double bond. However, Bakstad and co-workers increased the yield eight times by switching from the Makosza to the Seyferth procedure in the cyclopropanation of 2-bromo-3-(4-nitro-

phenoxy)propene (Scheme 3.6),[12] while 1,1,2-tribromo-2-(4-methylphenoxy)methylcyclopropane (**2j**) was prepared in good yields with the Makosza procedure at 50 ºC (Scheme 3.6), so the reaction conditions obviously affect the reactivity extensively.

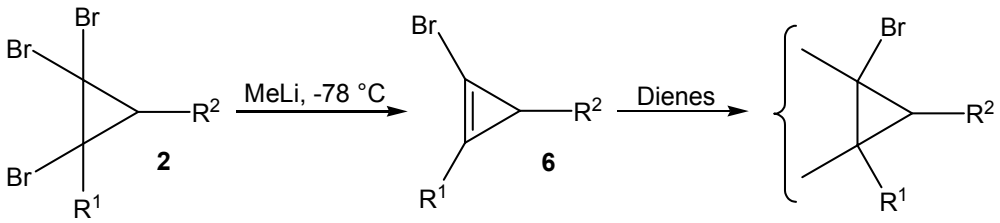


Scheme 3.6

Since deactivated 1-bromo-1-phenylethene furnished **2l** in acceptable yield with the Xu-Brinker method employing ultrasound irradiation to a slurry of bromoform, finely ground NaOH and olefin (Table 3.2; entry 5),[8] it would also be interesting to try this procedure in the preparation of **2i-2k**.

3.3 Metal-halogen exchange

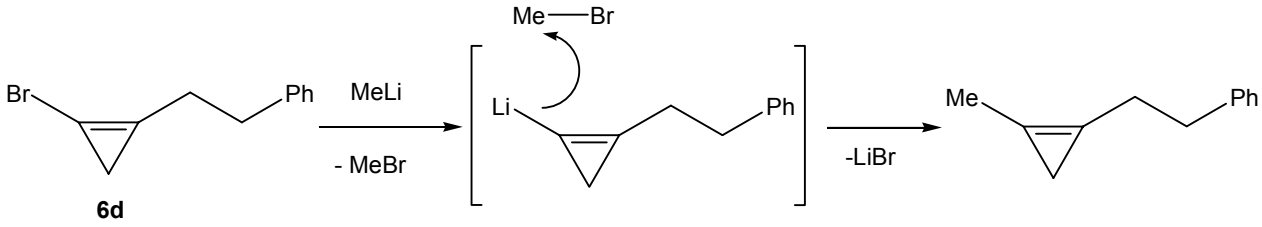
In order to find the optimum conditions for the whole process from the starting material **2**, via 1-bromocyclopropenes **6** to the [4+2] cycloadducts (Scheme 3.7), exploratory experiments were performed with some of the cyclopropanes, varying the relative amount of MeLi and the reaction temperatures.



Scheme 3.7

When the relative amount of MeLi was varied in the reaction with 1,1,2-tribromo-2-(2-phenylethyl)cyclopropane (**2d**), it appeared that even a moderate excess lead to lithiation of the primary product 1-bromo-2-(2-phenylethyl)cyclopropene (**6d**) and subsequent formation of by-products. Thus, when **2d** was treated with more than 1.2 equivalents of MeLi, 2-methyl-1-(2-phenylethyl)cyclopropene was obtained in addition to **6d**.

The hydrocarbon is conceivably formed in a two-step process, *i.e*. lithiation of **6d** and formation of 1-lithio-2-(2-phenylethyl)cyclopropene, which reacts with MeBr (Scheme 3.8), and its formation is no surprise when results reported in the literature are considered.[13,14] It was therefore decided to perform the conversion of **2** to **6** with a very small (1-3%) excess of MeLi.



Scheme 3.8

It was therefore important to standardise the MeLi on a regular basis to ensure that the concentration was accurate. This was done by performing double titrations of MeLi against butan-2-ol in xylene with *N*-phenyl-1-naphthylamine as an indicator giving a distinct change of colour from yellow to white at the point of equivalence.[15]

The methyl protons in 2-methyl-1-(2-phenylethyl)cyclopropene resonate at 1.96 ppm as a triplet. Since the methylene group in the cyclopropene ring gives rise to a singlet at 0.82 ppm, the 1.5 Hz coupling constant for the methyl group is probably due to a long-range coupling ($^5J_{H,H}$) out of the ring (Figure 3.1). In contrast to these findings, the methylene group in the ring of **6d** appeared as a triplet ($^4J_{H,H}$=0.5 Hz) at 1.55 ppm (Figure 3.2).

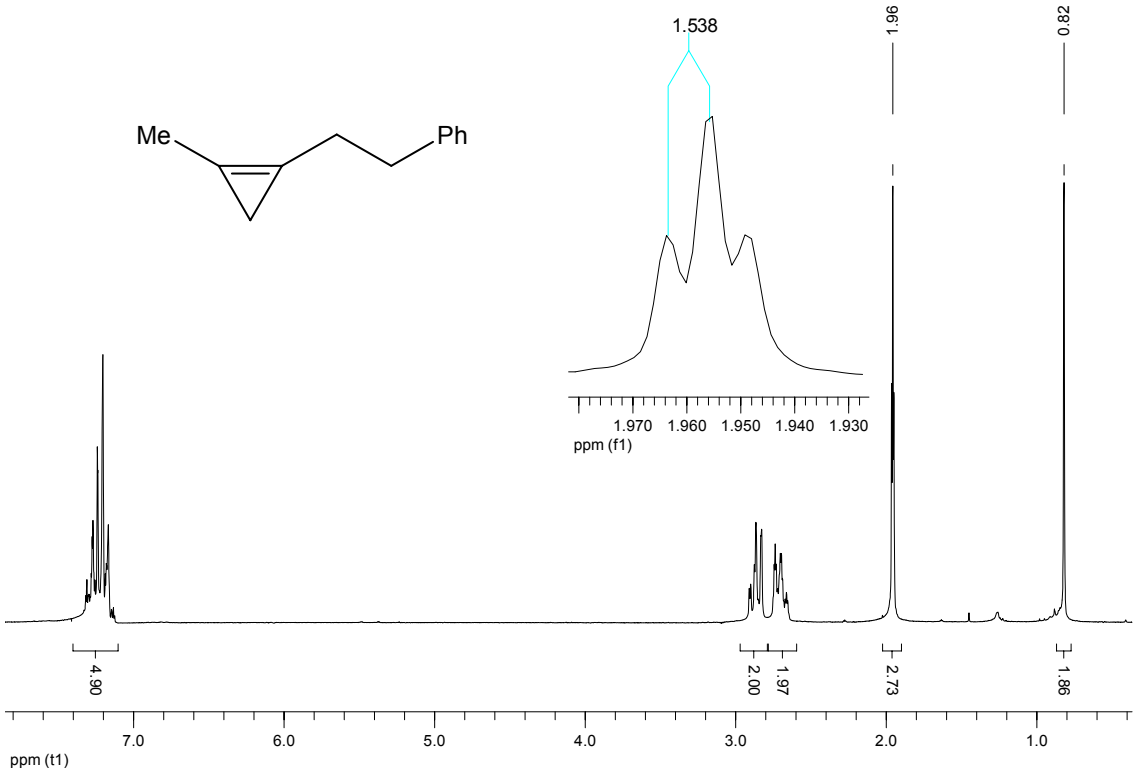


Figure 3.1 ^{1}H NMR spectrum of 2-methyl-1-(2-phenylethyl)cyclopropene.

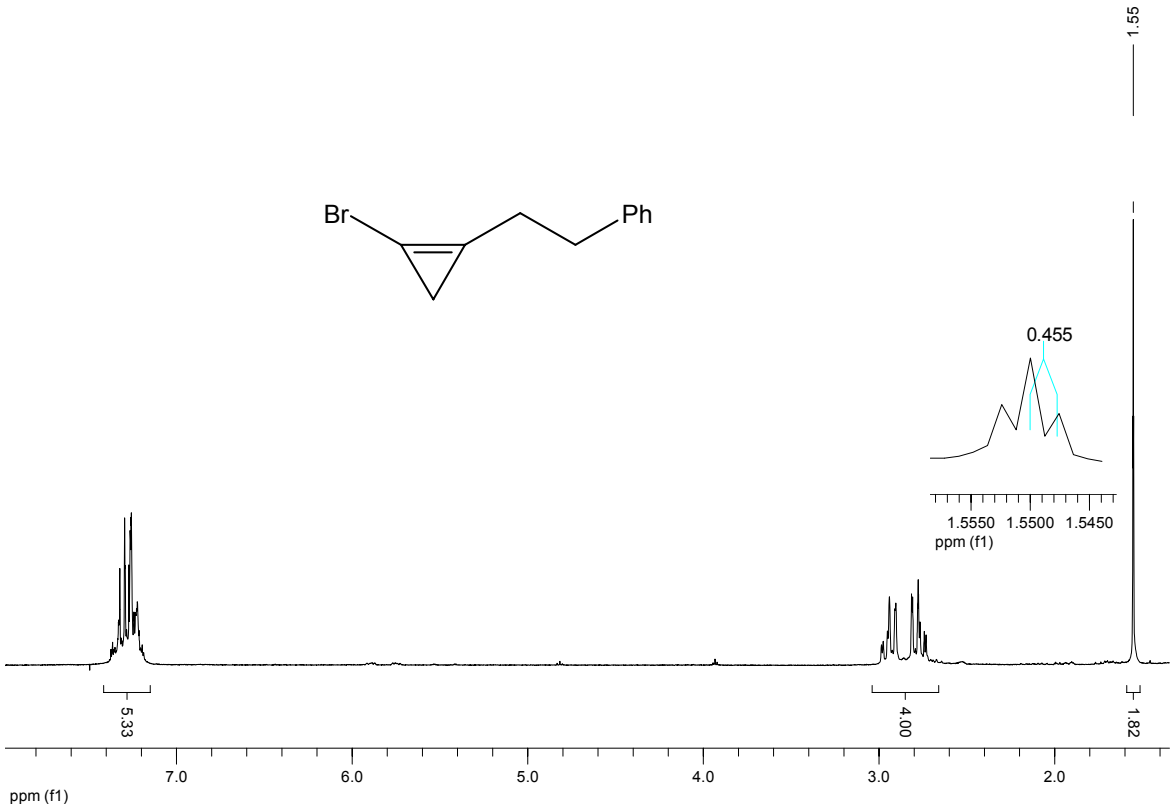
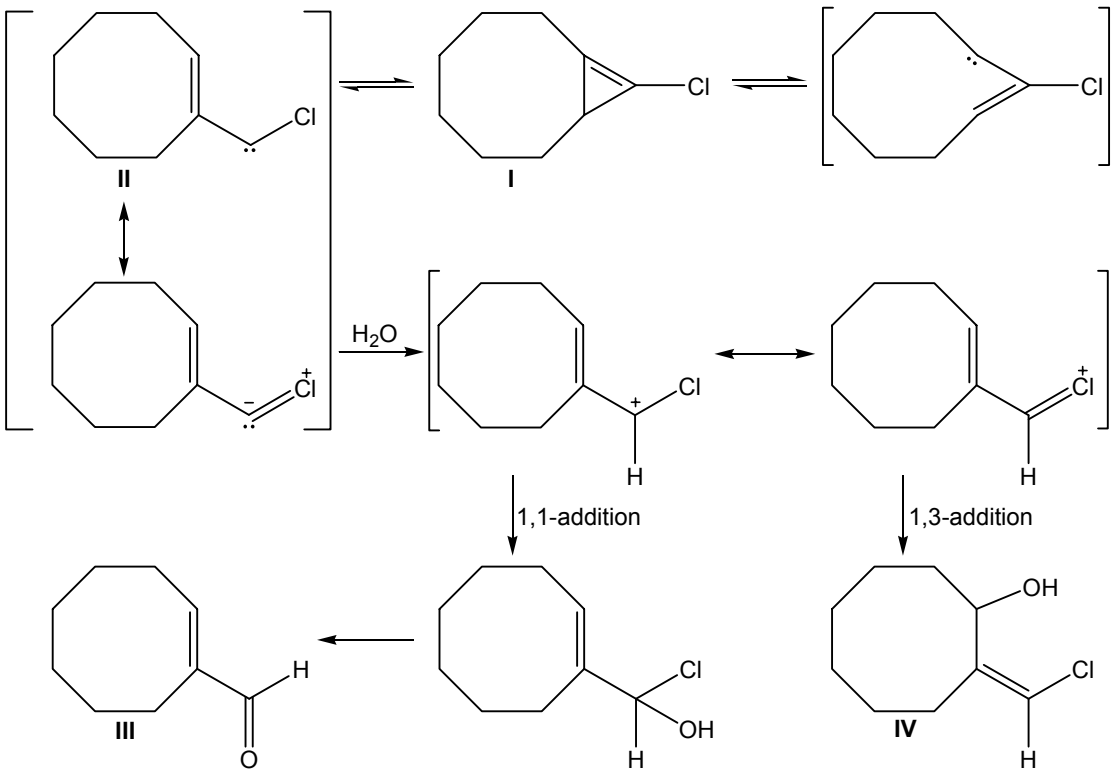


Figure 3.2 ^{1}H NMR spectrum of 1-bromo-2-(2-phenylethyl)cyclopropene (**6d**).

Secondly, when generating **6** from **2** it appeared to be important to control the reaction temperatures properly due to the somewhat limited stability of the primary products, *i.e.* 1-bromocyclopropene derivatives **6**. Treatment of 1,9,9-tribromobicyclo[6.1.0]nonane (**2h**) with MeLi afforded 9-bromobicyclo[6.1.0]non-1(9)-ene (**6h**) in quantitative yield. It decomposed rapidly at room temperature, but turned out to be stable at least for one week in the refrigerator.[16] The products from an analogous reaction with 9-chlorobicyclo[6.1.0]non-1(9)-ene have been studied by Lee *et al.*, who isolated an aldehyde (**III**) and an allylic alcohol (**IV**) when the compound was kept at room temperature in the presence of water (Scheme 3.9).[17] It therefore seems preferable to carry out the Diels-Alder reaction well below room temperature if the reaction rates so permit.



Scheme 3.9

Finally, it also appeared that the stability of some 1-bromocyclopropenes could be increased by storing the compounds as solutions in THF. For instance, treatment of 1,1,2-bromo-2-octylcyclopropane (**2c**) with 1.02 equivalents of MeLi gave 1-bromo-2-octylcyclopropene (**6c**), which was fairly stable in THF at room temperature for approximately five days (Chart 3.1), but which turned out to decompose in a matter of hours when kept neat under otherwise identical conditions.

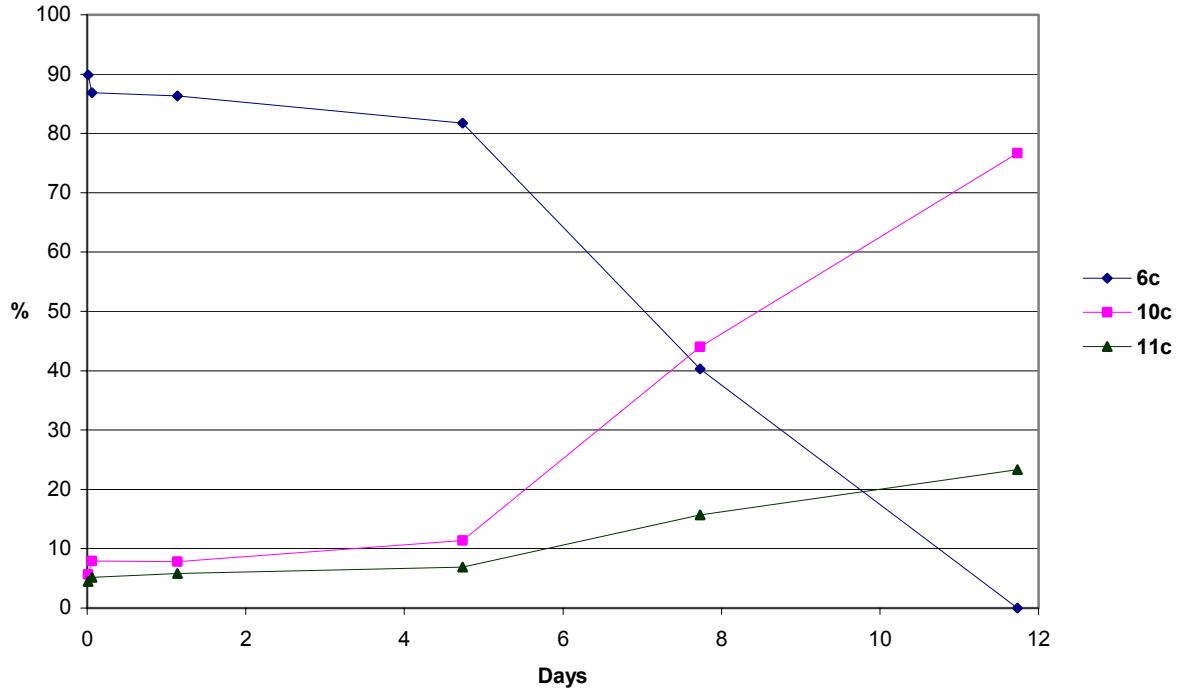
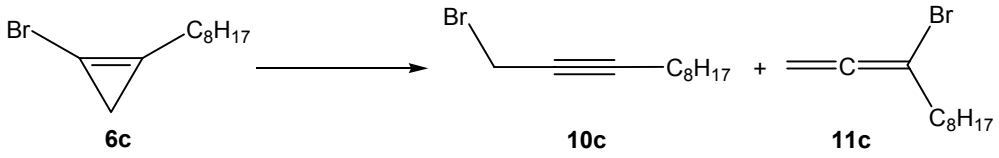


Chart 3.1 Decomposition of 1-bromo-2-octylcyclopropene (**6c**) in THF at room temperature. At the first point of measure, 15 minutes after the completion of the addition of MeLi, the relative amount of **6c** was approximately 90%.

Two rearrangement products, an acetylene and an allene, were formed in a 3:1 ratio and identified as 1-bromoundec-2-yne (**10c**) and 3-bromoundeca-1,2-diene (**11c**) on the basis of thorough spectroscopic analyses (Scheme 3.10).



Scheme 3.10

A characteristic frequency of 2233 cm^{-1} could be seen in the IR spectrum of the acetylene **10c**, due to the stretch of the substituted triple bond (Figure 3.3).[18] The cumulated double bond in allenes are reported to give rise to medium bands in the region 1900-2000 cm^{-1}, but in the IR spectrum of the allene **11c** this was only seen as a very weak absorption at 1957 cm^{-1} (Figure 3.4).[18]

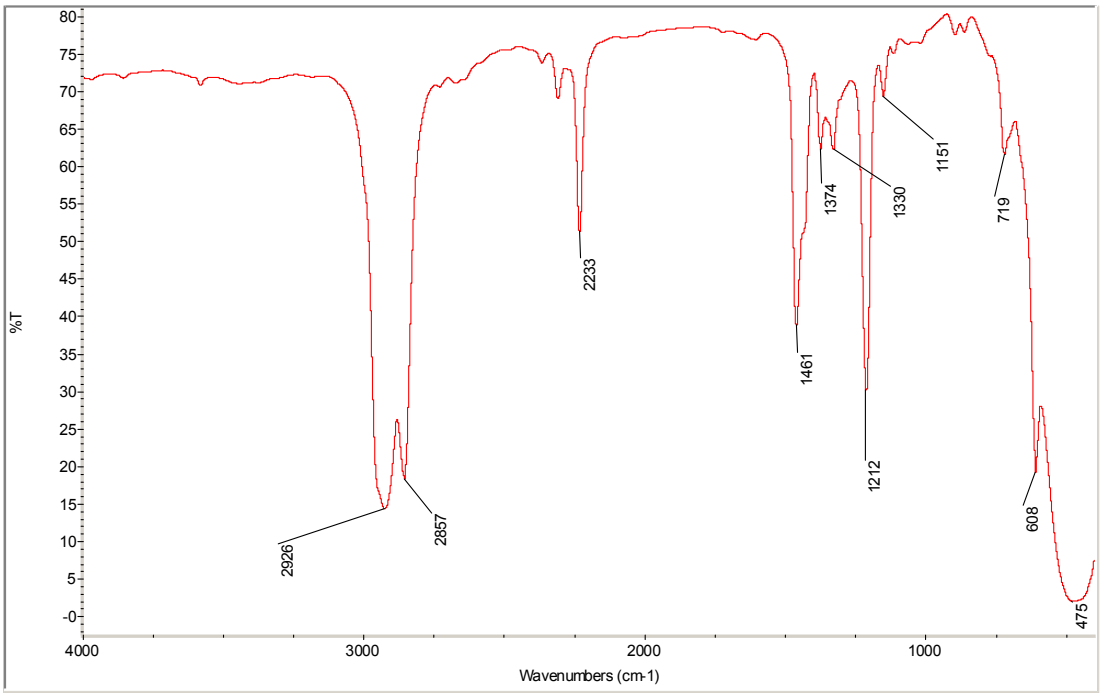


Figure 3.3 IR spectrum of 1-bromoundec-2-yne (**10c**) with the characteristic triple-bond stretch at 2233 cm^{-1}.

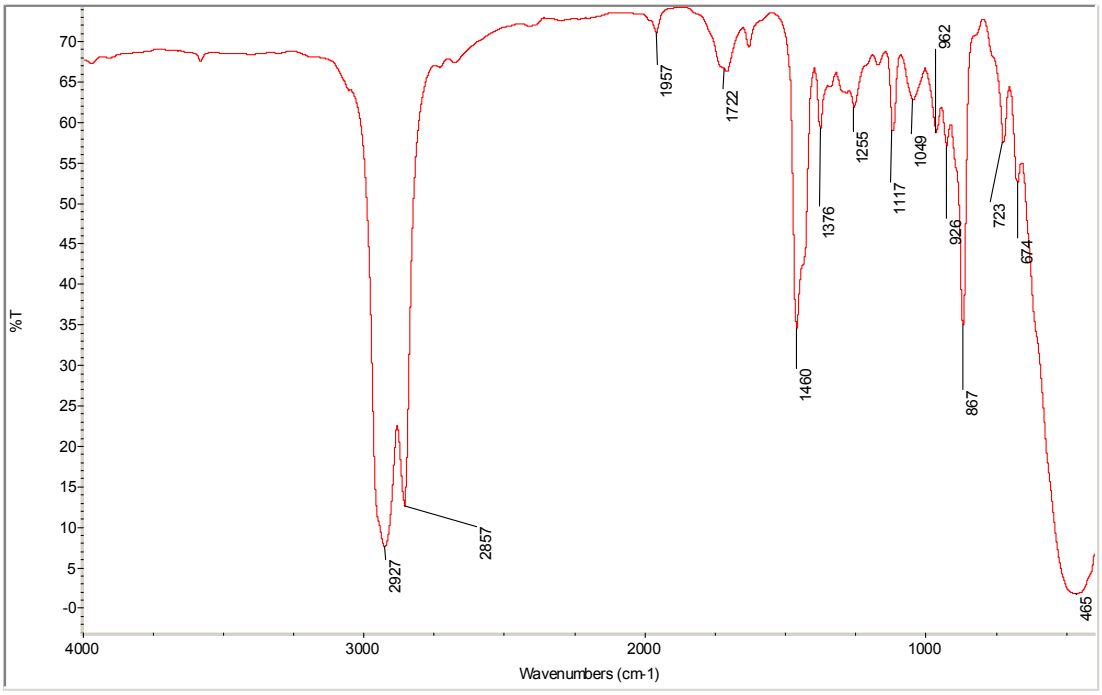


Figure 3.4 IR spectrum of 3-bromoundeca-1,2-diene (**11c**) with a very weak stretch from the cumulated double bond at 1957 cm^{-1}.

In the ^{13}C NMR spectrum of **10c** the quaternary carbon atoms appear at 88.2 and 75.1 ppm (Figure 3.5), while the quaternary carbon atoms in **11c** appear at 203.9 and 93.1 ppm (Figure 3.6). The low shielding, giving shift values between 215 and 195 ppm, is a striking feature for the central carbon atom of all allene derivatives.[19]

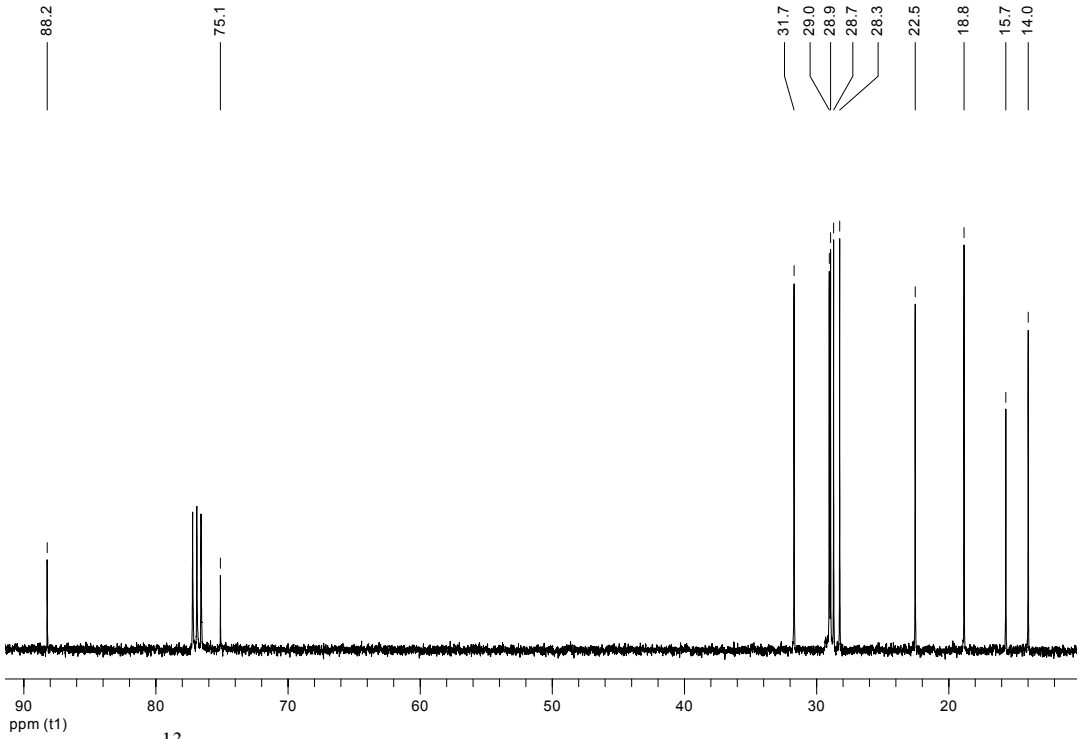


Figure 3.5 The ^{13}C NMR spectrum of 1-bromoundec-2-yne (**10c**) with the characteristic signals of the acetylenic carbon atoms at 88.2 and 75.1 ppm.

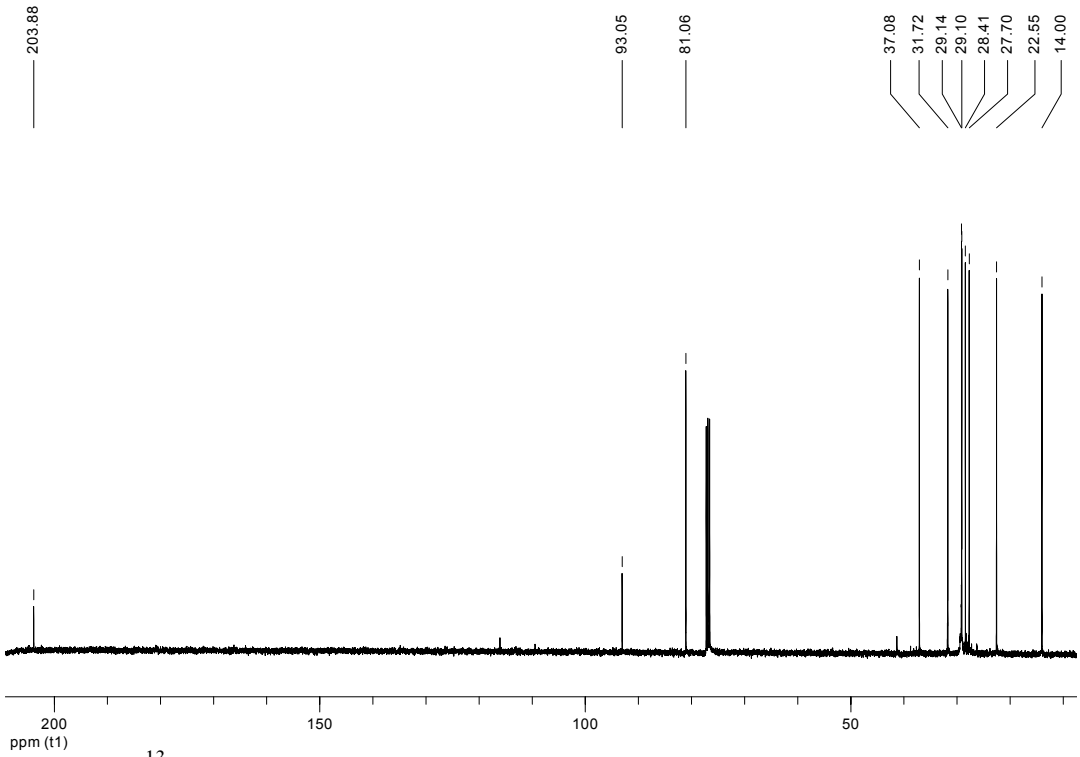


Figure 3.6 The ^{13}C NMR spectrum of 3-bromoundeca-1,2-diene (**11c**) with the characteristic signal at 203.9 ppm from the central quaternary carbon atom (C-2).

Another striking feature of both the acetylene **10c** an the allene **11c** is the long-range coupling ($^5J_{H,H}$) seen in the ^1H NMR spectra, through the triple bond and the cumulated double bonds of respectively 2.4 and 3.2 Hz (Figure 3.7 and 3.8).

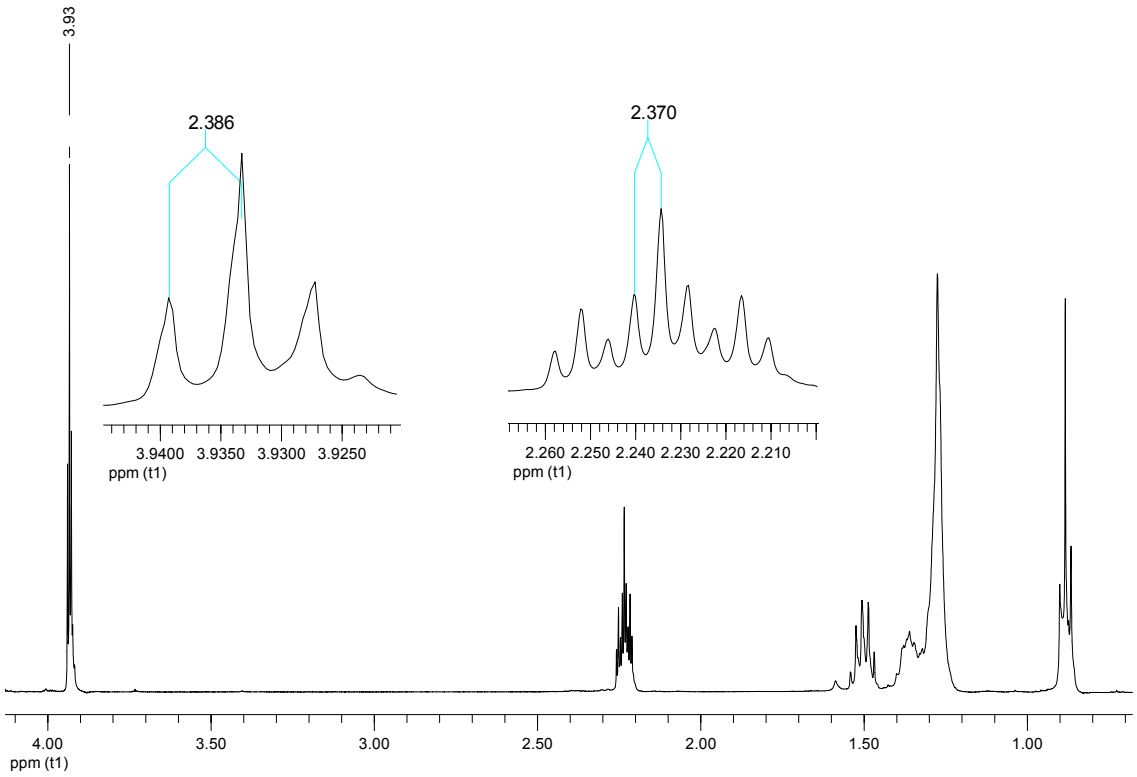


Figure 3.7 ^{1}H NMR spectrum of 1-bromoundec-2-yne (**10c**) with the characteristic long-range coupling through the triple bond.

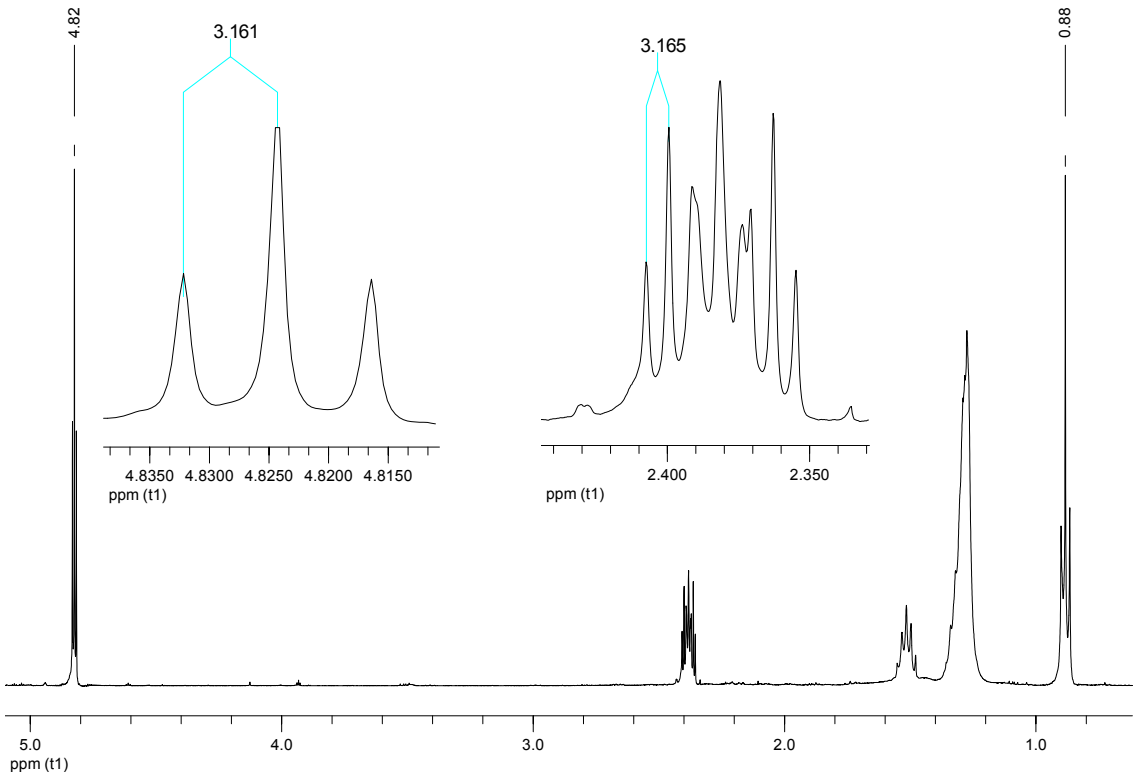
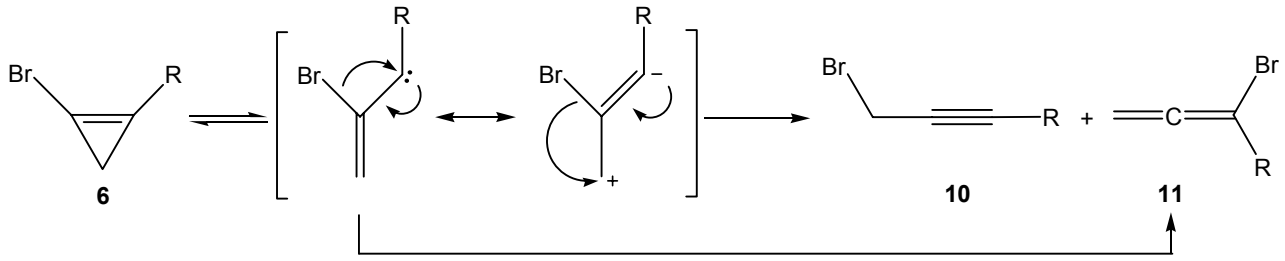


Figure 3.8 ^{1}H NMR spectrum of 3-bromoundeca-1,2-diene (**11c**) with a characteristic long-range coupling through the cumulated double bonds.

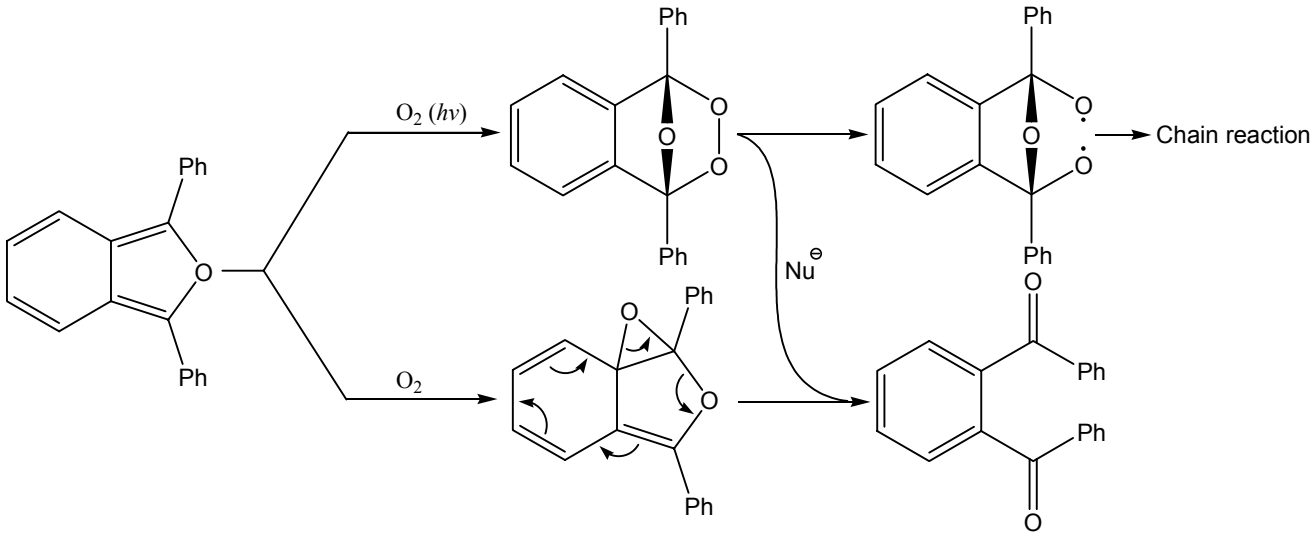
1-Bromo-2-pentylcyclopropene (**6b**), 1-bromo-2-cyclohexylmethylcyclopropene (**6e**) and 1-bromo-2-phenylcyclopropene (**6l**) rearranged in a similar fashion as **6c**, forming acetylenes (**10**) and allenes (**11**) in variable amounts. On the basis of reports published by Billups and Bachman,[20] and Baird and co-workers formation of both compounds may be explained in terms of a 1,2-bromo shift in an intermediate vinylcarbene as outlined in Scheme 3.11.[21] It is interesting to observe that 1-bromoalk-1-ynes, which conceivably could result from a 1,2-alkyl shift in the alternative vinylcarbene, carrying a bromo substituent at the divalent carbon, were not observed.



Scheme 3.11

3.4 Trapping of substituted 1-bromocyclopropenes

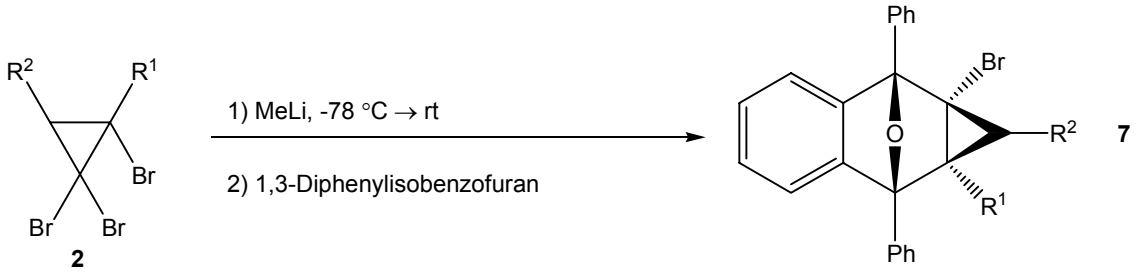
In order to minimise the possibility for the by-product formation discussed above, the Diels-Alder reactions were carried out below room temperature. Three dienes were employed, *viz*. 1,3-diphenylisobenzofuran (DPIBF), cyclopentadiene, and furan, which have been reported to react with some cyclopropene derivatives, albeit with different rates; thus, DPIBF and cyclopentadiene react smoothly with such dienophiles at room temperature,[22-24] whereas furan reacts more reluctantly and therefore can be used to uncover reactivity differences among the cyclopropene derivatives.[25] A deficiency of the diene was used in the experiments with both DPIBF and cyclopentadiene, because unreacted DPIBF proved difficult to remove, while dicyclopentadiene formation hampered the product isolation. Removal of DPIBF could be achieved by oxidation with air,[26,27] but the oxidation was slow and a complete conversion of DPIBF to *o*-benzoylbenzophenone took several days (Scheme 3.12).



Scheme 3.12

3.4.1 *Diels-Alder reactions with DPIBF*

When cyclopropenes **6a**-**6l** were reacted with DPIBF (Scheme 3.13), the corresponding cycloadduct (**7**) was isolated in good to excellent yield in all cases except one, *viz*. **7g** (R^1=*tert*-butyl) which was isolated in 33% only (Table 3.3).



Scheme 3.13

Table 3.3 1,2-Dehalogenation of 2-substituted 1,1,2-tribromocyclopropanes (**2**) with MeLi and subsequently trapping of **6** with DPIBF.

Entry	R^1	R^2	Cyclopropane	Yields of *exo*-**7** (%)
1	Propyl	H	**2a**	84
2	Pentyl	H	**2b**	86
3	Octyl	H	**2c**	80
4	2-Phenylethyl	H	**2d**	75
5	Cyclohexylmethyl	H	**2e**	82
6	Isobutyl	H	**2f**	63
7	*tert*-Butyl	H	**2g**	33
8	—$CH_2CH_2CH_2CH_2CH_2CH_2$—		**2h**	94
9	Phenoxymethyl	H	**2i**	81
10	(4-Methylphenoxy)methyl	H	**2j**	76
11	(4-Bromophenoxy)methyl	H	**2k**	—
12	Phenyl	H	**2l**	88

All cycloadducts were formed and isolated as a single isomer, which in all cases was assigned the *exo* configuration on the basis of spectroscopic evidence. ^{1}H NMR spectroscopy appeared to be particularly informative in the case of all compounds apart from 10-bromo-14-oxa-1,11-diphenyl-12,13-benzotetracyclo[9.2.1.$0^{2,9}$.$0^{2,10}$]tetradecane (**7h**) because one of the cyclopropyl protons appeared consistently at a much lower field than the other: The signal associated with the proton *anti* to the oxygen atom was found at 1.69-2.17 ppm, while the *syn* proton appeared between 2.80 and 3.09 ppm (Figure 3.7, Table 3.4). This difference may conceivably be attributed to the diamagnetic anisotropy of the oxygen atom, which causes a decrease in the shielding of the *syn* proton relative to the *anti* proton in the *exo*-cycloadduct (Figure 3.9).[28]

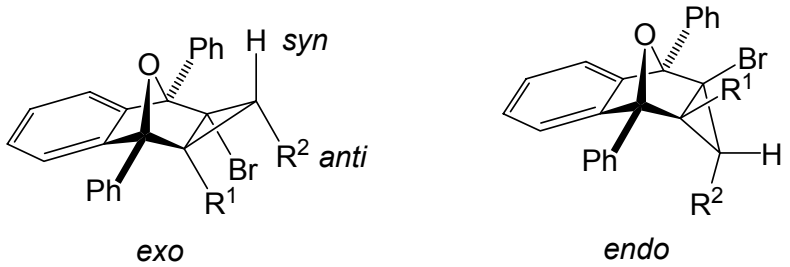


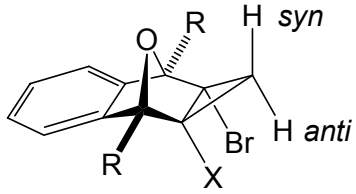
Figure 3.9 An illustration of two possible cycloadducts **7** from the Diels-Alder reaction between **6** and DPIBF.

Table 3.4 ^{1}H NMR data of DPIBF cycloadducts **7**.

Entry	*Exo*-cycloadducts	δ_H (ppm)	
		H_{syn}	H_{anti}
1	**7a**	2.80	1.69
2	**7b**	2.80	1.71
3	**7c**	2.80	1.70
4	**7d**	2.85	1.77
5	**7e**	2.93	1.76
6	**7f**	2.94	1.79
7	**7g**	3.04	2.17
8	**7i**	2.98	2.07
9	**7j**	2.96	2.06
10	**7k**	3.09	1.90

Additionally, the spectral data of cycloadducts **7** were in accordance with those previously reported in the literature for *exo*-cycloadducts produced in the Diels-Alder reaction between 1,2-disubstituted cyclopropenes and isobenzofurans (Table 3.5).[29]

Table 3.5 ^{1}H NMR data of *exo*-cycloadducts.[29]



Entry	R	X	δ_H (ppm)	
			H_{syn}	H_{anti}
1	Ph	Cl	3.20	2.18
2	Ph	Br	3.22	2.13
3	H	Cl	2.79	1.82
4	Ph	$SiMe_3$	2.96	1.98
5	H, $SiMe_3$	Cl	2.68	1.81

The *exo*-assignment of cycloadducts **7** was also in agreement with that reported by Binger *et al*.,[30] which showed that the formation of the *exo* isomer at the expense of *endo* was due to the lack of a favourable secondary orbital interaction (SOI) in the transition state. The importance of SOI in the Diels-Alder reaction is illustrated in Figure 3.10.

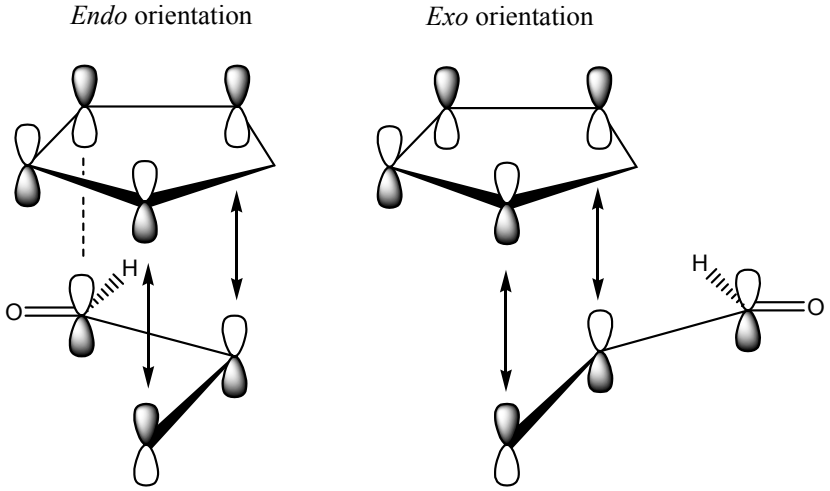
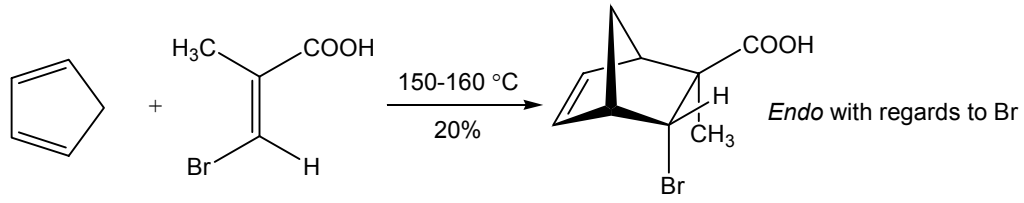


Figure 3.10 The *exo*- and *endo*-transition states in the Diels-Alder reaction between cyclopentadiene and 2-propenal. SOI is indicated by dotted lines (---), while primary orbital interactions leading to bonds between atoms are indicated by arrows (↔). The figure shows the overlap between $HOMO_{diene}$ and $LUMO_{dienophile}$.

Furthermore, it is noteworthy that halogen-substituted dienophiles are believed to favour *endo* addition to dienes, and in some cases the halogen substituent may even compete with carboxyl groups for the *endo* orientation (Scheme 3.14).[29,31,32]



Scheme 3.14

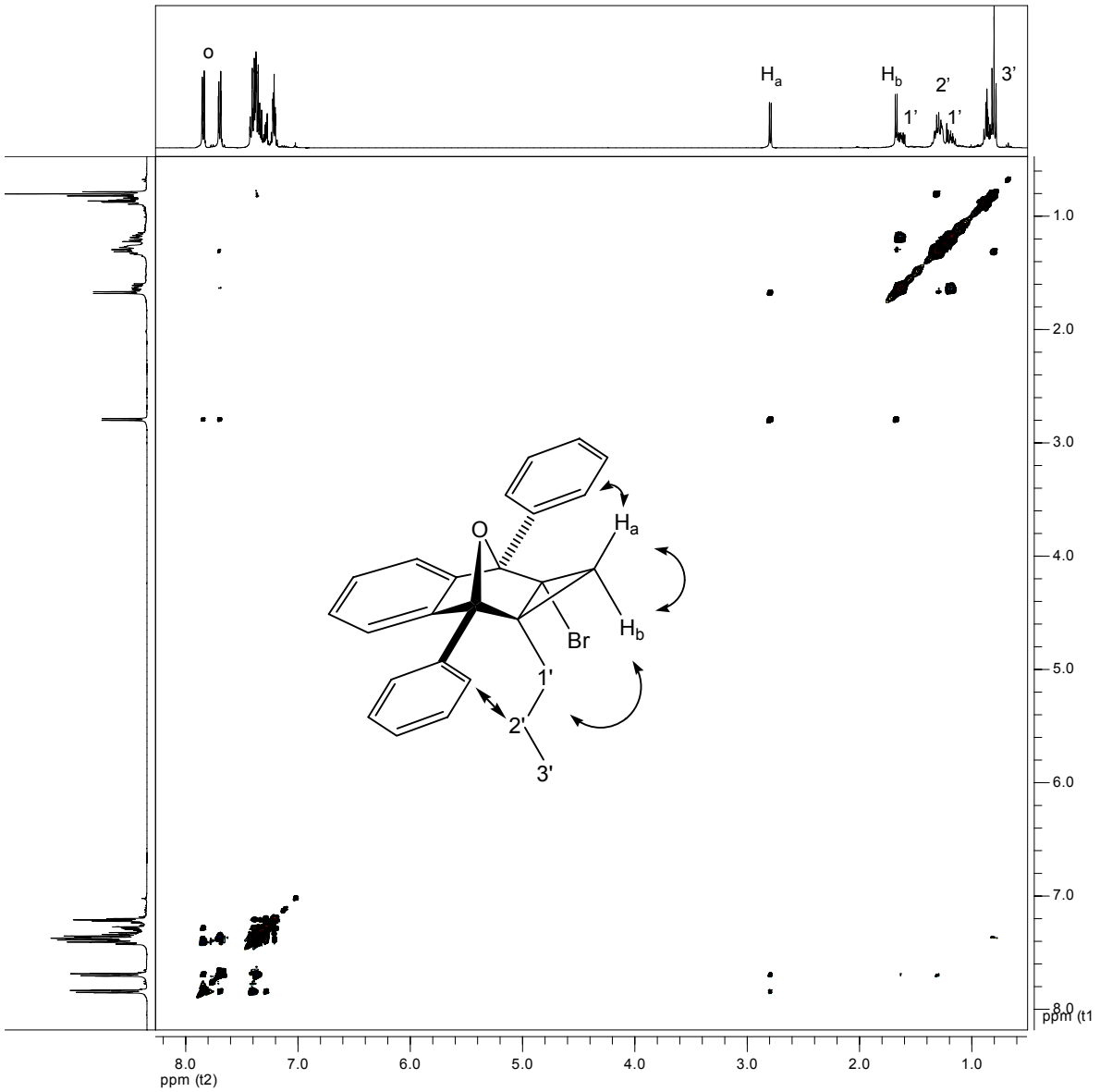


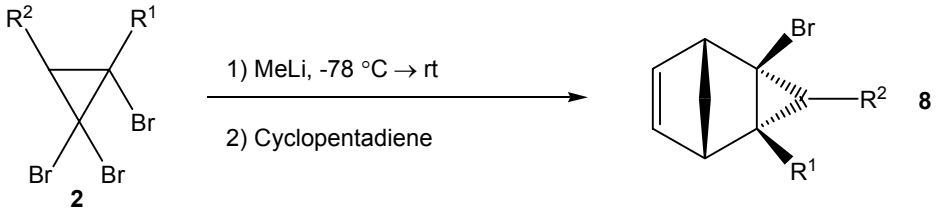
Figure 3.11 NOESY spectrum of 2-bromo-8-oxa-1,5-diphenyl-4-propyl-6,7-benzotricyclo-[3.2.1.$0^{2,4}$]octane (**7a**).

In order to support the assignment of the configuration of cycloadducts **7** a number of 2D experiments were performed, and especially the NOESY experiment of **7a**, which reveals direct (through-space) couplings in the molecule, gave some useful information (Figure 3.11). As expected in the *exo*-isomer, the *syn* proton H_a does not couple to the alkyl chain on the

other side of the molecule (H-1', H-2' and H-3'), but well-defined cross-peaks to the *ortho*-protons in both phenyl rings connected to C-1 and C-5 can be seen. There is also a through-space relationship between H_a and H_b, but due to overlap between the signals from H_b and H-1' it is difficult to determine whether H_b couples to the alkyl chain or not. However, a coupling between H-2' and the *ortho*-protons in the phenyl ring connected to C-5 can be seen. Hence, the multiplet at 7.68-7.72 might be assigned to these *ortho*-protons, while the multiplet at 7.82-7.86 originates from the *ortho*-protons in the phenyl ring connected to C-1.

3.4.2 *Diels-Alder reactions with cyclopentadiene*

When DPIBF was replaced by cyclopentadiene in the Diels-Alder reaction (Scheme 3.15), the addition to cyclopropenes **6a-6l** and the formation of the corresponding cycloadducts (**8a-8l**) proceeded much slower and were significantly less efficient than when DPIBF was used.



Scheme 3.15

Table 3.6 1,2-Dehalogenation of 2-substituted 1,1,2-tribromocyclopropanes (**2**) with MeLi and subsequently trapping of **6** with cyclopentadiene.

Entry	R^1	R^2	Cyclopropane	Yields of *endo*-**8** (%)
1	Propyl	H	**2a**	22
2	Pentyl	H	**2b**	29
3	Octyl	H	**2c**	35[a]
4	2-Phenylethyl	H	**2d**	56[a]
5	Cyclohexylmethyl	H	**2e**	19[a,b]
6	Isobutyl	H	**2f**	26
7	*tert*-Butyl	H	**2g**	12[c]
8	—$CH_2CH_2CH_2CH_2CH_2CH_2$—		**2h**	72
9	Phenoxymethyl	H	**2i**	70
10	(4-Methylphenoxy)methyl	H	**2j**	74
11	(4-Bromophenoxy)methyl	H	**2k**	—
12	Phenyl	H	**2l**	54

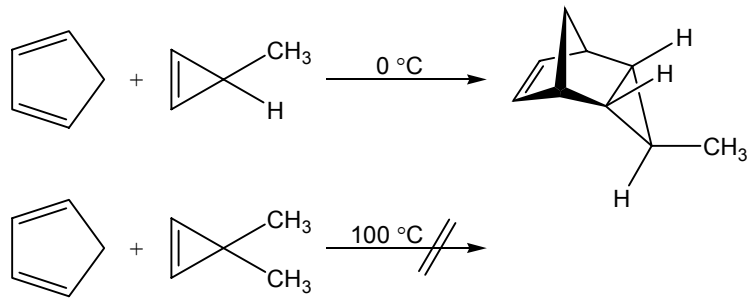
[a] 1-Bromocyclopropene (**6**) was isolated.
[b] 1-Bromo-4-cyclohexylbut-2-yne (**10e**) was isolated.
[c] The yield is based on ^{1}H NMR data from a 3:6:1 mixture of **2k**, and *endo*-**8k** and *exo*-**8k**.

The yields ranged from poor to good, but in all cases cycloadduct **8** was obtained in lower yield than the corresponding cycloadduct **7**. The best yields were furnished when substituent R^1 contained an aromatic moiety (Table 3.6; entries 4, 9, 10 and 12), and this trend clearly indicates the influence of some sort of π-π interaction, which overcomes the steric repulsion otherwise present (Table 3.6; entries 5-7). Since monitoring of the reaction by TLC and GC showed a rapid and complete conversion of **2** to **6**, the low yields of adducts **8** must be due to poor reactivity towards cyclopentadiene. It is therefore not surprising that considerable amounts of unreacted **6** were isolated in some cases (Table 3.6; entries 3-5; 39, 13, and 35%, respectively), and in the reaction with **2e** 1-bromo-4-cyclohexylbut-2-yne (**10e**, 5%) was also isolated.

The reactions with cyclopentadiene proceed in accordance with *Alder's endo* rule[33] in all cases except one, *viz.* the reaction with **2g** (R^1=*tert*-butyl) where the *endo* and *exo* isomers were formed in a 6:1 ratio (Figure 3.12).

Figure 3.12 Illustration of the *exo* and *endo* isomers of cycloadducts **8**.

The small difference in the shift values of the cyclopropyl protons in **8** supported the assignment. In **8l** (R^1=phenyl) the two protons even gave signals that overlapped so extensively that a broad singlet appeared at 1.78 ppm in the ^{1}H NMR spectrum. In addition to favourable secondary orbital interactions, steric hindrance caused by the methylene bridge is probably a decisive factor for the outcome of the reaction (Figure 3.12). This reasoning is supported by observations reported by Closs *et al*., who isolated only the *endo* adduct when 3-methylcyclopropene reacted with cyclopentadiene, whereas no adduct was observed at all when 3,3-dimethylcyclopropene was reacted under similar conditions (Scheme 3.16).[34,35]



Scheme 3.16

Some interesting multiplets were seen in the ^{1}H NMR spectra of cycloadducts **8a-8l** due to extensive indirect (through-bond) couplings between hydrogen nuclei; illustrated by the ^{1}H NMR spectrum of **8d** (R^{1}=2-phenylethyl) (Figure 3.13).

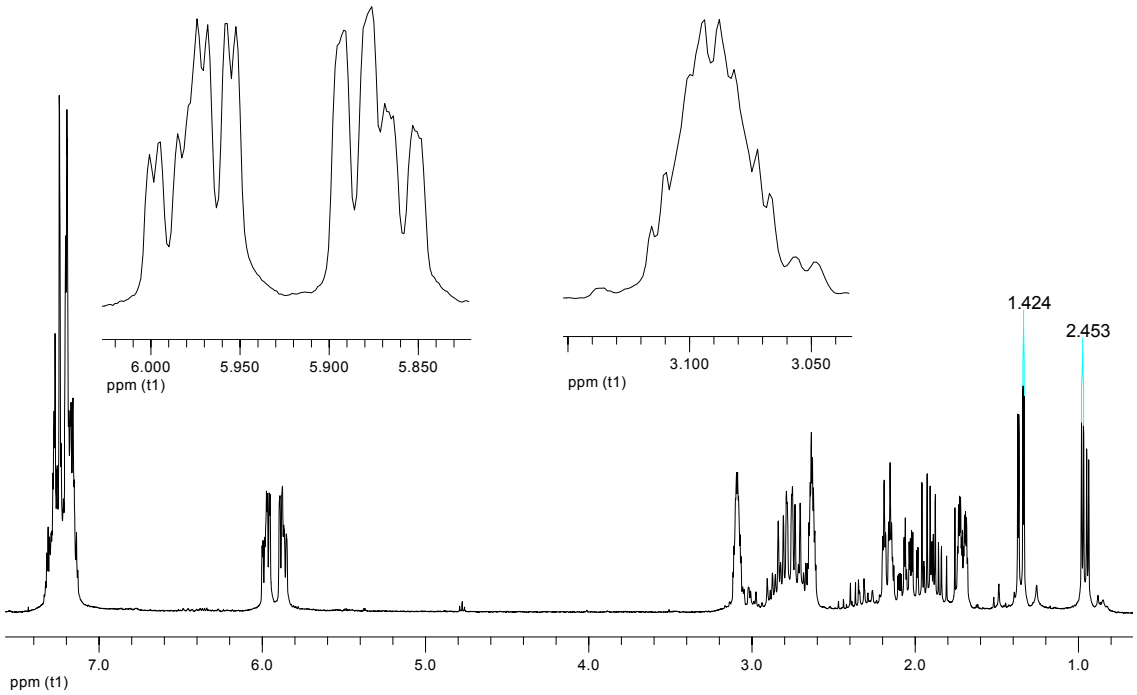


Figure 3.13 The ^{1}H NMR spectrum of 2-bromo-4-(2-phenylethyl)tricyclo[3.2.1.0^{2,4}]oct-6-ene (*endo*-**8d**) with expansion of some interesting multiplets with extensive coupling. Two long-range coupling constants of 1.4 and 2.5 Hz are also indicated.

The two protons connected to C-3 resonate at 0.96 and 1.35 ppm (Figure 3.13), and appear as double doublets due to *geminal* couplings to each other and long-range couplings within the bicyclic framework or to the alkyl side-chain. Many indirect couplings between the bridge-head protons connected to C-1 and C-5 and other protons in *endo*-**8d** may be visualised: Since H-1 and H-5 may take part in three *vicinal* couplings as well as four and six $^{4}J_{H,H}$ long-range couplings respectively, these protons can probably be assigned to the complex multiplets at

2.61-2.66 ppm and 3.07-3.12 ppm (Figure 3.13). The vinylic protons H-6 and H-7 resonate at 5.85-6.00 ppm (Figure 3.13), and may take part in two *vicinal* and three $^{4}J_{H,H}$ couplings each.

2D NMR experiments were crucial in the structure elucidation of this compound. The HSQC experiment, which correlates proton and carbon chemical shifts through single-bond couplings (optimised for $^{1}J_{C,H}$=150 Hz), showed that the multiplet at 1.68-1.74 ppm and the triple doublet at 2.17 ppm were connected to the same carbon atom at 59.8 ppm. The two multiplets at 2.61-2.66 and 3.07-3.12 ppm were connected to two different carbon atoms at respectively 48.1 and 54.7 ppm. This proves that the former multiplet and triple doublet can be attributed to the methylene-bridge protons connected to C-8, while the latter multiplets originate from the bridge-head protons connected to C-1 and C-5.

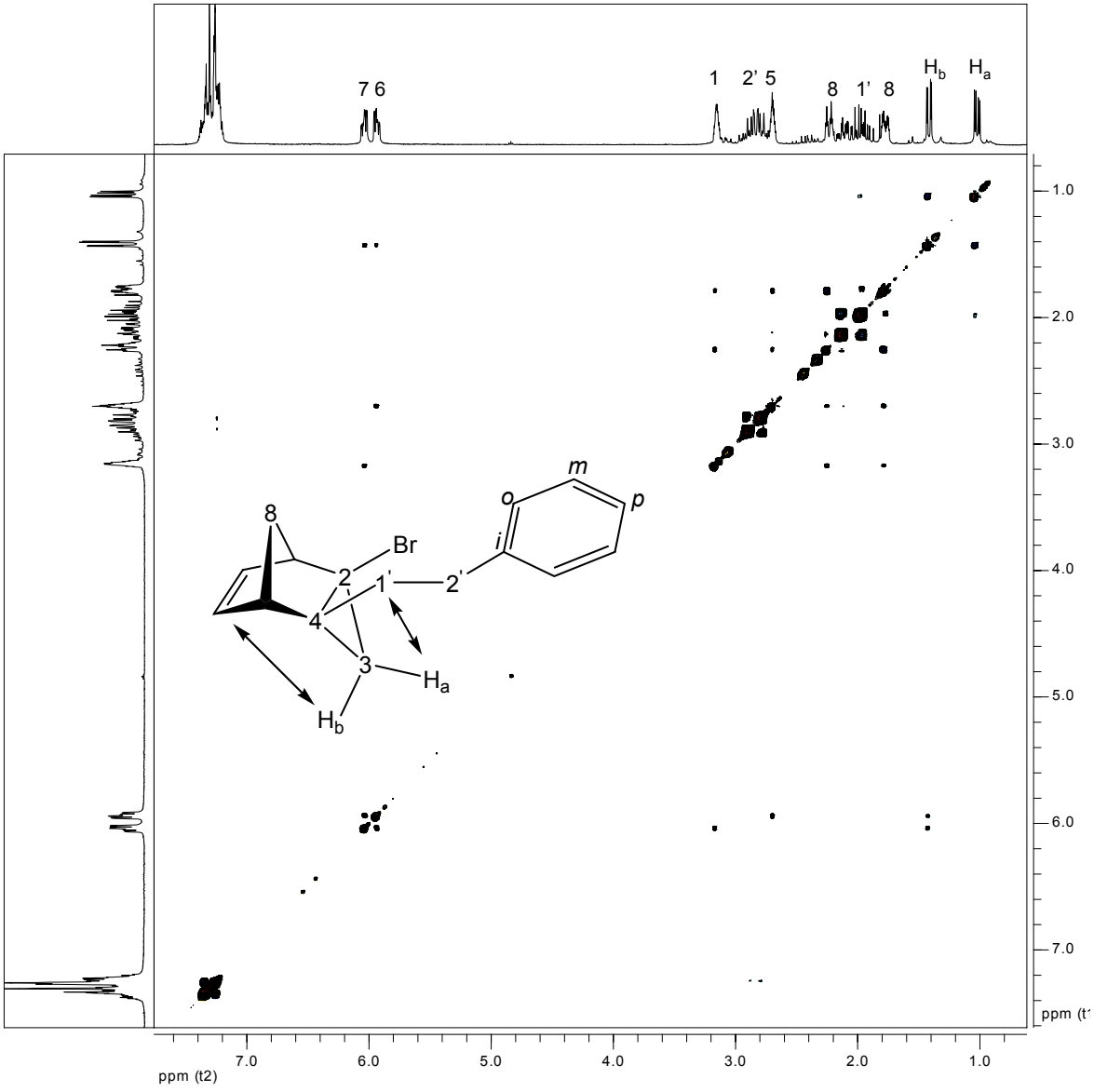


Figure 3.14 NOESY spectrum of *endo*-**8d**.

The HMBC experiment, which was optimised for long-range carbon-proton couplings of 8 Hz, showed that the multiplet at 1.81-2.14, attributed to the protons in the methylene group at C-1', coupled to the carbon atom at 48.1 ppm. Since a coupling to the carbon atom at 54.7 ppm is not seen it is therefore reasonable to assume that this carbon atom is C-1, while the one at 48.1 ppm may be attributed to C-5. In the HSQC spectrum C-1 was coupled to the multiplet at 3.07-3.12 ppm, while C-5 was coupled to the multiplet at 2.61-2.66 ppm.

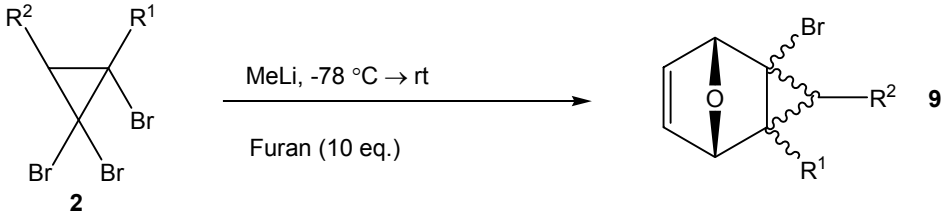
The NOESY spectrum of *endo*-**8d** shows that one of the cyclopropyl protons (H_b) is in close contact with both H-6 and H-7 in the double bond, thus giving rise to two strong cross-peaks (Figure 3.14). This coincides with the fact that the double doublet from H_b at 1.35 ppm appears at a higher field than the signal from H_b in the corresponding *exo*-**7d** at 1.77 ppm (Table 3.4; entry 4); which may be explained by increased shielding of H_b in *endo*-**8d** due to magnetic anisotropy from the close-encountering double bond. Cross-peaks between H-6 and H-7 and any of the protons connected to C-8 can not be seen, but there seems to be a strong cross-peak between H-1' and one of the proton connected to C-8 which resonates at 1.68-1.74. Cross-peaks between H-1' and H_a can also be observed, but H-2' does not exhibit this correlation to H_a. It is also interesting to note that the only direct coupling between the phenyl ring and the rest of the molecule is indicated by weak cross-peaks to H-2'. This indicates that the phenyl ring is orientated as far away as possible from both the cyclopropyl protons (H_a and H_b) and the protons in the methylene bridge at C-8.

The double doublet at 0.96 ppm from H_a is, besides a *geminal* coupling of 6.3 Hz to H_b on C-3, most likely coupled to one of the methylene-bridge protons on C-8, resonating at 1.68-1.75 with a long-range ($^5J_{H,H}$) coupling of 2.5 Hz. This assumption was strongly supported by the COSY experiment, which also showed that the same proton is involved in another long-range coupling ($^5J_{H,H}$) to H-1', besides two *vicinal* couplings to the bridge-head protons H-1 and H-5. However, neither the ^{1}H NMR nor the COSY spectrum clearly indicates to which nuclei the other cyclopropyl proton H_b couples ($J_{H,H}$=1.4 Hz, see Figure 3.13).

3.4.3 *Diels-Alder reactions with furan*

Furan, the least reactive of the dienes used in this study of Diels-Alder reactions, did not react with the cyclopropenes under the conditions employed for cyclopentadiene and DPIBF; this is not surprising considering the fact that Diels-Alder reactions involving furan are usually performed around 80 °C.[22] However, since such a high temperature is incompatible with the relatively low thermal stability of the cyclopropenes, we adopted a modified procedure,

developed by Baird and co-workers,[25] which makes use of a large excess of furan (10 eq.) that is present during the MeLi addition and the generation of **6**. In spite of this modification, however, cycloadduct formation was observed in three reactions only, *viz.* those involving 1-bromo-2-phenoxymethylcyclopropene (**6i**), 1-bromo-2-(4-methylphenoxy)methylcyclopropene (**6j**) and 1-bromo-2-(4-bromophenoxy)methylcyclopropene (**6k**). The corresponding cycloadducts **9i**, **9j** and **9k** were formed as mixtures of the *exo* and *endo* isomers (Scheme 3.17), but due to formation of at least four other products, complete analysis of the reaction mixtures and proper isolation of the cycloadducts were hampered.



Scheme 3.17

Table 3.7 1,2-Dehalogenation of 2-substituted 1,1,2-tribromocyclopropanes (**2**) with MeLi and subsequently trapping of **6** with furan.

Entry	R^1	R^2	Cyclopropane	Yields of *exo*-**9** (%)
1	Propyl	H	**2a**	0
2	Pentyl	H	**2b**	0
3	Octyl	H	**2c**	0[a]
4	2-Phenylethyl	H	**2d**	0[b]
5	Cyclohexylmethyl	H	**2e**	0[b]
6	Isobutyl	H	**2f**	0
7	*tert*-Butyl	H	**2g**	0
8	—$CH_2CH_2CH_2CH_2CH_2CH_2$—		**2h**	0[b]
9	Phenoxymethyl	H	**2i**	46[d]
10	(4-Methylphenoxy)methyl	H	**2j**	49
11	(4-Bromophenoxy)methyl	H	**2k**	46[e]
12	Phenyl	H	**2l**	0[f]

[a] By-products were isolated.
[b] 1-Bromocyclopropene (**6**) was isolated.
[c] The yield is based on ^{1}H NMR data from a 3:6:1 mixture of **2k**, and *endo*-**8k** and *exo*-**8k**.
[d] Pure *exo* (31%) and impure *endo*-**9b** (15%) were isolated.
[e] Pure *exo* (38%) and impure *endo*-**9k** (8%) were isolated.
[f] Traces of *exo*-**9l** was seen in the crude product mixture.

However, it was determined that *exo*-**9i**, *exo*-**9j** and *exo*-**9k** were formed in 31-49% yield (Table 3.7; entries 9-11) and that the corresponding *endo* isomers were obtained in

significantly lower yields (see Chapter 5.5.3). Furthermore, pure samples of *exo*-**9i**, *exo*-**9j** and *exo*-**9k** were isolated in 31, 49 and 38% yield, respectively.

Since cycloadducts **9** contain an oxygen bridge, instead of the methylene bridge in cycloadducts **8**, the ^{1}H NMR spectra of the former cycloadducts were easier to interpret. This is illustrated by the spectrum of *exo*-**9i** where all indirect couplings, apart from those in the aromatic moiety, were assigned (Figure 3.15).

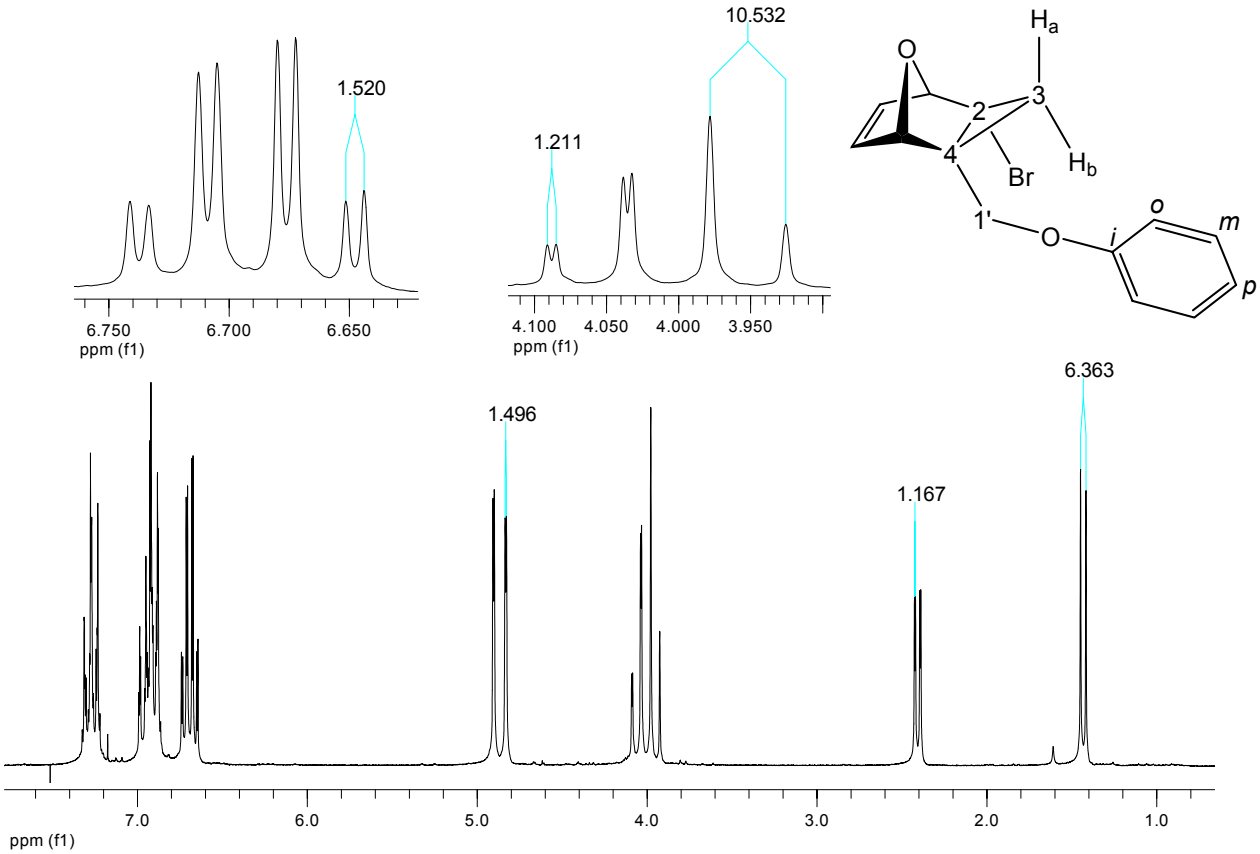


Figure 3.15 ^{1}H NMR spectrum of 2-bromo-8-oxa-4-phenoxymethyltricyclo[3.2.1.0^{2,4}]oct-6-ene (*exo*-**9i**) with some of the indirect coupling constants indicated.

It is fairly evident that H_b, which resonates at 1.44 ppm, is coupled to H_a at 2.41 ppm with a *geminal* coupling constant of 6.4 Hz. Furthermore, H_a is also coupled to one of the H-1' protons in the phenoxymethyl group at 4.05 ppm with a $^{4}J_{H,H}$-coupling constant of 1.2 Hz. This proton is also coupled to the other H-1' proton at 3.95 ppm with a *geminal* coupling constant of 10.5 Hz. The bridge-head protons connected to C-1 and C-5 resonates at 4.84 and 4.91 ppm, and they only couple to the vinylic protons on C-7 and C-6 by *vicinal* coupling constants of equal magnitude (1.5 Hz). Besides these couplings, H-6 and H-7 are also coupled to each other with a *vicinal* coupling constant of 5.7 Hz.

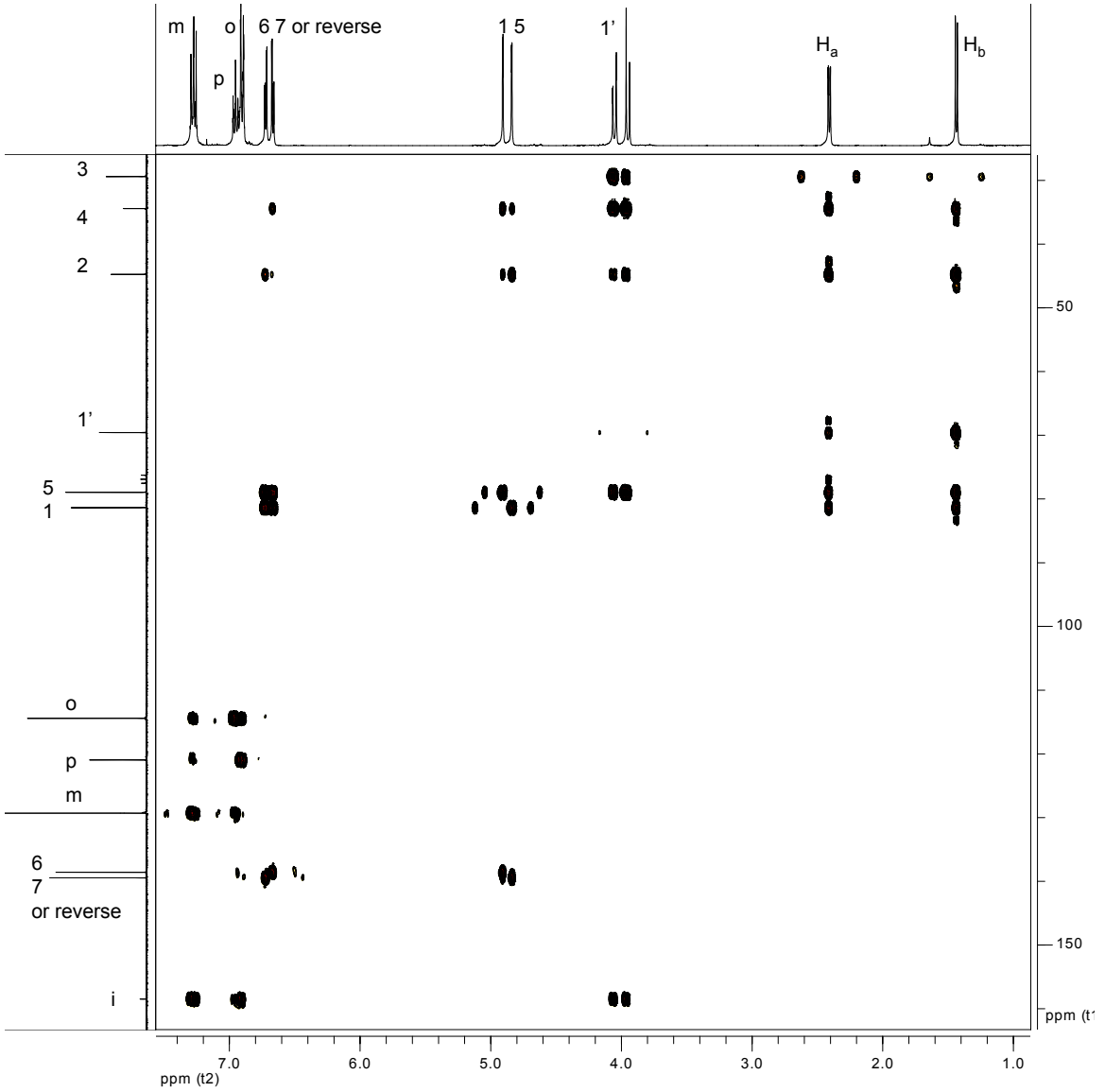


Figure 3.16 HMBC spectrum of *exo*-**9i** ($^1J_{C,H}$ couplings can be seen as doublets on the outside of the central signals).

The HMBC experiment was optimised to observe long-range correlations 8 Hz between proton and carbon nuclei by suppressing $^1J_{C,H}$ correlations of 150 Hz. However, in the HMBC spectrum of *exo*-**9i** some $^1J_{H,H}$ correlations can be seen and easily distinguished from the long-range correlations because their cross-peaks appear as doublets on the outside of the central signals (Figure 3.16). The most important information from this spectrum was that the bridge-head carbon atoms could be distinguished from each other. Since the signal at 79.0 ppm coupled to the signals from H-1' at 3.95 and 4.05 ppm, this signal may be attributed to C-5. The signal from C-5 also coupled to the proton doublet at 4.91 ppm, which probably belongs to H-1. Furthermore, since the H-1 signal coupled to the carbon atom at 138.6 ppm, it was

expected that this signal belonged to C-7, while the carbon signal at 139.5 ppm coupled to H-5 presumably belonged to C-6.

However, the NOESY spectrum of *exo*-**9i** supported another assumption. There were strong cross-peaks between H-1 and the double doublet at 6.67 ppm and H-5 and the double doublet at 6.72 ppm, indicating that these signals belonged to H-7 and H-6 respectively (Figure 3.17).

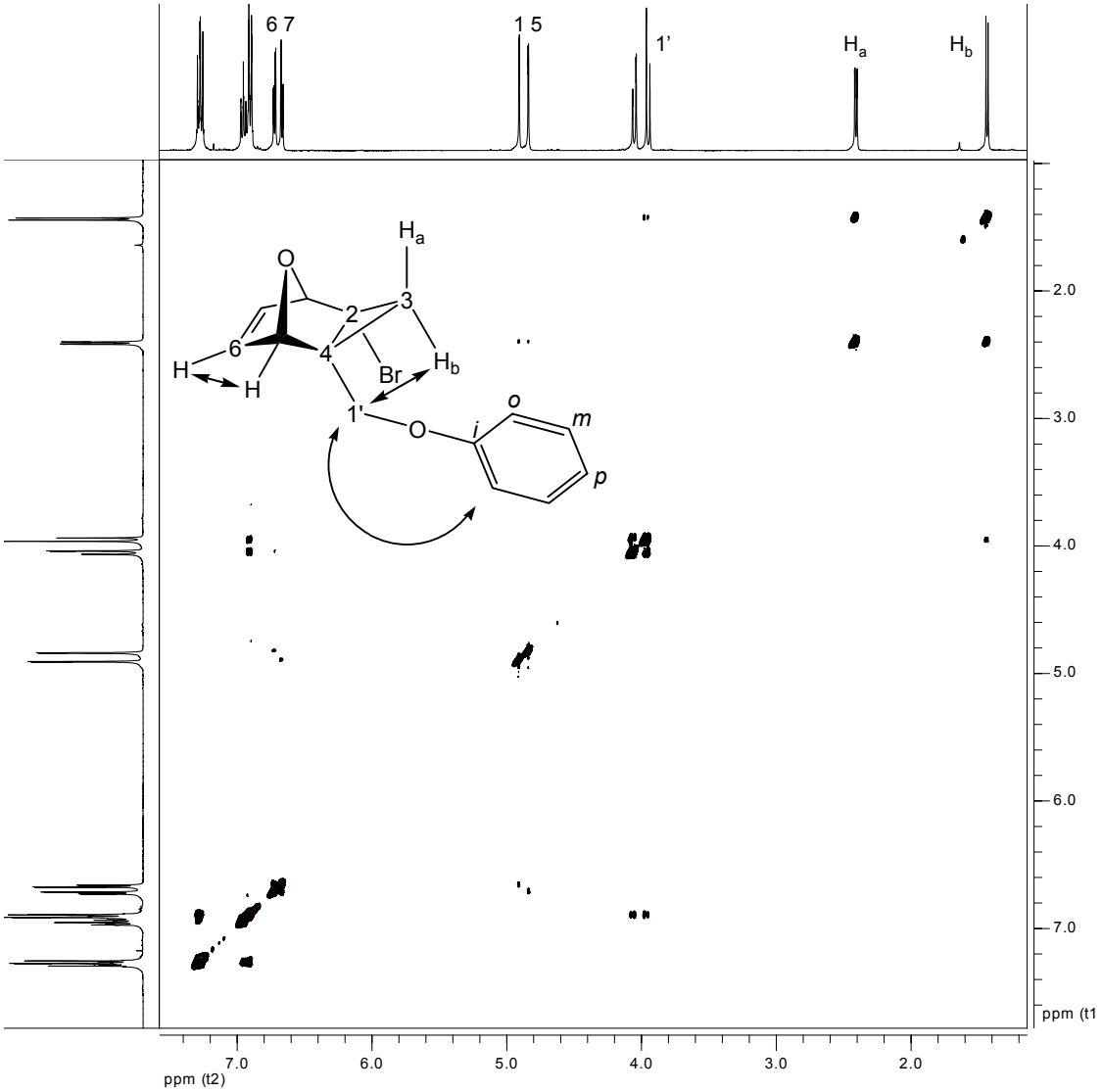


Figure 3.17 NOESY spectrum of *exo*-**9i**.

With these findings in mind the assignment of C-6 and C-7 in the HMBC spectrum was reversed in such a way that C-6 was associated with the signal at highest field (Figure 3.16). This also indicated that the cross-peaks from C-4 and C-2 in the topmost left corner of the HMBC spectrum must be due to $^{4}J_{C,H}$ couplings to H-7 and H-6 respectively, instead of $^{3}J_{C,H}$ coupling in a reverse fashion. This absence of *vicinal* carbon-proton couplings might be

explained by a dihedral angle close to 90° in H(6)-C-C-C(4) and H(7)-C-C-C(2) (Figure 3.18), although the exact magnitude of these angles are not known.

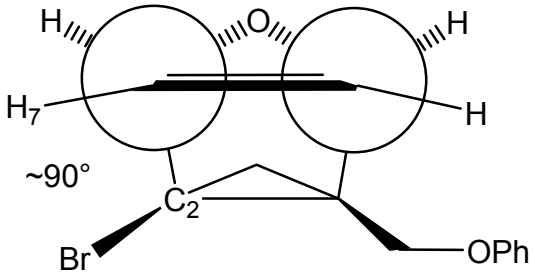
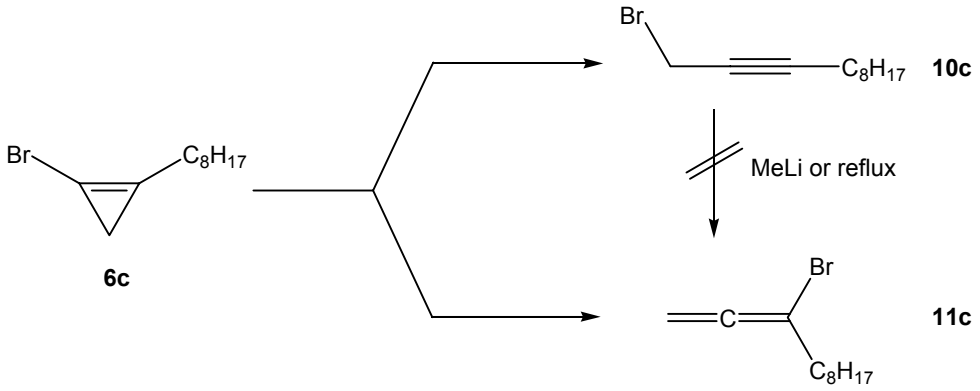


Figure 3.18 Illustration of the dihedral angle between H(7)-C-C-C(2) in *exo*-**9i**.

The NOESY spectrum of *exo*-**9i** also showed direct couplings between the *ortho*-protons in the phenyl ring and the methylene protons in the phenoxymethyl group (H-1') (Figure 3.17). H-1' exhibited also a through-space coupling to one of the cyclopropyl protons, namely H_b.

The Diels-Alder reactions with **2d**, **2e** and **2h**, and furan afforded no cycloadduct, but were nevertheless very clean and gave one product only. In each case the product appeared to be the corresponding cyclopropene, which was isolated in 96, 74 and 100% yield, respectively (Table 3.7; entries 4, 5 and 8). The rest of the 1,1,2-tribromocyclopropanes, however, gave complex reaction mixtures, from which it was generally very difficult to isolate pure samples of the individual compounds. One exception is the reaction involving furan and 1,1,2-tribromo-2-octylcyclopropane (**2c**) (Table 3.7; entry 3); from the product mixture 1-bromo-undec-2-yne (**10c**) and 3-bromoundeca-1,2-diene (**11c**) were isolated in 22 and 17% yield, respectively (Scheme 3.18). These products are most likely formed by a vinylcarbene rearrangement as previously outlined in Scheme 3.11, although formation of **11c** from **10c** can be envisaged by a 1,3-bromide shift. However, when pure **10c** in THF was refluxed in the presence and absence of MeLi, no allene was formed; hence, **11c** does not originate from the acetylene by rearrangement.



Scheme 3.18

3.5 Concluding remarks

In summary, it can be concluded that the 1-bromocyclopropenes (**6**) which were studied exhibit the same reactivity toward cyclopentadiene, DPIBF, and furan as cyclopropene and alkyl-substituted cyclopropenes,[30,34,36] *viz*. the reaction rate and the chemical yield vary in the order DPIBF > cyclopentadiene >> furan. Due to the reluctance of furan to react the thermal instability of **6** becomes important; as a result most of the product mixtures from the furan reactions contain several compounds formed by decomposition of the 1-bromocyclopropenes. Furthermore, it appears that the lack of SOI is decisive for the outcome in the reactions with DPIBF;[30] thus, in these cycloadditions *exo* cycloadducts are formed exclusively whereas Alder's *endo* rule is followed when cyclopentadiene is involved.[33,34] As well as stabilising SOI in the *endo* transition state, steric interactions in the *exo* adduct is probably important factors for the stereoselectivity in the Diels-Alder reaction. The transition state for the formation of the *exo* cycloadduct resembles a boat cyclohexane conformer. In Diels-Alder reactions with cyclopentadiene the flagpole 1,4-methylene interaction illustrated in Figure 3.19 destabilises the otherwise less hindered *exo* approach.[36]

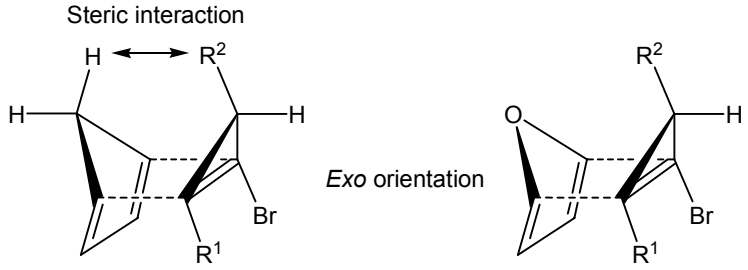


Figure 3.19 Illustration of the *exo* transition state in the formation of cycloadducts **8** from cyclopentadiene and cycloadducts **9** from furan.

Hence, it came as no surprise that when changing from cyclopentadiene to furan as the diene in the Diels-Alder reactions with 1-bromocyclopropenes **6**, the sterically less hindered *exo* cycloadduct prevailed.

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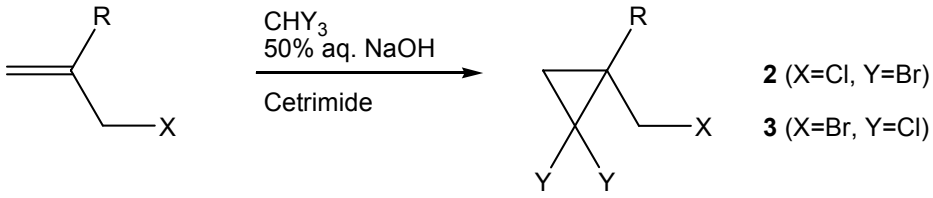
4 Pyrolyses of polyhalogenated cyclopropanes

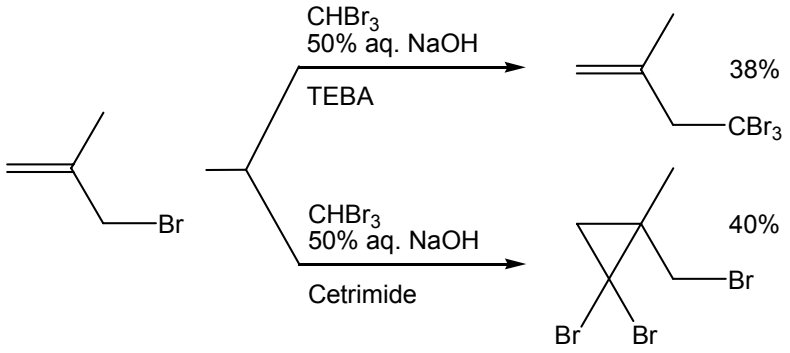
4.1 Synthesis of halogenated cyclopropanes

Three 1,1-dihalo-2-R-2-halomethylcyclopropanes (**2** and **3**) were synthesised from the corresponding allylic halides under PTC, with either bromoform or chloroform as the dihalocarbene precursor (Scheme 4.1).[1]



Scheme 4.1

The choice of phase-transfer catalyst in the reaction was crucial. Baird and co-workers showed that the reaction involving allylic bromide and bromoform with TEBA as the catalyst yielded 4,4,4-tribromo-2-methylbut-1-ene as the major primary product.[2] This unwanted by-product had probably arisen from nucleophilic substitution of bromide by the tribromomethyl anion generated from bromoform. However, when the reaction was repeated with Cetrimide as the phase-transfer catalyst, 1,1-dibromo-2-bromomethyl-2-methylcyclopropane was obtained as the single product in 40% yield (Scheme 4.2).



Scheme 4.2

The best yields of **2** and **3** were obtained when the allylic halide, NaOH and haloform ratio was 1:3:8 and the use of solvent was avoided (Table 4.1). The effect of Cetrimide on the yields in the cyclopropanation reactions seems apparent when the results are compared to

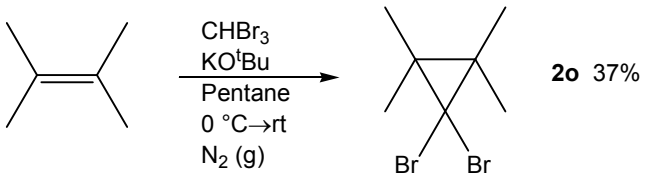
those obtained by Pettersen *et al.* with TEBA under otherwise identical conditions (Table 4.1).[3]

Table 4.1 Preparation of 1,1-dihalo-2-R-2-halomethylcyclopropanes from allylic halides under PTC.

Entry	R	X	Y	Product	Yields (%)	
						Pettersen *et al.*[a]
1	H	Cl	Br	**2m**	42	26
2	Methyl	Cl	Br	**2n**	90	58
3	Methyl	Br	Cl	**3n**	69	39

[a] TEBA was used as the phase-transfer catalyst.[3]

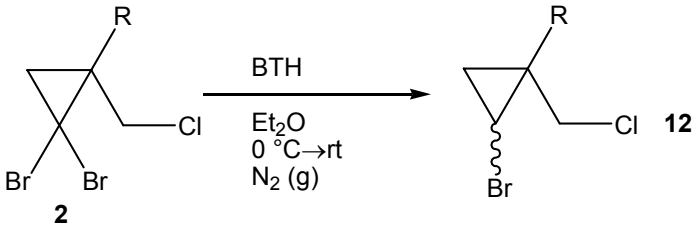
In order to test our pyrolysis procedure and apparatus, we wanted to repeat the pyrolysis of a halogenated cyclopropane which is known to give a clean pyrolysate and preferably high yields of ring-opening products (Chapter 4.3.1). Hence, 1,1-dibromo-2,2,3,3-tetramethyl-cyclopropane (**2o**) was synthesised, as previously described in the literature,[4,5] by the Doering-Hoffmann procedure by dropwise addition of bromoform to a slurry of the alkene and potassium *tert*-butoxide in pentane (Scheme 4.3).[6]



Scheme 4.3

4.2 Reduction of 1,1-dibromo-2-R-2-chloromethylcyclopropanes

The 1,1-dibromo-2-R-2-chloromethylcyclopropanes **2m** and **2n** were converted to the corresponding dihalides in moderate yields when treated with tributyltin hydride (BTH) in diethyl ether.[3] The reaction was completely regiospecific at low temperatures, leaving the chloromethyl side-chain unreacted when the *gem*-dibromo moiety was attacked by the hydride, furnishing mixtures of *cis* and *trans* isomers (**12**) in moderate yields (Scheme 4.4, Table 4.2).



Scheme 4.4

Table 4.2 Reduction of **2** with BTH.

Entry	R	Product	*cis*/*trans* ratio[a]	Boiling point (°C/mmHg)	Yields (%)
1	H	**12m**	41/59	54-56/12	57
2	Methyl	**12n**	33/67	48/10	74

[a] Based on GC and ^{1}H NMR analyses.

The products (**12**) were isolated as isomeric mixtures by fractional distillation through a 20-cm column packed with fine class cuttings (Table 4.2). GC analyses on a non-polar column indicated that the boiling points of the *cis* and *trans* isomers were coinciding and efforts on isolating the *cis* and *trans* isomers by preparative GC were not conducted. Since the peaks of the two isomers of **12n** partially overlapped in the chromatogram obtained on a HP 5890 II GC, equipped with a 25-m non-polar capillary column (Figure 4.1), it seemed difficult to separate the isomers on a Varian Aerograph 90-P preparative GC equipped with a 4-m packed column.

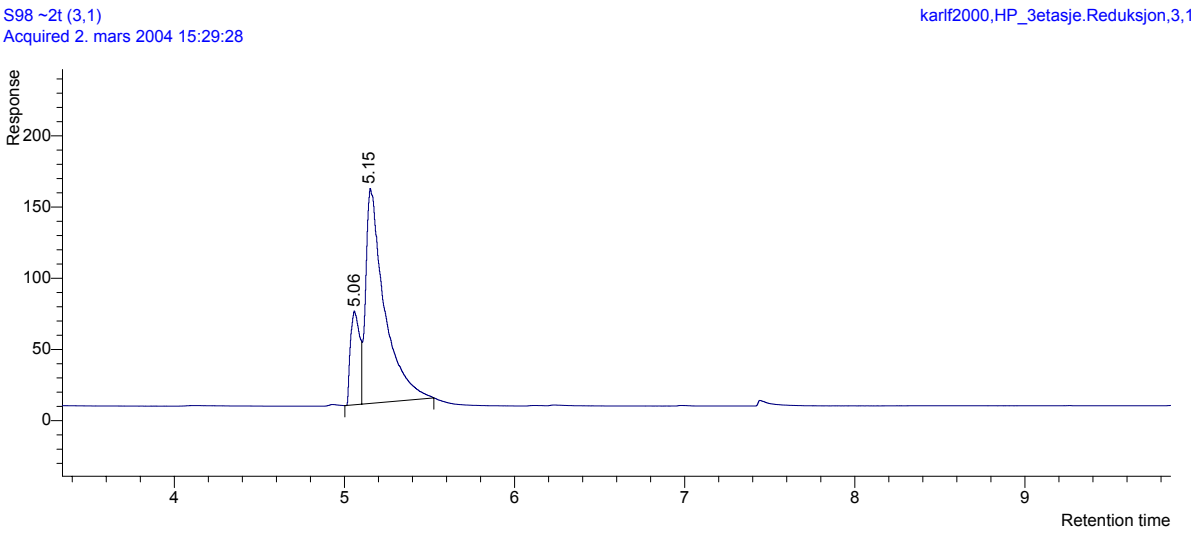


Figure 4.1 GC chromatogram of *cis*/trans-**12n** where the *cis* isomer has the shorter retention time. Temperature program: 50 ºC (2 min) $\xrightarrow{15\ ^\circ C/min}$ 200 ºC (0 min) $\xrightarrow{25\ ^\circ C/min}$ 290 ºC (5 min).

However, analyses of **12n** on an HPLC system with a reversed-phase column (Hypersil® ODS) connected to a UV-detector showed some promising results. When an isocratic separation was performed in a 1:1 mixture of acetonitrile and water, the two isomers were nicely separated (Figure 4.2). But when attempts at scaling up the separation were performed the two peaks overlapped severely, due to an overload of the analytic HPLC system, rendering the method unsuitable for our purpose (Figure 4.3).

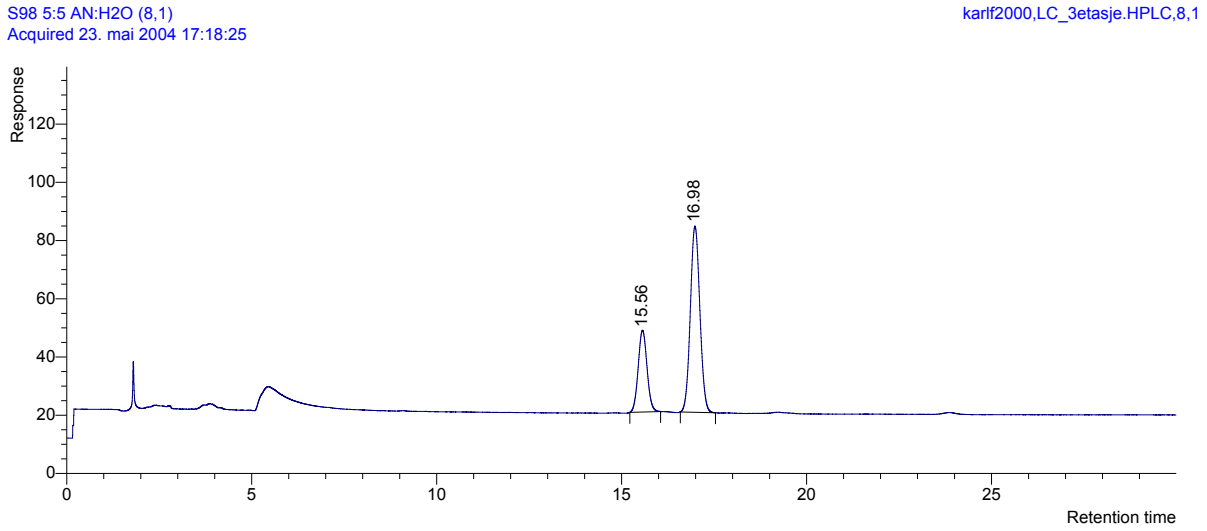


Figure 4.2 HPLC chromatogram of *cis*/*trans*-**12n** (λ_{max}=205 nm), when 10 µL of a 0.06 mM solution of the isomeric mixture was injected.

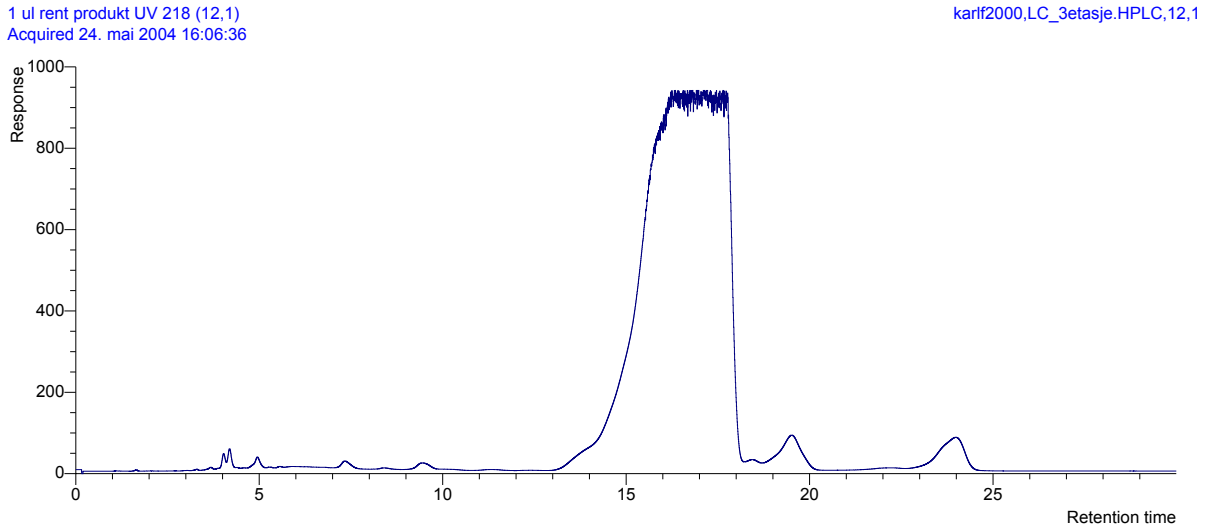


Figure 4.3 The chromatogram after injection of 1 µL of pure *cis*/*trans*-**12n**.

Since separation of the isomers appeared unsuccessful on any preparative scale the structure elucidation of *cis*- and *trans*-**12** were carried out with the mixture. Based on the assumption that van der Waals interactions between the bromine atom and its *cis*

neighbouring groups lead to a decreased shielding of the groups, the formation of the *trans* isomers was found to be preponderant in the reductions with BTH. Thus, the signal from the methyl group in *trans*-**12n** was shifted to a lower field (1.41 ppm) compared to the same signal (1.28 ppm) in the *cis* isomer (Figure 4.4).

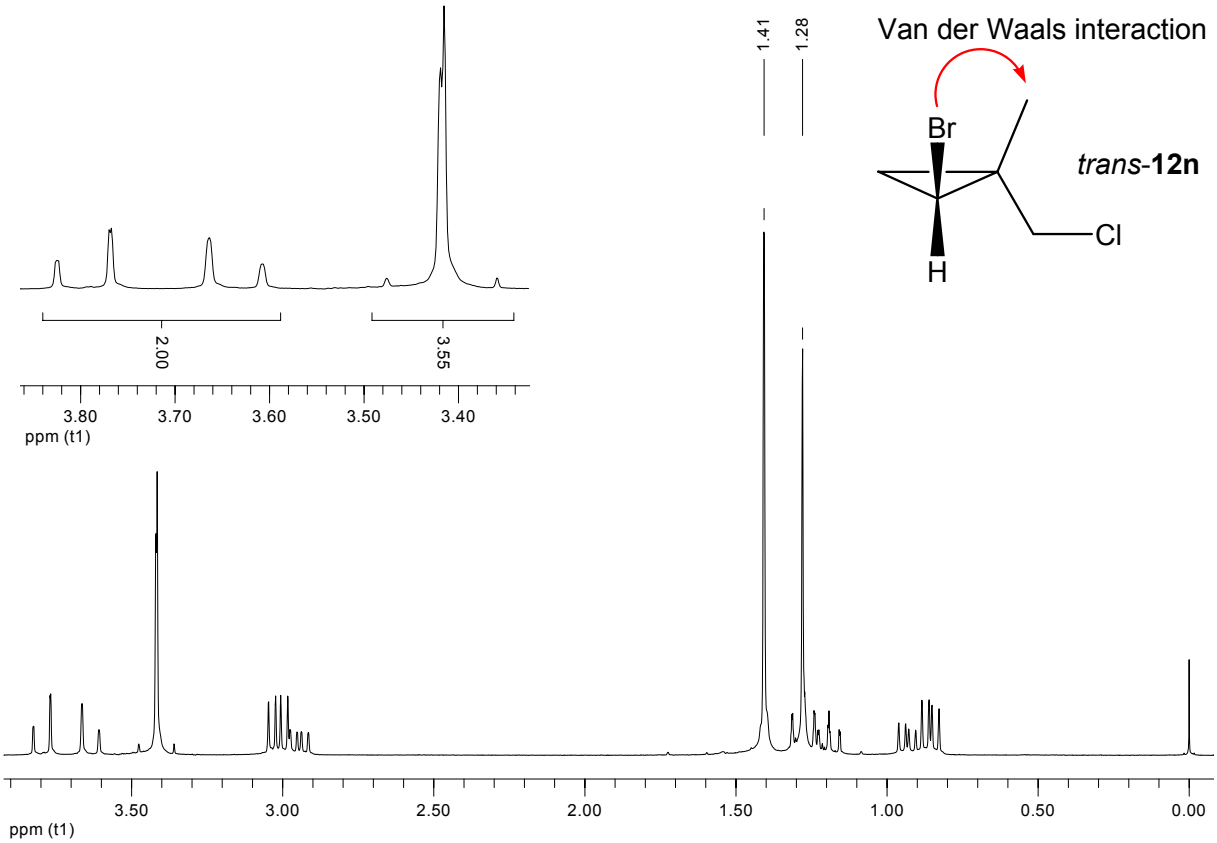


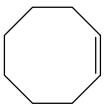
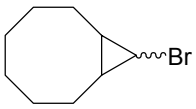
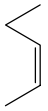
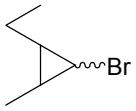
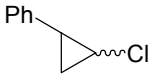
Figure 4.4 Electrostatic interaction between the bromine atom and the methyl group in *trans*-**12n** shifts the methyl signal to a lower field (1.41 ppm) compared to the same signal (1.28 ppm) in *cis*-**12n**.

Due to extensive couplings in the ^{1}H NMR spectrum of **12m** it was difficult to distinguish the signals from the *cis* and *trans* isomers from each other. However, Pettersen *et al.* confirmed the conclusion that the *trans* isomers predominated by independent syntheses of both *trans*-**12m** and *trans*-**12n**, which had the same retention time as the most abundant isomer in the GC chromatograms.[3]

Attempts were also made at making **12m** and **12n** by monobromocarbene addition to the corresponding alkenes, following Martel and Hiriart's procedure which showed promising stereospecificity in the syntheses of some monohalocyclopropanes (Table 4.3).[7] Martel and Hiriart attained the best stereoselectivity in the synthesis of 9-bromo-bicyclo[6.1.0]nonane

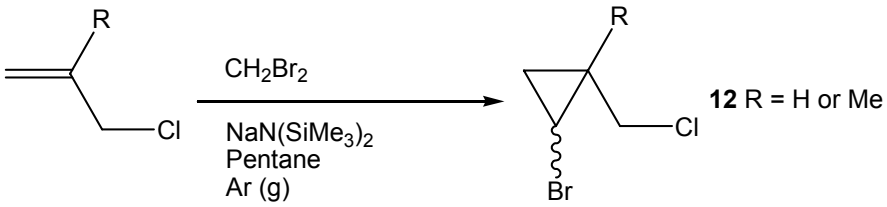
(Table 4.3; entry 1), although it should be mentioned that Seyferth *et al.* observed the same selectivity by partial reduction of 9,9-dibromobicyclo[6.1.0]nonane with BTH.[8]

Table 4.3 Preparation of monohalocyclopropanes by Martel and Hiriart.[7]

Entry	Alkene	Product	*cis*/*trans* ratio	Yield (%)
1			20[a]	40
2			3	30
3			2.12	40

[a] Dehmlow and Lustinetz achieved a *cis*/*trans* ratio of only 2.8.[9]

Monobromocarbene additions were performed under argon by slowly adding methylene bromide to a slurry of sodium bis(trimethylsilyl)amide and the olefin in pentane (Scheme 4.5). However, the yields were lower compared to the partial reduction of **2** with BTH, and **12m** and **12n** were difficult to separate from bis(trimethylsilyl)amine formed during the course of the reaction (Table 4.4). Moreover, ^{1}H NMR and GC analyses of the crude products showed that the stereoselectivity did not improve either (Table 4.4).



Scheme 4.5

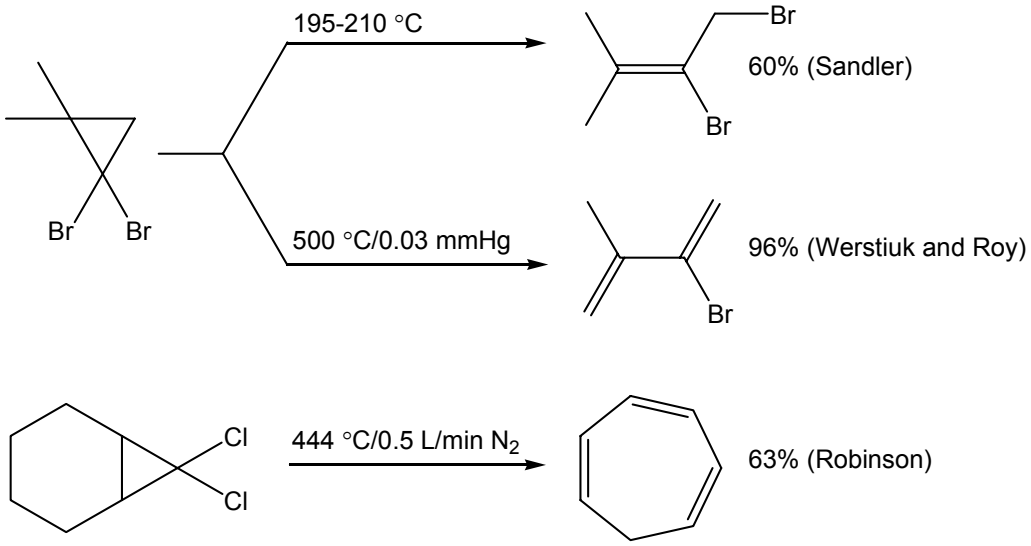
Table 4.4 Monobromocarbene addition to alkenes.

Entry	Alkene (R)	Product	*Cis*/*trans* ratio[a]	Yields (%)[a]
1	H	**12m**	41/59	8
2	Methyl	**12n**	37/63	11

[a] Based on GC and ^{1}H NMR analyses.

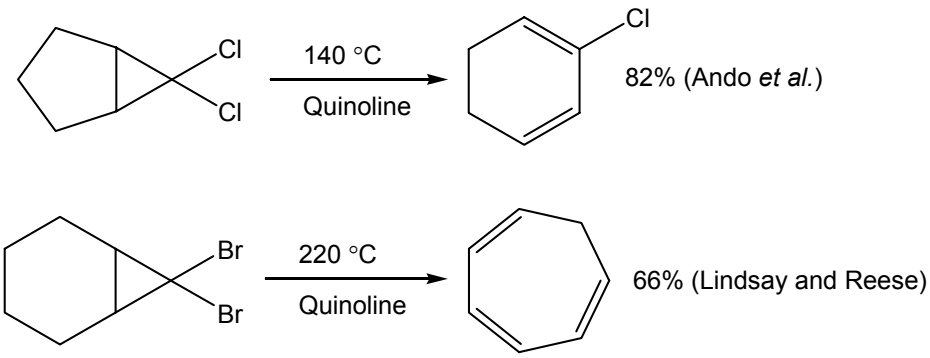
4.3 Pyrolysis of 1,1-dihalo-2-R-2-halomethylcyclopropanes

Pyrolysis of halogenated cyclopropanes have successfully been carried out in numerous ways: Sandler heated liquid 1,1-dibromo-2,2-dimethylcyclopropane under nitrogen between 195-210 °C and isolated sole 1,2-dibromo-3-methyl-2-butene in good yield (Scheme 4.6).[10] Gas-phase pyrolyses have been conducted in both horizontally and vertically orientated columns. Werstiuk and Roy afforded exclusively 2-bromo-3-methylbuta-1,3-diene in high yields when 1,1-dibromo-2,2-dimethylcyclopropane was passed through a horizontal electrically heated furnace at 500 ºC and high vaccum.[11] The results of Sandler and Werstiuk and Roy indicate that elimination occurs in concert with ring opening in the gas phase, while substitution is the preferred route at lower temperatures. Robinson converted 7,7-dichloronorcarane to cyclo-heptatriene in 63% yield by passing it through a vertical column, packed with calcium oxide and heated to 444 ºC, with a constant flow of nitrogen (Scheme 4.6).[12]



Scheme 4.6

These experimental results imply that the thermal ring opening of halogenated cyclopropanes is often accompanied by dehydrohalogenation and should therefore be assisted by the presence of a base like quinoline. Hence, Ando and co-workers isolated 2-chlorocyclohexa-1,3-diene in high yields when 6,6-dichlorobicyclo[3.1.0]hexane was heated at 140 °C in quinoline (Scheme 4.7),[13] while Lindsay and Reese converted the relatively thermolabile 7,7-dibromonorcarane to cycloheptatriene in quinoline at 220 °C.[14]



Scheme 4.7

On the basis of these observations it was decided to perform pyrolysis of polyhalogenated cyclopropanes in both quinoline and the gas phase.

4.3.1 *Pyrolysis in hot quinoline*

The pyrolyses of 1,1-dihalo-2-R-2-halomethylcyclopropanes (**2** and **3**) were carried out in hot quinoline in a microscale distillation unit under inert atmosphere, and the pyrolysates were collected in a dry-ice or liquid-nitrogen cooled flask connected to a gas inlet through a liquid-nitrogen cooled trap (Figure 4.5).

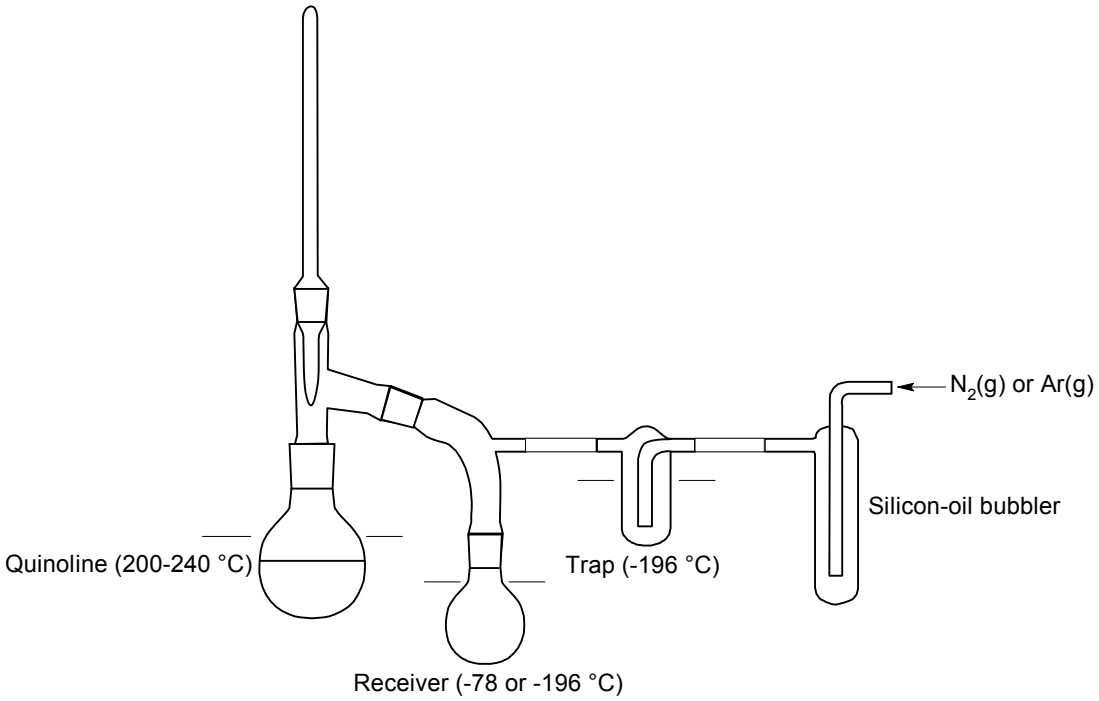
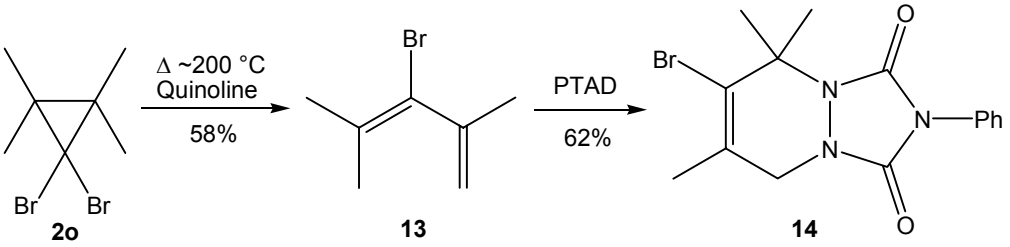


Figure 4.5 Apparatus for pyrolysis in quinoline.

In order to test our procedure and apparatus we repeated the pyrolysis of 1,1-dibromo-2,2,3,3-tetramethylcyclopropane (**2o**), which gave 82% pure 3-bromo-2,4-dimethyl-1,3-

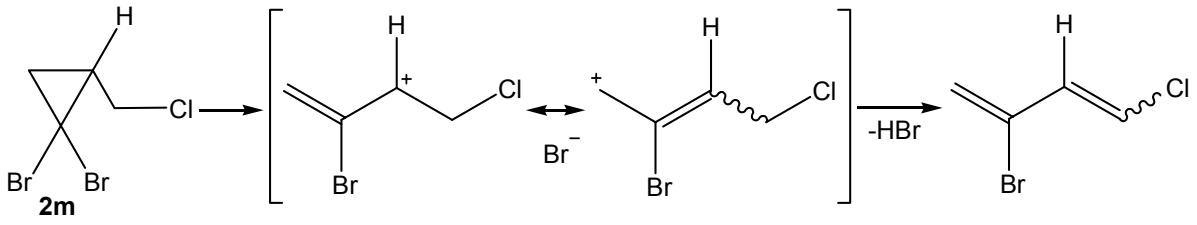
pentadiene (**13**) when Sandler heated the cyclopropane at 160-162 ºC.[10] When **2o** was heated in quinoline, for approximately 15 minutes, **13** was collected in a liquid-nitrogen cooled receiver flask in 58% yield as a colourless liquid.[10,15] Treatment of **13** with intensely red 4-phenyl-4*H*-1,2,4-triazole-3,5-dione (PTAD) furnished the yellowish cycloadduct 6-bromo-5,5,7-trimethyl-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]-pyridazine-1,3(5*H*,8*H*)-dione (**14**) in 62% yield (Scheme 4.8).



Scheme 4.8

This proved that the method should serve our purpose, and pyrolyses of trihalogenated cyclopropanes **2** and **3** were henceforth carried out as for **2o**, with a 1:3 ratio between the cyclopropane and quinoline. The reactions were monitored by GC to ensure a complete conversion of the cyclopropanes, and to trap any volatile dienes formed during the reactions the pyrolysates were immediately treated with PTAD because it is one of the most reactive dienophiles known towards a variety of dienes,[16] its strong red colour disappears upon reaction and it has no disturbing aliphatic signals in the ^{1}H NMR spectrum.

In preliminary pyrolysis experiments with **2** Diels-Alder cycloadducts were only isolated in scarce amounts, but some colourless liquid accumulated in the trap. This liquid was strongly acidic, and formation of a yellowish precipitate when treated with 0.1 M $AgNO_3$ strongly indicated that this was HBr formed during ring opening of **2** (Scheme 4.9).



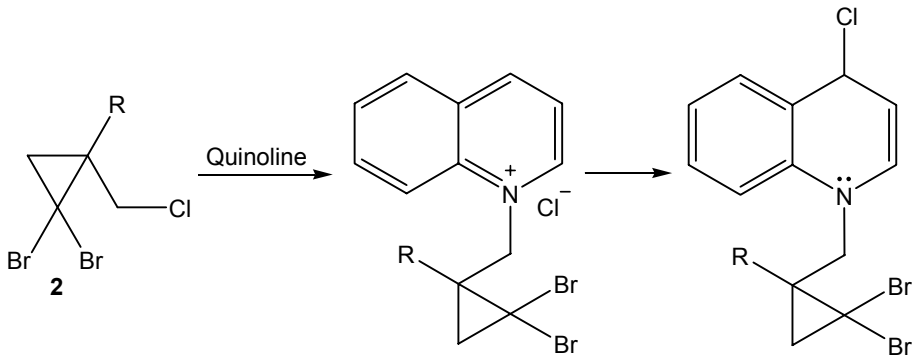
Scheme 4.9

The mass balance was calculated to see if any volatile products escaped from the apparatus during pyrolysis. When 2.099 g (8.45 mmol) of 1,1-dibromo-2-chloromethylcyclopropane (**2m**) was pyrolysed in 3.066 g (23.74 mmol) quinoline, 0.174 g of a liquid, colourless

pyrolysate was collected in the receiver flask, while 4.886 g tarry material was left in the reaction flask. Thus, only 0.105 g is unaccounted for, of which some was left in the distillation neck, giving a mass balance of approximately 98%.

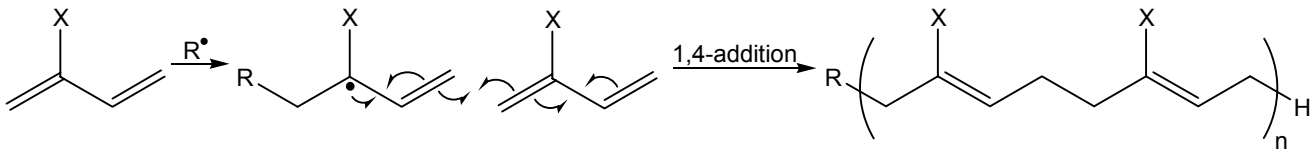
To isolate any products or unconverted cyclopropanes left in the quinoline residues after pyrolysis, the residues were acidified and extracted with ether, and the organic phases were treated with aqueous sodium carbonate and sodium chloride, before evaporation *in vacuo*. Nevertheless, no compounds were observed or isolated from the residues apart from impurities of quinoline.

In the harsh conditions during pyrolysis unexpected reactions may be envisaged, for example nucleophilic substitution of quinoline furnishing quaternary salts or 1,4-dihydroquinoline derivatives (Scheme 4.10). Such quaternary salts may have been transferred to the aqueous phases during the extraction of the residue, and were together with 1,4-dihydroquinoline derivatives not observed or isolated.



Scheme 4.10

Since the reaction mixtures generally changed colour from light brown to dark black and became viscous and tarry, the low yields of cycloadducts may have been caused by polymerisations of substituted 1,3-butadienes formed in the thermal ring opening of **2** (Scheme 4.11).

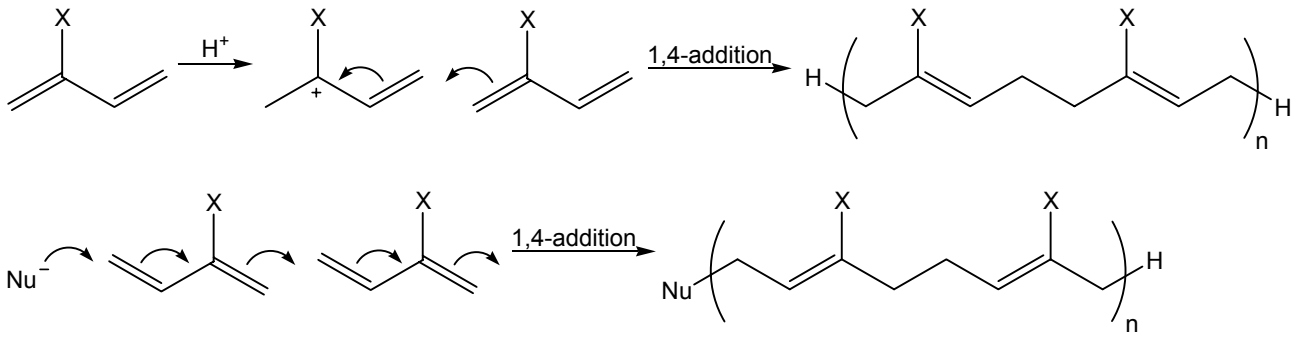


Scheme 4.11

Butadienes are commonly used as monomers in the production of synthetic rubbers, e.g. 2-chlorobuta-1,3-diene (chloroprene) which is used in the production of Neoprene.[17]

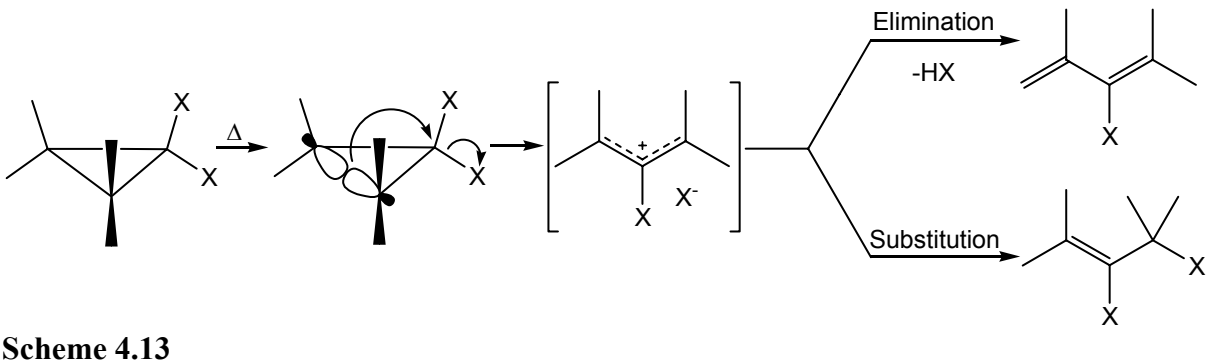
Chloroprene polymerises spontaneously at room temperature in aqueous emulsion, and the rate of this transformation is roughly 700 times greater than the analogous polymerisation of isoprene to rubber or gutta percha.[18]

The high mass balance in the pyrolysis of **2m** and the fact that no unconverted starting material was seen in the GC analysis of the crude mixture also support the proposition of polymerisation in the reaction flask. However, addition of the radical scavenger 4-*tert*-butylpyrocatechol[19] to the reaction mixture did not improve the yield. But polymerisations can occur through both radical and ionic mechanisms (Scheme 4.11 and 4.12), so this observation did not rule out the possibility for polymerisations.



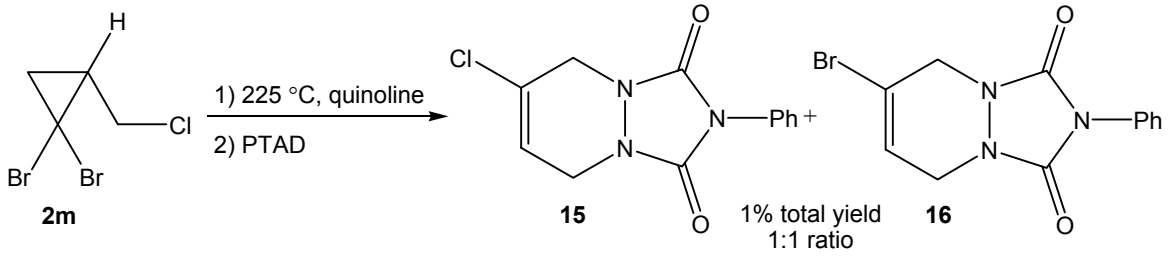
Scheme 4.12

Regardless of the low yields in the preliminary experiments pyrolyses of **2** and **3** were continued as a mechanistic study. In concerted electrocyclic ring-opening reactions of *gem*-dihalocyclopropanes at elevated temperatures it is expected that the expelled halide ion either functions as a base and abstracts a proton to give 1,3-dienes,[11,15] or as a nucleophile to give the corresponding allylic halide (Scheme 4.13).[10] However, in the pyrolysis of **2m** no substitution-products were observed or isolated. Furthermore, no products due to the elimination of HBr or HCl were observed; only dienes formed by formal elimination of Br_2 and BrCl were found.



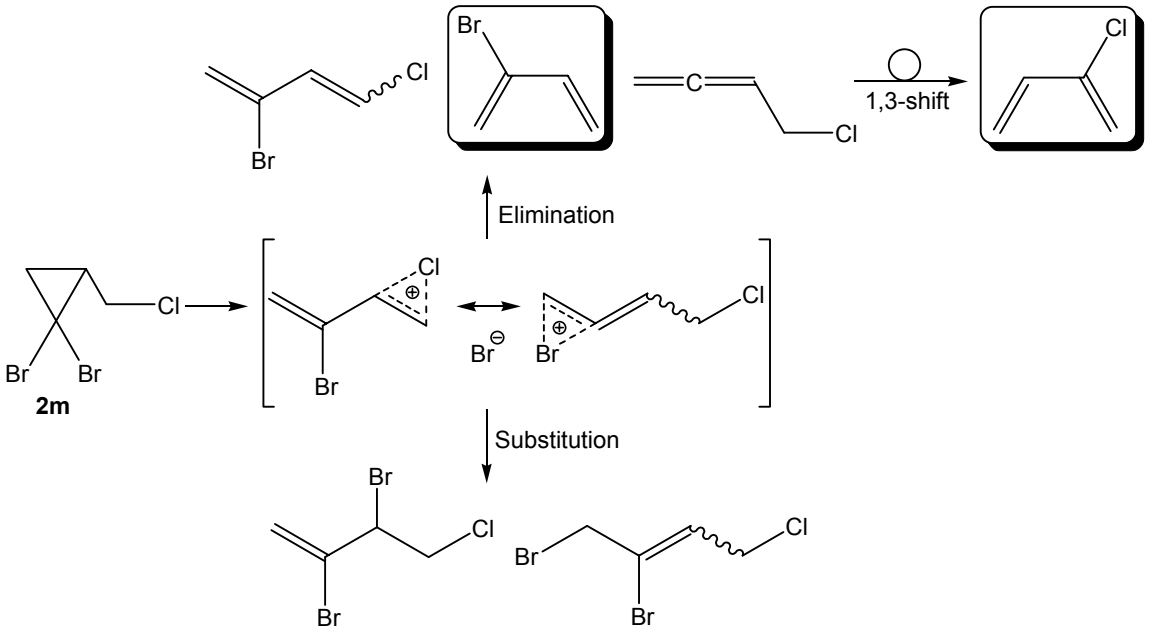
Scheme 4.13

The pyrolysate from **2m** was collected in a liquid-nitrogen cooled receiver flask as a colourless liquid, and subsequently treated with deeply red PTAD until the red colour persisted (Scheme 4.14).

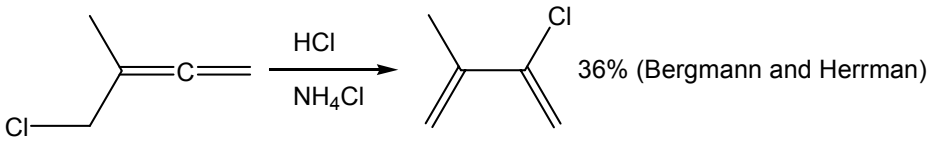


Scheme 4.14

Formation of chloroprene, which was trapped and isolated as cycloadduct **15**, may be visualised by elimination of Br_2 to give an intermediate allene, which can rearrange to chloroprene by a 1,3-chloride shift (Scheme 4.15). This reaction can be compared with the isomerisation of 4-chloro-3-methylbuta-1,2-diene to yield 2-chloro-3-methylbuta-1,3-diene under acidic conditions (Scheme 4.16).[20]



Scheme 4.15



Scheme 4.16

Formation of bromoprene, which was trapped and isolated as cycloadduct **16**, may be envisaged by an unexpected elimination of BrCl, which has not been described in the literature (Scheme 4.15).

Cycloadducts **15** and **16** were isolated by flash chromatography as a 1:1 mixture, which afforded a white powder upon evaporation. Signals from the vinylic protons in **15** and **16** could be seen in the ^{1}H NMR spectrum of the mixture as two multiplets between 6.06-6.31 ppm (Figure 4.6).

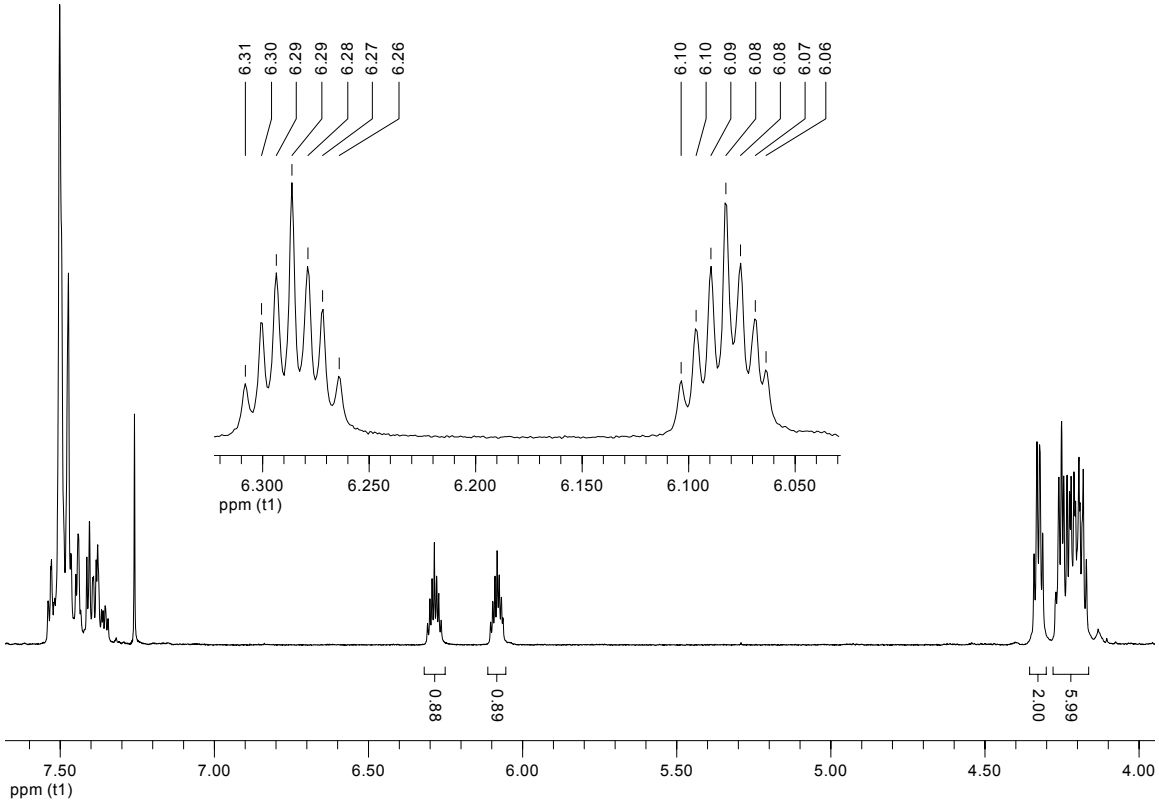


Figure 4.6 ^{1}H NMR spectrum of the 1:1 mixture of **15** and **16**.

The analysis of **15** and **16** was simplified by synthesis of an authentic sample of **15** from chloroprene.[21] In the ^{1}H NMR spectrum of pure **15** the vinylic protons gave rise to a multiplet at 6.05-6.07 ppm (Figure 4.7).

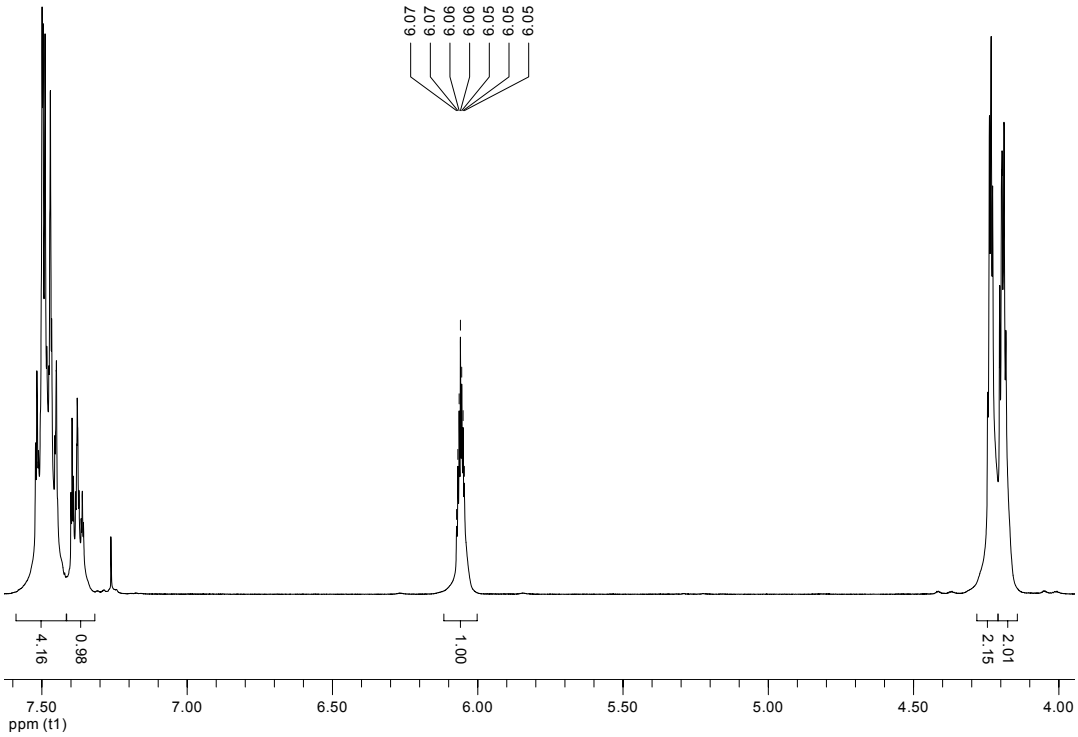


Figure 4.7 ^{1}H NMR spectrum of **15**, which was synthesised from chloroprene.

The IR spectrum of **15** showed a strong absorption at 1705 cm^{-1} due to the carbonylic groups in the triazolo ring, while the medium stretching at 1780 cm^{-1} possibly may be ascribed to the imide function in the same ring (Figure 4.8).

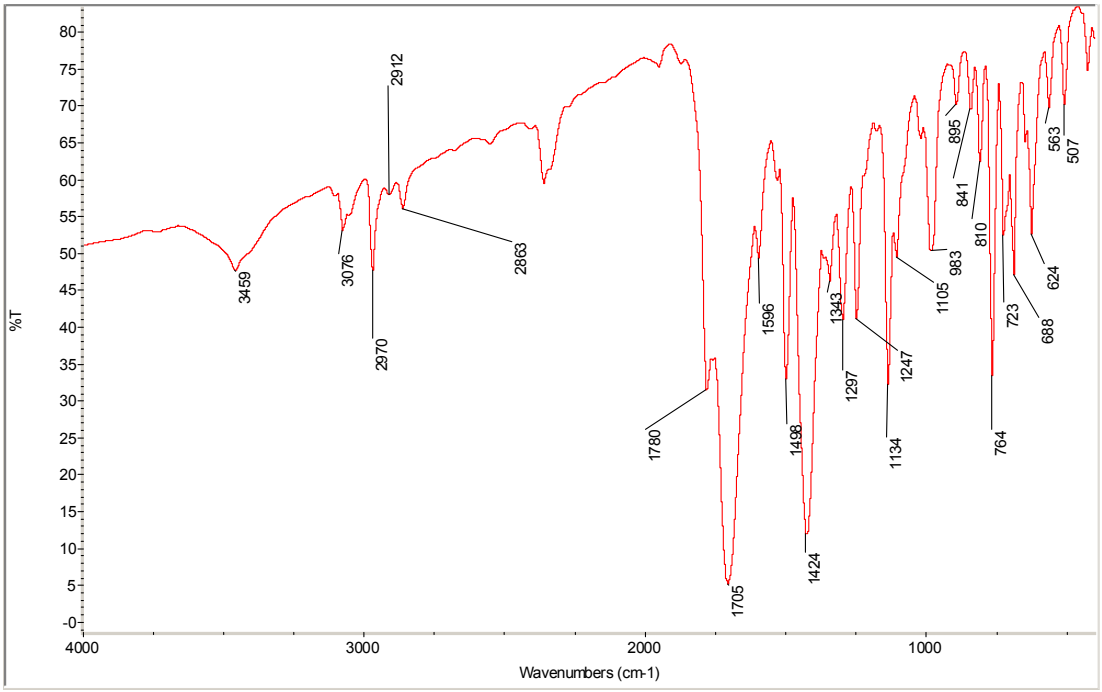
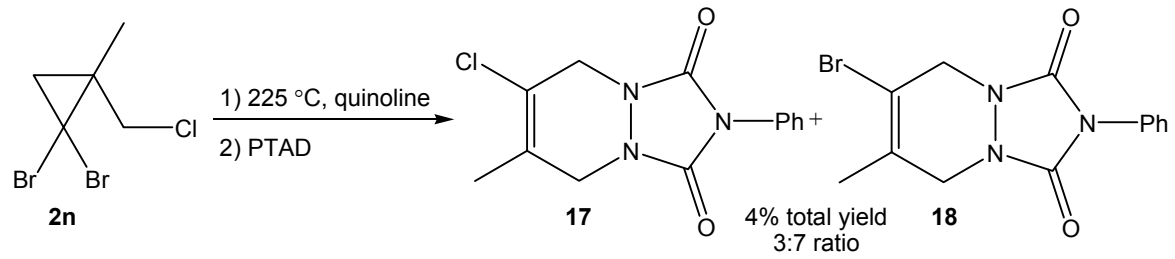


Figure 4.8 IR spectrum of pure **15**.

When 1,1-dibromo-2-chloromethyl-2-methylcyclopropane (**2n**) was pyrolysed under the same conditions and the pyrolysate was treated with PTAD, only **17** and **18** were observed and isolated as a 3:7 mixture by flash chromatography (Scheme 4.17).



Scheme 4.17

Evaporation of the solvent afforded a white powder with overlapping signals from the methyl groups at 1.93-1.97 ppm and the methylene groups at 4.13-4.26 ppm in the ^{1}H NMR spectrum (Figure 4.9). The isolation of the mixture of **17** and **18** showed that the ring opening of **2n** followed the same pathway as outlined for **2m** in Scheme 4.15, with formal elimination of Br_2 and BrCl furnishing substituted 1,3-butadienes.

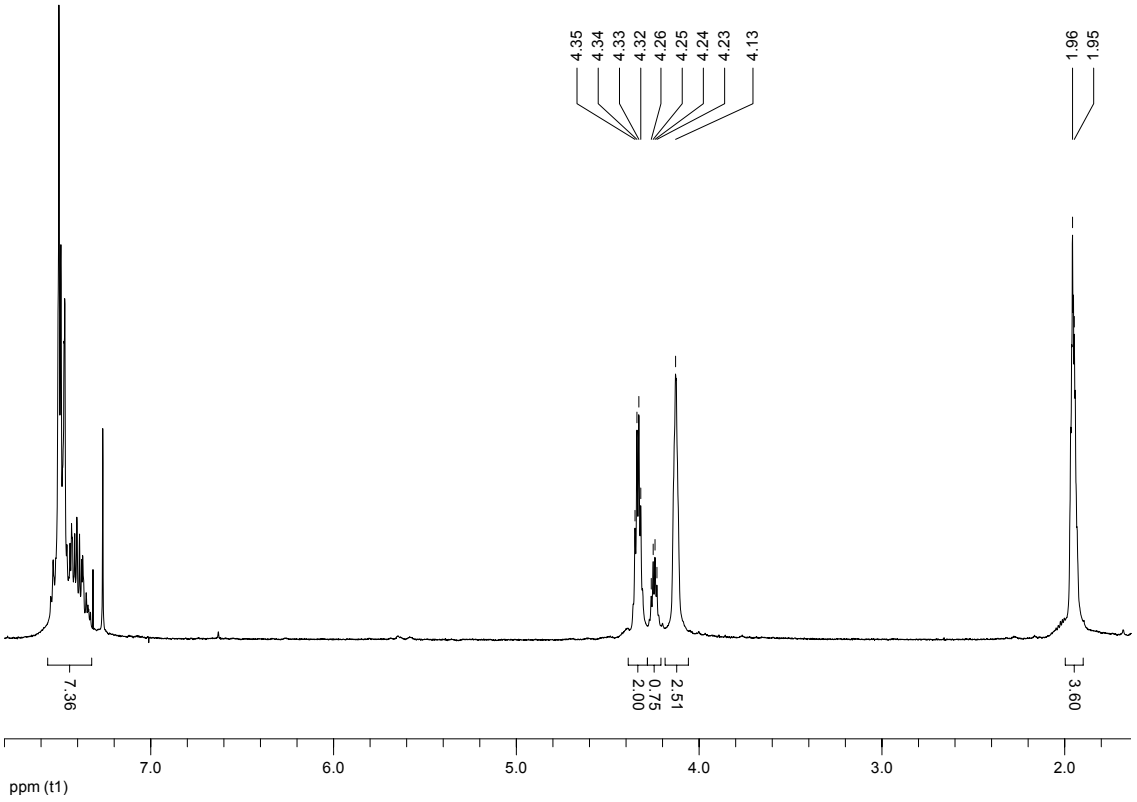
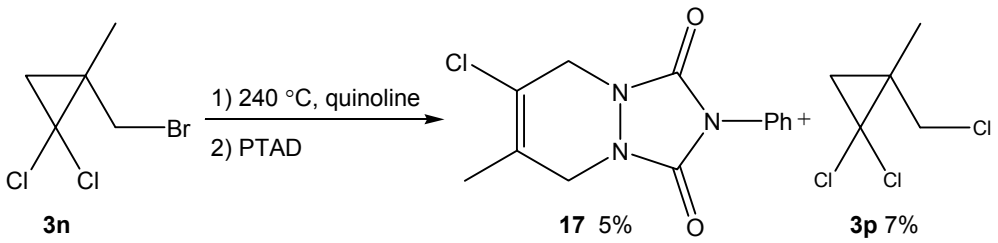


Figure 4.9 ^{1}H NMR spectrum of the 3:7 mixture of **17** and **18**.

The pyrolysis of 1-bromomethyl-2,2-dichloro-1-methylcyclopropane (**3n**) followed by subsequent treatment of the pyrolysate with PTAD afforded **17** (Scheme 4.18), an outcome which also simplified the assignment of the proton and carbon signals in the mixture of **17** and **18** from the pyrolysis of **2n**. When the ^{1}H and ^{13}C NMR spectra of pure **17** were compared to those of the mixture from the pyrolysis of **2n**, it was possible to extract most of the signals due to **18**.



3n **17** 5% **3p** 7%

Scheme 4.18

In the ^{1}H NMR spectrum of **17** the multiplet at 1.92-1.95 ppm was assigned to the methyl group, while the two methylene groups gave rise to multiplets at 4.11-4.13 and 4.21-4.26 ppm (Figure 4.10).

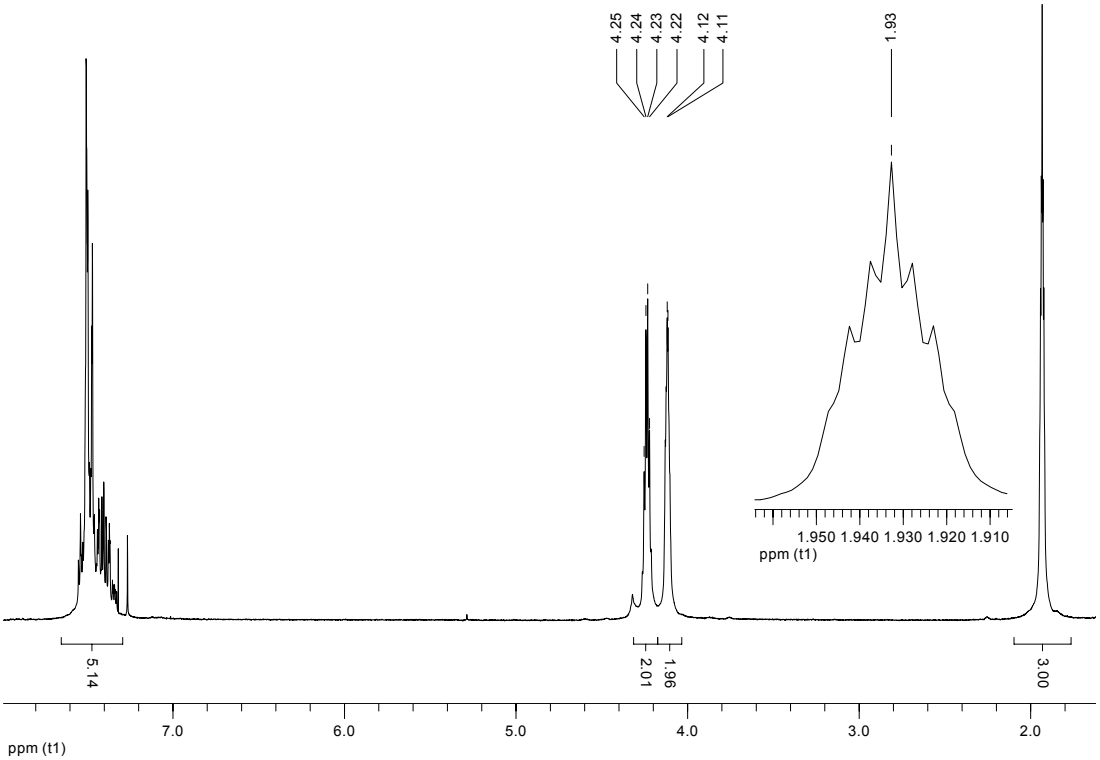


Figure 4.10 ^{1}H NMR spectrum of **17**, which was isolated after the pyrolysis of **3n**.

In addition to cycloadduct **17** 1,1-dichloro-2-chloromethyl-2-methylcyclopropane (**3p**) was also isolated from the crude product mixture. GC-MS analyses showed that the molecular ion

and fragmentation of the major peak from the crude product were in accordance with those expected from **3p** (Figure 4.11). Additional spectral data were also in agreement with those previously reported in the literature.[3] Trichloride **3p** probably results from an ionic substitution reaction of **3n** by chloride generated during the pyrolysis.

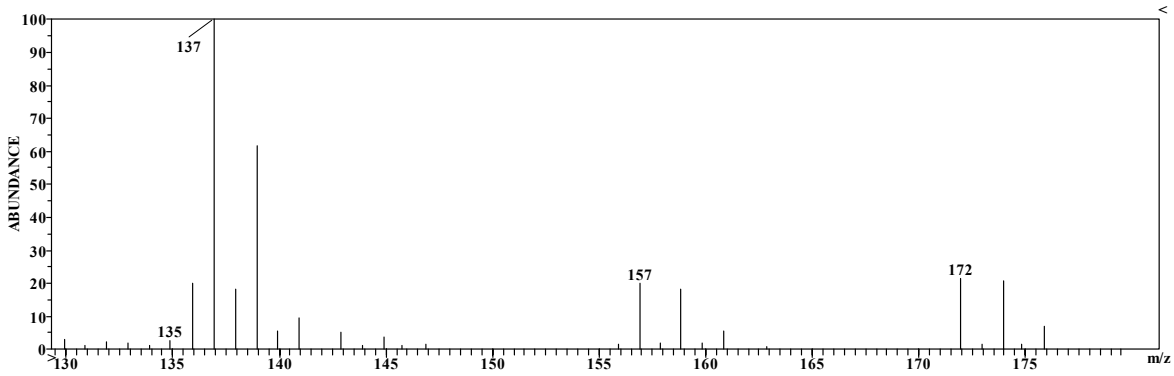
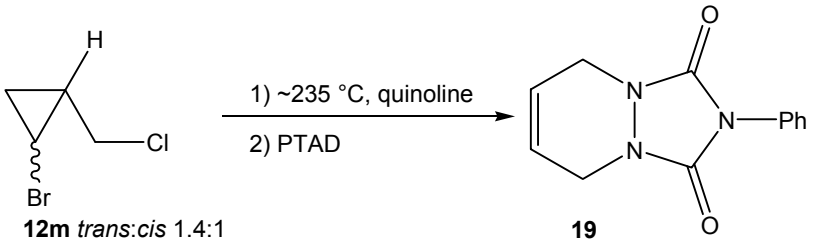


Figure 4.11 An expansion of the mass spectrum from the GC-MS analysis of **3p**, where *m*/*z* 172 is the molecular ion (the y-axis showing the abundance is only a relative scale).

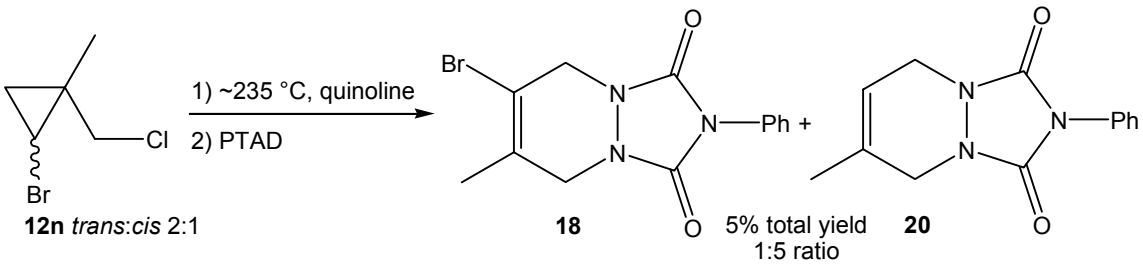
Pyrolyses of dihalogenated cyclopropanes (**12**) were expected to follow the same course as outlined for *gem*-dihalocyclopropanes in Scheme 4.13, with elimination of HX or nucleophilic substitution as the preferred transformations to give halogenated 1,3-butadienes or allylic halides. The receiver flask was filled with PTAD dissolved in methylene chloride, in such a way that the tip of the distillation adapter was immersed in the solution, to minimise the loss of volatile ring-opened products. Still, no halogenated 1,3-butadienes or allylic halides were isolated or trapped from the pyrolysate of 1-bromo-2-chloromethyl-cyclopropane (**12m**), only traces of **19** could be seen in the GC chromatogram of the crude product (Scheme 4.19). This was confirmed by analyses of an authentic sample of **19** which was synthesised by passing 1,3-butadiene through a solution of PTAD in methylene chloride.[22] Formation of 1,3-butadiene in the pyrolysis of **12m** may be visualised by an unforeseen elimination of BrCl (*vide supra*).



12m *trans*:*cis* 1.4:1 **19**

Scheme 4.19

The pyrolysis of 1-bromo-2-chloromethyl-2-methylcyclopropane (**12n**) and subsequent treatment of the pyrolysate with PTAD yielded a mixture of **18** and **20** in addition to unconverted **12n**. However, only **18** and **20** were isolated by flash chromatography in a 1:5 ratio (Scheme 4.20).



Scheme 4.20

Nevertheless, GC analyses of the crude product showed that unreacted **12n** was present as a 1.5:1 mixture of the *trans* and the *cis* isomers, indicating that the *trans* isomer reacts faster than the *cis* isomer (Figure 4.12). Since DePuy *et al.* suggested that R-groups *trans* to the leaving group rotate outwards in electrocyclic ring openings,[23] one plausible explanation for this reactivity difference is that the inward rotation of the chloromethyl group in the *cis* isomer leads to a less stable, sterically hindered cation (Figure 4.12).

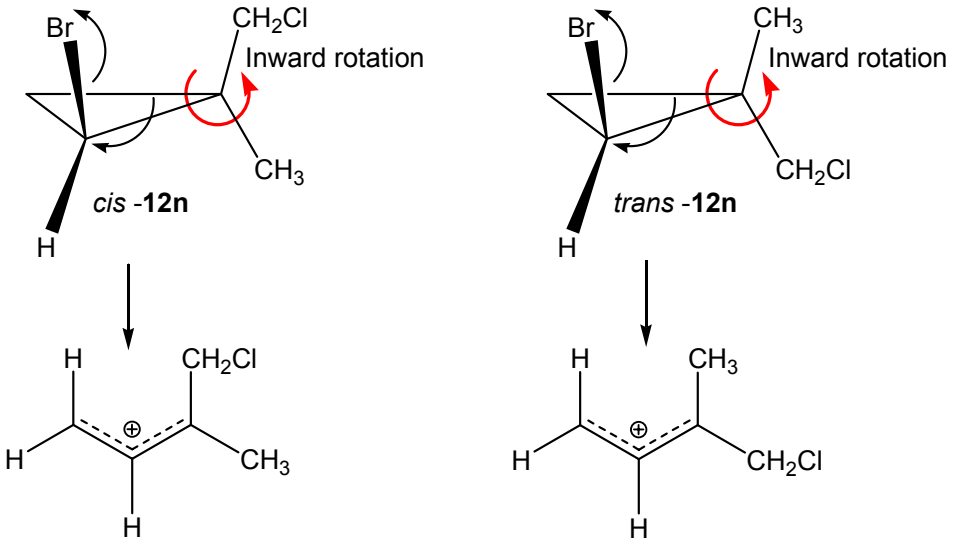
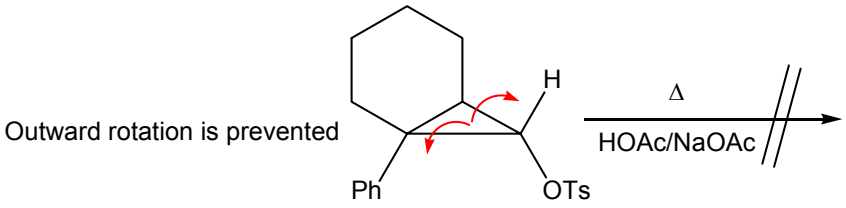


Figure 4.12 The *cis* isomer of **12n** seems to react slower than the *trans* isomer. This might be explained by the formation of a less stable cation in the electrocyclic ring opening.

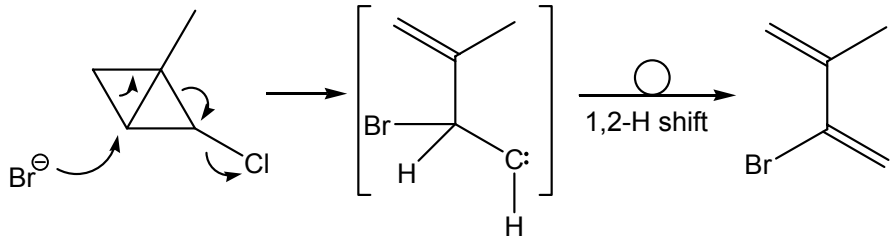
DePuy *et al.* observed the same reactivity difference between *cis*- and *trans*-2-phenylcyclopropyl tosylate in the solvolysis reaction in acetic acid and sodium acetate.[23] *Exo*-phenyl-

norcaranyl tosylate, in which outward rotation of the *trans* groups obviously is impossible, did not react at all when it was exposed to the same reaction conditions (Scheme 4.21).



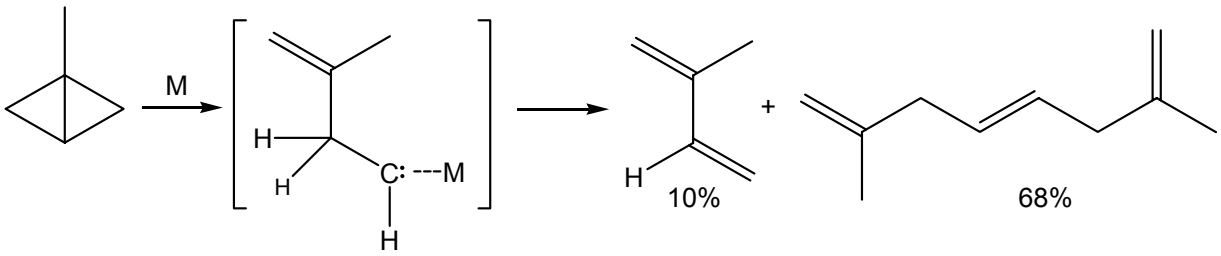
Scheme 4.21

The formation of isoprene, which was trapped by PTAD and gave **20**, followed the reaction pathway outlined in Scheme 4.15, but the formation of 2-bromo-3-methyl-1,3-butadiene, which was trapped and isolated as **18**, was not anticipated. The isolation of **18** could have been explained by impurities of **2n** in the substrate, but the ^{1}H NMR spectrum of **12n** showed absolutely no signals which could be ascribed to **2n** (see previous Figure 4.4). This means that the formation of 2-bromo-3-methyl-1,3-butadiene follows a different reaction pathway than outlined in Scheme 4.15. A possible explanation is the formation of 2-chloro-1-methylbicyclo[1.1.0]butane which can react with bromide present in the reaction mixture and rearrange to the 1,3-diene via an intermediate carbene (Scheme 4.22).



Scheme 4.22

This reaction has analogy in the literature: Gassman and Reitz observed a similar hydrogen shift in the metal-catalyzed cleavage of 1-methylbicyclo[1.1.0]butane.[24] In addition to the dimer 2,7-dimethylocta-1,4,7-triene Gassman and Reitz also isolated isoprene, which was formed by a 1,2-hydrogen shift in the intermediate metal-stabilised carbene (Scheme 4.23).



Scheme 4.23

4.3.2 *Flash-vacuum pyrolysis*

Flash-vacuum pyrolyses (FVP) of cyclopropane **2n** were accomplished by passing it through a packed Pyrex^{TM} tube, heated to between 450-500 °C, at a vacuum of between 0.8-1.2 mmHg. The pyrolysates were collected in a liquid-nitrogen cooled flask, connected to the vacuum inlet through a liquid-nitrogen cooled trap, and immediately treated with PTAD until the red colour persisted (Figure 4.13). Unfortunately the Winkler heating tape, which was used to heat the Pyrex^{TM} tube, short-circuited and prevented further pyrolysis experiments to be carried out.

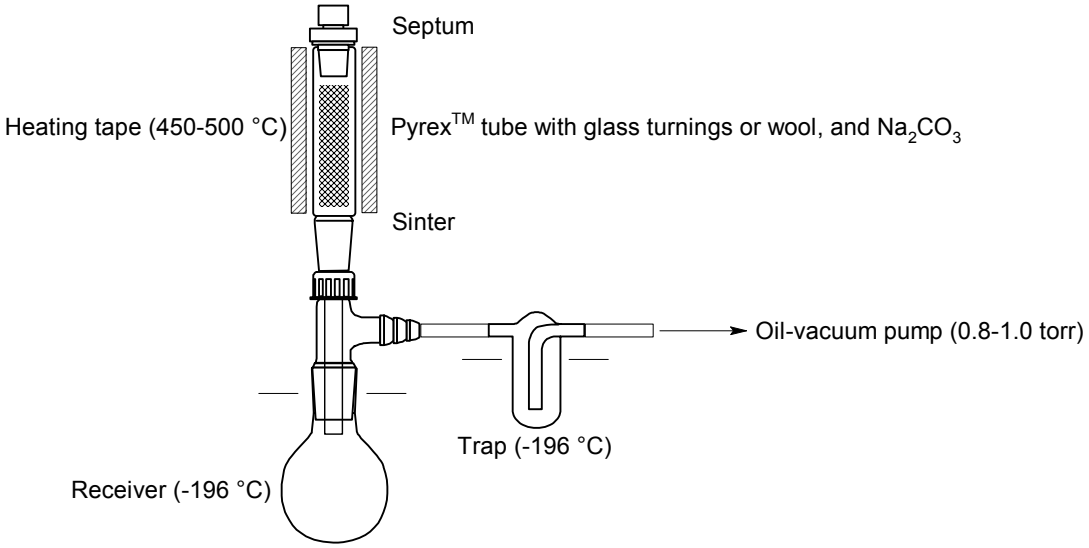
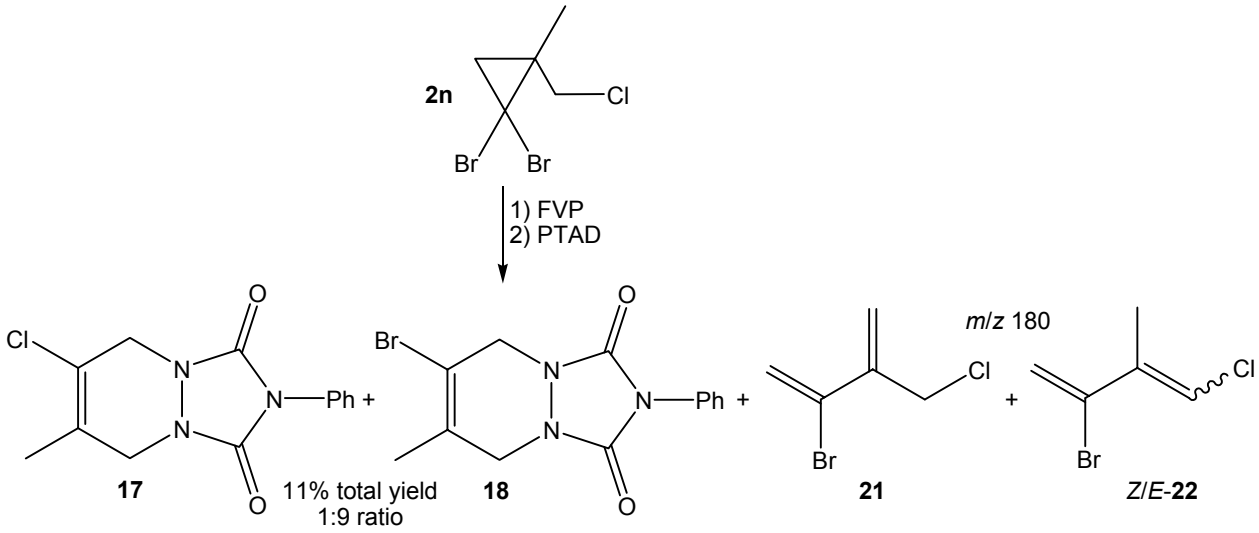


Figure 4.13 Apparatus used in flash-vacuum pyrolysis.

Generally, the pyrolysates after FVP were more coloured than the pyrolysates from the pyrolyses of **2n** in quinoline. Furthermore, the GC chromatograms of the former pyrolysates were more complex, containing more peaks than those of the latter, and when the pyrolysates were treated with PTAD the total yield of cycloadducts was greater after FVP than after pyrolyses in hot quinoline.

Flash chromatography of the crude product after FVP of **2n** and subsequent treatment with PTAD yielded a yellow liquid and a white solid consisting of **17** and **18** as a 1:9 mixture

in 11% yield (Scheme 4.24). According to GC-MS analyses the yellow liquid consisted of three isomers with *m*/*z* 180, probably 2-bromo-3-(chloromethyl)buta-1,3-diene (**21**), (*Z*)- and (*E*)-3-bromo-1-chloro-2-methylbuta-1,3-diene (**22**), generated from **2n** by HBr elimination (Scheme 4.24).



Scheme 4.24

The isomers appeared as three peaks with retention time 6.28, 6.92 and 7.37 minutes in a 1:1.6:3 ratio in the total ion chromatogram (TIC). The three peaks gave the same fragmentation of 180 (M^+), 147/145 (M^+-Cl) and 101 (M^+-Br) (Figure 4.14), but efforts on separating **21**, (*Z*)- and (*E*)-**22** by chromatography and distillation in a Fischer Spaltrohr® system were unsuccessful.

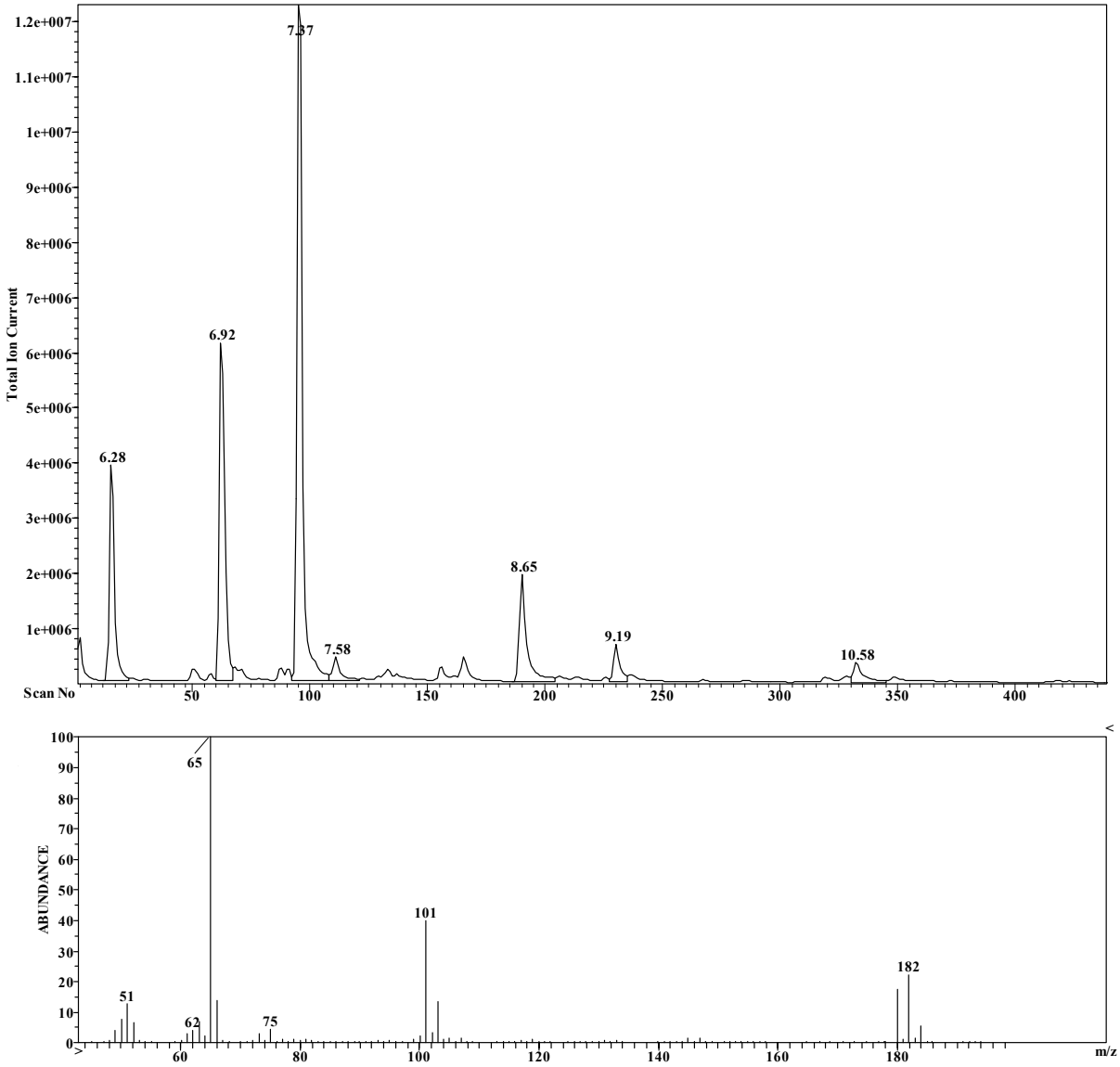
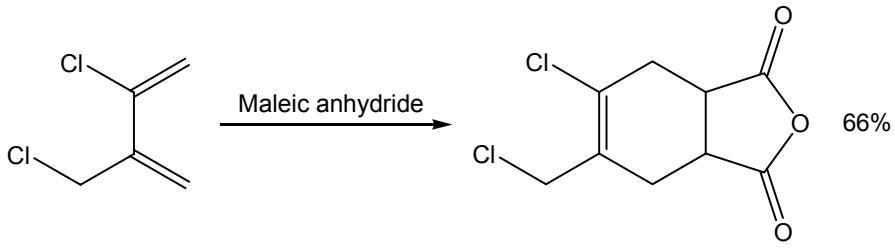


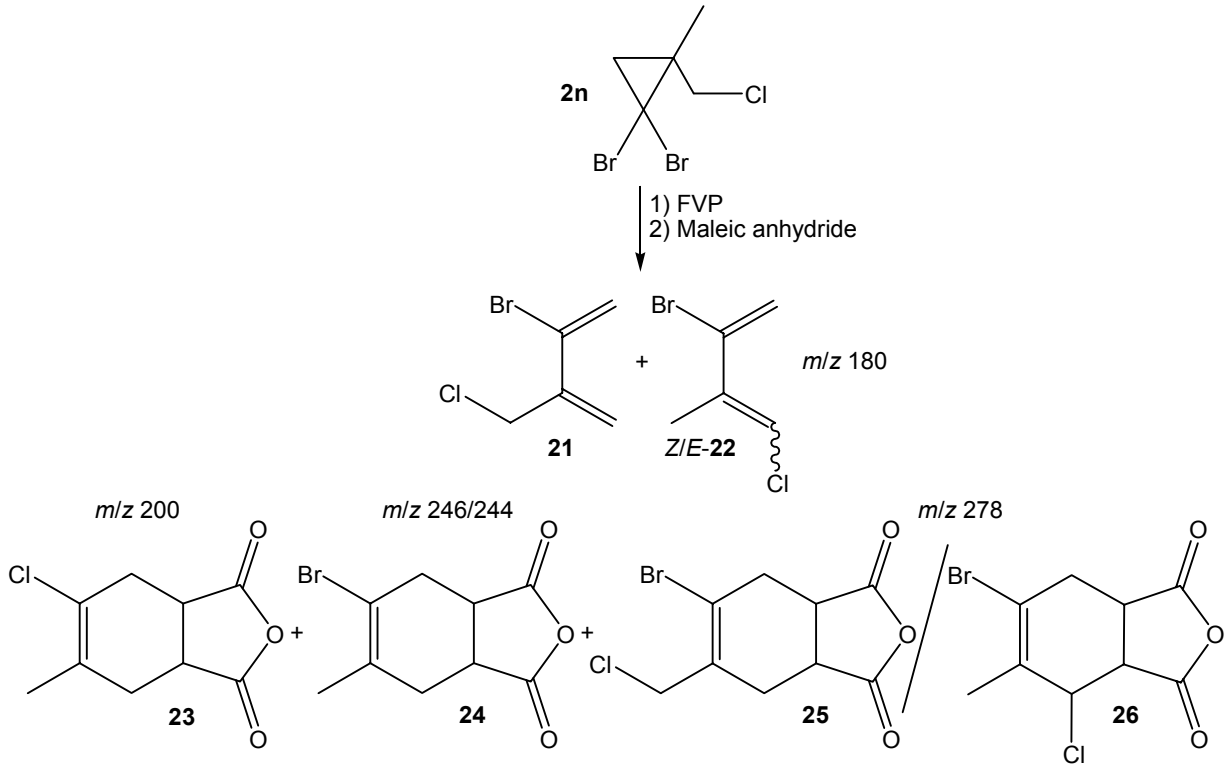
Figure 4.14 GC-MS analysis of the yellow mixture of isomers from the FVP of **2n**, showing the TIC and the mass spectrum of the peak at 6.28 minutes. Since the molecular ion contains both bromine and chlorine atoms it gave an isotope pattern of *m*/*z* 184/182/180 in a 27:100:81 relative ratio. This observation was in accordance with the literature.[25]

Apart from **17** and **18** no other cycloadducts were observed in the crude product. It therefore seems reasonable to believe that **21**, (*Z*)- and (*E*)-**22** react more slowly with PTAD than the 2-halo-3-methyl-1,3-butadienes which were trapped as **17** and **18**. No support was found for this proposition in the literature, but since Kaplanyan *et al.* isolated the cycloadduct in 66% yield in the Diels-Alder reaction between 2-chloro-3-chloromethylbuta-1,3-diene and maleic anhydride it was decided to try this dienophile as trapping agent instead of PTAD (Scheme 4.25).[26]



Scheme 4.25

When the experiment was repeated and the pyrolysate was treated with maleic anhydride the GC-MS chromatogram showed mainly six peaks, which according to the mass spectra were **21**, (*Z*)- and (*E*)-**22** and, in addition, three cycloadducts with *m*/*z* 200, 278 and 246/244 in a 1:2:6 ratio. The compounds with *m*/*z* 200 and 246/244 is most likely 5-chloro-3a,4,7,7a-tetrahydro-6-methylisobenzofuran-1,3-dione (**23**) and 5-bromo-3a,4,7,7a-tetrahydro-6-methylisobenzofuran-1,3-dione (**24**), while the compound with *m*/*z* 278 could either be 5-bromo-6-chloromethyl-3a,4,7,7a-tetrahydroisobenzofuran-1,3-dione (**25**) or 6-bromo-4-chloro-3a,4,7,7a-tetrahydro-5-methylisobenzofuran-1,3-dione (**26**) (Scheme 4.26).



Scheme 4.26

Successive attempts on separating the cycloadducts by flash chromatography failed. However, one fraction seemed to be a mixture of maleic anhydride, **23**, **24** and **25** or **26** with a 1:7:14 ratio between the cycloadducts. Based on the ^{1}H NMR spectrum of this fraction the major

cycloadduct with *m*/*z* 278 appears to be **25**. The two doublets at 4.12-4.28 ppm can probably be assigned to the methylene protons in the chloromethyl group in **25** (Figure 4.15).

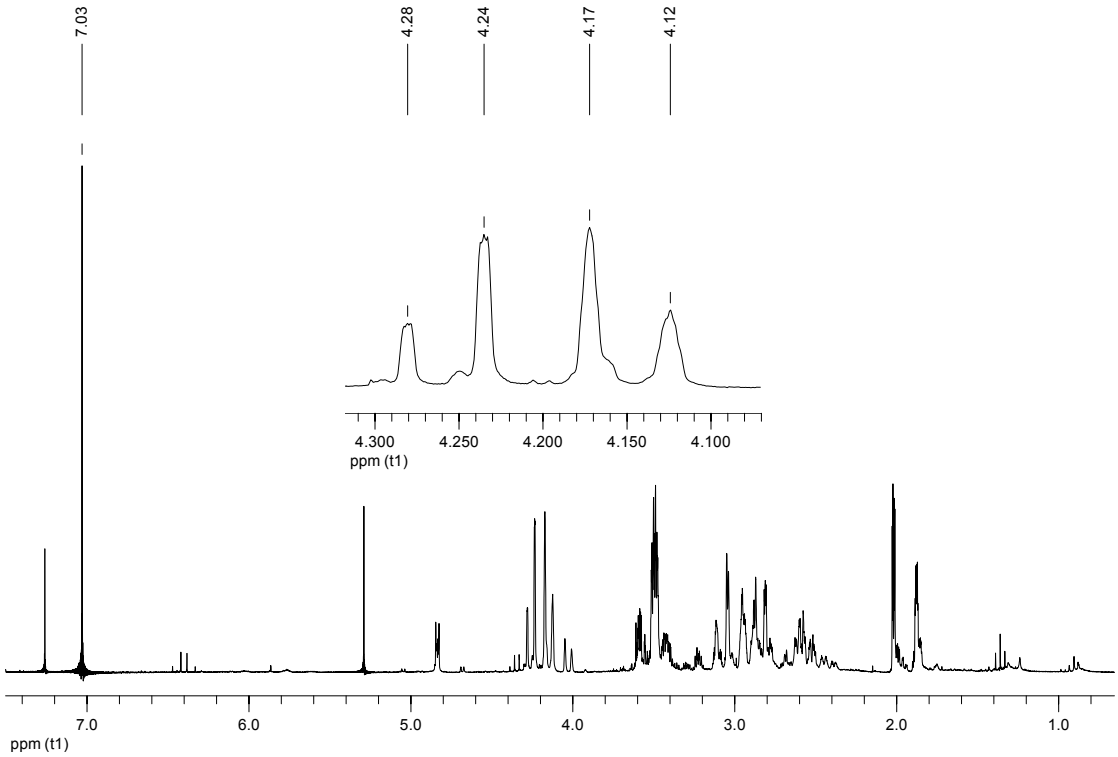


Figure 4.15 ^{1}H NMR of a flash chromatography fraction which probably contains maleic anhydride (singlet at 7.03 ppm), **23**, **24** and **25** (two doublets at 4.12-4.28 ppm).

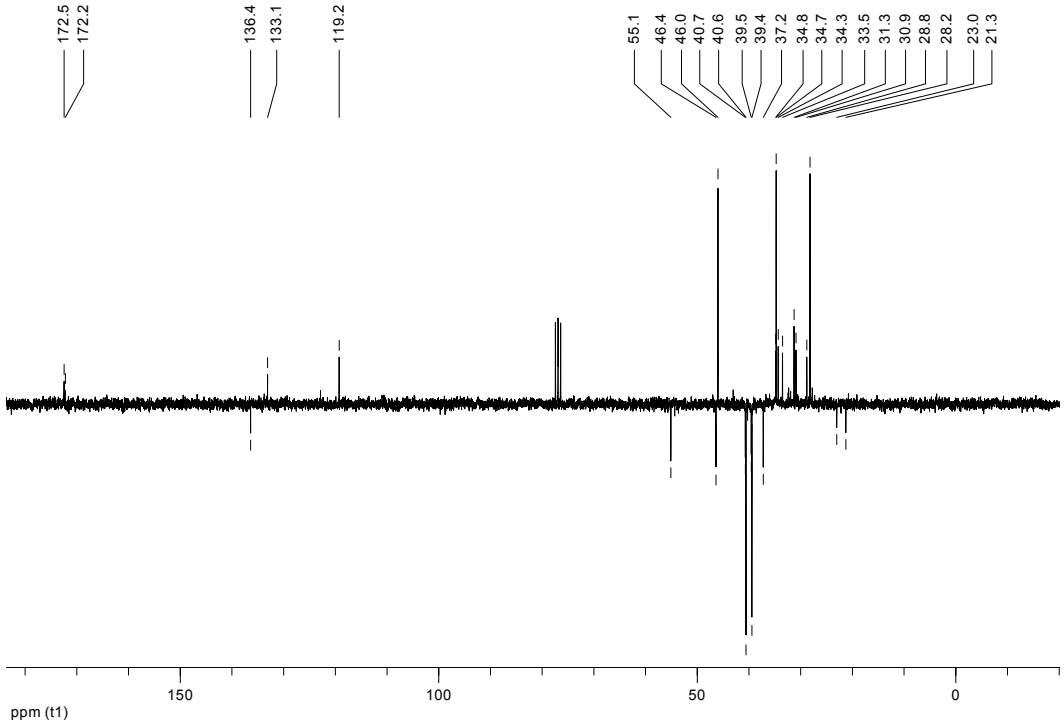


Figure 4.16 SEFT spectrum of a flash chromatography fraction which probably contains maleic anhydride, **23**, **24** and **25**. Quaternary and methylene carbons are phased in the positive direction.

In the SEFT spectrum of the same fraction the signals at 133.1 and 119.2 ppm may be assigned to the carbon atoms in the double bond of **25**, while the carboxylic carbon atom probably gives rise to either the signal at 172.5 or 172.2 ppm (Figure 4.16). Since maleic anhydride is symmetric it only gives rise to two signals in the SEFT spectrum. The negative signal at 136.4 ppm may be assigned to the carbon atom in the double bond, while one of the signals at approximately 172 ppm is due to the carbon atom in the carboxylic group.

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5 Experimental

General. IR spectra were recorded on a Nicolet Impact 410 infrared spectrophotometer, with the compounds as either a liquid between NaCl plates or as a solid in KBr discs. Absorptions are given in wave-numbers (cm^{-1}) and the intensities are indicated as (s) for strong, (w) for weak, (m) for medium and (br) for broad. A few spectra were recorded on a Nicolet Protege 460 FTIR spectrophotometer, with the attenuated total reflection (ATR) technique on a diamond crystal.

NMR spectra were recorded on a Bruker Spectrospin AC 200 F, a Bruker Spectrospin DPX 250, a Bruker Spectrospin DMX 400 or a Bruker Spectrospin DRX 600 spectrometer, with the field strengths of 200, 250, 400 and 600 MHz for ^{1}H nuclei and 50, 62.5, 100 and 150 MHz for ^{13}C nuclei. Chemical shifts are reported downfield from TMS and coupling constants are given in Hertz. Multiplicities are indicated as (s) for singlet, (d) for doublet, (t) for triplet, (q) for quartet, (dd) for double doublet, (dt) for double triplet, (td) for triple doublet and (m) for multiplet.

GC analyses were performed on an HP 5890 Gas Chromatograph with a FID (flame ionisation detection) detector and an HP Ultra 1 (100% dimethylpolysiloxane) 25 m, 0.2 mm i.d. and 0.33 μm column. The chromatograph was interfaced to a computer with Atlas 2000 (Labsystems, Altrincham, Cheshire, UK) software for Windows. No corrections were made for response ratios. The detector temperature was 300 ˚C, while the injector temperature was varied between 150 and 250 ˚C. Helium was used as the carrier gas (200 kPa, 20 mL/min), and a mixture of hydrogen (35 mL/min), air (350 mL/min) and nitrogen (30 mL/min) was used as the detector gas. In almost all cases the same temperature program was used: 50 ºC (2 min) $\xrightarrow{15\ ^{\circ}C/min}$ 200 ºC (0 min) $\xrightarrow{25\ ^{\circ}C/min}$ 290 ºC (5 min).

GC-MS analyses were performed on an HP 5890 II Gas Chromatograph with a dual column and detection system: FID in GC unit, especially for quantification, and mass sensitive detector HP 5971, run from a computer with a dedicated HP Chem Laboratory data system. Some analyses were also done on an HP6890 GC system without FID, connected to an HP5973 mass selective detector.

Mass spectra were obtained on a VG 7070 Micromass spectrometer operated in the EI mode at 70 eV. Melting points were determined on a Gallenkamp apparatus. All melting and boiling points are reported uncorrected. Elemental analyses were performed by Ilse Betz Micro analytical laboratory in Kronach in Germany.

Purification of crude products by flash chromatography was performed with Silica gel (230-400 mesh) as the stationary phase and usually different mixtures of hexane and ethyl acetate as the mobile phase. TLC analyses of the reaction mixtures were carried out with Silica gel (60 F_{254}) on aluminium sheets with mixtures of hexane and ethyl acetate, or chloroform as the mobile phase.

HPLC analyses were conducted through either Hypercarb® (100mm x 4.6mm, 5µ particle size) or Hypersil® ODS (250mm x 4.6 mm, 5µ particle size) Thermo Hypersil-Keystone columns. Samples were applied on the columns through a 10 µL injection loop, which was connected to a Perkin-Elmer Binary LC Pump operated at 1 $^{mL}/_{min}$. The solvents (HPLC grade) were degassed with ultrasonication before use and all analyses were performed with an isocratic program and monitored with an HP 1040A UV-detector, which was interfaced to a computer with Atlas 2000 (Labsystems, Altrincham, Cheshire, UK) software for Windows.

Chemicals. Methyllithium was obtained from commercial sources (Fluka) and standardised by double-titration against butan-2-ol in xylene with *N*-phenyl-1-naphthylamine as an indicator.[1] THF and diethyl ether was distilled from sodium-benzophenone ketyl under nitrogen immediately prior to use. Absolute ethanol was used without further purification. Super-dry ethanol was prepared from absolute ethanol and magnesium by the method developed by Lund and Bjerrum, and stored over type 4Å molecular sieves.[2] Both dichloromethane and acetone was dried over type 4Å molecular sieves prior to use. Magnesium turnings, used in the preparation of super-dry ethanol and Grignard reagents, were dried in a heat cupboard at 130 ˚C. Solutions of sodium methoxide was prepared immediately prior to use by dissolving sodium in methanol (pro analysis) at 0 ˚C, followed by gentle reflux for 1 h. Cyclopentadiene, which was used in the trapping of cyclopropenes, was distilled from dicyclopentadiene, bp. 42 ˚C/760 mmHg and stored in the freezer to prevent dimerisation.

5.1 Synthesis of alkanes

1,2-Dibromo-3,3-dimethylbutane was prepared from 3,3-dimethylbut-1-ene (77.79 g, 0.92 mol) and bromine (147.00 g, 0.92 mol), by dropwise addition of a mixture of bromine and chloroform (100 mL) to the alkene dissolved in chloroform (150 mL) with mechanical stirring under nitrogen atmosphere at -78 ˚C.[3] The stirring was continued for 1 h. The solution was

warmed to room temperature, before water was added (100 mL) and the aqueous phase was extracted with dichloromethane (5 x 100 mL). The combined organic phases were washed with saturated sodium hydrogencarbonate and dried with magnesium sulfate. After evaporation of the solvents, the residue was distilled through a packed column to give a colourless oil (198.28 g, 88%), bp. 72-76 ˚C/10 mmHg (lit.[3] 85 ˚C/12 mmHg).

ν_{max}(film)/cm^{-1} 2966br, 2909m, 2874m, 1470s, 1424w, 1397w, 1368m, 1319w, 1256m, 1227s, 1159w, 1130w, 900m, 875w and 664m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.12 (9 H, s, 3 x CH_3), 3.57 (1 H, dd, *J* 9.7 and 11.3, CHBr) and 3.95-4.09 (2 H, m, CH_2Br); δ_C(50 MHz; $CDCl_3$; Me_4Si) 27.4 (3 x CH_3), 35.8 (CH_2Br), 36.9 (C) and 69.0 (CHBr).

5.2 Synthesis of alkenes

2,3-Dibromopropene was synthesised from allyl bromide (130 mL, 1.5 mol) by addition of bromine (78 mL, 1.6 mol). Allyl bromide was dissolved in tetrachloromethane (250 mL) with mechanical stirring and cooled to -5 ˚C. Bromine was slowly added from a dropping funnel connected to a nitrogen inlet. The solution was stirred for half an hour at room temperature before the solvent was evaporated under reduced pressure. The crude product was immediately shaken with a mixture of sodium hydroxide (99.50 g, 2.5 mol) and water (20 mL). Distillation at high temperature (>200 ˚C) yielded a two-phased mixture of the product and water. The mixture was thoroughly washed with water (300 mL), dried with magnesium sulfate, filtrated and evaporated under reduced pressure. Distillation of the residue yielded 2,3-dibromopropene (192.67 g, 64%) as a colourless liquid, bp. 69-73 ˚C/75 mmHg (lit.[4] 73-76 ˚C/75 mmHg).

ν_{max}(film)/cm^{-1} 3017w, 2961w, 1621s, 1421s, 1384m, 1212s, 1192s, 1101s, 904s and 708m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 4.19 (2 H, d, *J* 1.0, CH_2Br), 5.63 (1 H, d, *J* 2.2, =CH) and 6.02-6.04 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 36.7 (CH_2Br), 121.1 (CH_2) and 127.5 (CBr).

5.2.1 *Preparation of 2-bromo-1-alkenes*

General procedure. Grignard reagents were prepared from alkyl bromide or alkyl chloride (0.25 mol), magnesium (6.08 g, 0.25 mol) and a few crystals of iodine in diethyl ether (10 mL) in a dry three necked round-bottomed flask equipped with condenser and dropping funnel under nitrogen atmosphere. A few drops of the halide were added and when the reaction started (indicated by the disappearance of the dark colour of iodine) the solution was diluted with more diethyl ether (approximately 50 mL). A mixture of halide and diethyl ether

(1:1) was added dropwise to achieve a gentle reflux of the solution. The reaction mixture was stirred for a couple of hours at room temperature before refluxing for another hour.

The concentration of some Grignard reagents were estimated by titration prior to use, while some reagents were used directly to synthesise 2-bromo-1-alkenes (**1**).

The freshly prepared Grignard reagent was added dropwise to a solution of 2,3-dibromopropene in diethyl ether or THF under nitrogen at 0 ˚C (in a few cases copper(I) cyanide was used as a catalyst). The solutions generally became discoloured and smoke developed in the flask. Two layers were formed and magnesium halide separated. After two hours reflux, with vigorously magnetic stirring, the solution was decanted into a beaker filled with ice and acidified with HCl (6 M). The products were extracted with diethyl ether and the organic phase was dried, filtrated and evaporated. Finally, the products (**1**) were isolated by either distillation, through a 20 cm packed column, or flash chromatography.

2-Bromopent-1-ene (**1a**) was obtained from ethylmagnesium bromide (1.21 M, 132 mL, 0.16 mol) and 2,3-dibromopropene (30.46 g, 0.15 mol) in THF (100 mL). A colourless oil (**1a**, 10.26 g, 46%) was isolated by distillation, bp. 68-70 ˚C/300 mmHg (lit.[5] 106 ˚C/760 mmHg).
ν_{max}(film)/cm^{-1} 2962s, 2935s, 2874m, 1630s, 1459m, 1431w, 1382w, 1233w, 1158s, 1130w, 1071w, 885s and 771w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.92 (3 H, t, *J* 7.3, CH_3), 1.49-1.68 (2 H, m, CH_2), 2.36-2.44 (2 H, m, CH_2), 5.39 (1 H, d, *J* 1.5, =CH) and 5.55-5.57 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 12.7 (CH_3), 21.0 (CH_2), 43.2 (CH_2), 116.3 (=CH_2) and 134.5 (CBr).

2-Bromohept-1-ene (**1b**) was synthesised from 1-chlorobutane (13.89 g, 0.15 mol), magnesium (3.65 g, 0.15 mol) and 2,3-dibromopropene (20.04 g, 0.10 mol) in diethyl ether (100 mL). Distillation of the residue yielded **1b** (9.32 g, 53%) as a colourless liquid, bp. 48 ˚C/16 mmHg (lit.[6] 34 ˚C/0.3 mmHg).
ν_{max}(film)/cm^{-1} 2931br, 2863s, 1630m, 1461m, 1380w, 1203w, 1156w, 1078w, 884s and 730w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.89-0.93 (3 H, m, CH_3), 1.26-1.36 (4 H, m, 2 x CH_2), 1.49-1.63 (2 H, m, CH_2), 2.37-2.45 (2 H, m, CH_2), 5.38 (1 H, d, *J* 1.7, =CH) and 5.54-5.56 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 22.3 (CH_2), 27.5 (CH_2), 30.5 (CH_2), 41.3 (CH_2), 116.1 (CH_2) and 134.8 (CBr).
Traces of octane, a Wurtz-coupling product, could be observed in the NMR spectra:[7]
δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.6 (CH_2), 29.2 (CH_2) and 31.8 (CH_2).

2-Bromodec-1-ene (**1c**) was synthesised from 1-bromoheptane (17.94 g, 0.10 mol), magnesium (2.43 g, 0.10 mol) and 2,3-dibromopropene (15.94 g, 0.08 mol) in diethyl ether (100 mL). By distilling the residue **1c** (7.28 g, 42%) was isolated as a colourless oil, bp. 58-62 ˚C/0.5 mmHg (lit.[8] 76-77 ˚C/3 mmHg).

ν_{max}(film)/cm^{-1} 2927br, 2857s, 1630m, 1461m, 1376w, 1178w, 1146w, 1091w, 883s and 723w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-0.92 (3 H, m, CH_3), 1.28 (10 H, m, 5 x CH_2), 1.51-1.58 (2 H, m, CH_2), 2.37-2.45 (2 H, m, CH_2), 5.38 (1 H, d, *J* 1.6, =CH) and 5.54-5.56 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.6 (CH_2), 27.8 (CH_2), 28.3 (CH_2), 29.1 (CH_2), 29.2 (CH_2), 31.7 (CH_2), 41.3 (CH_2), 116.1 (CH_2) and 134.8 (CBr).

In addition tetradecane (3.73 g, 18 mmol), bp. 69-79 ˚C/0.2 mmHg (lit.[9] 254 ˚C/760 mmHg), was isolated as a colourless liquid.

ν_{max}(film)/cm^{-1} 2923br, 2857s, 1462m, 1376w, 883w and 722w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-0.91 (6 H, m, 2 x CH_3) and 1.26 (24 H, br s, 12 x CH_2); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (2 x CH_3), 22.6 (2 x CH_2), 29.3 (2 x CH_2), 29.6 (2 x CH_2), 29.7 (4 x CH_2) and 31.9 (2 x CH_2).

2-Bromo-4-phenylbut-1-ene (**1d**) was prepared from benzyl chloride (12.66 g, 0.10 mol), magnesium (2.43 g, 0.10 mol) and 2,3-dibromopropene (15.99 g, 0.08 mol) in diethyl ether (80 mL).[8] Purification by flash chromatography (hexane) gave pure **1d** (10.36 g, 61%) as a colourless oil.

ν_{max}(film)/cm^{-1} 3062m, 3027m, 2934br, 2860w, 1629s, 1605w, 1496m, 1450m, 1430m, 1187m, 1114m, 1073w, 1029w, 888s, 746s and 699s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.65-2.74 (2 H, m, CH_2), 2.83-2.91 (2 H, m, CH_2), 5.37 (1 H, d, *J* 1.7, =CH), 5.48-5.50 (1 H, m, =CH) and 7.15-7.32 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 34.2 (CH_2), 43.1 (CH_2), 117.0 (CH_2), 126.0 (CH), 128.25 (2 x CH), 128.34 (2 x CH), 133.4 (CBr) and 140.2 (C).

In addition bibenzyl (3.14 g, 17 mmol), mp. 40-45 ˚C (lit.[9] 50-53 ˚C), was isolated as light yellow crystals.

ν_{max}(KBr)/cm^{-1} 3061m, 3026s, 2927br, 2856m, 1602w, 1495m, 1451m, 1071w, 748s and 699s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.9 (4 H, s, 2 x CH_2) and 7.09-7.32 (10 H, m, 10 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 37.8 (CH_2), 125.8 (CH), 128.2 (2 x CH), 128.3 (2 x CH) and 141.6 (C).

2-Bromo-3-cyclohexylpropene (**1e**) was prepared from cyclohexylmagnesium bromide (56 mL, 1.84 M, 103 mmol) and 2,3-dibromopropene (20.51 g, 103 mmol), with copper(I)

cyanide as catalyst, in diethyl ether (100 mL). Distillation yielded **1e** (11.67 g, 56%) as a colourless oil, bp. 84-92 ˚C/13 mmHg (lit.[10] 88-89 ˚C/14 mmHg).

ν_{max}(film)/cm^{-1} 2924br, 2850s, 1628m, 1448m, 1268w, 1206w, 1157m, 1096w, 1070w and 884s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.79-1.38 (5 H, m, CH and 2 x CH_2), 1.54-1.76 (6 H, m, 3 x CH_2), 2.27 (2 H, dd, *J* 0.8 and 6.7, CH_2), 5.40 (1 H, d, *J* 1.4, =CH) and 5.52 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 26.0 (2 x CH_2), 26.3 (CH_2), 32.3 (2 x CH_2), 35.4 (CH), 49.0 (CH_2), 117.2 (CH_2) and 133.4 (CBr).

Traces of bicyclohexyl (8% according to GC) could be observed in the NMR spectra:[7]

δ_C(50 MHz; $CDCl_3$; Me_4Si) 26.8 (4 x CH_2), 30.0 (2 x CH_2) and 43.3 (2 x CH).

2-Bromo-4-methylpent-1-ene (**1f**) was synthesised from 2-brompropane (18.45 g, 150 mmol), magnesium (3.69 g, 150 mmol) and 2,3-dibromopropene (23.97 g, 120 mmol) in THF (120 mL). Distillation yielded **1f** (8.72 g, 46%) as a colourless liquid, bp. 63-64 ˚C/100 mmHg (lit.[11] 126-127 ˚C/760 mmHg).

ν_{max}(film)/cm^{-1} 2957s, 2929s, 2873s, 1629s, 1463s, 1428m, 1387m, 1336w, 1234m, 1163s, 1083m, 885s and 822w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.92 (6 H, d, *J* 6.5, 2 x CH_3), 1.85-2.08 (1 H, m), 2.24-2.28 (2 H, m, CH_2), 5.41 (1 H, d, *J* 1.5, =CH) and 5.53-5.54 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 21.6 (2 x CH_3), 26.3 (CH), 50.4 (CH_2), 117.2 (CH_2) and 133.9 (CBr).

5.2.2 *Synthesis of some bromoalkenes*

2-Bromo-3,3-dimethylbut-1-ene (**1g**) was prepared from 1,2-dibromo-3,3-dimethylbut-1-ene (36.60 g, 0.15 mol) and sodium methoxide (180 mL, 1 M, 0.18 mol).[12] The dihalide was dissolved in dichloromethane (100 mL) and sodium methoxide was added dropwise at 0 ˚C. The solution was magnetically stirred for 1h, heated to room temperature and stirred for another hour. After reflux for 24 h, the reaction mixture was quenched with saturated ammonium chloride (50 mL) and extracted with pentane (4 x 150 mL). After evaporation of the solvents, the residue was distilled through a 20 cm packed column and **1g** (19.52 g, 80%) was isolated as a colourless oil, bp. 60-63 ˚C/96 mmHg (lit.[13] 60 ˚C/100 mmHg).

ν_{max}(film)/cm^{-1} 2967s, 2910s, 2874s, 1627m, 1608m, 1462br, 1365m, 1262w, 1240w, 1207w, 1093s, 945br, 888br and 740w.

GC and NMR studies proved that two isomers were formed (but not separately isolated):

2-Bromo-3,3-dimethylbut-1-ene (**1g**, 76%): δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.20 (9 H, s, 3 x CH_3), 5.38 (1 H, d, *J* 2.1, =CH) and 5.59 (1 H, d, *J* 2.1, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.0 (CH_3), 39.5 (C), 113.9 (=CH_2) and 147.0 (CBr).
(E)-*1-Bromo-3,3-dimethylbut-1-ene* (24%): δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.04 (9 H, s, 3 x CH_3), 5.97 (1 H, d, *J* 13.7, =CH) and 6.22 (1 H, d, *J* 13.7, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 28.9 (3 x CH_3), 35.6 (C), 101.7 (CHBr) and 148.3 (=CH).

1-Bromocyclooctene (**1h**) was obtained from cyclooctene (27.76 g, 252 mmol) dissolved in tetrachloromethane (100 mL), by dropwise addition of bromine (13 mL, 252 mmol) at –35 ˚C. The solution was evaporated *in vacuo* and the residue was dissolved in diethyl ether (150 mL). Potassium *tert*-butoxide (42.69 g, 380 mmol) was added in small portions to the magnetically stirred solution at 0 ˚C. Stirring was continued at room temperature for 1 h before the reaction was quenched with ice water (150 mL) and extracted with diethyl ether (3 x 50 mL). The organic phase was washed with sat. NaCl solution, dried over magnesium sulfate and evaporated under reduced pressure. The residue was distilled to give **1h** (32.42 g, 68%) as a colourless oil, bp. 80-88 ˚C/8 mmHg (lit.[14] 78-82 ˚C/10 mmHg).
ν_{max}(film)/cm^{-1} 2926br, 2853s, 1642m, 1455m, 1354w, 1212w, 1109m, 986w, 874w, 833m, 770w and 731w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.52 (8 H, br s, 4 x CH_2), 2.09 (2 H, m, CH_2), 2.61 (2 H, m, CH_2) and 6.03 (1 H, t, *J* 8.5, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 25.3 (CH_2), 26.3 (CH_2), 27.3 (CH_2), 28.5 (CH_2), 29.7 (CH_2), 35.0 (CH_2), 124.7 (CBr) and 131.5 (=CH).

5.2.3 *Preparation of 3-aryloxy-2-bromopropenes*

General procedure. 2,3-Dibromopropene (~40 g, 0.20 mol) was added to a mixture of a phenol (~0.20 mol) and anhydrous potassium carbonate (~32 g, 0.23 mol) in anhydrous acetone (200 mL) kept under nitrogen. The resulting mixture was stirred vigorously, refluxed and monitored by GC (approximately 26 h). The reaction was quenched with 2 M NaOH (200 mL) and diethyl ether (300 mL) was added. The organic phase was washed with 2 M NaOH (3 x 50 mL) and the combined water phases were washed with diethyl ether (2 x 100 mL). The combined organic phases were washed with 1 M HCl (50 mL) and water (50 mL), dried with anhydrous magnesium sulfate, filtrated and evaporated *in vacuo*. The products (**1**) were isolated by distillation.

2-Bromo-3-phenoxypropene (**1i**) was obtained from phenol and 2,3-dibromopropene (40.19 g, 0.20 mol), bp. 58-62 ˚C/0.3 mmHg (lit.[15] 98-99 ˚C/2.5 mmHg) as a colourless oil (33.16 g, 77%).

ν_{max}(film)/cm^{-1} 2921w, 2865w, 1640m, 1595s, 1493s, 1453m, 1384w, 1298m, 1233br, 1170m, 1127w, 1077w, 1043s, 898s, 827w, 755s and 687s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 4.62 (2 H, t, *J* 1.5, OCH_2), 5.64-5.66 (1 H, m, $=CH_2$), 5.97-5.98 (1 H, m, $=CH_2$), 6.89-6.92 (2 H, m, 2 x CH), 6.95-6.99 (1 H, m, CH) and 7.25-7.30 (2 H, m, 2 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 71.4 (OCH_2), 114.7 (2 x CH), 117.5 ($=CH_2$), 121.4 (CH), 126.9 (CBr), 129.4 (2 x CH) and 157.6 (C).

2-Bromo-3-(4-methylphenoxy)propene (**1j**) was synthesised from 4-methylphenol and 2,3-dibromopropene (40.01 g, 0.20 mol), bp. 74-78 ˚C/1 mmHg (lit.[15] 70-71 ˚C/1 mmHg) as a colourless oil (37.85 g, 83%).

ν_{max}(film)/cm^{-1} 3031m, 2922m, 2864m, 1640s, 1613s, 1591m, 1511s, 1451m, 1404w, 1383w, 1293s, 1231s, 1173m, 1119m, 1042s, 898s, 763w and 724w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.28 (3 H, s, CH_3), 4.61 (2 H, t, *J* 1.5, OCH_2), 5.64-5.67 (1 H, m, $=CH_2$), 5.97-6.00 (1 H, m, $=CH_2$), 6.79-6.85 (2 H, m, 2 x CH) and 7.06-7.11 (2 H, m, 2 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 20.3 (CH_3), 71.8 (CH_2), 114.8 (2 x CH), 117.4 ($=CH_2$), 127.3 (CBr), 129.9 (2 x CH), 130.8 (C) and 155.6 (C).

2-Bromo-3-(4-bromophenoxy)propene (**1k**) was obtained from 4-bromophenol and 2,3-dibromopropene (40.37 g, 0.20 mol), bp. 106-108 ˚C/0.25 mmHg (lit.[16] 171 ˚C/22 mmHg) as a colourless oil (43.12 g, 73%).

ν_{max}(film)/cm^{-1} 3070w, 2919w, 2866w, 1639m, 1585s, 1486s, 1451m, 1401w, 1289s, 1232br, 1170m, 1124w, 1072w, 1036br, 900s, 822s, and 686m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 4.60 (2 H, t, *J* 1.5, OCH_2), 5.66-5.69 (1 H, m, $=CH_2$), 5.95-5.98 (1 H, m, $=CH_2$), 6.76-6.84 (2 H, m, 2 x CH) and 7.34-7.42 (2 H, m, 2 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 71.7 (OCH_2), 113.7 (C), 116.6 (2 x CH), 117.9 ($=CH_2$), 126.4 (=CBr), 132.3 (2 x CH) and 156.7 (CBr).

In addition 4-hydroxy-4-methylpentan-2-one (1.45 g, 12 mmol), bp. 32 ˚C/0.25 mmHg (lit.[9] 166 ˚C/760 mmHg), was isolated as a colourless liquid.

δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.26 (6 H, s, 2 x CH_3), 2.19 (3 H, s, CH_3), 2.64 (2 H, s, CH_2) and 3.89 (1 H, br s, OH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.0 (2 x CH_3), 31.5 (CH_3), 53.6 (CH_2), 69.3 (C) and 210.6 (C=O).

5.3 Synthesis of trihalogenated cyclopropanes

General procedure. Most of the cyclopropanes (**2** and **3**) were synthesised on 50 mmol scale under phase-transfer conditions.[17] The appropriate alkenes (**1**) were treated with haloform (8 equivalents) and 50% aqueous sodium hydroxide (6 equivalents) at 0 °C with vigorous mechanical stirring and triethylbenzylammonium chloride (TEBA) or hexadecyltrimethyl-ammonium bromide (Cetrimide) as catalyst. The reactions were monitored by GC or TLC and the stirring was continued at room temperature for 15-36 h. After quenching with water and hydrochloric acid (6 M), the products were extracted with dichloromethane. The combined organic phases were dried with magnesium sulfate, filtrated and evaporated *in vacuo*. Finally, the products (**2** or **3**) were isolated by flash chromatography, distillation or recrystallisation.

1,1,2-Tribromo-2-propylcyclopropane (**2a**) was prepared from **1a** (7.49 g, 50 mmol), bromoform (100.59 g, 398 mmol), 50% aqueous sodium hydroxide (27.05 g, 338 mmol) and TEBA.[18] Purification by flash chromatography (hexane) gave **2a** (12.31 g, 77%) as a colourless oil.

ν_{max}(film)/cm^{-1} 2961br, 2872s, 1459s, 1421m, 1380w, 1145m, 1089w, 1051m, 1014s, 955w, 740w and 666br; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.00 (3 H, t, *J* 7.3, CH_3), 1.56-2.13 (6 H, m, 3 x CH_2); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.3 (CH_3), 21.0 (CH_2), 33.0 (CBr_2), 37.9 (CH_2), 43.4 (CH_2) and 45.5 (CBr); *m/z* (EI) 317.8268 (M^+, 4%, $C_6H_9Br_3^+$ requires 317.8254), 243/241/239 (6/12/6), 201/199/197 (16/32/16), 79 (56) and 51 (100).

1-Bromo-2,2-dichloro-1-propylcyclopropane (**3a**) was synthesised from **1a** (4.23 g, 28 mmol), chloroform (27.12 g, 227 mmol), 50% aqueous sodium hydroxide (13.65 g, 170 mmol) and TEBA.[18] The crude product was purified by flash chromatography (hexane) and **3a** (3.55 g, 55%) was isolated as a yellow oil.

ν_{max}(film)/cm^{-1} 2962s, 2934s, 2875s, 1460m, 1413m, 1382w, 1234w, 1153w, 1097m, 1046s, 961w, 904w, 836w, 762s and 609m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.99 (3 H, t, *J* 7.4, CH_3), 1.67-1.77 (3 H, m), 1.84 (1 H, d, *J* 8.9, CH) and 1.89-2.04 (2 H, m, CH_2); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.3 (CH_3), 20.9 (CH_2), 36.1 (CH_2), 41.3 (CH_2), 45.7 (CBr) and 63.6 (CCl_2).

1,1,2-Tribromo-2-pentylcyclopropane (**2b**) was synthesised from **1b** (9.00 g, 51 mmol), bromoform (101.38 g, 401 mmol), 50% aqueous sodium hydroxide (25.93 g, 324 mmol) and

TEBA.[18] Distillation of the residue yielded **2b** (12.48 g, 70%) as a colourless liquid, bp. 88-92 ˚C/0.4 mmHg.

ν_{max}(film)/cm^{-1} 2952s, 2930s, 2862s, 1459m, 1422m, 1378w, 1145w, 1051w, 1016m, 684s and 672s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.88-0.98 (3 H, m, CH_3), 1.28-1.42 (4 H, m, 2 x CH_2) and 1.62-2.16 (6 H, m, 3 x CH_2); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 22.4 (CH_2), 27.2 (CH_2), 31.0 (CH_2), 33.1 (CBr_2), 37.9 (CH_2), 41.6 (CH_2) and 45.7 (CBr)); *m/z* (EI) 345.8595 (M^+, 1%, $C_8H_{13}Br_3^+$ requires 345.8567), 201/199/197 (8/16/8), 189/187 (10/10), 107 (73) and 41 (100).

1,1,2-Tribromo-2-octylcyclopropane (**2c**) was synthesised from **1c** (7.16 g, 33 mmol), bromoform (66.32 g, 262 mmol), 50% aqueous sodium hydroxide (17.02 g, 213 mmol) and TEBA. Purification by flash chromatography (hexane) gave **2c** (9.28 g, 72%) as a colourless liquid.[19,20]

ν_{max}(film)/cm^{-1} 2925br, 2856s, 1459s, 1423m, 1375w, 1144w, 1052m, 1016m, 885w, 722w, 691s and 672m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-0.92 (3 H, m, CH_3), 1.28-1.31 (10 H, m, 5 x CH_2) and 1.55-2.15 (6 H, m, 3 x CH_2); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.5 (CH_2), 27.6 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 31.7 (CH_2), 33.1 (CBr_2), 37.9 (CH_2), 41.6 (CH_2) and 45.7 (CBr) *m/z* (EI); 393.8993 (M^+, 1%, $C_{11}H_{19}{}^{81}Br_3^+$ requires 393.8975), 201/199/197 (7/14/7), 69 (90) and 42 (100).

1,1,2-Tribromo-2-(2-phenylethyl)cyclopropane (**2d**) was prepared from **1d** (10.05 g, 48 mmol), bromoform (101.07 g, 400 mmol), 50% aqueous sodium hydroxide (26.46 g, 331 mmol) and TEBA.[18] Purification by flash chromatography (hexane) gave **2d** (14.07 g, 77%) as a colourless oil.

ν_{max}(film)/cm^{-1} 3066w, 3026m, 2951w, 2925w, 2860w, 1495w, 1450m, 1422w, 1180w, 1054w, 1009m, 748s and 695s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.73 (1 H, d, *J* 9.4, CH), 1.92 (1 H, dd, *J* 0.6 and 9.4, CH), 2.16-2.47 (2 H, m, CH_2), 2.86-3.16 (2 H, m, CH_2) and 7.15-7.35 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 32.6 (CBr_2), 33.8 (CH_2), 37.8 (CH_2), 43.6 (CH_2), 45.0 (CBr), 126.2 (CH), 128.37 (2 x CH), 128.39 (2 x CH) and 140.3 (C); *m/z* (EI) 300.9233 (M^+-Br, 3%, $C_{11}H_{11}Br_2^+$ requires 300.9227), 223/221 (33/33), 91 (100) and 65 (74).

1,1,2-Tribromo-2-cyclohexylmethylcyclopropane (**2e**) was synthesised from **1e** (10.16 g, 50 mmol), bromoform (103.58 g, 410 mmol), 50% aqueous sodium hydroxide (25.36 g, 317 mmol) and TEBA.[18] Purification by flash chromatography (hexane) gave **2e** (12.79 g, 68%) as

a colourless oil. In the freezer white crystals were formed and subsequently recrystallised (hexane), mp. 29-30 ˚C.

ν_{max}(film)/cm^{-1} 2924br, 2849s, 1446m, 1420m, 1346w, 1267w, 1207w, 1149w, 1054m, 1017m, 974m, 902w, 851w and 690m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.79-1.42 (6 H, m, 3 x CH_2) and 1.66-2.15 (9 H, m, 4 x CH_2 and CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 26.0 (CH_2), 26.2 (CH_2), 26.3 (CH_2), 32.1 (CH_2), 32.9 (CH_2), 33.5 (CBr_2), 38.0 (CH), 38.2 (CH_2), 44.3 (CBr) and 47.3 (CH_2); *m/z* (EI) 371.8732 (M^+, 1%, $C_{10}H_{15}Br_3^+$ requires 371.8724), 297/295/293 (2/4/2), 215/213 (13/13), 133 (45), 109 (60), 83 (98) and 55 (100).

1-Bromo-2,2-dichloro-1-cyclohexylmethylcyclopropane (**3e**) was prepared from **1e** (5.44 g, 27 mmol), chloroform (26.44 g, 221 mmol), 50% aqueous sodium hydroxide (13.34 g, 167 mmol) and TEBA.[18] Purification of the crude product by flash chromatography (hexane) yielded **3e** (4.58 g, 59%) as a colourless oil.

ν_{max}(film)/cm^{-1} 2926s, 2850s, 1447m, 1413m, 1348w, 1267w, 1209w, 1153w, 1039m, 978m, 888m, 853w, 762s and 623m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.85-1.35 (6 H, m, 3 x CH_2), 1.65-1.88 (8 H, m) and 1.99-2.04 (1 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 26.0 (CH_2), 26.1 (CH_2), 26.3 (CH_2), 32.2 (CH_2), 32.6 (CH_2), 36.3 (CH_2), 37.4 (CH), 44.6 (CBr), 45.2 (CH_2) and 63.5 (CCl_2).

1,1,2-Tribromo-2-isobutylcyclopropane (**2f**) was prepared from **1f** (8.48 g, 54 mmol), bromoform (108.47 g, 429 mmol), 50% aqueous sodium hydroxide (25.90 g, 322 mmol) and Cetrimide.[20] Purification of the crude product by flash chromatography (hexane) yielded **2f** (12.42 g, 69%) as a colourless liquid.

ν_{max}(film)/cm^{-1} 2957s, 2932s, 2870m, 1464m, 1419m, 1386m, 1369m, 1298w, 1239w, 1149m, 1120w, 1099w, 1055m, 1019m, 963br, 865w, 690s and 656m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.98 (3 H, d, *J* 6.6, CH_3), 1.06 (3 H, d, *J* 6.6, CH_3), 1.65-1.69 (1 H, m), 1.85 (1 H, d, *J* 9.2), 1.99 (1 H, dd, *J* 1.0 and 9.2) and 2.12-2.20 (2 H, m, CH_2); δ_C(50 MHz; $CDCl_3$; Me_4Si) 21.3 (CH_3), 22.4 (CH_3), 28.7 (CH), 33.3 (CBr_2), 38.2 (CH_2), 44.7 (CBr) and 48.4 (CH_2); *m/z* (EI) 335.8397 (M^+, 1%, $C_7H_{11}Br^{81}Br_2^+$ requires 335.8370), 257/255/253 (M^+-Br, 3/6/3), 201/199/197 (6/12/6), 175/173 (8/8), 150/148 (5/5), 69 (37) and 43 (100).

1,1,2-Tribromo-2-(1,1-dimethylethyl)cyclopropane (**2g**) was synthesised from **1g** (7.49 g, 46 mmol), bromoform (98.42 g, 361 mmol), 50% aqueous sodium hydroxide (22.24 g, 278

mmol) and TEBA. Flash chromatography (hexane) of the residue yielded **2g** (6.97 g, 60% based on the amount of **1g**) as a colourless liquid.[18,20,21]

ν_{max}(film)/cm^{-1} 2967s, 2875m, 1466br, 1410m, 1263w, 1211w, 1058m, 1032w, 1058br, 948w, 878w, 670s and 600s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.34 (9 H, s, 3 x CH_3), 1.90 (1 H, d, *J* 9.9, CH) and 2.21 (1 H, d, *J* 9.9, CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.8 (3 x CH_3), 30.6 (C), 34.7 (CH_2), 38.7 (CBr_2) and 55.8 (CBr); *m/z* (EI) 330.8333 (M^+-H, 1%, $C_7H_{10}Br_3^+$ requires 330.8333), 176/174 (2/2), 150/148 (55/55), 69 (77) and 41 (100).

1-Bromo-2,2-dichloro-1-(1,1-dimethylethyl)cyclopropane (**3g**) was prepared from **1g** (8.15 g, 50 mmol), chloroform (47.75 g, 400 mmol), 50% aqueous sodium hydroxide (24.15 g, 302 mmol) and TEBA.[18] Purification by distillation gave **3g** (5.46 g, 58% based on the amount of **1g**) as a colourless oil, bp. 74 ˚C/2.5 mmHg.

ν_{max}(film)/cm^{-1} 2968br, 2877s, 1467s, 1405m, 1368m, 1268m, 1211m, 1058m, 1008s, 957w, 894w, 755s, 726s and 634m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.30 (9 H, s, 3 x CH_3), 1.80 (1 H, d, *J* 9.6, CH) and 2.11 (1 H, d, *J* 9.6, CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.4 (3 x CH_3), 32.7 (CH_2), 38.2 (C), 56.7 (CBr) and 63.5 (CCl_2) ; *m/z* (EI) 165.0222 (M^+, 2%, $C_7H_{11}Cl_2^+$ requires 165.0238) and 69 (100).

1,9,9-Tribromobicyclo[6.1.0]nonane (**2h**) was prepared from **1h** (18.88 g, 0.10 mol), bromoform (201.95 g, 0.80 mol), 50% aqueous sodium hydroxide and TEBA. Purification by flash chromatography (hexane:ethyl acetate [97.5:2.5]) gave **2h** (26.08 g, 72%), which was subsequently recrystallised (hexane) to give light yellow crystals, mp. 41-43 ˚C (lit.[22] 41-43 ˚C).

ν_{max}(KBr)/cm^{-1} 2921s, 2853s, 1451m, 1358m, 1248w, 1201w, 1137m, 1086w, 1060m, 1025m, 895w, 866w, 827m, 769w, 756w and 719m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.16-1.35 (2 H, m), 1.49-1.88 (9 H, m), 2.03-2.10 (1 H, m) and 2.23-2.26 (1 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 25.3 (CH_2), 25.6 (CH_2), 26.9 (CH_2), 27.0 (CH_2), 27.9 (CH_2), 34.9 (CH_2), 41.3 (CBr_2), 43.5 (CH) and 49.4 (CBr); *m/z* (EI) 283/281/279 (M^+-Br, 5%), 119 (100), 91 (41), 79 (18) and 51 (14).

1,1,2-Tribromo-2-phenoxymethylcyclopropane (**2i**) was prepared from **1i** (10.69 g, 50 mmol), bromoform free of ethanol (101.85 g, 403 mmol), 50% aqueous sodium hydroxide (24.00 g, 300 mmol) and TEBA. Flash chromatography (hexane) and subsequently recrystallisation

(hexane and activated charcoal) gave pure **2i** (5.49 g, 28%) as light yellow crystals, mp. 45-47 ˚C (lit.[23] 44-46 ˚C).

ν_{max}(KBr)/cm^{-1} 3071w, 3039w, 2925w, 2871w, 1594s, 1494s, 1456w, 1386w, 1297w, 1240s, 1173w, 1052m, 1012w, 754m and 693m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.03 (1 H, dd, *J* 0.5 and 9.4, CH), 2.14 (1 H, d, *J* 9.4, CH), 4.39 (1 H, dd, *J* 0.5 and 11.1, OCH), 4.49 (1 H, d, *J* 11.1, OCH), 6.92-7.04 (3 H, m, Ph) and 7.27-7.36 (2 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.5 (CBr_2), 35.8 (CH_2), 40.9 (CBr), 74.8 (OCH_2), 115.0 (2 x CH), 121.6 (CH), 129.5 (2 x CH) and 157.9 (C).

1,1,2-Tribromo-2-(4-methylphenoxy)methylcyclopropane (**2j**) was prepared from **1j** (11.38 g, 50 mmol), bromoform (37.94 g, 150 mmol), 50% aqueous sodium hydroxide (32.08 g, 380 mmol) and TEBA. Purification by flash chromatography (hexane:ethyl acetate [97.5:2.5]), followed by recrystallisation (hexane and activated charcoal) yielded **2j** (4.48 g, 23%) as white crystals, mp. 37-39 ˚C (lit.[23] 35-37 ˚C).

ν_{max}(KBr)/cm^{-1} 3060m, 3016m, 2927m, 2865m, 1613w, 1587w, 1510s, 1458m, 1422w, 1387m, 1293m, 1247s, 1233s, 1182m, 1116w, 1064s, 1018m, 823w, 810s, 756w and 703m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.02 (1 H, dd, *J* 0.5 and 9.6, CH), 2.14 (1 H, d, *J* 9.6, CH), 2.29 (3 H, s, CH_3), 4.37 (1 H, dd, *J* 0.5 and 11.0, OCH), 4.47 (1 H, d, 11.0), 6.82-6.89 (2 H, m, 2 x CH) and 7.06-7.13 (2 H, m, 2 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 20.4 (CH_3), 29.5 (CBr_2), 35.8 (CH_2), 41.0 (CBr), 75.1 (OCH_2), 114.9 (2 x CH), 129.9 (2 x CH), 131.0 (C) and 155.9 (C).

1,1,2-Tribromo-2-(4-bromophenoxy)methylcyclopropane (**2k**) was synthesised from **1k** (14.66 g, 50 mmol), bromoform (103.37 g, 409 mmol), 50% aqueous sodium hydroxide (25.42 g, 318 mmol) and TEBA. Flash chromatography (hexane:ethyl acetate [95:5]) and recrystallisation (hexane) gave **2k** (5.74 g, 25%) as yellow crystals, mp. 84-86 ˚C (lit.[24] 84-86 ˚C).

ν_{max}(KBr)/cm^{-1} 3066w, 2923w, 2867w, 1581w, 1487s, 1450m, 1386w, 1286w, 1241s, 1172w, 1051s, 818m, 700w and 647m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.04 (1 H, d, *J* 9.4, CH), 2.14 (1 H, d, *J* 9.4, CH), 4.35 (1 H, dd, *J* 0.5 and 11.0, OCH), 4.47 (1 H, d, *J* 11.0, OCH), 6.80-6.88 (2 H, m, 2 x CH) and 7.36-7.44 (2 H, m, 2 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.3 (CBr_2), 35.8 (CH_2), 40.6 (CBr), 75.2 (OCH_2), 113.9 (C), 116.8 (2 x CH), 132.3 (2 x CH) and 157.0 (C).

1,1,2-Tribromo-2-phenylcyclopropane (**2l**) was prepared from 1-(1-bromovinyl)benzene (9.16 g, 50 mmol), bromoform (25.40 g, 100 mmol), finely ground NaOH (12.00 g, 300 mmol) and TEBA in dichloromethane (50 mL) by using the Xu-Brinker procedure.[25] The solution was ultrasonicated for 1 h, before some Celite® was added and the crude product was filtered through a bed of Celite®. The filtrate was extracted with dichloromethane (4 x 50 mL) and the combined extracts were concentrated on a rotavapor. Flash chromatography (hexane) and subsequently recrystallisation (hexane) yielded **2l** (10.04 g, 57%) as white crystals, mp. 89-90 °C (lit.[26] 88-89 °C).

ν_{max}(KBr)/cm^{-1} 3075w, 2995m, 1493m, 1445m, 1416m, 1313w, 1176w, 1159w, 1069m, 1056m, 989m, 936w, 914w, 889w, 756s, 693s and 619s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 2.24 (1 H, d, *J* 9.3), 2.50 (1 H, d, *J* 9.3) and 7.32-7.49 (5 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 31.7 (CBr_2), 37.0 (CH_2), 42.8 (CBr), 128.5 (2 x CH), 128.8 (CH), 129.0 (2 x CH) and 139.9 (C).

1,1-Dibromo-2-chloromethylcyclopropane (**2m**) was prepared from allyl chloride (7.65 g, 0.10 mol), bromoform (202.67 g, 0.80 mol), 50% aqueous sodium hydroxide (49.17 g, 0.61 mol) and Cetrimide. Distillation of the crude product, through a packed column, gave **2m** (10.35 g, 42%) as a colourless liquid, bp. 72 °C/6 mmHg (lit.[27] 84-86 °C/11 mmHg).

ν_{max}(film)/cm^{-1} 2962w, 1433m, 1373m, 1264m, 1218br, 1103br, 1049m, 1019m, 940w, 910w, 854w, 801w, 725s and 670s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.47-1.51 (1 H, m), 1.91-1.96 (1 H, m), 2.01-2.07 (1 H, m) and 3.64-3.66 (2 H, m, CH_2Cl); δ_C(100 MHz; $CDCl_3$; Me_4Si) 25.5 (CBr_2), 28.9 (CH_2), 32.2 (CH) and 45.9 (CH_2Cl); *m/z* (EI) 247.8419 (M^+, 4%, $C_4H_5Br_2Cl^+$ requires 247.8426), 215/213/211 (M^+-Cl, 13/26/13) and 201/199/197 (M^+-CH_2Cl, 50/100/50).

1,1-Dibromo-2-chloromethyl-2-methylcyclopropane (**2n**) was synthesised from 3-chloro-2-methylprop-1-ene (18.11 g, 0.20 mol), bromoform (404.48 g, 1.60 mol), 50% aqueous sodium hydroxide (96.23 g, 1.20 mol) and Cetrimide.[27,28] Distillation of the crude product, through a packed column, yielded **2n** (47.33 g, 90%) as a colourless liquid, bp. 67-70 °C/3.5 mmHg (lit.[27] 86 °C/9 mmHg).

ν_{max}(film)/cm^{-1} 2992m, 2964m, 2931m, 2872w, 1441s, 1382m, 1326w, 1273s, 1165w, 1079m, 1027s, 959m, 909w, 845w, 728s and 684s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.56 (3 H, s), 1.60 (1 H, d, *J* 7.8), 1.69 (1 H, d, *J* 7.8), 3.68 (1 H, d, *J* 11.4) and 3.82 (1 H, d, *J* 11.4); δ_C(50 MHz; $CDCl_3$; Me_4Si) 21.1 (CH_3), 30.4 (C), 34.5 (CH_2), 35.3 (CBr_2) and 52.6 (CH_2); *m/z* (EI) 261.8577 (M^+, 1%, $C_5H_7Br_2Cl^+$ requires 261.8583), 215/213/211 (M^+-CH_2Cl, 30/60/30), 181 (M^+-Br, 13), 133/131 (15/15), 65 (100) and 51 (54).

2-Bromomethyl-1,1-dichloro-2-methylcyclopropane (**3n**) was prepared from 3-bromo-2-methylprop-1-ene (6.76 g, 50 mmol), chloroform (50.30 g, 421 mmol), 50% aqueous sodium hydroxide (25.60 g, 320 mmol) and Cetrimide. Distillation, through a packed column, yielded **3n** (7.52 g, 69%) as a colourless liquid, bp. 68-69 °C/9 mmHg (lit.[27] 72-74 °C/10.5 mmHg). ν_{max}(film)/cm^{-1} 2992 (m), 2970 (m), 2930 (m), 1447 (s), 1424 (s), 1378 (m), 1324 (w), 1274 (m), 1224 (s), 1147 (m), 1079 (s), 1041 (br), 962 (m), 900 (w), 854 (m), 762 (s) and 643 (s); δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.45-1.51 (2 H, m, CH_2), 1.53 (3 H, s, CH_3), 3.52 (1 H, d, *J* 10.5 Hz, CH_2Br) and 3.67 (1 H, d, *J* 10.5 Hz, CH_2Br); δ_C(100 MHz; $CDCl_3$; Me_4Si) 19.8 (CH_3), 31.3 (C), 33.5 (CH_2), 39.5 (CH_2Br) and 67.1 (CCl_2).

1,1-Dibromo-2,2,3,3-tetramethylcyclopropane (**2o**) was synthesised from 2,3-dimethyl-2-butene (1.69 g, 20 mmol), bromoform (10.15 g, 40 mmol) and potassium *tert*-butoxide (4.45 g, 40 mmol) in pentane (20 mL) by the Doering-Hoffmann procedure.[29] Crystallisation from cold methanol gave **2o** (1.88 g, 37%) as a white powder, mp. 79-80 °C (lit.[30] 77-78 °C). ν_{max}(ATR)/cm^{-1} 3007m, 2956w, 2929w, 2870w, 1460m, 1444m, 1373m, 1175m, 1102m, 1032m, 992m, 951m, 862m and 768s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.26 (12 H, s, 4 x CH_3); δ_C(50 MHz; $CDCl_3$; Me_4Si) 21.6 (4 x CH_3), 29.6 (C) and 58.8 (C); *m/z* (EI) 177/175 (M^+-Br, 100%), 135/133 (12/12), 123/121 (19/19), 95 (57) and 67 (62).

5.4 Ring opening of trihalogenated cyclopropanes

5.4.1 *Phase-transfer conditions*

General procedure. To a mixture of **2** (5 mmol), TEBA (0.2 g) and ethanol (0.92 g, 20 mmol) in dichloromethane (15 mL), kept at 0 ˚C, was added 50% aqueous sodium hydroxide (3.26 g, 40 mmol). The resulting mixture was stirred vigorously at room temperature until all the starting material was consumed (monitored by GC or TLC). Water was added, the products were extracted with ether, and the combined extracts were dried with magnesium sulfate, filtrated and evaporated *in vacuo*. The products were isolated by flash chromatography.

1,1-Diethoxyhex-2-yne (**4a**) and *3,3-diethoxyhex-1-yne* (**5a**) and were synthesised from **2a** (1.63 g, 5 mmol), in a 55:45 ratio according to GC. Isolation by flash chromatography (hexane:ethyl acetate [97.5:2.5]) yielded the products as a yellow mixture (0.47 g, 55%), of which some pure **5a** (0.21 g, 25%) was obtained.

ν_{max}(film)/cm^{-1} 3302m, 2970s, 2933s, 2883s, 2116w, 1455m, 1388m, 1301m, 1286m, 1257m, 1152s, 1113s, 1059s, 988s, 845w, 806w and 652m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.95 (3 H, t, *J* 7.3, CH_3), 1.18-1.27 (6 H, m, 2 x C*H*$_3$CH$_2$O), 1.43-1.65 (2 H, m, CH_2), 1.75-1.84 (2 H, m, CH_2), 2.52 (1 H, s, ≡C*H*) and 3.48-3.73 (4 H, m, 2 x CH$_3$C*H*$_2$O); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.8 (CH_3), 15.0 (2 x *C*H$_3$CH$_2$O), 17.3 (CH_2), 40.1 (CH_2), 57.7 (2 x CH$_3$*C*H$_2$O), 72.6 (≡*C*H), 81.1 (≡C) and 98.2 ((EtO)$_2$C); *m/z* (EI) 125.0969 (M^+-OEt, 100%, $C_8H_{13}O^+$ requires 125.0966), 97 (40) and 41 (100).

1,1-Diethoxyoct-2-yne (**4b**) and *3,3-diethoxyoct-1-yne* (**5b**) were prepared from **2b** (1.75 g, 5 mmol), in a 64:36 ratio according to GC, and isolated by flash chromatography (hexane:ethyl acetate [98:2]) in a mixture as a yellow liquid (0.43 g, 43%), of which some pure **4b** (0.20 g, 20%) and **5b** (0.08 g, 8%) was isolated.

4b:

ν_{max}(film)/cm^{-1} 2967s, 2932s, 2877s, 2243w, 1457m, 1358m, 1332m, 1152s, 1056s, 1009s, 912w and 815w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.83-0.91 (3 H, m, CH_3), 1.18-1.59 (12 H, m), 2.22 (2 H, dt, *J* 1.6 and 7.0, CH_2), 3.47-3.80 (4 H, m, 2 x CH$_3$C*H*$_2$O) and 5.24 (1 H, t, *J* 1.6, (EtO)$_2$C*H*); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.7 (CH_3), 14.9 (2 x *C*H$_3$CH$_2$O), 18.4 (CH_2), 22.0 (CH_2), 27.8 (CH_2), 30.9 (CH_2), 60.4 (2 x CH$_3$*C*H$_2$O), 76.3 (C), 86.3 (C) and 91.3 ((EtO)$_2$*C*H); *m/z* (EI) 153.1268 (M^+-OEt, 100%, $C_{10}H_{17}O^+$ requires 153.1279), 103 (10), 81 (50) and 55 (40).

5b:

ν_{max}(film)/cm^{-1} 3303m, 2959s, 2931s, 2873s, 2112w, 1459m, 1386m, 1281m, 1227m, 1149s, 1057s, 1009s, 957m, 886w and 651m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.87-0.93 (5 H, m), 1.18-1.58 (12 H, m), 1.76-1.85 (2 H, m, CH_2), 2.52 (1 H, s, (≡C*H*) and 3.48-3.73 (4 H, m, 2 x CH$_3$C*H*$_2$O); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 15.1 (2 x *C*H$_3$CH$_2$O), 22.4 (CH_2), 23.6 (CH_2), 31.5 (CH_2), 37.9 (CH_2), 57.8 (2 x CH$_3$*C*H$_2$O), 72.6 (≡*C*H), 81.2 (≡C) and 98.4 (*C*(OEt)$_2$); *m/z* (EI) 153.1260 (M^+-OEt, 100%, $C_{10}H_{17}O^+$ requires 153.1279), 127 (98), 71 (57) and 55 (58).

1,1-Diethoxyundec-2-yne (**4c**) and *3,3-diethoxyundec-1-yne* (**5c**) were synthesised from **2c** (1.95 g, 5 mmol), in a 58:42 ratio according to ^{1}H NMR, and isolated as a yellow mixture (0.72 g, 61%). Further purification by flash chromatography (hexane:ethyl acetate [99:1]) yielded **4c** and **5c** as yellow liquids (0.12 g, 10% and 0.20 g, 17%).

4c:

ν_{max}(film)/cm^{-1} 2927s, 2861s, 2241w, 1459m, 1358m, 1331m, 1260w, 1152s, 1057s, 1009s, 910w and 811w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-0.91 (3 H, m, CH_3), 1.20-1.60 (18 H, m), 2.24 (2 H, dt, *J* 1.6 and 7.0, CH_2), 3.49-3.82 (4 H, m, 2 x CH_3CH_2O) and 5.26 (1 H, t, *J* 1.6, ($(EtO)_2CH$); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 14.9 (2 x CH_3CH_2O), 18.4 (CH_2), 22.4 (CH_2), 28.1 (CH_2), 28.7 (CH_2), 28.8 (CH_2), 29.0 (CH_2), 31.6 (CH_2), 60.3 (2 x CH_3CH_2O), 75.4 (C), 86.3 (C) and 91.3 ($(EtO)_2CH$); *m/z* (EI) 240 (M^+,1%), 195 (M^+-OEt, 100), 81 (45) and 55 (55).

5c:

ν_{max}(film)/cm^{-1} 3307m, 2927s, 2858s, 2115w, 1460m, 1386m, 1300m, 1278m, 1249m, 1148s, 1057s, 990s and 886w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-0.91 (3 H, m, CH_3), 1.18-1.53 (18 H, m), 1.78-1.85 (2 H, m, CH_2), 2.52 (1 H, s, ≡C*H*) and 3.48-3.74 (4 H, m, 2 x CH_3CH_2O); δ_C(50 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 15.0 (2 x CH_3CH_2O), 22.5 (CH_2), 23.9 (CH_2), 29.1 (CH_2), 29.3 (2 x CH_2), 31.7 (CH_2), 37.9 (CH_2), 57.7 (2 x CH_3CH_2O), 72.6 (≡*C*H), 81.2 (≡C) and 98.3 ($C(OEt)_2$); *m/z* (EI) 195.1765 (M^+-OEt, 100%, $C_{10}H_{17}O^+$ requires 195.1749) and 127 (93).

1,1-Diethoxy-5-phenylpent-2-yne (**4d**) and *3,3-diethoxy-5-phenylpent-1-yne* (**5d**) were prepared from **2d** (1.91 g, 5 mmol), in a 60:40 ratio according to GC, and isolated by flash chromatography (hexane:ethyl acetate [96:4]) as yellow liquids (0.40 g, 34% and 0.23 g, 20%).

4d:

ν_{max}(film)/cm^{-1} 3062w, 3028m, 2976s, 2928s, 2887s, 2240w, 1605w, 1494m, 1449m, 1357s, 1334s, 1150s, 1056br, 1009s, 911w, 746m and 700s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.21 (6 H, t, *J* 7.2, 2 x CH_3CH_2O), 2.49-2.58 (2 H, m), 2.81-2.88 (2 H, m), 3.45-3.76 (4 H, m, 2 x CH_3CH_2O), 5.24 (1 H, t, *J* 1.6, $(EtO)_2CH$) and 7.16-7.33 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.9 (2 x CH_3CH_2O), 20.6 (CH_2), 34.4 (CH_2), 60.4 (2 x CH_3CH_2O), 76.2 (C), 85.3 (C), 91.2 ($(EtO)_2CH$), 126.1 (CH), 128.16 (2 x CH), 128.18 (2 x CH) 140.2 (C); *m/z* (EI) 232 (M^+, 1%), 187 (M^+-OEt, 35), 91 (100) and 77 (8).

5d:

ν_{max}(film)/cm^{-1} 3287m, 3027m, 2975s, 2932s, 2890m, 2112w, 1600w, 1494w, 1450m, 1389m, 1292m, 1274m, 1222m, 1167s, 1114s, 1053br, 1009s, 961m, 878w, 822w, 745m, 700s and 659m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.22 (6 H, t, *J* 7.1, 2 x CH_3CH_2O), 2.09-2.17 (2

H, m), 2.58 (1 H, s, ≡CH), 2.79-2.88 (2 H, m), 3.52-3.79 (4 H, m, 2 x CH_3CH_2O) and 7.12-7.32 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 15.0 (2 x CH_3CH_2O), 30.4 (CH_2), 39.6 (CH_2), 58.0 (2 x CH_3CH_2O), 73.2 (≡CH), 80.8 (≡C), 98.0 ($C(OEt)_2$), 125.7 (CH), 128.2 (4 x CH) and 141.4 (C); *m/z* (EI) 187.1142 (M^+-OEt, 35%, $C_{13}H_{15}O^+$ requires 187.1123), 127 (56), 91 (100) and 77 (21).

1,1-Diethoxy-4-cyclohexylbut-2-yne (**4e**) and *3,3-diethoxy-4-cyclohexylbut-1-yne* (**5e**) were prepared from **2e** (1.87 g, 5 mmol), in a 64:36 ratio according to ^{1}H NMR. Isolation by flash chromatography (hexane:ethyl acetate [95:5]) yielded a yellow mixture (0.64 g, 57%), of which some pure **4e** (0.37 g, 33%) was isolated.

ν_{max}(film)/cm^{-1} 2975s, 2925s, 2855s, 2242w, 1448m, 1331m, 1152s, 1055s, 1007s, 912m and 817w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.83-1.83 (17 H, m), 2.14 (2 H, dd, *J* 1.7 and 6.8, CH_2), 3.50-3.82 (4 H, m, 2 x CH_3CH_2O) and 5.27 (1 H, t, *J* 1.7, $(EtO)_2CH$); δ_C(50 MHz; $CDCl_3$; Me_4Si) 15.0 (2 x CH_3CH_2O), 25.9 (2 x CH_2), 26.1 (CH_2), 26.3 (CH_2), 32.6 (2 x CH_2), 36.9 (CH), 60.2 (2 x CH_3CH_2O), 76.4 (C), 85.2 (C) and 91.4 ($(EtO)_2CH$); *m/z* (EI) 223 (M^+-H, 10%), 179.1441 (M^+-OEt, 100, $C_{12}H_{19}O^+$ requires 179.1436) and 55 (41).

Traces of *α,β*-unsaturated aldehyde could be observed both in the NMR spectra and the IR spectrum.

1,1-Diethoxy-5-methylhex-2-yne (**4f**) and *3,3-diethoxy-5-methylhex-1-yne* (**5f**) were synthesised from **2f** (1.68 g, 5 mmol), in a 78:22 ratio according to GC and ^{1}H NMR. Isolation by flash chromatography (hexane:ethyl acetate [97.5:2.5]) yielded **4f** (0.33 g, 36%) as a yellow liquid.

ν_{max}(film)/cm^{-1} 2964s, 2928br, 2241w, 1462m, 1361m, 1334m, 1279w, 1257w, 1151s, 1058br, 1009s, 911w and 817br; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.98 (6 H, d, *J* 6.5, 2 x CH_3), 1.23 (6 H, t, *J* 7.1, 2 x OCH_2CH_3), 1.74-1.94 (1 H, m, $(CH_3)_2CH$), 2.14 (2 H, dd, *J* 1.7 and 6.5, CH_2), 3.50-3.82 (4 H, m, 2 x OCH_2CH_3) and 5.27 (1 H, t, *J* 1.7, $(EtO)_2CH$); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.9 (2 x CH_3CH_2O), 21.8 (2 x CH_3), 27.55 (CH_2), 27.61 ($(CH_3)_2CH$), 60.3 (2 x CH_3CH_2O), 76.4 (C), 85.1 (C) and 91.3 ($(EtO)_2CH$); *m/z* (EI) 183.1388 (M^+-H, 2%, $C_{11}H_{19}O_2^+$ requires 183.1385), 139 (M^+-OEt, 100), 127 (4) and 57 (4).

Traces of **5f** and *α,β*-unsaturated aldehyde could be observed in some fractions.

1,1-Diethoxy-4,4-dimethylpent-2-yne (**4g**) was prepared from **2g** (1.67 g, 5 mmol). No traces of *3,3-diethoxy-4,4-dimethylpent-1-yne* (**5g**), only **4g** was observed by GC and isolated by dry-flash chromatography (hexane:ethyl acetate [97.5:2.5]) as a yellow liquid (0.34 g, 37%). ν_{max}(film)/cm^{-1} 2971s, 2932s, 2887s, 2243w, 1718m, 1672m, 1621m, 1456m, 1363m, 1332m, 1263m, 1204m, 1117s, 1054s, 1009s, 904w, 856w and 808m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.20-1.27 (15 H, m), 3.49-3.81 (4 H, m, 2 x CH_3CH_2O) and 5.26 (1 H, s, $(EtO)_2CH$); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.9 (2 x CH_3CH_2O), 27.1 (C), 30.5 (3 x CH_3), 60.3 (2 x CH_3CH_2O), 74.0 (C), 91.3 ($(EtO)_2CH$) and 94.1 (C); *m/z* (EI) 183 (M^+-H, 25%), 155 (72), 139.1124 (M^+-OEt, 100, $C_9H_{15}O^+$ requires 139.1123) and 57 (90).

1,1-Diethoxy-4-phenoxybut-2-yne (**4i**) and *3,3-diethoxy-4-phenoxybut-1-yne* (**5i**) were synthesised from **2i** (1.92 g, 5 mmol), in a 1:99 ratio according to GC and ^{1}H NMR, and isolated by flash chromatography as brown liquids (0.06 g, 5% and 0.59 g, 50%).[31,32]

4i:

ν_{max}(film)/cm^{-1} 3062m, 3041m, 2977s, 2934s, 2890s, 2190w, 1774w, 1595s, 1493s, 1453m, 1364m, 1335m, 1297m, 1220s, 1141s, 1051br, 911w, 886w, 818m, 756s and 692m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.21 (6 H, t, *J* 7.0, 2 x OCH_2CH_3), 3.48-3.78 (4 H, m, 2 x OCH_2CH_3), 4.75 (2 H, d, *J* 1.4, OCH_2), 5.30 (1 H, t, *J* 1.4, $(EtO)_2CH$), 6.93-7.07 (3 H, m) and 7.24-7.36 (2 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.9 (2 x OCH_2CH_3), 55.7 (OCH_2), 60.8 (2 x OCH_2CH_3), 80.1 (C), 82.4 (C), 91.0 ($(EtO)_2CH$), 114.8 (2 x CH), 121.4 (CH), 129.3 (2 x CH) and 157.4 (C).

5i:

ν_{max}(film)/cm^{-1} 3282s, 3063w, 3035w, 2977s, 2935s, 2892s, 2119w, 1760m, 1595s, 1493s, 1461m, 1388m, 1244s, 1200s, 1145s, 1058br, 958m, 885m, 828m, 756s and 691s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.24 (6 H, t, *J* 7.1, 2 x OCH_2CH_3), 2.59 (1 H, s, ≡C*H*), 3.62-3.86 (4 H, m, 2 x OCH_2CH_3), 4.12 (OCH_2), 6.92-7.02 (3 H, m) and 7.23-7.32 (2 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 15.0 (2 x OCH_2CH_3), 58.7 (2 x OCH_2CH_3), 70.3 (OCH_2), 73.8 (≡*C*H), 79.4 (C), 96.0 (C), 114.9 (2 x CH), 121.1 (CH), 129.2 (2 x CH) and 158.4 (C).

5.4.2 *DBU in super-dry ethanol; synthesis of acetylenic diethyl acetals*

General procedure. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (20 mmol) was added dropwise to a solution of **2** (5 mmol) in extremely dry ethanol (25 mL) under nitrogen. The resulting mixture was refluxed with vigorous stirring and monitored by GC. The reaction was

terminated after 24 h, although some unreacted starting material was still present. Water was added, the products were extracted with diethyl ether (4 x 50 mL) and worked up in the usual way. The products were isolated by flash chromatography.

1,1-Diethoxyhex-2-yne (**4a**) was synthesised from **2a** (1.60 g, 5 mmol) and DBU (1.53 g, 20 mmol). Isolation by flash chromatography (heptane:ethyl acetate [96:4]) gave **4a** (0.39 g, 46%) as a colourless liquid, along with recovered **2a** (0.21 g, 13%).
ν_{max}(film)/cm^{-1} 2971s, 2933s, 2881s, 2245w, 1455m, 1333m, 1152s, 1056s, 1009s, 914m and 816w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.91 (3 H, t, *J* 7.3, CH_3), 1.15 (6 H, t, *J* 7.2, 2 x C*H*$_3$CH$_2$O), 1.39-1.57 (2 H, m, CH_2), 2.14 (2 H, dt, *J* 1.6 and 7.0, CH_2), 3.41-3.73 (4 H, m, 2 x CH$_3$C*H*$_2$O) and 5.17 (1 H, t, *J* 1.6, (EtO)$_2$C*H*); δ_C(50 MHz; $CDCl_3$; Me_4Si) 12.9 (CH_3), 14.5 (2 x *C*H$_3$CH$_2$O), 20.0 (CH_2), 21.3 (CH_2), 60.0 (2 x CH$_3$*C*H$_2$O), 75.4 (C), 85.6 (C) and 91.0 ((EtO)$_2$*C*H); *m/z* (EI) 125.0981 (M^+-OEt, 100%, $C_8H_{13}O^+$ requires 125.0966), 103 (7) and 97 (62).
It was also possible to see traces of *α,β*-unsaturated aldehyde, indicated by peaks at 167.7 and 191 ppm in the ^{13}C NMR spectrum of the crude product.

5.4.3 *Sodium ethoxide in THF; synthesis of acetylenic diethyl ketals*

General procedure. Sodium ethoxide was either commercial or prepared from an excess of absolute ethanol (20 mL) and sodium (0.92 g, 40 mmol). Excess of absolute ethanol was carefully distilled off prior to use. To a mixture of sodium ethoxide (2.72 g, 40 mmol) in dry THF (25 mL), kept under nitrogen, was added **2** (5 mmol) in dry THF (10 mL) dropwise from a syringe pump in approximately half an hour. The resulting mixture was stirred vigorously at room temperature and monitored by GC. Water was added, the products were extracted with dichloromethane and work-up was completed in the usual way. The products were isolated by flash chromatography.

3,3-Diethoxyhex-1-yne (**5a**) was synthesised from **2a** (1.17 g, 5 mmol) and isolated by flash chromatography (hexane:ethyl acetate [97.5:2.5]) as a yellow liquid (0.34 g, 40%). The spectroscopic data were consistent with previous analyses (see Chapter 5.4.1).

3,3-Diethoxy-4-cyclohexylbut-1-yne (**5e**) was prepared from **2e** (1.87 g, 5 mmol) and isolated by flash chromatography (hexane:ethyl acetate [95:5]) as a light yellow liquid (0.51 g, 46%).

ν_{max}(film)/cm^{-1} 3306m, 2974s, 2925s, 2853s, 2114w, 1448m, 1388m, 1342m, 1279m, 1235m, 1180s, 1147s, 1111s, 1058s, 997s, 936w, 884w, 824w and 650m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.84-1.36 (12 H, m), 1.60-1.73 (5 H, m), 1.87-1.90 (2 H, m), 2.54 (1 H, s, ≡C*H*) and 3.52-3.68 (4 H, m, 2 x CH_3CH_2O); δ_C(100 MHz; $CDCl_3$; Me_4Si) 15.0 (2 x CH_3CH_2O), 26.2 (2 x CH_2), 26.3 (CH_2), 33.7 (CH), 34.1 (2 x CH_2), 44.9 (CH_2) 57.8 (2 x CH_3CH_2O), 73.1 (≡*C*H), 81.4 (≡C) and 98.3 ($(EtO)_2C$); *m/z* (EI) 179.1427 (M^+-OEt, 31%, $C_8H_{13}O^+$ requires 179.1436), 149 (10), 135 (35), 127 (15), 107 (41), 83 (20) and 41 (100).

3,3-Diethoxy-5-methylhex-1-yne (**5f**) was synthesised from **2f** (1.67 g, 5 mmol) and isolated by flash chromatography (hexane:ethyl acetate [95:5]) as a light yellow liquid (0.52 g, 57%). ν_{max}(film)/cm^{-1} 3306m, 2958s, 2894s, 2112w, 1464m, 1388m, 1361m, 1265m, 1148s, 1060br, 996s, 922w, 810br and 651m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.99 (6 H, d, *J* 6.5, 2 x CH_3), 1.20 (6 H, t, *J* 7.1, 2 x CH_3CH_2O), 1.73 (2 H, d, *J* 1.73, CH_2), 1.90-2.09 (1 H, m), 2.55 (1 H, s, ≡C*H*), 3.49-3.73 (4 H, m, 2 x CH_3CH_2O); δ_C(50 MHz; $CDCl_3$; Me_4Si) 15.0 (2 x CH_3CH_2O), 23.5 (2 x CH_3), 24.5 (CH), 46.0 (CH_2), 57.8 ((2 x CH_3CH_2O), 73.2 (≡*C*H), 81.3 (≡C) and 98.3 ($(EtO)_2C$); *m/z* (EI) 139 (M^+-OEt, 100%), 138.1051 (M^+-EtOH, 2, $C_9H_{14}O^+$ requires 138.1045), 127 (82), 111 (30) and 57 (6).

5.5 Trapping of 1-bromocyclopropenes

General procedure.[33] The cyclopropane **2** was dissolved in THF in a round-bottomed flask, equipped with a condenser connected to a nitrogen inlet. The solution was cooled to -78 ˚C (acetone/dry-ice or ethyl acetate/liquid nitrogen) with magnetic stirring and methyllithium (1.00-1.20 equivalents) was added dropwise with a syringe. Stirring was continued at room temperature for 1 h, before the diene was added at a temperature well below 0 °C. The reactions were monitored by either TLC or GC and quenched with a portion of water. The product was extracted with diethyl ether, dried with magnesium sulfate, filtrated and evaporated *in vacuo* and finally isolated by either flash chromatography or recrystallisation.

5.5.1 *Trapping with 1,3-diphenylisobenzofuran*

2-Bromo-8-oxa-1,5-diphenyl-4-propyl-6,7-benzotricyclo[3.2.1.0^{2,4}]octane (**7a**) was synthesised from **2a** (0.80 g, 2.50 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.55 g, 2.02 mmol) in THF (40 mL). Isolation by flash chromatography (hexane:ethyl acetate [98:2]) yielded *exo*-**7a** (0.72 g, 84%) as a light yellow oil.

ν_{max}(film)/cm^{-1} 3061s, 3041s, 2959s, 2931s, 2870s, 1604w, 1497m, 1453s, 1422m, 1348s, 1301s, 1181m, 1160w, 1093m, 1058w, 981br, 938m, 907br, 754br and 700s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.81 (3 H, t, *J* 7.0, CH_3), 1.10-1.37 (3 H, m), 1.57-1.64 (1 H, m), 1.69 (1 H, d, *J* 6.3), 2.80 (1 H, d, *J* 6.3), 7.22-7.48 (10 H, m), 7.68-7.72 (2 H, m) and 7.82-7.86 (2 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.2 (CH_3), 21.4 (CH_2), 27.6 (CH_2), 30.3 (CH_2), 36.9 (C), 50.7 (CBr), 90.26 (CO), 90.33 (CO), 121.8 (CH), 122.7 (CH), 126.1 (CH), 126.2 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.8 (CH), 128.9 (CH), 129.2 (CH), 133.6 (C), 134.5 (C), 147.2 (C) and 148.0 (C); *m/z* (EI) 430.0934 (M^+, 1%, $C_{26}H_{23}OBr^+$ requires 430.0932), 351 (M^+-Br, 75), 327 (15), 270 (6), 246 (30), 103 (100), 91 (63) and 77 (73).

2-Bromo-8-oxa-4-pentyl-1,5-diphenyl-6,7-benzotricyclo[3.2.1.0^{2,4}]octane (**7b**) was prepared from **2b** (0.87 g, 2.49 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.68 g, 2.51 mmol) in THF (40 mL). Flash chromatography (hexane:ethyl acetate [98:2]) and recrystallisation (hexane and activated charcoal) gave *exo*-**7b** (0.80 g, 70%) as white crystals, mp. 84-86 ˚C.

ν_{max}(KBr)/cm^{-1} 3064m, 3037m, 2932s, 2854s, 1600w, 1497w, 1451s, 1423w, 1347m, 1297s, 1180w, 1100w, 1004m, 982br, 934w, 909w, 875br, 753s and 699s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.80-0.84 (3 H, m, CH_3), 1.14-1.34 (7 H, m), 1.62-1.68 (1 H, m), 1.71 (1 H, d, *J* 6.2), 2.80 (1 H, d, *J* 6.2), 7.25-7.32 (3 H, m), 7.38-7.49 (7 H, m), 7.69-7.71 (2 H, m) and 7.83-7.85 (2 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (CH_3), 22.3 (CH_2), 27.6 (CH_2), 27.8 (CH_2), 27.9 (CH_2), 31.9 (CH_2), 37.0 (C), 50.8 (CBr), 90.3 (CO), 90.4 (CO), 121.8 (CH), 122.7 (CH), 126.1 (CH), 126.3 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.8 (CH), 128.9 (CH), 129.2 (CH), 133.7 (C), 134.6 (C), 147.3 (C) and 148.1 (C); *m/z* (EI) 458.1231 (M^+, 1%, $C_{28}H_{27}OBr^+$ requires 458.1245), 379 (M^+-Br, 100), 270 (25), 105 (96) and 77 (36).

2-Bromo-4-octyl-8-oxa-1,5-diphenyl-6,7-benzotricyclo[3.2.1.0^{2,4}]octane (**7c**) was prepared from **2c** (0.98 g, 2.50 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.54 g, 1.98 mmol) in THF (40 mL). Flash chromatography (hexane:ethyl acetate [97.5:2.5]) yielded *exo*-**7c** (0.80 g, 80%) as a viscous light yellow oil.

ν_{max}(film)/cm^{-1} 3061m, 3041m, 2926s, 2856s, 1497m, 1454s, 1349m, 1300s, 1178w, 1110w, 1058w, 982br, 935w, 909m, 879m, 756s and 700; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.82-0.88 (3 H, m, CH_3), 1.19-1.30 (13 H, m), 1.62-1.68 (1 H, m), 1.70 (1 H, d, *J* 6.2), 2.80 (1 H, d, *J* 6.2), 7.25-7.32 (3 H, m), 7.38-7.48 (7 H, m), 7.69-7.71 (2 H, m) and 7.83-7.85 (2 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.5 (CH_2), 27.6 (CH_2), 28.0 (CH_2), 28.1 (CH_2), 29.1

(CH_2), 29.2 (CH_2), 29.7 (CH_2), 31.7 (CH_2), 37.0 (C), 50.8 (CBr), 90.3 (CO), 90.4 (CO), 121.8 (CH), 122.7 (CH), 126.1 (CH), 126.2 (CH), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.8 (CH), 128.9 (CH), 129.2 (CH), 133.7 (C), 134.6 (C), 147.3 (C) and 148.1 (C); *m/z* (EI) 421.2530 (M^+-Br, 100%, $C_{31}H_{33}O^+$ requires 421.2531), 316 (32), 270 (20), 105 (48) and 77 (12).

2-Bromo-8-oxa-1,5-diphenyl-4-(2-phenylethyl)-6,7-benzotricyclo[3.2.1.$0^{2,4}$]octane (**7d**) was synthesised from **2d** (0.96 g, 2.50 mmol), methyllithium (1.6 mL, 1.6 M, 2.56 mmol) and DPIBF (0.54 g, 2.00 mmol) in THF (50 mL). Flash chromatography (hexane:ethyl acetate [97.5:2.5]) and recrystallisation (hexane) gave *exo*-**7d** (0.74 g, 75%) as white crystals, mp. 142-143 ˚C.

ν_{max}(KBr)/cm^{-1} 3065m, 3026m, 2929m, 2857m, 1496w, 1451m, 1348m, 1300m, 1156w, 978br, 910w, 754br and 699s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.48-1.64 (1 H, m), 1.77 (1 H, d, *J* 6.3, CH), 1.91-2.07 (1 H, m), 2.54-2.63 (2 H, m, CH_2), 2.85 (1 H, d, *J* 6.3, CH), 7.01-7.32 (7 H, m, 7 x CH), 7.41-7.52 (8 H, m, 8 x CH), 7.72-7.77 (2 H, m, 2 x CH) and 7.81-7.87 (2 H, m, 2 x CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 27.8 (CH_2), 30.3 (CH_2), 34.4 (CH_2), 36.9 (C), 50.5 (CBr), 90.2 (CO), 90.3 (CO), 121.8 (CH), 122.8 (CH), 125.8 (CH), 126.2 (CH), 126.4 (CH), 128.1 (2 x CH), 128.2 (2 x CH), 128.3 (2 x CH), 128.4 (2 x CH), 128.5 (2 x CH), 128.9 (CH), 129.0 (CH), 129.2 (2 x CH), 133.5 (C), 134.4 (C), 141.5 (C), 147.1 (C) and 148.0 (C); *m/z* (EI) 413.1902 (M^+-Br, 50%, $C_{31}H_{25}O^+$ requires 413.1905), 270 (19), 105 (100), 91 (34) and 77 (25).

In a preliminary experiment, with a greater excess of methyllithium, 2-methyl-1-(2-phenylethyl)cyclopropene (0.04 g, 0.3 mmol) was isolated as a colourless liquid.

ν_{max}(film)/cm^{-1} 3062m, 3027s, 2931br, 2861s, 1875w, 1603w, 1495m, 1447s, 1174m, 1080m and 1008s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.82 (2 H, s, CH_2), 1.96 (3 H, t, *J* 1.5, CH_3), 2.65-2.74 (2 H, m, CH_2), 2.83-2.91 (2 H, m, CH_2) and 7.13-7.33 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 8.2 (CH_2), 11.4 (CH_3), 27.9 (CH_2), 33.5 (CH_2), 106.2 (C), 109.1 (C), 125.7 (CH), 128.17 (2 x CH), 128.19 (2 x CH) and 141.8 (C).

2-Bromo-4-cyclohexylmethyl-8-oxa-1,5-diphenyl-6,7-benzotricyclo[3.2.1.$0^{2,4}$]octane (**7e**) was synthesised from **2e** (0.94 g, 2.50 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.54 g, 2.00 mmol) in THF (50 mL). Flash chromatography (hexane:ethyl acetate [98:2]) yielded *exo*-**7e** (0.80 g, 82%) as a white powder, mp. 54-56 ˚C.

ν_{max}(KBr)/cm^{-1} 3060br, 2921s, 2847s, 1497w, 1449m, 1347m, 1298m, 1174w, 1122w, 1078w, 981br, 906w, 874w, 754s and 697s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.76-0.84 (2 H, m),

0.99-1.25 (5 H, m), 1.49-1.70 (6 H, m), 1.76 (1 H, d, *J* 6.3), 2.93 (1 H, d, *J* 6.3), 7.27-7.32 (3 H, m), 7.39-7.48 (7 H, m), 7.74-7.76 (2 H, m) and 7.82-7.85 (2 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 26.1 (2 x CH_2), 26.3 (CH_2), 28.5 (CH_2), 33.5 (CH_2), 33.6 (CH_2), 35.1 (C), 35.4 (CH_2), 35.6 (CH), 50.3 (CBr), 90.2 (CO), 90.5 (CO), 122.1 (CH), 122.8 (CH), 126.1 (CH), 126.3 (CH), 128.3 (4 x CH), 128.8 (2 x CH), 128.9 (2 x CH), 129.3 (2 x CH), 133.6 (C), 134.6 (C), 147.1 (C) and 148.0 (C); *m/z* (EI) 484.1442 (M^+, 1%, $C_{30}H_{29}OBr^+$ requires 484.1402), 405 (M^+-Br, 100), 300 (20), 270 (26), 105 (71) and 77 (21).

2-Bromo-4-isobutyl-8-oxa-1,5-diphenyl-6,7-benzotricyclo[3.2.1.$0^{2,4}$]octane (**7f**) was synthesised from **2f** (0.84 g, 2.50 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.54 g, 2.00 mmol) in THF (40 mL). Isolation by flash chromatography (hexane:ethyl acetate [95:5]) gave *exo*-**7f** (0.56 g, 63%) as a colourless oil.

ν_{max}(film)/cm^{-1} 3061m, 2956s, 2926m, 2870m, 1497w, 1454m, 1348m, 1300m, 1271w, 1179w, 1105w, 983br, 908m, 754br, 701s and 650m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.84 (6 H, t, *J* 6.7, 2 x CH_3), 0.94-1.04 (1 H, m), 1.50-1.63 (2 H, m), 1.79 (1 H, d, *J* 6.3), 2.94 (1 H, d, *J* 6.3), 7.21-7.28 (3 H, m), 7.33-7.44 (7 H, m), 7.74-7.76 (2 H, m) and 7.83-7.86 (2 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 22.7 (CH_3), 22.8 (CH_3), 26.1 (CH), 28.2 (CH_2), 35.5 (C), 36.5 (CH_2), 50.3 (CBr), 90.1 (CO), 90.4 (CO), 121.9 (CH), 122.7 (CH), 126.1 (CH), 126.2 (CH), 128.22 (2 x CH), 128.23 (2 x CH), 128.6 (2 x CH), 128.80 (CH), 128.82 (CH), 129.1 (2 x CH), 133.6 (C), 134.6 (C), 147.0 (C) and 147.9 (C); *m/z* (EI) 446/444 (M^+, 2%), 403/401 (11), 365.1923 (M^+-Br, 100, $C_{27}H_{25}O^+$ requires 365.1905), 270 (30), 105 (83) and 77 (32).

*2-Bromo-4-*tert*-butyl-8-oxa-1,5-diphenyl-6,7-benzotricyclo[3.2.1.$0^{2,4}$]octane* (**7g**) was synthesised from **2g** (0.84 g, 2.50 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.54 g, 2.00 mmol) in THF (40 mL). Flash chromatography (hexane:ethyl acetate [97.5:2.5]) yielded *exo*-**7g** (0.29 g, 33%) as a colourless oil, from which some white crystals where isolated after recrystallisation (hexane), mp. 145-146 ˚C.

ν_{max}(KBr)/cm^{-1} 3059m, 3036m, 2958s, 2909m, 2872m, 1452m, 1396w, 1364w, 1342w, 1292m, 1203w, 1151w, 1004w, 979m, 905br, 874w, 756s and 698br; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.83 (9 H, s, 3 x CH_3), 2.17 (1 H, d, *J* 6.2), 3.04 (1 H, d, *J* 6.2), 7.31-7.46 (9 H, m), 7.70-7.72 (1 H, m), 7.78-7.80 (2 H, m) and 7.85-7.87 (2 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 28.8 (CH_2), 31.0 (3 x CH_3), 32.0 (C), 43.8 (C), 49.2 (CBr), 89.6 (CO), 90.9 (CO), 123.2 (CH), 123.8 (CH), 125.8 (CH), 126.3 (CH), 128.2 (2 x CH), 128.3 (2 x CH), 128.5 (2 x CH), 128.8 (CH), 128.9 (CH), 129.5 (2 x CH), 133.4 (C), 136.5 (C), 147.4 (C) and 148.6 (C); *m/z* (EI)

444.1090 (M^+, 3%, $C_{27}H_{25}OBr^+$ requires 444.1089), 390/388 (10/10), 365 (M^+-Br, 66), 270 (37), 105 (100), 77 (24) and 57 (81).
Traces of *endo*-**7g** could be seen in the ^1H NMR spectrum.

10-Bromo-14-oxa-1,11-diphenyl-12,13-benzotetracyclo[9.2.1.0^{2,9}.0^{2,10}]tetradecane (**7h**) was synthesised from **2h** (0.90 g, 2.49 mmol), methyllithium (1.6 mL, 1.6 M, 2.56 mmol) and DPIBF (0.54 g, 2.00 mmol). Recrystallisation (hexane) and flash chromatography (hexane:ethyl acetate [98:2]) afforded *exo*-**7h** (0.89 g, 94%) as white crystals, mp. 187-188 ˚C.
ν_{max}(KBr)/cm^{-1} 3036m, 2914s, 2852s, 1496w, 1454s, 1343m, 1295m, 1273m, 1168w, 989br, 916m, 753br and 700s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.90-1.10 (2 H, m), 1.28-1.56 (8 H, m), 1.64-1.68 (1 H, m), 1.95-2.00 (1 H, m), 2.54-2.58 (1 H, m), 7.24-7.51 (9 H, m), 7.75-7.78 (2 H, m) and 7.84-7.90 (3 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 25.5 (CH_2), 25.6 (CH_2), 25.9 (CH_2), 26.5 (CH_2), 26.8 (CH_2), 27.6 (CH_2), 32.4 (CH), 39.8 (C), 57.6 (CBr), 89.5 (CO), 89.8 (CO), 121.6 (CH_2), 122.7 (CH_2), 126.0 (CH), 126.2 (CH), 126.5 (CH), 127.9 (CH), 128.0 (CH), 128.3 (CH), 128.9 (CH), 129.7 (CH), 133.8 (C), 137.2 (C), 146.7 (C) and 148.4 (C); *m/z* (EI) 391.2083 (M^+-Br, 100%, $C_{29}H_{27}O^+$ requires 391.2062), 270 (25), 105 (80), 91 (16) and 77 (24).

2-Bromo-8-oxa-4-phenoxymethyl-1,5-diphenyl-6,7-benzotricyclo[3.2.1.0^{2,4}]octane (**7i**) was synthesised from **2i** (0.96 g, 2.49 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.54 g, 2 mmol). Flash chromatography (hexane:ethyl acetate [97.5:2.5]) yielded *exo*-**7i** (0.80 g, 81%) as a colourless oil. Subsequently recrystallisation (hexane) gave white crystals, mp. 146-148 ˚C.
ν_{max}(KBr)/cm^{-1} 3041m, 2907m, 2857m, 1595m, 1495m, 1452m, 1395w, 1337w, 1295m, 1242s, 1176w, 1124w, 1077w, 1033m, 982m, 945w, 895w, 755s and 695s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 2.07 (1 H, d, *J* 6.5), 2.98 (1 H, dd, *J* 0.7 and 6.5), 3.91 (1 H, d, *J* 10.7, OCH), 4.14 (1 H, dd, *J* 0.7 and 10.7, OCH), 6.77-6.81 (2 H, m), 6.91-6.95 (1 H, m), 7.21-7.51 (12 H, m) and 7.79-7.87 (4 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 28.2 (CH_2), 36.6 (C), 49.9 (CBr), 67.9 (OCH_2), 90.0 (CO), 90.3 (CO), 114.4 (CH), 120.9 (CH), 121.7 (CH), 122.9 (CH), 126.5 (CH), 126.6 (CH), 128.2 (CH), 128.4 (CH), 128.8 (CH), 128.9 (CH), 129.1 (CH), 129.2 (CH), 129.3 (CH), 133.2 (C), 133.9 (C), 147.6 (C), 148.0 (C) and 158.4 (C); *m/z* (EI) 415.1699 (M^+-Br, 30%, $C_{30}H_{23}O_2^+$ requires 415.1698), 321 (46), 270 (10), 105 (100) and 77 (35).

2-Bromo-4-(4-methylphenoxy)methyl-8-oxa-1,5-diphenyl-6,7-benzotricyclo[3.2.1.0^{2,4}]octane (**7j**) was prepared from **2j** (1.00 g, 2.5 mmol), methyllithium (2 mL, 1.5 M, 3 mmol) and DPIBF (0.51 g, 1.9 mmol). Flash chromatography (hexane:ethyl acetate [99:1]) gave *exo*-**7j** (0.68 g, 71%) as a colourless oil, from which some white crystals were isolated by recrystallisation (hexane), mp. 58-65 ˚C.

ν_{max}(KBr)/cm^{-1} 3030m, 2915m, 2855m, 1510s, 1449m, 1390w, 1298m, 1237s, 1175m, 1031m, 983m, 811br, 755s and 698s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 2.06 (1 H, d, *J* 6.3, CH), 2.26 (3 H, s, CH_3), 2.96 (1 H, d, *J* 6.3, CH), 3.88 (1 H, d, *J* 10.4, OCH), 4.11 (1 H, d, *J* 10.4, OCH), 6.67-6.70 (2 H, m, 2 x CH), 7.03-7.04 (2 H, m, 2 x CH), 7.27-7.50 (10 H, m, 10 x CH), 7.79-7.81 (2 H, m, 2 x CH) and 7.85-7.86 (2 H, m, 2 x CH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 20.3 (CH_3), 28.1 (CH_2), 36.7 (C), 49.9 (CBr), 68.0 (OCH_2), 90.0 (CO), 90.3 (CO), 114.2 (2 x CH), 121.7 (CH), 122.8 (CH), 126.4 (CH), 126.6 (CH), 128.2 (2 x CH), 128.4 (2 x CH), 128.8 (2 x CH), 128.9 (CH), 129.1 (CH), 129.2 (2 x CH), 129.7 (2 x CH), 130.1 (C), 133.2 (C), 133.9 (C), 147.7 (C), 148.0 (C) and 156.3 (C); *m/z* (EI) 508.1002 (M^+, 1%, $C_{31}H_{25}BrO_2^+$ requires 508.1038), 429 (26), 403/401 (13/13), 321 (100), 270 (14), 105 (83), 91 (7) and 77 (19).

2-Bromo-8-oxa-1,4,5-triphenyl-6,7-benzotricyclo[3.2.1.0^{2,4}]octane (**7l**) was synthesised from **2l** (0.89 g, 2.51 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and DPIBF (0.54 g, 2.00 mmol) in THF (40 mL). Flash chromatography (hexane:ethyl acetate [95:5]) yielded *exo*-**7l** (0.82 g, 88%) as a colourless oil, from which some white crystals where isolated after recrystallisation (hexane), mp. 134-136 ˚C.

ν_{max}(KBr)/cm^{-1} 3062m, 3028m, 2999m, 2954m, 2867m, 1495m, 1448m, 1345m, 1297m, 1177w, 1013w, 977s, 912w, 883m, 760br and 700s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.90 (1 H, d, *J* 5.8), 3.09 (1 H, d, *J* 5.8), 6.59-6.62 (2 H, m), 7.14-7.55 (15 H, m) and 7.91-7.94 (2 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 29.4 (CH_2), 44.4 (C), 49.1 (CBr), 90.1 (CO), 90.3 (CO), 122.1 (CH), 123.0 (CH), 126.2 (CH), 126.6 (CH), 126.7 (2 x CH), 127.48 (2 x CH), 127.50 (CH), 127.9 (3 x CH), 128.4 (2 x CH), 129.1 (CH), 129.3 (2 x CH), 131.7 (2 x CH), 133.7 (C), 134.8 (C), 135.2 (C), 147.7 (C) and 147.9 (C); *m/z* (EI) 466/464 (M^+, 2%), 385.1595 (M^+-Br, 100, $C_{29}H_{21}O^+$ requires 385.1592), 270 (27), 105 (48) and 77 (36).

5.5.2 *Trapping with cyclopentadiene*

2-Bromo-4-propyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8a**) was synthesised from **2a** (0.80 g, 2.49 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (40 mL). According to TLC at least eight products were formed, but isolation by flash chromatography (hexane) yielded only *endo*-**8a** (0.12 g, 22%) as a colourless liquid.

ν_{max}(film)/cm^{-1} 3063m, 2962s, 2931s, 2869s, 1456m, 1377w, 1322w, 1268w, 1245w, 1074m, 995w, 898w, 857w, 738m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.88-1.01 (5 H, m), 1.34-1.76 (5 H, m), 2.17 (1 H, td, *J* 7.3 and 1.7), 2.71-2.76 (1 H, m), 3.07-3.12 (1 H, m), 5.89-5.94 (1 H, m, =CH) and 5.97-6.02 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.2 (CH_3), 21.4 (CH_2), 28.7 (C), 33.6 (CH_2), 35.8 (CH_2), 46.7 (CBr), 48.1 (CH), 54.7 (CH), 59.7 (CH_2), 132.7 (=CH) and 135.1 (=CH); *m/z* (EI) 226.0369 (M^+, 3%, $C_{11}H_{15}Br^+$ requires 226.0357), 185/183 (16/16), 147 (M^+-Br, 80), 117 (40), 105 (96), 91 (100), 77 (48) and 51 (34).

2-Bromo-4-pentyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8b**) was prepared from **2b** (0.87 g, 2.50 mmol), methyllithium (2.35 mL, 1.27 M, 2.98 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (50 mL). TLC indicated that at least five compounds were formed, but purification by flash chromatography (hexane) yielded only *endo*-**8b** (0.18 g, 29%) as a colourless liquid.

ν_{max}(film)/cm^{-1} 3064m, 2960s, 2927s, 2860s, 1456s, 1375w, 1322m, 1256m, 1081s, 1052m, 1015m, 898m, 858m, 800w and 735; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.87 (4 H, m), 1.30-1.62 (8 H, m), 1.65-1.79 (2 H, m), 2.14-2.19 (1 H, m, CH), 2.70-2.75 (1 H, m, CH), 3.07-3.12 (1 H, m, CH), 5.89-5.93 (1 H, m, =CH) and 5.97-6.01 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.6 (CH_2), 27.8 (CH_2), 28.8 (C), 31.9 (CH_2), 33.6 (CH_2), 33.7 (CH_2), 46.8 (CBr), 48.0 (CH), 54.7 (CH), 59.7 (CH_2), 132.7 (=*C*H) and 135.1 (=*C*H); *m/z* (EI) 256/254 (M^+, 6%), 185/183 (23/23), 175.1486 (M^+-Br, 65, $C_{13}H_{19}^+$ requires 175.1487), 117 (44), 105 (100), 91 (96), 77 (40) and 55 (48).

2-Bromo-4-octyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8c**) was prepared from **2c** (0.99 g, 2.53 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (40 mL). According to TLC and GC analyses at least five compounds were formed. Isolation by flash chromatography (hexane) yielded only *endo*-**8c** (0.25 g, 34%) as a colourless liquid (R_f=0.73).

ν_{max}(film)/cm^{-1} 3064w, 2973s, 2926s, 2856s, 1458m, 1374w, 1321w, 1255w, 1085w, 1051w, 1034w, 897w, 857w, 737m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-1.00 (5 H, m), 1.29-1.75 (6 H, m), 2.14-2.19 (1 H, m), 2.71-2.74 (1 H, m), 3.08-3.11 (1 H, m), 5.89-5.93 (1 H, m, =CH) and 5.97-6.01 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.6 (CH_2), 28.2 (CH_2), 28.9 (C), 29.2 (CH_2), 29.5 (CH_2), 29.7 (CH_2), 31.8 (CH_2), 33.6 (CH_2), 33.7 (CH_2), 46.8 (CBr), 48.1 (CH), 54.8 (CH), 59.8 (CH_2), 132.7 (=CH) and 135.1 (=CH); *m/z* (EI) 298.1119 (M^+, 9%, $C_{16}H_{25}{}^{81}Br^+$ requires 298.1119), 217 (M^+-Br, 64), 185/183 (29/29), 117 (43), 105 (100), 91 (84), 77 (28) and 57 (42).

In addition 1-bromo-2-octylcyclopropene (**6c**, 0.23 g, 39%) was isolated as a light yellow liquid (R_f=0.90).

ν_{max}(film)/cm^{-1} 2927s, 2857s, 1836w, 1461m, 1375w, 1259w, 1106w, 1033m, 804w and 722w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.85-0.92 (3 H, m, CH_3), 1.28-1.43 (10 H, m, 5 x CH_2), 1.52 (2 H, t, *J* 0.5, CH_2), 1.53-1.62 (2 H, m, CH_2) and 2.42 (2 H, t, *J* 7.0, CH_2); δ_C(50 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 17.1 (CH_2), 22.6 (CH_2), 25.3 (CH_2), 26.2 (CH_2), 29.1 (CH_2), 29.2 (2 x CH_2), 31.7 (CH_2), 92.1 (CBr) and 117.9 (C); *m/z* (EI) 151 (M^+-Br, 11%), 134/132 (18/18), 109 (21), 95 (59), 81 (49), 67 (46), 55 (78) and 41 (100).

2-Bromo-4-(2-phenylethyl)tricyclo[3.2.1.0^{2,4}]oct-6-ene (**8d**) was synthesised from **2d** (0.96 g, 2.51 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (40 mL). TLC and GC indicated that at least seven compounds were formed, however only *endo*-**8d** (0.39 g, 54%) was isolated by flash chromatography (hexane) as a colourless liquid (R_f=0.22).

ν_{max}(film)/cm^{-1} 3063m, 3025m, 2967s, 2931s, 2861m, 1603w, 1495m, 1449m, 1357w, 1321m, 1256m, 1121w, 1091m, 1048m, 1027m, 959w, 900br, 856m, 795w, 742s and 701s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.96 (1 H, dd, *J* 2.5 and 6.3), 1.35 (1 H, dd, *J* 1.4 and 6.3), 1.68-1.74 (1 H, m), 1.81-2.14 (2 H, m, CH_2), 2.17 (1 H, td, *J* 1.7 and 7.3), 2.61-2.66 (1 H, m), 2.65-2.91 (2 H, m, CH_2), 3.07-3.12 (1 H, m), 5.85-5.89 (1 H, m, =CH), 5.95-6.00 (1 H, m, =CH) and 7.13-7.32 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 28.7 (C), 33.6 (CH_2), 34.6 (CH_2), 35.9 (CH_2), 46.7 (CBr), 48.1 (CH), 54.7 (CH), 59.8 (CH_2), 125.7 (CH), 128.2 (2 x CH), 128.4 (2 x CH), 132.8 (=CH), 135.0 (=CH) and 141.9 (C); *m/z* (EI) 290.0500 (M^+, 1%, $C_{16}H_{17}{}^{81}Br^+$ requires 290.0493), 209 (M^+-Br, 10), 117 (31), 105 (21), 91 (100), 77 (12), 65 (19) and 51 (10).

In addition 1-bromo-2-(2-phenylethyl)cyclopropene (**6d**, 0.07 g, 13%) was isolated as a light yellow liquid (R_f=0.34).

ν_{max}(film)/cm^{-1} 3062w, 3027m, 2963s, 2926s, 2880s, 1836w, 1603w, 1495m, 1451m, 1078w, 1034s, 746m and 699s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.55 (2 H, t, *J* 0.5, CH_2), 2.70-2.96 (4 H, m, 2 x CH_2) and 7.16-7.35 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 17.2 (CH_2), 27.3 (CH_2), 32.4 (CH_2), 92.9 (CBr), 117.1 (C), 126.1 (CH), 128.2 (2 x CH), 128.3 (2 x CH) and 140.7 (C); *m/z* (EI) 222.0028 (M^+, 1%, $C_{11}H_{11}Br^+$ requires 222.0044), 143 (M^+-Br, 40), 128 (25), 105 (5), 91 (100), 77 (6), 65 (20) and 51 (42).

2-Bromo-4-cyclohexymethyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8e**) was synthesised from **2e** (0.96 g, 2.56 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (40 mL). According to TLC at least 3 products were formed, but only *endo*-**8e** (0.13 g, 19%) was isolated by flash chromatography (hexane) as a colourless liquid (R_f=0.62).

ν_{max}(film)/cm^{-1} 3062w, 2923br, 2850s, 1448m, 1321w, 1257w, 1078br, 1006w, 966w, 902w, 857w and 738m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.03 (1 H, dd, 6.3 and 2.4), 1.07-1.39 (5 H, m), 1.42 (1 H, dd, *J* 1.7 and 6.3), 1.69-1.78 (9 H, m), 2.13-2.18 (1 H, m), 2.71-2.76 (1 H, m), 3.07-3.12 (1 H, m), 5.91-5.95 (1 H, m, =CH) and 5.97-6.02 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 26.2 (CH_2), 26.3 (CH_2), 26.5 (CH_2), 27.1 (C), 32.9 (CH_2), 34.0 (CH_2), 34.1 (CH_2), 37.6 (CH), 40.9 (CH_2), 46.7 (CBr), 48.7 (CH), 54.8 (CH), 59.6 (CH_2), 132.8 (=CH) and 134.9 (=CH); *m/z* (EI) 282/280 (M^+, 5%), 201.1650 (M^+-Br, 12, $C_{15}H_{21}^+$ requires 201.1643), 185/183 (8/8), 117 (29), 105 (70), 91 (37) and 55 (100).

Two by-products, 1-bromo-2-cyclohexylmethylcyclopropene (**6e**, 0.19 g, 35%) and 1-bromo-4-cyclohexylmethylbut-2-yne (**10e**, 0.03 g, 5%), were also isolated (R_f=0.79 and 0.42, respectively).

6e:

ν_{max}(film)/cm^{-1} 2924s, 2852s, 1834w, 1711br, 1615w, 1447m, 1266m, 1210m, 1076w, 1032s, 956w, 908w, 736br and 687w; δ_C(50 MHz; $CDCl_3$; Me_4Si) 17.3 (CH_2), 26.07 (2 x CH_2), 26.13 (CH_2), 32.99 (2 x CH_2), 33.03 (CH_2), 36.0 (CH), 92.6 (CBr) and 117 (C); *m/z* (EI) 135 (M^+-Br, 16%), 105 (14), 91 (23), 67 (94) and 55 (100).

10e:

ν_{max}(film)/cm^{-1} 2923s, 2851s, 2249w, 1448m, 1211m and 607m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.86-1.82 (11 H, m), 2.13 (2 H, td, *J* 2.4 and 6.6, CH_2) and 3.94 (2 H, t, *J* 2.4, CH_2Br); δ_C(50 MHz; $CDCl_3$; Me_4Si) 15.8 (CH_2), 26.0 (2 x CH_2), 26.1 (CH_2), 26.6 (CH_2), 32.5 (2 x CH_2), 37.0 (CH), 76.0 (C) and 87.2 (C); *m/z* (EI) 216/214 (M^+, 0.3%), 135 (M^+-Br, 26), 107 (6), 93 (17), 83 (98), 67 (24) and 55 (100).

2-Bromo-4-isobutyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8f**) was prepared from **2f** (0.83 g, 2.49 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (30 mL). TLC and GC indicated that at least nine compounds were formed, but purification by flash chromatography (hexane) yielded only *endo*-**8f** (0.15 g, 26%) as a colourless oil.

ν_{max}(film)/cm^{-1} 3063m, 2958br, 2871s, 2841m, 1462m, 1366w, 1324m, 1249w, 1081br, 1004w, 956w, 901w, 856m and 738m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 0.90 (3 H, d, *J* 6.5, CH_3), 0.97 (3 H, d, *J* 6.3, CH_3), 1.04 (1 H, dd, *J* 2.5 and 6.3), 1.25-1.38 (1 H, m), 1.44 (1 H, dd, *J* 1.6 and 6.3), 1.68-1.86 (3 H, m), 2.16 (1 H, td, *J* 1.7 and 7.3), 2.73-2.78 (1 H, m), 3.08-3.13 (1 H, m), 5.90-5.95 (1 H, m, =CH) and 5.98-6.03 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 22.2 (CH_3), 23.4 (CH_3), 27.6 (C), 28.1 (CH), 34.1 (CH_2), 42.2 (CH_2), 46.5 (CBr), 48.6 (CH), 54.8 (CH), 59.6 (CH_2), 132.8 (=CH) and 134.9 (=CH); *m/z* (EI) 240.0500 (M^+, 3%, $C_{12}H_{17}Br^+$ requires 240.0514), 185/183 (14/14), 161 (M^+-Br, 20), 117 (53), 105 (100), 91 (67), 77 (40) and 57 (39).

*2-Bromo-4-*tert*-butyltricyclo[3.2.1.0^{2,4}]oct-6-ene* (**8g**) was synthesised from **2g** (0.85 g, 2.54 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (40 mL). TLC and GC analyses showed that at least nine compounds were formed. Purification by flash chromatography (hexane) yielded a colourless oil (0.10 g, R_f=0.63), and NMR analysis proved that this was a mixture of **2g**, *endo*- and *exo*-**8g** in a 3:6:1 ratio. The cyclopropane ring protons in **2g** give rise to two doublets at 1.90 and 2.21 ppm in the ^{1}H NMR spectrum, while the two multiplets at 5.75-5.98 and 5.88-6.04 ppm are due to the vinylic protons in respectively the *endo* and *exo* isomers of **8g**.

10-Bromotetracyclo[9.2.1.0^{2,9}.0^{2,10}]tetradec-12-ene (**8h**) was prepared from **2h** (0.91 g, 2.52 mmol), methyllithium (1.6 mL, 1.5 M, 2.56 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol). TLC and GC indicated that at least four compounds were formed, but purification by flash chromatography (hexane) yielded only *endo*-**8h** (0.47 g, 70%) as a colourless oil.

ν_{max}(film)/cm^{-1} 3061w, 2973s, 2921s, 2856s, 1451m, 1356w, 1323w, 1250m, 1164w, 1096w, 1060br, 1034w, 948w, 887w, 797w and 736m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.01-1.04 (1 H, m), 1.28-1.44 (6 H, m), 1.51-1.76 (7 H, m), 2.08 (1 H, td, *J* 1.8 and 7.3), 2.74-2.76 (1 H, m), 3.09-3.11 (1 H, m), 5.88-5.90 (1 H, m, =CH) and 5.98-6.00 (1 H, m, =CH); δ_C(100 MHz;

$CDCl_3$; Me_4Si) 26.5 (CH_2), 26.8 (CH_2), 27.2 (CH_2), 27.6 (CH_2), 27.9 (CH_2), 28.6 (CH_2), 28.8 (C), 37.9 (CH), 48.3 (CH), 52.8 (CBr), 56.4 (CH), 58.6 (CH_2), 132.5 (=CH) and 134.1 (=CH); *m/z* (EI) 268/266 (M^+, 2%), 187 (M^+-Br, 41), 145 (14), 131 (22), 117 (44), 105 (49), 91 (100), 79 (57), 67 (69) and 55 (41).

2-Bromo-4-phenoxymethyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8i**) was synthesised from **2i** (1.02 g, 2.65 mmol), methyllithium (2.00 mL, 1.50 M, 3.00 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol). GC indicated that at least three compounds were formed. Isolation by flash chromatography (hexane:ethyl acetate [98:2]) gave only *endo*-**8i** (0.49 g, 70%) as a colourless liquid.

ν_{max}(film)/cm^{-1} 3063w, 2982m, 2937m, 2866w, 1599s, 1495s, 1388s, 1367s, 1300m, 1240s, 1172m, 1033s, 856w, 752s and 691s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.35 (1 H, dd, *J* 2.5 and 6.6), 1.59 (1 H, dd, *J* 1.1 and 6.6), 1.81-1.84 (1 H, m), 2.35-2.38 (1 H, m), 3.05-3.07 (1 H, m), 3.14-3.16 (1 H, m), 4.20 (1 H, d, *J* 9.9, OCH), 4.30 (1 H, dd, *J* 1.1 and 9.9, OCH), 6.01-6.07 (2 H, m, HC=CH), 6.91-6.98 (3 H, m, Ph) and 7.25-7.32 (2 H, m, Ph); δ_C(100 MHz; $CDCl_3$; Me_4Si) 28.5 (C), 33.6 (CH_2), 43.7 (CBr), 47.3 (CH), 54.5 (CH), 60.6 (CH_2), 72.4 (OCH_2), 114.7 (2 x CH), 120.8 (CH), 129.3 (2 x CH), 133.2 (=CH), 135.2 (=CH), 159.0 (C); *m/z* (EI) 290.0326 (M^+, 2%, $C_{15}H_{15}BrO^+$ requires 290.0306), 198/196 (21/21), 117 (100), 91 (44) and 77 (37).

After a couple of months in the freezer, white crystals were formed, mp. 38-39 ˚C.

2-Bromo-4-(4-methylphenoxy)methyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8j**) was prepared from **2j** (1.00 g, 2.51 mmol), methyllithium (2.00 mL, 1.50 M, 3.00 mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol). GC analyses indicated that at least five compounds were formed, but purification by flash chromatography (hexane:ethyl acetate [95:5]) yielded only *endo*-**8j** (0.55 g, 74%) as a light yellow oil.

ν_{max}(film)/cm^{-1} 3063w, 2982m, 2935m, 2865m, 1613w, 1585w, 1512s, 1458w, 1388w, 1290m, 1237s, 1175w, 1099w, 1026s, 856w, 814s, 742m and 717w; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.33 (1 H, dd, *J* 2.6 and 6.6), 1.57 (1 H, dd, *J* 1.1 and 6.6), 1.79-1.82 (1 H, m), 2.28 (3 H, s, CH_3), 2.34-2.36 (1 H, m), 3.03-3.06 (1 H, m), 3.12-3.15 (1 H, m), 4.16 (1 H, d, *J* 9.9, OCH), 4.26 (1 H, dd, *J* 1.1 and 9.9, OCH), 6.00-6.02 (1 H, m, =CH), 6.03-6.05 (1 H, m, =CH), 6.83-6.87 (2 H, m, 2 x CH) and 7.07-7.09 (2 H, m, 2 x CH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 20.4 (CH_3), 28.5 (C), 33.5 (CH_2), 43.6 (CBr), 47.3 (CH), 54.4 (CH), 60.5 (CH_2), 72.6 (OCH_2), 114.5 (2 x CH), 129.7 (2 x CH), 129.9 (C), 133.2 (=CH), 135.1 (=CH) and 156.9

(C); *m/z* (EI) 304.0465 (M^+, 4%, $C_{16}H_{17}BrO^+$ requires 304.0463), 198/196 (25/25), 117 (100), 108 (83), 91 (64) and 77 (28).

2-Bromo-4-phenyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**8l**) was synthesised from **2l** (0.96 g, 2.71 mmol), methyllithium (2.00 mL, 1.50 M, 3 .00mmol) and cyclopentadiene (0.20 mL, δ 0.80 g/mL, 2.42 mmol) in THF (40 mL). GC analyses indicated that at least six compounds were formed; however flash chromatography (hexane) gave only *endo*-**8l** (0.34 g, 54%) as a colourless oil.

ν_{max}(film)/cm^{-1} 3061m, 2979s, 2870w, 1600w, 1498m, 1448m, 1321m, 1255m, 1101m, 1058m, 1014m, 899w, 856m, 761m, 741s and 698s; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.78 (2 H, br s, CH_2), 1.91-1.93 (1 H, m), 2.62-2.64 (1 H, m), 3.05-3.07 (1 H, m), 3.24 (1 H, m), 6.08-6.10 (1 H, m, =CH), 6.17-6.19 (1 H, m, =CH) and 7.23-7.40 (5 H, m, Ph); δ_C(100 MHz; $CDCl_3$; Me_4Si) 32.6 (CH_2), 33.2 (C), 46.9 (CBr), 52.1 (CH), 54.7 (CH), 61.0 (CH_2), 126.4 (CH), 128.1 (2 x CH), 128.3 (2 x CH), 134.6 (=CH), 135.7 (=CH) and 140.2 (C); *m/z* (EI) 262/260 (M^+, 6%), 181.1008 (M^+-Br, 100, $C_{14}H_{13}^+$ requires 181.1017) and 77 (30).

5.5.3 *Trapping with furan*

General. The cyclopropane (**2**) and furan (~10 eq.) were dissolved in THF (40 mL) in a round-bottomed flask, equipped with a condenser connected to a nitrogen inlet. The solution was cooled to -78 ˚C (acetone/dry-ice or ethyl acetate/liquid nitrogen). MeLi (1.01-1.13 eq.) was added dropwise with a syringe with magnetic stirring. The reactions were monitored by either TLC or GC and quenched with a portion of water. The product (**9**) was extracted with diethyl ether, dried ($MgSO_4$), filtrated and evaporated *in vacuo* and finally isolated by flash chromatography.

Attempts at synthesising *2-bromo-8-oxa-4-propyltricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2a** (0.80 g, 2.51 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) failed. Work-up and evaporation *in vacuo* afforded an orange, bad smelling liquid (0.42 g) which according to TLC consisted of at least five compounds. Purification by flash chromatography (hexane:ethyl acetate [97.5:2.5]) was not successful.

Attempts at synthesising *2-bromo-8-oxa-4-pentyltricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2b** (0.87 g, 2.49 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) were unsuccessful. Work-up and evaporation *in vacuo* afforded an orange liquid (0.65 g) which according to TLC consisted of at least four compounds. Purification by flash chromatography (hexane) gave a colourless oil (0.42 g) which according to ^{1}H NMR consisted of some 1-bromooct-2-yne (**10b**) and 3-bromoocta-1,2-diene (**11b**) in a 1:6 ratio. The acetylene **10b** gives rise to a triplet at 3.92 ppm, which is assigned to the methylene group at C1; the same group in **11b** gives rise to a triplet at 4.82 ppm. However, isolation efforts were unsuccessful.

Attempts at synthesising *2-bromo-4-octyl-8-oxatricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2c** (0.98 g, 2.51 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) failed. Work-up and evaporation *in vacuo* afforded an orange liquid (0.60 g) which according to TLC consisted of at least five compounds. Purification by flash chromatography (hexane) afforded 1-bromoundec-2-yne (**10c**, 0.13 g, 22%) and 3-bromoundeca-1,2-diene (**11c**, 0.10 g, 17%) as colourless oils (R_f=0.44 and 0.70, respectively). Traces of the **6c** could also be seen in the ^{1}H NMR spectrum of some fractions, but efforts to isolate it failed.

10c:

ν_{max}(film)/cm^{-1} 2926s, 2857s, 2249w, 1461m, 1374w, 1330w and 1212m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.87-0.90 (3 H, m, CH_3), 1.28-1.40 (10 H, m, 5 x CH_2), 1.47-1.54 (2 H, m, CH_2), 2.21-2.26 (2 H, m, CH_2) and 3.93 (2 H, t, *J* 2.4, (CH_2)Br); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 15.7 (CH_2), 18.8 (CH_2), 22.5 (CH_2), 28.3 (CH_2), 28.7 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 31.7 (CH_2), 75.1 (C) and 88.2 (C); *m/z* (EI) 175/173 (M^+-Bu, 4%), 109 (26), 95 (100), 81 (54), 67 (43), 55 (43) and 41 (44).

11c:

ν_{max}(film)/cm^{-1} 2927s, 2857s, 1460m, 1376w, 1255w, 1117w, 1049w, 962w and 867m; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.88 (3 H, t, *J* 6.9, CH_3), 1.28-1.34 (10 H, m, 5 x CH_2), 1.48-1.55 (2 H, m, CH_2), 2.36-2.41 (2 H, m, CH_2) and 4.82 (2 H, t, *J* 3.2, $=CH_2$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (CH_3), 22.5 (CH_2), 27.7 (CH_2), 28.4 (CH_2), 29.10 (CH_2), 29.14 (CH_2), 31.7 (CH_2), 37.1 (CH_2), 81.1 ($=CH_2$), 93.1 (=CBr) and 203.9 (C); *m/z* (EI) 151 (M^+-Br, 14%), 134/132 (44), 109 (40), 95 (83), 81 (68), 67 (57), 55 (84) and 41 (100).

Attempts at synthesising *2-bromo-8-oxa-4-(2-phenylethyl)tricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2d** (0.96 g, 2.51 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) were unsuccessful. The crude product, a yellow liquid, was impure **6d** (0.54 g, 96%), which decomposed slightly on silica gel during purification with flash chromatography (hexane). The spectroscopic data were identical to those given previously (see Chapter 5.5.2).

Attempts at synthesising *2-bromo-4-cyclohexylmethyl-8-oxatricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2e** (0.93 g, 2.48 mmol), methyllithium (1.60 mL, 1.60 M, 2.56 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) failed. The crude product, an orange liquid, was impure **6e** (0.52 g, 74%), which decomposed slightly on silica gel during purification with flash chromatography (hexane:ethyl acetate [98:2]). The spectroscopic data were consistent with previous analyses (see Chapter 5.5.2).

Efforts to synthesise *2-bromo-4-isobutyl-8-oxatricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2f** (0.83 g, 2.48 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) were unsuccessful. Work-up and evaporation *in vacuo* afforded a yellow, bad smelling liquid (0.52 g) which according to TLC consisted of at least four compounds. Purification by flash chromatography (hexane:ethyl acetate [98:2]) was not successful.

Efforts to synthesise *2-bromo-4-*tert-*butyl-8-oxatricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2g** (0.84 g, 2.48 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) failed. Work-up and evaporation *in vacuo* afforded a yellow liquid (0.64 g) which according to TLC consisted of at least four compounds. Purification by flash chromatography (hexane:ethyl acetate [98:2]) was not successful.

Attempts at synthesising *10-bromo-14-oxatetracyclo[9.2.1.0^{2,9}.0^{2,10}]tetradec-12-ene* from **2h** (0.85 g, 2.36 mmol), methyllithium (2.00 mL, 1.50 M, 3.00 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) failed. The reaction mixture was ultrasonicated, with and without aluminium(III) chloride, but no product was formed. Instead, 9-bromobicyclo[6.1.0]non-1(9)-ene (**6h**, 0.47 g, 100%) was isolated as a yellow oil by evaporating the solvents *in vacuo*.[20,21,34]

ν_{max}(film)/cm^{-1} 2924s, 2855s, 1702m, 1452s, 1348w, 1319w, 1237w, 1059m, 1019m, 862w, 754w and 671w; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.19-1.67 (9 H, m), 1.79-1.88 (1 H, m), 2.12-2.23 (2 H, m) and 2.70 (1 H, ddd, *J* 3.9, 5.7 and 14.7); δ_C(100 MHz; $CDCl_3$; Me_4Si) 19.7 (CH_2), 24.7 (CH_2), 24.97 (CH_2), 24.99 (CH_2), 29.0 (CH), 29.4 (CH_2), 30.5 (CH_2), 97.1 (C) and 123.4 (C); *m/z* (EI) 202/200 (M^+, 25%), 121 (M^+-Br, 21), 105 (11), 93 (74), 91 (42), 79 (100) and 67 (38).

2-Bromo-8-oxa-4-phenoxymethyltricyclo[3.2.1.0^{2,4}]oct-6-ene (**9i**) was prepared from **2i** (0.96 g, 2.50 mmol), methyllithium (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL). According to TLC and GC at least eight compounds were formed, but purification by flash chromatography (hexane:ethyl acetate [98:2]) yielded only *exo*-**9i** (0.23 g, 31%) as a colourless oil. This was characterised as pure *exo* isomer, because of the large difference in the chemical shift of the doublet and double doublet at 1.44 and 2.41 ppm, which were assigned to the H atoms in the cyclopropane moiety.
ν_{max}(film)/cm^{-1} 3062w, 3006m, 2916w, 2869w, 1594s, 1494s, 1467m, 1429w, 1392m, 1295s, 1237br, 1174m, 1132m, 1081m, 1030s, 919s, 886m, 873s, 821w, 782w, 754s and 692; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.44 (1 H, d, *J* 6.4), 2.41 (1 H, dd, *J* 1.3 and 6.4), 3.95 (1 H, d, *J* 10.5, OCH), 4.05 (1 H, dd, *J* 1.3 and 10.5), 4.84 (1 H, d, *J* 1.5), 4.91 (1 H, d, *J* 1.5), 6.67 (1 H, dd, *J* 1.5 and 5.7, =CH), 6.72 (1 H, dd, *J* 1.5 and 5.7, =CH), 6.89-6.98 (3 H, m, Ph) and 7.25-7.30 (2 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.4 (CH_2), 34.4 (C), 44.8 (CBr), 69.6 (OCH_2), 79.0 (OCH), 81.4 (OCH), 114.4 (2 x CH), 121.0 (CH), 129.3 (2 x CH), 138.6 (=CH), 139.5 (=CH) and 158.5 (C); *m/z* (EI) 294/292 (M^+, 4%), 213 (M^+-Br, 3), 91 (100), 77 (20) and 65 (26).
In addition impure *endo*-**9i** (0.11 g, 15%) was isolated, but this sample was not pure enough to obtain satisfying spectra. However, in the ^{1}H NMR spectrum a doublet at 1.76 (*J*=6.9 Hz) ppm and a double doublet at 1.86 (*J*=6.9 and 1.4 Hz) ppm were also assigned to the H atoms in the cyclopropane moiety.

2-Bromo-4-(4-methylphenoxy)methyl-8-oxatricyclo[3.2.1.0^{2,4}]oct-6-ene (**9j**) was prepared from **2j** (1.04 g, 2.61 mmol), methyllithium (2.00 mL, 1.50 M, 3.00 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL). TLC and GC indicated that at least six compounds were formed, but purification by flash chromatography (hexane:ethyl acetate [97.5:2.5]) gave only *exo*-**9j** (0.38 g, 49%) as a colourless oil (R_f=0.16). This was characterised as pure *exo* isomer on the same grounds as for **9i**.

ν_{max}(film)/cm^{-1} 3004m, 2919m, 2866w, 1612m, 1587w, 1512s, 1464m, 1433w, 1391m, 1293s, 1235br, 1179m, 1127m, 1028s, 920br, 871s, 815s, 753w, 702m and 614w; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.44 (1 H, d, *J* 6.3), 2.28 (3 H, s, CH_3), 2.41 (1 H, dd, *J* 1.3 and 6.3), 3.94 (1 H, d, *J* 10.5, OCH), 4.04 (1 H, dd, *J* 1.3 and 10.5, OCH), 4.84 (1 H, d, *J* 1.7), 4.92 (1 H, d, *J* 1.5), 6.68 (1 H, dd, *J* 1.7 and 5.8, =CH), 6.74 (1 H, dd, *J* 1.5 and 5.8, =CH), 6.80-6.83 (2 H, m, 2 x CH) and 7.07-7.09 (2 H, m, 2 x CH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 20.4 (CH_3), 29.5 (CH_2), 34.5 (C), 44.8 (CBr), 69.9 (OCH_2), 79.1 (CO), 81.4 (CO), 114.4 (2 x CH), 129.8 (2 x CH), 130.3 (C), 138.7 (=CH), 139.5 (=CH) and 156.5 (C); *m/z* (EI) 306.0252 (M^+, 8%, $C_{15}H_{15}O_2Br^+$ requires 306.0255), 201/199 (4), 108 (26), 91 (100) and 77 (15).

Traces of the *endo* isomer were observed in the ^{1}H NMR spectrum of the crude product as a doublet at 1.75 ppm (*J*=6.9 Hz) and a double doublet at 1.85 ppm (*J*=6.9 and 1.4 Hz), which were assigned to the H atoms in the cyclopropane moiety. Isolation efforts were unsuccessful.

In addition impure 1-bromo-2-(4-methylphenoxy)methylcyclopropene (**6j**, 0.08 g, 13%) was isolated as a yellow oil (R_f=0.34).

δ_C(100 MHz; $CDCl_3$; Me_4Si) 9.2 (CH_2), 20.4 (CH_3), 63.9 (OCH_2), 105.9 (C), 110.8 (C), 114.5 (2 x CH), 129.7 (2 x CH), 129.8 (C) and 156.1 (C).

2-Bromo-4-(4-bromophenoxy)methyl-8-oxatricyclo[3.2.1.0^{2,4}]oct-6-ene (**9k**) was prepared from **2k** (1.16 g, 2.49 mmol), methyllithium (1.7 mL, 1.5 M, 2.55 mmol) and furan (2 mL, δ 0.94 g/mL, 28 mmol) in THF (40 mL). GC indicated that at least three compounds were formed, but flash chromatography (hexane:ethyl acetate [95:5]) yielded only *exo*-**9k** (0.35 g, 38%) as a yellow oil.

ν_{max}(film)/cm^{-1} 3079w, 3003w, 2921w, 2868w, 1585m, 1487s, 1429w, 1393m, 1289s, 1238br, 1174m, 1130w, 1073m, 1023s, 920s, 891br, 871m, 822s 747w, 708m, 688m and 635m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.45 (1 H, d, *J* 6.4), 2.43 (1 H, dd, *J* 1.2 and 6.4), 3.94 (1 H, d, *J* 10.4, OCH), 4.04 (1 H, dd, *J* 1.2 and 10.4, OCH), 4.85 (1 H, d, *J* 1.6), 4.95 (1 H, d, *J* 1.6), 6.71 (1 H, dd, *J* 1.6 and 5.7, =CH), 6.76 (1 H, dd, *J* 1.6 and 5.7, =CH), 6.78-6.82 (2 H, m) and 7.37-7.41 (2 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 29.5 (CH_2), 34.4 (C), 44.7 (CBr), 70.1 (OCH_2), 79.0 (CO), 81.5 (CO), 113.3 (CBr), 116.3 (2 x CH), 132.2 (2 x CH), 138.6 (=CH), 139.7 (=CH) and 157.7 (C); *m/z* (EI) 374/372/370 (M^+, 2%), 201/199 (4), 91 (100) and 65 (18).

Traces of *endo*-**9k** and 1-(4-bromobut-2-ynyloxy)-4-bromobenzene (**10k**) were observed in the ^{1}H NMR spectrum of the crude product, and purification by flash chromatography (hexane:ethyl acetate [9:1]) yielded almost pure *endo*-**9k** (0.07 g, 8%). However, small

impurities made it difficult to obtain satisfying spectra, but the doublet at 1.75 (*J*=7.0 Hz) ppm and the double doublet at 1.87 (*J*=7.0 and 1.3 Hz) were assigned to the cyclopropane H atoms.

Attempts on synthesising *2-bromo-8-oxa-4-phenyltricyclo[3.2.1.0^{2,4}]oct-6-ene* from **2l** (0.89 g, 2.51 mmol), MeLi (1.70 mL, 1.50 M, 2.55 mmol) and furan (2.00 mL, δ 0.94 g/mL, 27.61 mmol) in THF (40 mL) were unsuccessful. The brown crude product consisted of at least four compounds according to TLC. NMR analyses indicated that this was *exo*-**9l**, and 1-(3-bromoprop-1-ynyl)benzene (**10l**) and 1-(1-bromopropa-1,2-dienyl)benzene (**11l**) in a 2:3 ratio. The acetylene **10l** gives rise to a singlet at 4.05 ppm, which is assigned to the methylene group. The same group in the **11l** gives rise to a singlet at 5.29 ppm. Efforts to isolate the products by flash chromatography were unsuccessful. However, an impure sample of *exo*-**9l** (0.02 g) was obtained. The cyclopropane ring protons give rise to two doublets at 1.61 (*J*=5.9 Hz) and 2.69 (*J*=5.9 Hz) ppm, while the vinylic protons resonate as a multiplet at 6.75-6.84 ppm.

5.6 Reduction of trihalogenated cyclopropanes

Tributyltin hydride (BTH) was prepared from tributyltin chloride (162.70 g, 0.50 mol) and lithiumaluminium hydride (LAH) (9.49 g, 0.25 mol) in diethyl ether (500 mL) in a nitrogen atmosphere.[35] LAH was dissolved in diethyl ether and tributyltin chloride was added dropwise with mechanical stirring at 0 ˚C. The solution was stirred at room temperature over night, carefully quenched with cold water and extracted with diethyl ether (4 x 150 mL). The combined extracts were washed with water and dried ($MgSO_4$). Distillation through a Vigreux column yielded BTH (111.51 g, 77%) as a colourless liquid, bp. 64-69 ˚C/0.25 mmHg (lit.[35] 68-74 ˚C/0.3 mmHg).
ν_{max}(film)/cm^{-1} 2954s, 2922s, 2854s, 1810s, 1459s, 1421m, 1377m, 1342m, 1290m, 1251w, 1181w, 1152w, 1073m, 1049w, 1015m, 1006m, 961w, 870m, 698s and 675s; δ_H(200 MHz; shift values are not calibrated) 0.88-0.95 (9 H, m), 1.24-1.45 (12 H, m), 1.57-1.73 (6 H, m) and 5.27-5.28 (1 H, m); δ_C(50 MHz; shift values are not calibrated) 8.5, 14.1, 27.7 and 30.5.

cis/trans-*1-Bromo-2-chloromethylcyclopropane* (**12m**) was synthesised from **2m** (4.97 g, 20 mmol) and BTH (73% determined by ^{1}H NMR, 8.47 g, 21 mmol) in diethyl ether (30 mL) under nitrogen.[27,36] Distillation of the crude product, through a Vigreux column, gave **12m**

(1.94 g, 57%) as a colourless liquid, bp. 54-56 ˚C/12 mmHg. This was a mixture of the *cis*/*trans*-diastereomers in a 41:59 ratio, according to GC analyses.
ν_{max}(film)/cm^{-1} 3060 (w), 3003 (w), 2959 (m), 1439 (s), 1376 (m), 1274 (s), 1256 (s), 1242 (s), 1217 (m), 1114 (w), 1073 (w), 1040 (m), 998 (w), 973 (w), 921 (w), 906 (w), 863 (w), 823 (m), 796 (w) and 712 (s); δ_H(250 MHz; $CDCl_3$) 0.78-1.78 (m) and 2.77-3.83 (m) (approximately 1:1 ratio between the multiplets, but difficult to determine the *cis*/*trans* ratio); δ_C(62.5 MHz; $CDCl_3$) 15.7 (CH_2), 16.3 (CH_2), 18.1 (CH), 18.9 (CH), 22.0 (CH), 24.3 (CH), 46.3 (CH_2Cl) and 46.7 (CH_2Cl); *m/z* (EI) 169.9314 (M^+, 3%, $C_4H_6BrCl^+$ requires 169.9319), 135/133 (M^+-Cl, 9/9), 121/119 (M^+-CH_2Cl, 18/18), 89 (M^+-Br, 100) and 53 (58).

cis/trans-*1-Bromo-2-chloromethyl-2-methylcyclopropane* (**12n**) was prepared from **2n** (5.25 g, 20 mmol) and BTH (6.15 g, 21 mmol) in diethyl ether (30 mL) under nitrogen.[27,36] Distillation of the crude product, through a packed column, yielded **12n** (2.72 g, 74%) as a colourless liquid, bp. 48 ˚C/10 mmHg (lit.[27] 62-64 ˚C/11 mmHg). This was a mixture of the *cis*/*trans*-diastereomers in a 33:67 ratio, according to ^{1}H NMR and GC analyses.
ν_{max}(film)/cm^{-1} 3051w, 2961s, 2934s, 2872m, 1440s, 1384m, 1340m, 1303s, 1271s, 1218s, 1083w, 1039m, 957m, 917m, 890w, 842w, 720s and 607s; δ_H(250 MHz; $CDCl_3$) 0.84 (1 H (major), dd, *J* 4.7 and 6.6 Hz), 0.92 (1 H (minor), dd, *J* 4.6 and 6.7 Hz), 1.15-1.21 (1 H (minor), m), 1.24-1.30 (1 H (major), m), 1.27 (3 H (minor), s), 1.40 (3 H (major), s), 2.94 (1 H (minor), dd, *J* 4.6 and 7.5 Hz), 3.01 (1 H (major), dd, *J* 4.7 and 8.1 Hz), 3.38 (1 H (major), d, *J* 11.3 Hz), 3.43 (1 H (major), d, *J* 11.3 Hz), 3.63 (1 H (minor), d, *J* 11.3 Hz) and 3.78 (1 H (minor), d, *J* 11.3 Hz); δ_C(50 MHz; $CDCl_3$; Me_4Si) 18.7 (CH_3, major), 20.5 (CH_3), 22.58 (C), 22.61 (CH_2, major), 23.11 (C), 23.15 (CH_2), 27.7 (CH, major), 28.3 (CH), 52.5 (CH_2) and 52.6 (CH_2, major) ; *m/z* (EI) 183.9472 (M^+, 3%, $C_5H_8BrCl^+$ requires 183.9476), 149/147 (M^+-Cl, 4/4), 135/133 (M^+-CH_2Cl, 52/52), 103 (M^+-Br, 85), 84 (91) and 49 (100).

Attempts at making **12m** and **12n** by monobromocarbene addition to the corresponding olefins were also made, following a procedure by Martel and Hiriart.[37] Sodium bis(trimethylsilyl)amide (10 mmol) and olefin (30 mmol) were dissolved in dry pentane in a three-necked flask, connected to an argon inlet through a condenser. Methylene bromide (10 mmol) was added dropwise at room temperature with vigorous stirring. The stirring was continued for 4 hours before work-up with water, extraction (3 x 50 mL, diethyl ether) and drying ($MgSO_4$). After evaporation of the solvent, GC and ^{1}H NMR analyses indicated that the yields of **12m** and **12n** were respectively 8 and 11%. The crude products were difficult to

purify because of the similarity in boiling points to bis(trimethylsilyl)amine produced in the reaction. However, GC and NMR analyses showed that the stereoselectivity in these reactions were the same as with reduction of **2** with BTH.

5.7 Pyrolysis of halogenated cyclopropanes

5.7.1 *In hot quinoline*

General procedure. Pyrolyses of cyclopropanes **2**, **3** and **12** were performed in hot quinoline according to the procedure by Ando *et al*. at temperatures between 200-240 °C under nitrogen or argon.[38] GC and GC-MS monitoring ensured full conversion. The cyclopropanes were heated in quinoline (1:3 ratio) in a microscale distillation unit, with magnetic stirring, and the pyrolysate was collected in a dry-ice or liquid nitrogen cooled flask connected to the nitrogen inlet through a liquid nitrogen cooled U-tube. In order to simplify the analyses and isolation of dienes formed in the pyrolyses, they were immediately trapped in a Diels-Alder reaction with 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (PTAD) in CH_2Cl_2. The quinoline residues were acidified (diluted HCl) and extracted with diethyl ether. The organic phase was treated with solutions of sodium carbonate and sodium chloride, before evaporation *in vacuo*.

3-Bromo-2,4-dimethyl-1,3-pentadiene (**13**) was prepared by heating **2o** (0.77 g, 3 mmol) in quinoline at 200 °C for 15 minutes. After 10 minutes **13** (0.31 g, 58%) was collected in the dry-ice cooled receiver flask as a colourless liquid, bp. 152 °C (lit.[39] 47-48 °C/15 mmHg).
ν_{max}(ATR)/cm^{-1} 2916m, 2852w, 1443m, 1365m, 1093m, 980m, 906s, 879m, 851s, 801m and 781m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.80 (3 H, s, CH_3), 1.88-1.90 (6 H, m, 2 x CH_3), 4.90-4.92 (1 H, m, =CH) and 5.02-5.05 (1 H, m, =CH); δ_C(50 MHz; $CDCl_3$; Me_4Si) 21.5 (CH_3), 21.6 (CH_3), 24.3 (CH_3), 116.3 (=CH_2), 120.0 (C), 130.8 (C) and 143.9 (C); *m/z* (EI) 176/174 (M^+, 58%), 95 (M^+-Br, 100), 67 (73) and 55 (40).

*6-Bromo-5,5,7-trimethyl-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione* (**14**) was prepared from **13** (0.15 g, 0.87 mmol) and PTAD (3.5 mL, 0.251 M, 0.88 mmol) in dichloromethane. Flash chromatography (hexane:ethyl acetate [7:3]) yielded **14** (0.19 g, 62%) as a white solid, mp. 140-141 °C.
ν_{max}(ATR)/cm^{-1} 2949w, 1776m, 1714s, 1501m, 1410s, 1247m, 1173m, 1135m, 1076m, 943m, 765s, 739m and 689s; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.76 (6H, s, 2 x CH_3), 1.96 (3 H, t, *J* 0.8, CH_3), 4.07-4.08 (2 H, m, CH_2) and 7.33-7.53 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 20.9

(CH_3), 23.8 (2 x CH_3), 48.1 (CH_2), 64.1 (C), 125.1 (C), 125.4 (2 x CH_2), 126.1 (C), 128.1 (CH), 129.0 (2 x CH_2), 130.9 (C), 152.2 (CO) and 152.3 (CO); *m/z* (EI) 349.0420 (M^+, 75%, $C_{15}H_{16}BrN_3O_2^+$ requires 349.0426), 336/334 (M^+-CH_3, 100/100), 270 (M^+-Br, 12), 217/215 (82/82), 119 (47), 108 (82), 94 (50) and 67 (34).

1,1-Dibromo-2-chloromethylcyclopropane (**2m**, 1.96 g, 7.90 mmol) was heated in quinoline (3.10 g, 24.02 mmol) at 225 °C for 50 minutes and a colourless liquid was collected in the liquid nitrogen cooled receiver flask after 5 minutes. Addition of PTAD, until the red colour persisted, and purification with flash chromatography (hexane:ethyl acetate [7:3]) yielded a white powder (R_f=0.24, 0.03 g, 1%) which, according to ^{1}H NMR was a 1:1 mixture of 6-chloro-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione (**15**, *m/z* 263) and 6-bromo-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione (**16**, *m/z* 307). When the NMR spectra were compared to spectra from an authentic sample of **15** (see Chapter 5.7.3), it was possible to extract some signals due to **16**.
δ_H(250 MHz; $CDCl_3$; Me_4Si) 4.17-4.27 (6 H, m), 4.31-4.34 (2 H, m), 6.06-6.10 (1 H, m, **15,** =CH), 6.26-6.31 (1 H, m, =CH) and 7.35-7.54 (10 H, m); δ_C(62.5 MHz; $CDCl_3$; Me_4Si) 43.8 (**15**, CH_2), 45.1 (CH_2), 47.9 (**15**, CH_2), 49.6 (CH_2), 113.6 (C), 118.4 (**15**, CH), 122.3 (CH), 125.2 (**15**, CH), 125.4 (**15**, C), 128.2 (**15**, CH), 129.1 (**15**, CH), 130.8 (**15**, C), 151.7 (**15**, CO), 151.9 (CO), 152.26 (**15**, CO) and 152.32 (CO).
In addition **2m** (0.07 g, 4%) was recovered. Work-up of the quinoline residue did not yield any unreacted **2m** or ring-opening products.

1,1-Dibromo-2-chloromethyl-2-methylcyclopropane (**2n**, 2.10 g, 8.02 mmol) was heated in quinoline (3.10 g, 24.00 mmol) at 225 °C for 1 hour and smoke developed in the flask when a colourless liquid was collected in the liquid nitrogen cooled receiver flask after 10 minutes. Addition of PTAD until the red colour persisted yielded a mixture consisting of at least three different compounds. Flash chromatography (chloroform) yielded a light yellow solid (R_f=0.24, 0.09 g, 4%), which according to GC-MS and NMR was a 3:7 mixture of 6-chloro-7-methyl-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione (**17**, *m/z* 277) and 6-bromo-7-methyl-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione (**18**, *m/z* 321). The spectroscopic data were identical to later results (*vide infra*). Work-up of the quinoline residue did not yield any unreacted **2n** or ring-opening products.

2-Bromomethyl-1,1-dichloro-2-methylcyclopropane (**3n**, 0.88 g, 4.04 mmol) was heated in quinoline at 240 °C for 40 minutes and a colourless liquid was collected in the liquid nitrogen cooled receiver flask after 5 minutes. Addition of PTAD until the the red colour persisted yielded a mixture of at least two compounds. Flash chromatography (hexane:ethyl acetate [7:3]) yielded 1,1-dichloro-2-chloromethyl-2-methylcyclopropane (**3p**, R_f=0.72, 0.05 g, 7%), as a colourless liquid (the spectroscopic data coincided with the literature).[40]

δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.39-1.53 (2 H, m, CH_2), 1.51 (3 H, s, CH_3), 3.65 (1 H, d, *J* 11.5 Hz, CHCl) and 3.78 (1 H, d, *J* 11.5 Hz, CHCl); *m/z* (EI) 172 (M^+, 1%), 157 (M^+-CH_3, 1), 137 (M^+-Cl, 3), 123 (M^+-CH_2Cl, 100) and 87 (26).

In addition **17** (R_f=0.36, 0.05 g, 5%) was isolated, as a white solid, mp. 201-202 °C (decomposed).

ν_{max}(KBr)/cm^{-1} 3061w, 2965w, 2914w, 2852w, 1771m, 1717s, 1598w, 1503m, 1427br, 1345w, 1306w, 1261m, 1135m, 1082w, 940w, 913w, 798w, 750w, 690w and 642w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.92-1.94 (3 H, m, CH_3), 4.11-4.13 (2 H, m, CH_2), 4.21-4.26 (2 H, m, CH_2) and 7.33-7.55 (5 H, m); δ_C(50 MHz; $CDCl_3$; Me_4Si) 16.6 (CH_3), 47.5 (CH_2), 47.8 (CH_2), 119.3 (C), 124.6 (C), 125.2 (2 x CH), 128.1 (CH), 129.0 (2 x CH), 130.8 (C), 151.8 (CO) and 152.0 (CO); *m/z* (EI) 277.0617 (M^+, 61%, $C_{13}H_{12}N_3O_2Cl^+$ requires 277.0618), 242 (M^+-Cl, 11), 123 (100), 119 (66), 102 (21), 91 (26) and 67 (36).

Work-up of the quinoline residue did not yield any unreacted **3n**, **3p** or ring-opening products.

cis/trans-*1-Bromo-2-chloromethylcyclopropane* (**12m**, 0.56 g, 3.28 mmol, 1:1.4 ratio) was refluxed in quinoline at 237 °C for 30 minutes, followed by distillation at 20 °C/225 mmHg with the dry-ice cooled receiver flask filled with PTAD (4 mL, 0.251 M, 1.00 mmol). Traces of 2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione (**19**, *m/z* 229) could be seen in GC and GC-MS chromatograms. The chromatograms were compared with those of an authentic sample (see Chapter 5.7.3). However, isolation by flash chromatography (hexane:ethyl acetate [7:3]) failed, and work-up of the quinoline residue did not yield any unreacted **12m** or ring-opening products.

cis/trans-*1-Bromo-2-chloromethyl-2-methylcyclopropane* (**12n**, 0.55 g, 3.01 mmol, 1:2 ratio) was heated in quinoline at 240 °C for 30 minutes and a light yellow liquid was collected in the liquid nitrogen cooled receiver flask after 10 minutes. Addition of PTAD until the red colour persisted yielded a mixture of at least five compounds, according to GC and GC-MS, of which two where *cis*/*trans*-**12n** (1:1.5 ratio). Flash chromatography (hexane:ethyl acetate

[7:3]) yielded 6-methyl-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione (**20**, R_f=0.18, 0.029 g, 4%), as a yellow solid, mp. 99-100 °C (lit.[41] 110-112 °C). The spectral data were identical with those of an authentic sample (see Chapter 5.7.3).

In addition **18** (R_f=0.30, 0.008 g, 1%) was isolated as white solid, mp. 198 °C (decomposed). ν_{max}(KBr)/cm^{-1} 2955w, 2921m, 2851w, 1775m, 1710s, 1600w, 1503m, 1430br, 1338w, 1306w, 1261m, 1134m, 1089w, 1076w, 1024w, 907w, 792w, 745m, 715w and 687w; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.96-1.97 (3 H, m, CH_3), 4.13-4.14 (2 H, m, CH_2), 4.33-4.36 (2 H, m, CH_2) and 7.46-7.53 (5 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 19.6 (CH_3), 48.1 (CH_2), 49.8 (CH_2), 109.8 (C), 125.3 (2 x CH), 127.4 (C), 128.2 (CH), 129.1 (2 x CH), 130.8 (C), 151.7 (CO) and 152.1 (CO); *m/z* (EI) 321.0117 (M^+, 30%, $C_{13}H_{12}N_3O_2Br^+$ requires 321.0113), 242 (M^+-Br, 3), 207 (11), 123 (100), 119 (51), 91 (24) and 67 (53).

Work-up of the quinoline residue did not yield any unreacted **12n**, **18**, **20** or ring-opening products.

5.7.2 *In a vertical electrical furnace (flash-vacuum pyrolysis)*

General procedure. The cyclopropanes **2** were passed through a Pyrex^{TM} tube (14 cm long, 2.8 cm inner diameter) packed with glass wool or fine glass turnings and sodium carbonate, and maintained at between 450-500 °C/0.8-1.2 mmHg with a Winkler heating tape. The pyrolysates were collected in a dry-ice cooled flask, connected to the vacuum inlet through a liquid nitrogen cooled U-tube.

1,1-Dibromo-2-chloromethyl-2-methylcyclopropane (**2n**, 2.04 g, 7.78 mmol) was pyrolysed and the pyrolysate was immediately treated with a solution of PTAD until the red colour persisted. Flash chromatography of the crude product (hexane:ethyl acetate [7:3]) yielded a yellow, liquid mixture (1.39 g, R_f=0.80) of three compounds and another white, solid mixture of two compounds (R_f=0.34). The first spot contained, according to GC-MS, three isomers with *m/z* 180; most likely 2-bromo-3-(chloromethyl)buta-1,3-diene (**21**), (*Z*)-3-bromo-1-chloro-2-methylbuta-1,3-diene ((*Z*)-**22**) and (*E*)-3-bromo-1-chloro-2-methylbuta-1,3-diene ((*E*)-**22**), generated from **2n** by HBr elimination. However, efforts to separate the isomers failed. In the ^{1}H NMR spectrum of this mixture there were many peaks in the region between 5.50-6.10 ppm, which can be assigned to vinylic protons. The second spot was, according to GC-MS and ^{1}H NMR, a 1:9 mixture (0.28 g, 11%) of **17** and **18** (*vide supra*).

1,1-Dibromo-2-chloromethyl-2-methylcyclopropane (**2n**, 2.10 g, 8.00 mmol) was pyrolysed and the pyrolysate was immediately treated with maleic anhydride (0.76 g, 7.71 mmol). After magnetic stirring at room temperature over night, GC-MS analyses showed that, together with the three *m/z* 180 isomers, three adducts with *m/z* 200, 278 and 244 in a 1:2:6 ratio were formed. The compounds with *m/z* 200 and 246/244 is most likely 5-chloro-3a,4,7,7a-tetrahydro-6-methylisobenzofuran-1,3-dione (**23**) and 5-bromo-3a,4,7,7a-tetrahydro-6-methylisobenzofuran-1,3-dione (**24**), while the compound with *m/z* 278 could either be 5-bromo-6-chloromethyl-3a,4,7,7a-tetrahydro-isobenzofuran-1,3-dione (**25**) or 6-bromo-4-chloro-3a,4,7,7a-tetrahydro-5-methylisobenzofuran-1,3-dione (**26**), but efforts to separate them by flash chromatography (chloroform) failed.

5.7.3 *Synthesis of authentic samples*

*6-Chloro-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione* (**15**) was prepared from a partly polymerised sample of 2-chlorobuta-1,3-diene by addition of PTAD in CH_2Cl_2 until the red colour persisted. Evaporation and flash chromatography (hexane:ethyl acetate [7:3]) yielded **15** (R_f=0.24, 0.14 g) as a white solid, mp. 163-165 °C (lit.[42] 157-159 °C).
ν_{max}(KBr)/cm^{-1} 3080 (w), 2970 (w), 2864 (w), 1784 (m), 1706 (s), 1596 (w), 1494 (m), 1424 (m), 1341 (w), 1247 (w), 1131 (m), 1100 (w), 979 (br), 807 (w), 763 (m), 724 (w) and 685 (w); δ_H(400 MHz; $CDCl_3$; Me_4Si) 4.18-4.20 (2 H, m), 4.23-4.25 (2 H, m), 6.05-6.07 (1 H, m, =CH), 7.36-7.40 (1 H, m) and 7.45-7.52 (4 H, m); δ_C(100 MHz; $CDCl_3$; Me_4Si) 43.8 (CH_2), 47.8 (CH_2), 118.4 (CH), 125.2 (2 x CH), 125.3 (C), 128.1 (CH), 129.0 (2 x CH), 130.7 (C), 151.7 (CO) and 152.2 (CO); *m/z* (EI) 263.0467 (M^+, 66%, $C_{12}H_{10}ClN_3O_2^+$ requires 263.0462), 228 (M^+-Cl, 8), 119 (100), 109 (35), 91 (30), 77 (6) and 64 (17).

*2-Phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione* (**19**) was prepared by passing 1,3-butadiene through a solution of PTAD in dichloromethane, with magnetic stirring, until the red colour disappeared. Evaporation of the solvent yielded **19** (0.39 g) as an orange solid, mp. 144-145 °C (lit.[43] 158-159 °C).
ν_{max}(KBr)/cm^{-1} 2857w, 1766m, 1717s, 1596w, 1498m, 1426s, 1289m, 1257m, 1212w, 1134m, 964w, 764m and 710w; δ_H(200 MHz; $CDCl_3$; Me_4Si) 4.15 (4 H, br s, 2 x CH_2), 5.91 (2 H, s, 2 x =CH) and 7.34-7.55 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 43.1 (CH_2), 120.5 (CH), 125.2 (CH), 127.8 (CH), 128.8 (CH), 130.9 (C), 152.1 (CO); *m/z* (EI) 229,0846 (M^+,

100%, $C_{12}H_{11}N_3O_2^+$ requires 229,0851), 119 (95), 110 (13), 91 (34), 82 (49), 77 (8), 64 (23) and 54 (86).

*6-Methyl-2-phenyl-2*H*-[1,2,4]triazolo[1,2-*a*]pyridazine-1,3(5*H*,8*H*)-dione* (**20**) was synthesised from isoprene (0.07 g, 1.00 mmol) by addition of PTAD in CH_2Cl_2 until the red colour persisted. Evaporation of the solvent gave **20** (0.21 g, 86%) as an orange solid, mp. 98 °C (lit.[41] 110-112 °C).

ν_{max}(KBr)/cm^{-1} 2971w, 2916w, 2864w, 1774s, 1703br, 1596m, 1500s, 1418br, 1297m, 1250m, 1135m, 1055w, 987w, 948w, 902w, 850w, 765s, 732m and 688m; δ_H(200 MHz; $CDCl_3$; Me_4Si) 1.86-1.87 (3 H, m), 4.04-4.05 (2 H, m), 4.10-4.16 (2 H, m), 5.61-5.66 (1 H, m, =CH), 7.32-7.56 (5 H, m, Ph); δ_C(50 MHz; $CDCl_3$; Me_4Si) 20.1 (CH_3), 43.0 (CH_2), 46.4 (CH_2), 114.9 (CH), 125.3 (2 x CH), 128.0 (CH), 129.0 (2 x CH), 131.1 (C), 152.0 (CO) and 152.3 (CO); *m/z* (EI) 243.1005 (M^+, 100%, $C_{13}H_{13}N_3O_2^+$ requires 243.1008), 119 (63), 96 (25), 91 (21), 82 (7), 77 (7) and 68 (49).

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