Reactions and Reactivity of Allyl and Related Carbamates

by

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of the requirements for the degree of

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DECLARATION

I hereby certify that this research is a result of my own investigation which has not already been accepted in substance for any degree and is not being submitted in candidature for any other degree.

Signed: .....

P. H. Mason

I hereby certify that this statement is correct.

Signed: .....

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August 1997

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ABBREVIATIONS

acac	acetylacetonate
aq	aqueous
Ar	aryl, aromatic
b	broad
9-BBN	9-borabicyclo[3,3,1]nonane
b.p.	boiling point
bs	broad signal
Bu	butyl
BuLi	butyllithium
c	complex, concentrated
CAL	*Candida antarctica* lipase
cat.	catalyst, catalytic
d	doublet
D	deuterium
DABCO	1,4-diazabicyclo[2,2,2]octane
d.e.	diastereomeric excess
DIBAL	diisobutylaluminium hydride
DMG	directing metalation group
DNA	deoxyribonucleic acid
D*o*M	directed-*ortho*-metalation
E	electrophile
e.e.	enantiomeric excess
eq.	equivalents
Et	ethyl
ether	diethyl ether
g	gram, gaseous
GC/MS	gas chromatography - mass spectrometry

HMPTA	hexamethylphosphoric triamide
hr	hour
Hz	Hertz
i	iso
LDA	lithium diisopropylamide
m	meta, multiplet
M	metal, molar
$M^{+\cdot}$	molecular ion
mCPBA	*meta*-chloroperbenzoic acid
Me	methyl
min.	minute
ml	millilitre
mol.	mole
MOM	methoxymethyl
m.p.	melting point
MsOH	methanesulfonic acid
n	normal
naph	naphthyl
NMR	nuclear magnetic resonance
OAc	acetate
OCb	carbamate group
p	para, pentet
Ph	phenyl
ppm	parts per million
Pr	propyl
q	quartet
rt	room temperature
s	secondary, singlet
t	tertiary, triplet
T	temperature

TBDMS	*t*butyldimethylsilyl
TBDMSCl	*t*butyldimethylsilyl chloride
THF	tetrahydrofuran
TMEDA	N,N,N',N'-tetramethylethylenediamine
TMS	trimethylsilyl, tetramethylsilane
TMSCl	trimethylsilyl chloride
X	halide

SUMMARY

The research in this thesis is concerned with the reactions and reactivity of various allyl carbamates. It was found that cinnamyl carbamates (i) are readily silylated with TBDMSCl, and can then react further with a second electrophile to give 1,3-disubstituted cinnamyl carbamates (ii). The mono-substitution with alkyl halides and silylation of cinnamyl carbamates and ethers was also studied, giving predominantly γ-substitution. Overall, carbamates were found to give better regioselectivity. Simple allyl carbamates were found to give poor results in disubstitution reactions.

The dicarbamate (iii) was found to spontaneously eliminate one carbamate group on treatment with butyllithium to give the diene (iv), which can undergo further substitution in the 1-position to give 1,1-disubstituted 1,3-butadienes (v). This substitution is a result of deprotonation by the liberated diethyl amide from the fugitive carbamate group. It was found, however, that better results are obtained by isolating the unsubstituted diene, followed by reaction with a second electrophile. An improved preparation of mikanecic acid derivatives (vi) from α-hydroxyalkyl acrylates and carbamoyl chlorides *via* a DABCO mediated elimination-cycloaddition was also developed.

Treatment of cinnamyl carbamates with hydrogen halides, acetic acid or alcohols under acidic conditions results in the substitution of the carbamate group to give 1-substituted 3-phenylprop-2-enes (vii) by an S_N2 mechanism.

Finally, two related routes to oudemansin A (viii), a potent antifungal compound of considerable economic value, from cinnamaldehyde and *N,N*-diethyl crotyl carbamate were developed. The initial and critical step is the reaction between crotyl carbamate and cinnamaldehyde, which establishes the basic oudemansin skeleton (ix). Using either (*E*) or (*Z*) crotyl carbamate gives the *anti* and *syn* product respectively. Further elaboration

of (ix), involving methylation of the hydroxy group, reductive cleavage of the carbamate to the alcohol and Jones' oxidation of the alcohol to the carboxylic acid gives an intermediate which is easily converted to oudemansin A by published methods.

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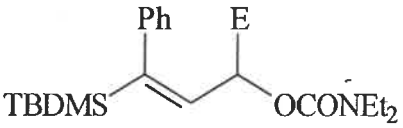

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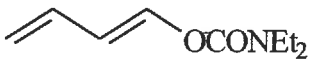

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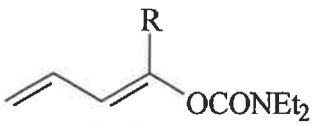

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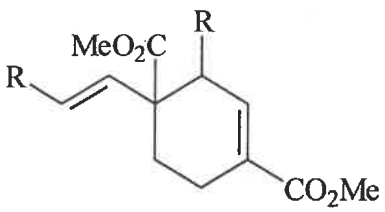

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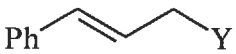

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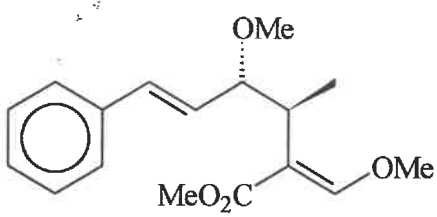

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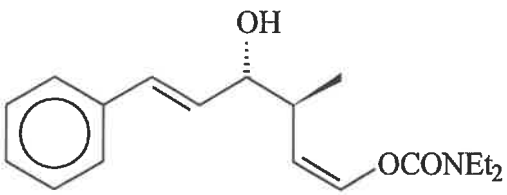


(ix)

PUBLICATIONS RESULTING FROM THIS THESIS

1) Paul H. Mason and Neville D. Emslie. Synthesis and Reactivity of 1-*N,N*-Diethylcarbamoyl-1,3-Butadiene. *Tetrahedron*. **1995**, *51*, 2673.

2) Paul H. Mason, Deborah K. Yoell, L. Frances van Staden and Neville D. Emslie. Bis-Silylation of *N,N*-Diethylbenzyl and Cinnamyl Carbamates. *Synthetic Communications*. **1995**, *25*, 3347.

3) Paul H. Mason and Neville D. Emslie. Preparation of Substituted Vinylsilanes from Cinnamyl Carbamates. *Synthetic Communications*. **1996**, *26*, 1473.

4) Danie Janse van Rensburg, Paul H. Mason and Neville D. Emslie. A Simple One-Pot Preparation of Mikanecic Acid Derivatives *via* Allylic Carbamates. *Synthetic Communications*. **1996**, *26*, 4403.

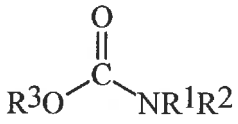
CHAPTER 1: INTRODUCTION

The subject of this thesis is the reactions and reactivity of allylic carbamates, so this review will cover those areas of the literature that relate to this topic. For the most part, the work presented involves the reaction of allylic anions with electrophiles, so most of the discussion involving the reactions of carbamates will be restricted to this field. Carbamates do, however, form an interesting and diverse group of compounds with many uses and reactions. For this reason any discussion of carbamates would be incomplete without a general overview of carbamates. This is, without a doubt, a very large area which covers fields as diverse as natural product chemistry, industrial, pharmaceutical, agricultural and synthetic organic chemistry. The first part of this review will be concerned with these varied and interesting applications of carbamates, although it will, unfortunately, be somewhat brief. The next section will cover the all important subject of the preparation and cleavage of carbamates, while the last section will be concerned with the reactions of carbamates. Again, this is a very broad topic, so the bulk of the discussion will only consider the reactions of carbamate anions. Since carbamate anions form the subject of this thesis, a discussion of other heteroatom stabilised anions is also included, for the sake of completeness and comparison.

1.1) Carbamates: A Brief Overview.

Carbamates, which are also known as urethanes or urethans, have wide and varied application. When considering carbamates in general it is convenient to think of them in two ways; one being as end products which contain one or more carbamate groups, and the other being as synthetic intermediates containing one or more carbamate groups. The former group consists of the industrial chemicals, including those used in the pharmaceutical and agricultural industries. The latter group includes protecting groups and other reactions involving carbamate containing compounds, but at this stage only their use as protecting groups will be considered.

Carbamates are derivatives of the unstable carbamic acid, and in simple terms contain a carbonyl group flanked on one side by an oxygen atom and on the other by a nitrogen atom (**1**).

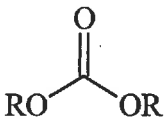


(1)

R^1, R^2 = H, aryl, alkyl, *etc.*

R^3 = Aryl, alkyl, *etc.*

Together with carbonates (**2**) and ureas (**3**), carbamates are part of a versatile and interesting group of compounds with unique reactivity, as will become apparent in this review.



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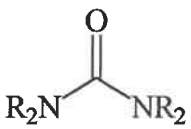

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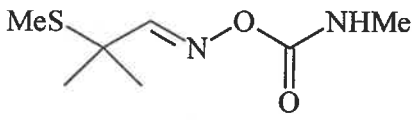
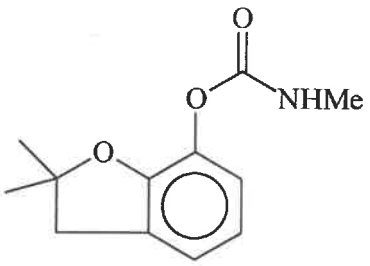
1.1.1) Industrial Application of Carbamates.

It is in the area of industrial, agricultural and pharmaceutical chemistry that carbamates are best known. Perhaps the largest use of carbamates by volume is as polyurethane polymers, which are usually prepared by the tertiary amine catalysed reaction of diols with di-isocyanates.[1] Carbamates also find use as plasticisers for natural and synthetic rubbers[2]. Ethyl and propyl carbamates, in particular, are used as plasticisers for melamine-isocyanate resins and laminates[3]. Carbamates are also used in crease-resistant cottons[4] and hair setting agents[5].

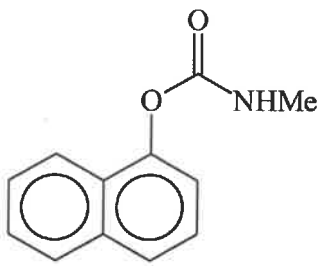
Typically, carbamates are toxic, and it is for this reason that they have found extensive use as insecticides, herbicides and fungicides[6, 7, 8]. Their major use in this area is as insecticides, where their mode of action is believed to be the inhibition of the enzyme acetylcholinesterase. This results in a build-up of acetylcholine in the neurons of the affected organism, resulting in the death of the organism. In a more general sense, carbamates are alkylating agents and thus have an effect on biological molecules that are sensitive to alkylation or acylation, such as DNA. It has been found that *N,N*-dimethyl- and, particularly, *N*-methyl carbamates are particularly effective, due to their ease of hydrolysis. Listed below are some of the more common carbamates that are used as insecticides (Scheme 1).



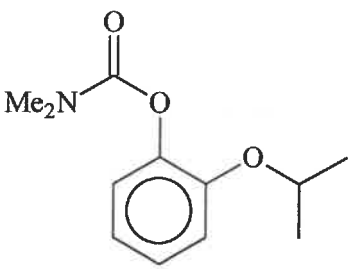
Aldicarb



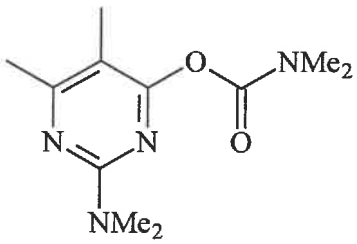
Carbofuran



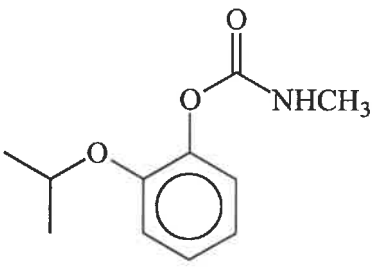
Carbaryl



Propoxur



Pirimicarb

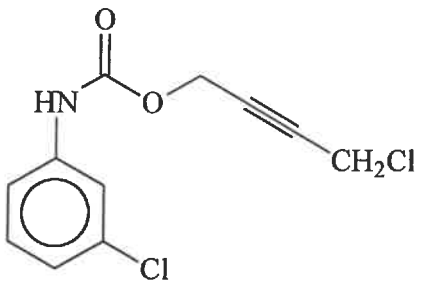


Baygon

Scheme 1

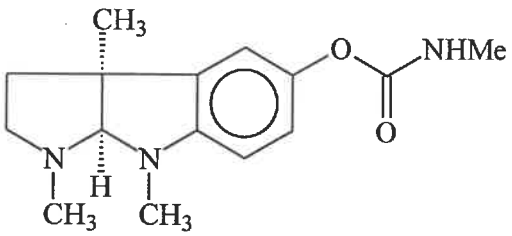
Carbamate pesticides are the compounds of choice since they are rapidly degraded in the environment[9] and do not, apparently, pose any of the ecological problems that many of the organophosphate and organohalide pesticides present. In particular, they are not accumulated in the tissue of exposed organisms and are thus not passed up the food chain. They are, however, highly toxic to mammals, but this is outweighed by their advantages, for example, the control of soil nematodes by aldicarb.

Barban is a herbicide commonly used in the control of wild-oats in cereal. It is thought that the mode of action involves inhibition of cell division.



Barban

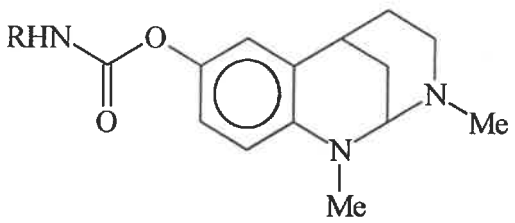
Pharmaceutical uses of carbamates are increasing due to the discovery that physostigmine (**4**) and its analogue HP290, which has an altered carbamate group, show promise as a treatment for Alzheimer's disease and are currently undergoing clinical trials.[10, 11, 12] It is also used for the treatment of glaucoma and for the relief of the symptoms of the muscular disease *myasthenia gravis*.[6]



(4)

Alzheimer's disease sufferers have too low a concentration of acetylcholine in the nerve synapses, so physostigmine is used to regulate the conversion of acetylcholine to choline by the inhibition of acetylcholinesterase.[8]

Other analogues (**5a - c**) have also been prepared, which also show activity.[13]

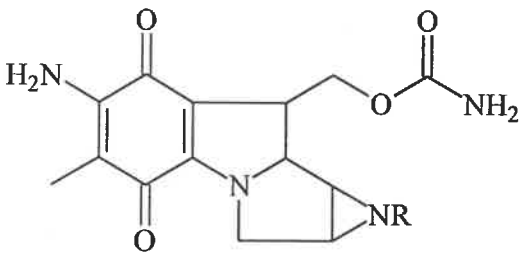


(5a) R = Me

(5b) R = cyclohexyl

(5c) R = 1-methylbenzyl

Mitomycin C (**6**) is a toxic antitumour compound that was isolated from *Streptomyces caespitosus*[14]. Mitomycin C and the structurally related porfiromycin (**7**) are used for the treatment of carcinomas of the breast, lung, colon and stomach. Their mode of action is due to their alkylating ability, whereby they cause interstrand cross-linking in DNA. Both (**6**) and (**7**) contain three carcinostatic groups, namely a carbamate, an aziridine and a quinone.



(**6**) R = H

(**7**) R = CH_3

Other medicinal uses of carbamates are:

- Antiseptics.[15]
- Anti-leukaemia treatment.[15]
- Local anaesthetics.[16]
- Anti-convulsants.[17]
- Muscle relaxants.[18]

1.1.2) Carbamates as Protecting Groups.

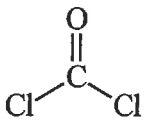
Carbamates have found numerous applications in organic synthesis, but their best known use is as a protecting group. Due to the general lack of absolute chemoselectivity of organic reactions, it is frequently necessary to protect various functional groups from reaction while carrying out a transformation at some other position in the molecule. Often, one needs to protect alcohols, thiols and amines, since they are potential nucleophiles and alkylation and acylation sites. It is in this capacity that carbamates have found important application, since they can be prepared from both alcohols and amines. Carbamates are relatively easily formed and exhibit varying stability to hydrolytic conditions, which makes them ideal candidates for protecting groups. The formation and cleavage of carbamates will be discussed later in the relevant section.

Carbamates are particularly useful as protecting groups for amines in peptide syntheses, since they minimize racemisation of the substrate. There are numerous examples of carbamate protecting groups, which are well documented by Greene and Wuts[19].

1.2) Preparation of Carbamates.

There are numerous published methods for the preparation of carbamates, but only a few are of widespread use. The main reasons for this are convenience and the commercial availability of suitable precursors. Only the more common methods will be considered since the research presented in this thesis only uses these common methods, so a detailed survey of the more exotic preparations is unnecessary.

Most of the more common preparations involve the use of phosgene (**8**), which is a toxic gas. Due to the difficulties encountered when using phosgene, two alternative phosgene equivalents have been introduced. These are diphosgene (trichloromethyl carbonate) (**9**), which is a liquid, and triphosgene [bis(trichloromethyl) carbonate] (**10**) which is a solid.[20, 21]



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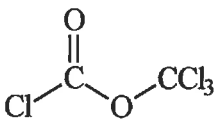

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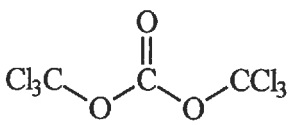
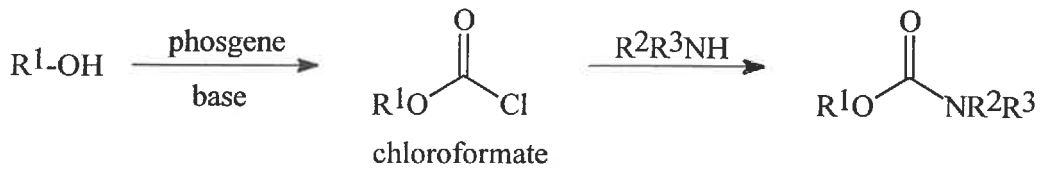


(10)

1.2.1) Preparation from Chloroformates and Amines.

This is a general, high yielding reaction which is commonly used due to the commercial availability of a wide range of chloroformates. The chloroformates themselves are prepared from phosgene, diphosgene or triphosgene and the relevant alcohol in the presence of a base. Chloroformates react readily with ammonia, primary and secondary amines (usually without the need for a base) to yield *N*-substituted, *N,N*-disubstituted and unsubstituted carbamates[22, 23] (Scheme 2).



chloroformate

R^1, R^2 = alkyl or aryl.

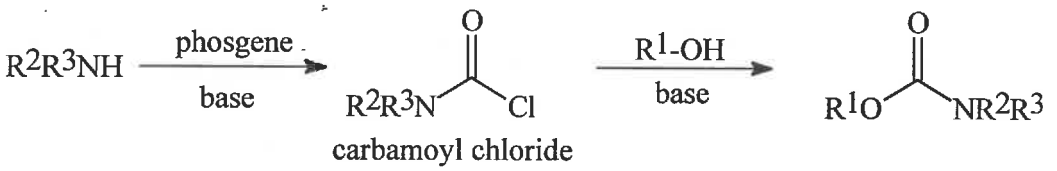
R^3 = alkyl, aryl or H.

Scheme 2

1.2.2) Preparation from Carbamoyl Chlorides and Alcohols.

This is another widely used preparation of carbamates, but suffers from the fact that relatively few carbamoyl chlorides are commercially available, forcing one to prepare them from amines and phosgene, diphosgene or triphosgene[15].

Carbamoyl chlorides react readily with alcohols in the presence of a base, usually pyridine or sodium hydride, to yield carbamates in good yield (Scheme 3).

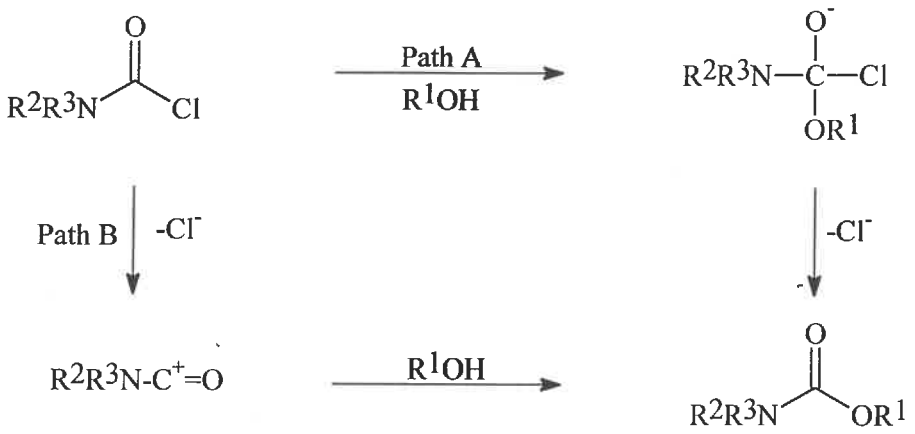


carbamoyl chloride

R^1, R^2, R^3 = alkyl, aryl.

Scheme 3

The reaction is believed to occur *via* one of two possible pathways, *i.e.* an addition-elimination (concerted displacement of the halide ion by the alcohol) reaction (Path A, Scheme 4) or unimolecular loss of chloride (Path B, Scheme 4).[24]



R^1, R^2, R^3 = alkyl, aryl.

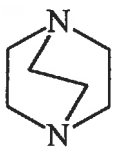
Scheme 4

1.2.3) Preparation from Isocyanates and Alcohols.

This is a rapid, high yielding reaction for the preparation of *N*-alkyl carbamates (Scheme 5). This method of preparation is used on an industrial scale in the preparation of polyurethanes. In most cases the reaction is accelerated by the presence of a tertiary amine[1], usually 1,4-diazabicyclo[2,2,2]octane (DABCO) (**11**).

$$R^1\text{-}N{=}C{=}O + R^2\text{-}OH \rightarrow R^1\text{-}NH\text{-}CO_2R^2$$

Scheme 5



(11)

A similar method involves the reaction of sodium cyanate with alcohols.[25]

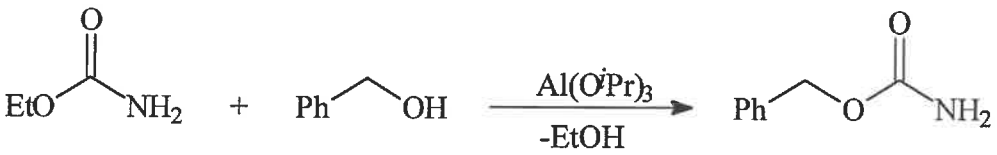
1.2.4) Preparation from Alcohols and Ureas.

This is the oldest method, dating back to 1840, when Wohler prepared ethyl carbamate from urea and ethanol[1]. This method is still used commercially for the preparation of methyl and ethyl carbamates (Scheme 6).

Scheme 6

1.2.5) Preparation from Alcohols and Carbamates (Transesterification).

Aluminium isopropoxide catalyses the transesterification between ethyl carbamate and benzyl alcohol to give benzyl carbamate (Scheme 7).

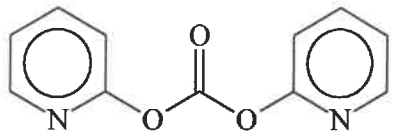


Scheme 7

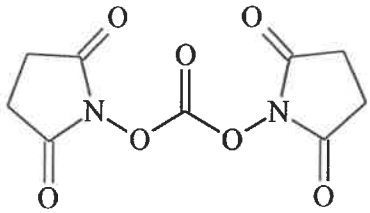
It has since been developed into a general method for the preparation of mono- and dicarbamates from alcohols and diols respectively.[1] *N*-Substituted or unsubstituted carbamates can be used in transesterification reactions.[26] Generally, most alcohols react, with the exception of phenols and tertiary alcohols.

1.2.6) Preparation from Amines and Carbonates.

Carbamates can also be prepared by the displacement of an alkoxy group on a carbonate by an amine. The most commonly used carbonates are di-(2-pyridyl) carbonate (**12**)[27] and *N,N*-di-succinimyl carbonate (**13**),[28] both of which are commercially available.

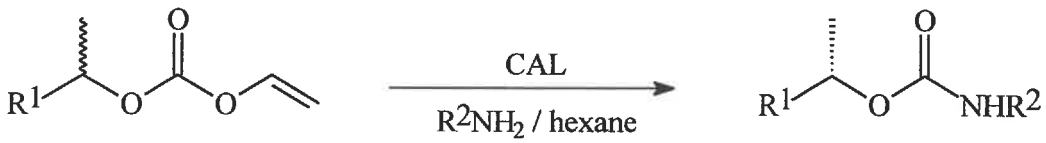


(12)



(13)

Candida antarctica lipase has been found to be effective in the preparation of chiral carbamates (and consequently chiral alcohols) by the resolution of racemic vinyl carbonates[10] (Scheme 8).



R1, R2 = alkyl, aryl

Scheme 8

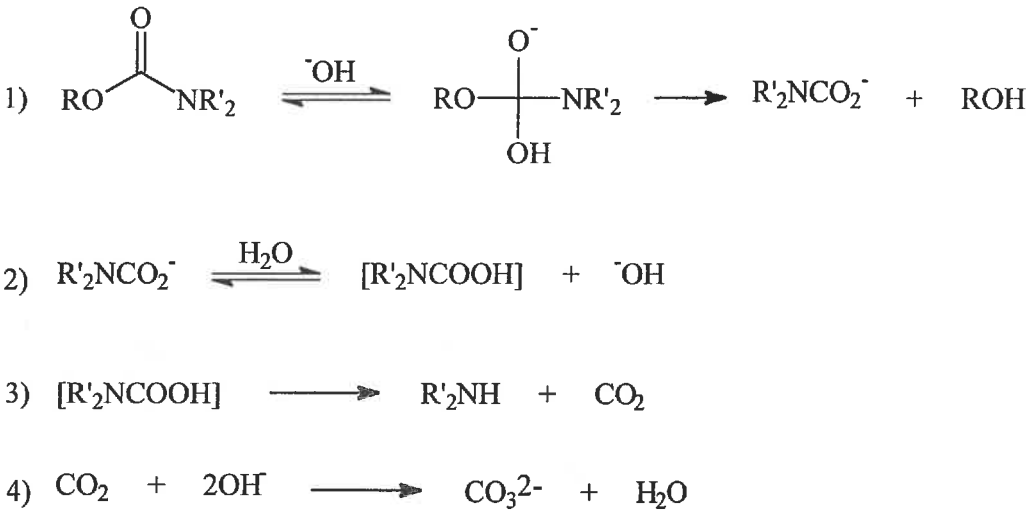
1.3) Reactions of Carbamates.

This section will discuss some of the more common reactions of carbamates, excluding the reactions of metalated carbamates. The reactions that fall into the latter catagory, which will be discussed in detail in the next section, include the reactions of metalated alkyl, alkynyl, allyl, aryl, benzyl and vinyl carbamates, as well as other

closely related systems. In this context, the reactions considered will include electrophilic substitutions, carbamate migrations and eliminations.

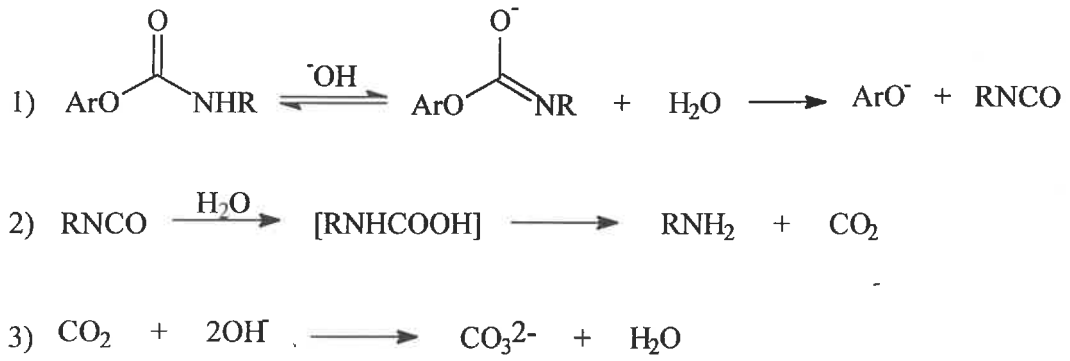
1.3.1) Hydrolysis of Carbamates.

The hydrolysis of carbamates is of fundamental importance if they are to be used successfully as synthetic intermediates. Unsubstituted and *N*-mono-substituted carbamates that are derived from aliphatic alcohols, as well as disubstituted carbamates, are hydrolysed in alkaline solution to give an amine, water and a carbonate[15] (Scheme 9).



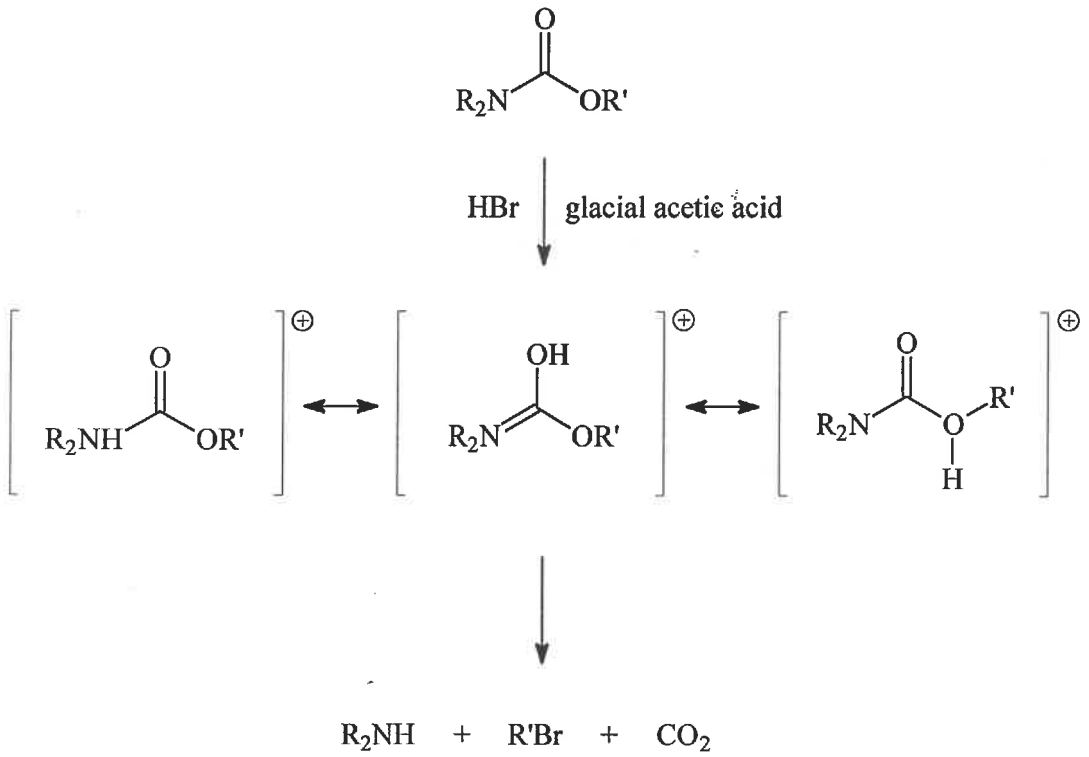
Scheme 9

Aryl carbamates are rapidly hydrolysed *via* an isocyanate intermediate (Scheme 10), except in the case of *N,N*-disubstituted aryl carbamates, which cannot form an isocyanate intermediate. In this case the normal mechanism (Scheme 9) operates.



Scheme 10

Carbamates are also hydrolysed under acidic conditions (hydrogen halides) yielding an alkyl halide, carbon dioxide and an amine. It is thought that the acid protonates the carbamate group, followed by attack on the alkoxy group by the halide ion[29] (Scheme 11).



Scheme 11

1.3.2) Thermal Decomposition of Carbamates.

Carbamates are susceptible to thermal decomposition, with unsubstituted carbamates being the least stable and *N,N*-disubstituted carbamates being the most stable. Unsubstituted carbamates decompose to cyanic acid derivatives, while *N*-substituted carbamates give mainly isocyanates. Generally speaking, *N,N*-disubstituted carbamates do not decompose cleanly. Metal salts have been found to enhance the rate of decomposition.[15]

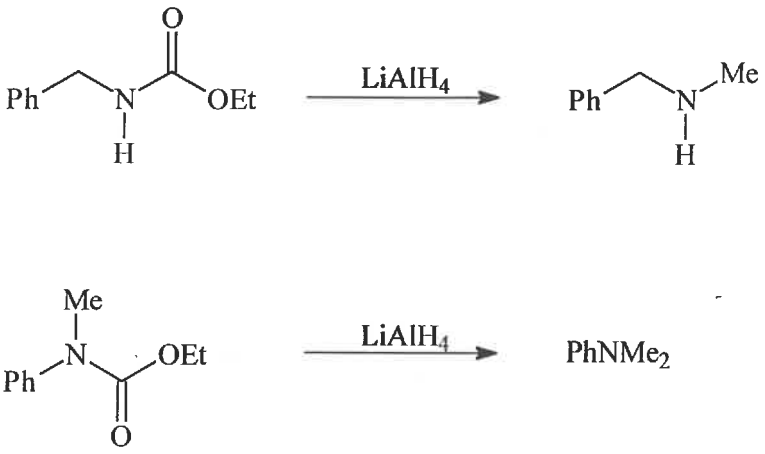
1.3.3) Reactions at the Carbonyl Group.

The carbonyl group of carbamates, like other carbonyl compounds is susceptible to nucleophilic attack. Carbon, nitrogen and oxygen and sulfur nucleophiles add to carbamates, giving various synthetically useful products.

Werner[30] found that heating ethyl carbamate to 150 °C in the presence of ammonia yielded urea in 33 % yield, together with ethanol (Scheme 12).

Scheme 12

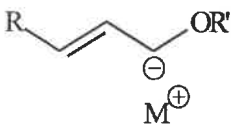
Carbamates are also readily reduced by lithium aluminium hydride to produce secondary and tertiary methyl amines in good yield[31, 32] (Scheme 13).



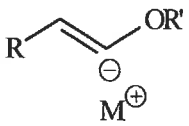
Scheme 13

1.4) Heteroatom Stabilised Carbanions.

The scope of the research presented in this thesis is the reactivity of α-oxo-allylic (**14**) and vinylic (**15**) anions, so this section will be concerned primarily with these and related systems, and not carbanions in general.

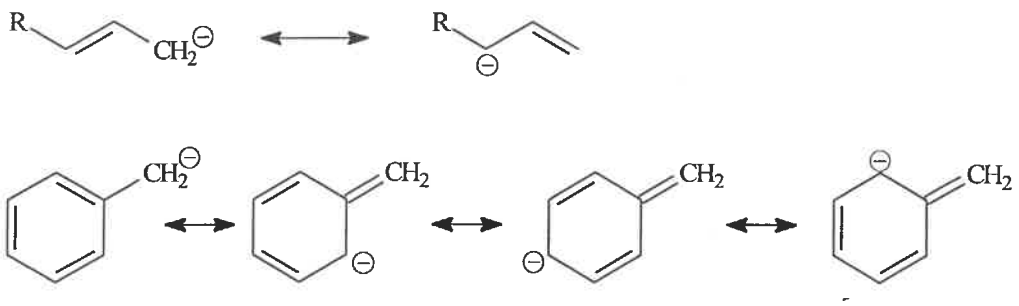


(**14**)



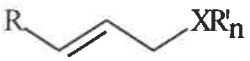
(**15**)

Simple anions are very unstable in solution, but when a double or triple bond is situated α to the carbanionic centre, the negative charge is stabilised by delocalisation. This is thought to be the primary stabilising effect accounting for the stability of allylic[33] and, to a lesser extent, benzylic carbanions[34] (Scheme 14).



Scheme 14

When the carbanionic carbon is in conjugation with a carbon-oxygen or carbon-nitrogen multiple bond even greater stability is afforded, but this is outside the scope of this review. Useful as these reactions may be, most molecules of interest contain heteroatoms (particularly N, O and S), so considerable research has gone into the study of α-substituted allylic compounds of type (**16**).



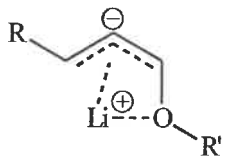
X = O, N or
n = 1 or 2

(16)

One of the earliest studies on such a system is the 1,2-Wittig rearrangement of allylic ethers[35] (Scheme 15).

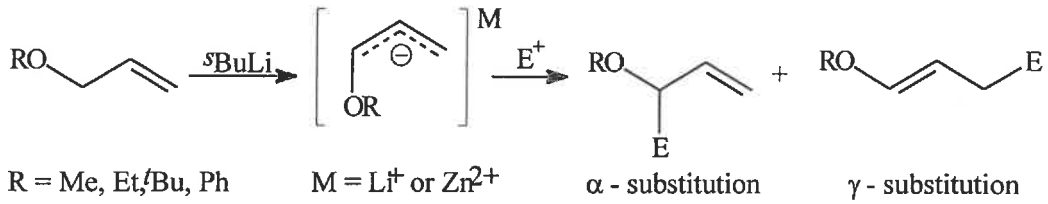
Scheme 15

This reaction occurs *via* the metalated anion (**17**), which is thought to be stabilised by coordination with the ether oxygen.[36]



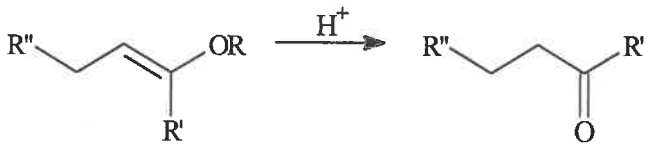
(17)

It was subsequently found, however, that these anions are quite stable at low temperatures (-78 °C) and the Wittig rearrangement does not occur to any appreciable extent. Due to this, the anions react with a variety of electrophiles to give a mixture of α- and γ-substituted products[37] (Scheme 16).



Scheme 16

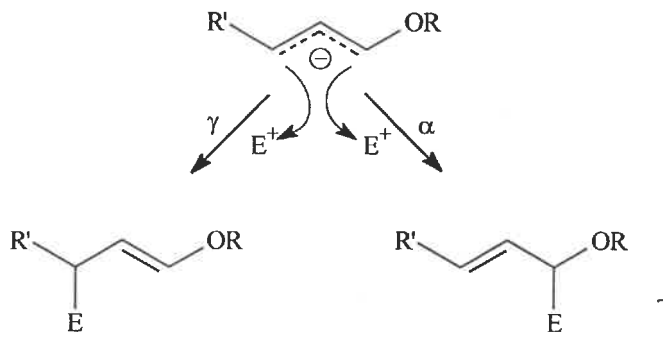
Allyl silyl ethers also undergo substitution in the same way. Cleavage of the resultant vinyl ethers, which result from γ-substitution, under acidic conditions gives aldehydes and ketones in good yield[38] (Scheme 17).



R', R" = H or alkyl
R = $SiMe_3$

Scheme 17

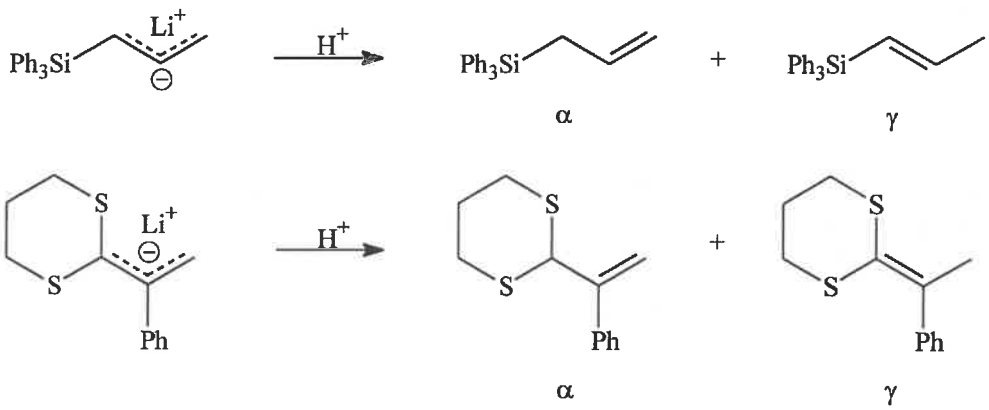
This mixture of α- and γ-substituted products is thought to be due to steric factors, since the anion is delocalised over three carbon atoms. Reaction can therefore occur at either the α- or the γ-position, with the ratio depending on the relative accessibility of the two sites and the steric bulk of the electrophile (Scheme 18).



Scheme 18

In most cases "R' > OR" favours α-substitution, and *vice-versa.*

A recent study involving the anions of allyl silanes and allyl thioacetals was carried out to determine the effect of the bulk of various proton sources (acids) on the product distribution[39] (Scheme 19).



Scheme 19

The results were varied, but generally the more bulky acids protonated the less sterically hindered position, while the less bulky acids were less selective. These, and other results, will be discussed in more detail at a later stage.

Since the pioneering work by Evans and Still, it has been recognised that heteroatom substituted allylic anions can serve as homo-enolate anion equivalents. For this

reason, much effort has been put into directing attack to the γ-position. A number of factors influencing the selectivity of heteroatom substituted allylic anions have been recognised.[40] These include:

- The size and the nature of the group(s) attached to the heteroatom.
- The metal counterion.
- The solvent.
- The presence of various additives, such as TMEDA, HMPA or cryptand [2.2.2].
- The reaction temperature.
- The reaction time.

Gompper and Wagner[41] have proposed that the selectivity in such kinetically controlled reactions can be explained by the concept of "allopolarisation", which permits a description of substituent effects in terms of their polarity. Factors affecting the regioselectivity and reactivity have also been reviewed by Schlosser.[42]

Other heteroatom substituted alkenes, such as those containing nitrogen, sulfur or silicon substituents react similarly, as reviewed by Werstiuk.[43]

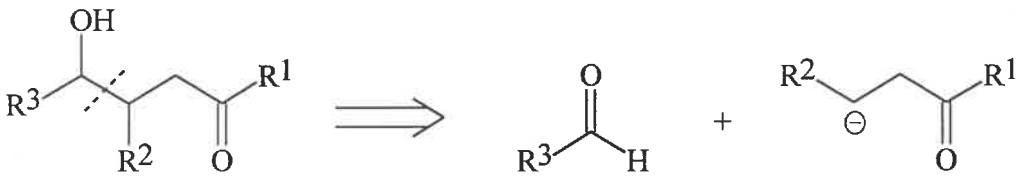
The previous section has been brief, since more detail will be provided in the following sections of this review. All discussion involving carbamates has been deferred to the following sections as well to avoid repetition.

1.5) Metalated Carbamates.

This section, which covers the background material that is directly applicable to the research presented in this thesis, is divided into a number of sections. The division is based simply on the structure of the starting carbamate, even though a common reactivity is described. There is, however, considerable overlap in the reactivity displayed by the various groups of carbamates.

1.5.1) Reactions of Allyl Carbamates.

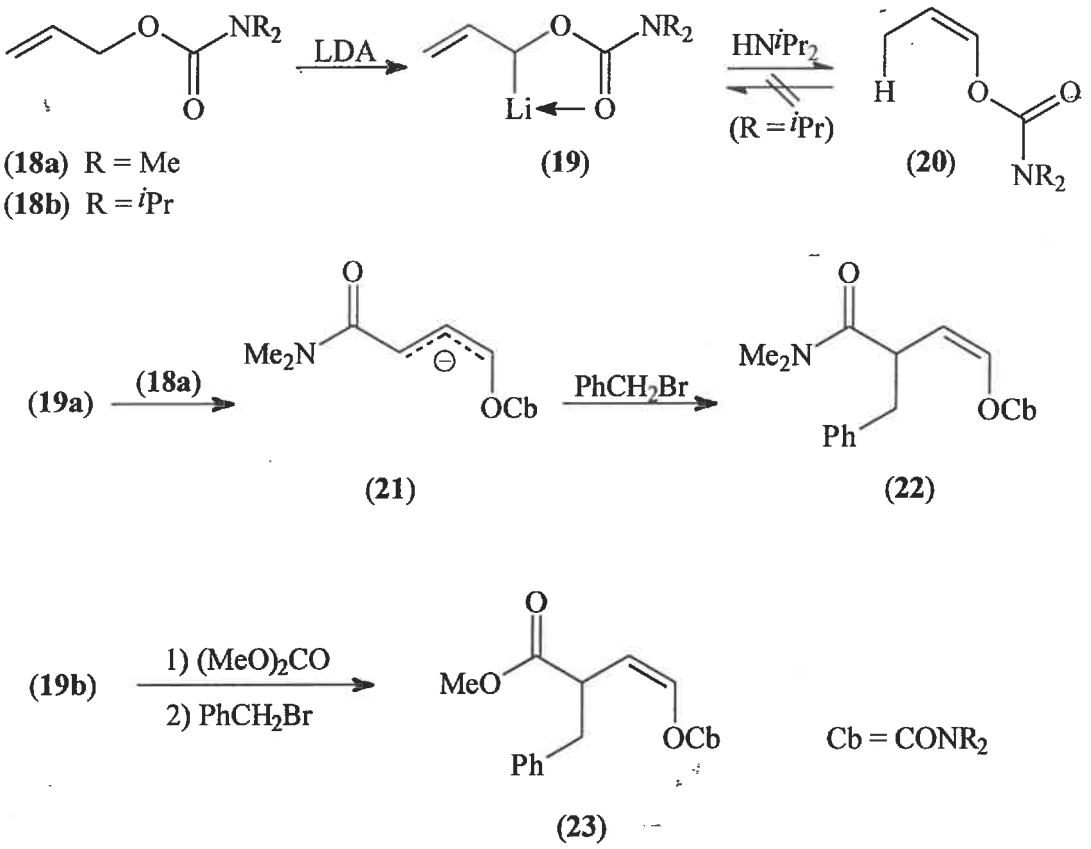
Metalated allyl carbamates have perhaps found their best application in "homo-aldol" reactions. The preparation of β-hydroxycarbonyl compounds by traditional aldol methodology is common-place, but the preparation of γ-hydroxycarbonyl compounds needs to follow "*umpolung*" methodology[44] (Scheme 20).



Scheme 20

Hoppe and co-workers, based on the work of Beak and others[45, 46, 47] on the importance of the "chelate effect" on directed lithiation, have carried out the bulk of the research on allylic carbamates. Hoffmann had also previously shown, using allylic boranes, that in non-polar solvents the regiochemistry of the addition to the carbonyl group of the electrophile is largely controlled by the position of the metal. It is the position of the metal which directs the incoming electrophile to the γ-position, with allylic inversion. In most cases, however, one also observes α-addition, as is observed in the reaction of allyl ether.[37, 38]

Hoppe's first reported reaction was 2-propenyl-*N,N*-dimethyl carbamate (**18**) with benzyl bromide using LDA as base[48] (Scheme 21). This early work is important because it demonstrates a number of features that are very relevant to the work presented in this thesis.



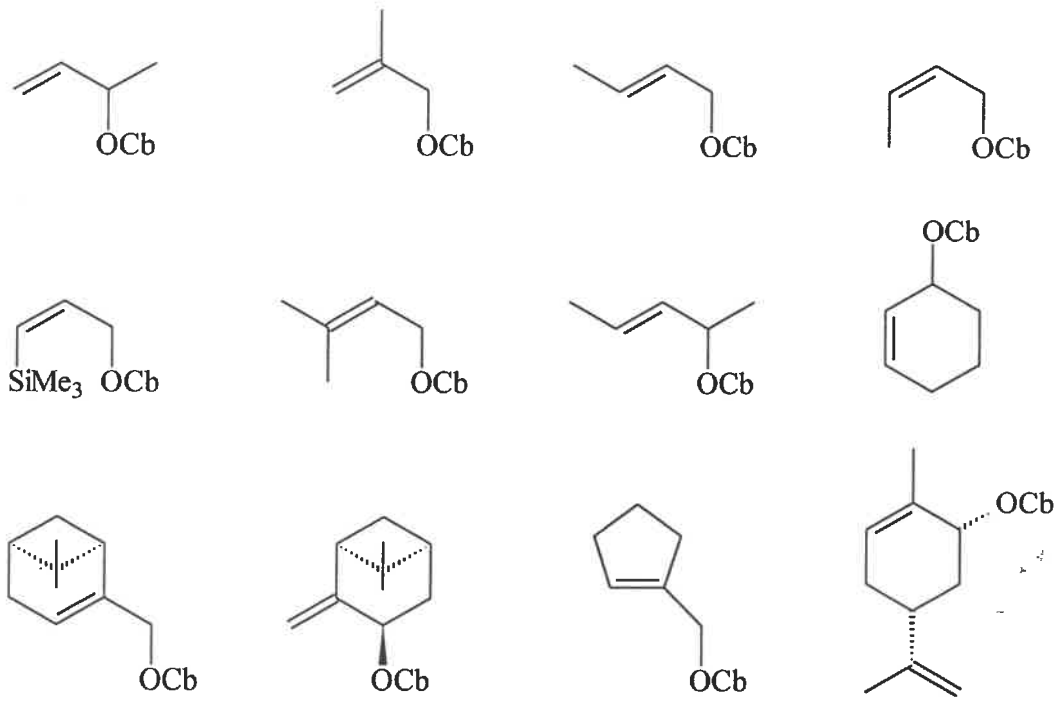
Scheme 21

The lithiated anion (**19a**) reacts rapidly with the starting material (**18a**) to give the amide anion (**21**), which then reacts with benzyl bromide to give (**22**). The problem of self-condensation is minimised by using bulkier alkyl groups on the carbamate. By using the *N,N*-diisopropyl carbamate (**18b**), Hoppe was able to eliminate this problem, while still maintaining an acceptable rate of reaction.

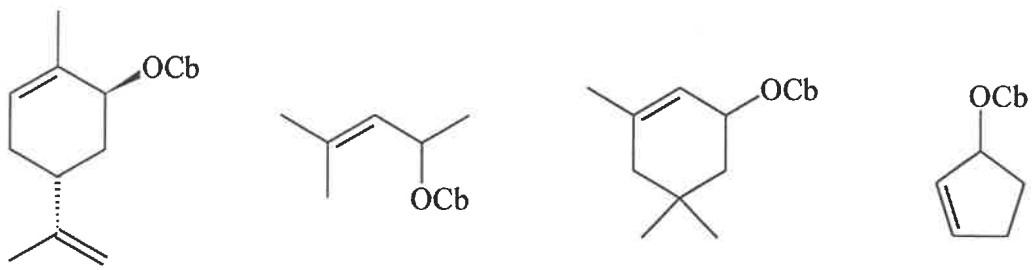
The ease of cleavage and the toxicity of *N,N*-dimethyl carbamates has resulted in a preference for other bulkier, less toxic carbamates for synthetic studies.

It has been found that n-butyllithium in the presence of 1.0 to 1.1 equivalents of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) in diethyl ether\hexane or n-butyllithium in tetrahydrofuran (THF) is the best reagent for deprotonating *N,N*-dialkyl allyl carbamates.[49] Deprotonation is rapid, typically being complete in less than 30 minutes.[50]

Various substitution patterns can be accommodated, as is illustrated by the range of allylic carbamates illustrated in Scheme 22.[44]



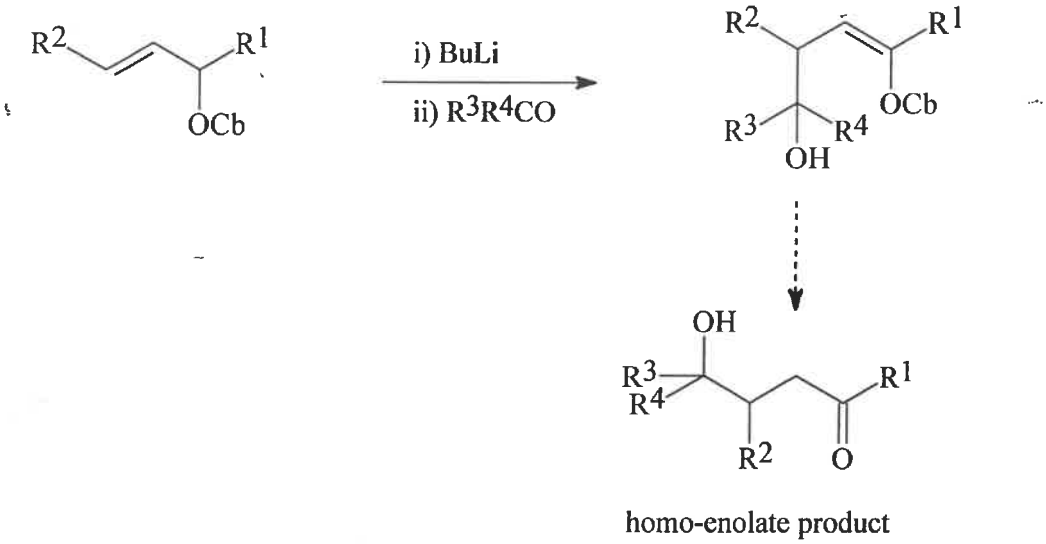
Deprotonated



No reaction

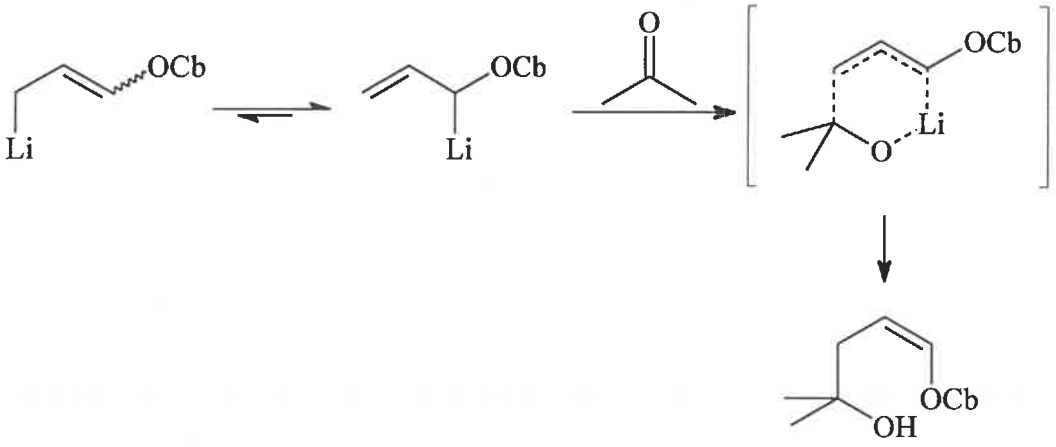
Scheme 22

Subsequent reaction of the lithiated carbamates with aldehydes or ketones provides a general route to 1-oxoallyl anions with varied structure,[49, 50] which are potential homo-enolate equivalents. γ-Substitution predominates, with varying amounts of α-substituted products (Scheme 23).



Scheme 23

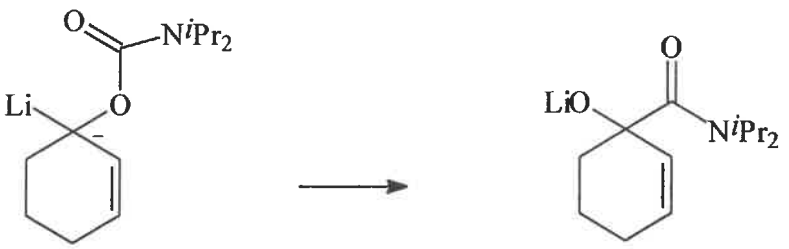
It was found that γ-selectivity increases with increased 3-substitution and decreasing 1-substitution, and also with decreasing reactivity of the carbonyl group in the electrophile. Ketones were also found to give better γ-selectivity than aldehydes. These factors are thought to be a result of a cyclic transition state (Scheme 24).



Scheme 24

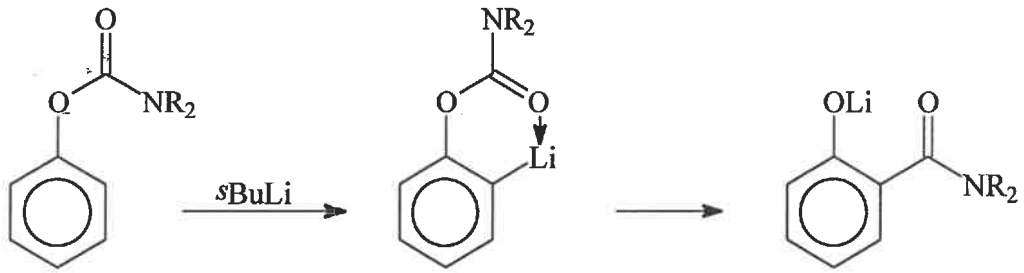
1.5.1.1) Structure and Properties of Lithiated Carbamates.

The abundance of experimental results has shown that lithiated carbamates are stable in non-polar solvents below -70 °C. In donating solvents such as THF, however, they slowly rearrange to give salts of α-hydroxyamides (Scheme 25). This undesirable migration is less pronounced with bulkier substituents on the carbamate.[51]



Scheme 25

This migration is analogous to the migration of the amide portion of aryl carbamates onto the *ortho* ring position[52] (Scheme 26).



Scheme 26

This rearrangement still occurs if the lithium counterion is exchanged for potassium. Reaction of metalated allyic carbamates with electrophiles give products with a (1-*Z*) double bond geometry, unless the starting carbamate has a 3-*cis*-substituent.

Addition of carbonyl compounds is highly γ-selective, while the addition of non-chelating groups such as alkyl halides is controlled predominantly by the alkyl groups present.[44]

The lithiated allyl carbamates are generally regarded as tight-ion pairs, since they exhibit properties that are characteristic of allyl anions[53] (delocalised anion) as well as covalent allyl metal compounds. This is represented diagramatically in Figure 1.[49]

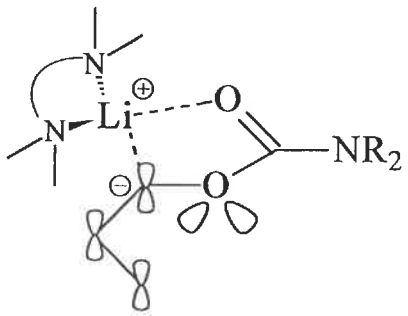


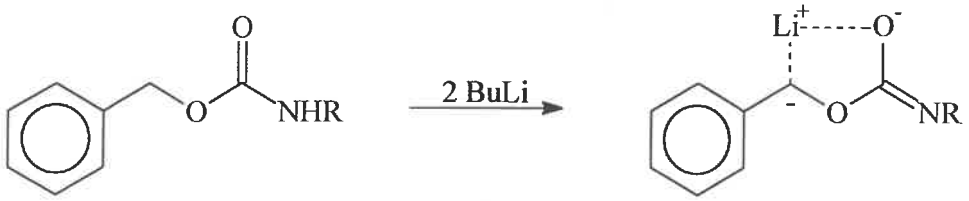
Figure 1

The additional two coordination sites on the lithium cation can be occupied by chelating amines, such as TMEDA, allowing for further stabilisation of the anion.[54]

It is thought that the high kinetic acidity of allyl carbamates is a direct result of the complexing ability of the carbamate group.

A major concern with the reaction of allyl as well as other carbamates is the tendency of the carbamate to be cleaved by the base (usually BuLi). The use of more sterically hindered bases, such as ^{s}BuLi, ^{t}BuLi and LDA reduces cleavage of the carbamate, but the rate of deprotonation is also adversely affected. Increasing the steric bulk of the carbamate is also effective, but again the rate of deprotonation can suffer. The use of bulkier carbamates also has the added disadvantage in that non-destructive removal of the carbamate group can be very difficult.

Barner and Mani[55] overcame this problem by using *N*-alkyl benzyl carbamates. The double lithiation effectively prevents cleavage of the carbamate group (Scheme 27).



Scheme 27

Hoppe extended this work to include allyl carbamates, but found it to have little synthetic scope.[56]

While the majority of the work done on allyl carbamates involves carbonyl electrophiles, other electrophiles have also been used. These include alkyl[56] and silyl halides[50], carbonates[48] and stannanes.[57]

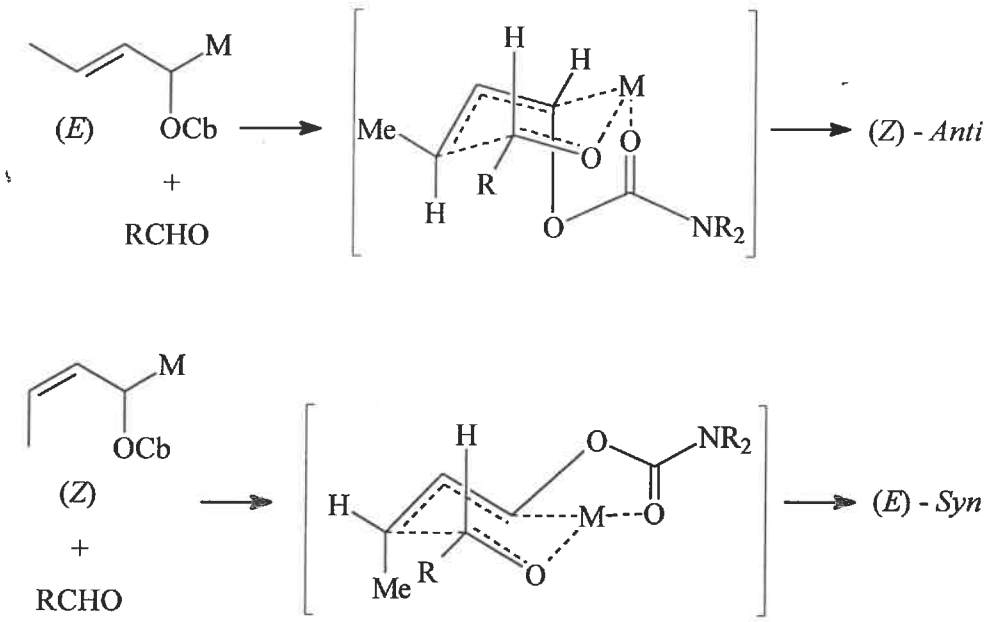
1.5.1.2) Diastereoselective Addition of Carbonyl Compounds.

When 3-substituted allyl carbamates, such as crotyl carbamate, react with aldehydes or unsymmetrical ketones, one gets the formation of two adjacent chiral centres. It is therefore of considerable importance that one can control the diastereoselectivity of the reaction.

As with other allyl metal compounds, metalated allyl carbamates exhibit appreciable diastereoselectivity in their reaction with aldehydes and unsymmetrical ketones. The stereochemical outcome of such additions are usually interpreted using the Zimmerman-Traxler model.[58, 59] The model involves addition *via* a six-membered chair transition-state (Scheme 28).

Based on this model, (2-*E*)-carbamates should give *anti*-products, while (2-*Z*)-carbamates should give *syn*-products. The energy difference between the transition states for lithiated carbamates, however, is insufficient to appreciably influence the stereochemical outcome of the reaction.[49, 50, 62, 63, 64]

Metal exchange with titanium compounds ($Ti(^{i}OPr)_3Cl$, $Ti(^{i}OPr)_4$, $Ti(NR_2)_3Cl$) give superior results, favouring the (*Z*)-*anti*-product.[60, 61]



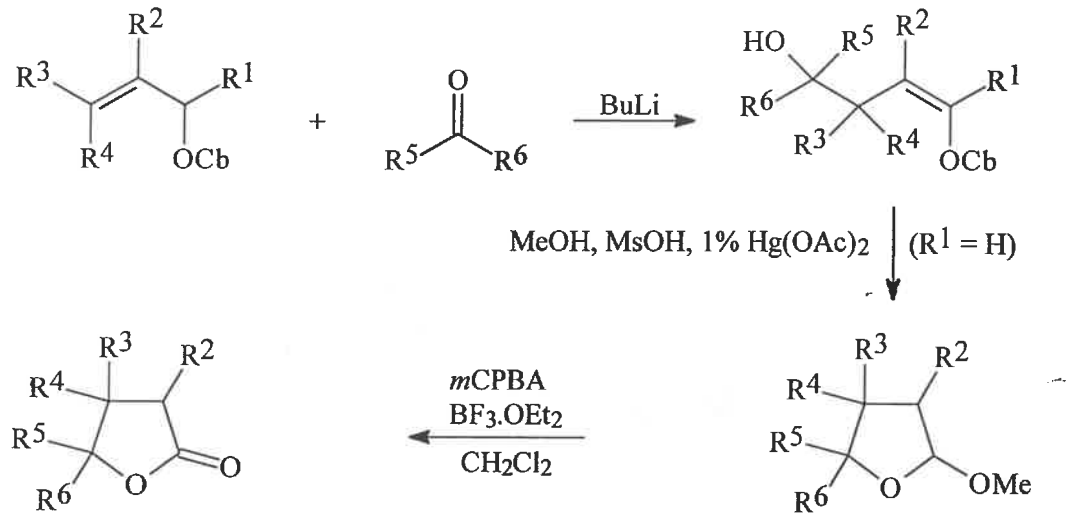
Scheme 28

Diisobutyl aluminium chloride has also been shown to be an effective exchange metal.[65]

1.5.1.3) Applications.

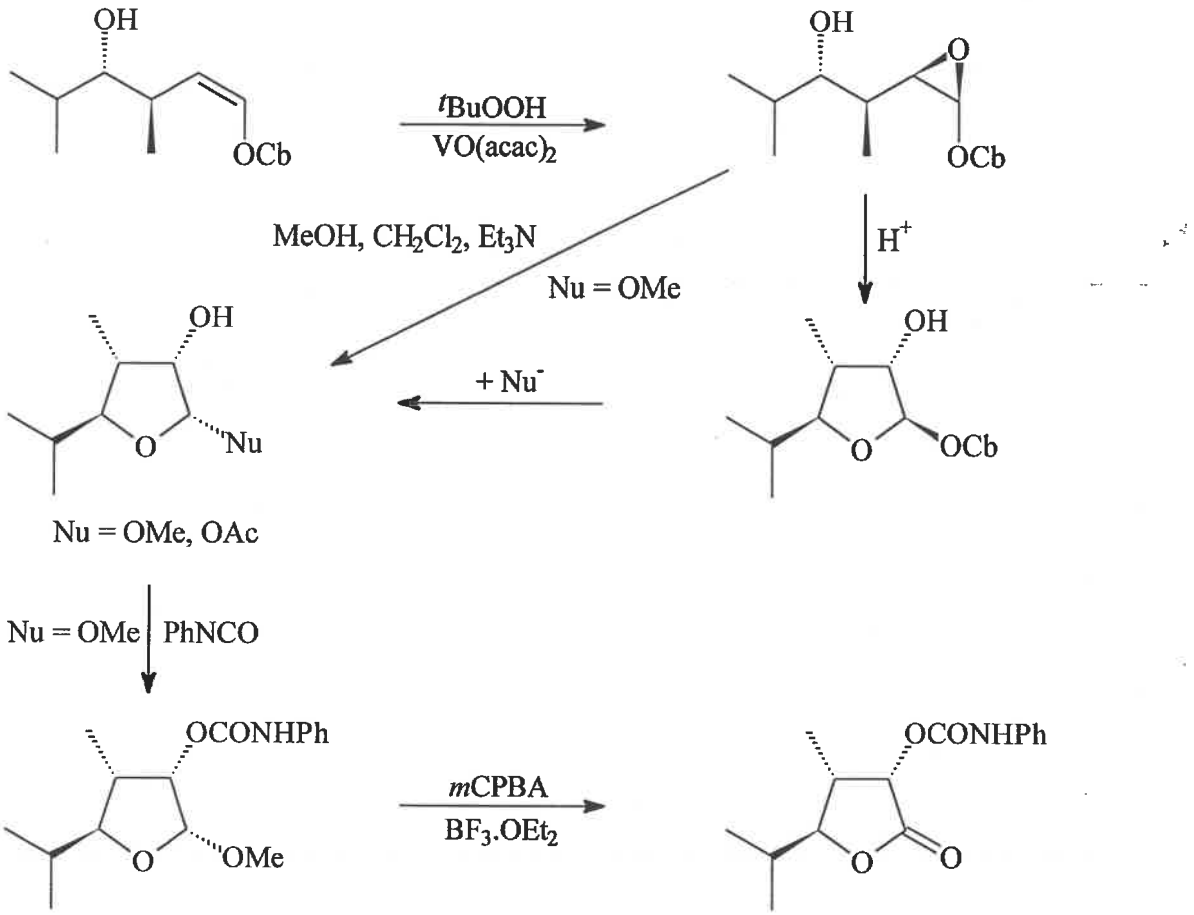
The homo-aldol products of the reaction of allyl carbamates and carbonyl compounds has proven to be a useful route to substituted tetrahydrofurans and butanolides.

Hoppe and co-workers produced a wide range of substituted butanolides, using the method shown in Scheme 29.[65 - 70]



Scheme 29

A similar approach was used in the preparation of 1-hydroxy lactones and lactols, *via* and epoxide intermediate[62, 71 - 73] (Scheme 30).

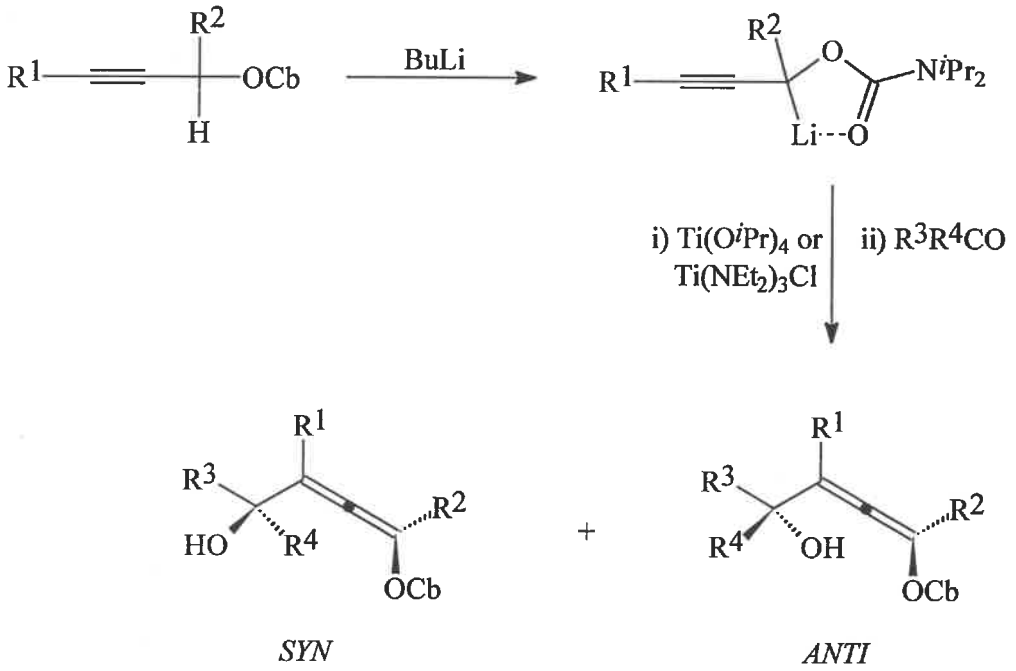


Scheme 30

1.5.2) Reactions of Alkynyl Carbamates.

Alkynyl carbamates have also been studied under similar conditions to allyl carbamates, but to a lesser extent. Alkynyl carbamates are easily deprotonated by strong bases to give α-lithiated carbamates, with the mechanistic aspects dealt with regarding allyl carbamates applying in this case as well.

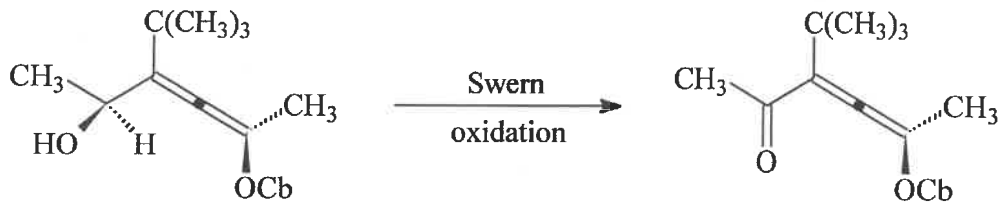
Reaction proceeds in an analagous manner to allyl carbamates with bond-migration, but in the case of alkynyl carbamates this results in allene derivatives[74, 75, 76] (Scheme 31).



R^1 = H, Me, $SiMe_3$, cC_6H_{11}, CMe_3, $SiMe_2Ph$; R^2 = H, nC_3H_7, Me, $CHMe_2$, CMe_3
R^3 = alkyl, aryl; R^4 = H, Me

Scheme 31

Further elaboration of the substituted products is, however, limited. Swern oxidation of (**24**) gives the allenic ketone (**25**)[76] (Scheme 32).

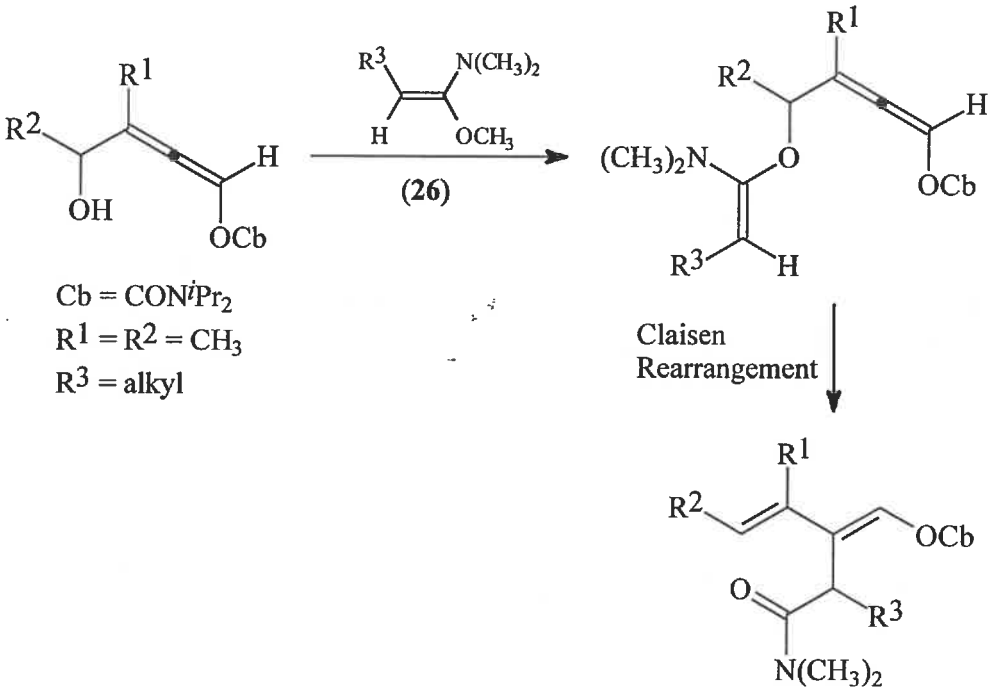


SYN and *ANTI*

(24) **(25)**

Scheme 32

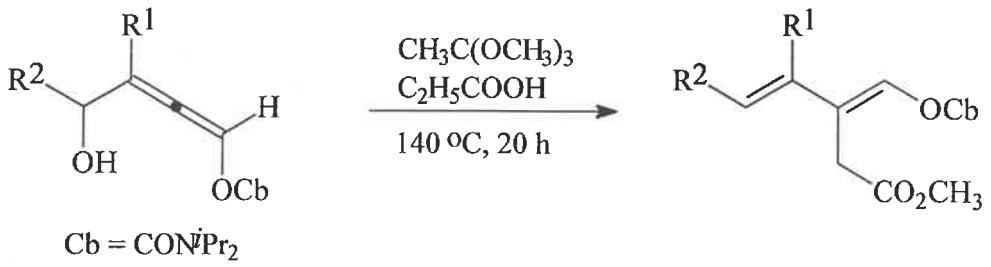
An interesting reaction is the preparation of substituted 1,3-butadienes from (**24**) *via* an allene Claisen Rearrangement using an amino ketene acetal (**26**)[77, 78] (Scheme 33).



Cb = $CON^{i}Pr_2$
$R^1 = R^2 = CH_3$
R^3 = alkyl

Scheme 33

Esters were prepared in a similar manner to the amides using the Johnson ortho ester Claisen Rearrangement[75] (Scheme 34).

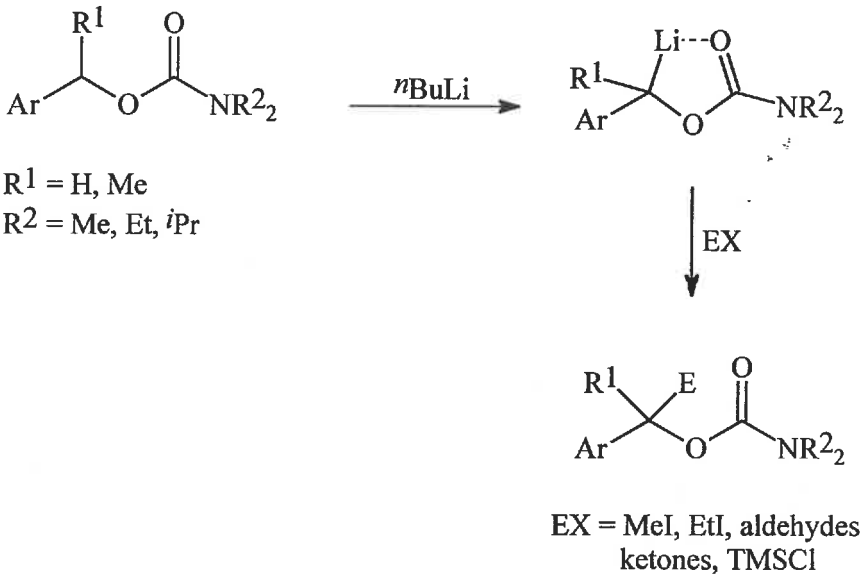


Cb = CON^{i}Pr$_2$

Scheme 34

1.5.3) Reactions of 1-Arylalkyl-N,N-Dialkyl (Benzyl-Type) Carbamates.

Shortly after the work on allyl carbamates, Hoppe[79, 80] reported that 1-arylalkyl-*N,N*-dialkyl (benzyl-type) carbamates could be deprotonated by strong bases and reacted with electrophiles in the same manner as allyl carbamates. The reaction conditions are the same, being THF or diethyl ether / TMEDA at -78 °C. LDA can also be used, but yields are lower than with alkyllithiums (Scheme 35).



R^1 = H, Me
R^2 = Me, Et, ^{i}Pr

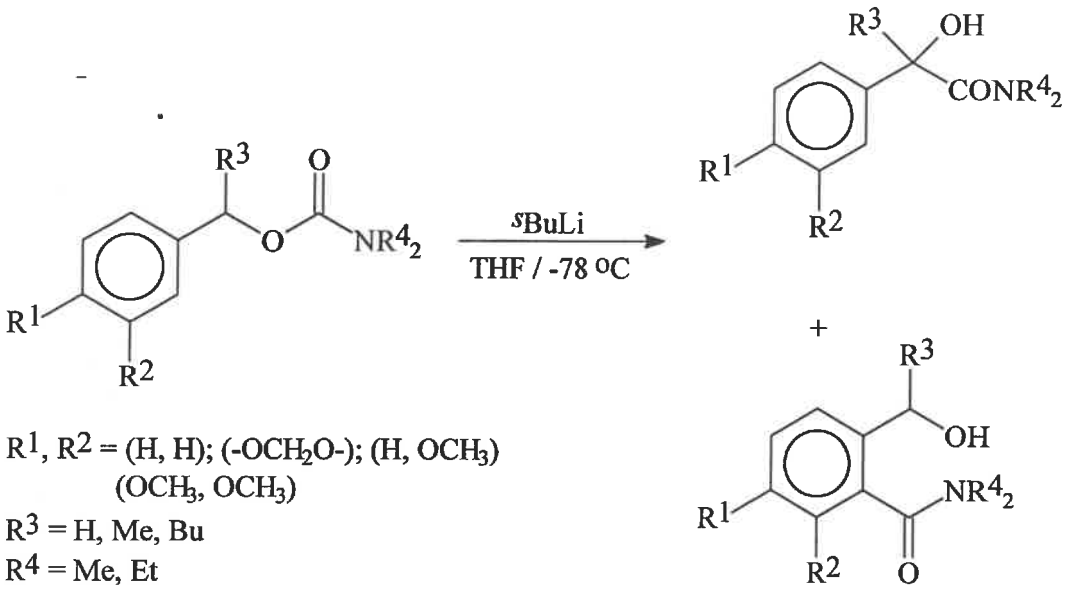
EX = MeI, EtI, aldehydes
ketones, TMSCl

Scheme 35

Like the allyl carbamates, *N,N*-dimethyl carbamates are susceptible to cleavage by the base. Donor groups on the ring, such as methoxy, do not appear to have any effect on

the reactivity of the carbamates. Theoretically, anion delocalisation onto the aromatic ring is possible , as a consequence ring substitution is possible. Electrophilic substitution has not, however, been observed by Hoppe.

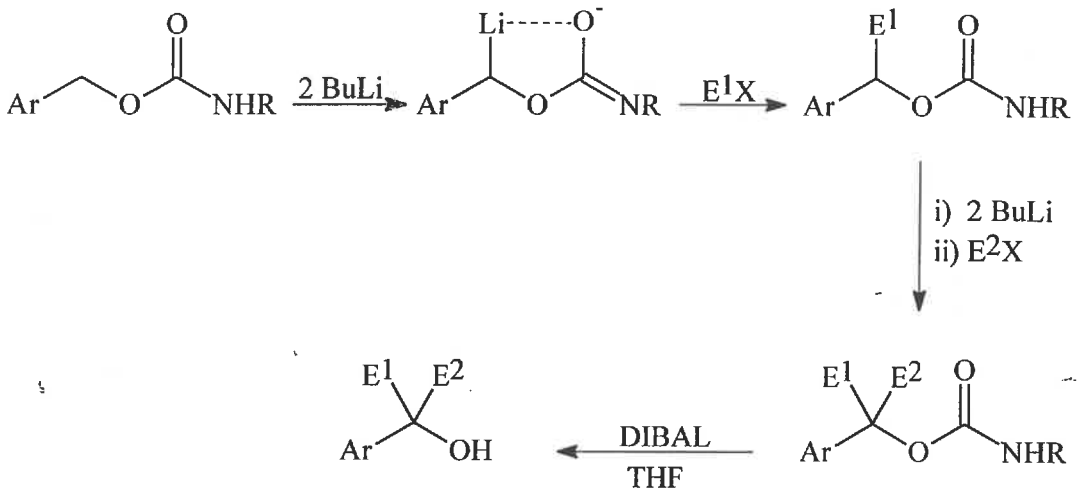
Gawley[81], on the other hand, has reported the migration of the amide portion of the carbamate onto the benzylic position and the *ortho* ring-position (Scheme 36).



R^1, R^2 = (H, H); ($-OCH_2O-$); (H, OCH_3)
(OCH_3, OCH_3)
R^3 = H, Me, Bu
R^4 = Me, Et

Scheme 36

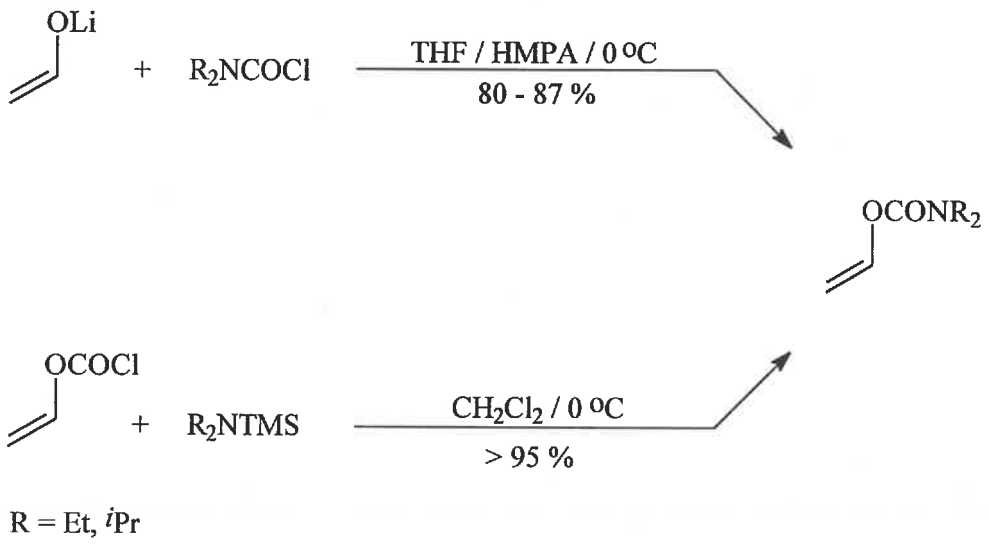
Studies in our laboratories[82] on similar systems have also shown similar migrations to those reported by Gawley. *N*-Alkyl benzyl carbamates can also be deprotonated, but require two equivalents of base due to the acidic amide proton[55] (Scheme 27). More importantly, from the point of view of the work presented in this thesis, is the fact that Barner and Mani recognised the possibility of electrophilic disubstitution of carbamates (Scheme 37).



Scheme 37

1.5.4) Reactions of Vinyl Carbamates.

Vinyl carbamates, like aryl carbamates which are covered in the next section, are a special case in that the abstracted proton is in a vinyl position and not in an allyl or benzyl position as was previously the case. Sengupta and Snieckus[83] were the first to report on the reaction of α-metalated enol carbamates (metalated vinyl carbamates), which were prepared from lithium enolates (Scheme 38).

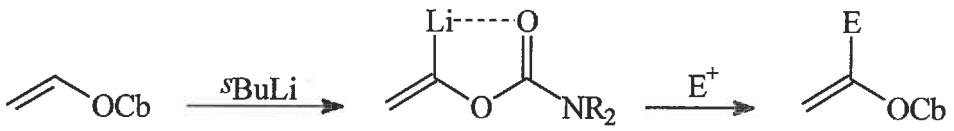


Scheme 38

α-Metalated vinyl carbamates are of considerable synthetic importance since they are acyl anion equivalents (Figure 2).

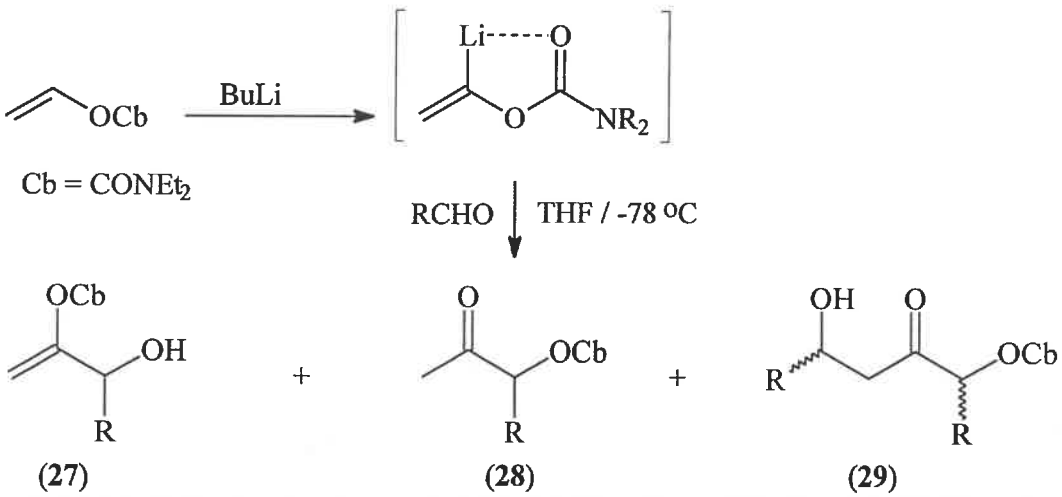
Figure 2

Vinyl carbamates are easily deprotonated under standard metalation conditions and react with a variety of electrophiles, including alkyl halides, silyl halides, epoxides, acid chlorides, isocyanates and carbonyl compounds, giving α-substituted vinyl carbamates (Scheme 39).



Scheme 39

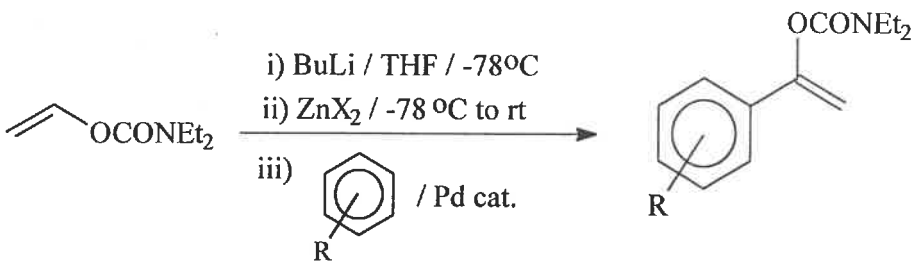
The reaction with aldehydes is interesting because one gets carbamate migration occurring as well, giving an α-carbamoyl ketone (**28**), which can react with a second equivalent of aldehyde to give the β-hydroxy ketone (**29**) (Scheme 40).



Scheme 40

Ketones react in a similar manner, but the second addition giving a β-hydroxy ketone does not occur.

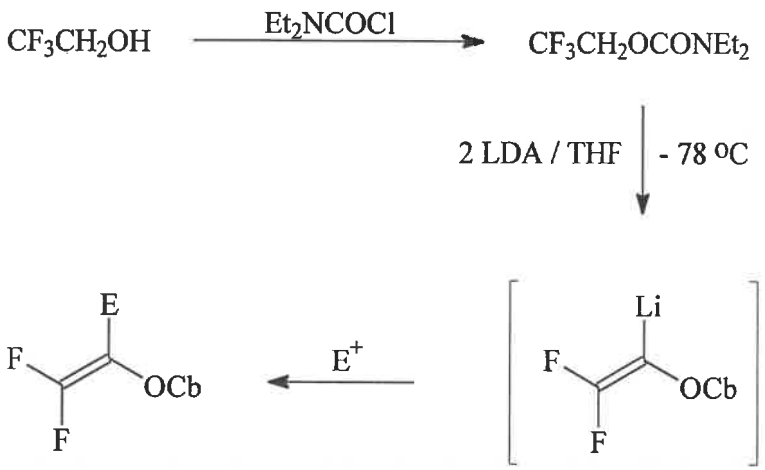
Snieckus and coworkers broadened the scope of this reaction to include reaction with aryl halides under Heck Reaction conditions[84, 85] (Scheme 41).



R = 2-Me, 2-OMOM, 2-$OCONEt_2$, 2-$CONEt_2$, 3-OMe, 3-NO_2, 3-$CONEt_2$, 4-Me, 4-OMe, 4-NO_2, 4-Cl.
X = Br or I.
Pd catalyst = $Pd(PPh_3)_4$ and $PdCl_2(dppf)$.

Scheme 41

2,2-Difluoro analogues have also been studied and undergo the same type of reactions with various electrophiles.[86, 87, 88] The metalated fluoro carbamate is generated *in situ* from 2,2,2-trifluoroethyl-*N,N*-diethylcarbamate[86] (Scheme 42).

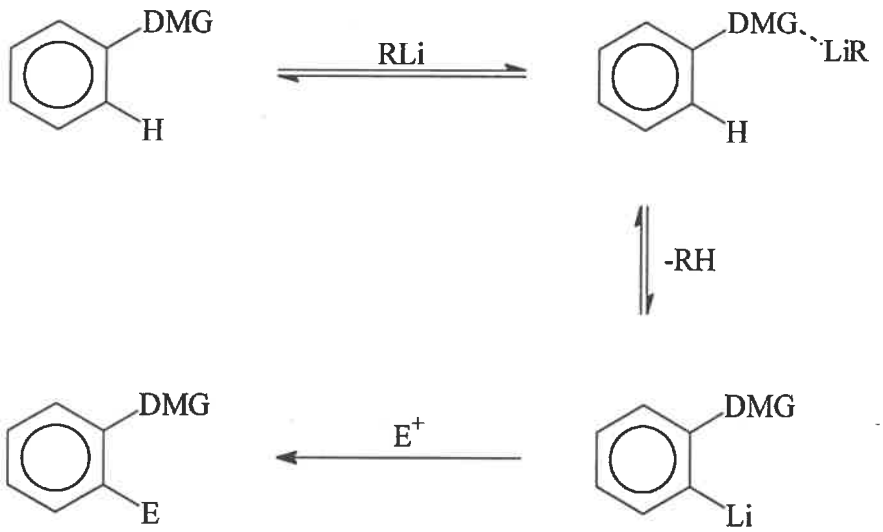


Scheme 42.

1.5.5) Beta-(Ortho)-Metalation.

Directed-*ortho*-metalation (DoM) was first reported, independently, by Gilman and Bebb[89] and Wittig and Fuhrmann.[90] Strong bases were found to deprotonate aromatic rings in the position *ortho* to the directing metalation group (DMG).[91] The reaction occurs in three steps, which are shown in Scheme 43.

1. Coordination of RLi to the heteroatom of the DMG.
2. Deprotonation to give the *ortho*-metalated intermediate.
3. Reaction with the electrophile.



Scheme 43.

For the reaction to be successful, the DMG needs to be a poor electrophilic site and a good coordinating site for metal complexation. The carbamate group has been found to be an excellent DMG, since carbamates, especially the more bulky types, are poor electrophiles and they can stabilise the metalated carbanion by complexation with the carbonyl group *via* a six-membered intermediate (Figure 3).

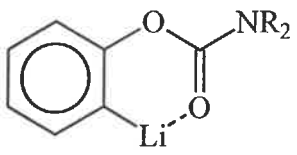


Figure 3.

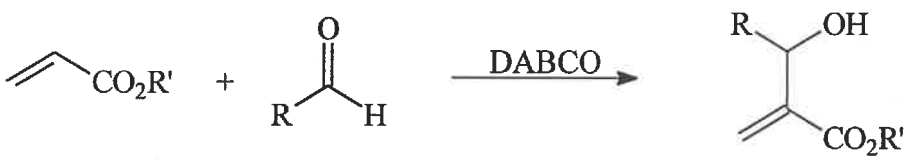
Hydrolysis of the carbamate group can be achieved by reduction with lithium aluminium hydride or treatment with sodium hydroxide in aqueous methanol.[92]

1.6) Other Reactions.

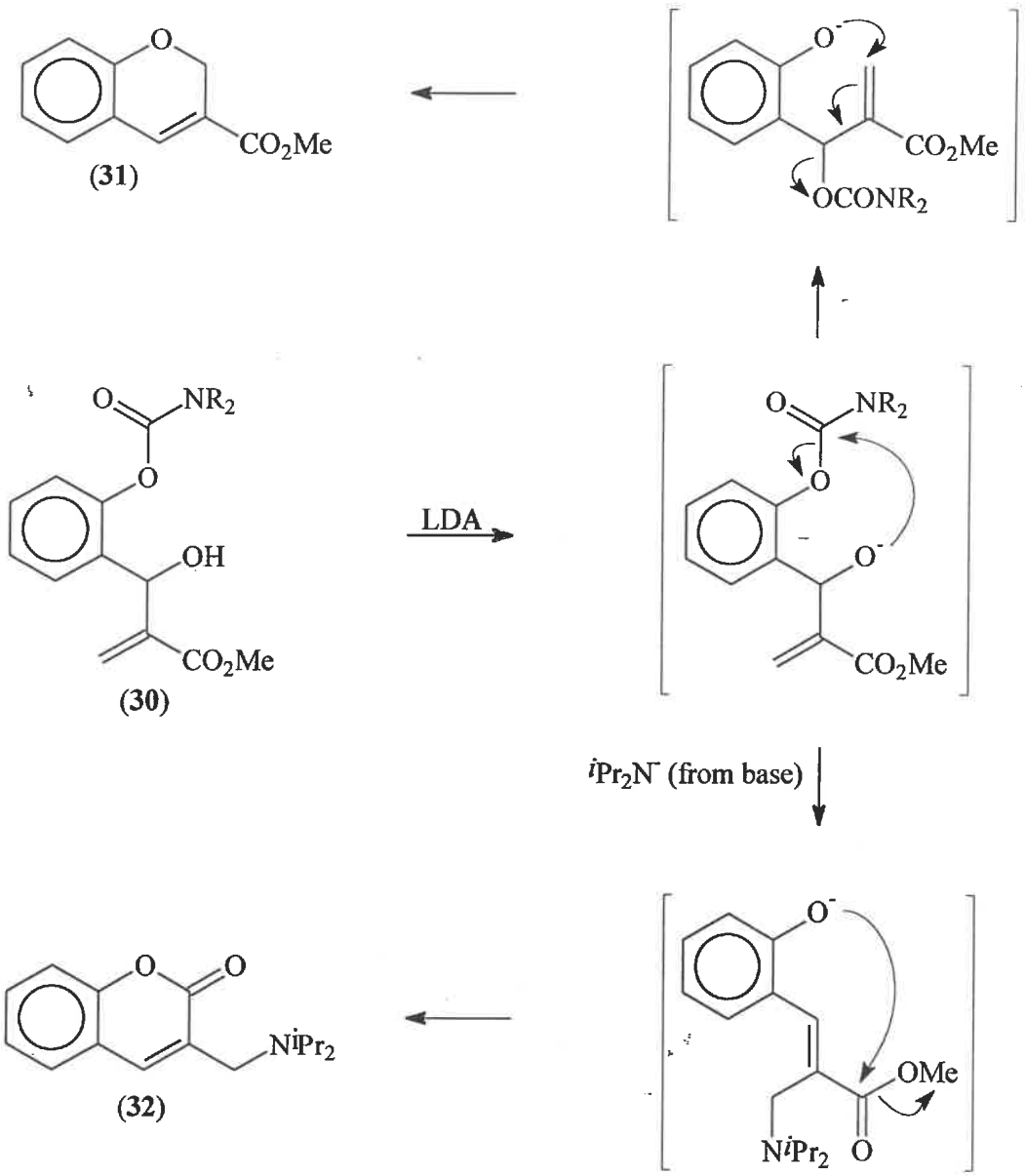
This section is simply a summary of some of the interesting results that have been obtained during the course of the studies conducted in our laboratories on the reactions and reactivity of various carbamates.

1.6.1) Preparation of Substituted Chromenes and Coumarins.

Substituted chromenes (**31**) and coumarins (**32**)[93] were prepared from substituted aryl carbamates (**30**) (Scheme 45). The allylic carbamates were prepared from the corresponding allylic alcohols, which had been prepared using the Baylis Hillman reaction (Scheme 44).[94]



Scheme 44

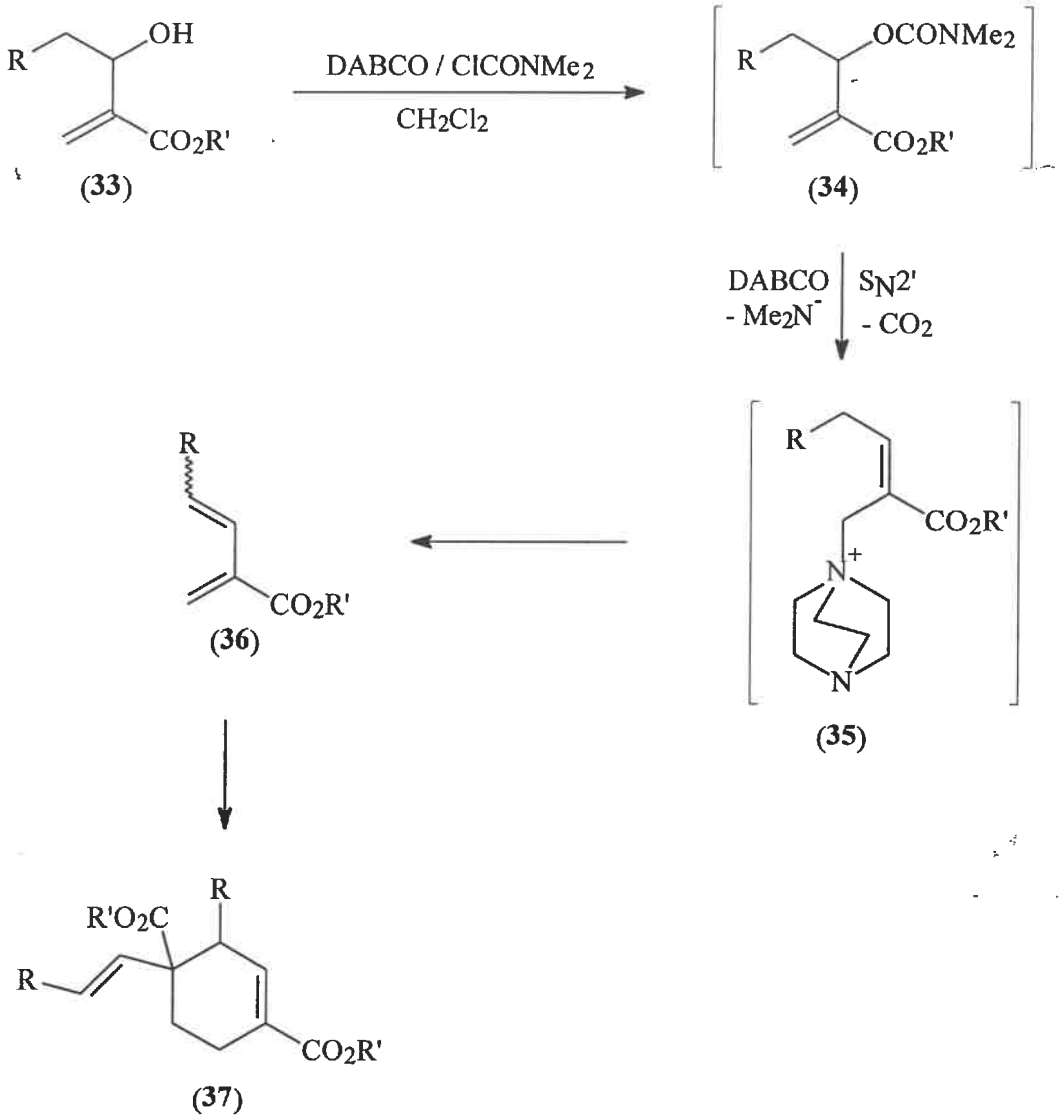


Scheme 45

1.6.2) Preparation of Mikanecic Acid Derivatives.

A particularly interesting synthesis is the preparation of mikanecic acid (**37**) derivatives *via* an *in situ* generated allylic carbamate.[93] Reaction of the allylic alcohol (**33**) with dimethylcarbamoyl chloride with three equivalents of DABCO in dichloromethane gives the allylic carbamate intermediate (**34**), which cannot be

isolated. S_N2' elimination of the carbamate group by DABCO gives the salt (**35**) which undergoes elimination to give the diene (**36**). Diels-Alder dimerisation gives the mikanecic acid derivatives (**37**) (Scheme 46). Mikanecic acid itself has R=R'= H.



R = H, Me, Et, $(CH_3)_2$
R = Me, Et, Pr

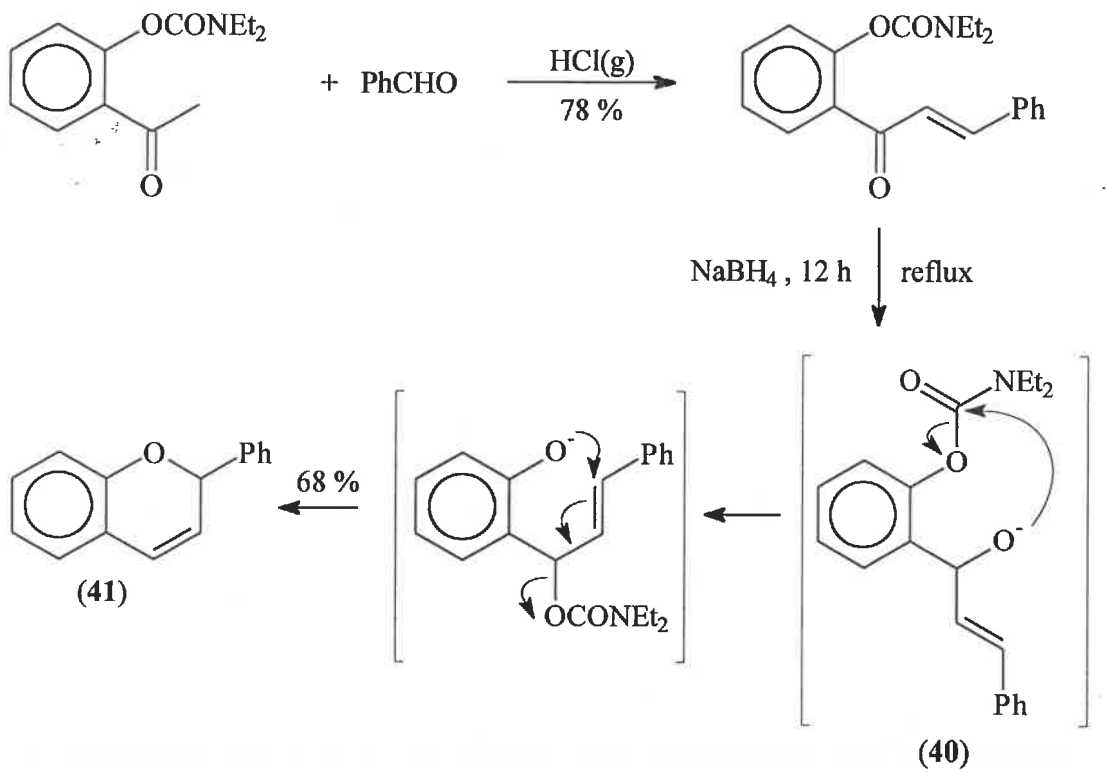
Scheme 46

α-Aryl allylic carbamates cannot react in this manner, since they do not have a proton *beta* to the carbamate group. The loss of this proton is required to form the diene (**36**). In the case of α-aryl allylic carbamates, the liberated dimethyl amide anion substitutes the quarternary DABCO salt (**38**) to give the allylic amine (**39**) (Scheme 47).

Scheme 47

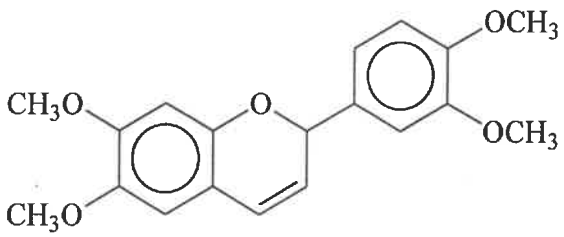
1.6.3) Synthesis of Flav-3-enes.

During the course of studies directed towards the leaving and migrational properties of carbamates, a useful preparation of flav-3-enes (**41**) was discovered[95] (Scheme 48).



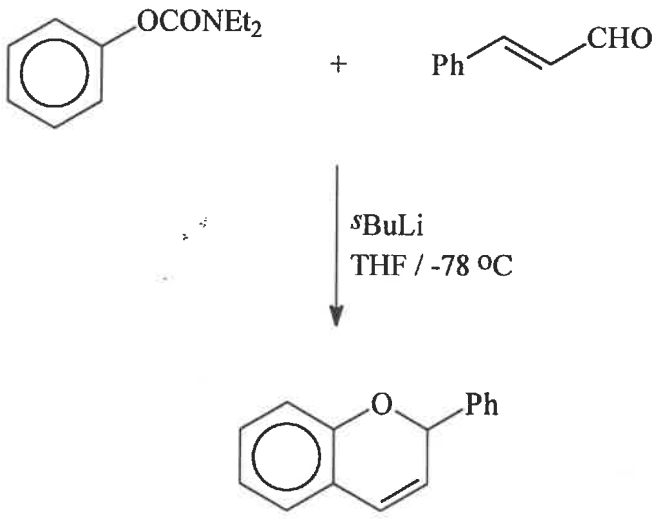
Scheme 48

The substituted flav-3-ene (**42**) was prepared as well as the unsubstituted flav-3-ene (**41**).



(**42**)

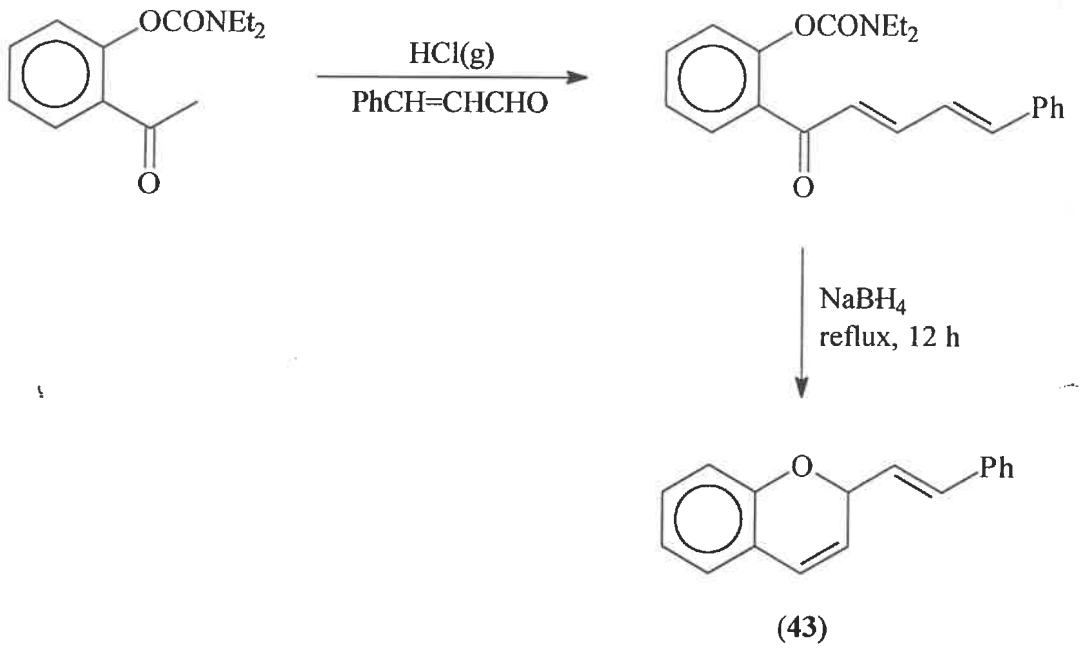
Flav-3-ene (**41**) was also prepared in low yield (10 %) *via* a directed-*ortho*-metalation reaction, through intermediate (**40**) (Scheme 49).



(**41**)

Scheme 49

The methodology outlined in Scheme 48 was extended to prepare other flavenoid compounds (**43**) (Scheme 50).



(43)

Scheme 50

1.7) Conclusion.

From this survey of the chemistry of carbamates it is obvious that the carbamate functionality is a useful intermediate in organic synthesis. They are not limited to protecting groups and have found fairly widespread use in the preparation of synthetically useful intermediates. The majority of the research published in this field has been in the area of carbamate stabilised metalated anions, which have been shown to have considerable synthetic importance as homo-enolate equivalents.

It is with this background that the research described in this thesis was carried out, in the field of carbamate stabilised allylic anions and related systems.

CHAPTER 2: RESULTS AND DISCUSSION

2.1) Introduction.

Allylic alcohols and α,β-unsaturated carbonyl compounds, which are the oxidised forms of allylic alcohols, are found in numerous organic compounds. They are particularly common in natural products and are useful synthetic intermediates. It comes as no surprise, therefore, that much effort has gone into developing synthetic routes to allylic alcohols and α,β-unsaturated carbonyl compounds.

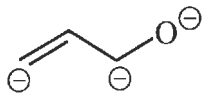
Of particular interest are methods to elaborate on simple allylic alcohols and their derivatives to give more substituted compounds, while keeping the allylic alcohol intact.

The aim of this research is to begin an investigation into the substitution of allylic carbamates (which are simply protected allylic alcohols) with a view to developing synthetic methodology that may be generally applicable to organic synthesis, and natural product synthesis in particular.

Obviously, at this stage, it is important to clarify the direction of this research. The main purpose is to develop general methodology in a number of related areas, which has to be done at the expense of a very detailed investigation in any one particular area. Furthermore, since the research in this field is part of a group effort, various closely related areas and obvious extensions of the work are the subject of other research projects, both in progress and envisioned. These areas will be identified where appropriate. Other workers are also very active in this field, so overlap of research was avoided.

The work on allylic carbamates that has been reported by other workers, particularly Hoppe, is fairly extensive and while it has been discussed in some detail already, some comparisons with the work presented in this thesis are required.

Taking the simplest allylic alcohol, allyl alcohol, one immediatly identifies the hydroxy group as a potential nucleophile. Less obvious are the α- and γ-carbons, which are also potential nucleophiles. The presence of the hydroxy group, however, prevents proton abstraction at these sites unless it is protected in some way.



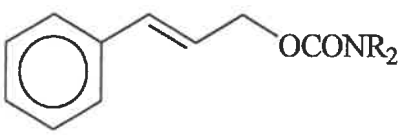
The three nucleophile sites on allyl alcohol

The hydroxy group, when protected appropriately, can play an important role in stabilising the resultant α- or γ-anion.

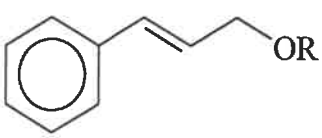
As was made clear in Chapter 1, the carbamate group is considered superior both as a protecting group and a stabilising group for α- and β-metalation reactions. For the purpose of this investigation, cinnamyl alcohol was chosen as the model allylic alcohol. This was for a number of reasons, which are outlined below.

- The cinnamyl fragment is found in a large number of natural products.
- The phenyl group in the γ-position limits the uncontrolled multiple substitution of the carbamates (to be expanded on later).
- Simple allylic ethers, are very volatile and are consequently difficult to work with, unlike cinnamyl ethers. The allyl ethers were required for comparative studies.

The first part of this investigation involves the cinnamyl carbamates (**45**) and the corresponding ethers (**46**).



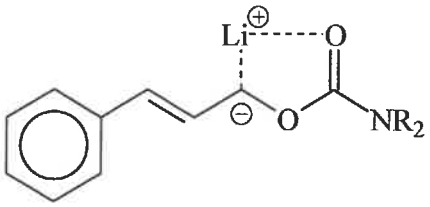
(**45a**): R = Et
(**45b**): R = ^{i}Pr



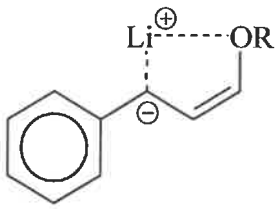
(**46a**): R = Me
(**46b**): R = Et

Further studies involve other allylic carbamates, but these will be discussed at the appropriate time.

The reason for studying the ethers as well as the carbamates initially is because both compounds are readily accessible and have similar reactivity, but at the same time a different mode of stabilisation of the allylic anion. While it is generally accepted that, in the case of allylic anions, the negative charge is delocalised, a lot of the reactivity of these compounds is explained in terms of a localised anion, which is stabilised in the α-position by a carbamate group (**47**) and in the γ-position by an ether group (**48**).



(**47**)

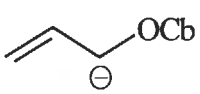


(**48**)

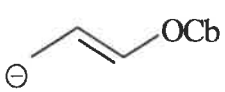
2.1.1) A Note on Nomenclature.

Discussions involving allylic anions can be problematic since the anion can be localised in the α- or the γ-position or delocalised over both positions. For this reason the term "allylic anion" is taken to refer to a delocalised anion, while "α-anion" or "γ-anion" refers to the respective localised anions. The carbamate group, OCb, refers to a generic *N,N*-dialkyl carbamoyl group, unless otherwise stated. In the context of this chapter, it invariably refers to either the *N,N*-diethyl- or the *N,N*-diisopropyl carbamoyl group.

"allylic anion"



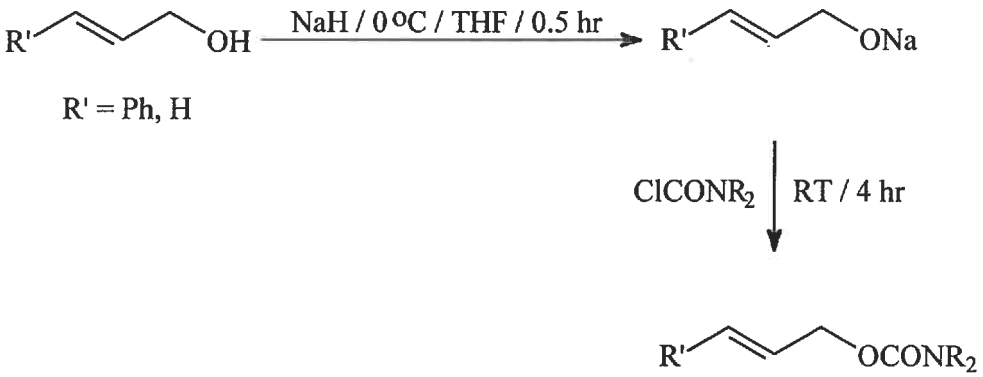
"α-anion"



"γ-anion"

2.2) Preparation of Allylic Carbamates and Ethers.

Numerous methods exist for the preparation of carbamates, as discussed in Section 1.2. Hoppe[96] prepared allyl and benzyl carbamates by refluxing the corresponding alcohols with carbamoyl chlorides in pyridine under nitrogen for 12 - 20 hours. We found that preparation of the sodium alkoxide from the alcohol and sodium hydride in tetrahydrofuran, followed by reaction with the carbamoyl chloride to be an excellent method for the preparation of simple allylic carbamates (Scheme 51). This method was also extended to the preparation of cinnamyl ethers, using the corresponding alkyl halide.



(45a): R' = Ph, R = Et
(45b): R' = Ph, R = ^{i}Pr
(49a): R' = H, R = Et
(49b): R' = H, R = ^{i}Pr
(49d): R' = Me, R = Et

Scheme 51

This simple approach allowed for the multigram preparation of carbamates (**45**) and (**49**) in good yield (Table 1). Workup is simple and the products are easily purified by distillation. All four of the above carbamates are stable for long periods of time under ambient conditions. Stored samples showed no signs of deterioration after three years. 1-*N*-^{t}butylcarbamoyloxyprop-2-ene (**49c**) (94 %) was prepared by treating allyl chloroformate with ^{t}butylamine in THF at 0 °C.

Table 1: Isolated yields of carbamates (**45**) and (**49**).

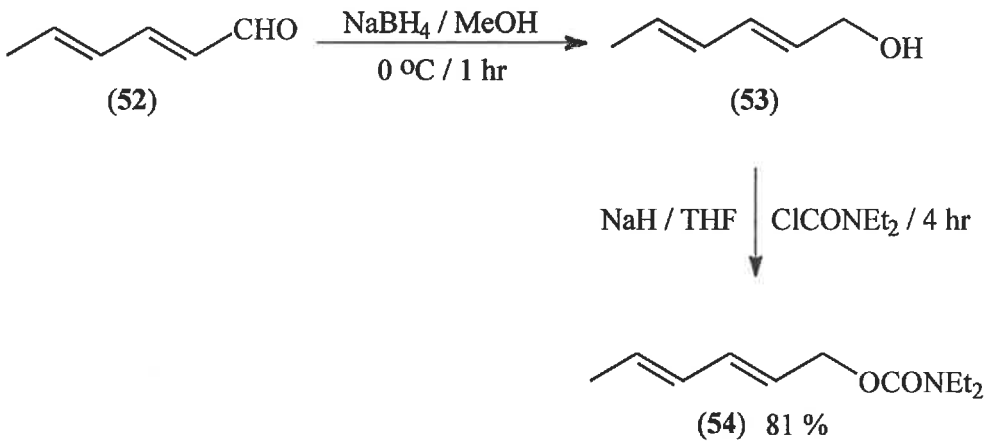
Carbamate	Yield (%)
45a	96
45b	92
49a	95
49b	93
49d	88

The dicarbamates (**50**) and (**51**) were prepared using the same method from the corresponding commercially available diols and two equivalents of sodium hydride and *N,N*-diethylcarbamoyl chloride.

(**50**) 93 %

(**51**) 89 %

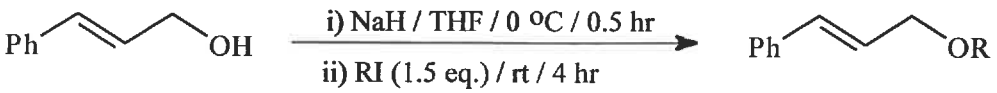
1-*N,N*-Diethylcarbamoyl-2,4-hexadiene (**54**) was prepared by the reduction of commercially available 2,4-hexadienal (**52**) to the alcohol (**53**), followed by reaction with *N,N*-diethylcarbamoyl chloride as described previously (Scheme 52).



(**52**) (**53**) (**54**) 81 %

Scheme 52

The cinnamyl ethers (**46a**) and (**46b**) were prepared similarly (Scheme 53).



R = Me (**46a**) 93 %; R = Et (**46b**) 89 %

Scheme 53

2.2.1) Characterisation and Spectroscopy.

All of the compounds described give well defined first order NMR spectra. It was found, however, that the *N*-alkyl substituents of the carbamates gave distinctive and diagnostic NMR signals.

The ethyl groups gave rise to two sets of two broad signals at *ca* 14 and 41 ppm on the ^{13}C spectrum and a triplet at *ca* 1.1 ppm and a broad quartet at *ca* 3.3 ppm on the ^{1}H NMR spectrum. The diisopropyl group gives rise to broad signals at *ca* 21 and 46 ppm on the ^{13}C NMR spectrum and a doublet and a broad signal at *ca* 1.2 and 3.9 ppm respectively on the ^{1}H NMR spectrum. These signals are of characteristically low intensity on the ^{13}C NMR spectrum, relative to other signals.

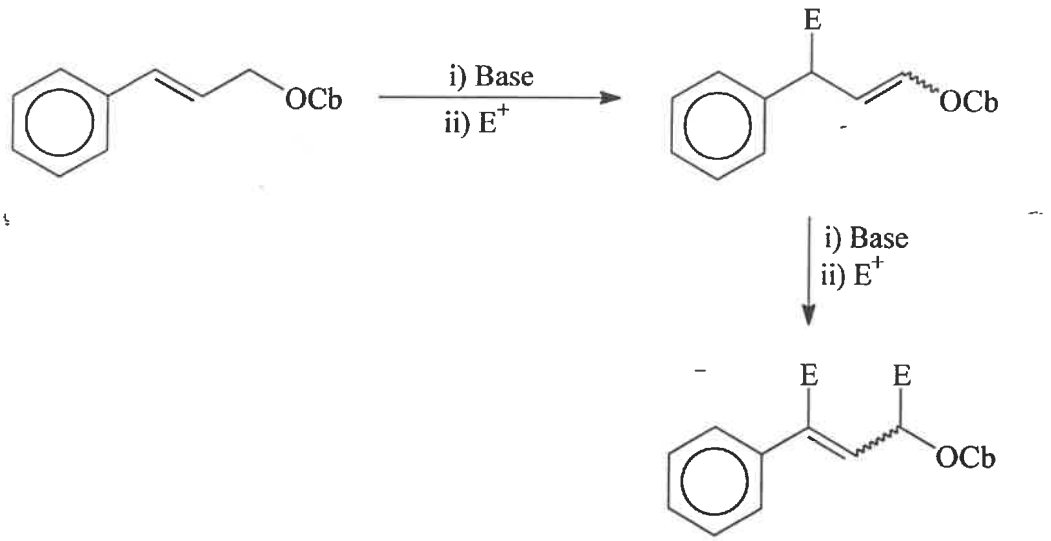
This effect, which is due to restricted rotation about the carbonyl carbon - nitrogen bond, is observed in all of the carbamate derivatives synthesised. The extent of signal broadening and loss of resolution varies with the ^{1}H NMR signals, but the ^{13}C signals all displayed the same broadening and non-equivalence.

2.3) Electrophilic Substitution of Cinnamyl Carbamates.

2.3.1) Aims.

The main objective of the study on cinnamyl carbamates was to investigate the possibility of disubstitution. Hoppe and coworkers have done considerable work on

the mono-substitution of allylic carbamates, and we felt that it was reasonable to extend this to disubstitution reactions (Scheme 54).



Scheme 54

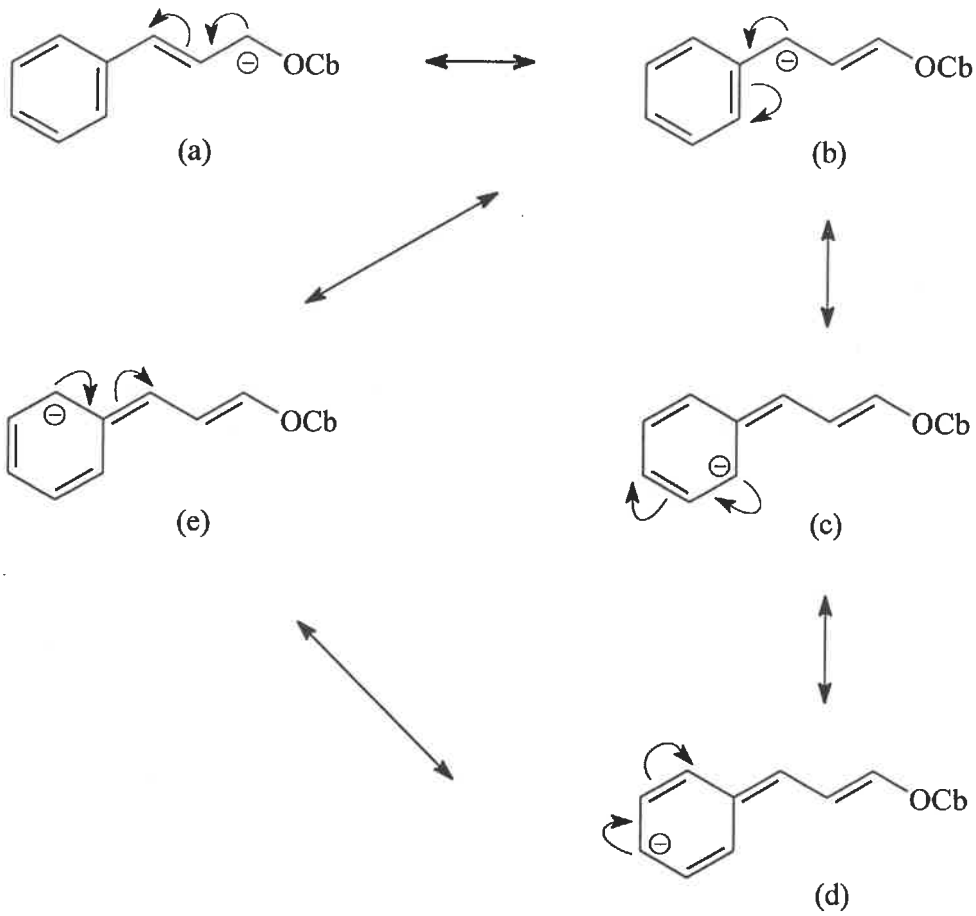
In the case of the cinnamyl carbamates, we envisioned the first substitution occurring at the γ-position and the second substitution occurring at the α-position, due to steric constraints.

Before the disubstitution reactions were attempted, however, it was necessary to determine the effect of the steric bulk of the electrophile on the α:γ substitution ratio and the yield of the reaction. The necessity for this is obvious, since allyl carbamates can undergo both α- and γ-substitution, with a complex interplay of various effects influencing the overall outcome of the reaction.

2.3.2) *Effect of the Steric Bulk of the Electrophile on the α:γ Ratio and Yield of Substitution Reactions of Cinnamyl Carbamates.*

As was shown in Chapter 1, allylic anions (in this case allylic carbamate anions) can undergo substitution in either the α- or the γ-position, due to the delocalisation of the negative charge.[33]

A number of factors influence the product distribution,[40] but the major effects are due to substituent steric effects, electrophile steric effects and various electronic effects. The most important electronic effects are the stabilisation and localisation of the negative charge by a group such as a carbamate or an ether. In the case of cinnamyl carbamates, the effect of the carbamate group at one end of the molecule and an aromatic group at the other is difficult to determine except by experiment. At the outset, however, we felt that the stabilising and delocalising effect of the aromatic group would favour enhanced γ-selectivity (Scheme 55).

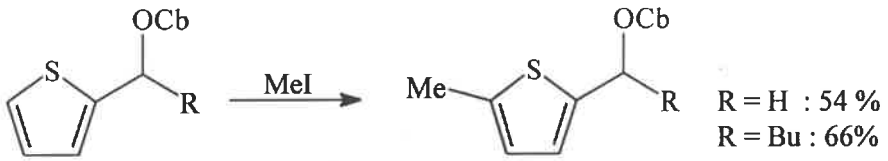


Scheme 55

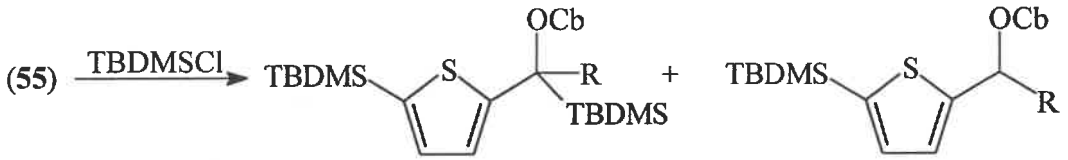
It is clear from resonance forms (c), (d) and (e) that the aromatic ring can stabilise the negative charge by delocalisation. This delocalisation also raises the possibility of electrophilic substitution on the aromatic ring. Ring substitution was not observed

during the course of these studies, but other investigations in these laboratories have shown examples of ring substitution.[97, 98]

Most of the ring substitution reactions observed have been trace by-products, where *para*- and ortho-substitution occurs.[97] The case of thenyl carbamates, however, is different.[98] Reaction of thenyl carbamates (**55**) with various electrophiles (MeI, TBDMSCl and TMSCl) gives various ring substituted products, in addition to the usual α-substituted products (Scheme 56).[98]

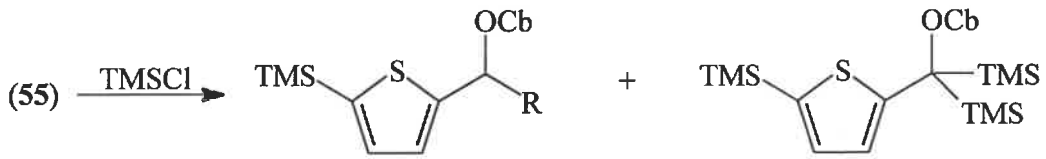


(55a) R = H : **(55b)** R = ^{n}Bu
(55c) R = Ph: **(55d)** R = Naph



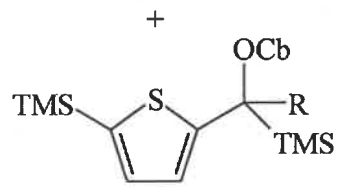
R = H : 29 %
R = Bu : 0 %

R = H : 2 %
R = Bu : 18 %



R = H : 28 %; R = Bu : 30 %
R = Ph : 22 %; R = Naph : 38 %

R = H : 6 %



R = H : 40 %; R = Bu : 20 %

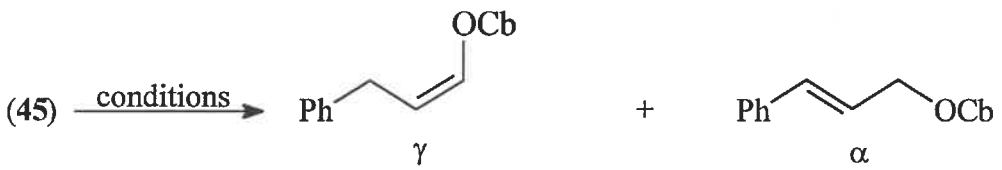
Scheme 56

Although a number of products are obtained, three main trends are observed:

- A bulky R group favours ring substitution (except when R is aromatic).
- The more reactive electrophiles tend to favour ring substitution.
- There is a decrease in ring substitution when R is aromatic. This is probably due to the delocalisation onto the aromatic ring, which results in an overall decrease in electron density on the thiophene ring.

In the case of the cinnamyl carbamates studied, both the α- and the γ-positions are open towards the approach of an electrophile, which accounts for the fact that no ring substitution was observed. The increased stability of the aromatic phenyl group also accounts for the lack of ring substitution. Trace amounts of *para*- and *ortho*-substituted products were observed with the reaction of benzyl carbamates[97], which is the subject of other investigations within our research group. This is due to the increased steric hinderance of the benzylic (α) position.

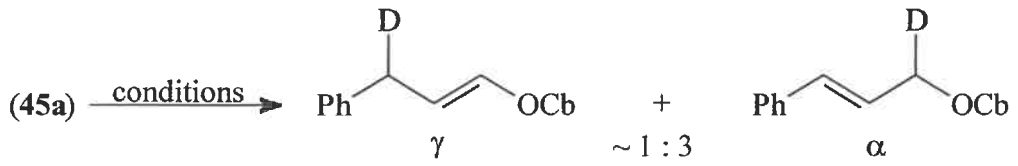
The simplest substitution reaction of this type is simply protonation of the anion.[39] The first part of this study was aimed at investigating the effect of the steric bulk of the proton source ("acid") (Scheme 57).



Conditions: i) ^{n}BuLi, solvent (THF or diethyl ether), -78 °C, 15 minutes.
ii) "H^{+}", 1 hour

Scheme 57

Deuterium labeling of the anion showed that deprotonation was complete after 10 minutes by quenching the reaction with D_2O or CD_3OD (both gave identical results) and measuring the proton NMR signal integrals (Scheme 58).



Conditions: i) ^{n}BuLi, THF, -78 °C
ii) D_2O or CD_3OD

Scheme 58

The results, which are shown in Tables 2 and 3, although not conclusive, do show a trend towards γ-substitution for the more bulky proton sources and the *N,N*-diisopropyl cinnamyl carbamate. In the case of bulkier carbon electrophiles, we felt that the steric bulk of the electrophile would override the conjugation effect (which results in overall α-selectivity in the protonation studies. Obviously, the choice of base, provided that complete deprotonation occurs, has no effect on the product ratio. The choice of base is, however, dictated by other factors, particularly hydrolysis of the carbamate.

Table 2: Proton source bulk and solvent effects on the α : γ ratio[a] for *N,N*-diethyl cinnamyl carbamate.

	Proton Source	α : γ (THF)[a]	α : γ (ether)[a]
1	H_2O	65 : 35	64 : 36
2	CH_3OH	61 : 39	61 : 39
3	PhOH	66 : 34	65 : 35
4	H_2SO_4	22 : 78[b]	30 : 70[b]
5	cyclohexanol	74 : 26	75 : 25
6	^{t}BuOH	56 : 44	60 : 40
7	CH_3CO_2H	62 : 38	60 : 40

[a] Ratio determined by proton nmr; average of three experiments.
[b] Decomposition.

Table 3: Proton source bulk and solvent effects on the α : γ ratio[a] for *N,N*-diisopropyl cinnamyl carbamate.

	Proton Source	α : γ (THF)[a]	α : γ (ether)[a]
1	H_2O	60 : 40	60 : 40
2	CH_3OH	59 : 41	60 : 40
3	PhOH	62 : 38	61 : 39
4	H_2SO_4	25 : 75[b]	30 : 70[b]
5	cyclohexanol	71 : 29	70 : 30
6	^tBuOH	55 : 45	61 : 39
7	CH_3CO_2H	61 : 39	60 : 40

[a] Ratio determined by proton nmr; average of three experiments.
[b] Decomposition.

All reactions were quenched at -78 °C and then allowed to warm to room temperature under an atmosphere of nitrogen because some product decomposition was found to occur on warming to room temperature in the presence of butyllithium.

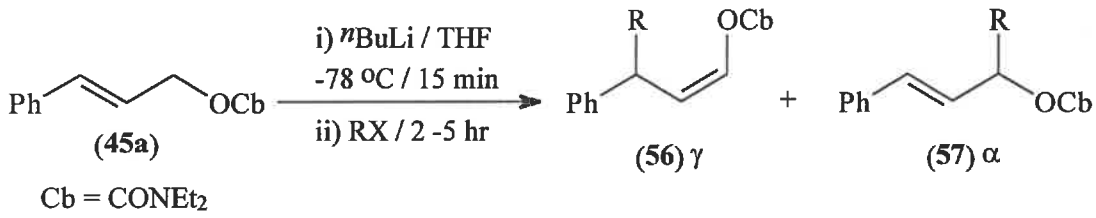
All other reactions involving carbamates and ethers were quenched with saturated aqueous ammonium chloride at -78 °C and then allowed to warm to room temperature, unless otherwise stated.

It became apparent during these initial studies that in the case of the cinnamyl carbamates, the diisopropyl group was too bulky and as a result the reaction yields were lower and reaction times longer compared to the analagous *N,N*-diethyl carbamates. For this reason, further investigations were limited, in most cases, to *N,N*-diethyl cinnamyl carbamates.

Although the study involving various proton sources shed some light on the effects of electrophile bulk on the product distribution, one needs to consider carbon electrophiles where the substituent groups vary but, hopefully, not the reactivity.

Simple alkyl halides fulfil these requirements, since a wide range is commercially available and their reactivity is less varied than most other classes of electrophiles. To this end various alkyl halides of differing steric bulk were reacted with cinnamyl carbamates after treatment with butyllithium at -78 °C.

The general reaction procedure is shown in Scheme 59 and the results in Table 4. The results shown in Table 4 are for reactions carried out in tetrahydrofuran only. Reaction in diethyl ether and diethyl ether/TMEDA gave essentially the same product ratio, but the yields were lower (see last two columns of Table 4).



Cb = $CONEt_2$

RX = MeI, EtI, isopropyl bromide, isobutylbromide, octyl bromide.

Scheme 59

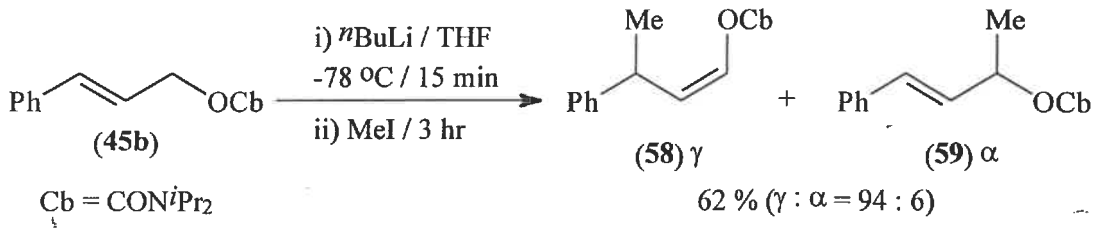
Table 4: Results of reaction of N,N-diethylcinnamyl carbamate with alkyl halides.

Product	Electrophile	α:γ Ratio[a] (THF)	% Yield (THF)	% Yield (ether)	% Yield (ether/TMEDA)
56a, 57a	MeI	0: 100	83	71	79
56b, 57b	EtI	1 : 99	72	62	65
56c, 57c	Isopropyl-Br	1 : 99	70	62	64
56d, 57d	Isobutyl-Br	8 : 92	32	12	30
56e, 57e	Octyl-Br	2 : 98	48	29	41

[a] Determined by proton nmr.

The results in Table 4 show that the yields are adversely affected by the bulk of the alkyl halide, but the decreased electrophilicity of the larger alkyl halides is also considered to be a contributing factor. There is also a slight increase in α-substitution with the bulkier alkyl halides, but this is minor, except in the case of isobutyl

bromide. As mentioned before, the *N,N*-diisopropylcinnamyl carbamate reacts more slowly and the yields are significantly lower (Scheme 60).



Scheme 60

Other bases, such as LDA, ^{s}BuLi and ^{t}BuLi, gave no significantly different results except that, again, longer reaction times were required with the more bulky bases.

From the proposed method of stabilisation of the allylic anion by the carbamate group, it is clear that attack would occur at the less hindered γ-position, since the α-position is more hindered due to the bulk of the complexed carbamate group (Figure 2).[49, 53]

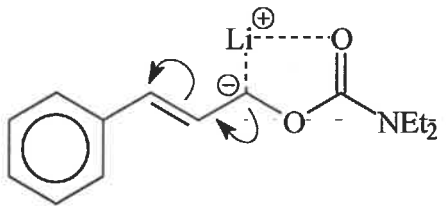


Figure 2

The increase in α-substitution observed with the *N,N*-diisopropylcinnamyl carbamate may be due to decreased coordination between the bulkier carbamate and the α-lithio group, making the α-position more accessible. The case when one uses isobutyl bromide as an electrophile (Scheme 59, Table 4) is an exception, and is an indication that other steric and electronic effects also operate. Based on these results, it is to be expected that disubstitution reactions will be very sensitive to the steric bulk of the electrophile, and this will be the dominant effect in the reaction.

2.3.2.1) Characterisation and Spectroscopy

The geometry of the isomerised double bond is easily assigned the *cis*-configuration based on the vicinal (H,H) coupling constant of *ca* 6 Hz (*e.g.* Figure 3).

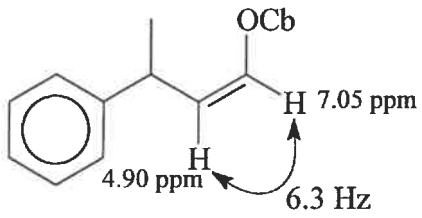
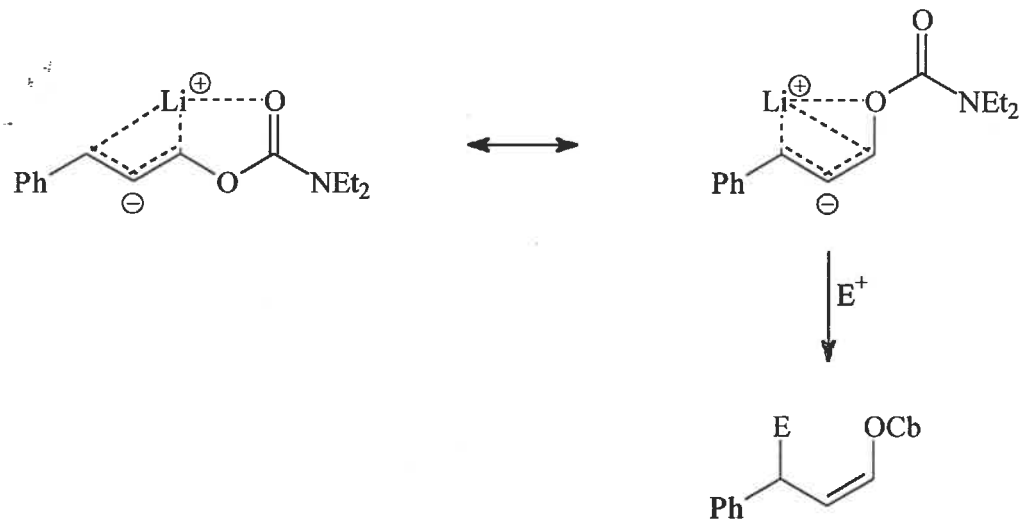


Figure 3

This coupling indicates that on reaction with the electrophile, the anion may be stabilised in the γ-position by the sp^3 hybridised carbamate oxygen (Scheme 61), leading to the observed *cis*-geometry, as is observed in the case of ether stabilised allylic anions.[37, 38]



Scheme 61

The α-substituted products have a *trans* double bond (Figure 4), based on a coupling constant of 15.9 Hz.

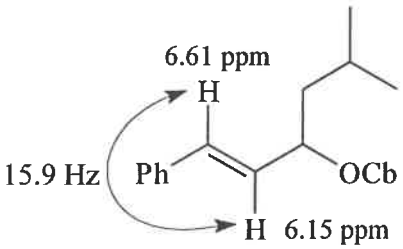
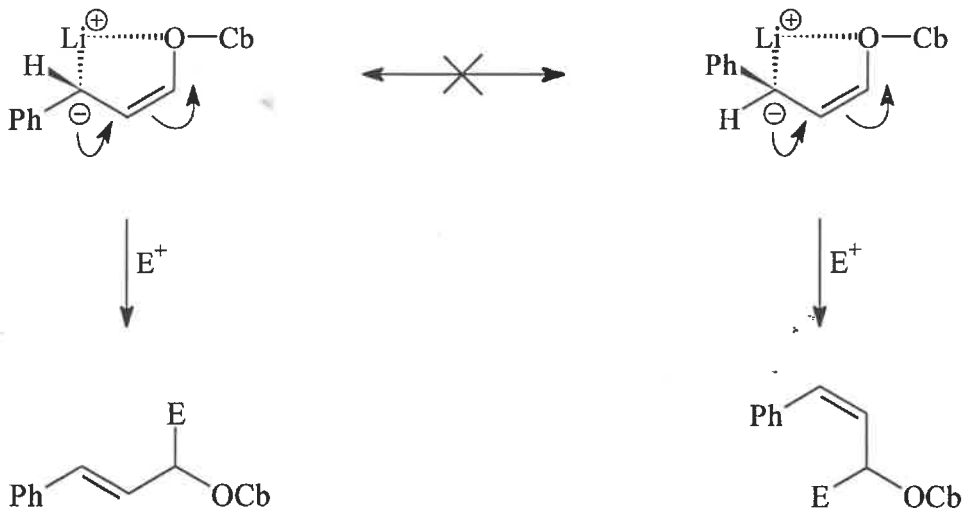


Figure 4

This indicates that only one of the two possible conformations of the stabilised γ-anion, which are "pseudo-diastereomers", exists (Scheme 62). The other conformation is disfavoured due to the decreased stabilisation and unfavourable steric interactions.

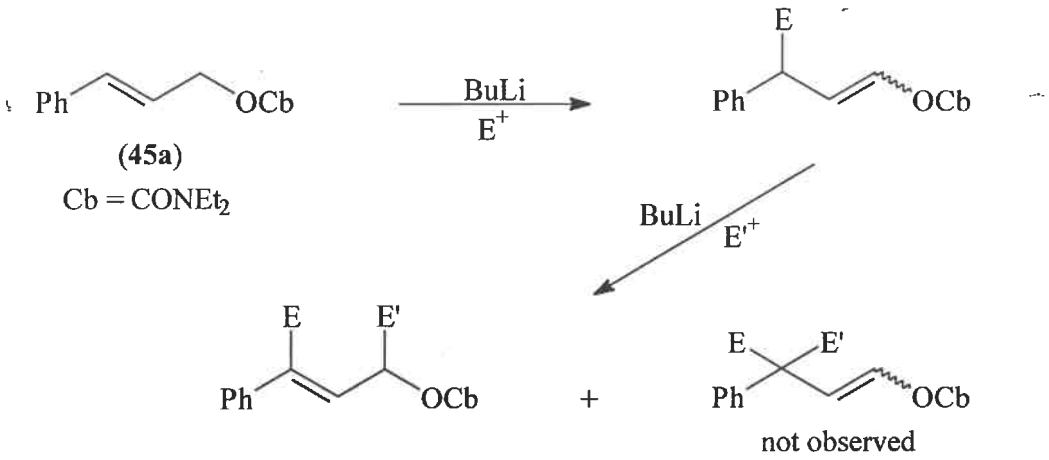


Scheme 62

2.3.3) Disubstitution Reactions of Cinnamyl Carbamates.

The work described thus far has been leading up to the disubstitution of cinnamyl carbamates, which will yield α,γ-disubstituted carbamates. The envisioned reaction

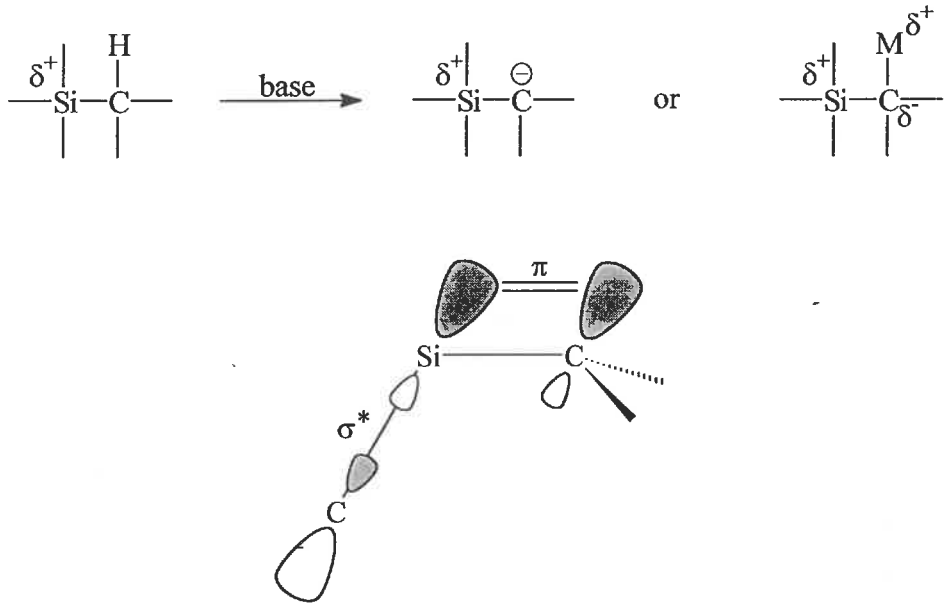
sequence, which is outlined in Scheme 63, involves the initial substitution at the γ-position, followed by a second substitution at the α-position. The second substitution could also occur at the γ-position, though this is unlikely, due to steric effects, which has been verified experimentally.



Scheme 63

The introduction of the first electrophile has been covered and is well documented in the literature (see Chapter 1), but for the purpose of the study involving the introduction of the second electrophile, we required the first group to be inert to butyllithium. We also felt that since the second anion would be generated α to the first electrophile, a group which could stabilise the second anion would enhance the reactivity.

A silyl group is an obvious choice, since a silyl group can stabilise an adjacent anion by orbital overlap with the d-orbitals on the silicon atom. More recent studies have, however, indicated that (n_c - σ^*_{SR}) charge transfer interactions of the carbon lone pair (anion) with the antibonding σ^* orbital of the adjacent anti-periplanar SR bond can contribute to carbanion stabilisation. The polarisation of the C - Si bond further enhances the stabilising effect of the overlap (Scheme 64).[99]



Scheme 64

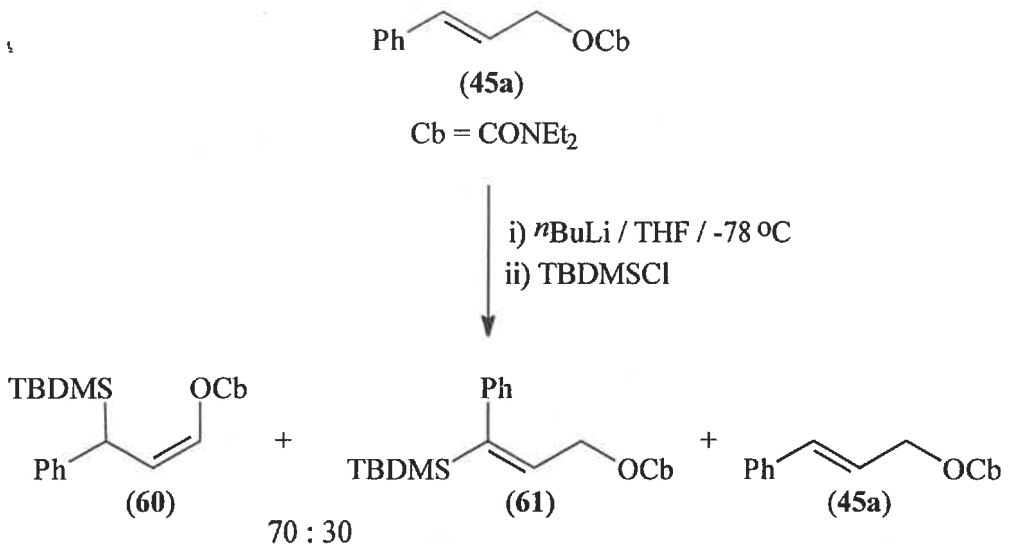
Additionally, the products will be vinyl silanes, which are synthetically useful, as is the allyl silane intermediate. The high reactivity of silyl halides is also an advantage. For the purpose of this investigation ^{t}butyldimethylsilyl chloride (TBDMSCl) and trimethylsilyl chloride (TMSCl) were used.

Since the introduction of the silyl group is central to the introduction of the second electrophile, a fairly detailed investigation into the silylation of cinnamyl carbamates was conducted.

2.3.3.1) Silylation of Cinnamyl Carbamates.

The initial silylation of the cinnamyl carbamates was thought to be fairly straight forward, much like the alkylations already discussed. At the onset, however, it became apparent that the reaction was more complicated than we had anticipated.

The first reaction that was attempted was the silylation of *N,N*-diethylcinnamyl carbamate (**45a**) using one equivalent of TBDMSCl and n-butyllithium. The required product (**60**) was obtained, but starting material (mixture of isomers, see Scheme 57) and the isomeric (β,γ-unsaturated) product (**61**) were also isolated (Scheme 65). The yield of the silylated product was also disappointingly low (30 % overall).



Scheme 65

Treatment of (**45a**) with two equivalents of n-butyllithium gave a mixture of (**60**) and (**61**) in 64 % yield with a ratio of 69 : 31. Changing the amount of butyllithium, rate of addition of the TBDMSCl, as well as the reaction solvent had some effect on the product distribution, but neither product could be prepared exclusively, as can be seen from Tables 5, 6, 7 and 8.

Table 5: Effect of the amount of base on the product ratio (THF).

	No. of Equiv. of n-Butyllithium	Ratio (60) : (61) (% Yield)
1	1	70 : 30 (30 %)
2	2	69 : 31 (64 %)
3	3[a]	67 : 33 (42 %)

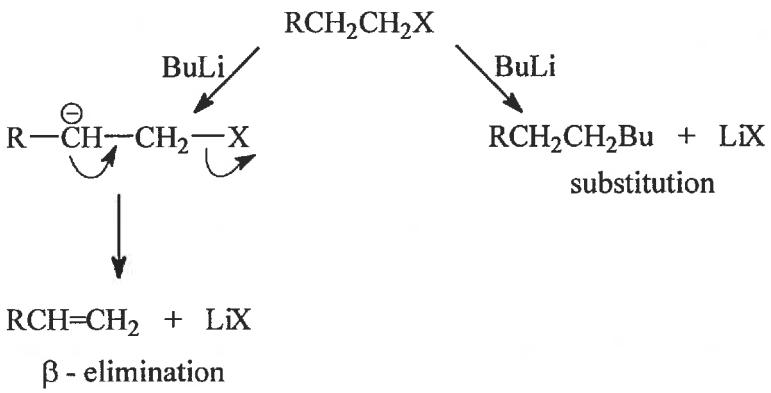
[a] Cleavage of carbamate also occurs.

When looking at these results, it appears that increasing the number of equivalents of n-butyllithium increases the proportion of (**61**). This is simply a coincidence, since the origin of the two isomers has nothing to do with the nature or the amount of base added. This will be discussed a little later in this section. The differences in product distribution are also too small to be considered significant. It is to be expected that excess free base (entry 3) will result in cleavage of the carbamate. At this stage it was interesting to note that two equivalents of *n*-butyllithium gave the optimum results, indicating that perhaps a dianion was involved.

Table 6: Effect of the rate of addition of TBDMSCl (THF, 2 equivalents of ^{n}BuLi, THF).

	Conditions	Ratio (60) : (61) (% Yield)
1	Add TBDMSCl before base	71 : 29 (66 %)
2	TBDMSCl added slowly after base	69 : 31 (64 %)
3	TBDMSCl added quickly after base	70 : 30 (63 %)

The rate and order of addition of the TBDMSCl also appears to have little, if any, effect on the yield and product ratio. Adding the TBDMSCl together with the carbamate starting material does, however, have the advantage of being more convenient than adding the TBDMSCl after the n-butyllithium. It must be remembered, however, that this approach does not apply to alkyl halide electrophiles, since they are either substituted by butyllithium or undergo a β-elimination reaction to afford an alkene (Scheme 66).



Scheme 66

Table 7: Effect of the solvent on the product distribution (2 eq. of ^{n}BuLi added to a mixture of carbamate and TBDMSCl).

	Solvent	Ratio (60) : (61) (% Yield)
1	THF	71 : 29 (66 %)
2	diethyl ether	- (0 %)[a]
3	diethyl ether / TMEDA (1.1 eq.)	65 : 35 (48 %)

[a] No reaction.

Clearly, tetrahydrofuran is the solvent of choice, but the fact that there is no reaction in diethyl ether is interesting. As will be shown later, the lack of reactivity in diethyl ether is limited to silyl halides. The carbamate is deprotonated in diethyl ether, which can be easily shown by quenching the anion with D_2O. The reaction is successful, although in lower yield, if a slight molar excess of TMEDA is added to the diethyl ether as a complexing agent. The TMEDA stabilises the metalated anion by further complexation of the lithium counterion (Figure 5).[54]

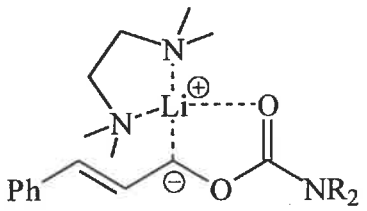


Figure 5

From these results one can assume that complexation of the anion by the solvent plays an important role in determining the reactivity towards silicon based electrophiles. The exact form and nature of this solvent effect is unknown, except to say that a stronger coordinating solvent, such as THF or TMEDA enhances the reactivity of the anion.

Table 8: Effect of the base on the product distribution (2 eq. of base added to a mixture of carbamate and TBDMSCl in THF).

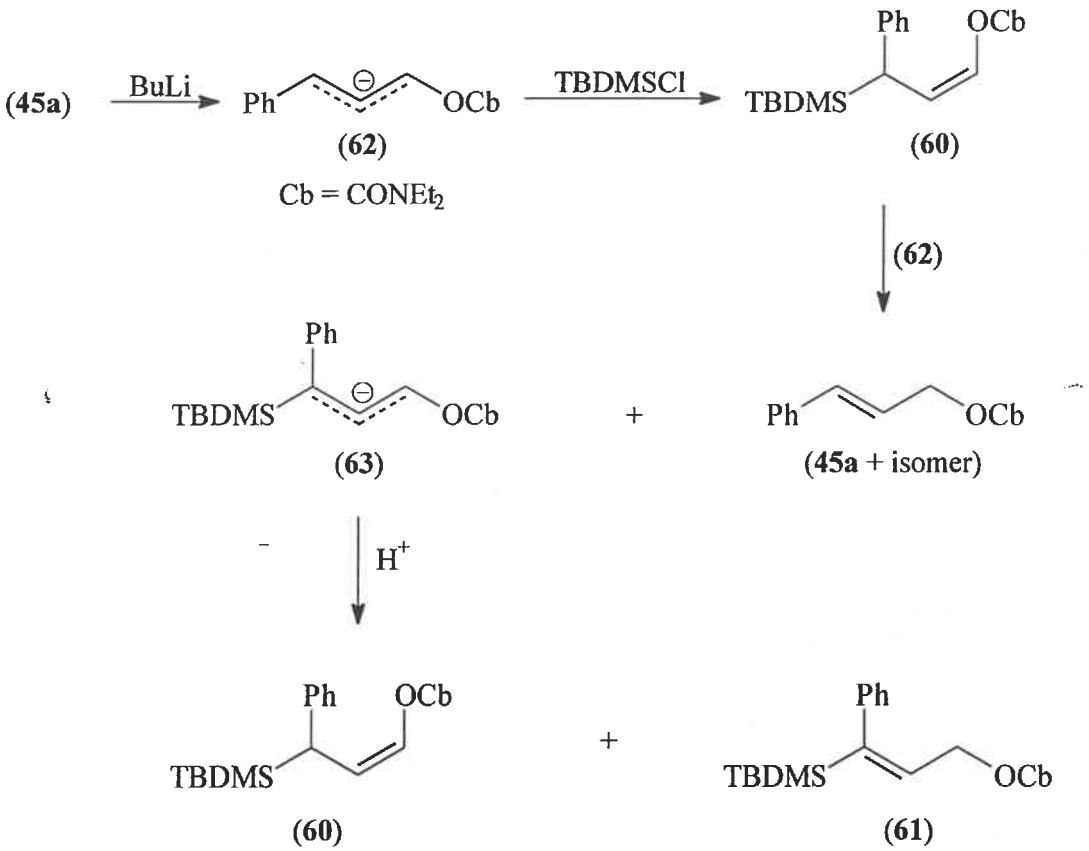
	Base	Ratio (60) : (61) (% Yield)
1	^{n}butyllithium	71 : 29 (66 %)
2	^{s}butyllithium	70 : 30 (67 %)
3	^{t}butyllithium	70 : 30 (61 %)
4	LDA	69 : 31 (65 %)

The effect of the base is slight, favouring n-butyllithium simply due to convenience and cost.

Based on these results, the best conditions for the preparation of the TBDMS carbamate is adding two equivalents of *n*-butyllithium to a 1 : 1 mixture of *N,N*-diethylcinnamyl carbamate and TBDMSCl in THF at -78 °C. These conditions were found to be optimum for other carbamates and TMSCl, except where otherwise noted.

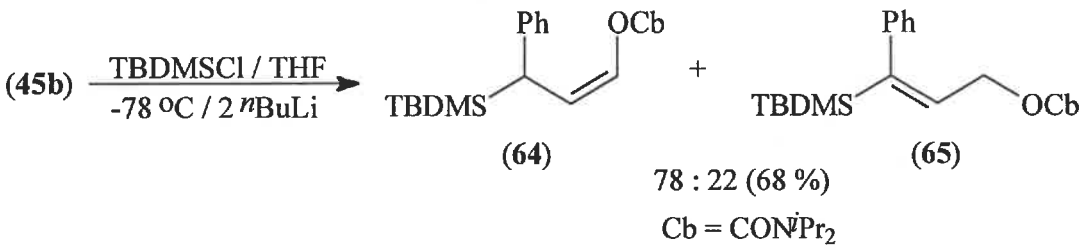
2.3.3.2) Mechanism of the Silylation of Cinnamyl Carbamates.

The reason for the mixture of products is that the proton on the silyl carbamate (**60**) (Scheme 67) is more acidic than the proton on the starting material (**45a**). Due to this, a proton exchange occurs, giving the silylated anion (**63**) which, on quenching, gives a mixture of (**60**) and (**61**) in a similar ratio to that observed in the studies involving the protonation of the carbamate anions (Scheme 57). Both isomers of the starting material, which is regenerated by proton transfer, are observed, although the α,β-unsaturated carbamate is only observed in trace quantities. This α,β-unsaturated isomer may, however, simply be a result of quenching unreacted starting material. The sequence of steps in the reaction are shown in Scheme 67.



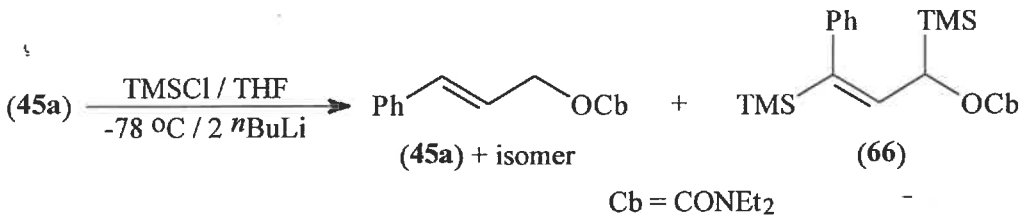
Scheme 67

Using two equivalents of butyllithium ensures complete formation of the second anion (**63**). The two isomers (**60**) and (**61**) can be separated by column chromatography, but both react with a second electrophile to give the same α,γ-disubstituted product (due to the delocalised anion (**63**)), so separation is not necessary. Reaction of the corresponding N,N-diisopropylcinnamyl carbamate gives a product mixture with a 78 : 22 ratio in 68 % yield (Scheme 68).



Scheme 68

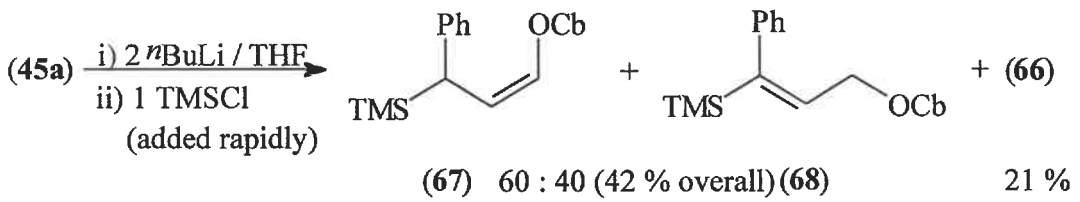
It seemed reasonable to assume that the same would occur using TMSCl, but again something unexpected happened, which in retrospect may have been anticipated. On treatment of the *N,N*-diethylcinnamyl carbamate with two equivalents of n-butyllithium and one equivalent of TMSCl, roughly equimolar amounts of starting material and the bis-TMS compound (**66**) (42 %) were isolated (Scheme 69).



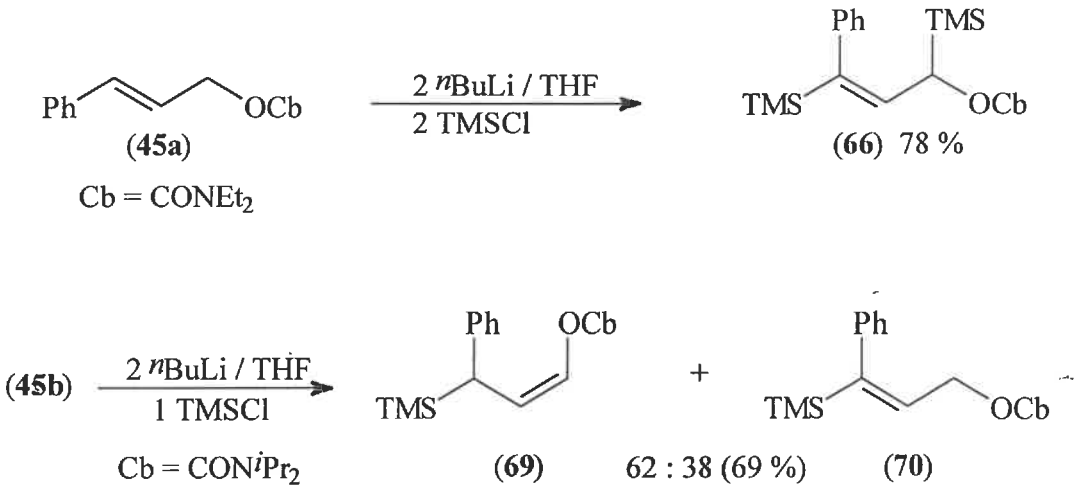
Scheme 69

The mechanism for this reaction is essentially the same as that described previously in Scheme 67, but in that case the TBDMSCl was too bulky to allow a second substitution on anion (**63**). In this case, however, the TMSCl is small enough to react with anion (**63**), giving the bis-TMS product (**66**).

Using two equivalents of TMSCl gave (**66**) in 78 % yield. Rapid quenching of the reaction with one equivalent of TMSCl gave a mixture of isomers of the mono-TMS compound in 42 % yield ($\gamma : \alpha = 60 : 40$) and the bis-TMS product (21 %). The *N,N*-diisopropylcinnamyl carbamate gave only the mono-TMS products, due to the increased steric bulk of the *N,N*-diisopropyl group (Scheme 70).



Scheme 70 (continued on next page)

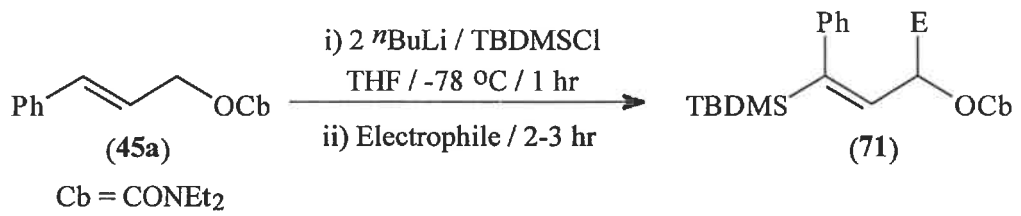


Scheme 70

The conditions given (*n*-butyllithium, THF, -78 °C) were found to be the optimum conditions for preparing the silyl carbamates. The results of the optimisation study are not given, since they are predictable, based on previous results.

2.3.3.3) One-Pot Disubstitution Reactions.

Since it was found that one needs two equivalents of n-butyllithium to prepare the silyl carbamate intermediate, it was thought that disubstitution could simply be effected by quenching the reaction with the second electrophile (Scheme 71).



Electrophile = MeI, EtI, TMSCl, PhCOCl and piperonal.

Scheme 71

These initial studies were successful, but the yields were very low. The main problem with the one-pot reactions, however, is that many by-products are formed, making purification difficult. The results are shown in Table 9.

Table 9: Results of one-pot disubstitution reactions.

(71)	Electrophile	% Yield
a	MeI	63
b	EtI	48
c	TMSCl	0[a]
d	PhCOCl	12
e	Piperonal	-[b]

[a] No reaction.
[b] Complex mixture of products.

From previous experience with the silylation of the cinnamyl carbamates, it was thought that the by-products that are formed during the silylation step (cleavage of the carbamate) and during the introduction of the second electrophile just compounds the problem. The obvious solution is simply to carry out the reaction as a two-pot preparation, where one isolates and purifies the silyl intermediate first.

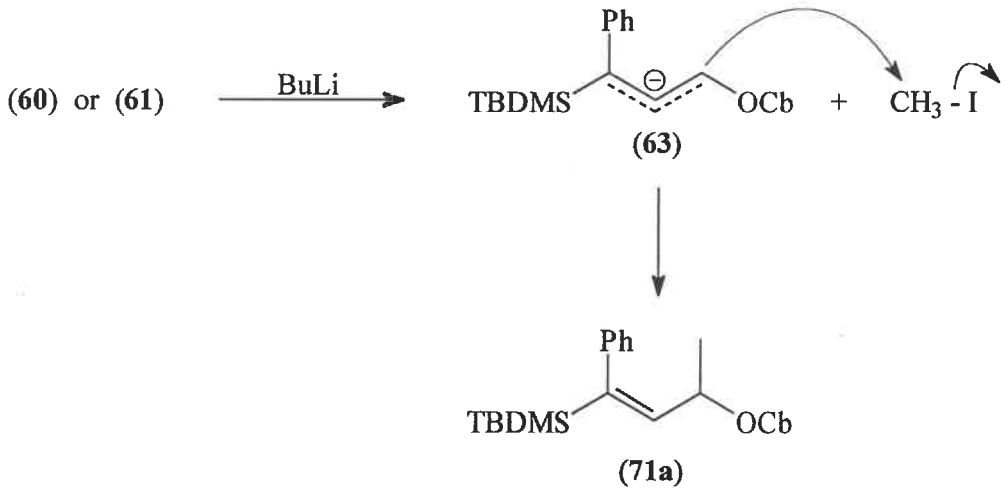
2.3.3.4) Two-Pot Disubstitution Reactions.

The first problem encountered was the fact that the silyl carbamate was a mixture of isomers, so separation was necessary to determine their individual reactivity. Since the separation is fairly tedious, reaction with a mixture of isomers was also undertaken. The results are shown in Table 10 for the reaction of (**60**), (**61**) and a mixture of the two isomers (70 : 30) with methyl iodide in THF.

Table 10: Reaction of (**60**) and (**61**) with Methyl Iodide.

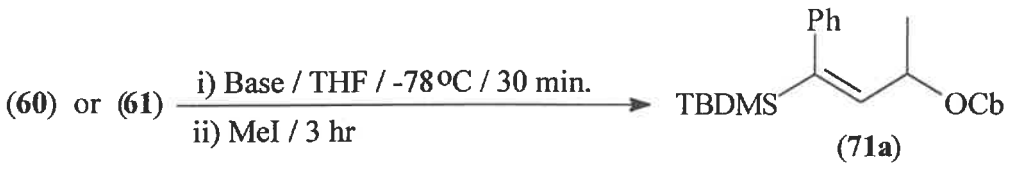
	Substrate	% Yield
1	(**60**)	86
2	(**61**)	78
3	(**60** + **61**) : (70 : 30)	84

Clearly, it makes no difference which isomer is used. This is because both isomers are deprotonated to give the same delocalised anion intermediate (**63**), which reacts at the less hindered α-position to give (**71a**) (Scheme 72). For this reason separation of the isomers is not necessary and all further studies were carried out on a mixture of the isomers.



Scheme 72

Reaction in different solvents, such as diethyl ether and diethyl ether / TMEDA had no discernable effect on the reaction yield. The nature of the base did, however, affect the yield. This is because the acidic proton on (**60**) is more hindered than the proton on (**61**), so abstraction by bulkier bases, such as *t*-butyllithium and LDA is more difficult, which has an adverse effect on the yield (Table 11, Scheme 73).



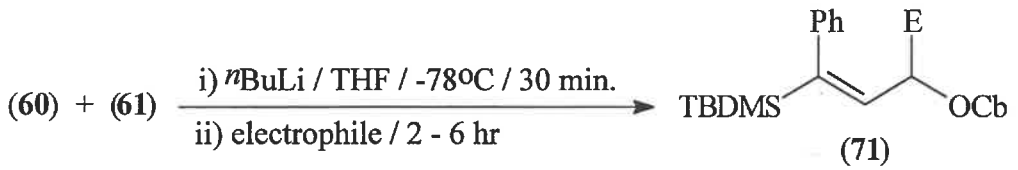
Scheme 73

Table 11: Effect of the base on the substitution of **(60)** and **(61)**.

	Substrate	Base	% Yield
1	**(60)**	n-BuLi	78
2	**(60)**	t-BuLi	75
3	**(60)**	LDA	69
4	**(61)**	n-BuLi	86
5	**(61)**	t-BuLi	85
6	**(61)**	LDA	79

Obviously, *n*-butyllithium was chosen for further studies since the other bases gave lower yields (although it is very slight), and *n*-butyllithium is more convenient to use.

The two-pot disubstitution reactions were simply carried out by treating a mixture of the silylated carbamates **(60)** and **(61)** with n-butyllithium in THF at -78 °C and then quenching the anion after 30 minutes with the appropriate electrophile (Scheme 74, Table 12).



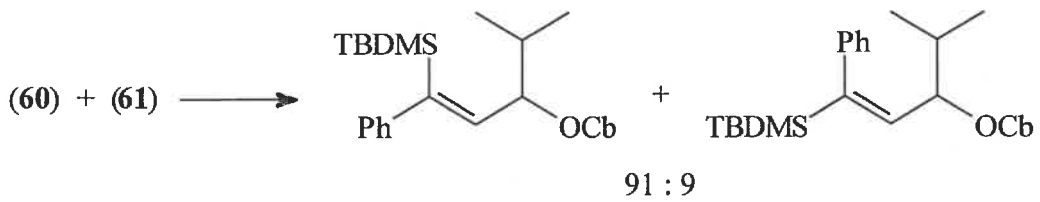
Scheme 74

Table 12: Results of the two-pot disubstitution reactions.

(71)	Electrophile	% Yield
a	MeI	89
b	EtI	81
c	TMSCl	0[a]
d	PhCOCl	64
e	Piperonal	-[b]
f	2-Bromopropane	45
g	iso-Butyl bromide	0[a]
h	Octyl bromide	19
i	Ethyl chloroformate	74
j	Benzophenone	0[a]
k	Allyl bromide	79

[a] No reaction.
[b] Complex mixture of products.

Again, the steric bulk of the electrophile plays an important role in the reaction, as can be seen from the entries relating to the addition of the alkyl halides (a, b, f, g, h and k). The bulky electrophiles, TMSCl, isobutyl bromide and benzophenone did not react due to their steric bulk. Acid chlorides and chloroformates, due to their high reactivity and sp^2 hybridisation, are particularly reactive. The high reactivity of allyl bromide may be due to the fact that it can undergo S_N2' as well as S_N2 substitution. The reaction of 2-bromopropane was particularly interesting because the major product was the (*Z*)-isomer (Scheme 75).



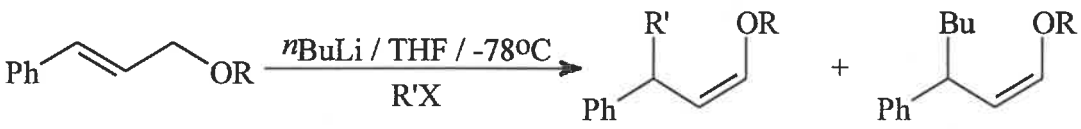
Scheme 75

2.4) Electrophilic Substitution of Cinnamyl Ethers.

A study was undertaken to investigate the analogous reactions using cinnamyl ethers, to determine whether or not there was any advantage in using carbamates. As previously mentioned, the methyl and ethyl ethers of cinnamyl alcohol were used since they are readily available, the preparation of which is described in Section 2.2. Simple allyl ethers are too volatile to be synthetically useful, so this fact alone precludes their use, in favour of allyl carbamates.

2.4.1) Reaction of Cinnamyl Ethers with Alkyl Halides.

The first reactions attempted were reactions of cinnamyl ether anions with alkyl halides. For this purpose methyl iodide and allyl bromide were chosen. Investigation of a wide range of alkyl halides was not necessary since a simple comparison was all that was required, besides which we were more interested in the silylation and di-substitution reactions of the cinnamyl ethers. Based on the results obtained during the study involving cinnamyl carbamates, *n*-butyllithium was the obvious choice of base for the deprotonation of the cinnamyl ethers. When the reactions were carried out, however, an inseparable mixture of the desired product and the *n*-butyl substituted ether was obtained. The source of the butyl group is the *n*-butyllithium (Scheme 76).



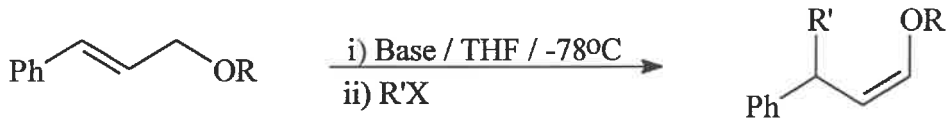
Scheme 76

The mechanism of this reaction is unclear and at first was thought to involve some kind of exchange with the alkyl halide to give a butyl halide (Scheme 77).

Scheme 77

The problem with this mechanism, however, is that it is independent of the cinnamyl ether, so one would expect the same reaction to have occurred in the case of the cinnamyl carbamates, which was not the case. Also, the amount of butyl substituted product that formed exceeded the amount of *n*-butyllithium left after deprotonation of the cinnamyl ether, which also rules out the exchange reaction. No support or evidence could be found for the substitution of an alkyl group.

Reaction of other alkyllithiums also gave the "exchange product" to some extent, and the only way to eliminate the formation of this undesirable side-product was to use LDA as the base (Scheme 78, Table 13).



R = Me : **46a**
R = Et : **46b**

R = Me, R' = Me : **72a**
R = Me, R' = $CH_2CH{=}CH_2$: **72b**
R = Et, R' = Me : **72c**
R = Et, R' = $CH_2CH{=}CH_2$: **72d**

Scheme 78

Table 13: Effect of different bases on the reaction between cinnamyl ethers and alkyl halides (continued on next page).

	Substrate	Base	Electrophile	Product	% Yield (72)[b]
1	**46a**	^{n}BuLi	MeI	**72a**	39[a]
2	**46a**	^{s}BuLi	MeI	**72a**	45[a]
3	**46a**	^{t}BuLi	MeI	**72a**	57[a]
4	**46a**	MeLi	MeI	**72a**	81
5	**46a**	LDA	MeI	**72a**	88
6	**46a**	^{n}BuLi	Allyl-Br	**72b**	38[a]
7	**46a**	^{s}BuLi	Allyl-Br	**72b**	42[a]
8	**46a**	^{t}BuLi	Allyl-Br	**72b**	52[a]
9	**46a**	MeLi	Allyl-Br	**72b**	27[a]

	Substrate	Base	Electrophile	Product	% Yield (72)[b]
10	**46a**	LDA	Allyl-Br	**72b**	91
11	**46b**	^{n}BuLi	MeI	**72c**	45[a]
12	**46b**	^{s}BuLi	MeI	**72c**	44[a]
13	**46b**	^{t}BuLi	MeI	**72c**	59[a]
14	**46b**	MeLi	MeI	**72c**	83
15	**46b**	LDA	MeI	**72c**	86
16	**46b**	^{n}BuLi	Allyl-Br	**72d**	46[a]
17	**46b**	^{s}BuLi	Allyl-Br	**72d**	48[a]
18	**46b**	^{t}BuLi	Allyl-Br	**72d**	61[a]
19	**46b**	MeLi	Allyl-Br	**72d**	37[a]
20	**46b**	LDA	Allyl-Br	**72d**	85

[a] "Exchange product" formed as well.

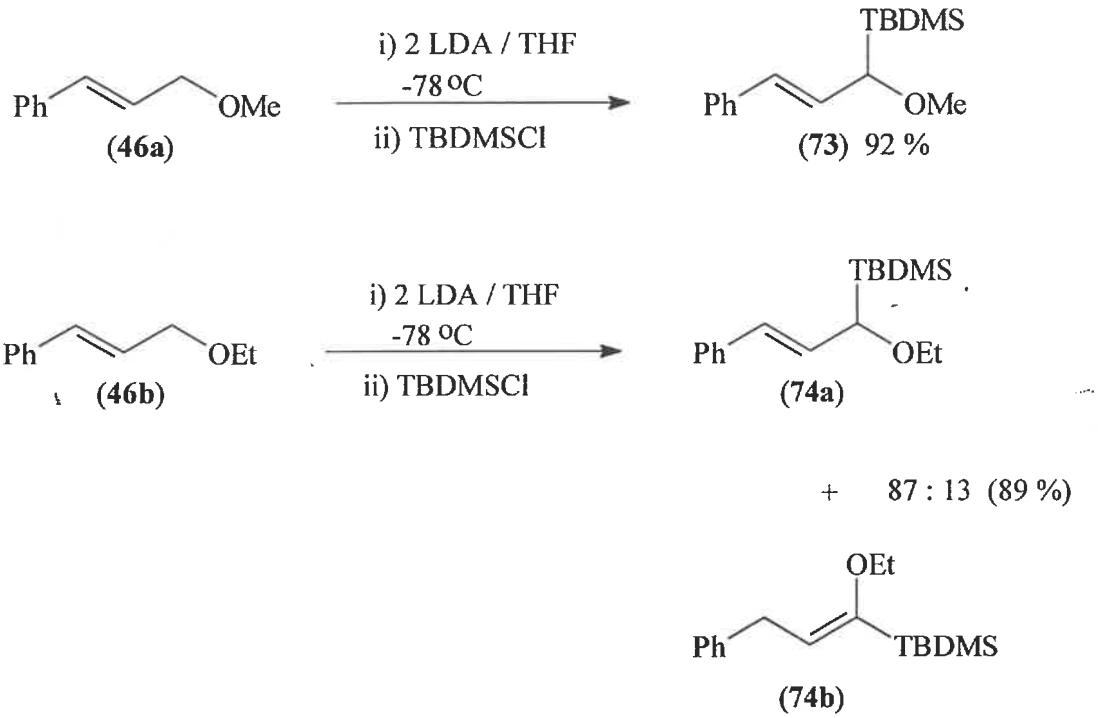
[b] Determined by H-NMR from a mixture of product and "exchange product".

Based on these results, cinnamyl carbamates are clearly superior due to the problems encountered using alkyllithiums. Obviously, using methyllithium when the electrophile is methyl iodide is acceptable since the "exchange product" product is the same as the desired product. The yields were also found to be lower in diethyl ether and diethyl ether / TMEDA by about 10 %.

2.4.2) Reaction of Cinnamyl Ethers with Silyl Halides.

It is in the reaction with silyl halides that one observes the greatest difference in reactivity between cinnamyl ethers and cinnamyl carbamates. It was anticipated that the same reactivity would be observed as was found with cinnamyl carbamates, except for the problem using alkyllithiums.

Reaction of the methyl and ethyl cinnamyl ethers with two equivalents of LDA and one equivalent of TBDMSCl gave exclusively the α-substituted products, and only the ethyl ether gave a mixture of isomers, which is the result of a second deprotonation (Scheme 79).



Scheme 79

The fact that only α-substitution occurred was very surprising, considering that the cinnamyl carbamates gave exclusively the γ-products. This could be attributed to the different mode of stabilisation of the allylic anion. The yields obtained with the ethers are also considerably higher than the yields obtained with the cinnamyl carbamates.

Since only the ethyl cinnamyl ether gave the isomeric product (**74b**), we felt that abstraction of the proton α to the silyl group may also be more difficult. Again, this is most likely due to the different stabilisation that occurs in the case of the ethers. Steric effects may also play a role, but the fact that the methyl ether is totally inert to a second deprotonation (shown by attempted deuterium labelling) seems to contradict this. There is no reaction in diethyl ether, as was the case with the corresponding carbamates.

The fact that silyl halides are essentially inert to alkyllithiums, under the reaction conditions employed, prompted us to investigate the deprotonation with alkyllithiums as well as LDA. This time, no "exchange product" was observed and *n*-butyllithium,

s-butyllithium and *t*-butyllithium all gave similar yields to LDA. This observation simply clouds the issue even more, because it seems to indicate an interaction between the alkyl halide and the alkyllithium; a possibility that was previously discarded. The results using different bases are shown in Table 14.

Table 14: Results of silylation of cinnamyl ethers using different bases.

Substrate	Base	Product	% Yield	Ratio (α,β-unsat : β,γ-unsat)
46a	^{n}BuLi	73	93	0 : 100
46a	^{s}BuLi	73	90	0 : 100
46a	^{t}BuLi	73	91	0 : 100
46b	^{n}BuLi	74	94	25 : 75
46b	^{s}BuLi	74	90	15 : 85
46b	^{t}BuLi	74	89	4 : 96

This study highlighted another interesting difference between the reactivity of the cinnamyl ethers and the cinnamyl carbamates. The isomer product ratio obtained in the case of the carbamates was essentially independent of the nature of the base (Table 8). In the case of the ethers, however, the bulkier bases result in a dramatic decrease in the amount of the isomeric product obtained.

The reason for using two equivalents of base in the first place was to counteract the tendency of the silylated product to undergo a proton exchange with the primary anion (Scheme 67). In the case of the ethers, however, the bulk of the primary anion may be too great to deprotonate the silylated product. The other possibility, of course, is simply that quenching the second anion favours the β,γ-unsaturated product.

Carrying out the reaction using a single equivalent of base clarified the situation. It was found that a single equivalent of base was all that was necessary (Table 15). Both the methyl and the ethyl cinnamyl ethers gave only the β,γ-unsaturated product with one equivalent of base.

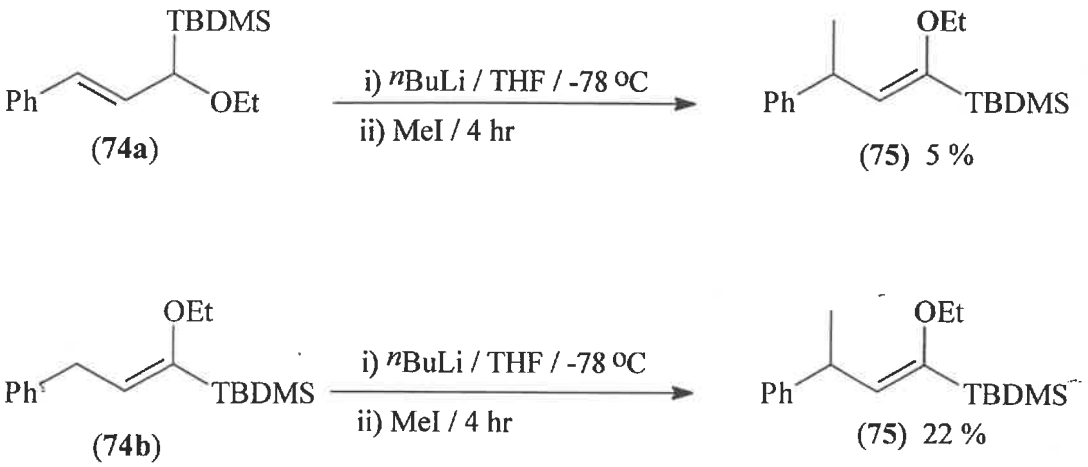
Table 15: Reaction with one equivalent of base.

Substrate	Base	Product	% Yield
46a	^{n}BuLi	73	95
46a	^{s}BuLi	73	92
46a	^{t}BuLi	73	90
46b	^{n}BuLi	74a	93
46b	^{s}BuLi	74a	93
46b	^{t}BuLi	74a	91

We now turned our attention to preparing TMS substituted ethers, since we felt that the bulk of the TBDMS group may have an adverse effect on the susceptibility of the ether to a second deprotonation, which is critical to the disubstitution reactions. Unfortunately, all reactions attempted using TMSCl failed, with only traces of the desired products being detected by GC\MS.

2.4.3) Disubstitution Reactions.

Based on our results from the silylation of the cinnamyl ethers, we felt that disubstitution reactions would not be possible. This was found to be the case with the TBDMS substituted methyl cinnamyl ether, which was unreactive under all conditions tried. The silylated ethyl cinnamyl ethers did react with methyl iodide to give the disubstituted product, although in very low yield (Scheme 80). The α,β-unsaturated silyl ether gave the higher yield, most probably due to the less hindered allylic proton.



Scheme 80

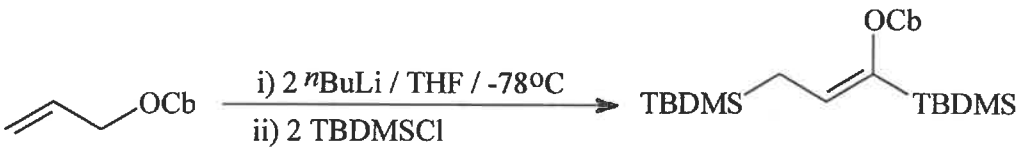
Other, more hindered bases (*s*-butyllithium, *t*-butyllithium and LDA), gave even lower yields, as is to be expected. Reactions with all other electrophiles (alkyl halides, acid chlorides, aldehydes, ketones and esters) were unsuccessful.

2.4.4) Conclusions.

These results clearly indicate that carbamates offer the more attractive solution as regards α-metalation reactions when it comes to both mono- and disubstitution reactions. The exclusive α-silylation of cinnamyl ethers is useful, however, since carbamates give the γ-product. Reaction of allyl ethers and carbamates have been extensively studied by other workers (see Chapter 1), with the general consensus being that carbamates give superior γ-selectivity in most instances.

2.5) Electrophilic Substitution of Allyl Carbamates.

The possibility of disubstitution of the simple allyl carbamates, 1-*N,N*-diethylcarbamoyloxyprop-2-ene **(49a)**, 1-*N,N*-diisopropylcarbamoyloxyprop-2-ene **(49b)** and 1-*N*-^{t}butylcarbamoyloxyprop-2-ene **(49c)** was investigated. None of the silylation reactions investigated gave significant yields, with a multitude of inseparable products being typical. Considerable time and effort was expended investigating these system, but only the bis-TBDMS carbamate **(76)** was obtained in reasonable yield (Scheme 81). The mechanism is essentially the same as that described for the formation of the bis-TMS cinnamyl carbamate (Section 2.3.3).

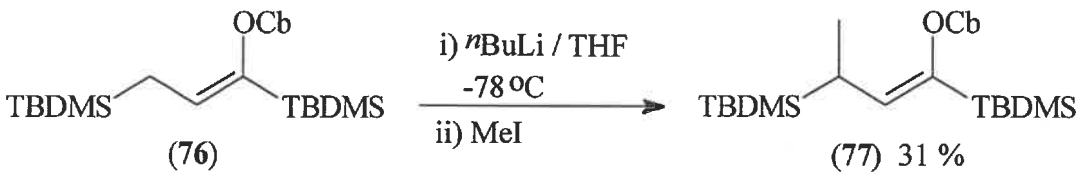


(49a) **(76)** 39 %

Cb = $CONEt_2$

Scheme 81

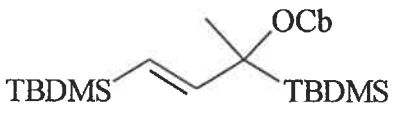
Treatment of **(76)** with *n*-butyllithium and methyl iodide afforded the methyl substituted product **(77)** in 31 % yield (Scheme 82).



(76) **(77)** 31 %

Scheme 82

In this case no double bond migration occurred, due to steric constraints. Migration of the double bond would result in the hindered quaternary product **(78)**.



(78)

2.5.1) Conclusions.

These results, and numerous other reactions that were attempted, are poor, so these studies were discontinued.

2.6) Reaction of Silyl Substituted Carbamates with Michael Acceptors.

One of the reasons for studying the bis-substitution of cinnamyl carbamates was to investigate the possibility of preparing oudemansin derivatives, which are potentially useful as antifungal agrochemicals (to be discussed in a later section). Towards this end we were interested in the possibility of 1,4-addition of silyl substituted carbamates to α,β-unsaturated carbonyl compounds.

Silicon, due to its electropositive nature, can coordinate to a carbonyl group (behave as a Lewis acid).[100 - 103] We hoped that the TBDMS group on the cinnamyl carbamate would coordinate with the carbonyl group of the α,β-unsaturated carbonyl compound electrophile, thereby promoting conjugate addition (Figure 6).

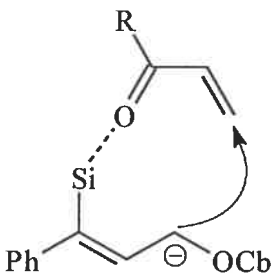
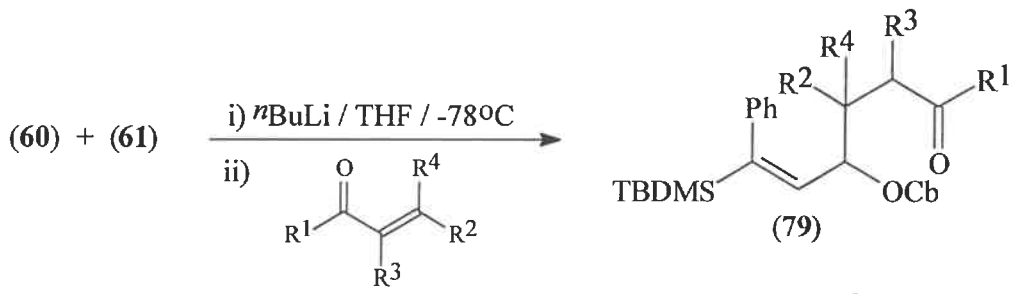


Figure 6

The reaction of silyl carbamates (**60**) and (**61**) with various α,β-unsaturated carbonyl compounds was investigated (Scheme 83, Table 16).



Scheme 83

Table 16: Reaction of (**60**) and (**61**) with α,β-unsaturated carbonyl compounds.

(79)	R^1	R^2	R^3	R^4	% Yield (1,4)	% Yield (1,2)	1,4 : 1,2
a	MeO	H	H	H	63	0	100 : 0
b	CH_2CH_2		H	H	0	0	-
c	$CH_2CH_2CH_2$		H	H	71	0	100 : 0
d	MeO	H	Me	H	0	56[a]	0 : 100
e	MeO	Me	H	H	0[b]	0[b]	-
f	MeO	Me	H	Me	0[b]	0[b]	-
g	EtO	Ph	H	H	0	0	-

[a] Mixture of (*E*) and (*Z*) isomers.
[b] Complex mixture of products.

Only methyl acrylate gave the desired 1,4-addition product (entry a) out of the non-cyclic α,β-unsaturated carbonyl compounds, while methyl crotonate and methyl 3-methylbut-2-enoate gave complex mixtures of products. Methyl methacrylate gave only the 1,2-addition product (entry d) and ethyl cinnamate was unreactive.

2.6.1) Conclusions.

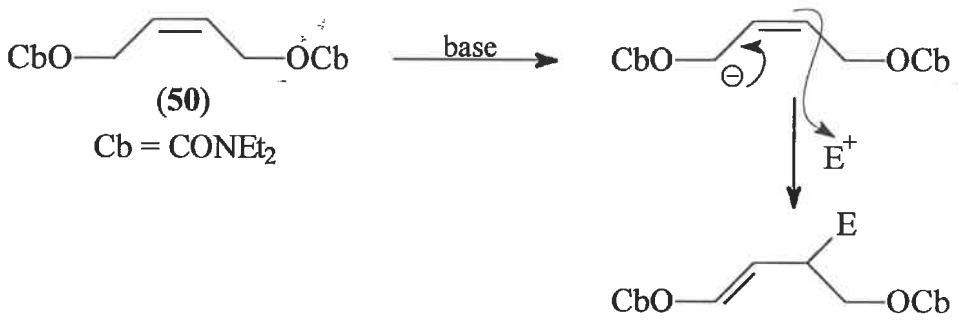
These results were very disappointing, especially the reaction of methyl crotonate, which was required for the preparation of oudemansin derivatives. From these results it can be concluded that a substituent in the β-position prevents 1,4-addition, as might be expected. The 1,4-addition to cyclohexenone (Table 16, entry c) was surprising,

since ketones usually favour 1,2-addition. Cyclopentenone (Table 16, entry b), on the other hand, was unreactive. Phenylvinylsulfone and phenylvinylsulfoxide were also unreactive.

The reaction of silylated cinnamyl carbamate anions with cyclic α,β-unsaturated carbonyl compounds, while useful in the case of methyl acrylate and cyclohexenone, fails with other electrophiles and is therefore of limited synthetic utility.

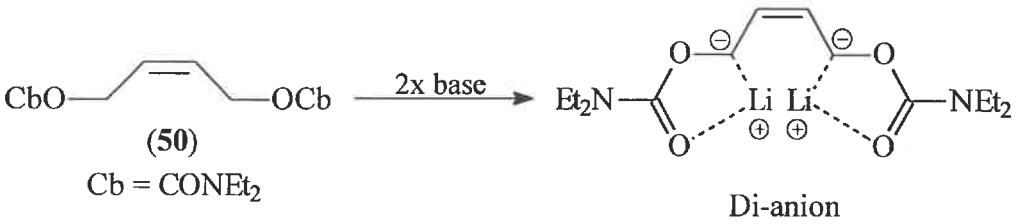
2.7) Reactivity of (*Z*)-1,4-bis(*N*,*N*-diethylcarbamoyloxy)-but-2-ene.

Based on the stabilising effect of the carbamoyl group, we decided to investigate whether or not a second carbamate group would afford better anion stabilisation. As a model system, (*Z*)-1,4-bis(*N*,*N*-diethylcarbamoyloxy)but-2-ene (**50**) (see Section 2.2) was prepared. It was envisioned that (**50**) would react in a similar manner to other allylic carbamates, in that the allylic anion would react with electrophiles in the γ-position, as shown in Scheme 84.



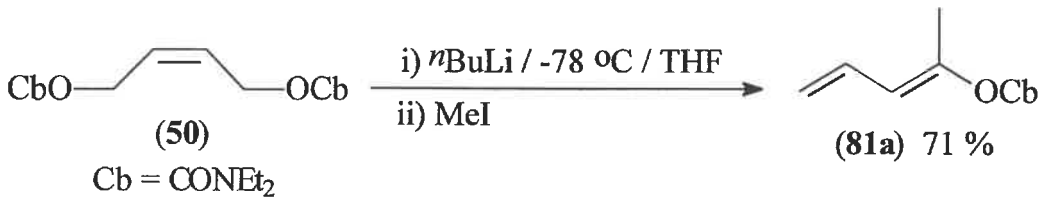
Scheme 84

We also thought that it may be possible to form a dianion using two equivalents of base (Scheme 85).



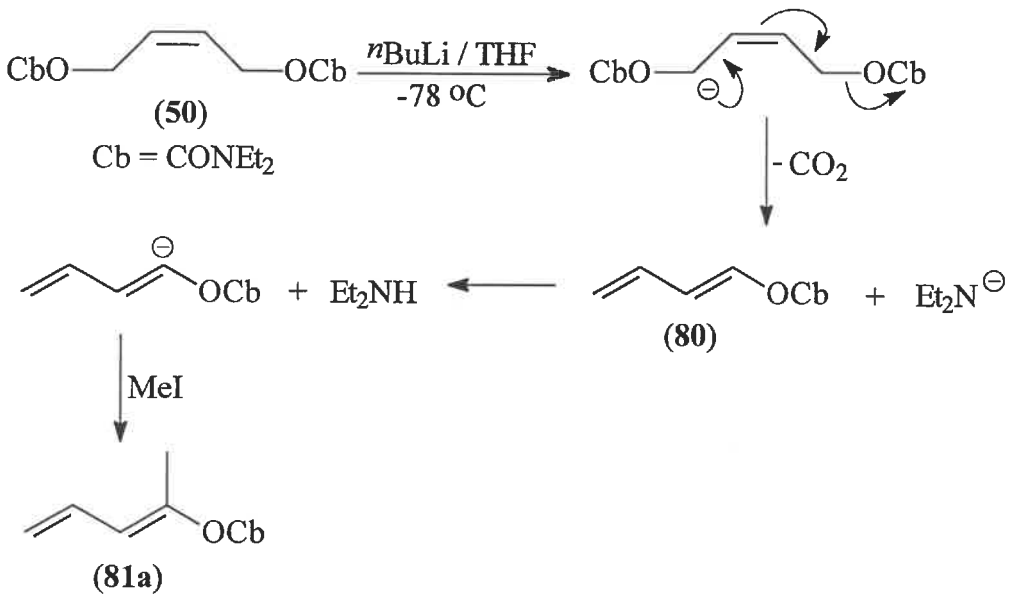
Scheme 85

It was found, however, that on reaction with methyl iodide, (*E,E*)-2-*N,N*-diethylcarbamoyloxy-2,4-pentadiene (**81a**) was isolated in good yield (Scheme 86), and none of the expected product (Scheme 84) was observed.



Scheme 86

The only way in which this product could be accounted for was the initial elimination of one of the carbamate groups, which then decarboxylates to yield the strong base lithium *N,N*-diethylamide. Abstraction of the α-vinyl proton on diene (**80**) leads to the observed methyl substituted diene (**81**), as outlined in Scheme 87.

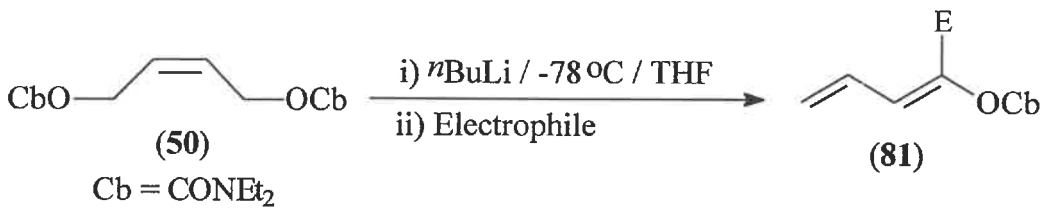


Scheme 87

Treatment of (**50**) with two equivalents of n-butyllithium and methyl iodide also results in the same product, and not the product from the expected dianion, indicating that the elimination of the carbamate group is rapid. This reaction is very similar to the work reported by Snieckus[83-85] and Percy[86-88] (see Section 1.5.4).

2.7.1) One-Pot Preparation of 1-Substituted (E,E)-1-N,N-Diethylcarbamoyloxy-1,3-butadienes.

Treatment of (*Z*)-1,4-bis(*N,N*-diethylcarbamoyloxy)but-2-ene (**50**) with one equivalent of *n*-butyllithium for 60 minutes in THF at -78 °C, followed by the addition of one equivalent of electrophile yielded 1-substituted (*E,E*)-1-*N,N*-diethylcarbamoyloxy-1,3-butadienes in low to moderate yield (Scheme 88, Table 17).



Scheme 88

Table 17: Yields of one-pot reactions.

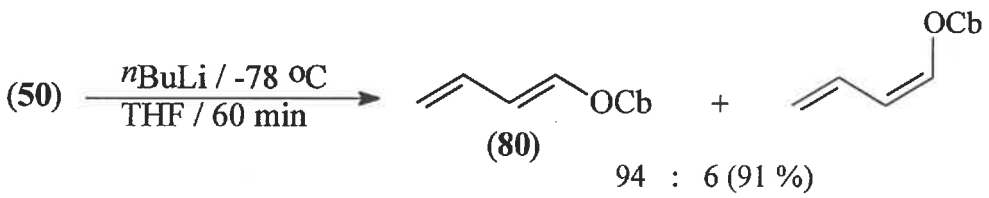
(81)	Electrophile	% Yield
a	MeI	71
b	EtI	0[a]
c	2-bromopropane	0[a]
d	octyl bromide	0[a]
e	TMSCl	45
f	TBDMSCl	0[a]
g	PhCOCl	33
h	$PhCO_2Et$	0[a]

[a] No reaction.

As can be seen from these results, most electrophiles were unreactive, which was especially surprising in the case of the alkyl halides. For this reason it was decided to use a two-pot procedure, with the isolation of the unsubstituted diene (**80**).

2.7.2) Two-Pot Preparation of 1-Substituted (E,E)-1-N,N-Diethylcarbamoyloxy-1,3-butadienes.

(*E,E*)-1-*N,N*-Diethylcarbamoyloxy-1,3-butadiene (**80**) was easily prepared on a multigram scale in 91 % yield by treating (**50**) with a slight excess of *n*-butyllithium in THF at -78 °C and distilling the crude product after workup (Scheme 89).



Scheme 89

The major product is the (*E,E*)-isomer, with 6 % of the (*Z,E*) isomer. The use of other bases and solvents had no appreciable effect on the reaction time and yield.

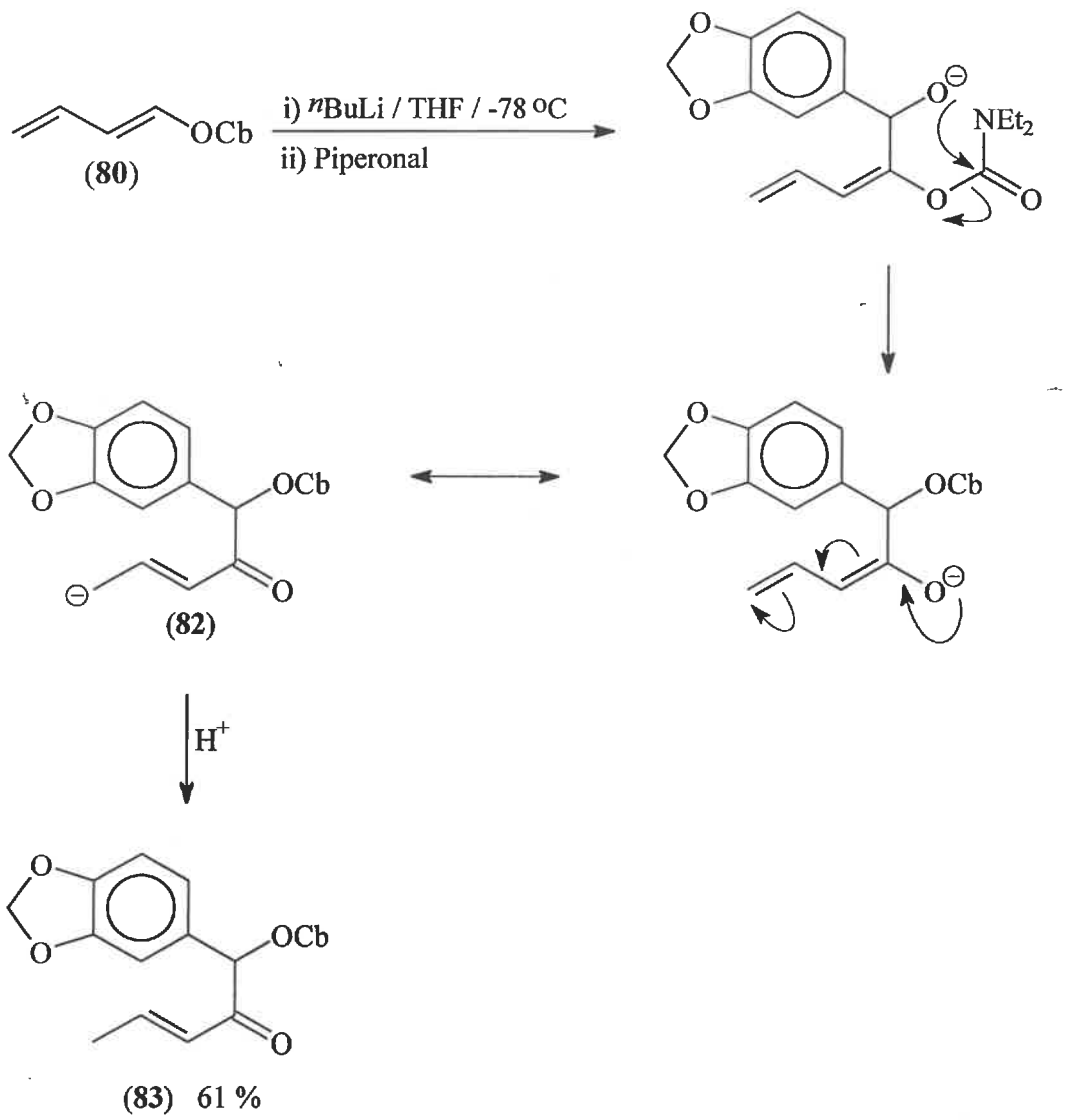
Treatment of diene (**80**) with a slight excess of n-butyllithium, followed by an electrophile gave fair to good yields of some products, but again all alkyl halides except for methyl iodide failed to react. TMSCl reacted readily, but TBDMSCl was too bulky. Benzyl bromide, allyl bromide, benzaldehyde and benzophenone all gave complex reaction mixtures. Acid chlorides, chloroformates and carbamoyl chlorides do, however, give reasonable yields (Table 18).

Table 18: Yields of two-pot reactions.

(81)	Electrophile	% Yield
a	MeI	85
b	EtI	0[a]
c	2-bromopropane	0[a]
d	octyl bromide	0[a]
e	TMSCl	69
f	TBDMSCl	0[a]
g	PhCOCl	55
h	$PhCO_2Et$	0[a]
i	allyl chloroformate	61
j	ethyl chloroformate	58
k	*N,N*-diethylcarbamoyl chloride	43
l	benzyl bromide	0[b]
m	allyl bromide	0[b]
n	benzaldehyde	0[b]
o	benzophenone	0[b]

[a] No reaction.
[b] Complex mixture of products.

The only aldehyde that reacted successfully with the diene (**80**) was piperonal, which gave the expected product as an intermediate, but this was followed by migration of the carbamate group and tautomerisation of the resulting enolate to give (**83**) in fair yield (Scheme 90).

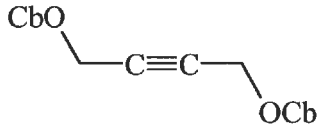


Scheme 90

All attempts to trap anion (**82**) with electrophiles were unsuccessful. Other aldehydes and ketones all gave complex mixtures of products that were of no synthetic use.

2.7.3) Attempted Reactions Using Related Systems.

As an extension of these reactions, we attempted similar reactions using the dicarbamoyloxy alkyne (**51**) and the diether (**84**). In both cases, however, no reaction occurred and the starting material was recovered.

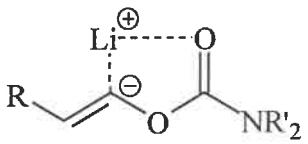


(51)

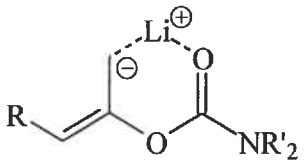
Cb = $CONEt_2$

(84)

The vinyl anion is stabilised *via* a five-membered transition state (**85**), as proposed by both Hoppe[79, 80, 104] and Snieckus.[83 - 85] We felt that the favourable six-membered transition state (**86**) would allow allylic deprotonation of (**81a**) and allow further substitution. Unfortunately (**81a**) was also unreactive.



(85)



(86)

2.7.4) Conclusions.

The preparation and reaction of (*E,E*)-1-*N,N*-diethylcarbamoyloxy-1,3-butadiene is interesting and synthetically useful in a limited number of cases. Consistent results in reactions with carbonyl compounds would make this reaction a useful preparation of α-hydroxy ketones.

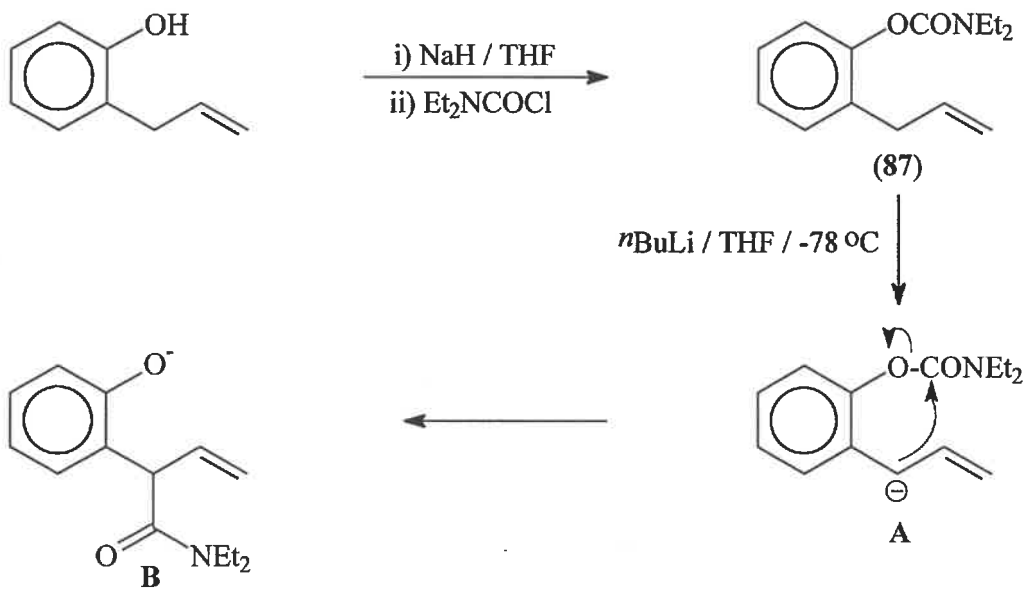
2.8) Miscellaneous Reactions.

This section describes some limited studies that were conducted as extensions of other work done in our laboratories. A brief description of any background material will be given where neccessary.

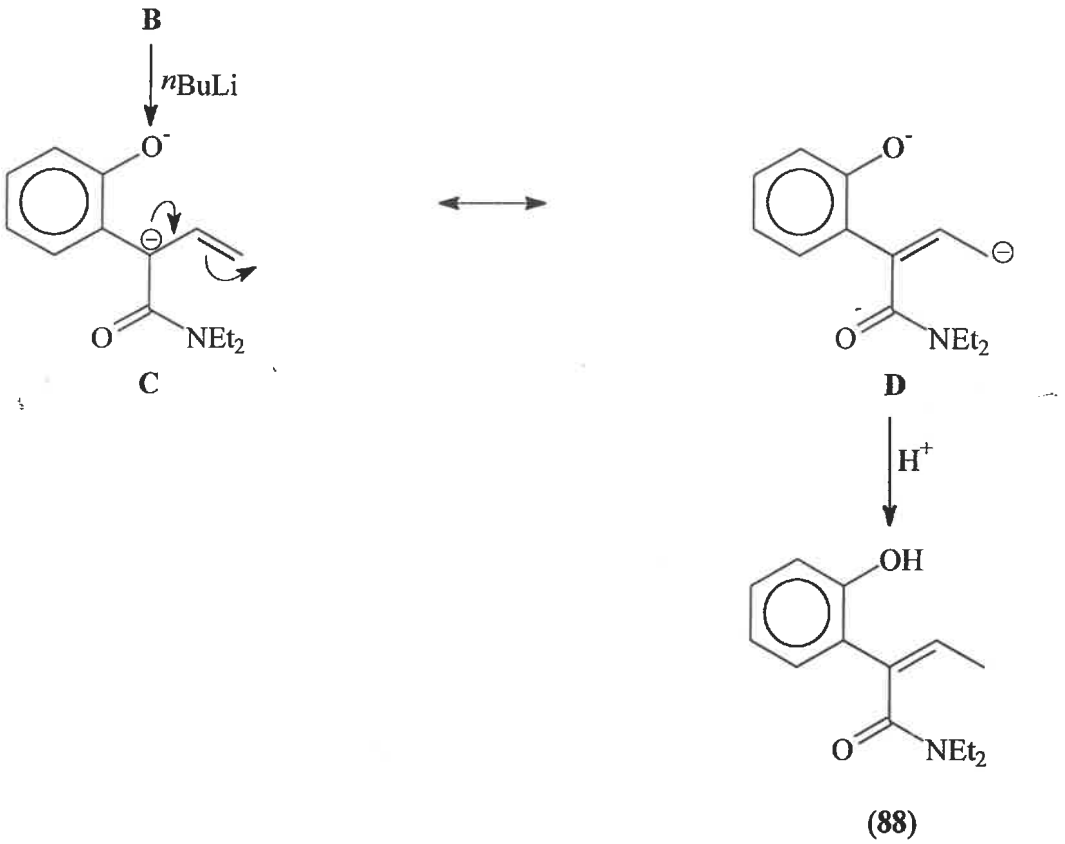
2.8.1) Migration of the Carbamate Group.

Under specific conditions, the amide portion of a carbamate group has been found to undergo intramolecular migration (see Chapter 2, Scheme 90). Migration onto a carbon atom, rather than an oxygen atom, *via* a carbanion is less common and is limited to the migration of the amide portion of *O*-aryl carbamates onto the ortho ring position[81] (Scheme 26) and the migration of the amide group of benzyl carbamates onto the ortho ring position and benzylic position (Scheme 36).[52]

We found that the amide portion of 3-(2'-*N,N*-diethylcarbamoyloxy)phenylpropene (**87**) migrates onto the 3-position of the allyl side chain, followed by migration of the double bond due to a second deprotonation or proton exchange. Thus, complete reaction requires two equivalents of base (Scheme 91).

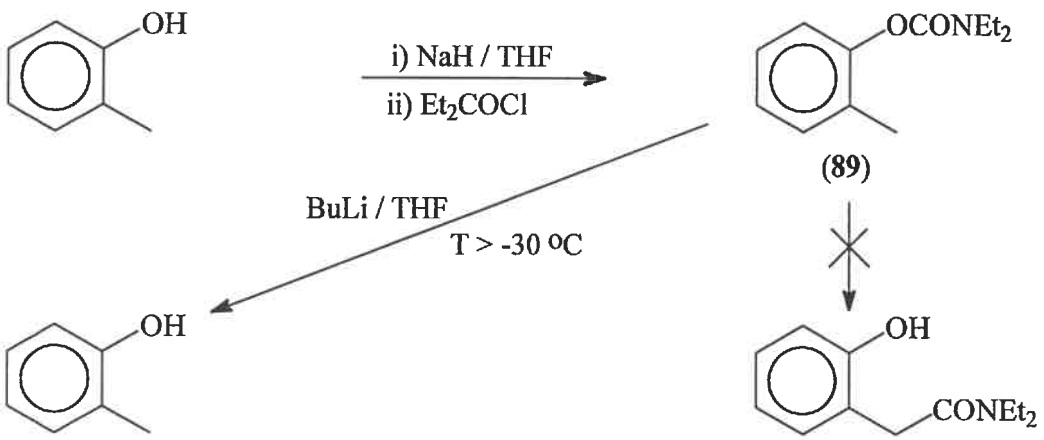


Scheme 91 (continued on next page)



Scheme 91 (continued from previous page)

The simpler 1-*N,N*-diethylcarbamoyloxy-2-methylbenzene (**89**), however, did not react at -78 °C. Raising the reaction temperature resulted in cleavage of the carbamate by the *n*-butyllithium. Other bases were also found to cleave the carbamate at higher temperatures (Scheme 92).

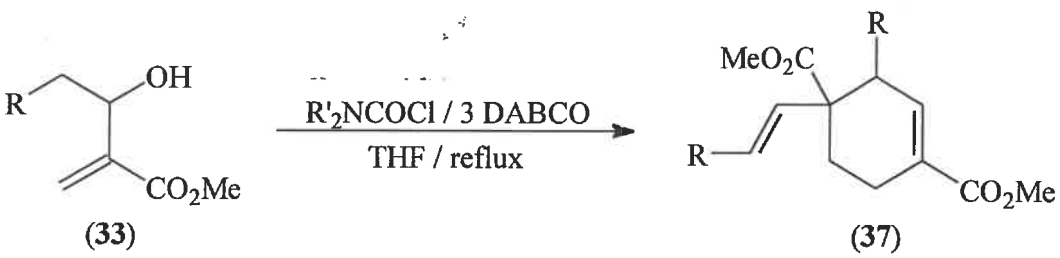


Scheme 92

2.8.2) An Improved Preparation of Mikanecic Acid Derivatives.

Previous studies in our laboratories have shown that mikanecic acid derivatives can be prepared in high yield from α-hydroxyalkyl acrylates and *N,N*-dimethylcarbamoyl chloride using DABCO as the base in dichloromethane (Scheme 46).[93] The reaction time is, however, long (24 hours) and employs the highly toxic *N,N*-dimethylcarbamoyl chloride.

This investigation was aimed at improving the reaction time and eliminating the use of *N,N*-dimethylcarbamoyl chloride in favour of *N,N*-diethylcarbamoyl chloride, which is cheaper and less toxic, but had previously given poor results. A key intermediate in the reaction is the *N,N*-dialkylamide base, which we felt would be better stabilised by a more polar solvent, such as THF. THF was found to be a far better reaction medium, especially under reflux, where reaction was complete in 3 hours. *N,N*-Diethylcarbamoyl chloride can also be used under these conditions, although the reaction time is somewhat longer (Scheme 93, Table 19). Allylic alcohols (**33**) were prepared by known methods.[94]



(**33**) (**37**)

Scheme 93

Table 19: Yields of Mikanecic Acid Derivatives (**37**) (continued on next page).

(33)	R	R'	Reaction Time	% Yield	d.c.
a	H	Me	3	98	-
b	CH_3	Me	3	95	59
c	CH_2CH_3	Me	3	91	60
d	$(CH_3)_2$	Me	3	0[a]	-

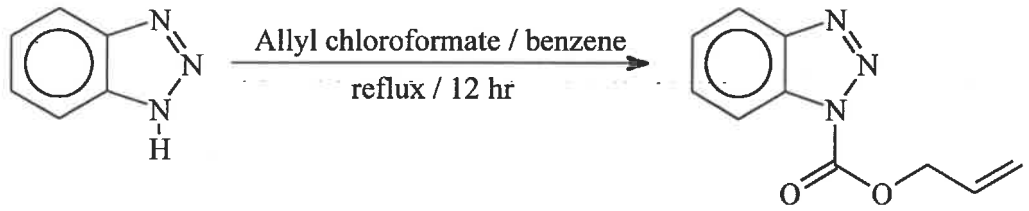
(33)	R	R'	Reaction Time	% Yield	d.e.
a	H	Et	4	97	-
b	CH_3	Et	4	95	60
c	CH_2CH_3	Et	4	92	60
d	$(CH_3)_2$	Et	4	0[a]	-

[a] No reaction.

Pyridine was also found to be an effective solvent, with pyridine playing the role of both solvent and base/nucleophile, with comparible yields to DABCO/THF. *N,N*-Diisopropylcarbamoyl chloride was unreactive under all conditions described.

2.8.3) Attempted Reaction of Benzotriazole Carbamates.

Work done by Katritsky and coworkers[105] has shown that the benzotriazole group is a very good leaving group and can be removed under relatively mild conditions. We prepared the carbamate (**90**) from benzotriazole and allyl chloroformate in moderate yield as a low melting solid (Scheme 94).



(90) 68 %

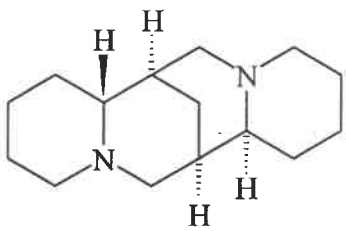
Scheme 94

Unfortunately, the carbamate was immediately hydrolysed under basic conditions (BuLi and aqueous base) and therefore is of no preparative use as far as electrophilic substitution reactions are concerned. Benzotriazole carbamates may, however, be useful protecting groups under certain reaction conditions, due to their ease of hydrolysis.

2.8.4) Attempts at Asymmetric Synthesis Using Cinnamyl Carbamates.

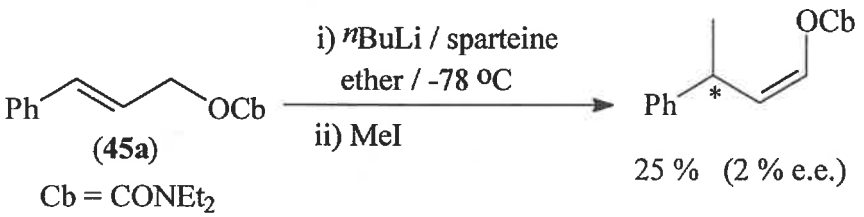
While not directly part of this project (other projects were concerned with the topic of asymmetric synthesis using carbamates), a number of attempts were made at (-)-sparteine (**91**) mediated chiral induction. Hoppe and coworkers have done considerable research into the use of sparteine in asymmetric electrophilic substitution reactions.[106 - 111]

Sparteine acts as a chiral complexing agent and has been shown to complex with butyllithium to give a chiral base, which can then be used for asymmetric deprotonations.[109, 112] In the case of carbamates, however, it is thought that the sparteine complexes to the α-metalated anion, with the sparteine blocking one face of the anion from approach by the electrophile.[108] Choice of solvent is critical, since competing solvent complexation lowers the selectivity. THF, being a strongly coordinating solvent, complexes in preference to sparteine, while reactions done in diethyl ether or hydrocarbons such as hexane or pentane, can give reasonable selectivity.[81]



(91)

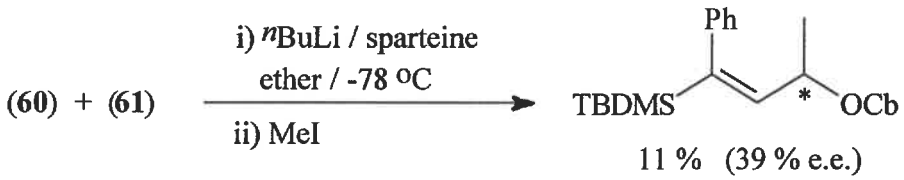
Our first attempt was the asymmetric introduction of a methyl group using the *N,N*-diethylcinnamyl carbamate, but the reaction yield was very low (25 %) and the e.e. negligible (*ca* 2 %) (Scheme 95).



Scheme 95

Other electrophiles were unreactive under these conditions, while silicon electrophiles gave no induction whatsoever. The lower yield may be due to the decreased polarity of the solvent and the bulk of the sparteine, which hinders approach by the electrophile. Longer reaction times, other bases and other solvents did not improve the results.

The TBDMS substituted *N,N*-diethylcinnamyl carbamates (**60**) and (**61**) gave a better e.e. (39 %), but the reaction yield was considerably lower (11 %). Again, only methyl iodide gave a positive result (Scheme 96). Changing the reaction conditions was also ineffective. The absolute stereochemistries were not determined and the e.e.'s were determined by NMR / chiral shift reagent.



Scheme 96

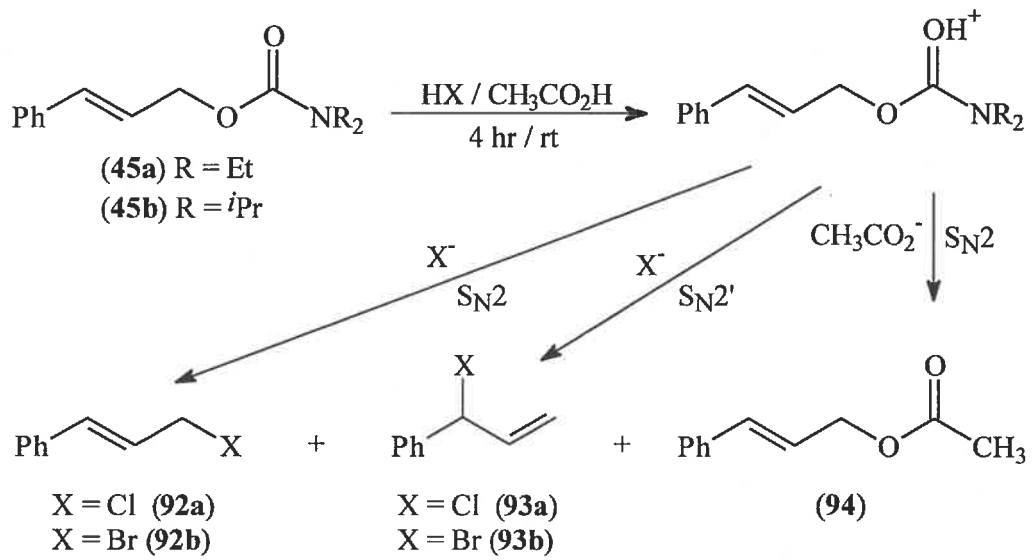
2.9) Nucleophilic Substitution Reactions of Cinnamyl Carbamates.

The cleavage of vinyl carbamates to give ketals has been extensively studied by Hoppe,[65 - 70] but allyl carbamates have proved to be somewhat more difficult to cleave under mild conditions. Alkyllithiums cleave allyl carbamates but the yields are usually low and variable, with numerous by-products being common. The disubstituted carbamates described previously could not be directly hydrolysed without further degradation of the molecule. Lithium aluminium hydride reduction resulted in reduction of susceptible groups, including the double bond. We therefore attempted to substitute the carbamate group with other more easily hydrolysed groups. The initial studies were conducted using *N,N*-diethyl and *N,N*-diisopropyl cinnamyl carbamates.

2.9.1) Substitution with a Halide.

A common method for the cleavage of amines protected as carbamates is treatment of the carbamate with hydrochloric or hydrobromic acid in glacial acetic acid, which gives the deprotected amine, carbon dioxide and an alkyl halide[29] (Scheme 11). Our work on carbamates considers them to be protected alcohols, not amines, so we were interested in preparing the allyl halides using the same reaction, which can then be hydrolysed under basic conditions to give the allyl alcohol. Previous studies, since they had been concerned with the deprotection of amines, paid little attention to the reactions of *O*-allyl carbamates in this sense.

Treatment of N,N-diethyl or N,N-diisopropyl cinnamyl carbamate with hydrochloric or hydrobromic acid in glacial acetic acid gave a mixture of the two isomeric allyl halides, which result from either an S_N2 or an S_N2' elimination of the protonated carbamate group, and cinnamyl acetate, which is a result of nucleophilic attack by an acetate anion. This was surprising, since the acetate anion is not usually considered a good nucleophile. Hydroiodic acid gave a complex mixture of products (Scheme 97, Table 20).



Scheme 97

Table 20: Results of reaction with hydrogen halide in glacial acetic acid.

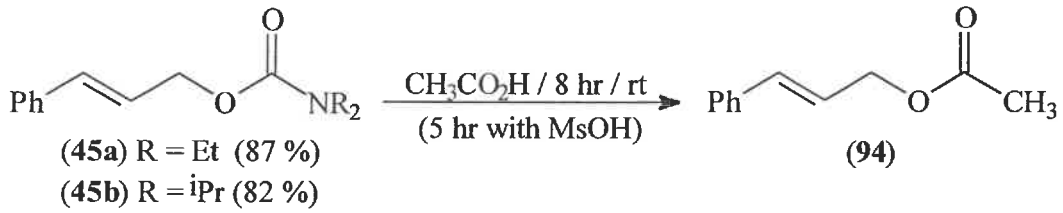
R	HX	Ratio (92 : 93 : 94)[a]	% Yield (92)
Et	HCl	74 : 12 :14	72
^{i}Pr	HCl	62 : 15 : 23	57
Et	HBr	47 : 25 : 28	40
^{i}Pr	HBr	45 : 18 : 37	37
Et	HI	-[b]	-[b]
^{i}Pr	HI	-[b]	-[b]

[a] Determined by H-NMR.
[b] Complex mixture of products.

From these results it can be seen that the smaller *N,N*-diethyl carbamate group and the smaller halide (Cl^-) favour formation of the cinnamyl halide (S_N2 reaction), while bulkier groups favour the formation of the acetate (**94**). Disubstituted cinnamyl carbamates were all unreactive under these conditions, probably due to the increased steric bulk of the additional groups.

2.9.2) Substitution with an Acetate Group.

The previous section described the preparation of cinnamyl halides which can be easily hydrolysed under basic conditions to give the corresponding alcohol, but the isomeric product lowers the yield (the acetate is also hydrolysed under the same conditions). The formation of the cinnamyl acetate, however, allows for a more direct path to the alcohol, since esters are also easily hydrolysed under basic conditions, especially since none of the isomeric S_N2' product is formed. Acetic acid was the only carboxylic acid which reacted. Addition of one equivalent of methane sulfonic acid decreased the reaction time, since it is a better proton source than acetic acid (Scheme 98).



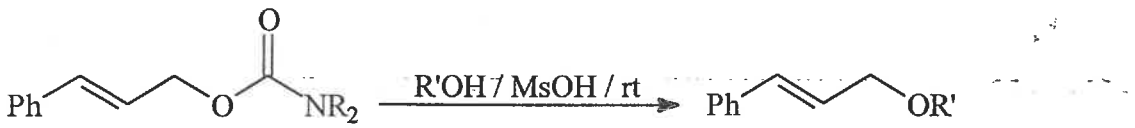
(**45a**) R = Et (87 %)
(**45b**) R = ^{i}Pr (82 %)

(**94**)

Scheme 98

2.9.3) Substitution with an Alcohol.

The fact that a weak nucleophile such as an acetate could displace a carbamate group under acidic conditions prompted us to investigate the use of alcohols as nucleophiles, which would give cinnamyl ethers as products. Only methanol and ethanol reacted, using methane sulfonic acid as a proton source. Methane sulfonic acid was used because a non-nucleophilic proton source was required to avoid a competing substitution reaction. Toluene sulfonic acid can also be used, but the reaction times are longer. The results are shown in Scheme 99 and Table 21. Again, bulky substituents increase the reaction time and decrease the yield slightly.



(**45a**) R = Et
(**45b**) R = ^{i}Pr

(**46a**) R' = CH_3
(**46b**) R' = CH_2CH_3

Scheme 99

Table 21: Yields of ethers (**46**)

R	R'	Reaction Time (hr)	% Yield
Et	CH_3	5	95
Et	CH_2CH_3	7	91
^{i}Pr	CH_3	7	90
^{i}Pr	CH_2CH_3	9	90

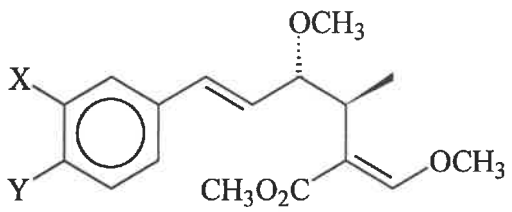
2.9.4) Conclusions.

These reactions, while interesting from a mechanistic point of view, are of limited synthetic use since they all failed when applied to the disubstituted cinnamyl carbamates described previously. This does not, however, rule out other systems as suitable substrates for these reactions. An in depth study was not conducted simply because it had already been shown conclusively that this methodology was not applicable to the products obtained during the course of these studies.

2.10) Synthesis of (±)-Oudemansin A.

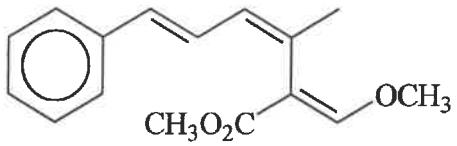
2.10.1) Introduction.

Oudemansins (**95a-c**), which are naturally occurring β-methoxyacrylates isolated from mycelial cultures of Basiomycetes, have attracted considerable interest due to their broad spectrum antibiotic and antifungal activity.[113, 114]

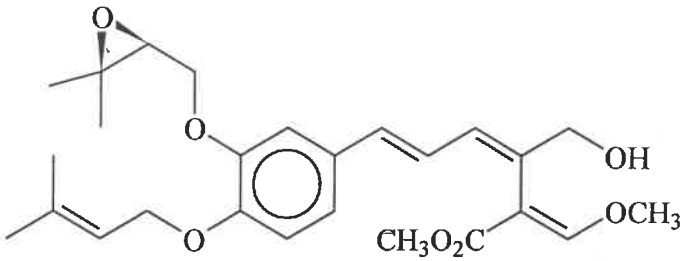


(95a)	X = Y = H	: Oudemansin A[115]
(95b)	X = OMe, Y = Cl	: Oudemansin B[116]
(95b)	X = H, Y = OMe	: Oudemansin X[117]

The oudemansins are structurally related to the strobilurins, of which there are eleven known members, the simplest being strobilurin A (**96**),[118] which is shown. The strobilurins are characterised by the (*E,Z,E*) triene system. All variation in the strobilurin group, apart from hydroxystrobilurin D (**97**),[119] is on the 3 and 4 ring positions.



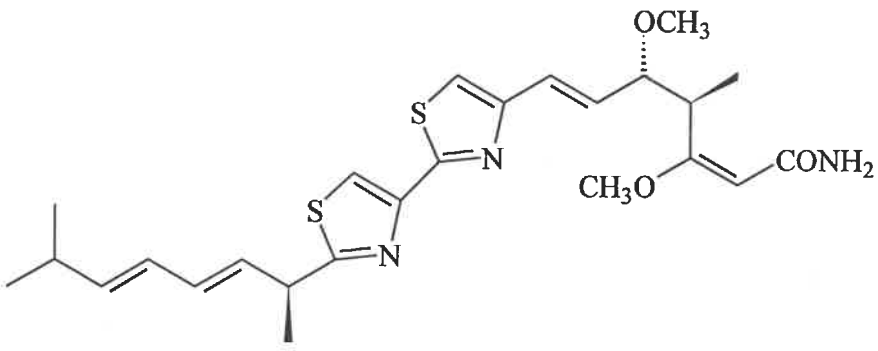
(**96**) Strobilurin A (mucidin)[118]



(**97**) Hydroxystrobilurin D[119]

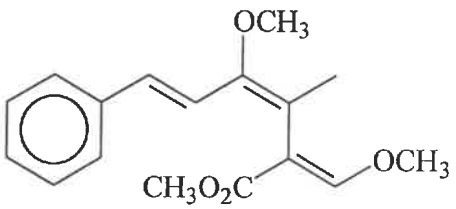
According to the Cahn-Ingold-Prelog rules, hydroxystrobilurin D (**97**) has the (*E,E,E*) configuration. Most of the literature from the early 1980's incorrectly shows strobilurins to have the (*E,Z,E*) configuration.

Another related group of compounds are the myxothiazols, with 24 different compounds having been identified. Myxothiazol A (**98**) was first described in a patent application in 1978.[120]

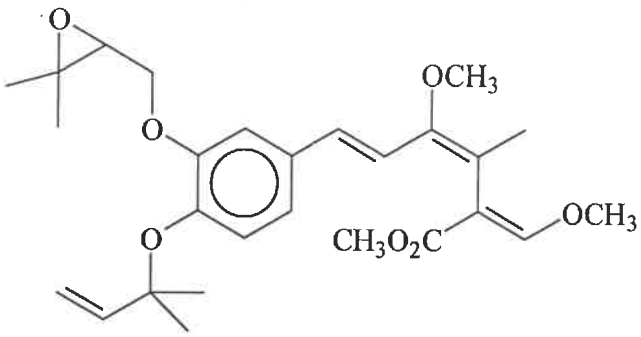


(**98**) Myxothiazol A[120]

More recently two 9-methoxystrobilurins (**99**) and (**100**) have been isolated.[121, 122]



(99)



(100)

2.10.2) The Oudemansins.

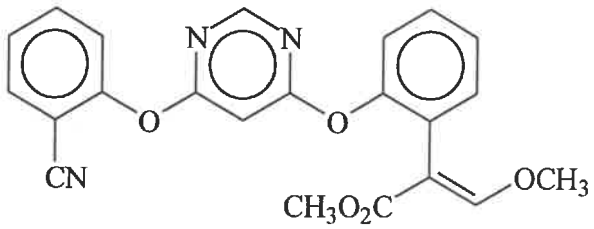
Only three oudemansins are known to occur naturally, which are called oudemansins A, B and X (**95a-c**). Oudemansin A, a colourless solid, was isolated from mycelial fermentations of *Oudemansiella mucida*, which also produces strobilurin A.[118] It has also been isolated from *Mycena polygramma*[123] and *Xerula melanotricha*.[116] Oudemansin B and strobilurin B were also isolated from *Xerula melanotricha* in 1983.[116] Oudemansin X was first isolated in 1990 from *Oudemansiella radicata*.[117]

Formally, oudemansins can be considered derivatives of strobilurins in which methanol has undergone *syn* addition across the central double bond (the formal relative stereochemistry is *syn*). All three known oudemansins are laevorotatory, with the (9S,10S) configuration.[124]

The biological activity of oudemansins is very similar to that of strobilurins in that they control the activity of fungi (but not bacteria) and show some anti-tumour

activity. It is the former property, however, that has attracted the most attention. Their potent antifungal property has led to considerable research into their use as antifungal agrochemicals, with some 250 patents regarding the synthesis and use of oudemansins and related compounds.[124]

Naturally occurring oudemansins suffer from limited water solubility and photo-degradation,[113] so various analogues have been developed to overcome these problems. One of the most promising analogues is ICIA5504 (**101**), which was developed by Zeneca Agrochemicals.[113]

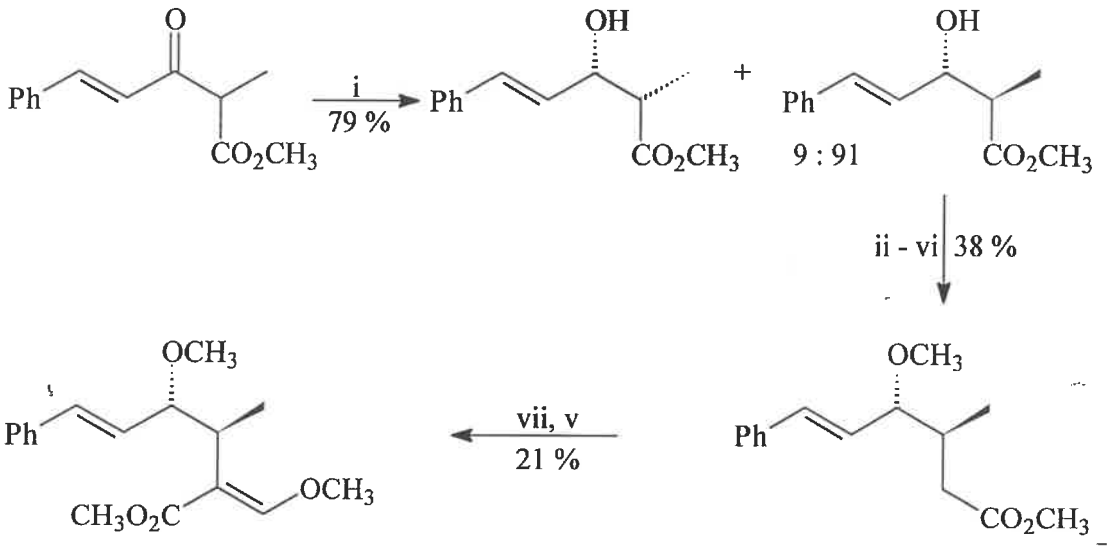


ICIA5504 (**101**)

It is interesting to note that it is only the β-methoxy acrylate unit that remains from the natural oudemansin and the molecule has no chiral centres, which indicates that the β-methoxy acrylate unit is the active site. This is consistent with the fact that both the oudemansins and the strobilurins are active in their own right and that no bioconversion appears to occur.

2.10.3) Published Syntheses of Oudemansins.

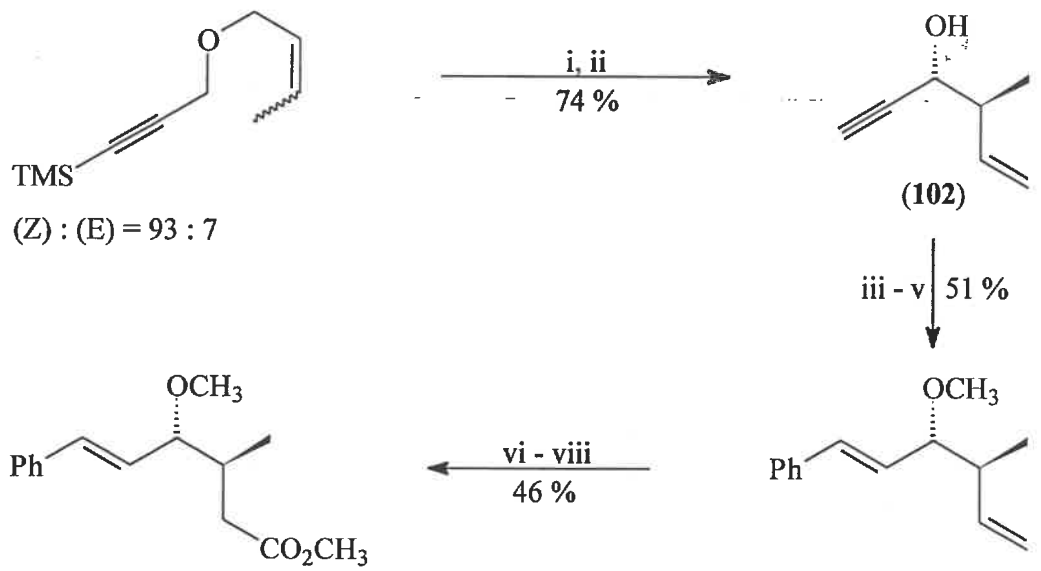
Three approaches for the preparation of racemic oudemansins have been published. The first of these employs a diastereoselective zinc borohydride reduction of an α-methyl-β-ketoester as the key step to achieving the required diastereoselectivity (Scheme 100).[125, 126]



i) $Zn(BH_4)_2$; ii) $Me_3O^+BF_4^-$; iii) LiOH; iv) $SOCl_2$; v) CH_2N_2; vi) $PhCO_2Ag$, Et_3N, MeOH; vii) HCO_2Me, LDA.

Scheme 100

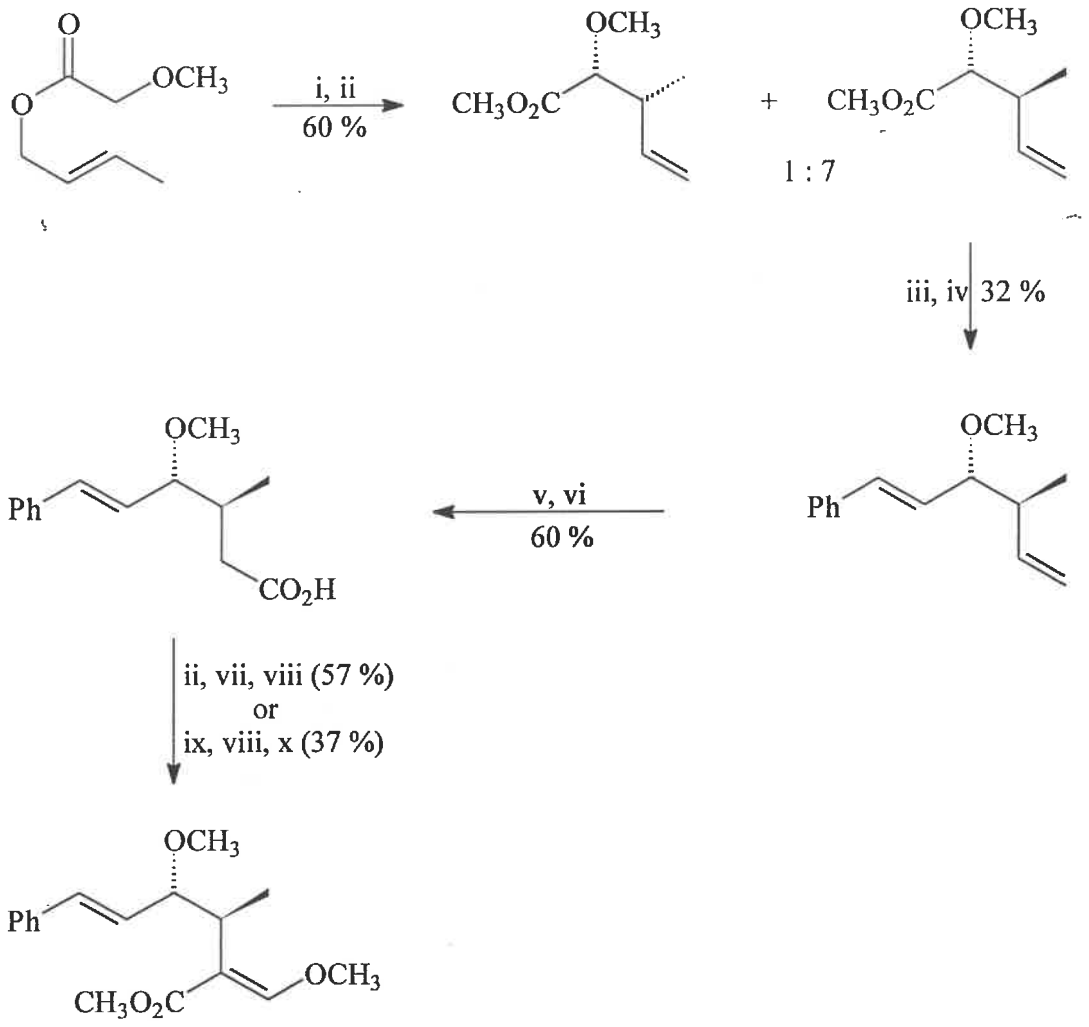
In the second approach a diastereoselective [2,3]-Wittig rearrangement gave the propargyl alcohol (**102**) in 94 % d.e., which was then converted into oudemansin A (Scheme 101).[127, 128]



i) ^{n}BuLi, -85 °C; ii) CsF; iii) PhI, Et_2NH, CuI, $(PPh_3)_2PdCl_2$; iv) $LiAlH_4$; v) MeI, NaH; vi) 9-BBN, then H_2O_2, NaOH; vii) O_2, Pt-C, $NaHCO_3$; viii) CH_2N_2.

Scheme 101

The last approach relies on a diastereoselective Claisen-Ireland rearrangement to give a 7 : 1 mixture of diastereomers (Scheme 102).[129, 130]

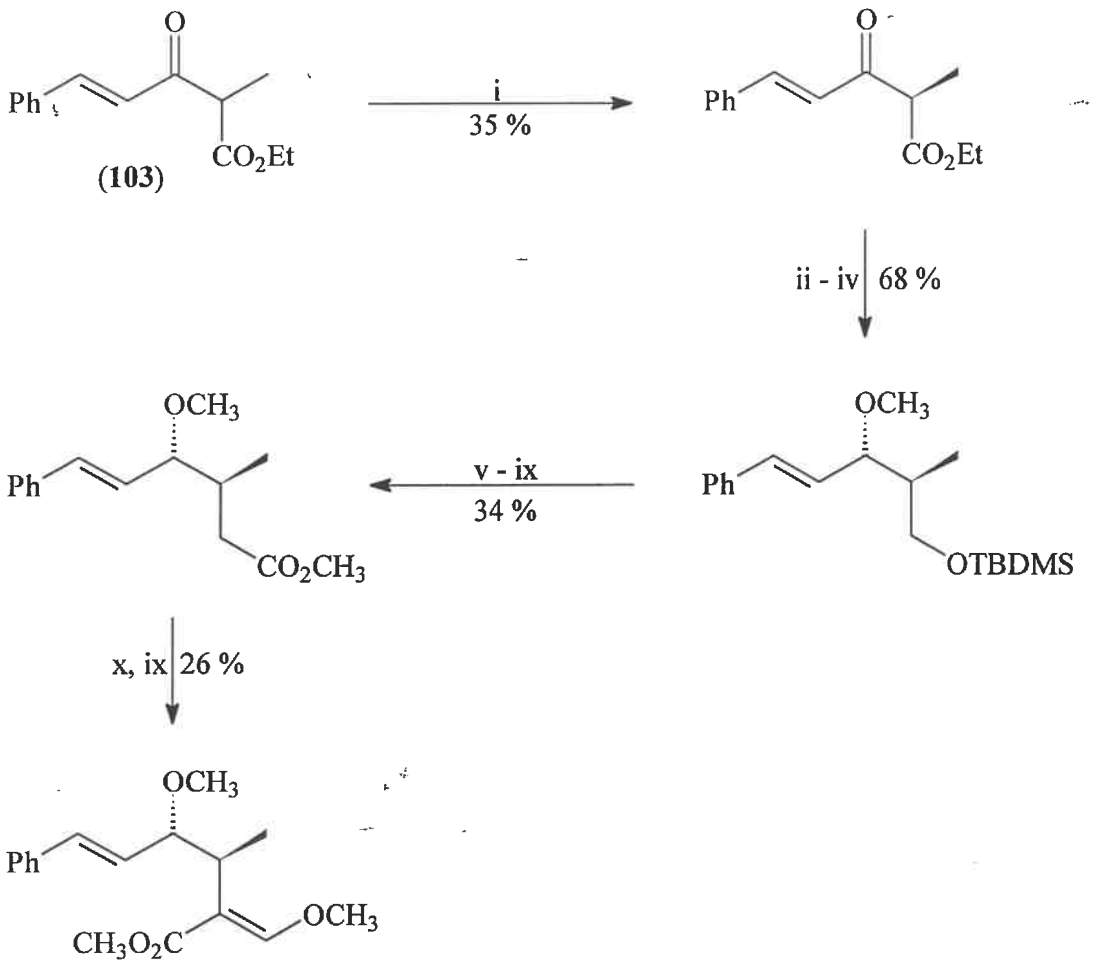


i) LDA, TMSCl, then aq. NH_4Cl; ii) CH_2N_2; iii) $PhCH_2P(O)Ph_2$, ^nBuLi; iv)$LiBH_4$; v) 9-BBN, then H_2O_2, NaOH; vi) Jones' oxidation; vii) LDA, *N*-formylimidazole; viii) Me_2SO_4, K_2CO_3; ix) HCO_2Me, 2 ^tBuLi; x) H^+, MeOH.

Scheme 102

It is obvious from these three syntheses of racemic oudemansins that the key step is the introduction of the correct relative stereochemistry of the two chiral centres.

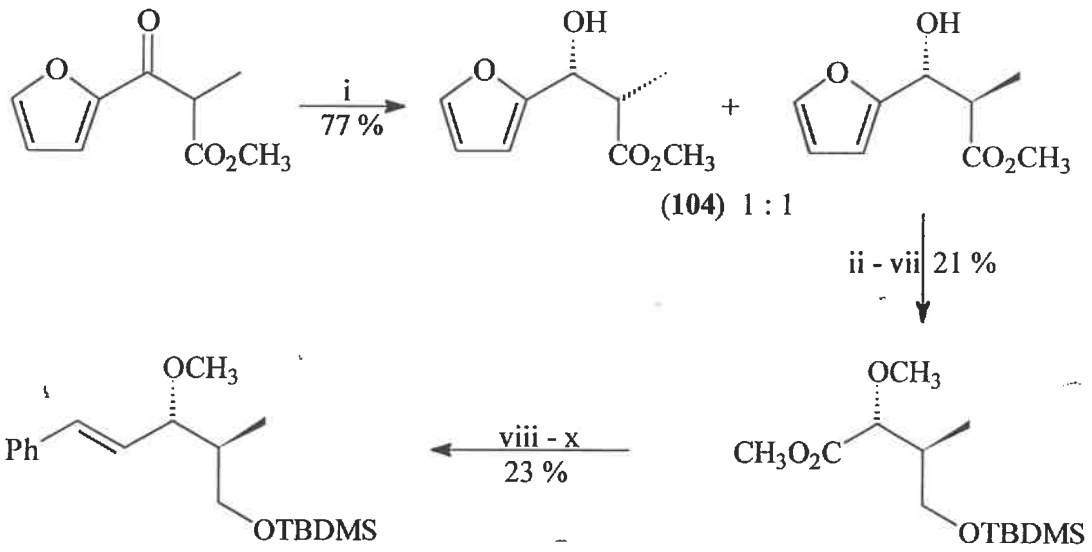
The first synthesis of (-)-oudemansin A was reported in 1983 by Akita and coworkers, who also started with an α-methyl-β-ketoester (**103**).[131] In this case, however, stereoselective reduction using *Candida albicans*, followed by conventional transformations, yielded (-)-oudemansin (Scheme 103).



i) *Candida albicans*; ii) $LiAlH_4$; iii) TBDMSCl, imidazole; iv) MeI, KH; v) AcOH; vi) TsCl, pyridine; vii) NaCN; viii) KOH, ix) CH_2N_2; x) HCO_2Me, LDA.

Scheme 103

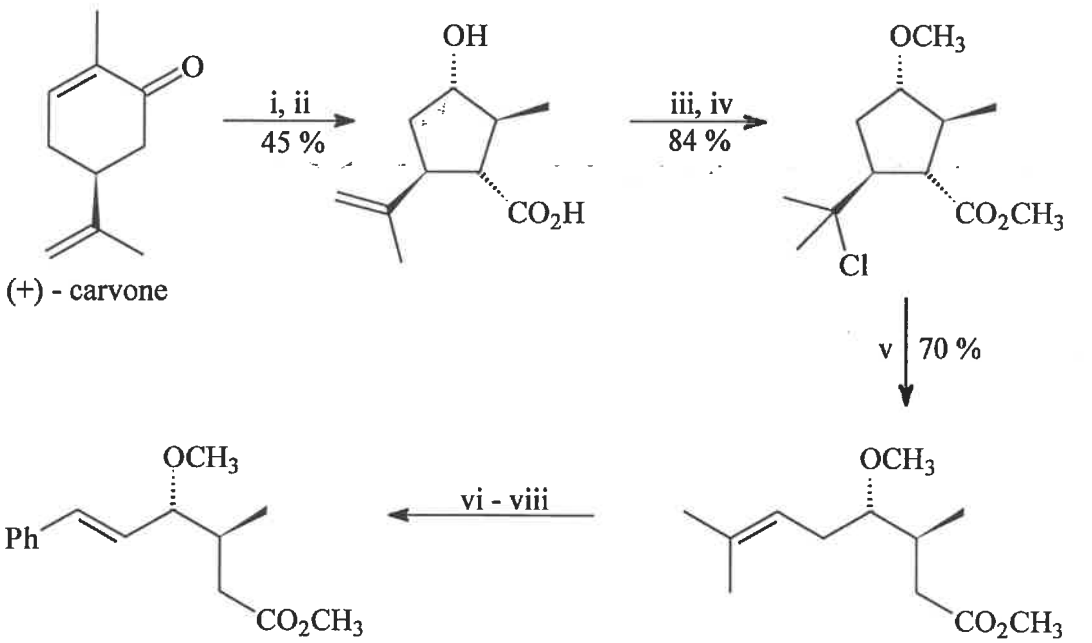
Another approach, also by Akita, employs another microbial reduction, giving equimolar amounts of the *syn* and *anti* diastereomers (**104**) in greater than 99 % e.e. The *syn* intermediate was then converted to oudemansin A (Scheme 104).[132]



i) *Saccharomyces fermentati*; ii) $LiAlH_4$; iii) TBDMSCl, imidazole; iv) MeI, NaH; v) O_3; vi) H_2O_2; vii) CH_2N_2; viii) DIBAL; ix) $Ph_3P^+{}^-CHPh$; x) separation.

Scheme 104

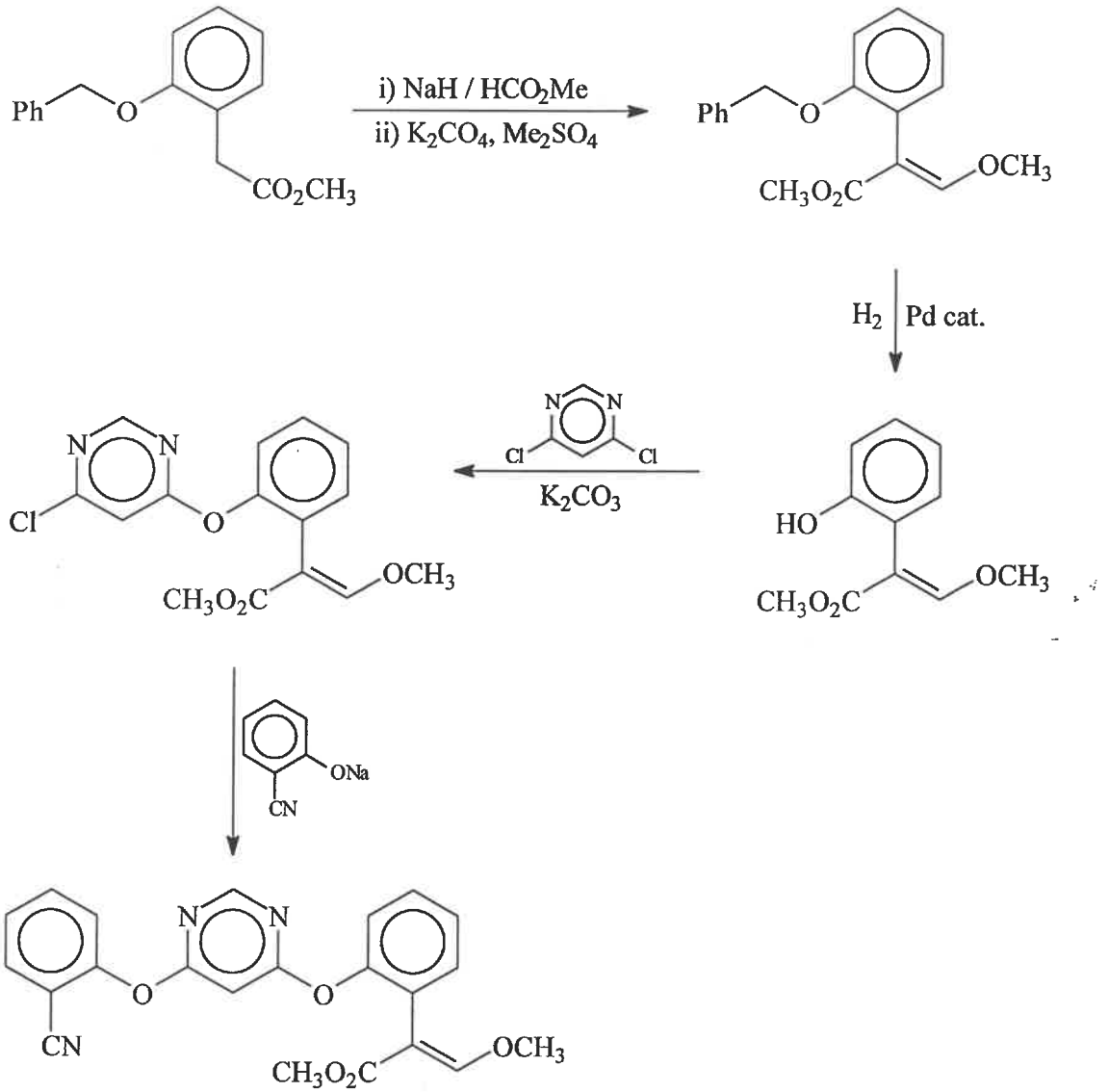
Honda and coworkers reported a particularly elegant synthesis of (-)-oudemansin A from (+)-carvone (Scheme 105).[133]



i) H_2O_2, NaOH; ii) NaOEt, then H_2O; iii) 2 MeI, 2 NaH; iv) HCl(g); v) SmI_2; vi) O_3, then Me_2S; vii) PhMgBr; viii) Me_2SO_4, DMAP.

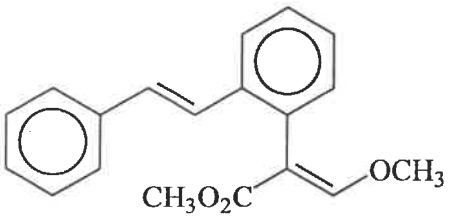
Scheme 105

A number of other syntheses have been reported, including preparations of oudemansins B and X. Information regarding the preparation of the various analogues is more scarce, since they are the subject of patent applications, but the preparation of ICIA5504 (**101**) has been reported.[113] The preparation of ICIA5504 (**101**) is relatively simple and is well suited to large scale preparation (Scheme 106), unlike the syntheses described previously. A conspicuous feature of ICIA5504 and the anologues (**105 - 107**) is the fact that none of them contain any chiral centres.[113]

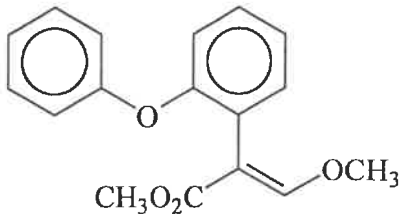


ICIA5504 (**101**)

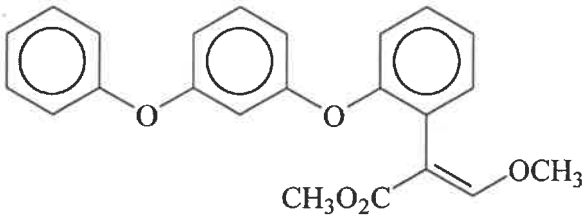
Scheme 106



(105)



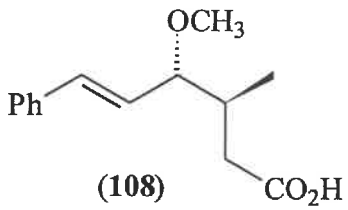
(106)



(107)

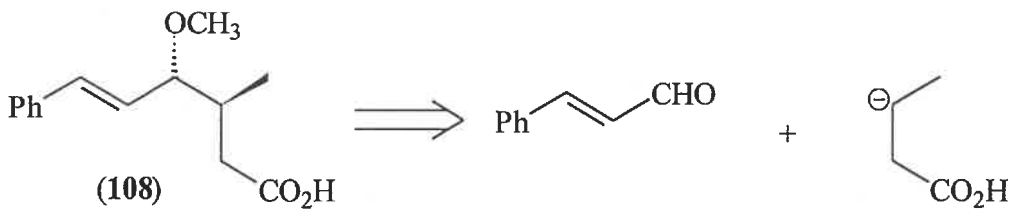
2.10.4) Preparation of (±)-Oudemansin A.

From the published syntheses of oudemansin A that were discussed, one finds that the acid (**108**) (or the methyl ester) is a key intermediate.



(108)

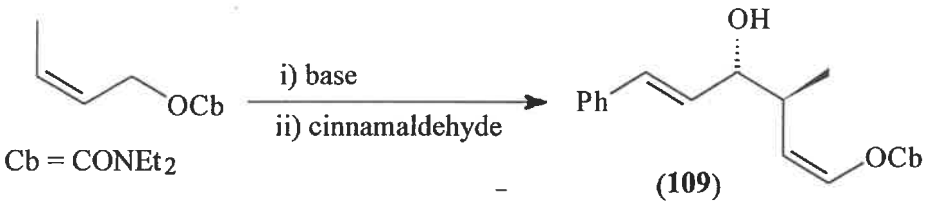
Further retrosynthetic analysis of this compound reveals that it is the product of a homoaldol reaction (Scheme 107).



(108)

Scheme 107

As discussed previously, the γ-substitution of allyl carbamates can be regarded as a homoaldol reaction, with the carbonyl group masked as a vinyl carbamate. Previous work by Hoppe (Scheme 28) indicates that the correct *syn*-stereochemistry will be obtained by using the (Z)-crotyl carbamate (Scheme 108). The (E)-crotyl carbamate gives the *anti*-isomer.[60, 61, 65]



Scheme 108

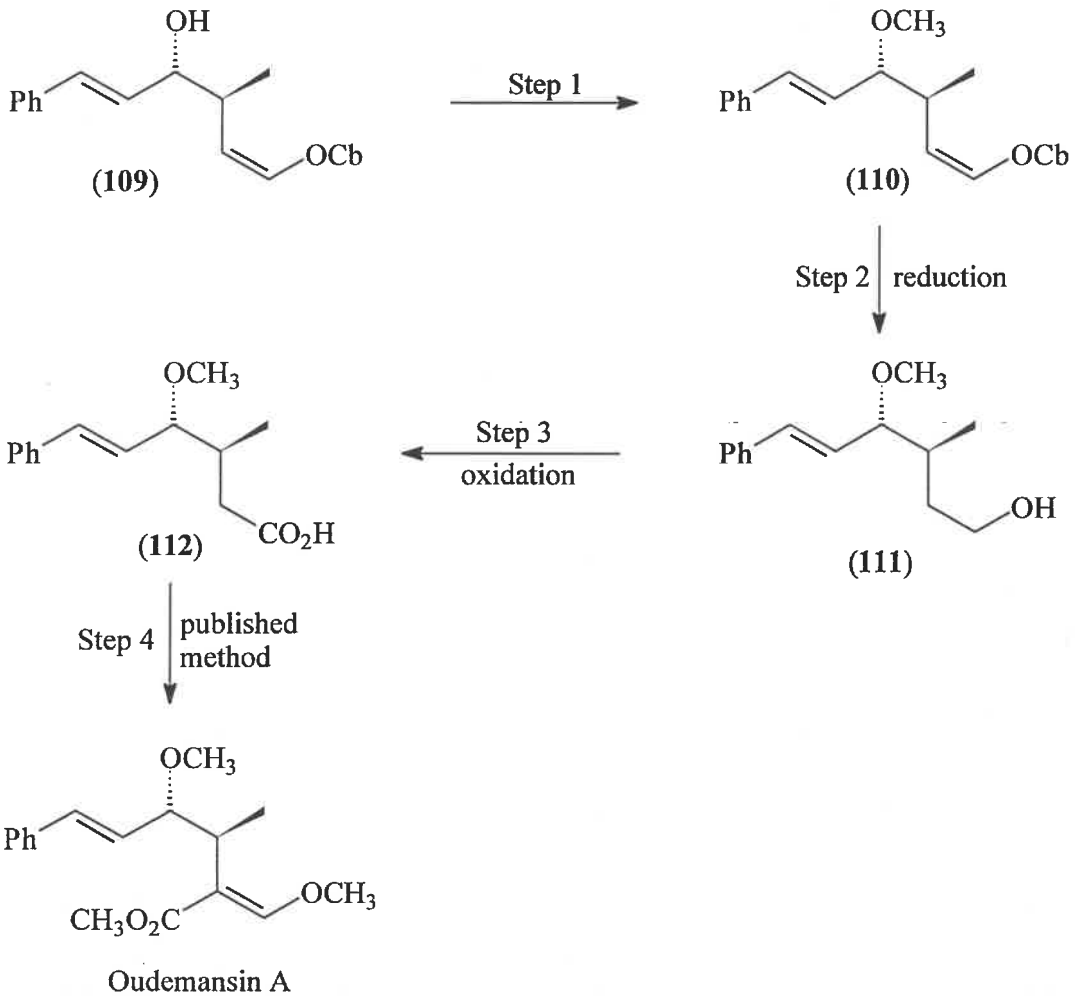
For the purpose of these preliminary studies we used a 2 : 1 mixture of (*E*)-crotyl carbamate and (*Z*)-crotyl carbamate to establish which isomer gave the correct relative stereochemistry. Reaction of *N,N*-diethylcrotyl carbamate proved somewhat problematic, with the simple reaction conditions described previously resulting in very poor yields. Optimum conditions were found to be deprotonation with *n*-butyllithium in diethyl ether/TMEDA, followed by metal exchange with diethylaluminium chloride, and then reaction with cinnamaldehyde (Table 22).[65]

Table 22: Yields of reaction between *N,N*-diethylcinnamyl carbamate and cinnamaldehyde to give (**109**).

Conditions	% Yield	*anti* : *syn*
^{n}BuLi / THF	0	-
^{n}BuLi / ether	0	-
^{n}BuLi / ether / TMEDA	18	57 : 43
^{n}BuLi / ether / TMEDA / Et_2AlCl	82	66 : 34

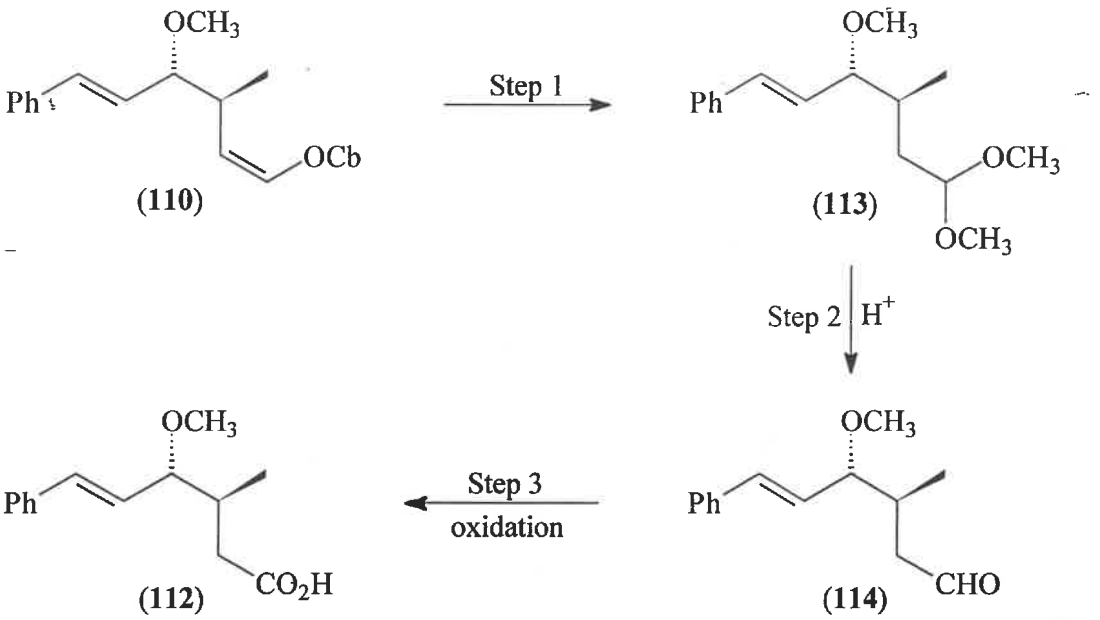
This reaction was the critical reaction in the synthesis of oudemansin A, since it established the correct relative stereochemistry. A 2:1 mixture of the *anti* and *syn* isomers was obtained, in accordance with Hoppe's observation that the (*Z*)-crotyl carbamate gives the *syn*-diastereomer.[65] This 2:1 mixture of isomers remained unchanged throughout all the subsequent transformations and a mixture of isomers is implied in all subsequent reactions, although only the *syn*-isomer is shown. All the remaining steps are simply the conversion of the vinyl carbamate into the β-methoxy acrylate group.

Conversion of (**109**) into (±)-oudemansin A was envisioned to occur using the following route (Scheme 109).



Scheme 109

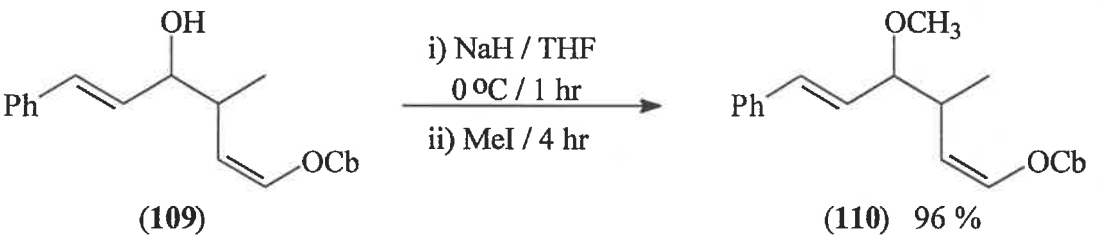
The reduction of the vinyl carbamate requires lithium aluminium hydride which, being a strong reducing agent, may limit the general applicability of the synthesis, so we devised a second route, which avoids the use of a strong reducing agent (Scheme 110). These two routes are designated "Route 1" and "Route 2".



Scheme 110

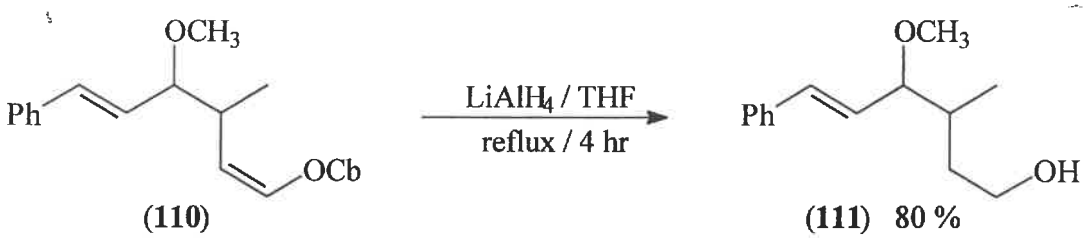
2.10.4.1) Route 1.

Step1: The methylation of **(109)** was simply carried out by abstraction of the hydroxy proton with sodium hydride in THF, followed by methylation with excess methyl iodide (Scheme 111).



Scheme 111

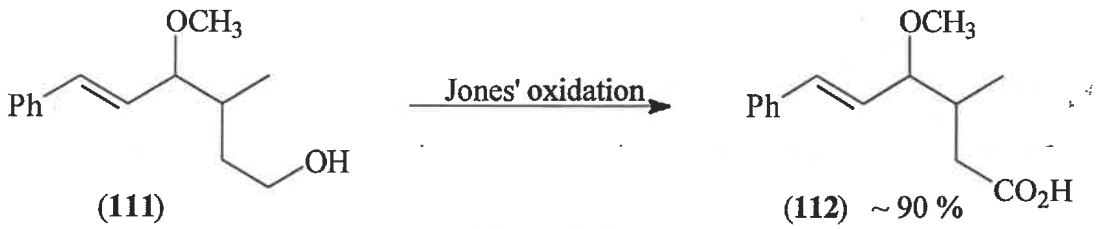
Step 2: The reduction of the vinyl carbamate (**110**) was most conveniently carried out by refluxing (**110**) in THF with one equivalent of lithium aluminium hydride (Scheme 112). Other milder reducing agents, namely $NaBH_4$, $Ca(BH_4)_2$ and $Zn(BH_4)_2$ were ineffective. The reaction proceeds by reductive cleavage of the carbamate, followed by tautomerisation of the intermediate vinyl alcohol to give the aldehyde which is reduced to the alcohol (**111**), which has been previously prepared.[129, 130]



(**110**) (**111**) 80 %

Scheme 112

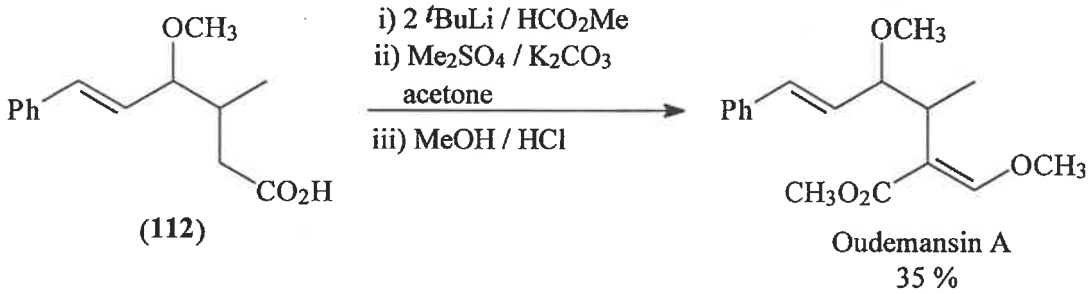
Step 3: Oxidation of alcohol (**111**) to the acid (**112**) was carried out by Jones' oxidation,[129, 130] which afforded the acid in high yield (Scheme 113). Peroxide oxidations were ineffective, since the reactions were not clean.



(**111**) (**112**) ~ 90 %

Scheme 113

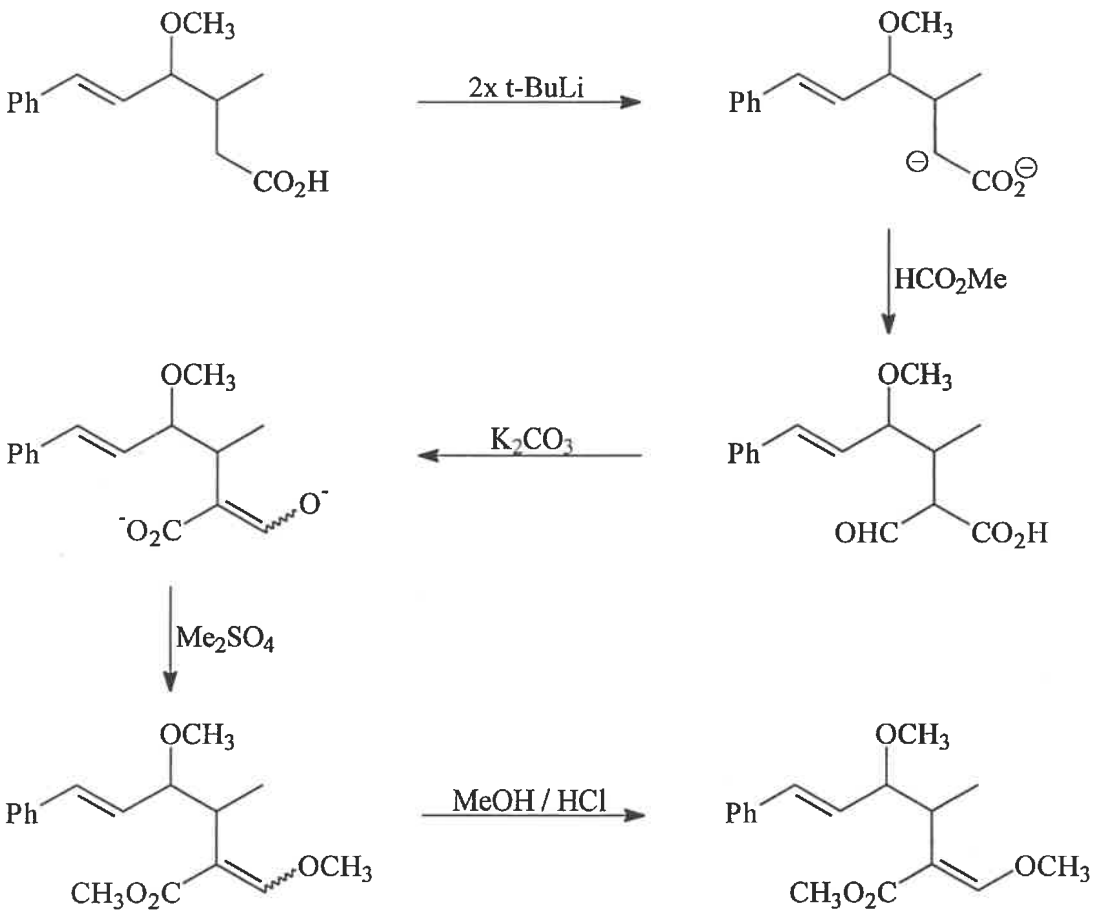
Step 4: Acid (**112**) can then be used according to the method of Kallmerten and Wittman to prepare (±)-oudemansin A (**95a**) (Scheme 114).[129, 130]



(**112**) Oudemansin A
35 %

Scheme 114

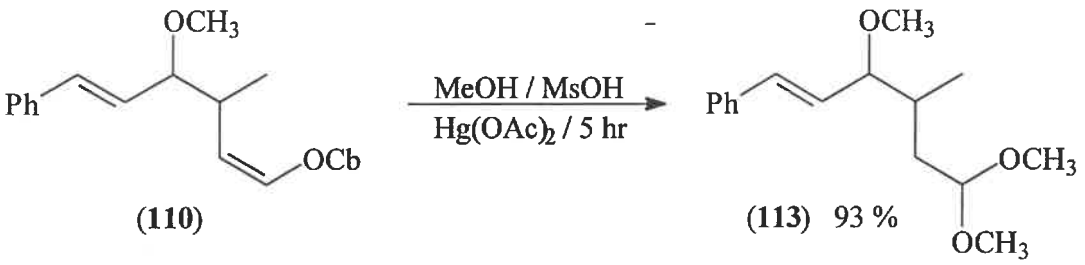
Scheme 115 shows the mechanism of the conversion of (**112**) to (±)-oudemansin A. Treatment of (**112**) with two equivalents of t-butyllithium results in abstraction of the acid proton and the acidic α-proton. This is followed by α-formylation using methyl formate. The α-formyl carboxylic acid is then treated with base to form the carboxylic acid salt and the enolate from the aldehyde which, when treated with dimethyl sulfate results in a double methylation. This results in a mixture of isomers which is isomerised in acidic methanol (Scheme 115).



Scheme 115

2.10.4.2) Route 2.

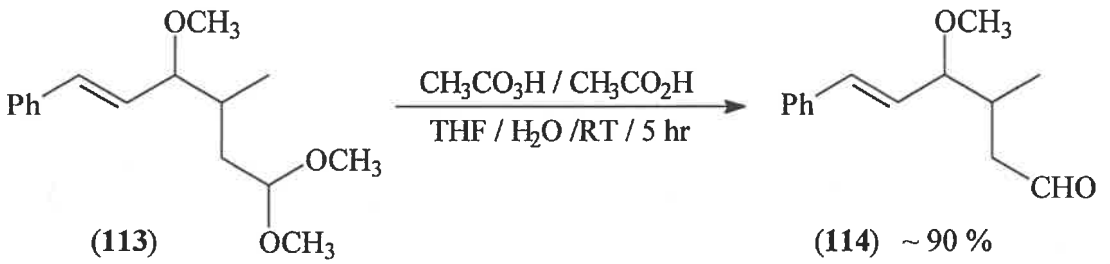
Step 1: Treatment of the methoxycarbamate (**110**) with acidic methanol and a catalytic amount of mercuric acetate afforded the dimethyl acetal (**113**) in good yield.[65 - 70] The reaction proceeds by the cleavage of the vinyl carbamate under the acidic conditions to the aldehyde, which is then converted to the dimethyl acetal *in situ*. Simply cleaving the vinyl carbamate to the aldehyde gave a very low yield, hence the dimethyl acetal route was chosen (Scheme 116).



(**110**) (**113**) 93 %

Scheme 116

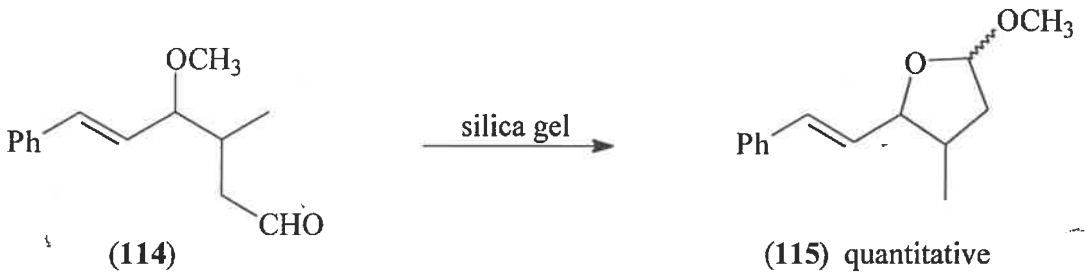
Step 2: The dimethyl acetal (**113**) was converted to the aldehyde (**114**) by stirring it with two equivalents of peracetic acid / acetic acid (38 %) in THF for 5 hours at room temperature. Acetic acid on its own was ineffective, while mineral acids resulted in considerable decomposition. In spite of using peracetic acid, however, no trace of any oxidation product (carboxylic acid) was found (Scheme 117).



(**113**) (**114**) ~ 90 %

Scheme 117

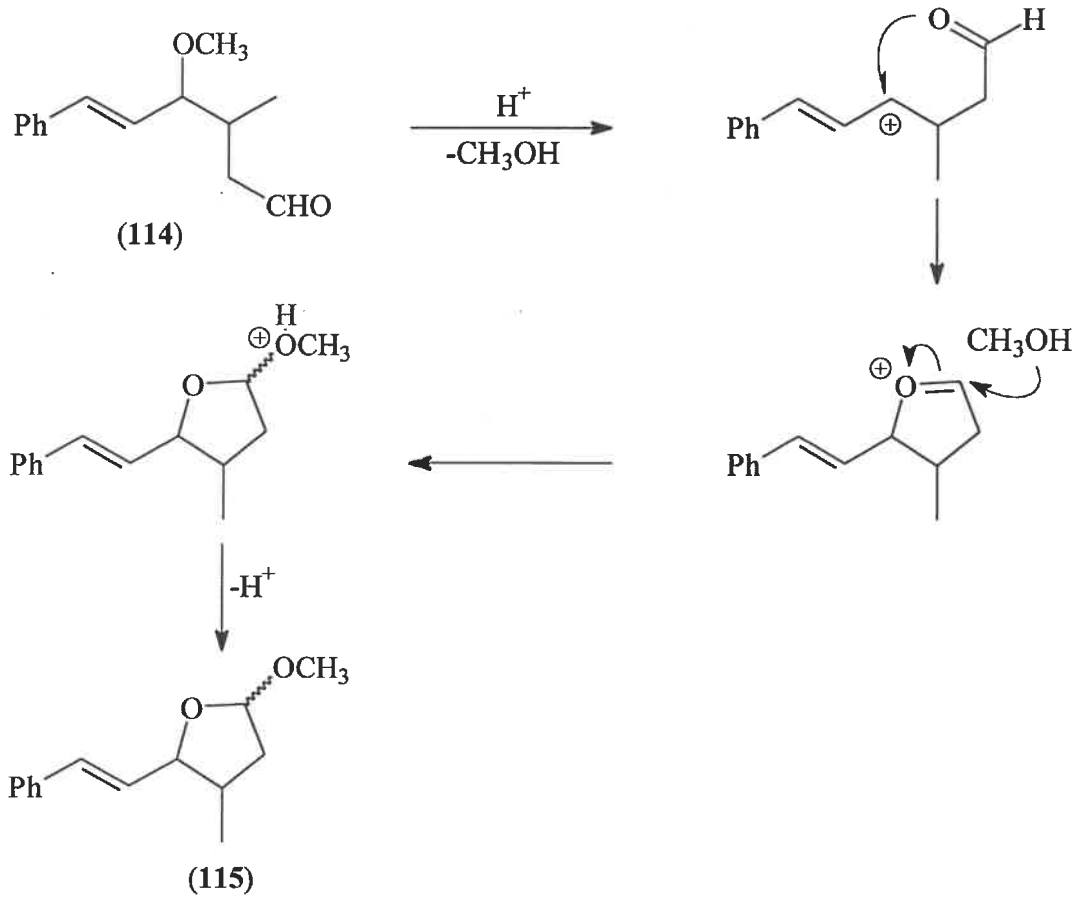
Aldehyde (**114**) was used without further purification since it was found to cyclise spontaneously on silica gel to give the cyclic acetal (**115**) (Scheme 118).



(**114**) (**115**) quantitative

Scheme 118

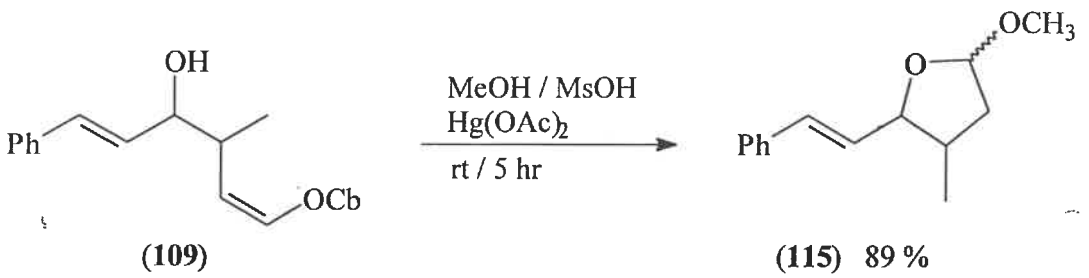
The cyclic acetal is obtained as an inseparable mixture of diastereomers. The cyclisation is rapid and complete within about five minutes during the course of column chromatography. A tentative mechanism for the reaction is shown in Scheme 119.



(**114**) (**115**)

Scheme 119

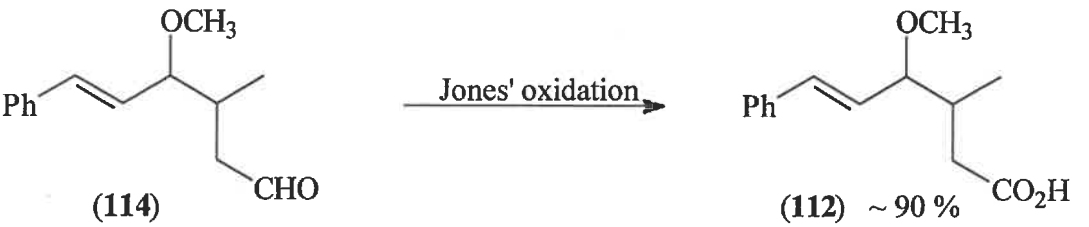
The indentity of this cyclic acetal was confirmed by preparing the same compound directly from (**109**), according to the method of Hoppe (Scheme 120).[65 - 70]



(**109**) (**115**) 89 %

Scheme 120

Step 3: Oxidation of the aldehyde (**114**) using the Jones' oxidation[129, 130] gave the acid (**112**), which is converted to oudemansin A using the method described in Step 4 of Route 1 (Scheme 121).

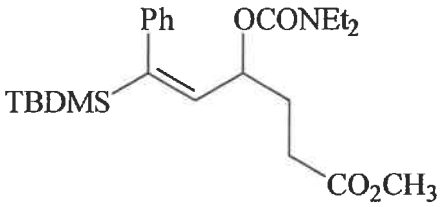


(**114**) (**112**) ~ 90 %

Scheme 121

2.10.5) Other Attempts at the Preparation of Oudemansin Derivatives.

It was mentioned previously (Section 2.6) that we had hoped to prepare oudemansin derivatives using the reaction of TBDMS substituted cinnamyl carbamates with α,β-unsaturated carbonyl compounds, particularly methyl crotonate. The only reaction that gave a satisfactory result was the reaction with methyl acrylate to give (**79a**)



(79a)

Unfortunately, we were unable to remove the carbamate group non-destructively. For these reasons, and the fact that the preparation from crotyl carbamates was successful, led to the discontinuation of these studies.

2.10.6) Conclusions.

These initial studies have resulted in the development of two related routes to oudemansins. We have shown that oudemansins can be easily prepared from (*Z*)-crotyl carbamates, while (*E*)-crotyl carbamates give the *anti*-diastereomer. While it is possible to prepare both diastereomers of natural oudemansins, studies on synthetic analogues have shown that the *syn* methoxy/methyl subunit is not necessary for antifungal activity, so the more easily prepared *anti*-diastereomer or a mixture of diastereomers may be equally effective. The overall yield is comparable to other published methods and the new preparation is also experimentally simple. From a synthetic point of view it is also significant that this is the first synthesis of an oudemansin that uses homoaldol methodology. Other investigations are underway to expand on these findings. These include:

- Other related routes, not necessarily involving carbamates.
- Preparation of other oudemansins.
- Asymmetric synthesis of oudemansins.
- Testing for antifungal activity. This will also be aimed at determining the effect of the relative and absolute stereochemistry of oudemansins.
- An improved preparation of the β-methoxyacrylate subunit.

CHAPTER 3: EXPERIMENTAL

3.1) Chemicals and Instrumentation.

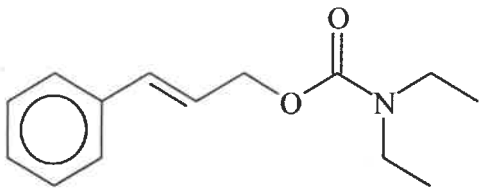
All solvents were dried using standard procedures and distilled before use. Flash column chromatography was carried out using Merck silica gel (230 - 400 mesh) by the technique of Still *et al.*[134] Pre-coated Kieselgel 60 F_{254} Merck plastic sheets were used for thin-layer chromatography. Melting points were measured on a Kofler hot-stage apparatus and are uncorrected.

NMR spectra (^{1}H 200 MHz and ^{13}C 50 MHz) were recorded on a Varian Gemini 200 instrument. All chemical shifts are reported in ppm downfield from TMS as internal standard, using $CDCl_3$ as solvent and coupling constants are reported in Hertz (Hz). Mass spectra were recorded on a Hewlett-Packard gas chromatographic-mass spectrometer (HP5988A) and high resolution mass spectra on a Kratos MS 9/50. Elemental analysis was carried out on a Perkin-Elmer 2400 CHN elemental analyser. Enantiomeric excesses (e.e.'s) were determined by NMR using $Eu(hfc)_3$ shift reagent.

All reactions involving the use of alkyllithiums and LDA were conducted under an atmosphere of dry nitrogen. All such reactions were repeatedly evacuated and flushed with nitrogen before addition of the reagents. All glassware used in moisture sensitive reactions was flame-dried. All other glass-ware was oven dried.

3.2) Starting Materials: Carbamates and Ethers.

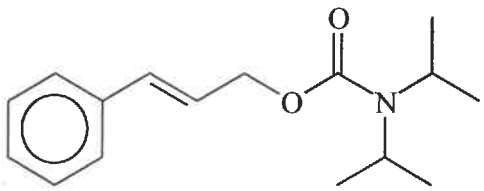
(E)-1-N,N-Diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**).



$C_{14}H_{19}NO_2 = 233.311$

To a solution of cinnamyl alcohol (24.82 g, 0.185 mol) in dry THF (200 ml) which was cooled in an ice bath, was added sodium hydride (0.200 mol) in portions with stirring. The reaction mixture was warmed to room temperature and stirred for 30 minutes. After cooling in an ice bath again, *N,N*-diethylcarbamoylchloride (25.11 g, 0.186 mol) in dry THF (100 ml) was added dropwise and the mixture stirred at room temperature for 4 hours. The reaction was quenched with saturated aqueous ammonium chloride (50 ml) and the THF removed. The residue was extracted with diethyl ether (2x 100 ml) and the combined organic extracts dried over anhydrous magnesium sulfate and distilled to give 3-*N,N*-diethylcarbamoyloxy-1-phenyl-propene (**45a**) as a colourless liquid (37.57 g, 87 %). b.p. 124 - 129 / 0.15 mmHg; (Found: C, 71.85; H, 8.40; N, 5.97; $C_{14}H_{19}NO_2$ requires C, 72.07; H, 8.21; N, 6.00 %; δ_H (200 MHz) 1.11 (6H, t, $N(CH_2CH_3)_2$), 3.28 (4H, bq, $N(CH_2CH_3)_2$), 4.73 (2H, dd, J = 1.28, 6.14, CH_2-O), 6.29 (1H, dt, J = 6.12, 15.86, Ph-CH=C*H*), 6.60 (1H, d, J = 15.92, Ph-C*H*=CH), 7.1 - 7.4 (5H, m, Ar-H); δ_C (50 MHz) 13.57 and 14.06 (2x q, $N(CH_2CH_3)_2$), 41.24 and 41.76 (2x t, $N(CH_2CH_3)_2$), 65.51 (t, CH_2-O), 124.50, 126.54, 128.53 (3x d, 5x Ar-C), 127.82 (d, Ph-CH=*C*H), 132.96 (d, Ph-*C*H=CH), 136.44 (s, Ar-C), 155.62 (s, C=O); *m/z* 233 (M^+, 7 %), 117 (100), 115 (28), 100 (22), 91 (11), 72 (9), 44 (7).

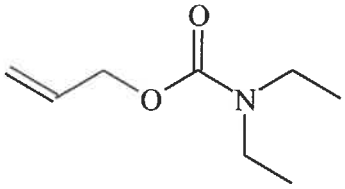
(E)-1-N,N-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**45b**).



$C_{16}H_{23}NO_2 = 261.365$

To a solution of cinnamyl alcohol (24.82 g, 0.185 mol) in dry THF (200 ml) which was cooled in an ice bath, was added sodium hydride (0.200 mol) in portions with stirring. The reaction mixture was warmed to room temperature and stirred for 30 minutes. After cooling in an ice bath again, *N,N*-diisopropylcarbamoylchloride (30.45 g, 0.186 mol) in dry THF (100 ml) was added dropwise and the mixture stirred at room temperature for 4 hours. The reaction was quenched with saturated aqueous ammonium chloride (50 ml) and the THF removed. The residue was extracted with diethyl ether (2x 100 ml) and the combined organic extracts dried over anhydrous magnesium sulfate and distilled to give 3-*N,N*-diisopropylcarbamoyloxy-1-phenyl-propene (**45b**) as a colourless liquid (40.15 g, 83 %). b.p. 189 - 191 / 0.1 mmHg; (Found: C, 73.41; H, 8.95; N, 5.40; $C_{16}H_{23}NO_2$ requires C, 73.53; H, 8.87; N, 5.36 %; δ_H (200 MHz) 1.22 (12H, d, J = 6.79 Hz, 4x CH_3), 3.90 (2H, bs, 2x $CH(CH_3)_2$), 4.75 (2H, dd, J = 1.34, 6.18, CH_2), 6.32 (1H, dt, J = 6.15, 15.86, Ph-CH=C*H*), 6.63 (1H, d, J = 15.93, Ph-C*H*=CH), 7.1 - 7.4 (5H, m, Ar-H); δ_C (50 MHz) 21.02 (q, 2x $CH(CH_3)_2$), 45.87 (d, $CH(CH_3)_2$), 65.17 (t, CH_2), 124.65, 126.54, 128.53 (3x d, 5x Ar-C), 127.79 (d, Ph-CH=*C*H), 132.95 (d, Ph-*C*H=CH), 136.54 (s, Ar-C), 155.33 (s, C=O); *m/z* 261 (M^+, 1 %), 117 (100), 115 (18), 91 (8), 86 (5), 43 (8).

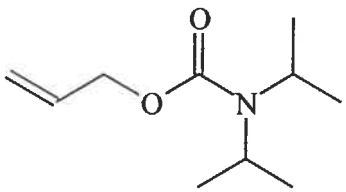
1-N,N-Diethylcarbamoyloxy-prop-2-ene (**49a**).



$C_8H_{15}NO_2 = 157.213$

To a solution of allyl alcohol 15.00 g, 0.258 mol) in dry THF (300 ml) which was cooled in an ice bath, was added sodium hydride (0.335 mol) in portions with stirring. The reaction mixture was warmed to room temperature and stirred for 30 minutes. After cooling in an ice bath again, *N,N*-diethylcarbamoylchloride (35.00 g, 0.258 mol) in dry THF (150 ml) was added dropwise and the mixture stirred at room temperature for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (75 ml) and the THF removed. The residue was extracted with diethyl ether (2x 100 ml) and the combined organic extracts dried over anhydrous magnesium sulfate and distilled to give 1-*N,N*-diethylcarbamoyloxy-prop-2-ene (**49a**) as a colourless liquid (38.55 g, 95 %). b.p. 62 - 63 °C / 0.2 mmHg; (Found: C, 61.31; H, 9.75; N, 9.09; $C_8H_{15}NO_2$ requires C, 61.12; H, 9.62; N, 8.91 %; δ_H (200 MHz) 1.13 (6H, t, $N(CH_2CH_3)_2$), 3.30 (4H, q, $N(CH_2CH_3)_2$), 4.58 (2H, dt, J = 1.47, 5.39, CH_2-O), 5.14 - 5.23 (1H, ddd, J = 1.42, 2.90, 10.35, $CH=CH_{trans}$), 5.25 - 5.36 (1H, ddd, J = 1.65, 3.31, 17.22, $CH=CH_{cis}$), 5.84 - 6.05 (1H, ddt, J = 5.40, 10.36, 17.23, $CH=CH_2$); δ_C (50 MHz) 13.97, 14.02 (2x q, $N(CH_2CH_3)_2$), 41.28, 41.79 (2x t, $N(CH_2CH_3)_2$), 65.61 (t, CH_2-O), 116.85 (t, $CH=CH_2$), 133.37 (d, $CH=CH_2$), 155.66 (s, C=O); *m/z* 157 (M^+, 62 %), 142 (100), 116 (63), 100 (91), 98 (90), 72 (97), 56 (90).

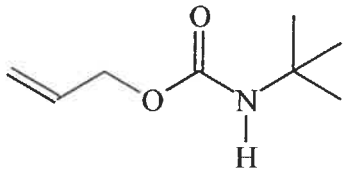
1-N,N-Diisopropylcarbamoyloxy-prop-2-ene (**49b**).



$C_{10}H_{19}NO_2 = 185.267$

To a solution of allyl alcohol 15.00 g, 0.258 mol) in dry THF (300 ml) which was cooled in an ice bath, was added sodium hydride (0.335 mol) in portions with stirring. The reaction mixture was warmed to room temperature and stirred for 30 minutes. After cooling in an ice bath again, *N,N*-diisopropylcarbamoylchloride (42.23 g, 0.258 mol) in dry THF (150 ml) was added dropwise and the mixture stirred at room temperature for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (75 ml) and the THF removed. The residue was extracted with diethyl ether (2x 100 ml) and the combined organic extracts dried over anhydrous magnesium sulfate and distilled to give 1-*N,N*-diisopropylcarbamoyloxy-prop-2-ene (**49b**) as a colourless liquid (44.51 g, 93 %). b.p. mmHg; (Found: C, 64.92; H, 10.68; N, 7.50; $C_{10}H_{19}NO_2$ requires C, 64.83; H, 10.34; N, 7.56 %; δ_H (200 MHz) 1.22 (12H, d, J = 6.79 Hz, 2x $CH(CH_3)_2$), 3.93 (2H, bs, 2x $CH(CH_3)_2$), 4.60 (2H, dt, J = 1.45, 5.40, CH_2O), 5.15 - 5.23 (1H, ddd, J = 1.38, 2.93, 10.39, $CH=CH_{trans}$), 5.25 - 5.36 (1H, ddd, J = 1.65, 3.30, 17.21, $CH=CH_{cis}$), 5.87 - 6.06 (1H, ddt, J= 5.45, 10.38, 17.25, $CH_2=CH$); δ_C (50 MHz) 20.96 (q, 4x CH_3), 45.70 (d, 2x $CH(CH_3)_2$), 65.29 (t, CH_2O), 116.90 (t, $CH_2=CH$), 133.46 (d, $CH_2=CH$), 155.30 (s, C=O); *m/z* 185 (M^+, 19 %), 170 (100), 128 (13), 102 (12), 84 (66), 41 (23).

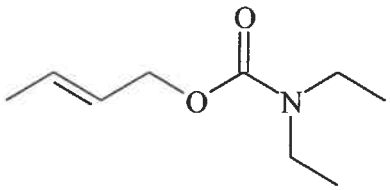
1-N-tert-Butylcarbamoyloxyprop-2-ene (**49c**).



$C_8H_{15}NO_2 = 157.213$

^{t}Butylamine (10.00 g, 0.0684 mol) was dissolved in dry dichloromethane (75 ml) and cooled in an ice-bath. Allyl chloroformate (9.08 g, 0.0753 mol) was added dropwise with stirring over 30 minutes. The reaction was allowed to warm to room temperature and stirred for a further 3 hours. The reaction was quenched with saturated aqueous sodium hydrogen carbonate (50 ml) and washed with saturated aqueous sodium hydrogen carbonate (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was distilled to afford 1-*N*-^{t}butylcarbamoyloxyprop-2-ene (**49c**) as a colourless liquid (10.11 g, 94 %). (Found: C, 60.99; H, 9.75; N, 9.09; $C_8H_{15}NO_2$ requires C, 61.12; H, 9.62; N, 8.91 %; δ_H (200 MHz) 1.32 (9H, s, C(CH_3)$_3$), 4.50 (2H, d, CH_2-O), 4.99 (1H, bs, N*H*), 5.18 (1H, ddd, J = 1.33, 2.84, 10.39, CH=CHH_{trans}), 5.28 (1H, ddd, J = 1.56, 3.20, 17.22, CH=CHH_{cis}), 5.91 (1H, ddt, J = 5.52, 10.43, 17.21, C*H*=CH$_2$); δ_C (50 MHz) 28.91 (q, C(CH_3)$_3$), 50.25 (s, *C*(CH_3)$_3$), 64.74 (t, *C*H$_2$-O), 117.22 (t, CH=*C*H$_2$), 133.23 (d, *C*H=CH$_2$), 154.82 (s, *C*=O); *m/z* 157 (M^+, 9 %), 142 (100), 98 (83), 57 (50), 41 (69).

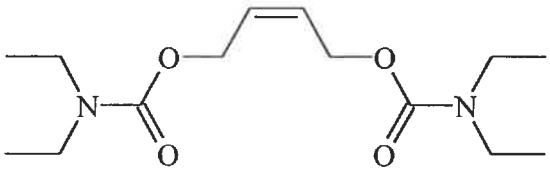
(E)-1-N,N-Diethylcarbamoyloxybut-2-ene (**49d**).



$C_9H_{17}NO_2 = 171.240$

To a solution of crotyl alcohol 10.00 g, 0.139 mol) in dry THF (150 ml) which was cooled in an ice bath, was added sodium hydride (0.208 mol) in portions with stirring. The reaction mixture was warmed to room temperature and stirred for 30 minutes. After cooling in an ice bath again, *N,N*-diethylcarbamoylchloride (20.69 g, 0.153 mol) in dry THF (75 ml) was added dropwise and the mixture stirred at room temperature for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (25 ml) and the THF removed. The residue was extracted with diethyl ether (2x 75 ml) and the combined organic extracts dried over anhydrous magnesium sulfate and distilled to give (*E*)-1-*N,N*-diethylcarbamoyloxybut-2-ene (**49d**) as a colourless liquid (20.91 g, 88 %). b.p. 58 - 59 °C / 0.13 mmHg; (Found: C, 63.19; H, 10.29; N, 8.31; $C_9H_{17}NO_2$ requires C, 63.13; H, 10.01; N, 8.18 %; δ_H (200 MHz) 1.12 (6H, t, $N(CH_2CH_3)_2$), 1.71 (3H, dd, J = 1.19, 6.05, CH_3-CH), 3.27 (4H, bq, $N(CH_2CH_3)_2$), 4.50 (2H, d, CH_2-O), 5.5 - 5.9 (2H, c, CH=CH); δ_C (50 MHz) 13.65, 14.06 (2x q, $N(CH_2CH_3)_2$), 17.80 (q, CH_3CH), 41.32, 41.75 (2x t, $N(CH_2CH_3)_2$), 65.64 (t, CH_2-O), 126.47 (d, CH_3CH), 129.72 (d, CH-CH_2), 155.82 (s, C=O); *m/z* 171 (M^+, 2 %), 100 (18), 72 (11), 58 (20), 55 (100).

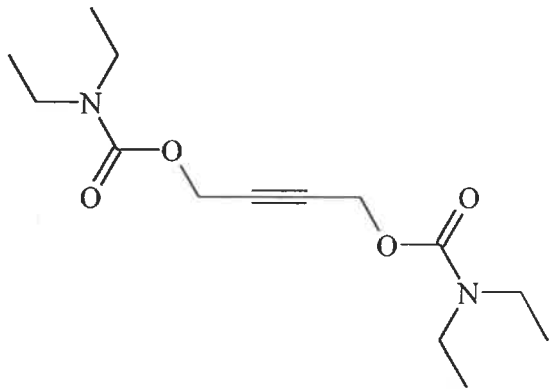
(Z)-1,4-Bis-(N,N-diethylcarbamoyloxy)but-2-ene (**50**).



$C_{14}H_{26}N_2O_4 = 286.372$

A solution of (*Z*)-1,4-dihydroxybut-2-ene (10.00 g, 0.1135 mol) in dry THF (50 ml) was added to a cooled (0 °C), stirred suspension of NaH (0.2838 mol) in dry THF (100 ml). The mixture was allowed to warm to room temperature and stirred for 30 minutes. The reaction mixture was cooled again and a solution of *N,N*-diethylcarbamoylchloride (32,33 g, 0.2384 mol) in dry THF (50 ml) was added drop-wise. The reaction was warmed to room temperature and stirred for a further 4 hours. The reaction was quenched with water (100 ml) and the THF removed. The reaction mixture was diluted with diethyl ether (100 ml) and washed with 10 % aqueous sodium hydrogen carbonate (2 x 50 ml) and water (1 x 50 ml). The organic phase was separated and dried over anhydrous $MgSO_4$. The solvent was removed and the residue distilled to yield (*Z*)-1,4-bis-(*N,N*-diethylcarbamoyl)but-2-ene (**50**) (30.30 g, 93 %). b.p. 165 °C / 5 mmHg; (Found: C, 58.58; H, 9.21, N, 9.63; $C_{14}H_{26}N_2O_4$ requires C, 58.72; H, 9.15, N, 9.78 %); δ_H (200 MHz) 1.12 (12H, t, 4 x CH_3), 3.28 (bq, 8H, 4 x CH_2CH_3), 4.70 (d, 4H, CH_2-CH=CH-CH_2), 5.76 (t, 2H, CH=CH); δ_C (50 MHz) 13.58, 14.00 (2 x q, 2 x CH_3), 41.28, 41.80 (2 x t, 2 x CH_2CH_3), 60.73 (t, CH_2-CH=CH-CH_2), 128.46(d, CH=CH), 155.63 (s, 2 x C=O); *m/z* 286 (M^+, <1 %), 117 (19), 100 (100), 72 (85), 54 (21), 44 (24).

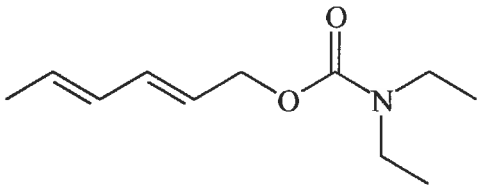
1,4-Bis-(N,N-diethylcarbamoyloxy)but-2-yne (**51**).



$C_{14}H_{24}N_2O_4 = 284.356$

A solution of 1,4-dihydroxybut-2-yne (10.00 g, 0.1162 mol) in dry THF (50 ml) was added to a cooled (0 °C), stirred suspension of NaH (0.2905 mol) in dry THF (100 ml). The mixture was allowed to warm to room temperature and stirred for 30 minutes. The reaction mixture was cooled again and a solution of *N,N*-diethylcarbamoylchloride (33.10 g, 0.2440 mol) in dry THF (50 ml) was added drop-wise. The reaction was warmed to room temperature and stirred for a further 4 hours. The reaction was quenched with water (100 ml) and the THF removed. The reaction mixture was diluted with diethyl ether (100 ml) and washed with 10 % aqueous sodium hydrogen carbonate (2 x 50 ml) and water (1 x 50 ml). The organic phase was separated and dried over anhydrous $MgSO_4$. The solvent was removed and the residue purified by column chromatography (silica, 10 % diethyl ether / hexane) to yield 1,4-bis-(*N,N*-diethylcarbamoyl)but-2-yne (**51**) (29.40 g, 89 %). (Found: C, 59.08; H, 8.66, N, 9.69; $C_{14}H_{24}N_2O_4$ requires C, 59.14; H, 8.51, N, 9.85 %); δ_H (200 MHz) 1.13 (12H, t, 2x $N(CH_2CH_3)_2$), 3.29 (8H, bd, 2x $N(CH_2CH_3)_2$), 4.74 (4H, s, 2x CH_2-O); δ_C (50 MHz) 13.46, 14.07 (q, 2x $N(CH_2CH_3)_2$), 41.39, 42.03 (t, 2x $N(CH_2CH_3)_2$), 52.83 (t, 2x CH_2-O), 81.18 (s, C≡C), 155.00 (s, 2x C=O); *m/z* 284 (M^+, < 1 %), 118 (26), 100 (100), 72 (85), 52 (21), 44 (18).

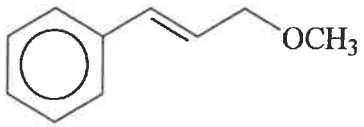
(E,E)-1-N,N-Diethylcarbamoyloxy-2,4-hexadiene (**54**).



$C_{11}H_{19}NO_2 = 197.278$

(*E,E*)-2,4-Hexadienal (4.00 g, 0.0416 mol) was dissolved in methanol (50 ml) and cooled in an ice-bath. Sodium borohydride (1.57 g, 0.0416 mol) was added in portions and the mixture stirred for 1 hour. The reaction was quenched with 2N HCl (20 ml) and extracted with diethyl ether (2x 100 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed. The crude alcohol was dissolved in dry THF (50 ml) and cooled in an ice-bath. Sodium hydride (0.0624 mol) was added slowly and the mixture stirred at room temperature for 30 minutes. The reaction was cooled again in an ice-bath and *N,N*-diethylcarbamoyl chloride (6.09 g, 0.0449 mol) was added. The reaction was allowed to warm to room temperature and stirred for a further 4 hours. The reaction was quenched with saturated aqueous ammonium chloride (20 ml) and the THF removed. The residue was dissolved in diethyl ether (50 ml) and washed with 10 % aqueous sodium hydrogen carbonate (2x 50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and distilled to afford (*E,E*)-1-*N,N*-diethylcarbamoyloxy-2,4-hexadiene (**54**) (6.65 g, 81 %). (Found: C, 66.89; H, 9.59, N, 7.21; $C_{11}H_{19}NO_2$ requires C, 66.97; H, 9.71, N, 7.10 %); δ_H (200 MHz) 1.12 (6H, t, $N(CH_2CH_3)_2$), 1.76 (3H, d, CH_3-CH), 3.25 (4H, bq, $N(CH_2CH_3)_2$), 4.58 (2H, d, CH_2O), 5.5 - 5.9 (2H, c, CH_3-CH=CH), 5.9 - 6.4 (2H, c, CH=CH-CH_2); δ_C (50 Mhz) 13.50, 13.88 (2x q, $N(CH_2CH_3)_2$), 18.11 (q, CH_3-CH), 41.29, 41.70 (2x t, $N(CH_2CH_3)_2$), 65.42 (t, CH_2-O), 125.14 (d, CH_3-CH), 130.50 (d, CH_3CH=CH), 130.73 (d, CH_2CH=CH), 133.71 (d, CH_2CH=CH), 155.77 (s, C=O); *m/z* 197 (M^+, 10 %), 100 (16), 81 (100), 79 (21), 72 (11), 41 (8).

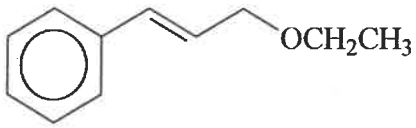
(E)-1-Methoxy-3-phenylprop-2-ene (**46a**).



$C_{10}H_{12}O = 148.205$

Cinnamyl alcohol (5.00 g, 0.0373 mol) was dissolved in dry THF (50 ml) and cooled in an ice-bath. Sodium hydride (0.0560 mol) was added, the reaction warmed to room temperature and stirred for 30 minutes. The reaction mixture was cooled again in an ice-bath and methyl iodide (7.95 g, 0.0560 mol) was added dropwise. The reaction was stirred at 5 °C for 3 hours and then quenched with water (50 ml). The THF was removed and the residue extracted with diethyl ether (2x 50 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed. Distillation afforded (*E*)-1-methoxy-3-phenylprop-2-ene (**46a**) as a colourless liquid (5.05 g, 93 %). b.p. 49-50 °C / 0.19 mmHg; δ_H (200 MHz) 3.33 (3H, s, OC*H*$_3$), 4.03 (2H, dd, *J* = 1.42, 5.89, C*H*$_2$), 6.24 (1H, dt, *J* = 5.86, 15.94, PhCH=C*H*), 6.58 (1H, d, *J* = 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 57.89 (q, O*C*H$_3$), 73.02 (t, *C*H$_2$), 125.89, 126.44, 128.52 (3x d, Ar*C*), 127.63 (d, PhCH=*C*H), 132.36 (d, Ph-*C*H), 136.66 (s, Ar*C*); *m/z* 148 (M^+, 100 %), 147 (41), 117 (68), 116 (47), 115 (88), 105 (32), 91 (22), 77 (21).

(E)-1-Ethoxy-3-phenylprop-2-ene (**46b**).



$C_{11}H_{14}O = 162.232$

Cinnamyl alcohol (5.00 g, 0.0373 mol) was dissolved in dry THF (50 ml) and cooled in an ice-bath. Sodium hydride (0.0560 mol) was added, the reaction warmed to room temperature and stirred for 30 minutes. The reaction mixture was cooled again in an ice-bath and ethyl iodide (8.73 g, 0.0560 mol) was added dropwise. The reaction was stirred at 5 °C for 3 hours and then quenched with water (50 ml). The THF was removed and the residue extracted with diethyl ether (2x 50 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed. Distillation afforded (*E*)-1-ethoxy-3-phenylprop-2-ene (**46b**) as a colourless liquid (5.33 g, 89 %). b.p. 101-103 °C / 0.55 mmHg; δ_H (200 MHz) 1.23 (3H, t, OCH_2CH_3), 3.51 (2H, q, OCH_2CH_3), 4.10 (2H, dd, J = 1.38, 5.93, $CHCH_2$), 6.28 (1H, dt, J = 5.91, 15.93, PhCH=C*H*), 6.59 (1H, d, J = 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 15.25 (q, CH_3), 65.66 (t, OCH_2CH_3), 71.19 (t, $CHCH_2$), 126.30, 126.44, 128.50 (3x d, Ar*C*), 127.57 (d, PhCH=*C*H), 132.10 (d, Ph-*C*H), 136.74 (s, Ar*C*); *m/z* 162 (M^+, 56 %), 133 (37), 118 (26), 117 (53), 115 (49), 105 (100), 91 (30), 77 (24).

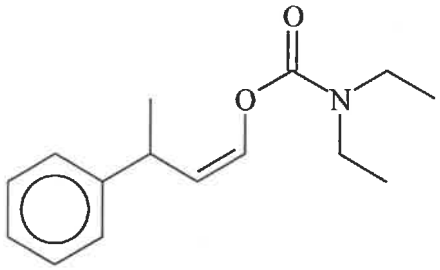
(Z)-1,4-Diethoxybut-2-ene (**84**)

$C_8H_{16}O_2 = 144.214$

(*Z*)-1,4-Dihydroxybut-2-ene (5.00 g, 0.0567 mol) was dissolved in dry THF (75 ml) and cooled in an ice-bath. Sodium hydride (0.1418 mol) was added, the reaction warmed to room temperature and stirred for 30 minutes. The reaction mixture was cooled again in an ice-bath and ethyl iodide (22.12 g, 0.1418 mol) was added dropwise. The reaction was stirred at 5 °C for 3 hours and then quenched with water (50 ml). The THF was removed and the residue extracted with diethyl ether (2x 50 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed. Distillation afforded (*Z*)-1,4-diethoxybut-2-ene (**84**) as a colourless liquid (7.06 g, 86 %). b.p. 118-120 °C / 0.50 mmHg. (Found: C, 66.75; H, 11.37; $C_8H_{16}O_2$ requires C, 66.63; H, 11.18 %); δ_H (200 MHz) 1.21 (6H, t, 2x OCH_2CH_3), 3.49 (4H, q, 2x OCH_2CH_3), 4.05 (4H, d, J = 4.78, 2x CH_2CH), 5.70 (2H, ddd, J = 1.11, 3.68, 6.65, *CH*=*CH*); δ_C (50 MHz) 15.23 (q, 2x OCH_2CH_3), 65.74 (t, 2x OCH_2CH_3), 66.28 (t, 2x CH_2-CH), 129.40 (d, *C*H=*C*H); *m/z* 144 (M^+, < 1 %), 98 (100), 85 (41), 71 (29), 70 (98), 69 (55), 57 (76).

3.3) Reaction of Cinnamyl Carbamates with Alkyl Halides.

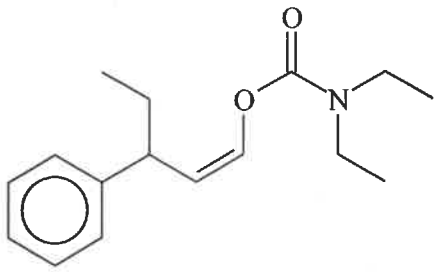
(Z)-1-N,N-Diethylcarbamoyloxy-3-phenylbutene (**56a**).



$C_{15}H_{21}NO_2 = 247.338$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (0.500 g, 0.0021 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0021 mol) was added dropwise and the mixture stirred for 15 minutes. Methyl iodide (0.370 g, 0.0027 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for 2 hrs at -78 °C. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The mixture was washed with water (2x 50 ml) and the organic phase separated and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*Z*)-1-*N,N*-diethylcarbamoyloxy-3-phenylbutene (**56a**) (0.433 g, 83 %). (Found: C, 72.78; H, 8.67; N, 5.69; $C_{15}H_{21}NO_2$ requires C, 72.84; H, 8.56; N, 5.66 %); δ_H (200 MHz) 1.11 (6H, t, $N(CH_2CH_3)_2$), 1.36 (3H, d, $CHCH_3$), 3.25 (4H, c, $N(CH_2CH_3)_2$), 3.92 (1H, p, $CHCH_3$), 4.90 (1H, dd, J = 6.38, 9.03, CH=CH-O), 7.05 (1H, dd, J = 1.17, 6.36, CHO), 7.1 - 7.3 (5H, m, Ar-*H*); δ_C (50 MHz) 13.02, 13.81 (2x q, $N(CH_2CH_3)_2$), 21.93 (q, $CHCH_3$), 35.07 (d, $CHCH_3$), 41.29, 41.79 (2x t, $N(CH_2CH_3)_2$), 115.59 (d, CH=CH-O), 125.67, 126.42, 128.08 (3x d, Ar-*C*), 133.89 (d, CH-O), 145.80 (s, Ar-*C*), 152.53 (s, C=O); *m/z* 247 (M^+, 2 %), 131 (6), 101 (7), 100 (100), 91 (10), 77 (6), 72 (51), 44 (8).

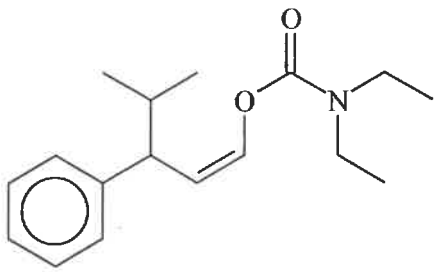
(Z)-1-N,N-Diethylcarbamoyloxy-3-phenylpent-1-ene (**56b**).



$C_{16}H_{23}NO_2 = 261.365$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (0.500 g, 0.0021 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0021 mol) was added dropwise and the mixture stirred for 15 minutes. Ethyl iodide (0.280 g, 0.0026 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for 2 hrs at -78 °C. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The mixture was washed with water (2x 50 ml) and the organic phase separated and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*Z*)-1-*N,N*-diethylcarbamoyloxy-3-phenylpent-1-ene (**56b**) (0.395 g, 72 %). (Found: C, 73.32; H, 8.69; N, 5.41; $C_{16}H_{23}NO_2$ requires C, 73.53; H, 8.87; N, 5.36 %); δ_H (200 MHz) 0.89 (3H, t, $CHCH_2CH_3$) 1.10 (6H, t, $N(CH_2CH_3)_2$), 1.68 (2H, m, $CHCH_2CH_3$), 3.23 (4H, c, $N(CH_2CH_3)_2$), 3.63 (1H, q, $CHCH_2CH_3$), 4.88 (1H, dd, J = 6.38, 9.38, *CH*=CH-O), 7.11 (1H, dd, J = 1.08, 6.40, *CH*O), 7.1 - 7.3 (5H, m, Ar-*H*); δ_C (50 MHz) 11.80 (q, $CHCH_2CH_3$) 12.93, 13.73 (2x q, $N(CH_2CH_3)_2$), 29.41 (t, $CHCH_2CH_3$); 41.20, 41.71 (2x t, $N(CH_2CH_3)_2$), 42.85 (d, $CHCH_2CH_3$) 114.01 (d, *C*H=CH-O), 125.59, 126.82, 127.95 (3x d, Ar-*C*), 134.60 (d, *C*H-O), 144.64 (s, Ar-*C*), 152.40 (s, *C*=O); *m/z* 261 (M^+, 2 %), 100 (100), 91 (6), 72 (40), 44 (6).

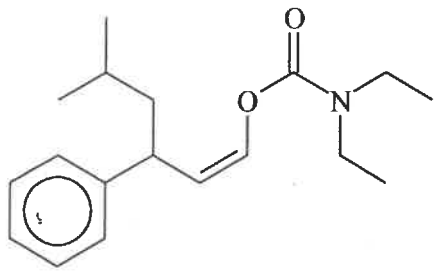
(Z)-1-N,N-Diethylcarbamoyloxy-4-methyl-3-phenylpent-1-ene **(56c).**



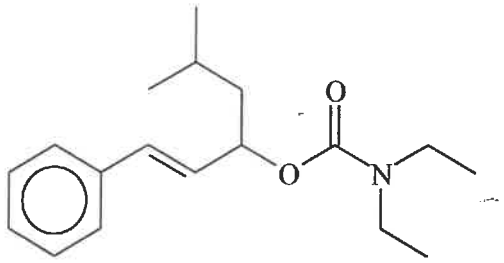
$C_{17}H_{25}NO_2 = 275.392$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (0.500 g, 0.0021 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0021 mol) was added dropwise and the mixture stirred for 15 minutes. 2-Bromopropane (0.320 g, 0.0026 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for 3 hrs at -78 °C. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The mixture was washed with water (2x 50 ml) and the organic phase separated and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*Z*)-1-*N,N*-diethylcarbamoyloxy-4-methyl-3-phenylpent-1-ene **(56c)** (0.415 g, 70 %). (Found: C, 74.41; H, 9.31; N, 5.27; $C_{17}H_{25}NO_2$ requires C, 74.14; H, 9.15; N, 5.09 %); δ_H (200 MHz) 0.79, 0.95 (6H, 2x d, $CH(CH_3)_2$), 1.07 (6H, c, $N(CH_2CH_3)_2$), 1.88 (1H, m, $CH(CH_3)_2$), 3.23 (4H, m, $N(CH_2CH_3)_2$), 3.44 (1H, t, Ph-C*H*), 4.97 (1H, dd, *J* = 6.50, 9.80, C*H*=CH-O), 7.0 - 7.3 (6H, m, Ar-*H*, C*H*-O); δ_C (50 MHz) 12.83, 13.65 (2x q, $N(CH_2CH_3)_2$), 19.77, 20.53 (2x q, $CH(CH_3)_2$), 32.12 (d, $CH(CH_3)_2$), 41.09, 41.60 (2x t, $N(CH_2CH_3)_2$), 48.54 (d, Ph-*C*H), 112.59 (d, *C*H=CH-O), 125.43, 127.29, 127.73 (3x d, Ar*C*), 134.74 (d, *C*H-O), 143.75 (s, Ar*C*), 152.24 (s, *C*=O); *m/z* 275 (M^+, < 1 %), 101 (6), 100 (100), 91 (3), 72 (32), 44 (6).

(Z)-1-N,N-Diethylcarbamoyloxy-5-methyl-3-phenylhex-1-ene (**56d**) *and (E)-3-N,N-Diethylcarbamoyloxy-5-methyl-1-phenylhex-1-ene* (**57d**).



(**56d**)



(**57d**)

$C_{18}H_{27}NO_2 = 289.419$

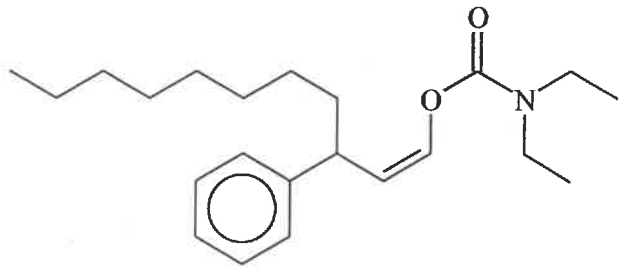
1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (0.500 g, 0.0021 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0021 mol) was added dropwise and the mixture stirred for 15 minutes. Isobutyl bromide (0.356 g, 0.0026 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for 5 hrs at -78 °C. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The mixture was washed with water (2x 50 ml) and the organic phase separated and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*Z*)-1-*N,N*-diethylcarbamoyloxy-5-methyl-3-phenylhex-1-ene (**56d**) and (*E*)-3-*N,N*-diethyl-carbamoyloxy-5-methyl-1-phenylhex-1-ene (**57d**) (92 : 8) (0.196 g, 32 % overall).

(**56d**) (Found: C, 74.57; H, 9.53; N, 4.94; $C_{18}H_{27}NO_2$ requires C, 74.70; H, 9.40; N, 4.84 %); δ_H (200 MHz) 0.91 (6H, dd, $CH(CH_3)_2$), 1.16 (6H, bs, $N(CH_2CH_3)_2$), 1.58 (3H, c, $CH_2CH(CH_3)_2$), 3.30 (4H, q, $N(CH_2CH_3)_2$), 3.88 (1H, q, Ph-C*H*), 4.87 (1H, dd, J = 6.36, 9.58, C*H*=CH-O), 7.07 (1H, dd, J = 0.98, 6.38, C*H*-O), 7.1 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) 13.32, 14.20 (2x q, $N(CH_2CH_3)_2$), 22.35, 22.79 (2x q, $CH(CH_3)_2$), 25.52 (d, $CH(CH_3)_2$), 39.15 (d, Ph-*C*H), 41.59, 42.12 (2x t, $N(CH_2CH_3)_2$), 46.15 (t, $CHCH_2$), 114.96 (d, *C*H=CH-O), 125.98, 127.16, 128.42 (3x d, Ar*C*), 134.61

(d, *C*H-O), 145.00 (s, Ar*C*), 152.60 (s, *C*=O); *m/z* 289 (M^+, < 1 %), 101 (6), 100 (100), 91 (4), 72 (29), 44 (4).

(57d) (Found: C, 74.45; H, 9.47; N, 4.99; $C_{18}H_{27}NO_2$ requires C, 74.70; H, 9.40; N, 4.84 %); δ_H (200 MHz) 0.96 (6H, d, $CH(CH_3)_2$), 1.12 (6H, t, $N(CH_2CH_3)_2$), 1.49 (1H, m, $CH(CH_3)_2$), 1.71 (2H, m, $CHCH_2$), 3.28 (4H, bq, $N(CH_2CH_3)_2$), 5.42 (1H, q, C*H*-O), 6.15 (1H, dd, *J* = 7.05, 15.93, PhCH=C*H*), 6.61 (1H, d, *J* = 15.90, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 14.00 (q, $N(CH_2CH_3)_2$), 22.65, 22.83 (2x q, $CH(CH_3)_2$), 24.64 (d, $CH(CH_3)_2$), 41.61 (t, $N(CH_2CH_3)_2$), 73.77 (d, *C*H-O), 126.53, 127.63, 128.47 (3x d, Ar*C*), 129.15 (d, PhCH=*C*H), 131.44 (d, Ph-*C*H), 136.70 (s, Ar*C*), 155.46 (s, *C*=O); *m/z* 289 (M^+, 1 %), 129 (20), 117 (100), 115 (17), 100 (70), 91 (23), 72 (20).

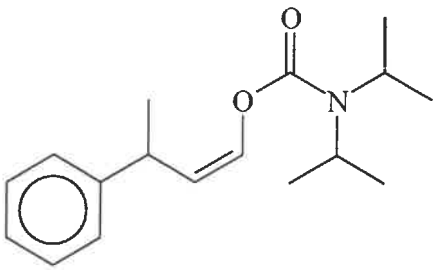
(Z)-1-N,N-Diethylcarbamoyloxy-3-phenylundec-1-ene (**56e**).



$C_{22}H_{35}NO_2 = 345.527$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (0.500 g, 0.0021 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0021 mol) was added dropwise and the mixture stirred for 15 minutes. 2-Bromo-octane (0.520 g, 0.0027 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for 4 hrs at -78 °C. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The mixture was washed with water (2x 50 ml) and the organic phase separated and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*Z*)-1-*N,N*-diethylcarbamoyloxy-3-phenylundec-1-ene (**56e**) (0.356 g, 48 %). (Found: C, 76.66; H, 10.35; N, 4.17; $C_{22}H_{35}NO_2$ requires C, 76.48; H, 10.21; N, 4.05 %); δ_H (200 MHz) 0.88 (3H, t, $(CH_2)_7CH_3$), 1.12 (6H, bt, $N(CH_2CH_3)_2$), 1.28 (12H, bs, $CH_2(CH_2)_6CH_3$), 1.69 (2H, bs, $CHCH_2$), 3.28 (4H, bs, $N(CH_2CH_3)_2$), 3.73 (1H, q, $CHCH_2$), 4.89 (1H, dd, J = 6.41, 9.43, C*H*=CH-O), 7.08 (1H, dd, J = 1.04, 6.37, C*H*-O), 7.1 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) 13.08, 13.91 (2x q, $N(CH_2CH_3)_2$), 13.86 (q, $(CH_2)_7CH_3$), 22.43, 27.35, 29.08, 29.29, 31.63, 36.66 (7x t, $(CH_2)_7CH_3$), 41.15 (d, $CH(CH_2)_7$), 41.35, 41.86 (2x t, $N(CH_2CH_3)_2$), 114.55 (d, *C*H=CH-O), 125.70, 126.92, 128.11 (3x d, Ar*C*), 134.56 (d, *C*H-O), 145.04 (s, Ar*C*), 152.60 (s, *C*=O); *m/z* 345 (M^+, 2%), 229 (7), 131 (6), 101 (5), 100 (100), 91 (6), 72 (21), 44 (5).

(Z)-1-N,N-Diisopropylcarbamoyloxy-3-phenylbut-1-ene (**58**).

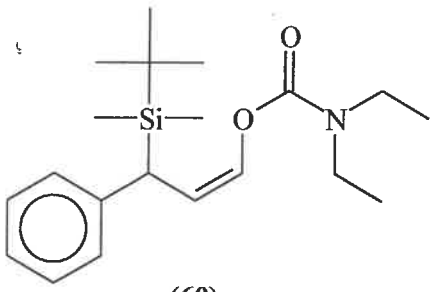


$C_{17}H_{25}NO_2 = 275.392$

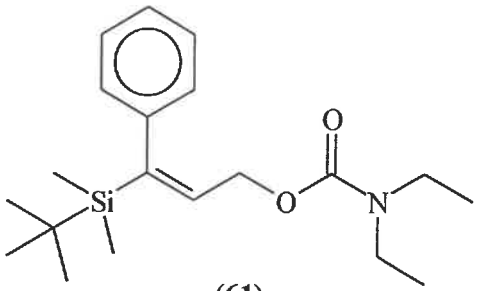
1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (0.500 g, 0.0018 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0018 mol) was added dropwise and the mixture stirred for 15 minutes. Methyl iodide (0.320 g, 0.0023 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for 3 hrs at -78 °C. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The mixture was washed with water (2x 50 ml) and the organic phase separated and dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*Z*)-1-*N,N*-diisopropylcarbamoyloxy-3-phenylbut-1-ene (**58**) (0.308 g, 62 %). (Found: C, 74.39; H, 9.25; N, 5.27; $C_{17}H_{25}NO_2$ requires C, 74.14; H, 9.15; N, 5.09 %); δ_H (200 MHz) 1.23 (12H, d, N(CH(C*H*$_3$)$_2$)$_2$), 1.38 (3H, d, CHCHC*H*$_3$), 3.88 (3H, c, N(C*H*(CH$_3$)$_2$)$_2$, CHC*H*CH$_3$), 4.90 (1H, dd, J = 6.45, 9.02, C*H*=CH-O), 7.08 (1H, dd, J = 1.15, 6.49, C*H*-O), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 20.30, 21.46 (2x q, N(CH(*C*H$_3$)$_2$)$_2$), 22.30 (q, CHCH*C*H$_3$), 35.58 (d, CH*C*HCH$_3$), 45.92, 46.81 (2x d, N(*C*H(CH$_3$)$_2$)$_2$), 114.52 (d, *C*H=CH-O), 125.98, 127.23, 128.38 (3x d, Ar*C*), 134.55 (d, *C*H-O), 145.26 (s, Ar*C*), 152.73 (s, *C*=O); *m/z* 275 (M^+, 1 %), 131 (4), 128 (100), 77 (6), 43 (9).

3.4) Preparation of Silyl Carbamates.

(Z)-3-^{t}Butyldimethylsilyl-1-N,N-diethylcarbamoyloxy-3-phenylprop-1-ene (**60**) *and (E)-1-^{t}butyldimethylsilyl-3-N,N-diethylcarbamoyloxy-1-phenylprop-1-ene* (**61**).



(**60**)



(**61**)

$C_{20}H_{33}NO_2Si = 347.575$

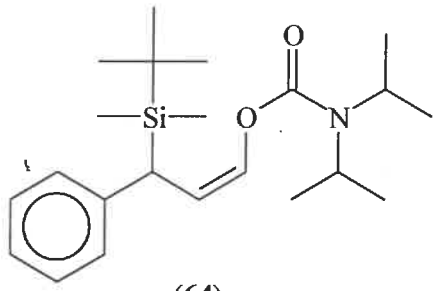
(*E*)-1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0021 mol) and TBDMSCl (0.348 g, 0.0023 mol) were dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0044 mol) was added dropwise and the mixture stirred at -78 °C for 2 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*Z*)-3-^{t}butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxy-3-phenylprop-1-ene (**60**) and (*E*)-1-^{t}butyldimethylsilyl-3-*N,N*-diethylcarbamoyloxy-1-phenylprop-1-ene (**61**).(71 : 29). (0.484 g, 66 %).

(**60**) (Found: C, 69.23; H, 9.81; N, 4.27; $C_{20}H_{33}NO_2Si$ requires C, 69.11; H, 9.57; N, 4.03 %); δ_H (200 MHz) 0.08, 0.11 (6H, 2x s, Si(CH_3)$_2$), 0.99 (9H, s, C(CH_3)$_3$), 1.20 (6H, bs, N(CH_2CH_3)$_2$), 3.37 (4H, bq, N(CH_2CH_3)$_2$), 5.46 (1H, d, J = 4.95, C*H*-Si), 6.2 - 6.5 (1H, c, C*H*=CHO), 7.1 - 7.4 (6H, m, Ar*H*, C*H*-O); δ_C (50 MHz) -8.14, -7.25 (2x q, Si(CH_3)$_2$), 13.49, 14.20 (2x q, N(CH_2CH_3)$_2$), 16.95 (s, *C*(CH_3)$_3$), 26.85 (q, C(CH_3)$_3$), 41.06, 41.89 (2x t, N(CH_2CH_3)$_2$), 68.87 (d, PhCH), 126.05, 126.46, 128.38

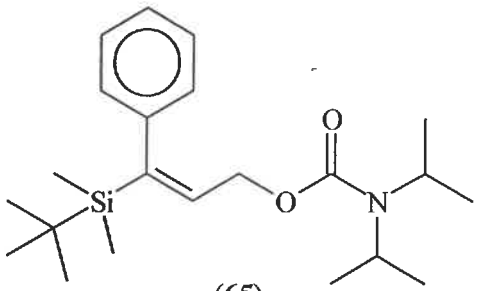
(3x d, Ar*C*), 126.82 (d, *C*H=CHO), 128.82 (d, *C*H-O), 137.39 (s, Ar*C*), 155.69 (s, *C*=O); *m/z* (CH_4) 349 (M^+ + 1, 13 %), 348 (M^+, 45), 347 (20), 332 (26), 232 (24), 231 (100), 115 (28).

(**61**) (Found: C, 69.27; H, 9.48; N, 4.09; $C_{20}H_{33}NO_2Si$ requires C, 69.11; H, 9.57; N, 4.03 %); δ_H (200 MHz) 0.09 (6H, s, $Si(CH_3)_2$), 0.91 (9H, s, $C(CH_3)_3$), 1.16 (6H, bs, $N(CH_2CH_3)_2$), 3.32 (4H, bq, $N(CH_2CH_3)_2$), 3.39 (2H, d, $CHCH_2$), 5.66 (1H, t, J = 7.04, C=C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) -6.41 (q, $Si(CH_3)_2$), 13.42, 14.31 (2x q, $N(CH_2CH_3)_2$), 16.82 (s, $C(CH_3)_3$), 26.55 (q, $C(CH_3)_3$), 32.11 (t, $CHCH_2$), 41.61, 41.93 (2x t, $N(CH_2CH_3)_2$), 125.94 (d, C=*C*H), 126.07, 128.37, 128.56 (3x d, Ar*C*), 140.22 (s, Ar*C*), 153.55 (s, *C*=CH), 153.95 (s, *C*=O); *m/z* 349 (M^+ + 1, 30 %), 348 (M^+, 100), 346 (7), 333 (15), 332 (55), 291 (12), 290 (52), 146 (5).

(Z)-3-^{t}Butyldimethylsilyl-1-N,N-diisopropylcarbamoyloxy-3-phenylprop-1-ene (**64**), *(E)-1-^{t}butyldimethylsilyl-3-N,N-diisopropylcarbamoyloxy-1-phenylprop-1-ene* (**65**).



(**64**)



(**65**)

$C_{22}H_{37}NO_2Si = 375.624$

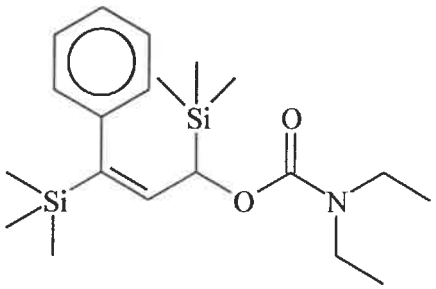
(*E*)-1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**45b**) (0.500 g, 0.0019 mol) and TBDMSCl (0.318 g, 0.0021 mol) were dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0040 mol) was added dropwise and the mixture stirred at -78 °C for 2 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*Z*)-3-^{t}butyldimethylsilyl-1-*N,N*-diisopropylcarbamoyloxy-3-phenylprop-1-ene (**64**) and (*E*)-1-^{t}butyldimethylsilyl-3-*N,N*-diisopropylcarbamoyloxy-1-phenylprop-1-ene (**65**). (78 : 22). (0.485 g, 68 %).

(**64**) (Found: C, 69.98; H, 9.77; N, 3.89; $C_{22}H_{37}NO_2Si$ requires C, 70.35; H, 9.93; N, 3.73 %); δ_H (200 MHz) 0.09, 0.11 (6H, 2x s, Si(CH_3)$_2$), 0.96 (9H, s, C(CH_3)$_3$), 1.26 (12H, d, N(CH(CH_3)$_2$)$_2$), 3.95 (2H, bs, N(C*H*(CH$_3$)$_2$)$_2$), 5.51 (1H, d, *J* = 5.11, C*H*-Si), 6.2 - 6.5 (1H, c, C*H*=CHO), 7.1 - 7.4 (6H, m, Ar*H*, C*H*-O); δ_C (50 MHz) -7.76, -7.15 (2x q, Si(*C*H$_3$)$_2$), 16.95 (s, *C*(CH$_3$)$_3$), 20.56, 21.41 (2x q, N(CH(*C*H$_3$)$_2$)$_2$), 26.92 (q, C(*C*H$_3$)$_3$), 45.92 (d, N(*C*H(CH$_3$)$_2$)$_2$), 68.28 (d, PhCH), 126.08, 126.69, 128.43 (3x d, Ar*C*), 126.85 (d, *C*H=CHO), 128.95 (d, *C*H-O), 137.50 (s, Ar*C*), 154.83 (s, *C*=O);

m/z 375 (M^+, < 1 %), 214 (11), 128 (19), 117 (9), 115 (40), 86 (50), 75 (13), 74 (10), 73 (100), 59 (10).

(**65**) (Found: C, 70.09; H, 10.08; N, 3.95; $C_{22}H_{37}NO_2Si$ requires C, 70.35; H, 9.93; N, 3.73 %); δ_H (200 MHz) 0.06 (6H, s, $Si(CH_3)_2$), 0.93 (9H, s, $C(CH_3)_3$), 1.27 (12H, d, $N(CH(CH_3)_2)_2$), 3.40 (2H, d, $CHCH_2$), 3.95 (2H, bs, $N(CH(CH_3)_2)_2$), 5.66 (1H, t, J = 6.96, C=CH), 7.1 - 7.4 (5H, m, ArH); δ_C (50 MHz) -6.30 (q, $Si(CH_3)_2$), 16.88 (s, $C(CH_3)_3$), 20.55, 21.43 (2x q, $N(CH(CH_3)_2)_2$), 26.62 (q, $C(CH_3)_3$), 32.26 (t, $CHCH_2$), 46.27 (d, $N(CH(CH_3)_2)_2$), 125.93 (d, C=CH), 126.01, 128.39, 128.60 (3x d, ArC), 140.33 (s, ArC), 153.30 (s, C=CH), 153.86 (s, C=O); *m/z* 375 (M^+, 1 %), 319 (25), 318 (100), 201 (31), 86 (17).

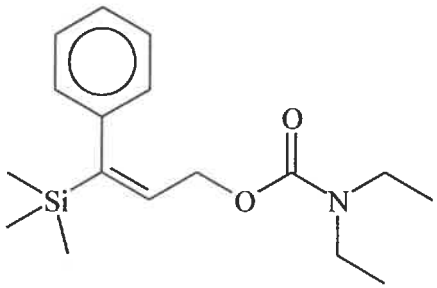
1-N,N-Diethylcarbamoyloxy-1,3-bis-trimethylsilylprop-2-ene (**66**).



$C_{20}H_{35}NO_2Si_2 = 377.670$

A solution of (*E*)-1-*N,N*-diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0021 mol) in dry THF (15 ml) was cooled to -78 °C. A solution of ^{n}butyllithium (0.0044 mol) was added dropwise and the solution stirred for 30 minutes. Trimethylsilylchloride (0.438 g, 0.0044 mol) was added dropwise and the reaction stirred for 2 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether. The organic phase was washed with water (2x 50 ml), dried over anhydrous magnesium sulfate and the solvent removed. The crude mixture was purified by chromatography (silica, 10 % diethyl ether / hexane) to afford 1-*N,N*-diethylcarbamoyloxy-1,3-bis-trimethylsilylprop-2-ene (**66**) as a colourless oil. (0.574 g, 72 %); (Found: C, 63.82; H, 9.25; N, 3.86; $C_{20}H_{35}NO_2Si_2$ requires C, 63.60; H, 9.34; N, 3.71 %); δ_H (200 MHz) 0.03, 0.20 (18H, 2x s, 2x $Si(CH_3)_3$), 1.18 (6H, m, $N(CH_2CH_3)_2$), 3.33 (4H, m, $N(CH_2CH_3)_2$), 3.57 (1H, d, C*H*-TMS), 5.73 (1H, d C*H*=C), 7.00-7.40 (5H, m, Ar*H*); δ_C (50 MHz) 0.13, 0.29 (2x q, 2x $Si(CH_3)_3$), 13.41, 14.29 (2x q, $N(CH_2CH_3)_2$), 36.38 (d, *C*H-TMS), 41.66, 41.84 (2x t, $N(CH_2CH_3)_2$), 124.37 (d, C=*C*H), 126.77, 127.34, 128.09 (3x d, Ar*C*), 141.58 (s, Ar*C*), 152.18 (s, *C*=CH), 154.15 (s, *C*=O); *m/z* 377 (M^+, 2 %), 174 (8), 100 (14), 75 (5), 73 (100) 44 (10).

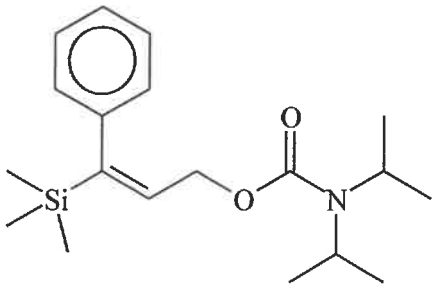
(E)-1-N,N-Diethylcarbamoyloxy-3-phenyl-3-trimethylsilyl-prop-2-ene (**68**)



$C_{17}H_{27}NO_2Si = 305.494$

(*E*)-1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0021 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0044 mol) was added dropwise and the mixture stirred at -78 °C for 30 minutes. TMSCl (0.228 g, 0.0021 mol) was added rapidly and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-*N,N*-diethylcarbamoyloxy-3-phenyl-3-trimethylsilyl-prop-2-ene (**68**) and its isomer (*Z*)-1-*N,N*-diethylcarbamoyloxy-3-phenyl-3-trimethylsilyl-prop-1-ene (**67**) as an inseparable mixture (40 : 60). (0.271 g, 42 %); (Found: C, 66.91; H, 8.96; N, 4.67; $C_{17}H_{27}NO_2Si$ requires C, 66.84; H, 8.91; N, 4.59 %); δ_H (200 MHz) 0.23 (9H, s, $Si(CH_3)_3$), 1.21 (6H, t, $N(CH_2CH_3)_2$), 3.37 (4H, q, $N(CH_2CH_3)_2$), 3.53 (2H, d, $CHCH_2$), 5.61 (1H, t, J = 7.06, C=C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) -0.98 (q, $Si(CH_3)_3$), 13.33, 14.14 (2x q, $N(CH_2CH_3)_2$), 31.69 (t, $CHCH_2$), 41.67, 41.83 (2x t, $N(CH_2CH_3)_2$), 125.74 (d, C=CH), 127.81, 128.20, 128.25 (3x d, Ar*C*), 140.08 (s, Ar*C*), 154.07 (s, *C*=CH), 155.39 (s, *C*=O); *m/z* 305 (M^+, < 1 %), 174 (17), 100 (100), 73 (45), 72 (56).

(E)-1-N,N-Diisopropylcarbamoyloxy-3-phenyl-3-trimethylsilyl-prop-2-ene (**70**)

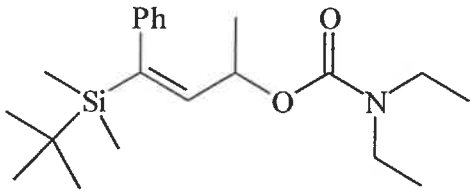


$C_{19}H_{31}NO_2Si$ = 333.548

(*E*)-1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0019 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / CO_2) with stirring. ^{n}Butyllithium (0.0040 mol) was added dropwise and the mixture stirred at -78 °C for 30 minutes. TMSCl (0.206 g, 0.0019 mol) was added rapidly and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-*N,N*-diisopropylcarbamoyloxy-3-phenyl-3-trimethylsilyl-prop-2-ene (**70**) and its isomer (*Z*)-1-*N,N*-diisopropylcarbamoyloxy-3-phenyl-3-trimethylsilyl-prop-1-ene (**69**) as an inseparable mixture (38 : 62). (0.435 g, 69 %); (Found: C, 68.52; H, 9.24; N, 4.37; $C_{19}H_{31}NO_2Si$ requires C, 68.42; H, 9.37; N, 4.20 %); δ_H (200 MHz) 0.17 (9H, s, Si(CH_3)$_3$), 1.27 (12H, bd, N(CH(CH_3)$_2$)$_2$), 3.47 (2H, d, CHCH_2), 3.96 (2H, bs, N(CH(CH$_3$)$_2$)$_2$) 5.54 (1H, t, J = 7.04, C=CH), 7.1 - 7.4 (5H, m, ArH); δ_C (50 MHz) -0.85 (q, Si(CH_3)$_3$), 20.38, 21.52 (2x q, N(CH(CH_3)$_2$)$_2$), 32.07 (t, $CHCH_2$), 45.62, 46.41 (2x d, N(CH(CH$_3$)$_2$)$_2$), 125.82 (d, C=CH), 127.77, 128.29, 128.38 (3x d, ArC), 140.26 (s, ArC), 153.89 (s, C=CH), 155.36 (s, C=O); *m/z* 333 (M^+, < 1 %), 128 (62), 86 (100), 75 (13), 73 (36), 43 (28).

3.5) One-Pot Disubstitution Reactions of Cinnamyl Carbamates.

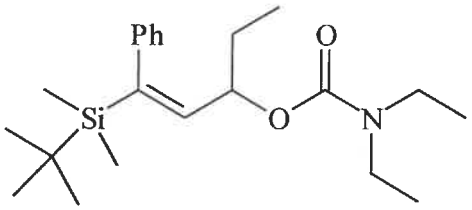
(E)-2-N,N-Diethylcarbamoyloxy-4-^{t}butyldimethylsilyl-4-phenylbut-3-ene (**71a**)



$C_{21}H_{35}NO_2Si = 361.602$

(*E*)-1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0021 mol) and ^{t}butyldimethylsilyl chloride (0.317 g, 0.0021 mol) were dissolved in dry THF (30 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0044 mol) was added dropwise and the mixture stirred at -78 °C for 1 hour. Methyl iodide (0.369g, 0.0026 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*E*)-2-*N,N*-diethylcarbamoyloxy-4-^{t}butyldimethylsilyl-4-phenylbut-3-ene (**71a**) as a colourless oil (0.480 g, 63 %); (Found: C, 69.69; H, 9.82; N, 3.97; $C_{21}H_{35}NO_2Si$ requires C, 69.75; H, 9.76; N, 3.87 %); δ_H (200 MHz) 0.15, 0.17 (6H, 2x s, Si(C*H*$_3$)$_2$), 0,97 (9H, s, C(C*H*$_3$)$_3$), 1.21 (6H, t, N(CH$_2$C*H*$_3$)$_2$), 1.43 (3H, d, CHC*H*$_3$), 3.34 (4H, m, N(C*H*$_2$CH$_3$)$_2$), 3.89 (1H, p, C*H*CH$_3$), 5.64 (1H, d, J = 9.15, C=C*H*), 7.33 (5H, m, Ar*H*); δ_C (50 MHz) -6.50, -6.36 (2x q, Si(*C*H$_3$)$_2$), 13.39, 14.24 (2x q, N(CH$_2$*C*H$_3$)$_2$), 16.85 (s, *C*(CH$_3$)$_3$), 20.76 (q, CH*C*H$_3$), 26.52 (q, C(*C*H$_3$)$_3$), 35.72 (d, *C*HCH$_3$), 41.57, 41.91 (2x t, N(*C*H$_2$CH$_3$)$_2$), 125.83, 126.92, 128.22 (3x d, Ar*C*), 138.18 (d, C=*C*H), 145.38 (s, Ar*C*), 151.65 (s, *C*=CH), 153.84 (s, *C*=O); *m/z* (CI - CH_4) 362 (M^+ + 1, 100 %), 346 (49), 304 (43), 284 (5), 174 (5).

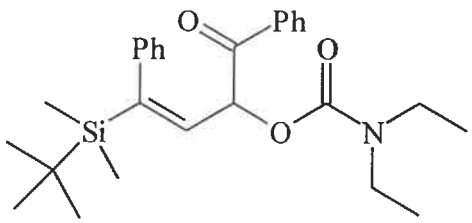
(E)-1-^{t}Butyldimethylsilyl-3-N,N-diethylcarbamoyloxy-1-phenylpent-1-ene (**71b**).



$C_{22}H_{37}NO_2Si = 375.629$

(*E*)-1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0021 mol) and ^{t}butyldimethylsilyl chloride (0.317 g, 0.0021 mol) were dissolved in dry THF (30 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0044 mol) was added dropwise and the mixture stirred at -78 °C for 1 hour. Ethyl iodide (0.406g, 0.0026 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-3-*N,N*-diethylcarbamoyloxy-1-phenylpent-1-ene (**71b**) as a colourless oil (0.382 g, 48 %); (Found : C, 70.21; H, 9.84; N, 3.89; $C_{22}H_{37}NO_2Si$ requires C, 70.35; H, 9.93; N, 3.73 %); δ_H (200 MHz) 0.10, 0.12 (6H, 2x s, Si(CH_3)$_2$), 0.90 (3H, t, $CHCH_2CH_3$), 0.91 (9H, s, C(CH_3)$_3$), 1.17 (6H, t, N(CH_2CH_3)$_2$), 1.75 (2H, m, $CHCH_2CH_3$), 3.32 (4H, m, N(CH_2CH_3)$_2$), 3.58 (1H, q, $CHCH_2CH_3$), 5.58 (1H, d, J = 9.32, C=C*H*), 7.24 (5H, m, Ar*H*); δ_C (50 MHz) -6.24, -6.20 (2x q, Si(CH_3)$_2$), 12.14 (q, $CHCH_2CH_3$), 13.48, 14.36 (2x q, N(CH_2CH_3)$_2$), 16.93 (s, $C(CH_3)_3$), 26.61 (q, C(CH_3)$_3$), 28.75 (t, $CHCH_2CH_3$), 41.63, 41.95 (2x t, N(CH_2CH_3)$_2$), 43.67 (d, $CHCH_2CH_3$), 125.88, 127.51, 128.26 (3x d, Ar*C*), 136.88 (d, C=CH), 144.40 (s, Ar*C*), 152.71 (s, *C*=CH), 153.84 (s, *C*=O); *m/z* (CI - CH_4) 376 (M^+ + 1, 100 %), 360 (50), 318 (47), 298 (5), 259 (4), 216 (3), 174 (8).

(E)-4-^{t}Butyldimethylsilyl-2-N,N-diethylcarbamoyloxy-1,4-diphenylbut-3-en-1-one (**71d**).

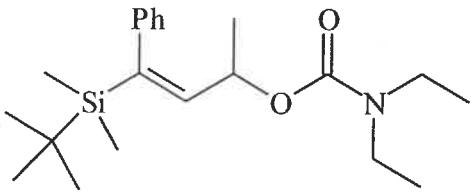


$C_{27}H_{37}NO_3Si = 451.683$

(*E*)-1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**45a**) (0.500 g, 0.0021 mol) and ^{t}butyldimethylsilyl chloride (0.317 g, 0.0021 mol) was dissolved in dry THF (30 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0044 mol) was added dropwise and the mixture stirred at -78 °C for 1 hour. Benzoyl chloride (0.366g, 0.0026 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 15 % diethyl ether / hexane) afforded (*E*)-4-^{t}butyldimethylsilyl-2-*N,N*-diethylcarbamoyloxy-1,4-diphenylbut-3-en-1-one (**71d**) as a colourless oil (0.113 g, 12 %); (Hrms calcd. for $C_{27}H_{37}NO_3Si$: 451.2540. Found: 451.2550); δ_H (200 MHz) 0.10, 0.11 (6H, 2x s, $Si(CH_3)_2$), 0.89 (9H, s, $C(CH_3)_3$), 1.08 (6H, q, $N(CH_2CH_3)_2$), 3.21 (4H, m, $N(CH_2CH_3)_2$), 5.65 (1H, d, J = 8.22, C=CHCH), 6.09 (1H, d, J = 8.22, C=CHCH), 7.10 - 7.60 (8H, m, ArH), 7.98 (2H, d, ArH)); δ_C (50 MHz) -6.48, -6.41 (2x q, $Si(CH_3)_2$), 13.35, 14.16 (2x q, $N(CH_2CH_3)_2$), 16.94 (s, $C(CH_3)_3$), 26.47 (q, $C(CH_3)_3$), 41.50, 41.89 (2x t, $N(CH_2CH_3)_2$), 50.44 (d, C=CHCH), 126.93, 128.32, 128.43, 128.73, 128.78, 132.90 (6x d, ArC), 131.51 (d, C=CH), 136.51, 138.63 (2x s, ArC), 153.32 (s, C=CH), 154.39 (s, OC=O), 198.20 (s, PhC=O); *m/z* 451 (M^+, 1 %), 174 (58), 105 (46), 100 (100), 73 (26), 72 (39).

3.6) Two-Pot Disubstitution Reactions of Cinnamyl Carbamates.

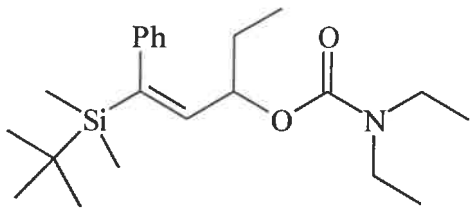
(E)-2-N,N-Diethylcarbamoyloxy-4-^{t}butyldimethylsilyl-4-phenylbut-3-ene (**71a**)



$C_{21}H_{35}NO_2Si = 361.602$

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of methyl iodide (0.114 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*E*)-2-*N,N*-diethylcarbamoyloxy-4-^{t}butyldimethyl-silyl-4-phenylbut-3-ene (**71a**) as a colourless oil (0.226 g, 89 %); (Found: C, 69.69; H, 9.82; N, 3.97; $C_{21}H_{35}NO_2Si$ requires C, 69.75; H, 9.76; N, 3.87 %); δ_H (200 MHz) 0.15, 0.17 (6H, 2x s, $Si(CH_3)_2$), 0,97 (9H, s, $C(CH_3)_3$), 1.21 (6H, t, $N(CH_2CH_3)_2$), 1.43 (3H, d, $CHCH_3$), 3.34 (4H, m, $N(CH_2CH_3)_2$), 3.89 (1H, p, $CHCH_3$), 5.64 (1H, d, J = 9.15, C=CH), 7.33 (5H, m, ArH); δ_C (50 MHz) -6.50, -6.36 (2x q, $Si(CH_3)_2$), 13.39, 14.24 (2x q, $N(CH_2CH_3)_2$), 16.85 (s, $C(CH_3)_3$), 20.76 (q, $CHCH_3$), 26.52 (q, $C(CH_3)_3$), 35.72 (d, $CHCH_3$), 41.57, 41.91 (2x t, $N(CH_2CH_3)_2$), 125.83, 126.92, 128.22 (3x d, ArC), 138.18 (d, C=CH), 145.38 (s, ArC), 151.65 (s, C=CH), 153.84 (s, C=O); *m/z* (CI - CH_4) 362 (M^+ + 1, 100 %), 346 (49), 304 (43), 284 (5), 174 (5).

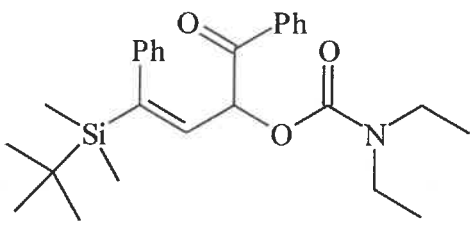
(E)-1-^{t}Butyldimethylsilyl-3-N,N-diethylcarbamoyloxy-1-phenylpent-1-ene (**71b**).



$C_{22}H_{37}NO_2Si = 375.629$

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of ethyl iodide (0.125 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-3-*N,N*-diethylcarbamoyl-oxy-1-phenylpent-1-ene (**71b**) as a colourless oil (0.214 g, 81 %); (Found : C, 70.21; H, 9.84; N, 3.89; $C_{22}H_{37}NO_2Si$ requires C, 70.35; H, 9.93; N, 3.73 %); δ_H (200 MHz) 0.10, 0.12 (6H, 2x s, $Si(CH_3)_2$), 0.90 (3H, t, $CHCH_2CH_3$), 0.91 (9H, s, $C(CH_3)_3$), 1.17 (6H, t, $N(CH_2CH_3)_2$), 1.75 (2H, m, $CHCH_2CH_3$), 3.32 (4H, m, $N(CH_2CH_3)_2$), 3.58 (1H, q, $CHCH_2CH_3$), 5.58 (1H, d, $J = 9.32$, C=CH), 7.24 (5H, m, ArH); δ_C (50 MHz) -6.24, -6.20 (2x q, $Si(CH_3)_2$), 12.14 (q, $CHCH_2CH_3$), 13.48, 14.36 (2x q, $N(CH_2CH_3)_2$), 16.93 (s, $C(CH_3)_3$), 26.61 (q, $C(CH_3)_3$), 28.75 (t, $CHCH_2CH_3$), 41.63, 41.95 (2x t, $N(CH_2CH_3)_2$), 43.67 (d, $CHCH_2CH_3$), 125.88, 127.51, 128.26 (3x d, ArC), 136.88 (d, C=CH), 144.40 (s, ArC), 152.71 (s, C=CH), 153.84 (s, C=O); *m/z* (CI - CH_4) 376 ($M^+ + 1$, 100 %), 360 (50), 318 (47), 298 (5), 259 (4), 216 (3), 174 (8).

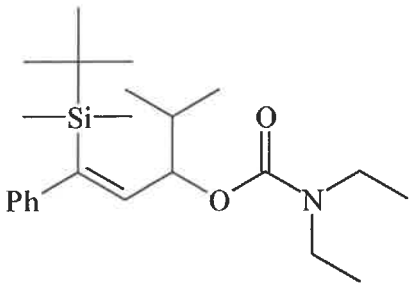
(E)-4-^{t}Butyldimethylsilyl-2-N,N-diethylcarbamoyloxy-1,4-diphenylbut-3-en-1-one (**71d**).



$C_{27}H_{37}NO_3Si = 451.683$

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of benzoyl chloride (0.112 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 15 % diethyl ether / hexane) afforded (*E*)-4-^{t}butyldimethylsilyl-2-*N,N*-diethylcarbamoyl-oxy-1,4-diphenylbut-3-en-1-one (**71d**) as a colourless oil (0.201 g, 64 %); (Hrms calcd. for $C_{27}H_{37}NO_3Si$: 451.2540. Found: 451.2550); δ_H (200 MHz) 0.10, 0.11 (6H, 2x s, Si(CH_3)$_2$), 0.89 (9H, s, C(CH_3)$_3$), 1.08 (6H, q, N(CH_2CH_3)$_2$), 3.21 (4H, m, N(CH_2CH_3)$_2$), 5.65 (1H, d, J = 8.22, C=CHC*H*), 6.09 (1H, d, J = 8.22, C=C*H*CH), 7.10 - 7.60 (8H, m, Ar*H*), 7.98 (2H, d, Ar*H*)); δ_C (50 MHz) -6.48, -6.41 (2x q, Si(CH_3)$_2$), 13.35, 14.16 (2x q, N(CH_2CH_3)$_2$), 16.94 (s, *C*(CH_3)$_3$), 26.47 (q, C(CH_3)$_3$), 41.50, 41.89 (2x t, N(CH_2CH_3)$_2$), 50.44 (d, C=CH*C*H), 126.93, 128.32, 128.43, 128.73, 128.78, 132.90 (6x d, Ar*C*), 131.51 (d, C=*C*H), 136.51, 138.63 (2x s, Ar*C*), 153.32 (s, *C*=CH), 154.39 (s, O*C*=O), 198.20 (s, Ph*C*=O); *m/z* 451 (M^+, 1 %), 174 (58), 105 (46), 100 (100), 73 (26), 72 (39).

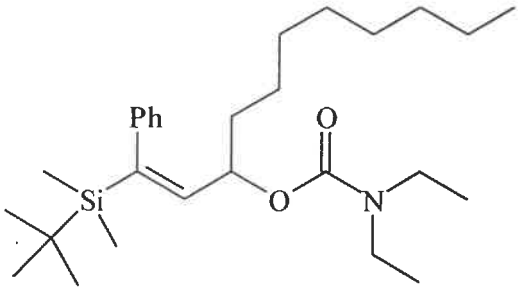
(Z)-1-^{t}Butyldimethylsilyl-3-N,N-diethylcarbamoyloxy-4-methyl-1-phenylpent-1-ene (**71f**).



$C_{23}H_{39}NO_2Si$ = 389.656

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of 2-bromopropane (0.098 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 5 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*Z*)-1-^{t}butyldimethylsilyl-3-*N,N*-diethylcarbamoyl-oxy-4-methyl-1-phenylpent-1-ene (**71f**) as a colourless oil (0.124 g, 45 %); (Found : C, 70.69; H, 10.21; N, 3.74; $C_{23}H_{39}NO_2Si$ requires C, 70.90; H, 10.09; N, 3.59 %); δ_H (200 MHz) 0.10, 0.12 (6H, 2x s, Si(CH_3)$_2$), 0.80 (3H, d, CHCH_3), 0.91 (9H, s, C(CH_3)$_3$), 0.98 (3H, d, CHCH_3), 1.17 (6H, t, N(CH_2CH_3)$_2$), 1.98 (1H, m, CH(CH$_3$)$_2$), 3.30 (4H, m, N(CH_2CH$_3$)$_2$), 3.36 (1H, t, CHCH(CH$_3$)$_2$), 5.69 (1H, d, J = 9.62, C=CH), 7.22 (5H, m, Ar-H); δ_C (50 MHz) -6.23, -6.15 (2x q, Si(CH_3)$_2$), 13.45, 14.35 (2x q, N(CH_2CH_3)$_2$), 16.98 (s, C(CH$_3$)$_3$), 20.44, 20.95 (2x q, CH(CH_3)$_2$), 26.60 (q, C(CH_3)$_3$), 33.08 (d, CH(CH$_3$)$_2$), 41.57, 41.87 (2x t, N(CH_2CH$_3$)$_2$), 49.43 (d, $CHCH$(CH$_3$)$_2$), 125.75, 128.01, 128.03 (3x d, ArC), 135.49 (d, C=CH), 143.66 (s, ArC), 153.10 (s, C=CH), 153.83 (s, C=O); *m/z* (CI - CH_4) 390 (M^+ + 1, 100 %), 374 (60), 332 (57), 273 (5), 174 (6).

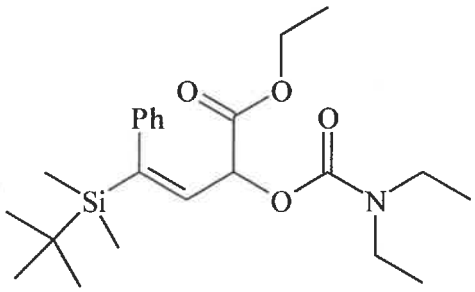
(E)-1-^{t}Butyldimethylsilyl-3-N,N-diethylcarbamoyloxy-1-phenylundec-1-ene (**71h**).



$C_{28}H_{49}NO_2Si = 459.791$

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of 1-bromo-octane (0.155 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 6 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-3-*N,N*-diethylcarbamoyl-oxy-1-phenylundec-1-ene (**71h**) as a colourless oil (0.061 g, 19 %); (Found : C, 72.98; H, 10.82; N, 2.98; $C_{28}H_{49}NO_2Si$ requires C, 73.14; H, 10.74; N, 3.05 %); δ_H (200 MHz) 0.08, 0.10 (6H, 2x s, Si(CH_3)$_3$), 0.88 (3H, t, $(CH_2)_7CH_3$), 0.90 (9H, s, C(CH_3)$_3$), 1.16 (6H, t, N(CH_2CH_3)$_2$), 1.24 (12H, bs, $CH_2(CH_2)_6CH_3$), 1.69 (2H, m $CH_2(CH_2)_6CH_3$), 3.30 (4H, m, N(CH_2CH_3)$_2$), 3.64 (1H, q, $CH(CH_2)_7CH_3$), 5.56 (1H, d, J = 9.34, C=C*H*), 7.23 (5H, m, Ar*H*); δ_C (50 MHz) -6.34, -6.27 (2x q, Si(CH_3)$_2$), 13.44, 14.34 (2x q, N(CH_2CH_3)$_2$), 14.09 (q, $(CH_2)_7CH_3$), 16.90 (s, $C(CH_3)_3$), 22.65 (t, $(CH_2)_6CH_2CH_3$), 26.55 (q, $C(CH_3)_3$), 27.39 (t, $(CH_2)_5CH_2CH_2CH_3$), 29.28 (t, $(CH_2)_4CH_2(CH_2)_2CH_3$), 29.47 (t, $(CH_2)_3CH_2(CH_2)_3CH_3$), 29.51 (t, $(CH_2)_2CH_2$-$(CH_2)_4CH_3$), 31.85 (t, $CH_2CH_2(CH_2)_5CH_3$), 35.74 (t, $CH_2(CH_2)_6CH_3$), 41.57, 41.83 (2x t, N(CH_2CH_3)$_2$), 41.84 (d, $CH(CH_2)_7CH_3$), 125.80, 127.44, 128.22 (3x d, Ar*C*), 137.16 (d, C=CH), 144.54 (s, Ar*C*), 152.30 (s, *C*=CH), 153.82 (s, *C*=O); *m/z* (CI - CH_4) 461 (M^+ + 1, 34 %), 460 (100), 444 (53), 402 (52), 346 (8), 174 (7).

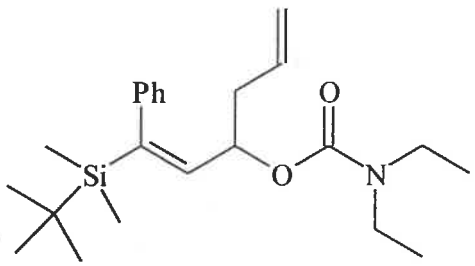
Ethyl (E)-4-^{t}butyldimethylsilyl-2-N,N-diethylcarbamoyloxy-4-phenylbut-3-en-1-oate (**71i**).



$C_{23}H_{37}NO_4Si = 419.638$

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of ethyl chloroformate (0.087 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded ethyl (*E*)-4-^{t}butyldimethylsilyl-2-*N,N*-diethylcarbamoyloxy-4-phenylbut-3-en-1-oate (**71i**) as a colourless oil (0.217 g, 74 %); (Hrms calcd. for $C_{23}H_{37}NO_4Si$: 419.2489. Found: 419.2503); δ_H (200 MHz) 0.11, 0.13 (6H, 2x s, Si(CH_3)$_2$), 0.91 (9H, s, C(CH_3)$_3$), 1.15 (6H, q, N(CH_2CH_3)$_2$), 1.21 (3H, t, OCH_2CH_3)), 3.28 (4H, m, N(CH_2CH_3)$_2$), 4.13 (2H, q, OCH_2CH_3), 4.63 (1H, d, J = 8.61, C=CHC*H*), 5.99 (1H, d, J = 8.59, C=C*H*CH), 7.29 (5H, m, Ar*H*); δ_C (50 MHz) -6.46, -6.37 (2x q, Si(CH_3)$_2$), 13.31, 14.15 (2x q, N(CH_2CH_3)$_2$), 14.00 (q, OCH_2CH_3), 16.90 (s, *C*(CH_3)$_3$), 26.46 (q, C(CH_3)$_3$), 41.54, 41.91 (2x t, N(CH_2CH_3)$_2$), 48.40 (d, C=CHCH), 60.91 (t, OCH_2CH_3), 126.98, 127.69, 128.48 (3x d, Ar*C*), 130.00 (d, C=*C*H), 138.39 (s, Ar*C*), 153.24 (s, *C*=CH), 154.96 (s, N*C*=O), 171.90 (s, CH*C*=O); *m/z* 419 (M^+, 6 %), 404 (79), 362 (100), 331 (6), 303 (61), 232 (5), 146 (7).

(E)-1-^{t}Butyldimethylsilyl-3-N,N-diethylcarbamoyloxy-1-phenylhexa-1,5-diene (**71k**).

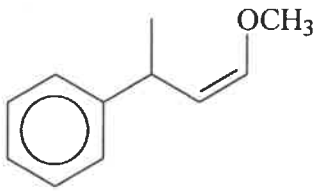


$C_{23}H_{37}NO_2Si = 387.640$

Silyl carbamate (**60**, **61** or a mixture of both) (0.250g, 0.0007 mol) was dissolved in dry THF (10 ml) and cooled to -78 °C (acetone / CO_2) under nitrogen. ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 30 minutes. A solution of allyl bromide (0.097 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride and diluted with diethyl ether (50 ml). The organic phase was washed with water (3x 25 ml), dried over anhydrous magnesium sulfate and the solvent removed. Purification by column chromatography (silica, 10 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-3-*N,N*-diethylcarbamoyl-oxy-1-phenylhexa-1,5-diene (**71k**) as a colourless oil (0.214 g, 79 %); (Hrms calcd. for $C_{23}H_{37}NO_2Si$: 387.2584. Found: 387.2597); δ_H (200 MHz) 0.08, 0.09 (6H, 2x s, $Si(CH_3)_2$), 0.89 (9H, s, $C(CH_3)_3$), 1.13 (6H, q, $N(CH_2CH_3)_2$), 2.48 (2H, t, $CH_2CH{=}CH_2$), 3.27 (4H, m, $N(CH_2CH_3)_2$), 3.76 (1H, q, $CHCH_2CH{=}CH_2$), 4.90, 5.10 (2H, m, $CH{=}CH_2$), 5.60 (1H, d, J = 9.15, C=CH), 5.65 - 6.00 (1H, m, $CH{=}CH_2$), 7.23 (5H, m, ArH); δ_C (50 MHz) -6.34, -6.28 (2x q, $Si(CH_3)_2$), 13.41, 14.29 (2x q, $N(CH_2CH_3)_2$), 16.85 (s, $C(CH_3)_3$),), 26.54 (q, $C(CH_3)_3$), 40.04 (t, $CH_2CH{=}CH_2$), 41.57, 41.91 (2x t, $N(CH_2CH_3)_2$), 41.71 (d, $CHCH_2$), 116.10 (t, $CH{=}CH_2$), 125.98, 127.48, 128.24 (3x d, ArC), 136.05 (d, $CH{=}CH_2$), 136.38 (d, C=CH), 143.65 (s, ArC), 152.77 (s, C=CH), 153.70 (s, C=O); *m/z* 388 (M^+, 1 %), 330 (10), 174 (100), 100 (76), 73 (53), 72 (60).

3.7) Electrophilic Substitution of Cinnamyl Ethers.

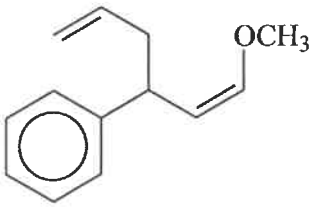
(Z)-1-Methoxy-3-phenylbut-1-ene (**72a**).



$C_{11}H_{14}O = 162.232$

N,N-Diisopropylamine (0.364g, 0.0036 mol) in dry THF (25 ml) was cooled in an ice-bath with stirring. ^{n}Butyllithium (0.0033 mol) was added dropwise and the mixture stirred for 30 minutes. The mixture was then cooled to -78 °C (acetone / CO_2) and cinnamyl methyl ether (0.500 g, 0.0033 mol) in dry THF (5 ml) was added dropwise. The mixture was stirred for 30 minutes and then methyl iodide (0.511 g, 0.0036 mol) in dry THF (2 ml) was added dropwise. The reaction was stirred for 2 hours and then quenched with saturated aqueous ammonium chloride (25 ml). The reaction was allowed to warm to room temperature, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and the residue purified by column chromatography (silica, 2 % diethyl ether / hexane) to afford (*Z*)-1-methoxy-3-phenylbut-1-ene (**72a**). (0.473 g, 88 %); (Found: C, 81.39; H, 8.97; $C_{11}H_{14}O$ requires C, 81.44; H, 8.70 %); δ_H (200 MHz) 1.32 (3H, d, CHC*H*$_3$), 3.57 (3H, s, OC*H*$_3$), 3.94 (1H, p, C*H*CH$_3$), 4.53 (1H, dd, *J* = 6.18, 9.48, C*H*=CH-O), 5.86 (1H, d, *J* = 6.21, CH=C*H*-O), 7.1 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) 22.29 (q, CHCH$_3$), 34.29 (d, *C*HCH$_3$), 59.59 (q, OCH$_3$), 112.20 (d, *C*H=CH-O), 125.71, 126.75, 128.28 (3x d, Ar*C*), 145.03 (d, CH=*C*H-O), 147.06 (s, Ar*C*); *m/z* (M^+, 35 %), 148 (11), 147 (100), 131 (22), 130 (23), 129 (13), 117 (13), 116 (9), 115 (58), 103 (9), 91 (15).

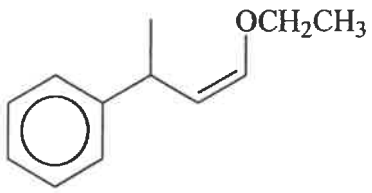
(Z)-1-Methoxy-3-phenylhexa-1,5-diene (**72b**).



$C_{13}H_{16}O = 188.270$

N,N-Diisopropylamine (0.364g, 0.0036 mol) in dry THF (25 ml) was cooled in an ice-bath with stirring. ^{n}Butyllithium (0.0033 mol) was added dropwise and the mixture stirred for 30 minutes. The mixture was then cooled to -78 °C (acetone / CO_2) and cinnamyl methyl ether (0.500 g, 0.0033 mol) in dry THF (5 ml) was added dropwise. The mixture was stirred for 30 minutes and then allyl bromide (0.436 g, 0.0036 mol) in dry THF (2 ml) was added dropwise. The reaction was stirred for 2 hours and then quenched with saturated aqueous ammonium chloride (25 ml). The reaction was allowed to warm to room temperature, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and the residue purified by column chromatography (silica, 2 % diethyl ether / hexane) to afford (*Z*)-1-methoxy-3-phenylhexa-1,5-diene (**72b**). (0.564 g, 91 %); (Found: C, 83.17; H, 8.66; $C_{13}H_{16}O$ requires C, 82.94; H, 8.57 %); δ_H (200 MHz) 2.41 (2H, m, CHCH_2), 3.54 (3H, s, OCH_3), 3.87 (1H, q, CHCH$_2$), 4.53 (1H, dd, J = 6.28, 9.56, CH=CH-O), 4.98 (2H, m, CH=CH_2), 5.72 (1H, m, CH=CH$_2$), 5.91 (1H, d, J = 6.20, CH-O), 7.1 - 7.3 (5H, m, ArH); δ_C (50 MHz) 40.11 (d, Ph-*C*H), 41.15 (t, CH*C*H$_2$), 59.57 (q, O*C*H$_3$), 109.97 (d, *C*H=CH-O), 115.68 (t, CH=*C*H$_2$), 125.85, 127.26, 128.29 (3x d, Ar*C*), 136.89 (d, *C*H=CH$_2$), 145.31 (s, Ar*C*), 145.85 (d, *C*H-O); *m/z* 188 (M^+, < 1 %), 147 (100), 117 (13), 115 (87), 103 (13), 91 (33), 77 (18).

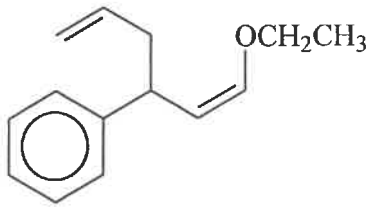
(Z)-1-Ethoxy-3-phenylbut-1-ene (**72c**).



$C_{12}H_{16}O = 176.259$

N,N-Diisopropylamine (0.344g, 0.0034 mol) in dry THF (25 ml) was cooled in an ice-bath with stirring. ^{n}Butyllithium (0.0031 mol) was added dropwise and the mixture stirred for 30 minutes. The mixture was then cooled to -78 °C (acetone / CO_2) and cinnamyl ethyl ether (0.500 g, 0.0031 mol) in dry THF (5 ml) was added dropwise. The mixture was stirred for 30 minutes and then methyl iodide (0.483 g, 0.0034 mol) in dry THF (2 ml) was added dropwise. The reaction was stirred for 2 hours and then quenched with saturated aqueous ammonium chloride (25 ml). The reaction was allowed to warm to room temperature, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and the residue purified by column chromatography (silica, 2 % diethyl ether / hexane) to afford (*Z*)-1-ethoxy-3-phenylbutene (**72c**). (0.471 g, 86 %); (Found: C, 81.66; H, 9.21; $C_{12}H_{16}O$ requires C, 81.77; H, 9.15 %); δ_H (200 MHz) 1.24 (3H, t, OCH_2CH_3), 1.33 (3H, d, $CHCH_3$), 3.78 (2H, q, OCH_2CH_3), 3.98 (1H, p, $CHCH_3$), 4.53 (1H, dd, J = 6.18, 9.38, C*H*=CH-O), 5.91 (1H, d, J = 6.20, CH=C*H*-O), 7.1 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) 15.30 (q, OCH_2CH_3), 22.17 (q, $CHCH_3$), 34.36 (d, $CHCH_3$), 67.62 (t, OCH_2CH_3), 112.38 (d, *C*H=CH-O); 125.65, 126.79, 128.24 (3x d, Ar*C*), 143.60 (d, CH=*C*H-O), 147.23 (s, Ar*C*); *m/z* 176 (M^+, 54 %), 161 (100), 133 (78), 130 (27), 115 (48), 105 (27), 91 (75), 77 (41).

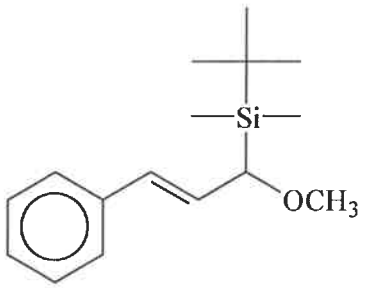
(Z)-1-Ethoxy-3-phenylhexa-1,5-diene (**72d**).



$C_{14}H_{18}O = 202.297$

N,N-Diisopropylamine (0.344g, 0.0034 mol) in dry THF (25 ml) was cooled in an ice-bath with stirring. ^{n}Butyllithium (0.0031 mol) was added dropwise and the mixture stirred for 30 minutes. The mixture was then cooled to -78 °C (acetone / CO_2) and cinnamyl ethyl ether (0.500 g, 0.0031 mol) in dry THF (5 ml) was added dropwise. The mixture was stirred for 30 minutes and then allyl bromide (0.411 g, 0.0034 mol) in dry THF (2 ml) was added dropwise. The reaction was stirred for 2 hours and then quenched with saturated aqueous ammonium chloride (25 ml). The reaction was allowed to warm to room temperature, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and the residue purified by column chromatography (silica, 2 % diethyl ether / hexane) to afford (*Z*)-1-ethoxy-3-phenylhexa-1,5-diene (**72d**). (0.536 g, 85 %); (Found: C, 83.09; H, 9.09; $C_{14}H_{18}O$ requires C, 83.12; H, 8.97 %); δ_H (200 MHz) 1.20 (3H, t, OCH_2CH_3), 2.42 (2H, m, $CHCH_2$), 3.74 (2H, q, OCH_2CH_3), 3.89 (1H, q, $CHCH_2$), 4.52 (1H, dd, J = 6.25, 9.57, C*H*=CH-O), 4.98 (2H, m, CH=CH_2), 5.75 (1H, m, C*H*=CH_2), 5.96 (1H, d, J = 6.22, C*H*-O), 7.1 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) 15.28 (q, OCH_2CH_3), 40.14 (d, Ph-*C*H), 41.03 (t, $CHCH_2$), 67.59 (t, OCH_2CH_3), 110.06 (d, *C*H=CH-O), 115.58 (t, CH=CH_2), 125.77, 127.28, 128.23 (3x d, Ar*C*), 136.99 (d, *C*H=CH_2), 144.41 (d, CH=*C*H-O), 145.44 (s, Ar*C*); *m/z* 202 (M^+, < 1 %), 161 (100), 115 (79), 91 (18).

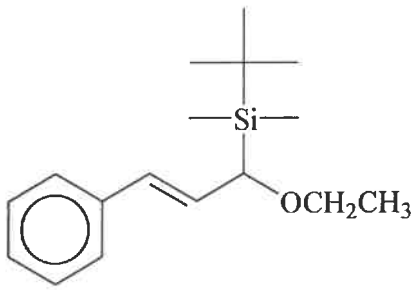
(E)-1-^{t}Butyldimethylsilyl-1-methoxy-3-phenylprop-2-ene (**73**).



$C_{16}H_{26}OSi$ = 262.469

Cinnamyl methyl ether (0.500 g, 0.003$\bar{3}$ mol) and ^{t}butyldimethylsilyl chloride (0.543 g, 0.0036 mol) was dissolved in dry THF (20 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0033 mol) was added dropwise and the mixture stirred at -78 °C for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was separated, dried over anhydrous magnesium sulfate and the solvent removed. Column chromatography (silica, 5 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-1-methoxy-3-phenylprop-2-ene (**73**) as a colourless liquid. (0.823 g, 95 %); (Found : C, 73.49; H, 10.17; $C_{16}H_{26}OSi$ requires C, 73.22; H, 9.99 %). δ_H (200 MHz) -0.04, 0.04 (6H, 2x s, Si(CH_3)$_2$), 0.96 (9H, S, C(CH_3)$_3$), 3.33 (3H, s, OCH_3), 3.72 (1H,dd, *J* = 1.15, 7.12, C*H*-O), 6.22 (1H, dd, *J* = 7.14, 15.95, PhCH=C*H*), 6.43 (1H, dd, *J* = 0.90,15.99, PhC*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) -8.64, -7.32 (2x q, Si(CH_3)$_2$), 17.08 (s, *C*(CH_3)$_3$), 26.99 (q, C(CH_3)$_3$), 58.86 (q, OCH_3), 77.59 (d, *C*H-O), 125.97, 126.82, 128.51 (3x d, Ar*C*), 127.62 (d, PhCH=*C*H), 129.88 (d, Ph-*C*H), 137.52 (s, Ar*C*); *m/z* 262 (M^+, 1 %), 247 (22), 147 (8), 115 (10), 89 (13), 74 (9), 73 (100), 59 (12), 45 (6).

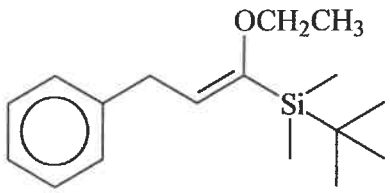
(E)-1-^{t}Butyldimethylsilyl-1-ethoxy-3-phenylprop-2-ene (**74a**).



$C_{17}H_{28}OSi = 276.496$

Cinnamyl ethyl ether (0.500 g, 0.0031 mol) and ^{t}butyldimethylsilyl chloride (0.513 g, 0.0034 mol) was dissolved in dry THF (20 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0031 mol) was added dropwise and the mixture stirred at -78 °C for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was separated, dried over anhydrous magnesium sulfate and the solvent removed. Column chromatography (silica, 5 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethyl-silyl-1-ethoxy-3-phenylprop-2-ene (**74a**) as a colourless liquid. (0.800 g, 93 %); (Found : C, 73.71; H, 10.25; $C_{17}H_{28}OSi$ requires C, 73.89; H, 10.21 %). δ_H (200 MHz) -0.05, 0.03 (6H, 2x s, $Si(CH_3)_2$), 0.96 (9H, S, $C(CH_3)_3$), 1.18 (3H, t, J = 7.00, OCH_2CH_3), 3.30, 3.70 (2H, 2x q, J = 6.95, OCH_2CH_3), 3.86 (1H, dd, J = 1.04, 6.80, CH-O), 6.24 (1H, dd, J = 6.78, 15.93, PhCH=C*H*), 6.42 (1H, dd, J = 0.72, 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) -8.59, -7.27 (2x q, $Si(CH_3)_2$), 15.50 (q, OCH_2CH_3), 17.14 (s, $C(CH_3)_3$), 27.01 (q, $C(CH_3)_3$), 66.37 (t, OCH_2CH_3), 75.22 (d, *C*H-O), 125.95, 126.70, 128.51 (3x d, Ar*C*), 126.95 (d, PhCH=*C*H), 130.78 (d, Ph*C*H), 137.70 (s, Ar*C*); *m/z* 276 (M^+, < 1 %), 247 (12), 161 (7), 73 (100).

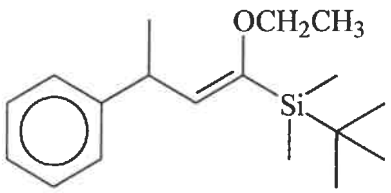
(E)-1-^{t}Butyldimethylsilyl-1-ethoxy-3-phenylprop-2-ene (**74b**).



$C_{17}H_{28}OSi = 276.496$

Cinnamyl ethyl ether (0.500 g, 0.0031 mol) and ^{t}butyldimethylsilyl chloride (0.513 g, 0.0034 mol) was dissolved in dry THF (20 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0062 mol) was added dropwise and the mixture stirred at -78 °C for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was separated, dried over anhydrous magnesium sulfate and the solvent removed. Column chromatography (silica, 5 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-1-ethoxy-3-phenylprop-2-ene (**74a**) as a colourless liquid (0.604 g, 71 %) and (*E*)-1-^{t}butyldimethylsilyl-1-ethoxy-3-phenylprop-1-ene (**74b**) as a colourless liquid (0.201 g, 23 %); (Found : C, 74.09; H, 10.38; $C_{17}H_{28}OSi$ requires C, 73.89; H, 10.21 %); δ_H (200 MHz) 0.15 (6H, s, Si(CH_3)$_2$), 0.99 (9H, s, C(CH_3)$_3$), 1.31 (3H, t, OCH_2CH_3), 3.60 (2H, d, J = 7.05, Ph-CH_2), 3.77 (2H, q, OCH_2CH_3), 5.40 (1H, t, J = 7.06, C=C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) -5.08, -4.97 (2x q, Si(CH_3)$_2$), 15.80 (q, OCH_2CH_3), 16.77 (s, *C*(CH_3)$_3$), 26.76 (q, C(CH_3)$_3$), 31.77 (t, Ph-CH_2), 66.91 (t, OCH_2CH_3), 125.70, 128.29, 128.35 (3x d, Ar*C*), 128.46 (d, *C*H=C), 141.30 (s, Ar*C*), 160.53 (s, *C*-O); *m/z* 276 (M^+, < 1 %), 88 (100), 75 (20), 59 (10).

(E)-1-^{t}Butyldimethylsilyl-1-ethoxy-3-phenylbut-1-ene (**75**).

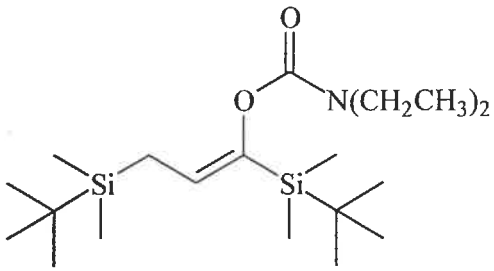


$C_{18}H_{30}OSi = 290.523$

A solution of (*E*)-1-^{t}butyldimethylsilyl-1-ethoxy-3-phenylprop-2-ene (**74a**) or (*E*)-1-^{t}butyldimethylsilyl-1-ethoxy-3-phenylprop-1-ene (**74b**) (0.250 g, 0.0009 mol) in dry THF (15 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0010 mol) was added dropwise and the mixture stirred for 1 hour. Methyl iodide (0.255 g, 0.0018 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for 4 hours. The reaction was quenched with saturated aqueous ammonium chloride (10 ml) and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 30 ml). The organic phase was separated, dried over anhydrous magnesium sulfate and the solvent removed. Colum chromatography (silica, 5 % diethyl ether / hexane) afforded (*E*)-1-^{t}butyldimethylsilyl-1-ethoxy-3-phenylbut-1-ene (**75**) as a colourless oil. (Starting with (**74a**): 0.014 g, 5 %; (**74b**): 0.057 g, 22 %); (Found : C, 74.22; H, 10.38; $C_{18}H_{30}OSi$ requires C, 74.42; H, 10.41 %); δ_H (200 MHz) 0.09 (6H, s, Si(CH_3)$_2$), 0.91 (9H, s, C(CH_3)$_3$), 1.23 (3H, t, OCH_2CH_3), 1.32 (3H, d, $CHCH_3$), 3.70 (2H, m, OCH_2CH_3), 4.16 (1H, p, $CHCH_3$), 5.32 (1H, d, $J = 9.45$, C=C*H*), 7.1 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) -5.06, -4.95 (2x q, Si(CH_3)$_2$), 15.81 (q, OCH_2CH_3), 16.84 (s, $C(CH_3)_3$), 22.38 (q, $CHCH_3$), 26.76 (q, $C(CH_3)_3$), 35.27 (d, $CHCH_3$), 67.03 (t, OCH_2CH_3), 125.70, 126.89, 128.27 (3x d, Ar*C*), 135.25 (d, *C*H=C), 146.69 (s, Ar*C*), 158.37 (s, CH=*C*-O); *m/z* 290 (M^+, < 1 %), 105 (38), 104 (10), 103 (100), 75 (28), 73 (31), 59 (16), 57 (8).

3.8) Reaction of Allyl Carbamates.

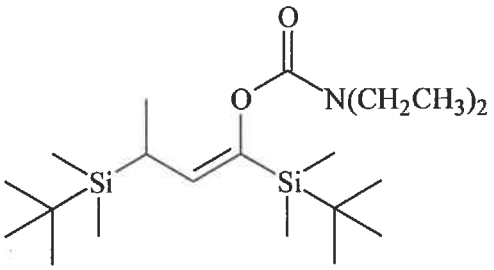
(E)-1,3-Bis-^{t}butyldimethylsilyl-1-N,N-diethylcarbamoyloxyprop-1-ene (**76**).



$C_{20}H_{43}NO_2Si_2 = 385.741$

N,N-Diethylcarbamoyloxyprop-2-ene (0.250 g, 0.0016 mol) and TBDMSCl (0.503 g, 0.0033 mol) was dissolved in dry THF (20 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0033 mol) was added and the reaction stirred for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (10 ml) and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E*)-1,3-bis-^{t}butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxyprop-1-ene (**76**) as a colourless oil. (0.241 g, 39 %); (Found : C, 62.59; H, 11.47; N, 3.99; $C_{20}H_{43}NO_2Si_2$ requires C, 62.27; H, 11.24; N, 3.63 %); δ_H (200 MHz) -0.08, 0.03 (12H, 2x s, 2x Si(CH_3)$_2$), 0.83, 0.87 (18H, 2x s, 2x C(CH_3)$_3$), 1.09 (6H, bs, N(CH_2CH_3)$_2$), 1.49 (2H, d, J = 8.68, CHCH_2), 3.28 (4H, bs, N(CH_2CH_3)$_2$), 5.50 (1H, t, J = 8.65, C=C*H*); δ_C (50 Mhz) -5.79, -5.70 (2x q, 2x Si(CH_3)$_2$), 13.65 (t, CHCH_2), 13.85, 14.77 (2x q, N(CH_2CH_3)$_2$), 17.19, 17.41 (2x s, 2x *C*(CH_3)$_3$), 26.85, 27.07 (2x q, 2x C(CH_3)$_3$), 41.79, 42.15 (2x t, N(CH_2CH_3)$_2$), 130.97 (d, C=*C*H), 151.46 (s, *C*=CH), 154.38 (s, *C*=O); *m/z* 385 (M^+, < 1 %), 174 (100), 100 (23), 73 (37), 72 (19).

(E)-1,3-Bis-^{t}butyldimethylsilyl-1-N,N-diethylcarbamoyloxybut-1-ene (**77**).

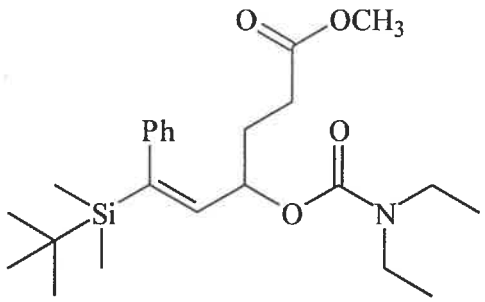


$C_{21}H_{45}NO_2Si_2 = 399.768$

(*E*)-1,3-Bis-^{t}butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxyprop-1-ene (**76**) (0.250 g, 0.0006 mol) was dissolved in dry THF (15 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0007 mol) was added dropwise and the mixture stirred for 1 hour. Methyl iodide (0.100 g, 0.0007 mol) in dry THF (1 ml) was added and the mixture stirred for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (10 ml) and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E*)-1,3-bis-^{t}butyldimethylsilyl-1-*N,N*-diethylcarbamoyloxybut-1-ene (**77**). (0.075 g, 31 %); (Found : C, 63.29; H, 11.46; N, 3.66; $C_{21}H_{45}NO_2Si_2$ requires C, 63.09; H, 11.35; N, 3.50 %); δ_H (200 MHz) -0.10, -0.09, 0.02, 0.05 (12H, 4x s, 2x Si(CH_3)$_2$), 0.86, 0.87 (18H, 2x s, 2x C(CH_3)$_3$), 1.04 (3H, d, J = 7.22, CHCH_3), 1.10 (6H, m, N(CH_2CH_3)$_2$), 2.05 (1H, dq, J = 7.23, 11.42, CHCH$_3$), 3.28 (4H, m, N(CH_2CH$_3$)$_2$), 5.31 (1H, d, J = 11.37, C=CH); δ_C (50 MHz) -7.58, -6.99, -6.25, -5.98 (4x q, 2x Si(CH_3)$_2$), 13.31, 14.27 (2x q, N(CH_2CH_3)$_2$), 15.85 (q, CHCH_3), 16.95, 17.53 (2x s, 2x C(CH$_3$)$_3$), 18.62 (d, CHCH$_3$), 26.62, 27.11 (2x q, 2x C(CH_3)$_3$), 41.32, 41.67 (2x t, N(CH_2CH_3)$_2$), 137.94 (d, C=CH), 149.15 (s, C=CH), 153.86 (s, C=O); *m/z* 399 (M^+, < 1 %), 343 (16), 342 (56), 174 (100), 100 (19), 73 (39), 72 (12), 44 (12).

3.9) Reactions with Michael Acceptors.

(E) Methyl 6-^{t}butyldimethylsilyl-4-N,N-diethylcarbamoyloxy-6-phenylhex-5-enoate (**79a**).

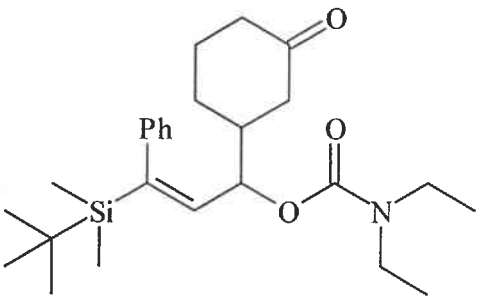


$C_{24}H_{39}NO_4Si = 433.665$

A mixture of (**60**) and (**61**) or the individual compounds (0.250 g, 0.0007 mol) was dissolved in dry THF (15 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0008 mol) was added dropwise and the mixture stirred for 1 hour. Methyl acrylate (0.069 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (10 ml) and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*) methyl 6-^{t}butyldimethylsilyl-4-*N,N*-diethylcarbamoyloxy-6-phenylhex-5-enoate (**79a**). (0.192 g, 63 %); (Found: C, 66.32; H, 9.01; N, 3.31; $C_{24}H_{39}NO_4Si$ requires C, 66.47; H, 9.07; N, 3.23 %); δ_H (200 MHz) 0.08, 0.10 (6H, 2x s, Si(CH_3)$_2$), 0.89 (9H, s, C(CH_3)$_3$), 1.15 (6H, t, N(CH_2CH_3)$_2$), 2.03 (2H, m, $CH_2CH_2CO_2CH_3$), 2.32 (2H, m, $CH_2CH_2CO_2CH_3$), 3.28 (4H, bs, N(CH_2CH_3)$_2$), 3.61 (3H, s, OCH_3), 3.67 (1H, dd, J = 7.00, 9.39, C*H*-O), 5.57 (1H, d, J = 9.43, C=C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) -6.30, -6.21 (2x q, Si(CH_3)$_2$), 13.45, 14.36 (2x q, N(CH_2CH_3)$_2$), 16.87 (s, $C(CH_3)_3$), 26.57 (q, C(CH_3)$_3$), 30.76 (t, $CH_2CH_2CO_2CH_3$), 32.00 (t, $CH_2CO_2CH_3$), 41.25 (d, C=CH-*C*H), 41.63, 41.95 (2x t, N(CH_2CH_3)$_2$), 51.34 (q, OCH_3), 126.23, 127.35, 128.43 (3x d, Ar*C*), 135.89 (d, C=*C*H), 143.44 (s, Ar*C*), 153.57, 153.68 (2x s,

N*C*=O, *C*=CH), 173.86 (s, O*C*=O); *m/z* CI (CH_4) 434 (M^+ + 1, 100 %), 419 (10), 418 (33), 377 (9), 376 (32), 317 (9).

(E) 3-^{t}Butyldimethylsilyl-1-(3'-cyclohexan-1'-one)-1-N,N-diethylcarbamoyloxy-3-phenylprop-2-ene (**79c**).

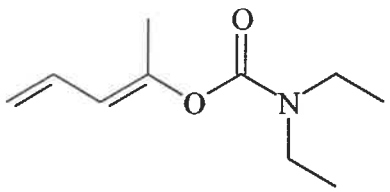


$C_{26}H_{41}NO_3Si = 443.686$

A mixture of (**60**) and (**61**) or the individual compounds (0.250 g, 0.0007 mol) was dissolved in dry THF (15 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0008 mol) was added dropwise and the mixture stirred for 1 hour. Cyclohexenone (0.077 g, 0.0008 mol) in dry THF (2 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (10 ml) and allowed to warm to room temperature. The mixture was diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*) 3-^{t}butyldimethylsilyl-1-(3'-cyclohexan-1'-one)-1-*N,N*-diethylcarbamoyloxy-1-phenyl prop-2-ene (**79c**). (0.220 g, 71 %); (Found: C, 70.55; H, 9.47; N, 3.29; $C_{26}H_{41}NO_3Si$ requires C, 70.38; H, 9.31; N, 3.16 %); δ_H (200 MHz) 0.04, 0.07 (6H, 2x s, Si(CH_3)$_2$), 0.83 (9H, s, C(CH_3)$_3$), 1.11 (6H, t, N(CH_2CH_3)$_2$), 1.2 - 2.4 (9H, c, cyclohexyl-*H*), 3.27 (4H, bs, N(CH_2CH_3)$_2$), 3.48 (1H, dd, J = 7.59, 9.56, C*H*-O), 5.66 (1H, d, J = 9.63, C=C*H*), 7.0 - 7.3 (5H, m, Ar*H*); δ_C (50 MHz) -6.45, -6.31 (2x q, Si(CH_3)$_2$), 13.28, 14.25 (2x q, N(CH_2CH_3)$_2$), 16.76 (s, *C*(CH_3)$_3$), 24.86 (t, *C*H_2CH$_2$C=O), 26.39 (q, C(CH_3)$_3$), 28.87 (t, *C*H_2(CH$_2$)$_2$C=O), 41.24 (t, CH$_2$*C*H$_2$C=O), 41.46, 41.79, (2x t, N(CH_2CH_3)$_2$), 43.73 (d, C=CH*C*H), 46.16 (t, (CH$_2$)$_2$*C*H$_2$C=O), 47.53 (d, C=CHCH*C*H), 126.17, 127.63, 128.28 (3x d, Ar*C*), 133.84 (d, C=*C*H), 141.61 (s, Ar*C*), 153.36 (s, *C*=CH), 154.05 (s, N*C*=O), 211.47 (s, CH$_2$*C*=O); *m/z* (CI: CH_4) 444 (M^+ + 1, 100), 428 (21), 386 (22), 327 (6), 232 (2).

3.10) One-Pot Preparation of 1-Substituted 1-N,N-Diethylcarbamoyloxybuta-1,3-dienes.

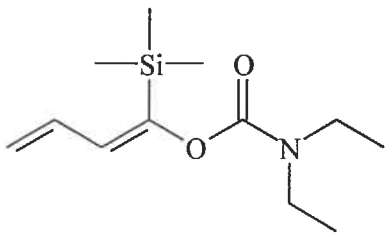
(E,E) 4-N,N-Diethylcarbamoyloxypenta-1,3-diene (**81a**).



$C_{10}H_{17}NO_2 = 183.251$

(*Z*)-1,4-Bis-(*N,N*-diethylcarbamoyloxy)but-2-ene (**50**) (0.500 g, 0.0017 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / solid CO_2) under nitrogen with stirring. ^{n}Butyllithium (0.0019 mol) was added drop-wise and the mixture was stirred at -78 °C for 1 hour. Methyl iodide (0.270 g, 0.0019 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*) 4-*N,N*-diethylcarbamoyloxypenta-1,3-diene (**81a**) as a colourless oil. (0.222 g, 71 %). (Found: C, 65.77; H, 9.09; N, 7.55; $C_{10}H_{17}NO_2$ requires C, 65.54; H, 9.35; N, 7.64 %); δ_H (200 MHz) 1.16 (6H, t, $N(CH_2CH_3)_2$), 2.02 (3H, s, C-CH_3), 3.31 (4H, q, $N(CH_2CH_3)_2$), 5.08 (2H, dd, CH_2=CH), 5.83 (1H, d, CH=C-CH_3), 6.40 (1H, dt, CH_2=CH); δ_C (50 MHz) 13.31, 14.00 (2x q, $N(CH_2CH_3)_2$), 15.99 (q, C-CH_3), 41.73, 41.78 (2x t, $N(CH_2CH_3)_2$), 116.34 (t, CH_2=CH), 118.39 (d, CH=C-CH_3), 131.14 (d, CH_2=CH), 148.56 (s, CH=C-CH_3), 153.83(s, C=O); *m/z* 183 (M^+, 3 %), 100 (100), 72 (45), 44 (12).

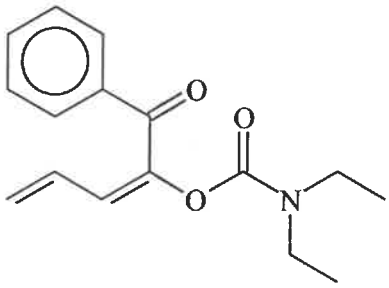
(E,E) 1-N,N-Diethylcarbamoyloxy-1-trimethylsilylbuta-1,3-diene (**81e**).



$C_{12}H_{23}NO_2Si = 241.407$

(*Z*)-1,4-Bis-(*N,N*-diethylcarbamoyloxy)but-2-ene (**50**) (0.500 g, 0.0017 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / solid CO_2) under nitrogen with stirring. ^{n}Butyllithium (0.0019 mol) was added drop-wise and the mixture was stirred at -78 °C for 1 hour. Trimethylsilyl chloride (0.207 g, 0.0019 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E,E*) 1-*N,N*-diethylcarbamoyloxy-1-trimethylsilylbuta-1,3-diene (**81e**) as a colourless oil. (0.184 g, 45 %). (Found : C, 59.84; H, 9.32; N, 5.59; $C_{12}H_{23}NO_2Si$ requires C, 59.70; H, 9.60; N, 5.80 %); δ_H (200 MHz) 0.25 (9H, s, $Si(CH_3)_3$), 1.16 (6H, m, $N(CH_2CH_3)_2$), 3.32 (4H, q, $N(CH_2CH_3)_2$), 5.18 (2H, 2x d, $CH=CH_2$), 6.50 (2H, c, $CH=CH$); δ_C (50 MHz) 0.00 (q, $Si(CH_3)_3$), 14.04, 14.74 (2x q, $N(CH_2CH_3)_2$), 42.36, 42.53 (2x t, $N(CH_2CH_3)_2$), 119.18 (t, $CH_2=CH$), 132.12 (d, $CH_2=CH$), 133.76 (d, $CH=C\text{-}SiMe_3$), 155.75 (s, $C\text{-}SiMe_3$), 160.09 (s, $C=O$); *m/z* 241 (M^+, <1 %), 174 (11), 100 (100), 73 (46), 72 (78), 44 (29).

(E,E) N,N-Diethylcarbamoyloxy-1-phenylpenta-2,4-dien-1-one (**81g**).

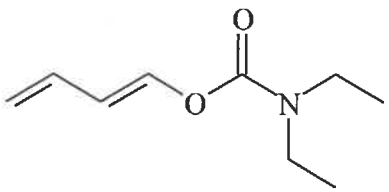


$C_{16}H_{19}NO_3 = 273.332$

(*Z*)-1,4-Bis-(*N,N*-diethylcarbamoyloxy)but-2-ene (**50**) (0.500 g, 0.0017 mol) was dissolved in dry THF (25 ml) and cooled to -78 °C (acetone / solid CO_2) under nitrogen with stirring. ^{n}Butyllithium (0.0019 mol) was added drop-wise and the mixture was stirred at -78 °C for 1 hour. Benzoyl chloride (0.267 g, 0.0019 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 4 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*) *N,N*-diethylcarbamoyloxy-1-phenylpenta-2,4-dien-1-one (**81g**) as a colourless oil. (0.155 g, 33 %). (Found : C, 70.16; H, 7.11; N, 5.14; $C_{16}H_{19}NO_3$ requires C, 70.31; H, 7.01; N, 5.12 %); δ_H (200 MHz) 0.96, 1.18 (6H, 2x t, $N(CH_2CH_3)_2$), 3.18, 3.33 (4H, 2x q, $N(CH_2CH_3)_2$), 5.10 - 5.50 (2H, dd, CH_2=CH), 6.30 - 6.60 (2H, m, CH=CH), 7.30 - 8.00 (5H, m, ArH); δ_C (50 MHz) 12.86, 13.88 (2x q, $N(CH_2CH_3)_2$), 41.74, 41.90 (2x t, $N(CH_2CH_3)_2$), 122.33 (t, CH_2=CH), 125.47, 128.18, 129.05 (3x d, ArC), 130.21 (d, CH_2=CH), 132.58 (d, CH_2=CH-CH), 137.19 (s, C-COPh), 144.64 (s, ArC), 153.30(s, $CONEt_2$), 190.19 (s, COPh); *m/z* 273 (M^+, 4 %), 105 (7), 101 (7), 100 (100), 77 (8), 72 (33), 44 (5).

3.11) Two-Pot Preparation of 1-Substituted 1-N,N-Diethylcarbamoyloxybuta-1,3-dienes.

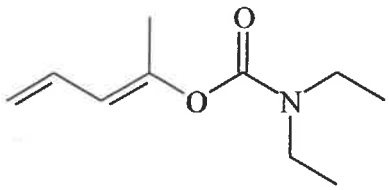
(E)-1-N,N-diethylcarbamoyloxy-1,3-butadiene (**80**).



$C_9H_{15}NO_2 = 169.224$

(*Z*)-1,4-bis-(*N,N*-diethylcarbamoyloxy)but-2-ene (5.000 g, 0.0175 mol) was dissolved in dry THF (75 ml) and cooled to -78°C (acetone / solid CO_2) under nitrogen with stirring. ^{n}Butyllithium (0.0210 mol) was added drop-wise and the mixture was stirred at -78 °C for 1 hour. The reaction was quenched with saturated aqueous ammonium chloride and the THF removed. The residue was dissolved in diethyl ether (100 ml) and washed with water (2 x 50 ml). The organic phase was separated, dried over anhydrous magnesium sulfate and the solvent removed. The residue was distilled to yield (*E*)-1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (**80**). (2.697 g, 91 %). b.p. 77 °C / 0.25 mmHg; (Found : C, 63.81; H, 8.99; N, 8.08; $C_9H_{15}NO_2$ requires C, 63.88; H, 8.93; N, 8.28 %); δ_H (200 MHz) 1.15 (6H, t, 2x C*H*$_3$), 3.33 (4H, q, 2 x C*H*$_2$CH$_3$), 4.99 (1H, dd, *J* = 1.73, 10.17, CH=CHH$_{trans}$), 5.13 (1H, dd, *J* = 1.74, 16.85, CH=CHH$_{cis}$), 5.96 (1H, dd, *J* = 11.04, 12.31, C*H*=CH-O), 6.28 (1H, dt, *J* = 10.66, 16.59, CH$_2$=C*H*), 7.38 (1H, d, *J* = 12.31, CH=C*H*-O); δ_C (50 MHz) 13.30, 14.18 (2x q, CH$_2$*C*H$_3$), 41.57, 42.20 (2x t, *C*H$_2$CH$_3$), 113.72 (d, CH$_2$=*C*H), 115.40 (t, *C*H$_2$=CH), 132.29 (d, *C*H=CH-O), 140.52 (d, *C*H-O), 152.77 (s, *C*=O); *m/z* 169 (M^+, 13 %), 100 (99), 72 (100), 56 (23).

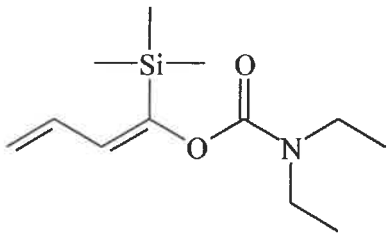
(E,E) 4-N,N-Diethylcarbamoyloxypenta-1,3-diene (**81a**).



$C_{10}H_{17}NO_2 = 183.251$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution methyl iodide (0.230 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 2 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*) 4-*N,N*-diethylcarbamoyloxypenta-1,3-diene (**81a**) as a colourless oil. (0.233 g, 85 %). (Found : C, 65.77; H, 9.09; N, 7.55; $C_{10}H_{17}NO_2$ requires C, 65.54; H, 9.35; N, 7.64 %); δ_H (200 MHz) 1.16 (6H, t, $N(CH_2CH_3)_2$), 2.02 (3H, s, C-CH_3), 3.31 (4H, q, $N(CH_2CH_3)_2$), 5.08 (2H, dd, CH_2=CH), 5.83 (1H, d, CH=C-CH_3), 6.40 (1H, dt, CH_2=CH); δ_C (50 MHz) 13.31, 14.00 (2x q, $N(CH_2CH_3)_2$), 15.99 (q, C-CH_3), 41.73, 41.78 (2x t, $N(CH_2CH_3)_2$), 116.34 (t, CH_2=CH), 118.39 (d, CH=C-CH_3), 131.14 (d, CH_2=CH), 148.56 (s, CH=C-CH_3), 153.83(s, C=O); *m/z* 183 (M^+, 3 %), 100 (100), 72 (45), 44 (12).

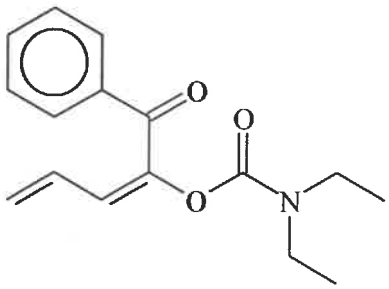
(E,E) 1-N,N-Diethylcarbamoyloxy-1-trimethylsilylbuta-1,3-diene (**81e**).



$C_{12}H_{23}NO_2Si = 241.407$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution trimethylsilylchloride (0.174 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed with water (2x 50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E,E*) 1-*N,N*-diethylcarbamoyloxy-1-trimethylsilylbuta-1,3-diene (**81e**) as a colourless oil. (0.250 g, 69 %). (Found : C, 59.84; H, 9.32; N, 5.59; $C_{12}H_{23}NO_2Si$ requires C, 59.70; H, 9.60; N, 5.80 %); δ_H (200 MHz) 0.25 (9H, s, $Si(CH_3)_3$), 1.16 (6H, m, $N(CH_2CH_3)_2$), 3.32 (4H, q, $N(CH_2CH_3)_2$), 5.18 (2H, 2x d, $CH=CH_2$), 6.50 (2H, c, *CH*=*CH*); δ_C (50 MHz) 0.00 (q, $Si(CH_3)_3$), 14.04, 14.74 (2x q, $N(CH_2CH_3)_2$), 42.36, 42.53 (2x t, $N(CH_2CH_3)_2$), 119.18 (t, CH_2=CH), 132.12 (d, CH_2=*C*H), 133.76 (d, *C*H=C-$SiMe_3$), 155.75 (s, *C*-$SiMe_3$), 160.09 (s, *C*=O); *m/z* 241 (M^+, <1 %), 174 (11), 100 (100), 73 (46), 72 (78), 44 (29).

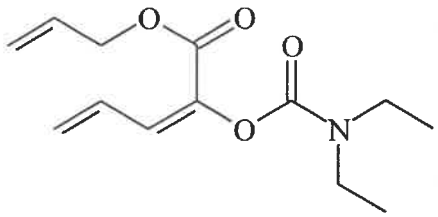
(E,E) N,N-Diethylcarbamoyloxy-1-phenylpenta-2,4-dien-1-one (**81g**).



$C_{16}H_{19}NO_3 = 273.332$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution benzoyl chloride (0.225 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 4 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*) *N,N*-diethylcarbamoyloxy-1-phenylpenta-2,4-dien-1-one (**81g**) as a colourless oil. (0.225 g, 55 %). (Found : C, 70.16; H, 7.11; N, 5.14; $C_{16}H_{19}NO_3$ requires C, 70.31; H, 7.01; N, 5.12 %); δ_H (200 MHz) 0.96, 1.18 (6H, 2x t, $N(CH_2CH_3)_2$), 3.18, 3.33 (4H, 2x q, $N(CH_2CH_3)_2$), 5.10 - 5.50 (2H, dd, CH_2=CH), 6.30 - 6.60 (2H, m, CH=CH), 7.30 - 8.00 (5H, m, Ar*H*); δ_C (50 MHz) 12.86, 13.88 (2x q, $N(CH_2CH_3)_2$), 41.74, 41.90 (2x t, $N(CH_2CH_3)_2$), 122.33 (t, CH_2=CH), 125.47, 128.18, 129.05 (3x d, Ar*C*), 130.21 (d, CH_2=CH), 132.58 (d, CH_2=CH-CH), 137.19 (s, *C*-COPh), 144.64 (s, Ar*C*), 153.30(s, *C*ONEt_2), 190.19 (s, *C*OPh); *m/z* 273 (M^+, 4 %), 105 (7), 101 (7), 100 (100), 77 (8), 72 (33), 44 (5).

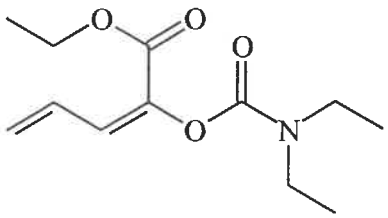
(E,E) 2-N,N-Diethylcarbamoyloxypenta-2,4-dienoic acid allyl ester (**81i**).



$C_{13}H_{19}NO_4 = 253.298$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution allyl chloroformate (0.193 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*) 2-*N,N*-diethylcarbamoyloxypenta-2,4-dienoic acid allyl ester (**81i**) as a colourless oil. (0.233 g, 61 %). (Found : C, 61.78; H, 7.51, N, 5.69; $C_{13}H_{19}NO_4$ requires C, 61.64; H, 7.56; N, 5.53 %); δ_H (200 MHz) 1.23 (6H, m, $N(CH_2CH_3)_2$), 3.36 (4H, m, $N(CH_2CH_3)_2$), 4.74 (2H, d, $OCH_2CH=CH_2$), 5.20 - 5.60 (4H, m, 2x $CH_2=CH$), 5.80 - 6.10 (1H, m, $OCH_2CH=CH_2$), 6.41 (1H, d, $CH_2=CH-CH$); δ_C (50 MHz) 13.32, 14.00 (2x q, $N(CH_2CH_3)_2$), 42.02, 42.27 (2x t, $N(CH_2CH_3)_2$), 65.68 (t, $OCH_2CH=CH_2$), 118.42 (t, $CH_2CH=CH_2$), 124.82 (t, $CH_2=CH-CH$), 130.94 (d, $CH_2CH=CH_2$), 130.98 (d, $CH_2=CH-CH$), 131.66 (d, $CH_2=CH-CH$), 137.32 (s, $CH=C-C=O$), 153.98 (s, $NC=O$), 161.98 (s, $OC=O$); *m/z* 253 (M^+, 1 %), 100 (100), 72 (35), 44 (4).

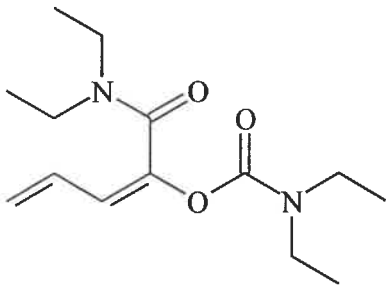
(E,E) 2-N,N-Diethylcarbamoyloxypenta-2,4-dienoic acid ethyl ester (**81j**).



$C_{12}H_{19}NO_4 = 241.287$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution ethyl chloroformate (0.174 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 3 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*) 2-*N,N*-diethylcarbamoyloxypenta-2,4-dienoic acid ethyl ester (**81j**) as a colourless oil. (0.211 g, 58 %). (Found : C, 59.84; H, 7.88; N, 5.87; $C_{12}H_{19}NO_4$ requires C, 59.73; H, 7.94; N, 5.81 %); δ_H (200 MHz) 1.20 (6H, m, $N(CH_2CH_3)_2$), 1.31 (3H, t, OCH_2CH_3), 3.34 (4H, m, $N(CH_2CH_3)_2$), 4.29 (2H, q, OCH_2CH_3), 5.44 (2H, dd, CH_2=CH-CH), 6.39 (1H, d, CH_2=CH-CH), 6.20 - 6.50 (1H, m, CH_2=CH-CH); δ_C (50 MHz) 13.34, 13.99 (2x q, $N(CH_2CH_3)_2$), 14.09 (q, OCH_2CH_3), 42.03, 42.28 (2x t, $N(CH_2CH_3)_2$), 61.16 (t, OCH_2CH_3), 124.54 (t, CH_2=CH), 130.54 (d, CH_2=CH), 130.99 (d, CH_2=CH-CH), 137.61 (s, CH_2=CH-CH=C), 154.01 (s, NC=O), 162.32 (s, OC=O); *m/z* 241 (M^+, 17 %), 196 (8), 100 (100), 72 (28), 44 (7).

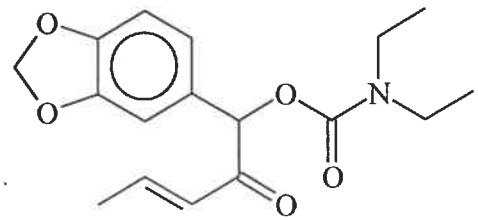
(E,E) N,N-Diethylcarbamoyloxypenta-2,4-dienoic acid diethyl amide (**81k**).



$C_{14}H_{24}N_2O_3 = 268.357$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution of *N,N*-diethylcarbamoyl chloride (0.217 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 4 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E,E*)- *N,N*-diethylcarbamoyloxypenta-2,4-dienoic acid diethyl amide (**81k**) as a colourless oil. (0.174 g, 43 %). (Found : C, 62.40; H, 8.89; N, 10.52; $C_{14}H_{24}N_2O_3$ requires C, 62.66; H, 9.01; N, 10.44 %); δ_H (200 MHz) 1.23 (12H, m, 2x N(CH_2CH_3)$_2$), 3.20 - 3.70 (8H, 2x m, 2x N(CH_2CH_3)$_2$), 5.10 - 5.40 (2H, dd, CH_2=CH), 6.07 (1H, d, CH_2=CH-C*H*), 6.20 - 6.50 (1H, dt, CH_2=C*H*); δ_C (50 MHz) 13.13, 13.27, 13.96, 14.11 (4x q, 2x N(CH_2CH_3)$_2$), 28.29, 41.97, 42.11, 43.01 (4x t, 2x N(CH_2CH_3)$_2$), 118.75 (d, CH_2=*C*H), 119.78 (t, *C*H_2=CH), 130.01 (d, CH_2=CH-*C*H), 142.99 (s, CH_2=CH-CH=*C*), 153.08 (s, N*C*=O), 164.18 (s, O*C*=O); *m/z*: 268 (M^+, 1%), 100 (100), 72 (51), 44 (12).

(E)-1-N,N-Diethylcarbamoyloxy-1-(3',4'-methylenedioxyphenyl)pent-3-en-2-one (**83**).

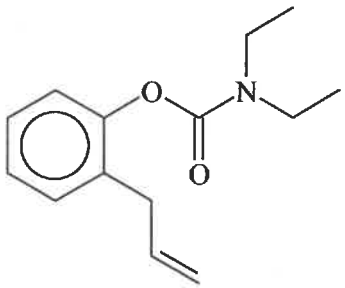


$C_{17}H_{21}NO_5 = 319.357$

A solution of 1-*N,N*-diethylcarbamoyloxy-1,3-butadiene (0.250 g, 0.0015 mol) in dry THF (10 ml) was cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0016 mol) was added dropwise and the mixture stirred for 1 hour. A solution of piperonal (0.240 g, 0.0016 mol) in dry THF (5 ml) was added dropwise and the mixture stirred for a further 5 hours. The reaction was quenched with saturated aqueous ammonium chloride, diluted with diethyl ether (50 ml) and washed 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and purified by column chromatography (silica, 15 % diethyl ether / hexane) to afford (*E*)-1-*N,N*-diethyl-carbamoyloxy-1-(3',4'-methylenedioxyphenyl)pent-3-en-2-one (**83**). (0.293 g, 61 %). (Found : C, 64.20; H, 6.79; N, 4.69; $C_{17}H_{21}NO_5$ requires C, 63.94; H, 6.63; N, 4.39 %); δ_H (200 MHz) 1.18 (6H, m, $N(CH_2CH_3)_2$), 1.84 (3H, d, $CHCH_3$), 3.36 (4H, m, $N(CH_2CH_3)_2$), 5.97 (2H, s, OCH_2O), 6.01 (1H, s, Ar-CHO), 6.21 (1H, d, J = 15.51, CH-C=O), 6.75 - 7.1 (4H, c, ArH, $CHCH_3$); δ_C (50 MHz) 13.43, 14.00 (2x q, $N(CH_2CH_3)_2$), 18.52 (q, $CHCH_3$), 41.58, 42.01 (2x t, $N(CH_2CH_3)_2$), 79.67 (d, Ar-CH-O), 101.33 (t, OCH_2O), 108.29, 108.54, 122.31 (3x d, ArC), 127.01 (d, $CHCH_3$), 127.85 (s, ArC), 144.75 (d, CHC=O), 148.08, 148.21 (2x s, ArC), 154.88 (s, OC=O), 193.57 (s, CHC=O); *m/z* 318 (M^+, 1 %), 246 (11), 101 (12), 100 (100), 72 (40).

3.12) Miscellaneous Reactions.

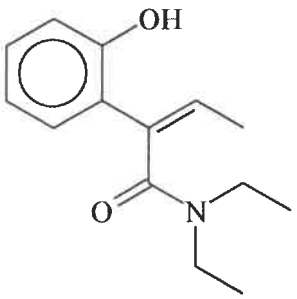
3-(2'-N,N-Diethylcarbamoyloxyphenyl)-prop-1-ene (**87**).



$C_{14}H_{19}NO_2 = 233.311$

2-Allylphenol (2.00 g, 0.015 mol) in dry THF (10 ml) was added dropwise over 15 minutes to a suspension of sodium hydride (0.020 mol) in dry THF (30 ml), which had been cooled in an ice-bath. The mixture was warmed to room temperature and stirred for 30 minutes. The mixture was cooled again and *N,N*-diethylcarbamoyl chloride (2.43 g, 0.018 mol) in dry THF (5 ml) was added dropwise. The mixture was then stirred at room temperature for a further 4 hours and then quenched with water (50 ml). The THF was removed and the residue extracted with diethyl ether (2x 30 ml). The combined organic extracts were dried over anhydrous magnesium sulfate, the solvent removed and distilled to afford 3-(2'-*N,N*-diethylcarbamoyloxyphenyl)-prop-1-ene (**87**). (2.57 g, 74 %). b.p. 107 °C / 0.25 mmHg; (Found : C, 72.31; H, 8.37; N, 5.98; $C_{14}H_{19}NO_2$ requires C, 72.07; H, 8.21; N, 6.00 %); δ_H (200 MHz) 1.18 (6H, t, $N(CH_2CH_3)_2$), 3.31 (2H, d, CH_2-CH=CH_2), 5.04 (2H, c, CH=CH_2), 5.8 - 6.1 (1H, c, CH=CH_2), 7.0 - 7.3 (4H, c, Ar*H*); δ_C (50 MHz) 13.18, 14.07 (2x q, $N(CH_2CH_3)_2$), 34.40 (t, CH_2-CH=CH_2), 41.64, 42.01 (2x t, $N(CH_2CH_3)_2$), 115.78 (t, CH=CH_2), 122.39, 125.30, 127.04, 129.89 (4x d, Ar*C*), 131.98 (s, ArC_1), 135.92 (d, *C*H=CH_2), 149.34 (s, ArC_2), 153.89 (s, *C*=O); *m/z* 233 (M^+, 1 %), 115 (3), 101 (6), 100 (100), 77 (3), 72 (56), 44 (16).

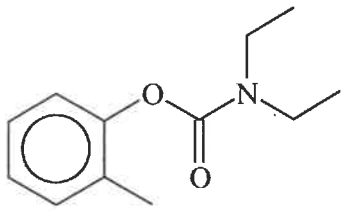
(E)-N,N-Diethyl-2-(2'-hydroxyphenyl)but-2-enamide (**88**).



$C_{14}H_{19}NO_2 = 233.311$

3-(2'-*N,N*-Diethylcarbamoyloxyphenyl)-prop-1-ene (**87**) (0.500 g, 0.0021 mol) was dissolved in dry THF (30 ml) and cooled to -78 °C (acetone / CO_2). ^{n}Butyllithium (0.0042 mol) was added dropwise and the mixture stirred at -78 °C for 4 hours. The reaction was quenched with saturated aqueous ammonium chloride and the THF removed. The residue was taken up in diethyl ether (50 ml) and washed with water (2x 50 ml). The organic layer was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 15 % diethyl ether / hexane) to afford (*E*)-*N,N*-diethyl-2-(2'-hydroxyphenyl)but-2-enamide (**88**). (0.299 g, 61 %); (Found : C, 72.29; H, 8.35; N, 6.21; $C_{14}H_{19}NO_2$ requires C, 72.07; H, 8.21; N, 6.00 %); δ_H (200 MHz) 1.16 (6H, dt, J = 2.87, 7.16, $N(CH_2CH_3)_2$), 1.65 (3H, d, J = 6.88, $CHCH_3$), 3.48 (4H, dq, J = 7.15, 20.43, $N(CH_2CH_3)_2$), 5.95 (1H, q, J = 6.87, $CHCH_3$), 6.8 - 7.3 (4H, c, Ar*H*), 10.50 (1H, bs, O*H*); δ_C (50 MHz) 12.53 (q, $CHCH_3$), 14.14, 14.17 (2x q, $N(CH_2CH_3)_2$), 39.53, 43.63 (2x t, $N(CH_2CH_3)_2$), 117.83 (d, C3'), 119.06 (d, C5'), 121.29 (s, C1'), 129.56 (d, C6'), 129.73 (d, C=CH), 130.30 (d, C4'), 134.61 (s, C=CH), 155.86 (s, C2'), 173.20 (s, C=O); *m/z* 233 (M^+, 2 %), 131 (6), 105 (7), 77 (6), 73 (26), 58 (100), 44 (6).

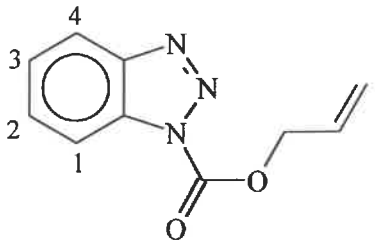
1-N,N-Diethylcarbamoyloxy-2-methylbenzene (**89**).



$C_{12}H_{17}NO_2 = 207.273$

o-Cresol (5.00 g, 0.0462 mol) was dissolved in dry THF (100 ml) and cooled in an ice-bath. Sodium hydride (0.0693 mol) was added in portions and the mixture stirred for 1 hour. *N,N*-Diethylcarbamoylchloride (7.84 g, 0.0578 mol) was added dropwise and the mixture then allowed to warm to room temperature. The mixture was stirred for a further 4 hours at room temperature and then quenched with water. The THF was removed and the residue diluted with diethyl ether (50 ml). The mixture was washed with 10 % aqueous sodium hydrogen carbonate (2x 50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was distilled to afford 1-*N,N*-diethylcarbamoyloxy-2-methylbenzene (**89**). (8.02 g, 84 %). b.p. 151 - 153 °C / 0.53 mmHg; (Found: C, 69.79; H, 8.38; N, 7.01; $C_{12}H_{17}NO_2$ requires C, 69.54; H, 8.27; N, 6.76 %); δ_H (200 MHz) 1.23 (6H, c, $N(CH_2CH_3)_2$), 2.22 (3H, s, Ar-CH_3), 3.42 (4H, bq, $N(CH_2CH_3)_2$), 7.0 - 7.3 (4H, c, Ar*H*); δ_C (50 MHz) 13.44, 14.28 (2x q, $N(CH_2CH_3)_2$), 16.29 (q, Ar-CH_3), 41.88, 42.22 (2x t, $N(CH_2CH_3)_2$), 122.20 (d, C_6), 125.31 (d, C_4), 126.74 (d, C_5), 130.42 (s, C_2), 130.90 (d, C_3), 150.02 (s, C_1), 153.96 (s, *C*=O); *m/z* 207 (M^+, 32 %), 107 (15), 101 (14), 100 (100), 91 (15), 77 (26), 72 (87), 56 (14).

Benzotriazole allyl carbamate (**90**).

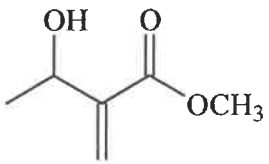


$C_{10}H_9N_3O_2 = 203.201$

Benzotriazole (0.500 g, 0.0042 mol) was dissolved in dry benzene (15 ml) and allylchloroformate (0.607 g, 0.0050 mol) was added. The mixture was refluxed overnight and then allowed to cool to room temperature. Water (30 ml) was added and the mixture extracted with diethyl ether (2x 30 ml). The combined organic extracts were dried over anhydrous magnesium sulfate and the solvent removed. The crude product was purified by column chromatography (silica, 15 % diethyl ether / hexane) to afford benzotriazole allyl carbamate (**90**) as a waxy solid. (0.580 g, 68 %). m.p. 33 - 34 °C; (Found : C, 58.98; H, 4.50; N, 20.48; $C_{10}H_9N_3O_2$ requires C, 59.11; H, 4.46; N, 20.68 %); δ_H (200 MHz) 5.11 (2H, dt, J = 1.22, 6.03, OCH_2), 5.45 (1H, ddd, J = 1.10, 2.18, 10.33, CH=CHH_{trans}), 5.58 (1H, ddd, J = 1.37, 2.68, 17.14, CH=CHH_{cis}), 6.16 (1H, ddt, J = 6.00, 10.28, 17.12, CH=CH$_2$), 7.50 (1H, ddd, J = 1.08, 7.17, 8.27, ArH_3), 7.66 (1H, ddd, J = 1.13, 7.16, 8.31, ArH_2), 8.11 (1H, ddd, J = 0.94, 0.94, 8.30, ArH_1), 8.13 (1H, ddd, J = 0.96, 0.96, 8.26, ArH_4); δ_C (50 MHz) 69.28 (t, OCH$_2$), 113.42, 120.41, 125.81, 130.24 (4x d, ArC), 121.00 (t, CH=CH$_2$), 130.31 (d, CH=CH$_2$), 131.72, 145.85 (2x s, ArC), 148.70 (s, C=O); *m/z* 203 (M^+, 3 %, 134 (26), 130 (38), 90 (55), 64 (16), 41 (100).

3.13) Synthesis of Mikanecic Acid Derivatives.

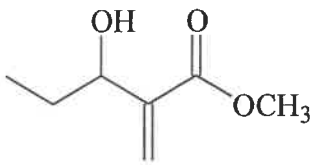
Methyl 3-hydroxy-2-methylenebutanoate (**33a**).



$C_6H_{10}O_3 = 130.143$

A mixture of acetaldehyde (22.00 g, 0.500 mol), methyl acrylate (30.00 g, 0.350 mol) and DABCO (10.00 g, 0.090 mol) was stirred in a sealed flask at room temperature for 7 days. The mixture was diluted with diethyl ether (150 ml) and washed with 3M HCl (2x 50 ml), 10 % aqueous sodium hydrogen carbonate (2x 50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and distilled to afford methyl 3-hydroxy-2-methylenebutanoate (**33a**). (36.81 g, 81 %). b.p. 55 °C / 5 mmHg; δ_H (200 MHz) 1.33 (3H, d, CHC*H*$_3$), 3.77 (3H, s, OC*H*$_3$), 4.11 (1H, s, O*H*), 4.63 (1H, q, C*H*CH$_3$), 5.90, 6.20 (2H, 2x s, C*H*$_2$=C); *m/z* 129 (M^+ - 1, < 1 %), 115 (64), 83 (100), 55 (45).

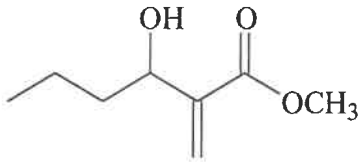
Methyl 3-hydroxy-2-methylenepentanoate (**33b**).



$C_7H_{12}O_3 = 144.170$

A mixture of propionaldehyde (29.00 g, 0.500 mol), methyl acrylate (30.00 g, 0.350 mol) and DABCO (10.00 g, 0.090 mol) was stirred in a sealed flask at room temperature for 7 days. The mixture was diluted with diethyl ether (150 ml) and washed with 3M HCl (2x 50 ml), 10 % aqueous sodium hydrogen carbonate (2x 50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and distilled to afford methyl 3-hydroxy-2-methylenepentanoate (**33b**). (41.75 g, 83 %). b.p. 80 °C / 6 mmHg; δ_H (200 Mhz) 0.90 (3H, t, CH_2CH_3), 1.68 (2H, m, CH_2CH_3), 3.34 (1H, s, O*H*), 3.77 (3H, s, OCH_3), 4.37 (1H, t, C*H*-OH), 5.84, 6.24 (2H, 2x s, CH_2=C); *m/z* 144 (M^+, < 1 %), 115 (74), 83 (100), 55 (27).

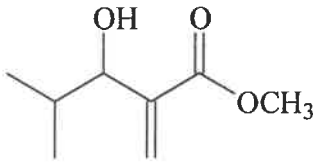
Methyl 3-hydroxy-2-methylenehexanoate (**33c**).



$C_8H_{14}O_3 = 158.197$

A mixture of n-butyraldehyde (36.00 g, 0.500 mol), methyl acrylate (30.00 g, 0.350 mol) and DABCO (20.00 g, 0.180 mol) was stirred in a sealed flask at room temperature for 14 days. The mixture was diluted with diethyl ether (150 ml) and washed with 3M HCl (3x 50 ml), 10 % aqueous sodium hydrogen carbonate (2x 50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and distilled to afford methyl 3-hydroxy-2-methylenehexanoate (**33c**). (44.23 g, 80 %). b.p. 95 °C / 2 mmHg; δ_H (200 MHz) 0.93 (3H, t, $CH_2CH_2CH_3$), 1.53 (4H, m, $CH_2CH_2CH_3$), 2.92 (1H, s, O*H*), 3.78 (3H, s, OCH_3), 4.40 (1H, t, C*H*-OH), 5.82, 6.22 (2H, 2x s, CH_2=C); *m/z* 157 (M^+ - 1, < 1 %), 115 (100), 98 (11), 87 (14), 83 (98), 55 (27).

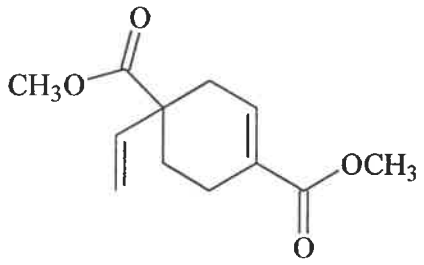
Methyl 3-hydroxy-4-methyl-2-methylenepentanoate (**33d**).



$C_8H_{14}O_3 = 158.197$

A mixture of ^{i}butyraldehyde (36.00 g, 0.500 mol), methyl acrylate (30.00 g, 0.350 mol) and DABCO (20.00 g, 0.180 mol) was stirred in a sealed flask at room temperature for 14 days. The mixture was diluted with diethyl ether (150 ml) and washed with 3M HCl (3x 50 ml), 10 % aqueous sodium hydrogen carbonate (2x 50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and distilled to afford methyl 3-hydroxy-4-methyl-2-methylenepentanoate (**33d**). (42.03 g, 76 %). b.p. 98 °C / 2 mmHg; δ_H (200 MHz) 0.90 (6H, 2x d, CH(C*H*$_3$)$_2$), 1.91 (1H, m, C*H*(CH$_3$)$_2$), 3.15 (1H, s, O*H*), 3.76 (3H, s, OC*H*$_3$), 4.14 (1H, t, C*H*-OH), 5.80, 6.25 (2H, 2x s, C*H*$_2$=C); *m/z* 157 (M^+ - 1, < 1 %), 115 (100), 84 (48), 83 (93), 55 (27).

Dimethyl 4-(1-ethenyl)-1-cyclohexene-1,4-dicarboxylate (**37a**).



$C_{12}H_{16}O_4 = 224.256$

Method A:

Methyl 3-hydroxy-2-methylenebutanoate (**33a**) (0.500 g, 0.0038 mol), *N,N*-dimethylcarbamoyl chloride or *N,N*-diethylcarbamoyl chloride (0.0042 mol) and DABCO (1.277 g, 0.0114 mol) were dissolved in dry THF (50 ml) and refluxed for 3 hours in the case of *N,N*-dimethylcarbamoyl chloride and 4 hours in the case of *N,N*-diethylcarbamoyl chloride. The reaction was quenched with 2M HCl (50 ml) after cooling and diluted with diethyl ether (50 ml). The organic phase was separated and washed with water (50 ml) and then dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford dimethyl 4-(1-ethenyl)-1-cyclohexene-1,4-dicarboxylate (**37a**). (*N,N*-dimethylcarbamoyl chloride: 0.418 g, 98 %; *N,N*-diethylcarbamoyl chloride: 0.412 g, 97 %).

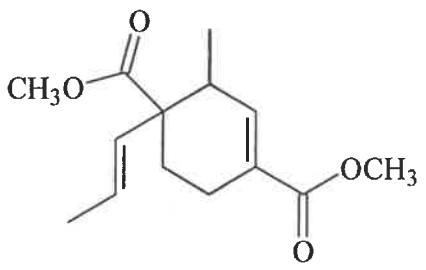
Method B:

Methyl 3-hydroxy-2-methylenebutanoate (**33a**) (0.500 g, 0.0038 mol) and *N,N*-dimethylcarbamoyl chloride or *N,N*-diethylcarbamoyl chloride (0.0042 mol) were dissolved in pyridine (10 ml) and refluxed for 5 hours. The pyridine was then removed under reduced pressure and the residue dissolved in diethyl ether (50 ml) and washed with 2M aqueous sulfuric acid (2x 50 ml), followed by water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and

the crude product purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford dimethyl 4-(1-ethenyl)-1-cyclohexene-1,4-dicarboxylate (**37a**). (*N,N*-dimethylcarbamoyl chloride: 0.406 g, 95 %; *N,N*-diethylcarbamoyl chloride: 0.389 g, 91 %).

δ_H (200 MHz) 1.74 - 2.32 (4H, m, C*H*$_2$C*H*$_2$), 2.33 - 2.87 (2H, m, C*H*$_2$CH), 3.68 (3H, s, CH$_2$CCO$_2$C*H*$_3$), 3.71 (3H, s, CH=CCO$_2$C*H*$_3$), 5.12 (2H, dd, C*H*$_2$=CH), 5.89 (1H, dd, CH$_2$=C*H*), 6.98 (1H, m, CH$_2$C*H*); δ_C (50 MHz) 21.78 (t, *C*H$_2$-C=CH), 29.51 (t, *C*H$_2$CH$_2$C=CH), 32.18 (t, *C*H$_2$CH), 47.26 (s, CH$_2$*C*CH$_2$), 51.52, 52.22 (2x q, 2x O*C*H$_3$), 115.14 (t, *C*H$_2$=CH), 129.38 (s, CH=*C*CO$_2$CH$_3$), 136.99 (d, CH$_2$*C*H), 139.49 (d, CH$_2$=*C*H), 167.14 (s, CH=C*C*O$_2$CH$_3$), 174.63 (s, C*C*O$_2$CH$_3$); *m/z* 224 (M^+, < 1 %), 192 (46), 165 (45), 133 (79), 105 (100), 91 (35).

Dimethyl 3-methyl-4-(1-propenyl)-1-cyclohexene-1,4-dicarboxylate (**37b**).



$C_{14}H_{20}O_4 = 252.310$

Method A:

Methyl 3-hydroxy-2-methylenepentanoate (**33b**) (0.500 g, 0.0035 mol), *N,N*-dimethylcarbamoyl chloride or *N,N*-diethylcarbamoyl chloride (0.0039 mol) and DABCO (1.176 g, 0.0105 mol) were dissolved in dry THF (50 ml) and refluxed for 3 hours in the case of *N,N*-dimethylcarbamoyl chloride and 4 hours in the case of *N,N*-diethylcarbamoyl chloride. The reaction was quenched with 2M HCl (50 ml) after cooling and diluted with diethyl ether (50 ml). The organic phase was separated and washed with water (50 ml) and then dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford dimethyl 3-methyl-4-(1-propenyl)-1-cyclohexene-1,4-dicarboxylate (**37b**). (*N,N*-dimethylcarbamoyl chloride: 0.421 g, 95 %; *N,N*-diethylcarbamoyl chloride: 0.416 g, 95 %).

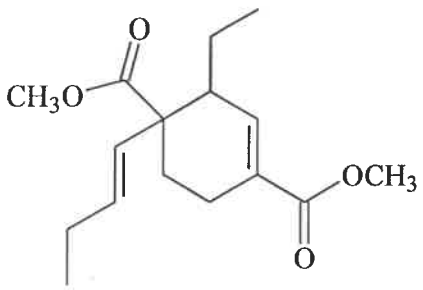
Method B:

Methyl 3-hydroxy-2-methylenepentanoate (**33b**) (0.500 g, 0.0035 mol) and *N,N*-dimethylcarbamoyl chloride or *N,N*-diethylcarbamoyl chloride (0.0039 mol) were dissolved in pyridine (10 ml) and refluxed for 5 hours. The pyridine was then removed under reduced pressure and the residue dissolved in diethyl ether (50 ml) and washed with 2M aqueous sulfuric acid (2x 50 ml), followed by water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and

the crude product purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford dimethyl 3-methyl-4-(1-propenyl)-1-cyclohexene-1,4-dicarboxylate (**37b**). (*N,N*-dimethylcarbamoyl chloride: 0.410 g, 93 %; *N,N*-diethylcarbamoyl chloride: 0.395 g, 89 %).

δ_H (200 MHz) 0.97 (3H, d, CHC*H*$_3$), 1.64 - 2.34 (4H, m, C*H*$_2$C*H*$_2$), 1.72 (3H, d, C*H*$_3$CH=CH), 3.00 (1H, m, C*H*CH$_3$), 3.65 (3H, s, CH$_2$CCO$_2$C*H*$_3$), 3.71 (3H, s, CH=CCO$_2$C*H*$_3$), 5.43 (1H, dd, *J* = 16.1, C*H*=CHCH$_3$), 5.53 (1H, dq, *J* = 16.1, 5.6, CH=C*H*CH$_3$), 6.93 (1H, m, CH$_3$CHC*H*); δ_C (50 MHz) 16.20 (q, CCH*C*H$_3$), 18.28 (q, CH=CH*C*H$_3$),) 22.57 (t, *C*H$_2$-C=CH), 24.72 (t, *C*H$_2$CH$_2$C=CH), 35.59 (d, *C*HCH=C), 50.17 (s, *C*CHCH$_3$), 51.57, 52.12 (2x q, 2x O*C*H$_3$), 126.45 (d, CH=*C*HCH$_3$), 128.00 (s, CH=*C*CO$_2$CH$_3$), 131.42 (d, CH*C*H=C), 143.71 (d, CH$_2$=*C*HCH$_3$), 167.61 (s, CH=C*C*O$_2$CH$_3$), 174.63 (s, C*C*O$_2$CH$_3$); *m/z* 252 (M^+, 7 %), 193 (57), 161 (90), 133 (75), 126 (100), 111 (64), 91 (6).

Dimethyl 4-(1-butenyl)-3-ethyl-1-cyclohexene-1,4-dicarboxylate (**37c**).



$C_{16}H_{24}O_4 = 280.364$

Method A:

Methyl 3-hydroxy-2-methylenehexanoate (**33c**) (0.500 g, 0.0032 mol), *N,N*-dimethylcarbamoyl chloride or *N,N*-diethylcarbamoyl chloride (0.0035 mol) and DABCO (1.075 g, 0.0096 mol) were dissolved in dry THF (50 ml) and refluxed for 3 hours in the case of *N,N*-dimethylcarbamoyl chloride and 4 hours in the case of *N,N*-diethylcarbamoyl chloride. The reaction was quenched with 2M HCl (50 ml) after cooling and diluted with diethyl ether (50 ml). The organic phase was separated and washed with water (50 ml) and then dried over anhydrous magnesium sulfate. The solvent was removed and the crude product purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford dimethyl 4-(1-butenyl)-3-ethyl-1-cyclohexene-1,4-dicarboxylate (**37c**). (*N,N*-dimethylcarbamoyl chloride: 0.410 g, 91 %; *N,N*-diethylcarbamoyl chloride: 0.413 g, 92 %).

Method B:

Methyl 3-hydroxy-2-methylenehexanoate (**33c**) (0.500 g, 0.0032 mol) and *N,N*-dimethylcarbamoyl chloride or *N,N*-diethylcarbamoyl chloride (0.0035 mol) were dissolved in pyridine (10 ml) and refluxed for 5 hours. The pyridine was then removed under reduced pressure and the residue dissolved in diethyl ether (50 ml) and washed with 2M aqueous sulfuric acid (2x 50 ml), followed by water (50 ml). The organic phase was dried over anhydrous magnesium sulfate, the solvent removed and

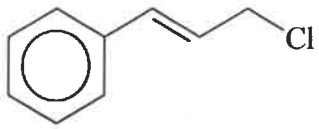
the crude product purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford dimethyl 4-(1-butenyl)-3-ethyl-1-cyclohexene-1,4-dicarboxylate (**37c**). (*N,N*-dimethylcarbamoyl chloride: 0.403 g, 90 %; *N,N*-diethylcarbamoyl chloride: 0.378 g, 84 %).

δ_H (200 MHz) 0.97, 1.01 (6H, 2x d, 2x CH_2CH_3), 1.60 - 2.40 (8H, m, CH_2CH_2, 2x CH_2CH_3), 2.77 (1H, m, $CHCH_2CH_3$), 3.65, 3.71 (6H, 2x s, 2x OCH_3), 5.46 (1H, dd, J = 16.1, CH=$CHCH_2$), 5.59 (1H, dt, J = 6.1, 16.1, CH=$CHCH_2$), 7.09 (1H, m, CH_2CHCH); δ_C (50 MHz) 12.37, 13.59 (2x q, 2x CH_2CH_3), 22.21 (t, CH_2-C=CH), 24.72 (t, CH_2CH_2C=CH), 25.44, 25.88 (2x t, 2x CH_2CH_3), 42.44 (d, $CHCH_2CH_3$), 50.44 (s, $CCHCH_2$), 51.56, 52.12 (2x q, 2x OCH_3), 128.58 (s, CCO_2CH_3), 129.20 (d, CH_2CH=CH), 133.35 (d, CHCH=C), 142.23 (d, CH_2CH=CH), 167.58 (s, CH=CCO_2CH_3), 175.52 (s, CCO_2CH_3); *m/z* 280 (M^+, 5 %), 189 (49), 139 (48), 125 (100), 105 (44), 91 (69), 59 (46).

3.14) Nucleophilic Substitution of Cinnamyl Carbamates.

(E)-1-Chloro-3-phenylprop-2-ene (**92a**).

Method A: From 1-*N,N*-diethylcarbamoyl-oxy-3-phenylprop-2-ene (**46a**).

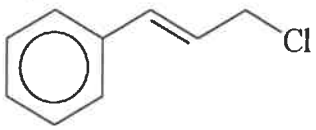


$C_9H_9Cl = 152.624$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**) (0.250 g, 0.0011 mol) was dissolved in glacial acetic acid (5 ml) and concentrated hydrochloric acid (0.5 ml) was added. The mixture was stirred at room temperature for 4 hours and then poured slowly into a 10 % aqueous solution of sodium hydrogen carbonate (100 ml). The mixture was extracted with diethyl ether (50 ml) and the organic layer washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-chloro-3-phenylprop-2-ene (**92a**). (0.121 g, 72 %). δ_H (200 MHz) 4.19 (2H, dd, J = 1.10, 7.15, CH_2), 6.28 (1H, dt, J = 7.14, 15.66, PhCH=C*H*), 6.61 (1H, d, J = 15.66, Ph-C*H*), 7.2 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 45.45 (t, CH_2), 124.84, 126.67, 128.61 (3x d, Ar*C*), 128.23 (d, Ph-CH=*C*H), 134.06 (d, Ph-*C*H), 135.82 (s, Ar*C*).

(E)-1-Chloro-3-phenylprop-2-ene (**92a**).

Method B: From 1-*N,N*-diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**).

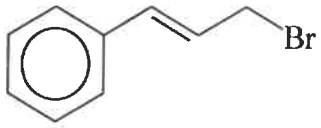


$C_9H_9Cl = 152.624$

1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**) (0.250 g, 0.0010 mol) was dissolved in glacial acetic acid (5 ml) and concentrated hydrochloric acid (0.5 ml) was added. The mixture was stirred at room temperature for 4 hours and then poured slowly into a 10 % aqueous solution of sodium hydrogen carbonate (100 ml). The mixture was extracted with diethyl ether (50 ml) and the organic layer washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-chloro-3-phenylprop-2-ene (**92a**). (0.087 g, 57 %). δ_H (200 MHz) 4.19 (2H, dd, J = 1.10, 7.15, CH_2), 6.28 (1H, dt, J = 7.14, 15.66, PhCH=C*H*), 6.61 (1H, d, J = 15.66, Ph-C*H*), 7.2 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 45.45 (t, *C*H_2), 124.84, 126.67, 128.61 (3x d, Ar*C*), 128.23 (d, Ph-CH=*C*H), 134.06 (d, Ph-*C*H), 135.82 (s, Ar*C*).

(E)-1-Bromo-3-phenylprop-2-ene (**92b**).

Method A: From 1-*N,N*-diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**).

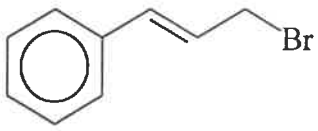


$C_9H_9Br = 197.075$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**) (0.250 g, 0.0011 mol) was dissolved in glacial acetic acid (5 ml) and concentrated hydrobromic acid (0.5 ml) was added. The mixture was stirred at room temperature for 4 hours and then poured slowly into a 10 % aqueous solution of sodium hydrogen carbonate (100 ml). The mixture was extracted with diethyl ether (50 ml) and the organic layer washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-bromo-3-phenylprop-2-ene (**92b**). (0.088 g, 40 %). δ_H (200 MHz) 4.15 (2H, dd, J = 0.78, 7.64, CH_2), 6.39 (1H, dt, J = 7.71, 15.56, PhCH=C*H*), 6.64 (1H, d, J = 15.59, Ph-C*H*), 7.2 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 45.45 (t, CH_2), 125.18, 126.74, 128.63 (3x d, Ar*C*), 128.34 (d, Ph-CH=*C*H), 134.52 (d, Ph-*C*H), 135.77 (s, Ar*C*).

(E)-1-Bromo-3-phenylprop-2-ene (**92b**).

Method B: From 1-*N,N*-diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**).

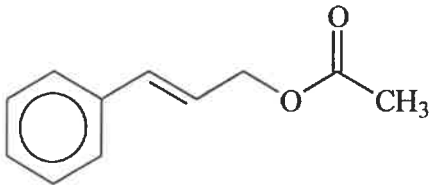


C_9H_9Br = 197.075

1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**) (0.250 g, 0.0010 mol) was dissolved in glacial acetic acid (5 ml) and concentrated hydrobromic acid (0.5 ml) was added. The mixture was stirred at room temperature for 4 hours and then poured slowly into a 10 % aqueous solution of sodium hydrogen carbonate (100 ml). The mixture was extracted with diethyl ether (50 ml) and the organic layer washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-bromo-3-phenylprop-2-ene (**92b**). (0.073 g, 37 %). δ_H (200 MHz) 4.15 (2H, dd, *J* = 0.78, 7.64, C*H*$_2$), 6.39 (1H, dt, *J* = 7.71, 15.56, PhCH=C*H*), 6.64 (1H, d, *J* = 15.59, Ph-C*H*), 7.2 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 45.45 (t, *C*H$_2$), 125.18, 126.74, 128.63 (3x d, Ar*C*), 128.34 (d, Ph-CH=*C*H), 134.52 (d, Ph-*C*H), 135.77 (s, Ar*C*).

(E)-1-Acetoxy-3-phenylprop-2-ene (**94**).

Method A: From 1-*N,N*-diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**).

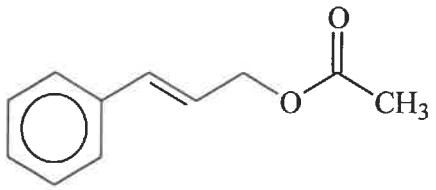


$C_{11}H_{12}O_2 = 176.215$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**) (0.250 g, 0.0011 mol) and methanesulfonic acid (0.106 g, 0.0011 mol) were dissolved in glacial acetic acid (5 ml). The mixture was stirred at room temperature for 5 hours and then poured slowly into a 10 % aqueous solution of sodium hydrogen carbonate (100 ml). The mixture was extracted with diethyl ether (50 ml) and the organic layer washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-acetoxy-3-phenylprop-2-ene (**94**). (0.169 g, 87 %). δ_H (200 MHz) 2.09 (3H, s, C*H*$_3$), 4.72 (2H, dd, *J* = 1.06, 6.38, C*H*$_2$), 6.28 (1H, dt, *J* = 6.41, 15.86, Ph-CH=C*H*), 6.65 (1H, d, *J* = 15.88, Ph-C*H*), 7.2 - 7.5 (5H, m, Ar*H*); δ_C (50 MHz) 20.99 (q, *C*H$_3$), 65.06 (t, *C*H$_2$), 123.13, 126.59, 128.59 (3x d, Ar*C*), 128.06 (d, Ph-CH=*C*H), 134.18 (d, Ph-*C*H), 136.16 (s, Ar*C*), 170.81 (s, *C*=O).

(E)-1-Acetoxy-3-phenylprop-2-ene (**94**).

Method B: From 1-*N,N*-diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**).

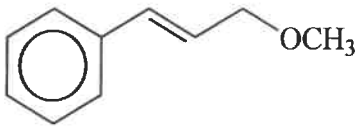


$C_{11}H_{12}O_2 = 176.215$

1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**) (0.250 g, 0.0010 mol) and methanesulfonic acid (0.096 g, 0.0010 mol) were dissolved in glacial acetic acid (5 ml). The mixture was stirred at room temperature for 5 hours and then poured slowly into a 10 % aqueous solution of sodium hydrogen carbonate (100 ml). The mixture was extracted with diethyl ether (50 ml) and the organic layer washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-1-acetoxy-3-phenylprop-2-ene (**94**). (0.144 g, 82 %). δ_H (200 MHz) 2.09 (3H, s, C*H*$_3$), 4.72 (2H, dd, *J* = 1.06, 6.38, C*H*$_2$), 6.28 (1H, dt, *J* = 6.41, 15.86, Ph-CH=C*H*), 6.65 (1H, d, *J* = 15.88, Ph-C*H*), 7.2 - 7.5 (5H, m, Ar*H*); δ_C (50 MHz) 20.99 (q, *C*H$_3$), 65.06 (t, *C*H$_2$), 123.13, 126.59, 128.59 (3x d, Ar*C*), 128.06 (d, Ph-CH=*C*H), 134.18 (d, Ph-*C*H), 136.16 (s, Ar*C*), 170.81 (s, *C*=O).

(E)-1-Methoxy-3-phenylprop-2-ene **(46a).**

Method A: From 1-*N,N*-diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**).

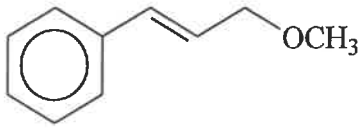


$C_{10}H_{12}O = 148.206$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**) (0.250 g, 0.0011 mol) and methanesulfonic acid (0.106 g, 0.0011 mol) were dissolved in methanol (10 ml) and stirred for 5 hours at room temperature. The mixture was then diluted with diethyl ether (50 ml) and washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The crude product was purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (E)-1-methoxy-3-phenylprop-2-ene (**46a**). (0.154 g, 95 %). δ_H (200 MHz) 3.33 (3H, s, OC*H*$_3$), 4.03 (2H, dd, *J* = 1.42, 5.89, C*H*$_2$), 6.24 (1H, dt, *J* = 5.86, 15.94, PhCH=C*H*), 6.58 (1H, d, *J* = 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 57.89 (q, O*C*H$_3$), 73.02 (t, *C*H$_2$), 125.89, 126.44, 128.52 (3x d, Ar*C*), 127.63 (d, PhCH=*C*H), 132.36 (d, Ph-*C*H), 136.66 (s, Ar*C*).

(E)-1-Methoxy-3-phenylprop-2-ene (**46a**).

Method B: From 1-*N,N*-diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**).

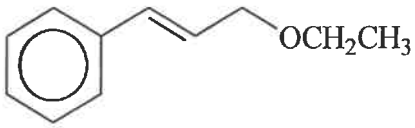


$C_{10}H_{12}O = 148.206$

1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**) (0.250 g, 0.0010 mol) and methanesulfonic acid (0.096 g, 0.0010 mol) were dissolved in methanol (10 ml) and stirred for 7 hours at room temperature. The mixture was then diluted with diethyl ether (50 ml) and washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The crude product was purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E*)-1-methoxy-3-phenylprop-2-ene (**46a**). (0.133 g, 90 %). δ_H (200 MHz) 3.33 (3H, s, OC*H*$_3$), 4.03 (2H, dd, *J* = 1.42, 5.89, C*H*$_2$), 6.24 (1H, dt, *J* = 5.86, 15.94, PhCH=C*H*), 6.58 (1H, d, *J* = 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 57.89 (q, O*C*H$_3$), 73.02 (t, *C*H$_2$), 125.89, 126.44, 128.52 (3x d, Ar*C*), 127.63 (d, PhCH=*C*H), 132.36 (d, Ph-*C*H), 136.66 (s, Ar*C*).

(E)-1-Ethoxy-3-phenylprop-2-ene (**46b**).

Method A: From 1-*N,N*-diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**).

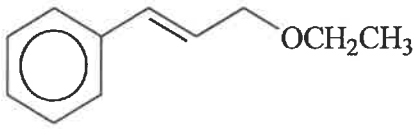


$C_{11}H_{14}O = 162.232$

1-*N,N*-Diethylcarbamoyloxy-3-phenylprop-2-ene (**46a**) (0.250 g, 0.0011 mol) and methanesulfonic acid (0.106 g, 0.0011 mol) were dissolved in ethanol (10 ml) and stirred for 7 hours at room temperature. The mixture was then diluted with diethyl ether (50 ml) and washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The crude product was purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E*)-1-ethoxy-3-phenylprop-2-ene (**46b**). (0.163 g, 91 %). δ_H (200 MHz) 1.23 (3H, t, OCH_2CH_3), 3.51 (2H, q, OCH_2CH_3), 4.10 (2H, dd, J = 1.38, 5.93, $CHCH_2$), 6.28 (1H, dt, J = 5.91, 15.93, PhCH=C*H*), 6.59 (1H, d, J = 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 15.25 (q, CH_3), 65.66 (t, OCH_2CH_3), 71.19 (t, $CHCH_2$), 126.30, 126.44, 128.50 (3x d, Ar*C*), 127.57 (d, PhCH=*C*H), 132.10 (d, Ph-*C*H), 136.74 (s, Ar*C*).

(E)-1-Ethoxy-3-phenylprop-2-ene (**46b**).

Method B: From 1-*N,N*-diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**).



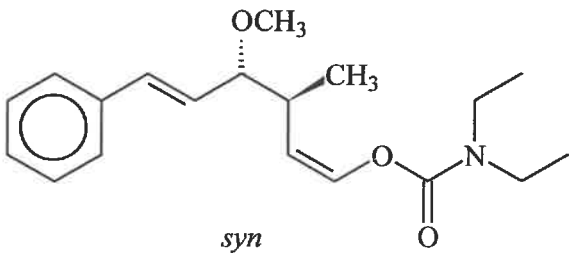
$C_{11}H_{14}O = 162.232$

1-*N,N*-Diisopropylcarbamoyloxy-3-phenylprop-2-ene (**46b**) (0.250 g, 0.0010 mol) and methanesulfonic acid (0.096 g, 0.0010 mol) were dissolved in ethanol (10 ml) and stirred for 9 hours at room temperature. The mixture was then diluted with diethyl ether (50 ml) and washed with 10 % aqueous sodium hydrogen carbonate (50 ml) and then water (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The crude product was purified by column chromatography (silica, 5 % diethyl ether / hexane) to afford (*E*)-1-ethoxy-3-phenylprop-2-ene (**46b**). (0.146 g, 90 %). δ_H (200 MHz) 1.23 (3H, t, OCH_2CH_3), 3.51 (2H, q, OCH_2CH_3), 4.10 (2H, dd, J = 1.38, 5.93, $CHCH_2$), 6.28 (1H, dt, J = 5.91, 15.93, PhCH=C*H*), 6.59 (1H, d, J = 15.96, Ph-C*H*), 7.1 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 15.25 (q, CH_3), 65.66 (t, OCH_2CH_3), 71.19 (t, $CHCH_2$), 126.30, 126.44, 128.50 (3x d, Ar*C*), 127.57 (d, PhCH=*C*H), 132.10 (d, Ph-*C*H), 136.74 (s, Ar*C*).

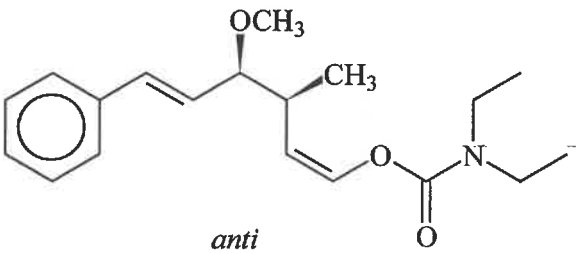
3.15) Synthesis of Oudemansin A.

All compounds listed consist of a 2 : 1 mixture of *anti : syn* isomers. NMR chemical shifts for the minor isomer are given in square brackets [ ] following the chemical shift of the major (*anti*) isomer. The two isomers were inseparable by column chromatography.

The *syn / anti* nomenclature refers to the relative position of the methyl and methoxy (hydroxy) group, as shown in the example below.

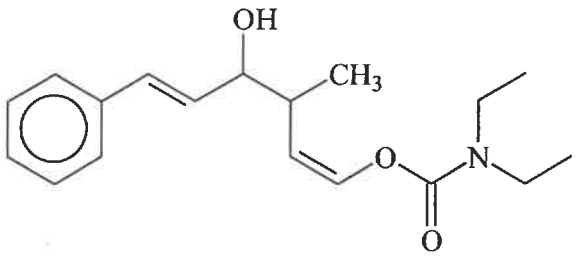


syn



anti

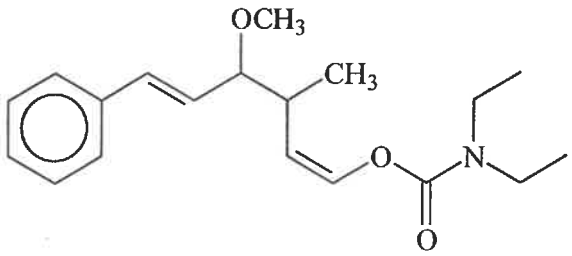
(Z,E) 1-N,N-Diethylcarbamoyloxy-4-hydroxy-3-methyl-6-phenyl-1,5-hexadiene (**109**).



$C_{18}H_{25}NO_3 = 303.402$

N,N-Diethylcarbamoyloxybut-2-ene (*E* : *Z* = 2 : 1) (0.500 g, 0.0029 mol) and TMEDA (0.373 g, 0.0032 mol) was dissolved in dry diethyl ether (30 ml) and cooled to -78 °C. ^{n}Butyllithium (0.0032 mol) was added dropwise and the mixture stirred for 30 minutes. Diethylaluminium chloride in toluene (0.0035 mol) was added dropwise and the mixture stirred for a further 1.5 hours. Cinnamaldehyde (0.424 g, 0.0032 mol) in dry diethyl ether (2 ml) was added dropwise and the mixture stirred at -78 °C for 4 hours. The reaction was quenched with 10 % aqueous sodium tartrate (10 ml) and then washed with 10 % aqueous sodium tartrate (2x 30 ml) and then water (30 ml). The organic phase was separated and dried over anhydrous magnesium sulfate. The solvent was removed and the residue purified by column chromatography (silica, 25 % diethyl ether / hexane) to afford (*Z,E*) 1-*N,N*-diethylcarbamoyloxy-4-hydroxy-3-methyl-6-phenyl-1,5-hexadiene (**109**) (0.723 g, 82 %). (*anti* : *syn* = 2 : 1); (Found: C, 71.51; H, 8.47; N, 4.81; $C_{18}H_{25}NO_3$ requires C, 71.26; H, 8.31; N, 4.62 %); δ_H (200 MHz) 1.11 (6H, t, $N(CH_2CH_3)_2$), 1.13 (3H, d, $CHCH_3$), 2.22 [2.02] (1H, bs, O*H*), 2.86 [2.37] (1H, m, C*H*CH_3), 3.29 (4H, bs, $N(CH_2CH_3)_2$), 4.07 (1H, bs, C*H*-OH), 4.72 [5.30] (1H, dd, *J* = 6.48, 9.64, C*H*=CHO), 6.21 [6.20] (1H, dd, *J* = 7.23, 15.92, PhCH=C*H*), 6.59 (1H, d, *J* = 15.97, Ph-C*H*), 7.1 - 7.4 (6H, m, Ar*H*, CH=C*H*-O); δ_C (50 MHz) 13.30, 14.08 (2x q, $N(CH_2CH_3)_2$), 16.81 (q, $CHCH_3$), 36.64 [39.30] (d, *C*HCH_3), 41.60, 42.11 (2x t, $N(CH_2CH_3)_2$), 76.60 (d, *C*H-OH), 112.63 [113.47] (d, *C*H=CHO), 126.48, 127.61, 128.51 (3x d, Ar*C*), 130.32 (d, PhCH=*C*H), 131.66 (d, Ph*C*H), 136.46 (d, CH=*C*H-O), 138.11 (s, Ar*C*), 152.98 (s, *C*=O); *m/z* 303 (M^+, < 1 %), 132 (78), 131 (100), 103 (66), 78 (41), 77 (58), 51 (38).

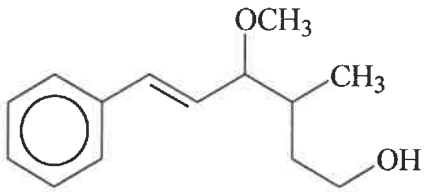
(Z,E) 1-N,N-Diethylcarbamoyloxy-4-methoxy-3-methyl-6-phenyl-1,5-hexadiene (**110**).



$C_{19}H_{27}NO_3 = 317.429$

(*Z,E*)-1-*N,N*-Diethylcarbamoyloxy-4-hydroxy-3-methyl-6-phenyl-1,5-hexadiene (**109**) (0.250 g, 0.0008 mol) was dissolved in dry THF (10 ml) and cooled to < 5 °C in an ice-bath. Sodium hydride (0.0012 mol) was added and the mixture stirred for 1.5 hours. Methyl iodide (0.226 g, 0.0016 mol) in dry THF (2 ml) was added and the mixture stirred for a further 4 hours. The reaction was quenched with water (10 ml) and then diluted with diethyl ether (50 ml). The mixture was washed with water (30 ml) and the organic phase dried over anhydrous magnesium sulfate. The solvent was removed and the residue purified by column chromatography (silica, 20 % diethyl ether / hexane) to afford (*Z,E*) 1-*N,N*-diethylcarbamoyloxy-4-methoxy-3-methyl-6-phenyl-1,5-hexadiene (**110**) (0.243 g, 96 %). (*anti : syn* = 2 : 1); (Found: C, 71.60; H, 8.43; N, 4.57; $C_{19}H_{27}NO_3$ requires C, 71.89; H, 8.57; N, 4.41 %); δ_H (200 MHz) 1.10 (3H, d, CHC*H*$_3$), 1.14 (6H, t, N(CH$_2$C*H*$_3$)$_2$), 2.95 [2.46] (1H, m, C*H*CH$_3$), 3.30 (4H, bs, N(C*H*$_2$CH$_3$)$_2$), 3.31 (3H, s, OC*H*$_3$), 3.60 (1H, bs, C*H*-OCH$_3$), 4.74 [5.36] (1H, ddd, *J* = 0.72, 6.42, 9.34, C*H*=CHO), 6.09 (1H, ddd, *J* = 0.72, 8.17, 15.97, PhCH=C*H*), 6.54 (1H, d, *J* = 15.97, PhC*H*), 7.06 (1H, d, *J* = 5.72, CH=C*H*O), 7.2 - 7.5 (5H, m, Ar*H*); δ_C (50 MHz) 13.32, 14.06 (2x q, N(CH$_2$*C*H$_3$)$_2$), 16.60 [16.81] (q, CH*C*H$_3$), 35.06 [37.56] (d, *C*HCH$_3$), 41.51, 42.02 (t, N(*C*H$_2$CH$_3$)$_2$), 56.56 (q, O*C*H$_3$), 86.08 [86.63] (d, *C*H-OCH$_3$), 112.99 [113.88] (d, *C*H=CHO), 126.47, 127.67, 128.54 (3x d, Ar*C*), 133.23 [133.48] (d, PhCH=*C*H), 135.26 (d, Ph*C*H), 136.58 (d, CH=*C*HO), 137.18 (s, Ar*C*), 153.00 (s, *C*=O); *m/z* 317 (M^+, < 1 %), 200 (5), 148 (17), 147 (100), 131 (4), 115 (12), 101 (3), 100 (50), 91 (3), 72 (14).

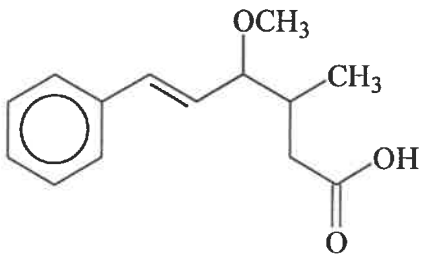
(E) 4-methoxy-3-methyl-6-phenylhex-5-en-1-ol (**111**).



$C_{14}H_{20}O_2 = 220.312$

(*Z,E*)-1-*N,N*-Diethylcarbamoyloxy-4-methoxy-3-methyl-6-phenyl-1,5-hexadiene (**110**) (0.250 g, 0.0008 mol) was dissolved in dry THF (15 ml) and lithium aluminium hydride (0.0008 mol) was added. The mixture was refluxed under an atmosphere of nitrogen for 4 hours and then allowed to cool to room temperature. The reaction was quenched with 10 % aqueous sodium tartrate (10 ml) and then diluted with diethyl ether (50 ml). The mixture was washed with 10 % aqueous sodium tartrate (2x 25 ml) and then water (25 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 20 % diethyl ether / hexane) to afford (*E*) 4-methoxy-3-methyl-6-phenylhex-5-en-1-ol (**111**) (0.142 g, 80 %). (*anti : syn* = 2 : 1); (Found: C, 76.07; H, 9.02; $C_{14}H_{20}O_2$ requires C, 76.33; H, 9.15 %); δ_H (200 MHz) 0.94 [0.96] (3H, d, CHC*H*$_3$), 1.35 - 2.05 (3H, c, C*H*C*H*$_2$), 2.58 (1H, bs, O*H*), 3.32 [3.33] (3H, s, OC*H*$_3$), 3.49 (1H, dd, C*H*-OCH$_3$), 3.68 (2H, m, C*H*$_2$-OH), 6.05 [6.13] (1H, dd, *J* = 8.28, 15.96, PhCH=C*H*), 6.53 (1H, d, *J* = 15.97, PhC*H*), 7.2 - 7.5 (5H, m, Ar*H*); δ_C (50 MHz) 16.67 (q, CH*C*H$_3$), 35.68 (d, *C*HCH$_3$), 36.64 (t, CH*C*H$_2$), 56.43 (q, O*C*H$_3$), 60.96 (t, *C*H$_2$OH), 87.30 (d, *C*H-OCH$_3$), 126.48, 127.78, 128.61 (3x d, Ar*C*), 128.36 (d, PhCH=*C*H), 133.59 (d, Ph*C*H), 136.47 (s, Ar*C*); *m/z* 220 (M^+, < 1 %), 148 (22), 147 (100), 115 (70), 91 (32).

(E)-4-Methoxy-3-methyl-6-phenylhex-5-enoic acid (**112**).



$C_{14}H_{18}O_3 = 234.295$

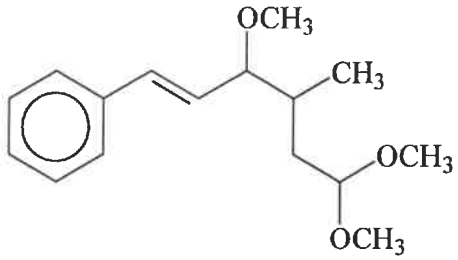
Route 1: (E) 4-methoxy-3-methyl-6-phenylhex-5-en-1-ol (**111**) (0.250 g, 0.0011 mol) was dissolved in acetone (10 ml) and Jones' reagent (1 ml) was added. The mixture was stirred at room temperature for 5 hours and then diluted with diethyl ether (50 ml). The mixture was washed with 1M HCl (30 ml) and the organic phase dried over anhydrous magnesium sulfate. The solvent was removed to afford crude (*E*)-4-methoxy-3-methyl-6-phenylhex-5-enoic acid (**112**) (*ca* 90 %).

Route 2: (*E*)-4-Methoxy-3-methyl-6-phenylhex-5-enal (**114**) (0.250 g, 0.0011 mol) was dissolved in acetone (10 ml) and Jones' reagent (1 ml) was added. The mixture was stirred at room temperature for 4 hours and then diluted with diethyl ether (50 ml). The mixture was washed with 1M HCl (30 ml) and the organic phase dried over anhydrous magnesium sulfate. The solvent was removed to afford crude (*E*)-4-methoxy-3-methyl-6-phenylhex-5-enoic acid (**112**) (*ca* 90 %).

Jones' Reagent: CrO_3 (1 g) and concentrated sulfuric acid (1 ml) was dissolved in water (3 ml).

δ_H (200 MHz) 0.99 (3H, d, CHC*H*$_3$), 2.1 - 2.7 (3H, c, C*H*C*H*$_2$), 3.28 (3H, s, OC*H*$_3$), 3.48 (1H, m, C*H*-OCH$_3$), 6.04 (1H, m, PhCH=C*H*), 6.56 (1H, d, PhC*H*), 7.2 - 7.7 (5H, m, Ar*H*), 8.09 (1H, bs, CO_2H); δ_C (50 MHz) 16.40 (q, CHCH$_3$), 35.20 (d, *C*HCH$_3$), 38.12 (t, *C*H$_2$), 56.59 (q, OCH$_3$), 86.48 (d, *C*H-OCH$_3$), 126.52, 127.81, 128.62 (3x d, Ar*C*), 127.88 (d, PhCH=*C*H), 134.03 (d, Ph*C*H), 136.33 (s, Ar*C*), 179.07 (s, *C*=O).

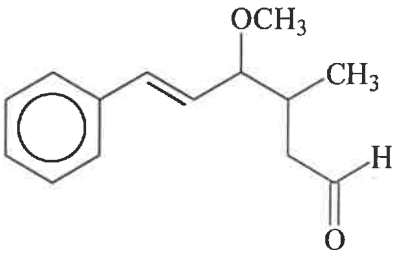
(E)-3-Methyl-6-phenyl-1,1,4-trimethoxyhex-5-ene (**113**).



$C_{16}H_{24}O_3 = 264.365$

(*Z,E*)-1-*N,N*-Diethylcarbamoyloxy-4-methoxy-3-methyl-6-phenyl-1,5-hexadiene (**110**) (0.250 g, 0.0008 mol) was dissolved in dry methanol (10 ml) and methane sulfonic acid (0.084 g, 0.0009 mol) and mercuric acetate (15 mg) were added. The mixture was stirred at room temperature for 5 hours, quenched with 10 % aqueous sodium hydrogen carbonate (25 ml) and then diluted with diethyl ether (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford (*E*)-3-methyl-6-phenyl-1,1,4-trimethoxyhex-5-ene (**113**) (0.197 g, 93 %). (*anti : syn* = 2 : 1); (Found: C, 72.95; H, 9.29; $C_{16}H_{24}O_3$ requires C, 72.69; H, 9.15 %); δ_H (200 MHz) 0.99 [0.95] (3H, d, CHC*H*$_3$), 1.38 (1H, m, C*H*CH$_3$), 1.91 (2H, m, C*H*$_2$), 3.31 (9H, c, 3x OC*H*$_3$), 3.53 (1H, m, CHC*H*-OCH$_3$), 4.52 (1H, c, C*H*(OCH$_3$)$_2$), 6.07 [6.05] (1H, dd, *J* = 7.86, 15.98, PhCH=C*H*), 6.53 (1H, d, *J* = 15.99, PhC*H*), 7.2 - 7.4 (5H, m, Ar*H*); δ_C (50 MHz) 15.66 (q, CHCH$_3$), 34.18 (t, *C*H$_2$), 35.63 (d, *C*HCH$_3$), 52.04 (q, CH(O*C*H$_3$)$_2$), 56.67 (q, CHCHO*C*H$_3$), 86.42 (d, CH*C*HOCH$_3$), 103.10 (d, *C*H(OCH$_3$)$_2$), 126.45, 127.64, 128.57 (3x d, Ar*C*), 128.19 (d, PhCH=*C*H), 133.14 (d, Ph*C*H), 136.62 (s, Ar*C*); *m/z* 264 (M^+, < 1 %), 174 (46), 148 (23), 147 (100), 115 (76), 91 (33), 75 (66).

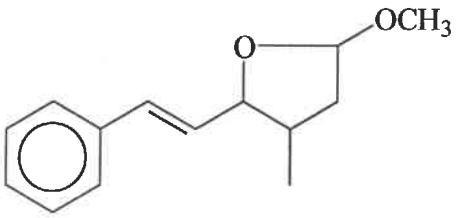
(E)-4-Methoxy-3-methyl-6-phenylhex-5-enal (**114**).



$C_{14}H_{18}O_2 = 218.296$

(*E*)-3-Methyl-6-phenyl-1,1,4-trimethoxyhex-5-ene (**113**) (0.250 g, 0.0009 mol), peracetic acid in glacial acetic acid (0.5 ml) and water (2 ml) was dissolved in THF (15 ml) and stirred at room temperature for 8 hours. The mixture was then diluted with diethyl ether (50 ml) and washed with 10 % aqueous sodium hydrogen carbonate (2x 30 ml) and then water (30 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed to afford crude (*E*)-4-methoxy-3-methyl-6-phenylhex-5-enal (**114**) (0.190 g, *ca* 90 %). δ_H (200 MHz) 0.98 (3H, d, CHC*H*$_3$), 1.7 - 2.8 (3H, c, C*H*C*H*$_2$), 3.26 [3.30] (3H, s, OC*H*$_3$), 3.97 (1H, c, C*H*-OCH$_3$), 6.04 (1H, c, PhCH=C*H*), 6.54 (1H, d, PhC*H*), 7.2 - 7.5 (5H, m, Ar*H*), 9.73 (1H, bs, C*H*O); δ_C (50 MHz) 16.83 (q, CH*C*H$_3$), 34.02 (d, *C*HCH$_3$), 48.28 (t, *C*H$_2$), 56.35 (q, OCH$_3$), 86.91 (d, *C*H-OCH$_3$), 126.50, 127.91, 128.63 (3x d, Ar*C*), 127.89 (d, PhCH=*C*H), 134.04 (d, Ph*C*H), 136.27 (s, Ar*C*), 202.04 (s, *C*=O).

1-Methoxy-3-methyl-4-styrylfuran (**115**).



$C_{14}H_{18}O_2 = 218.296$

(*Z,E*)-1-*N,N*-Diethylcarbamoyloxy-4-hydroxy-3-methyl-6-phenyl-1,5-hexadiene (**109**) (0.250 g, 0.0008 mol) was dissolved in dry methanol (10 ml) and methane sulfonic acid (0.084 g, 0.0009 mol) and mercuric acetate (15 mg) were added. The mixture was stirred at room temperature for 5 hours, quenched with 10 % aqueous sodium hydrogen carbonate (25 ml) and then diluted with diethyl ether (50 ml). The organic phase was dried over anhydrous magnesium sulfate and the solvent removed. The residue was purified by column chromatography (silica, 10 % diethyl ether / hexane) to afford 1-methoxy-3-methyl-4-styrylfuran (**115**) (0.144 g, 89 %). (mixture of isomers); (Found: C, 77.21; H, 8.47; $C_{14}H_{18}O_2$ requires C, 77.03; H, 8.31 %); δ_H (200 MHz) 1.07 (3H, d, CHC*H*$_3$), 1.4 - 2.6 (3H, c, C*H*$_2$, C*H*CH$_3$), 3.49 (3H, s, OC*H*$_3$), 4.08 (1H, c, C*H*-OCH$_3$), 5.02 (1H, c, CH-C*H*-O), 6.17 (1H, c, PhCH=C*H*), 6.59 (1H, c, PhC*H*), 7.1 - 7.5 (5H, m, Ar*H*); δ_C (50 MHz) 15.97 (q, CH*C*H$_3$), 37.74 (d, *C*HCH$_3$), 41.66 (t, *C*H$_2$), 54.59 (q, O*C*H$_3$), 88.19 (d, CH-*C*H-O), 104.78 (d, *C*H-OCH$_3$), 126.54, 127.60, 128.49 (3x d, Ar*C*), 130.47 (d, PhCH=*C*H), 131.69 (d, Ph*C*H), 136.68 (s, Ar*C*); *m/z* 218 (M^+, 2 %), 143 (5), 129 (8), 128 (6), 115 (9), 104 (6), 91 (14), 86 (35), 85 (100), 77 (8), 71 (75).

CHAPTER 4: REFERENCES

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