Transition metal-catalysed oxidative additions to alkenes

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Transition metal catalysed oxidative additions to alkenes

by

Adam David Warrington

A Doctoral Thesis
Submitted in partial fulfilment of the requirements
For the award of
Doctor of Philosophy of Loughborough University
(September 2007)

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Acknowledgements

Firstly a massive thank you to Dr. Steve Christie for giving me the opportunity to study towards a Ph.D. His guidance, enthusiasm and friendship over the last 4 years have allowed me to develop my love of chemistry and have made this work possible. A big thank you also of course to the rest of the Christie group, all have contributed to making my time at Loughborough a happy one and their help and support is truly appreciated. Special thanks to Poults and Kaz whose friendship has been invaluable to me and to Jaime who taught me never to leave my glassware unattended.

I would also like to acknowledge all the organic lecturers for their assistance and who have always been approachable and happy to answer my queries. The laboratory technicians and especially technical staff have all been essential in the evolution of my work including Dr. Mark Edgar, John Kershaw, Alistair Daley and John Spray. Everyone in laboratories F001, F009, F113 and F402 deserve a big thank you for making life fun even when things weren't going my way.

I would like to take the opportunity to thank my family, Elaine, Stephen, Nicola, Paul and Sue for their everlasting help, advice and friendship throughout my studies but especially my wife Claire who has always been there for me no matter how I'm feeling and without whose support and love none of this would be possible.

Finally I would like to thank both the EPSRC and GSK for their financial support which has enabled this research term to be completed.
Abstract

This thesis describes the development of new methods towards the stereoselective synthesis of oxazolidinones and [3,3] sigmatropic rearrangements to allylamines from allylic carbamate starting materials. Unlike previous protocols found in the literature the oxazolidinones formed do not have a protected nitrogen atom.

The stereoselective formation of chlorohydroxylated products is demonstrated with the view to utilise this reaction as part of an alternative to the tethered aminohydroxylation.

A novel diastereoselective iodine mediated cyclisation of allylic carbamates and allylic ureas to oxazolidinones and imidazolidinones respectively is described. The reaction has also been telescoped from an aldehyde completing three reactions in a one pot environment.

The use of palladium (II) catalysis for oxazolidinone formation is also shown in an attempt to devise an enantioselective reaction analogous to the highly acclaimed tethered aminohydroxylation. Palladium (II) catalysis is also utilised for the diastereoselective conversion of allylic carbamates to allylic amines.

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Chapter 2: Highlights our research into the formation of oxazolidinone rings from and [3,3] sigmatropic rearrangements of allylic carbamates.

Chapter 3: Provides experimental data for our studies.
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X-ray crystallographic data for Carbamic acid 2,6-dichloro-3,7-dihydroxy-3,7-dimethyl-octyl ester.
Abbreviations

Ac  acetyl
AcOH acetic acid
Ar  aryl
atm. atmosphere
aq. aqueous
BINAP binaphthalene
Bn  benzyl
bp  boiling point
Bu  butyl
nBu normal butyl
iBu iso-propyl
tBu tertiary butyl
cat. catalyst
cm³ cubic centimetre
cm⁻¹ wavenumber
conc. concentration
°C  degrees Celsius
Cp  cyclopentadiene
δ  chemical shift
Δ  heat
DCM dichloromethane
d.e. diastereomeric excess
d.r. diastereomeric ratio
DMF dimethyl formamide
DMSO dimethylsulfoxide
e.e. enantiomeric excess
EI  electron ionisation
eq. (equiv.) equivalent
Et  ethyl

v
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1.0 Introduction

This literature review will cover transition metal activation of alkenes. This subject is vast and as such this review could not encompass all known reactions. Therefore it will focus on two of the most important metals used in this area of organic synthesis, osmium and palladium.

1.1 Osmium

Osmium was discovered in 1803 by Smithson Tennant.\(^1\) When he dissolved crude platinum in aqua regia (a mixture of hydrochloric acid and nitric acid) a dark coloured residue was left containing both osmium and iridium. Osmium resides in group eight of the periodic table and is one of the precious metals. It is an incredibly dense solid and long before it was seen as a catalyst in organic synthesis was used to fashion phonograph needles because of its outstanding resistance to chipping and wear.\(^1\)

For catalysis it is more or less exclusive employed as osmium tetroxide and is widely used for the oxidation of alkenes through dihydroxylation and aminohydroxylation pathways. These reactions are two of the most important transformations used in organic synthesis and will now be discussed along with oxidative cyclisations of dienes in further detail.

1.1.1 Dihydroxylations

The osmium mediated dihydroxylation is one of the most well known and synthetically useful reactions in modern day chemistry. The basic premise of the reaction is to deliver two hydroxyl groups \(\text{syn}\) across a carbon-carbon double bond. The hydroxyls will add \(\text{syn}\) regardless of the geometry \((E\) or \(Z)\) of the double bond meaning that the confirmation of the double bond in the starting material will control which diastereoisomer of the product is obtained, (Scheme 1).\(^2\)
The mechanism of the reaction is still debated, but can be viewed in its simplest form as follows. The first step is thought to be a cycloaddition between the osmium tetroxide (OsO₄) and the alkene to yield an osmate ester, 1, which can then be hydrolysed to generate the desired diol. As the oxygen atoms were both added in one concerted step during the cycloaddition their relative stereochemistry remains syn, (Scheme 2).

As the mechanism is written an entire equivalent of expensive and toxic osmium tetroxide would be needed for the reaction to progress and this is indeed how early examples of the dihydroxylation were performed. Scientists wished to make the process catalytic however and a great deal of study went into making this a reality. The most famously developed catalytic reaction conditions were discovered at Upjohn and bear its name. The Upjohn process involves the use of NMO as a stochiometric oxidant lowering the amount of osmium catalyst required, (Scheme 3).
The catalytic version of the dihydroxylation greatly increased the interest of scientists and the osmium mediated reactions use. One obstacle still remaining for scientists to conquer, was to introduce enantioselectivity to make the reaction asymmetric. The discovery of the asymmetric reaction was a major break-through in this area of chemistry and saw the osmium catalysed reaction soar in popularity.

1.1.1 The Asymmetric Dihydroxylation

Initial work towards an enantioselective variant of the dihydroxylation reaction was conducted by Criegee in which he studied stoichiometric reactions of OsO₄ with olefins. Work by Sharpless and co-workers showed that the addition of pyridine to the system increased the rate of reaction. This gave rise to the ligand acceleration effect (LAE) upon which the process is dependant, This ensures that the reaction is funneled through a pathway involving a chiral catalyst, (Scheme 4).

![Scheme 4]

The enantioselectivity that is observed for these reactions comes from the use of the chiral ligands; these favour the addition to one face of the alkene. Examples of these are the Cinchona alkaloid derived ligands [(DHQ)₂PHAL] and [(DHQD)₂PHAL] where [(DHQ)₂PHAL] favours addition to the α-face and [(DHQD)₂PHAL] the β-face, (Fig. 1).
As mentioned earlier, the mechanism for the dihydroxylation is not fully known and still debated to this day. For the case of the asymmetric reaction two pathways have been suggested. The first pathway suggested was a concerted [3 + 2] pathway by Böseken and Criegee\(^5\), Scheme 5, Path A, the second a [2 + 2]-like addition of the olefin 2 across an Os=O bond, Scheme 5, Path B followed by rearrangement of the resulting osmaoxetane 3 intermediate to the glycolate product 4 suggested by Sharpless.\(^7\)

Enantiomeric excesses of diol products under catalytic conditions were initially found to be lower than those produced by stoichiometric reactions. The origin of this discrepancy was found to be the presence of a second catalytic cycle\(^8\) which gave only low or no enantioselectivity, yielding a mechanistic scheme for the reaction, (Scheme 6).
Elimination of the secondary cycle was achieved by conducting the reaction under two-phase conditions with K₃Fe(CN)₆ as the stoichiometric reoxidant. (Scheme 7).⁹

Under these reaction conditions there is no oxidant other than the OsO₄ present in the organic layer (the co-oxidant (K₃Fe(CN)₆) is kept away by the liquid/liquid boundary),
this contrasts with the homogeneous NMO conditions of scheme 6. The osmylation now therefore takes place in the organic layer and thus the resulting osmium(VI) monoglycolate ester 5 undergoes hydrolysis releasing the diol 6 and the ligand into the organic layer and the Os(VI) into the aqueous layer before its reoxidation can occur. This means that the entry of osmium glycolate into the second cycle is prevented.

It has been shown that MeSO₂NH₂ (a sulphonamide) can accelerate the hydrolysis of the osmium (VI) glycolate. The reaction time could be as much as 50 times shorter with the additive¹⁰ and thus the scope of the reaction has been increased to more sterically hindered substrates. The “sulfonamide effect” allows most AD reactions to be carried out at 0 °C as opposed to at room temperature which can help selectivity.¹¹ An exception is terminal olefins which can show a reduction in reaction rate on addition of MeSO₂NH₂.

Synthetic examples of the osmium catalysed dihydroxylation reaction range in the thousands. Therefore only a few selected examples will be discussed. An interesting example of its use is with polyunsaturated olefins. Polyunsaturated olefins have considerable synthetic potential, since they are highly functionalised compounds and each sp² centre may in principle be prochiral. The asymmetric dihydroxylation can be used to add stereospecifically two hydroxyl groups in suprafacial fashion across each double bond. For these molecules the initial dihydroxylation can be predicted based on previous studies.¹² Subsequent dihydroxylation steps can be controlled by the choice of an appropriate ligand. Thus, the reaction can be directed to effect either polydihydroxylation or regioselective mono-dihydroxylation of polyenes, leading to polyols or ene diols, respectively. Exhaustive dihydroxylation of polyenes can be achieved either in two ways. A single step process can be employed using the homogeneous N-methylmorpholine N-oxide process which will dihydroxylate all the double bonds with each new dihydroxylation occurring adjacent to the previous and on the opposite face, (Scheme 8).¹³
The second method is stepwise, carrying out sequential mono-dihydroxylations using heterogeneous ferricyanide conditions\textsuperscript{14} which allow better diastereoselectivity. This method has been taken to the extreme with the exhaustive dihydroxylation of squalene 7 to form the dodecaol 8, (Scheme 9).\textsuperscript{14}

\[
\text{Scheme 9}
\]

One final important example in the development of the dihydroxylation reaction is its selectivity with allylic alcohols. In 1983 Kishi produced a thorough study of the dihydroxylation of allylic alcohols and showed that the double bond is oxidized from the face opposite to the hydroxyl group under standard conditions, (Scheme 10).\textsuperscript{15}

\[
\text{Scheme 10}
\]

The existence of conditions to allow the formation of the \textit{syn} diol did not appear until 1996 when Donohoe \textit{et al.} displayed the use of an osmium tetroxide tetramethylethylenediamine (TMEDA) complex, (Scheme 11).\textsuperscript{16}

\[
\text{Scheme 11}
\]
The observed syn selectivity is believed to come about due to hydrogen bonding.\textsuperscript{17} The TMEDA forms a chelate with the osmium and donates electron density to the metal centre which in turn also increases the electron density on the oxygen ligands. This makes the oxy ligands better hydrogen bonding acceptors and thus the dihydroxylation is directed to take place on the same face as the hydroxyl group of the allylic alcohol. An important point here is that an equivalent of OsO\textsubscript{4} is required for the reaction, i.e. it is not catalytic. The creation of a catalytic variant using TMEDA has not been found; the osmate ester, 9, formed during the reaction has proven too stable to allow the formation of a catalytic cycle, (Fig. 2).\textsuperscript{17}

![Fig. 2](attachment:fig2.png)

The use of monodentate amine ligands provided the answer, complexation of quinuclidine to OsO\textsubscript{4} produced a catalyst capable of directing syn diol formation.\textsuperscript{18} Quinuclidine-N-oxide (QNO) was introduced into a dihydroxylation as an oxidant in the presence of catalytic OsO\textsubscript{4}. As the reaction proceeded QNO was reduced and quinuclidine released which allowed it to coordinate to the OsO\textsubscript{4}. This catalytic variant has been showed to work well when powerful trichloroacetamide directors are used (Scheme 12).\textsuperscript{18}

\[
\begin{align*}
\text{NHCOC\textsubscript{3}} & \quad \text{OsO}_4, \\
\text{QNO, } & \quad \text{H}_2\text{O}_2, \\
\text{CH}_2\text{Cl} & \quad \text{H}_{\text{2O}}, \\
\text{NHCOC\textsubscript{3}} & \quad \text{NHCOC\textsubscript{3}} \\
\text{82} & \quad \text{18}
\end{align*}
\]

Scheme 12

The directed dihydroxylation reaction has been used to synthesise a number of different natural sugars.\textsuperscript{19,20}
1.1.2 Aminohydroxylation

The aminohydroxylation reaction is the addition of an amino and hydroxyl group across a carbon double bond. It was first reported in its stochiometric version in 1975 by Sharpless. In his paper he showed that the reactions of monoimido complexes, 10 and 11, with α-methyl styrene, 12, yielded aminoalcohols as the major products, (Scheme 13).

$$\text{O}_2\text{O} + \text{CH}_2\text{Cl}_2 \rightarrow \text{HO} - \text{NHR}$$

Scheme 13

Sharpless found that generally the aminohydroxylation reactions carried out using 10 were cis stereoselective and that they preferred terminal alkenes. Interestingly Sharpless reports in his first paper that the reactions occurred with high regioselectivity, with the amino group favouring addition at the more accessible terminal carbon atom. As with the fore mentioned dihydroxylation, the use of pyridine as the reaction solvent increased the yields of the aminoalcohol products formed. For sterically hindered alkenes the major products of the reactions were diols. Pyridine once again showed its benefits as a solvent affecting the chemoselectivity of these reactions and increasing the amount of aminoalcohol product seen, (Scheme 14).

$$\text{O}_2\text{O} + \text{C}_4\text{H}_9 \rightarrow \text{HO} - \text{C}_4\text{H}_9 $$

Scheme 14

To further expand the reaction an asymmetric variation was investigated and achieved. Sharpless made a brief mention of the Cinchona alkaloid ligands in his 1980 paper, stating that they were capable of promoting an asymmetric reaction pathway similar to that seen for the dihydroxylation reaction. Rubinstein and Svendsen built on this
observation reporting the use of 4-chlorobenzoyl substituted dihydroquinine (DHQ) and dihydroquinidine (DHQD).\textsuperscript{23} Using these \textit{Cinchona} alkaloid derived ligands the aminoalcohol:dil ratio for the reaction of styrene with 10, was raised from 40:60 to 97:3 and 92:8 in favour of the desired aminoalcohols.

The stochiometric aminohydroxylation was now a useful reaction in the chemists toolkit but there were major drawbacks. Firstly, as seen for the dihydroxylation the use of stochiometric amounts of expensive osmium was required, in addition quaternary alkyl substituents at nitrogen and the use of strong reducing agents such as \textit{NaBH}_4 or \textit{LiAlH}_4 to liberate the aminoalcohol were also necessary.\textsuperscript{24}

\textbf{1.1.2.1 Catalytic Aminohydroxylations}

Using their knowledge of the catalytic asymmetric dihydroxylation,\textsuperscript{25} where oxo-transfer reagents such as NMO had been employed, Sharpless \textit{et al.} suggested that a nitrene based terminal oxidant would be ideal. Investigation showed that chloramine-T trihydrate, 13, was a viable reagent as it was cheap and importantly, left no organic by-products, (Scheme 15).\textsuperscript{26,27}

\[
\text{TsNCiNa}_3\text{H}_\text{2O} + \begin{array}{c} \text{R} \\ \text{OsO}_4, \text{tBuOH, 60} \degree \text{C} \end{array} \rightarrow \begin{array}{c} \text{HO} \\ \text{R} \end{array} \begin{array}{c} \text{TsHN} \\ \text{R} \end{array} + \text{NaCl}
\]

\textbf{Scheme 15}

The use of \textit{N}-chloro salts of carbamates were reported as alternative nitrene precursors.\textsuperscript{28,29} These reagents have been shown to be more favoured, as the aminoalcohol products obtained with these have more easily cleavable nitrogen protecting groups, (Scheme 16).\textsuperscript{28,29,30}

\[
\text{R'}\text{O} + \text{OsO}_4, \begin{array}{c} \text{CH}_2\text{CN, H}_2\text{O, RT} \end{array} \rightarrow \begin{array}{c} \text{HO} \\ \text{R} \end{array} \begin{array}{c} \text{R'} \text{O} \\ \text{AgN}_3 \end{array} + \text{AgCl + NaNO}_3
\]

\textbf{Scheme 16}

An interesting and noteworthy point for both catalytic reactions is, that the addition of silver or mercury salts has been seen to increase yields.\textsuperscript{28,29}
With the reaction now catalytic an asymmetric variant was greatly desired.

1.1.2.2 The Asymmetric Aminohydroxylation

The long sought after catalytic asymmetric aminohydroxylation was finally realised in 1996. Sharpless et al. reported that the use of an osmium (VI) salt in combination with chloramine-T and a chiral Cinchona alkaloid, (Fig 1), catalysed the oxidation of various olefins in both alcohol/water and acetonitrile/water solvent mixtures, (Scheme 17).\(^{31}\)

With the publication of Sharpless's paper, interest in the asymmetric aminohydroxylation grew and investigations into the improvement and understanding of the reaction began.

Different nitrogen sources have been studied with several different nitrene precursors compatible with the general conditions of the asymmetric aminohydroxylation seen, (Fig. 3).\(^{32-36}\)
The first nitrogen sources to be looked at were the sulfonamides, 14, starting as seen, with chloramine-T. Chloramine-T still is the most commonly used sulfonamide due to its low cost and wide availability. A common alternative to chloramine-T used in the literature is chloramine-M [MsN(Na)Cl]. Chloramine-M has been observed to give higher yields along with greater enantio- and regio-selectivities than chloramine-T. The superiority of this reagent is thought to be due to its smaller substituent on the sulfur.\(^{32}\) This trend is illustrated for the major AA products derived from methyl cinnamate, (Fig. 4).

The use of carbamate based nitrogen sources, 15, 17, allowed the scope of the asymmetric aminohydroxylation reaction to be increased to include many styrenes and terminal alkenes.\(^{33}\) In contrast to the sulfonamide case the nitrene precursor is generated \textit{in situ} by reaction with tert-butyl hypochlorite, giving the carbamate sources another advantage. One downside to the carbamate based asymmetric aminohydroxylation reaction is the removal of unreacted carbamate, extensive column chromatography is often required.\(^{37}\) Possibly the best carbamate reported to date is the 2-(trimethylsilyl)ethyl reagent,17, as it has been shown to give generally the best yields.
and selectivities. The reagent has also provided the fastest reaction rates which have allowed for the use of reduced osmium catalyst loading. Of the three major nitrogen sources reported for the asymmetric aminohydroxylation reaction, the most recently developed contain the amide moiety. The scope of the amide variant is very similar to that of the carbamate variant with the amides frequently giving better yields for comparative reactions. Initially N-bromoacetamide was used as the oxidant here as N-chlorocarbamides are susceptible to Hoffman rearrangement. The available amide sources, were increased by the development of a facile monobromination method for primary amides. Unfortunately as with sulfonamides the nitrene precursors formed from the amides have to be prepared in advance, they cannot be prepared in situ. However, the use of amide based nitrenes has allowed reactions to be performed with only a slight excess of oxidant, in contrast to both sulfonamide and carbamate cases where 3 equivalents is often necessary.

The mechanism of the asymmetric reaction has been the source of much debate and as for its predecessor the asymmetric dihydroxylation it is not wholly agreed on. Proposals for the asymmetric aminohydroxylation reaction mechanism have been closely related to the asymmetric dihydroxylation reaction due to their similarities. The intermediate that has been implicated in the key bond forming step of the reaction is the imidotrioxoosmium(VII) species. This is believed to add to an alkene with syn-stereospecificity to yield an azaglycolate complex. Two possible pathways have been suggested for the process; both agree the preference of to effect aminohydroxylation rather than dihydroxylation, (Scheme 18).
Sharpless proposed that upon coordination of the imidotrioxoosmium species 19 to an alkene, a [2+2] cycloaddition may occur to give the osmaazetide 21. The sequence is believed to be reversible until the coordination of a chiral ligand forming 22 this triggers an irreversible 1,2-migration of the carbon-osmium bond to yield 20, the osmium azaglycolate product. Sharpless's proposal utilizes electronic arguments to account for the observed preference of the nitrogen to add to the β-carbon of alkenes that bear an electron withdrawing group. The second proposed mechanistic pathway involves a concerted [3+2] cycloaddition of 23 to the alkene to form the product 20. Compounds 19 and 23 exist in equilibrium but 23 is believed to react faster due to the ligand acceleration effect observed for osmium oxidants and as such the reaction progresses via a chiral pathway rather than an achiral one. This proposal is analogous to the Criegee mechanism for osmium-mediated dihydroxylation. For this mechanistic proposal, catalyst-substrate interactions control the selectivity of the addition. Despite the existence of two mechanistic pathways for the formation of 20 catalytic cycles similar to those seen for the asymmetric dihydroxylation have been constructed, (Scheme 19).

The primary cycle is mediated by the ligand and in virtually all reported AA methods to date the presence of the ligand has been observed to improve the catalytic turnover relative to the non-ligand mediated reaction. The ligand mediates (i.e. is intervening)
the addition of the imidotrioxyosmium(vm) species 19 to the alkene to give the azaglycolate species 20. Reoxidation of 20 then occurs by the nitrogen source to give 24 which in turn can undergo hydrolysis to regenerate the initial osmium species 19 and yield the product (another possible pathway is the hydrolysis of 20 followed by oxidation to 19). The oxidised azaglycolate species 24 can however also enter a secondary cycle and addition of a second alkene can occur to give the bis(azaglycolate)osmium species 25. This cycle’s addition step is independent of the alkaloid derived ligand and thus results in addition products which have low enantioselectivity. Hydrolysis of 25 leads back to 20, which is then free to re-enter either the primary or secondary cycle. The turnover-limiting step in both of the cycles is the hydrolysis of azaglycolate complexes 24 or 25.\(^\text{45}\) The oxidation pathway is controlled by carrying out the reactions in aqueous solvent mixtures, this has the effect of making the hydrolysis of 24 more favourable than addition to an alkene and thus brings about the dominance of the primary cycle.\(^\text{22,43}\) The existence and the key stages of the two cycles is generally accepted among chemists and accounts for many of the observations made during the investigation of the asymmetric aminohydroxylation.

Despite the increase in knowledge, the asymmetric aminohydroxylation still has one major downfall, its lack of regioselectivity. It is easy to see that for an unsymmetrical olefin, 26, there is the possibility of two regioisomers, 27 and 28 depending on which atoms the nitrogen and oxygen add to, (Scheme 20).

\[
\begin{align*}
\text{ROCONH}_2 & \quad (\text{DHQ})_2\text{PHAL} \\
K_2\text{OsO}_2(\text{OH})_4 \\
\text{NaOH, } \text{tBuOOCl}, \\
\text{ROH, } H_2O \\
\text{R}^1\text{CHR}^2 & \quad \text{NHCOOR} \\
\text{R}^1 \quad \text{OH} & + \quad \text{R}^1 \quad \text{NHCOOR} \\
\text{R}^2 & \quad \text{OH} \\
\text{Scheme 20}
\end{align*}
\]

Solutions for certain, although limited, substrates have been discovered.\(^\text{44,46}\) Interestingly the choice of chiral ligand has shown in some cases to control the regioselectivity of the reaction. As previously mentioned the Cinchona alkaloids allow for the enantioselectivity of the reaction. For a chiral ligand used in the asymmetric aminohydroxylation it has an aromatic linker, the two most common being phthalazine (PHAL) and anthraquinone (AQN), (Fig. 5).
The reversal in regioselectivity observed by changing the linker is illustrated in the asymmetric aminohydroxylation of methyl cinnamate, (Scheme 21).23,47

The reason for the reversal of regioselectivity observed is not fully understood, one proposal is that the changing of the ligand structure favours an alternative substrate orientation with respect to the osmium-ligand complex.48

One of the most successful investigations into the inherent problem of regioselectivity in aminohydroxylation reactions has been reported by Donohoe et al.49 Reported first in 2001, Donohoe’s strategy is to use a tethered carbamate as the nitrogen source for the reaction.50 Using this approach complete regioselectivity was seen for the intramolecular reaction, (Scheme 22).
Carbamates such as 29 are formed from their respective allylic alcohols via isocyanate addition and cleavage reactions. When these substrates were subjected to common asymmetric aminohydroxylation reaction conditions oxazolidinone products, 30, were afforded as single regioisomers. This reaction was a major step in the development towards a regioselective asymmetric aminohydroxylation but the regioselectivity observed came at a cost. Using (DHQ)$_2$PHAL as the ligand for the reaction gave material that was racemic, there was no enantioselectivity. The scope of the tethered carbamate approach was extended by examining the stereoselectivity in cyclic systems, (Scheme 23).

The reaction of cyclic substrates provided the desired oxazolidinone products with complete chemo and stereoselectivity in moderate to high yields. The reaction shows only a slight increase in rate in the presence of tertiary amines. As with acyclic substrates the use of *Cinchona* alkaloid derived ligands did not induce enantioselectivity. Two possible reasons for this outcome could be, either the olefin face distinction does not apply in the intramolecular version of the asymmetric aminohydroxylation or the carbamoylimido osmium intermediate releases the ligand in a step prior to olefin functionalisation. Recently Donohoe *et al.* has introduced a new nitrene precursor for the tethered aminohydroxylation. Lebel *et al.* had introduced
NHOTs derivatives of carbamates as effective nitrene precursors for C-H insertion and alkene aziridination. Donohoe has shown that similar N-sulfonyloxy derivatives can be used for tethered aminohydroxylations, (Scheme 24).

![Scheme 24](image)

The use of N-sulfonyloxy derivatives for the reaction has seen improved yields for some substrates. It is important to note that these conditions do not require the base or oxidant seen in previous examples.

With the development of firstly a catalytic version of the aminohydroxylation and then subsequently an asymmetric variant the reaction has been used in an increasing array of synthetic methods. The earliest known application of the asymmetric aminohydroxylation, a short synthesis of the Taxol® C-13 side chain, 32, is shown to give an example of the reactions use in natural product synthesis, (Scheme 25).

![Scheme 25](image)

The asymmetric aminohydroxylation product, 31, from the reaction of methyl cinnamate (see fig. 4), was elaborated to 32 in two steps.

1.1.3 Oxidative Cyclisations of 1,5-Dienes

A final example of osmium’s impressive résumé is its use in the oxidative cyclisations of 1,5-dienes. Oxidative cyclisation reactions of 1,5-dienes to produce tetrahydrofurans are well established. These types of reactions provide a unique way to form these heterocycles. The reaction involves suprafacial addition of two oxygen atoms across
each of the two alkenes of a diene, as well as stereoselective formation of a cis-substituted tetrahydrofuran ring, (Scheme 26).\textsuperscript{55}

\[
\begin{align*}
\text{R}_1 & \quad \text{R}_2 \quad \text{R}_3 \quad \text{R}_4 \quad \text{R}_5 \quad \text{R}_6 \quad \text{[O]} = \text{KMnO}_4, \text{OsO}_4, \text{RuO}_4
\end{align*}
\]

Scheme 26

The first examples of this reaction typically used stoichiometric amounts of the oxidant involved, such as KMnO\textsubscript{4}\textsuperscript{56} or CrO\textsubscript{3} derivatives.\textsuperscript{57} Osmium was first introduced in 2000 by Piccialli \textit{et al.} who reported conditions for accomplishing the desired cyclisation using catalytic OsO\textsubscript{4} in conjugation with NaI\textsubscript{O} as a reoxidant, (Scheme 27)\textsuperscript{58}

\[
\begin{align*}
\text{[O]} & \quad \text{= OsO}_4 (5\%), \text{NaIO}_4 (4 \text{eq.}), \text{DMF, 16 h}
\end{align*}
\]

Scheme 27

More recently Donohoe \textit{et al.} have made significant advancements in the development of the reaction. The group initially showed that using a combination of OsO\textsubscript{4} and tetramethylethlenediamine (TMEDA) with a diene, 33, yielded an osmate ester, 34, which could then cyclise under acidic conditions, (Scheme 28).\textsuperscript{55}

\[
\begin{align*}
\text{R} & \quad \text{OsO}_4 (1 \text{ eq.)}, \text{TMEDA, CH}_2\text{Cl}_2
\end{align*}
\]

Scheme 28

Stochiometric osmium was used for this reaction and Donohoe sought a catalytic variant of the acid catalysed reaction. The breakthrough came when the oxidative
cyclisation of a number of 1,5-dienes using catalytic OsO₄ (5%), Me₂NO (4 eq.) and either camphorsulphonic acid (CSA; 6 eq.) or trifluoroacetic acid (TFA; excess) were attempted. Under these conditions the desired tetrahydrofurans were furnished in good yields.\(^{55}\)

The mechanism of the reaction has been postulated, (Scheme 29).\(^{55}\)

Initially dihydroxylation of \(\text{35}\) yields the osmate ester, \(\text{36}\), which under acidic conditions is believed to pass through the transition stage, \(\text{37}\), yielding the tetrahydrofuran product, \(\text{38}\), before the osmium is reoxidised back to Os\(^{\text{VIII}}\). The acid is thought to promote cyclisation by protonation of an oxo ligand on the osmium, this makes it more electron-deficient in the ensuing cycloaddition.
1.2 Palladium

Palladium was discovered in 1803, the same year as osmium, by the English chemist and physicist William Hyde Wollaston.\textsuperscript{59} It has found many applications within human society, it has been used for instrumental parts, in dentistry and it has been used for watch springs.

Palladium is probably the most widely used of all metal catalysts. It is incredibly versatile, promoting or catalysing a huge array of reactions including carbon-carbon and carbon-heteroatom bond formations, as well as rearrangement reactions. Due to the sheer volume of palladium literature, this review could never hope to cover all areas, indeed several books have been written on the subject.\textsuperscript{60,61,62} Fundamental reactions with alkenes involving both palladium (0) and palladium (II) catalysis will be discussed with special consideration given to reactions complementary to those seen with osmium.

1.2.1 Palladium (0)

Of the two aforementioned palladium species, palladium (0) is the most widely used and investigated. Although many transition metals are known to catalyse carbon-carbon bond forming reactions non surpass the generality and range of reactions mediated by palladium (0). It is used in many famous and synthetically useful reactions including: the Stille,\textsuperscript{63,64,65} Suzuki,\textsuperscript{66,67,68} and Sonogashira\textsuperscript{69,70} couplings. Reactions with alkenes include the Heck reaction and \(\pi\)-allyl chemistry, these will be discussed separately.

1.2.1.1 The Heck Reaction

The Heck reaction involves arylation or alkenylation of alkenes catalyzed by palladium (0). The reaction was first reported by Mizoroki in 1971\textsuperscript{71} and in 1972 by Heck\textsuperscript{72} whose name has since been attributed to the reaction. The general reaction is shown, (Scheme 30).

\[
R^1-X + \overset{\text{Pd(0)}}{\text{base}} \xrightarrow{\text{base}} R^1\equiv R^2 + \text{base.HX}
\]

Scheme 30
Initially interest in the reaction was low but grew rapidly in the late 1980's. The Heck reaction today is considered the most important reaction in the formation of carbon-carbon bonds involving sp² carbons.

The traditionally portrayed mechanism for the reaction is shown, (Scheme 31).

**Scheme 31**

Oxidative addition of R¹X occurs generating a *cis*-RPdXL₂ species which isomerises to the more stable *trans* configuration. To allow the alkene to insert, one of the ligands is released to generate a neutral palladium complex to which the alkene can coordinate. Insertion into the Pd-R bond results in the formation of an unstable σ-bond. Carbon-carbon bond rotation and β-hydride elimination follow to yield the new substituted alkene, which leaves the cycle. Regeneration of the palladium (0) catalyst is effected by the addition of base, reductive elimination occurs removing HX from the system and allowing palladium (0) to re-enter the cycle.⁷³ Thorough investigations into the finer points of the mechanistic cycle have been carried out.⁷⁴,⁷⁵

The Heck reaction is still used extensively with many new publications involving it coming out each year. Two recent publications by Xiao et al.⁷⁶,⁷⁷ show that the Heck reaction is still very much at the forefront of research, (Scheme 32).
Pd(OAc)$_2$ (2 mol%), mBDP (4 mol%), NEt$_3$ (1.5 eq.), DMSO, 115 ºC, 36 h.

Pd-mBDPP-Catalyzed Regioselective Internal Arylation of Electron-Rich Olefins by Aryl Halides

The Heck Reaction of Electron-Rich Olefins with Regiocontrol by Hydrogen-Bond Donors

1.2.1.2 π-Allylpalladium Chemistry

An important class of reactions involving alkenes and a palladium (0) catalyst are those of allylic compounds via π-allylpalladium complexes, (Scheme 33).

The palladium catalyst after initial coordination displaces the leaving group, X, to from a π-allylpalladium complex. These electrophilic species react with various kinds of pronucleophiles of carbon, oxygen and nitrogen to form new products. Many allylic compounds are known to form π-allylpalladium complexes by oxidative addition, (Fig. 6).

Fig. 6
The reaction can be represented as a catalytic cycle as for the Heck reaction, (Scheme 34).2

![Diagram](image)

Scheme 34

An important point as shown in the scheme 34, is that the intermediate $\pi$-allyl complex is in equilibrium between the neutral version, 39, and the cationic $\pi$-allyl 40. Controlling regioselectivity can be a problem with these reactions, (Scheme 35).

![Diagram](image)

Scheme 35

Once the $\pi$-allyl complex has been formed the nucleophile can attack from either end allowing both regioisomers to form. To overcome this problem the use of steric hinderance,79 electron-withdrawing groups80 and ligands has been seen.81 For non-symmetric allyl substrates substitution normally occurs at the least hindered allylic position, (Scheme 36).79
By employing an electron withdrawing group such as an ester, regioselectivity can be controlled. Substitution occurs at the allylic position furthest from the group, (Scheme 37).\(^8\)

Regioselectivity has been controlled via the use of chiral ligands. Trost et al. has developed a number of catalysts that can be used for the reaction.\(^8\) One interesting example is shown, (Scheme 38).\(^8\)

The number of ligands synthesized and screened in addition to those of Trost to control the enantioselectivity of the reaction is vast.\(^8\) One group of ligands that has found
success for different groups are those incorporating a 4,5-dihydrooxazole group, (Fig. 7).

![Fig. 7]

Pfaltz et al. has reported the use of ligands containing the backbones of 41 and 43. Helmchen et al. have also reported the use of 43, in allylpalladium reactions. Williams et al. have made significant contributions to this area investigating the use of ligands containing the backbones 42, 43 and 44. The enantioselectivity and the rate of reaction are greatest for allylpalladium substitutions that employ the phosphine/nitrogen combination, 43. An example reaction is shown, (Scheme 39).

\[
\text{CH}_2(\text{SO}_2\text{Ph})_2 + \text{Ph} \rightarrow \text{Ph} \xrightarrow{\text{Pd}(\eta^3-\text{C}_8\text{H}_5)\text{Cl}_2, \text{N/P ligand, THF, RT.}} \text{Ph} \rightarrow \text{Ph} \quad 92\%, 94\% \text{ e.e.}
\]

![Scheme 39]

The choice of nucleophile for this reaction can also have an impact on the product formed by altering the pathway a particular reaction takes, (Scheme 40).
\( \pi \)-allyl complex, 46, is formed from, 45, with inversion of stereochemistry. If a 'soft' nucleophile is used such as a malonate then this attacks 46 from the back of the palladium yielding 47. This attack gives inversion in stereochemistry again so that overall retention in configuration is seen. However, if a 'hard' nucleophile is used, such as a Grignard reagent, then formation of 48 via transmetallation is seen. Subsequent reductive elimination yields 49, with the overall configuration inverted.

As with the Heck reaction there are many examples of \( \pi \)-allyl complexes in synthesis. Some select examples highlighting the reactions use in ring formation as well as some more recent publications will be shown. Nitrogen containing heterocycles have successfully been synthesized using \( \pi \)-allyl complexes.\(^{90,91,92}\) Alper et al. developed a very clever synthesis of 4-vinyltetrahydropyrimidin-2-one from \( N \)-cyclohexyl-2-vinylazetidine and phenyl isocyanate, (Scheme 41).\(^{91}\)

\[
\text{N} + \text{Ph-N} = \text{C} = \text{O} \\
\stackrel{\text{Pd(OAc)}_2,}{\text{PPh}_3,} \text{THF, RT.} \\
\text{Ph-N} = \text{C} = \text{O} \\
\text{Cy}^{89\%}
\]

Scheme 41

The total synthesis of uvaricin, 50, was achieved by employing a double cyclisation of, 51, using \( \pi \)-allyl chemistry to form a known intermediate, 52. By using a Trost chiral ligand, 52, was synthesized as a single diastereoisomer, (Scheme 42).\(^{93}\)
Recently Narsihmulu et al. have used palladium mediated π-allyl chemistry to convert allylic alcohols to allyl phenyl sulfones, (Scheme 43).94

\[
\text{R} = \text{OAc} \quad \text{Pd}_2(\text{dba})_3, (R,R)-\text{Trost Ligand, THF.}
\]

Scheme 42

\[
\text{R} = \text{OAc}
\]

Scheme 43

1.2.2 Palladium (II)

Palladium (II) has been frequently used as a precursor to palladium (0). Palladium (II) salts (e.g. PdCl₂) are generally much more stable than palladium (0) catalysts and as such have been reduced within reactions to form palladium (0) in situ. Palladium (II) catalysts however have been shown to be unique oxidizing agents and the list of useful reactions specific to palladium (II) catalysts continues to grow.

A major problem with using palladium (II) was that after oxidation of an organic compound, palladium (II) is reduced to palladium (0). Stochiometric reactions involving expensive metal catalysts are never favourable and few publications were made.95,96 Real interest in palladium (II) as a catalyst began with the development in 1959 of the Wacker process, (Scheme 44).97,98,99

\[
\text{PdCl}_2, \text{CuCl}_2, \text{O}_2, \text{H}_2\text{O} \rightarrow \text{O}\text{H}
\]

Scheme 44

28
The Wacker process is an industrial reaction to oxidize ethylene to acetylaldehyde but with it came the first example of \textit{in situ} reoxidation of Palladium (0) to Palladium (II). Copper (II) chloride is used as the reoxidant itself being reduced to copper (I) chloride in the process. The clever part to this reaction is that the copper (I) is readily oxidized back to copper (II) by oxygen creating a complete catalytic cycle. Since this monumental reaction, publications involving palladium (II) as a catalyst have grown vast and select areas involving alkenes will be discussed in more detail.

Firstly palladium (II) interactions with alkenes must be considered. Alkenes can coordinate to electrophilic palladium (II) compounds to form \( \pi \)-complexes. This coordination to palladium (II) effectively causes a drop in electron density on the alkene allowing nucleophiles to attack. This behaviour is the opposite to that seen for uncomplexed alkenes, electrophilic attack is common. The addition of a nucleophile is followed by the formation of a carbon-palladium \( \sigma \)-bond, 53, the overall process is called palladation. Palladation products are unstable and generally decompose by one of two pathways. The first pathway is \( \beta \)-hydride elimination. In this pathway \( \text{H-Pd-X} \) is eliminated from 53 to form vinyl compounds, 54, the result being the nucleophilic substitution of an alkene, (Scheme 45).\(^{100}\) The second pathway is the displacement of the \( \text{Pd} \) by another nucleophile, the overall result being nucleophilic addition to the alkene, 55, (Scheme 45).\(^{100}\) The pathway adopted can be controlled in many cases via the choice of reactants and reaction conditions.

\[
\text{R} + \text{AH} + \text{PdX}_2 \xrightarrow{\text{palladation}} \xrightarrow{\text{nucleophilic substitution}} \xrightarrow{\text{B}^- \text{nucleophilic addition}} \text{AH, BH = nucleophiles e.g. H}_2\text{O, ROH} \]

\text{Scheme 45}
Both inter- and intramolecular reactions are known incorporating nucleophiles such as water, carboxylic acids, ammonia and amines. This review will consider the two areas separately; catalyzed rearrangement reactions will also be discussed individually.

1.2.2.1 Intermolecular Reactions

Intermolecular reactions have received less investigation than intramolecular variations. However, this does not mean that the number of publications for this area is small. Both oxygen and nitrogen nucleophiles will be considered with the use of select examples.

1.2.2.1.1 Oxygen Nucleophiles

As seen for the Wacker process one of the earliest nucleophiles used in these reactions was water.\textsuperscript{97,98,99} An early example of the use of water is shown, (Scheme 46).\textsuperscript{101}

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {\textbf{Scheme 46}};
  \node (b) at (-2,0) {\text{PdCl$_2$, CuCl, O$_2$, H$_2$O, DMF}};
  \node (c) at (2,0) {68\%};
  \node (d) at (-2,-1) {56};
  \node (e) at (2,-1) {57};

  \draw[->] (b) -- (a);
  \draw[->] (b) -- (c);
  \draw[->] (d) -- (a);
  \draw[->] (d) edge[double] (e);
  \draw[->] (e) edge[double] (c);
\end{tikzpicture}
\end{center}

Tsuji \textit{et al.} demonstrated the use of water as a nucleophile in the formation of 1,4-diketones such as, 57, from allylated ketones, 56.\textsuperscript{101} The attack of OH is observed to follow the Markovnikov rule. Recently the reaction was used as a key step in the synthesis of the fungal metabolite (+)-decarestrictine L, 59, (Scheme 47).\textsuperscript{102}
PdCl₂, I₂, CuCl₂, O₂, H₂O, DMF, MeOH, K₂CO₃, MeOH, H₂O, R.T.

Scheme 47

58, was formed using the established palladium (II) chemistry and this was successfully cyclised to yield 59.

Alcohols have been used as nucleophiles in palladium (II) chemistry. In an intermolecular fashion they have been used to carry out acetalization of alkenes, a recent example employs polymer supported (PS) benzoquinone as a co-catalyst and supercritical CO₂ as a solvent, (Scheme 48).

1.2.2.1.2 Nitrogen Nucleophiles

When amines were used as the nucleophiles in reactions, enamine formation was expected. However when amines were first employed in the reaction a major problem arose. Aliphatic amines were found to coordinate to the palladium (II) catalyst, they are strong ligands, and this meant that they could not be employed in the reaction. To overcome the problem of complexation the ability of the amine to coordinate had to be reduced. One way is to form amides such as tosylamide and carbamates. Examples of intermolecular reactions are far fewer than intramolecular cases (see page 36) however, they are becoming more prominent.
An important development in the area of palladium (II) mediated reactions with alkenes has been the use of iodobenzendiacetate (PhI(OAc)₂). The use of this oxidant has caused palladium (II) to be oxidized to palladium (IV) within the reaction which has facilitated C-O formation, (Scheme 49).106

Stahl et al. reported regioselective intermolecular palladium catalyzed aminoacetoxylation for alkenes forming compounds such as 60, (Scheme 49).106 This reaction is an incredibly important discovery, it is analogous to the intermolecular osmium catalyzed aminohydroxylation and as seen this often forms regioisomeric mixtures (see section 1.1.2). The reaction is believed to follow the pathway shown, (Scheme 50).106

Compound 61, is believed to form as following the normal reaction pathway (see Scheme 45). The inclusion of PhI(OAc)₂ facilitates the oxidation of palladium (II) to (IV), 62, subsequent reductive elimination yields the product but also regenerates palladium (II). Stahl’s publication demonstrates the only example of an intermolecular reaction however, PhI(OAc)₂ has found more use in the intramolecular reaction discussed later.

One final select example for the use of nitrogen based nucleophiles is the intermolecular diamination reaction. Booker-Milburn et al. have reported the use of dialkyl ureas to effect 1,2-diamination of 1,3-dienes, (Scheme 51).107
1.2.2.2 Intramolecular Reactions

Palladium (II) mediated intramolecular reactions have been a great source of research for many different groups. This is largely due to the fact that the use of tethered nucleophiles has allowed the construction of many heterocycles. There are far too many publications to cover all in this section so as with the intermolecular reactions both oxygen and nitrogen nucleophiles will be considered using select examples.

1.2.2.2.1 Oxygen Nucleophiles

The use of oxygen based tethers to allow the formation of oxygen containing heterocycles has been readily investigated over the past few decades. In 1976 Hosokawa et al. reported one of the first examples of an intramolecular reaction showing the cyclisation of γ,δ-unsaturated alcohols, 63, to 2-vinyltetrahydrofurans, 64, (Scheme 52).108

A very elegant synthesis of bicyclic structure, 65, was reported by Andersson et al. utilising molecular oxygen as a reoxidant, (Scheme 53).109
Oxazolidinone formation has been achieved.\textsuperscript{110} Hiemstra \textit{et al.} have published several papers describing the synthesis of the five-membered rings. They have demonstrated importantly that only 5-\textit{exo} cyclisation occurs, a select example is shown, (Scheme 54).\textsuperscript{110}

Heterocycle formation is not limited to 5-membered rings, de Koning \textit{et al.} successfully demonstrated the synthesis of benzoisochromene, 66, (Scheme 55).\textsuperscript{111}

Olefinic phenols have been used as suitable starting materials for a number of cyclisations. Larock \textit{et al.} showed that the chemoselectivity for the cyclisation of 2-allylphenol, 67, could be controlled by varying the catalytic species, (Scheme 56).\textsuperscript{112}

Through careful selection of the catalyst \textit{exo} or \textit{endo} cyclisation can be effected.\textsuperscript{112}
The palladium catalysed cyclisation of carboxylic acids has been shown. The reaction is extremely useful allowing the formation of unsaturated lactones in a single step. Hegedus et al. showed in 1977 that isocoumarins 68, could be synthesised via a palladium promoted cyclisation of 2-vinylbenzoic acid, 69, the five-membered lactone was not observed. (Scheme 57).\textsuperscript{113}

![Scheme 57](image)

A very important and clever development in the area of palladium (II) catalyzed reactions has been reported by Wolfe et al.\textsuperscript{114} Wolfe described a new stereoselective method for the synthesis of substituted tetrahydrofurans from $\gamma$-hydroxy alkenes. The published procedure forms both a carbon-carbon bond and a carbon-oxygen bond when forming both 2,5- and 2,3-disubstituted tetrahydrofurans. What is most interesting about this process however, is the novel use of the palladium catalyst. An example reaction is shown, (Scheme 58).\textsuperscript{114}

![Scheme 58](image)

As shown in scheme 58, it is not a palladium (II) catalyst that is used in this reaction but a palladium (0) catalyst. Wolfe has suggested two possible mechanisms for the reaction based on the observed stereochemistry of the products, (Scheme 59).
For both paths A and B the first step is the formation of the palladium (II) species \( \text{L}_n\text{Pd(Ar)}\text{Br} \) formed by the oxidative addition of palladium (0) into the aromatic carbon-bromine bond. Chelation is believed to be occurring in these reactions delivering the high diastereo- and regioselectivities observed. Reaction of the alcohol, 70, leads to the formation of the intermediate, 71, which could undergo insertion of the olefin into the palladium-oxygen bond (Path A) followed by carbon-carbon bond forming reductive elimination to generate the product, 72. The other suggested route (Path B) would see 71, undergoing insertion of the olefin into the palladium-carbon bond followed by sp\(^3\) carbon-oxygen bond forming reductive elimination to give, 72. Both mechanisms generate the product with the correct observed stereochemistry.\(^{114}\)

### 1.2.2.2 Nitrogen Nucleophiles

As mentioned previously (see section 1.2.2.1) intermolecular reactions involving nitrogen nucleophiles have proven difficult. In contrast there are many examples of intramolecular reactions as these occur much more readily.

The earliest examples of carbon-nitrogen bond formation via intramolecular reactions were published by Hegedus et al. in 1976.\(^{115}\) They described the synthesis of 2-methylindoles, 73, from \( \sigma \)-allylic anilines, 74, (Scheme 60).
Stochiometric palladium (II) was used in this early example. Hegedus utilised a catalytic variant to synthesize indoloquinones, 75, (Scheme 61).  

Acyclic starting materials have been successfully cyclised, a nice example of this which also shows molecular oxygen as the oxidant was reported by Stahl et al., (Scheme 62).  

Recently Stahl et al. building on their previous work have used palladium(II) to catalyze the oxidative coupling of allyl tosylamides with butyl vinyl ether and various styrene derivatives to produce 2,4-substituted pyrrolidine products, 76 and 77, at room temperature employing molecular oxygen together with a copper(II) cocatalyst as the reoxidant, (Scheme 63).
A novel way of regenerating the palladium (II) catalyst has been described by Hirai et al.\textsuperscript{119,120} It has been used as the key step in the synthesis of natural products (+)-prosopinine\textsuperscript{119} and 1-deoxymannojirimycin, (Scheme 64).\textsuperscript{120}

After initial attack of the nitrogen nucleophile on the coordinated alkene, intermediate, 78, is formed. Elimination of the $\beta$-OH group regenerates the palladium (II) catalyst allowing the reaction to progress with a catalytic amount of palladium (II) chloride with no oxidant.\textsuperscript{120} As shown in scheme 45, the palladium-carbon bond can be cleaved via the attack of a second nucleophile to give overall nucleophilic addition. This approach has been utilised by Lu et al. in intramolecular haloamination reactions, (Scheme 65).\textsuperscript{121}
Carbamates were successfully cyclised to generate oxazolidinone structures, 79a and 79b. These reactions can be classed as similar to the tethered asymmetric aminohydroxylation reaction; here a halogen is added to the outside of the double bond instead of a hydroxyl group. Interestingly complete regiocontrol is seen for the reaction, 80, is not observed. Equally important is the observation that the potential β-hydride product, 81, is not formed. This is believed to occur due to the excess of halide ions within the reaction, favouring the formation of 79, over 81. Intramolecular haloamination reactions were also reported by Chemler et al. in the same year, (Scheme 66).122

The lithium salt is not present here; instead potassium carbonate is used in the reaction. PhI(OAc)₂ has been used as an oxidant for intramolecular reactions as well as intermolecular. Sorensen et al. reported in 2005 the aminoacetoxylation of alkenes, forming products such as 82, (Scheme 67).123

Sorensen’s reaction is the closest comparison to the osmium mediated tethered aminohydroxylation present in the literature. A very important point to mention here is
the necessity of a protecting group on the nitrogen atom which can not easily be
removed. However, this reaction was an incredibly important breakthrough in the field
of palladium (II) catalysed reactions.

Muniz et al. have described a novel intramolecular diamination reaction allowing the
formation of two nitrogen containing heterocycles, (Scheme 68).\textsuperscript{124}

![Scheme 68](image)

The first heterocycle is formed as expected placing the palladium on the end of the
alkene. The palladium-carbon bond is broken by the attack of the second nitrogen
forming the second ring, under oxidative conditions the palladium (II) catalyst is
regenerated. PhI(OAc)\textsubscript{2} has been found to be the only highly efficient reoxidant for the
reaction, an example is shown, (Scheme 69).\textsuperscript{124}

![Scheme 69](image)

The final example in this section comes from Wolfe et al. who have applied their novel
chemistry (see page 35) to perform carboamination reactions.\textsuperscript{125} A select example
showing the cyclisation of N-allylureas to form imidazolidi-2-ones is given, (Scheme
70).

![Scheme 70](image)
1.2.2.3 Pd (II) cat. [3,3] Sigmatropic Rearrangements

Palladium (II) has been extensively utilised to facilitate the formations of carbon-carbon and carbon-heteroatom bonds via [3,3] sigmatropic rearrangement reactions. [3,3] sigmatropic rearrangements are important as these reactions take place in a stereochemically defined manner. These types of rearrangement reactions have been around for a long time but traditionally have been carried out thermally requiring high temperatures. Palladium (II) has been shown to catalyse these reactions removing the need for harsh conditions.

As with previous sections this area of palladium catalysed reactions is large. Considered here is the reaction most associated with the work in this thesis, the [3,3] sigmatropic rearrangement of allylic imidates, a variant of the aza-Claisen rearrangement.

1.2.2.3.1 Allylic Imidates

An aza-Claisen rearrangement is classed as the [3,3] sigmatropic rearrangement of an N-allyl N-vinyl amine, (Scheme 71).126

\[
\text{HN} \quad \text{[3,3]} \quad \text{NH} \quad \text{R} \\
\text{R} \quad \text{R} \quad \text{NH}_2 \quad \text{R}
\]

Scheme 71

The aza-Claisen rearrangement has been employed in organic synthesis126 but the variant; the [3,3] sigmatropic rearrangement of allylic imidates has seen much greater interest. In particular, the rearrangement of allylic trichloroacetimidates has been employed as the key step in the synthesis of many nitrogen containing molecules including alkaloids, antibiotics and drug molecules.127-130 The rearrangement allows excellent transfer of chirality to and generates clean amide products making it a popular reaction.

The first reported example of an allylic imidate rearrangement was by Mumm and Möller in 1937.131 Here the rearrangement was achieved under thermal conditions.
Despite this early introduction for allylic imidates it was not until 1982 that palladium (II) was used to catalyze the rearrangement of the imidates to yield allyl amides, (Scheme 72).\textsuperscript{132}

\[
\text{PdCl}_2(\text{PhCN})_2 \rightarrow \text{O} \rightarrow \text{N} \rightarrow \text{Ph}
\]

\[
\text{PdCl}_2(\text{PhCN})_2 \rightarrow \text{O} \rightarrow \text{N} \rightarrow \text{Ph}
\]

Scheme 72

As shown in scheme 72, Ikariya et al. also indicated in their paper the differing selectivities of palladium (II) and palladium (0). Using palladium (II) yields exclusively a [3,3] rearrangement product whereas palladium (0) generates predominantly a [1,3]. The generally accepted mechanism for the [3,3] sigmatropic rearrangement is shown, (Scheme 73).\textsuperscript{133}

The reaction is suggested to proceed through a cyclization-induced rearrangement mechanism via a cyclic carbocation intermediate, 83. As the understanding of the rearrangement reaction increased, the development of an enantioselective reaction was desired.

Overman et al. were the first to report successful asymmetric catalysis in 1997 using palladium (II) complexes containing chiral diamine ligands.\textsuperscript{134} The best of these, 84, was used successfully in the rearrangement of \textit{N}-(4-trifluorophenylbenzimidate), 85, to yield the allylic benzamide, 86, in 60% e.e., (Scheme 74).\textsuperscript{134}
A significant problem however was identified when using a cationic catalyst such as 84. A competing ionisation pathway was observed leading to [1,3] rearranged products and a lower yield for the desired [3,3] rearranged products. To suppress this competing pathway Overman et al. synthesized neutral palladium (II) complexes containing ferrocenyl amines as ligands. These ligands improved yields as expected but did not heighten the observed e.e. Other early examples showed little improvement including the use of tridentate ligands. Improvement in enantioselectivity was shown by Donde and Overman in 1999, when they used ferrocenyl oxazoline catalysts giving 77-96% e.e. The most significant advance in chiral catalysts for allylic imidates has been the development of cobaltocenyl oxazoline palladaecyles as catalysts, reported by both Kang and Overman. Catalyst, 87, has now emerged as the optimal catalyst for enantioselective sigmatropic rearrangements, (Fig. 8).

The use of 87, in combination with simple allylic trichloroacetimidates has shown rearrangement reactions occurring with excellent enantioselectivity. The ease with
which the trichloroacetyl group can be removed allows the formation of allylic amines. A good example of this chemistry is seen in the formation of (S)-vigabatrin, 88, (Scheme 75).

The stereoselectivity of the [3,3] sigmatropic rearrangements has also been controlled via the use of chiral substrates. By using a chiral directing group within the starting substrate the palladium (II) catalyzed rearrangement can be directed to occur on one face of the alkene, giving a highly diastereoselective reaction. Bellúš et al. demonstrated the power of this approach, using α-amino alcohols as starting materials, to achieve rearranged products with diastereoselectivities >99 : 1, (Scheme 76).

Jamieson and Sutherland have reported the use of ether groups to direct the palladium (II) catalysed rearrangement of trichloroacetimidates. They tested a number of different groups and observed the methoxymethyl (MOM) ether to be the most selective. When investigating the scope of the reaction it was discovered that as the side chain of the substrate increased, the formation of [1,3] products was observed. This was overcome by the incorporation of p-benzoquinone which oxidized any palladium (0) formed to palladium (II), (Scheme 77).
The product, 89, observed by Sutherland et al. was converted to the corresponding β-hydroxy-α-amino acid, 90, by oxidation of the alkene followed by a one-pot deprotection step.\textsuperscript{144}

Finally, Sutherland et al. used their developed chemistry in an enantioselective synthesis of (2S,3S,4R)-γ-hydroxyisoleucine, 91, the amino acid component of the natural product funebrine, 92, (Fig. 9).

![Fig. 9](image)

In their paper Sutherland et al. showed the benefit of using the palladium (II) catalysed reaction over the thermal rearrangement. Heating the allylic acetimidate, 93, gave a 3 : 2 mixture of diastereoisomers, whereas using a palladium (II) catalyst generated the desired isomer, 94, in a 7 : 1 ratio, which was taken on to 91, (Scheme 78).\textsuperscript{145}
2.0 Results and Discussion

2.1 Osmium catalyzed aminohydroxylations

2.1.1 Background

Donohoe introduced the tethered aminohydroxylation in 2001.\textsuperscript{50} When this PhD began, investigations involving the reaction and dienes were not abundant. In particular desymmetrisation of \textit{meso} allylic alcohols appeared an interesting goal in order to access enantiomerically enriched compounds, which could be of use in organic synthesis.

2.1.2 Tethered aminohydroxylations of allylic alcohols

The first system chosen for investigation was 1,4-pentadiene-3-ol, 95, (Fig. 10).

\begin{center}
\includegraphics[width=0.3\textwidth]{fig10.png}
\end{center}

\textbf{Fig. 10}

To allow study of the tethered aminohydroxylation reaction conversion of the alcohol into its respective carbamate was necessary. Utilising conditions outlined by Donohoe,\textsuperscript{50} the carbamate was furnished \textit{via} a two step reaction, (Scheme 79).

\begin{center}
\includegraphics[width=0.6\textwidth]{scheme79.png}
\end{center}

\textbf{Scheme 79}

Initially trichloroacetyl isocyanate is added to yield 96, subsequent cleavage of the trichloroacetyl group in basic conditions yields the desired carbamate, 97. It was found that if the isocyanate was added too quickly in these reactions then the yield of 96,
could be drastically reduced, falling from 90+% to 50%. With the successful formation of 97, aminohydroxylation was attempted.

The oxidant used in tethered aminohydroxylation reactions was tert-butyl hypochlorite, 98. This is readily formed from the reaction of sodium hypochlorite (household bleach) with tert-butyl alcohol, 99, and acetic acid, 100, (Scheme 80). The hypochlorite, 98, is both heat and light sensitive. Storing in a silver foil covered flask at 0 °C allowed the reagent to be used for a month before reactivity decreased.

\[
\begin{align*}
\text{OH} + \text{COOH} & \xrightarrow{\text{Sodium hypochlorite}} \text{OCl} \\
99 & \quad 100 \\
\end{align*}
\]

Scheme 80

The aminohydroxylation of 97, was now attempted, (Scheme 81).

\[
\begin{align*}
\text{O} & \xrightarrow{\text{K}_2\text{Os(OH)}_2\text{O}_4, \text{NaOH, } \text{tBuOCl, } \text{Pr}_2\text{NEt}, \text{nPrOH/H}_2\text{O, RT.}} \text{O} \\
97 & \quad 101 \\
\end{align*}
\]

Scheme 81

Work up of the reaction proved problematic due to the formation of an intractable black liquid, which was not easily parted from the organic phase during aqueous extraction. A product spot was isolated for the reaction which by NMR analysis appeared to be our desired product 101, (d.r. 3 : 1) but the yield for the reaction was a very disappointing 6%. The poor yield was initially attributed to the difficult work up; repeating the experiment and exhaustively washing the aqueous layer however, did not greatly raise the yield, 11% was isolated. Conditions were altered to try and improve the yield, (Table 1).
<table>
<thead>
<tr>
<th>Entry</th>
<th>K₂Os(OH)₂O₄ (%)</th>
<th>NaOH (eq.)</th>
<th>¹BuOCl (eq.)</th>
<th>¹Pr₂NEt (%)</th>
<th>³PrOH/H₂O</th>
<th>Temp. (oC)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1:1</td>
<td>RT.</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1:1</td>
<td>RT.</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1:1</td>
<td>40</td>
<td>12</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>1:1</td>
<td>reflux</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>10</td>
<td>1:1</td>
<td>RT.</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>1:1</td>
<td>RT.</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>1:1</td>
<td>RT.</td>
<td>19</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>2:1</td>
<td>RT.</td>
<td>61</td>
</tr>
</tbody>
</table>

Table 1

As shown in table 1, changing the catalyst concentration, temperature and amount of diisopropylethylamine (Hünig's base) made little to no difference on the product yield. A more appreciable gain was made by increasing the concentrations of sodium hydroxide and tert-butyl hypochlorite. For all these cases, the work up was still difficult, however, the reaction where the solvent ratio was changed to 2 : 1 ³propanol/water was far easier. With an easier extraction step the yield for the product rose to 61%. The yield for the reaction was now comparable to the literature.⁴⁹ A d.r. of 3 : 1 was seen for each reaction, this clearly indicated a preferred stereochemistry for the product. Based on results published by Donohoe⁴⁹ for cyclic carbamates we believed the major product would be 102, as the cyclisation is believed to occur facially, (Fig. 11).

With conditions found to promote the desired reaction, a second substrate was investigated. Commercially available 1,5-hexadiene-3,4-diol, 103, was chosen introducing the existence of a second hydroxyl function. The diol 103, was not available as a single isomer, instead it exists as a mixture of meso, + and – isomers.
Again effective desymmetrisation was desired, so initially the conversion of only one of the hydroxyl groups to a carbamate was attempted, utilising the same conditions shown for 1,4-pentadiene-3-ol, (Scheme 82).

Despite several attempts 104, could not be isolated, interestingly monitoring the reaction by TLC, the spot due to trichloroacetyl isocyanate was observed to remain undiminished. The obvious difference between 95 and 103 is the presence of an extra hydroxyl group. To nullify any effect from the second group it was decided to mono protect 103, as its benzyl ether, this would also desymmetrise the molecule, (Scheme 83).

Benzylated compound, 105, was produced in 64% isolated yield. Carbamate formation was attempted on the protected substrate, (Scheme 84).

The carbamate, 107, was formed in good yield allowing aminohydroxylation to be attempted. The conditions that had proven best for 97, were used (see table 1), (Scheme 85).
The reaction yielded a complex polar mixture by both TLC and NMR and despite numerous attempts 108, could not be isolated. To aid the isolation of a reaction product an in situ TBDMS protection was attempted, (Scheme 86).

Unfortunately protection did not allow the isolation of the desired cyclisation product, 109. The results for this substrate were very disappointing, leaving the single ring formation behind, the possibility of achieving a double cyclisation for 1,5-hexadiene-3,4-diol, 103 was now investigated.

Using the standard carbamate formation steps the dicarbamate, 110, was formed in high yield, (Fig. 12).

Aminohydroxylation was attempted on 110, to form the double cyclised product, 111, (Fig. 13). Unfortunately as seen for 107, a complex mixture from which no product could be isolated was observed.
Disappointed with the lack of success using the diol substrate, attention was refocused back to single alcohols. Having observed a d.r. for the reaction of 97, an answer to the question ‘what controls the stereochemistry of the reaction?’ was sought. 1,3 allylic strain was believed to hold the answer to which isomer of the tethered aminohydroxylation formed preferentially, (Fig. 14).

Conformations where the starting carbamate suffers 1,3-allylic strain 112, 113, 114, rather than 1,2-allylic strain 115, 116, 117, is preferred due to its lower energy state. Of the possible conformations undergoing 1,3-allylic strain 112, should be the lowest in energy and thus the favoured as the interaction is between the two smallest substituents, the protons. Assuming 112, is the conformation adopted then as shown the hydrogens of carbons 2 and 3 have a trans relationship. The tethered aminohydroxylation cyclisation is believed to occur syn, this would mean that the stereochemistry present in the starting material would be present in the product. Based on this argument the two isomers expected would be 118 and 119, (Fig. 15).
To investigate this theory a range of allylic alcohols, 120a-d, were synthesised with different R groups, ultimately allowing the formation of their respective carbamates. The allylic alcohols were formed readily via vinyl magnesium bromide addition to the desired aldehyde, (Table 2).

![Diagram](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>120a</td>
<td>81</td>
</tr>
<tr>
<td>2</td>
<td>Et</td>
<td>120b</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>'Pr</td>
<td>120c</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>NO2Ph</td>
<td>120d</td>
<td>79</td>
</tr>
</tbody>
</table>

The isolated alcohols were rapidly converted to their respective carbamates, 121a-d following the already outlined procedure. Carbamate, 121e, formed from commercially available 1,5-hexadien-3-ol was also synthesized, (Table 3).
Yields obtained for nearly all substrates were good and a d.r. was seen for each with bulkier R-substituents giving a greater diasteromeric ratio. The exception was the carbamate, 121d, which failed to yield an isolatable product. Oxazolidinone, 122e, was the one product that had also been synthesised by Donohoe et al. Interestingly, the
NMR data collected for the compound, \(122e\), did not match that reported by Donohoe. Following further study (see table 6) the products were accurately identified as the chlorohydroxylated compounds, \(123\) and not the desired oxazolidinones, \(122\). This reaction is discussed in detail in section 2.4.1.

During these studies a paper by Donohoe et al.\(^{51}\) was published showing that the stereochemistry for the tethered aminohydroxylation was indeed controlled by 1,3-allylic strain confirming the outlined thoughts above, (Fig. 14). In light of this publication and the formation of the chlorohydroxylated products, \(123\), the decision was taken to move away from osmium catalysed aminohydroxylations.

2.1.3 Tethered aminohydroxylation of allylic amines

Running alongside studies into allylic alcohols, investigations into the possibility of using ureas in the tethered aminohydroxylation reaction were also carried out. Ureas such as, \(125\), were a hitherto unutilised substrate in the reaction. The starting materials for the required ureas were allylic amines, studies began with symmetrical diallylamine, \(124\). Using the protocol for carbamate synthesis, formation of the urea, \(125\), was attempted, (Scheme 87).

As nitrogen is more nucleophilic than oxygen, isocyanate addition to form \(126\), was rapid. Unfortunately, however, cleavage via the normal route proved unsuccessful, \(126\), was too stable. Heating the reaction and using stronger bases such as sodium hydride also proved fruitless. Consulting the literature it was discovered that zinc dust had previously been used to cleave similar groups.\(^{147}\) Reaction with zinc generated a small amount of \(125\), (approximately 5% yield), but still left the majority of \(126\), intact. Spurred on by this small breakthrough a more active source of zinc was sought. Following a suggestion by Dr Andrew Poulton a zinc/copper couple, \(127\), which can be easily synthesized, was tried, (Scheme 88).
Utilizing this new reagent 126, was converted to 125, in 80% yield. With easy access to the urea now accomplished, aminohydroxylation was attempted using the same conditions developed for carbamates, (Scheme 89).

Scheme 88

\[ \text{HCI, } \text{H}_2\text{O, } \text{CuSO}_4, \text{Zn/Cu} \] \[ \text{EtOH, } \text{Et}_2\text{O} \]

Scheme 89

\[ \text{H}_2\text{N} - \text{N} - \text{O} \]

\[ \text{K}_2\text{Os(OH}_2\text{)}\text{O}_4, \text{NaOH, } \text{BuOCl, } \text{Pr}_2\text{Net, } \text{PrOH/H}_2\text{O, RT.} \]

Unfortunately as for the diols (see section 2.1.2) the reaction only returned a complicated mixture of largely unidentifiable products. The starting material, 125, was re-isolated but no cyclisation product could be distinguished. Commercially available allyl urea, 129, (Fig. 16) was also tried under the conditions, but this did not react with only starting material recovered from the reaction.

Fig. 16

Increasing the concentrations of the various reactants and the use of elevated temperature all proved ineffective for both 125 and 129.

The outcomes of the attempted reactions were disappointing. However, the use of ureas in the tethered aminohydroxylation reaction has still not been reported in the literature despite lots of interest in the area. The observation of chlorohydroxylated product formation from the carbamate reaction (see section 2.1.4) coincided with the findings detailed here. This discovery took the research in a new direction, moving away from this area of study.
2.1.4 Chlorohydroxylation reactions

While investigating the tethered aminohydroxylation reactions of carbamates (see section 2.1.2) an interesting discovery was made. For the product of the reaction of 97, (see scheme 81) a crystal was obtained suitable for x-ray crystallography. The expected oxazolidinone product of the reaction, 101, had not been formed, instead the chlorohydroxylated structure, 130, was observed, (Fig. 17).

![Diagram of compounds 101 and 130](image)

Chlorohydroxylated products had not been previously mentioned as potential by-products in these reactions, this made the observed result very surprising. Interestingly only one isomer was afforded by crystallisation and seen by x-ray. This result is very...
intriguing as NMR spectra for the pre-crystallisation product clearly shows that both exist from the reaction. Based on the data observed, a mechanism for the formation of 130, was postulated, (Scheme 90).

Mechanistically for the progression of an aminohydroxylation reaction it is accepted that the formation of a nitrene is required (see scheme 19). Nitrene formation occurs via a chlorocarbamate structure similar to 131. The chlorine present on the nitrogen atom in 131, could potentially be attacked by the double bond. Addition of the chlorine in this fashion would account for the favoured stereochemistry observed in the final product as the chlorine would be added to the same face as the carbamate. The chloronium ion may form, and as the reaction is carried out in the presence of water and base addition of a hydroxyl group as shown is very probable and would yield the correct structure, 130. If the proposed mechanism was correct the inclusion of an osmium catalyst would not be required for the reaction to progress. The conditions required for the formation of 130, were now investigated, (Table 5).
Entry 1 shows the original reaction giving 130, in a yield of 61%. As expected the omission of the osmium catalyst has little impact on the reaction, removing NaOH however totally shuts it down. Hüning's base is insufficient at its low concentration to facilitate the reaction and can be removed without affecting the yield. Solvent selection is seen to be important, reducing the ratio of alcohol to water lowers the yield and both are necessary to obtain the higher yields. Finally, increasing the equivalents of NaOH and 'BuOCl did not convert more starting material; the yield obtained in entry 9 is comparable to that of entry 8.

The generality of the reaction was tested by using the optimised conditions with various carbamates to see if chlorohydroxylation was possible, (Table 6).
The reactions proceeded well allowing the generation of chlorohydroxylated products, 123a-d in reasonable yields and diastereomeric ratios, 123b and 123d were afforded as single diastereoisomers. Importantly, the results and spectra obtained here proved the formation of the chlorohydroxylated products, 123, over the oxazolidinones, 122, in the attempted osmium catalysed tethered aminohydroxylation reaction shown earlier, (Table 4). Pleasingly, as for 130, recrystallisation of the reaction mixture using ethyl acetate and hexane afforded, by NMR, only the major isomer from the reaction leaving the minor in solution. A particularly interesting example of the reaction was when the conditions were applied to the carbamate formed from geraniol, 132. Carbamate 132, contains two carbon-carbon double bonds and surprisingly both undergo chlorohydroxylation, (Scheme 91).

Initial NMR studies confirmed that a double chlorohydroxylation had taken place forming, 133. When the material was recrystallised, NMR suggested the presence of only one diastereoisomer. This result was certainly not expected as the reaction forms three chiral centres. Fortunately recrystallisation from ethyl acetate afforded crystals...
good enough for x-ray crystallography to be performed. The structure, 134, elucidated by this analysis is shown, (Fig. 18).

X-ray crystallography confirmed the existence of a single diastereoisomer with well-defined stereochemistry clearing showing the two chlorine atoms having been added to the same face.

The outcome of the chlorohydroxylation reactions was intriguing but, more interesting was its potential to allow a new route to the desired oxazolidinone structures shown earlier. Cyclisation of the chlorohydroxylated substrates, 130, via reaction with a suitable base was envisaged. This chemistry could potentially lead to the synthesis of a range of oxazolidinones complementary to those desired earlier; however the oxazolidinone stereochemistry would now be trans, (Scheme 92)
As shown in scheme 92, upon addition of base, deprotonation of the carbamate is expected to occur to yield the intermediate, 135, which could then cyclise via an S$_{N}$2 route to yield the trans oxazolidinone, 136. There is however another possible pathway for cyclisation, (Scheme 93).

It can not be ruled out that the deprotonated hydroxyl group could displace the chlorine first, 137. This would form the intermediate, 138, which could be attacked by the carbamate to open the newly formed yet strained epoxide ring. This pathway would lead to, 101, where stereochemistry across the desired oxazolidinone would now be cis as for the tethered aminohydroxylation reaction. It is important to note here that the chlorohydroxylated product, 130, was first resubmitted to the standard tethered aminohydroxylation conditions to determine whether the product was simply an intermediate for the cyclisation reaction. The starting material, 130, was re-isolated from the reaction, cyclisation did not occur. This outcome disproved the theory that the formed chlorohydroxylated products, 130 and 133, could actually be intermediates of the tethered aminohydroxylation reaction. To affect cyclisation, a number of bases were tested using 130, as the starting material, (Table 7).
Very disappointingly, cyclisation did not occur with any of the bases tried. It is very hard to believe that deprotonation would not occur under the conditions attempted; therefore it must be assumed that it is the $S_N2$ reaction that will not progress. One possible hypothesis for cyclisation failure is that the nitrogen must attack from the backside of the chlorine but cannot as it is held on the same face by the tether. Therefore, attack from the opposite face may not be viable and as such cyclisation is not realised.

After being very hopeful that the chlorohydroxylation reaction would generate a novel route to oxazolidinones, its failure meant other ways of formation had to be investigated. After much discussion it was decided that an iodine mediate reaction might allow access to the desired oxazolidinone structures.
2.2 Iodine mediated cyclisations

2.2.1 Background

Halogens are useful reagents because of their ability for electrophilic addition to an alkene, indeed the use of bromine is a classic test for the presence of a carbon-carbon double bond. Bromine is probably still the most widely employed halogen for electrophilic addition as products formed with bromine are generally more stable than those formed with iodine. However, iodine chemistry involving alkenes is vast, with many different examples of its use reported in journals due to its greater reactivity. A general reaction utilising iodine as a reactant is shown, (Scheme 94).

![Scheme 94](image)

Iodine adds to the double bond to form an iodonium ion. This allows a nucleophile to attack with the overall result a 1,2 addition across the carbon-carbon bond. This basic reaction forms the fundamental principal for iodine catalysis involving alkenes. If the nucleophile and alkene involved are part of the same molecule, then we see an intramolecular reaction and the formation of a cyclic structure. The most common use of this reaction is iodolactonisation, (Scheme 95).

![Scheme 95](image)

Cyclisation via a tethered nitrogen group have been reported in the literature. One such group are imidates which have been used as cyclisation precursors to allow the formation of both five and six membered rings, (Scheme 96).
Of great importance to work studied in this thesis is the published findings of Hirama et al who showed that submitting preformed allylic and homoallylic carbamates to iodocyclisation conditions mediated attack via the oxygen atom yielding carbonates and hydroxycarbarnates, (Scheme 97).^{150}

Cyclisation via the nitrogen atom of a carbamate has been observed to allow the formation of nitrogen containing heterocycles. To accomplish this, increased substitution of the nitrogen atom has been required. Initial research was used to form 6-membered cycles,^{139,140} and indicated that sulphonyl group substitution is most effective at promoting the desired reaction, (Table 8).^{151}
The reaction has also been found to work equally well for the formation of 5-membered oxazolidinone rings, 141,142 (Table 9).151

Utilising the iodine chemistry shown would allow the desired oxazolidinone structures to be formed. However, with a wealth of literature and research in this area a novel approach was required. With this in mind investigations into the formation of free oxazolidinones was undertaken. Eradication of the need for a protecting group or substitution of the problematic sulphonyl group was targeted.
2.2.2 Iodine mediated oxazolidinone formation

Previous literature indicated that the need for a protecting group on the nitrogen was crucial to obtain the desired cyclisation. For our work an easily removable group was desired, our initial attempts utilised a trichloroacetyl group. As shown previously (see scheme 79) the addition of trichloroacetyl isocyanate to 1,4-pentadiene-3-ol, 95, yielded the protected carbamate, 96 an intermediate in the formation of carbamate, 97. Knowing the ease with which the group could be removed it seemed a good starting point especially as in a single step we could go from the alcohol, 95, to carbamate, 96. Carbamate 96, was readily synthesised using the previously mentioned procedure and isolated in good yield. For cyclisation, conditions used in the literature for tosylated carbamates \cite{151} were utilised, (Scheme 98).

![Scheme 98]

The reaction was monitored by TLC and pleasingly a strong product spot was observed for the reaction. The product, isolated in 73\% yield was analysed and the disappearance of an alkene was observed, however the infrared spectra showed only a single carbonyl signal and worryingly not in the expected region for an oxazolidinone ring. After comparison to literature products for iodine cyclisations and mass spectrometry the product was accurately identified as 144, (Fig. 19).

![Fig. 19]

The outcome was disappointing but perhaps not surprising. From the literature (see scheme 97) \cite{150} it was known that a free carbamate would cyclise via the oxygen to yield
a carbonate. Also we had shown (see scheme 79) the removal of the trichloroacetyl protecting group could be achieved in basic aqueous conditions. With these two pieces of information it was obvious that cleavage of the protecting group had occurred prior to cyclisation. To overcome this undesirable reaction anhydrous conditions were attempted, (Scheme 99).

In this first test, the reaction was attempted without the addition of a base but the nitrogen appeared to not be nucleophilic enough to cyclise. This outcome was put down to the presence of the electron-withdrawing group, starting material was simply retrieved. The base used for the reaction could not be overly strong as deprotection would occur, with this in mind potassium carbonate was chosen, (Scheme 100).

Once again monitoring the reaction by TLC a product spot was observed. As before the infrared spectrum for the isolated product displayed only a single carbonyl signal, however this time it was in the correct region for an oxazolidinone. As the various pieces of data for the product were obtained it became clear that oxazolidinone, 145, had been synthesized, (Fig. 20).
This result was very pleasing; the protection was stable enough to mediate cyclisation via the nitrogen but also was removed during the work up for the reaction yielding the free oxazolidinone without the need for a deprotection step. With methodology now established several other allylic carbamates, 146a-e, were synthesized and subjected to the cyclisation conditions, (Table 10).

All carbamates reacted delivering the respective oxazolidinone products, 147a-e, in high yields. A diastereomeric ratio was seen for entries 1 and 3 and only a single isomer was produced when \( R = \text{Pr} \) (entry 2). It should be noted here that the carbamate, 146e, where \( R = \text{Ph} \) which successfully cyclised is unstable and must be submitted to the reaction conditions directly after its isolation. The same 1,3-allylic strain argument indicated for the tethered aminohydroxylation (see figs. 14 and 15) can account for the observed stereochemistry. All substrates used up to that point contained external double bonds. In order to test whether the reaction could be extended to internal alkenes commercial cis-pent-2-en-1-ol and hept-2-en-1-ol were acquired and converted to carbamates, 148a-b, respectively. These were then subjected to the iodine reaction conditions, (Table 11).
The reaction proceeds as smoothly for internal alkenes as for terminal alkenes. Single diastereoisomers are observed for both examples, this can be explained by considering the mechanism of formation, (Scheme 101).

Activation of the alkene occurs via iodonium ion formation (see scheme 94) and as a base is required deprotonation of the nitrogen is believed to occur to give intermediates, 150a and b. The iodonium ion can form on either enantiotopic face of the alkene but attack of the nitrogen nucleophile will occur from the opposite face in an S_N2 reaction. This means that the relationship between the two added groups will always be \textit{trans} as shown, (Scheme 101).

To improve the reaction overall the process was attempted as a one pot procedure thus removing the carbamate isolation step, (Table 12).
Oxazolidinone products were isolated for each of the allylic alcohols subjected to the reaction conditions. This was an excellent result; the overall yield obtained for each reaction was greater than the equivalent stepwise process, the isocyanate addition appearing to go quantitatively. With this novel one pot procedure achieved attempts were made to extend the scope of the reaction, by incorporating another step, namely a Grignard addition to form the allylic alcohol, (Scheme 102).

The scheme was ambitious but initial test reactions showed that the Grignard reaction could indeed be quenched by the addition of the trichloroacetyl isocyanate. The reaction was attempted using 4-methyl-pent-1-en-3-ol where \( R = \text{tPr} \) as relatively high yields had been seen for the individual reactions with this group and the product had
always been a single isomer making structural elucidation easier. Following the reaction by TLC the oxazolidinone, **147b**, was observed to form. Isolation of the product was problematic due to other materials present, including the starting aldehyde and carbamate, **121c**. Despite this presence of other products **147b**, was isolated in an overall yield of 51% proving the principle that the three reactions could be performed in a single pot.

Searching the literature, it was discovered that the pendant iodine may be substituted for an OAc group. If this transformation could be realised then a metal free reaction analogous to an aminohydroxylation reaction would have been accomplished, (Scheme 103).

The previously synthesized oxazolidinones were subjected to the literature conditions, (Table 13).

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et</td>
<td>151a</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>'Pr</td>
<td>151b</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>H₂C=CHCH₂</td>
<td>151c</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>H</td>
<td>151d</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>H₂C=CH</td>
<td>151e</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 13

Unfortunately reactions did not progress as hoped and in all cases only starting material was isolated. This outcome was unexpected based upon the literature precedent for the
reaction. Conditions were varied in an attempt to push the reaction forward but, the desired products could not be realised which was very disappointing.

The iodine mediated cyclisation is not only limited to carbamates and has been shown to work with ureas, 152, accessible from trichloroacetyl isocyanate addition to diallylamine, (Table 14).

![Chemical Reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂C=CHCH₂</td>
<td>153</td>
<td>76</td>
</tr>
</tbody>
</table>

Table 14

Imidazolidinone, 153, is formed in comparable yields to the oxazolidinone products previously seen. Interestingly the protecting group is removed from the nitrogen during the reaction, after the difficulties involved in urea formation for the tethered aminohydroxylation (see section 2.1.3) it may have been expected to have survived the conditions.

Overall, a new method for the formation of free oxazolidinones and imidazolidinones via an iodine mediated cyclisation has been developed. A major drawback however with the reaction is the lack of enantioselectivity, though as demonstrated it can be diastereoselective for internal alkenes. The next area of research for this PhD therefore became the development of an enantioselective oxazolidinone forming reaction and a movement into palladium chemistry.
2.3 Palladium mediated cyclisations

2.3.1 Background

Palladium is probably the most utilised catalyst in modern day organic chemistry due to its incredible versatility. It has been shown to catalyse the attack of alkenes by nucleophiles and indeed has been used to synthesize oxazolidinones (see section 1.2.2). Many chiral ligands are known for palladium (0) and (II) which have been shown to introduce enantioselectivity for reactions (see section 1.2). Wishing to develop an enantioselective oxazolidinone forming reaction, palladium presented itself as an ideal catalyst for investigation. Strangely the use of chiral ligands in oxazolidinone formation via carbamate cyclisation has not been previously investigated despite palladium's popularity.

2.3.2 Palladium (II) catalyzed haloamination reactions

Lu et al. had briefly reported the cyclisation of tosyl protected carbamates via palladium (II) mediated haloamination reaction in 2004. The reaction provided similar structures to those obtained with the iodine mediated reactions. Initial investigations therefore centred around this area. The first substrate investigated was that of α-vinylbenzyl alcohol, 120a. Free amines have been shown to cause problems for palladium (II) mediated reactions due to the affinity they have displayed for each other. However, amides have been used to overcome this phenomenon (see section 1.2.2), therefore initially the carbamate, 121a, was used. Free carbamates had not been investigated previously in the reaction and would remove the need for a deprotection step. 121a, readily accessible (see table 3) was synthesized and subjected to the literature conditions proposed by Lu, (Scheme 104).

```
O
|\   |
|   |
|   |
O        NH

O
|\   |
|   |
|   |
O        NH

Pd(OAc)\_2, CuCl\_2, LiCl, THF, RT.

Scheme 104
```
Disappointingly the reaction failed to progress and only 121a, was recovered from the reaction mixture. A range of conditions were attempted to facilitate the reaction, (Table 15).

```
<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd(OAc)$_2$ (%)</th>
<th>CuCl$_2$ (eq.)</th>
<th>LiCl (eq.)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>0</td>
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<tr>
<td>3</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>CH$_3$CN</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>DMF</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>DMF</td>
<td>0</td>
</tr>
</tbody>
</table>
```

Table 15

Entry 1 indicates the literature conditions. Increasing the quantity of the reagents had no effect on the reaction as did changing the solvent used for the reaction. The final variable to change was the temperature and this did have an effect. Increasing the temperature of the reaction to 40°C saw the formation of a product. Unfortunately the product obtained from the reaction was not the desired oxazolidinone, 154. Very interestingly instead of cyclising the carbamate, 121a, had undergone a [3,3] sigmatropic rearrangement reaction to yield cinnamyl carbamate, 155, in a 60% yield (Fig. 21).

![Chemical structure](image)

The [3,3] sigmatropic rearrangement will be discussed more fully later (see section 2.4). The outcome of the reaction was a setback but did indicate that protection of the nitrogen was necessary for cyclisation. The literature reported protection was a tosyl...
group, this had been successfully switched for a trichloroacetyl group in the iodine mediated reactions and the same approach was attempted here, (Scheme 105).

![Scheme 105](image)

The starting carbamate, 96, failed to cyclise under the reaction conditions and was recovered alongside some deprotected carbamate; 97. Once again various conditions were investigated, a shortened summary is shown, (Table 16).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd(OAc)$_2$ (%)</th>
<th>CuCl$_2$ (eq.)</th>
<th>LiCl (eq.)</th>
<th>Solvent</th>
<th>Temp. (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>RT.</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>RT.</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>THF</td>
<td>RT.</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>CH$_3$CN</td>
<td>RT.</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>5</td>
<td>2</td>
<td>DMF</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 16

As had been found for 121a, increases in reagent concentration and/or temperature failed to facilitate cyclisation. Surprisingly for the elevated temperature reactions a [3,3] sigmatropic rearrangement product was not observed despite the formation of the carbamate, 97. With the failure of the reaction attention was turned to the discovery of a different protecting group for the reaction but, before heavy investigations began the problem was solved serendipitously. Having exhaustively changed the variables for the
reaction a final attempt was made whereby the order of addition was altered. Amazingly if the copper (II) chloride and lithium chloride are added first and allowed to stir for 5 mins at room temperature, then palladium (II) acetate added and the reaction temperature increased to 40 °C cyclisation occurs. As seen for the iodine mediated reactions the loss of the protecting group is observed in the product, 157, (Fig. 22).

![Fig. 22](image)

Why the order of addition for the reagents is so important is unclear but if not followed the product was not isolated. The carbamates 97 and 121a were subjected to the new conditions to test whether the change in method could facilitate the cyclisation of unprotected carbamates. These reactions did not furnish a cyclised product, protection is required. The newly developed conditions were applied to a range of carbamates, (Table 17).

![Reaction Scheme](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
<th>d.r.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂C=CH</td>
<td>157</td>
<td>69</td>
<td>12 : 1</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>154</td>
<td>70</td>
<td>&gt;25 : 1</td>
</tr>
<tr>
<td>3</td>
<td>H₂C=CHCH₂</td>
<td>158a</td>
<td>67</td>
<td>&gt;25 : 1</td>
</tr>
<tr>
<td>4</td>
<td>Et</td>
<td>158b</td>
<td>70</td>
<td>&gt;25 : 1</td>
</tr>
<tr>
<td>5</td>
<td>iPr</td>
<td>158c</td>
<td>73</td>
<td>&gt;25 : 1</td>
</tr>
<tr>
<td>6</td>
<td>PhCH₂CH₂</td>
<td>158d</td>
<td>75</td>
<td>&gt;25 : 1</td>
</tr>
</tbody>
</table>

Table 17
Entry 1 displays the result obtained for the reaction of 96, cyclising to yield 157 with a d.r. of 12 : 1. This result is intriguing as it is the only substrate for which a d.r. is visible in the NMR spectra. Amazingly for all other reacted substrates only a single diastereoisomer is observed. Based on the previously stated 1,3 allylic strain argument and results obtained for the iodine mediated reactions the trans oxazolidinone with respect to the protons across the ring was expected to be the major isomer, 159, (Fig. 23).

![Fig. 23](image)

However the minor isomer, 160, would still be expected for the reaction. This result was an unexpected but much welcomed bonus for the reaction. Propelled by the success of the terminal alkenes, interest was turned to internal alkenes, (Table 18).

![Reaction Scheme](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et</td>
<td>151a</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>H₃C(H₂C)₂CH₂</td>
<td>151b</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 18

Disappointingly the reaction failed to occur when using carbamates, 148, some cleavage of the protecting group was observed but only in very small quantity (< 3%). This outcome was a major setback for the reaction potentially limiting its usefulness in synthesis. Unperturbed, alterations to the conditions were attempted, in all cases the order of addition was maintained, (Table 19).
Despite increases in reagent concentration and temperature, cyclisation was never realised. It should be noted that all reaction conditions shown in table 19 were also attempted on 148f, with no success. The failure to cyclise onto an internal bond was very disappointing but with further study this obstacle should be overcome. With the finishing point for the study period of this PhD rapidly approaching investigations were continued on the terminal alkene containing carbamates only.

The requirement of lithium chloride was investigated, it was thought that the chloride ions needed for the quenching of the palladium-carbon bond should be available from the excess of copper (II) chloride present in the reaction. However, cyclisation was not observed if the extra chloride source was removed from the mixture. A one pot procedure, similar to that observed for the iodine reactions (see table 12), has been realised, (Table 20).
The overall yields for the reactions are good allowing oxazolidinones to be synthesized directly from the corresponding allylic alcohol. Attempts to include the Grignard step incorporated successfully for the iodine mediated reactions failed. Grignard addition and quench with trichloracetyl isocyanate progressed as expected but disappointingly in all cases cyclisation did not occur.

Despite setbacks, the reaction methodology was now in place to quickly and efficiently produce free oxazolidinone structures. Chloride ions had been utilised to quench the palladium-carbon bond thus far, other possibilities were now considered.

2.3.3 Palladium (II) catalyzed acetoxylations reactions

To truly consider the palladium mediated reaction as an alternative to the tethered aminohydroxylation an oxygen containing group was desired as a quench. The first group considered was that of OAc. The group had not been used in the literature previously for these reactions and it was thought that it could be employed easily via the use of sodium acetate and copper (II) in the reaction, (Scheme 106).

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H₂C=CH</td>
<td>157</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>154</td>
<td>66</td>
</tr>
<tr>
<td>3</td>
<td>H₂C=CH₂</td>
<td>158a</td>
<td>62</td>
</tr>
<tr>
<td>4</td>
<td>Et</td>
<td>158b</td>
<td>69</td>
</tr>
<tr>
<td>5</td>
<td>iPr</td>
<td>158c</td>
<td>73</td>
</tr>
<tr>
<td>6</td>
<td>PhCH₂CH₂</td>
<td>158d</td>
<td>73</td>
</tr>
</tbody>
</table>

Table 20
The first carbamate subjected to the conditions was compound, 96. The reaction did not proceed as desired and 162, was not isolated. The reaction mixture became very viscous and dark during the reaction; by TLC several faint spots were observed along with the starting material. Crude NMR was complicated and separation extremely difficult. Repeats of the reaction yielded the same results, the use of fresh reagents also made no difference to the outcome. This result was very disappointing however, during this time Sorensen et al. published a paper on aminoacetoxylation.\textsuperscript{123} They had reported the formation of oxazolidinones, and had succeeded in incorporating the addition of OAc. Although disappointed at being beaten to the post their paper did confirm the above results reported. They had been unable to facilitate the reaction using a traditional OAc cation source. Indeed the quenching of the palladium-carbon bond was believed to occur by a different pathway, (Scheme 107).

Initial cyclisation is believed to occur but instead of conventional S\textsubscript{N}2 quenching the palladium is oxidized to a palladium (IV) species, 163, via the acceptance of an OAc group from iodobenzene diacetate (PhI(OAc)\textsubscript{2}) also used in the reaction. Reductive elimination generates the product, 164, and releases the palladium to re-enter the catalytic cycle. Sorensen’s reported conditions varied depending on the substrate used but in all cases a sulfonyl protecting group was employed on the nitrogen.

The conditions which had expressed the greatest generality in Sorensen’s paper were used initially to try and effect the cyclisation of the protected carbamate, 96. These
conditions failed to facilitate the reaction, a summary of other variations that were attempted are shown, (Table 21).

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd(OAc)$_2$ (%)</th>
<th>Phi(OAc)$_2$ (eq.)</th>
<th>OAc source</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>2</td>
<td>-</td>
<td>AcOH:Ac$_2$O (1:1)</td>
<td>RT.</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>2</td>
<td>-</td>
<td>AcOH:Ac$_2$O (1:1)</td>
<td>40</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>3</td>
<td>-</td>
<td>AcOH:Ac$_2$O (1:1)</td>
<td>60</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>2</td>
<td>NaOAc</td>
<td>CH$_3$CN</td>
<td>40</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>2</td>
<td>NaOAc</td>
<td>CH$_3$CN</td>
<td>40</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>2</td>
<td>NaOAc</td>
<td>DCM</td>
<td>RT.</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>3</td>
<td>NaOAc</td>
<td>DCM</td>
<td>Reflux</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
<td>2</td>
<td>'BuOAc</td>
<td>CH$_3$CN</td>
<td>RT.</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>10</td>
<td>2</td>
<td>'BuOAc</td>
<td>CH$_3$CN</td>
<td>60</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>3</td>
<td>'BuOAc</td>
<td>CH$_3$CN</td>
<td>60</td>
<td>12</td>
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<td>11</td>
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<td>4</td>
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<td>CH$_3$CN</td>
<td>60</td>
<td>24</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 21**

Entry 1 shows the initial conditions attempted for the reaction. For these conditions a further source of acetate is not required as the reaction is performed in acetic acid.
These conditions failed to give the desired product even with increased temperatures, quantity of iodobenzene diacetate and reaction time. Sorensen had indicated that for some substrates an organic solvent with an external extra source of OAc was required. Sodium acetate was used first but once again the reaction failed to progress, both dichloromethane and acetonitrile were used as the solvent. Finally in an attempt to facilitate the reaction the more expensive tert-butyl acetate was employed but again no reaction was observed. As shown each variable was altered but to no avail, cyclisation of the carbamate could not be realised.

Sorensen’s paper clearly showed the fickle nature of the conditions for the reaction. This could simply mean that the conditions required for cyclisation of 96, were not found due to the capricious nature of the reaction. Further investigation including the testing of other starting materials is needed to assess whether the reaction could be made viable. Disappointingly this work had to be moved away from due to the ending of the laboratory section of this PhD.

2.3.4 Palladium (II) catalyzed tandem N-arylations/carboaminations

While continuing to investigate other groups that could be added to the outside of the alkene, a very interesting reaction by Wolfe was discovered. Wolfe et al. reported the use of N-arylation/carboamination reactions to allow the cyclisation of amines, alcohols and ureas onto alkenes. Interestingly in these reactions, a carbon-carbon bond is formed at the terminal end of the alkene, (Scheme 108).

![Scheme 108]

Importantly as with other literature reported reactions, Wolfe has to protect the nitrogen involved in the cyclisation. The use of this chemistry with carbamate substrates was, and still is unreported. Carbamate, 96, was subjected to varying cyclisation conditions, (Table 22).
Table 22

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd$_2$(dba)$_3$ (%)</th>
<th>dppe (%)</th>
<th>KOTBu (eq.)</th>
<th>PhBr (eq.)</th>
<th>Temp. (°C)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1.2</td>
<td>1.1</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1.2</td>
<td>1.1</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1.2</td>
<td>1.1</td>
<td>110</td>
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<td>10</td>
<td>2</td>
<td>1.2</td>
<td>1.1</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>10</td>
<td>1.2</td>
<td>1.1</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td>10</td>
<td>1.2</td>
<td>2</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>10</td>
<td>1.2</td>
<td>2</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

Entry 1 shows conditions similar to those utilised for urea substrates displayed in the literature.\textsuperscript{125} All conditions shown were attempted, orders of addition were also changed. The reaction failed to proceed as desired in all cases and 166 was not isolated. In all reactions a small amount of carbamate, 97, was formed alongside many unknown products. Disappointed with the outcome of these reactions, the use of tosyl protection was considered. Although removal of a tosyl group is very problematic the reactions were attempted as, as mentioned no example of carbamate cyclisation was known. Tosyl isocyanate is commercial and the required starting material, 167, was formed easily from 1,4-pentadiene-3-ol, 95, (Table 23). Cyclisation was attempted as a one-pot procedure and stepwise using the conditions shown, (Table 23).
As had been observed for the trichloroacetyl protected carbamate, 96, cyclisation failed to occur under all conditions.

It is unclear at this time why the reaction appears to more problematic for carbamate structures. Further investigation would be required to establish whether they could be utilised with this chemistry. Unfortunately, due to the time constraints of this PhD full investigation could not be undertaken.
2.4 Palladium mediated [3,3] sigmatropic rearrangements

2.4.1 Background

As mentioned in section 2.3.2 when carbamate, 121a, was subjected to the initially attempted cyclisation conditions, (see table 15), cinnamyl carbamate, 155, was formed, (Scheme 109).

\[
\text{Pd(OAc)}_2, \quad \text{CuCl}_2, \quad \text{LiCl}, \quad \text{THF}, 40^\circ C.
\]

Scheme 109

[3,3] sigmatropic rearrangement reactions are well established for palladium (II) catalysis, the most famous being that of the Overmann rearrangement, (see section 1.2.2.3).

This serendipitous discovery was intriguing and further investigations were initiated.

2.4.2 Carbamate forming rearrangements

The rearrangement of 121a, to yield 155, was envisaged simplistically to occur \textit{via} the following mechanism, (Scheme 110).

Based on known reactions palladium (II) is assumed to coordinate to the alkene present in the molecule facilitating attack \textit{via} the oxygen atom, 169, to form the intermediate, 170. This could then breakdown to yield the product, 155. If the reaction truly progressed as shown then the need for the copper (II) oxidant used in the first reaction...
(see scheme 109) would be unnecessary. Another important point to make at this stage is the possibility of a π-allyl type reaction (see scheme 34) pathway, (Scheme 111).

\[
\begin{align*}
\text{Ph} & \quad \text{PdL}_2 \\
\text{O} & \quad \text{NH}_2 \\
\text{171} & \quad \text{Ph} \\
\text{Ph} & \quad \text{L}_2\text{Pd} \\
\text{O} & \quad \text{NH}_2 \\
\text{155} & \quad \text{Ph}
\end{align*}
\]

Scheme 111

π-allyl reactions are attributed to palladium (0), it is conceivable that some may be present in the reaction mixture. However, the nucleophile required to form the observed product (see scheme 111) would be incredibly unstable and is unlikely to be present. Because of this the reaction is most likely to occur via the palladium (II) pathway but, the palladium (0) can not be discounted. Building on the premise that an oxidant would not be required, test reactions were carried out, (Table 24).

\[
\begin{align*}
\text{Pd(OAc)}_2 & \quad \text{CuCl}_2 \\
\text{Ph} & \quad \text{NH}_2 \\
\text{121a} & \quad \text{Ph} \\
\text{O} & \quad \text{NH}_2 \\
\text{155} & \quad \text{Ph}
\end{align*}
\]

As shown in the above table the copper oxidant was not required for the reaction to proceed. Increases in temperature made little difference to the yield obtained; extra
equivalents of lithium chloride also only afford a negligible increase in product. The catalytic loading of palladium was reduced without detrimental effect to the yield of the reaction. Interestingly, lithium chloride was necessary to facilitate the reaction, no product was observed without it.

Optimised conditions (entry 8) were now available for the rearrangement of the carbamate, 121a, via the oxygen atom. These conditions were also shown to work for carbamate, 121b to yield 172, (Scheme 112).

The rearrangement reaction had been shown to successfully progress through the oxygen atom of the carbamate. Of more interest however, was the possibility of rearrangement via the nitrogen and subsequent formation of allylic amines.

2.4.3 Allylic amine forming rearrangements

As shown (see section 1.2.1) formation of allylic amines, 174, could be obtained from the use of palladium (0) catalyzed \( \pi \)-allyl chemistry. The drawback to this approach has been the potential for the formation of two regioisomers, (see scheme 35). If a \([3,3]\) sigmatropic rearrangement reaction could be realised via the nitrogen atom then a potentially regioselective reaction could be achieved, (Scheme 113).

Based on the literature for the iodine mediated reactions and observations made in this thesis, it was conceived that to facilitate rearrangement via the nitrogen atom,
protection would be required. The first substrate tested was that of the trichloroacetyl protected carbamate, 96, (Scheme 114).

![Scheme 114](image)

The reaction proceeded as expected yielding the protected allylic amine in a 92% yield. Pleasingly the reaction had progressed at room temperature unlike the oxygen mediated rearrangement. Consulting the literature a similar reaction had been reported by Lu et al., (Scheme 115).\textsuperscript{153}

![Scheme 115](image)

They had shown that the use of a tosyl group had generated protected allylic amines \textit{via} a [3,3] sigmatropic rearrangement. The conditions used for the reactions outlined in Lu's paper where in general quite harsh requiring 100 °C and the use of 4 equivalents of lithium bromide. Again as has been seen for many literature reported reactions a sulfonyl protecting group had been utilised which could not easily be removed. With distinct advantages evident for the use of the trichloroacetyl protection investigations continued.

One of the most interesting aspects of the reaction is that the reagents used for the reaction are nearly identical to those used for the cyclising haloamination reactions. The need for a copper oxidant is removed and the reaction is run at room temperature.

For a direct comparison the reaction was attempted at an elevated temperature of 40 °C, (Scheme 116).
Rearrangement was still observed for the reaction conditions with no cyclised product, 157, generated. This result was very interesting, either the oxazolidinone or allylic amine product could be synthesised simply by the inclusion or exclusion of copper (II) chloride.

Two further carbamates, 146, were subjected to the room temperature conditions, (Table 25).

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et</td>
<td>178a</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>&quot;Pr</td>
<td>178b</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 25

Rearrangement was not observed for either of the protected carbamate starting materials, 146a-b, utilised. Both experiments were run for 48 h but still rearrangement was not seen. In an attempt to facilitate the reaction the protected carbamate, 146a, was subjected to various conditions, (Table 26).
Entry 1 shows the initially attempted conditions. Increasing the temperature for the reaction did facilitate the rearrangement, with only a small increase above room temperature to 40 °C giving the product, 178a, in a yield of 42%. Increasing the temperature further to 60 °C also saw a rise in the isolated yield, indeed 60 °C was seen to be the optimal temperature for the reaction. Switching the solvent to DMF to allow higher temperatures to be used gave no significant benefit. At 100 °C a slight improvement was observed for the yield of 178a, but this small increase could easily be attributed to better experience of working up the reaction. Increasing the length of time for the reaction to 5 h, (entry 7), saw the yield rise significantly. However, increasing the time further gave no further improvement. Finally, increasing the concentrations of both the palladium catalyst and lithium chloride gave no increase in the yield for the reaction, entry 7, was chosen as the optimum conditions for the rearrangement reaction. With conditions found for the ethyl carbamate, 146a, a range of carboxamides were screened, (Table 27).
Sigmatropic rearrangement occurred readily for all tested substrates in good yields. The whole process could be carried out as a one-pot procedure as previously seen for both the iodine and palladium mediated cyclisations (see tables 12 and 20) to allow the formation of allyl amines directly from the corresponding allylic alcohol, (Table 28).

The reactions proceeded as expected affording the protected allyl amines, 178, in good yields over the two steps.

91
Initial investigations for the rearrangement reaction were carried out on terminal alkenes. The possibility of its use on internal double bonds was very interesting as a [3,3] sigmatropic rearrangement on a carbamate containing an internal carbon-carbon double would generate a new chiral centre, 179, (Scheme 117).

Using the optimised conditions developed, rearrangement reactions were attempted for two internal carbon-carbon double bond containing carbamates, (Table 29).

Unfortunately, as had been observed for the attempted chloroamination reactions with internal carbon-carbon double bonds, (see table 18), moving to an internal double bond from a terminal one shuts down the reaction. Again as observed for the chloroamination reactions, (see table 19) more vigorous conditions made no difference. The inability of the carbamates containing internal double bonds to undergo rearrangement was very disappointing, but gave further weight to the argument that a trichloroacetyl protecting group perhaps could not be utilised for these types of palladium (II) catalyzed reactions, although it had worked very well for the iodine mediated reactions (see table 12).

While on CASE placement at GlaxoSmithKline, the opportunity to investigate microwave chemistry presented itself. Microwaves were a different way to introduce
energy into the reactions and its potential to facilitate rearrangements was investigated. Initially, carbamate, 146a, was used as it had rearranged by employing heat (see table 26). Investigations began with the use of dimethylformamide as the reaction solvent, (Table 30).

\[
\begin{array}{ccccccc}
\text{Entry} & \text{Pd(OAc)} & \text{LiCl} & \text{Solvent} & \text{Temp} & \text{Time} & \text{Yield} \\
& (%) & (\text{eq.}) & & (^\circ\text{C}) & (\text{min}) & (\%) \\
1 & 5 & 2 & \text{DMF} & 60 & 10 & 50 \\
2 & 5 & 2 & \text{DMF} & 80 & 10 & 60 \\
3 & 5 & 2 & \text{DMF} & 100 & 10 & 65 \\
4 & 5 & 2 & \text{DMF} & 100 & 20 & 66 \\
\end{array}
\]

Table 30

Dimethylformamide was utilised first as it is a solvent well known to absorb microwave radiation. Rearrangement product 178a was seen for the reaction with a yield of 50% being observed in just 10 minutes at 60 °C. Raising the temperature to 80 °C saw an increase in the observed yield. Further increases had little effect however with only minimal improvement to the isolated yield, reacting for longer also made little difference. Disappointingly the yields obtained for the reaction in dimethylformamide were lower than those observed with regular heating, (Table 26). In an attempt to improve the yields obtained with microwave irradiation both acetonitrile and tetrahydrofuran were investigated as possible solvents, (Table 31).
Acetonitrile, another well known solvent for palladium catalyzed microwave reactions showed no improvement with similar yields to dimethylformamide observed. Tetrahydrofuran is less widely employed as a solvent for microwave reactions as it absorbs very little microwave radiation, when it was used for the rearrangement reactions however, significant increases in yield were seen. At 60 °C for 10 minutes 178a, was isolated in a 65% yield, raising the temperature to 100 °C saw this result rise to 80% a result comparable to the thermally heated cases (see table 26) but with the time required for the reaction reduced from 5 hours to 10 minutes. Reducing the amounts of either the palladium catalyst or the lithium chloride (entries 7 and 8) saw the yield decrease. The optimum conditions found for the reaction are shown (entry 9), increasing the reaction time to 15 minutes facilitated the formation of 178a in 98%.

As for the thermally heated cases, the newly found conditions were applied to a range of starting materials, (Table 32).

Table 31

<table>
<thead>
<tr>
<th>Entry</th>
<th>Pd(OAc) (%)</th>
<th>LiCl (eq.)</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>2</td>
<td>CH₃CN</td>
<td>60</td>
<td>10</td>
<td>53</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>2</td>
<td>CH₃CN</td>
<td>80</td>
<td>10</td>
<td>58</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>2</td>
<td>CH₃CN</td>
<td>100</td>
<td>10</td>
<td>66</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>60</td>
<td>10</td>
<td>65</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>80</td>
<td>10</td>
<td>72</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>100</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td>2</td>
<td>THF</td>
<td>100</td>
<td>10</td>
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</tr>
<tr>
<td>8</td>
<td>5</td>
<td>1</td>
<td>THF</td>
<td>100</td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>2</td>
<td>THF</td>
<td>100</td>
<td>15</td>
<td>98</td>
</tr>
</tbody>
</table>
In all cases the reactions progressed as expected and the desired allylic amines were obtained in excellent isolated yields in a fraction of the time required for the thermally heated cases, (see table 27).

With a new protocol now in place for these reactions, rearrangements of starting materials containing an internal double bond were once again attempted to see if the use of microwave radiation could increase the scope of the reaction, (Table 33).
The internal alkene starting materials tried previously (see table 29) once again failed to rearrange despite increasing the time of the reaction to 25 minutes. However, when R = Ph (entries 5 and 6) some product was isolated at extended reaction times. Initial happiness at this mini breakthrough was short lived as, despite increasing reaction times further and also catalyst loading an isolated yield of greater than 5% could not be achieved and indeed even this result was capricious the low yield making reproducibility very poor.

The main reason considered for the failure of these reactions was that of steric hindrance, perhaps the bulky trichloroacetyl group made attack at the internal alkene very unfavourable. It was decided to attempt the reaction using cyclic starting material, 180, (Fig. 24).

![Fig. 24](image)

Carbamate, 180, contains a cis double bond within the rigid structure of the ring much more accessible than the previously used trans alkenes. The reaction was attempted as before, (Table 34).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>93</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>95</td>
</tr>
</tbody>
</table>

Table 34

Rearrangement of 180, occurred readily with an optimum reaction time of 15 minutes observed. The success of this reaction pointed to the fact that perhaps steric strain was
the Achilles heel of the reaction. cis-Cinnamyl alcohol, 182, was rapidly synthesized by the shown procedure, (Scheme 118).

Phenylacetylene, 183, was reacted with "butyl lithium and para-formaldehyde to form 3-phenyl-prop-2-yn-1-ol, 184, which was successfully converted to the desired cis-cinnamyl alcohol, 182, by hydrogenation with Lindlar's catalyst. The newly synthesised alcohol was converted to the corresponding protected carbamate, 185, by the usual procedure (see scheme 79) and then subjected to microwave rearrangement conditions, (Table 35).

Rearrangement failed to occur for 185, which was a disappointment even though the alkene was cis the reaction still failed to deliver any amine product. The result observed for 185, suggested that the more rigid cyclic structure may have been the reason for the success seen with 180. With this in mind, the cyclic alcohol, 187, was synthesized from commercially available cyclopentenone, 188, (Scheme 119).
With cyclopent-2-enol, 187, synthesized, conversion was attempted to its corresponding protected carbamate, 189, (Fig. 25).

[Chemical structure image]

Monitoring the reaction, the starting material, 187, was consumed and the reaction worked up to isolate the product. Unfortunately the orangey solid yielded from the reaction did not appear to be the desired product, it was highly insoluble. A small amount was dissolved in dimethylsulfoxide but NMR and IR analysis gave very messy spectra, structural elucidation was not possible. The unsuccessful formation of 189, remains a quandary.

An important aspect of the observed rearrangements was the ability to cleave the trichloroacetyl group from the products to yield free allyl amines. The products formed were analogous to those formed by the Overman reaction. With this in mind cleavage of the protecting group was found to be documented in several papers. Interestingly, the first attempted deprotection step failed for the rearrangement products. The trichloroacetyl group had previously been shown to readily cleave to form carbamate, 97, via reaction with potassium carbonate, water and methanol, (Scheme 79). These reaction conditions however failed to produce any of the desired allyl amine, the protected species being too stable. Deprotection was achieved with the zinc/copper couple previously used successfully for the formation of urea, 125. Protected allyl amines 178e, 178f and 181 were successfully deprotected, (Table 36).
\[
\begin{align*}
\text{Entry} & \quad \text{R}^1 & \quad \text{R}^2 & \quad \text{Product} & \quad \text{Yield} \\
1 & \text{PhCH}_2\text{CH}_2 & \text{H} & \text{190a} & 86 \\
2 & \text{H} & \text{H} & \text{190b} & 90 \\
3 & -(\text{CH}_2)_4- & & \text{190c} & 87 \\
\end{align*}
\]

Table 36
2.5 Conclusion

2.5.1 Osmium catalyzed aminohydroxylations

While studying tethered aminohydroxylation reactions, the discovery of chlorohydroxylated product formation over the desired oxazolidinones was observed, (Scheme 120).

![Chemical structure](image)

Formation of these products was unreported in the literature, however it was proven in this PhD that they are not intermediates for the cyclisation reaction proving stable when resubmitted to the above conditions. Separation of the two diastereoisomers formed in the reaction has been shown to be straight forward. Recrystallisation from ethyl acetate via the slow addition of hexane yields the cis isomer, 130, leaving the trans in solution, this was proven by x-ray crystallography and NMR experiments.

2.5.2 Iodine mediated cyclisations

An iodine mediated cyclisation was investigated as an alternative to the tethered aminohydroxylation reaction to allow the formation of oxazolidinones. Previous studies of carbamates suggested the requirement of sulfonyl protecting groups to allow cyclisation via the nitrogen atom, (see tables 8 and 9)\textsuperscript{151} This requirement has been removed for the reaction and conditions allowing the formation of oxazolidinone rings were achieved, (Scheme 121).
The reaction conditions have been successfully employed for both internal and terminal alkenes starting from the corresponding allylic alcohol, (see table 12). A single experiment has also been conducted showing that the reaction can be telescoped from an aldehyde, completing three steps in one pot, (see scheme 93). Disappointingly substitution of the iodine atom with an oxygen containing nucleophile proved unsuccessful, (see table 13), despite literature precedent for this type of substitution. The cyclisation reaction was however, also successfully utilized in the formation of imidazolidinones, (see table 14).

2.5.3 Palladium mediated cyclisations

Palladium (II) was investigated as another alternative catalyst for the formation of oxazolidinone rings. With the vast array of chiral ligands available for palladium it was hoped that enantioselective cyclisation could be achieved. Initial chloroamination investigations using a free carbamate produced not cyclisation but rearrangement via the carbonyl oxygen, (see table 15). The trichloroacetyl protection was employed and conditions were successfully found to facilitate oxazolidinone formation, (Scheme 122).

As with the iodine mediated cyclisations a one-pot procedure was found to be useable starting from the allylic alcohol, (see table 20). A major problem for these reactions is
the apparent lack of reactivity for internal alkene starting materials. In all attempted cases cyclisation was not possible, (see table 18). Attempts were made to increase the scope of the palladium mediated reaction to include aminoacetoxylations, (see section 2.3.3) and carboaminations, (see section 2.3.4) changing the second bond formation to C-OAc and C-C respectively also proved fruitless.

2.5.4 Palladium mediated [3,3] sigmatropic rearrangements

This area of interest sprung from the serendipitous discovery of a rearrangement occurring when investigations into cyclising chloroamination reactions were underway, (see fig. 21). This initial rearrangement saw simple migration of the carbamate functionality, however upon incorporation of a trichloroacetyl protection rearrangement occurred via the nitrogen amount allowing the formation of allylic amines, (Scheme 123).

\[
\text{Scheme 123}
\]

Yields were good for the initially tested reactions, (see table 27) and further improved by the use of microwave radiation which also slashed reaction times, (see table 32). As had been demonstrated with the palladium mediated cyclisation reactions a one-pot procedure was successfully employed transforming an allylic alcohol to its corresponding amine in good yield, (see table 28). Unfortunately the use of carbamate starting materials posed a problem again. Some progress has been made in this area with the reaction of cyclic material, (see table 34). General conditions for internal alkene containing materials however were not found.
2.6 Future Plans

Two separate systems have been demonstrated in this thesis to mediate the formation of free oxazolidinones via oxidative addition across a carbon-carbon double bond. Both the palladium (II) and iodine system show a major advantage over previously reported studies due to \textit{in situ} removal of the protecting group attached to the nitrogen. A natural step for either system would be the incorporation of a chiral catalyst to make the reactions enantioselective.

The iodine system has been shown to be diastereo- and regioselective, but there is very little literature precedent for enantioselective reactions. However, a paper published by Kang \textit{et al.} \cite{Kang2015} reporting the catalytic enantioselective iodocyclization of $\gamma$-Hydroxy-\textit{cis}-alkenes, 191, indicates that perhaps our reaction could also be made enantioselective, (Scheme 124).

Chiral salen–cobalt complexes, 193, were used in the enantioselective intramolecular iodoetherification of $\gamma$-hydroxy-(Z)-alkenes, 191, to yield 2-substituted tetrahydrofurans, 192, in up to 90% ee. The possibility of using a similar catalyst to introduce enantioselectivity into our reactions would indeed be interesting.

The products obtained from the iodine mediated reactions, 147 and 149, are also very useful molecules due to the possibility of substitution of the iodine. Briefly investigated in this thesis was the substitution of the iodine functionality with an OAc group. This transformation is very desirable as its facilitation would generate structures equivalent
to those obtained via the tethered aminohydroxylation reaction and if enantioselectivity could be achieved this would give the iodine reaction a significant advantage over the osmium mediated system.

For the palladium (II) chemistry described in this thesis the next desirable step would also be the incorporation of enantioselectivity. There is a much greater array of literature to be found when considering the development of an enantioselective palladium system, indeed there is a vast array of chiral ligands known which could potentially be applied to our reaction systems. By the appropriate choice of a chiral palladium (II) catalyst either enantiomer could be exclusively synthesised, (Scheme 125).

![Scheme 125](image)

Importantly, the reduced reactivity of both the [3,3] sigmatropic rearrangement and cyclisation palladium mediated reactions to internal alkenes has to be addressed. Causes for the apparent decrease when moving from terminal alkenes are believed to be steric. A change from the trichloroacetyl group to a chemically similar yet less sterically demanding protecting group may be necessary and will be investigated.

The failure to introduce an oxygen atom in place of the chlorine for the palladium mediated cyclisation reaction was particularly disappointing. Oxygen should however be able to replace the chlorine atom for the terminal alkene substrates, (Scheme 126).

![Scheme 126](image)

The Kornblum reaction first reported in 1957 is well known to convert a primary halide, 194, into an aldehyde, 195, via reaction with DMSO and triethylamine. The reaction is closely linked to the Swern oxidation and should allow the incorporation on
the desired oxygen atom. Conversion to the primary alcohol or the addition of extra functionality could now be carried out. The potential of this conversion will be investigated within the group.
Experimental

General Information:

Solvents and Reagents:

Commercial dry solvents were used in all reactions except for light petroleum 40-60 °C fraction, and ethyl acetate, which were distilled from CaCl₂, tetrahydrofuran which was distilled over sodium and benzophenone and dichromomethane which was distilled over phosphorous pentoxide or calcium chloride. Sodium hydride was obtained in 60% dispersion oil. Dimethylformamide, benzene and toluene were bought as anhydrous solvents in Sure-Seal® bottles.

The reagents used were bought from Sigma-Aldrich Chemical Co. Ltd, Lancaster Synthesis Ltd and Strem Chemical Co. Ltd.

Spectra and Analysis:

Melting points were determined on a Leica Galen III hot stage melting point apparatus and are uncorrected.

Infrared spectra were recorded on a Perkin-Elmer Paragon 1000 FT-IR spectrophotometer on NaCl plates as thin films of pure liquid, deuteriochloroform solution or Nujol® mulls.

¹H (400.15 MHz) and ¹³C (100.62 MHz) NMR spectra were recorded using a Brucker AC-400 spectrometer, ¹H (200.15 MHz) spectra were recorded using a Brucker AC-250 spectrometer. The internal standards used in the ¹H NMR spectra were either the residual chloroform peak, in deuteriochloroform assigned as 7.26 ppm, the residual dimethylsulfoxide peak, in deuteriodimethylsulfoxide assigned as 2.54 ppm, the residual methanol peak in deuteriomethanol assigned as 3.34 ppm or the peak due to tetramethylsilane assigned as 0 ppm. In the ¹³C NMR spectra the internal standards were the central peak of the deuteriochloroform triplet assigned as 77.4 ppm, the central peak of the deuteriodimethylsulfoxide heptet assigned as 40.5 ppm or the
central peak of the deuteriomethanol heptet assigned as 49.9 ppm. Chemical shifts are given in parts per million (ppm) and $J$ values in Hertz (Hz). Multiplicities are assigned as singlets (s), doublets (d), triplets (t), quartets (q), multiplets (m), and combinations of these, for example, double doublet (dd), or a double triplet (dt).

High resolution mass spectrometry was carried out on a Jeol SX 102 machine, using the fast atom bombardment (FAB) ionisation technique. For FAB spectroscopy a matrix of 1,3-nitrobenzylalcohol (NOBA) or octadecane was used to dissolve the compounds under investigation, prior to ionisation.

**Chromatography:**

TLC using silica gel as absorbent was carried out with aluminium backed plates coated with silica gel (Merck Kieselgel 60 F254), and TLC using alumina as absorbent was carried out with aluminium backed plates coated with neutral aluminium oxide (Merck 150 F254, Type I). The plates were analysed under UV light or stained with iodine or potassium permanganate.

Silica gel (Merck Kieselgel 60 H silica) was used for column chromatography unless otherwise specified. Samples were applied as liquids, saturated solutions of the appropriate solvent system, or pre-adsorbed onto flash silica gel.

Column chromatography using alumina was carried out with Aldrich aluminium oxide, activated neutral, Brockmann 1, STD Grade, 150 mesh size. Prep-TLC was carried out using aluminium oxide (Merck 60 PF254, Type E).

**General Procedures:**

Anhydrous reactions were flame-dried under an atmosphere of nitrogen. Concentration or evaporation *in vacuo* refers to the removal of solvent under reduced pressure on a rotary evaporator.

Yields are calculated from the mass of the immediate synthetic precursor used, unless otherwise specified.
Nomenclature and Numbering of Compounds:

The compounds produced during the course of this work are named according to systematic nomenclature. However, the numbering system used to illustrate the structure of these compounds is one used for convenience and is not meant to reflect the systematic numbering of these compounds.
General reaction procedures:

**General allylic alcohol formation**

![Chemical structure](image)

To a solution of aldehyde (1 eq.) in tetrahydrofuran (30 ml) cooled to -75 °C in a cardice/acetone bath was added drop wise vinylmagnesium bromide (3 eq.) as a tetrahydrofuran solution. The mixture was stirred for 4 h, while warming to room temperature and monitored by thin layer chromatography. Ammonium chloride (excess) was then added to the reaction mixture and stirring continued for a further 10 min. The reaction mixture was then extracted with diethyl ether (3 x 25 ml) and water (3 x 25 ml), the organic layers collected, dried with MgSO₄, filtered and concentrated *in vacuo* to yield the crude product which was purified by flash silica chromatography as indicated.

**General procedure for allyl carbamate formation**

![Chemical structure](image)

To a solution of an allylic alcohol (1 eq.) in dichloromethane (20 ml) cooled to 0 °C in an ice bath was added drop wise trichloroacetyl isocyanate (1.1 eq.). The mixture was stirred for 4 h, and monitored by thin layer chromatography (TLC). Upon consumption of starting material the dichloromethane was evaporated *in vacuo* off to afford a residue. This residue was dissolved in methanol (20 ml) and the solution cooled to 0 °C upon which water (10 ml) and potassium carbonate (excess) were added. The mixture was stirred for 6 h, while monitoring by TLC. Upon consumption of starting material the methanol was removed via rotary evaporation, an aqueous extraction with DCM performed and the organic layers collected. The combined organic layers were dried
over MgSO₄, filtered and concentrated in vacuo to yield the crude product which was purified by flash silica chromatography as indicated.

**General procedure for chlorohydroxylated product formation**

![Structure of chlorohydroxylated product]

To a solution of allyl carbamate (1 eq.) in propanol : water (2:1) was added aqueous sodium hydroxide (2 eq.). The reaction was stirred for 10 mins upon which tert-butyl hypochlorite (2 eq.) was added. The mixture was stirred for 6 h, while monitoring by thin layer chromatography (TLC). Upon reaction completion, sodium sulphite (excess) was added and the reaction stirred for a further 30 mins. An aqueous extraction with ethyl acetate was performed and the organic layers collected. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo to yield the crude product which was purified by flash silica chromatography as indicated.

**General procedure for (2,2,2-Trichloro-acetyl)-carbamic acid formation**

![Structure of (2,2,2-Trichloro-acetyl)-carbamic acid]

To a solution of an allylic alcohol (1 eq.) in dichloromethane (20 ml) cooled to 0 °C in an ice bath was added drop wise trichloroacetyl isocyanate (1.1 eq.). The mixture was stirred for 4 h, while monitoring by thin layer chromatography (TLC). Upon consumption of starting material the dichloromethane was evaporated off to afford the crude product, which was purified by flash silica chromatography as indicated.
General procedure for iodoamination cyclisation

To a solution of allylic alcohol (1 eq.) in diethyl ether (10 ml) cooled to 0 °C in an ice bath was added drop-wise trichloroacetyl isocyanate (1.1 eq.). The reaction was warmed slowly to rt., with stirring and monitored by TLC. Upon consumption of the starting material, iodine (2 eq.) and potassium carbonate (2 eq.) were added in a single portion and stirring maintained for 5 h. The reaction mixture was then extracted with sodium thiosulphate and ether and the organic layers collected. The combined organic layers were dried over MgSO₄, filtered and concentrated \textit{in vacuo}. The crude product was purified by flash silica chromatography as indicated.

General procedure for the palladium (II) catalyzed chloroamination cyclisation

To a solution of allylic alcohol (1 eq.) in dry THF (10 ml) cooled to 0 °C in an ice bath was added drop-wise trichloroacetyl isocyanate (1.1 eq.). The reaction was warmed slowly to rt., with stirring and monitored by TLC. Upon consumption of the starting material, lithium chloride (2 eq.) and copper (II) chloride (4 eq.) were added in a single portion and the reaction stirred for 5 min. Palladium (II) acetate (0.1 eq.) was then added and stirring maintained for 12 h. The reaction mixture was concentrated \textit{in vacuo} and the crude product purified by flash silica chromatography as indicated.
**General procedure for Palladium catalyzed [3,3] sigmatropic rearrangement**

![Chemical Structure](https://via.placeholder.com/150)

(2,2,2-Trichloro-acetyl)-carbamic acid (1 eq.), palladium (II) chloride (0.05 eq.), and lithium chloride (2 eq.) were weighed into a microwave vial and THF (2 ml) added. The vessel was subjected to the stated microwave conditions and monitored by TLC. Upon consumption of starting material the crude product was purified by flash silica chromatography as indicated.
Experimental data:

(2,2,2-Trichloro-acetyl)-carbamic acid 1-vinyl-allyl ester (96)

1,4-Pentadiene-3-ol (1.00 g, 11.89 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:1) to yield the title complex as a yellow oil (2.59 g, 80%).

\[
\text{\textbf{Carbamic acid 1-vinyl-allyl ester (97)}}
\]

1,4-Pentadiene-3-ol (1.00 g, 11.89 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white powdery solid (1.28 g, 85%).
(2H, dt, J 16.9, 1.3Hz, H1 trans), 5.23 (2H, dt, J 10.4, 1.3Hz, H1 cis), 4.71 (2H, bs, NH2); δC (100.62 MHz; CDCl3) 156.4 (q, C4), 135.3 (2 x CH, C2), 117.1 (2 x CH2, Cl), 75.6 (CH, C3).

No mass ion observed

**Tertiary-butyl hypochlorite (98)**

![Tertiary-butyl hypochlorite (98)](image)

Sodium hypochlorite (200 ml) was placed into a round bottomed flask covered in silver foil, in subdued light. The flask was placed in an ice bath and rapidly stirred until the temperature dropped below 10 °C. The lights in the vicinity were then turned off. A solution of tert-butyl alcohol (11.47 g, 154.75 mmol) and glacial acetic acid (10.28 g, 171.19 mmol) was added in a single portion to the rapidly stirred bleach solution. Stirring was continued for a further 3 min. The reaction mixture was then poured into a separating funnel and the lower aqueous layer discarded. The oily yellow organic layer was washed, first with 10% aqueous sodium carbonate (50 ml) then water (50 ml). The organic product was then dried with calcium chloride and filtered to yield the title complex as a yellow oil (9.60 g, 57%). The product was stored in the freezer.

δH (250.15 MHz; CDCl3) 1.21 (9H, s, H1).

Spectroscopic data is in agreement with that published by Mintz et al.146

**4-Benzyllox-hexa-1,5-dien-3-ol (105)**

![4-Benzyllox-hexa-1,5-dien-3-ol (105)](image)

Sodium hydride (0.170 g, 4.38 mmol) was weighed into a flask and this placed into an ice bath. A second flask was charged with 1,5-hexadiene-3,4-diol (0.500 g, 4.38 mmol) and THF (5.0 ml). This mixture was then syringed slowly into the sodium hydride
containing flask. The reaction mixture was stirred for 10 minutes, maintaining the temperature at 0 °C. Benzyl bromide (0.52 ml, 4.38 mmol) was weighed into a third flask and dissolved in THF (5.0 ml). This solution was then slowly added to the reaction mixture. Stirring was maintained at 0 °C for a further 5 mins and then slowly warmed to room temperature, where stirring was maintained for a further 6 h. Aqueous extraction was performed with dichloromethane and the organic layers collected. The combined organic layers were dried over MgSO4, filtered and concentrated \textit{in vacuo} to yield the crude product which was purified by flash silica chromatography eluting in diethyl ether-petroleum ether (1:5) to yield the \textit{title complex} as a colourless oil (0.57 g, 64%, 1:1 d.r.).

\[ \nu_{\text{max}} \text{(neat)/cm}^{-1} 3453 (\text{OH}); \]

(1\textsuperscript{st} isomer) \( \delta_H \) (250.15 MHz; CDCl\textsubscript{3}) 7.40-7.25 (5H, m, H9,H10,H11), 5.82-5.68 (2H, m, H2,H5), 5.42-5.18 (4H, m, H1,H6), 4.66 (1H, d, \( J \) 12.0Hz, 1 x H7), 4.39 (1H, dd, \( J \) 8.3, 3.7Hz, 1 x H7), 4.24-4.22 (1H, bdd, H4), 4.08 (1H, t, \( J \) 12.9Hz, H3); \( \delta_C \) (100.62 MHz; CDCl\textsubscript{3}) 137.5 (q, C8), 136.2 (CH, C2 or C5), 134.2 (CH, C2 or C5), 128.6 (2 x CH, C10), 127.8 (2 x CH, C9), 127.7 (CH, C11), 120.2 (CH\textsubscript{2}, C1 or C6), 116.8 (CH\textsubscript{2}, C1 or C6), 83.1 (CH, C3), 74.5 (CH, C4), 70.2 (CH\textsubscript{2}, C7).

(2\textsuperscript{nd} isomer) \( \delta_H \) (250.15 MHz; CDCl\textsubscript{3}) 7.40-7.25 (5H, m, H9,H10,H11), 5.82-5.68 (2H, m, H2,H5), 5.42-5.18 (4H, m, H1,H6), 4.66 (1H, d, \( J \) 12.0Hz, 1 x H7), 4.39 (1H, dd, \( J \) 8.3, 3.7Hz, 1 x H7), 3.85 (1H, dd, \( J \) 4.1, 3.7Hz, H4), 3.67 (1H, t, \( J \) 15.0Hz, H3); \( \delta_C \) (100.62 MHz; CDCl\textsubscript{3}) 137.2 (q, C8), 136.0 (CH, C2 or C5), 134.1 (CH, C2 or C5), 128.2 (2 x CH, C10), 127.3 (2 x CH, C9), 127.2 (CH, C11), 119.8 (CH\textsubscript{2}, C1 or C6), 116.5 (CH\textsubscript{2}, C1 or C6), 82.8 (CH, C3), 74.3 (CH, C4), 70.1 (CH\textsubscript{2}, C7).

Spectroscopic data is in agreement with that published by Fujioka \textit{et al.}\textsuperscript{157}
Carbamic acid 2-benzzyloxy-1-vinyl-but-3-enyl ester (107)

4-Benzzyloxy-hexa-1,5-dien-3-ol (0.500 g, 2.45 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as yellow crystals (0.424 g, 70%, 2:1 d.r.).

mp 151.3-153.4 °C; νmax (neat)/cm⁻¹ 4219 (NH₂), 4156 (NH₂), 1695 (C=O), 1653 (C=C);

(Major isomer): δH (250.15 MHz; CDCl₃) 7.26-7.18 (5H, m, H₁₀,H₁₁,H₁₂) 5.84-5.67 (2H, m, H₂,H₅), 5.28-5.18 (4H, m, H₁,H₆), 4.88 (1H, bs, NH₂), 4.82 (1H, bs, NH₂), 4.58 (1H, dd, J 4.1, 3.7Hz, H₃ or H₄), 4.35 (1H, dd, J 7.6, 1.4Hz, H₃ or H₄); δC (100.62 MHz; CDCl₃) 156.4 (q, C₇), 138.6 (q, C₉), 134.7 (CH, C₂ or C₅), 133.3 (CH, C₂ or C₅), 128.7 (3 x CH, C₁₀,C₁₂), 128.0 (2 x CH, C₁₁), 120.2 (CH₂, C₁ or C₆), 118.7 (CH₂, C₁ or C₆), 81.7 (CH, C₃), 76.9 (CH, C₄), 70.8 (CH₂, C₈).

(Minor isomer): δH (250.15 MHz; CDCl₃) 7.26-7.18 (5H, m, H₁₀,H₁₁,H₁₂) 5.84-5.67 (2H, m, H₂,H₅), 5.28-5.18 (4H, m, H₁,H₆), 4.88 (1H, bs, NH₂), 4.82 (1H, bs, NH₂), 4.58 (1H, dd, J 4.1, 3.7Hz, H₃ or H₄), 4.35 (1H, dd, J 7.6, 1.4Hz, H₃ or H₄); δC (100.62 MHz; CDCl₃) 156.5 (q, C₇), 138.4 (q, C₉), 134.5 (CH, C₂ or C₅), 133.7 (CH, C₂ or C₅), 128.2 (3 x CH, C₁₀,C₁₂), 127.9 (2 x CH, C₁₁), 120.1 (CH₂, C₁ or C₆), 118.1 (CH₂, C₁ or C₆), 81.3 (CH, C₃), 76.6 (CH, C₄), 70.9 (CH₂, C₈).
Carbamic acid 2-carbamoyloxy-1-vinyl-but-3-enyl ester (110)

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{O} & \quad \text{O} & \quad \text{N}\text{H}_2 \\
\text{2} & \quad \text{3} & \quad \text{4} & \quad \text{5} \\
\text{1} & \quad & \quad & \quad \\
\text{6} & \quad & \quad & \quad 
\end{align*}
\]

1,5-hexadiene-3,4-diol (0.500 g, 4.38 mmol) was subjected to a modified general allyl carbamate formation procedure, trichloroacetyl isocyanate (2 eq.) used. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (3:1) to yield the title complex as a powdery white solid (0.656 g, 75%).

mp 163.2-165.2 °C; \( \nu_{\text{max}} \) (neat)/cm\(^{-1} \) 3427 (NH\(_2\)), 3358 (NH\(_2\)), 1698 (C=O), 1615 (C=C); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 5.80-5.68 (2H, m, H\(_2\),H\(_5\)), 5.27-5.05 (6H, m, H\(_1\),H\(_3\),H\(_4\),H\(_6\)); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 158.9 (2 x q, C\(_7\), C\(_8\)), 134.4 (CH, C\(_2\) or C\(_5\)), 134.1 (CH, C\(_2\) or C\(_5\)), 118.9 (CH\(_2\), C\(_1\) or C\(_6\)), 118.8 (CH\(_2\), C\(_1\) or C\(_6\)), 76.3 (CH, C\(_3\) or C\(_4\)), 75.3 (CH, C\(_3\) or C\(_4\)); \( m/z \) (FAB) 201.0878 (M\(^+\), C\(_8\)H\(_{12}\)N\(_2\)O\(_4\) requires 201.0875) 201 (34%), 140 (71).

\( \alpha \)-Vinylbenzyl alcohol (120a)

Benzaldehyde (1.00 g, 9.42 mmol) was subjected to the general allylic alcohol formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (0.1:1) to yield the title complex as a pale yellow oil (1.02 g, 81%).

\( \nu_{\text{max}} \) (neat)/cm\(^{-1} \) 3357 (OH), 1642 (C=C); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 7.38-7.26 (6H, m, H\(_1\),H\(_2\),H\(_3\),H\(_4\),H\(_5\)), 6.10-6.02 (1H, m, H\(_6\)), 5.36 (1H, d, \( J \) 16.8Hz, H\(_{3\text{trans}}\)), 5.20 (1H, d, \( J \) 10.4Hz, H\(_{7\text{cis}}\)), 2.31 (1H, bs, OH); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 142.6 (q, C\(_4\)), 140.2 (CH, H\(_6\)), 128.6 (2 x CH, C\(_2\)), 127.8 (CH, C\(_1\)), 126.3 (2 x CH, C\(_3\)), 115.2 (CH\(_2\), C\(_7\)), 75.4 (CH, C\(_6\)).
Spectroscopic data is in agreement with that published by Mąkosza et al.\textsuperscript{158}

**Pent-1-en-3-ol (120b)**

\[
\begin{align*}
\text{OH} \\
1 & \quad 2 & \quad 3 & \quad 4 & \quad 5 \\
\end{align*}
\]

Propional (0.580 g, 8.75 mmol) was subjected to the general allylic alcohol formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as a pale yellow oil (0.538 g, 74%).

\(\nu_{\text{max}}\text{ (neat)/cm}^{-1} 3391 \text{ (OH)}, 1511 \text{ (C=C)}; \delta_H (250.15 \text{ MHz}; \text{CDCl}_3) 5.81 (1H, ddd, J 17.3, 10.4, 6.2Hz, H4), 5.17 (1H, dt, J 17.3, 1.5Hz, H5\text{trans}), 5.06 (1H, dt, J 10.4, 1.5Hz, H5\text{cis}), 4.01-3.93 (1H, m, H3), 2.28 (1H, bs, OH), 1.58-1.45 (2H, m, H2), 0.88 (3H, t, J 7.4Hz, H1); \delta_C (100.62 \text{ MHz}; \text{CDCl}_3) 141.0 (CH, C4), 114.7 \text{CH}_2, C5), 74.1 (CH, C3), 68.0 (CH\_2, C2) 9.6 (CH\_3, Cl).\)

Spectroscopic data is in agreement with that published by Johnson et al.\textsuperscript{159}

**4-Methyl-pent-1-en-3-ol (120c)**

\[
\begin{align*}
\text{OH} \\
1 & \quad 2 & \quad 3 & \quad 4 & \quad 5 \\
\end{align*}
\]

Isobutyraldehyde (0.400 g, 5.50 mmol) was subjected to the general allylic alcohol formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as a pale yellow oil (0.518 g, 94%).

\(\nu_{\text{max}}\text{ (neat)/cm}^{-1} 3432 \text{ (OH)}, 1643 \text{ (C=C)}; \delta_H (400.15 \text{ MHz}; \text{CDCl}_3) 5.84-5.76 (1H, m, H4), 5.18 (1H, dt, J 15.8, 1.2Hz, H5\text{trans}), 5.09 (1H, dt, J 10.8, 1.2Hz, H5\text{cis}), 3.70-3.67 (1H, m, H3), 2.01 (1H, bs, OH), 1.80-1.77 (1H, m, H2), 0.87 (3H, d, J 6.0Hz, H1 or
H6), 0.84 (3H, d, J 6.0Hz, H1 or H6); δC (100.62 MHz; CDCl₃) 139.5 (CH, C4), 115.7 (CH₂, C5), 78.3 (CH, C3), 33.6 (CH, C2), 18.2 (CH₃, C1 or C6), 17.8 (CH₃, C1 or C6). Spectroscopic data is in agreement with that published by Mąkosza et al.¹⁵⁸

1-(4-Nitrophenyl)-prop-2-en-1-ol (120d)

4-Nitrobenzaldehyde (1.00 g, 6.67 mmol) was subjected to the general allylic alcohol formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as pale yellow crystals (0.940 g, 79%).

mp 47.4-48.6 °C (lit. 48-49 °C)¹⁶⁰; vmax (neat)/cm⁻¹ 3388 (OH), 1606 (C=O); δH (400.15 MHz; CDCl₃) 8.13 (2H, d, J 8.9Hz, H2), 7.48 (2H, d, J 8.9Hz, H3), 5.92 (1H, ddd, J 16.9, 10.4, 6.6Hz, H6), 5.38 (1H, d, J 16.9Hz, H7trans), 5.34-5.28 (1H, m, H5), 5.27 (1H, d, J 10.4Hz, H7cis); δC (100.62 MHz; CDCl₃) 149.6 (q, C1), 146.8 (q, C4), 139.2 (CH, H6), 127.0 (2 x CH, C3), 123.7 (2 x CH, C2), 116.8 (CH₂, C7), 74.6 (CH, C5).

Spectroscopic data is in agreement with that published by Hu et al.¹⁶⁹

5-Phenyl-pent-1-en-3-ol (120e)

Hydrocinnamaldehyde (1.00 g, 7.45 mmol) was subjected to the general allylic alcohol formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a pale yellow oil (0.846 g, 70%).
Phenylacetaldehyde (1.00 g, 8.33 mmol) was subjected to the general allylic alcohol formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a pale yellow oil (0.370 g, 30%).

Data in agreement with that published by Okawara et al.\textsuperscript{162}
Carbamic acid 1-phenyl-allyl ester (121a)

\[
\begin{align*}
\text{O} & \quad \text{NH}_2 \\
2 & \quad 3 \\
\text{1} & \quad \text{4} \\
\text{1} & \quad \text{5} \\
\text{1} & \quad \text{6} \\
\text{1} & \quad \text{7}
\end{align*}
\]

α-Vinylbenzyl alcohol (0.500 g, 3.73 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a powdery white solid (0.660 g, 81%).

mp 126.7-129.3 °C; \( \nu_{\text{max}} \) (nujol)/cm\(^{-1} \) 3425 (NH\(_2\)), 3335 (NH\(_2\)), 1684 (C=O), 1609 (C=C); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 7.44-7.27 (5H, m, H1, H2, H3), 6.19-6.15 (1H, m, H5), 6.02 (1H, ddd, J 17.1, 10.4, 5.9Hz, H6), 5.31 (1H, dt, J 17.1, 1.3Hz, H7\(_{\text{trans}}\)), 5.26 (1H, dt, J 10.4, 1.3Hz, H7\(_{\text{cis}}\)), 4.79 (2H, bs, NH\(_2\)); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 156.0 (q, C8), 139.0 (q, C4), 136.4 (CH, H6), 126.8 (2 x CH, C2), 126.2 (CH, C1), 127.1 (2 x CH, C3), 116.8 (CH\(_2\), C7), 77.1 (CH, C5); \( m/z \) (FAB) 178.0864 (M\(^+\), C\(_{10}\)H\(_{11}\)NO\(_2\) requires 178.0868) 178 (1%), 117 (100), 115 (18).

Carbamic acid 1-ethyl-allyl ester (121b) 

\[
\begin{align*}
\text{O} & \quad \text{NH}_2 \\
1 & \quad \text{2} \\
\text{1} & \quad \text{3} \\
\text{1} & \quad \text{4} \\
\text{1} & \quad \text{5}
\end{align*}
\]

1-penten-3-ol (0.250 g, 2.90 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a white crystalline solid (0.322 g, 86%).

mp 85.6-86.2 °C; \( \nu_{\text{max}} \) (neat)/cm\(^{-1} \) 3431 (NH\(_2\)), 3320 (NH\(_2\)), 1688 (C=O), 1615 (C=C); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 5.64 (1H, ddd, J 17.3, 10.5, 6.5Hz, H4), 5.11 (1H, dt, J 17.3, 1.4Hz, H5\(_{\text{trans}}\)), 5.03 (1H, dt, J 10.5, 1.4Hz, H5\(_{\text{cis}}\)), 4.92-4.86 (1H, m, H3), 4.54 (2H, bs,
4-methyl-1-pentene-3-ol (0.250 g, 2.50 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as off-white crystals (0.336 g, 94%).

$$\text{mp } 69.4-71.3 \degree C; \nu_{\max} (\text{neat})/\text{cm}^{-1} 3420 (\text{NH}_2), 3342 (\text{NH}_2), 1734 (\text{C} = \text{O}), 1653 (\text{C} = \text{C});$$

$$\delta_{\text{H}} (400.15 \text{ MHz}; \text{CDCl}_3) 5.83-5.69 (1\text{H}, \text{m}, \text{H}_4), 5.28-5.17 (2\text{H}, \text{m}, \text{H}_5), 4.94-4.89 (1\text{H}, \text{m}, \text{H}_3) 4.71 (2\text{H}, \text{bs}, \text{NH}_2), 1.92-1.82 (1\text{H}, \text{m}, \text{H}_2), 0.95-0.92 (6\text{H}, \text{m}, \text{H}_1, \text{H}_7); \delta_{\text{C}} (100.62 \text{ MHz}; \text{CDCl}_3) 156.7 (q, \text{C}_6), 135.0 (\text{CH}, \text{C}_4), 117.2 (\text{CH}_2, \text{C}_5), 80.1 (\text{CH}, \text{C}_3), 32.0 (\text{CH}, \text{C}_2), 18.0 (\text{CH}_3, \text{H}_1 \text{ or } \text{H}_7), 17.9 (\text{CH}_3, \text{H}_1 \text{ or } \text{H}_7).$$

No mass ion observed

**Carbamic acid 1-isopropyl-allyl ester (121c)**

![Diagram](attachment:diagram.png)

**Carbamic acid 1-(4-nitro-phenyl)-allyl ester (121d)**

1-(4-Nitro-phenyl)-prop-2-en-1-ol (0.300 g, 1.67 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica
chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the **title complex** as pale yellow crystals (0.372 g, 82%).

mp 141.2-144.3 °C; $v_{\text{max}}$ (nujol)/cm$^{-1}$ 3451 (NH$_2$), 3340 (NH$_2$), 1698 (C=O), 1615 (C=C); $\delta_H$ (250.15 MHz; CDCl$_3$) 8.16 (2H, d, $J$ 8.9Hz, H2), 7.47 (2H, d, $J$ 8.9Hz, H3), 6.16 (1H, d, $J$ 6.0Hz, H5), 5.92 (1H, ddd, $J$ 16.3, 10.2, 6.0Hz, H6), 5.31 (1H, dt, $J$ 16.3, 1.2Hz, H7$_{\text{trans}}$), 5.25 (1H, dt, $J$ 10.2, 1.2Hz H7$_{\text{cis}}$); $\delta_C$ (100.62 MHz; CDCl$_3$) 155.9 (q, C8), 147.5 (q, C1), 146.5 (q, C4), 135.3 (CH, C6), 127.6 (2 x CH, C3), 123.7 (2 x CH, C2), 118.2 (CH$_2, C7$), 75.7 (CH, C5).

No mass ion observed

**Carbamic acid 1-vinyl-but-3-enyl ester (121e)**

Hexa-1,5-dien-3-ol (0.300 g, 3.06 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the **title complex** as yellow/orange oil (0.432 g, 86%).

$v_{\text{max}}$ (neat)/cm$^{-1}$ 3428 (NH$_2$), 3358 (NH$_2$), 1684 (C=O), 1597 (C=C); $\delta_H$ (250.15 MHz; CDCl$_3$) 5.84-5.65 (2H, m, H2,H5), 5.28-5.02 (5H, m, H1,H4,H6), 2.40-2.34 (2H, m, H3); $\delta_C$ (100.62 MHz; CDCl$_3$) 157.2 (q, C7), 136.0 (CH, C5), 133.1 (CH, C2), 118.0 (CH$_2$, C6), 116.7 (CH$_2$, C1), 77.1 (CH, C4), 38.8 (CH$_2$, C3).

Spectroscopic data is in agreement with that published by Donohoe et al.$^{163}$
Carbamic acid 2-chloro-3-hydroxy-1-phenyl-propyl ester (123a)

Carbamic acid 1-phenyl-allyl ester (0.100 g, 0.565 mmol) was subjected to the general chlorohydroxylated product formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as a white solid (0.0882 g, 68%, 5:1 d.r.).

mp 166.7-169.1 °C; \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 3430 (NH\(_2\)), 3350 (NH\(_2\)), 3142 (OH), 1711 (C=O);

(Major isomer): \( \delta_H \) (400.15 MHz; \( \text{C}_3\text{D}_6\text{O} \)) 7.41-7.24 (5H, m, C1,C2,C3), 6.05 (1H, d, \( J = 5.0 \text{Hz} \), C5), 4.36 (1H, t, \( J = 6.3 \text{Hz} \), OH), 4.26-4.22 (1H, m, C6), 3.77-3.71 (1H, m, 1 x C7), 3.64-3.57 (1H, m, 1 x C7); \( \delta_C \) (100.62 MHz; \( \text{C}_3\text{D}_6\text{O} \)) 156.9 (q, C8), 139.7 (q, C4), 129.1 (2 x CH, C2), 128.9 (CH, C1), 127.5 (2 x CH, C3), 74.6 (CH, C5), 66.8 (CH, C6), 63.8 (CH, C7).

(Minor isomer): \( \delta_H \) (400.15 MHz; \( \text{C}_3\text{D}_6\text{O} \)) 7.41-7.24 (5H, m, C1,C2,C3), 5.62 (1H, d, \( J = 5.0 \text{Hz} \), C5), 4.36 (1H, t, \( J = 6.3 \text{Hz} \), OH), 4.26-4.22 (1H, m, C6), 3.77-3.71 (1H, m, 1 x C7), 3.64-3.57 (1H, m, 1 x C7); \( \delta_C \) (100.62 MHz; \( \text{C}_3\text{D}_6\text{O} \)) 156.9 (q, C8), 139.7 (q, C4), 129.1 (2 x CH, C2), 128.9 (CH, C1), 127.5 (2 x CH, C3), 74.6 (CH, C5), 66.8 (CH, C6), 63.8 (CH, C7).

Carbamic acid 2-chloro-1-ethyl-3-hydroxy-propyl ester (123b)

Carbamic acid 1-ethyl-allyl ester (0.0500 g, 0.774 mmol) was subjected to the general chlorohydroxylated product formation procedure. The crude product was purified by
flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as a white solid (0.0829 g, 59%, 7:1 d.r.).

mp 126.5-128.9 °C; νmax (neat)/cm⁻¹ 3425 (NH₂), 3363 (NH₂), 3130 (OH), 1716 (C=O);
(Major isomer): δ_H (400.15 MHz; C₃D₆O) 6.05 (2H, bs, NH₂), 4.79-4.75 (1H, m, H3), 4.08 (1H, dd, J 6.8, 6.0Hz, H4), 3.68-3.50 (2H, m, H5), 1.70-1.46 (2H, m, H2) 0.91 (3H, t, J 7.4Hz, H1); δ_C (100.62 MHz; C₂D₆O) 156.7 (q, C6), 75.2 (CH, C3), 63.6 (CH, C4), 63.3 (CH₂, C5), 24.2 (CH₂, C2), 9.3 (CH₃, Cl).
(Minor isomer): δ_H (400.15 MHz; C₂D₆O) 6.05 (2H, bs, NH₂), 4.87-4.81 (1H, m, H3), 4.18 (1H, dd, J 6.8, 6.0Hz, H4), 3.68-3.50 (2H, m, H5), 1.70-1.46 (2H, m, H2) 0.91 (3H, t, J 7.4Hz, H1); δ_C (100.62 MHz; C₂D₆O) 156.7 (q, C6), 77.2 (CH, C3), 65.8 (CH, C4), 65.7 (CH₂, C5), 24.2 (CH₂, C2), 9.3 (CH₃, Cl).

Carbamic acid 2-chloro-3-hydroxy-1-isopropyl-propyl ester (123c)

Carbamic acid 1-isopropyl-allyl ester (0.100 g, 0.699 mmol) was subjected to the general chlorohydroxylated product formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as a white solid (0.0861 g, 63%).

mp 118.2-120.5 °C; νmax (neat)/cm⁻¹ 3417 (NH₂), 3360 (NH₂), 3134 (OH), 1713 (C=O);
δ_H (400.15 MHz; C₃D₆O) 4.63 (1H, dd, J 8.2, 3.9Hz, H3), 3.94-3.89 (2H, m, H4,OH), 3.70-3.64 (1H, m, 1 x H5), 3.61-3.55 (1H, m, 1 x H5), 2.14-2.07 (1H, m, H2), 0.82 (3H, d, J 6.80, H1 or H7), 0.78 (3H, d, J 6.80, H1 or H7); δ_C (100.62 MHz; CDCl₃) 158.2 (q, C6), 77.2 (CH, C3), 63.9 (CH₂, C5), 63.5 (CH, C4), 19.8 (CH, C2), 16.0 (2 x CH₃, Cl,C7).
Carbamic acid 1-(1-chloro-2-hydroxy-ethyl)-but-3-enyl ester (123e)

Carbamic acid 1-vinyl-but-3-enyl ester (0.200 g, 1.42 mmol) was subjected to the general chlorohydroxylated product formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:1) to yield the title complex as a colourless oil (0.192 g, 70%).

mp 132.4-134.3 °C; \(v_{\text{max}}\) (neat)/cm\(^{-1}\) 3405 (NH\(_2\)), 3342 (NH\(_2\)), 3201 (OH), 1720 (C=O), 1632 (C=C); \(\delta_H\) (250.15 MHz; CD\(_3\)OD) 5.88 (1H, ddd, \(J_{17.2, 10.6, 5.7}\)Hz, H2), 5.35-5.31 (1H, m, H4), 5.28 (1H, dt, \(J_{17.2, 1.4}\)Hz, 1 x H1), 5.15 (1H, dt, \(J_{10.6, 1.4}\)Hz, 1 x H1), 3.95-3.87 (1H, m, H5), 3.58-3.49 (2H, m, H6), 1.91-1.84 (1H, m, 1 x H3), 1.73-1.66 (1H, m, 1 x H3); \(\delta_C\) (100.62 MHz; CD\(_3\)OD) 159.4 (q, C7), 138.8 (CH, C2), 115.9 (CH\(_2\), C1), 72.7 (CH, C4), 68.7 (CH, C5), 50.3 (CH\(_2\), C6), 40.5 (CH\(_2\), C3).

1,1-Diallyl-urea (125)

To a solution of an diallyl amine (0.500 g, 5.15 mmol) in dichloromethane (20 ml) cooled to 0 °C in an ice bath was added drop wise trichloroacetyl isocyanate (1.07 g, 5.66 mmol). The mixture was stirred for 4 h, monitoring by thin layer chromatography (TLC). Upon consumption of starting material the dichloromethane was evaporated \textit{in vacuo} off to afford a yellow residue. This residue was dissolved in methanol (20 ml) and the solution cooled to 0 °C upon which Zinc/Copper couple (excess) was added and the cooling bath removed. The mixture was then stirred at room temperature for 3-4 h, monitoring by TLC. Upon consumption of starting material excess Zn/Cu couple was filtered off, the methanol removed \textit{via} rotary evaporation, an aqueous extraction
performed with ethyl acetate and the organic layers collected. The combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo to yield the crude product which was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (3:1) to yield the title complex as a white powdery solid (0.590 g, 80%).

mp 118.2-120.4 °C; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3400 (NH$_2$), 3363 (NH$_2$), 1617 (C=O), 1522 (C=C); $\delta_H$ (400.15 MHz; CDCl$_3$) 5.85-5.76 (2H, m, H$_2$, H$_5$), 5.31 (4H, dd, J 12.6Hz, 3.2Hz, H$_1$,H$_6$), 3.90 (4H, d, J 5.3Hz, H$_3$,H$_4$); $\delta_C$ (100.62 MHz; CDCl$_3$) 157.2 (q, C$_7$), 133.1 (2 x CH, C$_2$,C$_5$), 117.9 (2 x CH$_2$, C$_1$,C$_6$), 49.9 (2 x CH$_2$, C$_3$,C$_4$); $m/z$ (FAB) 141.1026 (M$^+$, C$_7$H$_{12}$N$_2$O requires 141.1028) 141 (100%), 98 (16), 41 (12).

Spectroscopic data is in agreement with that published by Yale.$^{164}$

Zinc/Couple (127)

Zn/Cu

Zinc dust (1.25 g, 18.81 mmol) was placed into an Erlenmeyer flask containing a stirrer bar. Hydrochloric acid (20 ml, 1 M) was added to the flask and the reaction mixture stirred rapidly for 1 min. The supernatant was then decanted away and the process repeated with three more portions of hydrochloric acid. Distilled water (50 ml) was added to the flask, the solution stirred rapidly for 1 min and the supernatant decanted away. This distilled water wash was repeated a further four times. Aqueous copper (II) sulphate (20 ml) was then added to the reaction flask, the solution stirred rapidly for 1 min and the supernatant decanted away. The copper (II) sulphate wash was then repeated once more, followed by another wash with distilled water (50 ml). Ethanol (50 ml) was added to the zinc in the flask and this solution stirred. The supernatant was decanted directly onto a sintered funnel to which a vacuum was applied. This process was repeated three more times. Diethyl ether (50 ml) was then added to the flask, the solution stirred and the supernatant decanted directly onto the sintered funnel. The ether wash was repeated four more times and on the final wash all zinc/copper couple was transferred to the sintered funnel to dry under vacuum. The zinc/copper couple was then dried in a desiccator to yield the title complex as a dark grey solid (2.31 g, 95%).
Carbamic acid 1-(1-chloro-2-hydroxy-ethyl)-allyl ester (130)

Carbamic acid 1-vinyl-allyl ester (0.400 g, 3.15 mmol) was subjected to the general chlorohydroxylated product formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (3:2) to yield the title complex as a white solid (0.280 g, 61%, 3:1 d.r.).

mp 125.6-128.4 °C; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3428 (NH$_2$), 3348 (NH$_2$), 3180 (OH), 1702 (C=O), 1622 (C=C);

(Major isomer): $\delta$$_H$ (250.15 MHz; CDCl$_3$) 5.97-5.82 (1H, m, H2), 5.56-5.52 (1H, m, H3), 5.44-5.30 (2H, m, H1), 4.14-3.99 (1H, m, H4), 3.80-3.53 (2H, m, H5); $\delta$$_C$ (100.62 MHz; CDCl$_3$) 157.1 (q, C6), 135.2 (CH, C2), 117.9 (CH$_2$, Cl), 73.3 (CH, C3), 64.9 (CH, C4), 63.8 (CH$_2$, C5).

(Minor isomer): $\delta$$_H$ (250.15 MHz; CDCl$_3$) 5.94-5.77 (1H, m, H2), 5.56-5.52 (1H, m, H3), 5.44-5.30 (2H, m, H1), 4.14-3.99 (1H, m, H4), 3.80-3.53 (2H, m, H5); $\delta$$_C$ (100.62 MHz; CDCl$_3$) 157.1 (q, C6), 135.2 (CH, C2), 117.9 (CH$_2$, Cl), 73.3 (CH, C3), 64.9 (CH, C4), 63.8 (1C, C5).

Carbamic acid 3,7-dimethyl-octa-2,6-dienyl ester (132)

Geraniol (0.500 g, 3.24 mmol) was subjected to the general allyl carbamate formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as white needles (0.590 g, 92%).
Carbamic acid 2,6-dichloro-3,7-dihydroxy-3,7-dimethyl-octyl ester (133)

Carbamic acid 3,7-dimethyl-octa-2,6-dienyl ester (0.100g, 0.507mmol) was subjected to the general chlorohydroxylated product formation procedure. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (6:1) to yield the title complex as a white crystalline solid (0.104 g, 68%, 3:1 d.r.).

mp 289.3-292.1 °C; \( \nu_{max} \) (nujol)/cm\(^{-1} \) 3426 (NH\(_2\)), 3350 (NH\(_2\)), 3361 (OH), 1715 (C=O);  

(Major isomer): \( \delta_H \) (400.15 MHz; C\(_3\)D\(_6\)O) 4.49-4.45 (1H, m, 1 x H8), 4.47 (1H, dd, J 5.8, 2.8Hz 1 x H8), 3.91-3.89 (1H, m, H7), 3.63-3.59 (1H, m, H3), 2.09-2.04 (2H, m, H4 or H5), 1.61-1.45 (2H, m, H4 or H5), 1.22 (3H, s, H1 or H11), 1.18 (3H, s, H1 or H11), 1.17 (3H, s, H10); \( \delta_C \) (100.62 MHz; C\(_3\)D\(_6\)O) 159.5 (q, C9), 74.5 (q, C2), 73.9 (q, C6), 73.6 (CH, C3), 67.0 (CH, C7), 66.8 (CH\(_2\), C8), 39.5 (CH\(_2\), C5), 27.6 (CH\(_2\), C4), 27.4 (CH\(_3\), C1 or C11), 25.1 (CH\(_3\), C11 or C1), 23.0 (CH\(_3\), C10).

(Minor isomer): \( \delta_H \) (400.15 MHz; C\(_3\)D\(_6\)O) 4.49-4.45 (1H, m, 1 x H8), 4.47 (1H, dd, J 5.8, 2.8Hz 1 x H8), 3.91-3.89 (1H, m, H7), 3.63-3.59 (1H, m, H3), 2.09-2.04 (2H, m, H4 or H5), 1.61-1.45 (2H, m, H4 or H5), 1.22 (3H, s, H1 or H11), 1.18 (3H, s, H1 or H11), 1.16 (3H, s, H10); \( \delta_C \) (100.62 MHz; C\(_3\)D\(_6\)O) 159.5 (q, C9), 74.5 (q, C2), 73.9 (q, C6), 73.8 (CH, C3), 66.8 (CH, C7), 66.8 (CH\(_2\), C8), 39.1 (CH\(_2\), C5), 27.7 (CH\(_2\), C4), 27.3 (CH\(_3\), C1 or C11), 25.2 (CH\(_3\), C1 or C11), 22.6 (CH\(_3\), C10).
To a solution of (2,2,2-Trichloro-acetyl)-carbamic acid 1-phenyl-allyl ester (0.100 g, 0.310 mmol) in diethyl ether (10 ml), iodine(0.157 g 0.620 mmol) and 1M aqueous sodium hydrogen carbonate solution (10ml) were added and the reaction stirred for 5 h at room temperature monitoring by TLC. When the reaction had reached completion by TLC, the mixture was extracted with aqueous sodium thiosulphate and ether and the organic layers collected. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a yellow oil (0.069 g, 73%, 4:1 d.r.).

νmax (neat)/cm⁻¹ 1760 (C=O);

(Major isomer): δH (400.15 MHz; CDCl₃) 7.38-7.24 (5H, m, H1,H2,H3), 5.01 (1H, d, J 4.8Hz, H5), 3.89-3.83 (1H, m, H6), 3.37 (2H, d, J 5.6Hz, H7); δC (100.62 MHz; CDCl₃) 152.7 (q, C8), 137.5 (q, C4), 128.7 (4 x CH, C2,C3), 125.6 (CH, C1), 75.9 (CH, C5), 75.1 (CH, C6), 7.3 (CH₂, C7).

(Minor isomer): δH (400.15 MHz; CDCl₃) 7.38-7.24 (5H, m, H1,H2,H3), 5.46 (1H, d, J 7.6Hz, H5), 4.35-4.28 (1H, m, H6), 3.37 (2H, d, J 5.6Hz, H7); δC (100.62 MHz; CDCl₃) 152.7 (q, C8), 132.9 (q, C4), 129.1 (4 x CH, C2,C3), 126.3 (CH, C1), 72.4 (CH, C5), 72.1 (CH, C6), 5.8 (CH₂, C7).

m/z (FAB) 304.9596 (M⁺, C₁₆H₉O₃I requires 304.9596) 305 (100%), 253 (11).
4-Iodomethyl-5-vinyl-oxazolidin-2-one (145)

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1,4-Pentadiene-3-ol (0.0370 g, 0.440 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0813 g, 73%, 2:1 d.r.).

\[
\nu_{\text{max}} (\text{nujol})/\text{cm}^{-1} 3266 (\text{NH}), 1751 (\text{C} = \text{O});
\]

(Major isomer): \(\delta_H\) (400.15 MHz; CDCl\(_3\)) 7.16 (1H, bs, NH), 6.02-5.89 (1H, m, H2), 5.51-5.46 (1H, m, H1), 5.36 (1H, d, \(J = 10.4\text{Hz}\), H1), 5.15-5.08 (1H, m, H3), 4.27-4.19 (1H, m, H4), 3.20-3.11 (2H, m, H5); \(\delta_C\) (100.62 MHz; CDCl\(_3\)) 158.5 (q, C6), 129.1 (CH, C2), 121.4 (CH\(_2\), C1), 79.7 (CH, C3), 57.2 (CH, C4), 4.7 (CH\(_2\), C5).

(Minor isomer): \(\delta_H\) (400.15 MHz; CDCl\(_3\)) 6.93 (1H, bs, NH), 6.02-5.89 (1H, m, H2), 5.60-5.46 (2H, m, H1), 4.73-4.68 (1H, m, H3), 3.74-3.69 (1H, m, H4), 3.28 (2H, d, \(J = 6.0\text{Hz}\), H5); \(\delta_C\) (100.62 MHz; CDCl\(_3\)) 158.7 (q, C6), 133.8 (CH, C2), 119.2 (CH\(_2\), C1), 82.5 (CH, C3), 58.5 (CH, C4), 8.2 (CH\(_2\), C5);

\(m/z\) (FAB) 253.9682 (M\(^+\), C\(_6\)H\(_{10}\)NO\(_2\)I requires 253.9681) 254 (100%).

(2,2,2-Trichloro-acetyl)-carbamic acid 1-ethyl-allyl ester (146a)

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1-penten-3-ol (0.250 g, 2.90 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a white powdery solid (0.757 g, 95%).
mp 131.3-132.6 °C; $\nu_{\text{max}}$ (nujol)/cm$^{-1}$ 3271 (NH), 1782 (C=O), 1721 (C=O); $\delta_H$ (400.15 MHz; CDCl$_3$) 8.41 (1H, bs, NH), 5.85-5.73 (1H, m, H4), 5.37 (1H, d $J$ 17.2 Hz, H$_5$$_{\text{trans}}$), 5.29 (1H, d $J$ 10.4 Hz, H$_5$$_{\text{cis}}$), 5.24 (1H, q, $J$ 6.8 Hz, H3), 1.84-1.66 (2H, m, H2), 0.96 (3H, t, $J$ 7.4 Hz, H1); $\delta_C$ (100.62 MHz; CDCl$_3$) 157.7 (q, C6 or C7), 149.1 (q, C6 or C7), 134.7 (CH, C4), 119.0 (CH$_2$, C5), 80.2 (CH, C3), 27.0 (CH$_2$, C2), 9.3 (CH$_3$, C1); m/z (FAB) 273.9810 (M$^+$, C$_8$H$_{10}$NO$_3$Cl$_3$ requires 273.9805) 298 (39%), 296 (41), 274 (6), 261 (13).

(2,2,2-Trichloro-acetyl)-carbamic acid 1-isopropyl-allyl ester (146b)

4-methyl-1-pentene-3-ol (0.250 g, 2.50 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a white semi-crystalline solid (0.691 g, 96%).

mp 128.4-131.2 °C; $\nu_{\text{max}}$ (nujol)/cm$^{-1}$ 3274 (NH), 1782 (C=O), 1721 (C=O); $\delta_H$ (400.15 MHz; CDCl$_3$) 8.41 (1H, bs, NH), 5.84-5.75 (1H, m, H4), 5.39-5.29 (2H, m, H5), 5.10 (1H, t, $J$ 8.0 Hz, H3), 1.98 (1H, dq, $J$ 8.0, 5.9 Hz, H2), 0.97 (6H, d, $J$ 5.9 Hz, H1,H6); $\delta_C$ (100.62 MHz; CDCl$_3$) 157.1 (q, C7 or C8), 148.9 (q, C7 or C8), 132.7 (CH, C4), 119.2 (CH$_2$, C5), 83.2 (CH, C3), 31.3 (CH, C2), 17.5 (CH$_3$, C1 or C6), 17.4 (CH$_3$, C1 or C6); m/z (FAB) 287.9968 (M$^+$, C$_8$H$_{12}$NO$_3$Cl$_3$ requires 287.9961) 312 (21%), 310 (22), 288 (3), 171 (4).
(2,2,2-Trichloro-acetyl)-carbamic acid 1-vinyl-but-3-enyl ester (146c)

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1,5-hexadiene-3-ol (0.250 g, 2.55 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a clear oil (0.620 g, 85%).

\[\nu_{\text{max}} \text{(nujol)} / \text{cm}^{-1} 3274 (\text{NH}), 1785 (\text{C=O}), 1718 (\text{C=O}); \delta_H (400.15 \text{ MHz; CDCl}_3) 8.44 (1\text{H, bs, NH}), 5.88-5.71 (2\text{H, m, H}_2/\text{H}_5), 5.42-5.28 (3\text{H, m, H}_1/\text{H}_4/\text{H}_6), 5.18-5.12 (2\text{H, m, H}_1/\text{H}_6), 2.49 (2\text{H, t, J}\ 6.0 \text{Hz, H}_3); \delta_C (100.62 \text{ MHz; CDCl}_3) 157.6 (q, \text{C}_7 \text{ or C}_8), 149.0 (q, \text{C}_7 \text{ or C}_8) 134.3 (\text{CH}, \text{C}_5), 132.2 (\text{CH}, \text{C}_2), 118.9 (2 \text{ x CH}_2, \text{C}_1/\text{C}_6), 78.1 (\text{CH}, \text{C}_4), 38.5 (\text{CH}_2, \text{C}_3); m/z (\text{FAB}) 285.9809 (\text{M}^+, \text{C}_9\text{H}_{10}\text{NO}_3\text{Cl}_3 \text{ requires } 285.9805) 308 (16\%), 288 (7\%), 286 (8\%), 171 (9)\].

(2,2,2-Trichloro-acetyl)-carbamic acid allyl ester (146d)

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\]

Allyl alcohol (0.500 g, 8.61 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a pale yellow oil (1.87 g, 88%).

\[\nu_{\text{max}} \text{(nujol)} / \text{cm}^{-1} 3282 (\text{NH}), 1789 (\text{C=O}), 1715 (\text{C=O}); \delta_H (400.15 \text{ MHz; CDCl}_3) 8.52 (1\text{H, bs, NH}), 5.99-5.89 (1\text{H, m, H}_2), 5.42 (1\text{H, dq, J} 17.2, 1.2 \text{Hz, H}_1_{\text{trans}}), 5.33 (1\text{H, dq, 10.4, 1.2Hz, H}_1_{\text{cis}}), 4.74 (2\text{H, dt, J} 6.0, 1.2 \text{Hz, H}_3); \delta_C (100.62 \text{ MHz; CDCl}_3) 157.7 (q, \text{C}_4 \text{ or C}_5), 149.5 (q, \text{C}_4 \text{ or C}_5) 130.6 (\text{CH}, \text{C}_2), 120.3 (\text{CH}_2, \text{C}_1), 67.9 (\text{CH}_2, \text{C}_3).\]

No mass ion observed.
(2,2,2-Trichloro-acetyl)-carbamic acid 1-phenyl-allyl ester (146e)

\[
\text{\includegraphics[width=0.2\textwidth]{image}}
\]

α-Vinylbenzyl alcohol (0.0500 g, 0.373 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure, yielding the crude title complex as a yellow oil. Due to instability purification was not attempted on the material, it was used crude.

(2,2,2-Trichloro-acetyl)-carbamic acid 1-(4-nitro-phenyl)-allyl ester (146f)

\[
\text{\includegraphics[width=0.2\textwidth]{image}}
\]

1-(4-Nitrophenyl)-prop-2-en-1-ol (0.200 g, 1.12 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a white oily solid (0.328 g, 80%).

mp 263.2-265.7 °C; \(\nu_{\text{max}}\) (neat)/cm\(^{-1}\) 3269 (NH), 1780 (C=O), 1725 (C=O); \(\delta_{\text{H}}\) (400.15 MHz; CDCl\(_3\)) 8.54 (1H, bs, NH), 8.26 (2H, d, \(J\) 8.6Hz, H2), 7.61 (2H, d, \(J\) 8.6Hz, H3), 6.39 (1H, d, \(J\) 6.6Hz, H5), 6.08-5.98 (1H, m, H6), 5.46 (2H, dd, \(J\) 17.0, 12.4Hz, H7); \(\delta_{\text{C}}\) (100.62 MHz; CDCl\(_3\)) 157.1 (q, C8 or C9), 148.5 (q, C8 or C9), 147.6 (q, C1), 143.8 (q, C4), 133.2 (CH, C6), 127.5 (2 x CH, C3) 123.6 (2 x CH, C2), 119.8 (CH\(_2\), C7), 78.1 (CH, C5).

No mass ion observed.
(2,2,2-Trichloro-acetyl)-carbamic acid 1-(3-phenylethane)-allyl ester (146g)

5-Phenyl-pent-1-en-3-ol (0.500 g, 3.08 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a pale yellow oil (0.703 g, 65%).

$\nu_{\text{max}} \text{(neat)/cm}^{-1}$ 3279 (NH), 1779 (C=O), 1722 (C=O); $\delta_H$ (400.15 MHz; CDCl$_3$) 8.39 (1H, bs, NH), 7.36-7.32 (2H, m, H2), 7.29-7.23 (3H, m, H1,H3), 5.97-5.87 (1H, m, H8), 5.50-5.37 (3H, m, H7,H9), 2.79 (2H, t, $J$ 7.9Hz, H5), 2.25-2.04 (2H, m, H6); $\delta_C$ (100.62 MHz; CDCl$_3$) 157.1 (q, C10 or C11), 148.6 (q, C10 or C11), 140.3 (q, C4), 134.2 (CH, C8) 128.1 (2 x CH, C2), 127.9 (2 x CH, C3), 125.7 (CH, C1), 118.6 (CH, C9), 78.0 (CH, C7), 34.9 (CH$_2$, C6), 30.8 (CH$_2$, C5); $m/z$ (FAB) 350.0039 (M$^+$, C$_{14}$H$_{14}$NO$_2$Cl$_3$ requires 350.0039) 374 (36%), 372 (40), 350 (10), 146 (8).

(2,2,2-Trichloro-acetyl)-carbamic acid 1-benzyl-allyl ester (146h)

1-Phenyl-but-3-en-2-ol (0.500 g, 3.37 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a pale yellow oil (0.852 g, 75%).

$\nu_{\text{max}} \text{(neat)/cm}^{-1}$ 3277 (NH), 1780 (C=O), 1724 (C=O); $\delta_H$ (400.15 MHz; CDCl$_3$) 8.25 (1H, bs, NH), 7.26-7.14 (5H, m, H1,H2,H3), 5.85-5.74 (1H, m, H7), 5.47-5.42 (1H, m, H6) 5.29-5.19 (2H, m, H8), 3.01 (1H, dd, $J$ 14.0, 7.2Hz, H5), 2.91 (1H, dd, $J$ 14.0,
6.4Hz, H5); δC (100.62 MHz; CDCl3) 157.2 (q, C9 or C10), 148.9 (q, C9 or C10), 140.2 (q, C4), 136.3 (CH, C7) 128.4 (2 x CH, C2), 127.9 (2 x CH, C3), 125.6 (CH, C1), 118.8 (CH2, C8), 78.2 (CH, C6), 38.6 (CH2, C5).

5-Ethyl-4-iodomethyl-oxazolidin-2-one (147a)

Pent-1-en-3-ol (0.0345 g, 0.401 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a pale yellow powdery solid (0.0808 g, 79%, 4 : 1 d.r.).

mp 92.0-93.4 °C; ν max (nujol)/cm⁻¹ 3239 (NH), 1735 (C=O);

(Major isomer): δH (400.15 MHz; CDCl3) 7.02 (1H, bs, NH), 4.24-4.19 (1H, m, H3), 3.67-3.63 (1H, m, H4), 3.29-3.14 (2H, m, H5), 1.85-1.72 (2H, m, H2), 1.04 (3H, t, J 7.6Hz, H1); δC (100.62 MHz; CDCl3) 158.9 (q, C6), 83.7 (CH, C3), 57.8 (CH, C4), 28.0 (CH2, C2), 8.9 (CH3, Cl), 8.7 (CH2, C5).

(Minor isomer): δH (400.15 MHz; CDCl3) 6.63 (1H, bs, NH), 4.54-4.48 (1H, m, H3), 4.13-4.08 (1H, m, H4), 3.29-3.14 (2H, m, H5), 1.85-1.72 (2H, m, H2), 1.10 (3H, t, J 7.6Hz, H1); δC (100.62 MHz; CDCl3) 158.7 (q, C6), 81.1 (CH, C3), 57.2 (CH, C4), 21.9 (CH2, C2), 10.5 (CH3, C1), 4.2 (CH2, C5);

m/z (FAB) 255.9765 (M⁺, C6H10NO2I requires 255.9765) 256 (100%), 195 (11), 128 (7).
4-Iodomethyl-5-isopropyl-oxazolidin-2-one (147b)

4-Methyl-pent-1-en-3-01 (0.0416 g, 0.416 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a white solid (0.0851 g, 76%).

mp 104.0-106.0 °C; νmax (nujol)/cm⁻¹ 3235 (NH), 1703 (C=O); δ H (400.15 MHz; CDCl₃) 7.06 (1H, bs, NH), 3.96 (1H, dd, J 6.0, 4.0Hz, H3), 3.64-3.60 (1H, m, H4), 3.16 (2H, dd, J 6.4, 1.6Hz, H5), 1.92-1.81 (1H, m, H2), 0.94 (6H, dd, J 6.8, 1.2Hz, H1,H6); δC (100.62 MHz; CDCl₃) 159.1 (q, C7), 86.9 (CH, C3), 55.8 (CH, C4), 32.2 (CH, C2), 17.7 (CH₃, C1 or C6), 16.7 (CH₃, C1 or C6), 9.9 (CH₂, C5); m/z (FAB) 269.9991 (~, C₁₀N₀₂I requires 269.9991) 270 (100%), 214 (39), 209 (14).

5-allyl-4-iodomethyl-oxazolidin-2-one (147c)

1,5-Hexadiene-3-01 (0.0377 g, 0.384 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0738 g, 77%, 5 : 1 d.r.).

νmax (nujol)/cm⁻¹ 3273 (NH), 1749 (C=O), 1641 (C=C);
(Major isomer): δ H (400.15 MHz; CDCl₃) 7.25 (1H, bs, NH), 5.89-5.75 (1H, m, H2), 5.27-5.17 (2H, m, H1), 4.34 (1H, dt, J 6.0, 5.2Hz, H4), 3.71-3.66 (1H, m, H5), 3.27-3.19 (2H, d, J 2.4 Hz, H6), 2.54-2.50 (2H, m, H3); δC (100.62 MHz; CDCl₃) 158.9 (q,
C7), 131.0 (CH, C2), 120.0 (CH2, C1), 81.4 (CH, C4), 57.0 (CH, C5), 38.9 (CH2, C3), 9.2 (CH2, C6).

(Minor isomer): $\delta_H$ (400.15 MHz; CDCl3) 7.02 (1H, bs, NH), 5.89-5.75 (1H, m, H2), 5.27-5.17 (2H, m, H1), 4.72-4.65 (1H, dt, $J$ 8.0, 6.0 Hz, H4), 4.17-4.08 (1H, m, H5), 3.23 (2H, d, $J$ 4.0 Hz, H6), 2.65-2.46 (2H, m, H3); $\delta_C$ (100.62 MHz; CDCl3) 158.7 (q, C7), 132.2 (CH, C2), 118.9 (CH2, C1), 78.7 (CH, C4), 56.8 (CH, C5), 32.8 (CH2, C3), 4.1 (CH2, C6);

$m/z$ (FAB) 267.9832 ($M^+$, C6H10NO2I requires 267.9835) 268 (100%), 207 (10), 80 (10).

4-Iodomethyl-oxazolidin-2-one (147d)

Allylalcohol (0.0306 g, 0.528 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow solid (0.0875 g, 73%).

$\text{mp } 51-54 \degree C$ (lit. 52-54 \degree C)$^{165}$; $\nu_{\text{max}}$ (nujol)/cm$^{-1}$ 3252 (NH), 1761 (C=O); $\delta_H$ (400.15 MHz; CDCl3) 7.16 (1H, bs, NH), 4.51 (1H, t, $J$ 8.6 Hz, H3), 4.16-4.09 (2H, m, H2,H3), 3.31-2.59 (2H, m, H1); $\delta_C$ (100.62 MHz; CDCl3) 159.7 (q, C4), 70.6 (CH2, C3), 53.2 (CH, C2), 8.6 (CH2, C1); $m/z$ (FAB) 227.9522 ($M^+$, C6H10NO2I requires 227.9522) 228 (100%).

Data in agreement to that published by Knochel et al.$^{165}$
4-Iodomethyl-5-phenyl-oxazolidin-2-one (147e)

α-Vinylbenzyl alcohol (0.0541 g, 0.403 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0928 g, 76%, 3:1 d.r.).

$\nu_{\max}$ (nujol)/cm$^{-1} 3254$ (NH), 1751 (C=O);

(Major isomer): $\delta_{H}$ (400.15 MHz; CDCl$_3$) 7.41-7.26 (5H, m, H1,H2,H3), 5.25 (1H, d, J 4.8Hz, H5), 3.90-3.87 (1H, m, H6), 3.35 (2H, d, J 5.6Hz, H7); $\delta_{C}$ (100.62 MHz; CDCl$_3$) 158.7 (q, C8), 137.8 (q, C4), 128.9 (4 x CH, C2,C3), 125.7 (CH, C1), 83.1 (CH, C5), 61.0 (CH, C6), 8.1 (CH$_2$, C7).

(Minor isomer): $\delta_{H}$ (400.15 MHz; CDCl$_3$) 7.41-7.26 (5H, m, H1,H2,H3), 5.71 (1H, d, J 7.6Hz, H5), 4.40-4.35 (1H, m, H6), 3.35 (2H, d, J 5.6Hz, H7); $\delta_{C}$ (100.62 MHz; CDCl$_3$) 158.7 (q, C8), 133.1 (q, C4), 129.2 (4 x CH, C2,C3), 126.1 (CH, C1), 80.2 (CH, C5), 58.4 (CH, C6), 6.3 (CH$_2$, C7);

$m/z$ (FAB) 303.9756 (M$^+\text{C}_{10}\text{H}_{10}\text{NO}_2\text{l}$ requires 303.9756) 304 (100%), 243 (12).

(2,2,2-Trichloro-acetyl)-carbamic acid pent-2-enyl ester (148a)

Cis-2-pentene-1-ol (0.500 g, 5.81 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a pale yellow oil (1.19 g, 75%).

$\nu_{\max}$ (neat)/cm$^{-1} 3273$ (NH), 1781 (C=O), 1722 (C=O); $\delta_{H}$ (400.15 MHz; CDCl$_3$) 8.53 (1H, bs, NH), 5.77-5.68 (1H, m, H4), 5.57-5.48 (1H, m, H3), 4.79 (2H, d, J 6.8Hz, H5),

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2.19-2.09 (2H, m, H2), 0.99 (3H, t, J 7.8Hz, H1); δc (100.62 MHz; CDCl3) 157.2 (q, C6 or C7), 149.2 (q, C6 or C7), 138.4 (CH, C4), 120.6 (CH, C3), 62.4 (CH2, C5), 20.4 (CH2, C2), 13.5 (CH3, C1); m/z (FAB) 274.9700 (M+, C8H16NO3Cl3 requires 274.9697) 297 (17%), 275 (9), 158 (8).

(2,2,2-Trichloro-acetyl)-carbamic acid hept-2-enyl ester (148b)

\[
\begin{align*}
\text{C} & \quad \text{O} \\
\text{H} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]

Trans-2-heptene-1-ol (0.500 g, 4.38 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:1) to yield the title complex as a clear oil (1.06 g, 80%).

νmax (neat)/cm⁻¹: 3269 (NH), 1779 (C=O), 1720 (C=O); δH (400.15 MHz; CDCl3) 8.46 (1H, bs, NH), 5.93-5.83 (1H, m, H6), 5.64-5.55 (1H, m, H5), 4.68 (2H, d, J 6.6Hz, H7), 2.07 (2H, q, J 7.0 Hz), 1.43-1.27 (4H, m, H2, H3), 0.89 (3H, t, J 7.2Hz, H1); δc (100.62 MHz; CDCl3) 157.2 (q, C8 or C9), 149.1 (q, C8 or C9), 138.5 (CH, C6), 121.7 (CH, C5), 67.7 (CH2, C7), 31.4 (CH2, C4), 30.3 (CH2, C3), 21.7 (CH2, C2), 13.4 (CH3, C1); m/z (FAB) 302.0039 (M+, C10H14NO3Cl3 requires 302.0039) 323 (24%), 302 (8), 171 (7).

(2,2,2-Trichloro-acetyl)-carbamic acid 3-phenyl-allyl ester (148c)

\[
\begin{align*}
\text{C} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]

Cinnamyl alcohol (0.600 g, 4.47 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a white powdery solid (1.23 g, 85%).
mp 210.3-213.1 °C; \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 3246 (NH), 1774 (C=O), 1720 (C=O); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 8.42 (1H, bs, NH), 7.45-7.26 (5H, m, ArH), 6.77 (1H, d, J 16.0Hz, H5), 6.33 (1H, dt, J 16.0, 6.2Hz, H6), 4.94 (2H, d, J 6.2Hz, H7); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 157.1 (q, C8 or C9), 149.0 (q, C8 or C9), 135.9 (CH, C5), 135.2 (q, C4), 128.2 (2 x CH, C2), 128.1 (CH, C1), 126.3 (2 x CH, C3), 120.7 (CH, C6), 67.5 (CH\(_2\), C7); \( m/z \) (FAB) 321.9726 (M\(^+\), C\(_{12}\)H\(_{10}\)NO\(_3\)Cl\(_3\) requires 321.9726) 343 (18%), 322 (10), 118 (6).

4-(1-Iodo-propyl)-oxazolidin-2-one (149a)

Cis-pent-2-en-1-ol (0.0439 g, 0.510 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow crystalline solid (0.0937 g, 72%).

mp 86.6-87.8 °C; \( \nu_{\text{max}} \) (nujol)/cm\(^{-1}\) 3264 (NH), 1746 (C=O); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 7.16 (1H, bs, NH), 4.51 (1H, t, J 8.8Hz, H5), 4.23 (1H, dd, J 8.8, 4.4Hz, H5), 4.01-3.96 (2H, m, H3,H4), 1.84-1.71 (2H, m, H2), 1.08 (3H, t, J 7.2Hz, H1); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 160.0 (q, C6), 69.3 (CH\(_3\), C5), 57.6 (CH, C4), 42.8 (CH, C3), 28.1 (CH\(_2\), C2), 14.6 (CH\(_3\), C1); \( m/z \) (FAB) 255.9839 (M\(^+\), C\(_6\)H\(_9\)NO\(_2\)I requires 255.9838) 256 (100%), 195 (7).
4-(1-Iodo-pentyl)-oxazolidin-2-one (149b)

Hept-2-en-1-ol (0.0717 g, 0.628 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as white needles (0.132 g, 74%).

mp 105.8-107.8 °C; \( \nu_{\text{max}} \) (nujol)/cm\(^{-1}\) 3259 (NH), 1742 (C=O); \( \delta \)\( \text{H} \) (400.15 MHz; CDCl\(_3\)) 7.58 (1H, bs, NH), 4.53-4.49 (1H, m, H7), 4.20-4.16 (1H, m, H7), 4.03-3.97 (2H, m, H5,H6), 1.74-1.69 (2H, m, H4), 1.63-1.51 (1H, m, H3), 1.45-1.29 (3H, m, H3,H2) 0.92 (3H, t, \( J \) 8.0Hz, H1); \( \delta \)\( \text{C} \) (100.62 MHz; CDCl\(_3\)) 160.2 (q, C8), 71.2 (CH\(_2\), C7), 58.0 (CH, C6), 40.7 (CH, C5), 35.0 (CH\(_2\), C4), 31.3 (CH\(_2\), C3), 21.8 (CH\(_2\), C2), 13.9 (CH\(_3\), C1); m/z (FAB) 284.0148 (M\(^+\), C\(_8\)H\(_{14}\)NO\(_2\)I requires 284.0148) 284 (100%), 223 (5).

1-Allyl-4-iodomethyl-imidazolidin-2-one (153)

Diallylamine (0.0442 g, 0.455 mmol) was subjected to the general iodoamination cyclisation conditions. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0920 g, 76%).

\( \nu_{\text{max}} \) (nujol)/cm\(^{-1}\) 3272 (NH), 1765 (C=O); \( \delta \)\( \text{H} \) (400.15 MHz; CDCl\(_3\)) 6.48 (1H, bs, NH), 5.80-5.70 (1H, m, H2), 5.24-5.19 (2H, m, H1), 3.92-3.85 (1H, m, H5), 3.78 (2H, d, \( J \) 6.0Hz, H3), 3.54 (1H, t, \( J \) 9.2Hz, H4), 3.26-3.10 (3H, m, H4,H6); \( \delta \)\( \text{C} \) (100.62 MHz; CDCl\(_3\)) 161.2 (q, C7), 132.9 (CH, C2), 117.9 (CH\(_2\), C1), 50.9 (CH, C5), 50.8 (CH\(_2\), C3), 46.0 (CH\(_2\), C4), 10.2 (CH\(_2\), C6); m/z (FAB) 266.9997 (M\(^+\), C\(_8\)H\(_{16}\)NO\(_2\)I requires 266.9994) 267 (100%), 266 (13), 265 (15).
α-Vinylbenzyl alcohol (0.0541 g, 0.403 mmol) was subjected to the general palladium (II) catalyzed chloroamination cyclisation. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as an off-white powder (0.0563 g, 66%).

mp 125.1-128.4 °C; v_{max} (nujol)/cm^{-1} 3285 (NH), 1751 (C=O), 1023 (CO); δ_{H} (400.15 MHz; CDCl₃) 7.44-7.35 (5H, m, ArH), 7.10 (1H, bs, NH), 5.37 (1H, d, J 4.8Hz, H5), 4.02-3.98 (1H, m, H6), 3.67 (2H, d, J 5.6Hz, H7); δ_{C} (100.62 MHz; CDCl₃) 159.1 (q, C8), 137.9 (q, C4), 129.2 (CH, C1), 129.1 (2 x CH, C2), 125.6 (2 x CH, C3), 80.8 (CH, C5), 61.2 (CH, C6), 45.4 (CH₂, C7); m/z (FAB) 212.0479 (M'ClOHN0₂Cl requires 212.0478) 214 (33%), 212 (100).

Carbamic acid 3-phenyl-allyl ester (155)

To a solution of carbamic acid 1-phenyl-allyl ester (0.200 g, 1.13 mmol) in dry THF was added palladium diacetate (0.0127 g, 0.0564 mmol) and lithium chloride (0.958 g 2.26 mmol) as a single portion. Stirring was started at the reaction monitored by TLC. Upon consumption of the starting material the solvent was removed via rotary evaporation and the crude product purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a clear oil (0.120 g, 60%).

v_{max} (nujol)/cm^{-1} 3409 (NH₂), 3331 (NH₂), 1682 (C=O), 1608 (C=C); δ_{H} (400.15 MHz; CDCl₃) 7.33-7.16 (5H, m, ArH), 6.58 (1H, d, J 16.0Hz, H5), 6.22 (1H, dt, J 16.0, 6.4Hz, H6), 4.71 (2H, bs, NH₂), (2H, dd, J 6.4, 1.6Hz, H7); δ_{C} (100.62 MHz; CDCl₃).
4-Chloromethyl-5-vinyl-oxazolidin-2-one (157)

1,4-Pentadiene-3-ol (0.0309 g, 0.367 mmol) was subjected to the general palladium (II) catalyzed chloroamination cyclisation. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0385 g, 65%, 12:1 d.r.).

$\nu_{\text{max}}$ (nujol)/cm$^{-1}$: 3286 (NH), 1751 (C=O), 1240 (CO);

(Major isomer): $\delta_{H}$ (400 MHz; CDCl$_3$) 6.63 (1H, bs, NH), 5.97-5.89 (1H, m, H2), 5.48 (1H, dt, $J$ 16.8, 1.2Hz H$_{1\text{trans}}$), 5.36 (1H, dt, $J$ 10.4, 1.2Hz, H$_{1\text{cis}}$), 4.83-4.79 (1H, m, H3), 3.84 (1H, q, $J$ 5.6Hz, H4), 3.60 (2H, d, $J$ 5.6Hz, H5); $\delta_{C}$ (100 MHz; CDCl$_3$) 158.6 (q, C6), 133.7 (CH, C2), 119.3 (CH$_2$, C1), 80.2 (CH, C3), 58.8 (CH, C4), 45.2 (CH$_2$, C5).

(Minor isomer): $\delta_{H}$ (400.15 MHz; CDCl$_3$) 6.63 (1H, bs, NH), 5.97-5.89 (1H, m, H2), 5.56 (1H, dt, $J$ 16.8, 1.2Hz H$_{1\text{trans}}$), 5.44 (1H, dt, $J$ 10.4, 1.2Hz, H$_{1\text{cis}}$), 5.19-5.14 (1H, m, H3), 4.17-4.11 (1H, m, H4), 3.60 (2H, d, $J$ 5.6Hz, H5); $\delta_{C}$ (100.62 MHz; CDCl$_3$) 158.6 (q, C6), 129.23 (CH, C2), 121.3 (CH$_2$, C1), 79.1 (CH, C3), 56.8 (CH, C4), 43.9 (CH$_2$, C5);

$m/z$ (FAB) 162.0321 ($M^+$, C$_8$H$_7$NO$_2$Cl requires 162.0322) 164 (33%) 162 (100), 149 (21), 120 (5), 118 (10).
5-Allyl-4-chloromethyl-oxazolidin-2-one (158a)

1,5-Hexadiene-3,4-diol (0.0377 g, 0.384 mmol) was subjected to the general palladium (II) catalyzed chloroamination cyclisation. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0674 g, 62%).

$\nu_{\text{max}}$ (nujol)/cm$^{-1}$ 3300 (NH), 1751 (C=O), 1240 (CO); $\delta_H$ (400.15 MHz; CDCl$_3$) 6.70 (1H, bs, NH), 5.82-5.71 (1H, m, H2), 5.26-5.19 (2H, m, H1), 4.50-4.45 (1H, m, H4), 3.82 (1H, q, $J$ 6.0Hz, H5), 3.54 (2H, d, $J$ 6.0Hz, H6), 2.58-2.46 (2H, m, H3); $\delta_C$ (100.62 MHz; CDCl$_3$) 159.4 (q, C7), 130.5 (CH, C2); 120.4 (CH$_2$, C1), 79.4 (CH, C4), 57.4 (CH, C5), 45.5 (CH$_2$, C6), 38.8 (CH$_2$, C3); $m/z$ (FAB) 176.0477 ($M^+$, C$_7$H$_{10}$NO$_2$Cl requires 176.0478) 178 (33%), 176 (100), 124 (5), 122 (15).

Data in agreement with that published by Bach et al.$^{166}$

4-Chloromethyl-5-ethyl-oxazolidin-2-one (158b)

Pent-1-en-3-ol (0.0345 g, 0.401 mmol) was subjected to the general palladium (II) catalyzed chloroamination cyclisation. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a yellow oil (0.0453 g, 69%).

$\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3295 (NH), 1749 (C=O), 1024 (CO); $\delta_H$ (400.15 MHz; CDCl$_3$) 6.96 (1H, bs, NH), 4.38-4.31 (1H, m, H3), 3.77-3.72 (1H, m, H4), 3.61-3.51 (2H, m, H5), 1.85-1.69 (2H, m, H2), 1.04 (3H, t, $J$ 7.4Hz, H1); $\delta_C$ (100.62 MHz; CDCl$_3$) 159.2 (q,
4-Chloromethyl-5-isopropyl-oxazolidin-2-one (158c)

4-Methyl-pent-1-en-3-ol (0.0416 g, 0.416 mmol) was subjected to the general palladium (II) catalyzed chloroamination cyclisation. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a colourless solid (0.0539 g, 73%).

mp 66-70 °C (lit. 65-67 °C)\(^{166}\); \(\nu_{\text{max}}\) (nujol)/cm\(^{-1}\) 3279 (NH), 1735 (C=O), 1240 (CO);
\(\delta_{\text{H}}\) (400.15 MHz; CDCl\(_3\)) 6.92 (1H, bs, NH), 4.16 (1H, dd, \(J\) 6.4, 4.4Hz, H3), 3.86-3.82 (1H, m, H4), 3.55 (2H, d, \(J\) 5.6Hz, H5), 1.94 (1H, dq, \(J\) 7.2, 6.4Hz, H2), 1.01 (6H, d, \(J\) 7.2Hz, H1,H6); \(\delta_{\text{C}}\) (100.62 MHz; CDCl\(_3\)) 159.6 (q, C7), 84.8 (CH, C3), 56.0 (CH, C4), 46.3 (CH\(_2\), C5), 32.2 (CH, C2), 17.3 (CH\(_3\), C1 or C6), 16.7 (CH\(_3\), C1 or C6).

Data in agreement with that published by Bach et al.\(^{166}\)

4-Chloromethyl-5-phenethyl-oxazolidin-2-one (158d)

5-phenyl-pent-1-en-3-ol (0.100 g, 0.000616 mmol) was subjected to the general palladium (II) catalyzed chloroamination cyclisation. The crude product was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:2) to yield the title complex as a colourless oil (0.108 g, 73%).
\[ \nu_{\text{max}} \text{(neat)/cm}^{-1} \ 3278 \text{ (NH)}, \ 1750 \text{ (C=O)}; \ \delta_H \text{ (400.15 MHz; CDCl}_3) \ 7.25-7.12 \text{ (5H, m, ArH)}, \ 6.66 \text{ (1H, bs, NH)}, \ 4.33-4.26 \text{ (1H, m, H7)}, \ 3.70-3.65 \text{ (1H, m, H8)}, \ 3.51-3.39 \text{ (2H, m, H9)}, \ 2.83-2.62 \text{ (2H, m, H5)}, \ 2.09-1.85 \text{ (2H, m, H6)}; \ \delta_C \text{ (100.62 MHz; CDCl}_3) \]

Missing q C10, 140.2 (q, C4), 128.6 (2 x CH, C3), 128.5 (2 x CH, C2), 126.4 (CH, C1), 79.6 (CH, C7), 58.5 (CH, C8), 45.6 (CH2, C9) 36.8 (CH2, C6) 30.8 (CH2, C5); m/z (FAB) 240.0791 (M+, C12H14NO2Cl requires 240.0791) 242 (34%), 240 (100), 122 (7), 120 (10).

Data in agreement with that published by Bach et al.\textsuperscript{166}

\textbf{Carbamic acid pent-2-enyl ester (172)}

![Structure of Carbamic acid pent-2-enyl ester](image)

To a solution of carbamic acid 1-ethyl-allyl ester (0.150g, 1.16 mmol) in dry THF was added palladium diacetate \((0.0127 \text{ g, 0.0564 mmol})\) and lithium chloride \((0.958 \text{ g 2.26 mmol})\) as a single portion. Stirring was started at the reaction monitored by TLC. Upon consumption of the starting material the solvent was removed via rotary evaporation and the crude product purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the \textit{title complex} as a white crystalline solid \((0.087 \text{ g, 58%})\).

mp 95.3-96.7 °C; \(\nu_{\text{max}}\) (nujol)/cm\(^{-1}\) 3427 (NH2), 3325 (NH2), 1696 (C=O); \(\delta_H\) (400.15 MHz; CDCl\(_3\)) 5.67-5.59 (1H, m, H4), 5.52-5.44 (1H, m, H3), 4.75 (2H, d, \(J\ 7.2\text{Hz, H5)}), 2.17-2.05 (2H, m, H2), 1.05 (3H, t, \(J\ 8.0\text{Hz, H1)}); \(\delta_C\) (100.62 MHz; CDCl\(_3\)) 156.3 (q, C6) 135.6 (CH, C4), 122.8 (CH, C3), 65.2 (CH2, C5), 23.4 (CH2, C2), 14.1 (CH3, C1).

Data in agreement with that published by Hiemstra et al.\textsuperscript{167}
2,2,2-Trichloro-N-penta-2,4-dienyl-acetamide (175)

(2,2,2-Trichloro-acetyl)-carbamic acid 1-vinyl-allyl ester (0.0500 g, 0.183 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 20 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white powdery solid (0.0386 g, 92%).

mp 46.7-48.2 °C; \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 3296 (NH), 1700 (C=O); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 6.30-6.19 (2H, m, H3, H4), 5.75-5.68 (1H, m, H2), 5.21-5.17 (1H, m, H1), 5.10-5.06 (1H, m, H1), 4.58 (2H, bs, NH\(_2\)), 4.53 (2H, d, J 6.8Hz, H5); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 161.8 (q, C6), 135.9 (CH, C2), 134.4 (CH, C3), 127.4 (CH, C4), 118.6 (CH\(_2\), C1), 46.2 (CH\(_2\), C5).

No mass ion observed

2,2,2-Trichloro-N-penta-2-enyl-acetamide (178a)

(2,2,2-Trichloro-acetyl)-carbamic acid 1-ethyl-allyl ester (0.0500 g, 0.182 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 20 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white powdery solid (0.0412 g, 98%).

mp 49.3-51.4 °C; \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 3233 (NH), 1696 (C=O); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 6.69 (1H, bs, NH), 5.83-5.73 (1H, m, H4), 5.53-5.44 (1H, m, H3), 3.94 (2H, t, J 5.8Hz, H5), 2.14-2.03 (2H, m, H2), 1.02 (3H, t, J 7.4Hz, H1); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 160.6 (q, C6), 138.8 (CH, C4), 126.1 (CH, C3), 44.6 (CH\(_2\), C5), 25.8(CH\(_2\), C2), 14.0 (CH\(_3\), C1); \( m/z \) (FAB) 229.9828 (M\(^+\), C\(_7\)H\(_{10}\)NOCl\(_3\) requires 229.9828) 232 (53%) 230 (92), 228 (31), 162 (21), 145 (100).
(2,2,2-Trichloro-acetyl)-carbamic acid 1-isopropyl-allyl ester (0.0500 g, 0.173 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 10 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white powdery solid (0.0400 g, 95%). mp 45.1-47.3 °C; ν_{max} (neat)/cm^{-1} 3228 (NH), 1693 (C=O); δ_H (400.15 MHz; CDCl₃) 6.72 (1H, bs, NH), 5.69 (1H, dd, J 15.4, 5.4Hz, H3), 5.43 (1H, dt, J 15.4, 6.0Hz, H4), 3.93 (2H, t, J 6.0Hz, H5), 2.38-2.24 (1H, m, H2), 1.00 (6H, d, J 7.2Hz, H1,H7); δ_C (100.62 MHz; CDCl₃) 162.0 (q, C6), 142.5 (CH, C4), 120.7 (CH, C3), 43.4 (CH₂, C5), 30.8 (CH, C2), 22.1 (2 x CH₃, C1,C7); m/z (FAB) 243.9990 (M⁺, C₉H₁₁NOCI₃ requires 243.9985) 246 (64%), 244 (90), 242 (37), 167 (25), 149 (100), 113 (19).

(2,2,2-Trichloro-acetyl)-carbamic acid 1-phenyl-allyl ester (0.0500 g, 0.155 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 20 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a yellow oil (0.0397 g, 92%). ν_{max} (nujol)/cm^{-1} 3230 (NH), 1691 (C=O); δ_H (400.15 MHz; CDCl₃) 7.34-7.19 (5H, m, ArH), 6.54 (1H, d, J 15.9Hz, H5), 6.28 (1H, dt, J 15.9, 5.8Hz, H6) 4.92 (1H, bs, NH), 4.24 (2H, d, J 5.8Hz, H7); δ_C (100.62 MHz; CDCl₃) Missing q C8, 136.7 (q, C4), 131.5 (CH, C5) 128.5 (2 x CH, C2), 128.2 (CH, C1 or C6) 127.8 (CH, C1 or C6), 126.8 (2 x CH, C3), 63.4 (CH₂, C7).
2,2,2-Trichloro-N-[3-(4-nitro-phenyl)-allyl]-acetamide (178d)

(2,2,2-Trichloro-acetyl)-carbamic acid 1-(4-nitro-phenyl)-allyl ester (0.0500 g, 0.136 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 20 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a orange oil (0.0352 g, 80%).

\[
\begin{align*}
\text{V}_{\text{max}} \text{ (nujol)/cm}^{-1} &\quad 3236 \text{ (NH), 1697} \text{ (C=O); } \\
\delta_{\text{H}} \text{ (400.15 MHz; CDCl}_3) &\quad 8.18 \text{ (2H, d, } J 7.6 \text{Hz, C2), 7.51} \text{ (2H, d, } J 8.2 \text{Hz, C3), 7.04} \text{ (1H, bs, NH), 6.67} \text{ (1H, d, } J 15.8 \text{Hz, C5), } \\
&\quad 6.41 \text{ (1H, dt, } J 15.8, 5.8 \text{Hz, H6), 4.22} \text{ (2H, t, } J 5.8 \text{Hz, H7); } \\
&\quad \delta_{\text{C}} \text{ (100.62 MHz; CDCl}_3) \\
&\quad 161.6 \text{ (q, C8), 146.8} \text{ (q, C1), 142.0} \text{ (q, C4), 130.6} \text{ (CH, C5), 127.9} \text{ (CH, C6), 126.6} \text{ (2 x CH, C3), 123.6} \text{ (2 x CH, C2), 42.6} \text{ (CH}_2\text{, C7);} \\
&\quad m/z \text{ (FAB) 322.9680 (M}^+\text{, C}_{11}\text{H}_{9}\text{N}_{2}\text{O}_{3}\text{Cl}_3 \text{ requires 322.9679) 323 (69%), 321 (86), 163 (35), 144 (100). }
\end{align*}
\]

2,2,2-Trichloro-N-(5-phenyl-pent-2-enyl)-acetamide (178e)

(2,2,2-Trichloro-acetyl)-carbamic acid 1-(3-phenylethane)-allyl ester (0.0500 g, 0.143 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 20 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white/yellow solid (0.0393 g, 90%).
mp 121.3-124.0 °C; \( v_{\text{max}} \) (neat)/cm\(^{-1}\) 3230 (NH), 1689 (C=O); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 7.31-7.23 (2H, m, ArH), 7.22-7.12 (3H, m, ArH), 6.61 (1H, bs, NH), 5.79-5.69 (1H, m, H7), 5.53-5.43 (1H, m, H8), 3.90 (2H, t, \( J \) 6.0Hz, H9), 2.70 (2H, t, \( J \) 7.6Hz, H5), 2.38 (2H, q, \( J \) 7.6Hz, H6); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 161.1 (q, C10), 140.8 (q, C4), 134.0 (CH, C8), 128.0 (2 x CH, C3 or C2), 127.9 (2 x CH, C3 or C2), 125.5 (CH, C1), 124.0 (CH, C7), 42.7 (CH\(_2\), C9), 34.8 (CH\(_2\), C5), 33.4 (CH\(_2\), C6); m/z (FAB) 306.0225 (M\(^+\), C\(_{13}\)H\(_{14}\)NOCl\(_3\) requires 306.0219) 308 (46%), 306 (49), 289 (14), 253 (13), 251 (14).

**N-allyl-2,2,2-trichloro-acetamide (178f)**

\[ \begin{align*}
\text{O} & \quad \text{CCl}_3 \\
1 & \quad 2 \quad 3 \\
\end{align*} \]

(2,2,2-Trichloro-acetyl)-carbamic acid allyl ester (0.0500 g, 0.203 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 20 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the **title complex** as a white powdery solid (0.0366 g, 89%).

mp 29-31 °C (lit. 28-31 °C\(^{164}\); \( v_{\text{max}} \) (nujol)/cm\(^{-1}\) 3396 (NH), 1724 (C=O); \( \delta_H \) (400.15 MHz; CDCl\(_3\)) 6.87 (1H, bs, NH), 5.85-5.63 (1H, m, C2), 5.47-5.06 (2H, m, H1), 3.95 (2H, t, \( J \) 5.5Hz, H3); \( \delta_C \) (100.62 MHz; CDCl\(_3\)) 160.5 (q, C4), 132.1 (CH, C2), 116.7 (CH\(_2\), C1), 44.0 (CH\(_2\), C3).

Data in agreement with that published by Overman et al.\(^{169}\)

**2,2,2-Trichloro-N-(4-phenyl-but-2-enyl)-acetamide (178g)**

\[ \begin{align*}
\text{O} & \quad \text{CCl}_3 \\
1 & \quad 2 \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \quad 8 \\
\end{align*} \]

1-Phenyl-but-3-en-2-ol (0.0500 g, 0.149 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 15 mins. The crude
product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white powdery solid (0.0391 g, 90%).

mp 119.7-122.1 °C; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3335 (NH), 1696 (C=O); $\delta_{\text{H}}$ (400.15 MHz; CDCl$_3$) 7.38-7.17 (5H, m, ArH), 6.72 (1H, bs, NH), 5.93-5.86 (1H, m, H6), 5.60-5.54 (1H, m, H7), 3.97 (2H, t, $J$ 6.0Hz, H8), 3.40 (2H, d, $J$ 6.4Hz, H5); $\delta_{\text{C}}$ (100.62 MHz; CDCl$_3$) 162.1 (q, C9), 139.4 (q, C4), 133.9 (2 x CH, C2), 128.6 (3 x CH, C1,C3), 126.3 (CH, C7), 125.0 (CH, C6), 43.1 (CH$_2$, C8), 38.6 (CH$_2$, C5); m/z (FAB) 291.9985 (M$^+$, C$_{12}$H$_{12}$NOCl$_3$ requires 291.9985) 294 (54%), 292 (92), 147 (34), 144 (100), 132 (15).

2,2,2-Trichloro-N-(1-phenyl-allyl)-acetamide (179c)

(2,2,2-Trichloro-acetyl)-carbamic acid 3-phenyl-allyl ester (0.0500 g, 0.155 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 25 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:1) to yield the title complex as a pale yellow solid (0.00216 g, 5%).

mp 52.7-54.3 °C (lit. 56-58 °C)\textsuperscript{164}; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3257 (NH), 1689 (C=O); $\delta_{\text{H}}$ (400.15 MHz; CDCl$_3$) 7.41-7.25 (5H, m, ArH), 6.64 (1H, bs, NH), 6.20-5.98 (1H, m, H6), 5.64-5.54 (1H, m, H7), 5.30-5.08 (2H, m, H5); $\delta_{\text{C}}$ (100.62 MHz; CDCl$_3$) 159.2 (q, C8), 143.5 (q, C4), 128.6 (2 x CH, C2), 127.4 (2 x CH, C3), 126.3 (CH, C1), 134.7 (CH, C6), 116.2 (CH$_2$, C7), 50.3 (CH, C5).

Data in agreement with that published by Overman et al.\textsuperscript{169}
(2,2,2-Trichloro-acetyl)-carbamic acid cyclohex-2-enyl ester (180)

2-cyclohexene-1-ol (0.500 g, 5.09 mmol) was subjected to the general (2,2,2-trichloroacetyl)-carbamic acid formation procedure. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (2:1) to yield the title complex as a white solid (1.37 g, 94%).

mp 164.3-166.1 °C; $\nu_{\text{max}}$ (nujol)/cm$^{-1}$ 3271 (NH), 1779 (C=O), 1720 (C=O); $\delta_H$ (400.15 MHz; CDCl$_3$) 8.46 (1H, bs, NH), 6.06 (1H, dt, J 12.0, 6.0Hz, H4), 5.81-5.75 (1H, m, H5), 5.37-5.31 (1H, m, H3), 2.17-1.62 (6H, m, H1,H2,H6); $\delta_C$ (100.62 MHz; CDCl$_3$) 158.2 (q, C7 or C8), 149.8 (q, C7 or C8), 134.9 (CH, C4), 124.5 (CH, C5), 72.2 (CH, C3), 28.4 (CH$_2$, C2), 25.2 (CH$_3$, C6), 18.8 (CH$_2$, C1); $m/z$ (FAB) 285.9726 ($M^+$, C$_9$H$_{16}$NO$_2$Cl$_3$ requires 285.9726) 309 (38%), 307 (37), 286 (10).

2,2,2-Trichloro-N-cyclohex-2-enyl-acetamide (181)

(2,2,2-Trichloro-acetyl)-carbamic acid cyclohex-2-enyl ester (0.0500 g, 0.175 mmol) was subjected to the general [3,3] sigmatropic rearrangement conditions, microwaving at 100°C for 15 mins. The crude product was purified by flash silica chromatography eluting in cyclohexane-ethyl acetate (1:2) to yield the title complex as a white powdery solid (0.161 g, 95%).

mp 84.2-87.0 °C (lit. 85.5-87 °C)$^{154}$; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3226 (NH), 1689 (C=O); $\delta_H$ (400.15 MHz; CDCl$_3$) 6.59 (1H, bs, NH), 6.02-5.94 (1H, m, H4), 5.68-5.62 (1H, m, H3), 4.51-4.41 (1H, m, H5), 2.11-2.03 (2H, m, H2), 2.02-1.92 (1H, m, H6), 1.75-1.61 (3H, m, H1,H6); $\delta_C$ (100.62 MHz; CDCl$_3$) 160.6 (q, C7), 132.2 (CH, C4), 125.2 (CH,
C3), 46.2 (CH, C5), 26.3 (CH2, C6), 21.4 (CH2, C2), 18.8 (CH2, C1); m/z (FAB) 241.9901 (M+, C6H10NOCl3 requires 241.9906) 242 (6%), 167 (26), 149 (100), 113 (21), 95 (11).

Data in agreement with that published by Overman et al.169

cis-Cinnamyl alcohol (182)

3-phenyl-prop-2-yn-1-01 (0.300 g, 2.27 mmol) and Lindlar's catalyst (0.0600 g) were vigorously stirred in toluene (20 ml) at 0 °C under a hydrogen atmosphere monitoring by TLC. When the reaction was complete the mixture was concentrated in vacuo and purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:4) to yield the title complex as a yellow oil (0.151 g, 50%).

\( \nu_{\text{max}} \) (nujol)/cm\(^{-1}\) 3331 (OH); \( \delta_{\text{H}} \) (400.15 MHz; CDCl3) 7.57-7.22 (5H, m, H1, H2, H3), 6.58 (1H, d, J 11.8 Hz, H5), 5.90 (1H, dt, J 11.8, 6.4 Hz, H6), 4.46 (2H, dd, J 6.4, 1.7 Hz, H7), 2.75 (1H, bs, OH); \( \delta_{\text{C}} \) (100.62 MHz; CDCl3) 136.6 (q, C4), 131.2 (CH, C5 or C6), 130.7 (CH, C5 or C6), 128.8 (2 x CH, C2), 128.5 (2 x CH, C3), 126.5 (CH, C1), 59.6 (CH2, C7).

Data in agreement with that published by Denis et al.170

3-Phenyl-prop-2-yn-1-ol (184)

To a flame dried RBF (50 ml) was added phenylacetylene (1.00 g, 9.77 mmol) in THF (10 ml) under a nitrogen atmosphere. The reaction flask was cooled to 0 °C and \( \text{^t} \)butyl lithium (0.626 g, 9.77 mmol) added dropwise. The reaction was stirred at 0 °C for 30 mins. Paraformaldehyde (0.586 g, 19.5 mmol) was then added and the reaction
gradually warmed to rt. monitoring by TLC. When the reaction was complete, water was slowly added to kill excess butyl lithium followed by an extraction with diethyl ether. The combined organic layers were dried over MgSO₄, filtered, concentrated in vacuo and purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (1:4) to yield the title complex as a yellow/orange oil (1.17 g, 91%).

\n
\[ v_{\text{max}} \ (\text{nujol})/\text{cm}^{-1} \]

\[ 3334 \ (\text{OH}), \ 2237 \ (\text{C}-\text{C}, \text{alkyne}); \]

\[ \delta_{\text{H}} \ (400.15 \text{ MHz; CDCl}_3) \]

\[ 7.33-7.28 \ (2\text{H, m, H3}), \ 7.22-7.15 \ (3\text{H, m, H1, H2}), \ 4.37 \ (2\text{H, s, H7}), \ 2.14 \ (1\text{H, bs, OH}); \]

\[ \delta_{\text{C}} \ (100.62 \text{ MHz; CDCl}_3) \]

\[ 131.7 \ (2 \times \text{CH, C3}), \ 128.5 \ (\text{CH, C1}), \ 128.4 \ (2 \times \text{CH, C2}), \ 122.6 \ (q, \text{C4}), \ 87.3 \ (q, \text{C5 or C6}), \ 85.6 \ (q, \text{C5 or C6}), \ 51.6 \ (\text{CH}_2, \text{C7}). \]

Data in agreement with that published by Denis et al.¹⁷⁰

(2,2,2-Trichloro-acetyl)-carbamic acid 3-phenyl-allyl ester (185)

\begin{center}
\includegraphics[width=0.2\textwidth]{structure}
\end{center}

To a solution of dichloromethane (20 ml) was added 3-phenyl-prop-2-en-1-ol (0.100 g, 0.746 mmol). The reaction was cooled to 0 °C upon which trichloroacetyl isocyanate (0.169 g, 0.895 mmol) was added drop wise. Once addition was complete the reaction was gradually warmed to rt. monitoring by thin layer chromatography. When the reaction was complete the mixture was concentrated in vacuo to yield the title complex as a cream/yellow solid (0.219 g, 91%).

\[ \text{mp} \ 208.7-209.9 \text{ °C}; \]

\[ v_{\text{max}} \ (\text{nujol})/\text{cm}^{-1} \]

\[ 3210 \ (\text{NH}), \ 1773 \ (\text{C}=\text{O}), \ 1692 \ (\text{C}=\text{O}), \]

\[ \delta_{\text{H}} \ (400.15 \text{ MHz; CDCl}_3) \]

\[ 7.35-7.12 \ (5\text{H, m, H1, H2, H3}), \ 6.71 \ (1\text{H, d, J} \ 11.6\text{Hz, H5}), \ 5.79 \ (1\text{H, dt, J} \ 11.6, 6.8\text{Hz, H6}), \ 4.97 \ (2\text{H, dd, J} \ 6.8, 1.6\text{Hz, H7}); \]

\[ \delta_{\text{C}} \ (100.62 \text{ MHz; CDCl}_3) \]

\[ 157.7 \ (q, \text{C8 or C9}), \ 149.5 \ (q, \text{C8 or C9}), \ 135.5 \ (q, \text{C4}), \ 131.2 \ (\text{CH, C5 or C6}), \ 130.7 \ (\text{CH, C5 or C6}), \ 128.8 \ (2 \times \text{CH, C2}), \ 128.5 \ (2 \times \text{CH, C3}), \ 127.9 \ (\text{CH, C1}), \ 64.1 \ (\text{CH}_2, \text{C7}); \]

\[ m/z \ (\text{FAB}) \]

\[ 321.9726 \ (M^+, \text{C}_{12}\text{H}_{10}\text{NO}_3\text{Cl}_3 \text{ requires} \ 321.9726) \ 343 \ (32%), \ 322 \ (20), \ 118 \ (15). \]

155
Cyclopent-2-enol (187)

Cyclopentenone (0.500 g, 6.09 mmol) was dissolved in a 0.4 M cerium (III) chloride heptahydrate methanol solution (15 ml) and sodium borohydride (0.230 g, 6.09 mmol) slowly added with stirring. The reaction was monitored by thin layer chromatography. Upon consumption of the starting material water (20 ml) was added very slowly and the reaction mixture stirred for a further 10 minutes. The reaction mixture was then extracted with ether (3 x 25 ml) and water (3 x 25 ml), the organic layers collected, dried with MgSO₄, filtered, concentrated in vacuo and purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a colourless oil (0.476 g, 93%).

ν<sub>max</sub> (nujol)/cm⁻¹ 3401 (OH), 1598 (C=C); δ<sub>H</sub> (400.15 MHz; CDCl₃) 6.12-6.09 (1H, m, H₁ or H₂), 5.83-5.80 (1H, m, H₁ or H₂), 5.71-5.66 (1H, m, H₅), 2.55-2.46 (1H, m, H₃ or H₄), 2.34-2.24 (2H, m, H₃ or H₄), 1.84-1.77 (1H, m, H₃ or H₄); δ<sub>C</sub> (100.62 MHz; CDCl₃) 137.6 (CH, C₁ or C₂), 129.3 (CH, C₁ or C₂), 80.5 (CH, C₅), 31.1 (CH₂, C₃ or C₄) 29.8 (CH₂, C₃ or C₄).

Data in agreement with that published by Luche et al.<sup>171</sup>

5-Phenyl-pent-2-enylamine (190a)

2,2,2-Trichloro-N-(5-phenyl-pent-2-enyl)-acetamide (0.150 g, 0.489 mmol) was dissolved in methanol (20 ml) and the solution cooled to 0 °C upon which Zinc/Copper couple (excess) was added and the cooling bath removed. The mixture was then stirred at room temperature for 3-4 h, monitoring by TLC. Upon consumption of starting material excess Zn/Cu couple was filtered off, the methanol removed via rotary evaporation, an aqueous extraction performed with ethyl acetate and the organic layers
collected. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo to yield the crude product which was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a pale yellow oil (0.0694 g, 88%).

\[ \text{v}_{\text{max}} \text{(neat)/cm}^{-1} 3283 (\text{NH}), 3082 (\text{NH}), 1649 (\text{C} = \text{C}); \delta_{\text{H}} (400.15 \text{ MHz; CDCl}_3) 7.33-7.25 (2\text{H, m, H2}), 7.20-7.13 (3\text{H, m, H1, H3}), 5.68-5.60 (1\text{H, m, H7 or H8}), 5.49-5.41 (1\text{H, m, H7 or H8}) 3.78 (2\text{H, t, J 6.0Hz, H9}), 2.68 (2\text{H, t, J 7.2Hz, H5}), 2.37-2.30 (2\text{H, m, H6}); \delta_{\text{C}} (100.62 \text{ MHz; CDCl}_3) 141.6 (\text{q, C4}), 132.7 (\text{CH, C7}), 128.5 (2 \times \text{CH, C2 or C3}), 128.3 (2 \times \text{CH, C2 or C3}), 126.4 (\text{CH, C8}), 125.9 (\text{CH, C1}), 41.5 (\text{CH}_2 \text{ C9}), 35.5 (\text{CH}_2, \text{C5}), 34.0 (\text{CH}_2, \text{C6}). \]

No mass ion observed.

Allylamine (190b)

\[
\begin{align*}
\begin{array}{c}
1 \\
2 \\
3 \\
\end{array}
\end{align*}
\text{NH}_2
\]

N- Allyl-2,2,2-trichloro-acetamide (0.100 g, 0.494 mmol) was dissolved in methanol (20 ml) and the solution cooled to 0 °C upon which Zinc/Copper couple (excess) was added and the cooling bath removed. The mixture was then stirred at room temperature for 3-4 h, monitoring by TLC. Upon consumption of starting material excess Zn/Cu couple was filtered off, the methanol removed via rotary evaporation, an aqueous extraction performed with ethyl acetate and the organic layers collected. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo to yield the crude product which was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (4:1) to yield the title complex as a clear oil (0.0282 g, 86%).

\[ \text{v}_{\text{max}} \text{(neat)/cm}^{-1} 3396 (\text{NH}), 3082 (\text{NH}), 1643 (\text{C} = \text{C}); \delta_{\text{H}} (400.15 \text{ MHz; CDCl}_3) 5.70-5.58 (1\text{H, m, H2}), 5.12-4.98 (2\text{H, m, H1}), 4.58 (1\text{H, bs, NH2}), 3.52-3.47 (2\text{H, m, H3}); \delta_{\text{C}} (100.62 \text{ MHz; CDCl}_3) 140.0 (\text{CH, C2}), 113.5 (\text{CH}_2, \text{C1}), 44.8 (\text{CH}_2, \text{C3}). \]

Data in agreement with that published by Aldrich.\textsuperscript{172}
Cyclohex-2-enylamine (190c)

2,2,2-Trichloro-N-cyclohex-2-enyl-acetamide (0.100 g, 0.412 mmol) was dissolved in methanol (20 ml) and the solution cooled to 0 °C upon which Zinc/Copper couple (excess) was added and the cooling bath removed. The mixture was then stirred at room temperature for 3-4 h, monitoring by TLC. Upon consumption of starting material excess Zn/Cu couple was filtered off, the methanol removed via rotary evaporation, an aqueous extraction performed with ethyl acetate and the organic layers collected. The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo to yield the crude product which was purified by flash silica chromatography eluting in ethyl acetate-petroleum ether (2:1) to yield the title complex as a clear oil (0.0361 g, 90%).

v_{max} (nujol)/cm⁻¹ 3354 (NH₂), 3085 (NH₂), 1625 (C=C); δH (400.15 MHz; CDCl₃) 5.71-5.62 (1H, m, H3 or H4), 5.56-5.48 (1H, m, H3 or H4), 3.29-3.20 (1H, m, H5), 1.98-1.19 (6H, m, H1, H2, H6); δC (100.62 MHz; CDCl₃) 131.7 (1C, CH, C3 or C4), 129.2 (1C, CH, C3 or C4), 46.8 (1C, CH, C5), 32.2(1C, CH₂, C6), 24.7 (1C, CH₂ C1 or C2), 19.9 (1C, CH₂, C1 or C2).

Data in agreement with that published by Adam et al.¹⁷³
4.0 References

(1) http://elements.vanderkrogt.net/elem/os.html


(59) www.platinuminfo.net/palladium200.html


(172) www.sigmaaldrich.com/catalog/search/ProductDetail/ALDRICH/241075.

Table 1. Crystal data and structure refinement for sdrc8.

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<th>Identification code</th>
<th>sdrc8</th>
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</tr>
<tr>
<td>Temperature</td>
<td>150(2) K</td>
</tr>
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<td>Radiation, wavelength</td>
<td>MoKα, 0.71073 Å</td>
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<td>Crystal system, space group</td>
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<td></td>
<td>b = 13.8128(14) Å, β = 90°</td>
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<tr>
<td></td>
<td>c = 23.679(2) Å, γ = 90°</td>
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<td>Absorption coefficient μ</td>
<td>0.421 mm⁻¹</td>
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<tr>
<td>F(000)</td>
<td>752</td>
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<td>Crystal colour and size</td>
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<td>5912 (θ range 2.95 to 28.32°)</td>
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</tr>
<tr>
<td>θ range for data collection</td>
<td>ω rotation with narrow frames</td>
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<td>Index ranges</td>
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<td>Min. and max. transmission</td>
<td>0.727 and 0.971</td>
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<td>direct methods</td>
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<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
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<tr>
<td>Weighting parameters a, b</td>
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<td>Data / restraints / parameters</td>
<td>2039 / 0 / 101</td>
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<td>R indices (all data)</td>
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Goodness-of-fit on $F^2$
Largest and mean shift/su
Largest diff. peak and hole

1.275
0.000 and 0.000
0.345 and $-0.536$ e Å$^{-3}$
Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å²) for sdr8. $U_{eq}$ is defined as one third of the trace of the orthogonalized $U^i$ tensor.

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<th>z</th>
<th>$U_{eq}$</th>
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Table 3. Bond lengths [Å] and angles [°] for sdrc8.

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<th>Length [Å]</th>
<th>Bond</th>
<th>Length [Å]</th>
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Table 4. Anisotropic displacement parameters (Å²) for sdrc8. The anisotropic displacement factor exponent takes the form: 
\(-2\pi^2 [h^2 a^*^2 U^{11} + \ldots + 2hka*b*U^{12}]\)

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<th>U¹¹</th>
<th>U²²</th>
<th>U³³</th>
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<tr>
<td></td>
<td>-0.0019(9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 5. Hydrogen coordinates and isotropic displacement parameters (Å²) for sdrc8.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(1)</td>
<td>0.2402</td>
<td>0.7720</td>
<td>0.4447</td>
<td>0.050</td>
</tr>
<tr>
<td>H(1A)</td>
<td>0.6558</td>
<td>0.6883</td>
<td>0.4181</td>
<td>0.034</td>
</tr>
<tr>
<td>H(1B)</td>
<td>0.5304</td>
<td>0.7773</td>
<td>0.3836</td>
<td>0.034</td>
</tr>
<tr>
<td>H(2)</td>
<td>0.2659</td>
<td>0.6696</td>
<td>0.3306</td>
<td>0.029</td>
</tr>
<tr>
<td>H(3)</td>
<td>0.2128</td>
<td>0.5424</td>
<td>0.3958</td>
<td>0.029</td>
</tr>
<tr>
<td>H(4)</td>
<td>0.1504</td>
<td>0.4917</td>
<td>0.2986</td>
<td>0.036</td>
</tr>
<tr>
<td>H(5A)</td>
<td>0.5681</td>
<td>0.3727</td>
<td>0.3299</td>
<td>0.044</td>
</tr>
<tr>
<td>H(5B)</td>
<td>0.3620</td>
<td>0.3558</td>
<td>0.2770</td>
<td>0.044</td>
</tr>
<tr>
<td>H(1C)</td>
<td>0.7557</td>
<td>0.3644</td>
<td>0.4923</td>
<td>0.032</td>
</tr>
<tr>
<td>H(1D)</td>
<td>0.9175</td>
<td>0.4341</td>
<td>0.4563</td>
<td>0.032</td>
</tr>
</tbody>
</table>
Table 6. Torsion angles [°] for sdrc8.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Torsion Angle (°)</th>
<th>Bond</th>
<th>Torsion Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(1)–C(1)–C(2)–C(3)</td>
<td>−59.4(3)</td>
<td>O(1)–C(1)–C(2)–Cl(1)</td>
<td>177.56(17)</td>
</tr>
<tr>
<td>C(1)–C(2)–C(3)–O(2)</td>
<td>−56.2(3)</td>
<td>Cl(1)–C(2)–C(3)–O(2)</td>
<td>64.4(2)</td>
</tr>
<tr>
<td>C(1)–C(2)–C(3)–C(4)</td>
<td>179.6(2)</td>
<td>Cl(1)–C(2)–C(3)–C(4)</td>
<td>−59.8(3)</td>
</tr>
<tr>
<td>O(2)–C(3)–C(4)–C(5)</td>
<td>0.7(4)</td>
<td>C(2)–C(3)–C(4)–C(5)</td>
<td>122.3(3)</td>
</tr>
<tr>
<td>C(4)–C(3)–O(2)–C(6)</td>
<td>−82.6(3)</td>
<td>C(2)–C(3)–O(2)–C(6)</td>
<td>152.5(2)</td>
</tr>
<tr>
<td>C(3)–O(2)–C(6)–O(3)</td>
<td>−1.4(3)</td>
<td>C(3)–O(2)–C(6)–N(1)</td>
<td>178.4(2)</td>
</tr>
</tbody>
</table>

Table 7. Hydrogen bonds for sdrc8 [Å and °].

<table>
<thead>
<tr>
<th>D–H...A</th>
<th>d(D–H)</th>
<th>d(H...A)</th>
<th>d(D...A)</th>
<th>&lt;(DHA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(1)–H(1)...O(3')</td>
<td>0.84</td>
<td>1.90</td>
<td>2.729(3)</td>
<td>171.1</td>
</tr>
<tr>
<td>N(1)–H(1C)...O(1&quot;)</td>
<td>0.88</td>
<td>2.00</td>
<td>2.868(3)</td>
<td>168.4</td>
</tr>
<tr>
<td>N(1)–H(1D)...O(3*)</td>
<td>0.88</td>
<td>2.09</td>
<td>2.855(3)</td>
<td>144.3</td>
</tr>
</tbody>
</table>

Symmetry operations for equivalent atoms

' −x+1/2,y+1/2,z  " −x+1,−y+1,−z+1  * x+1,y,z
Table 1. Crystal data and structure refinement for sdrc9.

<table>
<thead>
<tr>
<th>Identification code</th>
<th>sdrc9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical formula</td>
<td>C11H2Cl2NO4</td>
</tr>
<tr>
<td>Formula weight</td>
<td>302.19</td>
</tr>
<tr>
<td>Temperature</td>
<td>150(2) K</td>
</tr>
<tr>
<td>Radiation, wavelength</td>
<td>MoKα, 0.71073 Å</td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>monoclinic, P21/c</td>
</tr>
</tbody>
</table>
| Unit cell parameters | \[
a = 9.9893(9) \text{ Å} \quad \alpha = 90° \\
b = 16.6692(15) \text{ Å} \quad \beta = 104.734(2)° \\
c = 9.1645(8) \text{ Å} \quad \gamma = 90° \\
\] |
| Cell volume         | 1475.8(2) Å³ |
| Z                   | 4 |
| Calculated density  | 1.360 g/cm³ |
| Absorption coefficient μ | 0.446 mm⁻¹ |
| F(000)              | 640 |
| Crystal colour and size | colourless, 1.02 × 0.43 × 0.40 mm³ |
| Reflections for cell refinement | 6014 (θ range 2.30 to 28.36°) |
| Data collection method | Bruker SMART 1000 CCD diffractometer |
| θ range for data collection | ω rotation with narrow frames |
| Index ranges        | 2.11 to 28.87° |
| Completeness to θ = 26.00° | h −13 to 12, k −22 to 22, l −11 to 11 |
| Intensity decay     | 100.0 % |
| Reflections collected | 0% |
| Independent reflections | 12497 |
| Reflections with F²>2σ | 3520 (Rint = 0.0294) |
| Absorption correction | 2850 |
| Min. and max. transmission | semi-empirical from equivalents |
| Structure solution  | 0.659 and 0.842 |
| Refinement method   | direct methods |
| Weighting parameters a, b | Full-matrix least-squares on F² |
| Data / restraints / parameters | 0.0425, 0.6777 |
| Final R indices [F²>2σ] | 3520 / 0 / 184 |
| R indices (all data) | R1 = 0.0377, wR2 = 0.0916 |
| Goodness-of-fit on F² | R1 = 0.0498, wR2 = 0.0985 |
|                     | 1.055 |
Largest and mean shift/su
Largest diff. peak and hole

0.001 and 0.000
0.389 and -0.249 e Å⁻³
Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å²) for sdr9. Ueq is defined as one third of the trace of the orthogonalized Uij tensor.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Ueq</th>
</tr>
</thead>
<tbody>
<tr>
<td>N(1)</td>
<td>0.00885(16)</td>
<td>0.40199(9)</td>
<td>0.12261(17)</td>
<td>0.0326(3)</td>
</tr>
<tr>
<td>O(1)</td>
<td>0.02555(16)</td>
<td>0.35453(8)</td>
<td>0.35857(15)</td>
<td>0.0499(4)</td>
</tr>
<tr>
<td>C(1)</td>
<td>0.05341(17)</td>
<td>0.35140(10)</td>
<td>0.23694(18)</td>
<td>0.0281(3)</td>
</tr>
<tr>
<td>O(2)</td>
<td>0.13442(12)</td>
<td>0.29330(6)</td>
<td>0.20321(12)</td>
<td>0.0273(2)</td>
</tr>
<tr>
<td>C(2)</td>
<td>0.18341(17)</td>
<td>0.23498(9)</td>
<td>0.32129(17)</td>
<td>0.0282(3)</td>
</tr>
<tr>
<td>C(3)</td>
<td>0.24594(15)</td>
<td>0.16635(9)</td>
<td>0.25292(17)</td>
<td>0.0236(3)</td>
</tr>
<tr>
<td>Cl(1)</td>
<td>0.41088(4)</td>
<td>0.19682(3)</td>
<td>0.22610(5)</td>
<td>0.03925(13)</td>
</tr>
<tr>
<td>C(4)</td>
<td>0.26114(15)</td>
<td>0.08891(9)</td>
<td>0.34851(17)</td>
<td>0.0243(3)</td>
</tr>
<tr>
<td>C(5)</td>
<td>0.34337(17)</td>
<td>0.10243(11)</td>
<td>0.51148(17)</td>
<td>0.0317(4)</td>
</tr>
<tr>
<td>O(3)</td>
<td>0.12287(11)</td>
<td>0.06617(7)</td>
<td>0.35494(12)</td>
<td>0.0264(2)</td>
</tr>
<tr>
<td>C(6)</td>
<td>0.32686(17)</td>
<td>0.01996(10)</td>
<td>0.28100(18)</td>
<td>0.0288(3)</td>
</tr>
<tr>
<td>C(7)</td>
<td>0.25693(17)</td>
<td>-0.00180(10)</td>
<td>0.11801(18)</td>
<td>0.0287(3)</td>
</tr>
<tr>
<td>C(8)</td>
<td>0.29408(16)</td>
<td>-0.08521(10)</td>
<td>0.07536(18)</td>
<td>0.0293(3)</td>
</tr>
<tr>
<td>Cl(2)</td>
<td>0.47449(6)</td>
<td>-0.09903(4)</td>
<td>0.10237(7)</td>
<td>0.03513(19)</td>
</tr>
<tr>
<td>Cl(2X)</td>
<td>0.29962(17)</td>
<td>-0.15614(9)</td>
<td>0.21065(18)</td>
<td>0.0393(5)</td>
</tr>
<tr>
<td>C(9)</td>
<td>0.21556(17)</td>
<td>-0.11486(11)</td>
<td>-0.08326(18)</td>
<td>0.0305(4)</td>
</tr>
<tr>
<td>O(4)</td>
<td>0.07056(12)</td>
<td>-0.10114(9)</td>
<td>-0.09768(13)</td>
<td>0.0391(3)</td>
</tr>
<tr>
<td>C(10)</td>
<td>0.25171(19)</td>
<td>-0.06624(13)</td>
<td>-0.2083(2)</td>
<td>0.0406(4)</td>
</tr>
<tr>
<td>C(11)</td>
<td>0.2401(3)</td>
<td>-0.20402(13)</td>
<td>-0.1027(3)</td>
<td>0.0555(6)</td>
</tr>
</tbody>
</table>
Table 3. Bond lengths [Å] and angles [°] for sdrc9.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length [Å]</th>
<th>Bond</th>
<th>Length [Å]</th>
<th>Bond</th>
<th>Length [Å]</th>
</tr>
</thead>
<tbody>
<tr>
<td>N(1)--C(1)</td>
<td>1.330(2)</td>
<td>O(1)--C(1)</td>
<td>1.217(2)</td>
<td>O(1)--C(1)--O(2)</td>
<td>125.85(16)</td>
</tr>
<tr>
<td>C(1)--O(2)</td>
<td>1.3475(18)</td>
<td>O(2)--C(2)</td>
<td>1.4444(18)</td>
<td>C(1)--O(2)--C(2)</td>
<td>112.03(13)</td>
</tr>
<tr>
<td>C(2)--C(3)</td>
<td>1.514(2)</td>
<td>C(3)--C(4)</td>
<td>1.546(2)</td>
<td>C(2)--C(3)--C(4)</td>
<td>107.19(12)</td>
</tr>
<tr>
<td>C(3)--Cl(1)</td>
<td>1.7997(15)</td>
<td>C(4)--O(3)</td>
<td>1.4478(18)</td>
<td>C(3)--Cl(1)</td>
<td>109.37(11)</td>
</tr>
<tr>
<td>C(4)--C(5)</td>
<td>1.527(2)</td>
<td>C(4)--C(6)</td>
<td>1.530(2)</td>
<td>C(4)--C(5)</td>
<td>106.28(12)</td>
</tr>
<tr>
<td>C(6)--C(7)</td>
<td>1.523(2)</td>
<td>C(6)--C(8)</td>
<td>1.516(2)</td>
<td>C(6)--C(7)</td>
<td>109.05(12)</td>
</tr>
<tr>
<td>C(8)--C(9)</td>
<td>1.547(2)</td>
<td>C(8)--Cl(2X)</td>
<td>1.704(2)</td>
<td>C(8)--C(9)</td>
<td>115.89(13)</td>
</tr>
<tr>
<td>C(8)--Cl(2)</td>
<td>1.7708(17)</td>
<td>C(9)--O(4)</td>
<td>1.439(2)</td>
<td>C(9)--Cl(2X)</td>
<td>112.15(13)</td>
</tr>
<tr>
<td>C(9)--O(4)</td>
<td>1.520(2)</td>
<td>C(9)--C(11)</td>
<td>1.524(3)</td>
<td>C(9)--C(10)</td>
<td>112.15(15)</td>
</tr>
</tbody>
</table>

O(1)--C(1)--N(1) 112.03(13) O(1)--C(1)--O(2) 114.88(12) N(1)--C(1)--O(2) 107.19(12) O(2)--C(2)--C(3) 112.83(12) C(2)--C(3)--Cl(1) 110.60(10) O(3)--C(4)--C(5) 106.28(12) O(3)--C(4)--C(6) 106.53(11) C(5)--C(4)--C(6) 112.86(12) O(3)--C(4)--C(3) 112.96(13) C(5)--C(4)--C(3) 114.43(13) C(5)--C(4)--C(6) 112.96(13) C(7)--C(6)--C(4) 112.96(13) C(7)--C(6)--C(4) 114.43(13) C(7)--C(6)--C(4) 112.96(13) C(7)--C(8)--Cl(2) 87.96(9) C(7)--C(8)--Cl(2) 112.99(12) C(7)--C(8)--Cl(2) 87.96(9) C(9)--C(8)--Cl(2) 112.99(12) C(9)--C(8)--Cl(2) 87.96(9) C(9)--C(8)--Cl(2) 112.99(12) Cl(2)--C(8)--Cl(2) 87.96(9) Cl(2)--C(8)--Cl(2) 112.99(12) Cl(2)--C(8)--Cl(2) 87.96(9) O(4)--C(9)--C(11) 107.06(13) O(4)--C(9)--C(11) 110.40(16) O(4)--C(9)--C(8) 107.06(13) O(4)--C(9)--C(8) 110.40(16) O(4)--C(9)--C(8) 107.06(13) C(10)--C(9)--C(8) 111.30(15) C(10)--C(9)--C(8) 111.30(15)
Table 4. Hydrogen bonds for sdrc9 [Å and °].

<table>
<thead>
<tr>
<th>D–H...A</th>
<th>d(D–H)</th>
<th>d(H...A)</th>
<th>d(D...A)</th>
<th>&lt;(DHA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N(1)–H(1A)...O(3')</td>
<td>0.84(2)</td>
<td>2.18(2)</td>
<td>3.0030(19)</td>
<td>164.8(19)</td>
</tr>
<tr>
<td>N(1)–H(1B)...O(3'')</td>
<td>0.87(2)</td>
<td>2.22(2)</td>
<td>3.0662(18)</td>
<td>163.8(19)</td>
</tr>
<tr>
<td>O(3)–H(3A)...O(4*)</td>
<td>0.84</td>
<td>1.87</td>
<td>2.7045(16)</td>
<td>173.0</td>
</tr>
<tr>
<td>O(4)–H(4)...O(1+)</td>
<td>0.84</td>
<td>1.88</td>
<td>2.7091(17)</td>
<td>168.6</td>
</tr>
</tbody>
</table>

Symmetry operations for equivalent atoms

* x, y+1/2, z-1/2  " -x, y+1/2, -z+1/2  * -x, -y, -z
+ -x, y-1/2, -z+1/2
Table 5. Hydrogen coordinates and isotropic displacement parameters (Å²) for sdrc9.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U</th>
</tr>
</thead>
<tbody>
<tr>
<td>H(1A)</td>
<td>0.044(2)</td>
<td>0.4014(12)</td>
<td>0.048(2)</td>
<td>0.039</td>
</tr>
<tr>
<td>H(1B)</td>
<td>-0.041(2)</td>
<td>0.4429(13)</td>
<td>0.135(2)</td>
<td>0.039</td>
</tr>
<tr>
<td>H(2A)</td>
<td>0.1058</td>
<td>0.2155</td>
<td>0.3607</td>
<td>0.034</td>
</tr>
<tr>
<td>H(2B)</td>
<td>0.2539</td>
<td>0.2593</td>
<td>0.4056</td>
<td>0.034</td>
</tr>
<tr>
<td>H(3)</td>
<td>0.1832</td>
<td>0.1544</td>
<td>0.1515</td>
<td>0.028</td>
</tr>
<tr>
<td>H(5A)</td>
<td>0.2974</td>
<td>0.1435</td>
<td>0.5580</td>
<td>0.048</td>
</tr>
<tr>
<td>H(5B)</td>
<td>0.4372</td>
<td>0.1203</td>
<td>0.5130</td>
<td>0.048</td>
</tr>
<tr>
<td>H(5C)</td>
<td>0.3483</td>
<td>0.0522</td>
<td>0.5681</td>
<td>0.048</td>
</tr>
<tr>
<td>H(3A)</td>
<td>0.0671</td>
<td>0.0751</td>
<td>0.2711</td>
<td>0.040</td>
</tr>
<tr>
<td>H(6A)</td>
<td>0.4244</td>
<td>0.0342</td>
<td>0.2874</td>
<td>0.035</td>
</tr>
<tr>
<td>H(6B)</td>
<td>0.3276</td>
<td>-0.0283</td>
<td>0.3442</td>
<td>0.035</td>
</tr>
<tr>
<td>H(7A)</td>
<td>0.1553</td>
<td>0.0017</td>
<td>0.1024</td>
<td>0.034</td>
</tr>
<tr>
<td>H(7B)</td>
<td>0.2841</td>
<td>0.0378</td>
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<td>0.034</td>
</tr>
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<td>H(8)</td>
<td>0.2665</td>
<td>-0.1224</td>
<td>0.1482</td>
<td>0.035</td>
</tr>
<tr>
<td>H(8X)</td>
<td>0.3923</td>
<td>-0.0802</td>
<td>0.0695</td>
<td>0.035</td>
</tr>
<tr>
<td>H(4)</td>
<td>0.0485</td>
<td>-0.1202</td>
<td>-0.0222</td>
<td>0.059</td>
</tr>
<tr>
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<td>0.1964</td>
<td>-0.0852</td>
<td>-0.3064</td>
<td>0.061</td>
</tr>
<tr>
<td>H(10B)</td>
<td>0.3503</td>
<td>-0.0728</td>
<td>-0.2031</td>
<td>0.061</td>
</tr>
<tr>
<td>H(10C)</td>
<td>0.2317</td>
<td>-0.0095</td>
<td>-0.1959</td>
<td>0.061</td>
</tr>
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<td>0.2091</td>
<td>-0.2346</td>
<td>-0.0259</td>
<td>0.083</td>
</tr>
<tr>
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<td>-0.2135</td>
<td>-0.0914</td>
<td>0.083</td>
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<td>0.1878</td>
<td>-0.2213</td>
<td>-0.2033</td>
<td>0.083</td>
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</table>
Table 6. Torsion angles [°] for sdrc9.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Torsion Angle</th>
<th>Bond</th>
<th>Torsion Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(1)–C(1)–O(2)–C(2)</td>
<td>0.8(2)</td>
<td>N(1)–C(1)–O(2)–C(2)</td>
<td>-178.42(14)</td>
</tr>
<tr>
<td>C(1)–O(2)–C(2)–C(3)</td>
<td>168.45(13)</td>
<td>O(2)–C(2)–C(3)–C(4)</td>
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<td>61.04(16)</td>
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<td>Cl(2)–C(3)–C(4)–C(5)</td>
<td>-55.00(17)</td>
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<td>Cl(2)–C(3)–C(4)–C(6)</td>
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<td>O(3)–C(4)–C(6)–C(7)</td>
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<td>C(6)–C(7)–C(8)–C(9)</td>
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