Bisphosphine Ligands, Metallamacrocycles And A Solid-Supported Alkene Metathesis Catalyst

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ABSTRACT

The aim of this work was to develop a solid-supported alkene metathesis catalyst. The initial strategy involved two new bisphosphine ligands, DPEN **I** and DPPN **II**, and the short and efficient syntheses of these ligands from 2,7-dihydroxynaphthalene are described. The platinum, palladium and ruthenium complexes of ligands **I** and **II** were investigated. The ligands were found to favour bridging metal centres to form dimeric or oligomeric complexes. The isolation and structures of three metallamacrocycles formed with platinum(II) are discussed. It was found that the thermodynamically favoured structures were the *cis*, *cis*-dimers and that isomerisation to these was catalysed by excess ligand.

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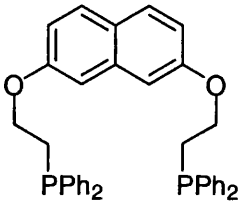
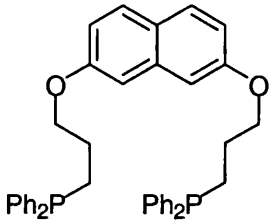
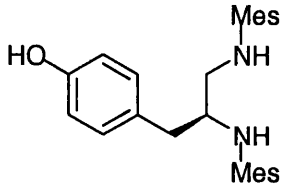




II

Ths bisphosphine ligands were not suitable for use in a solid-supported metathesis catalyst and so a new strategy was adopted. This involved the synthesis of a solid-supported N-heterocyclic carbene ligand. The synthesis of bis-mesityl diamine **III** from L-tyrosine methyl ester is described. Diamine **III** was immobilised on polystyrene resin and then converted to metathesis catalyst **IV**. The extensive optimisation carried out in the solid phase synthesis of **IV** is discussed. A number of diene substrates were synthesised and the supported catalyst was tested for ring closing metathesis activity with good results. However, no enantioselectivity was observed when using the catalyst for RCM of prochiral trienes.



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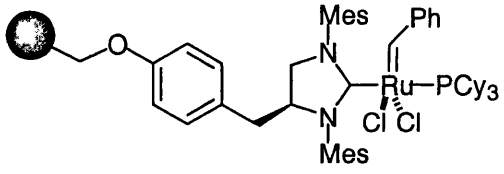

IV

BISPHOSPHINE LIGANDS, METALLAMACROCYCLES AND A SOLID-SUPPORTED ALKENE METATHESIS CATALYST

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DECLARATION

The work presented in this thesis is the original work of the author, except where stated otherwise, and was carried out in the Loudon Laboratory within the Chemistry Department of the University of Glasgow between October 1999 and October 2002 under the supervision of Dr. Susan K. Armstrong.

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ABBREVIATIONS

Ac	acetyl
Ad	adamantyl
AES	atomic emission spectroscopy
Ar	aryl
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bu	butyl
br	broad
Bn	benzyl
Cbz	benzyloxycarbonyl
CI	chemical ionisation
CM	cross metathesis
Cp	cyclopentadienyl
Cy	cyclohexyl
Cyp	cyclopentyl
d	doublet
dba	dibenzylidineacetone
DCC	1,3-dicyclohexylcarbodiimide
DEAD	diethyl azodicarboxylate
DMAP	4-(dimethylamino)pyridine
DMF	*N,N*-dimethylformamide
DMSO	dimethyl sulfoxide
DPEN	2,7-bis(2-diphenylphosphinoethoxy)naphthalene
DPPN	2,7-bis(3-diphenylphosphinopropoxy)naphthalene
EI	electron impact
Et	ethyl
FAB	fast atom bombardment
GC	gas chromatography
hfc	3-(heptafluoropropylhydroxymethylene)-(+)-camphorate
HRMS	high resolution mass spectrum
i	ipso, iso
IMes	*N,N'*-bis(mesityl)imidazol-2-ylidene

IR	infrared
m	multiplet (NMR), medium (IR)
m	meta
m.p.	melting point
Me	methyl
Mes	mesityl, 2,4,6-trimethylphenyl
Ms	mesyl, methanesulfonyl
MS	mass spectrum
NMR	nuclear magnetic resonance
n	normal
o	ortho
p	para
Ph	phenyl
Phth	phthaloyl
Pr	propyl
py	pyridine
q	quartet
RCM	ring closing metathesis
ROCM	ring opening cross metathesis
ROMP	ring opening metathesis polymerisation
RT	room temperature
s	singlet (NMR), strong (IR)
sec	secondary
t	triplet
t, tert	tertiary
TBAI	tetra-*n*-butylammonium iodide
TBDMS	*tert*-butyldimethylsilyl
THF	tetrahydrofuran
TLC	thin layer chromatography
Ts	tosyl, 4-toluenesulfonyl
w	weak

1. INTRODUCTION

1.1 AIMS

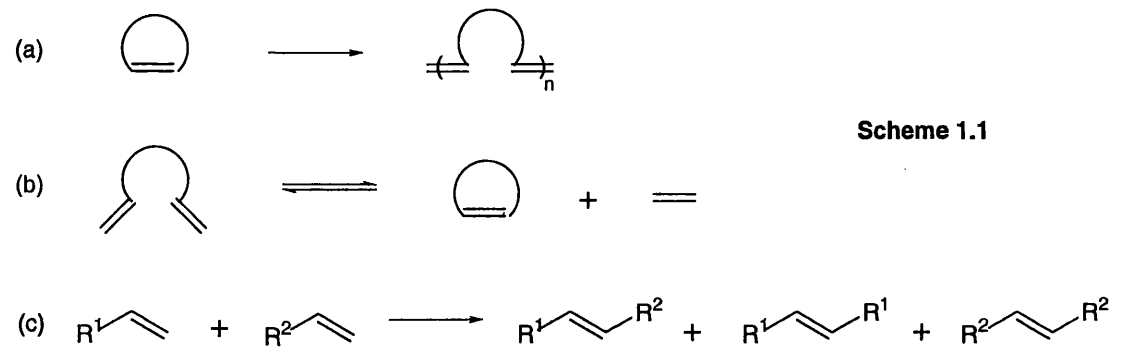
The ultimate aim of this work was to develop a solid-supported catalyst for carrying out alkene metathesis reactions.

The initial strategy investigated involved the use of bidentate phosphine ligands. After synthesising the ligands, they were found to be unsuitable for use in a metathesis catalyst. However, investigation of the ligands' chelation preferences with transition metals produced some interesting platinum-containing metallamacrocycles.

The second strategy involved synthesising a solid-supported N-heterocyclic carbene ligand and using it to form an immobilised alkene metathesis catalyst. After success and optimisation of this approach, the aim was to investigate the properties of the catalyst and test its activity for alkene metathesis.

1.2 THE ALKENE METATHESIS REACTION

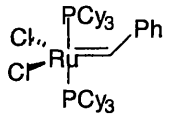
Alkene metathesis is a powerful method of carbon-carbon bond formation consisting of three closely related types of reaction (**Scheme 1.1**): (a) ring opening metathesis polymerisation (ROMP); (b) ring closing metathesis (RCM) and the reverse, ring opening metathesis (ROM) and (c) cross metathesis (CM) of two acyclic alkenes.



Scheme 1.1

Until recently, the application of alkene metathesis was almost solely restricted to polymerisation (ROMP) reactions catalysed by poorly understood mixtures of organometallic reagents. It is since the discovery, in the early 1990s, of well-defined metal alkylidene complexes which catalyse alkene metathesis that the full potential of this reaction for polymer chemistry and organic synthesis has begun to be realised.

The catalysts that have been most widely used for alkene metathesis are ruthenium complexes **1**[1] and **2**,[2] and molybdenum-based catalyst **3**.[3] However, many other well-defined complexes have been synthesised and shown to be active metathesis catalysts. Recent years have seen intense activity in this area and the publication of numerous catalytic systems aiming to extend the scope of the metathesis reaction by achieving increased activity with a wider range of substrates. Other important considerations are the catalyst's stability and ease of synthesis.



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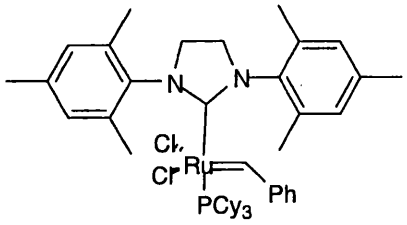

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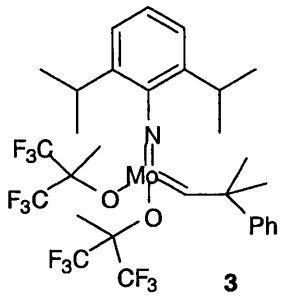


3

The advent and subsequent rapid development of well-defined and more active catalysts has resulted in correspondingly intense activity in the application of alkene metathesis to organic synthesis.

Ring closing metathesis (RCM) has developed rapidly over the past decade to become a valuable and widely used synthetic technique with applications reported in many areas of organic synthesis. The specificity of alkene metathesis has allowed RCM to be used in practically all types of molecules; natural products, cyclic peptides, macromolecules and combinatorial libraries (in solution and on solid support) have all been made by RCM. RCM has proved to be a particularly valuable technique for the preparation of medium and large sized rings.

Early work on cross metathesis (CM) between two acyclic alkenes was not particularly successful as a lack of regio- and stereochemical control led to a mixture of products. However, the development of more active and selective catalysts, such as **2**, has meant that with careful choice of substrates synthetically useful CM can be performed. Ring opening cross metathesis (ROCM), in which a cyclic alkene is opened and then undergoes cross metathesis with an acyclic alkene to form a monomeric product, has also been used as a synthetic technique.

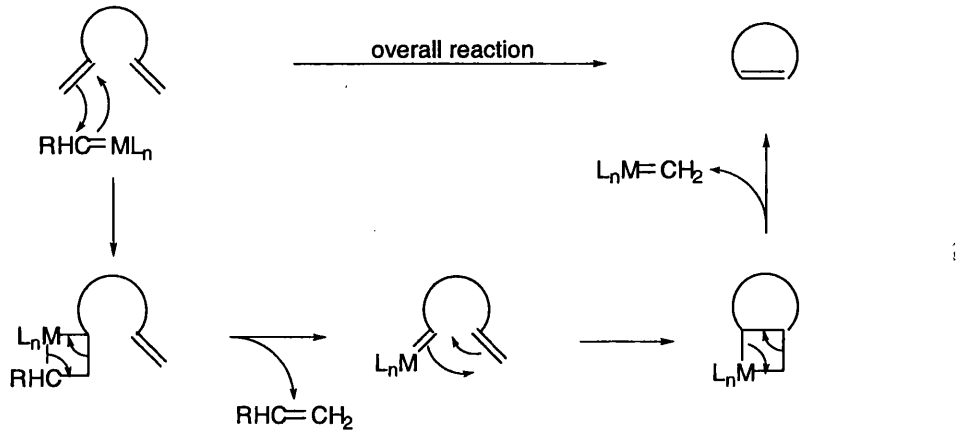
Another useful variant of the metathesis reaction is enyne metathesis. RCM or CM of an alkene and an alkyne produces a conjugated diene.

A number of reviews on the alkene metathesis reaction and its applications in organic synthesis have been published.[4]

Mechanism

Alkylidene complexes such as **1,2** and **3** are more correctly referred to as initiators or pre-catalysts as they are not usually regenerated by the first round of the catalytic cycle. Also, in many cases a ligand must first dissociate to form the catalytically active species.

The general mechanism of alkene metathesis involves a number of metal alkylidene and metallacyclobutane species. **Scheme 1.2** illustrates this for ring closing metathesis where $L_nM{=}CHR$ is a general metal alkylidene catalyst.



Scheme 1.2

In the first turn of the catalytic cycle, the alkene by-product depends on the R group in the original catalyst whereas in subsequent cycles it depends on the substrate. Therefore, when the substrate is a terminal alkene, the by-product is ethene and the propagating species is the methylidene $L_nM{=}CH_2$.

A kinetic study was carried out on the ring closing metathesis of diethyl diallylmalonate catalysed by the ruthenium methylidene $(PCy_3)_2Cl_2Ru{=}CH_2$.[5] This had the advantage of making every turn of the catalytic cycle identical. The conclusion was that, in this case, the major reaction pathway involved dissociation of one of the phosphine ligands to form an electron-deficient, four-coordinate 14-electron species before coordination of the substrate and metallacyclobutane formation. Subsequent studies have provided further

evidence for this dissociative mechanism and proved that the ligand dissociation and alkene coordination pre-equilibria are very important in determining relative catalyst activities.[6]

Studies on a number of catalysts have shown that, in addition to the initiation and propagation rates, the lifetimes of the complexes are also highly dependent on the ligands present.[7] Methylidene complexes, which are usually the catalytic species present during the reaction, are susceptible to unimolecular decomposition whereas other alkylidenes tend to undergo bimolecular decomposition.

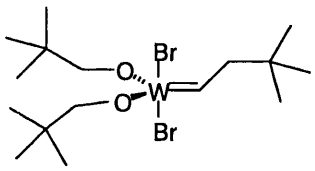
An understanding of how altering catalyst structure affects the relative rates of the processes involved in metathesis has led to the development of better catalysts and will undoubtedly continue to do so. As the number of available catalysts with different characteristics continues to grow, so too will the vast range of applications for the alkene metathesis reaction.

1.3 ALKENE METATHESIS CATALYSTS

The past decade has seen much work focused on the development of new metal alkylidene complexes in an effort to improve the activity, stability and tolerance of alkene metathesis catalysts. What follows is a summary of the most important developments in catalyst design.

Molybdenum and tungsten catalysts

The earliest stable metal alkylidene complexes found to catalyse alkene metathesis were based on tungsten, for example **4**[8] and **5**,[9] but it was molybdenum complex **3**, introduced by Schrock and co-workers,[3] which was the first to be widely used for synthetic purposes due to the high activity it exhibited in ring closing metathesis reactions.



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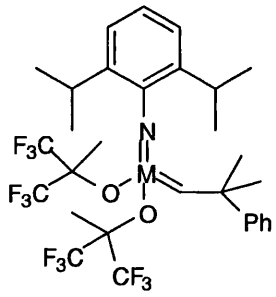
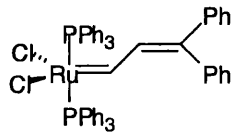


3 M = Mo
5 M = W

Alkylidene **3** suffers in comparison with ruthenium catalysts such as **1** in that it is much more difficult to synthesise, store and use. Although it is commercially available, it must be handled in a glove box and is extremely sensitive to air and moisture. It is also intolerant of polar functional groups such as alcohols, aldehydes and carboxylic acids but does have the advantage of rapid reaction rates and the ability to form rings in sterically demanding situations. However, the development of the latest generation of ruthenium catalysts, which have activities rivalling that of **3** combined with a much greater stability, means that Schrock catalyst **3** is now rarely used for synthetic applications.

Ruthenium catalysts

Ruthenium alkylidene complexes have proved to be by far the most versatile as alkene metathesis catalysts. The first ruthenium-based alkene metathesis catalyst was alkylidene **6**, reported by Grubbs in 1992.[10] Although **6** is a good catalyst for the ROMP of highly strained cyclic alkenes, it is not active for the ROMP of low-strain cyclic alkenes or for RCM reactions. However, substitution of the triphenylphosphine ligands with better σ-donating tricyclohexylphosphine ligands produced complex **7** which was found to exhibit high metathesis activity with low-strain cyclic and acyclic alkenes.[11] Alkylidene **7** is easier to prepare and handle than molybdenum complex **3**, and tolerates a wider range of functionalities. Therefore, it has been widely applied to a variety of systems for ring closing metathesis in organic synthesis.



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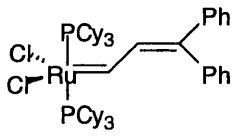
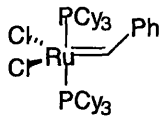


7

In 1995, Grubbs reported the synthesis of benzylidene catalyst **1**.[12] This commercially available complex rapidly become the metathesis catalyst of choice and has been used in the majority of applications reported. Catalyst **1**, generally referred to as Grubbs's first generation catalyst, is reasonably stable to air and moisture and is significantly faster initiating than catalyst **7**. It is tolerant of most functional groups, although can have problems with those containing 'soft' electron pairs (e.g. sulfides, amines). One disadvantage is that it has difficulty forming trisubstituted alkenes and is unable to form tetrasubstituted double bonds.[13]

The original synthesis of complex **1** was a one-pot two step synthesis involving the treatment of $RuCl_2(PPh_3)_3$ with phenyldiazomethane followed by ligand substitution with

tricyclohexylphosphine.[1] Although this gives almost quantitative yields, the method is limited, particularly on a large scale, by the danger of handling explosive diazo compounds. Therefore, alternative approaches to **1**[14] and other alkylidenes,[15] such as catalyst **8** which is also commercially available, have been developed.



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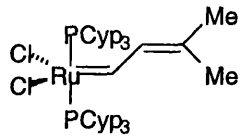


8

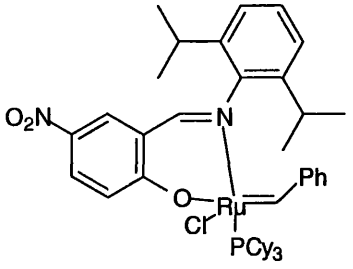
Since the development of Grubbs's catalyst **1**, many other ruthenium alkylidene complexes have been synthesised with different ligands around the metal centre in an effort to modify the properties and activities of the catalysts.

A systematic variation of ligands around the ruthenium centre was carried out by Grubbs's group to study the effects on catalytic activity.[5] Catalysts of the general form $(PR_3)_2X_2Ru{=}CHCHCPh_2$ were tested for the RCM of diethyl diallylmalonate, and the following order of increasing activity was observed: X = I < Br < Cl and $PR_3 = PPh_3 << P^iPr_2Ph < PCy_2Ph < P^iPr_3 < PCy_3$. In summary, phosphines which were larger and more electron donating, and halogens which were smaller and more electron withdrawing, were found to lead to more active catalysts. In fact, widely used catalyst **7** was found to be the most active of all the variants and this is consistent with the generally proposed mechanism.

One of the disadvantages of benzylidene catalyst **1** is that it is not soluble in polar, protic solvents such as methanol. Grubbs and co-workers prepared a series of complexes based on **1** in which one phosphine ligand and one chloride ligand are replaced by a bidentate Schiff-base ligand, for example **9**.[16] These complexes were air, moisture and thermally stable and exhibited high metathesis activity in methanol.

Grubbs's group also showed that by utilising water-soluble phosphines, it was possible to synthesise water soluble ruthenium alkylidene complexes **10** and **11** which catalyse ROMP and RCM reactions in methanol or water.[17] However, α,ω-dienes cannot be

cyclised due to the instability of the methylidene intermediates generated in the catalytic cycle. Catalyst **12** with sulfone-containing phosphine ligands has been shown to carry out RCM in methanol and methanol-water as well as in less polar solvents.[18]



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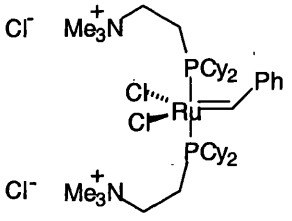

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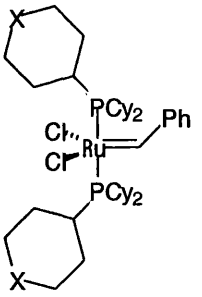
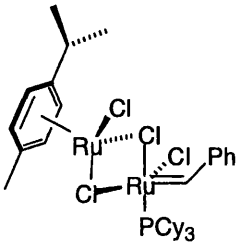


11 X = $NMe_2^+Cl^-$
12 X = SO_2

Several homo- and hetero-bimetallic ruthenium alkylidenes such as **13**,**14** and **15** have been synthesised by Grubbs.[19] All of them are air-stable and exhibit higher catalytic activity than the parent compound **1**. However, the complexes have relatively short lifetimes and so can sometimes fail to take reactions to completion despite their high initial activity.[7] It is thought that these bimetallic catalysts operate by an associative mechanism with no dissociation of the phosphine ligand.



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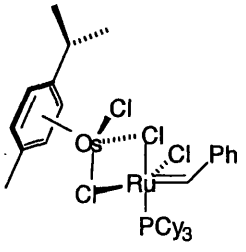

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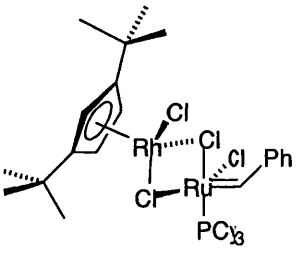
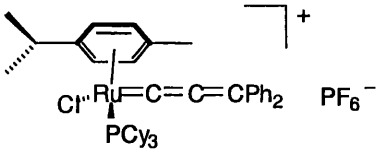


15

A new class of alkene metathesis catalysts, developed by Dixneuf, Fürstner and Hill, are ruthenium allenylidene complexes. Cationic 18-electron complex **16** was

synthesised and shown to be a good catalyst for RCM.[20,21] It was reported that the neutral 16-electron coordinatively unsaturated complex **17** had also been synthesised and found to exhibit similar activities and yields in RCM reactions to Grubbs's benzylidene **1**.[22,23] This would be expected as the propagating species should be the same methylidene, $(PCy_3)_2Cl_2Ru{=}CH_2$, in both cases. It was later realised[24,25] that the complex isolated had the rearranged structure **18**, but the important point is that the synthesis is straightforward, involving the reaction of $RuCl_2(PPh_3)_3$ with $HC{\equiv}CCPh_2OH$ followed by phosphine substitution.



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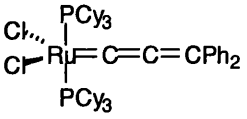

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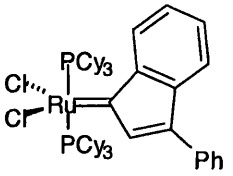
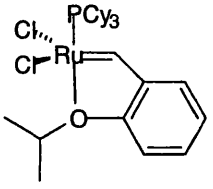


18

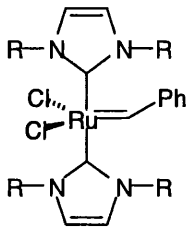
A significant variant of Grubbs's catalyst **1** is catalyst **19**, discovered by Hoveyda and co-workers, which contains an internal ruthenium-oxygen chelate.[26] The most noteworthy feature of **19** is that after carrying out a RCM reaction, the catalyst can be recovered in high yield by column chromatography, and then reused with no noticeable loss of activity. A dendritic version of catalyst **19** has also been developed to facilitate the chromatographic recovery.[27]



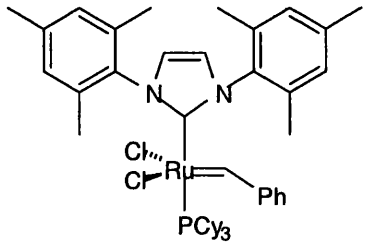
19

In 1998, Herrmann and co-workers reported that the phosphine ligands on catalyst **1** could be replaced by N-heterocyclic carbene (NHC) ligands and that the resulting stable complexes such as **20** were also active metathesis catalysts.[28] Following this discovery, the groups of Herrmann,[29-32] Grubbs[23] and Nolan[24,25,34-36] reported numerous new catalysts

incorporating NHC ligands with varying N- and C-substituents. It was found that the best results were obtained when only one phosphine was replaced. The complex that has been most studied is **21** which contains the sterically demanding *N*,*N*'-bis(mesityl)imidazol-2-ylidene (IMes) ligand.



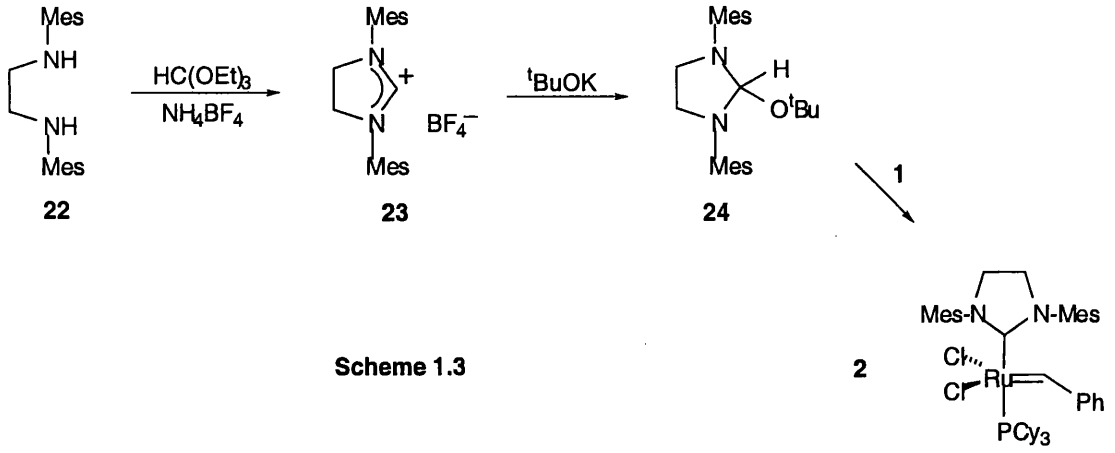
20 R = ^{i}Pr, Cy



21

Complex **21** was shown to exhibit greater RCM activity than the parent compound **1**, particularly at elevated temperatures.[33] The increased thermal stability of **21** allowed it to catalyse RCM in cases where **1** did so poorly or not at all. Of particular note were the formation of tri- and tetrasubstituted alkenes,[25,31,33] previously the domain of Schrock's molybdenum catalyst **3**, the metathesis of electron-deficient alkenes[25] and an increased tolerance of heteroatoms.[37] The IMes ligand is known to be a better σ-donor than PCy_3, hence enhancing catalyst performance, and its steric bulk is thought to help prevent bimolecular decomposition of the alkylidene.

Despite the increasing use of catalyst **21** for alkene metathesis, it was quickly superseded by its saturated analogue **2**.[2] Grubbs reasoned that saturated NHC ligands should be more basic than the unsaturated versions which in turn would translate to increased activity of the resulting catalyst. Starting from diamine **22**, imidazolinium salt **23** was formed by reaction with triethyl orthoformate and ammonium tetrafluoroborate (**Scheme 1.3**). Alkoxy derivative **24** is formed *in situ* and then heated in the presence of benzylidene **1**. *Tert*-butoxy adduct **24** undergoes α-elimination to generate the free carbene ligand which displaces a phosphine from **1** to give compound **2**.



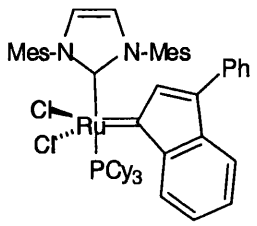
Scheme 1.3

Application of this new catalyst to RCM confirmed that it exhibited exceptional catalytic activity, readily cyclising sterically demanding substrates and even outperforming molybdenum complex **3**. Furthermore, in certain cases excellent yields were obtained with a catalyst loading as low as 0.05 mol%.

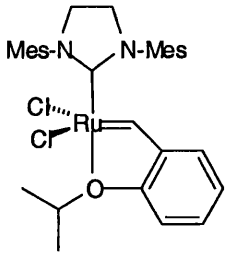
Complex **2** is now commercially available and is known as Grubbs's second-generation catalyst. Despite being more expensive than first-generation catalyst **1**, catalyst **2** is now frequently used as the catalyst of choice for synthetic applications due to the superior activity it displays in almost all circumstances. This greater activity has also increased the range of metathesis reactions possible, particularly in the area of cross metathesis allowing it to develop into a synthetically useful technique.[38]

It was originally thought that the greater activity of catalyst **2** over catalyst **1** was due to the more bulky and more basic NHC ligand accelerating phosphine dissociation to form the four-coordinate, 14-electron active species (see **Section 1.2**). However, an extensive mechanistic and kinetic study carried out by Grubbs showed that phosphine dissociation in complex **2** was two orders of magnitude *slower* than with complex **1**.[6] The higher activity was shown to be due to the increased propensity (by four orders of magnitude) of the NHC-containing 14-electron intermediate to bind alkene substrate rather than recoordinate free phosphine. Therefore, once the phosphine has dissociated many more turnovers are achieved before the catalyst rebinds the phosphine and returns to its resting state.

Since the discovery that an NHC ligand imparts increased activity on a ruthenium metathesis catalyst, examples of 'updated' versions of previously reported phosphine-containing catalysts have appeared such as **25**[39] and **26**.[40] Catalyst **26** is now commercially available and has a different reactivity profile to **2** being particularly useful for cross metathesis with electron-deficient alkenes.



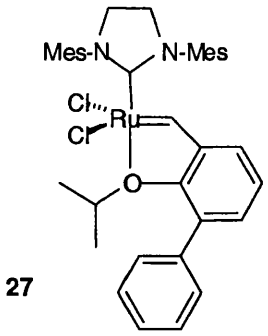
25



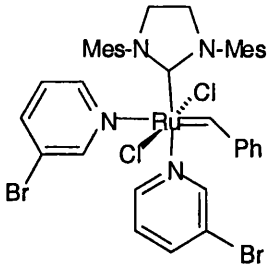
26

The most recent developments in catalyst design have led to even more active catalysts. Although complex **26** is generally a slower catalyst than Grubbs's second-generation catalyst **2**, Blechert reported that the related biphenyl based complex **27** was significantly more active than them both.[41] RCM reactions were complete within minutes. It was thought that the steric bulk of the ligand caused its rapid dissociation to form the catalytically active species.

The most active catalyst to date is bispyridine complex **28**, easily prepared from catalyst **2**.[42] Initial investigations by Grubbs have shown that this catalyst initiates at least six orders of magnitude faster than **2**. As with catalyst **27**, it was proposed that the 3-bromopyridine ligand dissociates extremely rapidly and rebinds slowly, both of which contribute to favourable turnover conditions.



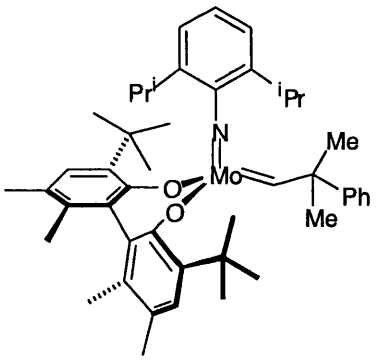
27



28

Chiral catalysts

Several chiral metathesis catalysts have been synthesised and tested for their ability to carry out asymmetric RCM and ROCM. Molybdenum catalysts such as **29**[43] and **30**,[44] prepared by Schrock and Hoveyda, have been used to effect kinetic resolution of racemic dienes and, more successfully, desymmetrisation of achiral trienes achieving greater than 99% enantiomeric excess in some cases (e.g. **Scheme 1.4**).[45]



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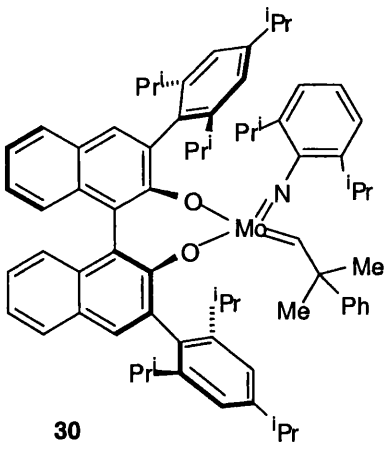

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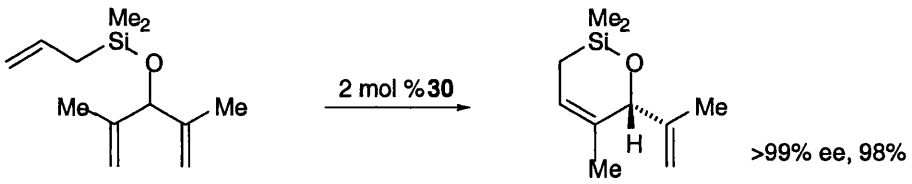
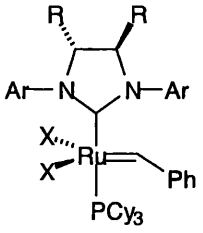


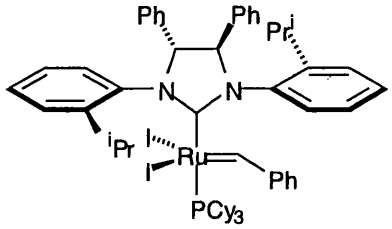
Scheme 1.4

The first chiral ruthenium catalysts were complexes of general form **31** with enantiopure NHC ligands, prepared by Grubbs and co-workers.[46] The results for desymmetrisation of achiral trienes varied greatly with the catalyst ligands and were dependent on substrate substitution and geometry. The best results, up to 90% enantiomeric excess, were achieved with catalyst **32** (converted to the diiodide analogue *in situ* by addition of sodium iodide).



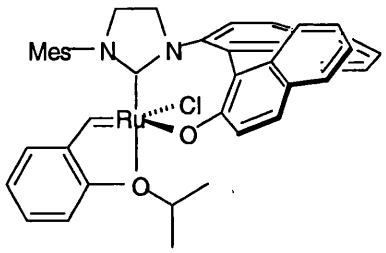
R = Ph, $-(CH_2)_4-$
Ar = mesityl, *o*-tolyl, *o*-isopropylphenyl
X = Cl, Br, I

31

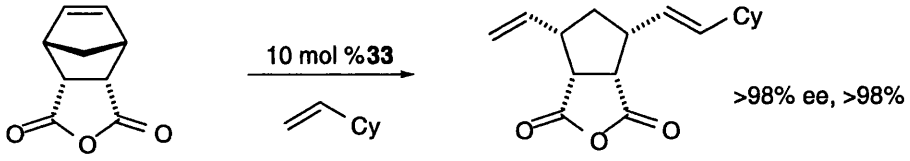


32

Hoveyda and co-workers have reported catalyst **33** which contains a bidentate chiral NHC ligand and a stereogenic ruthenium centre.[47] The catalyst was prepared in greater than 98% diastereo- and enantiomeric purity and, like other isopropoxystyrene-containing complexes, could be recovered by chromatography and reused. Preliminary results showed that the catalyst **33** displayed high enantioselectivity, over 98% enantiomeric excess, in the ROCM of norbornene derivatives with terminal alkenes (e.g. **Scheme 1.5**).



33



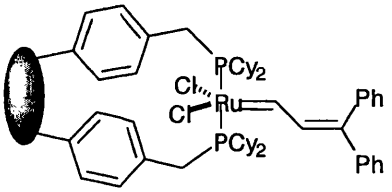
>98% ee, >98%

Scheme 1.5

1.4 SOLID-SUPPORTED METATHESIS CATALYSTS

The concept of immobilising organometallic catalysts onto solid supports has attracted much interest in recent years.[48] Despite the remarkable success and development of the alkene metathesis reaction, there are some disadvantages that could be overcome by the use of a supported catalyst. The available catalysts are expensive and in most cases not recyclable, restricting their use on a large industrial scale. Hoveyda's isopropoxystyrene-containing complexes can be recycled but require chromatography to recover the catalyst (**see Section 1.3**). A solid-supported, recyclable catalyst could allow the valuable metal complex to be easily recovered and reused. A heterogeneous system in which the ruthenium remained bound to a support would also minimise the ruthenium residues that usually contaminate the products of metathesis reactions.

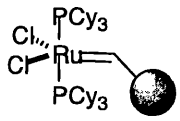
When this work began, only one example of a solid-supported well-defined alkene metathesis catalyst had been published. This was a 1995 report from Grubbs of the original vinylcarbene catalyst **7**, immobilised on a polystyrene support.[49] Ligand exchange of ruthenium complex **7** with randomly phosphine-functionalised polystyrene-divinylbenzene produced catalyst **34**. When this polymer complex was tested for ROMP, turnover numbers were found to be two orders of magnitude lower than with the homogeneous analogues. On attempting to recycle the catalyst, a loss of activity of 20% was observed after each cycle. The problems were attributed to incomplete phosphine substitution when forming the catalysts, reduced dissociation of the phosphine in areas of high ligand concentration, and slow diffusion of the polymeric substrate to and from the catalyst. The activity loss on recycling was possibly due to ruthenium leaching from the support and the formation of catalytically inactive complexes with *cis*-related phosphine ligands.



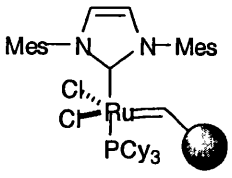
34

While this work was in progress, a number of other solid-supported metathesis catalysts were reported, utilising a variety of strategies. These different approaches are reviewed below.

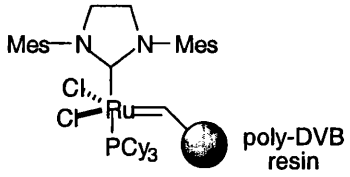
Among the simplest polymer-supported catalyst systems were 'boomerang' catalysts **35**[50] and **36**[51] developed by Barrett and co-workers. These were formed by cross metathesis of the corresponding ruthenium benzylidene complexes with vinyl polystyrene. When employed in a ring closing metathesis reaction, the first turn of the catalytic cycle released the ruthenium complex into solution where the propagating species is the same as that generated with a homogeneous catalyst, therefore resulting in comparable reactivity. After consumption of the substrate, the homogeneous complex was recaptured by the resin and could then be removed by filtration to give products with low ruthenium residues. Recycling catalysts **35** and **36** resulted in a much reduced activity in the second run. However, better results were achieved by adding a terminal alkene to the reaction mixture to generate more stable alkylidene complexes in solution than the propagating methylidene which is prone to decomposition.[7] The addition of triphenylphosphine prior to filtering the reaction mixture was also found to prolong catalyst lifetimes. Catalyst **36** retained high activity in up to four runs of RCM reactions when 1-octene and triphenylphosphine were used as additives.



35



36

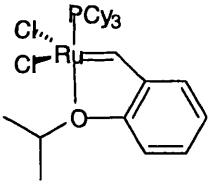


37

Nolan investigated similar 'boomerang' catalysts immobilised on a poly-divinylbenzene (poly-DVB) support.[52] This is a macroporous polymer which, unlike lightly

cross-linked polystyrene resins, has a permanent pore structure allowing access to sites in all solvents, without the need for swelling. It has a very large surface area and a large number of free vinyl groups available for cross metathesis with ruthenium carbene complexes. Poly-DVB versions of catalysts **35** and **36** were prepared along with complex **37** containing a saturated NHC ligand. The macroporous support was found to improve the recyclability of the catalysts. For example, the poly-DVB version of **36** still gave similarly high conversions (>80%) in the fourth run of the RCM of diethyl diallylmalonate to polystyrene-bound **36**, but without the use of any additives. Catalyst **37** performed even better, still giving quantitative conversion in the fourth run, again without the use of additives. However, on more demanding substrates activity and recyclability were considerably poorer.

The most popular approach to immobilisation of a metathesis catalyst was based on Hoveyda's ruthenium complex **19**, recyclable by chromatography.[26] It was thought by several groups that the robustness of this catalyst would result in an immobilised version exhibiting good activity and recyclability. Using the isopropoxystyrene moiety to immobilise the catalyst results in a 'boomerang' style catalyst similar to those described above where the catalysis occurs in solution and the active ruthenium species is then recaptured.

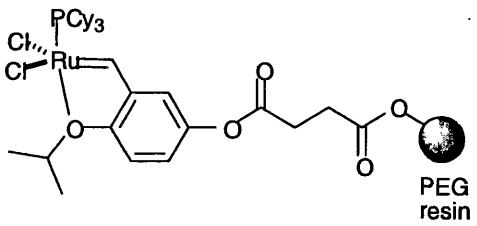


19

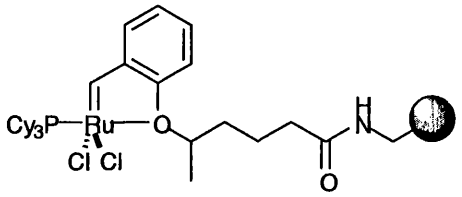
The first example of such a catalyst was complex **38** reported by Yao.[53] The support used was the soluble polymer poly(ethylene glycol) (PEG). This allowed the RCM reaction to be carried out under homogenous conditions in dichloromethane before diethyl ether was added to precipitate the polymer catalyst for recovery and reuse. The catalyst demonstrated excellent recyclability with only a slight loss of activity over 8 cycles; the 98% formation of a seven-membered nitrogen heterocycle in the first run dropped to 92% on the eighth

run. It was also demonstrated that the recovered catalyst could be used for the cyclisation of a different substrate without contamination from the previous reaction.

Catalyst **39** was prepared by Dowden and co-workers using polystyrene resin as the support.[54] RCM of several substrates was demonstrated in non-degassed dichloromethane in an air atmosphere. Recycling of the catalyst for RCM of benzyl diallylcarbamate resulted in steadily decreasing activity from 91% conversion for the first run to 63% for the fifth run. An attempt was made to make the catalyst suitable for use in polar protic solvents be preparing **39** on a TentaGel support. However, RCM in non-degassed methanol gave poor results.



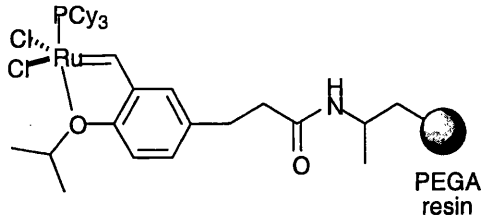
38



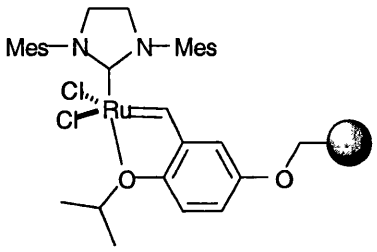
39

Blechert attempted to carry out RCM and CM in methanol and water using catalyst **40** with hydrophilic PEGA resin as the solid support.[55] The catalytic activity was variable and with some substrates a competing cycloisomerisation reaction was observed (see **Section 3.4**).

Blechert and co-workers also reported catalyst **41**, based on a polystyrene Wang resin, that gave high activity for cross metathesis with electron deficient alkenes.[56] Recycling of the catalyst was tested for the cross metathesis of methyl vinyl ketone with 1-pentenyl benzoate. Quantitative conversion was achieved in five runs although the reaction time required increased from four hours for the first two runs to two days in the fifth run.

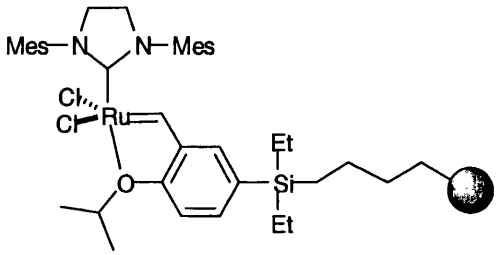


40



41

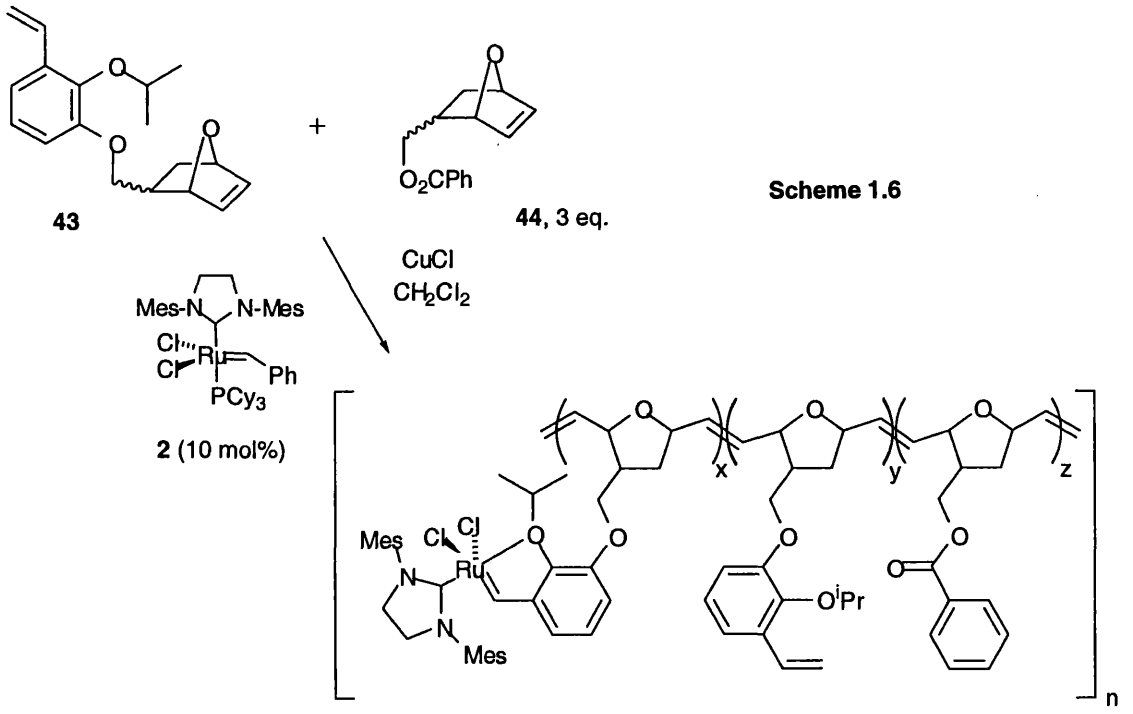
Another variation, from Grela and co-workers, was the use of a silyl linker in catalyst **42**.[57] This had the advantage that the carbene complex could be easily cleaved from the polystyrene support with tetrabutylammonium fluoride making determination of the ruthenium loading easier and more reliable. In many of the other supported catalysts the loading was determined only from indirect measurements such as elemental analysis of other elements or mass increase of the polymer. Catalyst **42** gave good results for RCM and CM of several substrates tested. The catalyst resin could be recycled up to five times with only a slight loss of activity but not if used in non-degassed solvent under air. The recycled catalyst was also used sequentially in five different reactions without any cross-contamination.



42

Another paper from Blechert's group described an innovative approach to a soluble polymer-bound catalyst.[58] Treatment of oxonorbornenes **43** and **44** with Grubbs's second generation catalyst **2** resulted in a ROMP reaction to form a co-polymer backbone and the isopropoxystyrene groups then chelated the ruthenium catalyst to give polymer **45**, in a one-pot reaction (**Scheme 1.6**). Supported catalyst **45** is soluble in most organic solvents but can be precipitated with diethyl ether or hexane. The catalyst displayed excellent

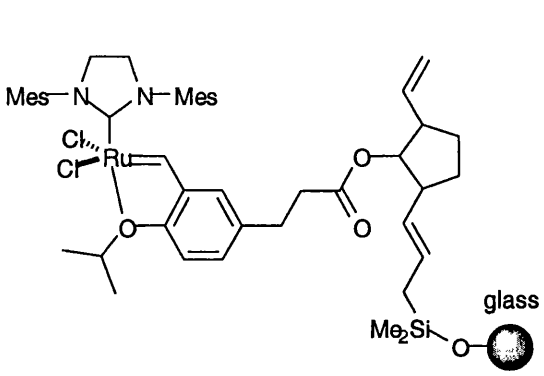
metathesis activity with 1 mol% of **45** at room temperature giving quantitative conversion for the RCM and ROCM of a range of substrates. Recyclability was also excellent; the RCM of *N*-tosyldiallylamine was quantitative in seven consecutive cycles. The most impressive feature of catalyst **45** was the very low ruthenium residues left in the products. This was an order of magnitude lower than achieved with the best methods for ruthenium removal from metathesis products and two orders lower than other solid-supported catalysts.



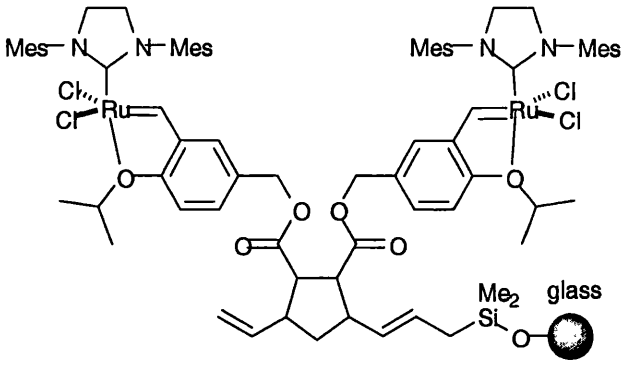
Scheme 1.6

45 x:y:z = 1:9:30

Fittingly, Hoveyda and co-workers produced the most impressive immobilisation of their catalyst. They used a porous sol-gel glass to make monolithic pellets supporting ruthenium complexes such as **46** and **47**.[59] The activity of the catalyst pellets was demonstrated with a range of substrates including the synthesis of two 25-member libraries of RCM and ROCM products. Catalyst recovery was simply carried out by removing the pellet with a pair of tweezers.

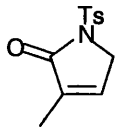


46

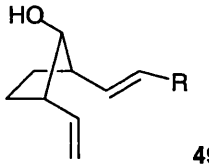


47

Recyclability of catalyst **47** was excellent. Trisubstituted alkene **48** was quantitatively formed in *fifteen* cycles when the catalyst was used in dry solvent under nitrogen (three cycles were achieved in air with reagent grade solvent). It was also shown that the catalyst, after carrying out RCM to form **48** in four cycles, could then be used for four cycles of a ROCM reaction to quantitatively form **49**. A different cross metathesis substrate was used in each cycle but no contamination from previous reactions was observed in the products.



48

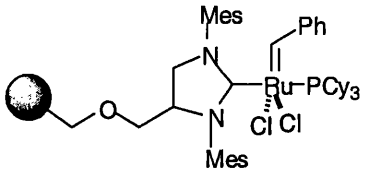


49

1. R = phenyl
2. R = *n*-hexyl
3. R = ferrocenyl
4. R = H

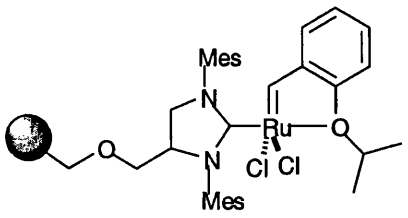
Another strategy for immobilisation of a metathesis catalyst has been to use the N-heterocyclic carbene ligand of Grubbs's second generation catalyst **2** as an attachment point. This results in the ruthenium complex being permanently attached to the support because the NHC does not dissociate during the catalytic cycle.

Blechert and co-workers used this approach to synthesise catalyst **50** on a cross-linked polystyrene support.[60] The catalyst was demonstrated to carry out RCM and enyne cross metathesis reactions with several substrates. The attempted recycling of catalyst **50** was reported to give variable results. In the best case, complete cyclisation to a seven-membered nitrogen heterocycle was achieved in four runs but the time required increased from 1.5 hours in the first run to two days in the fourth run.

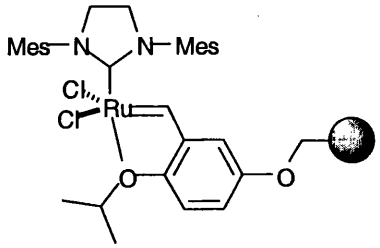


50

Blechert also used the same method to immobilise the Hoveyda catalyst.[56] The activity of catalyst **51** was compared with previously discussed catalyst **41** which is immobilised through the isopropoxystyrene moiety. Although both catalysts gave comparable results for RCM, catalyst **51** performed considerably poorer in the cross metathesis of electron-deficient alkenes. It was postulated that the difference was diffusion related because the catalytically active species from **51** remains bound to the resin whereas that from **41** is released into solution. In the case of catalyst **51**, decomposition of the electron-deficient intermediates may be competitive with metathesis. This also explains why there is little difference in RCM activity because there is only one substrate and so diffusion effects are less important.



51

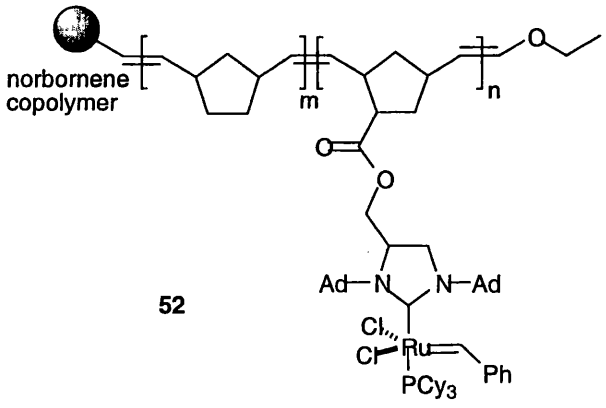


41

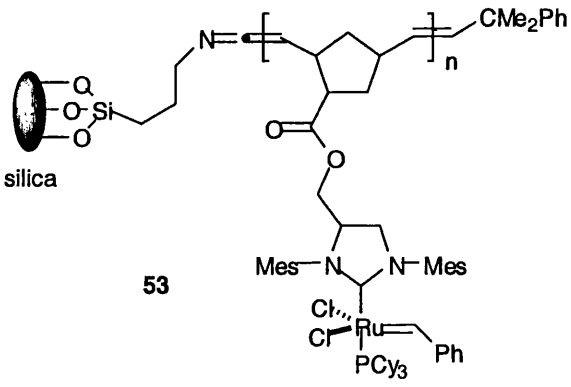
Buchmeiser and co-workers used the NHC ligand to immobilise a metathesis catalyst onto functionalised monolithic columns.[61] A porous polymer matrix was generated by ROMP within a borosilicate column and then derivatised with an adamantyl-substituted imidazolium salt as the carbene precursor, before being loaded with Grubbs's catalyst **1**. The resulting catalyst was of the form represented by structure **52**. Metathesis reactions were carried out by passing a solution of the substrate through the column. The preliminary results reported suggest that the monoliths exhibit high activity for RCM and ROMP

reactions. *Cis*-1,4-diacetoxybut-2-ene was used as an additive to convert intermediate ruthenium methylidenes to more stable species. This improved the lifetime of the catalyst and allowed the column to be used consecutively for different metathesis reactions.

Buchmeiser also reported a metathesis catalyst immobilised on silica.[62] A polynorbornene with pendant imidazolium groups and endcapped with a triethoxysilyl group was grafted onto silica. The free carbene was then generated and reacted with Grubbs's catalyst **1** to give supported catalyst **53**. Silica catalyst **53** was tested as a slurry for the RCM of diethyl diallylmalonate. It was reported that regardless of solvent, temperature or reaction times, the maximum turnover number achieved was approximately 80. More challenging substrates gave poorer results suggesting that diffusion of the substrate through the support was too slow resulting in decomposition of the catalytic species.



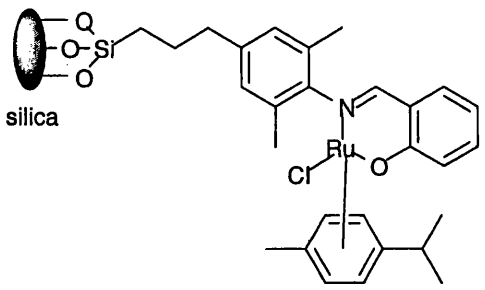
52



53

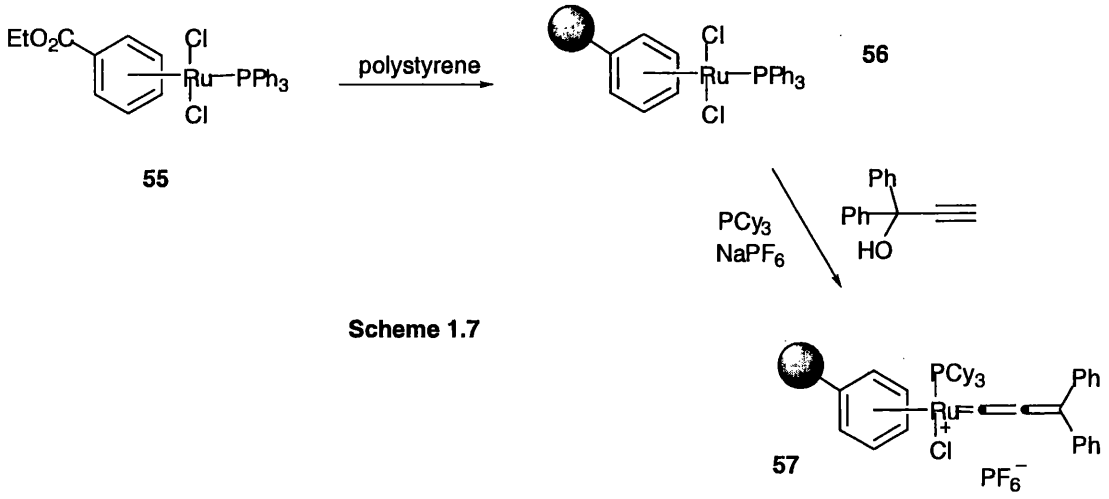
A few metathesis catalysts based on different parent structures were reported.

Verpoort described silica-supported complex **54**[63] based on his corresponding homogeneous catalyst.[64] The initiating species for alkene metathesis was formed by treating complex **54** *in situ* with a catalytic amount of trimethylsilyldiazomethane. The RCM activity of catalyst **54** was found to be comparable to the homogeneous analogue. The catalyst was successfully recycled for four runs of the RCM of diethyl diallylmalonate.



54

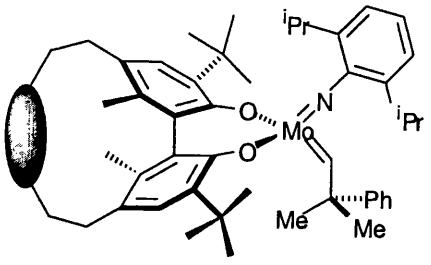
A novel approach to a supported catalyst was reported by Kobayashi.[65] Treatment of polystyrene with ruthenium-containing precursor **55** formed polymer **56** in which the ruthenium was coordinated to the aromatic rings of the polystyrene (**Scheme 1.7**). This ruthenium complex was then converted to polymer-supported catalyst **57** which was found to be moderately active for the RCM of several substrates. The catalyst could be recovered and reused but needed to be treated with tricyclohexylphosphine and sodium hexafluorophosphate to maintain its activity.



55 56 57

Scheme 1.7

One example of a solid-supported molybdenum metathesis catalyst was also reported. Hoveyda, Schrock and co-workers prepared chiral catalyst **58** on a polystyrene support.[66] Although catalyst **58** was less active than homogeneous version **29**, it exhibited comparably high enantioselectivity in RCM and ROCM reactions. After filtering under an inert atmosphere the catalyst could be reused once but in subsequent cycles activity decreased and increased molybdenum leaching from the support was observed.

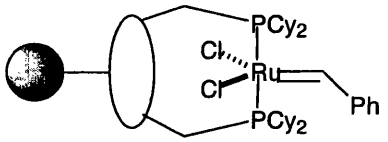


58

2. BISPHOSPHINE LIGANDS AND METALLAMACROCYCLES

2.1 INTRODUCTION

The initial strategy for developing a solid-supported alkene metathesis catalyst was as shown in structure **59**. The aim was to use the phosphine ligands of a ruthenium alkylidene complex to attach the catalyst to a solid-support. However, unlike previous attempts by Grubbs in which each phosphine was separately attached to the support (see **Section 1.4**), the idea was that the ligands would be *trans*-coordinating bidentate phosphines, with a rigid backbone providing the point of attachment. This approach was designed to avoid the problems encountered by Grubbs such as incomplete phosphine exchange when forming the supported complex, and the phosphine ligands recoordinating in a *cis* manner during the catalytic cycle giving inactive species. Catalyst leaching from the resin would also be reduced as the ruthenium remains attached to the support when one phosphine ligand dissociates during the catalytic cycle.

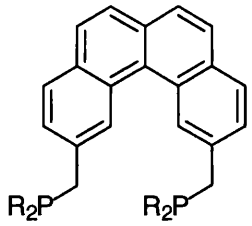


59

The first objective was to synthesise bisphosphine ligands with a definite preference for *trans* chelation across transition metal centres. Few such ligands have been described in the literature. Although a number of bisphosphine ligands have been shown to form *trans*-coordinated complexes, these are often formed as mixtures or in equilibria with other geometries. The geometry of the complexes is also often highly dependent on the reaction conditions and the transition metal used. A recent review discusses these *trans*-spanning bisphosphine complexes in detail.[67]

Venanzi's bisphosphines **60**, based on a rigid benzo[c]phenanthrene backbone, are the most reliable *trans* chelating ligands.[68] Ligand **60a**, which has been most studied shows a marked preference for *trans* chelation and readily forms 5-coordinate trigonal bipyramidal complexes with transition metals such as ruthenium.[69] However, whilst trialkylphosphines **60b** and **60c** may be suitable for forming a ruthenium alkylidene

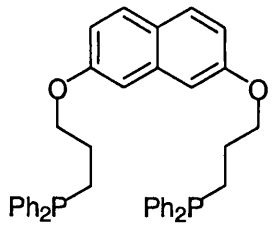
metathesis catalyst, they require a long and comparatively difficult synthesis which would be exacerbated by the addition of an attachment point for anchoring onto a solid support.

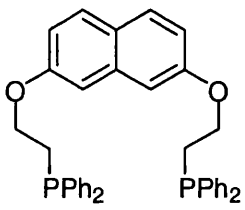


60a R = Ph
60b R = ^{t}Bu
60c R = Cy

Therefore, two new bisphosphine ligands **61** and **62** were designed to allow similar separation between the phosphorus atoms to that found in the Venanzi ligands **60**, but with a more flexible ligand backbone. It was hoped that the flexibility would allow one of the phosphines to dissociate during the catalytic cycle but that the rigid naphthalene backbone would help maintain the required *trans* geometry. Importantly, it was considered that the ligands would be amenable to short and straightforward syntheses. Although the ligands would require alkyl groups on the phosphines to produce active catalysts for ring closing metathesis, the aim was to first synthesise ligands containing phenyl groups and determine whether they had the correct geometry for *trans* chelation. Aryl phosphines are cheaper, easier to handle as they are much less prone to oxidation, and still allow the resulting complexes to be tested for ring opening metathesis polymerisation.

61

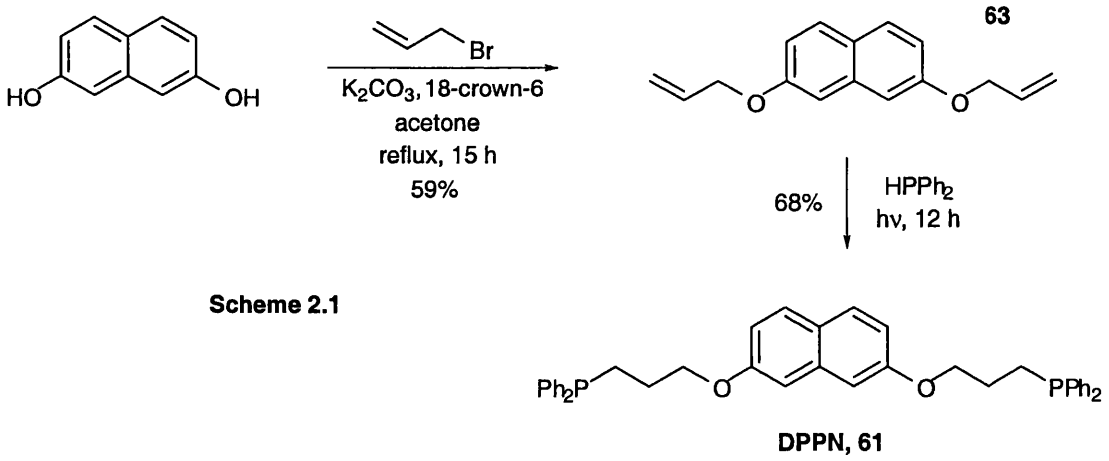




62

2.2 SYNTHESIS OF BISPHOSPHINE LIGANDS

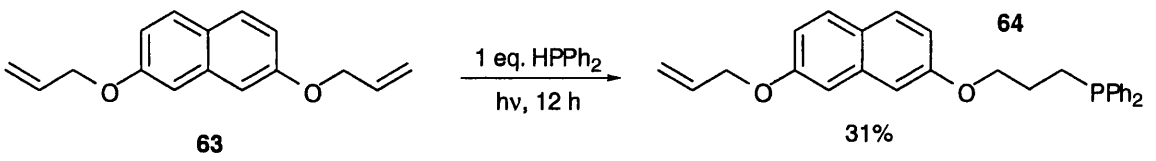
Bisphosphine **61** was obtained by the short, two-step synthesis shown in **Scheme 2.1**, beginning from 2,7-dihydroxynaphthalene. The first reaction, etherification with allyl bromide, had been described twice in the literature but with poor yields (27%[70] and 45% crude[71]). After a couple of attempts, it became apparent that the main problem lay in the work-up and purification. Small amounts of several highly coloured by-products were formed which proved hard to separate from the desired product by recrystallisation. The reaction was tried again with a small amount of 18-crown-6 added to help solvate the potassium carbonate, and the crude product was purified by column chromatography before recrystallisation. This enabled pure allyl ether **63** to be obtained in 59% yield. When diene **63** was dissolved in diphenylphosphine and subjected to ultraviolet radiation, addition to the double bonds occurred as expected, with the phosphine adding to the less hindered end. Bisphosphine **61** was obtained after chromatography as a very viscous oil which oxidised slowly in air and more rapidly in solution. Ligand **61**, 2,7-bis(3'-diphenylphosphinopropoxy)naphthalene, was given the abbreviation DPPN.



Scheme 2.1

Carrying out the photochemistry with one equivalent of diphenylphosphine was also tried, to obtain monophosphine ligand **64** with an alkene as a chelating group (**Scheme 2.2**). Predictably, using this statistical method gave a mixture of starting material,

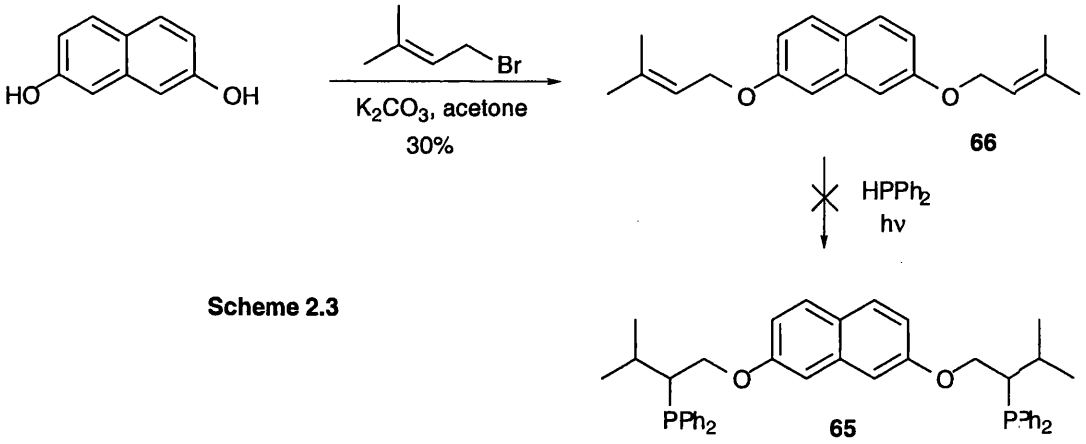
monophosphine and bisphosphine. Chromatographic separation allowed the isolation of monophosphine **64**, although no further work was carried out with this ligand.



Scheme 2.2

+ **61** 19% + **63** 34%

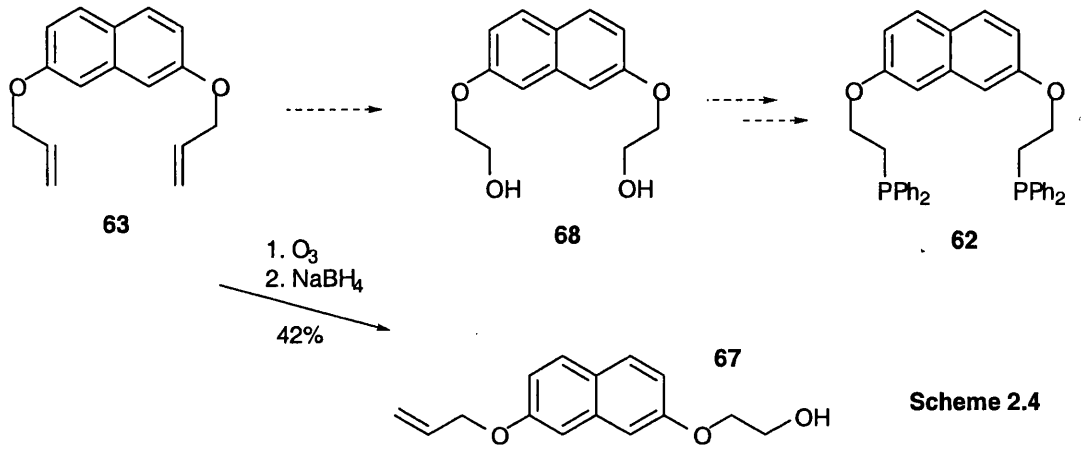
It was hoped that the more hindered bisphosphine ligand **65** could be obtained by a similar photochemical addition to prenyl ether **66**, the phosphine again adding to the less hindered end of the double bond (**Scheme 2.3**). Compound **66** was prepared from dihydroxynaphthalene and prenyl bromide but in this case the photochemistry was unsuccessful. Even after irradiation for several days, no addition product was detected and only starting material was recovered.



Scheme 2.3

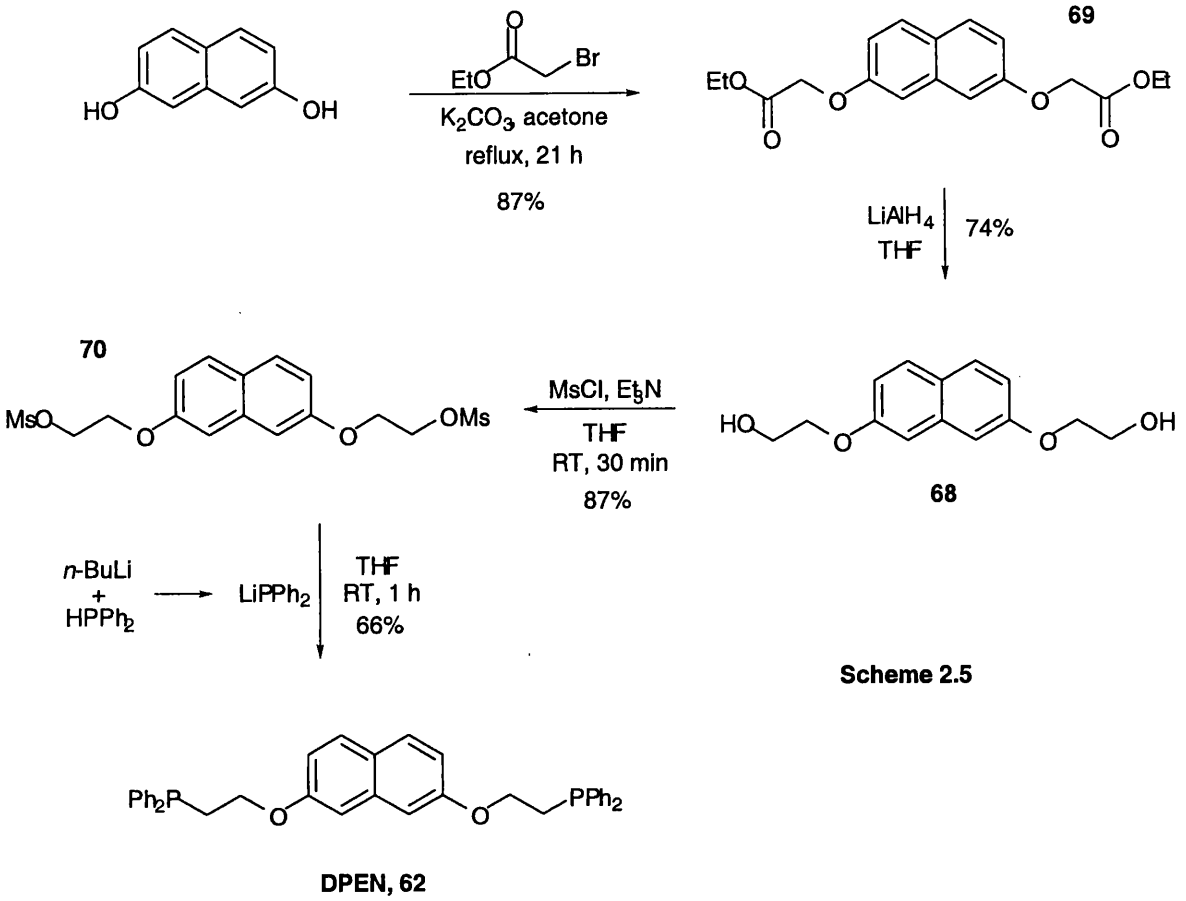
Another target ligand was bisphosphine **62** with shorter connections to the naphthalene backbone. It was initially thought that diene **63** would also be used as a precursor to bisphosphine **62**, by reductive ozonolysis and subsequent transformation of the hydroxyl groups to phosphines (**Scheme 2.4**). The first attempted ozonolysis, with sodium borohydride subsequently added to reduce the ozonide, did not proceed to completion. A

large proportion of starting material was recovered by column chromatography but surprisingly the only product isolated was compound **67**, in which only one double bond had reacted. A second attempt at the reaction was left longer but a mixture of products was formed and no alcohol or diol could be isolated.



Scheme 2.4

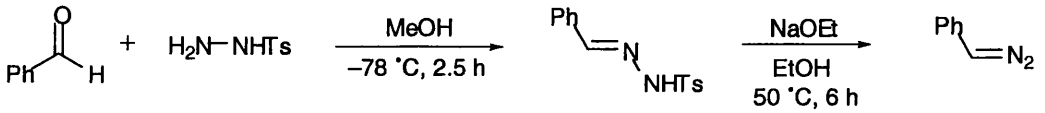
An alternative route to known diol **68**, modified from a literature procedure,[72] gave very good results and so was subsequently used instead (**Scheme 2.5**). In contrast to the reaction of dihydroxynaphthalene with allyl bromide, the reaction with ethyl bromoacetate proceeded cleanly, in high yield, producing diester **69**[73] pure enough to use without recrystallisation. Diester **69** was reduced with lithium aluminium hydride to give the required diol **68**, which was then treated with methanesulfonyl chloride and triethylamine to produce dimesylate **70**. These two reactions also proceeded in high yield giving crude products of high purity, although dimesylate **70** was usually recrystallised before further use. When dimesylate **70** was treated with lithium diphenylphosphide (prepared *in situ* from *n*-butyl lithium and diphenylphosphine), substitution proceeded as expected to give bisphosphine **62** in good yield after recrystallisation, and complete the synthesis. Ligand **62**, 2,7-bis(2'-diphenylphosphinoethoxy)naphthalene (DPEN) was a crystalline air-stable solid which oxidised slowly in solution.


HO
OH
EtO
O
Br
K_2CO_3, acetone
reflux, 21 h
87%
69
EtO
OEt
$LiAlH_4$
THF
74%
70
MsO
OMs
MsCl, Et_3N
THF
RT, 30 min
87%
HO
OH
68
n-BuLi
+
$HPPh_2$
$LiPPh_2$
THF
RT, 1 h
66%
Ph_2P
PPh_2
DPEN, 62

Scheme 2.5

2.3 RUTHENIUM COMPLEXES AND ALKENE METATHESIS CATALYSTS

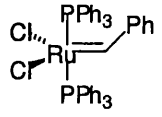
With the synthesis of two new bisphosphine ligands established, attention turned to preparing ruthenium alkylidene complexes with the ligands and investigating their potential for catalysing alkene metathesis. The ruthenium precursor for the alkylidene complexes was $RuCl_2(PPh_3)_3$. This was prepared from ruthenium trichloride hydrate and triphenylphosphine by the standard literature procedure.[74] The alkylidene moiety came from phenyldiazomethane **71** which due to its instability and explosive potential had to be prepared immediately before it was required. It was made by basic decomposition of benzaldehyde tosylhydrazone **72**,[75] which was prepared from benzaldehyde and tosylhydrazine (**Scheme 2.6**).[76]



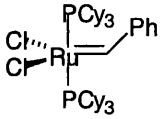
72 71

Scheme 2.6

The preparation of ruthenium alkylidene **73** is difficult as it is unstable in solution and must be obtained by precipitation and cannula filtration.[1] For this reason, an immediate ligand substitution is usually carried out with tricyclohexylphosphine to obtain Grubbs's benzylidene catalyst **1**, which is more stable. However, a sample of **73**, which will catalyse ring opening polymerisation but not ring closing metathesis, was required to compare with any new alkylidene complex. Therefore, the reaction was carried out and complex **73** prepared by the reaction of phenyldiazomethane with $RuCl_2(PPh_3)_3$.



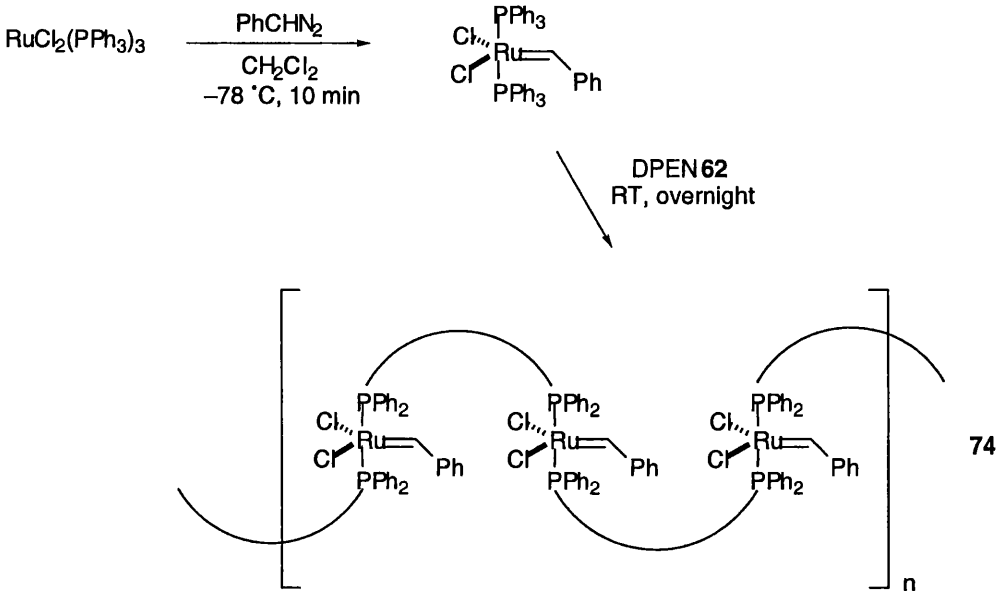
73



1

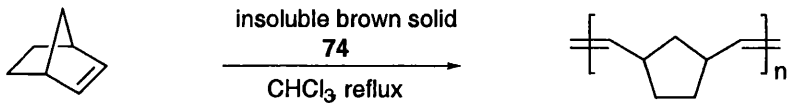
The ^{1}H NMR spectrum showed that the complex was not very clean but the formation of **73** was evident from the characteristic downfield resonance of the proton on the alkylidene moiety (δ 19.3). Alkylidene **73** was then tested for ring opening metathesis polymerisation (ROMP) activity using norbornene on an NMR tube scale to verify that this method could be used to test any new catalysts prepared. It was clearly observed that within 90 minutes the sample of **73** had completely polymerised 150 equivalents of norbornene.

An attempt was then made to prepare an alkylidene complex containing bisphosphine DPEN **62**. This involved a one-pot procedure, adding DPEN shortly after $RuCl_2(PPh_3)_3$ had been treated with phenyldiazomethane (**Scheme 2.7**). While stirring overnight, a brown solid precipitated from the reaction mixture. Unfortunately, when this product was isolated, it was found to be completely insoluble in all solvents investigated, preventing satisfactory characterisation. However, the infrared spectrum contained a strong band at 1209 cm^{-1} attributed to Ar–O–C bond stretching, indicating the presence of the ligand. (The band occurs at 1211 cm^{-1} in the free ligand). From the results subsequently obtained with other metals (**Sections 2.4 and 2.5**), it seems likely that the product was an oligomeric or polymeric complex such as that represented by structure **74**.



74

To determine whether this solid displayed any catalytic activity despite its insolubility, the ROMP of norbornene was attempted using a sample suspended in dichloromethane. After stirring for three hours at room temperature, no polymerisation was observed. However, an attempt at higher temperature was more successful, even though there was no evidence of dissolution of the catalyst: a suspension of **74** in refluxing chloroform polymerised 45 equivalents of norbornene in 15 hours (**Scheme 2.8**). This was evidence that **74** was indeed a novel ruthenium alkylidene complex. The catalytic activity could not have been due to the presence of **73** as an impurity because otherwise some polymerisation would have occurred at room temperature and in any case the solid had been well washed.



Scheme 2.8

It was decided that before continuing work with ruthenium complexes, it would be instructive to investigate the complexes of the ligands with some other, easier to handle, transition metals to determine whether they were capable of *trans* coordination.

2.4 PALLADIUM COMPLEXES

It was thought that platinum and palladium complexes, being easily prepared and more stable, would be suitable for investigating the coordination preferences of the ligands.

The palladium starting material used was $PdCl_2(MeCN)_2$. This was prepared by simply stirring palladium(II) chloride in acetonitrile.[77] $PdCl_2(MeCN)_2$ and DPEN **62** were then stirred overnight in dichloromethane at room temperature and removal of the solvent yielded a bright yellow solid. The crude ^1H NMR spectrum showed several complex signals where the methylene groups of the ligand would be expected suggesting that possibly more than one compound or isomer had been formed. The ^{31}P NMR spectrum consisted of two main signals, close together and of equal intensity, plus several smaller signals. Attempts to recrystallise the crude product were hampered by its erratic solubility characteristics. For example, on occasions the whole sample would readily dissolve in CH_2Cl_2 or $CHCl_3$ but then, on removing the solvent and repeating, a precipitate would remain even in a much larger volume of solvent.

It was concluded that the compound was exhibiting fluxional behaviour in solution. This is consistent with studies of palladium(II) complexes with long-chain bisphosphine ligands $R_2P–(CH_2)_n–PR_2$.[78,79] These reactions have often resulted in the formation of numerous, inseparable products with the same empirical formula, although monomeric and dimeric products have sometimes been isolated.[80,81] A detailed study into the lability of the palladium(II) centre in several complexes with long-chain bisphosphines found that dynamic equilibria existed in solution between *cis* and *trans* complexes and also between monomers and oligomers.[79] Similar behaviour by a DPEN complex would explain the solubility observations. No single isomer could be isolated although a FAB mass spectrum of the product mixture provided evidence that the main species present was actually dimeric, i.e. $Pd_2Cl_4(DPEN)_2$. It appeared that it would be difficult to obtain useful information about the ligands from palladium complexes and so these were not investigated further.

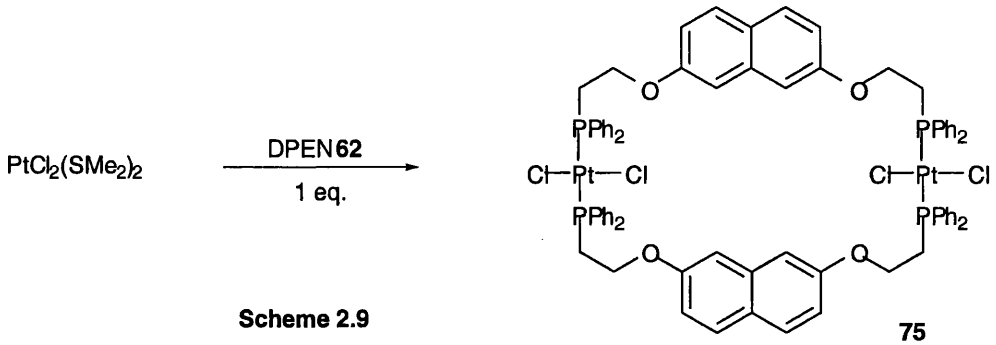
2.5 PLATINUM COMPLEXES

In contrast to palladium(II) complexes, the platinum(II) metal centre is relatively inert and its reactions with bisphosphine ligands therefore generally occur under kinetic control. This means that the products formed are dependent on a number of factors such as the donor properties of the ligand, reaction conditions, and the metal precursor employed.[82]

An advantage of platinum-phosphine complexes is that their geometry can be determined from the coupling constants in the ^{31}P NMR spectra. The separation between the ^{195}Pt satellites gives the value of $^{1}J_{Pt\text{-}P}$ which allows the assignment of the geometry around the platinum centre. For complexes of the general formula $PtCl_2(PR_3)_3$, the *trans* isomers have $^{1}J_{Pt\text{-}P}$ about 2500 Hz whereas the *cis* isomers have $^{1}J_{Pt\text{-}P}$ about 3500 Hz.[83]

The initial reaction carried out was to stir $PtCl_2(SMe_2)_2$ (*cis/trans* mixture) with one equivalent of DPEN **62** in dichloromethane at room temperature. Rather unpromisingly, the ^{31}P NMR spectrum of the crude product consisted of about ten signals of varying intensities, with their associated ^{195}Pt satellites. Analysis of the coupling constants showed that it contained signals due to both *cis*- and *trans*-coordinated phosphines.

Only one compound, significantly less polar than the rest, could be isolated pure from the mixture by column chromatography. The ^{31}P NMR spectrum of this complex gave $^{1}J_{Pt\text{-}P}$ = 2562 Hz indicating *trans* coordination of the ligand. A FAB mass spectrum indicated that the complex was dimeric. Slow diffusion of ether into a dichloromethane solution of the complex produced yellow prisms suitable for single-crystal X-ray analysis, which was carried out by Dr. Louis Farrugia. This confirmed that the complex was the metallamacrocycle *trans*, *trans*-$Pt_2Cl_4(DPEN)_2$ **75** (**Scheme 2.9**). The yield of **75** was only 5% but the remaining products in the mixture could not be separated.



Scheme 2.9

75

Figure 2.1 shows the dimeric structure of **75** with the two DPEN ligands bridging the square-planar platinum centres in a mutually *trans*, *trans* arrangement. As can be seen from the space-filling diagram (**Figure 2.2**), the 28-membered macrocycle has a central cavity with a radius of approximately 5 Å.

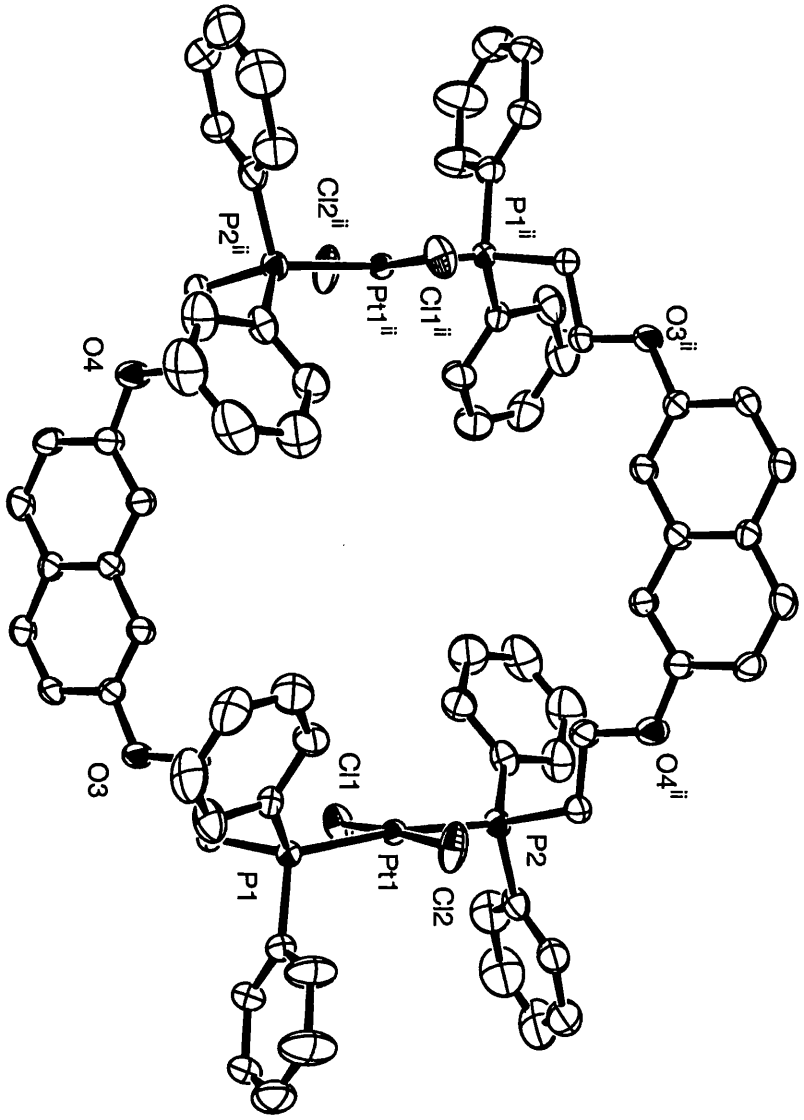


Figure 2.1 Ortep plot of *trans*, *trans*-$Pt_2Cl_4(DPEN)_2$ **75** with thermal ellipsoids shown at the 30% probability level. Atoms with primed labels are related to unprimed atoms by the symmetry operation $(1-x, 2-y, 1-z)$. Selected bond lengths (Å) and angles (°): Pt–Cl(1), 2.2982(15); Pt–Cl(2), 2.2879(16); Pt–P(1), 2.3113(14); Pt–P(2), 2.3057(15); Pt...Pt^{ii}, 10.692(1). Cl(1)–Pt–P(1), 92.02(5); Cl(1)–Pt–P(2), 88.70(6); Cl(2)–Pt–P(1), 87.75(6); Cl(2)–Pt–P(2), 91.27(6); Cl(1)–Pt–Cl(2), 177.29(8); P(1)–Pt–P(2), 174.32(5).

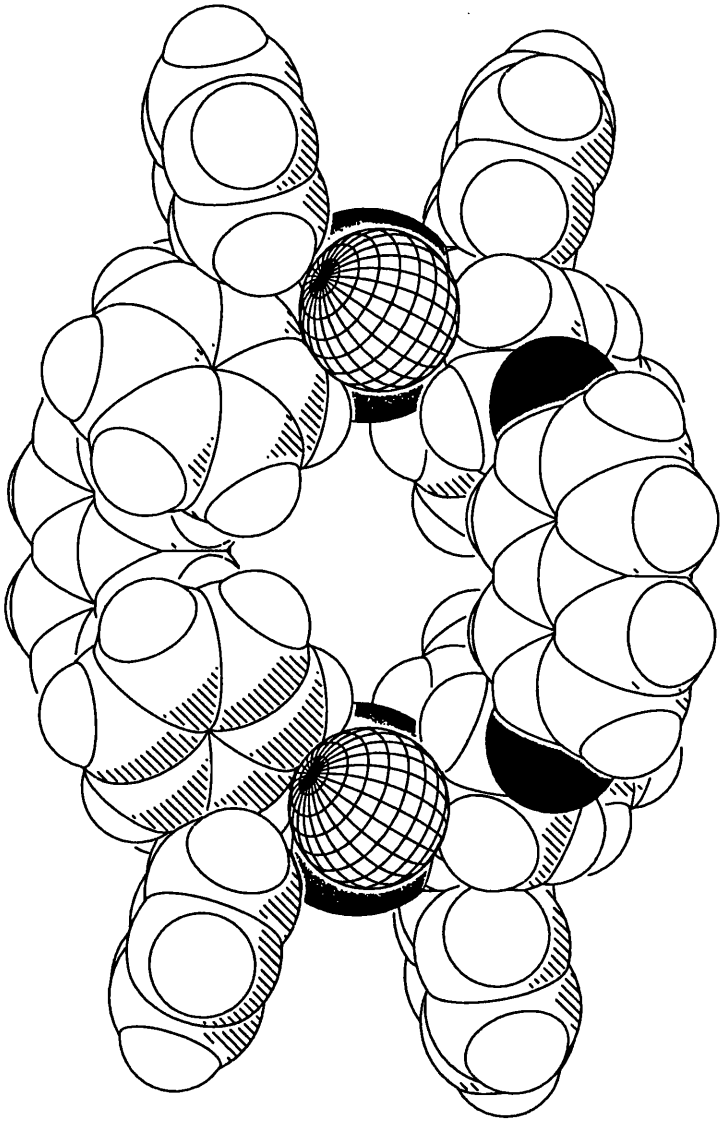
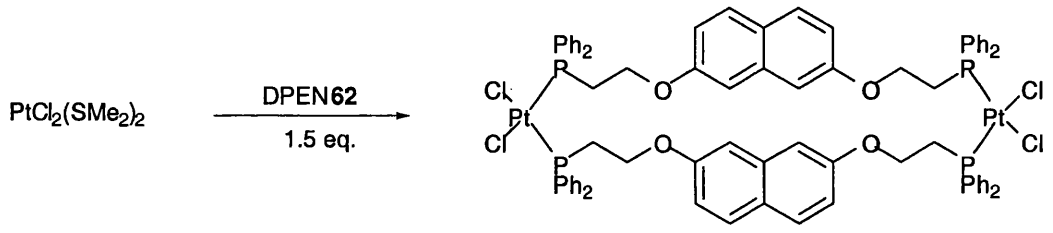


Figure 2.2 Space-filling plot of *trans*, *trans*-$Pt_2Cl_4(DPEN)_2$ **75**

The reaction was repeated but under high dilution conditions to try to prevent the formation of oligomeric complexes. On removal of the solvent a white solid remained. The ^{31}P NMR spectrum of this product consisted of two main signals, both with platinum satellites indicating *cis* geometry, and a FAB mass spectrum suggested that the dimer was the predominant species. However, no pure compound could be isolated for further identification. It was then realised that, by mistake, an excess of the ligand (1.5 equivalents) had been used. Excess phosphine present in the reaction mixture could catalyse the isomerisation of the initially formed kinetic products so that the complexes eventually obtained would be the thermodynamic products. The reaction was only left for 45 minutes and this may not have been long enough to allow equilibration to the most stable product.

The reaction was again carried out with 1.5 equivalents of ligand and high dilution but this time stirred overnight in toluene. The white solid precipitated was filtered off and found to consist almost entirely of a single product by ^{31}P NMR with $^{1}J_{Pt\text{-}P} = 3627$ Hz, indicating *cis* coordination of the ligand. A FAB mass spectrum showed that the complex was dimeric. Colourless prisms were grown from a concentrated chloroform solution and the X-ray crystal structure confirmed the identification of the product as *cis, cis*-$Pt_2Cl_4(DPEN)_2$ **76** (**Scheme 2.10**).



Scheme 2.10

76

The crystal structure of **76** is shown in **Figure 2.3**. The *cis, cis* arrangement of the two bridging DPEN ligands can be clearly seen. The Pt–P bonds are shorter and the Pt–Cl bonds longer than observed for complex **75**, consistent with the differing *trans* influences. The naphthalene rings of the DPEN ligands are approximately parallel to each other and nearly in van der Waals contact, as shown in the space-filling plot (**Figure 2.4**).

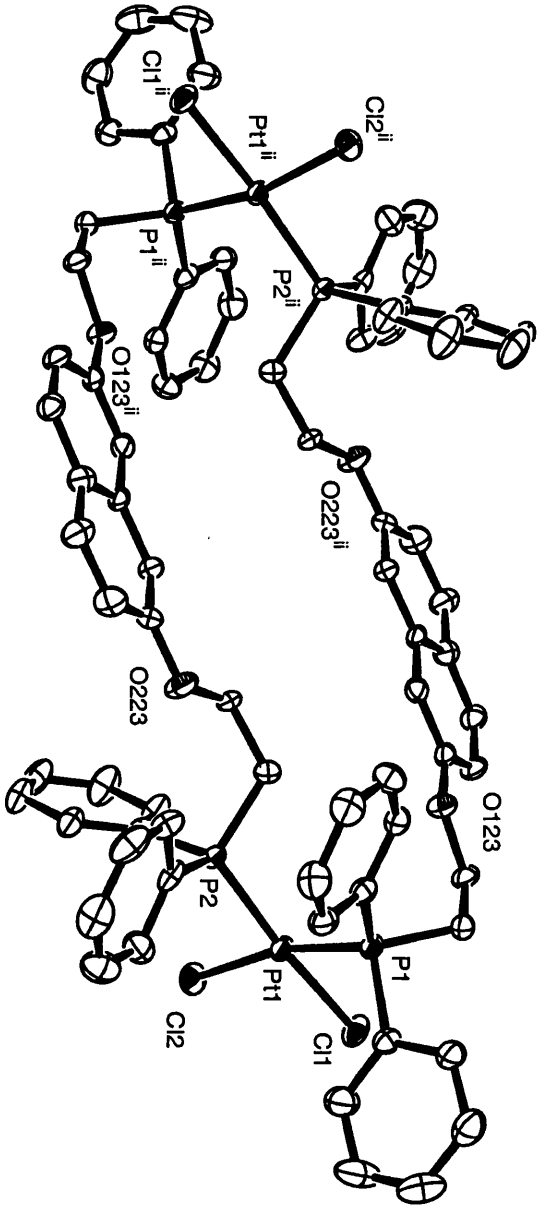


Figure 2.3 Ortep plot of *cis*, *cis*-$Pt_2Cl_4(DPEN)_2$ **76** with thermal ellipsoids shown at the 50% probability level. Atoms with primed labels are related to unprimed atoms by the symmetry operation $(1 - x, 1 - y, - z)$. Selected bond lengths (Å) and angles (°): Pt–Cl(1), 2.3495(19); Pt–Cl(2), 2.3566(18); Pt–P(1), 2.2567(18); Pt–P(2), 2.2479(19); Pt...Pt^{ii}, 14.174(1). Cl(1)–Pt–Cl(2), 87.56(7); P(1)–Pt–P(2), 97.54(7).

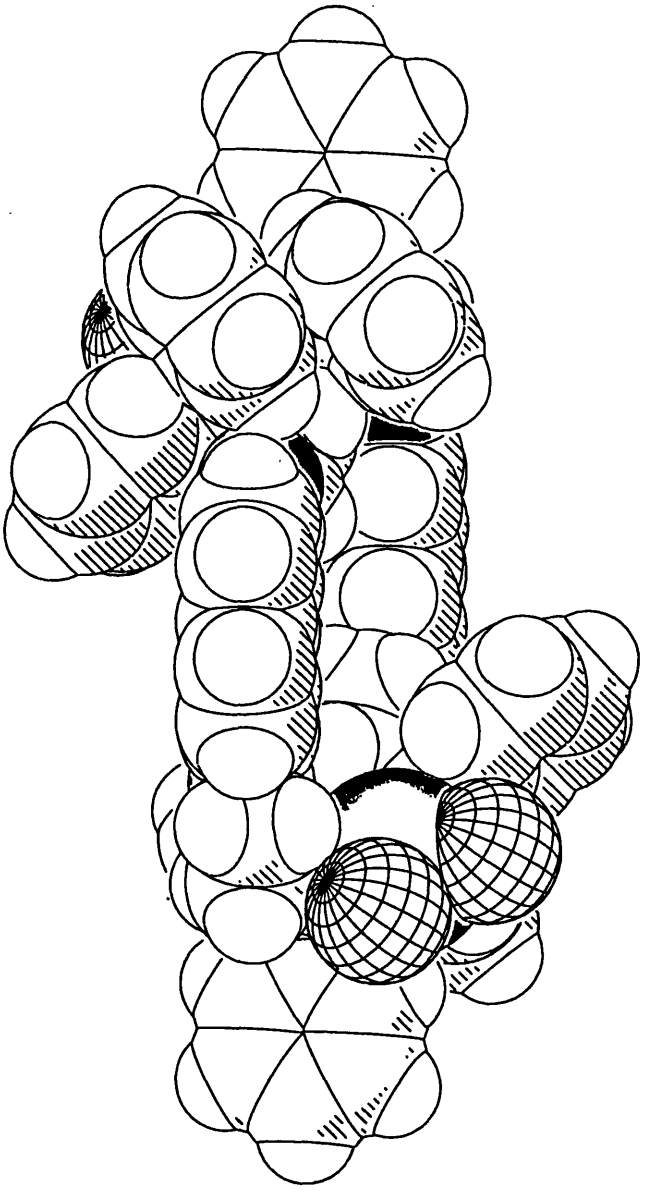


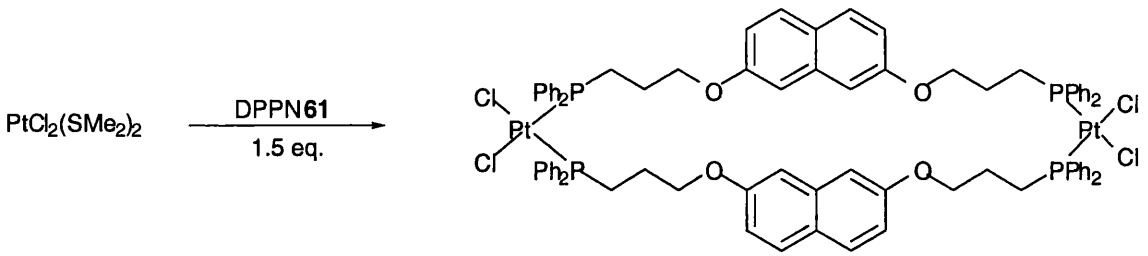
Figure 2.4 Space-filling plot of *cis*, *cis*-$Pt_2Cl_4(DPEN)_2$ **76**

It appeared that *cis, cis* complex **76** was the thermodynamic product and equilibration to it was catalysed by an excess of the phosphine ligand. Even under high dilution conditions, and in a non-polar solvent (which can promote *trans* coordination[80]), the *cis, cis*-dimer was the favoured product. The mixture formed in the first reaction with one equivalent of DPEN was a mixture of kinetic and thermodynamic products, of which the *trans, trans*-dimer **75** was the only one isolated.

An undergraduate project student, Alexis Perry, carried out some further investigations to confirm these conclusions.[84] He showed that *cis, cis* complex **76** was also formed as the major product if just one equivalent of DPEN was used but under inverse addition, i.e. the platinum precursor was added slowly to the ligand so there was always an excess of phosphine present to catalyse the isomerisation. Taking the kinetic mixture of products formed by 'normal' addition of one equivalent of DPEN and treating it with excess ligand also resulted in the formation of complex **76** as the only product.

I had observed by ^{31}P spectroscopy that treatment of a solution of pure *trans, trans*-dimer **75** with a small amount of DPEN at room temperature rapidly converted it to the *cis, cis*-dimer **76** in the few minutes taken to obtain a spectrum. However, Alexis carried out a low temperature NMR study which allowed observation of the isomerisation process. At 203 K, the *trans, trans*-dimer was fairly stable in the presence of excess phosphine. On gradually warming to 243 K, the signal was observed to broaden and then vanish, eventually being completely replaced by a signal due to the *cis, cis*-dimer.

I obtained similar results to those described above with the longer chain ligand DPPN **61**. Stirring $PtCl_2(SMe_2)_2$ with one equivalent of DPPN in dichloromethane at high dilution produced a mixture exhibiting eight signals in the ^{31}P NMR spectrum. The platinum satellites indicated a mixture of *cis* and *trans* geometries but no pure compounds could be isolated by chromatography. However, reaction with 1.5 equivalents of DPPN gave a white solid which was identified by ^{31}P NMR ($^1J_{Pt\text{-}P}$ = 3646 Hz) and FAB-MS as being predominately *cis, cis*-$Pt_2Cl_4(DPPN)_2$ **77** (**Scheme 2.11**). A small amount of a closely similar compound presumed to be a *cis, cis, cis*-trimer was also present.



Scheme 2.11

77

Alexis Perry replicated these results and grew crystals of complex **77** for X-ray analysis (**Figure 2.5**). The crystal structure is slightly different from that of DPEN complex **76**. The longer reach of the DPPN ligands allows the $PtCl_2$ groups to lie interior to the metallamacrocycle resulting in a close contact between the two inward-orientated chlorine atoms (**Figure 2.6**).

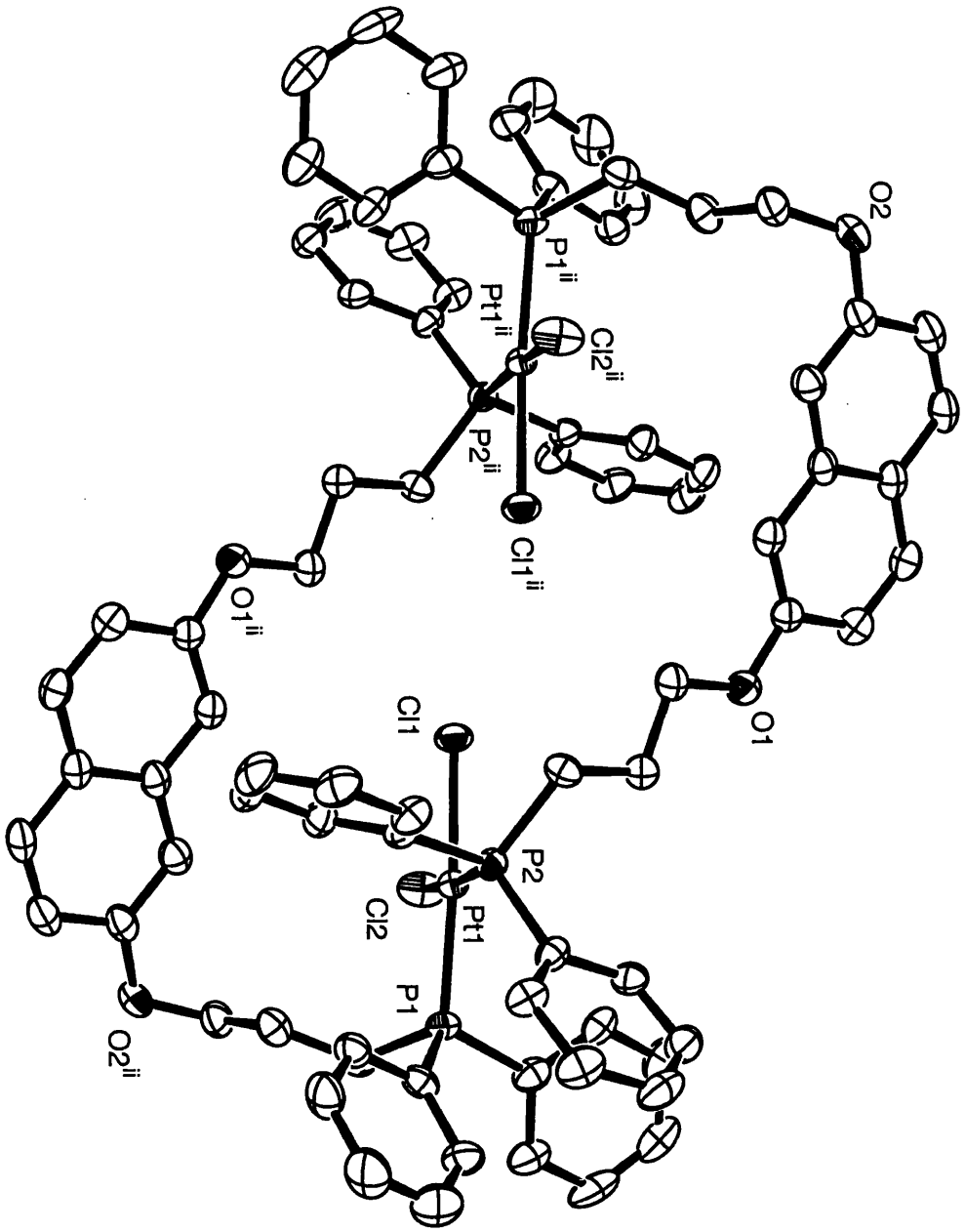


Figure 2.5 Ortep plot of *cis*, *cis*-$Pt_2Cl_4(DPPN)_2$ **77** with thermal ellipsoids shown at the 50% probability level. Atoms with primed labels are related to unprimed atoms by the symmetry operation ($-x, -y, 1-z$). Selected bond lengths (Å) and angles (°): Pt–Cl(1), 2.3500(9); Pt–Cl(2), 2.3467(10); Pt–P(1), 2.2544(9); Pt–P(2), 2.2510(9); Pt...Pt^{ii}, 8.369(1); Cl(1)...Cl(1)^{ii}, 3.942. Cl(1)–Pt–Cl(2), 86.20(7); P(1)–Pt–P(2), 98.41(7).

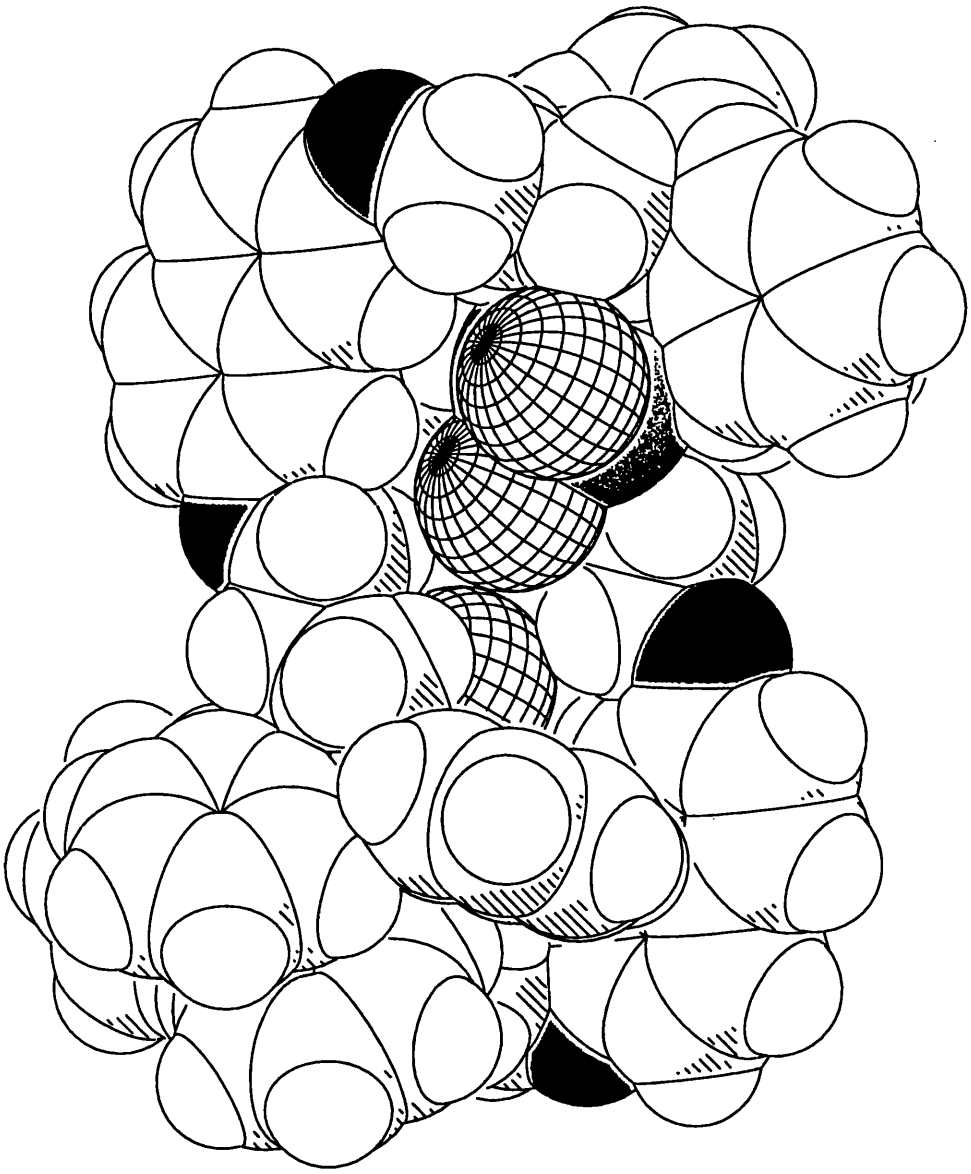


Figure 2.6 Space-filling plot of *cis*, *cis*-$Pt_2Cl_4(DPPN)_2$ **77**

2.6 CONCLUSIONS

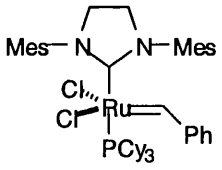
It was apparent that neither DPPN **61** or DPEN **62** were suitable for *trans* chelation across a transition metal. Both ligands favoured bridging metal centres to form dimeric or oligomeric complexes and showed a strong preference for *cis* chelation. No monomeric complexes were observed. It is unclear why the *cis, cis*-dimers formed with platinum(II) were so favoured as the thermodynamic products. One possibility could be π-stacking of the naphthalene rings, as suggested by their orientation in the crystal structure of *cis, cis*-$Pt_2Cl_4(DPEN)_2$ **76** (**Figure 2.3**).

Bisphosphines DPEN and DPPN were clearly not rigid enough to force the formation of *trans*-coordinated monomeric complexes such as those favoured by Venanzi's related ligands and as such would be unsuitable for use in a ruthenium alkene metathesis catalyst. However, the investigation of the ligands' chelation preferences produced interesting results with the formation of unusual platinum metallamacrocycles and the observation of equilibration between the isomers. A paper describing this work has recently been published.[85]

3. A SOLID-SUPPORTED ALKENE METATHESIS CATALYST

3.1 INTRODUCTION

While the work on the phosphine ligands was in progress, it became apparent from the increasing number of reports in the literature that Grubbs's second-generation catalyst **2** offered superior activity and was quickly becoming the catalyst of choice for many applications. At this stage, Barrett's 'boomerang' catalyst **35** was the only supported metathesis catalyst additional to Grubbs's early attempts (**Section 1.4**). No supported metathesis catalysts containing N-heterocyclic carbene ligands had been reported. Herrmann had described the first immobilised unsaturated NHC ligands and reported good results for catalysing Heck reactions with palladium complex **78**.[86] However, this approach with immobilisation via the N-substituents was considered to be unsuitable for a ruthenium metathesis catalyst because bulky aromatic N-substituents are usually required to give the most stable and active complexes.



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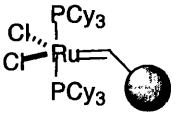

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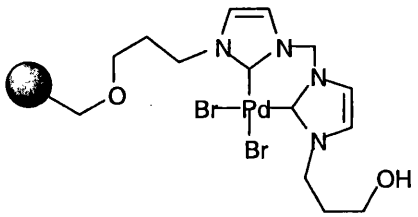
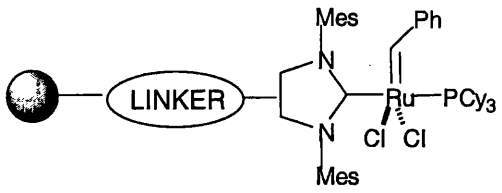


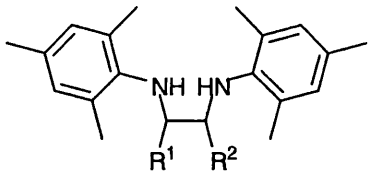
78

Therefore, with the bisphosphine approach proving unsuccessful, it was decided to adopt a new strategy with the aim of developing a solid-supported version of Grubbs's second-generation catalyst **2**. The N-heterocyclic carbene was to be modified to provide a point of attachment to a polymer support resulting in a structure such as **79**. In these catalysts, the NHC ligand remains bound to the metal centre and it is the phosphine that dissociates during the catalytic cycle. Therefore, it was hoped that as well as resulting in a more active catalyst, this approach would minimise leaching, as the ruthenium would remain permanently bound to the support.



79

The key intermediate that had to be synthesised to form the required solid-supported N-heterocyclic carbene ligand was bis-mesityl diamine **80**. This had to be prepared so that one, or both, of the R groups were linked to a polymer support at some stage in the synthesis. It was hoped that the polymer-bound diamine could then be cyclised to an imidazolinium salt and converted to a ruthenium alkylidene complex by methods analogous to those described by Grubbs for the synthesis of second-generation catalyst **2** (**Section 1.3**).[2]

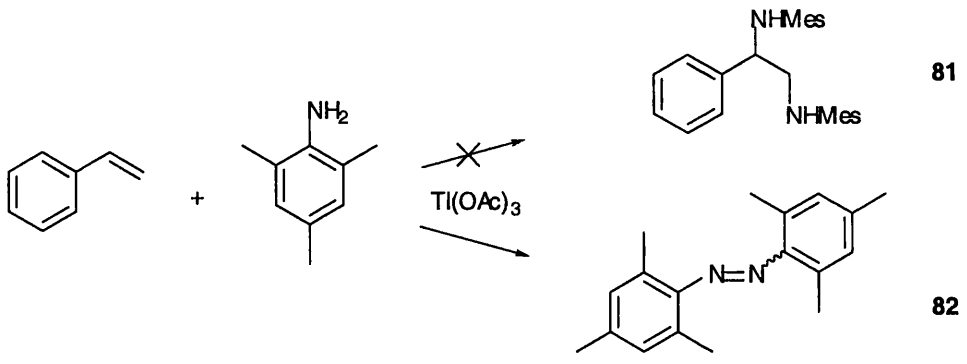


80

3.2 INITIAL APPROACHES TO A SOLID-SUPPORTED N-HETEROCYCLIC CARBENE LIGAND

Several synthetic routes were investigated in solution to determine a method to make a bis-mesityl diamine, which was suitable for transfer to solid phase.

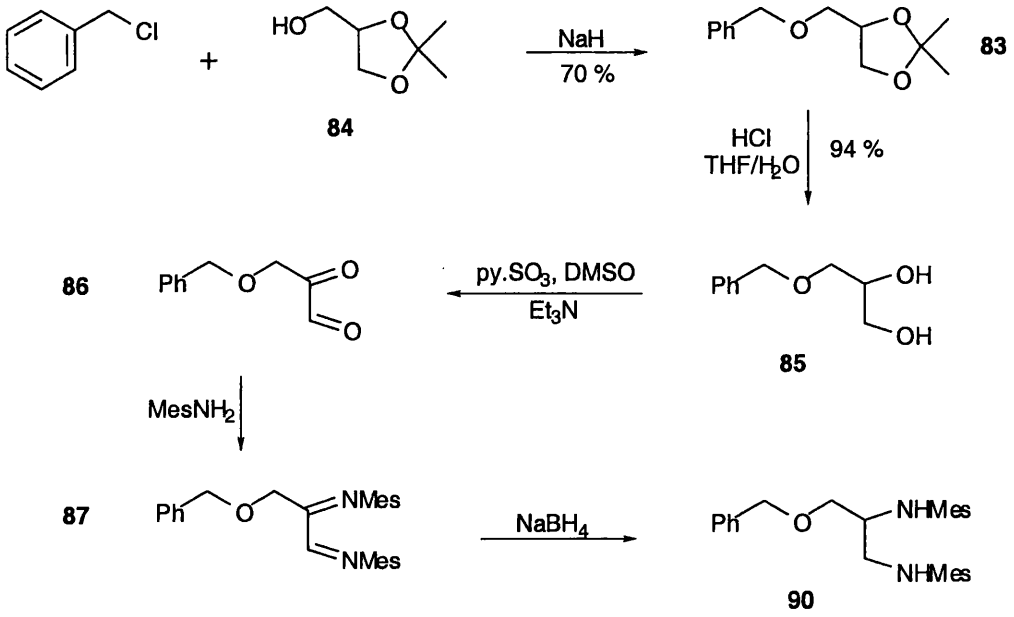
One direct route was diamination of a suitable alkene. Styrene was chosen as the polymer-bound analogue is commercially available. Two methods for the diamination of alkenes with aromatic amines have been reported in the literature. The methods are similar, one using a mercury(II) compound as the promoter,[87] and the other using thallium(III) acetate.[88] However, the first procedure produces elemental mercury which would make it difficult to transfer to solid phase. The thallium though is reduced to thallium(I) acetate which would be able to be washed away from the resin. Unfortunately, none of the desired product **81** was observed during attempts at the reaction between styrene and mesidine (**Scheme 3.1**). The reaction mixtures quickly took on an intense red/purple colour due to the formation of azo compound **82**, which was subsequently isolated by column chromatography. It is known that other oxidising agents can convert primary aromatic amines to azo compounds.[89] The reaction of aniline and styrene was reported to proceed in good yield so the failure can probably be attributed to the hindered nature of the amine.



Scheme 3.1

Another route to diamines is from 1,2-dicarbonyl compounds via the diimine. The transformation can be done in two steps or as a one-pot reductive amination. It was thought

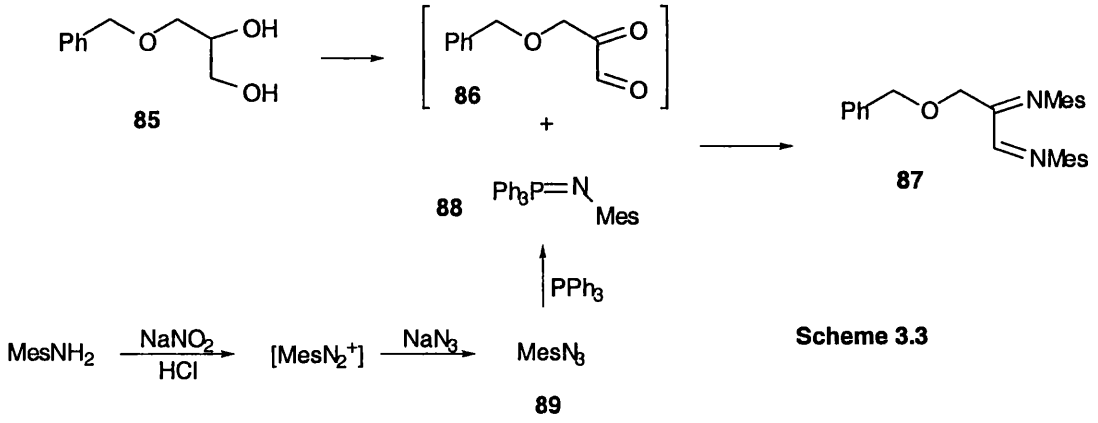
that a suitable 1,2-dicarbonyl compound could be obtained by oxidation of a vicinal diol. The route shown in **Scheme 3.2** was first considered. This was based on the fact that the polymer-bound analogue of ketal **83** is commercially available or could be easily prepared from chloromethylated polystyrene and solketal **84**. The resulting ligand would end up attached to the resin by a robust ether linkage.



Scheme 3.2

To test the feasibility of this route, diol **85** was prepared as shown from benzyl chloride and solketal with subsequent hydrolysis of ketal **83**. Aliphatic α-keto aldehydes such as **86** are very reactive, being prone to oxidation, hydration and polymerisation. It was rather optimistically thought that addition of mesidine to the crude oxidation mixture might allow imine formation to trap carbonyl compound **86** and form diimine **87**. The oxidation method used was a modified Swern oxidation with dimethylsulfoxide activated by pyridine-sulfur trioxide complex.[90] Unfortunately, attempts at either the one-pot reaction to **87**, or at isolation of keto aldehyde **86**, resulted in intractable mixtures with no clear product identifiable. It seemed likely that compound **86** was unstable and decomposed on formation.

An alternative method of imine formation is the aza-Wittig (or Staudinger) reaction of a carbonyl compound with an iminophosphorane (**Scheme 3.3**). One-pot Swern oxidation/Wittig reaction procedures have been used to trap unstable carbonyl compounds[91] and it was thought that a similar result might be possible with an aza-Wittig reaction. The preparation of the desired iminophosphorane **88** was straightforward involving formation of mesityl azide **89** via the diazonium salt,[92] and then reaction with triphenylphosphine.[93] Some attempts were made at a one-pot oxidation/aza-Wittig reaction using the original Swern oxalyl chloride method and adding the iminophosphorane while the mixture was still at –78 °C. However, again no clear products could be identified from the crude mixtures suggesting that even if the imine or diimine did form then it may have polymerised or decomposed.

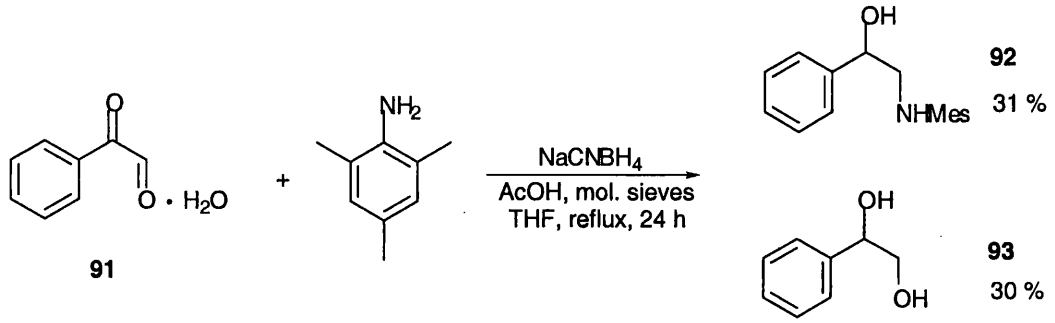


Scheme 3.3

It was decided that despite diol **85** being readily accessible in its solid-supported form, the conversion to diamine **90** would not be easily achieved, if at all, and so this approach was not pursued further.

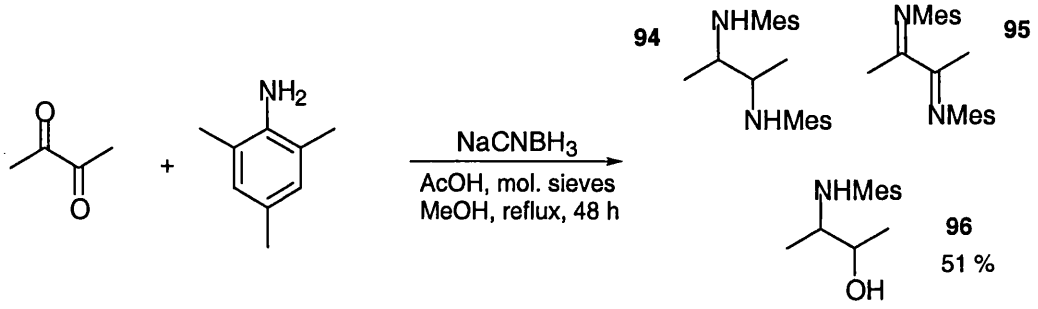
The polymer-bound analogue of phenylglyoxal or its hydrate **91** could be obtained by the dihydroxylation of solid-supported styrene followed by oxidation of the diol. However, imine formation from aryl ketones is generally difficult, with long reaction times and high temperatures being required. The fact that the required amine is both aromatic and hindered exacerbates the problem possibly rendering this approach unsuitable for transfer to solid phase. An attempt at the reductive amination of phenylglyoxal hydrate **91** in

refluxing THF was nevertheless made, with molecular sieves and acetic acid present to promote imine formation, but produced none of the desired product, only compounds **92** and **93** (**Scheme 3.4**). Sodium cyanoborohydride is used in reductive aminations as it reduces imines readily but ketones and aldehydes only slowly.[94] It appears that under these conditions, reduction of the ketone competes with the difficult imine formation resulting in amino alcohol **92**. More surprising is the formation of diol **93**, as it would be expected that even the hindered, aromatic mesidine should react readily with the aldehyde.



Scheme 3.4

It appeared that as imine formation from aryl ketones was difficult, and as aliphatic α-keto aldehydes were too unstable, the solution would be to use an aliphatic 1,2-diketone. However, an attempt with 2,3-butanedione and mesidine to determine whether a successful transformation from diketone to diamine was possible in such systems gave similar results to above. The reaction gave small amounts of diamine **94** and diimine **95** but the main product was amino alcohol **96** (**Scheme 3.5**).

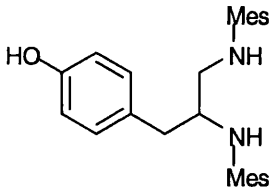


Scheme 3.5

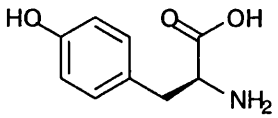
It became apparent that it would be hard to form the required vicinal diamine from a 1,2-dicarbonyl compound and consequently difficult to successfully achieve this on solid phase. Therefore, it was decided to adopt a different approach to forming the bis-mesityl diamine.

3.3 SYNTHESIS OF BIS-MESITYL DIAMINE

A new approach to the solid-supported N-heterocyclic carbene ligand was devised with the synthetic target being diamine **97**. The aim was to synthesise **97** from the natural amino acid L-tyrosine, using a palladium-catalysed Hartwig-Buchwald coupling reaction to install the *N*-mesityl groups. The phenol group could then be used to immobilise the diamine onto a polymer support.

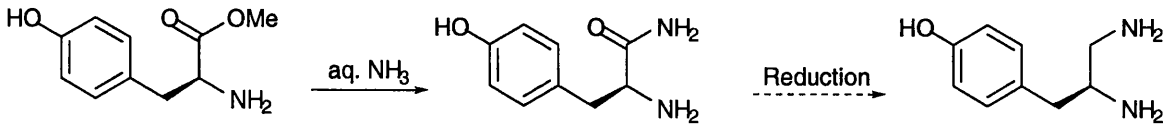


97



L-Tyrosine

L-Tyrosine methyl ester **98** was used as the starting material and treated with aqueous ammonia to form amide **99** (**Scheme 3.6**).[95] Attempts were then made to reduce the amide and form diamine **100**. Despite literature precedent, no product could be isolated from reductions using lithium aluminium hydride[96] or borane.[97] The main problem was the polarity and low organic solubility of both the reactant, amide **99,** and the desired product, diamine **100**, which made work-up of the reactions difficult.

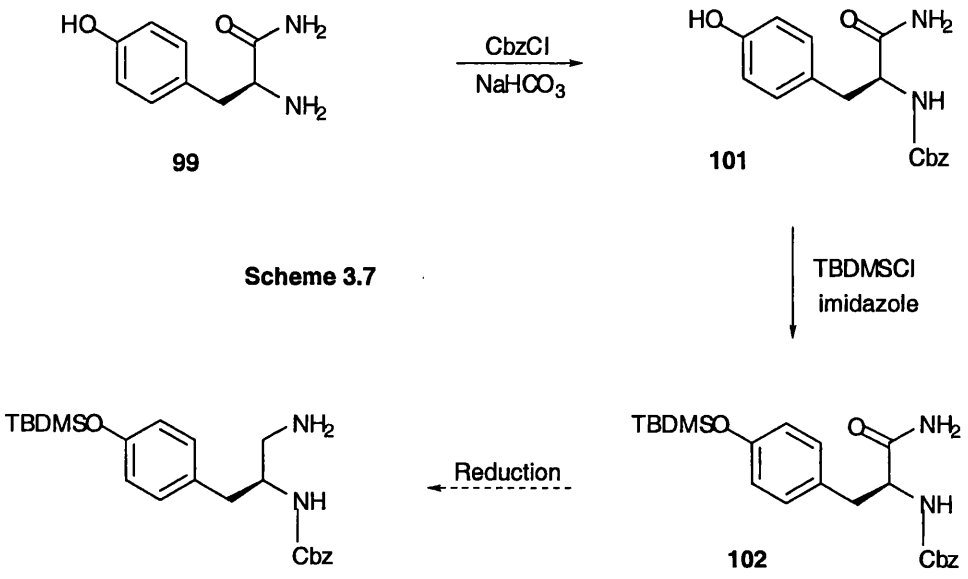


98 **99** **100**

Scheme 3.6

It was thought that protection of the phenol as a *tert*-butyldimethylsilyl (TBDMS) ether would help solve the solubility and isolation problems. However, the amino group had to first be protected before the silyl ether could be formed. A benzyl carbamate (Cbz)

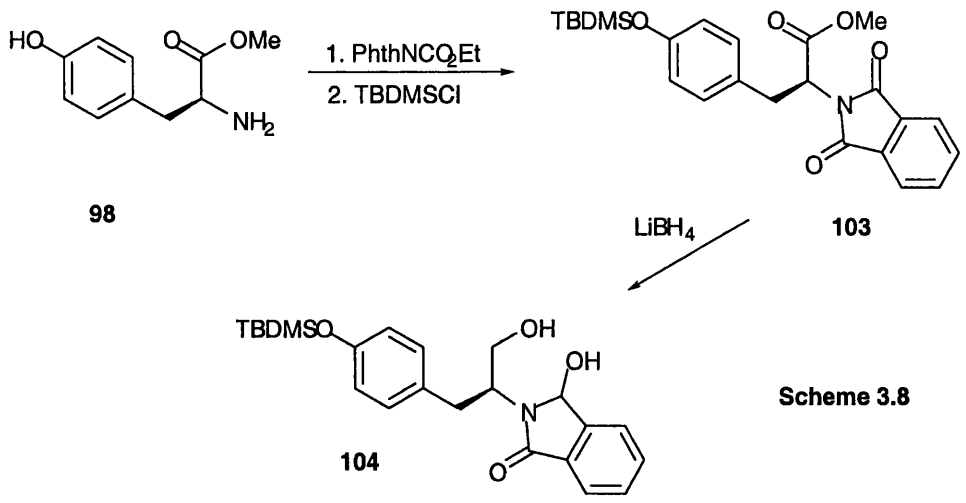
protecting group was chosen as this could be later removed without affecting the TBDMS group. Tyrosinamide **99** was reacted with benzyl chloroformate and sodium bicarbonate to give carbamate **101** (Scheme **3.7**). Treatment with *tert*-butyldimethylsilyl chloride and imidazole then gave doubly protected amide **102**. Unfortunately, reduction of **102** also proved difficult and could not be successfully achieved.



Scheme 3.7

As access to the diamine by reduction of an amino amide was proving troublesome, it was decided to investigate a different approach: forming the diamine from an amino alcohol. The strategy was to use a Mitsunobu reaction with phthalimide followed by hydrazinolysis to transform the hydroxyl group to an amino group and hence form the required diamine. This approach proved to be much more successful and ultimately led to the synthesis of the target molecule, diamine **97**.

Starting from L-tyrosine methyl ester **98**, protection of the nitrogen with a phthaloyl group was initially investigated with the aim of later deprotecting both amino groups at the same time. However, it was found that reduction of one half of imide **103** occurred at a similar rate to reduction of the ester to give compound **104** (**Scheme 3.8**). Therefore, a benzyl carbamate protecting group was chosen instead.

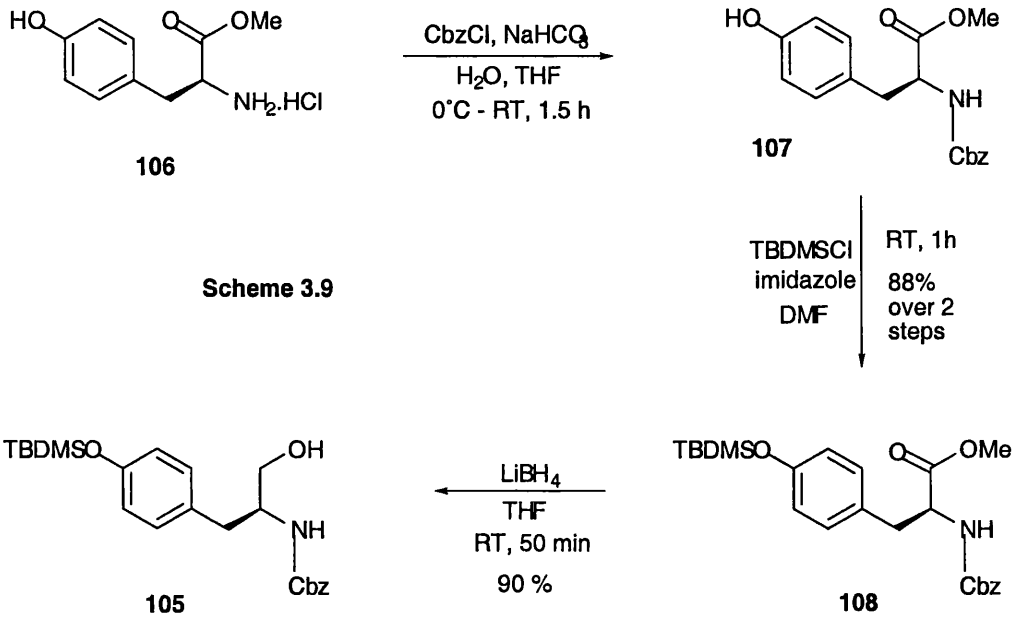


98 103 104

Scheme 3.8

Successful synthesis of diamine 97

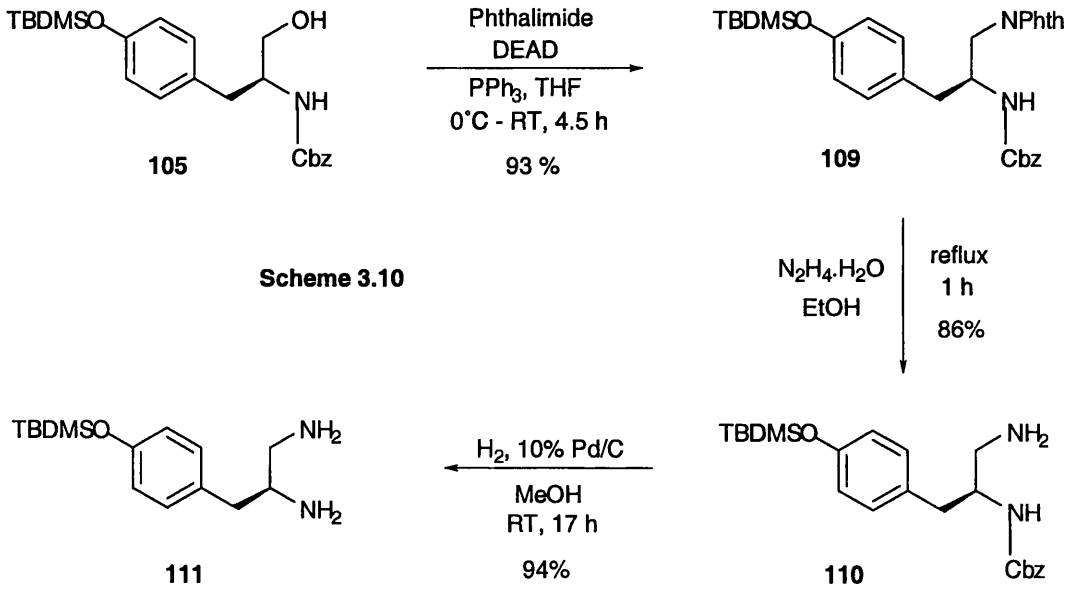
The optimised route to protected amino alcohol **105** is shown in **Scheme 3.9**. The starting material was inexpensive L-tyrosine methyl ester hydrochloride **106**. (Initially the free base was used but the salt is cheaper.) The first step was the benzyloxycarbonyl (Cbz) protection of the amine using benzyl chloroformate and sodium bicarbonate. This proceeded cleanly and the crude carbamate **107** was then treated with *tert*-butyldimethylsilyl chloride and imidazole to protect the phenol as a silyl ether. Ester **108** was then reduced with lithium borohydride to give amino alcohol **105**. These steps all proceeded smoothly in very good yields.



106 107 105 108

Scheme 3.9

The hydroxyl group was converted to the required amino group by a two-step procedure (**Scheme 3.10**). Reaction of alcohol **105** with phthalimide under Mitsunobu conditions using diethyl azodicarboxylate (or diisopropyl azodicarboxylate) and triphenylphosphine gave phthalimidocarbamate **109** in high yield. The phthaloyl group was then removed by refluxing with hydrazine hydrate to give protected diamine **110**. The benzyloxycarbonyl group was removed by catalytic hydrogenation to cleanly give diamine **111**.

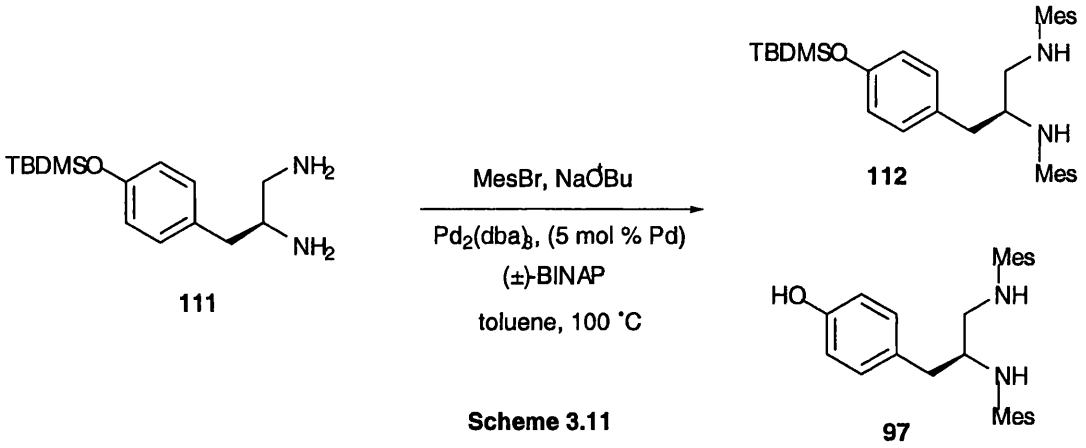


Scheme 3.10

The yields given up to aminocarbamate **110** are those obtained after purification by column chromatography. However, the synthesis was also readily carried out on a multi-gram scale with purification required only at the last step to ensure good yields in the hydrogenation step. Diamine **111** did not require purification and was used promptly as prolonged storage resulted in decomposition.

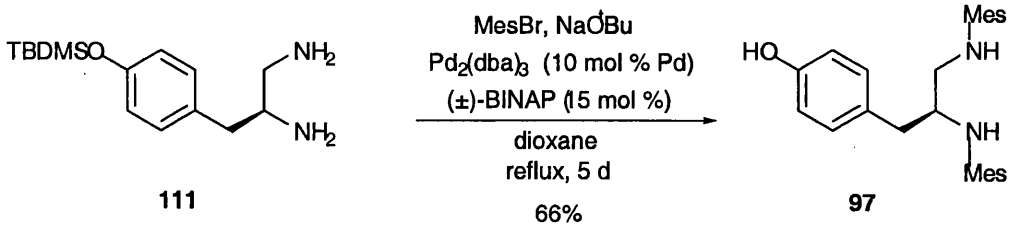
Several initial attempts to carry out a palladium-catalysed Hartwig-Buchwald coupling reaction on diamine **111** gave poor results. The standard conditions for the coupling of primary amines with aryl bromides[98] were used but very low yields of bis-mesityl diamine **112** were obtained, particularly on a larger scale (**Scheme 3.11**). However,

small amounts of deprotected product **97** were obtained, which suggested the possibility of avoiding a separate deprotection step.



Scheme 3.11

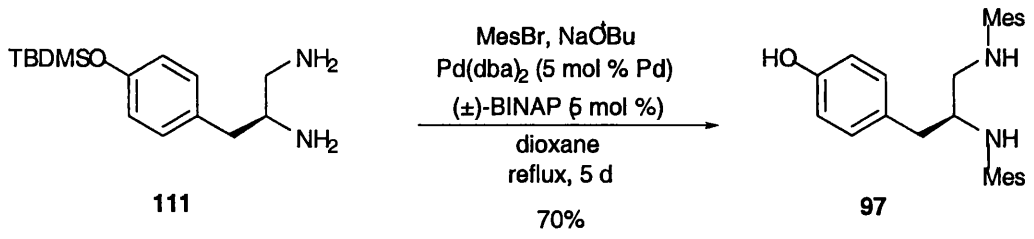
It was thought that a change of solvent would be beneficial as polar, deprotected intermediates may come out of solution before both couplings are accomplished. It was also decided to leave the reaction longer to try to effect complete removal of the TBDMS group. These modifications proved to be successful; increasing the reaction time and the amount of palladium, and changing the solvent to dioxane, resulted in a pleasing 66% yield of the required phenol **97** (**Scheme 3.12**).



Scheme 3.12

Further runs of the reaction in dioxane showed that similar yields, up to 70%, could be achieved with smaller amounts of palladium and BINAP (**Scheme 3.13**). $Pd(dba)_2$ prepared from palladium chloride and dibenzylideneacetone[99] performed as well as commercial $Pd_2(dba)_3$. The reaction mixture was refluxed until TLC analysis indicated the absence of TBDMS protected bis-mesityl diamine **112**, which typically took four or five days. The reaction could be performed on several grams of material and the product was

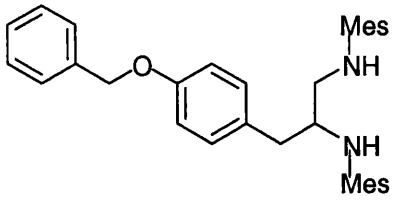
obtained pure after column chromatography of the reaction mixture, but was usually recrystallised to give colourless prisms before storage and use in subsequent immobilisation reactions.



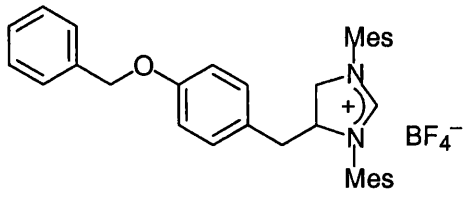
Scheme 3.13

Confirmation of enantiopurity

As the starting material was L-tyrosine methyl ester, the resulting *N*-heterocyclic carbene ligand and hence final catalyst were expected to be enantiopure, leading to the possibility of carrying out enantioselective alkene metathesis. Therefore, although it was unlikely that any racemisation had occurred during the synthesis of mesityl diamine **97**, and the compound exhibited optical rotation, it still needed to be verified that **97** was actually enantiopure. Diamine **97** only gave one peak when analysed on two different chiral HPLC columns. However, on analysing the racemic analogue of **97**, prepared from racemic tyrosine by undergraduate student Iain Rudkin,[100] it was found that the enantiomers failed to separate and also gave only a single peak. Racemic benzyl ether **113** and tetrafluoroborate salt **114** were also prepared by Iain to provide solution phase analogues of the intermediates in the synthesis of the solid-supported catalyst. Unfortunately, the enantiomers of these compounds could also not be separated by chiral HPLC. Attempts to distinguish the enantiomers of compounds **97**, **113** and **114** by using the chiral NMR shift reagent $Eu(hfc)_3$ also proved unsuccessful.

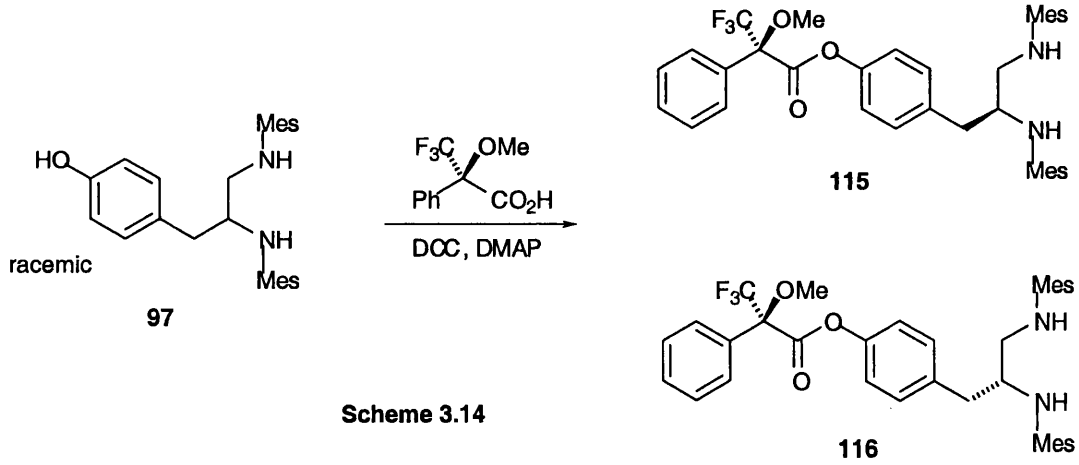


113



114

The enantiopurity of diamine **97** was finally proved by analysing its Mosher's ester by ^{19}F NMR spectroscopy. Racemic **97** was converted to the diastereomeric esters **115** and **116** by reaction with (R)-Mosher's acid, and two signals of equal intensity were observed in the ^{19}F NMR spectrum (**Scheme 3.14**). Diamine **97** prepared from L-tyrosine methyl ester was then similarly treated with (R)-Mosher's acid. The ^{19}F NMR spectrum of the product showed a single peak due to ester **115** therefore confirming the enantiopurity of diamine **97**.

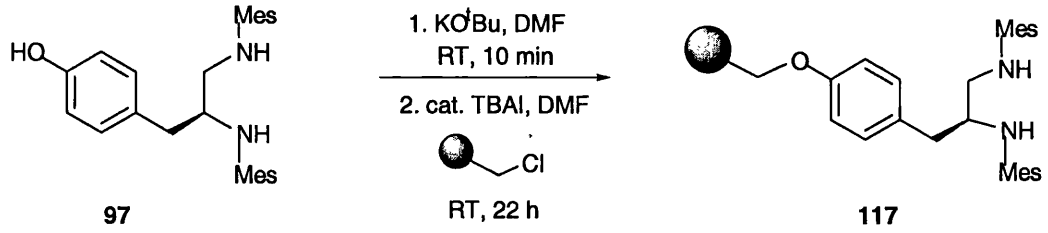


Scheme 3.14

3.4 SYNTHESIS OF SOLID-SUPPORTED CATALYST

The first step in synthesising the solid-supported catalyst was the immobilisation of mesityl diamine **97** on a suitable polymer support. Merrifield resin, chloromethylated polystyrene, was chosen as the support because it is the simplest and cheapest resin, and the ether linkage that was to be generated on attachment of the diamine to the support would be robust and secure to all the succeeding reaction conditions.

The immobilisation was accomplished by treating diamine **97** with potassium *tert*-butoxide to generate the phenolate and then adding this to Merrifield resin in the presence of tetra-*n*-butylammonium iodide (**Scheme 3.15**). Initially the reaction was performed at 40 °C but subsequent optimisation showed that the coupling also worked well, and was more convenient to carry out, by shaking in a cartridge at room temperature. Two equivalents of the phenolate are used but the excess can be recovered by quenching and then extracting the reaction solution drained off from the resin. The efficiency of the coupling was judged from nitrogen microanalysis of resin **117** and the quantity of recovered diamine **97** to be greater than 90 %.



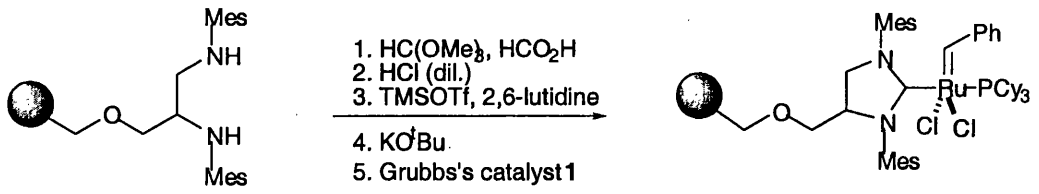
97 **117**

Scheme 3.15

The remaining steps to the solid-supported catalyst proved to be problematic and very difficult to optimise to reliably and repeatedly produce good quality catalyst. The main obstacle was the limited characterisation possible when working on solid phase. It was difficult to quantitatively determine what effect, if any, changes to the reaction conditions had on the efficiency of the attempted transformations. The only practical way to optimise the synthesis was to try and take each batch of resin through to the final catalyst and then

test it on a standard ring closing metathesis reaction to determine the quality of the polymer-bound catalyst.

A communication from Blechert and co-workers, which appeared during this work, described the synthesis of a similar solid-supported metathesis catalyst **50** from polymer-bound diamine **118 (Scheme 3.16)**.[60] According to their brief experimental details, their diamine was cyclised to the imidazolinium salt by heating with trimethyl orthoformate and a catalytic amount of formic acid, under vacuum, followed by washing with dilute hydrochloric acid. Although the cyclisation was described as going to completion, a capping step was then carried out with trimethylsilyl triflate. In a similar procedure to that used by Grubbs,[2] the salt was then treated with potassium *tert*-butoxide before being heated with Grubbs's catalyst to give the final polymer-bound ruthenium alkylidene.

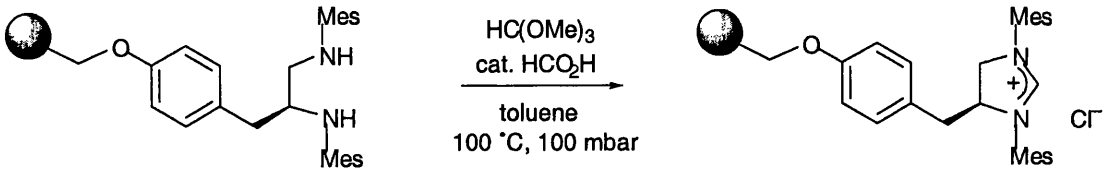


118 **50**

Scheme 3.16

This method was reported to result in active metathesis catalyst with a relatively high loading suggesting good conversion in all the steps. Therefore, this was used as the basis for attempting to convert resin-bound diamine **117** to a solid-supported catalyst.

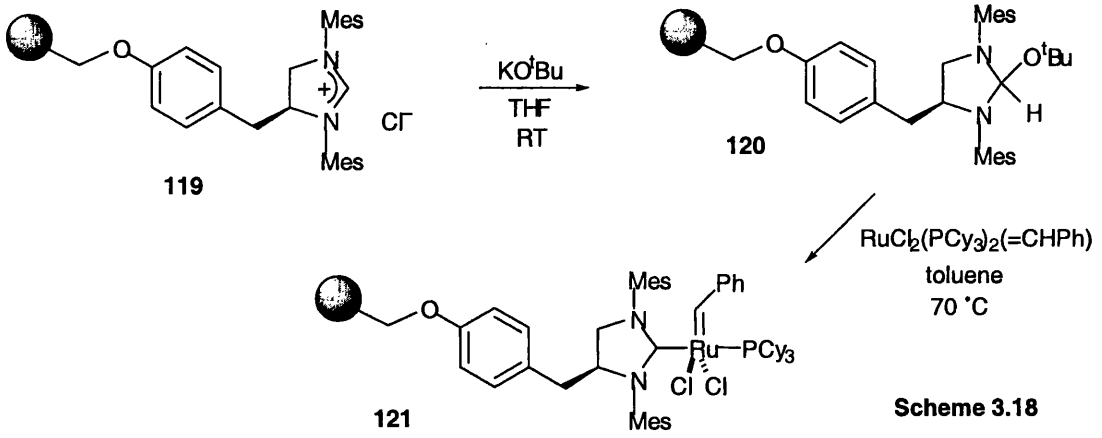
After a few initial attempts to replicate Blechert's method, two practical problems became apparent. The first involved applying a vacuum during the cyclisation step, in which immobilised diamine **117** was heated with trimethyl orthoformate in toluene with a catalytic amount of formic acid to form supported imidazolinium salt **119 (Scheme 3.17)**. Heating the reaction mixture to 100 °C under a vacuum of 100 mbar (applied via a vacuum controller) caused the mixture to regularly bump, depositing resin beads up the sides of the condenser and therefore no longer in contact with the reagents.



117 119

Scheme 3.17

The second problem involved removing the potassium *tert*-butoxide solution from the resin, and then washing the resin before adding Grubbs's catalyst, while keeping the sensitive *tert*-butoxide adduct **120** protected from air and moisture (**Scheme 3.18**).



119 120 121

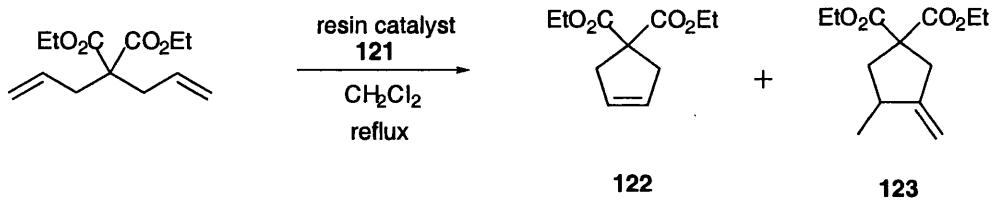
Scheme 3.18

Initially, the first problem was dealt with by simply attempting to wash as much resin as possible back into the flask by adding additional solvent down the sides of the condenser at regular intervals. However, this was tedious and only partially successful.

Resin **119** prepared in this way was treated with trimethylsilyl triflate and 2,6-lutidine as described by Blechert.[60] The resin was then sealed in Irori MiniKans™ to solve the second problem. This allowed the potassium *tert*-butoxide solution to be easily removed by syringe from the reaction vessel and fresh, dry tetrahydrofuran added to wash the resin. After vigorous stirring, the solvent was again removed by syringe and the process repeated several times thereby thoroughly washing all excess *tert*-butoxide from the resin while maintaining an inert atmosphere. Toluene and Grubbs's catalyst were then added and the

mixture heated to generate the free carbene, to displace a tricyclohexylphosphine ligand from the ruthenium complex, and form polymer-bound complex **121**.

After thorough washing, and drying under vacuum, the dark purple/brown resin **121** was tested for catalytic activity by attempting the ring closing metathesis of diethyl diallylmalonate in refluxing dichloromethane (**Scheme 3.19**). The resin was removed by filtration, the solvent was removed and the residue was analysed by ^{1}H NMR. The catalyst effected good conversion to ring-closed product **122** but a significant amount of another product was observed and the product mixture was a dark grey colour indicating that some leaching of ruthenium from the resin had occurred. An attempt at recycling the catalyst, by carrying out the same reaction using the recovered resin, produced none of the desired product but only a mixture of starting material and the same by-product. This was then identified as the *exo*-methylene cyclopentane **123**.



122 **123**

Scheme 3.19

This cycloisomerisation reaction is known to be catalysed by ruthenium hydride complexes.[101] Also, ruthenium hydride complexes have previously been observed as by-products when forming N-heterocyclic carbene containing metathesis catalysts from imidazolinium salt precursors.[102] Therefore, it seemed possible that the cycloisomerisation by-product was being formed by competing catalysis from ruthenium hydride complexes generated as an impurity on the resin.

It was thought that the problem step might be the treatment with potassium *tert*-butoxide. Blechert's procedure stated a reaction time of one hour to form the *tert*-butoxide adduct, before washing and heating with Grubbs's catalyst.[60] However, a published preparation of Grubbs's second-generation catalyst **2** specified a reaction time as short as possible before adding the ruthenium complex, and stated that prolonged exposure to the

tert-butoxide resulted in incomplete conversion to the desired product.[27] Therefore, the reaction time in this step was shortened to 30 minutes or just five minutes to try and improve the quality of the resin catalyst, but on testing both batches, by-product **123** was still observed.

A new batch of resin was then brought through the synthesis from the immobilisation of diamine **97** on Merrifield resin. The cyclisation and capping steps were carried out using the same methods as the previous batch, and then the immobilised imidazolinium salt was converted to resin catalyst, allowing five minutes reaction time with the potassium *tert*-butoxide solution. On testing this batch of catalyst, the results were much better. Diethyl diallylmalonate was cleanly cyclised and no trace of by-product **123** was observed. In addition, the product was colourless indicating minimal ruthenium leaching from the resin. Catalyst formed allowing 35 minutes reaction time with the *tert*-butoxide performed equally well suggesting that the time allowed in this step is not crucial. However, all the steps were performed in an identical manner to the previous batch so the reason for the difference in quality of the final catalyst is unclear.

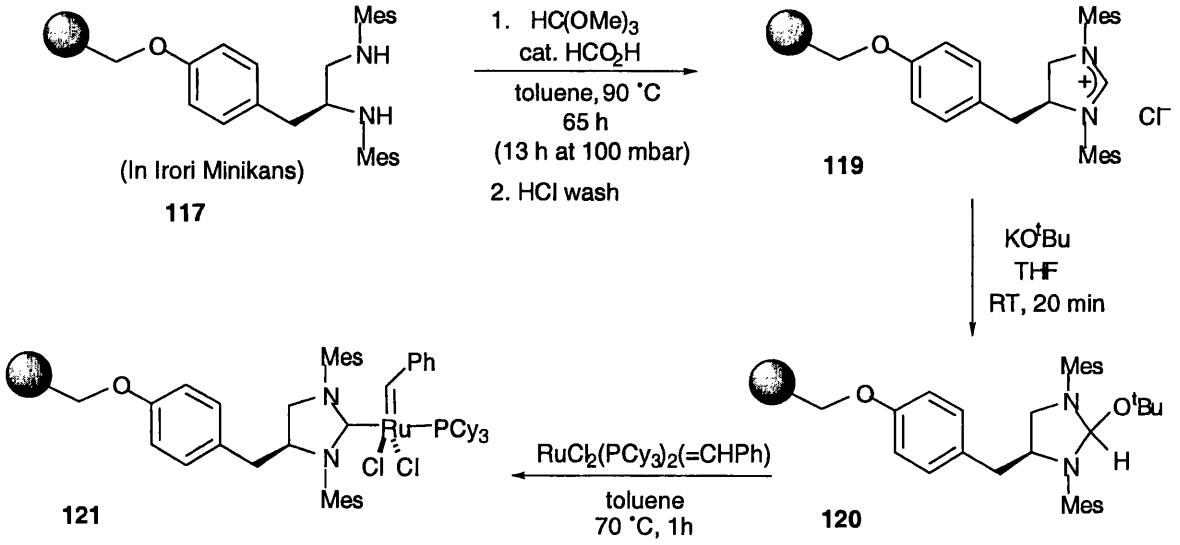
Although the goal of synthesising a solid-supported alkene metathesis catalyst had been achieved, much optimisation remained to be done. For the initial tests described above, the final catalyst loading of the resin had been estimated by comparison with Blechert's results which suggested good conversion in all the steps. However, using 5 mole percent of the resin catalyst, resulted in only low conversion to the ring-closed product. This indicated that the catalyst loading of the resin was much lower than expected and at least one of the steps was not proceeding in high yield. Up to this point, Merrifield resin with a loading of 1.6 mmol/g had been used. This was a higher loading than that used in Blechert's work, which was between 0.5 and 0.9 mmol/g, so it was thought that changing to a lower loaded resin might help to improve the synthesis. Therefore, subsequent syntheses began with Merrifield resin having a loading of 0.9 mmol/g.

To solve the problem of resin bumping up the condenser while under vacuum, it was decided to seal the resin into MiniKans before attempting the cyclisation step. Although Irori recommend that the Kans are not suitable for use at high temperature, it was

found that they survived well enough to contain the resin under the required reaction conditions – heating to 90 °C in toluene for several days with the vacuum applied for part of the time.

Polymer-bound imidazolinium salt prepared in this way was then used to test whether the trimethylsilyl capping step used by Blechert was effective. It was thought that although the cyclisation might not proceed to completion, the presence of some hindered, aromatic secondary amine groups would probably not affect the quality and activity of the final catalyst. Also, it was doubted whether an *N*-trimethylsilyl group would be sufficiently robust. One kan containing polymer-bound salt was subjected to the capping procedure while another was not treated. Both were then converted to resin catalyst in the same reaction vessel and therefore under identical conditions. When tested on the RCM of diethyl diallylmalonate, catalyst from the kan that had not undergone the capping step performed as well as the catalyst that had. Moreover, both batches of catalyst exhibited a higher activity than previously observed so better results had been achieved by using the lower loading resin. It was concluded that the capping step was unnecessary and so this was omitted in the synthesis of subsequent batches of catalyst.

The procedure for synthesising the resin catalyst using Kans is given in **Scheme 3.20**.

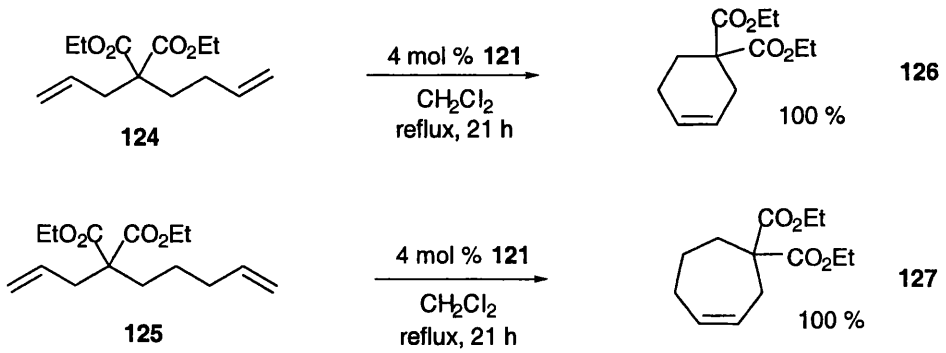


Scheme 3.20

With a fairly reliable method developed for making small quantities of catalyst, it was decided to try and obtain a value for the final catalyst loading on the resin. This was done by analysing the ruthenium content of the resin by atomic emission spectroscopy (AES). Samples of the resin were digested by boiling with concentrated sulfuric acid and then adding hydrogen peroxide solution to give clear solutions free of solid. These were then diluted and atomic emission spectroscopy was used to measure the ruthenium content in parts per million by comparison with standards of known concentration. The quantity of ruthenium in mmol per gram of resin could then be calculated and this was taken to be the catalyst loading. Values of between 0.06 and 0.10 mmol/g were obtained, although there was some variation between batches and samples of resin suggesting that the technique was not very accurate. Nevertheless, this allowed metathesis reactions to be carried out with a more certain mole percentage of catalyst added.

Up to this point, the catalyst had only been tested for the RCM of diethyl diallylmalonate so several other substrates were synthesised to further investigate the activity of the catalyst (see **Section 3.5** for details of synthesis).

The catalyst performed well on dienes **124** and **125** (**Scheme 3.21**). After refluxing overnight with 4 mol% of catalyst, complete conversions to six-membered ring **126** and seven-membered ring **127** were observed from the ^{1}H NMR of the crude products. The reactions were clean and after filtering off the resin catalyst and removing the solvent, the products were almost colourless.



Scheme 3.21

Although a synthesis of the solid-supported alkene metathesis catalyst had now been developed, and the initial results had been promising, some problems were preventing further investigation into the activity and properties of the catalyst. The loading of active catalyst on the resin was low with the consequence that large amounts of the catalyst had to be prepared and used to get complete conversion in the metathesis reactions. However, using MiniKans to contain the resin was expensive and only allowed small quantities of the catalyst to be prepared at a time. The challenge then, was to scale up the synthesis so that sufficient quantities of catalyst could be prepared, and simultaneously to try and improve the efficiency of the reactions to result in a higher loading final catalyst.

It was clear that to scale up the synthesis it would be necessary to develop methods to carry out the reactions without the need to use Kans. As discussed previously, the Kans were required in the cyclisation step to prevent bumping of the resin when a vacuum was applied to drive the reaction. This had originally been adapted from the procedure described by Blechert but it was thought, by comparison with similar solution phase reactions, that the vacuum might not be required and that prolonged heating should be sufficient to effect the cyclisation.[103] Therefore, the synthesis was modified and the reaction was carried out by suspending the loose resin in trimethyl orthoformate, toluene, and formic acid and heating to 100 °C for four days. Resin prepared in this way was then used to investigate methods for carrying out the final steps to the solid-supported catalyst without the use of Kans.

It was not possible to analyse each batch of resin for ruthenium content by AES to determine the catalyst loading, as this would have used up significant amounts of the small quantities of catalyst prepared. Therefore, the metathesis activity of each batch of resin was assessed by using an excess of diethyl diallylmalonate. The conversion was determined by NMR of the crude mixture and then the activity was calculated as millimoles of diethyl diallylmalonate converted per milligram of resin.

An attempt was made to treat resin **119** with potassium *tert*-butoxide and then carry out the washing with THF in air, before heating with Grubbs's catalyst, to test the stability of the *tert*-butoxide adduct **120**. The resulting catalyst carried out RCM but exhibited low activity, similar to that prepared in Kans. However, the metathesis was not clean with by-

products evident from NMR, and the product was discoloured indicating ruthenium leaching from the resin.

An improved procedure by Grubbs and co-workers for preparation of ruthenium carbene complexes involves replacing potassium *tert*-butoxide with potassium hexafluoro-*tert*-butoxide.[46] This does not react with Grubbs's catalyst and so it was hoped that it might be possible to avoid the need to wash the resin prior to the addition of the catalyst. Potassium hexafluoro-*tert*-butoxide was prepared from potassium hydride and the corresponding alcohol, and the resin catalyst was prepared in one pot from the imidazolinium salt. RCM with the resulting catalyst was again not very clean and the activity was even lower than previously observed.

After further trials, the method that worked best was to stir loose resin **119** in a Schlenk tube with the potassium *tert*-butoxide solution and then carefully syringe out the solution, trying to avoid removing the resin beads at the same time. Dry THF was then added, the mixture stirred, left to settle and the solvent removed again. This was repeated several times to remove all the *tert*-butoxide before the ruthenium complex and toluene were added. The resin was then heated to 70 °C in the presence of Grubbs's catalyst for an hour to form the resin catalyst.

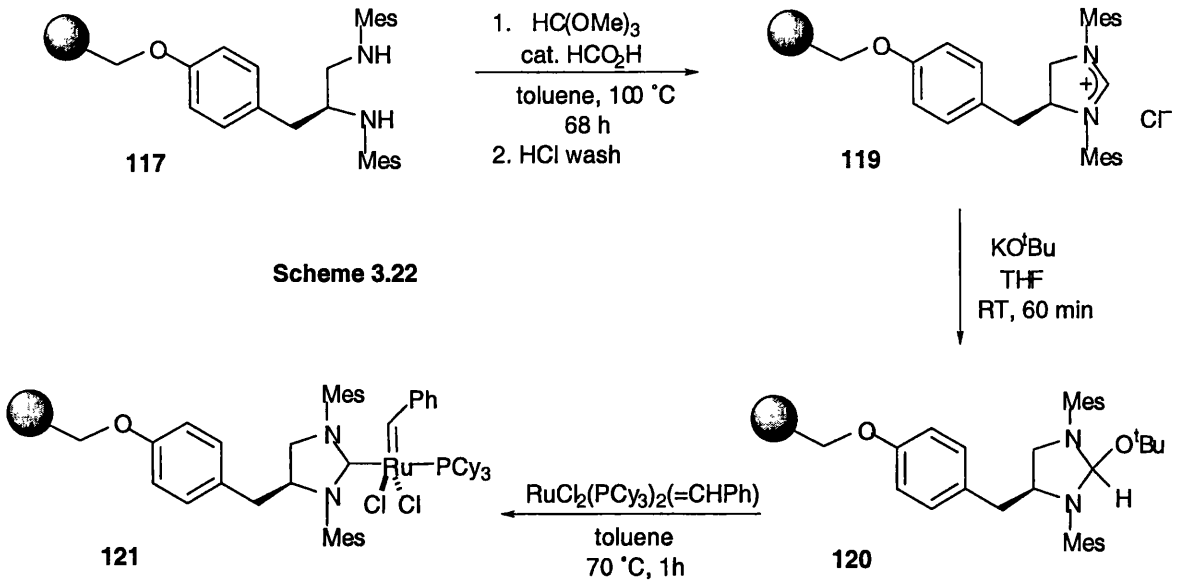
This method formed catalyst resin that carried out clean ring closing metathesis with minimal ruthenium leaching but unfortunately the loading was still low. However, the use of Kans was no longer required so the procedure was amenable to scaling up to produce larger quantities of catalyst.

It was thought that the problem of low catalyst loading on the resin was caused by a poor yield in the cyclisation of diamine **117** to imidazolinium salt **119**. Therefore, several attempts were made to try and improve this step by using different conditions for the cyclisation. The polymer-bound diamine **117** was suspended in neat triethyl orthoformate with ammonium tetrafluoroborate and heated to 130 °C to imitate the conditions used in similar solution phase reactions.[103] The resulting resin was converted to catalyst using the optimised conditions described above and then tested for RCM activity on diethyl diallylmalonate. Although the catalyst exhibited slightly higher activity for RCM than that

prepared by the other methods described, a large quantity of cycloisomerisation by-product **123** was also formed. The cyclisation was also tried by first treating resin diamine **117** with dilute hydrochloric acid to form the salt and then heating in neat triethyl orthoformate. In one attempt, a distillation head was fitted to the flask and periodically heated to try and remove any ethanol formed and drive the reaction. On testing, the catalysts formed from these batches also had slightly higher metathesis activity but again the reactions were not clean and large amounts of by-product **123** contaminated the product.

As discussed earlier, it seems probable that a ruthenium hydride species is responsible for the competing cycloisomerisation reaction that forms by-product **123**. From my results, it appears that the cyclisation of diamine **117** to imidazolinium salt **119** is the key step in determining whether the final resin catalyst effects clean metathesis or gives rise to by-products. However, how this step relates to the formation of ruthenium hydride species is unclear. Similar cycloisomerisation products have previously been observed with other metathesis catalysts.[21,55,104]

With time running out, it was decided to settle for the method of synthesis that gave resin catalyst producing clean metathesis and accept the low loading. The goal of modifying the synthesis to avoid using Kans had been achieved so sufficient quantities of the catalyst could now be prepared for further investigation. The optimised conditions are shown in **Scheme 3.22**. These were used to synthesise larger batches of catalyst (up to 1.5 g in the final step).



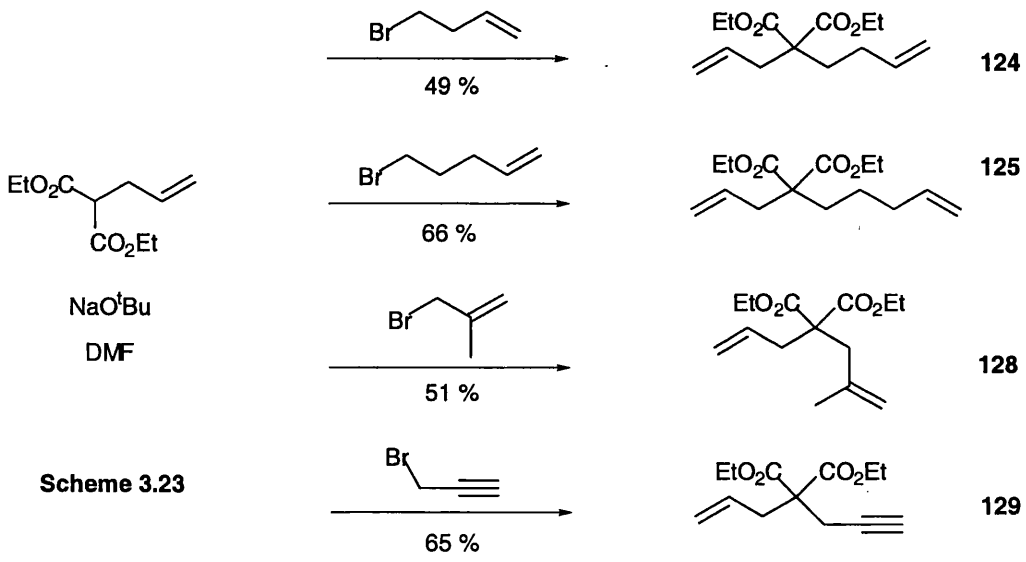
Scheme 3.22

The ruthenium loading of the final catalyst was measured by atomic emission spectroscopy as previously described. As before, there was some variation between samples of resin but an average value of 0.1 mmol/g was obtained and so this was used as the catalyst loading in all subsequent reactions.

3.5 SYNTHESIS OF SUBSTRATES

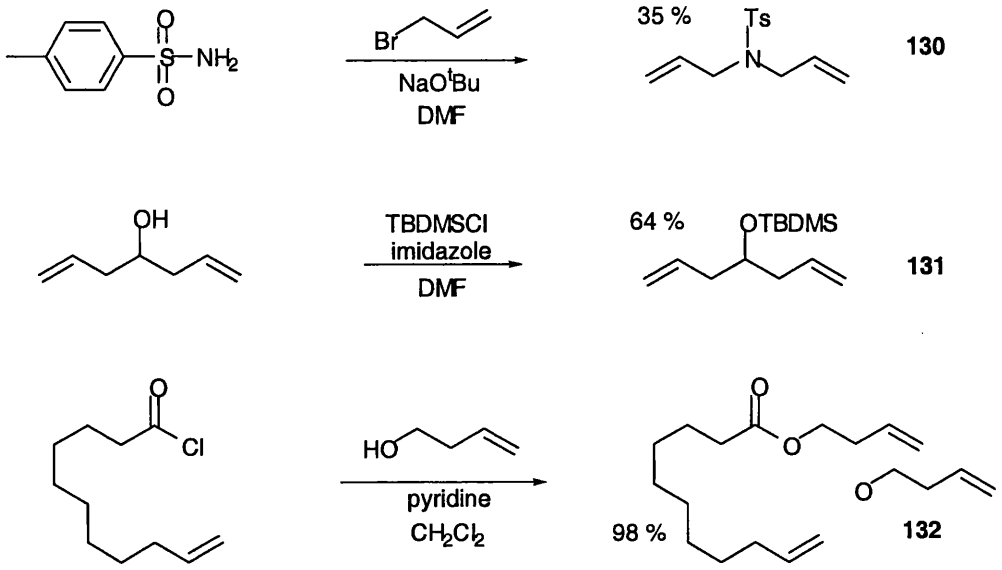
With a reliable method developed to make sufficient quantities of catalytically active resin, attention turned to testing the catalyst on a range of substrates. The syntheses of these substrates are described below. In most cases, the yields given are not optimised as the reactions were only carried out once to obtain sufficient material for testing.

Several substrates were synthesised by the alkylation of diethyl allylmalonate using sodium *tert*-butoxide as the base (**Scheme 3.23**). Reaction with 4-bromo-1-butene and 5-bromo-1-pentene gave dienes **124** and **125** respectively. Alkylation with methallyl bromide gave more substituted diene **128**. Substrate **129**, for attempted enyne metathesis, was prepared using propargyl bromide.



Scheme 3.23

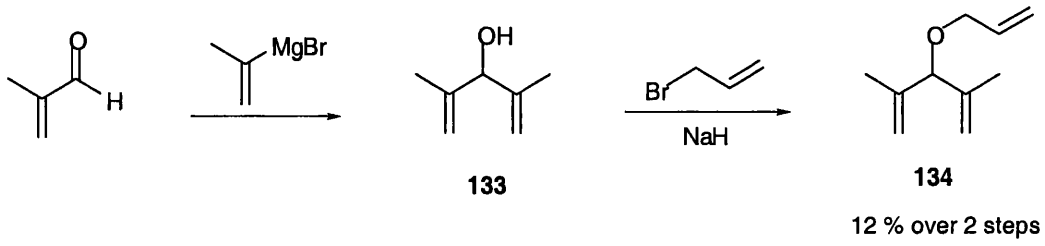
Diene **130** was prepared by the dialkylation of *p*-toluenesulfonamide with allyl bromide (**Scheme 3.24**). Silyl ether **131** was prepared by protection of 1,6-heptadien-4-ol under standard conditions. Ester **132**, to test macrocyclic ring formation, was readily formed in almost quantitative yield from 10-undecenoyl chloride and 3-buten-1-ol in a mixture of dichloromethane and pyridine.[105]



Scheme 3.24

As the resin catalyst contained an enantiopure N-heterocyclic carbene ligand, two prochiral trienes were synthesised to investigate whether the catalyst could promote enantioselective metathesis. Although the substrates have been used for this purpose several times before,[46,106] the syntheses of them have not been described in the literature. The trienes and their precursors were not easy to handle due to their volatility. However, with careful work-up and purification, and despite having to sacrifice yield for purity, sufficient quantities were prepared.

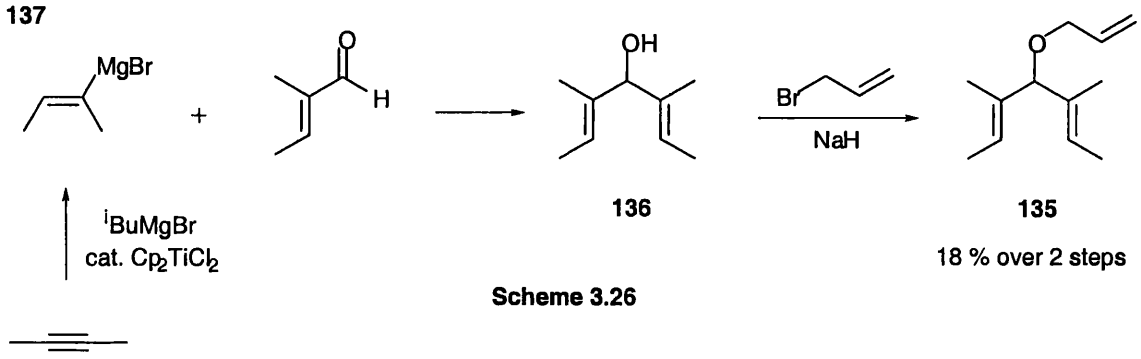
To make the less-substituted substrate, methacrolein was treated with isopropenylmagnesium bromide to give alcohol **133** (**Scheme 3.25**). The crude alcohol was then alkylated with allyl bromide to form triene **134**. The product was obtained pure by careful column chromatography eluting with pentane.



Scheme 3.25

The synthesis of triene **135** was slightly more difficult as the alkene geometry had to be taken into account. However, the synthesis of alcohol **136** has been reported from *E* Grignard reagent **137** and propyl formate, where the configurational purity and stability of the Grignard reagent were ensured by forming it from 2-butyne using a hydromagnesiation reaction.[107] This approach was modified to use the aldehyde *trans*-2-methyl-2-butenal instead of an ester.

The Grignard reagent was formed by treating 2-butyne with isobutylmagnesium bromide and a catalytic amount of titanocene dichloride (**Scheme 3.26**).[108] The aldehyde was then added and alcohol **136** was obtained as the only isomer. The crude alcohol was alkylated with allyl bromide and triene **135** was obtained pure after careful chromatography.



Scheme 3.26

3.6 APPLICATION OF SOLID-SUPPORTED CATALYST

Resin catalyst **121**, synthesised by the large scale route described in **Section 3.4**, was tested on a range of substrates. A summary of the results with achiral dienes is given in **Table 3.1** and discussed below.

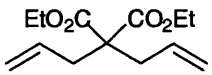
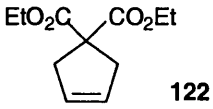
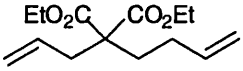
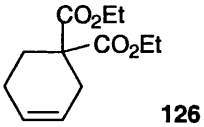
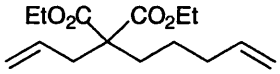
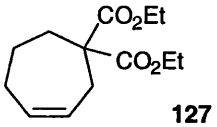
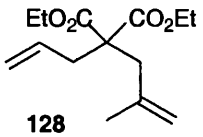
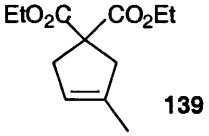
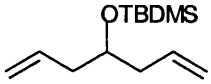
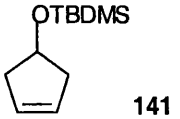
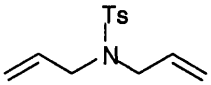
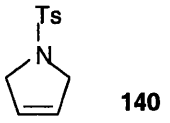
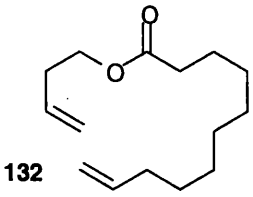
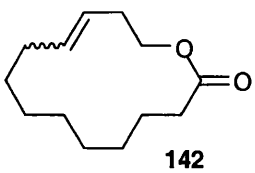
ENTRY	SUBSTRATE	PRODUCT	RESULT
1	 **138**	 **122**	100 %
2	 **124**	 **126**	90 %
3	 **125**	 **127**	92 %
4	 **128**	 **139**	91 %
5	 **131**	 **141**	100 %
6	 **130**	 **140**	95 %
7	 **132**	 **142**	60 % *E*/*Z*= 4

Table 3.1

All of the reactions above were carried out with 10 mol % of catalyst resin **121** in refluxing dichloromethane under nitrogen for 19 h except for entry 1 (5 mol %, 25 h) and entry 2 (5 mol %, 18 h). The percentage conversion was determined from the ^{1}H NMR spectrum of the crude reaction mixture.

Diethyl diallylmalonate **138** was the test substrate used throughout the optimisation of the catalyst. Unsurprisingly, the catalyst seems to be most active with this substrate. When overloading the catalyst with substrate to determine the activity of particular batches of catalyst, the highest activity observed was 0.0078 mmol of diethyl diallylmalonate cyclised per milligram of resin. With a catalyst loading of 0.1 mmol/g this corresponds to a turnover number of 78.

As previously described in **Section 3.4**, resin catalyst formed in MiniKans effected the complete cyclisation of dienes **124** and **125**. However, complete conversion was not achieved using the resin catalyst made without the use of Kans on a larger scale. Even using 10 mol % of catalyst as in entry 3 did not quantitatively form seven-membered ring **127**.

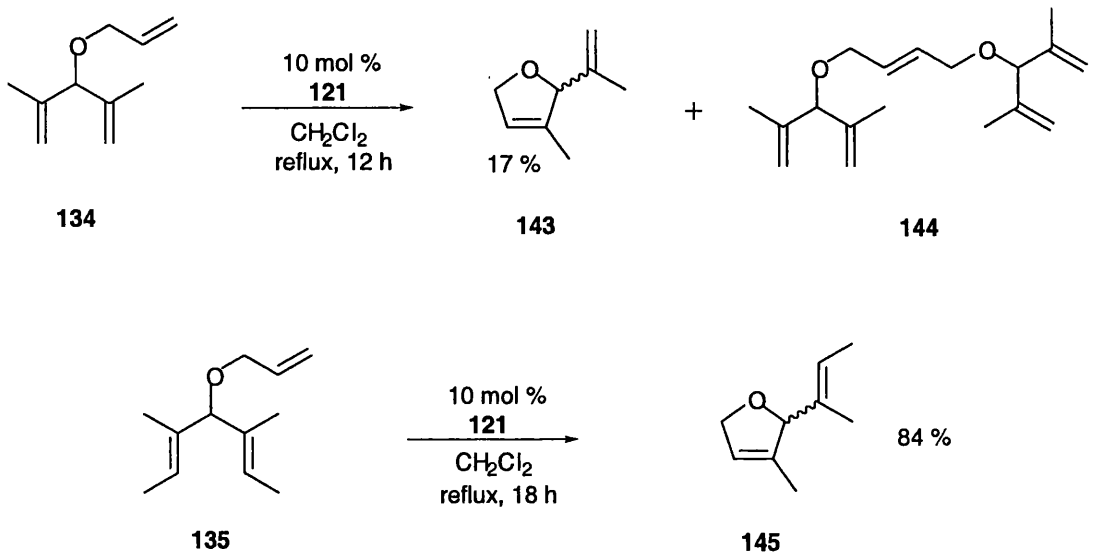
The catalyst performed well on other substrates though, giving a very good 91% yield for formation of the more demanding, trisubstituted alkene **139**, and excellent yields of sulfonamide **140** and silyl ether **141**.

A very good conversion of 60 % was achieved in the formation of 14-membered lactone **142** under high dilution conditions (4.5 mM in substrate). At normal concentration (46 mM), conversion was low and another compound, presumed to be dimer, was formed.

In most of the reactions, after removing the catalyst by filtration, the remaining solution was almost colourless indicating minimal leaching of ruthenium from the resin. The notable exception was entry 7 in which the macrocyclic product was quite badly discoloured.

Attempts at enyne metathesis with substrate **129** were unsuccessful, returning only starting material.

The two prochiral triene substrates were used to investigate whether the catalyst could promote enantioselective metathesis. Racemic samples of the products were first prepared using Grubbs's second-generation catalyst **2** and analysed by chiral GC to determine conditions to separate the enantiomers. Metathesis of the trienes with resin catalyst **121** was then attempted (**Scheme 3.27**). The reactions were worked up carefully as the products (and starting materials) are fairly volatile. After ^{1}H NMR of the crude reaction mixture to determine the conversion, the ring-closed product was isolated by column chromatography and then analysed by chiral GC.



Scheme 3.27

The conversion to ring-closed product **143** of triene **134** was low, with dimer **144** isolated as the main product. Chiral GC analysis of **143** showed that it was racemic. More substituted triene **135** however gave a much better conversion to desired product **145**. Again though, analysis of the product showed that no enantioselectivity had been obtained.

Grubbs's investigations with chiral ruthenium catalysts (**Section 1.3**) also found that conversions were higher when the more-substituted triene was used as the substrate.[46] He also found that the extent of chiral induction was very dependent on the groups imparting the chirality to the N-heterocyclic carbene ligand. In the case of resin catalyst **121**, the

para-substituted benzyl group on the chiral centre is clearly not sufficient to favour one diastereomeric transition state over the other.

Time allowed only a preliminary investigation into the recyclability of the resin catalyst. A sample of resin catalyst **121** which carried out RCM of diethyl diallylmalonate with 100% conversion was used for the same reaction, under the same conditions, after recovery by filtration in air and washing with reagent grade solvent. The conversion to cyclic product in the second run was 11%. This showed that some residual activity of the catalyst remained and suggested that recycling of the catalyst would be feasible. Obviously, methods for improving the recycling process would need to be investigated to improve the yield in subsequent cycles. For example, filtration under an inert atmosphere or using additives to regenerate the catalyst.

4. CONCLUSIONS AND FURTHER WORK

4.1 BISPHOSPHINES AND METALLAMACROCYCLES

Short and efficient syntheses of the two bisphosphine ligands, DPPN **61** and DPEN **62**, were successfully developed. Investigation of the transition metal complexes of these ligands showed that they did not exhibit the required *trans*-spanning coordination but, despite this, a number of interesting results were obtained. The ligands favoured bridging metal centres to form dimeric or oligomeric complexes and the thermodynamically favoured complexes of both ligands with platinum(II) were the *cis*, *cis* dimers.

As the ligands were not suitable for preparing a solid-supported alkene metathesis catalyst, I did not go on to carry out a more detailed investigation into their chelation properties. However, there is clearly further work that could be done with the two bisphosphine ligands.

As previously mentioned (**Section 2.5**), undergraduate student Alexis Perry carried out some experiments to confirm my conclusions on the isomerisation of the platinum complexes including a low temperature NMR study. He also demonstrated that *cis*, *cis*-$Pt_2Cl_4(DPEN)_2$ **76** was an active catalyst, displaying good linear selectivity, for the hydroformylation of 1-octene.

The bisphosphine ligands could potentially form complexes with a large number of metals and the stoichiometry, geometry and possible catalytic activity of these would be interesting to investigate. Alexis made a start on this by forming a complex from molybdenum hexacarbonyl. This was shown from the X-ray crystal structure to be *cis*, *cis*-dimer $Mo_2(CO)_8(DPEN)_2$, with the DPEN ligands adopting a similar conformation to that in the corresponding platinum complex. Details of this further work carried out are given in Alexis Perry's project report[84] and in our paper.[85]

4.2 SOLID-SUPPORTED ALKENE METATHESIS CATALYST

The ultimate aim of this work was to develop a solid-supported alkene metathesis catalyst and this target was successfully achieved. The synthesis of the catalyst was optimised as far as possible in the time available and the catalyst was then tested for the ring closing metathesis of a range of substrates with good results.

Further work that could be carried out would be to investigate in more detail the final steps in the synthesis of the resin catalyst. The practical techniques required and the limited analysis available for solid-phase chemistry made it difficult to optimise the reactions and further work might allow the catalyst to be made more efficiently and with a higher final loading.

Although the final supported catalyst was tested with several substrates, I did not have time to carry out a more detailed investigation into the properties and applications of the catalyst. Some further work in this area has been done by undergraduate project students. Unfortunately, they found it difficult to carry out the solid phase synthesis of the catalyst. Therefore, most of their testing was done with resin catalyst that was considerably less active than I used, making it hard to draw conclusions from many of the results.

However, some useful observations were made by investigating the RCM of diethyl diallylmalonate.[109] This was attempted in several solvents and at different temperatures to find the optimum conditions for the catalyst. It was found that refluxing dichloromethane, as I had used, gave the best results. Also, for this substrate at least, similar conversions were achieved using reagent grade solvent in air to using dry solvent under nitrogen, demonstrating the robustness of the catalyst. Attempting to recycle the catalyst by filtration under an inert atmosphere showed that the catalyst retained activity over four cycles although the conversion was significantly reduced after the first run (99% conversion in the first run, 22% in the second, 13% in the third and 6% in the fourth).

Further work that could be carried out on the supported catalyst would be to test its ability to carry out different types of metathesis such as cross metathesis and ring opening cross metathesis. Other work would include a more detailed investigation into recycling the

catalyst by using additives to regenerate the active species and the quantification of ruthenium residues in the products to determine the amount of catalyst leaching from the support.

5. EXPERIMENTAL

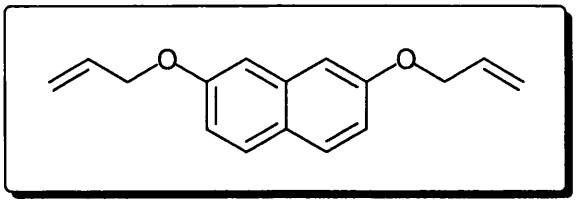
5.1 GENERAL

All air or moisture sensitive reactions were carried out using oven-dried glassware and dry solvents under a nitrogen atmosphere.

THF and dioxane were freshly distilled from sodium/benzophenone. Dichloromethane and toluene were freshly distilled from calcium hydride. Methanol was freshly distilled from magnesium. DMF was stored over 4 Å molecular sieves. Triethylamine was distilled from CaH_2 and stored over KOH. Pyridine was distilled from CaH_2 and stored over CaH_2. Trimethyl orthoformate was Aldrich anhydrous grade. Formic acid was dried by distillation. Pet. ether refers to petroleum ether boiling between 40 and 60 °C. Other reagents and starting materials were used as supplied without further purification. All column chromatography was carried out on silica.

All NMR spectra were obtained from $CDCl_3$ solutions unless stated otherwise. ^1H and ^{13}C NMR spectra were recorded using a Bruker DPX 400 spectrometer operating at 400 and 100 MHz respectively. ^{31}P spectra were recorded using a Bruker WP 200 SY spectrometer operating at 81 MHz. Chemical shifts (δ) are given in ppm relative to residual $CHCl_3$ (7.27) for ^1H, $CDCl_3$ (77.0) for ^{13}C, and 85% H_3PO_4 (0.0) for ^{31}P. ^{13}C and ^{31}P spectra were proton decoupled. Coupling constants (J) are given in Hz. Infra red spectra were recorded as KBr discs, unless stated otherwise, using a Jasco 410 spectrometer. Absorbances are quoted in wavenumbers (cm^{-1}). Mass spectra were obtained using a JMS 700 spectrometer. Melting points were recorded on a Kohfler hot stage and are uncorrected. Chiral GC was carried out on a HP6890 system with a Supelco β-DEX 120 column.

5.2 BISPHOSPHINE LIGANDS AND METALLAMACROCYCLES



2,7-Diallyloxynaphthalene[71] (63)

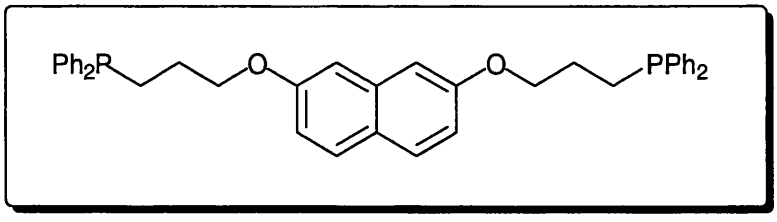
Potassium carbonate (3.80 g, 27.5 mmol) and 18-crown-6 (496 mg, 1.88 mmol) were added to a solution of 2,7-dihydroxynaphthalene (2.00 g, 12.5 mmol) in acetone (30 ml). The mixture was refluxed for 1 h and then allyl bromide (2.7 ml, 31 mmol) was added and the mixture refluxed for a further 15 h. The reaction mixture was allowed to cool, filtered and then concentrated. The crude product was purified by column chromatography (5% EtOAc/hexane) and recrystallised from hexane to give diether **63** as colourless plates (1.76 g, 59%): m.p. 60-62 °C [lit.[71] 62.5-63 °C (MeOH)].

^{1}H NMR: δ 4.65 (4H, dt, J = 5.3, 1.4, CH_2O), 5.33 (2H, dq, J = 10.5, 1.4, CH_AH_B=CH), 5.48 (2H, dq, J = 17.3, 1.5, CH_AH_B=CH), 6.13 (2H, ddt, J = 17.2, 10.5, 5.3, CH_2=C*H*), 7.02-7.05 (4H, m, $C_{3,6}$H, $C_{1,8}$H), 7.66 (2H, d, J = 8.6, $C_{4,5}$H).

^{13}C NMR: δ 68.8 (CH_2O), 106.5 (C_3, C_6), 116.4 (C_1, C_8), 117.7 (CH_2=CH), 124.4 (C_{4a}), 129.1 (C_4, C_5), 133.2 (CH_2=CH), 135.8 (C_{8a}), 157.1 (C_2, C_7).

IR: 3084 w, 2921 w, 2866 w, 1631 m (C=C), 1514 m, 1425 m, 1387 m, 1250 m, 1209 s (Ar–O–C), 1017 m, 936 m, 823 m.

MS (EI): *m/z* 240 (M^+, 100%), 212 (M^+ – CO, 13), 199 (M^+ – allyl, 24), 185 (39), 171 (M^+ – allyl – CO, 94), 143 (25), 128 (35), 102 (26).



2,7-Bis(3-diphenylphosphinopropoxy)naphthalene, DPPN (61)

Diallyloxynaphthalene **63** (400 mg, 1.67 mmol) was dissolved in diphenylphosphine (0.63 ml, 3.7 mmol) and the resulting solution was irradiated with ultraviolet light from a medium-pressure mercury lamp for 12 h. The gelatinous mass was then washed with pentane, dissolved in ethyl acetate and concentrated. The crude product was purified by column chromatography (5% EtOAc/hexane) to give DPPN **61** as a very viscous colourless oil (695 mg, 68%).

^{1}H NMR: δ 1.99-2.05 (4H, m, C*H*$_2$CH$_2$P), 2.27-2.31 (4H, m, CH$_2$P), 4.13 (4H, t, J = 6.3, CH$_2$O), 6.97-7.00 (4H, m, C$_{1,8}$H, C$_{3,6}$H), 7.32-7.38 (12H, m, Ph) 7.44-7.50 (8H, m, Ph), 7.64 (2H, d, J = 9.6, C$_{4,5}$H).

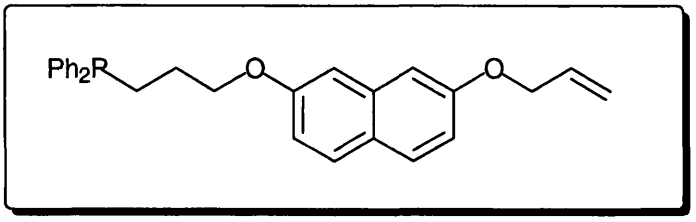
^{13}C NMR: δ 24.5 (d, J = 12, *C*H$_2$CH$_2$P), 25.8 (d, J = 17, CH$_2$P), 68.2 (d, J = 14, CH$_2$O), 106.1 (s, C$_3$, C$_6$), 116.2 (s, C$_1$, C$_8$), 124.2 (s, C$_{4a}$), 128.4-128.6 (m, Ph *p*-C and Ph *m*-C), 129.0 (s, C$_4$, C$_5$), 132.7 (d, J = 18, Ph *o*-C), 135.9 (s, C$_{8a}$), 138.4 (d, J = 13, Ph *i*-C), 157.4 (s, C$_2$, C$_7$).

^{31}P NMR: δ –16.4 (s, PPh$_2$).

IR (neat): 3069 m, 2944 m, 1627 s, 1514 s, 1434 s (Ph–P), 1387 s, 1253 m, 1210 s (Ar–O–C), 1159 m, 1026 m, 832 m, 751 s, 699 s.

MS (EI): *m/z* 612 (M$^+$, 11%), 582 (M$^+$ – CH$_2$O, 13), 496 (M$^+$ – C$_6$H$_{12}$O$_2$, 64), 227 [Ph$_2$P(CH$_2$)$_3^+$, 29], 199 (CH$_2$PPh$_2^+$, 100), 183 (50).

HRMS (EI): Calculated for C$_{40}$H$_{38}$O$_2$P$_2$: 612.2347. Found 612.2347.



2-Allyloxy-7-(3'-diphenylphosphinopropoxy)naphthalene (64)

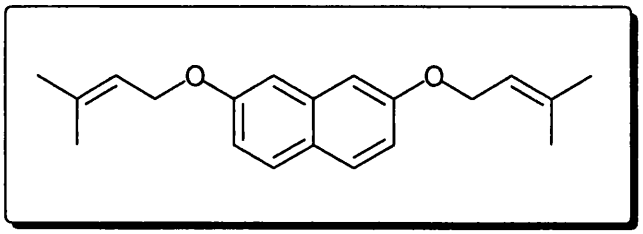
Diallyloxynaphthalene **63** (200 mg, 0.83 mmol) was dissolved in diphenylphosphine (0.14 ml, 0.83 mmol) and the resulting solution was irradiated with ultraviolet light from a medium-pressure mercury lamp for 12 h. The gelatinous mass was then washed with pentane, dissolved in EtOAc and concentrated. The crude product mixture was separated by

column chromatography (5% EtOAc/hexane) to give starting material **63** (67 mg, 34%), bisphosphine **61** (98 mg, 19%) and monophosphine **64** as a very viscous colourless oil (111 mg, 31%).

^{1}H NMR: δ 1.99 (4H, m, C*H*$_2$CH$_2$P), 2.28 (4H, m, CH$_2$P), 4.13 (4H, t, *J* = 6.3, CH$_2$O), 6.98 (4H, m, C$_{1,8}$H, C$_{3,6}$H), 7.36 (12H, m, Ph), 7.45 (8H, m, Ph), 7.64 (2H, d, *J* = 9.6, C$_{4,5}$H).

^{13}C NMR: δ 24.5 (d, *J* = 12, *C*H$_2$CH$_2$P), 25.8 (d, *J* = 17, CH$_2$P), 68.2 (d, *J* = 14, CH$_2$O), 106.1 (s, C$_3$, C$_6$), 116.2 (s, C$_1$, C$_8$), 124.2 (s, C$_{4a}$), 128.4 (d, *J* = 6, Ph *m*-C), 128.6 (s, Ph *p*-C), 129.0 (s, C$_4$, C$_5$), 132.7 (d, *J* = 18, Ph *o*-C), 135.9 (s, C$_{8a}$), 138.4 (d, *J* = 13, Ph *i*-C), 157.4 (s, C$_2$, C$_7$).

^{31}P NMR: δ –16.5 (s, PPh$_2$).



2,7-Diprenyloxynaphthalene (66)

Potassium carbonate (4.31 g, 31.3 mmol) and prenyl bromide (0.79 ml, 6.9 mmol) were added to a solution of 2,7-dihydroxynaphthalene (500 mg, 3.13 mmol) in acetone (15 ml) and the resulting mixture was stirred at room temperature for 3 h. The reaction mixture was allowed to cool, filtered and then concentrated. The crude product was purified by column chromatography (5% EtOAc/hexane) and recrystallised from ethanol to give diether **66** as colourless plates (280 mg, 30%): m.p. 74-75 °C.

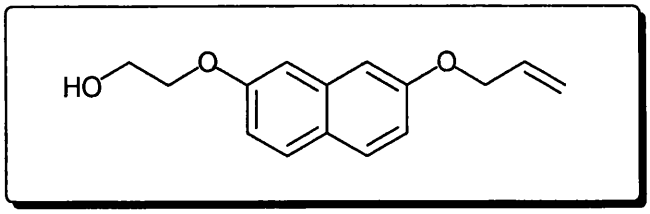
^{1}H NMR: δ 1.81 (6H, s, CH$_3$), 1.85 (6H, s, CH$_3$), 4.64 (4H, d, *J* = 6.7, CH$_2$O), 5.60 (2H, t, *J* = 6.1, CH=C), 7.04 (2H, dd, *J* = 8.9, 2.4, C$_{3,6}$H), 7.10 (2H, d, *J* = 2.3, C$_{1,8}$H), 7.67 (2H, d, *J* = 8.9, C$_{4,5}$H).

^{13}C NMR: δ 18.2 (CH$_3$), 25.8 (CH$_3$), 64.7 (CH$_2$O), 106.2 (C$_3$, C$_6$), 116.4 (C$_1$, C$_8$), 119.7 (Me$_2$C=*C*), 124.2 (C$_{4a}$), 129.0 (C$_4$, C$_5$), 135.8 (C$_{8a}$), 138.2 (Me$_2$*C*=C), 157.4 (C$_2$, C$_7$).

IR: 2978 m, 2932 m, 1629 s, 1513 s, 1387 s, 1209 s (Ar–O–C), 1016 s, 859 s, 832 s.

MS (EI): *m/z* 296 (M^+, 10%), 160 ($M^+ - C_{10}H_{16}$, 100).

Microanalysis: Calculated for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 81.02; H, 8.15.



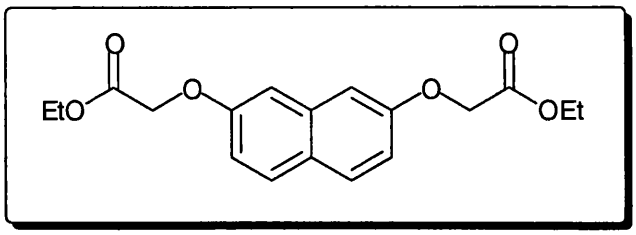
Attempted ozonolysis of diene 63

A solution of 2,7-diallyloxynaphthalene **63** (800 mg, 3.33 mmol) in methanol (15 ml) and dichloromethane (30 ml) was cooled to -78 °C. Ozone (in O_2) was bubbled through the solution for 2 h. The system was flushed with O_2, then N_2, and then sodium borohydride (629 mg, 16.7 mmol) was added carefully over 30 min. The mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched with 1 M aq. HCl, extracted with Et_2O, dried (Na_2SO_4) and concentrated. The crude product mixture was separated by column chromatography (10-50% EtOAc/hexane) to give starting material **63** (467 mg, 58%) and alcohol **67** (142 mg, 42% based on recovered **63**). Recrystallisation from hexane gave alcohol **67** as a white microcrystalline solid: m.p. 90-91 °C.

^{1}H NMR: δ 2.07 (1H, t, J = 6.1, OH), 4.03 (2H, dt, J = 4.1, 5.3, CH_2OH), 4.20 (2H, t, J = 4.5, CH_2CH$_2$OH), 4.65 (2H, dt, J = 5.3, 1.4, CH_2CH=CH$_2$), 5.33 (1H, dd, J = 10.5, 1.3, CH_AH$_B$=CH), 5.47 (1H, dd, J = 17.3, 1.5, CH$_A$$H_B$=CH), 6.13 (1H, ddt, J = 17.2, 10.5, 5.3, CH$_2$=CH), 7.02 (2H, d, J = 8.4, ArH), 7.05 (2H, s, ArH), 7.66 (2H, d, J = 8.9, ArH).

^{13}C NMR: δ 61.5 (CH$_2$OH), 68.8 (*C*H$_2$CH=CH$_2$), 69.1 (*C*H$_2$CH$_2$OH), 106.3 and 106.5 (C$_3$, C$_6$), 116.1 and 116.6 (C$_1$, C$_8$), 117.8 (*C*H$_2$=CH), 124.5 (C$_{4a}$), 129.2 and 129.3 (C$_4$, C$_5$), 133.2 (CH$_2$=*C*H), 135.7 (C$_{8a}$), 157.2 (C$_2$, C$_7$).

MS (EI) : m/z 244 (M^+, 95%), 200 (33), 185 (39), 175 (M^+ – allyl – CO, 18), 131 (100).



2,7-Bis(ethoxycarbonylmethoxy)naphthalene[73] (69)

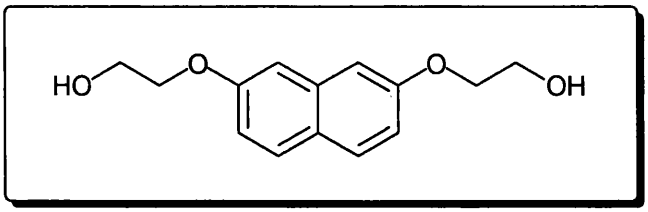
Potassium carbonate (34.5 g, 250 mmol) and ethyl bromoacetate (6.1 ml, 55 mmol) were added to a solution of 2,7-dihydroxynaphthalene (4.00 g, 25.0 mmol) in acetone (100 ml) and the mixture was refluxed for 21 h. The reaction mixture was allowed to cool, filtered and then concentrated to give diester **69** (7.19 g, 87%). A portion was recrystallised from ethanol to give diester **69** as a white microcrystalline solid: m.p. 124-125 °C [lit.[73] 126 °C (EtOH)].

^{1}H NMR: δ 1.31 (6H, t, J = 7.1, CH_3CH$_2$O), 4.30 (4H, q, J = 7.1, CH$_3$CH_2O), 4.72 (4H, s, CH$_2$C=O), 6.98 (2H, d, J = 2.5, C$_{1,8}$H), 7.10 (2H, dd, J = 8.9, 2.5, C$_{3,6}$H), 7.69 (2H, d, J = 8.9, C$_{4,5}$H).

^{13}C NMR: δ 14.1 (*C*H$_3$CH$_2$O), 61.4 (CH$_3$*C*H$_2$O), 65.4 (*C*H$_2$C=O), 106.7 (C$_3$, C$_6$), 116.4 (C$_1$, C$_8$), 125.2 (C$_{4a}$), 129.4 (C$_4$, C$_5$), 135.3 (C$_{8a}$), 156.5 (C$_2$, C$_7$), 168.8 (C=O).

IR: 2993 w, 2916 w, 1760 s (C=O), 1629 m, 1203 s (Ar–O–C), 1076 m, 847 w, 834 w.

MS (EI): *m/z* 332 (M$^+$, 100%).



2,7-Bis(2-hydroxyethoxy)naphthalene[72] (68)

A solution of lithium aluminium hydride (0.85 g, 22 mmol) in THF (50 ml) was cooled to 0 °C and a solution of diester **69** (6.84 g, 20.6 mmol) in THF (85 ml) was added. The resulting mixture was stirred for 1 h and then allowed to warm to room temperature and stirred overnight. Further portions of LiAlH$_4$ (1.3 g in total) were added until the reaction had gone to completion as indicated by TLC. The reaction mixture was quenched with

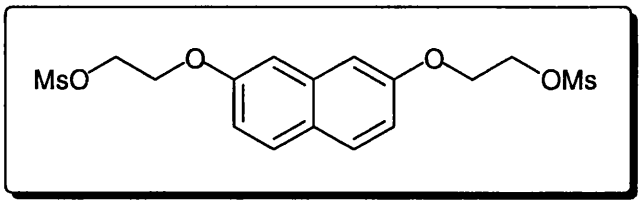
EtOAc and then satd. aq. potassium sodium tartrate solution was added. The mixture was filtered, extracted with EtOAc, dried (Na_2SO_4) and concentrated to give diol **68** (3.79 g, 74%). A portion was recrystallised from methanol to give diol **68** as a white microcrystalline solid: m.p. 151-152 °C [lit.[72] 152-153 °C].

^{1}H NMR: δ 2.04 (2H, t, J = 6.1, OH), 4.03 (4H, td, J = 4.2, 5.3, CH_2OH), 4.20 (4H, t, J = 4.5, CH_2CH_2OH), 7.03 (2H, dd, J = 8.8, 2.5, $C_{3,6}$H), 7.07 (2H, d, J = 2.4, $C_{1,8}$H), 7.68 (2H, d, J = 8.9, $C_{4,5}$H).

^{13}C NMR: δ 61.5 (CH_2OH), 69.2 (CH_2CH_2OH), 106.3 (C_3, C_6), 116.3 (C_1, C_8), 125.2 (C_{4a}), 129.3 (C_4, C_5), 135.4 (C_{8a}), 157.2 (C_2, C_7).

IR: 3334 br, 2931 w, 2882 w, 1631 s, 1387 m, 1213 s (Ar–O–C), 1081 m, 838 m.

MS (EI): *m/z* 248 (M^+, 77%), 204 (35), 160 (100).



2,7-Bis(2-hydroxyethoxy)naphthalene bis(methanesulfonate)ester (70)

Methanesulfonyl chloride (1.6 ml, 21 mmol) and triethylamine (2.9 ml, 21 mmol) were added to a solution of diol **68** (2.17 g, 8.75 mmol) in THF (100 ml) and the mixture was stirred for 30 min at room temperature. The reaction mixture was then filtered and the solvent removed. The residue was dissolved in EtOAc, washed with water, dried (Na_2SO_4) and concentrated. The crude product was recrystallised from dichloromethane and methanol to give dimesylate **70** as colourless plates (3.09 g, 87%): m.p. 134-135 °C.

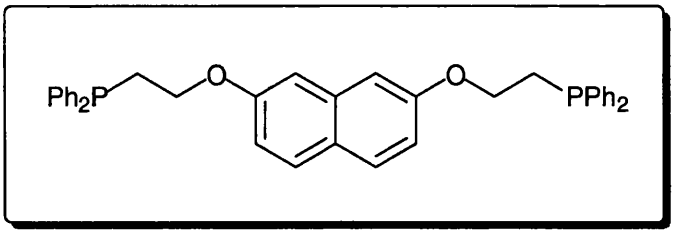
^{1}H NMR: δ 3.12 (6H, s, CH_3S), 4.36-4.38 (4H, m, CH_2CH_2OS), 4.64-4.66 (4H, m, CH_2OS), 7.01-7.05 (4H, m, $C_{3,6}$H, $C_{1,8}$H), 7.70 (2H, d, J = 8.7, $C_{4,5}$H).

^{13}C NMR: δ 37.8 (CH_3SO_2), 65.8 (CH_2), 67.9 (CH_2), 106.5 (C_3, C_6), 116.3 (C_1, C_8), 125.0 (C_{4a}), 129.5 (C_4, C_5), 135.5 (C_{8a}), 156.7 (C_2, C_7).

IR: 3025 w, 2941 w, 1629 s, 1517 m, 1353 s, 1256 m, 1216 s (Ar–O–C), 1171 s, 1069 m, 1024 m, 981 s, 930 s, 822 s.

MS (EI): *m/z* 404 (M^+, 57%), 123 ($C_2H_4OMs^+$, 100), 79 ($SO_2CH_3^+$, 28).

Microanalysis: Calculated for $C_{16}H_{20}O_8S_2$: C, 47.51; H, 4.98. Found: C, 47.49; H, 4.88.



2,7-Bis(2-diphenylphosphinoethoxy)naphthalene, DPEN (62)

n-Butyl lithium (1.6M solution in hexanes, 1.8 ml, 2.8 mmol) was added to a solution of diphenylphosphine (0.49 ml, 2.8 mmol) in THF (3 ml). After stirring at room temperature for 15 minutes, a solution of dimesylate **70** (520 g, 1.29 mmol) in THF (30 ml) was added and the mixture stirred for a further 1 h. The solvent was removed and the residue dissolved in dichloromethane, washed with water, dried (Na_2SO_4) and concentrated. The crude product was recrystallised from ethyl acetate and washed with pentane to give DPEN **62** as white needles (493 mg, 66%): m.p. 137-138 °C.

^{1}H NMR: δ 2.65 (4H, t, J = 7.7, CH_2P), 4.22 (4H, q, J = 7.5, CH_2O), 6.80 (2H, d, J = 2.2, $C_{1,8}H$), 6.90 (2H, dd, J = 8.9, 2.3, $C_{3,6}H$), 7.35-7.42 (12H, m, Ph), 7.51-7.55 (8H, m, Ph), 7.60 (2H, d, J = 8.9, $C_{4,5}H$).

^{13}C NMR: δ 28.3 (d, J = 13, CH_2P), 65.2 (d, J = 27, CH_2O), 106.0 (s, C_3, C_6), 116.3 (s, C_1, C_8), 124.3 (s, C_{4a}), 128.6 (d, J = 7, Ph *m*-C), 128.8 (s, Ph *p*-C), 129.0 (s, C_4, C_5), 132.7 (d, J = 19, Ph *o*-C), 135.7 (s, C_{8a}), 137.9 (d, J = 12, Ph *i*-C), 156.9 (s, C_2, C_7).

^{31}P NMR: δ –22.8 (s, PPh_2).

IR: 3066 w, 2914 w, 1630 s, 1514 m, 1433 s (Ph–P), 1211 s (Ar–O–C), 1168 m, 1018 m, 834 m, 741 s, 697 s.

MS (EI): *m/z* 584 (M^+, 4%), 553 ($M^+ - CH_3O$, 5), 371 ($M^+ - C_2H_4PPh_2$, 23), 341 ($M^+ - C_2H_4PPh_2$, 42), 328 (21), 212 ($C_2H_3PPh_2^+$, 83), 183 ($C_{13}H_{11}O^+$, 100).

HRMS (EI): Calculated for $C_{38}H_{34}O_2P_2$: 584.2034. Found: 584.2037.

Dichlorotris(triphenylphosphino)ruthenium (II), $RuCl_2(PPh_3)_3$

Following the method of Stephenson and Wilkinson,[74] triphenylphosphine (3.16 g, 12.1 mmol) was added to a solution of ruthenium trichloride hydrate (500 mg, 2.41 mmol) in methanol (100 ml). The mixture was shaken vigorously for 10 min, filtered and then refluxed for 7 h. After cooling, the dark brown precipitate of $RuCl_2(PPh_3)_3$ was collected by filtration and washed with ether (1.53 g, 72%) : m.p. 132-134 °C (lit.[74] 132-134 °C).

Benzaldehyde tosylhydrazone (72)

Following the method of Gloss and Moss,[76] a solution of tosylhydrazine (4.00 g, 21.5 mmol) in warm methanol (25 ml) was added slowly to benzaldehyde (2.2 ml, 21 mmol) at -78 °C. After addition was complete, the mixture was stirred at -78 °C for 2.5 h. The solvent was removed and the crude product recrystallised from methanol to give tosylhydrazone **72** as an off-white solid (4.14 g, 70%) : m.p. 128-129 °C (lit.[76] 128 °C).

Phenyldiazomethane (71)

Following the method of Bamford and Stevens,[75] sodium (100 mg, 4.4 mmol) was added to absolute ethanol (25 ml) and when it had all dissolved, benzaldehyde tosylhydrazone **72** (600 mg, 2.19 mmol) was added. The solution was stirred at 50 °C for 6 h. Ice-cold water was added and the mixture extracted with pentane. The extracts were decanted from a white precipitate and then concentrated to approx. 5 ml at 0 °C. The red solution of crude phenyldiazomethane **71** was not analysed but was used immediately, assuming a 50% yield.

$RuCl_2(=CHPh)(PPh_3)_2$ (73)

Following the method of Grubbs and co-workers,[1] a solution of $RuCl_2(PPh_3)_3$ (262 mg, 0.27 mmol) in dichloromethane (5 ml) at -78 °C was treated with a solution of phenyldiazomethane **71** (65 mg, 0.55 mmol) in pentane (5 ml). The mixture was stirred while warming to room temperature and then the solvent was removed. The residue was dissolved in dichloromethane (1 ml) and then pentane (20 ml) was added to precipitate a

dark green solid. The mother liquor was removed by cannula filtration and the procedure was repeated three times by which time the mother liquor was nearly colourless. The remaining grey-green solid was dried under vacuum (144 mg, 67%).

^{1}H NMR: δ 6.60-7.88 (m, all ArH), 19.0-19.4 (m, Ru=CH). [Lit.[1] (C_6H_6): δ 6.66-6.99 and 7.64-7.80 (m, all ArH), 19.56 (t, Ru=CH)]

IR: 3054 m, 1930 w, 1625 w, 1482 m, 1435 s, 1112 m, 1092 m, 746 m, 695 s, 515 s.

ROMP of norbornene by $RuCl_2(=CHPh)(PPh_3)_2$ 73

Degassed $CDCl_3$ was added to norbornene (36 mg, 0.38 mmol) and catalyst **73** (2 mg, 2.5 μmol, 0.7 mol%) in an NMR tube. A ^{1}H NMR spectrum was recorded after 105 min by which time the mixture had solidified in the tube.

^{1}H NMR: δ 1.00-1.12 (m), 1.27-1.46 (m), 1.70.1.92 (m), 2.44 (br s), 2.80 (br s), 5.17-5.26 (m), 5.32-5.40 (m). [Norbornene : δ 0.99 (m), 1.09 (d), 1.33 (m), 1.64 (m), 2.86 (s), 6.01 (s)]

Polymeric DPEN ruthenium alkylidene (74)

A solution of $RuCl_2(PPh_3)_3$ (262 mg, 0.27 mmol) in dichloromethane (5 ml) at -78 °C was treated with a solution of phenyldiazomethane (65 mg, 0.55 mmol) in pentane (5 ml). The mixture was stirred for 10 min and then a solution of DPEN **62** (176 mg, 0.30 mmol) in dichloromethane (4 ml) at 0 °C was added. The mixture was allowed to warm to room temperature and then stirred overnight during which time a dark brown solid precipitated. The solvent was removed and the product was washed with pentane (2 x 20 ml) which was removed by cannula filtration. The brown solid remaining was dried under vacuum.

IR: 3051 m, 2884 w, 1954 w, 1629 s, 1511 s, 1435 s (P–Ph), 1253 m, 1208 s (Ar–O–C), 1155 m, 1113 m, 1095 m, 997 m, 909 w, 831 m, 740 s, 693 s, 510 s.

ROMP of norbornene by polymeric DPEN ruthenium alkylidene 74

Degassed $CHCl_3$ was added to norbornene (60 mg, 0.64 mmol) and catalyst **74** (5.4 mg, 6.4 μmol, 1 mol%) and the suspension was refluxed for 15 h. The mixture was allowed to cool,

filtered and concentrated. Polynorbornene (27 mg, 45%) was identified from the ^{1}H NMR spectrum which was identical to that obtained in the test of catalyst **73**.

Palladium DPEN complexes

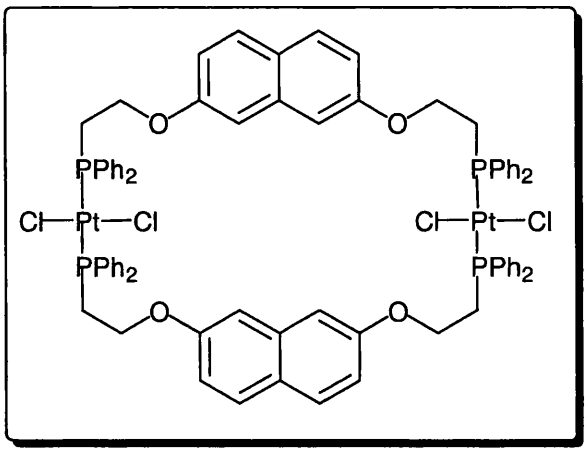
Dichloromethane (5 ml) was added to $PdCl_2(MeCN)_2$ (40 mg, 0.15 mmol) and DPEN **62** (91 mg, 0.15 mmol) and the resulting solution stirred overnight at room temperature. The solvent was then removed to yield a bright yellow solid.

^{1}H NMR: δ 2.86-2.94 (m), 2.96-3.07 (m), 4.32-4.53 (m), 4.60-4.70 (m), 6.61-7.85 (m).

^{31}P NMR: δ 12.1 (Rel. intensity 1) 12.8 (12), 12.9 (12), 13.2 (2), 16.4 (1), 26.2 (1), 29.3 (1).

MS (FAB) : 1523 ($Pd_2Cl_4(dpen)_4^+$, 2%), 1488 ($M^+ - Cl$, 5), 1451 ($M^+ - Cl_2$, 1.5).

IR: 3054 w, 2924 w, 1631 s, 1513 m, 1435 s (P-Ph), 1254 m, 1209 s (Ar-O-C), 1158 m, 1100 m, 749 m, 691 m.



***trans,trans*-$Pt_2Cl_4(DPEN)_2$ (75)**

A solution of DPEN **62** (100 mg, 0.17 mmol) in dichloromethane (3 ml) was added to a solution of $PtCl_2(SMe_2)_2$ (67 mg, 0.17 mmol) in dichloromethane (2 ml). The mixture was stirred at room temperature for 70 min and then the solvent was removed. Column chromatography (CH_2Cl_2) of the crude product mixture gave **75** as a yellow solid (8 mg, 5%). Slow diffusion of Et_2O into a CH_2Cl_2 solution of **75** produced yellow prisms suitable for X-ray analysis.

^{31}P NMR: δ 9.00 (J_{Pt-P} = 2563).

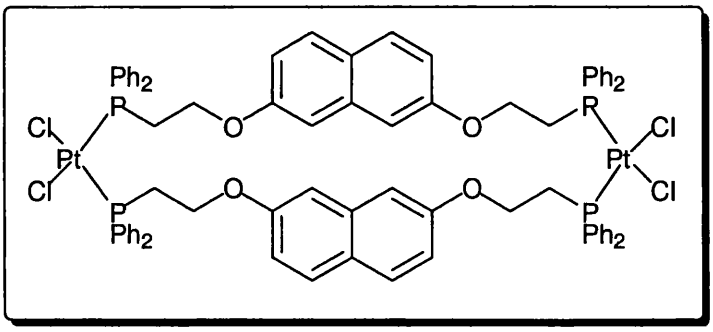
^{1}H NMR: δ 3.08-3.15 (8H, m, CH_2P), 4.00-4.05 (8H, m, CH_2O), 6.70 (4H, d, J = 2.3, $C_{1,8}H$), 6.85 (4H, dd, J = 8.8, 2.4, $C_{3,6}H$), 7.42 (16H, t, J = 7.6, Ph *o*-H), 7.50 (8H, t, J = 7.4, Ph *p*-H), 7.54 (4H, d, J = 8.9, $C_{4,5}H$), 7.81 (16H, dt, J = 7.0, 5.6, Ph *m*-H).

^{13}C NMR: δ 28.9 (CH_2P), 62.4 (t, J = 4, CH_2O), 105.0 ($C_{3,6}$), 115.8 ($C_{1,8}$), 123.6 (C_{4a}), 127.6 (t, J = 5, Ph *m*-C), 128.3 ($C_{4,5}$) 128.8 (Ph *ipso*-C), 130.1 (Ph *p*-C), 133.0 (t, J = 6, Ph *o*-C), 134.9 (C_{8a}), 156.1 ($C_{2,7}$).

IR: 3053 w, 2919 w, 1631 s, 1513 m, 1435 s , 1253 m, 1209 s (Ar–O–C), 1158 m, 1101 m, 740 m, 691 s.

MS (FAB): 1701 [$Pt_2Cl_4(DPEN)_2^+$, 1.8%], 1665 (M^+ – Cl, 1.3) 1628 (M^+ – 2Cl, 0.8).

HRMS: Calculated for $C_{76}H_{69}Cl_4O_4P_4Pt_2$: 1701.2200 Found: 1701.2217.



***cis,cis*-$Pt_2Cl_4(DPEN)_2$ (76)**

A solution of DPEN **62** (150 mg, 0.26 mmol) in dichloromethane (8 ml) was added dropwise to a solution of $PtCl_2(SMe_2)_2$ (67 mg, 0.17 mmol) in toluene (90 ml) and dichloromethane (15 ml) and the mixture was stirred for 18 h at room temperature. The white precipitate formed was collected by filtration to obtain *cis,cis*-$Pt_2Cl_4(DPEN)_2$ **76** (104 mg, 72%). Recrystallisation from a concentrated chloroform solution of **76** gave colourless prisms.

^{31}P NMR: δ 6.49 ($J_{Pt\text{-}P}$ = 3627).

^{1}H NMR: δ 2.88-2.94 (8H, m, CH_2P), 4.56 (8H, quintet, J = 6.4, CH_2O), 6.76 (4H, d, J = 2.2, $C_{1,8}H$), 6.83 (4H, dd, J = 8.8, 2.3, $C_{3,6}H$), 7.22 (16H, br t, J = 6.9, Ph *o*-H), 7.37 (8H, t, J = 7.3, Ph *p*-H), 7.48 (4H, d, J = 8.9, $C_{4,5}H$), 7.57, (16H, dd, J = 10.7, 8.1, Ph *m*-H).

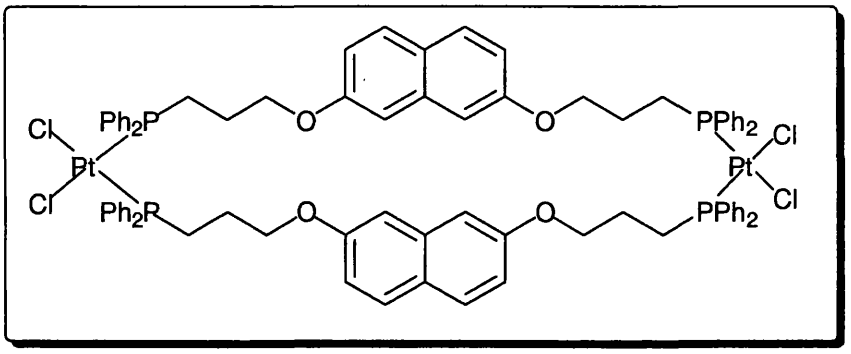
^{13}C NMR: δ 30.3 (5-line m, J_{P-C} = 22, CH_2P), 64.8 (CH_2O), 107.2 ($C_{3,6}$), 116.3 ($C_{1,8}$), 124.9 (C_{4a}), 128.8 (t, J = 5, Ph *m*-C), 129.4 ($C_{4,5}$), 130.1 (4 line m, J_{P-C} = 32, Ph *i*-C), 131.5 (br s, *p*-C), 133.7 (t, J = 5, *o*-C), 135.9 (C_{8a}), 156.6 (C_2).

IR: 1631 s, 1436 m, 1209 m (Ar–O–C), 694 m.

MS (FAB): 1701 [$Pt_2Cl_4(DPEN)_2^+$, 2.5%], 1665 (M^+ – Cl, 13) 1629 (M^+ – 2Cl, 2).

HRMS: Calculated for $C_{76}H_{68}Cl_3O_4P_4Pt_2$: 1665.2433 Found: 1665.2432.

Microanalysis: Calculated for $C_{76}H_{68}Cl_4O_4P_4Pt_2$: C, 53.7; H, 4.03. Found: C, 52.9; H, 3.97.



***cis,cis*-$Pt_2Cl_4(DPPN)_2$ (77)**

$PtCl_2(SMe_2)_2$ (143 mg, 0.37 mmol) was added to a solution of DPPN **61** (270 mg, 0.44 mmol) in chloroform (15 ml). The mixture was stirred at room temperature for 14 h and then filtered. The solvent was removed and the residue was washed with THF to give *cis,cis*-$Pt_2Cl_4(DPPN)_2$ **77** as a white solid (301 mg, 93%) which contained small quantities of a closely similar compound, presumed from NMR and MS evidence to be a *cis,cis,cis*-trimer.

^{31}P NMR: δ 7.18 (J_{Pt-P} = 3646).

^1H NMR (CD_2Cl_2): δ 2.20-2.30 (8H, m, CH_2CH_2P), 2.45-2.55 (8H, m, CH_2P), 4.15 (8H, t, J = 6.1, CH_2O), 6.91 (4H, dd, J = 8.8, 2.4, $C_{3,6}H$), 7.10-7.14 (16H, m, Ph *m*-H), 7.21 (4H, s, $C_{1,8}H$), 7.29 (8H, t, J = 7.0, Ph *p*-H), 7.41 (16H, dd, J = 10.0, 8.2, Ph *o*-H), 7.62 (4H, d, J = 8.9, $C_{4,5}H$).

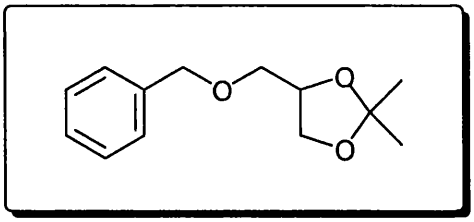
MS (FAB): 1757 [$Pt_2Cl_4(DPPN)_2^+$, 1.3%], 1721 [$Pt_2Cl_3(DPPN)_2^+$, 9.5%], 1685 [$Pt_2Cl_2(DPPN)_2^+$, 2.5%].

5.3 A SOLID-SUPPORTED ALKENE METATHESIS CATALYST

Attempted diamination of styrene with mesidine[88]

Styrene (0.24 ml, 2.1 mmol) and mesidine (1.79 ml, 12.7 mmol) were added to thallium(III) acetate (809 mg, 2.12 mmol) in dioxane (10 ml) and the resulting mixture was heated at reflux for 5 h. The reaction mixture was allowed to cool, filtered, washed with 0.5 M aq. NaOH, extracted with Et_2O, dried (Na_2SO_4) and concentrated. Column chromatography (5% EtOAc/pet. ether) of the crude mixture allowed the isolation of *trans* azomesitylene **82** (174 mg). Recrystallisation from ethanol gave red needles: m.p. 75-76 °C (lit.[110] 74-75 °C). Further fractions contained mixtures of *trans* and *cis* azomesitylene along with other unidentified products.

^{1}H NMR: *trans* **82** δ 2.35 (6H, s, *p*-CH_3), 2.43 (12H, s, *o*-CH_3), 2.35 (4H, s, ArH); *cis* **82** δ 1.90 (12H, s, *o*-CH_3), 2.25 (6H, s, *p*-CH_3), 6.76 (4H, s, ArH).

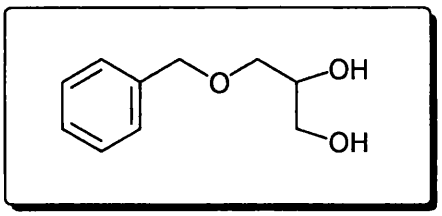


4-(Benzyloxymethyl)-2,2-dimethyl-1,3-dioxolane (83)

Solketal **84** (5.4 ml, 43 mmol) and benzyl chloride (5.0 ml, 43 mmol) were added to a suspension of sodium hydride (1.15 g, 47.8 mmol) in THF (50 ml) and the mixture was stirred at room temperature for 19 h. Monitoring by TLC showed starting material remained so further portions of NaH (1.7 g in total) and benzyl chloride (1 ml) were added over the next 6 h and the mixture was then heated at reflux for 16 h. The reaction mixture was allowed to cool and then quenched with isopropanol (5 ml). The solvent was removed and then the residue was dissolved in CH_2Cl_2, washed with water, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (10% EtOAc/pet. ether) to give ketal **83** as a colourless oil (6.78 g, 70%).

^{1}H NMR: δ 1.38 (3H, s, CH_3), 1.44 (3H, s, CH_3), 3.49 (1H, dd, J = 9.8, 5.5, CH_AH$_B$), 3.57 (1H, dd, J = 9.8, 5.7, CH$_A$$H_B$), 3.76 (1H, dd, J = 8.2, 6.3, CH_AH$_B$), 4.07 (1H, dd, J = 8.2, 6.4, CH$_A$$H_B$), 4.31 (1H, m, CH), 4.56 (1H, d, J = 12.2, PhCH_AH$_B$), 4.61 (1H, d, J = 12.2, PhCH$_A$$H_B$), 7.26-7.42 (5H, m, ArH).

This was consistent with literature data.[111]



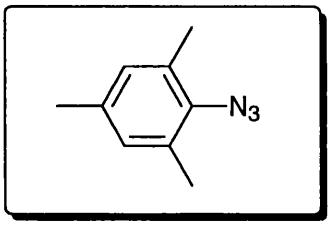
3-Benzyloxypropane-1,2-diol (85)

2 M aq. HCl (5 ml) was added to a solution of ketal **83** (2.53 g, 11.4 mmol) in THF (25 ml) and the mixture was stirred at room temperature for 15 h. The reaction mixture was quenched with satd. aq. $NaHCO_3$ (5 ml), extracted with EtOAc, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (EtOAc) to give diol **85** as a colourless oil (1.95 g, 94%).

^{1}H NMR: δ 2.22 (1H, t, J = 5.9, CH_2OH), 2.71 (1H, d, J = 4.5, CHOH), 3.53-3.77 (4H, m, CH_2CH(OH)CH_2OH), 3.90 (1H, m, CH), 4.57 (2H, s, $PhCH_2$), 7.28-7.39 (5H, m, ArH).

^{13}C NMR: δ 64.1 (CH_2), 70.6 (CH), 71.8 (CH_2), 73.6 (CH_2), 127.8, 127.9, 128.5 (all Ar CH), 137.9 (Ar C).

This was consistent with literature data.[112]

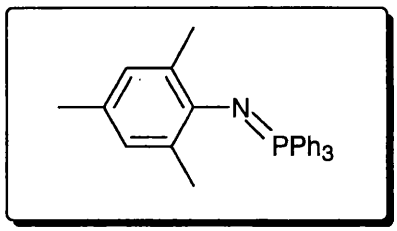


Mesityl azide (89)

Following the method of Murata and co-workers,[92] a mixture of conc. HCl (3 ml) and water (24 ml) was added to a solution of mesidine (1.00ml, 7.12 mmol) in THF (14 ml). The

mixture was stirred for 15 min at 0 °C and then a solution of sodium nitrite (982 mg, 14.2 mmol) in water (11 ml) was added dropwise, keeping the temperature below 5 °C. The mixture was then stirred for 15 min at 0 °C before urea (1 g) was added. Then, a solution of sodium azide (1.16 g, 17.8 mmol) in water (12 ml) was added dropwise and the mixture was allowed to warm to room temperature and stirred for 45 min. The reaction mixture was extracted with Et_2O, washed with 0.1 M aq. HCl, dried ($MgSO_4$) and concentrated to give azide **89** as a yellow oil (1.10 g, 96%) which was used without purification.

^{1}H NMR: δ 2.26 (3H, s, *p*-CH_3), 2.34 (6H, s, *o*-CH_3), 6.85 (2H, s, ArH).



***N*-Mesitylimino triphenylphosphorane (88)**

Following the method of Kasukhin and co-workers,[93] a solution of triphenylphosphine (1.80 g, 6.85 mmol) in THF (5 ml) was added dropwise to a solution of azide **89** (1.10 g, 6.85 mmol) in THF (5 ml) at 0 °C. The mixture was stirred for 1 h and then a further 30 min at room temperature before the solvent was removed. The crude product was recrystallised from methanol to give iminophosphorane **88** as yellow prisms (1.96 g, 72%): m.p. 145-147 °C [Lit.[93] 144-145 °C (THF)].

^{1}H NMR: δ 1.94 (6H, d, J = 1.6, *o*-CH_3), 2.20 (3H, d, J = 2.5, *p*-CH_3), 6.71 (2H, s, mesityl ArH), 7.39-7.63 (15H, m, phenyl ArH).

Attempted reductive amination of phenylglyoxal hydrate

A solution of phenylglyoxal hydrate **91** (200 mg, 1.31 mmol) in THF (15 ml) was stirred over 4 Å molecular sieves for 15 min. Mesidine (0.92 ml, 6.6 mmol), acetic acid (0.15 ml, 2.6 mmol) and sodium cyanoborohydride (165 mg, 2.6 mmol) were then added and the mixture was heated at reflux for 25 h. The reaction mixture was allowed to cool, filtered, poured into water, extracted with CH_2Cl_2, dried ($MgSO_4$) and concentrated. Column

chromatography (10% EtOAc/pet. ether → EtOAc) of the crude product mixture produced amino alcohol **92** as a colourless oil (102 mg, 31%) and diol **93** (54 mg, 30%) which was recrystallised from hexane to give colourless needles: m.p. 65-67 °C (lit.[113] 65 °C).

92: ^{1}H NMR: δ 2.28 (9H, s, CH_3), 3.12 (1H, dd, J = 12.6, 8.5, CH_AH$_B$N), 3.24 (1H, dd, J = 12.6, 3.7, CH$_A$$H_B$N), 3.12-3.29 (2H, br, OH, NH), 4.83 (1H, dd, J = 8.5, 3.7, CH), 6.86 (2H, s, mesityl ArH), 7.31-7.44 (5H, m, phenyl ArH).

^{13}C NMR: δ 18.2 (*o*-CH_3), 20.5 (*p*-CH_3), 55.8 (CH_2), 73.1 (CH), 125.8, 127.8, 128.4, 129.5 (All Ar CH), 130.0, 131.7, 142.2, 142.4 (all Ar C).

93: ^{1}H NMR: δ 2.49 (1H, br s, OH), 2.92 (1H, br s, OH), 3.66 (1H, dd, J = 11.3, 8.2, CH_AH$_B$OH), 3.76 (1H, dd, J = 11.2, 2.9, CH$_A$$H_B$OH), 4.82 (1H, dd, J = 8.2, 3.5, CH), 7.23-7.47 (5H, m, ArH).

^{13}C NMR: δ 67.9 (CH_2), 74.6 (CH), 126.0, 127.8, 128.4 (all Ar CH), 140.4 (Ar C).

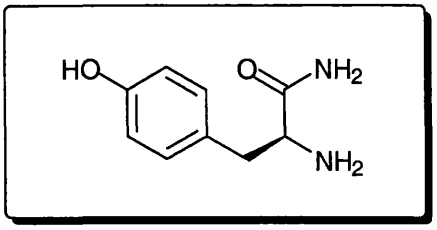
Attempted reductive amination of butanedione

Mesidine (3.2 ml, 23 mmol), acetic acid (0.26 ml, 4.5 mmol), sodium cyanoborohydride (287 mg, 4.57 mmol) and powdered 4 Å molecular sieves were added to a solution of 2,3-butanedione (0.20 ml, 2.3 mmol) in methanol (15 ml) and the mixture was heated at reflux for 48 h. The reaction mixture was allowed to cool, quenched with water, extracted with CH_2Cl_2, dried ($MgSO_4$) and concentrated. Most of the excess mesidine was removed by Kugelrohr distillation. Column chromatography (5–10% EtOAc/pet. ether) of the residue produced amino alcohol **96** as a pale brown oil (106 mg, 51%) and a number of mixed fractions containing diamine **94** and diimine **95**.

96 ^{1}H NMR: δ 1.02 (3H, d, J = 6.4, CH_3), 1.32 (3H, d, J = 6.2, CH_3), 2.27 (3H, s, *p*-CH_3), 2.29 (6H, s, *o*-CH_3), 3.03-3.10 (1H, m, CHN), 3.60-3.67 (1H, m, CHO), 6.86 (2H, s, ArH).

94 ^{1}H NMR: δ 1.19 (6H, d, J = 6.3, CH_3), 2.27 (12H, s, *o*-CH_3), 2.29 (6H, s, *p*-CH_3), 3.06 (2H, br s, NH), 3.36-3.42 (2H, m, CH), 6.86 (4H, s, ArH).

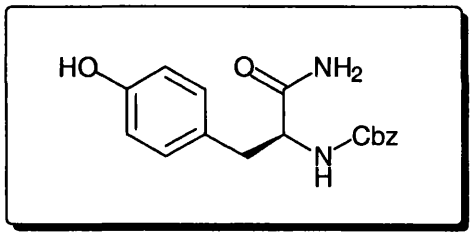
95 ^{1}H NMR: δ 2.01 (12H, s, *o*-CH_3), 2.04 (6H, s, *p*-CH_3), 2.30 (6H, s, CH_3), 6.90 (4H, s, ArH).



Tyrosinamide[95](99)

35% aq. NH_3 solution (15 ml) was added to L-tyrosine methyl ester **98** (1.02 g, 5.23 mmol) and the mixture was stirred at room temperature for 16 h. The solvent was removed to give amide **99** as a white solid (935 mg). The crude product contained ~5% tyrosine but was used without purification.

^{1}H NMR (D_2O): δ 2.75 (1H, dd, J = 13.7, 6.9, CH_AH_B), 2.81 (1H, dd, J = 13.7, 6.7, CH_AH_B), 3.54 (1H, dd, J = 6.8, 6.8, CH), 6.76 (2H, d, J = 8.4, ArH), 7.05 (2H, d, J = 8.4, ArH).

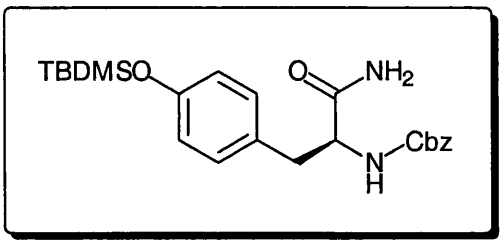


***N*-Benzyloxycarbonyl tyrosinamide (101)**

Benzyl chloroformate (0.58 ml, 4.1 mmol) was added to a suspension of tyrosinamide (731 mg, 4.06 mmol) and sodium bicarbonate (682 mg, 8.11 mmol) in water (21 ml) and THF (7 ml) at 0 °C. The mixture was stirred for 1h then allowed to warm to room temperature and stirred for a further 18 h. Aq. satd. NH_4Cl (5 ml) was added and the reaction mixture was extracted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated to give carbamate **101** as a white solid (1.12 g, 88%) which was used without purification.

^{1}H NMR (d_6-acetone): δ 2.87 (1H, dd, J = 13.9, 9.0, CH_AH_B), 3.10 (1H, dd, J = 13.9, 5.1, CH_AH_B), 4.40-4.45 (1H, m, CH), 4.98 (1H, d, J = 12.7, PhCH_AH_B), 5.05 (1H, d, J = 12.7, PhCH_AH_B), 6.31 (1H, br d, J = 8.0, NHCbz), 6.45 (1H, br s, $CONH_2$), 6.75 (2H, d, J = 8.5, ArH), 6.97 (1H, br s, $CONH_2$), 7.09 (2H, d, J = 8.5, ArH), 7.27-7.35 (5H, m, Cbz), 8.15 (1H, br s, ArOH).

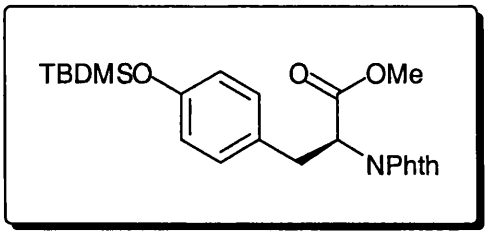
This was consistent with literature data.[114]



N-Benzyloxycarbonyl-O-(*tert*-butyldimethylsilyl) tyrosinamide (102)

Tert-butyldimethylsilyl chloride (584 mg, 3.87 mmol) and imidazole (549 mg, 8.07 mmol) were added to a solution of crude carbamate **101** (1.01 g, 3.23 mmol) in DMF (4 ml). The resulting solution was stirred at room temperature for 3.5 h then diluted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated to give silyl ether **102** as a white solid (1.29 g, 93%). The crude product was used without purification.

^{1}H NMR: δ 0.18 (6H, s, Me_2Si), 0.98 (9H, s, Me_3C), 2.95-3.03 (2H, m, CH_2CH), 4.38-4.42 (1H, m, CH), 5.08 (2H, s, CH_2O), 5.46 (1H, br d, J = 7.4, NHCbz), 5.64 (1H, br s, $CONH_2$), 5.83 (1H, br s, $CONH_2$), 6.77 (2H, d, J = 8.4, ArH), 7.07 (2H, d, J = 8.2, ArH), 7.30-7.38 (5H, m, Cbz).



N-Phthaloyl-O-(*tert*-butyldimethylsilyl)tyrosine methyl ester (103)

N-ethoxycarbonylphthalimide (387 mg, 1.76 mmol) and triethylamine (0.24 ml, 1.8 mmol) were added to a solution of L-tyrosine methyl ester **98** (313 mg, 1.60 mmol) in THF (12 ml). The mixture was stirred at room temperature for 25 h and then the solvent was removed. The residue was dissolved in EtOAc, washed with water and aq. satd. NaCl, dried ($MgSO_4$) and concentrated to give the *N*-phthaloyl compond as a colourless oil. This was dissolved in DMF (5 ml) and *tert*-butyldimethylsilyl chloride (287 mg, 1.90 mmol) and imidazole (270 mg, 3.97 mmol) were added. The resulting solution was stirred at room

temperature for 1.5 h then diluted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (10% EtOAc/pet. ether) to give silyl ether **103** as a colourless oil (522 g, 74% over two steps).

^{1}H NMR: δ 0.09 (6H, s, Me_2Si), 0.91 (9H, s, Me_3C), 3.44-3.55 (2H, m, CH_2CH), 3.79 (3H, s, CH_3O), 5.11 (1H, dd, J = 11.1, 5.7, CH), 6.64 (2H, d, J = 8.4, ArH), 7.00 (2H, d, J = 8.4, ArH), 7.68-7.71 (2H, m, Phth), 7.75-7.79 (2H, m, Phth).

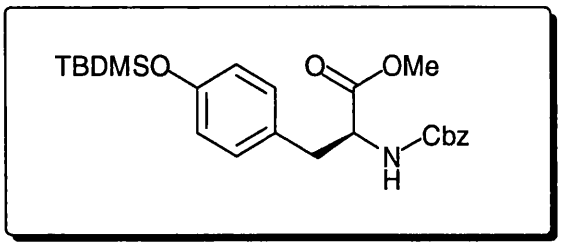
^{13}C NMR: δ –4.6 (Me_2Si), 18.1 (Me_3C), 25.6 (Me_3C), 33.9 (CH_2), 52.8 (CH_3O), 53.3 (CH), 120.2 (aryl CH), 123.4 (Phth CH), 129.3 (Phth C), 129.8 (aryl CH), 131.6 (aryl C), 134.0 (Phth CH), 154.4 (aryl CO), 167.4 (Phth C=O), 169.4 (CO_2CH_3).

Reduction of ester 103

Lithium borohydride (36 mg, 1.7 mmol) was added to a solution of ester **103** (362 mg, 0.82 mmol) in THF (3 ml) and the mixture was stirred at room temperature for 3.5 h. The reaction mixture was quenched with methanol (1 ml) and the solvent was removed. The residue was dissolved in EtOAc, washed with water, dried ($MgSO_4$) and concentrated to give a colourless oil (265 mg). This was identified by NMR as consisting primarily of alcohol **104**.

^{1}H NMR: δ 0.14 (6H, s, Me_2Si), 0.95 (9H, s, Me_3C), 3.05-3.09 (2H, m, CH_2), 3.29 (1H, br s, OH), 3.82-3.88 (2H, m, CH_2OH), 3.96 (1H, br s, OH), 4.52-4.55 (1H, m, CH_2CH), 5.80-5.84 (1H, m, CHOH), 6.72 (2H, d, J = 8.4, ArH), 7.09 (2H, d, J = 8.4, ArH), 7.43-7.56 (3H, m, Phth), 7.67-7.69 (1H, m, Phth).

^{13}C NMR: δ –4.5 (Me_2Si), 18.2 (Me_3C), 25.6 (Me_3C), 33.9 (CH_2), 54.9 (CH_2CH), 63.7 (CH_2OH), 80.7 (CHOH), 120.2 (aryl CH), 123.1 (Phth CH), 123.4 (Phth CH), 129.7 (Phth CH), 129.9 (aryl CH), 130.3 (Phth C), 131.1 (aryl C), 132.4 (Phth CH), 143.6 (Phth C), 154.3 (aryl CO), 168.3 (C=O).



_N_-Benzyloxycarbonyl-_O_-(_tert_-butyldimethylsilyl)tyrosine methyl ester[115] (108)

Sodium bicarbonate (4.57 g, 54.4 mmol) was added to a solution of L-tyrosine methyl ester hydrochloride **106** (4.20 g, 18.1 mmol) in water (80 ml) and THF (20 ml). The mixture was stirred and cooled to 0 °C. Benzyl chloroformate (2.6 ml, 18.1 mmol) was added and the mixture was allowed to warm to room temperature and stirred for 1.5 h. The reaction mixture was diluted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated to give carbamate **107** as a colourless oil. This was dissolved in DMF (20 ml) and *tert*-butyldimethylsilyl chloride (3.28 g, 21.8 mmol) and imidazole (3.09 g, 45.3 mmol) were added. The resulting solution was stirred at room temperature for 1 h then diluted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (20% EtOAc/pet. ether) to give silyl ether **108** as a colourless oil (7.09 g, 88% over two steps).

^{1}H NMR: δ 0.21 (6H, s, Me_2Si), 1.01 (9H, s, Me_3C), 3.00-3.07 (2H, m, CH_2CH), 3.71 (3H, s, CH_3O), 4.61-4.67 (1H, m, CH), 5.08-5.15 (2H, m, CH_2O), 5.32 (1H, br d, J = 8.2, NH), 6.77 (2H, d, J = 8.4, ArH), 6.98 (2H, d, J = 8.4, ArH), 7.31-7.40 (5H, m, Cbz).

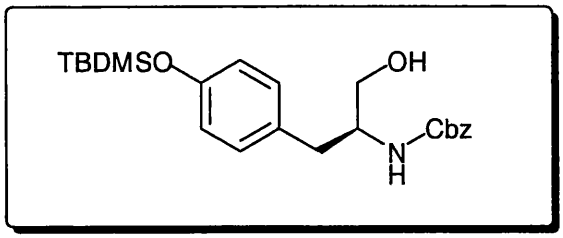
^{13}C NMR: δ –4.5 (Me_2Si), 18.1 (Me_3C), 25.6 (Me_3C), 37.4 (CH_2CH), 52.1 (CH_3O), 54.9 (CH), 66.8 (CH_2O), 120.1 (aryl CH), 128.0 (Cbz CH), 128.0 (Cbz CH), 128.2 (Cbz C), 128.4 (Cbz CH), 130.1 (aryl CH), 136.2 (aryl C), 154.7 (aryl CO), 155.5 (NHC=O), 172.0 (CH_3OC=O).

IR (neat): 3344 br, 2954 s, 2931 s, 2858 s, 1727 s, 1608 m, 1511 s, 1261 s, 1213 s, 1058 m, 916 s, 841 s, 782 s.

MS (EI): *m/z* 433 (M^+, 3%), 335 (M^+ – BnOH, 3), 292 (M^+ – $CbzNH_2$, 8), 278 (5), 221 (TBDMSO-C_6H_4-CH_2^+, 100).

HRMS (EI): Calculated for $C_{24}H_{33}NO_5Si$: 443.2128. Found: 443.2128.

$[\alpha]^{22}_D$ +44° (c = 1.4, $CHCl_3$)



_N_-Benzyloxycarbonyl-_O_-(_tert_-butyldimethylsilyl)tyrosinol (105)

Lithium borohydride (675 mg, 31.0 mmol) was added to a solution of ester **108** (6.87 g, 15.5 mmol) in THF (40 ml) and the mixture was stirred at room temperature for 50 min and then quenched with water (5 ml). The solvent was removed and the residue was dissolved in EtOAc, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (50% EtOAc/pet. ether) to give alcohol **105** as a colourless oil (5.82 g, 90%).

^{1}H NMR: δ 0.21 (6H, s, Me_2Si), 1.00 (9H, s, Me_3C), 2.77-2.81 (2H, m, CH_2CHCH_2OH), 2.87 (1H, br, OH), 3.54-3.56 (1H, m, CH_AH_BOH), 3.61-3.63 (1H, m, CH_AH_BOH), 3.88-3.91 (1H, m, CH), 5.08 (2H, s, $PhCH_2O$), 5.21 (1H, br, NH), 6.78 (2H, d, J = 8.2, ArH), 7.06 (2H, d, J = 8.2, ArH), 7.30-7.38 (5H, m, Cbz).

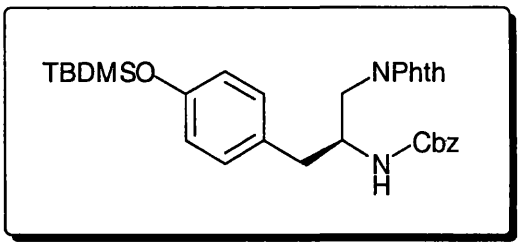
^{13}C NMR: δ –4.5 (Me_2Si), 18.1 (Me_3C), 25.6 (Me_3C), 36.4 (CH_2CHCH_2OH), 54.1 (CH), 63.7 (CH_2OH), 66.7 ($PhCH_2O$), 120.0 (aryl CH), 127.9 (Cbz CH), 128.0 (Cbz CH), 128.4 (Cbz C), 128.4 (Cbz CH), 130.1 (aryl CH), 136.3 (aryl C), 154.2 (aryl CO), 156.5 (NHC=O).

IR (neat): 3400 br, 2930 s, 2858 s, 1697 s, 1609 m, 1511 s, 1256 s, 1059 s, 919 s, 840 s, 780 s, 697 m.

MS (EI): *m/z* 415 (M^+, 10%), 264 (M^+ – $CbzNH_2$, 49), 250 (73), 221 (TBDMSO-C_6H_4-CH_2^+, 91).

HRMS (EI): Calculated for $C_{23}H_{33}NO_4Si$: 415.2179 Found: 415.2178.

$[\alpha]^{22}_D$ –22° (c = 1.3, $CHCl_3$)



3-[4-(*tert*-Butyldimethylsiloxy)phenyl]-N^1-phthaloyl-N^2-benzyloxycarbonyl-propane-1,2-diamine (109)

Phthalimide (3.02 g, 20.5 mmol) and triphenylphosphine (10.8 g, 41.0 mmol) were added to a solution of alcohol **105** (5.68 g, 13.7 mmol) in THF (90 ml). The resulting solution was cooled to 0 °C and diethyl azodicarboxylate (5.4 ml, 34.2 mmol) was added dropwise over 10 min. The mixture was then allowed to warm to room temperature and stirred for 4.5 h. The solvent was removed and the crude product was purified by column chromatography (30% EtOAc/pet. ether) to give **109** as a colourless gel (6.92 g, 93%).

^{1}H NMR: δ 0.21 (6H, s, Me_2Si), 1.00 (9H, s, Me_3C), 2.85 (2H, d, J = 6.5, CH_2CHCH_2N), 3.69-3.82 (2H, m, CH_2N), 4.27-4.31 (1H, m, CH), 4.90-4.98 (2H, m, CH_2O), 5.04 (1H, br d, J = 8.8, NH), 6.78 (2H, d, J = 8.3, ArH), 7.09 (2H, d, J = 8.3, ArH), 7.21-7.31 (5H, m, Cbz), 7.68-7.72 (2H, m, Phth), 7.80-7.84 (2H, m, Phth).

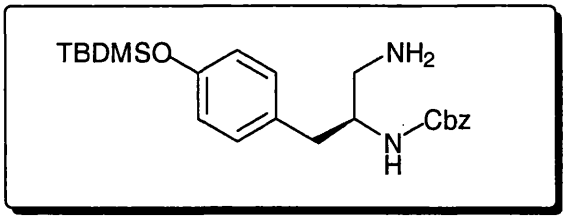
^{13}C NMR: δ –4.5 (Me_2Si), 18.1 (Me_3C), 25.6 (Me_3C), 38.2 (CH_2CHCH_2N), 41.3 (CH_2N), 51.5 (CH), 66.3 (CH_2O), 120.1 (aryl CH), 123.3 (Phth CH), 127.7 (Cbz CH), 127.8 (Cbz C), 128.3 (Cbz CH), 129.2 (Cbz CH), 130.2 (aryl CH), 131.8 (Phth C), 133.9 (Phth CH), 136.5 (aryl C), 154.4 (aryl CO), 155.9 (NHC=O), 168.4 (Phth C=O).

IR (neat): 3357 br, 3062 m, 3033 m, 2955 s, 2857 s, 1773 s, 1717 s, 1609 s, 1508 s, 1397 s, 1264 s, 1039 s, 921 s, 844 s, 780 s, 723 m.

MS (CI, NH_3): *m/z* 562 $(M + NH_4)^+$, 21%), 545 (6), 501 (8), 454 [$(M + NH_4)^+$ – BnOH, 100), 437 (28).

HRMS (EI): Calculated for $C_{31}H_{36}N_2O_5Si$: 544.2394 Found: 544.2393.

$[\alpha]^{22}_D$ +39° (c = 1.3, $CHCl_3$)



3-[4-(*tert*-Butyldimethylsiloxy)phenyl]-N^2-benzyloxycarbonyl-propane-1,2-diamine (110)

Hydrazine monohydrate (3.0 ml, 62.7 mmol) was added to a solution of phthalimidocarbamate **109** (6.83 g, 12.5 mmol) in ethanol (100 ml). The mixture was refluxed for 1 h then allowed to cool and filtered. The solids were washed well with Et_2O and the filtrate was washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (20:2:1 EtOAc/MeOH/aq. NH_3) to give aminocarbamate **110** as a pale orange oil (4.48 g, 86%).

^{1}H NMR: δ 0.20 (6H, s, Me_2Si), 0.99 (9H, s, Me_3C), 1.33 (2H, br, NH_2), 2.60-2.79 (4H, m, CH_2CHCH_2), 3.80-3.84 (1H, m, CH), 5.08 (2H, s, CH_2O), 5.10 (1H, br, NH), 6.76 (2H, d, J = 8.4, ArH), 7.03 (2H, d, J = 8.4, ArH), 7.29-7.38 (5H, m, Cbz).

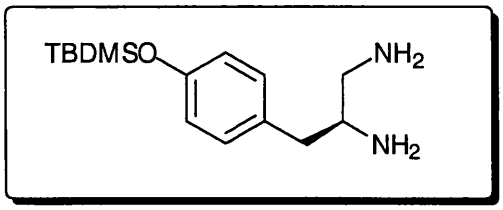
^{13}C NMR: δ –4.5 (Me_2Si), 18.1 (Me_3C), 25.6 (Me_3C), 37.8 (CH_2CHCH_2N), 44.4 (CH_2N), 54.5 (CH), 66.5 (CH_2O), 120.0 (aryl CH), 127.9 (Cbz CH), 128.0 (Cbz CH), 128.4 (Cbz CH), 130.1 (aryl CH), 130.3 (Cbz C), 136.5 (aryl C), 154.2 (aryl CO), 156.2 (NHC=O).

IR (neat): 3313 br, 3061 w, 3032 w, 2930 s, 2858 s, 1701 s, 1608 s, 1510 s, 1471 m, 1259 s, 1028 m, 917 s, 840 s, 780 s, 697 m.

MS (CI, *i*-butane): *m/z* 415 $(M + H)^+$, 15%), 347 (11), 307 [$(M + H)^+$ – BnOH, 100), 263 (37), 222 (73).

HRMS (CI, *i*-butane): Calculated for $C_{23}H_{35}N_2O_3Si$, $(M + H)^+$: 415.2417 Found: 415.2414.

$[\alpha]^{24}_D$ –5.7° (c = 2.1, $CHCl_3$)



3-[4-(*tert*-Butyldimethylsiloxy)phenyl]-propane-1,2-diamine (111)

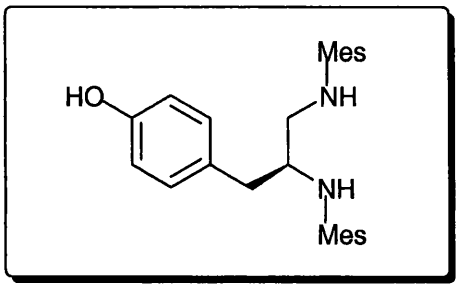
10% Palladium on carbon (270 mg) was added to a solution of aminocarbamate **110** (1.34 g, 3.23 mmol) in methanol (20 ml). Hydrogen was bubbled through the mixture for 1 h and then the mixture was stirred for a further 16 h at room temperature under 1 atm of hydrogen. The reaction mixture was filtered through celite, washing well with methanol, and concentrated to give diamine **111** as a pale yellow oil (851 mg, 94%). The product was used promptly without purification as storage or chromatography resulted in decomposition.

^{1}H NMR: δ 0.16 (6H, s, Me_2Si), 0.96 (9H, s, Me_3C), 2.45-2.50, 2.55-2.60, 2.67-2.72, 2.82-2.87 (all 1H, m, CH_2CHCH_2), 2.99-3.04 (1H, m, CH), 3.20 (4H, br, 2 × NH_2), 6.74 (2H, d, J = 8.4, ArH), 7.02 (2H, d, J = 8.4, ArH).

^{13}C NMR: δ –4.5 (Me_2Si), 18.1 (Me_3C), 25.6 (Me_3C), 40.9 (CH_2CHCH_2N), 46.5 (CH_2N), 53.9 (CH), 120.0 (aryl CH), 130.1 (aryl CH), 130.9 (aryl C), 154.1 (aryl CO).

MS (CI, *i*-butane): *m/z* 281 [$(M + H)^+$, 44%], 250 (44), 222 (14).

HRMS (CI, *i*-butane): Calculated for $C_{15}H_{29}N_2OSi$, $(M + H)^+$: 281.2049 Found: 281.2046.



3-(4-Hydroxyphenyl)-N^1,N^2-bismesityl-propane-1,2-diamine (97)

To diamine **111** (1.63 g, 5.81 mmol) was added mesityl bromide (1.78 ml, 11.6 mmol), sodium *tert*-butoxide (2.79 g, 29.1 mmol), (±)-BINAP (271 mg, 0.44 mmol, 7.5 mol %),

$Pd_2(dba)_3$ (133 mg, 0.15 mmol, 5 mol % Pd) and dioxane (60 ml). The mixture was refluxed for 7 days and then allowed to cool. The solvent was removed and the crude product was purified by column chromatography (20% EtOAc/pet. ether) to give **97** as an off-white solid (1.58 g, 68%). Recrystallisation from methanol gave colourless prisms: m.p. 161-163 °C.

^{1}H NMR: δ 2.14 (6H, s, *o*-CH_3), 2.23 (3H, s, *p*-CH_3), 2.27 (3H, s, *p*-CH_3), 2.29 (6H, s, *o*-CH_3), 2.46 (1H, dd, J = 13.4, 9.6 , CH_AH$_B$CHCH$_2$N), 2.76 (1H, dd, J = 12.1, 7.5 , CH_AH$_B$N), 2.85 (1H, dd, J = 13.4, 4.1 , CH$_A$$H_B$CHCH$_2$N), 3.20 (1H, dd, J = 12.1, 4.0 , CH$_A$$H_B$N), 3.64-3.72 (1H, m, CH), 6.67 (2H, d, J = 8.4 , ArH), 6.80 (2H, s, MesH), 6.87 (2H, s, MesH), 6.94 (2H, d, J = 8.4 , ArH).

^{13}C NMR: δ 18.4 (*o*-CH_3), 19.2 (*o*-CH_3), 20.5 (2 × *p*-CH_3), 39.1 (*C*H$_2$CHCH$_2$N), 52.2 (CH_2N), 59.0 (CH), 115.3 (aryl CH), 129.1 (Mes C), 129.4 (Mes C), 129.5 (Mes CH), 129.8 (Mes CH), 130.1 (aryl CH), 130.6 (aryl C), 131.0 (Mes C), 131.2 (Mes C), 141.3 (Mes CN), 143.3 (Mes CN), 154.1 (aryl CO).

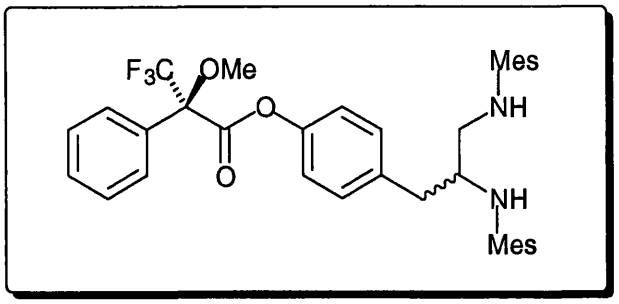
IR: 3339 w, 3302 m, 2960 br, 1610 m, 1588 m, 1513 s, 1482 s, 1441 s, 1379 m, 1351 m, 1218 s, 1014 m, 1052 s, 827 m, 740 m, 697 m.

MS (EI): m/z 402 (M^+, 2%), 295 [M^+ – (HO-C_6H_4-CH_2), 5], 254 (M^+ – MesNHCH$_2$, 100).

HRMS (EI): Calculated for $C_{27}H_{34}N_2O$: 402.2671 Found: 402.2672.

Microanalysis: Calculated for $C_{27}H_{34}N_2O$: C, 80.55; H, 8.51; N, 6.96. Found: C, 80.39; H, 8.53; N, 6.94.

$[\alpha]^{24}_D$ –7.6° (c = 1.0, CH_2Cl_2)



Preparation of Mosher's esters

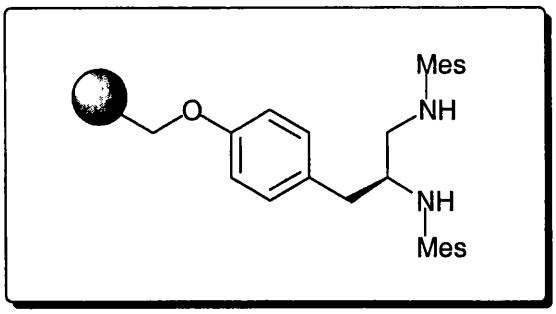
Dicyclohexylcarbodiimide (29 mg, 0.14 mmol) and 4-(dimethylamino)pyridine (2.4 mg, 0.020 mmol) were added to a solution of racemic phenol **97** (40 mg, 0.10 mmol) and (R)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (35 mg, 0.15 mmol). The mixture was stirred at room temperature for 19 h and then passed through a short plug of silica eluting with 20% EtOAc/pet. ether. The crude product was purified by column chromatography (10% EtOAc/pet.ether) to give a mixture of diastereomeric esters **115** and **116** (59 mg, 96%).

Enantiopure phenol **97** treated in the same way gave only ester **115**.

^{19}F NMR: **115** δ –71.88 (s, CF_3), **116** δ –71.90 (s, CF_3).

^{1}H NMR: δ 2.17 (6H, s, *o*-CH_3), 2.25 (3H, s, *p*-CH_3), 2.30 (3H, s, *p*-CH_3), 2.32 (6H, s, *o*-CH_3), 2.63 (1H, dd, J = 13.4, 9.2, $CH_AH_BCHCH_2N$), 2.84 (1H, dd, J = 12.1, 7.3, CH_AH_BN), 2.92 (1H, dd, J = 13.4, 4.5, $CH_AH_BCHCH_2N$), 3.18 (1H, dd, J = 12.1, 4.0, CH_AH_BN), 3.36 (2H, br s, NH), 3.70-3.75 (1H, m, CH), 3.75 (3H, s, CH_3O), 6.82 (2H, s, MesH), 6.89 (2H, s, MesH), 7.07 (2H, d, J = 8.5, ArH), 7.17 (2H, d, J = 8.5, ArH), 7.49-7.52 (3H, m, ArH), 7.70-7.72 (2H, m, ArH).

^{13}C NMR: δ 18.3 (*o*-CH_3), 19.2 (*o*-CH_3), 20.5 (*p*-CH_3), 39.5 (CH_2CHCH_2N), 52.2 (CH_2N), 55.7 (CH_3O), 59.1 (CH), 84.9 (q, CF_3), 120.9 (aryl CH), 121.2, 124.7, 127.2 (aryl CH), 128.6 (aryl CH), 129.1, 129.4 (Mes CH), 129.8 (Mes CH), 130.2 (aryl CH), 131.1 (Mes C), 131.1 (Mes C), 132.0, 137.5, 141.2 (Mes CN), 143.4 (Mes CN), 148.3 (aryl CO), 165.1 (C=O).

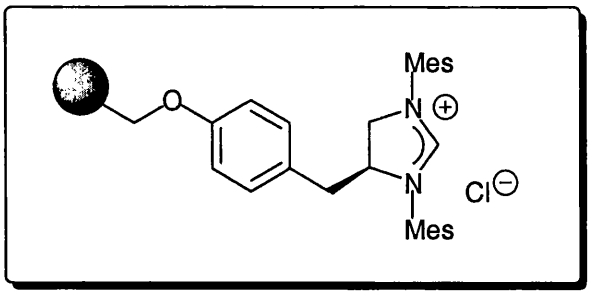


Immobilised bis-mesityl diamine (117)

DMF (15 ml) was added to diamine **97** (1.22 g, 3.03 mmol) and potassium *tert*-butoxide (340 mg, 3.03 mmol) and the mixture was stirred at room temperature for 10 min. The solution was then transferred by syringe to a cartridge containing Merrifield resin (1.68 g, 0.9 mmol/g, 1.52 mmol), tetrabutylammonium iodide (560 mg, 1.52 mmol) and DMF (5 ml). The mixture was then shaken at room temperature for 22 h. The resin was collected by filtration, washed (DMF, MeOH, THF, THF/H_2O (1:1), H_2O, THF/H_2O (1:1), THF, MeOH, CH_2Cl_2, pentane) and dried to give **117** as an off-white resin (2.23 g).

IR: 3372 br, 2919 br, 1602 m, 1509 s, 1483 s, 1451 s, 1228 s, 1016 m, 853 m, 820 m, 758 m, 698 s.

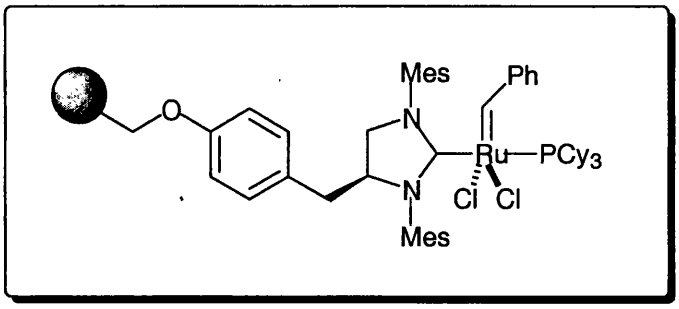
Excess diamine **97** was recovered from the filtrate and DMF washings. These were quenched with satd. aq. NH_4Cl, diluted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated to give **97** as an off-white solid.



Polymer-bound imidazolinium salt (119)

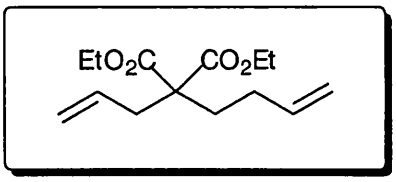
Polymer **117** (2.06 g) was suspended in toluene (40 ml), trimethyl orthoformate (10 ml), and formic acid (0.5 ml) and heated to 100 °C for 66 h. The mixture was allowed to cool and the resin was collected by filtration, washed (PhMe, CH_2Cl_2, MeOH, THF, THF/0.1M HCl (1:1), THF, MeOH, CH_2Cl_2, MeOH, CH_2Cl_2, pentane) and dried to give **119** as an off-white resin (1.84 g).

IR: 3649 w, 3389 br, 2920 s, 1622 s, 1511 s, 1451 s, 1251 m, 1016 m, 699 s.



Polymer-bound catalyst (121)

Polymer **119** (800 mg) was suspended in THF (5 ml) and potassium *tert*-butoxide (1M in THF, 15 ml) was added. The mixture was stirred for 60 min. The solvent was then removed carefully by syringe and fresh THF (15 ml) was added. The mixture was stirred, the resin was left to settle, and then the solvent was again removed carefully by syringe. This washing was repeated five times. Then Grubbs's catalyst (263 mg, 0.32 mmol) and toluene (4 ml) were added to the resin and the mixture was heated to 70 °C for 1 h. After allowing to cool, the resin was collected by filtration, washed (PhMe, CH_2Cl_2, MeOH, CH_2Cl_2, MeOH, CH_2Cl_2, pentane) and dried to give polymer-bound catalyst **121** as a brown resin (682 mg).

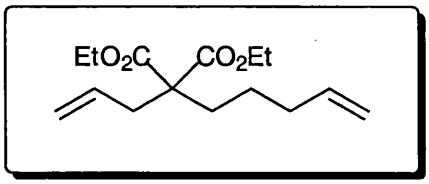


4,4-Di(ethoxycarbonyl)-1,7-octadiene (124)

Diethyl allylmalonate (0.39 ml, 2.0 mmol) was added to a solution of sodium *tert*-butoxide (288 mg, 3.0 mmol) in DMF (3 ml). The mixture was stirred at room temperature for 15 min and then 4-bromo-1-butene (0.22 ml, 2.2 mmol) was added and the mixture stirred for a further 17 h. The reaction mixture was quenched with water, diluted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (5% EtOAc/hexane) to give diene **124** as a colourless oil (250 mg, 49%).

^{1}H NMR: δ 1.26 (6H, t, J = 7.1, CH_3), 1.94-2.04 (4H, m, CH_2CH_2) 2.67 (2H, d, J = 7.4, $CH_2CH{=}CH_2$), 4.19 (4H, q, J = 7.1, CH_3CH_2), 4.96-5.14 (4H, m, $CH_2{=}CH$), 5.61-5.83 (2H, m, $CH_2{=}CH$).

This was consistent with literature data.[116]

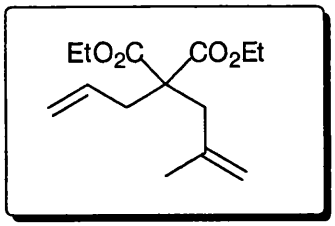


4,4-Di(ethoxycarbonyl)-1,8-nonadiene (125)

Diethyl allylmalonate (0.39 ml, 2.0 mmol) was added to a solution of sodium *tert*-butoxide (288 mg, 3.0 mmol) in DMF (3 ml). The mixture was stirred at room temperature for 15 min and then 5-bromo-1-pentene (0.28 ml, 2.4 mmol) was added and the mixture stirred for a further 68 h. The reaction mixture was quenched with water, diluted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (5% EtOAc/pet. ether) to give diene **125** as a colourless oil (354 mg, 66%).

^{1}H NMR: δ 1.25 (6H, t, J = 7.1, CH_3), 1.25-1.34 (2H, m, CH_2), 1.86-1.90 (2H, m, CH_2), 2.03-2.09 (2H, m, CH_2), 2.65 (2H, d, J = 7.4, $CH_2CH{=}CH_2$), 4.19 (4H, q, J = 7.1, CH_3CH_2), 4.95-5.13 (4H, m, $CH_2{=}CH$), 5.60-5.83 (2H, m, $CH_2{=}CH$).

This was consistent with literature data.[39]

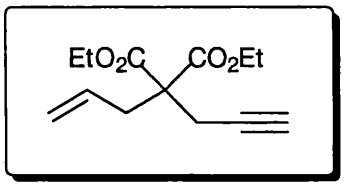


4,4-Di(ethoxycarbonyl)-2-methyl-1,6-heptadiene (128)

Diethyl allylmalonate (0.39 ml, 2.0 mmol) was added to a solution of sodium *tert*-butoxide (288 mg, 3.0 mmol) in DMF (3 ml). The mixture was stirred at room temperature for 20 min and then methallyl bromide (0.25 ml, 2.4 mmol) was added and the mixture stirred for a further 68 h. The reaction mixture was quenched with water, extracted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (5% EtOAc/pet. ether) to give diene **128** as a colourless oil (255 mg, 51%).

^{1}H NMR: δ 1.26 (6H, t, J = 7.1, CH_3CH_2), 1.68 (3H, s, CH_3C=C), 2.67-2.72 (4H, m, CH_2CCH_2), 4.12-4.24 (4H, m, CH_3CH_2), 4.77 (1H, s, C=CH_AH$_B$), 4.88 (1H, s, C=CH$_A$$H_B$) 5.08-5.12 (2H, m, CH_2=CH), 5.65-5.75 (1H, m, CH_2=CH).

This was consistent with literature data.[13]



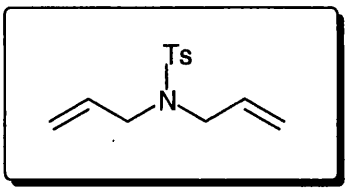
Diethyl 2-allyl-2-propargylmalonate (129)

Diethyl allylmalonate (0.39 ml, 2.0 mmol) was added to a solution of sodium *tert*-butoxide (288 mg, 3.0 mmol) in DMF (3 ml). The mixture was stirred at room temperature for 15 min and then propargyl bromide (80 wt% in toluene, 0.27 ml, 2.4 mmol) was added and the mixture stirred for a further 67 h. The reaction mixture was quenched with water, extracted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was

purified by column chromatography (5% EtOAc/pet. ether) to give enyne **129** as a colourless oil (312 mg, 65%).

^{1}H NMR: δ 1.26 (6H, t, J = 7.1, CH_3), 2.02 (1H, t, J = 2.7, C≡CH), 2.79-2.84 (4H, m, CH_2CCH_2), 4.22 (4H, q, J = 7.1, CH_2O), 5.13-5.22 (2H, m, CH=CH_2), 5.59-5.69 (1H, m, CH=CH_2).

This was consistent with literature data.[117]

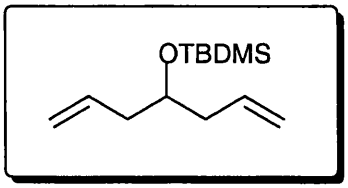


***N*-Tosyl diallylamine (130)**

Sodium *tert*-butoxide (1.39 g, 14.5 mmol) was added to a solution of *p*-toluenesulfonamide (989 mg, 5.78 mmol) in DMF (12 ml) and the mixture was stirred at room temperature for 10 min. Allyl bromide (1.10 ml, 12.7 mmol) was then added dropwise over 15 min and the mixture was stirred at room temperature for 18 h. The reaction mixture was quenched with water, extracted with EtOAc, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (10% EtOAc/pet. ether) to give diene **130** as a colourless oil (503 mg, 35%).

^{1}H NMR: δ 2.44 (3H, s, CH_3), 3.81 (4H, d, J = 6.1, CH_2NCH_2), 5.15 (4H, dd, J = 13.6, 1.1, CH=CH_2), 5.57-5.67 (2H, m, CH=CH_2), 7.30 (2H, d, J = 7.9, ArH), 7.71 (2H, d, J = 8.1, ArH).

This was consistent with literature data.[55]

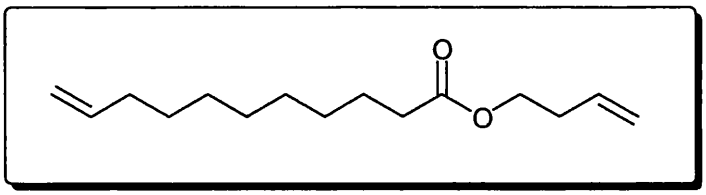


4-(*tert*-Butyldimethylsiloxy)-1,6-heptadiene (131)

Imidazole (655 mg, 9.63 mmol) and *tert*-butyldimethylsilyl chloride (697 mg, 4.62 mmol) were added to a solution of 1,6-heptadien-4-ol (0.50 ml, 3.9 mmol) in DMF (2 ml) and the mixture was stirred at room temperature for 24 h. The reaction mixture was then diluted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (pentane) to give silyl ether **131** as a colourless oil (556 mg, 64%).

^{1}H NMR: δ 0.06 (6H, s, Me_2Si), 0.90 (9H, s, Me_3C), 2.16-2.28 (4H, m, CH_2CCH_2), 3.71-3.78 (1H, m, CHO), 5.03-5.07 (4H, m, $CH{=}CH_2$), 5.77-5.88 (2H, m, $CH{=}CH_2$).

This was consistent with literature data.[118]

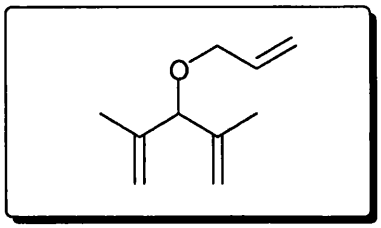


3-Butenyl 10-undecenoate (132)

10-Undecenoyl chloride (0.80 ml, 3.7 mmol) was added to a solution of 3-buten-1-ol (0.34 ml, 4.0 mmol) in dichloromethane (8 ml) and pyridine (2 ml) at 0 °C. The mixture was stirred for 5 min then allowed to warm to room temperature and stirred for a further 18 h. The reaction mixture was passed through a short plug of silica eluting with 5% EtOAc/pet. ether and concentrated. The residue was twice dissolved in hexane and concentrated to remove remaining pyridine and give ester **132** as a colourless oil (874 mg, 98%).

^{1}H NMR: δ 1.25-1.43 (10H, m, CH_2), 1.54-1.67 (2H, m, CH_2), 2.02-2.07 (2H, m, $CH_2CH{=}CH_2$), 2.30 (2H, t, J = 7.5, $CH_2C{=}O$), 2.37-2.42 (2H, m, $CH_2CH{=}CH_2$), 4.13 (2H, t, J = 6.7, CH_2O), 4.92-5.14 (4H, m, $CH{=}CH_2$), 5.75-5.87 (2H, m, $CH{=}CH_2$).

This was consistent with literature data.[105]

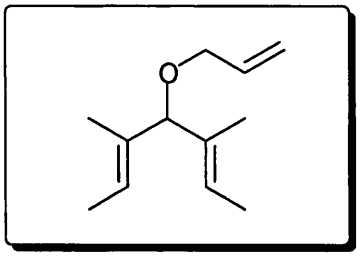


3-Allyl-(2,4-dimethyl-1,4-pentadienyl) ether (134)

Isopropenylmagnesium bromide (0.5M solution in THF, 30 ml, 15 mmol) was added over 10 min to a solution of methacrolein (1.03 ml, 12.5 mmol) in THF (5 ml) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 3 h. The reaction mixture was then quenched with water, extracted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated to give alcohol **133**. The crude alcohol was dissolved in THF (20 ml) and sodium hydride (600 mg, 25.0 mmol) was added. The mixture was stirred at room temperature for 15 min then allyl bromide (2.7 ml, 31 mmol) was added and the mixture was refluxed for 19 h. The reaction mixture was then allowed to cool, quenched with water, extracted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (pentane) to give triene **134** as a colourless oil (236 mg, 12% over 2 steps).

^{1}H NMR: δ 1.63 (6H, s, CH_3), 3.93 (2H, d, J = 5.3, CH_2O), 4.08 (1H, s, CHO), 4.97 (2H, s, CH_AH_B=C), 5.07 (2H, s, CH_AH_B=C), 5.16 (1H, dd, J = 10.4, 1.4, CH_AH_B=CH), 5.30 (1H, dd, J = 17.2, 1.6, CH_AH_B=CH), 5.89-5.98 (1H, m, CH_2=C*H*).

This was consistent with literature data.[106]



4-Allyl-(3,5-dimethyl-(2*E*,5*E*)-heptadienyl) ether (135)

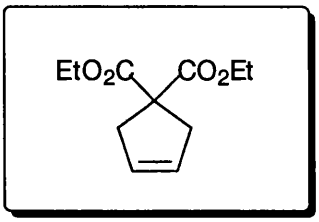
Isobutylmagnesium bromide (2.0M solution in Et_2O, 10.8 ml, 21.6 mmol) was added to a solution of 2-butyne (1.41 ml, 18.0 mmol) in diethyl ether (5 ml). Titanocene dichloride (134 mg, 0.54 mmol) was added and the mixture was stirred for 1 h and then cooled to 0

°C. A solution of *trans*-2-methyl-2-butenal (1.56 ml, 16.2 mmol) in THF (15 ml) was then added over 10 min. The mixture was allowed to warm to room temperature, stirred for 2.5 h, then quenched with water. 2 M HCl was added to dissolve the gel precipitate and then the mixture was extracted with Et_2O, washed with satd. aq. $NaHCO_3$ and water, dried ($MgSO_4$) and concentrated to give alcohol **136**. The crude alcohol was dissolved in THF (30 ml) and sodium hydride (578 mg, 24.1 mmol) was added. The mixture was stirred at room temperature for 15 min then allyl bromide (2.6 ml, 30 mmol) was added and the mixture was refluxed for 16 h. TLC indicated that there was still alcohol present so further sodium hydride (289 mg, 12.0 mmol) and allyl bromide (1.0 ml, 12.0 mmol) were added and the mixture was refluxed for a further 20 h. The reaction mixture was then allowed to cool, quenched with water, extracted with Et_2O, washed with water, dried ($MgSO_4$) and concentrated. The crude product was purified by column chromatography (pentane) to give triene **135** as a colourless oil (533 mg, 18% over 2 steps).

^{1}H NMR: δ 1.48 (6H, d, J = 1.0, CH_3), 1.65 (6H, dd, J = 6.7, 0.9, CH_3), 3.86 (2H, d, J = 5.4, CH_2O), 3.95 (1H, s, CHO), 5.14 (1H, d, J = 10.4, CH_AH_B=CH), 5.27 (1H, d, J = 17.2, CH_AH_B=CH), 5.54-5.59 (2H, m, CH_3CH=C), 5.88-5.98 (1H, m, CH_2=C*H*).

^{13}C NMR: δ 12.1 (CH_3), 13.1 (CH_3), 68.6 (CH_2O), 88.2 (CHO), 116.0 (CH_2=CH), 121.0 (CH_3CH=C), 134.1 (CH_3CH=*C*), 135.4 (CH_2=*C*H).

This was consistent with literature data.[106]



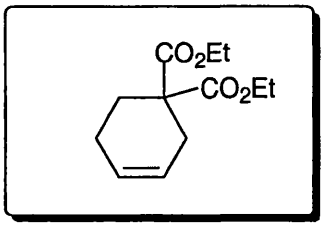
RCM of diethyl diallylmalonate

Dichloromethane (1 ml) was added to diethyl diallylmalonate **138** (20 µl, 0.083 mmol) and resin catalyst **121** (45 mg, 0.0045 mmol, 5 mol %). The mixture was refluxed for 25 h then

allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 100% conversion to cyclopentene **122**.

^{1}H NMR: δ 1.25 (6H, t, J = 7.1, CH_3), 2.97-3.06 (4H, m, CH_2CCH_2), 4.20 (4H, q, J = 7.1, CH_2O), 5.58-5.63 (2H, m, CH=CH).

This was consistent with literature data.[118]

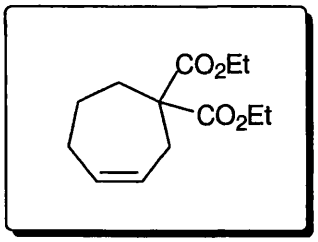


RCM of 4,4-di(ethoxycarbonyl)-1,7-octadiene

Dichloromethane (0.8 ml) was added to diene **124** (22 mg, 0.087 mmol) and resin catalyst **121** (43 mg, 0.0043 mmol, 5 mol %). The mixture was refluxed for 18 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 90% conversion to cyclohexene **126**.

^{1}H NMR: δ 1.24 (6H, t, J = 7.1, CH_3), 2.04-2.17 (4H, m, CH_2CH_2), 2.52-2.58 (2H, m, CH_2CH=CH), 4.19 (4H, q, J = 7.1, CH_2O), 5.64-5.70 (2H, m, CH=CH).

This was consistent with literature data.[119]

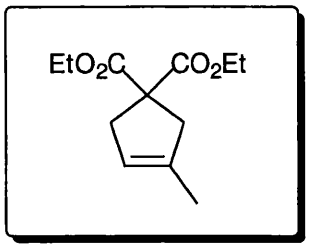


RCM of 4,4-di(ethoxycarbonyl)-1,8-nonadiene

Dichloromethane (1 ml) was added to diene **125** (10 mg, 0.037 mmol) and resin catalyst **121** (37 mg, 0.0037 mmol, 10 mol %). The mixture was refluxed for 19 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 92% conversion to cycloheptene **127**.

^{1}H NMR : δ 1.24 (6H, t, J = 7.1, CH_3), 1.62-1.68 (2H, m, CH_2), 2.14-2.18 (2H, m, CH_2), 2.22-2.25 (2H, m, CH_2), 2.67 (2H, d, J = 6.4, CH_2CH=CH), 4.17 (4H, q, J = 7.1, CH_2O), 5.66-5.71 (1H, m, CH=CH), 5.82-5.88 (1H, m, CH=CH).

This was consistent with literature data.[39]

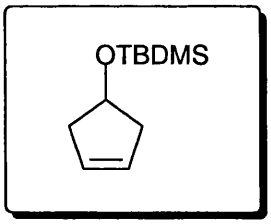


RCM of 4,4-di(ethoxycarbonyl)-2-methyl-1,6-heptadiene

Dichloromethane (1 ml) was added to diene **128** (10 mg, 0.039 mmol) and resin catalyst **121** (39 mg, 0.0039 mmol, 10 mol %). The mixture was refluxed for 19 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 91% conversion to cyclopentene **139**.

^{1}H NMR: δ 1.25 (6H, t, J = 7.1, CH_3CH_2), 1.71 (3H, s, CH_3C=C), 2.91-2.98 (4H, m, CH_2CCH_2), 4.20 (4H, q, J = 7.1, CH_2O), 5.18-5.20 (1H, m, C=CH).

This was consistent with literature data.[120]

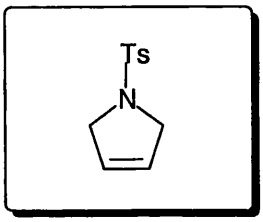


RCM of 4-(*tert*-butyldimethylsiloxy)-1,6-heptadiene

Dichloromethane (1 ml) was added to diene **131** (10 mg, 0.044 mmol) and resin catalyst **121** (44 mg, 0.0044 mmol, 10 mol %). The mixture was refluxed for 19 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 100% conversion to cyclopentene **141**.

^{1}H NMR: δ 0.07 (6H, s, Me_2Si), 0.90 (9H, s, Me_3C), 2.25-2.31 (2H, m, CH_AH$_B$C=C), 2.54-2.61 (2H, m, CH$_A$$H_B$C=C), 4.49-4.59 (1H, m, CHO), 5.67 (2H, s, C*H*=C*H*).

This was consistent with literature data.[118]

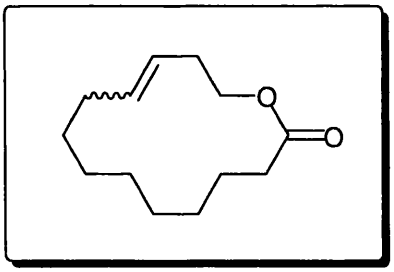


RCM of *N*-tosyl diallylamine

Dichloromethane (1 ml) was added to diene **130** (10 mg, 0.040 mmol) and resin catalyst **121** (40 mg, 0.0040 mmol, 10 mol %). The mixture was refluxed for 19 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 95% conversion to pyrroline **140**.

^{1}H NMR: δ 2.43 (3H, s, CH_3), 4.10-4.18 (4H, m, CH_2NCH_2), 5.58-5.68 (2H, m, C*H*=C*H*), 7.32 (2H, d, J = 8.2, ArH), 7.72 (2H, d, J = 8.2, ArH).

This was consistent with literature data.[21]



RCM of 3-butenyl 10-undecenoate

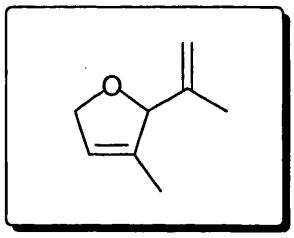
Resin catalyst **121** (67 mg, 0.0067 mmol, 10 mol %) was added to a solution of diene **132** (16 mg, 0.067 mmol) in dichloromethane (15 ml). The mixture was refluxed for 19 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude reaction product showed 60% conversion to lactone **142**. A pure sample was obtained by column chromatography (2% EtOAc/pet. ether).

^{1}H NMR: δ 1.26-1.40 (10H, m, CH_2), 1.56-1.68 (2H, m, CH_2), 2.00-2.05 (2H, m, CH_2CH=C), 2.34-2.45 (4H, m, CH_2CH=C, CH_2C=O), 4.13 (1.6H, dd, J = 5.4, 5.4, CH_2O, *E* isomer), 4.24 (0.4H, dd, J = 5.3, 5.3, CH_2O, *Z* isomer), 5.31-5.57 (2H, m, CH=CH).

^{13}C NMR: All signals in *E*/*Z* mixture; δ 23.5, 23.8, 23.9, 25.2, 25.5, 25.6, 25.7, 25.9, 26.0, 26.1, 26.2, 26.7, 27.5, 27.7, 31.3, 31.9, 33.3, 35.1 (all CH_2), 63.7 (CH_2O, *Z*), 64.3 (CH_2O, *E*), 127.1 (C=C, *Z*), 127.8 (C=C, *E*), 132.3 (C=C, *Z*), 132.8 (C=C, *E*), 174.1 (C=O).

MS (EI): *m/z* 210 (M^+, 7%).

The isomers were assigned by comparison with literature data.[105]



2-Isopropenyl-3-methyl-2,5-dihydrofuran (143)

Grubbs's catalyst **1**(14 mg, 0.017 mmol, 5 mol %) was added to a solution of triene **134** (52 mg, 0.34 mmol) in dichloromethane (3 ml) and the mixture was stirred at room temperature for 20 h. The solvent was removed and the crude mixture was separated by column chromatography (2% Et_2O/pentane) to give RCM product **143** (<5 mg), dimer **144** (30 mg) and starting material. The racemic RCM product **143** was then analysed by chiral GC to determine conditions that separated the enantiomers: Oven temp. 50 °C for 5 min then 1 °C/min increase to 100 °C. Retention times: 18.9 and 19.3 min.

143 ^{1}H NMR: δ 1.62 (6H, s, CH_3), 4.59-4.70 (2H, m, CH_2O), 4.91 (1H, s, C=CH_AH$_B$), 4.95-5.00 (2H, m, C=CH$_A$$H_B$, CHO), 5.58-561 (1H, m, CH_2C*H*=C).

^{13}C NMR: δ 12.1 (CH_3), 15.8 (CH_3), 75.6 (CH_2O), 92.9 (CHO), 113.6 (C=*C*H_2), 121.5 (CH_2*C*H=C), 136.4 (C=C), 144.9 (C=C).

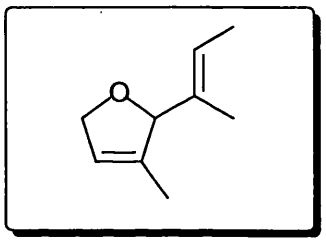
This was consistent with literature data.[106]

144 ^{1}H NMR: δ 1.62 (12H, s, CH_3), 3.88-3.96 (4H, m, CH_2O), 4.08 (2H, s, CHO), 4.97 (4H, s, CH_AH$_B$=C), 5.06 (4H, s, CH$_A$$H_B$=C), 5.82 (2H, s, C*H*=C*H*).

^{13}C NMR: δ 18.0 (CH_3), 68.0 (CH_2O), 85.7 (CHO), 112.7 (C=CH_2), 129.0 (*C*H=*C*H), 143.0 (*C*=CH_2).

Attempted enantioselective RCM of triene 134

Dichloromethane (3 ml) was added to triene **134** (18 mg, 0.12 mmol) and resin catalyst **121** (118 mg, 0.012 mmol, 10 mol %). The mixture was refluxed for 12 h then allowed to cool, filtered and concentrated. ^{1}H NMR analysis of the crude product mixture showed 17% conversion to RCM product **143** as well as dimer and starting material. After column chromatography (2% Et_2O/pentane), a sample of product **143** was analysed by chiral GC which showed it be racemic.



2-(2*E*-*sec*-Butenyl)-3-methyl-2,5-dihydrofuran (145)

Grubbs's second generation catalyst **2** (12 mg, 0.014 mmol, 5 mol %) was added to a solution of triene **135** (50 mg, 0.28 mmol) in dichloromethane (5 ml) and the mixture was refluxed for 2.5 h. The mixture was allowed to cool, the solvent was removed and column chromatography of the residue (2% Et_2O/pentane) gave RCM product **145** (28 mg, 73%). The racemic RCM product **145** was then analysed by chiral GC to determine conditions that separated the enantiomers: Oven temp. 75 °C for 5 min then 1 °C/min increase to 125 °C. Retention times: 15.4 and 15.6 min. (Alternatively, constant 60 °C gave retention times of 41.7 and 43.0 min).

^{1}H NMR: δ 1.49 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.65 (3H, d, J = 6.7, CH_3), 4.56-4.68 (2H, m, CH_2O), 4.89 (1H, s, CHO), 5.50-5.60 (2H, m, CH_2CH=C, CH_3CH=C).

^{13}C NMR: δ 9.9 (CH_3), 12.2 (CH_3), 13.2 (CH_3), 75.4 (CH_2O), 94.8 (CHO), 121.3 (*C*H=C), 123.5 (*C*H=C), 135.3 (C=C), 136.9 (C=C).

This was consistent with literature data.[106]

Attempted enantioselective RCM of triene 135

Resin catalyst **121** (105 mg, 0.011 mmol, 10 mol %) was added to a solution of triene **135** (19 mg, 0.11 mmol) in dichloromethane (15 ml) and the mixture was refluxed for 18 h. The mixture was allowed to cool, filtered, and concentrated. ^{1}H NMR analysis of the crude product mixture showed 84% conversion to RCM product **145**. After column chromatography (2% Et_2O/pentane), a sample of the product was analysed by chiral GC which showed it to be racemic.

6. REFERENCES

6. REFERENCES

1. P. Schwab, R. H. Grubbs and J. W. Ziller, *J. Am. Chem. Soc.*, 1996, **118**, 100.
2. M. Scholl, S. Ding, C. W. Lee and R. H. Grubbs, *Org. Lett.*, 1999, **1**, 953.
3. R. R. Schrock, J. S. Murdzek, G. C. Bazan, J. Robbins, M. DiMare and M. O'Regan, *J. Am. Chem. Soc.*, 1990, **112**, 3875.
4. S. K. Armstrong, *J. Chem. Soc., Perkin Trans. 1*, 1998, 371.

   R. H. Grubbs and S. Chang, *Tetrahedron*, 1998, **54**, 4413.

   M. Schuster and S. Blechert, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2036.

   T. M. Trnka and R. H. Grubbs, *Acc. Chem. Res.*, 2001, **34**, 18.
5. E. L. Dias, S. T. Nguyen and R. H. Grubbs, *J. Am. Chem. Soc.*, 1997, **119**, 3887.
6. M. S. Sanford, J. A. Love and R. H. Grubbs, *J. Am. Chem. Soc.*, 2001, **123**, 6543.
7. M. Ulman and R. H. Grubbs, *J. Org. Chem.*, 1999, **64**, 7202.
8. J. Kress, J. A. Osborn, R. M. E. Greene, K. J. Ivin and J. J. Rooney, *J. Chem. Soc., Chem. Commun.*, 1985, 874.
9. C. J. Schaverien, J. C. Dewan and R. R. Schrock, *J. Am. Chem. Soc.*, 1986, **108**, 2771.
10. S. T. Nguyen, L. K. Johnson and R. H. Grubbs, *J. Am. Chem. Soc.*, 1992, **114**, 3974.
11. S. T. Nguyen, R. H. Grubbs and J. W. Ziller, *J. Am. Chem. Soc.*, 1993, **115**, 9858.
12. P. Schwab, M. B. France, J. W. Ziller and R. H. Grubbs, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2039.
13. T. A. Kirkland and R. H. Grubbs, *J. Org. Chem.*, 1997, **62**, 7310.
14. T. R. Belderrain and R. H. Grubbs, *Organometallics*, 1997, **16**, 4001.

   P. A. van der Schaaf, R. Kolly and A. Hafner, *J. Chem. Soc., Chem. Commun.*, 2000, 1045.

   M. Gandelman, B. Rybtchinski, N. Ashkenazi, R. M. Gauvin and D. Milstein, *J. Am. Chem. Soc.*, 2001, **123**, 5372.
15. T. E. Wilhelm, T. R. Belderrain, S. N. Brown and R. H. Grubbs, *Organometallics*, 1997, **16**, 3867

16. S. Chang, L. Jones, C. Wang, L. M. Henling and R. H. Grubbs, *Organometallics*, 1998, **17**, 3460.

17. B. Mohr, D. M. Lynn and R. H. Grubbs, *Organometallics*, 1996, **15**, 4317.
D. M. Lynn, B. Mohr and R. H. Grubbs, *J. Am. Chem. Soc.*, 1998, **120**, 1627.
T. A. Kirkland, D. M. Lynn and R. H. Grubbs, *J. Org. Chem.*, 1998, **63**, 9904.
D. M. Lynn, B. Mohr, R. H. Grubbs, L. M. Henling and M. W. Day, *J. Am. Chem. Soc.*, 2000, **122**, 6601.

18. T. Rölle and R. H. Grubbs, *J. Chem. Soc., Chem. Commun.*, 2002, 1071.

19. E. L. Dias and R. H. Grubbs, *Organometallics*, 1998, **17**, 2758.

20. A. Fürstner, M. Picquet, C. Bruneau and P. H. Dixneuf, *J. Chem. Soc., Chem. Commun.*, 1998, 1315.

21. A. Fürstner, M. Liebl, C. W. Lehmann, M. Picquet, R. Kunz, C. Bruneau, D. Touchard, P. H. Dixneuf, *Chem. Eur. J.*, 2000, **6**, 1847.

22. A. Fürstner, A. F. Hill, M. Liebl and J. D. E. T. Wilton-Ely, *J. Chem. Soc., Chem. Commun.*, 1999, 601.

23. K. J. Harlow, A. F. Hill and J. D. E. T. Wilton-Ely, *J. Chem. Soc., Dalton Trans.*, 1999, 285.

24. L. Jafarpour, H-J. Schanz, E. D. Stevens and S. P. Nolan, *Organometallics*, 1999, **18**, 5416.

25. A. Fürstner, O. R. Thiel, L. Ackermann, H-J. Schanz and S. P. Nolan, *J. Org. Chem.*, 2000, **65**, 2204.

26. J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus and A. H. Hoveyda, *J. Am. Chem. Soc.*, 1999, **121**, 791.

27. S. B. Garber, J. S. Kingsbury, B. L. Gray and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2000, **122**, 8168.

28. T. Weskamp, W. C. Schattenmann, M. Spiegler and W. A. Herrmann, *Angew. Chem., Int. Ed. Engl.*, 1998, **37**, 2490.

29. T. Weskamp, F. J. Kohl, W. Hieringer, D. Gleich and W. A. Herrmann, *Angew. Chem., Int. Ed. Engl.*, 1999, **38**, 2416.

30. T. Weskamp, F. J. Kohl and W. A. Herrmann, *J. Organomet. Chem.*, 1999, **582**, 362.

31. L. Ackermann, A. Furstner, T. Weskamp, F. J. Kohl and W. A. Herrmann, *Tetrahedron Lett.*, 1999, **40**, 4787.

32. U. Frenzel, T. Weskamp, F. J. Kohl, W. C. Schattenmann, O. Nuyken and W. A. Herrmann, *J. Organomet. Chem.*, 1999, **586**, 263.

33. M. Scholl, T. M. Trnka, J. P. Morgan and R. H. Grubbs, *Tetrahedron Lett.*, 1999, **40**, 2247.

34. J. Huang, E. D. Stevens, S. P. Nolan and J. L. Petersen, *J. Am. Chem. Soc.*, 1999, **121**, 2674.

35. L. Jafarpour, J. Huang, E. D. Stevens and S. P. Nolan, *Organometallics*, 1999, **18**, 3760.

36. J. Huang, H-J. Schanz, E. D. Stevens and S. P. Nolan, *Organometallics*, 1999, **18**, 5375.

37. A. Briot, M. Bujard, V. Gouverneur, S. P. Nolan and C. Mioskowski, *Org. Lett.*, 2000, **2**, 1517.

38. A. K. Chatterjee, D. P. Sanders and R. H. Grubbs, *Org. Lett.*, 2002, **4**, 1939.
A. K. Chatterjee and R. H. Grubbs, *Org. Lett.*, 1999, **1**, 1751.
T.-L. Choi, C. W. Lee, A. K. Chatterjee and R. H. Grubbs, *J. Am. Chem. Soc.*, 2001, **123**, 10417.

39. A. Fürstner, O. Guth, A. Düffels, G. Seidel, M. Liebl, B. Gabor and R. Mynott, *Chem. Eur. J.*, 2001, **7**, 4811.

40. S. B. Garber, J. S. Kingsbury, B. L. Gray and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2000, **122**, 8168.

41. H. Wakamatsu and S. Blechert, *Angew. Chem. Int. Ed.*, 2002, **41**, 2403.

42. J. A. Love, J. P. Morgan, T. M. Trnka and R. H. Grubbs, *Angew. Chem. Int. Ed.*, 2002, **41**, 4035.

43. J. B. Alexander, D. S. La, D. R. Cefalo, A. H. Hoveyda and R. R. Schrock, *J. Am. Chem. Soc.*, 1998, **120**, 4041.

44. S. S. Zhu, D. R. Cefalo, D. S. La, J. Y. Jamieson, W. M. Davies, A. H. Hoveyda and R. R. Schrock, *J. Am. Chem. Soc.*, 1999, **121**, 8251.

45. G. S. Weatherhead, J. H. Houser, G. J. Ford, J. Y. Jamieson, R. R. Schrock and A. H. Hoveyda, *Tetrahedron Lett.*, 2000, **41**, 9553.

46. T. J. Seiders, D. W. Ward and R. H. Grubbs, *Org. Lett.*, 2001, **3**, 3225.

47. J. J. Van Veldhuizen, S. B. Garber, J. S. Kingsbury and A. H. Hoveyda, *J. Am. Chem. Soc.*, 2002, **124**, 4954.

48. *Recoverable Catalysts and Reagents*, ed. J. A. Gladysz, *Chem. Rev.*, 2002, **102**, 3215.

49. S. T. Nguyen and R. H. Grubbs, *J. Organomet. Chem.*, 1995, **497**, 195.

50. M. Ahmed, A. G. M. Barrett, D. C. Braddock, S. M. Cramp and P. A. Procopiou, *Tetrahedron Lett.*, 1999, **40**, 8657.

51. M. Ahmed, T. Arnauld, A. G. M. Barrett, D. C. Braddock and P. A. Procopiou, *Synlett.*, 2000, 1007.

52. L. Jafarpour, M-P. Heck, C. Baylon, H. M. Lee, C. Mioskowski and S. P. Nolan, *Organometallics*, 2002, **21**, 671.

53. Q. Yao, *Angew. Chem. Int. Ed.*, 2000, **39**, 3896.

54. J. Dowden and J. Savovic, *J. Chem. Soc., Chem. Commun.*, 2001, 37.

55. S. J. Connon and S. Blechert, *Bioorg. Med. Chem. Lett.*, 2002, 1873.

56. S. Randl, N. Buschmann, S. J. Connon and S. Blechert, *Synlett*, 2001, 1547.

57. K. Grela, M. Tryznowski and M. Bieniek, *Tetrahedron Lett.*, 2002, **43**, 9055.

58. S. J. Connon, A. M. Dunne and S. Blechert, *Angew. Chem. Int. Ed.*, 2002, **41**, 3835.

59. J. S. Kingsbury, S. B. Garber, J. M. Giftos, B. L. Gray, M. M. Okamoto, R. A. Farrer, J. T. Fourkas and A. H. Hoveyda, *Angew. Chem. Int. Ed.*, 2001, **40**, 4251.

60. S. C. Schürer, S. Gessler, N. Buschmann and S. Blechert, *Angew. Chem. Int. Ed.*, 2000, **39**, 3898.

61. M. Mayr, B. Mayr and M. R. Buchmeiser, *Angew. Chem. Int. Ed.*, 2001, **40**, 3839.

62. M. Mayr, M. R. Buchmeiser and K. Wurst, *Adv. Synth. Catal.*, 2002, **344**, 712.

63. B. De Clercq, F. Lefebvre and F. Verpoort, *New. J. Chem.*, 2002, **26**, 1201.

64. B. De Clercq and F. Verpoort, *Tetrahedron Lett.*, 2001, **42**, 8959.

65. R. Akiyama and S. Kobayashi, *Angew. Chem. Int. Ed.*, 2002, **41**, 2602.

66. K. C. Hultzsch, J. A. Jernelius, A. H. Hoveyda and R. R. Schrock, *Angew. Chem. Int. Ed.*, 2002, **41**, 589.

67. C. A. Bessel, P. Aggarwal, A. C. Marschilok and K. J. Takeuchi, *Chem. Rev.*, 2001, **101**, 1031.

68. N. J. DeStefano, D. J. Johnson, R. M. Lane and L. M. Venanzi, *Helv. Chim. Acta*, 1976, **59**, 2674.

69. H.-B. Bürgi, J. Murray-Rust, M. Camalli, F. Caruso and L. M. Venanzi, *Helv. Chim. Acta*, 1989, **72**, 1293.

70. N. P. Buu-Hoi and D. Lavit, *J. Chem. Soc.*, 1956, 1743.

71. L. Prajer-Janczewska and J. Wroblewski, *Pol. J. Chem.*, 1980, **54**, 1431.

72. G. T. Crisp, Y-L. Jiang, P. J. Pullman and C. De Savi, *Tetrahedron*, 1997, **53**, 17489.

73. M. Janczewski, B. Dabrowska and B. Florkiewicz, *Przemysl. Chem.*, 1958, **37**, 784. (*Chem. Abs.* 1959, 17983).

74. T. A. Stephenson and G. Wilkinson, *J. Inorg. Nucl. Chem.*, 1966, **28**, 945.

75. W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 1952, 4735.

76. G. L. Gloss and R. A. Moss, *J. Am. Chem. Soc.*, 1964, **86**, 4042.

77. M. A. Andrews, T. C. Chang, C. F. Cheng, T. J. Emge, K. P. Kelly and T. F. Koetzle, *J. Am. Chem. Soc.*, 1984, **106**, 5913.

78. W. E. Hill, C. A. McAuliffe, I. E. Niven and R. V. Parish, *Inorg. Chim. Acta*, 1980, **38**, 273.

79. D. C. Smith, Jr. and G. M. Gray, *Inorg. Chem.*, 1998, **37**, 1791.
D. C. Smith, Jr. and G. M. Gray, *J. Chem. Soc., Dalton Trans.*, 2000, 677.

80. W. E. Hill, J. G. Taylor, C. P. Falshaw, T. J. King, B. Beagley, D. M. Tonge, R. G. Pritchard and C. A. McAuliffe, *J. Chem. Soc., Dalton Trans.*, 1986, 2289.

81. A. Pryde, B. L. Shaw and B. Weeks, *J. Chem. Soc., Dalton Trans.*, 1976, 322.

82. W. E. Hill, D. M. A. Minahan and C. A. McAuliffe, *Inorg. Chem.*, 1983, **22**, 3382.

83. S. O. Grim, R. L. Keiter and W. McFarlane, *Inorg. Chem.*, 1967, **6**, 1133.

84. A. Perry, Final Year Project Report, University of Glasgow, 2001.

85. S. K. Armstrong, R. J. Cross, L. J. Farrugia, D. A. Nichols and A. Perry, *Eur. J. Inorg. Chem.*, 2002, 141

86. J. Schwarz, V. P. W. Böhm, M. G. Gardiner, M. Grosche, W. A. Herrmann, W. Hieringer and G. Raudaschl-Sieber, *Chem. Eur. J.*, 2000, **6**, 1773.

87. J. Barluenga, L. Alonso-Cires and G. Asensio, *Synthesis*, 1979, 962.

88. V. Gomez Aranda, J. Barluenga and F. Aznar, *Synthesis*, 1974, 504.

89. J. March, *Advanced Organic Chemistry*, 4th ed., Wiley-Interscience, New York, 1992, 1205.

90. J. R. Parikh, E. W. Van Doering, *J. Am. Chem. Soc.*, 1967, **89**, 5505.

91. R. E. Ireland and D. W. Norbeck, *J. Org. Chem.*, 1985, **50**, 2198.

92. S. Murata, S. Abe and H. Tomioka, *J. Org. Chem.*, 1997, **62**, 3055.

93. L. F. Kashukhin, M. P. Ponomarchuk, L. S. Sologub, A. A. Kisilenko and V. P. Kukhar, *J. Gen. Chem. USSR*, 1983, **53**, 491.

94. R. F. Borch, P. A. Bernstein, T. Durst, *J. Am. Chem. Soc.*, 1971, **93**, 2897.

95. D. J. Ager and I. Prakash, *Synth. Comm.*, 1996, **26**, 3865.

96. H. Brunner, R. Kroiss, M. Schmidt and H. Schönenberger, *Eur. J. Med. Chem. Chim. Ther.*, 1986, **21**, 333.

97. S. M. Yeh, D. G. Sherman and C. F. Meares, *Anal. Biochem.*, 1979, **100**, 152.

98. J. P. Wolfe, S. Wagaw and S. L. Buchwald, *J. Am. Chem. Soc.*, 1996, **118**, 7215.

99. T. Ukai, H. Kawazura, Y. Ishii, J. J. Bonnet and J. A. Ibers, *J. Organomet. Chem.*, 1974, **65**, 253.

100. I. Rudkin, Final Year Project Report, University of Glasgow, 2002.

101. Y. Yamamoto, Y. Nakagai, N. Ohkoshi and K. Itoh, *J. Am. Chem. Soc.*, 2001, **123**, 6372.

102. A. Fürstner, L. Ackerman, B. Gabor, R. Goddard, C. W. Lehmann, R. Mynott, F. Stelzer and O. R. Thiel, *Chem. Eur. J.*, 2001, **7**, 3236.

103. A. J. Arduengo III, R. Krafczyk and R. Schmutzler, *Tetrahedron*, 1999, **55**, 14523.

104. B. Çetinkaya, S. Demir, I. Özdemir, L. Toupet, D. Sémeril, C. Bruneau and P. H. Dixneuf, *New J. Chem.*, 2001, **25**, 519.

105. A. Fürstner and K. Langemann, *Synthesis*, 1997, 792.

106. D. S. La, J. B. Alexander, D. R. Cefalo, D. D. Graf, A. H. Hoveyda and R. R. Schrock, *J. Am. Chem. Soc.*, 1998, **120**, 9720.

107. C. M. Garner and M. E. Price, *Tetrahedron Lett.*, 1994, **35**, 2463.

108. F. Sato, H. Ishikawa and M. Sato, *Tetrahedron Lett.*, 1981, **22**, 85.

109. G. Marchbank, Final Year Project Report, University of Glasgow, 2003.

110. C. L. Forber, E. C. Kelusky, N. J. Bunce and M. C. Zerner, *J. Am. Chem. Soc.*, 1985, **107**, 5884.

111. K. Matsumoto, S. Fuwa, M. Shimojo and H. Kitajima, *Bull. Chem. Soc. Jpn.*, 1996, **69**, 2977.

112. F. Marguet, J-F. Cavalier, R. Verger and G. Buono, *Eur. J. Org. Chem.*, 1999, 1671.

113. I. Nongkynrih and M. K. Mahanti, *J. Org. Chem.*, 1993, **58**, 4925.

114. A. Zamri, F. Sirockin and M. A. Abdallah, *Tetrahedron*, 1999, **55**, 5157.

115. A. McKillop, L. McLaren, R. J. K. Taylor, R. J. Watson and N. J. Lewis, *J. Chem. Soc., Perkin Trans. 1*, 1996, 1385.

J. E. Jacobsen, M. A. Mitchell, S. K. Hendges, K. L. Belonga et. al., *J. Med. Chem.*, 1999, **42**, 1525.

116. R. Grigg, J. F. Malone, T. R. B. Mitchell, A. Ramasubbu and R. M. Scott, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1745.

117. M. E. Krafft, L. V. R. Bonaga and C. Hirosawa, *J. Org. Chem.*, 2001, **66**, 3004.

118. W. A. Nugent, J. Feldman and J. C. Calabrese, *J. Am. Chem. Soc.*, 1995, **117**, 8992.

119. M. W. Wright, T. L. Smalley, M. E. Welker and A. L. Rheingold, *J. Am. Chem. Soc.*, 1994, **116**, 6777.

120. E. E. Schweizer and G. J. O'Neill, *J. Org. Chem.*, 1965, **30**, 2082.