Towards Polymer-Supported Schrock-type Initiators for Olefin Metathesis

Thesis submitted for the Degree of
Doctor of Philosophy

By

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Statement

This thesis is based on work conducted by the author, in the Department of Chemistry at the University of Leicester, during the period October 2000 to December 2003.

All the work described in this thesis is original, unless otherwise acknowledged in the text or in the references. None of this work has been submitted for another degree in this or any other University.

Signed:  Date: 10.12.05

Samuel Suhard

Abstract

Title: Towards Polymer-Supported Schrock-type Initiators for Olefin Metathesis

Author: Samuel Suhard

This thesis describes the synthesis of supported Schrock-type initiators immobilised *via* polymer-bound alcohol and their activity in olefin metathesis, together with a parallel study of the synthesis and reactivity of their model homogeneous counterparts.

Chapter 1 presents an overview of the inorganic and organic supports used in order to achieve the heterogeneisation of a range of different homogenous catalysts. A review of the nature of various organic supports and examples of supported metal-ligand complexes are given. The terms olefin metathesis, and their corresponding metathesis reactions such as ROMP, RCM, ADMET, ROM, and cross metathesis are defined. A review of previously reported classical multi-component initiator systems, well-defined single component initiators, together with well-defined supported initiators for use in olefin metathesis reactions is given.

Chapter 2 describes the synthesis of diol ligands such as TADDOL and those based upon a pentanediol skeleton together with that of their supported counterparts. The synthesis of supported tetrafluorophenol *via* microwave-assisted Suzuki-Miyaura cross coupling is discussed. Strategies for the synthesis of polymer supports bearing TADDOL, pentanediol, and tetrafluorophenol unist with a built-in 'spacer' are examined.

Chapter 3 describes the synthesis of new Schrock-type olefin metathesis initiators, based on discrete soluble ligands described in chapter 2. Their formation is monitored by VT-NMR ^{1}H NMR experiments. Evidence of the ring-closing metathesis reactivity of the newly synthesised Schrock initiators is presented.

Chapter 4 describes the synthesis of polymer-supported Schrock-type olefin metathesis initiators based on resins outlined in chapter 2. The activity of such supported initiator system for ring-closing metathesis is examined. Strategies for the "on-beads" synthesis of a Schrock-type metathesis initiator are discussed.

Acknowledgements

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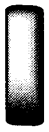
I would also like to thank all my colleagues and friends for making the experience of the last three years a pleasant one. A special mention goes to Toby and Chris (my colleagues), Ben and Mike (my roommates in 2002), for teaching me words you don't learn in France and enjoying the "exiting" English nightlife.

Most of all I would like to thank my wife Linlin as she has to endure all the crisis, during the writing-up of the thesis and my family for their endless support in every way possible.

Contents

Abbreviations and Symbols

	=	Lightly cross-linked (1-2 %) PS-DVB resin (unless stated otherwise)
	=	Generic polymer
δ	=	Chemical shift
18-crown-6	=	1,4,7,10,13,16-Hexaoxacyclooctadecane
AES	=	Atomic emission spectroscopy
AIBN	=	α,α'-Azoisobutyronitrile
Ar	=	Generic aryl group
ATR	=	Attenuated total internal reflectance
BINAP	=	[1,1'-Binaphthalene]-2,2'-diylbis(diphenylphosphine)
BINOL	=	Binaphthol
bm	=	Broad multiplet
Bn	=	Benzyl
bs	=	Broad singulet
COD	=	Cyclooctadiene
Cp	=	Cyclopentadienyl
Cy	=	Cyclohexyl
d	=	Doublet
DABCO	=	1,4-Diazabicyclo[2.2.2]octane
DCM	=	Dichloromethane
dd	=	Doublet of doublets
dhd	=	dimethyl hexane dione
DIOP	=	4,5-bis(diphenylphosphinomethyl)-2,2-dimethyl-1,3-dioxolane
DME	=	1,2-Dimethoxyethane
DMF	=	N,N-Dimethylformamide
DMP	=	2,2-Dimethoxypropane
DMSO	=	Dimethyl sulphoxide
dt	=	Doublet of triplets

DVB	=	Divinylbenzene
ee	=	Enantiomeric excess
EI	=	Electron impact
Et	=	Ethyl
GC	=	Gas chromatography
h	=	Hour
HOMO	=	Highest occupied molecular orbital
ICP	=	Inductively coupled plasma
^{i}Pr	=	*iso*-Propyl
IR	=	Infra-red
LUMO	=	Lowest unoccupied molecular orbital
m	=	Multiplet
m/z	=	Mass / charge ratio
MAO	=	Methylaluminoxane
Me	=	Methyl
MeCN	=	Acetonitrile
MeOH	=	Methanol
Mes	=	2,4,6-Trimethylphenyl (Mesityl)
MOM	=	Methoxymethyl
MS	=	Mass spectrometry
^{n}Bu	=	*n*-Butyl
NMR	=	Nuclear magnetic resonance
OAc	=	Acetate
PEG	=	Polyethylene glycol
Ph	=	Phenyl
ppm	=	Parts per million
PPTS	=	Pyridinium *p*-toluene sulfonate
PS	=	Polystyrene
p-TSA	=	*p*-Toluenesulphonic acid
py	=	Pyridine
q	=	Quartet
quint	=	Quintet
R	=	Generic alkyl or aryl group
RT	=	Room Temperature

s	=	Singlet
sept	=	Septet
SPOS	=	Solid phase organic synthesis
t	=	Triplet
TADDOL	=	α, α, α', α'-Tetraaryl-1,3-dioxolane-4,5-dimethanol
TBDMS	=	*tert*-Butyldimethylsilyl
^{t}Bu	=	*tert*-Butyl
THF	=	Tetrahydrofuran
TLC	=	Thin layer chromatography
TMS	=	Trimethylsilyl
tol	=	Toluene
Ts	=	Toluenesulphonyl
VT NMR	=	Variable temperature nuclear magnetic resonance

Chapter 1

Introduction

I Introduction

In the world of industrial catalysis there are two main approaches to undertaking reactions: either in a *homogeneous* or in a *heterogeneous* fashion.[1] In the homogeneous case, there is one phase (typically a single solution), whereas for heterogeneous systems there are at least two phases. Generally, for the homogeneous situation the starting material, the catalyst, and the final products are all soluble in the same solvent. In theory, this is ideal for studying initiator action and for the elucidation of a catalytic cycle since reactions can be probed using standard techniques like solution-state NMR, IR, *etc.* In practice, however, their detailed study can be problematic since the catalytically active species are often very reactive and difficult to observe or isolate. Thus, it is essential to verify that the kinetics of the reactivity of any proposed catalytically-active species match those of the catalytic cycle as a whole. Only if the kinetics are identical can a species truly be implicated in the catalytic cycle.

I.1 Homogeneous Catalysis

The homogeneous catalysis approach has some other specific disadvantages. In particular, catalyst separation and recovery can be problematic. For example, the isolation of the products can be difficult, especially if there is still unreacted reactants remaining, forming complex mixtures of species in solution. Even if the catalyst exhibits high selectivity and high activity, difficulties may be encountered in separating the initiator from the products, potentially making the purification process long, time consuming, and inefficient.

Since many of the most useful transition metal-based catalysts employ 'tailored' ligands a further complication arises when ligand dissociation occurs in solution. Not only are the beneficial properties of the ligands lost from the complex (*e.g.* providing solubility, conferring selectivity, *etc.*), but contamination of the product stream can occur. Ligand dissociation can result in the loss of often costly metals and can lead to the formation of potentially toxic metallic deposits that can be difficult to remove. Equally, the ligands themselves may be hard/expensive to prepare making their loss of some financial significance. This is particularly the case in asymmetric catalytic processes where chiral ligands are employed. Thus, it is often very desirable to retain, without loss, both the organic and metallic components of a catalytic system. One area in which this type of contamination by ligand/metal has become especially significant is with the use of metal-catalysed reactions in the pharmaceuticals and fine products industries when the highest purities are required.

I.2 Heterogeneous catalysis

Heterogeneous catalytic systems often comprise liquid-gas, solid-gas, liquid-liquid, or solid-liquid combinations. Broadly, heterogeneous catalytic system can be divided into three classes as illustrated in Figure **1** below.

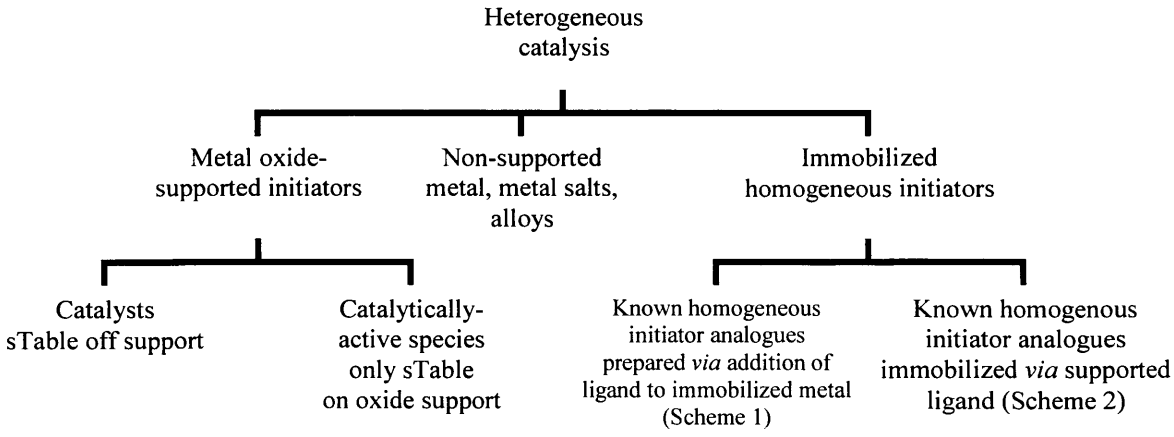
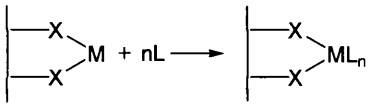
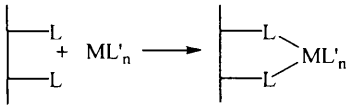


Figure 1 An overview of heterogeneous catalysis



Scheme 1



Scheme 2

Generally, heterogeneous systems, immobilized homogenous initiators and metal oxide-supported initiators in particularly, offer a number of advantages over their homogeneous counterparts as the initiators remain on the support. Thus only a simple separation or a filtration is needed for the work-up; the possibility of subsequent initiator recycling and re-use in an another catalytic cycle, can make the process less expensive. In addition, the heterogeneous initiators are generally more environmentally friendly, with initiator contamination of products being minimised so long as levels of leaching are low.

Despite these benefits, the heterogeneous catalytic approach also has some disadvantages. In particular, the elucidation of either the identity or the mode of action of surface-bound species can be complicated since analysis is a far from trivial exercise. Simple solution-state approaches are no longer appropriate and more elaborate, non-routine analytical techniques are required. An overview of a number of the more common methodologies and the data that they provide is given in Table **1.**

Technique	Application
Auger (AES)	Analysis of surface composition and electronic features
Secondary Ion Mass Spectrometry (SIMS)	Analysis of surface composition
X-Ray Photoelectron Spectroscopy (XPS)	Analysis of surface composition (elements) and of surface atom oxidation state
Ultraviolet Photoelectron Spectroscopy (UPS)	Electronic structure and orientation of chemisorbed molecules
Low Energy Electron Diffraction (LEED)	Symmetry features of surface atom environments, unit cell dimensions and structural features of the surface
X-Ray Fluorescence	Elements present at or near surface
Scanning Electron Microscopy (SEM)	Surface topography
Scanning Tunnelling Microscopy (STM)	Surface topography
Temperature Programmed Desorption (TPD)	Chemical identification of adsorbates
CPMAS NMR	Chemical identification of support or initiator components
IR/Raman spectroscopy	Identification/quantification of IR- or Raman-active species

Table 1 Analytical techniques for the study of heterogeneous initiator systems

In part, many of the advantages and disadvantages associated with heterogeneous initiator systems can be attributed to the nature of the solid support. In attempts to get around some of these problems a wide range of different types of support have been employed. In the following sections some discussion of the various support options will be given.

I.3 The solid support

Broadly speaking, there are two major kinds of initiator support: inorganic supports (*e.g.* metal oxides such as SiO_2, Al_2O_3, *etc.*) and organic supports (*e.g.* polymer resins). A short overview of each class will now be presented.

I.3.1 Inorganic supports

The principal inorganic supports are the silica and aluminium oxides. Silica adopts a three-dimensional polymeric structure built up from SiO_4 tetrahedra that are arranged in various ways.[1] Many silicas used for initiator supports are synthetic and are produced in one of two main ways. The first involves the acidification of silicate solutions, with changes in reaction conditions used to vary the nature of the resultant silica. Two types of oxide can be produced this way: sol-gel and precipitated silicas, which differ in agglomerate size, the former having a

large well-defined internal surface and the latter a large external surface. Lastly, fumed silica (*e.g.* Aerosil) is formed when a volatile silicon compound, such as $SiCl_4$ is injected into an oxygen/hydrogen flame. This generates a high external surface area silica.

All normal silica surfaces possess reactive hydrophilic silanol groups (Si-OH) and hydrophobic siloxane bridges (Si-O-Si).[2] The surface structure is made more complicated by various different types of silanol-silanol interactions being possible as indicated in Figure **2.**

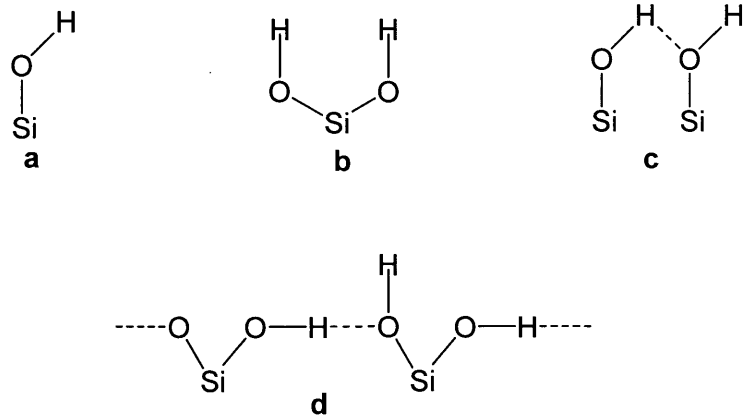


Figure 2 Classification of silanol groups: (a) isolated single group, (b) geminal group, (c) hydrogen-bonded vicinal groups and (d) hydrogen-bonded geminal groups

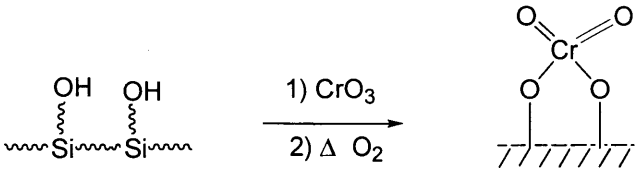
One of the most important properties of the silica support is the surface hydroxyl (silanol) density. This controls the number and dispersity of catalytically active species that can be bound to the surface, as metals are typically attached to the oxide through siloxide bonds, (Si-O-M). Siloxane bonds (Si-O-Si) are less reactive, and don't play a role in anchoring metals or metal complexes. Thermal treatment of the silica can affect the silanol density. At 200°C physically bound water is removed, although at this temperature the silanol density is not really affected, remaining around 5 OH groups nm^{-2}.[2] The precise value of the silanol density between silicas differs as the density is dependant upon the method used to prepare the silica. At temperatures of 800°C the number of silanols decreases dramatically to reach approximately 1 OH nm^{-2} mmol, as the neighbouring silanol groups combine and form geminal functionalities (Figure **2**).[2] Thus the surface of silica is generally regarded as being reactive (Si-OH bonds present) although there is some scope to modify this surface using heat treatments.

Alumina exists in two forms, α and the β-Al_2O_3. The oxide layers are close-packed in three dimensions, but every fifth layer has three quarters of its oxygens missing. Alumina is very similar to silica in terms of its properties as a support in catalysis.

Both silica and alumina are not particularly well-defined and can be regarded as complex supports with highly reactive surfaces. However, these oxides are still widely used especially in industry, since they are cheap, readily available and robust.

An example of relevance to this thesis is the use of alumina in metal-catalysed olefin metathesis (explained below) with several initiators having been supported in this way. The first system to be reported consists of a rhenium oxide on an alumina support, Re_2O_7/Al_2O_3.[3] This initiator works very well although its mode of action is not very well understood. It has been used mainly to prepare "commodity" compounds such as those used to manufacture detergents.

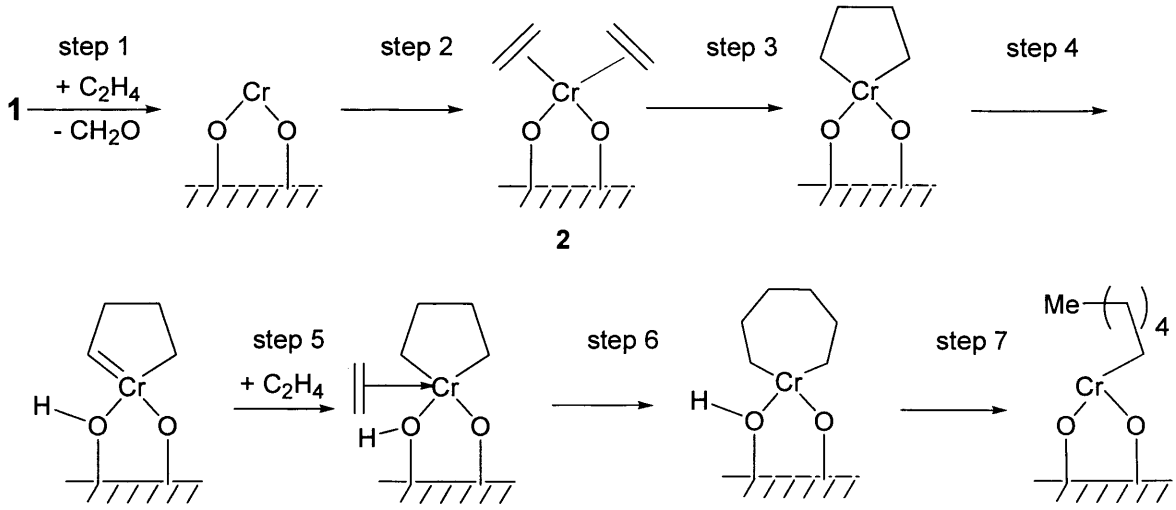
Another well-used heterogeneously-catalysed reaction is the Phillips process for the polymerisation of ethylene,[4] this particular example is informative as it illustrates how the support itself can be involved in the mode of action of the initiator. Species **1** is produced through aqueous impregnation of chromic acid onto silica followed by calcinations (Scheme **3**). The polymerisation-active species **2** is generated from **1** on addition of ethylene and subsequent elimination of formaldehyde (Scheme **4**). **2** is subsequently reduced by more ethylene.



1

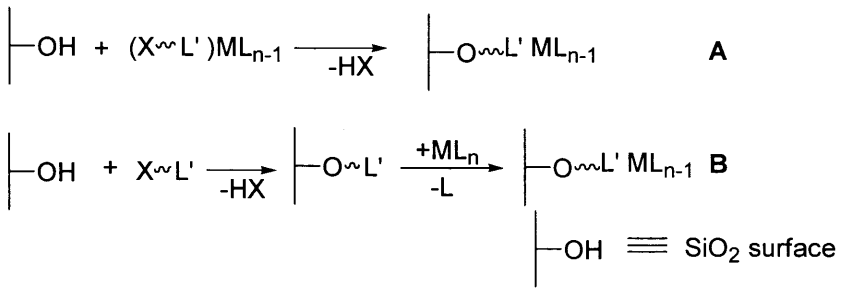
Scheme 3

Coordinatively unsaturated chromium (II) species such as **2** are not known to exist off support (*i.e.* without being bound to the silica surface) highlighting the stabilising effect that the silica support can induce. All these reaction steps (1-7) are believed to be involved in the initiation of the polymerisation process, with chain propagation consisting of coordination and migratory-insertion into the surface-bound metal alkyl formed in the last of these steps.



Scheme 4

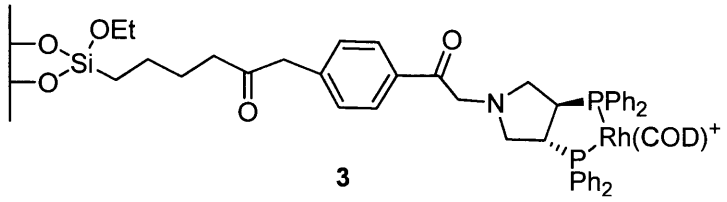
Despite their often ill-defined and reactive nature, today, silica supports are increasingly being used for the heterogenisation of preformed, well-defined homogeneous initiators *via* a spacer or a tether which distances the catalytically-active metal centre from the support. In general, the principles of the grafting are as follows: X is chosen to react with surface hydroxyl groups and L', a donor ligand functionality, is chosen for its ability to bind to the desired metal and hence anchor the initiator (Scheme **5**). There are two possibilities for achieving the grafting: either the initiator bearing X-L' is directly fixed to the surface *via* a hydroxyl group by the elimination of HX (**A**) or the ligand tether X-L' are fixed *via* the silanol functions by elimination of HX, and then the initiator is coordinated (**B**).[5]



Scheme 5

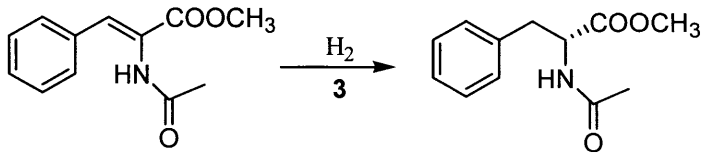
Below, an example of the application of this type of methodology for immobilising a homogenous initiator for the hydrogenation of methyl acetanimidecinnamate is described (Figure **3**), and illustrates the use of methodology **B** (Scheme **5**).[6] This system affords a product with an ee of 100% which is as good as the homogeneous version of the initiator. It is

interesting to note that this supported initiator **3** possesses a "spacer", which effectively holds the active component away from the support. Hence, the initiator can be regarded as being a kind of *pseudo* homogeneous environment, something which has been used to explain its high enantioselectivity (Scheme **6**).



3

Figure 3



Scheme 6

The above example demonstrates that silica can be used to heterogenise homogeneous initiators, which provides numerous advantages such as the benefits of soluble initiators (known mode of action, selectivity, activity) with those of heterogeneous catalysis (robustness ease of separation). It should be noted that the method used for the example described above works only for specific cases where the initiator is sTable to the poorly defined and reactive surface of silica. This oxide is not innocent, much of the time they can become involved in the catalytic process due to their acidic or basic nature. For a well-defined initiator which is unsTable to protic reagents, the silica is likely to react with the initiator in a unproductive way. So it is desirable to find a well-defined support and of course, an inert support. Hence, systems based around well-defined organic polymers are an ideal choice.

I.3.2 Organic supports[7]

In 1950 ionic exchange resins were developed, with sulfonic acid-functionalised polymers quickly becoming the main focus of research.[8] In addition to their exchange properties, these types of material have found numerous applications as heterogeneous acid catalysts. However, the development of organic polymers as insoluble reagent supports really took off in 1963 when Merrifield used a functionalised polystyrene for the solid phase

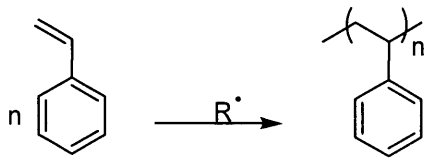
synthesis of peptides.[9] More recently, new disciplines, such as combinatorial chemistry, combined with an ever-growing need for the use of more environmentally friendly chemistries, have led to the use of organic supports becoming much more widely employed in numerous different applications.[10]

These type of organic supports can be divided into two distinct categories: *linear* and *cross-linked* polymers, the latter including gel-type resins, macroporous resins, and composite polymers. A brief description of the different structural types of organic supports that have found use in chemical synthesis will now be presented.

I.3.2.1 Linear polymers

Linear polymers are the simplest materials possible, and are usually obtained *via* a radical polymerisation reaction of, for example, styrene (Scheme **7**). The polymer obtained can be thought of as a mass of random, intertwined strands (Figure **4**). Linear polymers are easily functionalised, by introduction of the desired functional group by copolymerisation. To achieve this functionalisation and hence to make these materials suiTable for solid phase chemistry, it is important that the monomers are not incorporated at the same rate, in order to obtain the adequate linear polymer with the appropriate loading of the functional group.

At room temperature the linear polymer is below its glass transition temperature (Tg) where only rotation A is permitted (Figure **4**). As a result the polymer is amorphous and glass-like. When the temperature is raised above the polymer's Tg (around 100°C for polystyrene) rotation B is also permitted (Figure **4**), and the polymer becomes pliable. Above 250°C all movements are possible, making the polymer a viscous solid.[11]



Scheme 7

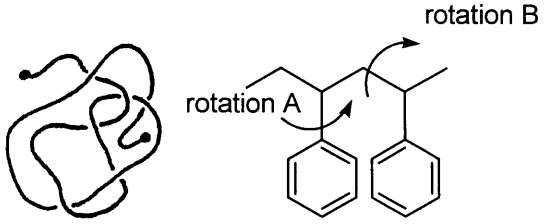


Figure 4 Linear polymer network and their rotations permitted in function of the temperature

The same physical changes can be observed at room temperature when the linear polymer is solvated, the effectiveness of which depends intimately on the nature of the solvent employed. Solvents for linear organic polymers can be divided into two distinct groups, often called "good" and "bad" solvents. The so-called "good" solvents allow the "plastification" of the polymer, inducing a change from a glass-like solid to a soft plastic material. Each network of random strands becomes independent and the polymer dissolves completely. In contrast, some solvents hardly interact with the organic support, the polymer remaining in an anamorphous state, with no dissolution of the polymer; by definition these are "bad" solvents. Below, Table **2** summarises the so-called "bad" and "good" solvents.[12]

"Good" solvents	"Bad" solvents
Aromatic hydrocarbons	*Aliphatic alcohols*
Benzene	Methanol
Toluene	2-Ethylhexanol
Xylenes	*Aliphatic hydrocarbons*
Chlorocarbons	Hexane
1,2 Dichloroethane	Dodecane
Chloroform	*Other solvents*
Cyclic ethers	Diethyl ether
Tetrahydrofuran	Acetic acid
Dioxane	

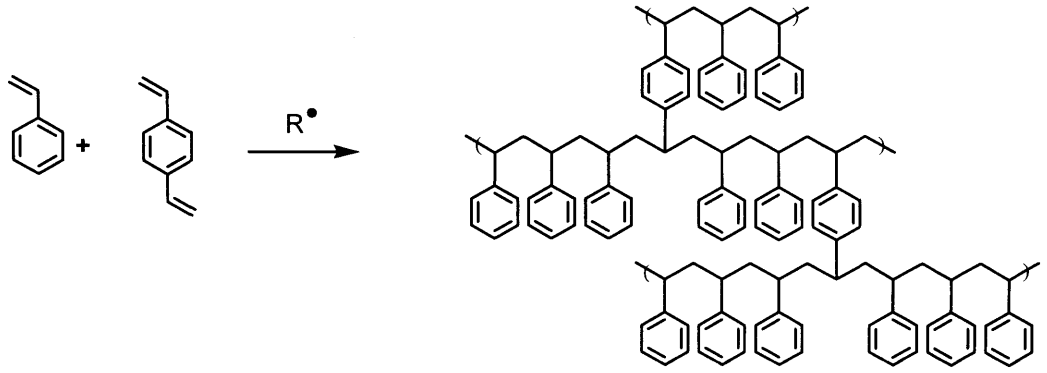
Table 2 Bad and good solvents for linear and cross-linked polymers

In theory, linear polymers could be very interesting as supports for initiators since they can dissolve completely in the presence of an appropriate solvent.[7] These supports could combine the advantages of heterogeneous systems, namely their ready separation using, for example ultrafiltration, with those of homogeneous systems since all the reactants are in the solution phase. However, for a given polymer only a limited choice of solvents are useful for their dissolution, according to Table **2** above, and a significant volume of solvent is needed to achieve good dilution and separation of the randomly interpenetrating "wires". Furthermore, efficient recovery of the polymer is not straight-forward, ultra filtration processes are required, but these are time consuming and expensive to carry out.[7]

I.3.2.2 Cross-linked polymers

I.3.2.2.1 Gel-type resins

Cross-linked polymers can be regarded as an infinite interconnected network.[7] A good example of this kind of structure is that obtained by the copolymerisation of styrene and divinylbenzene (DVB) as shown in Scheme **8** below. Other useful crosslinking monomers can be used including ethylene glycol dimethylacrylate (EGMA), trimethylopropane trimethacrylate (TRIM), and N,N-methylenebisacrylamide (MBA), giving rise to polymeric materials with a range of physical and chemical properties, something that can be used to tailor a particular material for a specific application .



Scheme 8

One of the most common ways to synthesize this type of cross-linked polymer is to employ a radical chain propagation reaction (often initiated by AIBN).[7] This reaction must be controlled since the shape and the size of the polymer beads are crucial. Modulation of these properties can be used to provide the polymer with better resistance to mechanical shock, which is very important as it can influence the reactivity of supported species and hence affect the reproducibility of the supported chemistry. The most common industrial and laboratory polymerisation process used to achieve the desired polymer morphology is called *suspension polymerisation.*[13] A styrene and divinyl benzene mixture that also contains a source of free radicals and a suspension stabilizer is dispersed as liquid droplets in an excess of an immiscible water phase. The suspension is stirred for 12h and heated at 80°C. Under these conditions the liquid monomer droplets are converted into a hard glassy polymer.

In just the same way that there are "good" and "bad" solvents for linear polymers, similar terms have been introduced for crosslinked polymers and signify the extent to which the polymer matrix is swollen or expanded on contact with a particular solvent. "Good" solvents swell the polymer to its elastic limit, forming a porous gel. As a result, these types of

support material are often called gel-type resins. "Bad" solvents do not swell the polymer and leave a solid structure. Gel-types resins are composed of an amorphous cross-linked network of interpenetrating polymer chains that have no long-range fine structure.[12] The polymer chains are in molecular contact with each other in the dry state. The degree of cross-linking is controlled by the amount of divinylbenzene (DVB) incorporated during the polymerisation process. High levels of divinylbenzene (>5%) leads to the generation of a rigid matrix of cross-linked polymer chains. This form of material is mechanically strong, but does not swell enough to allow all the network to be penetrated by the traditional "good" solvents (Table **2**) and thus usefully exploited in any subsequent reactions. As a result, highly cross-linked networks are not very good for supporting initiators, because they are difficult to functionalise in a reproducible manner.[7]

In contrast, the introduction of low levels of divinylbenzene (<1%) leads to a weakly crosslinked polymer network, which is easily damaged. So, the most commonly employed polymer supports for organic synthesis and catalysis are thus polystyrene beads cross-linked with ≈2% of divinylbenzene. These materials swell sufficiently such that the entire resin network can be penetrated by solvent (and hence reagents) and subsequently be exploited in chemical reactions and catalysis. Since this type of polymer is not soluble, the recovery of the supported species is easier than that with the linear support materials as a simple filtration allows the resin to be recovered.[7]

I.3.2.2.2 Macroporous resins

Often, there exists a fine balance between a solvent suiTable for swelling a resin and a solvent that is compatible with the reagent necessary for a particular transformation to be achieved using the resin, or for grafting to the resin. One solution to this problem is to synthesise a "permanently-swelled resin". This idea led to the development of *macroporous* resins.

Macroporous polymer resins are prepared by the copolymerisation of styrene with divinylbenzene *via* a free radical reaction in the presence of solvent, also called a porogen.[14] Macroporous resins are formed when the porogen is present in the comonomer mixture causing phase separation of the polymer matrix. When the reaction is complete, each polymer bead is composed of a cross-linked polymer phase and a discrete porogen phase, the latter acting as a template for the permanent porous structure of the resin. After removal of the solvent, permanently porous beads are obtained. As a result, these resins do not necessarily

need a solvent in order to swell, because they possess a permanently porous structure. Thus, water can be used as a solvent for reactions involving macroporous resins something that is not readily possible for related hydrophobic cross-linked gel-type resins. Furthermore, if a "good" solvent is added, the matrix will swell quickly as the pores are already "open", and the solvent will penetrate the whole resin rapidly. Since the solvent can easily penetrate the support, the use of macroporous resins overcomes the problems of swelling and deswelling that often lead to physical damage of the beads in gel-type resins.[7] In other words, macroporous resins have a better resistance to osmotic shock.

Macroporous resins can be regarded as a mass of very small gel-type particles that are enclosed in a complex pore structure.[14] Thus, an important characteristic of macroporous resins is the size of the pores. These can be controlled by the choice of the porogen, in particular, by the quantity used, and by the level of the cross-linker incorporated.

I.3.2.2.3 New polymer morphologies[15]

New kinds of polymers have been developed to offer the advantages of both macroporous and gel-type resins, largely with a view to affording an increased compatibility with various solvent systems. A number of these types of hybrid resin are outlined below.

I.3.2.2.3.1 Solvent-expanded gel-type resins

These types of polymer are prepared by the inclusion of large volumes of a compatible solvent in the polymerisation process, but without inducing any phase separation at the low levels of cross-linker (typically of the order of 2 weight %) used in gel-type resin synthesis. The resulting product is a swollen or "solvent-expanded" gel-type resin. The main advantage of these types of polymer is that they exhibit a greater swelling ability than a resin with the same cross-linked ratio prepared in the absence of solvents.[16]

I.3.2.2.3.2 Tentagel® and ArgoGel® resins

Tentagel®resins consist of a 2% cross-linked polystyrene polymer with a long polyethylene glycol (PEG) chain grafted to its surface and were originally designed for peptide synthesis.[17] This long PEG chain (that has both hydrophobic and hydrophilic properties) allows the polymer to swell in a diverse range of various protic solvents including water. Furthermore, the reactive sites associated with this type of resin for further functionalisation are located at the end of the spacer arms, meaning that they are much more

accessible and hence, behave kinetically like they were in solution rather than a polymer. In the past, one disadvantage of this type of resin was the possible cleavage of the long chains during use. Nowadays, this problem has been resolved by Argonaut Technologies Inc., by replacing the benzylic ether linkage with an aliphatic linkage and by utilising bifurcated PEG chains, which increases the branching and the overall loading capacity of the resin (Figure **5**).[18]

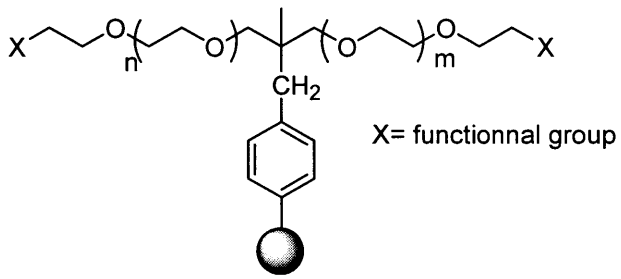


Figure 5 ArgoGel® resin

I.3.2.2.3.3 Self-supporting cylinders

The synthesis of self-supporting monolithic cylinders (Figure **6**) containing a functionalisable resin has been undertaken with a view to their being readily manipulated by a robot arm, making them very useful for the automation of the synthesis of chemical libraries.[19] However, these structures suffer from a restriction of the pore volume that results from the need for an adequate mass of polymer in order to provide mechanical solidity to the monolithic cylinder. As a result of this pore volume restriction, mass transfer into and chemical reaction within the inner parts of these self-supporting cylinders are also very restricted.[20]

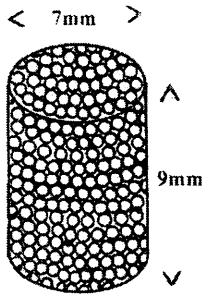


Figure 6 Schematic representation of a Self-Supported polymer cylinder (Stratosphere Plugs™)

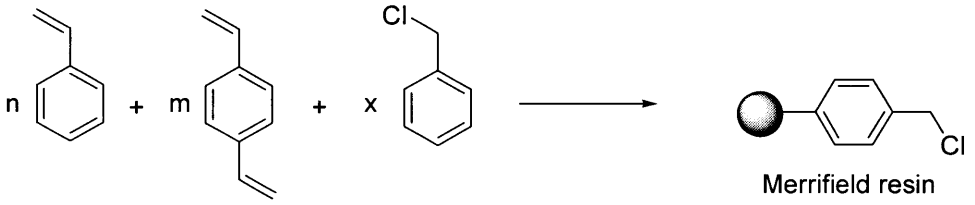
Recently, to overcome these problems, the synthesis of Stratosphere Plugs™ has been achieved: a polystyrene resin has been sintered and melted in the presence of a polyalkene.

The level of polyalkene incorporation is low enough to provide access for solvent and reagent into the core of the plugs.[20]

I.3.3 Application of organic-supported reagents

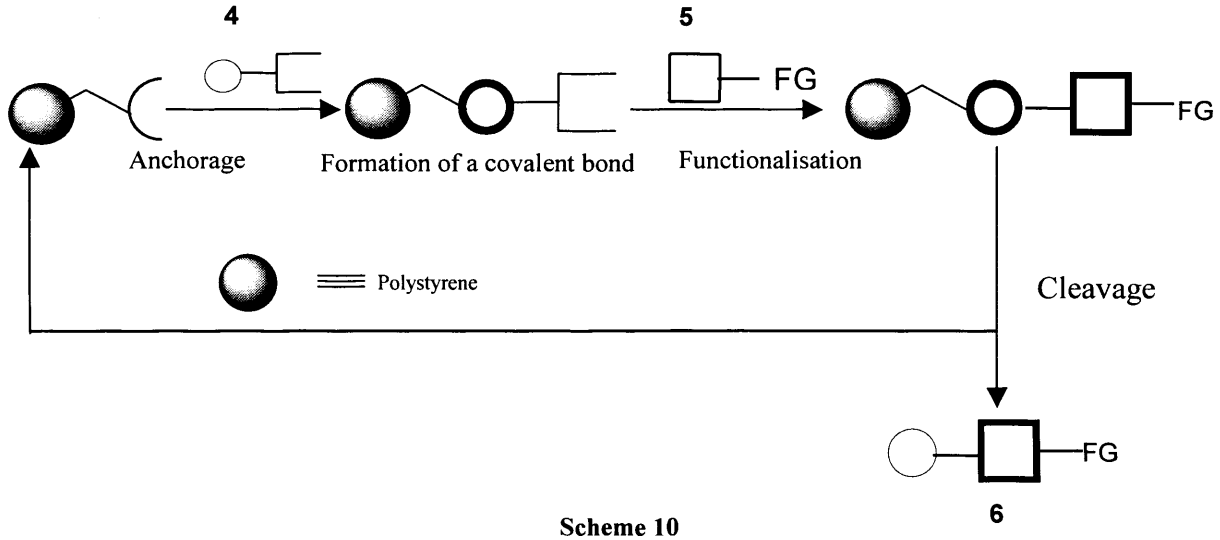
In recent years, chemistry on organic supports or using supported reagents has undergone a significant expansion with numerous important developments having been made. The growth in the use of supported chemistry can be attributed largely to the numerous advantages and benefits that are provided by solid-phase-type reagents (easy separation/recovery of desired products, recycling of the supported species, *etc.*). In particular, polystyrene supports are generally regarded as being totally inert and are also relatively easy to functionalise with a wide variety of different organic and inorganic species, often with near-stoichiometric reactions being possible, using standard synthetic methodologies. In this regard, one of the most commonly used resins is gel-type chloromethyl polystyrenes or Merrifield resins.[9]

This type of polymer resin is easily prepared by the copolymerisation of styrene, divinylbenzene and chloro methyl benzene (Scheme **9**). The resulting lightly cross-linked polymer (2% DVB) possesses a loading of chloromethyl function which can be modulated by the amount of chloromethyl benzene originally engaged in the reaction. Usually the loading of Merrifield resin is kept to *ca.* 1 mmol/g of chloromethyl function.



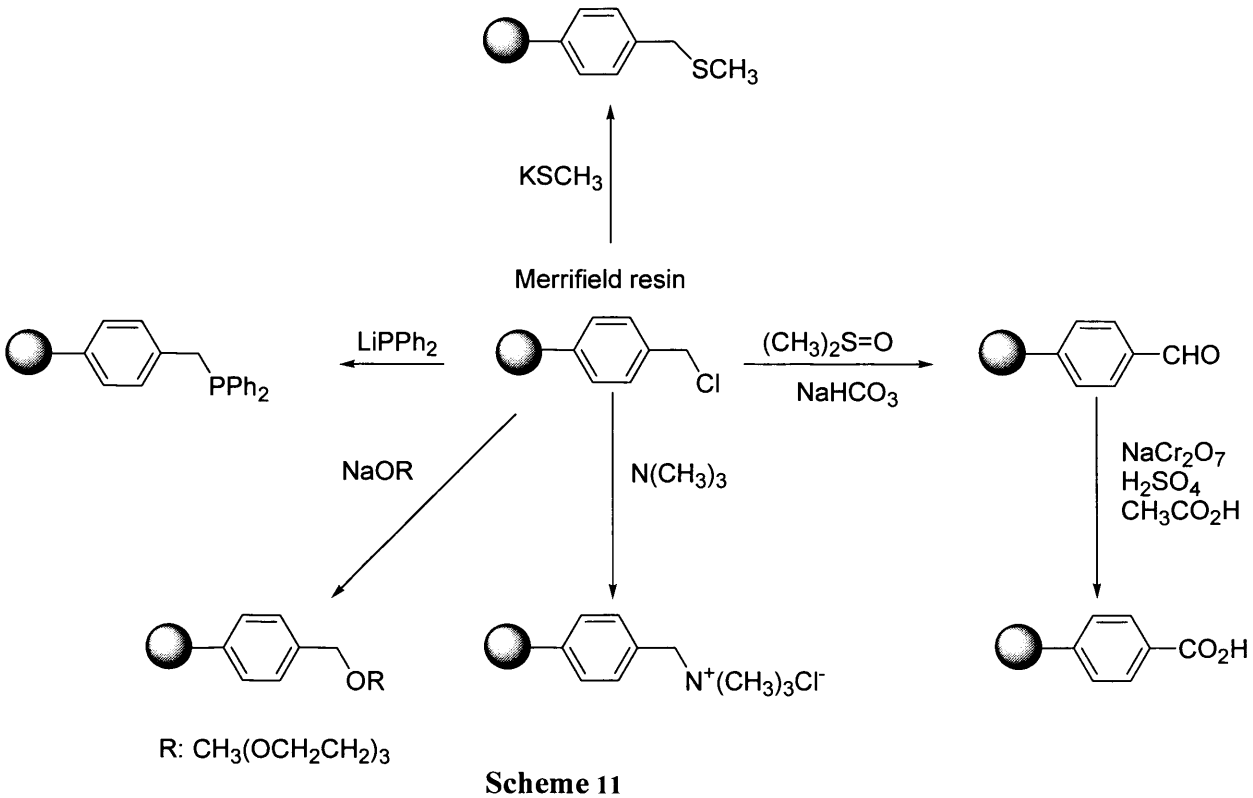
Scheme 9

In part, the success of this particular resin is historic, since this type of lightly cross-linked polymer was developed by Merrifield for use in the solid-phase synthesis of peptides, the principle behind this being outlined in Scheme **10**.[9] First, molecule **4** is fixed by a covalent bond to the support, then the resulting material functionalised by addition of another molecule **5**, a process which is repeated until the desired molecule has been prepared on-resin. Finally, in order to recover the desired product **6**, all that is required is a simple cleavage step to afford the product free from the resin (which can be recovered /removed by filtration).



Scheme 10

The polymer-bound chloromethyl group of Merrifield resin is a very reactive and versatile functionality. A number of very common synthetically useful functional groups such as carboxylic acids, aldehydes, and phosphines can be prepared on resin, therefore allowing the support and synthesis of a variety of chemical compounds. Examples of the chemical transformations possible with Merrifield resin are given in Scheme **11** below.[8]



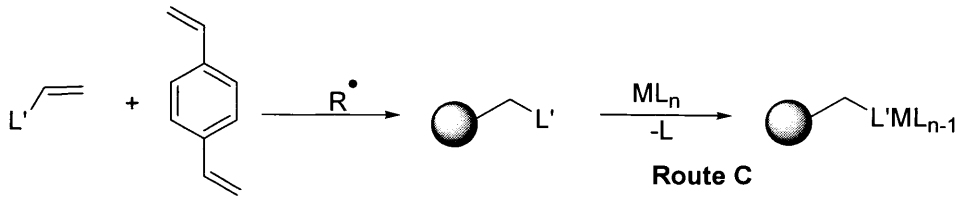
Scheme 11

I.3.4 Examples of polymer-supported initiators

In a similar way to the methods used to build up organic molecules on polymeric materials (namely in a post-resin modification approach), functionalised resins can be prepared (as in Scheme **12**) that can subsequently be used to anchor known, well-defined homogeneous transition metal initiators as discussed above (Figure **1**).

Scheme 12

Instead of post-functionalising a previously prepared organic support like an appropriately modified Merrifield resin with a initiator precursor, an alternative way to obtain polymer-supported species is to synthesise a variant of one of the metal's ligands such that it possesses a readily polymerisable functionality (such as a vinyl group) and then to induce its polymerisation in the presence of a comonomer (such as styrene) (Scheme **13**). The main advantage of route **C** is that of achieving a known level of functionalisation, but it is still difficult to obtain a good polymer in terms of its physical properties, morphology and size of the beads.



Scheme 13

Despite there being a number of potentially different approaches for the preparation of polymer-immobilised initiators, the vast majority of the work reported in the literature has involved the method described by route **B** (Scheme **12**) and its closely-related variant, method **C** (Scheme **13**).

The area of supported reagents, ligands and catalysts is now huge. As a result it is impossible to give a detailed overview of such a broad area of chemistry. Hence in the following sections an outline of some of the chemistry directly relevant to this thesis will be given. In particular a brief discussion of the preparation of some very common polymer-supported ligands such as phosphines, diols and metallocenes for applications in heterogenised

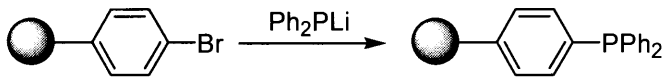
initiator synthesis and their use in catalysis for key reactions such as cross-coupling, epoxidation, Diels-Alder and olefin polymerisation will be given.

I.3.4.1 Supported metal phosphine complexes

I.3.4.1.1 Supported monodentate phosphines

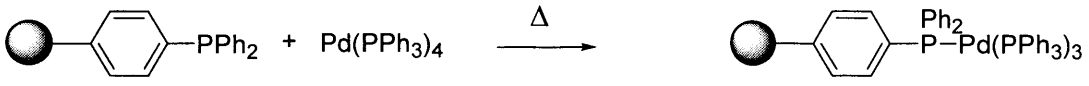
Phosphines (PR_3) are widely used as ligands throughout coordination chemistry, not least because they are known to bind to elements throughout the transition series and because they constitute one of the few families of ligands in which both steric and electronic parameters can be systematically altered by changing the nature of the substituents R.[21] The wide-range of applications using these ligands is aided by their facile synthesis, usually from commercially available halophosphines that behave as versatile building materials.[22] Furthermore, the ^{31}P nucleus has nuclear spin I = ½, 100% natural abundance and good receptivity, facilitating study by NMR spectroscopy.

Naturally, there have been many studies directed toward the immobilisation of such phosphorus-based ligands, something that has subsequently led to a wide range of supported phosphine-bearing species being prepared. Firstly, monodentate phosphines were supported, with perhaps most studies involving analogues of triphenylphosphine. The preparation of a polymer-bound variant of Ph_3P is simple to achieve, the most straightforward synthesis being outlined in Scheme **14**.[23]



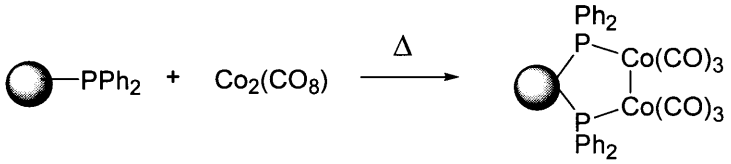
Scheme 14

Using this type of polymer-bound phosphine Pittman and co-workers prepared an immobilised variant of the well-known and synthetically versatile reagent palladium *tetrakis*(triphenylphosphine) by heating $[Pd(PPh_3)_4]$ with PS-PPh_2.[23] The resulting polymer has been shown to contain between 1.5% to 2.5% of palladium (Scheme **15**). The resulting supported palladium phosphine complex has been used frequently in cross coupling reactions.[23]



Scheme 15

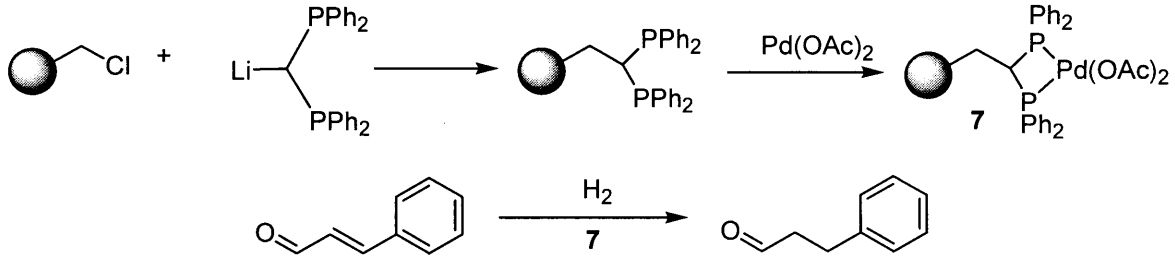
The utility of this polymer-bound phosphine has not just been limited to palladium. A vast range of other metal complexes including those of cobalt for the support of $Co_2(CO)_6$, which has been proven active in the Pauson-Khand reaction (Scheme **16**),[24] and ruthenium in the form of a supported arene complex, used as a initiator for enol formate synthesis and olefin cycloproanation amongst many others reactions.[25]



Scheme 16

I.3.4.1.2 Supported polydentate phosphines

More recently, the synthesis of polymer-supported polydentate phosphines has been achieved. These show better ligand properties over their monodentate analogues: their chelate behaviour is particularly important since simple entropic effects favour both initial metal complexation and help to retain the ligand in the metal's coordination sphere, while controlling coordination number. One of the first successful experiments in this respect was performed by Carlini and co-workers,[26] who treated standard Merrifield resin with lithiated *bis*(diphenylphosphino) methane. A supported Pd-initiator **7** (Scheme **17**) was then synthesised by reaction with palladium acetate, which has been shown to be an effective system for the selective hydrogenation of cinnamaldehyde to hydrocinnamaldehyde.[27]

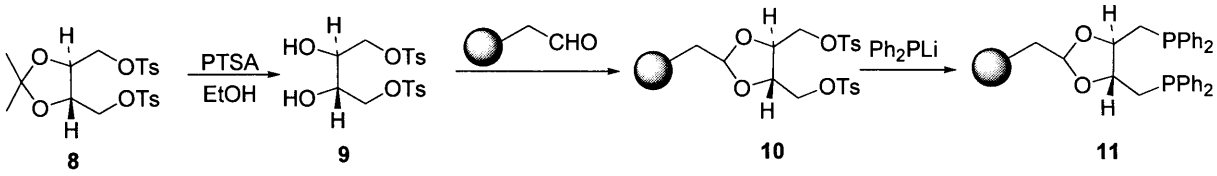


Scheme 17

In the last decade, many other polydentate phosphines have been supported with particular emphasis on asymmetric polydentate phosphines as their synthesis can be very demanding, expensive in compounds and time. Their immobilisation on a well-defined solid support affords the advantages of easy recovery and of possible reuse. A number of such systems are described below.

I.3.4.1.2.1 Supported DIOP

One of the first asymmetric supported phosphine ligands was reported by Kagan and co-workers in 1973, namely polymer-supported DIOP {2,3-o-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane}.[28] The ligand precursor **9** was prepared by ethanolysis of the corresponding acetonide **8** and anchored to a supported benzaldehyde resin to afford **10**, then treated with PPh_2Li to obtain the supported DIOP **11** (Scheme **18**).



Scheme 18

This supported diphosphine **11** has been used in the synthesis of a range of rhodium complexes. For example, treatment of **11** with rhodium compounds such as $[RhCl(C_2H_4)_2]_2$ under an atmosphere of CO led to the formation of immobilised systems such as **12** (Figure 7).

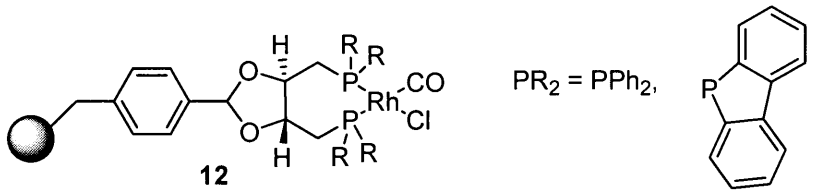
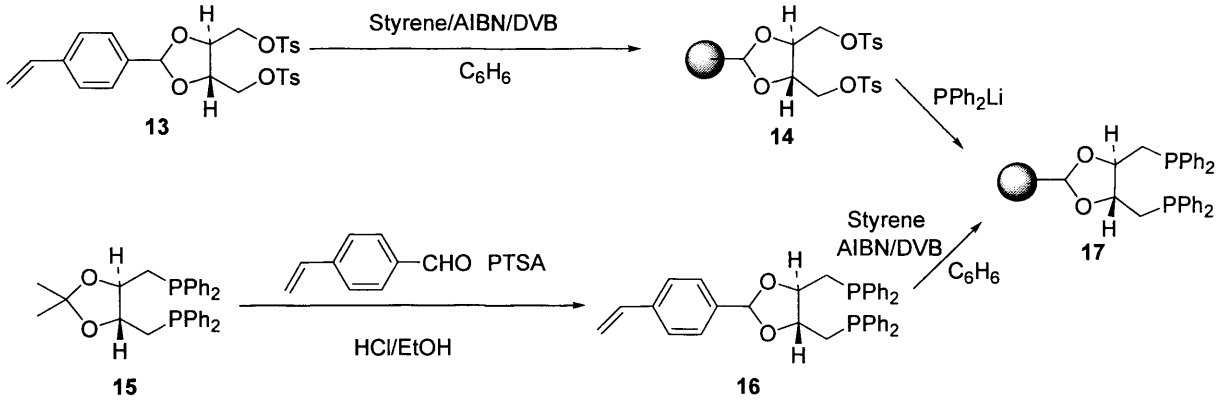


Figure 7 Supported rhodium initiator

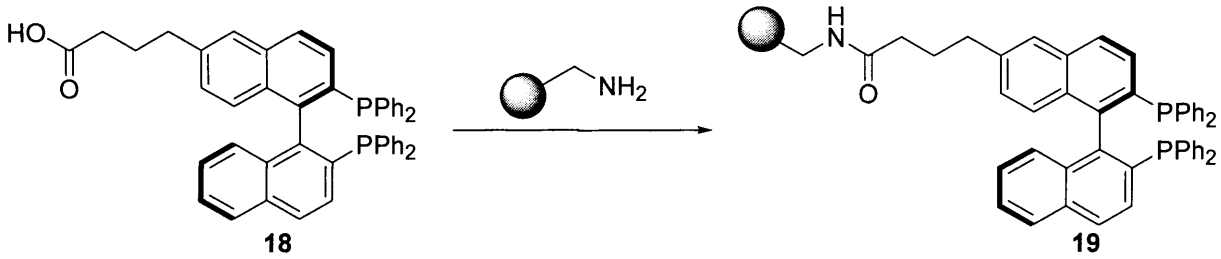
Although the supported species **12** has not been fully characterised, it has been shown to be an efficient initiator in asymmetric hydrogenation and hydrosilylation reactions.[28] Stille and coworkers have synthesised a similar initiator by the polymerisation of the monomer **13** (Scheme **19**) giving the functionalised species **14**, which was treated with Ph_2PLi to afford the supported DIOP **17**.[29] An alternative route was achieved by the synthesis of the bis(phosphine) compound **15**, which was used to prepare derivative **16**, which bears a vinyl function that was subsequently polymerised to afford the supported DIOP ligand **17**.



Scheme 19

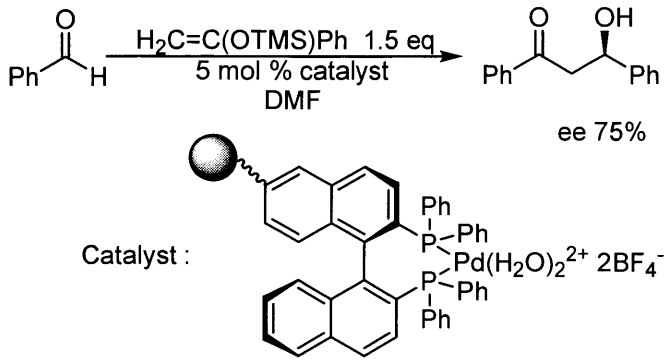
I.3.4.1.2.2 Polymer-supported BINAP

The immobilization of the versatile and well-known BINAP ligand has caught the interest of many research teams. The first synthesis of a polymer-supported variant was performed by Baystons and co-workers.[30] They synthesised a functionalised BINAP ligand with a carboxylic acid function **18**. The BINAP motif was then anchored to an amine cross-linked polymer by the formation of a peptide link to afford **19** (Scheme **20**).



Scheme 20

An alternative approach for the preparation of a similar ligand was taken by Chapuis and coworkers who immobilized a BINAP variant with a hydroxyl group by the formation of an ester linkage on a TentaGel® resin carrying a carboxylic acid functionality. Reaction between the supported BINAP and a palladium salt gave an efficient initiator system for asymmetric aldol reaction as illustrated in Scheme **21**.[31]

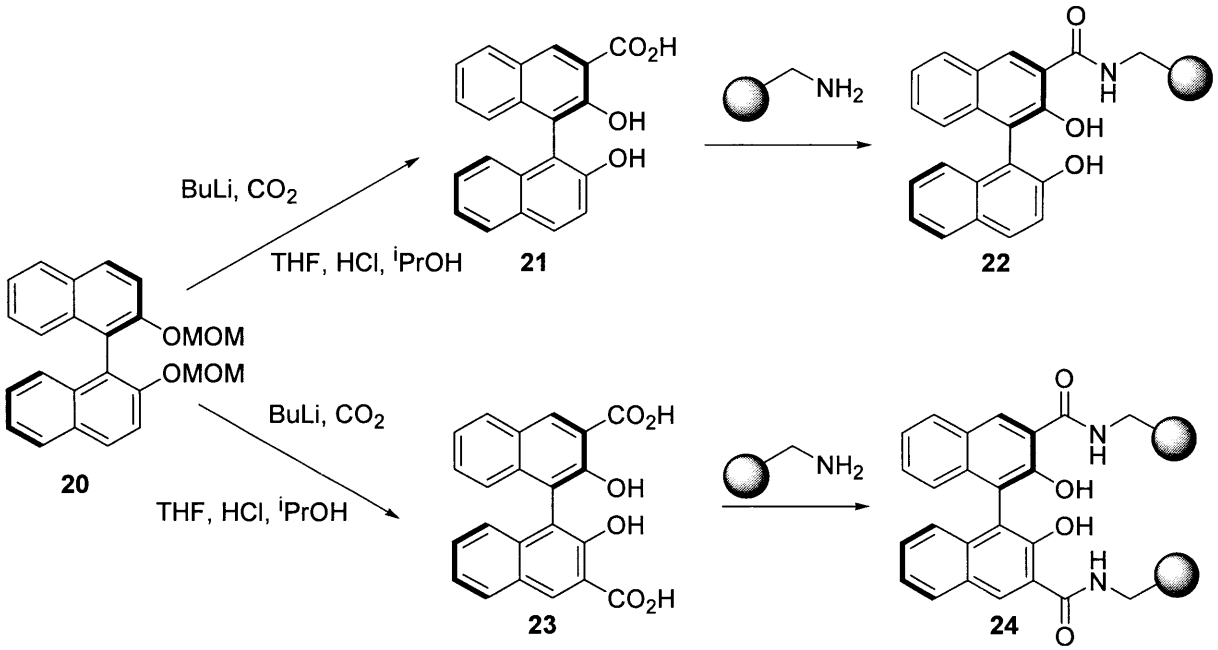


Scheme 21

I.3.4.2 Polymer-supported metal diol complexes

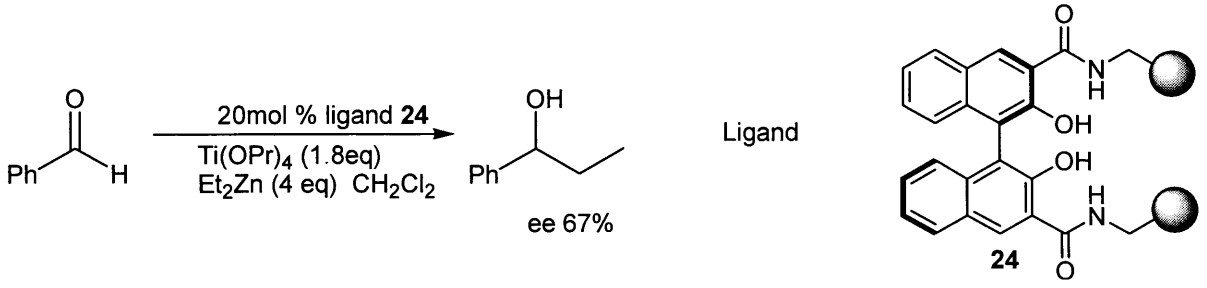
I.3.4.2.1 Supported BINOL

Like phosphines, alcohols (diols in particular) and their anionic equivalents are very important ligands in a variety of catalytic applications.[32] An area of some importance is that directed towards the synthesis of immobilized asymmetric diol ligands, especially BINOL ligands. In order to prepare such a polymer-bonded system, Chan and coworkers[33] started from the di-protected MOM-BINOL **20** (Scheme **22**), a carboxylation was then performed to obtain **21** and **23**, which were anchored to an amino-methylated polystyrene by the formation of peptide links yielding **22** and **24**.



Scheme 22

When **24** is used in combination with $Ti(O^iPr)_4$, an active initiator for the alkylation of aldehydes with diethyl zinc is obtained (Scheme **23**). It is noteworthy that the polymer-supported system affords a considerably greater enantioselectivity than was achieved with the corresponding homogeneous initiator analogue.[33]



Scheme 23

I.3.4.2.2 Polymer-supported TADDOL

Another example of an important diol ligand that has found application in a range of enantioselective metal-catalysed processes is α,α,α',α',-tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL).[34] One of the main feature of this ligand is its relatively easy synthesis and its great tuneability achieved by changing the R, R' and Ar groups (Figure **8**).

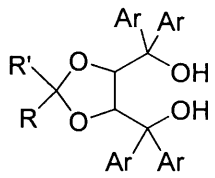
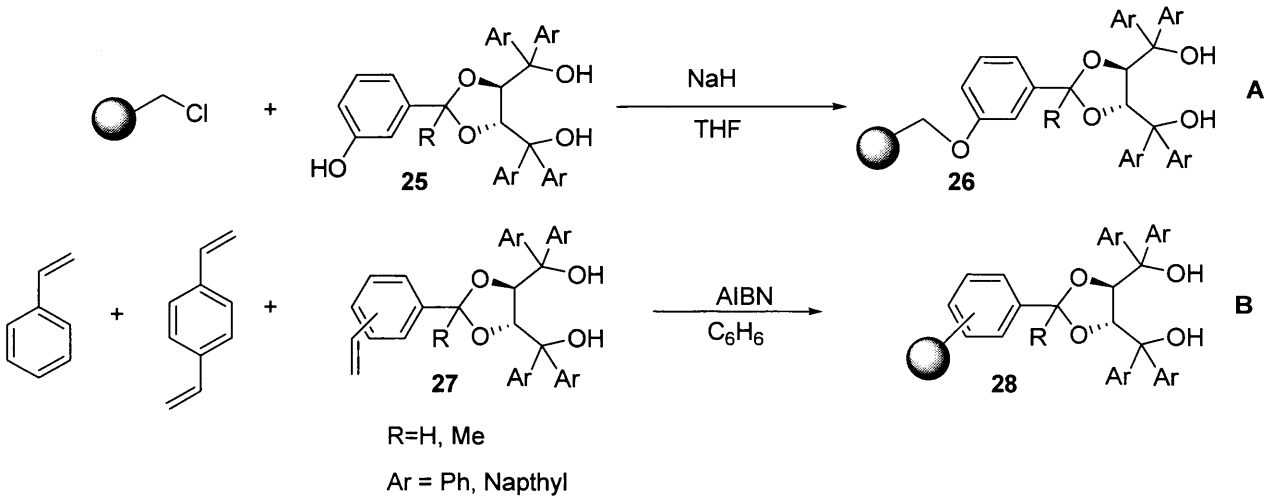


Figure 8 TADDOL

Therefore, TADDOL-type ligands with their dioxolane rings have been anchored onto a solid support.[35] This have been done by the synthesis of the TADDOL ligands **25** and their subsequent anchorage on the support, **26** (route A) or by the synthesis of TADDOL ligand with a vinyl function **27** and its consequent copolymerisation with styrene and divinyl benzene to afford **28** route B (Scheme **24**).[34]



Scheme 24

Supported TADDOL ligands have been shown to demonstrate good activity in the enantioselective Lewis acid-catalysed addition of diethylzinc to aldehydes, as well as in [3+2] cycloaddition reactions. The re-usability of the supported TADDOL has been demonstrated.[35] More description of TADDOL and its synthesis will be presented in chapter 2.

I.3.4.2.3 Polymer-supported salen

From an initiator preparation view point, another interesting diol is the salen ligand,[36] which has been used to synthesise many different complexes and in particular the manganese Jacobsen initiators that are highly active in enantioselective alkene epoxidation reactions (Figure **9**).

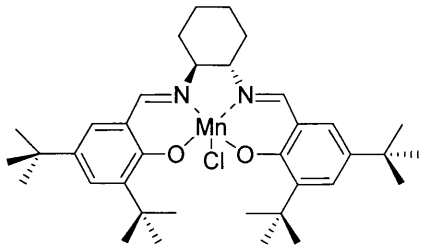
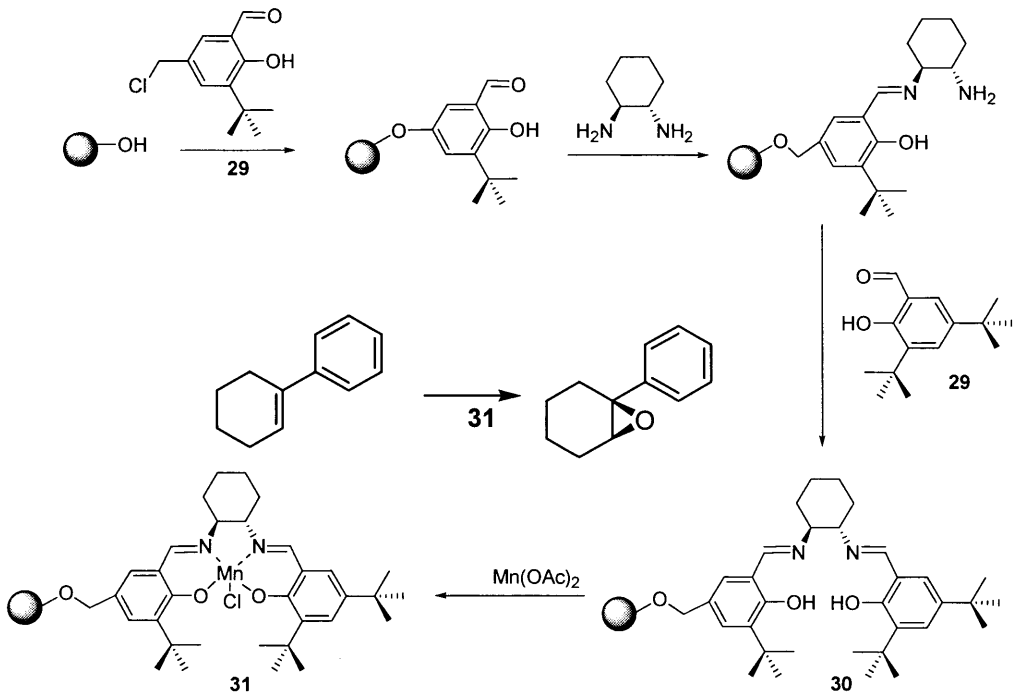


Figure 9 Chiral Mn (III) salen complex

Sherrington *et al.* have reported polymer-supported complexes where a Mn(salen)Cl derivative has been immobilised through one of its aromatic rings to a polystyrene-based support.[37] The choice of strategy adopted by Sherrington was based on four basic principles: the local molecular structure of the metal complex should mimic its homogeneous counterpart; the complex should be attached to the support through a single flexible linkage; a low ligand

loading is preferred to limit dimerisation of the metal complex; and the support should maximise the availability of the active sites.

Sherrington subsequently synthesised this supported Mn-ligand complex in four steps. First was the immobilisation of the aldehyde **29** (Scheme **25**); second condensation with 1,2-diaminohexane was performed; thirdly a second condensation with the salicylaldehyde **29** was carried out; and finally the resulting supported ligand **30** was reacted with $Mn(OAc)_2$ to yield the immobilised salen-supported initiator **31**. The resulting polymer-bound complex initiates the epoxydation of 1-phenylcyclohexene with relatively good enantioselectivity in the range 61-91%.[37]

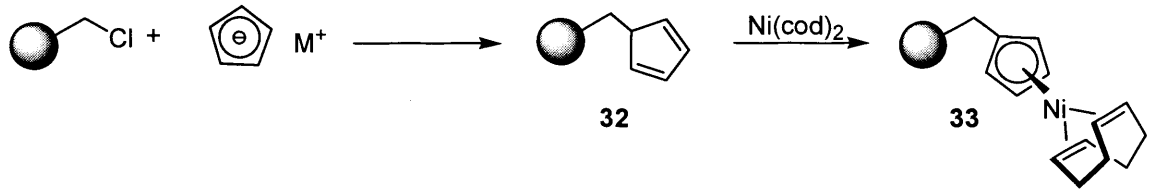


Scheme 25

I.3.4.3 Polymer-supported metallocene complexes

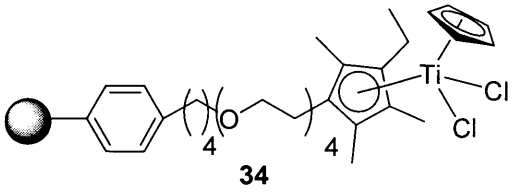
Metallocene complexes are very versatile reagents in the world of catalysis. These systems have been used to achieve a variety of different reactions such as hydrogenation, hydroformylation, and olefin polymerisation, amongst others.[38] As for the supported complexes and ligands discussed above, there has been a drive to produce immobilised analogues of simple metallocenes. The most straightforward way in which this has been done is through the preparation of an anchored cyclopentadiene **32**, which can easily be obtained

starting with a commercial Merrifield resin. This was then reacted with $Ni(cod)_2$ to afford the immobilised initiator **33** (Scheme **26**).[39]



Scheme 26

This particularly supported initiator **33** has shown some activity in ethylene polymerisation. It is interesting to note that the reactivity of the supported initiator is very different from its homogeneous analogue, [NiCp(cod)]. The homogeneous system gives high-density polyethylene, while its immobilised counterpart gives oligomers of ethylene. Using a similar strategy, that is to say, the immobilisation of a cyclopentadiene ligand, Barrett and De Miguel have prepared a supported titanium-based metal complex **34** (Figure **10**). This supported initiator has been shown to exhibit moderate activity in ethylene polymerisation when activated with MAO.[40] The low activity was explained by the lack of swelling of the polymer, something which consequently afforded limited access of ethylene to the metal centers.



34

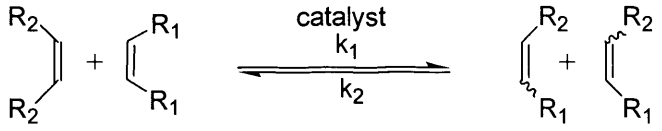
Figure 10 Supported cyclopentadiene titanium complex

The examples of supported ligands described above (section I.3.4) have been used to demonstrate the wide-ranging application and benefits of organic solid supports in catalysis. Today, a particularly important area of catalysis is that of olefin metathesis for both polymerisation (using, for example, Ring Opening Metathesis Polymerisation, ROMP) and for organic ring synthesis (using Ring Closing Metathesis, RCM). The importance of such systems has naturally led to attempts to prepare immobilised initiator systems. The next section will give a brief overview of the various types of olefin metathesis processes that are used widely for synthetic purposes, the initiators employed, and the supported variants that have already been synthesised and described in the literature.

I.4 Olefin metathesis

I.4.1 Introduction

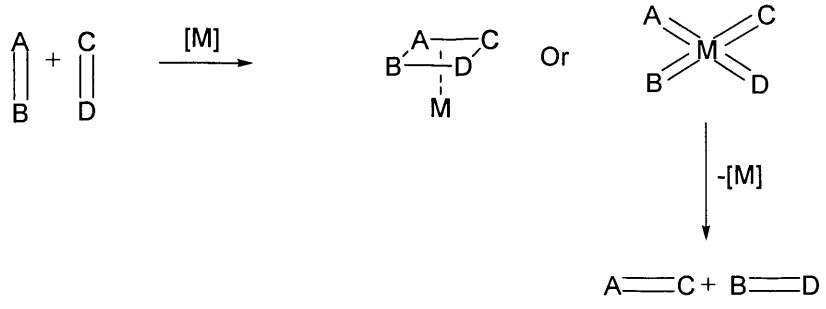
In its simplest form, the olefin metathesis reaction can be regarded as a transition metal-catalysed process in which there is a mutual exchange between two substituted alkenes (Scheme **27**).[41] All possible reactions of this general type are reversible, and can thus lead to the reformation of the starting olefin (so-called *unproductive* metathesis). The course of the overall reaction depends on the relative rates of the forward (k_1) and reverse (k_2) reactions as illustrated (Scheme **27**).



Scheme 27

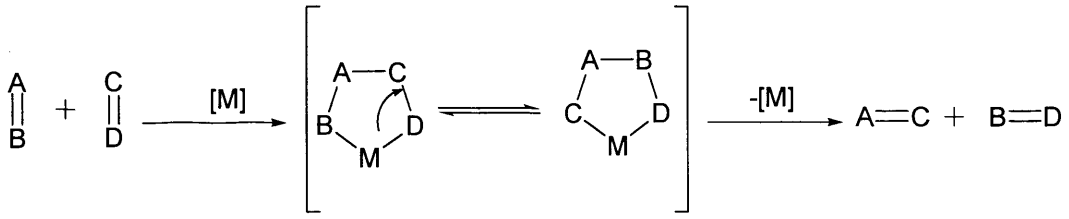
The metathesis reaction is not only capable of forming just one single C=C double bond, but is also capable of polymerisation, macrocyclisation, and C=C bond cleavage. Thus, it is a very important reaction for organic polymer and organometallic chemists alike.

Fundamental studies towards gaining an understanding of this reaction were performed by Calderon *et al.*[42] and Mol *et al.*[43] using labelled olefins and a metal initiator. These revealed that there was an exchange of alkylidene groups between olefins. Up until this point it was thought that the alkene rearrangement proceeded by a bis(alkylidene) metal intermediate in which both olefin ligands were coordinated to the metal center as shown below (Scheme **28**).



Scheme 28

Following this new insight into the mechanism, a second mechanism was proposed in which a metallocyclopentane intermediate was invoked (Scheme **29**):[44]



Scheme 29

These two mechanisms are both pair-wise, that is to say, both olefins coordinate to the metal simultaneously. Subsequently, detailed studies involving unsymmetrical olefins and the isolation of a metallacylobutene have shown that olefin metathesis is in fact not a pair-wise process.[44]

A better understanding of the metathesis process came about following the work of Fisher who prepared the first sTable metal carbene in 1964 (a so-called Fisher carbene), which was later followed by the synthesis by Schrock of another type of sTable metal carbene (a so-called Schrock carbene) as illustrated in Figure **11**.[45,46,47]

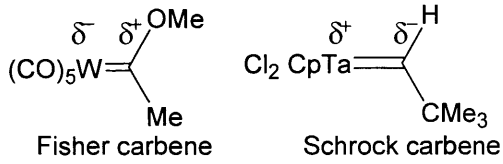


Figure 11 Metal carbene: Fisher, and Schrock Carbene.

Fisher-type carbenes are generally found with low oxidation state, late-transition metals, having π-acceptor ligands (*e.g.* CO) and with π donor substituents on the carbene carbon. Thus, the multiply bonded carbon is therefore electrophilic in nature. In contrast, Schrock carbenes are formed with higher-oxidation state, early-transition metals, having non π-acceptor ligands (*e.g.* Cl, alkyl, Cp) and no π–donor substituents on the carbene carbon. This second type of carbene is thus nucleophilic in nature. The relative energies of the M (d_π) orbitals and the C (p_z) orbitals control the electrophilic or the nucleophilic character of the carbene. Hence, if the M (d_π) levels are the lower in energy than the frontier orbirtals of the carbon, a Fisher carbene will result. If the M (d_π) levels are the higher in energy, a Schrock carbene will result (Figure **12**).

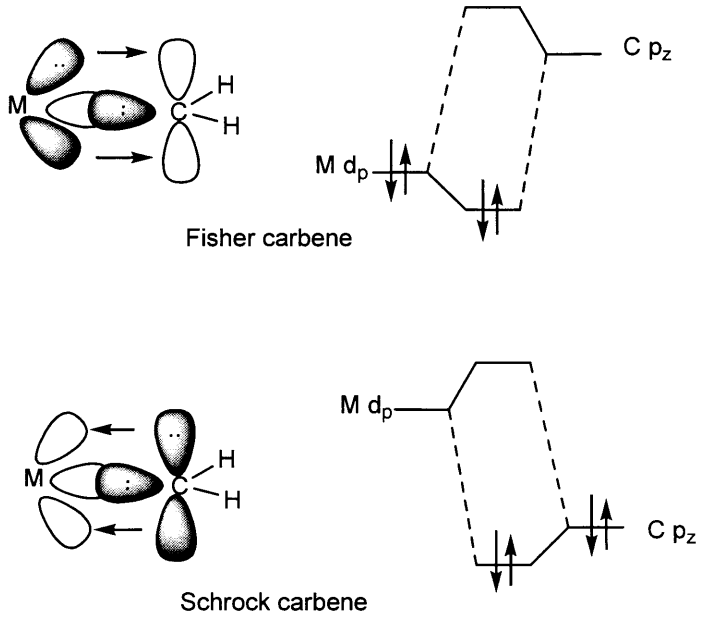
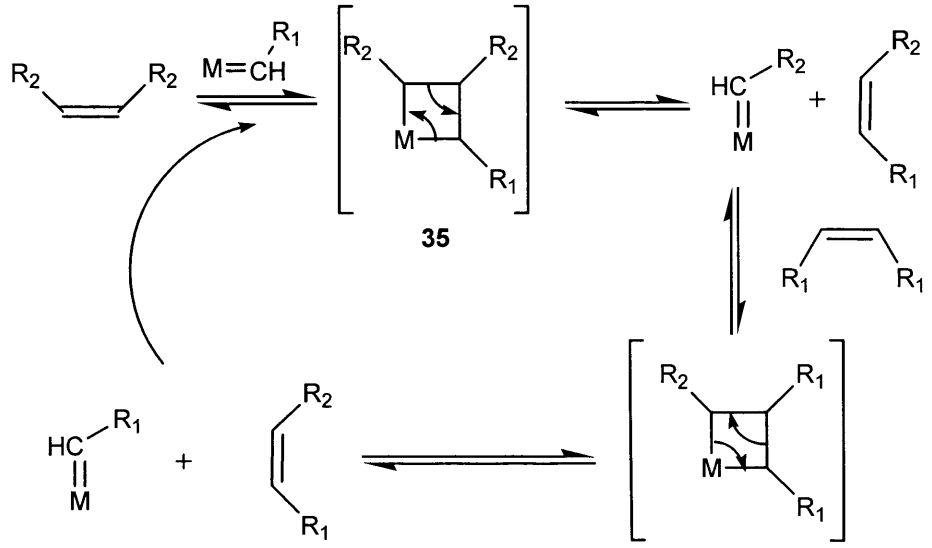


Figure 12 A comparaison of the frontier orbitals of Fisher, and Schrock carbenes

The π–bond in Fisher-type carbenes is best described as resulting from a M (d_π) to C(p_z) back donation. The electron pair remains largely on the metal because the M(d_π) orbital is considerably more sTable than the C(p_z). For Schrock-type carbenes the π bond is polarized ($M^{\delta+}$-$C^{\delta-}$) because the M(d_π) level lies above the Cp_z level.

Once metal carbene complexes had been prepared and isolated and their chemistry probed, the way was open to further investigate metal–catalysed olefin metathesis process in detail. The challenge was taken up by Chauvin *et al.* who used labelling studies, to show, that the metathesis reaction really involved a non-pair-wise mechanism.[48] This type of process is described in Scheme **30**.



Scheme 30

Chauvin proposed that the mechanism proceeds by the formation of a metallocyclobutane intermediate, **35**, formed *via* a [2+2] cycloaddition and that the subsequent olefin metathesis works by a similar [2+2] cycloaddition both between the C=C bond of an olefin and the metal-carbon double bond of a carbene complex, following a ring-opening of **35**. The conformation of the olefin formed is not stereocontrolled with the conformation depending on the nature of the starting material, the nature of the final product and the geometry of the initiator. This "Chauvin" mechanism is still valid and widely accepted today as being the true mechanism for olefin metathesis.

I.4.2 Initiators for olefin metathesis reactions

There are a variety of initiators capable of inducing olefin metathesis that have been developed and can operate under both heterogeneous and homogeneous conditions, a brief overview of some of these systems is given below.

1.4.2.1 Heterogeneous olefin metathesis initiators

In the heterogeneous systems, many of the initiators which have been discovered to date, are based on metal oxides and include: MoO_3/Al_2O_3, $WO_3/SiO_2/Al_2O_3$, Re_2O_7/Al_2O_3. These initiators often only work at very high temperatures, and are hence required to be very sTable and are used mainly (section 1.1) for the large scale synthesis of "simple" bulk products. As indicated before, the silica and alumina interact with the transition metal component stabilising the catalytically reactive species in metathesis. A nice example of the stabilising effect of these types of support materials is given by Weiss who supported a tungsten alkylidyne complex, $W(\equiv CCMe_3)(OCMe_3)_3$, on silica to produce an active metathesis initiator system.[49] Notably the soluble tungsten precursor complex is inactive for olefin metathesis in the absence of SiO_2, but when it reacts with the silica it becomes active, probably as a result of the following reaction:

$$W(\equiv CCMe_3)(OCMe_3)_3 + 2SiOH \longrightarrow (SiO)_2W(\equiv CCMe_3)(OCMe_3) + 2Me_3COH.$$

The surface-bound carbyne is electronically unsaturated and the electrophilic character of the tungsten is increased. As a result, the immobilised alkylidyne shows good activity, but the selectivity of this kind of initiator is very poor.

I.4.2.2 Homogeneous olefin metathesis initiators

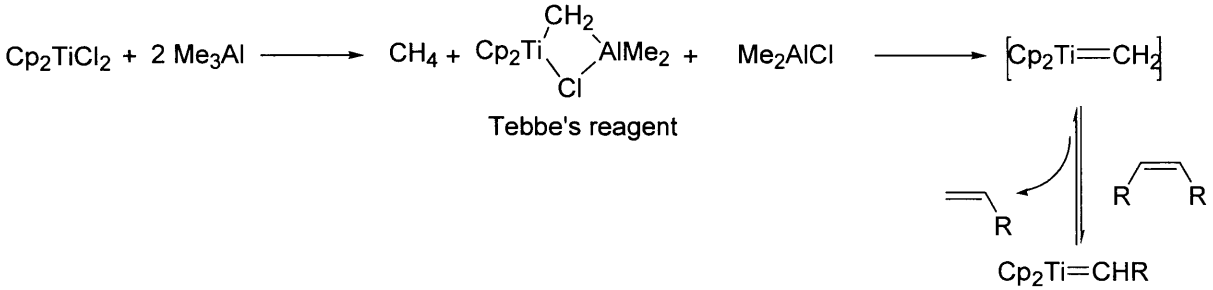
The first homogeneous initiators to be used for olefin metathesis were formed from a combination of a transition metal salt (*e.g.* WCl_6, $MoCl_5$, $ReCl_5$, ...) with a main group organometallic compound like $RAlCl_2$, SnR_4, *etc.*, to give a multi-component homogenous initiator system of the type: WCl_6 / EtOH / $EtAlCl_2$, WCl_6 / Et_2O / SnR_4, $MoCl_2(NO)_2(PR_3)_2$ / $RAlCl_2$, and $ReCl_5$ / Al_2O_3, *etc.* The introduction of a small amount of an oxygen-containing compound has been shown to increase the reactivity although the role of this additional component is far from being well understood.[44] It must be noted that although these initiators are soluble, the exact nature of the catalytically active species remains largely unclear. Hence, there still remains the problem with all these initiators that they are largely poorly defined and there is always the possibility that only a part of the transition metal component is directly involved in the catalytic process, something which can severely complicate their use in a specific reaction.

In the synthesis of natural products or drugs *via* RCM for example, the use of metathesis became more viable with the development of sTable metal alkylidene complexes with a well-defined molecular structure. The majority of these species contain a discrete metal-carbon double bond or alkylidene, formally a metal-bound carbene, as discussed in section I.4.1. Thus, the next section will outline these types of initiator.

I.4.2.3 Metal-bound carbene initiators

I.4.2.3.1 Tebbe's reagent

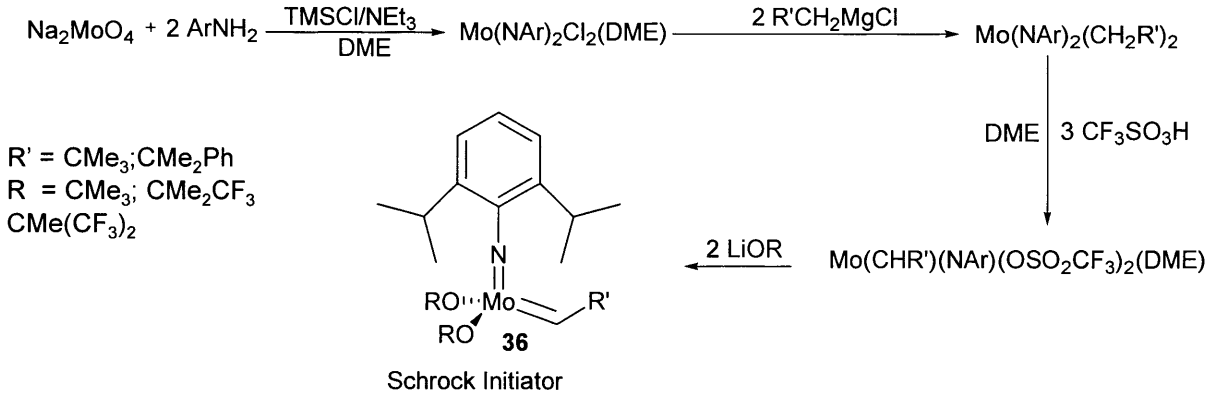
One of the first well-defined olefin metathesis initiators was the so-called Tebbe's reagent, prepared from Cp_2TiCl_2 by reaction with two equivalents of Me_3Al as shown in Scheme **31**.[50] Tebbe's reagent was employed for olefin metathesis (*e.g.* by Grubbs for the synthesis of natural products[51]), but the use of this initiator is limited since a strained olefin is required to execute the initial ring opening step.



Scheme 31

I.4.2.3.2 Schrock's initiator

Subsequently, other well-defined metal carbenes capable of supporting olefin metathesis have been developed, one of the first being the oxo-alkylidene complexes of molybdenum and tungsten, *e.g.* pseudo-octahedral $W(O)(CH\text{-}^tBu)(PR_3)Cl_2$.[52] However, these types of initiator were very unsTable. Thus, in a development of this work, related imido-alkylidene complexes were developed such as $W(NR)(CH\text{-}^tBu)(O^tBu)_2$. The imido ligands were introduced in order to block bimolecular decomposition that could occur with the oxo-alkylidene complexes and with a view to preventing dimerisation; the imido substituent R was generally 2,6-diisopropylphenyl, which is extremely sterically demanding. In addition, bulky alkoxides where introduced to further improve the stability.[53] Finally, the metal was changed to molybdenum, which was found to give more reactive complexes than the earlier tungsten versions. This led to the development of the now well-known and used alkylidene complex **36** namely, the so-called "Schrock initiator," which can be synthesized as shown in Scheme **32**.[54]

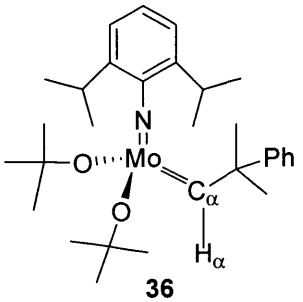


Scheme 32

It is important to note that this type of molybdenum Schrock-type initiator is dependant upon the presence of bulky substituants for its stability, largely in order to block intermolecular dimerisation of the Mo=C bond.[53] The bulky imido group also lends a degree of electronic flexibility to the system, due to its potential to act as either a two- or a four-electron donor ligand, in addition to providing steric bulk.

Schrock initiator **36** adopts a pseudo-tetrahedral structure (Figure **13**) in which Mo, N C_α and H_α all lie in a plane and in which the *tert*-butyl groups point toward the imido-ligands. The alkoxide groups provide a ready means of tuning the behaviour of the initiator. For example, the introduction of electro-attractive groups such as $OCMe_2CF_3$, $OCMe(CF_3)_2$, and OCF_3 makes the metal more electrophilic and the initiator more reactive for metathesis.

Depending on the nature of the alkoxide ligands, the Schrock initiator has been observed to adopt two different rotameric structures, namely the *syn* and *anti* forms which differ in the orientation of the CHR' unit with respect to the imido moiety (Scheme **33**).

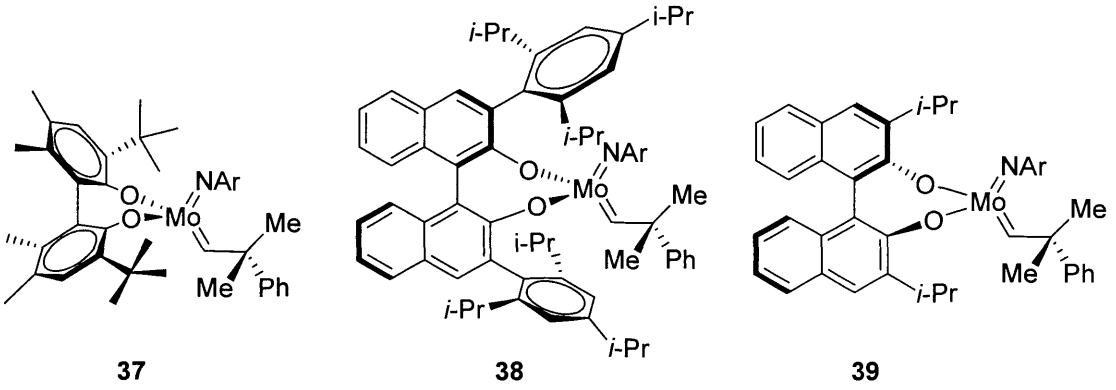


36

Figure 13 Schrock Initiator

Scheme 33

More recently, a number of variants of the Schrock initiator have been prepared that bear chiral ligands with a view to performing asymmetric catalytic olefin metathesis reactions (Figure **14**).[55,56,57] The three related systems **37-39** all employ chelating dialkoxide ligands, in part to help to retain the ligand (and hence the chiral elements) in the metal's coordination sphere (chelate effect), and also as a means of introducing the desired chiral element through an axially-chiral hindered biaryl.

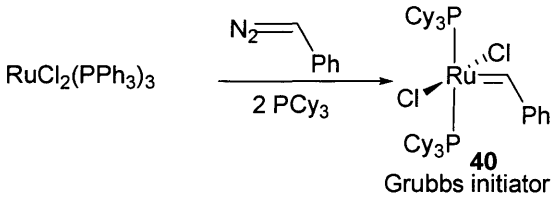


37 **38** **39**

Figure 14 Chiral variants of the Schrock-type initiators

I.4.2.3.3 Grubbs' initiator

In 1990 Grubbs discovered another family of metal carbene complexes **40** based on ruthenium that underwent olefin metathesis.[58,59] There are a number of significant benefits of these ruthenium complexes over the Schrock systems including their air/moisture stability and their comparatively facile synthesis (Scheme **34**).



Scheme 34

It has been shown that the metathesis activity of the Grubbs' initiator depends significantly upon the nature of the phosphine ligands.[58] For example, significantly better metathesis activity is observed on employing tricyclohexylphosphine than with triphenylphosphine. This can be explained in terms of the relative cone angles of the two different ligands. Tricyclohexylphosphine has a bigger cone angle (170°) than triphenylphosphine (145°), which accelerates the dissociation of the former from the metal centre, a step that is essential during the catalysis process.

The stability of this type of complex **40** is quite unusual since the carbene is not stabilized by any heteroatom. Indeed the behaviour of this metal bound carbene must be described as intermediate between that of a Fischer and a Schrock system since the ruthenium centre is generally regarded as being in the +II oxidation state. This makes the carbene a formally neutral fragment. Indeed, it has been shown that these systems are very reactive towards a variety of olefins, but are fairly inactive towards water and oxygen, and tolerate a variety of functional groups that include carboxylic acid, alcohols, aldehyde ether silyl ethers and acetal esters. Grubbs has even demonstrated that metathesis reactions can be done using such solvents as methanol and water, with judicious choice of ligands, like water-soluble phosphines.[60] In all these examples, the actual reactive species is thought to be a 14-electron metal complex of the type $[Ru(CHR)(Cl)_2(PCy_3)]$ although it has not been observed directly.

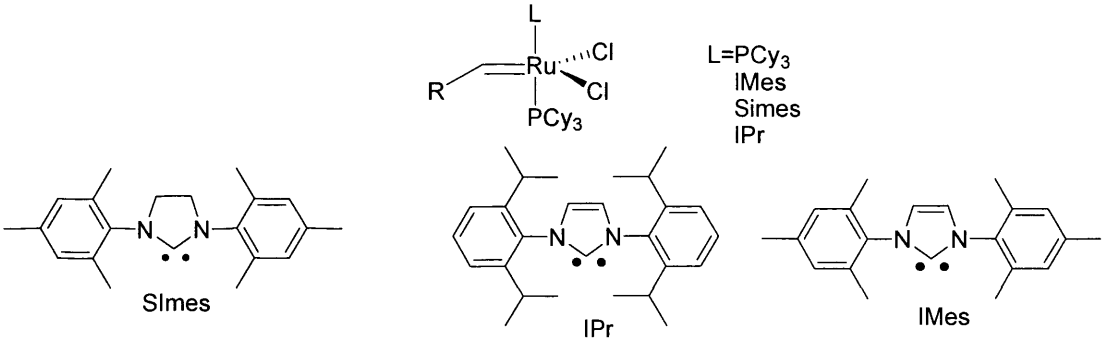


Figure 15 Carbene-based ligands: variations of Grubbs' initiator

A significant amount of work has been done to replace one of the phosphines by a stabilized N-heterocyclic carbene (NHC) (Figure **15**).[61] The NHC does not take place in the

metathesis reaction, behaving just as a very bulky ligand, with a strong donor ability, features which therefore protect the intermediate species from decomposing in a bimolecular fashion.[62] Since heterocyclic carbenes are such a strong σ-donors,[63] its high *trans*-influence slows the reassociation of the phosphine to the metal complex and therefore increases the availability of the 14-electron species and boosts the catalytic reaction.

More recently, Hoveyda has made a further variant of the Grubbs' initiator by replacing the remaining phosphine, while retaining an NHC ligand, by an ether donor that is itself linked to the carbene carbon *via* an aryl unit (Figure **16**).[64] This initiator is highly active yet remarkably sTable and can be recovered by chromatography, effectively making it recyclable.

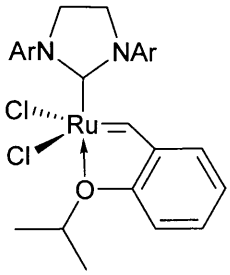


Figure 16 Hoveyda initiator

I.4.3 Olefin Metathesis processes

Now that the most efficient initiators for metathesis have been outlined, some description of their potential metathesis reactivity will be described in more detail. There are five sub-metathesis processes that are extremely useful in synthesis. These are:

ROMP: Ring Opening Metathesis Polymerisation

ADMET: Acyclic Diene METathesis

RCM: Ring Closing Metathesis

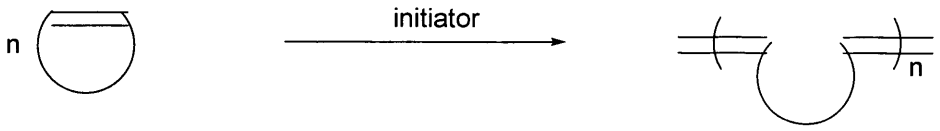
CM: Cross Metathesis

ROM: Ring Opening cross Metathesis

The following section will give just an example of each type of process using both a Schrock and Grubbs initiators rather than an extensive review.

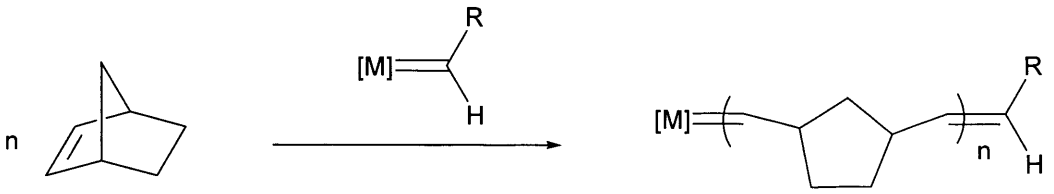
I.4.3.1 ROMP:

The ROMP (Ring Opening Metathesis Polymerisation) process, as expected from its name, achieves the formation of a polymer by ring-opening a cyclic monomer (Scheme **35**):



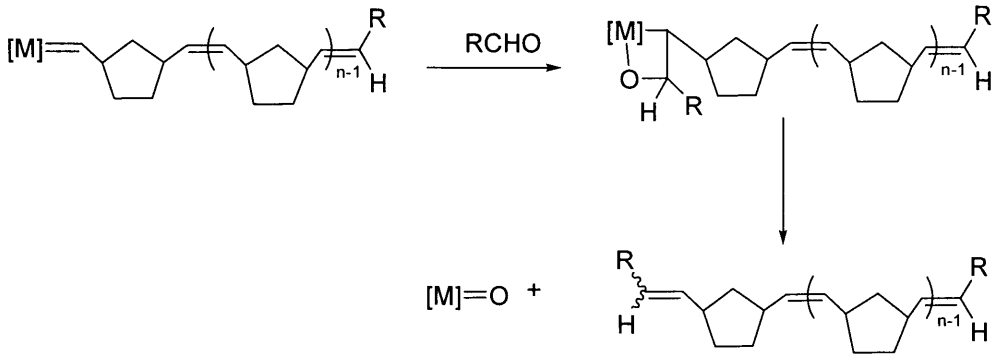
Scheme 35

Many of the studies concerning ring opening metathesis have employed norbornene or norbornadiene as the monomer, because these substrates usually react irreversibly with a metal alkylidene. Formation of poly-norbornene (Scheme **36**) is often used as the bench mark test reaction for ROMP activity.[65]



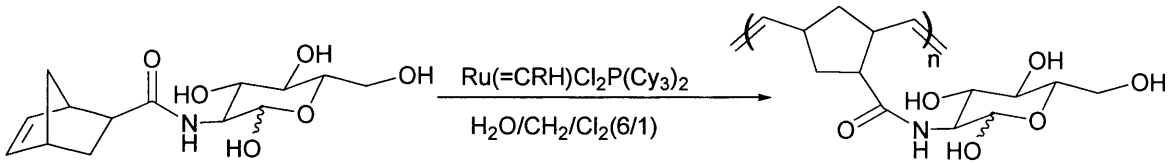
Scheme 36

The development of sTable metal alkylidenes that are more reactive than the classical metal salts (WCl_6, $MoCl_5$, $ReCl_5$) allows for a "living polymerisation" with no accompanying chain termination process.[66] Here, the rate of polymerisation (k_p) is greater than the rate of termination (k_t), that is to say $k_p >>> k_t$, consequently, the metal remains on the polymer . This creates a "living" process, as a metal alkylidene is always present at the end of the polymer chain ready to undergo reaction with additional monomer. This can be used to give very precise control over polymer molecular weight and also allows for the preparation of block co-polymers. The alkylidene is usually cleaved from the polymer through addition of an aldehyde in a Wittig-like process; an oxygen atom transfer occurs to the initiator forming a metal oxo species (Scheme **37**).[67]



Scheme 37

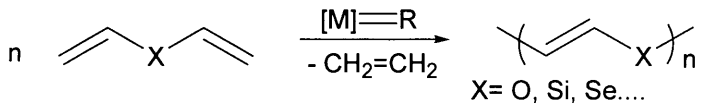
The following example shows the ROMP of an unprotected sugar-substituted norbornene (Scheme **38**) by the Grubbs' initiator.[68] This highlights the good tolerance of this type of system towards a variety of functional groups and their ability to achieve the desired metathesis reactions in water.



Scheme 38

I.4.3.2 ADMET

In its simplest form the ADMET (Acyclic Diene METathesis) reaction converts an α,ω–acyclic diene into the corresponding unsaturated linear polymer with elimination of a small molecule (*e.g.* ethylene, Scheme **39**). Terminal dienes are the preferred monomers in the ADMET reaction due to both entropic and steric considerations.[52] ADMET is a versatile method of preparing a variety of hydrocarbon and heteroatom-containing polymers that also have unsaturation in their backbone.[69]



Scheme 39

I.4.3.3 RCM

Ring closing metathesis (RCM) is a very useful tool for the preparation of a range of unsaturated rings and heterocycles, making it of wide utility for the organic chemist. The overall mechanism of RCM is usually believed to proceed *via* an alternating series of formal [2+2] cyclo-addition/cyclo-reversion steps according to the more general Chauvin mechanism (Figure **17**).[48] The driving force for the reaction is the gain in entropy resulting from the loss of ethene. Thus, it is clear to see that there will always be a competition between RCM and ADMET (outlined above). Which of these two reactions occurs depends on the size of the ring, the dilution of the reaction medium, the starting material, and the nature of the initiator; high dilution favours the ADMET reaction.[44]

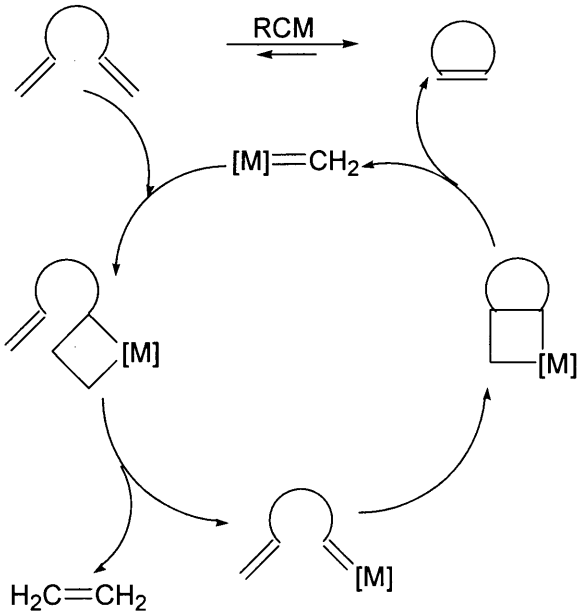
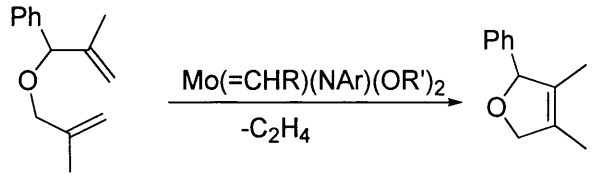
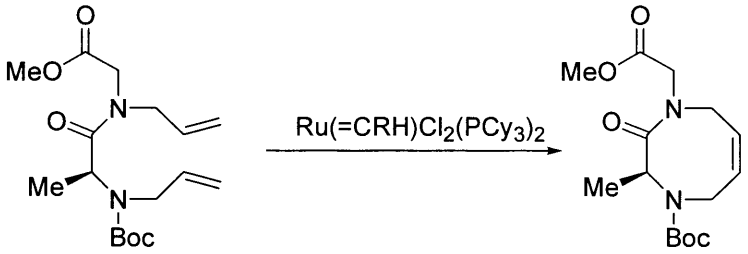


Figure 17 General mechanism for RCM reactions

It is now very well established that the RCM reaction (catalysed by Schrock and Grubbs' initiators) can be used for the preparation of a range of heterocycles, affording especially ready access to medium and large size rings (*e.g.* Schemes **40** and **41**).[70, 71]



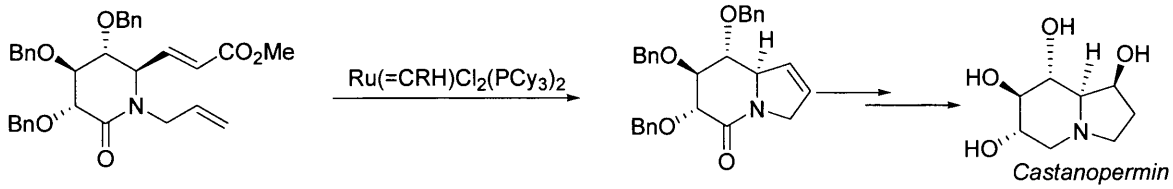
Scheme 40



Scheme 41

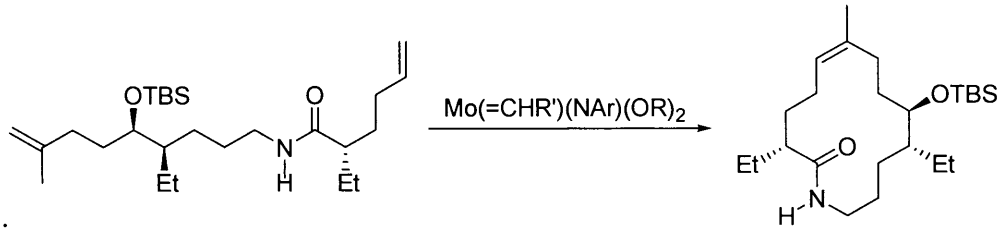
In general, the successful formation of an unsaturated cyclic compound depends on the size of the ring and on the conformation of the double bond formed. This conformation can be controlled by the choice of the initiator.[41]

The RCM reaction has proven to be a powerful tool for the synthesis of natural products as illustrated by the preparation of Castanopermin (Scheme **42**), which belongs to the family of polyhydroxylated alkaloids, *aza* analogues of saccharides.[72]



Scheme 42

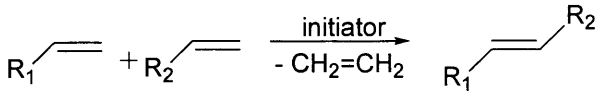
Another example of the use of the RCM reaction is the enantioselective total synthesis of an antifungal agent by Hoveyda *et al.* (Scheme **43**),[52] which is achieved with a Schrock-type initiator.



Scheme 43

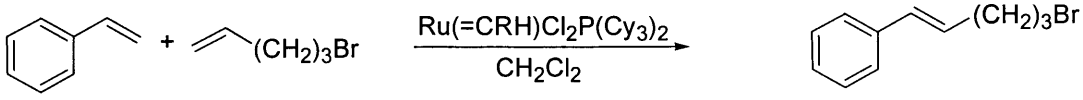
I.4.3.4 Cross Metathesis

This reaction achieves a coupling between two different olefins to afford a more substituted olefinic product (Scheme **44**). Unfortunately, this transformation is problematic since there is the possibility of forming homo-product olefins (R_1R_1, R_2R_2) because the stereoselectivity is hard to control.[73] The conformation of the new double bond depends on the starting material, the nature of the initiator, and on any steric effects during the cross coupling.



Scheme 44

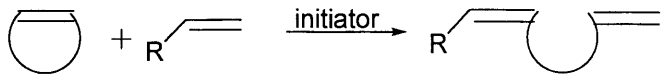
An example of cross metathesis is the synthesis of a substituted styrene performed by Crowe, as outlined in Scheme **45**.[74]



Scheme 45

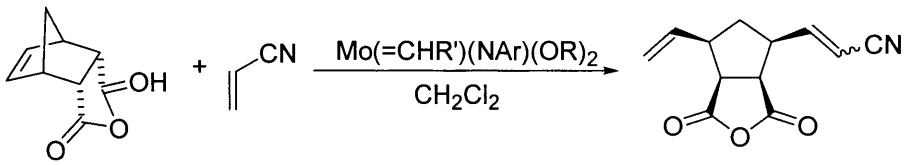
I.4.3.5 ROM

The ring opening metathesis reaction (ROM) (Scheme **46**) is a combination of the ROMP and cross metathesis reactions and is an economically atom efficient process, where no ethylene is lost during the reaction.



Scheme 46

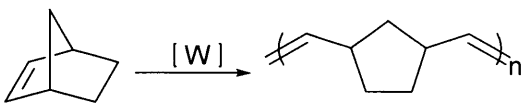
As in cross metathesis, there is no great selectivity in the formation of the double bond, it depends on steric effects, the initiator, and the starting materials. Nevertheless, it is an interesting reaction for the conversion of well-defined cyclic compounds into their acyclic analogues as shown in Scheme **47**.[75]



Scheme 47

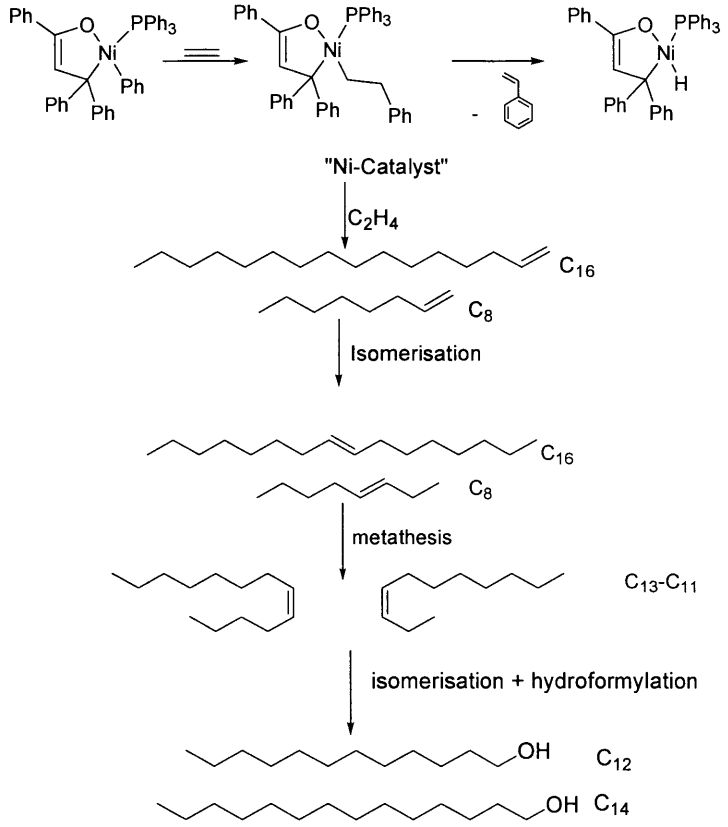
I.4.4 Industrial applications of metathesis[44]

The examples given in sections I.4.3 have demonstrated the use of the metathesis reactions for the preparation of fine chemicals such as natural products and drugs. Additionally, these metathesis reactions have also found some larger-scale applications. On an industrial scale, the most frequently employed metathesis reaction is based on ROMP, one of the most important uses being the preparation of a polymer derived from norbornene (Scheme **48**).[76] This material is produced in very large quantities (over 45000 tons a year) and is sold as a moulding powder under the name Norsorex and was developed by CdF chimie of France. The vulcanised product has important applications, for example in the manufacture of engine mountings and flexible couplings.



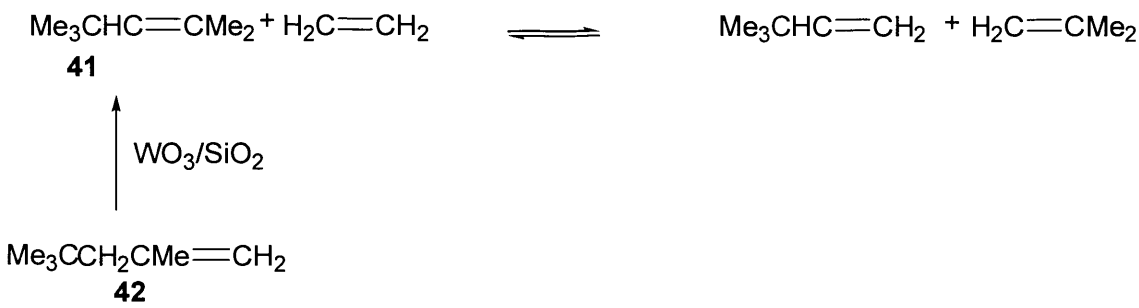
Scheme 48

Olefin metathesis also plays a crucial part in the Shell Higher Olefins Process, (SHOP) (Scheme **49**). This consists of oligomerization of ethylene, to form a range of terminal α-olefins. Subsequently, these olefins are isomerised to give the corresponding internal olefins. Next, an alumina-supported cobalt molybdate is used to metathesise the internal olefins, something that is followed by a joint isomerisation and hydroformylation step. The resulting products (long chain alcohols) are used as detergents. These types of material are produced on a scale of *ca.* 590,000 tons per year.[44]



Scheme 49

Finally, another example of the use of metathesis in industry is in the production of neohexene (3,3-dimethylbut-1-ene), an important intermediate in the synthesis of musk perfume. The process is based on the use of the dimer of isobutene, which consists of a mixture of 2,4,4-trimethylpent-2-ene **41** and 2,4,4-trimethylpent-1-ene **42**. Compound **42** is converted into **41** with an initiator. Then cross-metathesis is undertaken with **41** and ethene with a 1:3 initiator mixture of WO_3/SiO_2 and MgO as shown in Scheme **50**.[77]



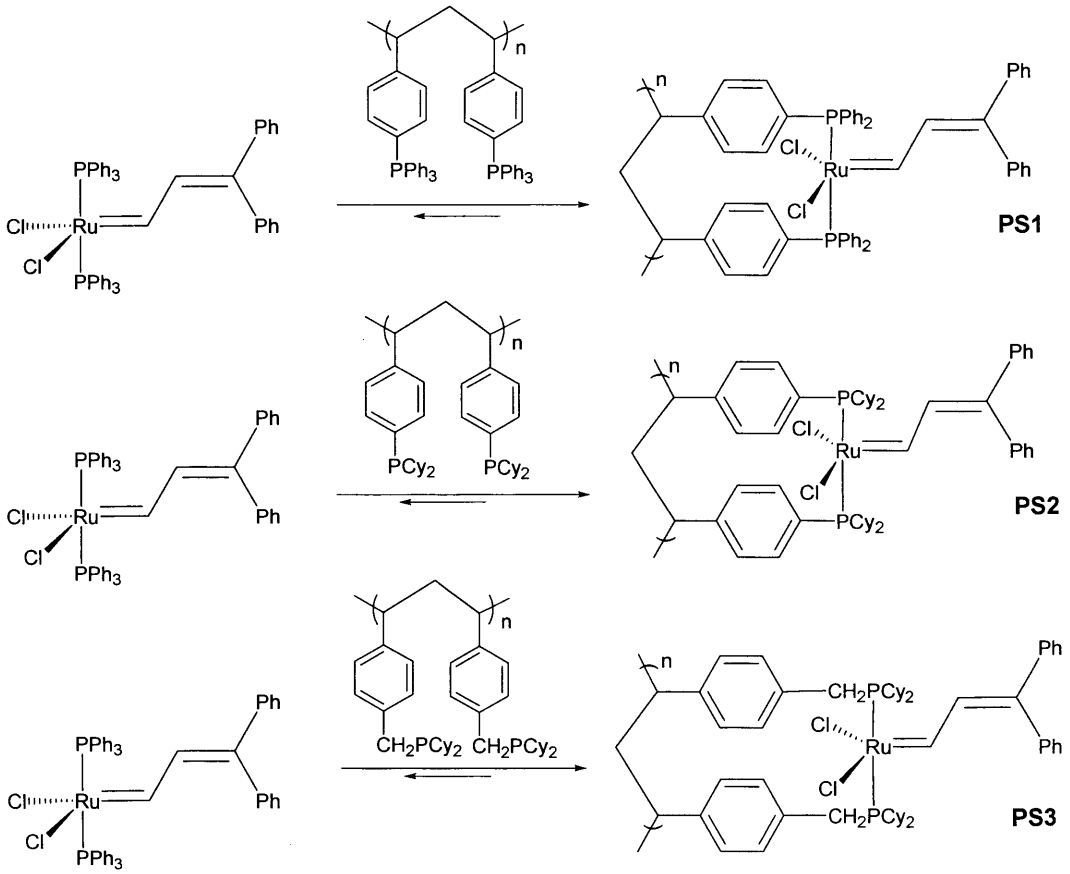
Scheme 50

I.5 Supported well-defined olefin metathesis initiators

As illustrated in sections I.4.3 the metathesis reaction is a very important tool for chemists. The success of these transformations in synthesis can be attributed to the existence of well-defined and well-established homogeneous initiators such as those described by Grubbs and Schrock. One limiting factor in the proliferation of such initiators is their often demanding synthesis and, especially for the Schrock system, their air and moisture sensitivity. Therefore, the immobilisation of such systems would be very interesting, potentially allowing re-use and easy work-up. However, by the nature of these very reactive species, any matrix used for the heterogenisation would need to be a well-defined, inert support. Thus, those derived from organic polymers are very attractive.

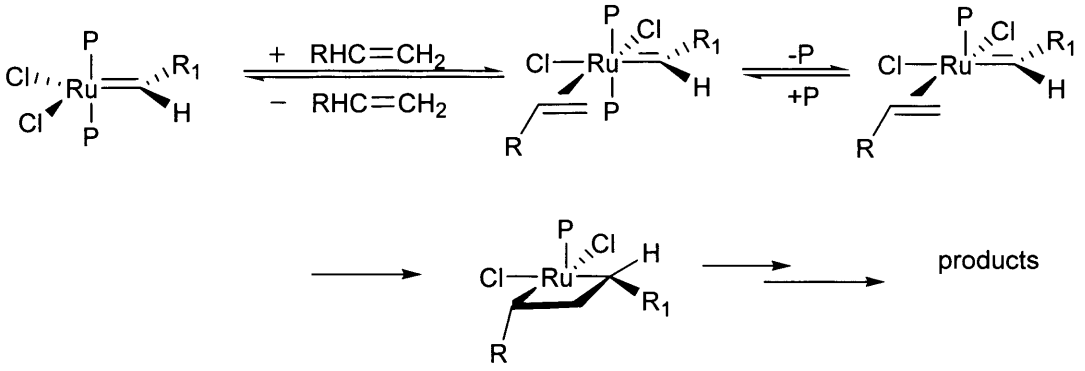
I.5.1 Supported Grubbs' initiator using an organic support

The first attempts to support this type of complex were made by Grubbs *et al.*[78] He supported a phosphine ligand on a Merrifield resin, then *via* ligand exchange with the soluble initiator, obtained a polymer-bound version (Scheme **51**).



Scheme 51

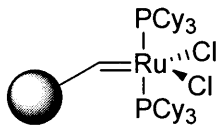
According to Grubbs, these initiators (**PS1**, **PS2**, **PS3**, Scheme **51**) show similar activities to their soluble analogues, and have been shown to initiate similar types of metathesis reactions with related substrates.[78] However, in contrast to conventional homogeneous systems, the rates of the reactions are very slow. Grubbs has explained this observation in three ways. For the first system (**PS1**), there was an incomplete substitution of the phosphine, because the ligand exchange is an equilibrium process. This was confirmed by the observation of the mixed-phosphine initiator $Cl_2(PolyPPh_2)(PPh_3)Ru{=}CH\text{-}CH{=}CH_2$ in the soluble phase.[78] Grubbs indicated that a large percentage of the new ruthenium complexes can potentially be mixed-phosphine species, which are very slow initiators. Secondly, the diffusion of the products is not as good through the cavities of the cross-linked polystyrene, as it would be in a solution environment. According to Grubbs, there were similar problems observed for supported rhodium hydrogenation initiators.[78] Finally, there is a phosphine chelation effect, something that is explained as follows. The mechanism of olefin metathesis (Scheme **52**) is dissociative in nature and thus the presence of a local high concentration of phosphine is going to slow down the rate of the reaction.



Scheme 52

High phosphine concentrations are inherent in the type of support package employed by Grubbs, as formally the phosphine-functionalised polystyrene resembles a bidentate chelating phosphine. Despite these disadvantages, the resulting immobilised initiator has a better lifetime than its homogeneous counterpart and can be re-used.

Barrett *et al.*[79] have reported another method for the immobilization of a Grubbs-type initiator *via* the reactive carbene functionality as outlined in Figure **18**:



43

Figure 18 Grubbs-type initiator 42 immobilised *via* its alkylidene function

During the metathesis reaction, the initiator **43** will be cleaved from the support as a result of the all important [2+2] cycloadddition reaction occurring at the Ru=C unit as a matter of course in the metathesis process. Thus, during the reaction the system will once again become a homogeneous initiator, however it is hoped that at the end of the reaction the initiator will become re-attached to the support, something that has been called the "boomerang effect" (Figure **19**). Perhaps as a consequence of this process, the initiator was unfortunately shown to leach from the support. It was demonstrated that this supported system can be reused only three times before significant loss of activity is evident after the third cycle.

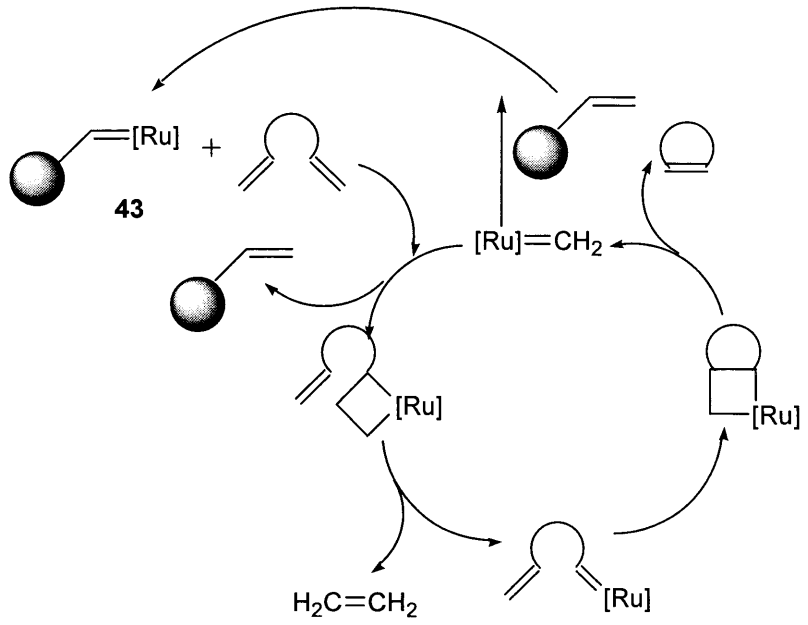


Figure 19 Supported Grubbs' initiator using the "Boomerang" effect

Nolan has improved this method of heterogenisation by using a macroporous resin in the place of the standard Merrifield resin (Figure **20** Scheme **53**).[80] The main advantage of this type of polymer is that pre-swelling is not necessary, to ensure the accessibility of pore sites.

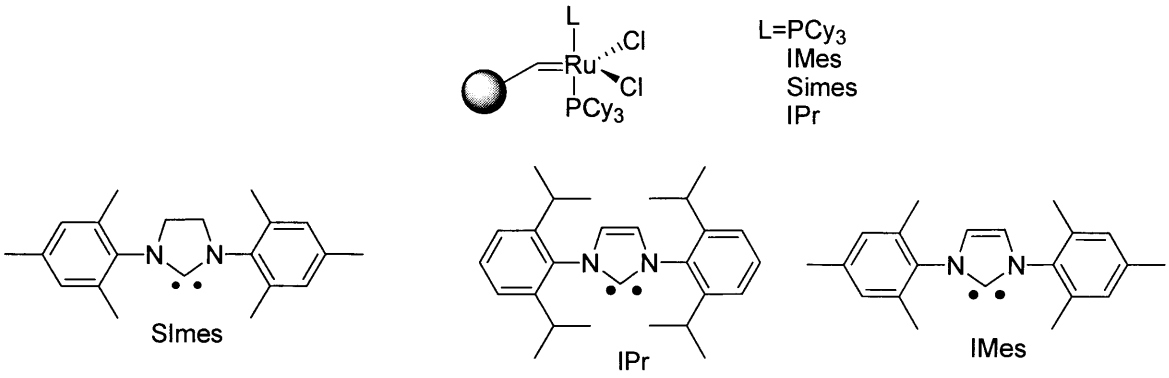
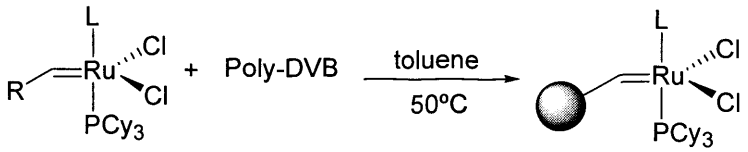


Figure 20 Various Grubbs-type initiators immobilised *via* their alkylidene function

Here, the desired supported initiator was prepared by simply mixing the polymer (cross-linked polymer with 50% toluene as porogen) with the starting Grubbs' initiator and heating at 50°C for one hour. This induced a metathesis reaction between the ruthenium complex initiator, and the polymer, to afford in a straightforward manner, the supported initiator (Scheme **53**).



44

R = Ph, CHCH=C(Me)$_2$

Scheme 53

The loading of this supported system is linked directly to the activity of the starting homogeneous initiator; the more reactive the complex is in this first metathesis step, the greater the loading. This approach is quite successful; the supported reagent exhibits the same reactivity and activity in simple ring closing metathesis reactions as its homogeneous counterpart.[80] The degree of leaching of the initiator is low (compared to the Barrett system), this alternative supported system remaining active even after four use cycles without significant loss of activity.

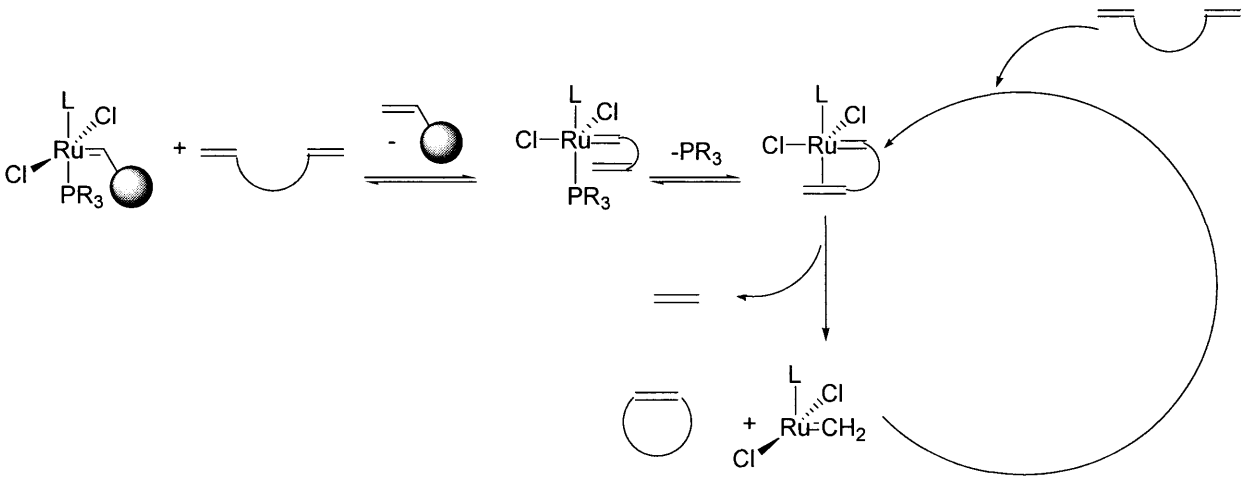
A further beneficial modification described by Nolan involved the addition of CuCl to the reaction, which acts as a phosphine sponge.[81] This led to an improvement in the reactivity, but the recyclability of the initiator was not very good as the phosphine can not rebind to the metal center. As a result, the active ruthenium species decomposed quickly.

In contrast to simple olefinic substrates, the ring closing metathesis activity of hindered olefins, especially those containing potential donor atoms like oxygen, was poor or even impossible for supported initiator **44**. Nolan and co-workers explained these observations on the existence of a competing coordination mode to the "free" initiator by oxygen, forming a sTable entity less reactive than the initial ruthenium catalyst which stayed in solution rather than re-binding to the polymer resin (Figure **21**).[80] Therefore this competing binding reduced the active sites in the polymer supported-initiator leading to a decrease in activity in consequent cycles.

Figure 21 Competing coordination between oxygen and the ruthenium metal centre

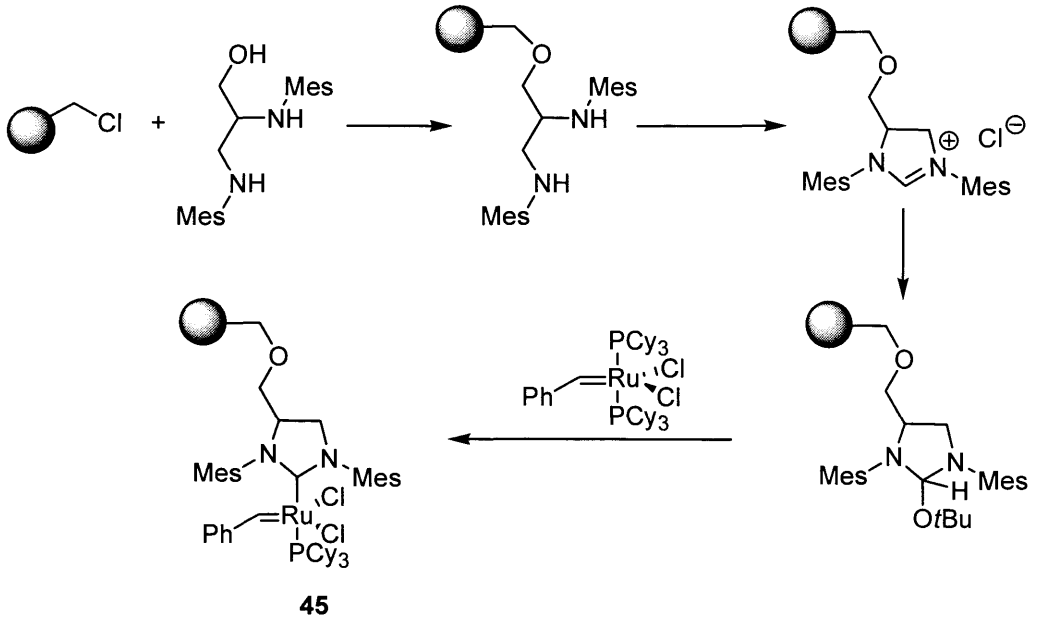
A better understanding of the workings of this type of catalysis was afforded by Nolan[80] who outlined a mechanism that is based on the dissociative phosphine mechanism proposed by Grubbs and the "boomerang " mechanism proposed by Barrett, as shown in Scheme **54**. The initiator became a homogeneous species when reacted with olefin, and

became an active initiator by the loss of one phosphine. The recovery of the active complex is possible when reassociated with the phosphine and is recaptured on the support by the "boomerang effect".



Scheme 54

In an alternative approach, Blechert and co-workers immobilized the Grubbs' initiator on Merrifield resin using a different tether.[82] They chose to prepare a polymer-grafted N-heterocyclic carbene (NHC) ligand and subsequently used this to coordinate to a ruthenium complex as outlined in Scheme **55**.

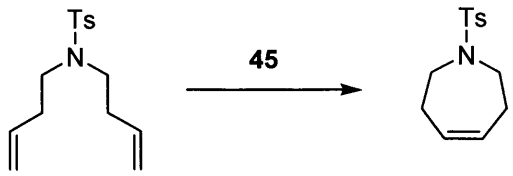


45

Scheme 55

Blechert's supported initiator has been employed in various RCM, and cross-coupling reactions.[82] The immobilised system demonstrated similar performance to that of an analogous

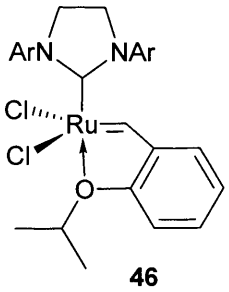
homogeneous Grubbs' system and, in cross coupling reactions involving alkenes and alkynes, the anchored variant was found to out perform its homogeneous counterpart. Initial testing of the efficiency of the initiator recycling has been done using a simple RCM reaction (Scheme **56**).



Scheme 56

Complete conversion of the diene substrate for each of four sequential runs was achieved, but the initiator's turn over frequency dropped dramatically: 1.5h is needed to complete the first run, then 4h for the second, 12h for the third, and finally 48h for the fourth. It is interesting to note that the supported ligand is obtained only in 4 steps, and that the NHC species acts as a spacer "insulating" the active metal component from the polymer matrix, something that can possibly explain the relatively good performance of this system.

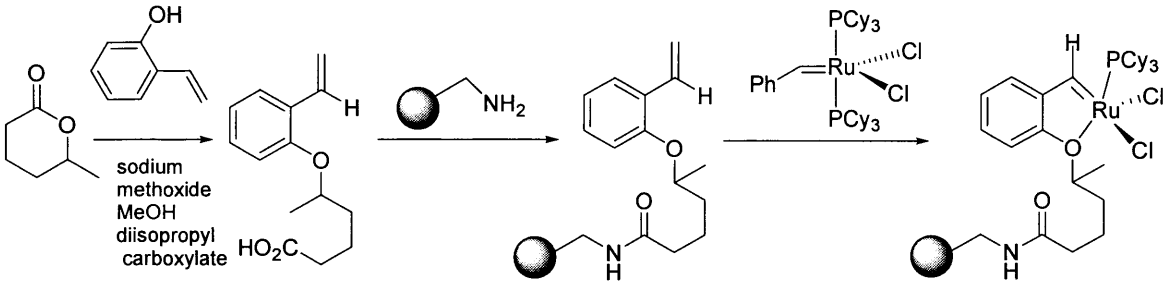
Similar heterogenisation routes have been reported by Dowden and co-workers.[83] Their aim was to support a variant of the Grubbs initiator, namely the so-called Hoveyda initiator **46** (Figure **22**).



46

Figure 22 Hoveyda initiator

This complex has been shown to be more sTable than other traditional or NHC-substituted Grubbs' initiators, something that avoids the contamination of the reaction by any decomposition products. Dowden has explored the synthesis of the supported Hoveyda system and its activity in non-degassed solvents under air. The anchored initiator was obtained in four steps. The first three stages are the synthesis and the anchorage of the ligand, with the last step being the immobilisation of the metal complex (Scheme **57**). Such supported initiators could make possible the automation of catalytic metathesis reactions due to the easy work-up, and very accessible reaction conditions.



Scheme 57

This supported Hoveyda-type initiator has been tested for RCM. The system's activity is modest, but it has to be kept in mind that the reactions are conducted under air and in non-degassed solvent.[83] The recycling of the initiator has again been tested by undertaking simple RCM reactions. The supported system dramatically lost its activity after four runs. The authors further attributed their relatively modest activities to be due to the low functional group loading provided by the commercial amino-TentaGel resin whose maximum capacity is 0.3 mmol/g.[83]

Blechert has also reported a polymer-supported variant of the Hoveyda initiator using the same NHC ligand as describe above. The support used was a readily swelled Wang resin, preferred in order to maximize the accessibility to the metal centre.[84] The supported initiator has shown a good activity in RCM, but a lower activity in CM, the specific reaction for which this particular supported initiator was designed for. Therefore an alternative means of supporting the ruthenium complex was designed. Instead of using the NHC ligand as a means to anchor the metal complex, a styrene ligand was used (Figure **23**). This second initiator has shown both a good activity in CM and a good recyclability.

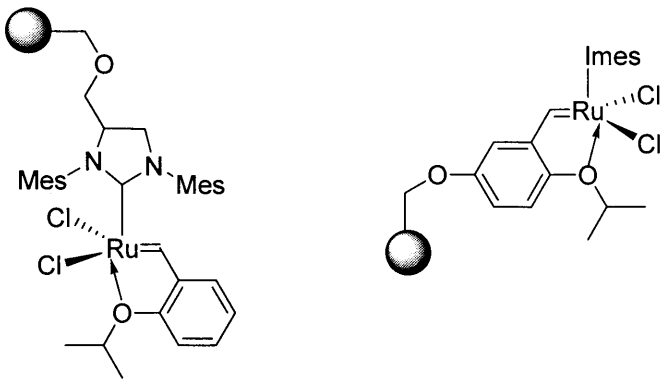
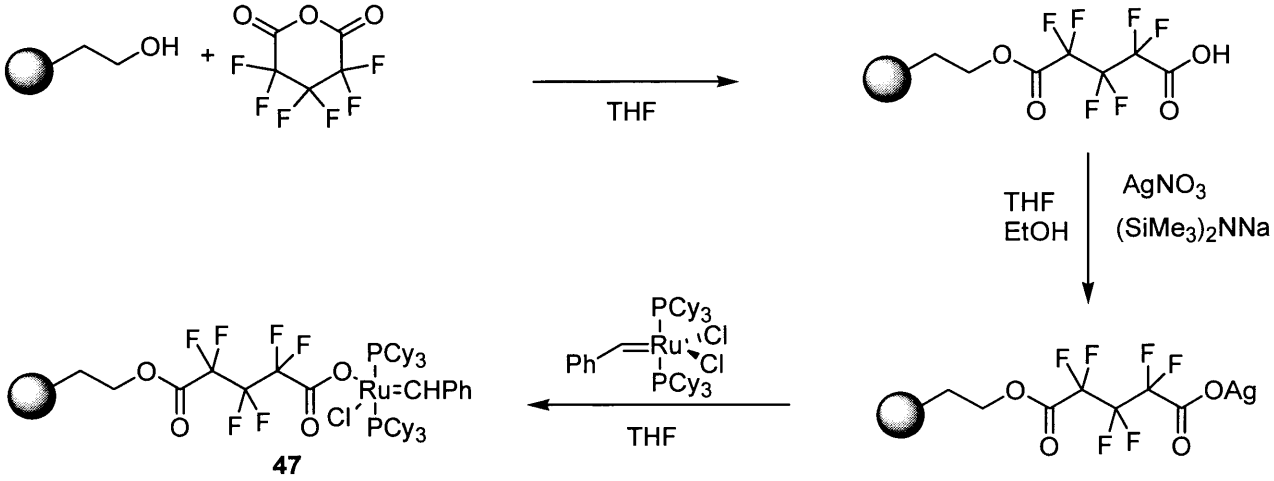


Figure 23 Examples of supported Hoveyda initiators

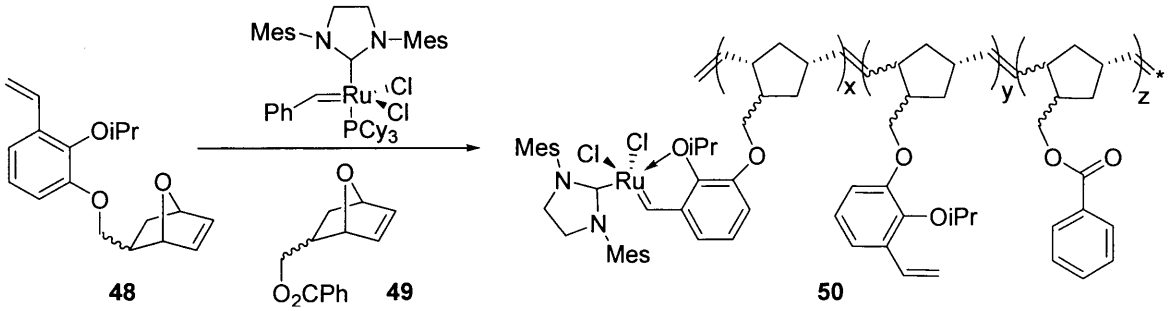
Early work has been done on substituting one of the chloride ligands at ruthenium with a carboxylate group in order to produce a six coordinate dimeric complex of the type $[Ru_2(=CHR)_2(R'CO_2)_2(PCy_3)_2]$,where R' is a strongly electron withdrawing group (*e.g.* CF_3, C_2F_5, CCl_3). These initiators were found to be very active in metathesis reactions.[85] Mol and Buchowicz have published a report in which they employ a much longer spacer than Blechert and Dowden, to isolate the active metal species from the polymer as illustrated in Scheme **58**.[86] The first step was the treatment of a hydroxyethyl polystyrene resin with hexafluoroglutaric anhydride, the second was the formation of the carboxylate silver salt, and finally the last step was the immobilisation of the Grubbs initiator.



Scheme 58

This supported initiator **47** has been used mainly in self-metathesis reactions of internal alkenes such has *trans*-4-decene and has shown a better activity than the traditional Grubbs' initiator under the same conditions, although the conversion is not great (39%).[86] The recyclability has been also tested and the supported system showed a decrease of 19% in its activity after the first cycle. The authors of this work explained this poor performance as resulting from leaching of the initiator from the resin.

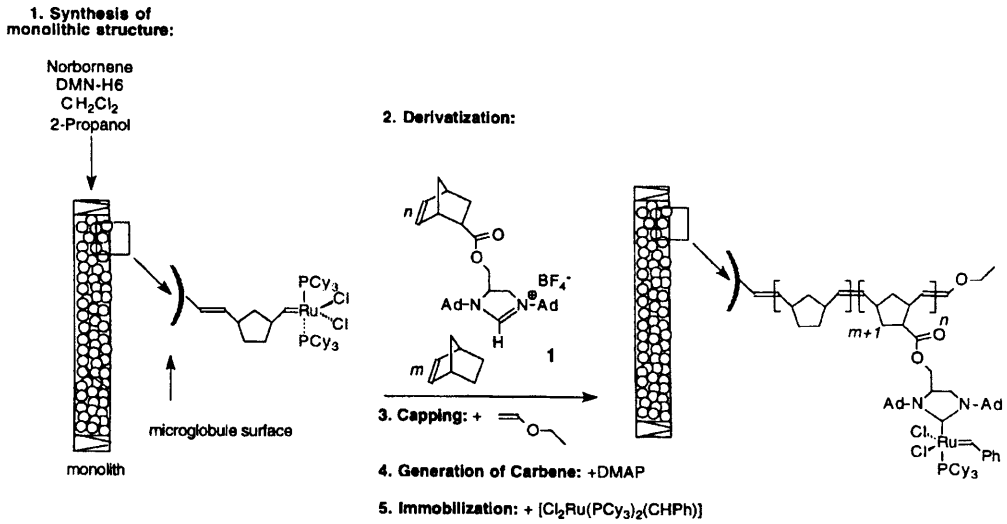
Less conventional ways for anchoring the Hoveyda-type initiators have also been described. For example, Blechert and coworkers undertook a living polymerisation of compound **48** in the presence of a soluble Grubbs initiator, CuCl (a phosphine scavenger) and compound **49**, which acts as a spacer preventing a close approach of the metal centers.[87] The living polymerisation is terminated by the final anchorage of the initiator. Overall, this gives rise to a supported Hoveyda-type system **50** as illustrated in Scheme **59**.



Scheme 59

This supported initiator **50** displays good efficiency in simple RCM reactions for substrates such as heptadienol and activated dienes such as 2-(1-allyl-but-3-enyl)-malonic acid diethyl ester.[87] The recyclability of **50** has also been tested, with a decrease in its activity only being observed after eight runs. This support has got the advantage of being soluble in most organic solvents (except diethyl ether and hexane), which can ease its separation from the reaction medium, and also help retain its level of reactivity. However, unfortunately the initiator loading is low, between 0.08 and 0.01 mmol/g.

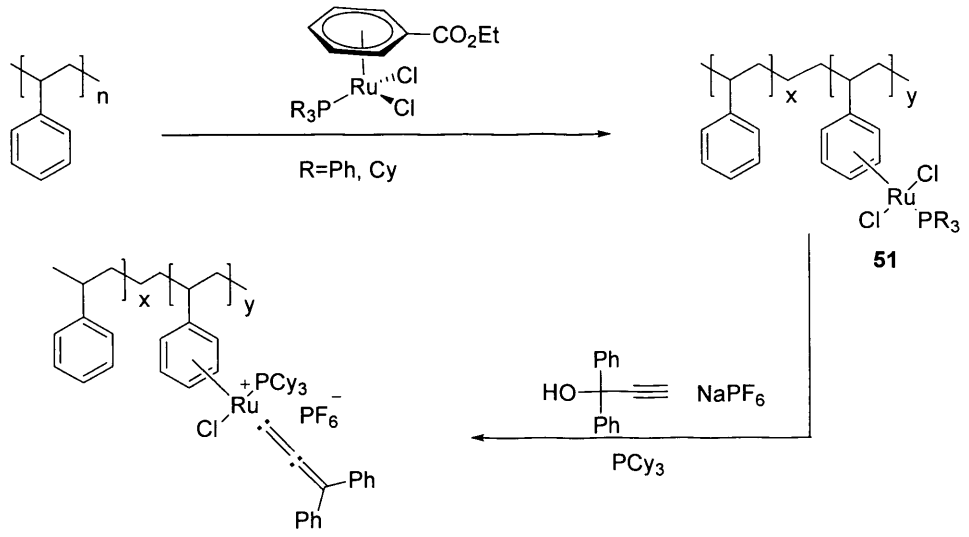
A similar synthesis to the one described by Blechert has also been described by Buchmeiser for the immobilisation of a Grubbs-type initiator.[88] Here the strategy involves the use of a functionalised organic monolithic support, itself synthesised by a living polymerisation catalysed by a soluble Grubbs initiator, followed by another living polymerisation, in order to introduce a spacer. The first Grubbs initiator is quenched and an NHC-based Grubbs initiator is added in order to obtain the desired supported ruthenium metal complexes (Scheme **60**).



Scheme 60

This monolithic organic supported initiator has also been tested in simple RCM and ROMP reactions. The system performed well, the supported reagent affords the desired products with comparable yields to those obtained from the homogeneous variant. One drawback here, however, are the problems associated with the nature of the monolithic support, that is to say its pore size and physical properties in general. The synthesis of this support by its very nature is also extremely costly in initiator!

An alternative strategy has been used to anchor a half-sandwich arene metathesis initiator *via* the arene ligand.[89] Kobayashi used polystyrene to support a ruthenium dichloride complex **51** and subsequently modified the complex on-resin using a method described by Fürstner and Dixneuf,[90] to afford the active olefin metathesis initiator (Scheme **61**).



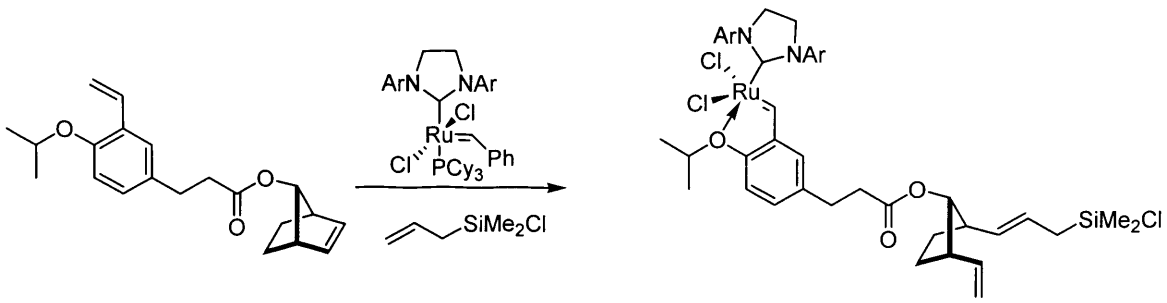
Scheme 61

This supported arene initiator has shown good activity in RCM reactions. According to Kobayashi, the immobilised reagent can be fully recovered after use and can be reused without any loss of activity. One advantage of this methodology is that **51** is a valuable intermediate that can be transformed into a wide range of complexes. This is significant because arene ruthenium complexes are well-known pre-initiators for organic reactions such as transfer hydrogenation, Diels-Alder reactions, and olefin cyclopropanation.[89]

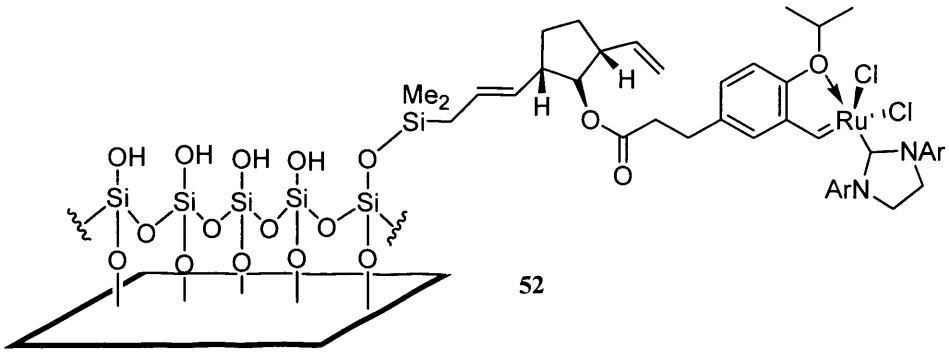
I.5.2 Supported Grubbs' initiator on inorganic supports

Up to this point, all the immobilised supported initiators discussed have used organic support materials. As it has been said before, tuned organic supports are inert and therefore

should not react detrimentally with any immobilised species. However, Hoveyda and co-workers have immobilised a ruthenium olefin metathesis initiator on an inorganic oxide-based monolithic sol-gel support **52**.[91] According to Hoveyda, the main advantages of using this type of silica support are that the porous glass will retain a rigid and exposed surface area; that surface functionalisation of a monolithic gel results in a bulk initiator sample; and that gelation occurs after a sol-gel is cast into a mould. In order to achieve this type of heterogenisation, Hoveyda has chosen a commercially available glass monolith and designed his strategy as shown in Scheme **62**. The first step was a tandem ROM/cross metathesis performed using a standard Grubbs-type initiator in order to obtain a new complex with a functionalised alkylidene ligand at the ruthenium metal centre, giving rise to a variant of the Hoveyda-type initiators. The final step was the immobilisation of the initiator on the sol gel *via* the functional tether by simply heating the reaction at 40°C for five days, forming the monolithic sol-gel-supported Hoveyda initiator (Figure **24**).



Scheme 62



52

Figure 24 Immobilised Hoveyda initiator

This initiator has displayed very good activity in RCM reactions, particularly those involving trisubstitued olefins. The recycling of this supported system has also been monitored, remaining active and not showing any decrease of activity even after eight cycles.

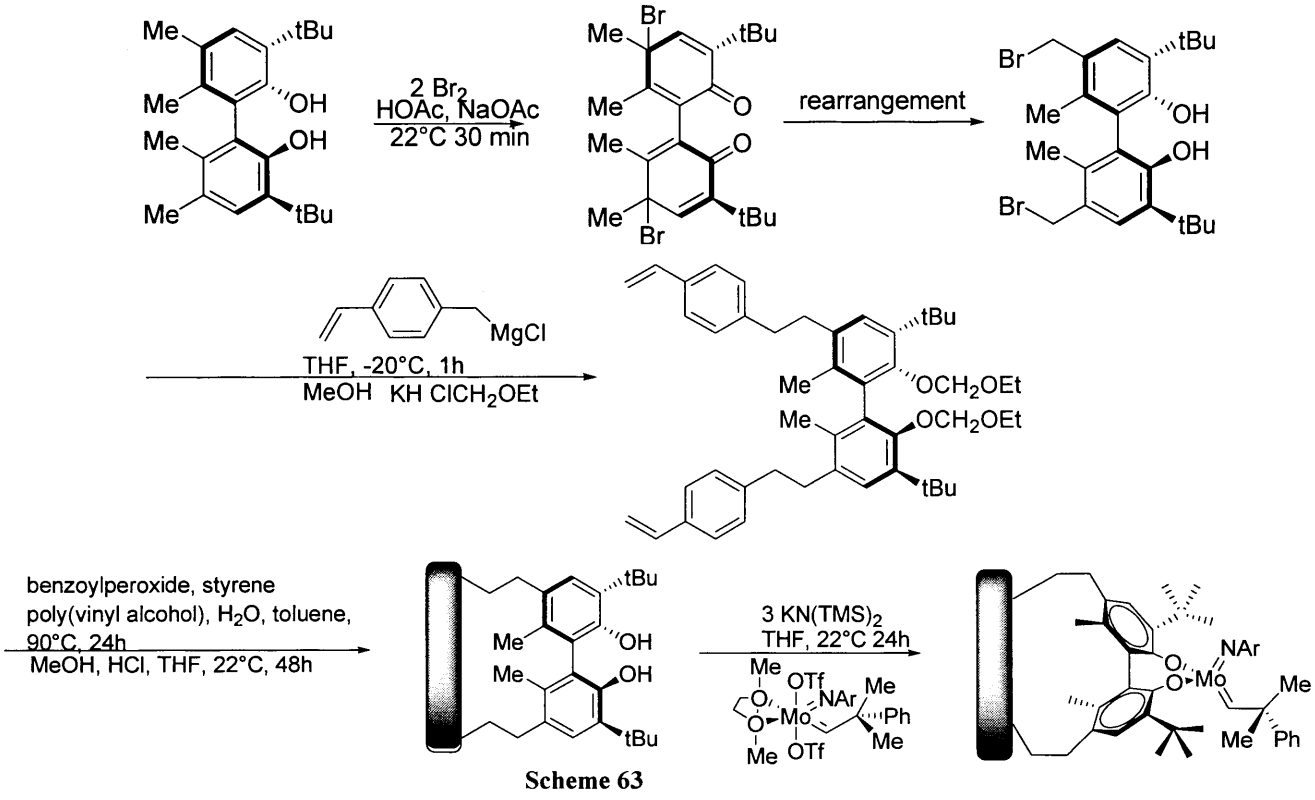
This has made the initiator very useful in combinatorial chemistry and has led to its use for the preparation of a number of chemical libraries.[91]

Although this supported system displays many good qualities, *i.e.* stability, recyclability, and good activity, it has to be kept in mind that the initiator that has been supported, a Hoveyda-type system, is itself very robust and sTable, which explains how anchorage on a very reactive silica surface could be achieved without initiator degradation. Indeed, Dowden has even done reactions of supported Hoveyda systems in non-degassed methanol.[83] Furthermore, the ligand used by Hoveyda to attach his initiator to the surface can be regarded as a very long spacer, something that could explain the very good activity of this inorganic oxide-supported initiator. It would be interesting to have a similar initiator on an organic support to see how its performance compared with that immobilised on an inorganic-support.

I.5.3 Supported Schrock initiators

A number of supported initiators have been developed from the original Grubbs' system, and its derivatives such as the Hoveyda initiator. Their prevalence can be explained by their relatively good stability, straightforward synthesis and ease of handling. On the other hand, Schrock-type initiators are very reactive, non-trivial to synthesise and difficult to handle. Therefore their immobilisation could attract a significant amount of interest, especially since the reactivity of Schrock-type systems is complementary to that of Grubbs systems for certain types of substrate.[92]

So far, three examples have been described of the anchorage of the Schrock systems, work that has been reported by Hoveyda, Schrock and Buchmeiser.[93,94,95] Although they chose to employ a synthetic organic polymer support, they did not use a conventional system, *e.g.* a Merrifield resin, but they prepared an oligomeric support based on BINOL, as shown in Scheme **63**. The strategy chosen was to synthesise a functionalised BINOL motif, which was then protected. Secondly, the protected BINOL motif was coupled with vinyl magnesium bromide and the resulting vinyl-BINOL polymerised. After deprotection of the BINOL motif the supported Schrock initiator was synthesised by reaction of $Mo(NAr)(CHCMe_2Ph)(OSO_3CF_3)_2(DME)$ with the newly functionalised support.



Scheme 63

This initiator was designed specifically for catalysing the ARCM (Asymmetric Ring Closing Metathesis) and has shown a good activity and selectivity, although it should be noted that these parameters are lower than those of a related soluble version. Its recycling has also been tested, but the results are quite modest: in RCM reactions the activity decreased by 30% after the second run, while for ROM the activity decreased by 44% after the third run. Schrock and Hoveyda insist on the necessity of the polymer to be properly swollen.[93] For one reaction, a solvent that effectively swelled the polymer was employed and the reaction proceeded to total conversion; whereas the use of a non-swelling solvent led to no conversion after 24h.

In a very similar fashion, a binaphtholate-based Schrock-type metal-alkylidene has also been reported by Schrock, Hoveyda *et al* (Figure **25**).[95] This supported system has shown good activity in ARCM and AROM which are comparable to the homogenous version of this initiator. Schrock and Hoveyda have synthesised the supported initiator with variation of the cross-linking, and have established the fact that a highly cross-linked polymer reduced the reactivity and the selectivity of the supported initiator. Hoveyda *et al.* suggested when the degree of cross-linking is high this reduces the ease of diffusion of substrates toward the Mo metal centre is more difficult as the polymer is more rigid and less swollen.

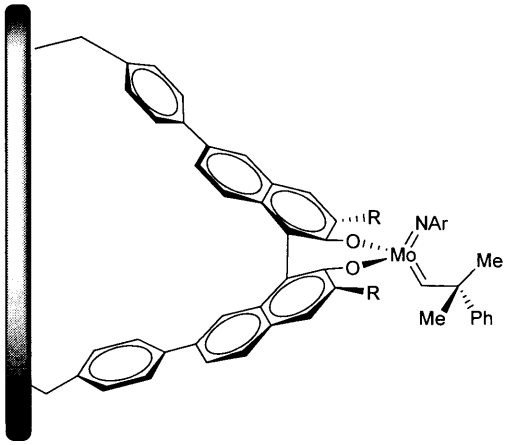
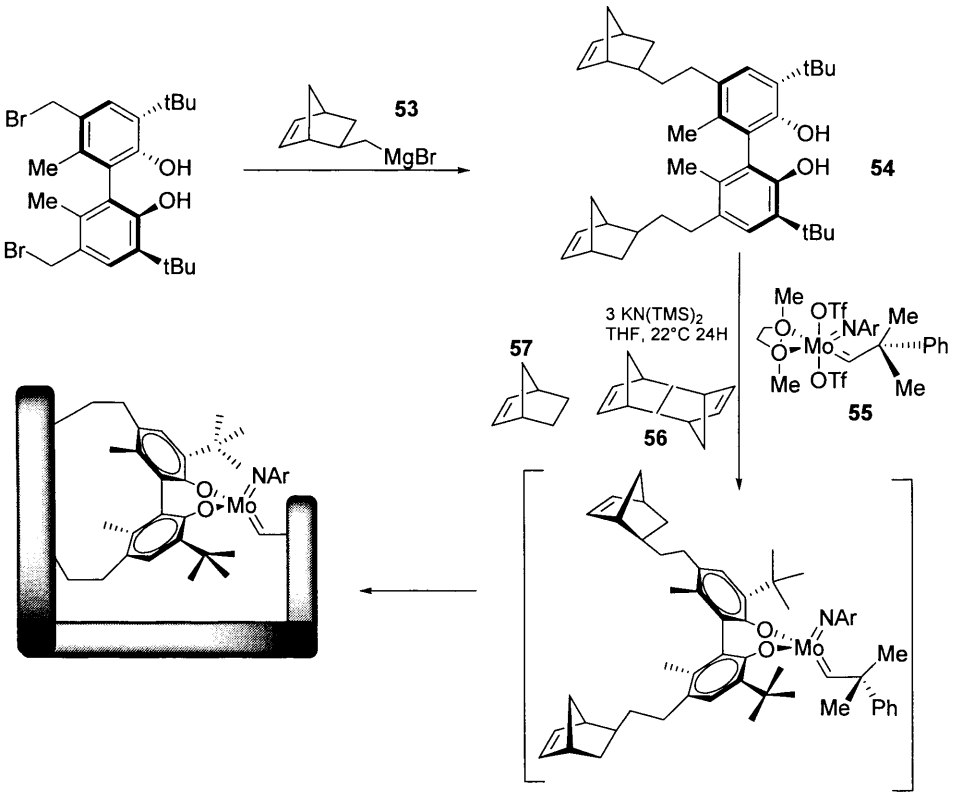


Figure 25 Supported binaphtholate Schrock-type initiator

The same team have reported the synthesis of a supported Schrock-type metal alkylidene initiator immobilised on polynorbonene units generated by the initiator itself, as described in Scheme **64**.[95] The starting material is the binol unit whose synthesis is described in Scheme **63**, which was reacted with **53** to afford compound **54** that bears two norbornene functions, which are subsequently reacted with the bis(triflate) molybdenum complex **55** and various amounts of norbornene compounds **56** and **57**, in order to afford polymer-supported Schrock-type metal-alkylidene complexes with various degree of cross-linking.

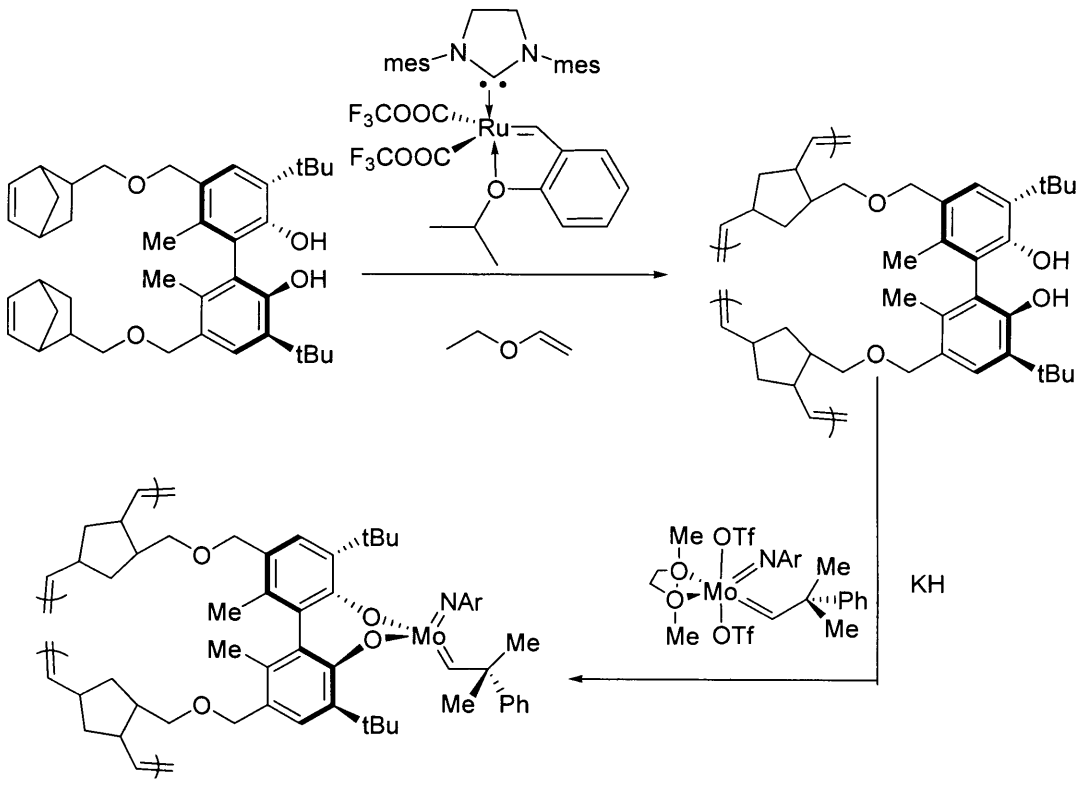


Scheme 64

The supported initiators have shown activity in ARCM and AROM that are comparable to their soluble counter-parts although in some reactions the enantioselectivity was lower than the homogenous systems. Again Schrock *et al.* have demonstrated that a high degree of cross-linking decreases the reactivity of the initiator.[95]

Unfortunately, all the Schrock-type initiators described in this section have shown a decrease in their activity usually after three runs, therefore the recyclability of the supported systems is not very good and the initiators therefore still undergo decomposition.

In a related strategy Buchmeiser achieved a very similar goal by synthesising a BINOL derivative bearing a norbornene function that was polymerised by performing a ROMP reaction in order to obtain the support for the metal-alkylidene Schrock-type complex.[94] His approach is surprising as the support is generated by a Hoveyda metal alkylidene initiator, which is destroyed in order to support another metathesis initiator, namely a Schrock-type metathesis initiator (Scheme **65**). Again RCM and ROMP have been performed and the supported system has shown good activity, but its recyclability is not very good as a significant decrease in activity is observed after the second run.



Scheme 65

These latter overall methodologies, although successful, are complex, and in particularly the synthesis and the polymerisation of the functionalised BINOL and NAPHTOL are very difficult, and the ratio of difficulty/activity is not very good. An alternative approach would be to synthesise a supported initiator using a previously functionalised resin made from a commercial product like a Merrifield resin and to introduce the active initiator in a one-step manner. It is this type of approach that has been considered in this thesis, and will now be discussed.

I.6 References

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Chapter 2

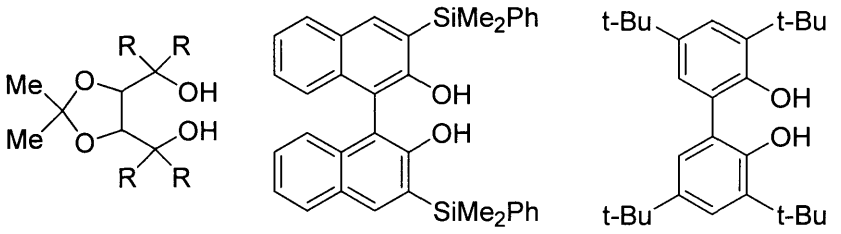
Synthesis of Ligands and Supports

II Synthesis of ligands and supports

In this chapter, the synthesis of TADDOL (and its derivatives) together with the synthesis of some simpler, yet analogous diols and tetrafluorophenol will be presented. Subsequently, their immobilisation with a view to synthesising Schrock-type initiators will be discussed.

II.1 Synthesis of TADDOL ligands

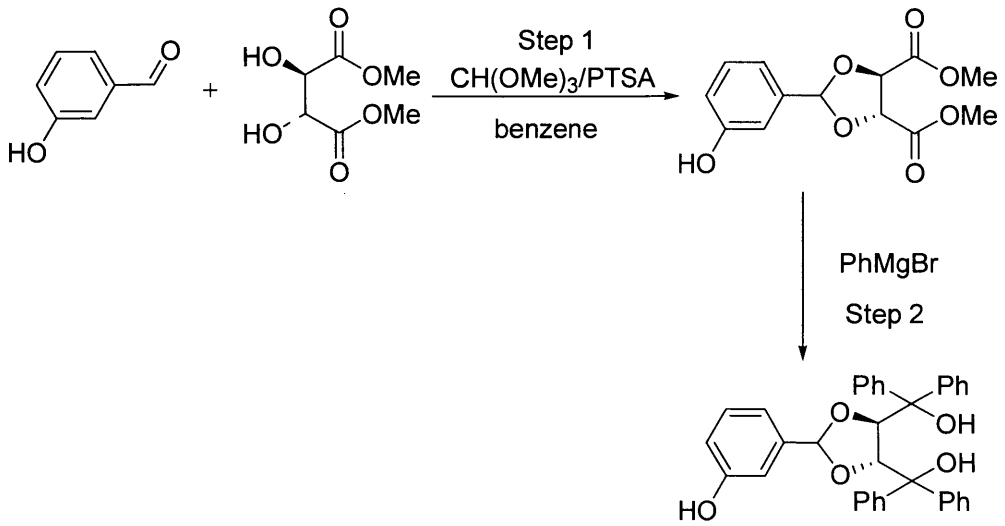
In 1993 Schrock reported the synthesis of an asymmetric molybdenum imido-alkylidene-based initiator for asymmetric ring closing metathesis (ARCM) and for ROMP.[1] He chose to include the chiral element in the alkoxide ligand necessary to stabilise these highly reactive molybdenum complexes. The chiral ligands chosen at this time were BINOL- and TADDOL-derivatives (Figure **1**). The resulting molybdenum complexes were shown to be very active for ROMP, and provided good control over the tacticity of the resulting polymers (over 90%).



R_4tartH_2 $BINO(SiMe_2Ph)_2H_2$ $Bipheno(t\text{-}Bu_4)H_2$

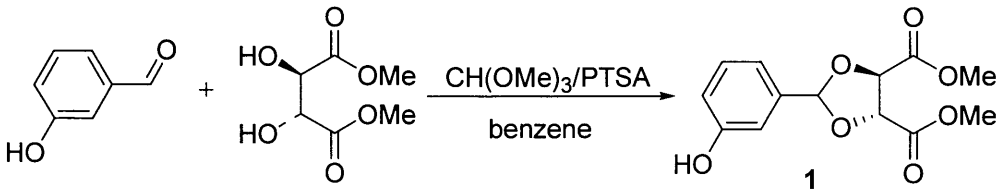
Figure 1 Examples of diols used as precursors to alkoxides in olefin metahesis

A natural extension to the work decribed above is to use polymer-supported variants of these ligands to prepare immobilised Schrock metathesis initiator complexes. Polymer-supported TADDOL, as has already been shown, was developed by Seebach,[2,3] and has been used very effectively for catalysing Diels-Alder reactions, when complexed to various Ti-containing fragments.[2] Seebach used Merrifield resin to first immobilize the chiral ligands and then to support the Ti complex. Other groups have also developed related methodologies for the preparation of similar polymer-bound ligands. For example, Burguette *et al.* have proposed an apparently easier synthesis of supported TADDOL.[4] This synthesis proceeds in two steps as shown in Scheme **1**.



Scheme 1

Building on this previous work, it was of interest for us to prepare polymer-supported TADDOL with a view to subsequently generating an immobilised Schrock-type metal alkylidene. Thus, initially the methodology outlined in the literature was followed in order to obtain the desired resin.

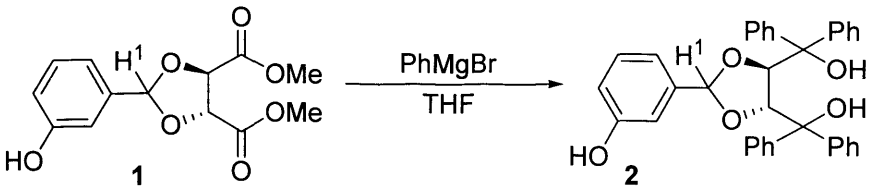


Scheme 2

The first step in the synthesis reported by Burguette (Scheme **1**) is the reaction of 3-hydroxy-benzaldehyde with trimethylorthoformate followed by the addition of D,L-dimethyl tartrate in the presence of a catalytic amount of *para*-toluene sulfonic acid (PTSA) in benzene (Scheme **2**). During the reaction methanol is formed, which was removed by the constant distillation of its azeotrope with benzene. Secondly, triethylamine was added to neutralize the PTSA, before the desired product **1** was purified by column chromatography. Despite a large number of attempts, in our hands, a yield of only 15% was obtained, which is significantly lower than that reported (84%).[4] Initially, it was believed that the removal of methanol azeotropically, was not very efficient. Hence, a number of methods for removing methanol were attempted including Dean-Stark apparatus and activated molecular sieves held within a Soxhlet extractor, without any greater success.

Despite this disappointing yield the next stage in the synthesis was attempted. Thus to complete the synthesis of the TADDOL **2**, a solution of compound **1** in THF was treated

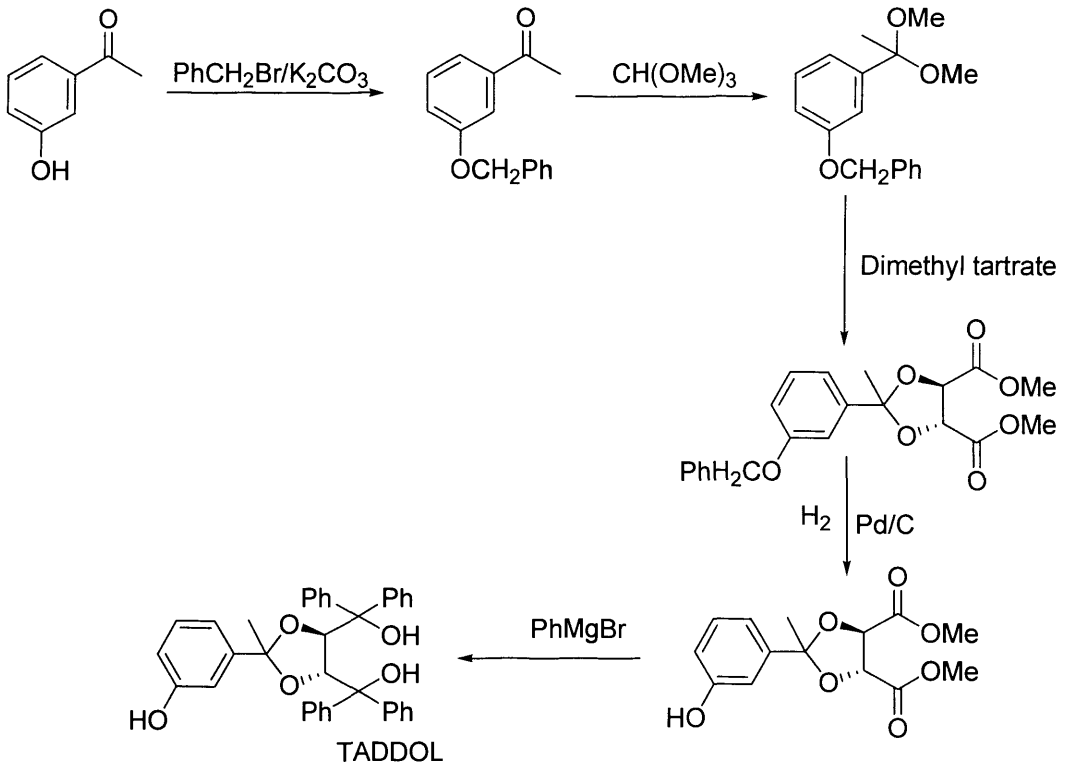
with phenyl magnesium bromide in large excess, itself prepared by a standard Grignard reaction (Scheme **3**).



Scheme 3

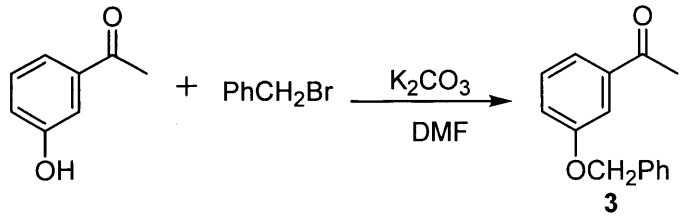
Again, a poor yield was obtained in our hands: around 30%, although this is similar to that reported by Burguette *et al.* (25%).[4] It seemed likely to us that this poor yield could be explained by the rather acidic proton H^1 (Scheme **3**), which could react rapidly and detrimentally with the phenyl Grignard.

Additionally, it was thought that the low yield could be attributed to a competing reaction between the alcohol function of the 3-hydroxy-benzaldehyde and those of the tartrate during step 1 (Scheme **1**) of the synthesis. Hence, the protection of the phenol group was undertaken. This strategy was combined with replacement of the acidic H^1 proton, something that made 3-hydroxy-acetophenone an ideal starting point. Indeed, Irurre *et al.*[5] have described a related synthesis of this type of TADDOL (achieved in 5 steps, Scheme **4**) for use in enantioselective Diels-Alder reactions.



Scheme 4

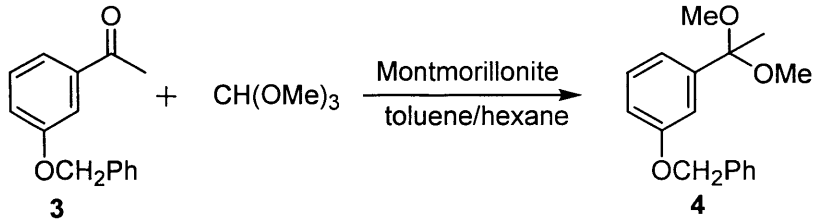
Thus, a similar approach to that used by Irrure was utilised for the preparation of the TADDOL. The first step of this synthesis is the protection of 3-hydroxy-acetophenone as its benzyl ether, achieved through reaction with benzyl bromide in the presence of K_2CO_3 in DMF at room temperature (Scheme **5**).



3

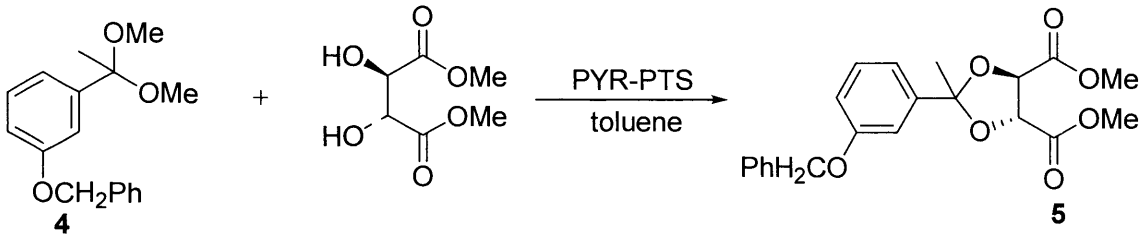
Scheme 5

The reaction afforded compound **3** with a yield of 97%. Subsequently, **3** was reacted with trimethylorthoformate to give the acetal **4** in the presence of a Montmorillonite clay catalyst (Scheme **6**). This afforded acetal **4**, which was isolated with a yield of 95%.



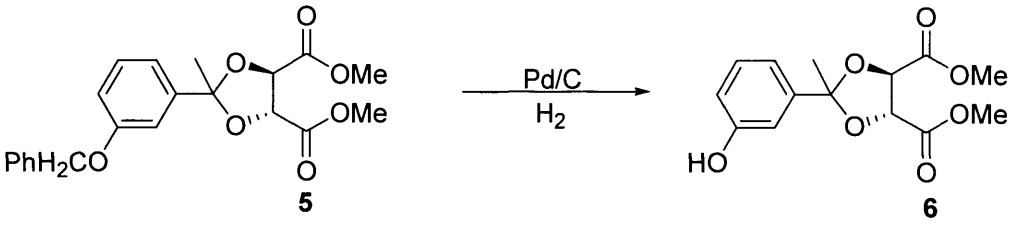
Scheme 6

Next, a toluene solution of the acetal **4** was reacted with the D,L-dimethyl tartrate, eliminating methanol, which was removed by a Dean-Stark apparatus. Here, rather than using a catalytic amount of PTSA as done by Seebach,[2] a catalytic amount of PYR-PTS (pyridinium *para*-toluene sulfonate), made by simple addition of pyridine to PTSA, was utilised. This was found necessary as when this synthesis was attempted using PTSA, the yield of the desired product **5** in our hands was poor (47%). PYR-PTS is a well known alternative for preparing related types of heterocycle.[6] Using this reaction modification, compound **5** was obtained (Scheme **7**) with a yield of 80% following purification by chromatography on silica gel.



Scheme 7

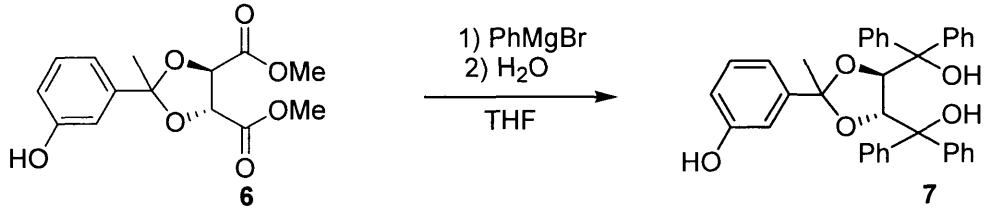
The next step in the TADDOL synthesis required the removal of the benzyl protecting group. Thus, product **5** was reduced to the unprotected alcohol **6** with hydrogen (1 atm) in the presence of palladium on charcoal (Scheme **8**). This reaction was almost quantitative. The product **6** was obtained with a yield of 95%.



5 **6**

Scheme 8

The last step of the TADDOL synthesis is the reaction between a tetrahydrofuran solution of compound **6** with excess phenyl magnesium bromide followed by addition of water, according to Scheme **9**.

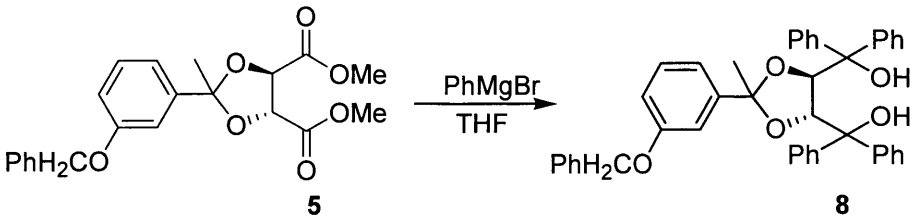


6 **7**

Scheme 9

This time the desired compound **7** was obtained with a good yield, 79%, which is vastly improved compared to the poor 30% of the first attempt (Scheme **3**). This confirmed that the removal of the H^1 hydrogen atom present in compound **1** was the key to the success of the final reaction of the diester **6** with phenyl Grignard. Although the synthesis of the desired TADDOL was achieved in five steps, the overall yield is still better (around 55%) than even the best two-step synthesis described by Burguette *et al.* who obtained TADDOL with an overall 21% yield.[3]

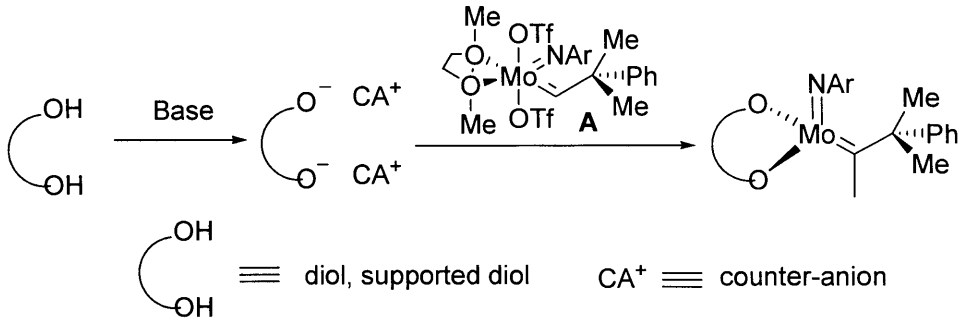
In order to synthesize an exact homogeneous analogue of what will be the supported TADDOL, the protected intermediate compound **5** was also treated with phenyl Grignard under the same experimental conditions described above (Scheme **10**). This afforded the benzyl-protected TADDOL **8** with a yield of 67% following work-up and isolation.



Scheme 10

II.2 Synthesis of diol ligands

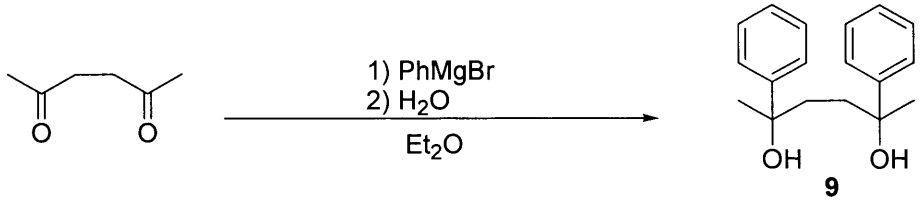
To synthesise a supported Schrock metathesis initiator, one approach is to take the soluble initiator precursor **A** (Scheme **11**) and to react this with a chelating dialkoxide, which results from the deprotonation of the corresponding alcohol by a base.



Scheme 11

II.2.1 Synthesis of fluorine-based diol.

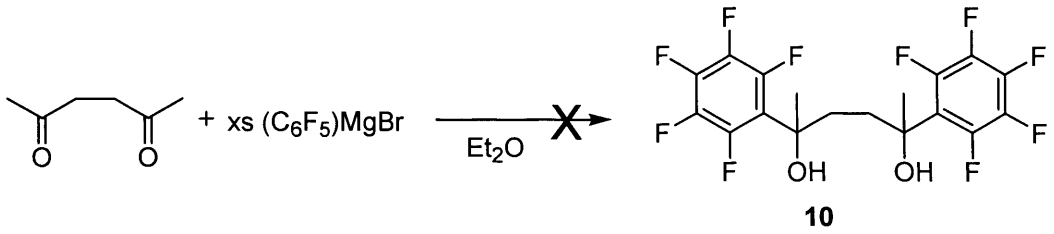
As well as looking at the use of TADDOL derivatives as a means of supporting the desired molybdenum complexes, some alternative diols (both soluble models and polymer-bound species) have also been investigated. As a starting point, a simple analogue **9** of TADDOLS **7** and **8** was studied (Scheme **12**). To the best of our knowledge, these types of ligand have never been used as a chelating dialkoxide framework on molybdenum. The desired diol was made by reacting phenyl Grignard with hexane dione. After hydrolysis, the resulting compound was recrystallised from a solution of dichloromethane to afford **9** with a yield of 74%.



Scheme 12

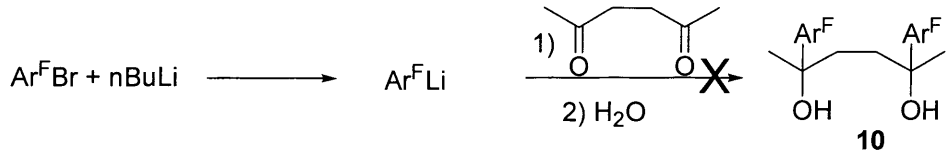
With a view to introducing more electronegative groups in order to obtain a more activated and reactive Schrock initiator (see chapter 1 section I.4.2.3.2), a perfluoro-phenyl

derivative of **9** was envisaged to be an attractive target to potentially mimic systems such as $Mo(NAr)(CHMe_2Ph)(OCF_3)_2$. Its synthesis was attempted in a similar fashion to that used for the preparation of compound **9**: 2,5-hexane dione was treated with four equivalents of tetrafluorophenyl magnesium bromide (Ar^FMgBr) [7] in diethyl ether according to Scheme **13**.



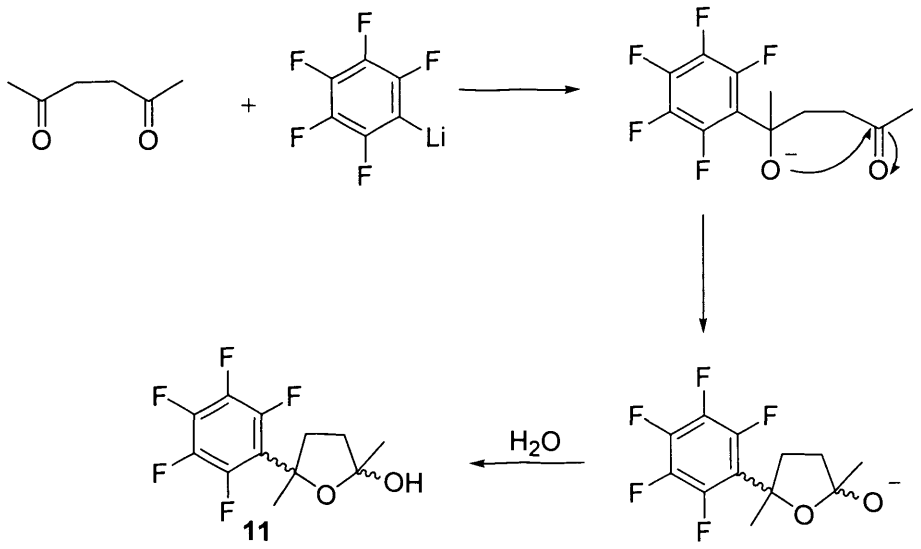
Scheme 13

After hydrolysis, the desired compound **10** was not obtained, somewhat surprisingly, only unreacted starting material was isolated instead, so the synthetic strategy was changed. A hexane solution of bromo-pentafluorobenzene (Ar^FBr) was treated with a 1.6 M hexane solution of butyl lithium at -78°C in order to prepare the lithium *penta*-fluorophenyl reagent (Ar^FLi).[8] Then an ether solution of the hexane dione was added at -78°C to the resulting lithium salt, before the reaction was left to warm slowly to room temperature overnight (Scheme **14**).



Scheme 14

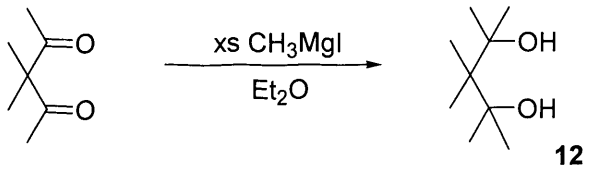
Once again, after hydrolysis and work-up, the desired product **10** was not obtained. Analysis of the NMR data revealed the presence of a new cyclic compound **11** (Scheme **15**). A possible mechanism for the formation of **11** is that one equivalent of lithium pentafluorobenzene attacks one ketone as expected, but under anhydrous conditions the resulting alkoxide (stabilised by the electron withdrawing aromatic ring) undergoes an *intra*-molecular nucleophilic attack at the adjacent ketone moiety (Scheme **15**). This occurs rapidly, the resulting heterocycle thus blocking any further reaction from the aryl lithium reagent. Indeed, following hydrolysis **11** was obtained with a yield of 64%. As a result of this unexpected side reaction. The synthesis of fluorinated 1,4-diols was not pursued any further.



Scheme 15

II.2.2 Synthesis of 2,3,3,4-tetramethyl-pentane-2,4-diol

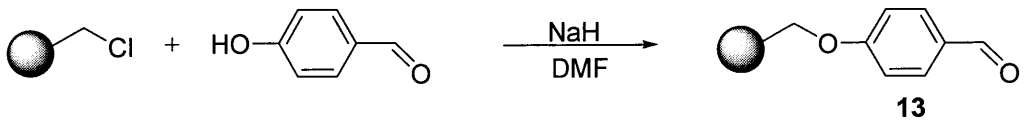
With a view to preparing a substituted 1,3-diol as a dialkoxide precursor, the synthesis of compound **12** (as illustrated in Scheme **16**), was undertaken. Diol **12** has been chosen for its straight-forward synthesis, and the possible formation of the resulting six-membered-chelate Schrock-type initiators. To the best of our knowledge, no work has been published concerning the use of this kind of ligand. The synthesis was achieved by reacting methyl dimethyl malonate with an excess of methyl magnesium iodide in diethyl ether, the product **12** being obtained following hydrolysis and work-up (62%).



Scheme 16

II.3 Immobilisation of TADDOL on a polystyrene support

The synthesis of a TADDOL derivative **7** has been performed following a literature procedure.[3] The next goal was its immobilization on a Merrifield resin *via* its hydroxy group. An alternative novel approach for the preparation of a supported TADDOL was to use the polymer support as a protecting group itself for the condensation of the tartrate with hydroxy-benzaldehyde, to give the immobilized TADDOL directly. This was undertaken by the immobilisation of an excess of 4-hydroxy-benzaldehyde on Merrifield resin using NaH as base in DMF (Scheme **17**).

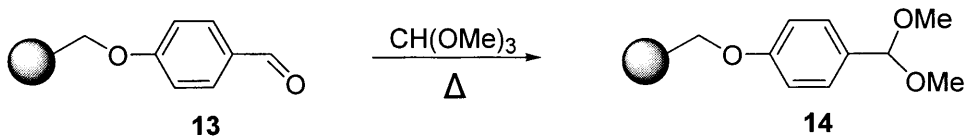


13

Scheme 17

The resulting modified Merrifield resin derivative **13** was analysed by gel-phase ^{13}C NMR spectroscopy. Although hard to interpret, peaks corresponding to the aldehyde function at 196.8 ppm can be assigned to the desired species **13**. Infrared spectroscopy also revealed the presence of a band at 1628 cm^{-1} consistent with the formation of the supported aldehyde **13** (*cf. para*-hydroxy benzaldehyde 1649 cm^{-1}). The loading of the supported aldehyde was 1 mmol/g of resin, something which was ascertained by elemental analysis.

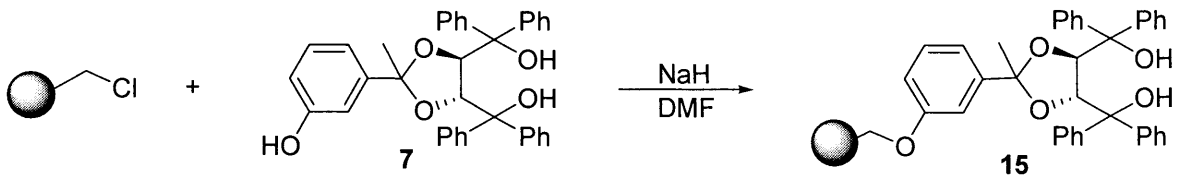
Subsequently, resin **13** was treated with neat trimethylformate in large excess to afford acetal-protected derivative **14** (Scheme **18**). The IR spectrum of the new material **14**, revealed no band corresponding to the aldehyde **13**. The gel phase NMR data were, however, not very helpful and could not be used to confirm, unambiguously, the nature of **14**.



13 14

Scheme 18

As a result of the problems to confirm the successful transformation of **13** into **14** and hence to follow the course of this reaction, it was deemed better to support TADDOL **7**, prepared using standard organic protection methodologies, rather than using a polymer protecting group. Therefore TADDOL derivatives **7** were immobilized on a Merrifield resin *via* its alcohol function with the help of sodium hydride as base. The synthesis was done following a procedure described in the literature (Scheme **19**).[4] This was achieved by heating a mixture of Merrifield resin **7** and NaH in DMF 80°C for five days. The resulting polymer was isolated by filtration and was washed several times with water, THF, and a mixture of water and THF (1:1).



7 15

Scheme 19

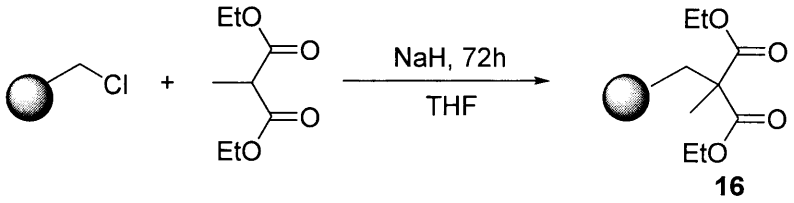
The loading was determined by elemental analysis by looking at the loss of chlorine and was found to be 0.66 mmol/g, which is higher than the literature, reported to

be 0.45 mmol/g. This could be a result of the slightly higher temperature (originally the reaction was done at 70°C) and a longer reaction time (the original time was three days).

II.4. Synthesis of supported malonate-type ligands

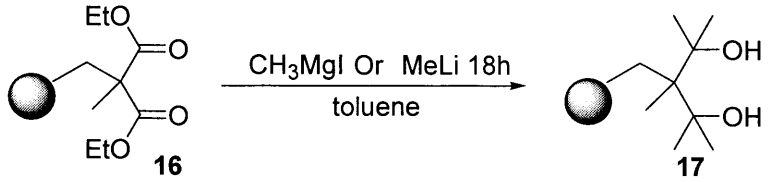
To the best of our knowledge few chelating ligands have been used for the synthesis of Schrock-type catalysts.[1,,9, 10,11] When deprotonated TADDOL is employed, in reaction with the bis(triflate) derivative **A** described in Scheme **11**, the resulting complex should possess a seven-membered metallacycle, which is not necessarily the most favourable arrangement. It was thought that a six-membered cycle might be better, forming a more stable initiator. Thus, it was of interest to investigate the possibility of using malonate-derived ligands in this respect, since they are cheap, easy to prepare and potentially structurally versatile, in addition to being easy to immobilise on a polymer support.

The synthesis of a supported diketone was achieved by the reaction of commercial Merrifield resin with an excess of diethyl malonate in the presence of sodium hydride at room temperature in THF for 72h (Scheme **20**). The ^{13}C NMR spectroscopic analysis of the resulting polymer (swollen by C_6D_6) showed the presence of the desired carbonyl moiety (δ 194.4 ppm). Elemental analysis confirmed the complete loss of chloride and revealed the loading of the new resin as being 0.88 mmol/g.



Scheme 20

The supported diethyl malonate **16** was immediately engaged in the next step of the synthesis, namely its reaction with an excess of methyl magnesium iodide in toluene, and left to stir at room temperature for 18h (Scheme **21**). The resulting resin was washed with THF, diethyl ether, water, and methanol to afford the supported diol **17**.

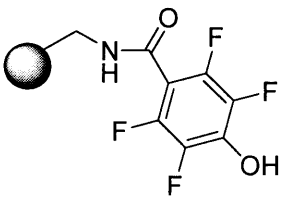


Scheme 21

Gel-phase ^{13}C NMR spectroscopy showed no evidence of a resonance corresponding to the starting carbonyl, while IR revealed the appearance of the desired hydroxyl function (υ = 3391 cm^{-1}). It has been shown that methyl lithium can be used instead of methyl magnesium iodide in order to obtain the supported tri-methyl pentane diol **17**. Indeed this modification was undertaken in order to ensure that none of the supported ester **16**, remained exploiting the greater reactivity of the lithium over the magnesium reagent. The free ester could be problematic for the later synthesis of a Schrock type-initiator.

II.5. Supported tetrafluorophenol ligands.

Fluorinated ligands have been used extensively for the synthesis of Schrock-type initiators, mainly because their electron withdrawing character has been shown to make these molybdenum and tungsten complexes more reactive for metathesis.[12,13,14]Thus, it was desirable to try to support potential fluorinated alcohols with a view to generating new immobilised alkoxide-tethered initiators. An additional advantage of employing fluorine-containing ligands is the possibility of using ^{19}F NMR spectroscopy as a reaction probe, consequently the functionalisation of the resin can be monitored using this technique. The use of gel-phase ^{19}F NMR spectroscopy has already been described in the literature[15] and looks to be a very effective analytical tool. This was developed by Irving *et al.* for ChemRx Advanced Technologies.[15] As shown in Figure **2**, the fluorine signals obtained from the solvent-swelled resin **B** have narrow line widths and can be attributed unambiguously to this supported fluorine compound.



B

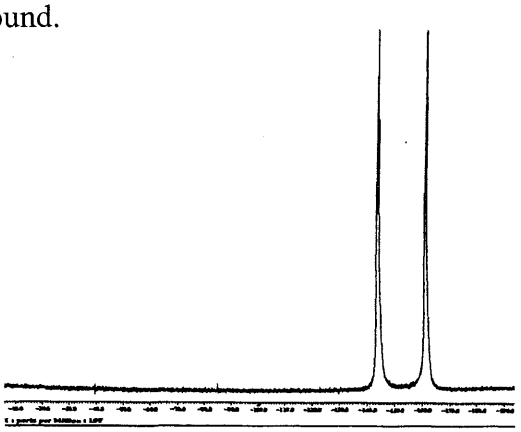
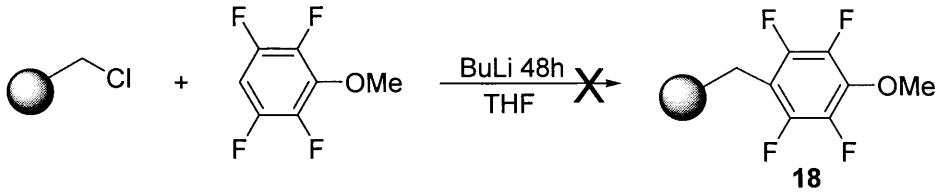


Figure 2 ^{19}F NMR spectrum of supported tetrafluorophenol[12]

The resin described by Irving *et al.* is interesting as it is very close to our target, which is a supported tetrafluorophenol ligand. This type of fluorinated phenol will be used in order to immobilise a Schrock-type complex. This chemistry will be described in chapter 4. The use of support **B** (Figure **2**) was considered in order to achieve this goal, but was discarded for the following reasons. Firstly, the presence of free secondary amide could be problematic since it could interact detrimentally with the Schrock initiator or its

precursors. Secondly, the synthesis of this functionalised amide is very costly in terms of the starting materials. Therefore a different methodology was explored with a view of obtaining a similar product.

The first alternative strategy proposed consists of the reaction of standard Merrifield resin with commercially available tetrafluoroanisole in the presence of butyl lithium, using THF as solvent (Scheme **22**).



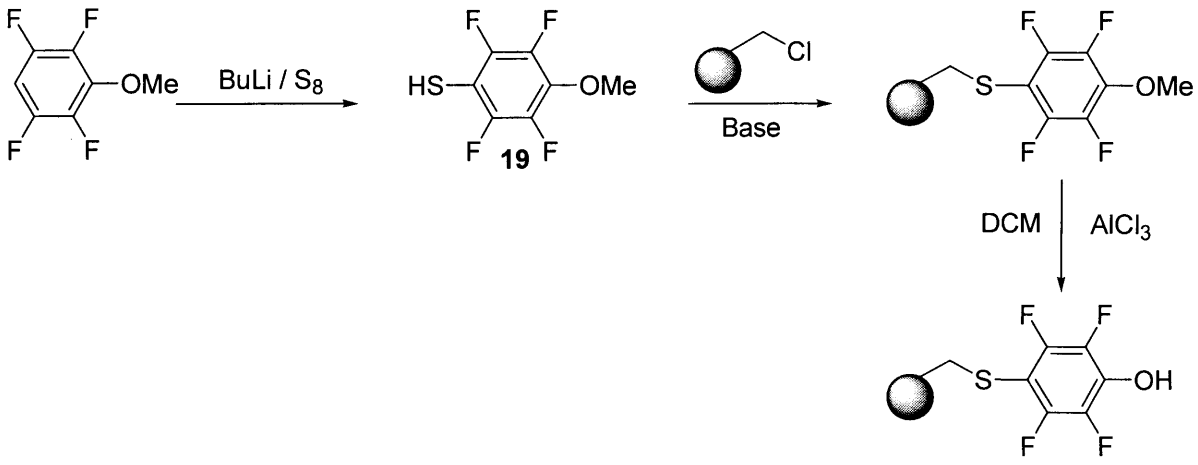
18

Scheme 22

The reaction was monitored by taking aliquots of the THF solution of the reaction mixture and by then using standard solution-phase ^{19}F NMR spectroscopy. Over a period of 72h it was observed that none of the tetrafluoroanisole was consumed. At this point the polymer was isolated by filtration and washed. Subsequent gel-phase ^{19}F NMR spectroscopic analysis of this resin and elemental analysis confirmed that no fluorine–containing species were present.

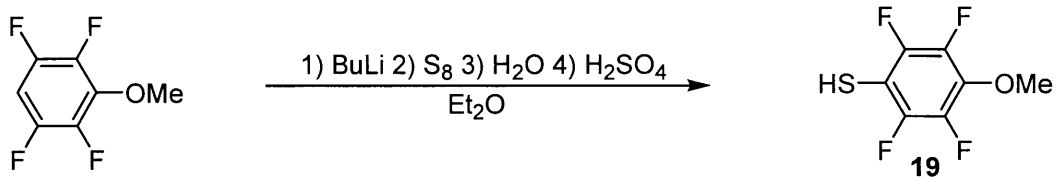
It has been shown that tetraflurophenol reacts clearly with butyllithium to afford the corresponding aryl lithium species, since it will be demonstrated (Scheme **24**) that sequential treatment of tetrafluoroanisole with butyl lithium and the bromine affords *para*-bromo tetrafluoroanisole. Therefore the failure of the reaction outlined in Scheme **22** could be explained by the relative lack of reactivity of the starting Merrifield resin.

Consequently another strategy for the preparation of a related product **19** (Figure **7**) has been developed. This time thiol **19** will be deprotonated at sulphur and the resulting lithium salt that should be more reactive, treated with the starting Merrifield resin. This strategy is divided into three steps. The first is the formation of a thiol function on the tetrafluoroanisole prepared by following a literature procedure described by Chambers.[16] The second step is the anchoring of the fluorine-containing compound by its thiol function and the final step being the deprotection of the fluoro derivative to afford the supported tetrafluorophenol (Scheme **23**).



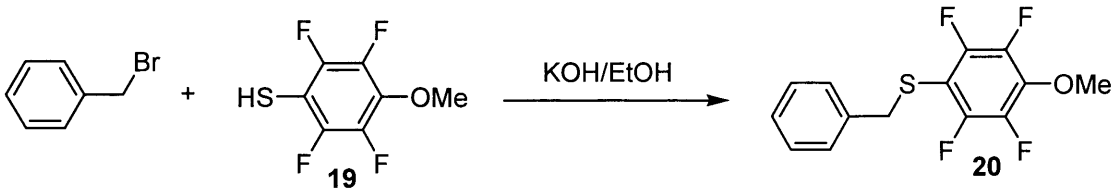
Scheme 23

The formation of the thiol function was performed by the reaction of tetrafluoroanisole with S_8 in the presence of butyllithium in diethylether.[10] The desired product **19** was obtained with a yield of 61%, following workup (Scheme **24**).



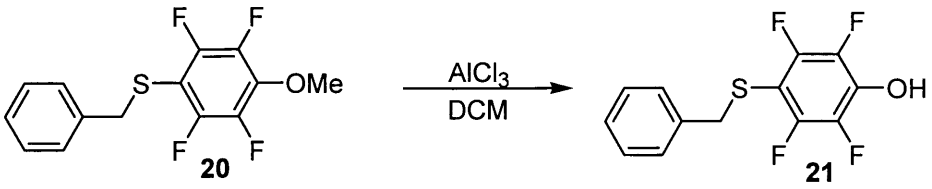
Scheme 24

Before the anchoring of **19** to a polymer resin was attempted, a model "homogeneous grafting" reaction was undertaken to ensure the validity of the proposed methodology. The synthesis of a homogeneous analogue of the desired polymer-supported tetrafluorophenol precursor **20** was obtained by reacting **19** with benzyl bromide in ethanol in the presence of potassium hydroxide (Scheme **25**).



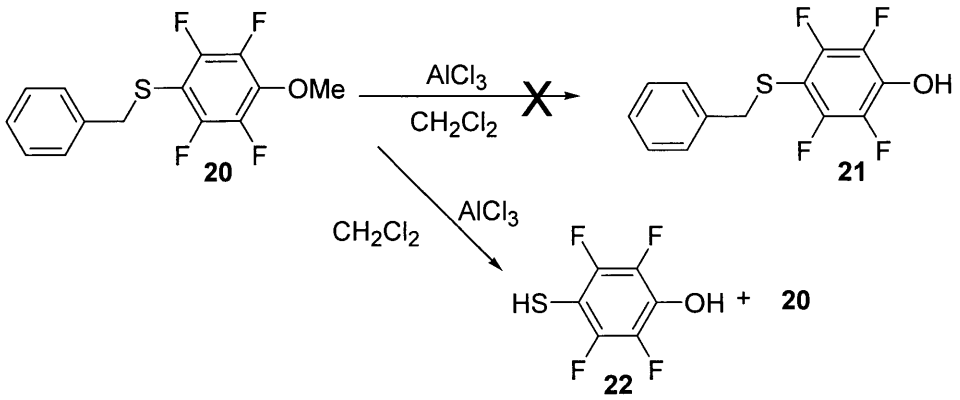
Scheme 25

The resulting anisole **20** was obtained quantitatively and was subsequently engaged in a deprotection reaction with $AlCl_3$ in solution in DCM at room temperature (Scheme **26**), according to the method described in the literature for a related reaction involving the transformation of an alkoxide into the corresponding hydroxide.[17,18]



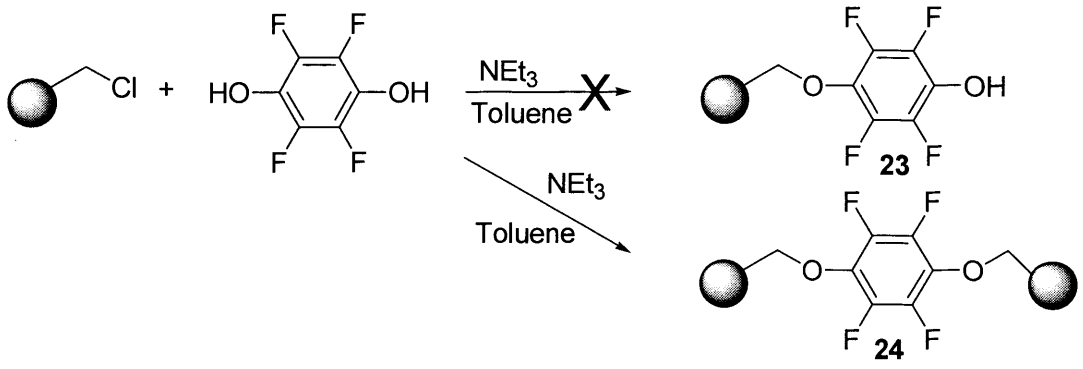
Scheme 26

Surprisingly however, the expected alcohol **21** was not isolated, instead a mixture of the starting material and 2,3,5,6-tetrafluoro-4-mercapto-phenol **22** was identified by GC-MS. Hence, another method of deprotection involving the use of NaI and TMSCl in acetonitrile[19] was employed without any improvement, the same products being obtained (Scheme **27**).



Scheme 27

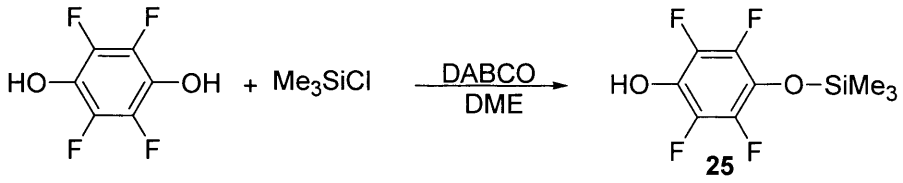
Therefore, in order to access the desired supported tetrafluorophenol, another strategy was attempted using a different starting material, namely tetrafluorohydroxyquinone. As the loading of the commercial Merrifield resin used throughout this thesis is fairly low (1 mmol/g), the immobilisation of tetrafluorohydroxyquinone *via* just one of its hydroxyl groups was tried without using a protecting group as the reaction could be done using pseudo high-dilution conditions. This was deemed necessary in order to try and prevent polymer "cross-linking" occurring as a result of the bifunctional nature of the hydroxyquinone, *i.e. via* the two hydroxyl groups. Therefore, commercial Merrifield resin was simply reacted with tetrafluorohydroxyquinone in the presence of one equivalent of NEt_3 in toluene (Scheme **28**).



Scheme 28

However, contrary to expectations, this experiment demonstrated the need for a protecting group, none of the desired product **23** formed, something which was confirmed by elemental analysis: the percentage of fluorine can only be assigned to the formation of **24**, what is assumed to be the cross-linked resin, suggesting that an effective cross-linking had occurred. This idea was supported by the fact that the polymer **24** exhibited dramatically reduced swelling behaviour consistent with high cross-linking (see chapter 1 section I.4.2). Therefore, different methods of protecting the tetrafluorohydroxyquinone have been investigated in order to achieve the objective of anchoring a tetrafluorophenol-type function to a polymer resin.

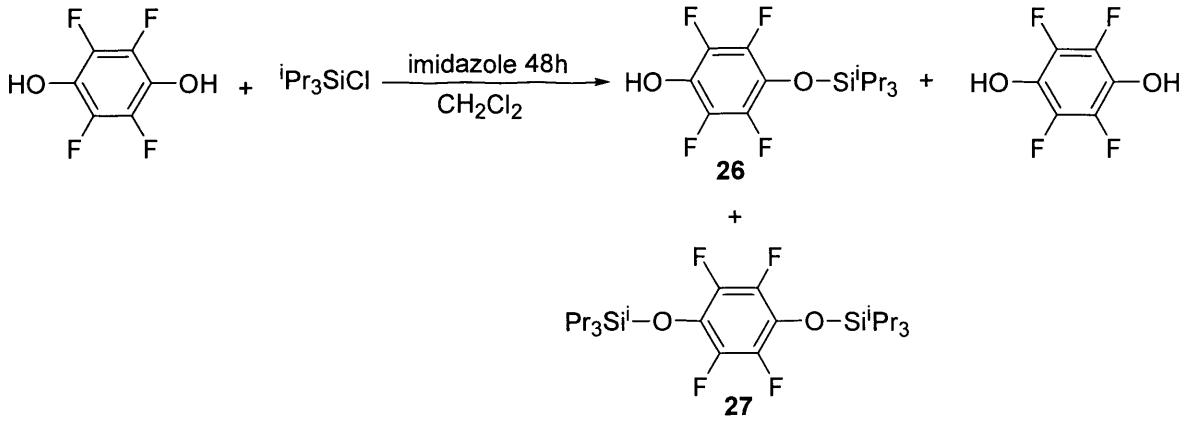
The first protection strategy attempted was achieved by reaction of tetrafluorohydroxyquinone with one equivalent of trimethylsilyl chloride (TMSCl) in DME solution, in the presence of the base DABCO (Scheme **29**). The use of DABCO (1,4-diaza-bicyclo-[2-2-2]-octane) is important since monoprotection of this base results in the formation of a very insoluble salt that precipitates rapidly from solution. This should help to prevent double deprotonation of the hydroxyquinone.[20]



Scheme 29

Unfortunately, it was difficult to characterize **25** with precision as it was very unstable and difficult to isolate although ^{1}H NMR data were consistent with its formation. A possible explanation for this instability could be the removal of the protecting group from **25** by protonation from any residual starting material as tetrafluorohydoroxyquinone is very acidic. Thus, the use of a more bulky, less reactive protecting group, would be logical in an effort to achieve the mono-protection of the tetrafluorohydroxyquinone.

Subsequently, a second attempt was made using one equivalent of triisopropylsilylchloride with imidazole in DCM solution at reflux (Scheme **30**). The progress of the reaction was monitored by GC-MS; after 48h only a mixture of unreacted starting materials, mono-protected derivative **26** and di-protected derivative **27** could be observed in the respective proportions 50%, 25%, 25%.

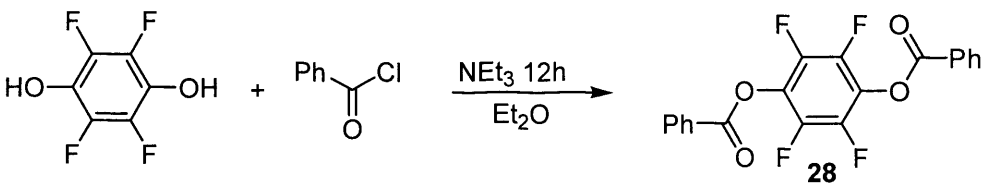


Scheme 30

In a last attempt to achieve monoprotection, the reaction of the tetrafluorohydoroxyquinone with triisopropylsilyl triflate in THF was carried out with triethylamine. Again, a mixture of unreacted starting materials together with monoprotected compound **26** and di-protected derivative **27** were observed in the same proportions.

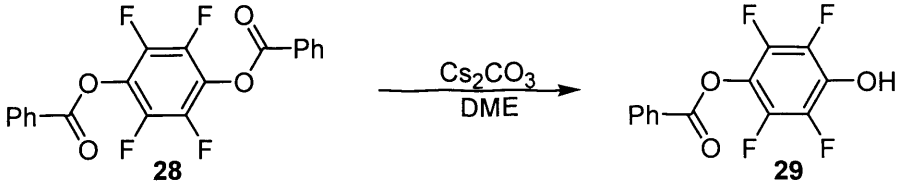
With hindsight these results were not very surprising. The use of strictly one equivalent of a protective group, with a view to obtaining the monoprotection of one hydroxyl function of a perfectly symmetrical molecule is extremely difficult to achieve since there is no control of selectivity, each hydroxyl function being identical.

In contrast, there is precedent for the removal of only one protecting group of a symmetrically-protected compound.[21] As a consequence, it was decided to use this method in order to try to prepare the desired monohydroxy compounds required as ligand precursors. The two hydroxyl groups of tetrafluorohydroxyquinone were deliberately protected with benzoyl chloride in the presence of NEt_3 in diethyl ether at reflux temperature for 12h (Scheme **31**).



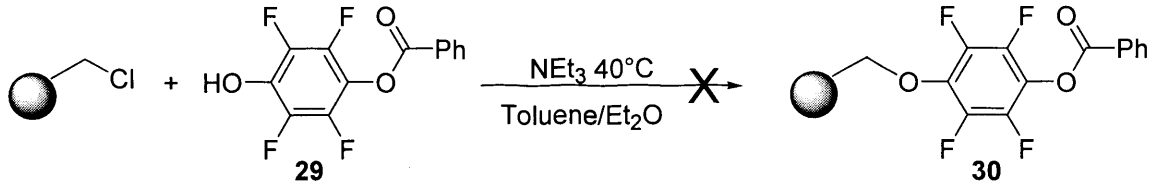
Scheme 31

The di-protected product **28** was obtained quantitatively, following work-up, and was subsequently engaged in a mono-deprotection reaction with caesium carbonate in DME, for five days, at reflux (Scheme **32**).[21] After recystallisation from petroleum ether and a minimum of DCM, the mono-benzyl-protected compound **29** was obtained with a yield of 45%.



Scheme 32

Now it was possible to undertake the last step of the desired synthesis of a supported highly fluorinated phenol, namely resin anchorage of the monoprotected tetrafluorophenol. Merrifield resin was stirred with **29** in a mixture of toluene and diethyl ether in order to dissolve **29** in the presence of triethylamine as base (Scheme **33**).



Scheme 33

Following isolation by filtration, the resulting resin was washed three times with water, toluene and a mixture of water and toluene. According to the elemental analysis of the resulting polymer beads the reaction was not successful, as only a very low level of fluorine was observed (<0.3 %) in comparison to the expected level of fluorine (13%). One possible explanation for this lack of success could be as a result of the formation of a very stable salt with NEt_3 and the product **29** as shown in Figure **3**. Consequently the Merrifield resin did not have the possibility to react with the phenol **29**.

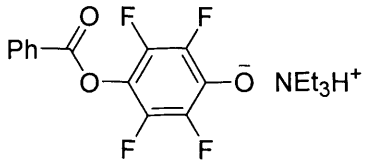


Figure 3

Further optimisation could have been done in these attempts at the immobilisation of tetrafluoroanisole motif, *e.g.* by the use of other bases for examples. However, the last synthesis of the precursor **29** gave only a very modest yield (under 50%), and the reaction

time is very long. For all these reasons, a totally different strategy has been developed with the aim of the synthesis of a supported tetrafluorophenol.

Thus, attempts were made to immobilise a tetrafluorophenol motif on Merrifield resin by modifying and exploiting an approach that has been developed by Hodge and co-workers.[22] The main idea behind his work is the immobilisation of organic molecules on a solid support by using a Suzuki-Miyaura-coupling.

This reaction was developed in 1982, for making carbon-carbon bonds using Pd^0 as catalyst.[23,24] The mechanism of this reaction can be explained using the catalytic cycle described in Figure **4**. The first stage is the oxidative addition reaction of an organo-halogen compound to a source of palladium (0), which is followed by a transmetallation reaction and, finally, a reductive elimination, to yield the coupling product and regenerate the palladium (0).

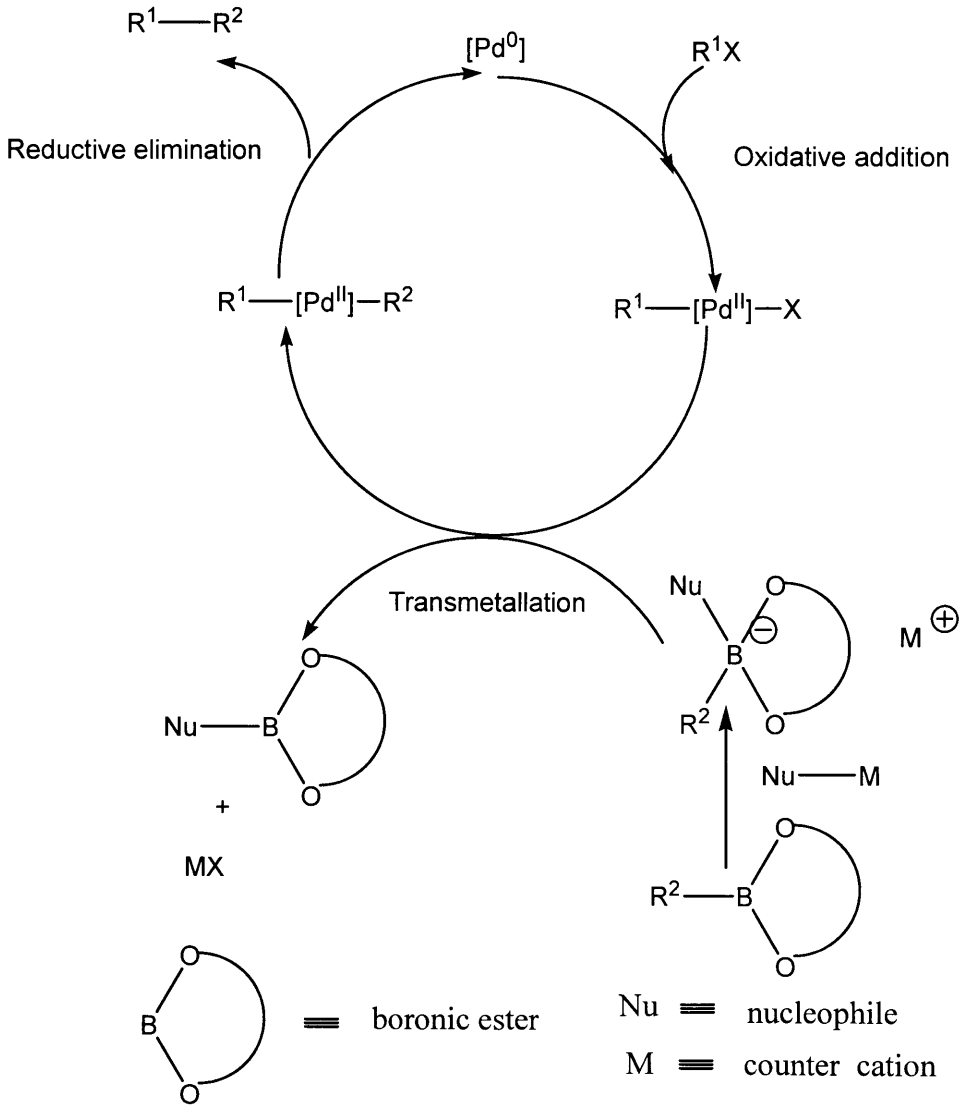
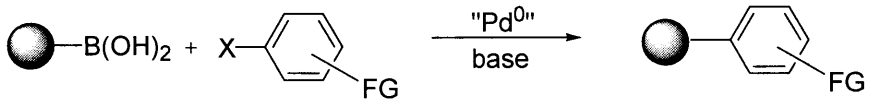


Figure 4 Suzuki –Miyaura cross-coupling reaction

The work developed by Hodge *et al.* outlines the synthesis of a functionalised polystyrene *via* a Suzuki-Miyaura coupling reaction with an immobilised boronic acid.[22] Hodge has demonstrated the feasibility of this method through the synthesis of a wide variety of functionalised polymers (Scheme **34**).



X= Cl, Br; FG= CO_2Et, NO_2 CO_2Bz,etc..

Scheme 34

The advantage of this method of functionalisation is the good conversions obtained and the efficiency of the immobilisation. In a traditional anchorage on a solid support (*e.g.* polystyrene) at least three to five equivalents of the desired substrate to be supported are necessary. Recovery of unreacted substrate is difficult and it is generally lost.[22] In the method described by Hodge, it has been shown that only one equivalent of the desired substrate is needed for its immobilisation on the solid support.

As a result, a strategy for the synthesis of supported tetrafluorophenol using a Suzuki-Miyaura coupling has been developed. Preliminary experiments in solution were carried out to determine the best conditions for the formation of the desired cross-coupling product *via* the Suzuki-Miyaura method (Figure **5**). Two different approaches are possible for the cross-coupling and were examined (routes **A** and **B**).

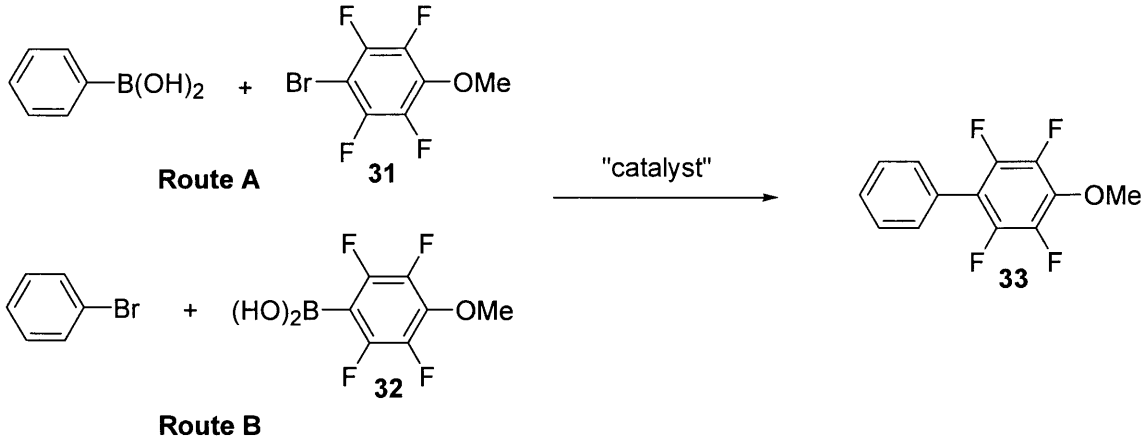
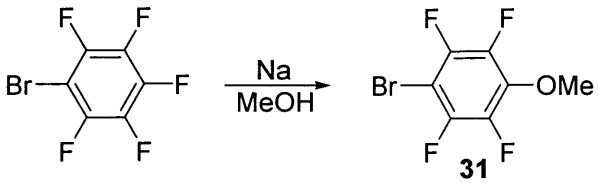


Figure 5 synthetic strategy for the preparation of anisole 33

Route A

The first step was the synthesis of the tetrafluoroanisole **31**, which was prepared according to a literature procedure.[25] This involved reaction of bromopentafluorobenzene in methanol with sodium at room temperature overnight (Scheme **35**).

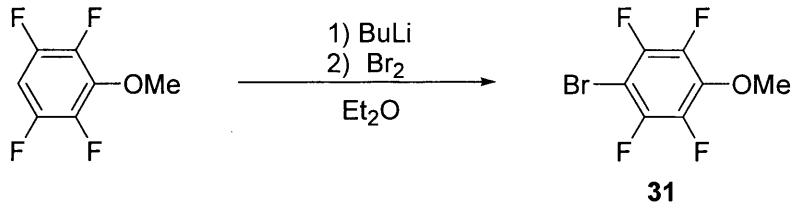


31

Scheme 35

The desired product **31** was obtained, but only as a mixture with unwanted *ortho* and *meta* OMe isomers, as observed by ^{1}H NMR spectroscopy. The best way to remove these undesirable species was to perform a distillation. Sadly, their boiling points are very close which made the separation of the different isomers very difficult. In the literature the separation of the different isomer was done by preparative HPLC, a technique unavailable to us. Thus, an alternative synthesis has been designed with the aim of obtaining exclusively the desired product **31**.

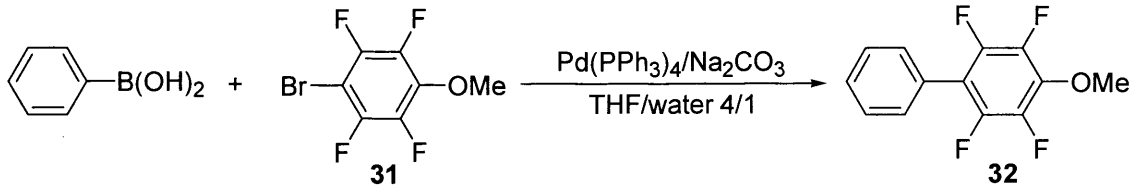
Tetrafluoroanisole was treated with butyl lithium at -78°C for 2 hours in diethylether, which was followed by the addition of 2 equivalents of Br_2, as a solution in hexane, the reaction mixture was then left for a further 2 hours. Finally, the reaction was allowed to return to room temperature (Scheme **36**). Using this approach, the reaction went to completion and the product **31** was obtained pure with a yield of 76%, following work-up.



31

Scheme 36

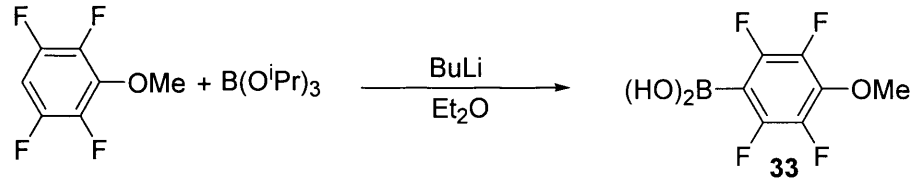
In order to probe the reactivity of **31** in the type of Pd catalysed reactions being attempted, a model off-resin was examined. The product **31** was used in a number of Suzuki-Miyaura reactions with phenyl boronic acid with a catalytic amount of $Pd(PPh_3)_4$ (10 mol %), sodium carbonate (stoichiometric amount) in a variety of different solvents at reflux temperature for 4 days (Scheme **37**). The best yield was obtained with a mixture of THF and water as solvents, conditions which were therefore used in all the subsequent Suzuki-Miyaura coupling reactions. Using this system the product **32** was obtained with a yield of 89%.



Scheme 37

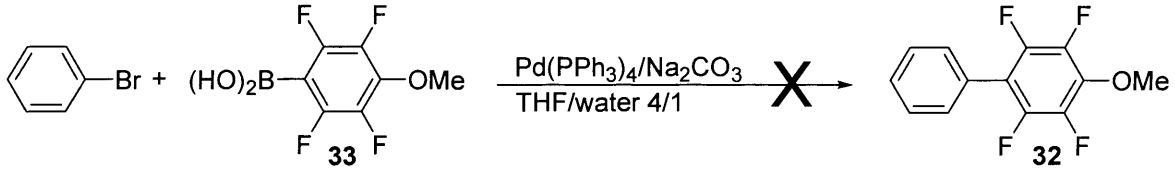
Route B

The *para*-boronic acid-substituted anisole **33** has been synthesised by the reaction of commercially available tetrafluoroanisole, in a diethylether solution at -78°C with butyl lithium for two hours and was consequently reacted with tri-isopropyl borate for 12h at room temperature (Scheme **38**).



Scheme 38

Novel compound **33** was obtained with a yield of 61% and was immediately engaged in the Suzuki coupling using exactly the same conditions as those described in route **A** above (Scheme **39**).

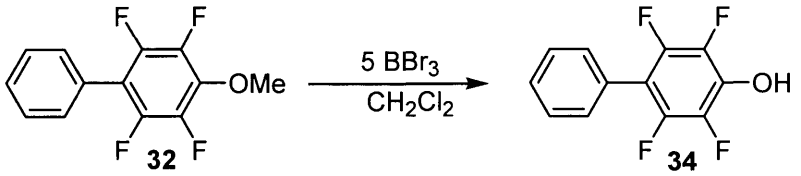


Scheme 39

However, this time no formation of the desired compound **32** was observed. One plausible explanation for this lack of reactivity compared with that observed by Route **A** is that the strong electronegativity of fluorine weakens the bromine-carbon bond of **31** used in route **A** and encourages the oxidative addition step in the catalytic cycle of the Suzuki-Miyaura reaction combined with the high stability of the "ate" complex formed from **33**.

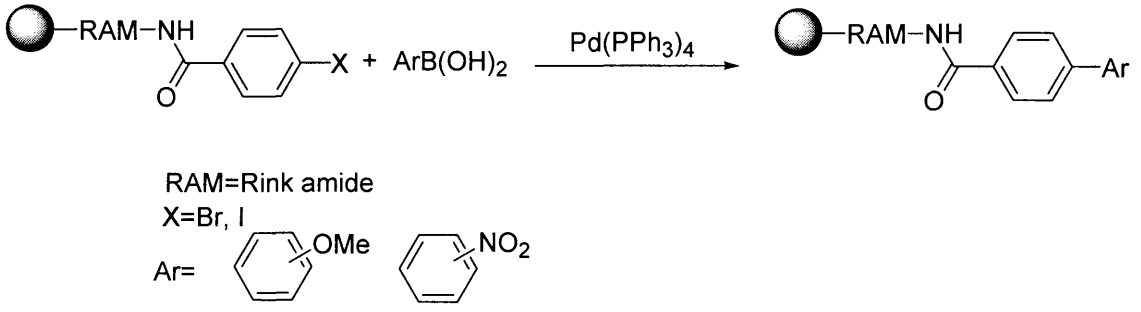
Since the model compound **32** was obtained conveniently by the Suzuki-Miyaura coupling *via* route **A**, the next step in the synthesis of the homogeneous analogue of supported fluorophenol, namely the phenol **34** will be the deprotection of the compound **32**. This was attempted by treating compound **32** with five equivalents of BBr_3 in dichloromethane at room temperature overnight in order to transform the ether group to a hydroxyl functionality (Scheme **40**).[17] This reaction was successful, the new product **34**

was obtained with a yield of 76% following work-up. Thus, this approach would seem ideally suited for the grafting of a highly fluorinated phenol to a polymer resin. The only disadvantage of the method **A** employed for the cross-coupling, is the relatively long reaction time necessary (48h).



Scheme 40

One way to try and decrease the reaction time is to use a modern heating technique, *i.e.* microwave dielectric heating, which has proven successful in providing faster reaction times, increased conversions and yields in several organic reactions.[26] Microwave-assisted palladium catalysed assisted reactions were first reported in 1999.[27] In this particularly example the authors have described a successful Suzuki-cross couplings reaction which was performed on a supported aryl halide. (Scheme **41**) Good conversion (>85%) were obtained in all attempts, for a very small period of time (3.8 min).



Scheme 41

Similar work have been described in the literature for supported halide ester, and good conversions were obtained (>90%), and the time reaction was improved from 2 hours using conventional heating methods, to 2 minutes using microwave heating.[28] According to these good examples described previously, it seemed interesting to use the microwave oven as the heating system.

The principle of the microwave oven which operates at frequencies between IR and radio frequencies (Figure **6**), is the following; in an electric field a molecule with a dipole aligns with this field. If the field oscillates very quickly, the molecules will be agitated since they try to realign themselves to the field. An extreme internal heat is thus created that can escalate at 10°C per second.[29] When undertaking reactions in a microwave, the use

of a polar solvent like water is desirable, because its dipoles can align with the electric field and hence also heat rapidly.

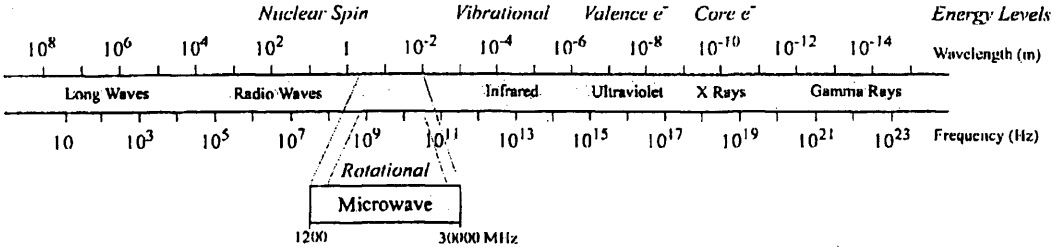


Figure 6 Microwave frequency

Two types of microwave oven exist: multimode and monomode ovens (Figure 7). The multimode oven is the most common oven and is the type used in domestic applications. These kinds of microwave oven have been used for performing chemical reactions mainly because they are cheap and readily available. However, they suffer from a number of disadvantages; the electric field created is not homogeneous, creating "hot spots" in some parts of the oven and more significantly, the cavity temperature cannot be set or controlled. These problems lead to poor experimental reproducibility. Thus, the monomode oven has been developed in which the electromagnetic waves generated by the magnetron, are focussed with a waveguide, leading to a homogeneous distribution of energy inside the reaction cavity.[30] The temperature can be controlled, leading to a good reaction reproducibility, the only negative point is that these latter systems are very expensive

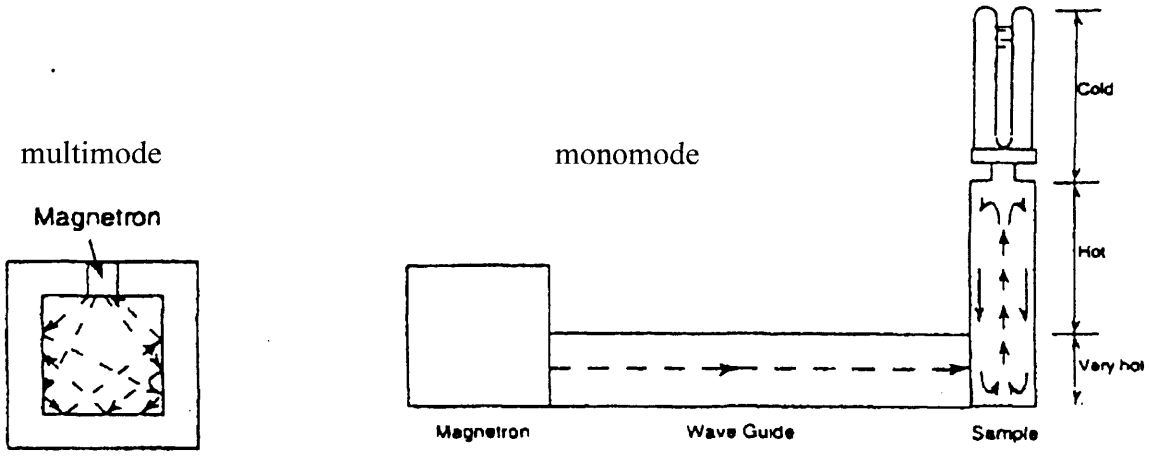
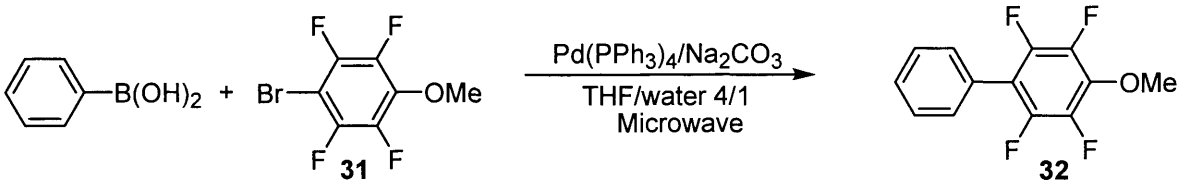


Figure 7 Principle of multimode and monomode microwave

The length of time required to undertake the Suzuki-Miyaura cross coupling reactions attempted in this thesis suggested that they were ideal candidates for being undertaken in a microwave oven in order to reduce the reaction time. This was indeed attempted in a momomode microwave and the chemical conditions employed were similar

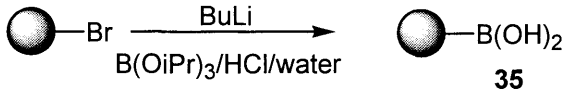
to the conditions used when using traditional heating methods as previously described (Scheme **42**).



Scheme 42

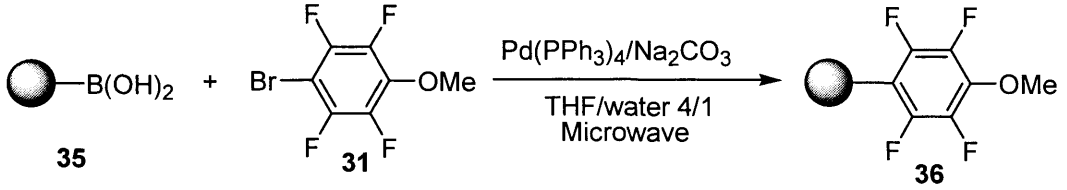
Various temperatures and reaction times have been tested, with a time of 25 minutes and a temperature of 120°C appearing to be the optimal combination. The reaction outlined in Scheme **42** has been very successful, the bromo derivative **31** was totally converted to the desired cross-coupling product **32**.[31]

As the synthesis of a homogeneous analogue of the intended supported tetraflurophenol has been successfully achieved, Suzuki-Miyaura cross-coupling reactions were attempted using the supported boronic acid. This reactive polymer was prepared according to a literature method, starting from commercially available bromopolystyrene.[22] The bromine was exchanged with lithium, by treating the resin with an excess of BuLi at reflux for 5h in toluene. Subsequently, the solvent and the excess BuLi were removed, *via* a canula, the support was swollen in THF, triisopropyl borate was added *via* a syringe, and the reaction left to stir overnight at room temperature (Scheme **43**). After hydrolysis, the supported boronic acid **35** was obtained. Elemental analyses were consistent with successful conversion to the supported boronic acid **35** with a loading of 3.95 mmol/g.



Scheme 43

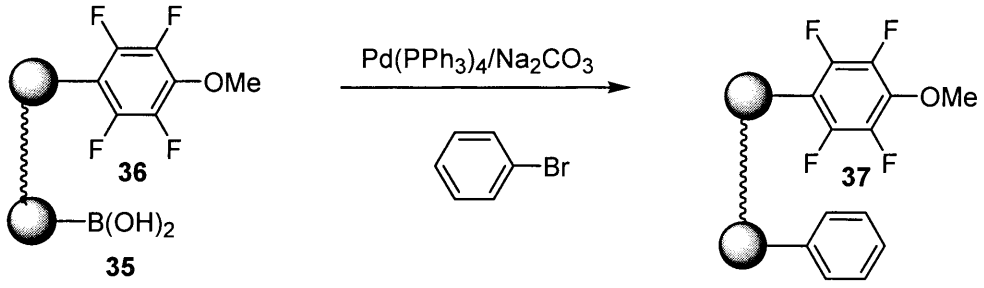
Boronic acid-derivatised resin **35** was then engaged in a reaction with bromo-tetrafluorophenol **31** and sodium carbonate in the presence of a catalytic amount of palladium tetrakis(triphenylphosphine) in a mixture of THF/water as used in the homogeneous cross-coupling reactions (Scheme **42**) this new reaction being described in Scheme **44**.



Scheme 44

The reaction was monitored by GC-MS analysis of the solution phase of the reaction mixture. The reaction was undertaken using a temperature of 110°C, and a reaction time of 1h as previously optimised for the microwave. It is important to note the reaction time and the temperature are related to the Personel Chemistry monomode microwave oven. When the reaction was performed with a monomode CEM microwave, the reaction only achieved completion at a temperature of 170°C after a time of 1h and 40 minutes. Although GC-MS indicated the total disappearance of anisole **31** for the CEM microwave, which implied the total conversion of supported boronic acid **35** into **36**, elemental analysis has indicated a loading of only 1.12 mmol/g for the supported tetrafluorophenol. A possible explanation for this lower loading than that expected (3 mmol/g) may be the very high temperature necessary when using the CEM[32] oven in order to achieve complete disappearance of **31** by GC-MS. Bromotetrafluoroanisole **31** could decompose to give tetrafluoroanisole.

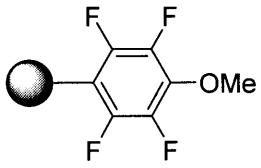
Although the conversion was not as good as hoped for, the loading of the supported tetrafluorophenol was still acceptable. However as a result of incomplete reaction, it was assumed that unreacted boronic acid groups would remain on the resin. Therefore, another Suzuki-Miyaura reaction has been performed with bromobenzene in order to eliminate any remaining boronic acid from the polymer (Scheme **45**).[22]



Scheme 45

For comparison, the reaction described in Scheme **37** has also been undertaken using traditional heating methods, *i.e.* heating at reflux for 5 days. A very poor conversion was achieved according to elemental analysis of the resulting resin, which revealed a very low amount of fluorine incorporation (<2%) compared to the expected amount of fluorine (15%).

A useful feature of having a supported fluoro compound is the ability to be able to monitor reaction chemistry by ^{19}F NMR in the solid state. The gel-phase ^{19}F NMR spectrum of **37** was obtained and revealed two peaks at -158.7 and -144.9 ppm, which correspond well with those of tetrafluoroanisole **32** that displays resonnances at -158.07 and -145.60 ppm (Figure **8**).



37

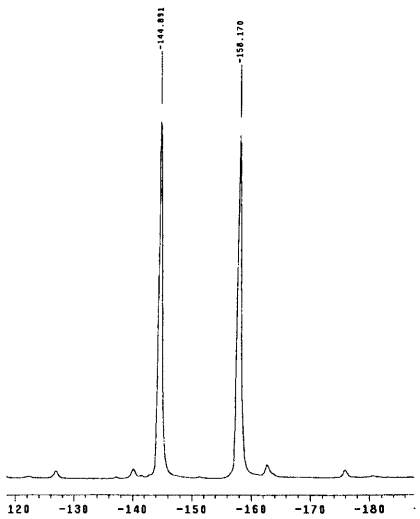
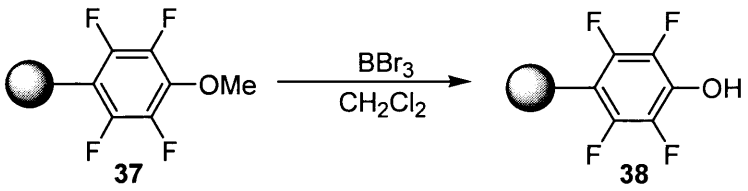


Figure 8 ^{19}F NMR spectrum of supported tetrafluoroanisole

The final stage of the synthesis of a supported tetrafluorophenol motif is to perform a deprotection of the OMe group of resin **37**. This has been carried out using the same experimental parameters used for the off-bead synthesis (Schemes **40**). Thus, supported tetrafluoroanisole was treated with a large excess of BBr_3 (12 equivalents) in dichloromethane and the mixture stirred for 5 days at room temperature (Scheme **46**).



Scheme 46

Following filtration and washing, an alcohol function was observed for the new resin as a broad band at 3478 cm^{-1} according to IR spectroscopy. This is consistent with that observed for compound **34**.

II.6 Synthesis of spacer resins

Until now, the supported TADDOL, pentane diol, and tetrafluorophenol ligands (Figure **9** species **15**, **17**, **38**) prepared have the potential metal tether points close to the polymer matrix. When used as ligands bound to a polymer, the metal will be immobilised, however the resulting supported catalyst will be very close to the polymer matrix (Figure **9 A**). A way to improve the performance of the catalyst is to introduce a spacer group between the polymer resin and the active catalyst component (Figure **9 B**).[33, 34,35,36,37] As a result, the catalyst moiety will be held away from the insoluble polymer backbone and therefore it will hopefully be in a more solution-like environment since the mobility of the supported catalyst will be increased.

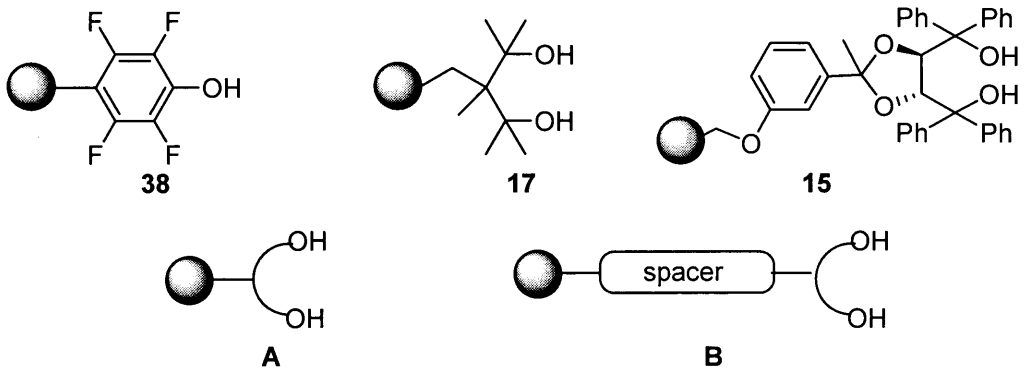
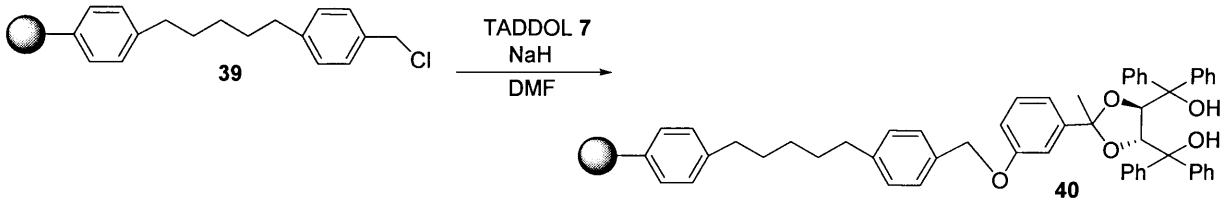


Figure 9 spacer resins

II.6.1 Synthesis of spacer-modified TADDOL resins

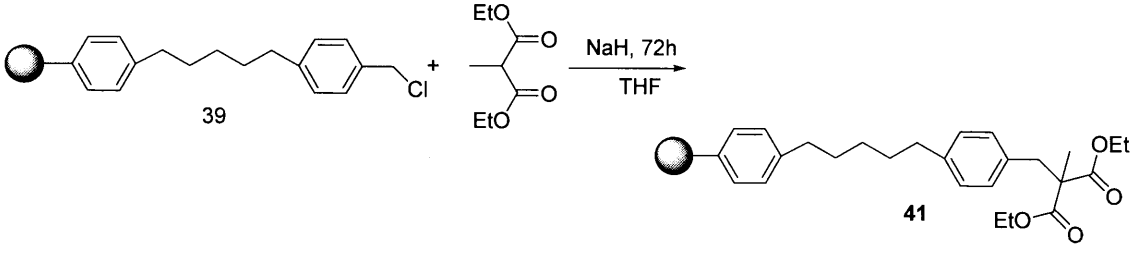
A synthesis of a Merrifield resin-supported TADDOL with a built-in spacer **40** has been described in the literature.[5] For simplicity, this procedure has been followed in order to obtain the supported TADDOL **40**. The experimental conditions used were analogous to those employed without a spacer (Scheme **47**), that is to say stirring the commercially available polymer **39** for 48h at 70°C with TADDOL **7**. Again using a longer reaction time, 5 days, the resin **39** was obtained with a better loading (0.54 mmol/g) than described in the literature (0.35 mmol/g).[4,5]



Scheme 47

II.6.2 Attempted synthesis of spacer-functionalised diol resins

The same commercial tether-modified polymer **39** was engaged in a reaction with 2-methyl-malonic acid diethyl ester, using the same conditions as those described before in Scheme **16**, to afford the supported ester **41** (Scheme **48**).



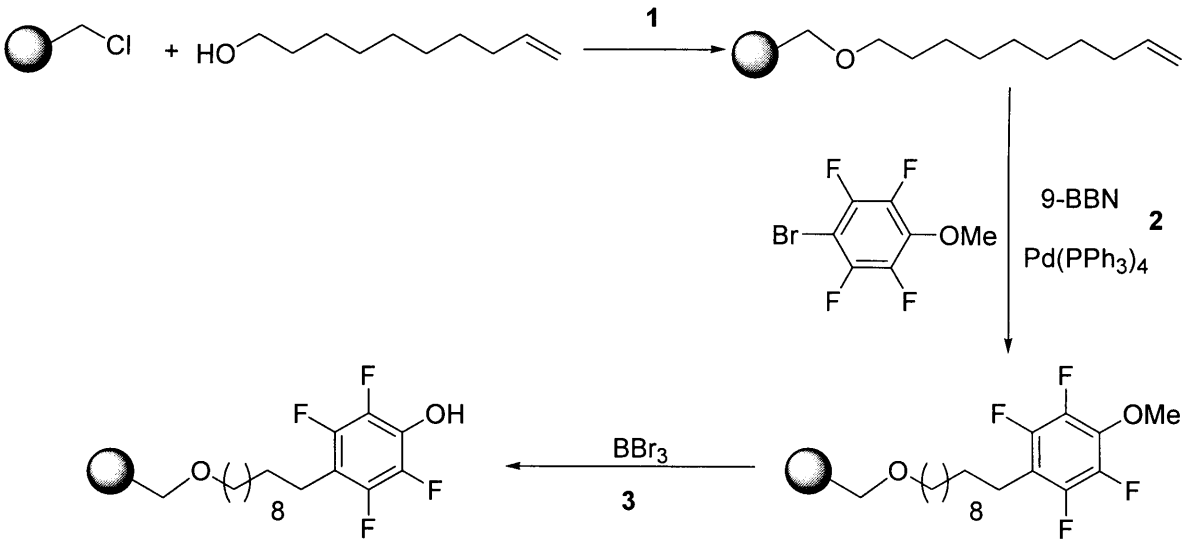
Scheme 48

The best loading obtained for functionalised polymer **41** was 0.42 mmol/g. The loading is low, and the ester motif is very light weight compared to the TADDOL motif, therefore the mass of the resin **41** should be lighter than the resin **39**, which carried the TADDOL motif. As a result the loading should be higher which is not the case here. A number of attempts were made to optimise this resin synthesis in order to try and increase the loading, mostly by increasing the temperature and the reaction time, but no better loading was obtained. It has been shown that the commercially available resin **39** swells very poorly.[38] As a consequence, diffusion of reactants into the polymer matrix is significantly hindered, something that can seriously affect grafting reactions, which is believed to be the origin of the low loading obtained here for **41**.

Although the next step of the synthesis of a supported pentanediol with a built-in spacer would be the reaction with a Grignard using the same condition as exposed in Scheme **17**, this was not attempted due to the low loading of the polymer **41**.

II.6.3 Attempted synthesis of spacer-modified tetrafluorophenol ligands

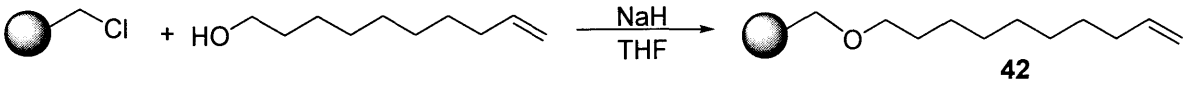
A strategy has been designed for the preparation of spacer-modified tetrafluorophenol ligands based on our success with Suzuki-Miyaura cross-coupling reactions in the synthesis of a supported tetrafluorophenol **38**, and by a Suzuki-Miyaura cross-coupling reaction "on-beads" described in the literature.[39] As presented in Scheme **49**, the synthesis of the spacer-modified tetrafluorophenol was attempted by initial immobilisation of a long chain alkene (step **1**), followed by a hydroboration, a Suzuki-Miyaura cross coupling (step **2**) and, finally, deprotection of the hydroxyl function (step **3**).



Scheme 49

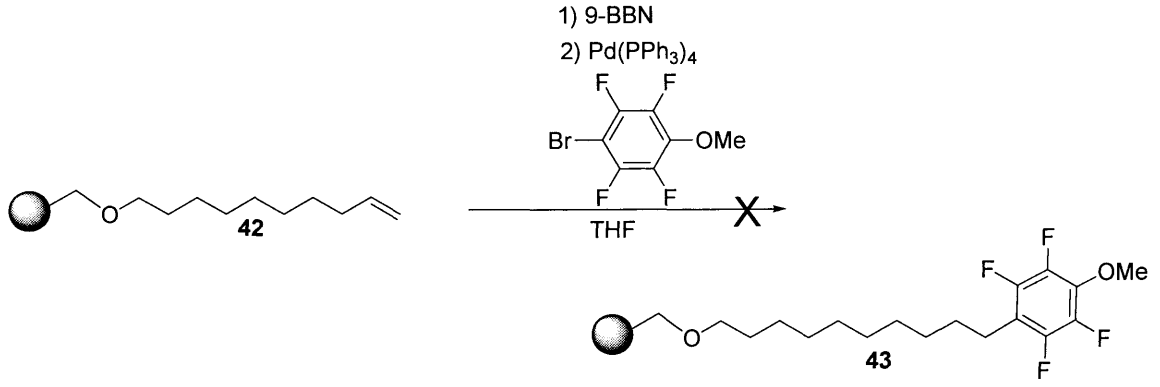
Step **1** was achieved through the reaction of decen-1-ol with standard Merrifield resin using sodium hydride as a base and THF as solvent, the reaction being stirred for 72h

at room temperature. The loading of the resulting novel resin **42** was determined by elemental analysis and was found to be 0.85 mmol/g (Scheme **50**). Its structure was further supported by gel-phase ^{13}C NMR spectroscopy which revealed the presence of the double bond (139.1 ppm (CH=CH_2), 114.1 ppm (CH=CH_2)).



Scheme 50

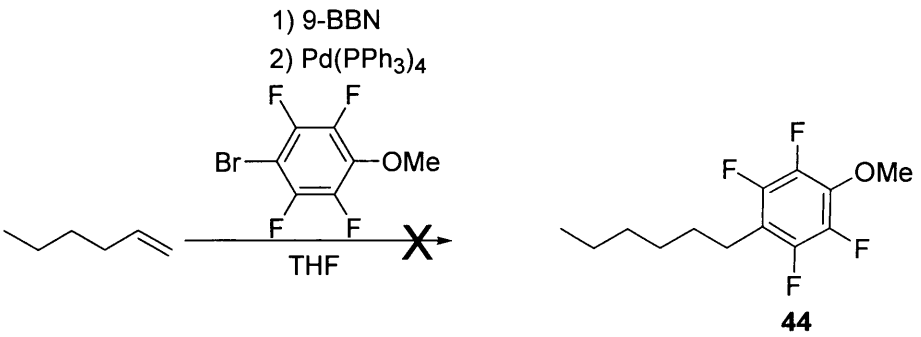
The supported alkene **42**, swelled in THF was engaged in a reaction with an excess of 9-BBN and was stirred for 24h. The solution containing excess 9-BBN was removed *via* a canula. The resulting polymer was reswelled in THF and used straight away in a Suzuki-Miyaura cross-coupling reaction with palladium tetrakis(triphenylphosphine) and bromotetrafluoroanisole (Scheme **51**).



Scheme 51

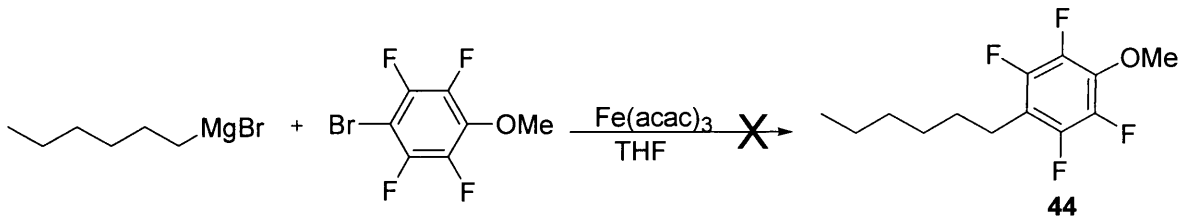
Unfortunately, elemental analyses revealed the presence of only a very small amount of fluorine, therefore the formation of the resin **42** was deemed to have been unsuccessful. An alternative method for its synthesis was attempted using microwave-assisted heating, the solution phase being monitored by GC-MS. Again, the desired product **43** was not obtained. Instead, the debromination of the tetrafluorophenol was observed to have taken place.

In order to try and explain the failure of this reaction, an attempt was made to perform cross-coupling between a soluble alkene and bromotetrafluorophenol to demonstrate the feasibility of such a cross-coupling with similar experimental conditions as described in Scheme **52**. However, only a very small amount of the desired product was observed. Again, the side product tetrafluoroanisole was detected, following debromination.



Scheme 52

An alternative methodology for the synthesis of **44** is illustrated in Scheme **53**, as described by Fürstner,[40] and involved a cross-coupling with a Grignard reagent and a halogen compound catalysed by $Fe(acac)_3$. This method was adapted to the synthesis of compound **44** as described in Scheme **52**.

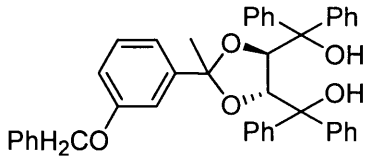


Scheme 53

Sadly, this last attempt was also unsuccessful. Once again formation of a number of by products such as tetrafluoroanisole were observed. One explanation for this lack of success in this Grignard-aryl cross-coupling is that the bromotetrafluoroanisole possesses a very deactivated ring. In addition, the literarure[40] describes successful examples of catalytic Grignard-aryl cross-couplings involved only activated rings such as benzophenone. Following this lack of success and due to the time consuming nature of the chemistry, the synthesis of a supported tetrafluorophenol with a built-in spacer was therefore abandoned.

II.7 Summary and Conclusions

Diols **8** and **12** have been synthesised and will be used to generate new Schrock-type metal-alkylidene initiators, and their possible catalytic activity will be tested for RCM. This work will be fully described in chapter three. In addition, their supported analogues **15** and **17** have been synthesized. Their coordination chemistry with molybdenum in order to give supported Schrock-type metal-alkylidene initiators will be discussed in chapter four, along with their catalytic activity. Finally, this chapter has presented a reliable way to synthesise supported tetrafluorophenol **37** with the use of microwave dielectric heating combined with Suzuki-Miyaura cross-coupling. Compound **38** will also be used to synthesise a Schrock-type metathesis initiator, and this work will be described in chapter four. Sadly, despite numerous attempts, the synthesis of support with a built-in spacer was not successful, only support **40** was synthesised.



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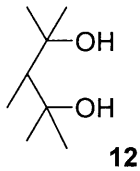

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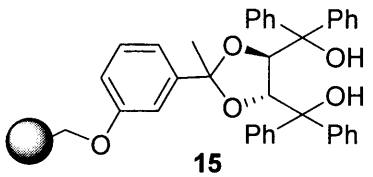

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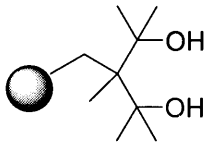

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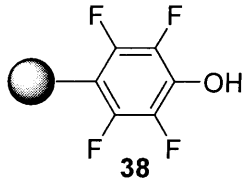

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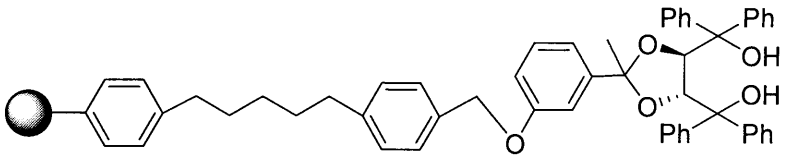

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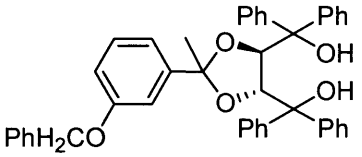
Chapter 3

Syntheses of Novel Homogenous Schrock-type Initiators

III Synthesis of Novel Soluble Schrock-type Initiators:

In chapter two, the synthesis of the TADDOL, **8**, and pentanediol, **12**, ligands (Figure **1**) has been described. Here, their coordination chemistry with molybdenum alkylidene-containing complexes will be studied with a view to obtaining new metal alkylidene initiators (Figure **2**), whose activity for olefin-metathesis will be tested. In order to prepare the new metal alkylidene complexes, precursors described previously for the synthesis of Schrock-type initiators will be employed. Their synthesis is revised here.



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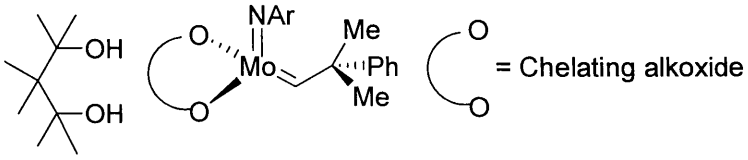

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Figure 1 Alkoxide ligand precursors

Figure 2 New alkylidene complexes

III.1 Synthesis of Schrock initiator precursors

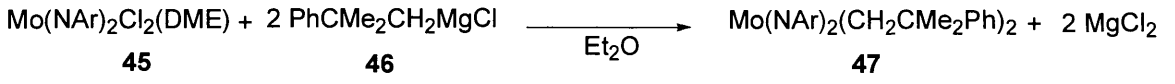
III.1.1 Synthesis of mono-imido-based molybdenum complexes

The necessary alkylidene-containing precursors were made following the procedures described by Schrock[1] except for the first step, namely the synthesis of $Mo(NAr)_2Cl_2(DME)$, which was achieved following the procedure of Gibson *et al.*[2] Thus sodium molybdate was reacted with trimethylsilyl chloride and 2,6-diisopropylphenyl amine ($ArNH_2$), in the presence of triethylamine in the coordinating solvent DME (Scheme **1**). This introduces the bulky 2,6-diisopropylphenyl imido ligands at molybdenum, which help to stabilise the later mono-metallic molybdenum alkylidene-containing complexes by preventing dimerisation. This reaction routinely gives the complex $Mo(NAr)_2Cl_2(DME)$ with a yield of *ca.* 90% following workup. Although it works very well, the mechanism of this reaction is still unknown.[2]

$$Na_2MoO_4 + 2\,ArNH_2 + 8\,TMSCl + 4\,NEt_3 \xrightarrow[DME]{70^\circ C} \underset{\mathbf{45}}{Mo(NAr)_2Cl_2(DME)} + 2\,NaCl + 4\,TMS_2O + 4\,HNEt_3Cl$$

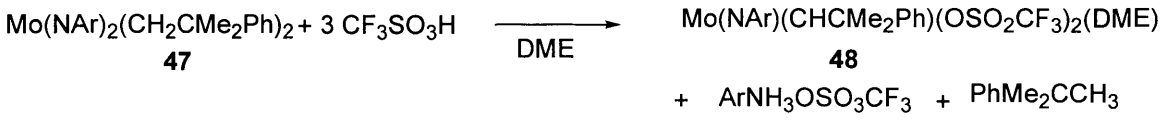
Scheme 1

Subsequently, the bis(imido) derivative is alkylated using a salt elimination reaction. The Grignard reagent **46** was made by the addition of neophyl chloride to magnesium in dry diethylether according to a standard literature procedure.[1] Following addition of the Grignard to the imido dichloride **45**, the reaction was heated at reflux for 18h. The resulting mixture was filtered and the filtrate concentrated, which afforded red crystals of **47** with a yield of 80%, comparable to the literature (Scheme **2**).[1]



Scheme 2

Dialkyl complex **47** was engaged in the next step in which the alkylidene is formed. This is achieved through protonation of one of the imido ligands followed by α-H abstraction between the two *cis*-dialkyl ligands with triflic acid in DME (Scheme **3**). This afforded compound **48** that was obtained with a yield of 75%, again consistent with the literature.[1]



Scheme 3

The complex formed is electron deficient, so DME is retained in the coordination sphere of molybdenum. X-Ray studies show that **48** is a pseudooctahedral species, in which the imido and alkylidene ligands are *cis* to one another, and the triflate ligands are mutually *trans*.[1] This compound is a useful precursor to a range of Schrock-type initiators.

III.1.2 Synthesis of bis(imido)-based molybdenum complexes

In addition to the synthesis of Schrock precursor **48**, another Schrock catalyst precursor has been synthesised, namely the unsymmetrical molybdenum *bis*(imido) derivative Mo(NAr)(N^{t}Bu)Cl$_2$(DME), by following the standard literature procedure.[3] This involved treating sodium molybdate with triethyl amine, trimethyl silyl chloride, and finally with *tert*-butylamine and 2,6-diisopropylaniline all in DME, these experimental conditions being very similar to those used for the synthesis of imido complex **48** (Scheme **4**). In order to obtain a good yield of the product **49**, and to limit the formation of symmetrical bis(imido)

molybdenum complex **45**, the less reactive *tert*-butylamine was added before the more reactive 2,6-di-isopropylaniline.

$$Na_2MoO_4 + {}^tBuNH_2 + ArNH_2 + 8\ TMSCl + 4\ NEt_3 \xrightarrow[70°C]{DME} \underset{\mathbf{49}}{Mo(NAr)(N^tBu)Cl_2(DME)} + 2\ NaCl + 4\ TMS_2O + 4\ HNEt_3Cl$$

Scheme 4

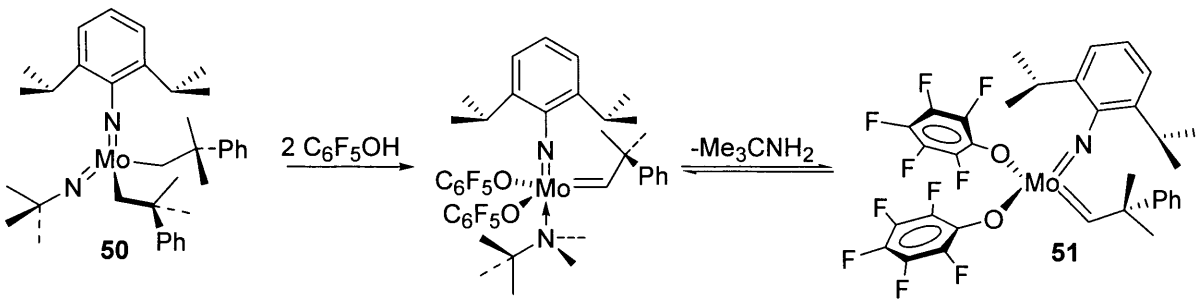
The product **49** was obtained in a good yield: 87%. Subsequently, the bis(imido) compound **49** was engaged in a reaction with Grignard reagent **46** to afford the unsymmetrical dialkyl bis-(imido) complex **50** (Scheme **5**).

$$\underset{\mathbf{49}}{Mo(NAr)(N^tBu)Cl_2(DME)} + 2\ \underset{\mathbf{46}}{PhCMe_2CH_2MgCl} \xrightarrow{Et_2O} \underset{\mathbf{50}}{Mo(NAr)(N^tBu)(CH_2CMe_2Ph)_2} + 2\ MgCl_2$$

Scheme 5

Although the desired product **8** is described in the literature as a red solid,[3] in our hands, a brown oil was repeatedly obtained despite recrystalisation from acetonitrile. However, both ^1H and ^{13}C NMR analysis of this oil revealed it to be of sufficient purity for further reactions.

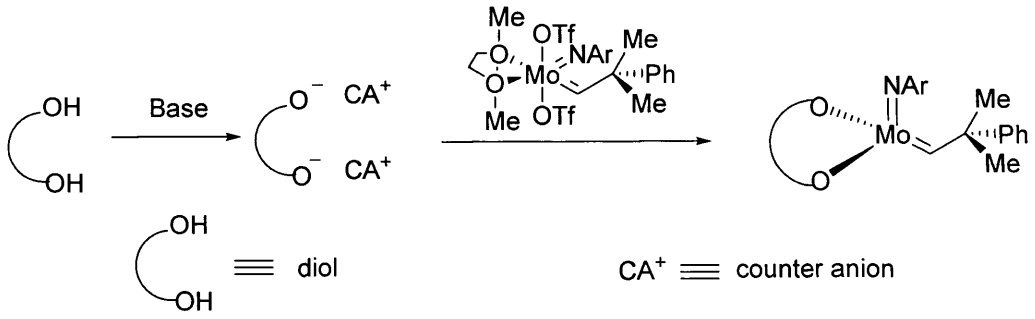
Compound **50** can be used as a one-step precursor to an imido-alkylidene complex **51** that has been shown to be active for ROMP.[3] This metal-based transformation is achieved by reaction of **50** with the very acidic alcohol C_6F_5OH that selectively protonates the *tert*-butylimido, which is more basic than the arylimido unit. This affords a Schrock-type complex bearing ($C_6F_5O^-$) ligands (Scheme **6**). The principle advantage of this methodology is the generation of a Schrock-type initiator in only three steps that avoids using triflic acid (CF_3SO_3H), which is expensive, very toxic, and difficult to handle.



Scheme 6

III.2. Synthesis of Schrock-type metal-alkylidene initiators.

The usual way to synthesise an active Schrock-type catalyst is to react an alkoxide generated by deprotonation from the corresponding alcohol with molybdenum precursors such as **48** (Scheme 7).



Scheme 7

III.2.1 Synthesis of lithium salts

In the original synthesis of the Schrock initiator described in the literature *tert*-butanol was treated with butyl lithium in order to give the resulting alkoxide **52**.[1] Thus lithium salts from *tert*-butanol, together with those from diols **53** and **54** were synthesised in the same manner, and were all isolated as white powders (Table **1**).

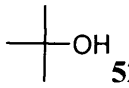
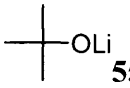
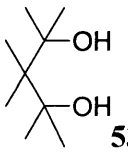
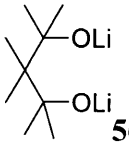
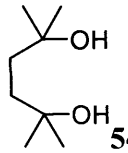
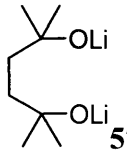
Diol	Lithium salt	Yield
 **52**	 **55**	61%
 **53**	 **56**	74%
 **54**	 **57**	76%

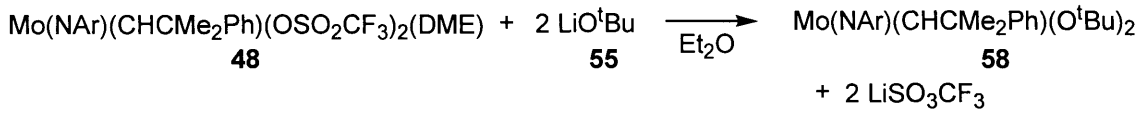
Table 1 Synthesis of alkoxide

Diol **53** was used as a potentially chelating version of *tert*-butanol, while diol **54** can be regarded as a simplistic model of TADDOL. It is important to note that once both diols **53** and **54** have been doubly deprotonated at oxygen and then bound to molybdenum, then neither will

have β hydrogens (relative to the metal) something which should prevent any β-H elimination reactions from occurring.

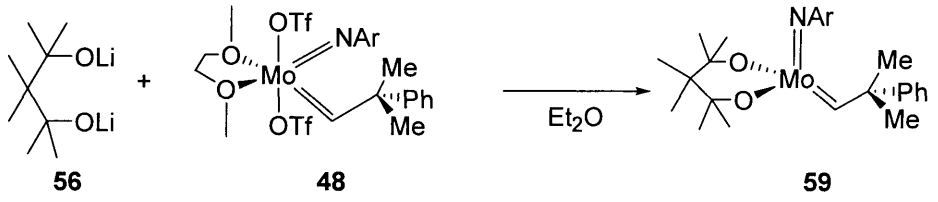
III.2.2 Attempted synthesis of alkoxide-functionalised Schrock initiators

The traditional Schrock initiator **58** has been synthesised according to a known literature procedure by the addition of the lithium salt **55** to a solution of the product **48** in diethylether at -30°C. The metal alkylidene complex **58** was isolated with a yield of 74%, which is comparable to the value quoted in the literature (Scheme 8).[1]



Scheme 8

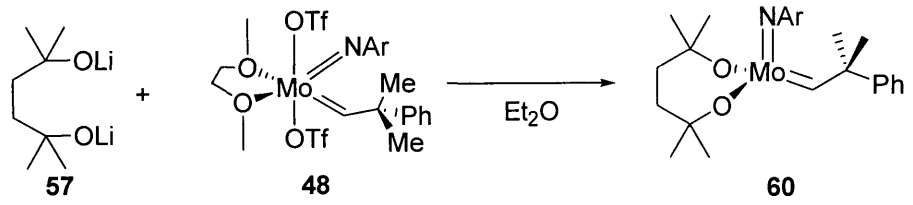
In the same manner as described for the synthesis of the original Schrock initiator **16**, lithium salt **56** has been engaged in a reaction with the bis(triflate) molybdenum complex **6** in diethylether at -30°C, then allowed to warm to room temperature (Scheme **9**). Since no crystals of the resulting product could be obtained despite prolonged cooling of a concentrated solution of the products, all volatile components were removed *in vacuo*. The resulting brown oil was subjected to ^{1}H NMR spectroscopic analysis, but did not reveal the formation of the desired complex. Instead a mixture of not readily identifiable or separable products was obtained.



56 **48** **59**

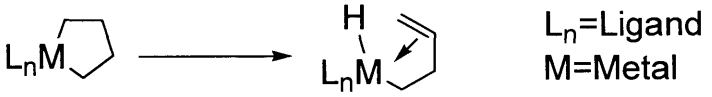
Scheme 9

A similar reaction as to that tried between **56** and **48** was attempted this time with the dialkoxide **57** (Scheme **10**) with a view to investigating the effect of chelate ring size upon ease of synthesis and complex stability. Again, analysis of the reaction mixture by ^{1}H NMR spectroscopy revealed a complex mixture of products had been formed, none of which could be attributed to the formation of the desired product.



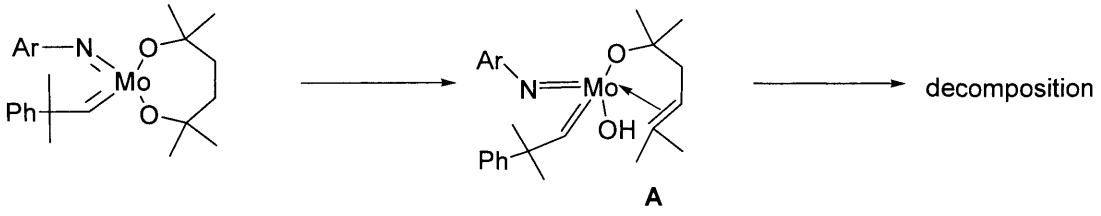
Scheme 10

A possible explanation for the lack of success in isolating the new Schrock-type initiator **60**, is the instability of these particular alkoxide derivatives, which could decompose rapidly, possibly as a result of an H atom migration from the alkoxide despite the choice of chelating systems used to try and block H-elimination using geometric constraints. Indeed, Zhenyang Lin *et al.* have demonstrated that β-elimination is possible even with five-membered ring metallacycles (Scheme **11**).[4] Hence, this type of elimination process may be even more likely for a flexible seven-membered ring.



Scheme 11

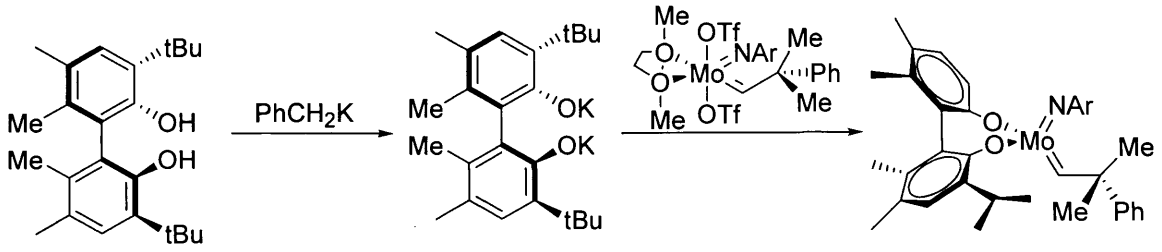
The desired cyclo alkoxide complex **60** possesses a flexible ring which could bend round and allow an H migration to take place. Therefore, **A** (Scheme **12**) could be formed, which would initiate the decomposition of the Schrock-type complex **60**, by protonation of the alkylidene or by reaction of the newly formed, highly reactive molybdenum-oxo complex. Free amine ($ArNH_2$) was observed by ^1H NMR spectroscopy, something that indicates that a protonation reaction may be involved in the decomposition process.



Scheme 12

In an attempt to see whether the desired alkylidene-alkoxide complexes were indeed being formed, but decomposing rapidly, the formation reactions were monitored by variable temperature NMR spectroscopy. These experiments were performed by allowing samples of the reactants to warm from liquid nitrogen temperature in a controlled fashion within the probe of the NMR spectrometer.

Schrock and Hoveyda published a paper about the synthesis of BINOL Schrock-type complexes (Scheme **13**).[5] The base chosen to deprotonate the diol was $PhCH_2K$. Therefore similar strategies have been used here in order to try and generate the desired chelating dialkoxide molybdenum complexes, **59** and **60** (Scheme **14-16**).



Scheme 13

III.2.3 Synthesis of potassium salts

Benzyl potassium was synthesised following a standard preparation[6] and was subsequently used for the synthesis of the dipotassium salts of diols **8**, **B**, and **12** as shown in Table **2** below.

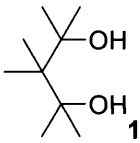
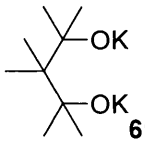
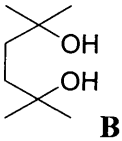
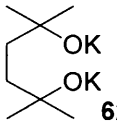
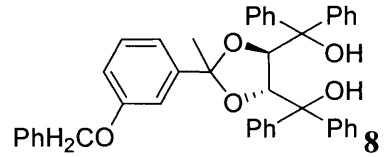
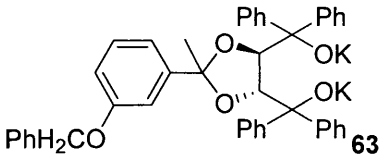
Diol	Potassium salts	Yield
 **12**	 **61**	91%
 **B**	 **62**	88%
 **8**	 **63**	89%

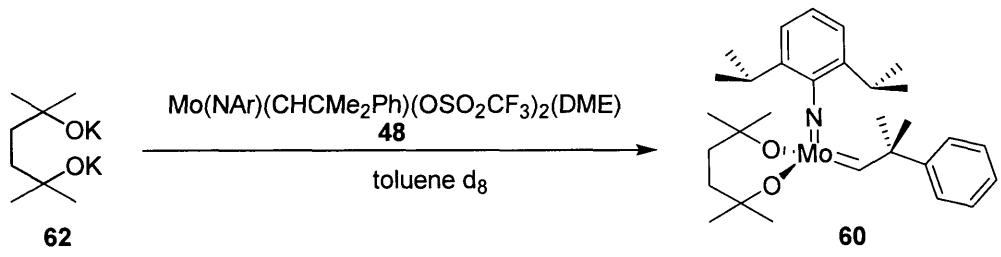
Table 2 Synthesis of potassium salts

The resulting potassium salts **61**, **62** and **63** were engaged in reactions with the molybdenum bis(triflate) complex **48** in an attempt to obtain new Schrock-type initiators. Each of the reactions was performed in dry degassed toluene d_8. The reagents were mixed in the solid state and the deuterated solvent added by syringe to the NMR tube, which had

previously been immersed in liquid nitrogen. The tube was then allowed to warm to -20°C, before being introduced into the probe of the NMR spectrometer.

III.2.4 Synthesis of Schrock initiator via potassium alkoxide salts

Using the procedure above, the Schrock-type metal alkylidene **60** was synthesised from potassium salt **62** and compound **48** (Scheme **14**). VT-NMR spectroscopic results are presented in Figure **3.**



62 **60**

Scheme 14

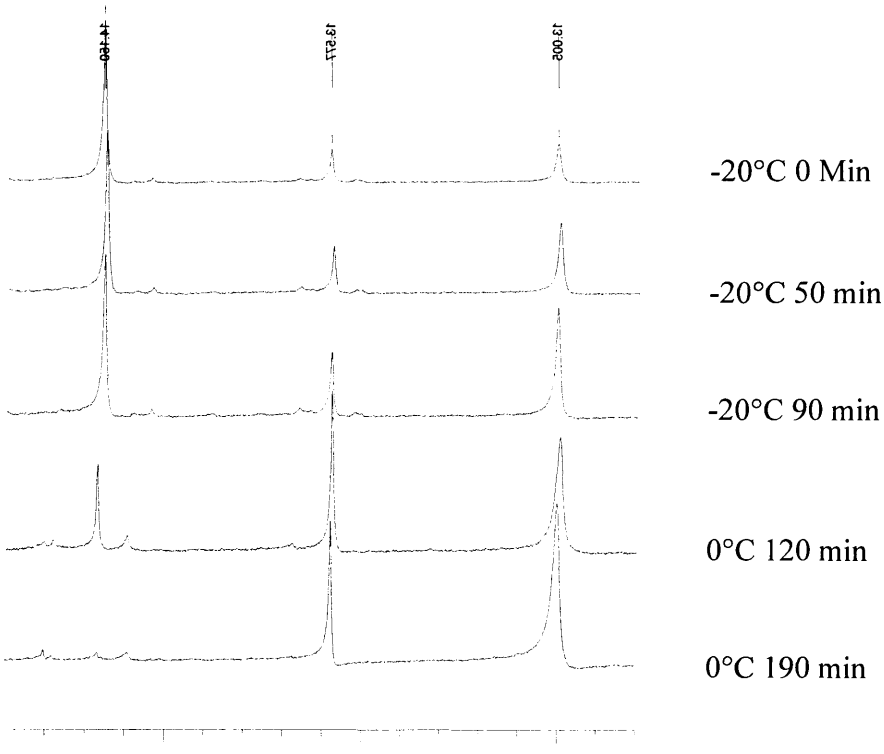
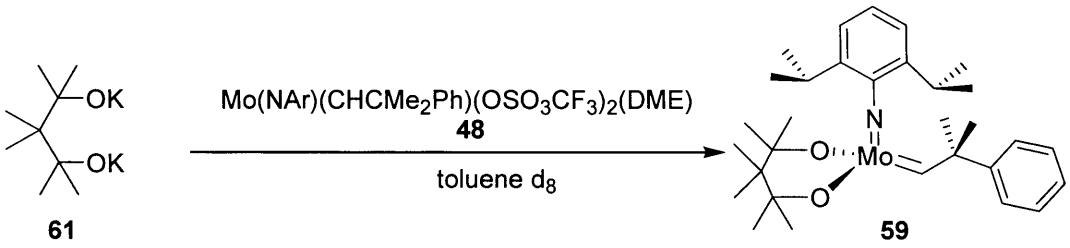


Figure 3 ^{1}H VT-NMR (toluene d_8 400 MHz) for the attempted synthesis of initiator 60 (alkylidene region only)

The resonances observed at 14.15, 13.58, and 13.01 ppm at 0 min are, respectively, those corresponding to the alkylidene signal of the starting bis(triflate) **48** and two new

alkylidene signals that have been attributed to the new Schrock-type alkylidene complex **60**. As the temperature of the probe is increased, the starting bis(triflate) is slowly consumed with concomitant increases in the amounts of each of the other two species. After 190 minutes at 0°C the starting complex **48** has essentially been totally consumed, leaving the two new alkylidene peaks at 13.01 and 13.56 ppm. Since two peaks are observed, this corresponds to the formation of two distinct new alkylidene complexes.

In the same manner as to that described above, the potassium salt **61** was allowed to react with molybdenum compound **48** (Scheme **15**). The results of this study are shown in the Figure **4**.



61 **59**

Scheme 15

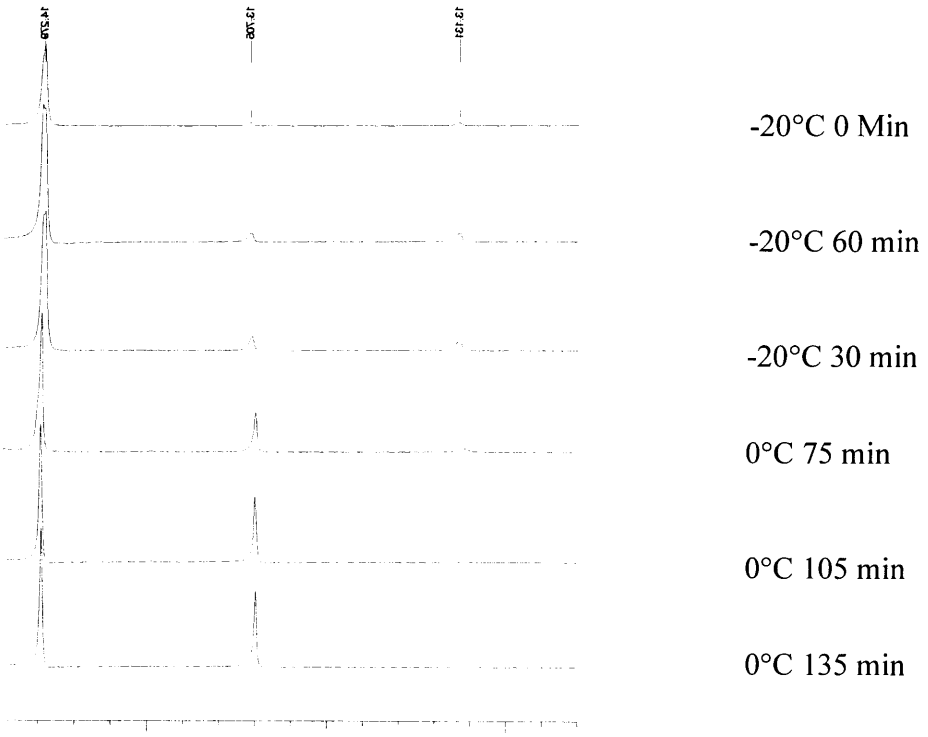
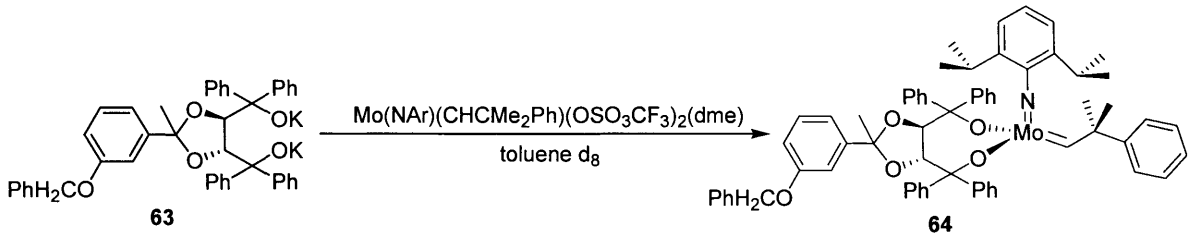


Figure 4 ^{1}H VT-NMR (toluene d_8 400 MHz) for the attempted synthesis of initiator 59 (alkylidene region only)

In this second example, again two resonances are observed at 13.71 and 13.13 ppm, in addition to the signal arising from unreacted **6** at -20°C. On allowing the tube to stand at -20°C for thirty minutes the resonances from the two minor reaction components clearly start to grow in as indicated by integration. On standing at 0°C for a further 75 minutes the resonance at 13.13 ppm almost completely disappeared leaving a peak at 13.70 ppm along with unreacted **48.**

Using an identical experimental approach, the potassium salt **23** derived from TADDOL was allowed to react with molybdenum compound **48** (Scheme **16**). The results of this study are given in Figure **5**.



Scheme 16

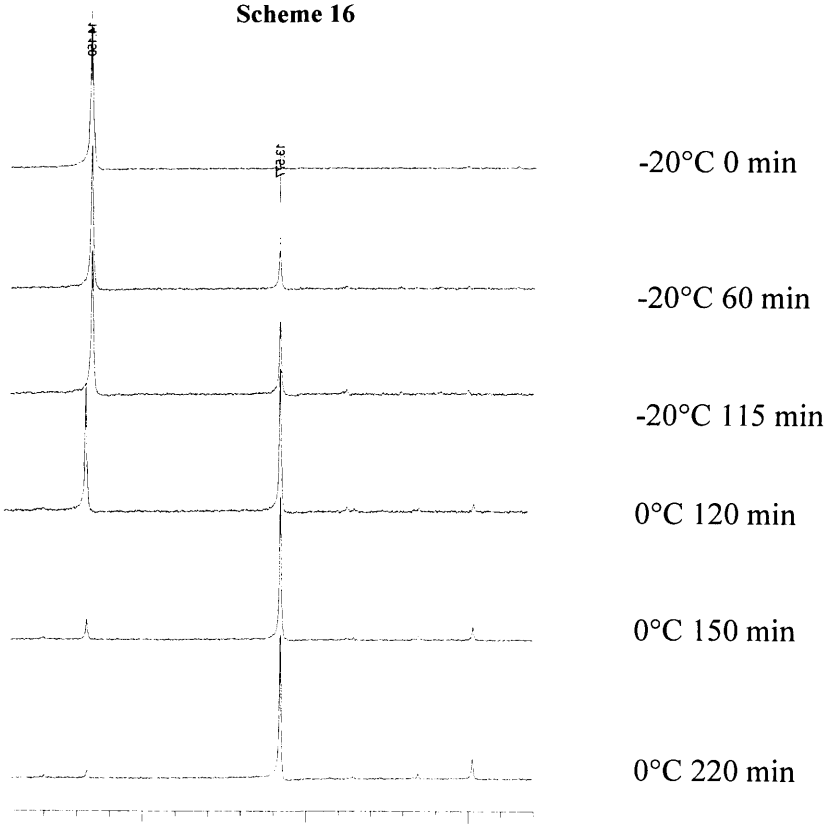
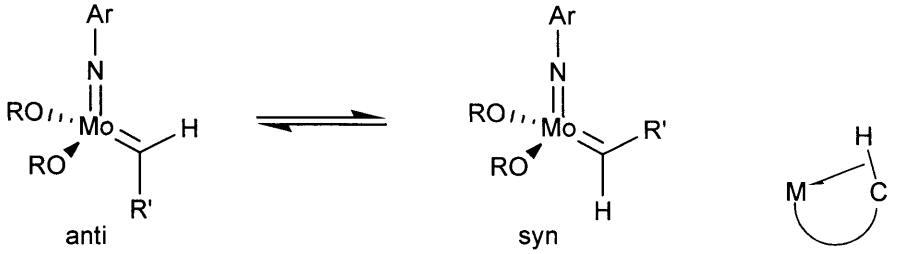


Figure 5 ^{1}H NMR (toluene $d_8$400MHz) for the attempted synthesis of catalyst 64 (alkylidene region only)

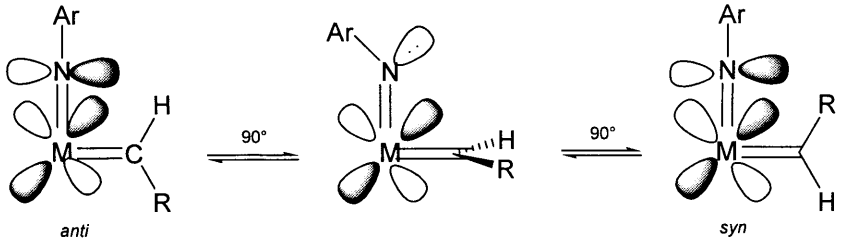
For this system, one major new alkylidene resonance was seen to appear with near total loss of starting complex **48** after 220 minutes. The formation of a new alkylidene-containing product peak started at -20°C after *ca.* sixty minutes. The reaction accelerated dramatically on warming the sample to 0°C and, after 220 minutes at this temperature, the starting molybdenum complex **48** has completely reacted. At 0°C t=120 minutes a resonance peak appeared and become larger at t=220 minutes, a result that is discussed below.

In the literature, the Schrock initiator has been observed to adopt two different rotomeric structures, namely the *syn* and *anti* forms (Scheme **17**). However, it should be noted that the *syn* rotamer is generally regarded as being more sTable than its *anti* counterpart since for the former, agostic ($MC_{\alpha}H$) interactions are possible.[7],[8] An agostic interaction which take place when an hydrogen atom is covalently bonded simultaneously to both a carbon atom and to a transition metal center. Agostic interaction generally occurs for high oxidation state, electron deficient systems, the C-H bond providing additional electron density to the metal (Figure **6**).[9]



Scheme 17 **Figure 6 Agostic interaction**

With very electron-attracting ligands such as fluoro-based alkoxides present at molybdenum, it is possible to observe both rotamers.[7] However, with less electro-attracting groups, such as *tert*-butoxide, the interconversion between the two rotamers is very quick, making it difficult to observe the two distinct forms. This has been explained in the following terms. When the metal is relatively electron-rich, the alkylidene, which has rotated by 90°, can be stabilized by the d orbital of the metal that lies in the NMC plane (Scheme **18**).[6] When the metal centre is more electron-poor, the d orbital is energetically more closely matched with the energy of a p orbital on the imido nitrogen atom, and then is involved in forming the pseudo triple bond to the imido ligand. Thus, it is clear that the rate of *syn*/*anti* interconversion will also be linked to the nature of the substituents of both the imido and alkylidene moieties.[6]



Scheme 18

The two resonances observed in each reactions of the dipotassium salts of **61**, **62** and **63** (Figures **3**, **4**, **5**) could be assigned to the *syn* and *anti* rotamers of a single new Schrock-type initiator. In the literature determination of the coupling constant J_{-CH} was undertaken in order to assign the chemical shift of the *syn* and *anti* rotamers since the coupling constants are different for these two rotamers.[10, 11] Unfortunately in our case, the ^{13}C NMR spectroscopy under the VT-NMR conditions described in Figures **4** and **5** proved impossible since the time required to acquire the ^{13}C [^{1}H] NMR spectra was long and decomposition occurred during this period. Nevertheless, in the literature, the *anti* rotamer has systematically been reported to exhibit a more downfield ^{1}H NMR chemical shift than the *syn* rotamer.[10,11] Therefore it is reasonable to attribute the signal at 13.5 ppm to be the *anti* rotamer and the signal at 13.01 ppm to be the *syn* rotamer. In Figure **3**, this assignment is supported by the integration, as the major product is at higher field and so is likely to be due to the more sTable *syn* rotamer, something that is in accordance with the literature.[5,9,10,] A probable hypothesis that accounts for the fact that two alkylidene peaks are observed is that on the NMR time scale the rate of interconversion of the two rotamers is slow at the temperatures employed.

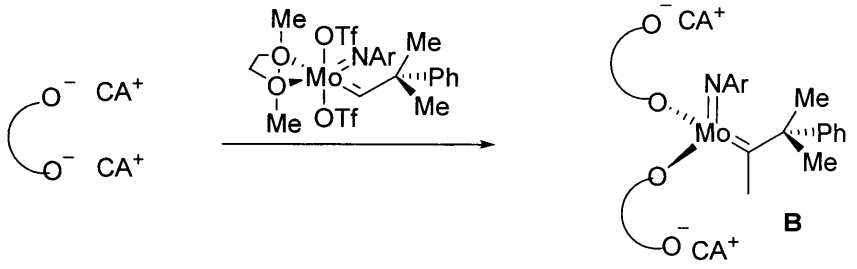
In all the VT-NMR experiments, a peak at 13.01 ppm was observed that has been attributed to a *syn* alkylidene (with the peak at 13.5 ppm being assigned to the *anti*). The major alkylidene product *(i.e.* the most sTable) obtained for this type of molybdenum imido system should be the *syn* rotamer. However, in the literature BINOL-type ligands have been described that display what has been assigned as an *anti* rotamer (13.46 ppm).[5] This is comparable to the chemical shifts obtained here for the simpler chelating dialkoxides. In the literature no experiments have described the formation of Schrock-type initiators at low temperature like the VT-NMR experiments described in this thesis. Possible observation of *syn*/*anti* rotamers have been either described at room temperature or have been indirectly observed by adding donor ligands such as trimethylphosphine, THF, or pyridine or the isomers generated by photolysis.[5,9,10] Although the major rotamer appeared to be the *anti* rotamer in Figure **5**, the *syn* rotamer seems to grow in. Thus, it is reasonable to propose that at higher temperatures the

syn rotamer could become the major species. This hypothesis is confirmed by the experiment described in Figure **3**, as the signal identified as being the *syn* rotamer grows in as the temperature is increased.

In Figure **4** the two NMR signals which could be attributed to the *anti* and *syn* rotamers have been observed at the beginning of the experiment, but surprisingly it appears that this reaction yields only the *anti* rotamer as the *syn* signals disappeared. It is important to note that in this particularly case the reaction did not got to completion as the peak corresponding to the starting material is still observed at 14.15 ppm. One explanation for this could be the poor solubility of the dipotassium salt, making the formation of the desired compound slow (especially at low temperature), which could therefore prevent the clean formation and interconversion from one rotamer to the other.

Finally a TADDOL-based Schrock–type catalyst has been described similar to **64**, but only one alkylidene resonance has been reported that was attributed to the *syn* rotamer.[11] Again, the observations have been made at room temperature and no study has been formally undertaken in order to try and observe both *syn* and *anti* rotamers which therefore makes any comparison very difficult.

Another hypothesis to account for the observation of two peaks in the VT-NMR spectra described in Figures **3**, **4** and **5** could be the reaction of two alkoxides species instead of one during the synthesis as described in Scheme **19**. Thus, the two peaks observed in the VT-NMR experiments could be a mixture of the dialkoxide together with the desired chelated dialkoxide Schrock-type complex.



Scheme 19

This hypothesis is highly improbable as the alkoxides used are diol-based systems which benefit from the chelate effect, therefore there is a bigger probability to observe the expected mono-dialkoxide species. Furthermore the formation of **B** would be very difficult as all the di-alkoxides are sterically hindered, something that would severely limit binding two

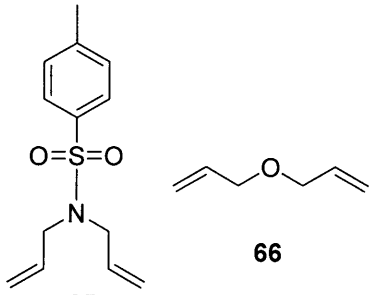
ligands to molybdenum. Most importantly, no unreacted bis(triflate) **48** was observed at the end of the reaction sequence, as would be the case if species such as **B** had formed.

Further experiments could be done to probe the formation of the *anti* and *syn* rotamer such as adding donor ligands as described in the literature or by photolysis, but our objective was just to obtain new Schrock-type compounds and the VT-NMR experiments described above (Figures **3**, **4**, **5**) do illustrate the success of the strategy as new alkylidene resonances are clearly observed, albeit that the new systems produced are only sTable below 0°C, as in all experiments described in Figures **3-5** all complexes **59**, **60** ,**64** were seen to decompose at room temperature.

As new Schrock-type complexes have been synthesised (**59**, **60**, **64**) their reactivity in ring closing metathesis (RCM) will be discussed in the following section.

III.3 Catalytic testing: RCM

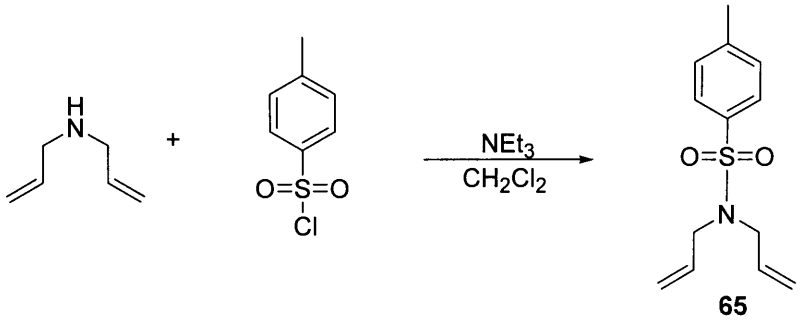
To demonstrate the activity of the new Schrock-type complexes for metathesis, investigations into their reactivity with dienes **65** and **66** were undertaken (Figure 7). These substrate were chosen for their very simple structure and well-known RCM behaviour, in order to facilitate the observation of products resulting from metathesis; they have already been used as substrates for RCM with Schrock-type initiators.[12]



65 **66**

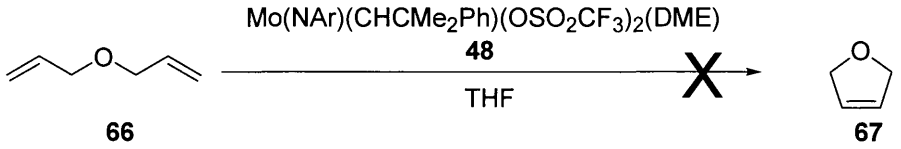
Figure 7 Dialkenes used for RCM testing

Compound **65** was synthesised by the reaction of diallyl amine with *para*-toluene sulphonyl chloride using triethyl amine as base in dichloromethane.[13] The desired compound was obtained as a colourless oil with a yield of 85% (Scheme **20**) comparable to that reported in the literature. Diallylether was obtained commercially and distilled prior to use.



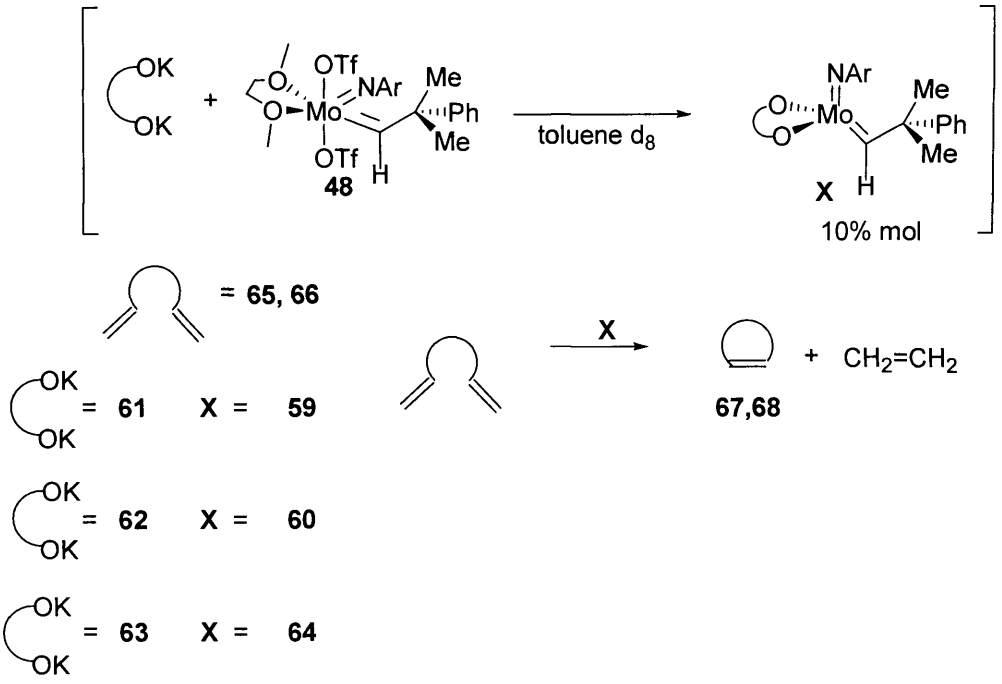
Scheme 20

Before the RCM study was undertaken it was desirable to show whether **48**, which is itself a metal alkylidene complex and involved in the synthesis of the new Schrock-type metal alkylidenes, could support RCM. Consequently **66** was allowed to react with a catalytic amount of **48** in THF (Scheme **21**). The bis(triflate) molybdenum compound **48** did not show any activity in RCM coupling. Therefore any observation of RCM activity with the new initiators prepared *in situ* must be a direct result of reaction of the new Schrock-type complexes **59**, **60** and **64**.



Scheme 21

The VT-NMR spectroscopic studies (Figure **3-5**) underlined the instability of the initiators **59**, **60** and **64**. Therefore RCM reactions were attempted with their preparation *in situ*. In a Young's tap NMR tube were placed molybdenum compound **48**, dialkenes (**65**, **66**) and toluene-d_8. A solution of the corresponding dipotassium dialkoxides (**61**, **62**, **63**) were subsequently introduced *via* a canula to the mixture at -78°C. The reaction was allowed to warm to -10°C, and this temperature was maintained for 24h (Scheme **22**).



Scheme 22

*III.3.1 RCM catalysis with complex **60***

RCM reactions have been attempted with dialkenes **65** and **66** with the new dialkoxide complex **60** that was prepared *in situ* as described in Scheme **22** with the results being described in Table **3**.

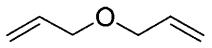
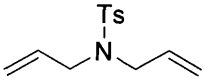
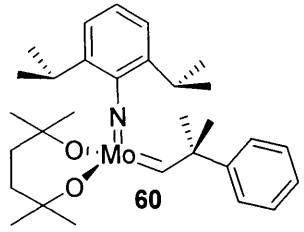
Initiator \ Dialkenes		
 **60**	 RCM product **67** Conversion: 15.2%	No product

Table 3 Catalytic tests for 60

It was found that complex **60** did not catalyse the RCM reaction of N,N-diallyl-4-methyl-benzenesulfonamide **66**, according to ^{1}H NMR spectroscopy. A possible explanation is the presence of S=O bonds which could interact with the catalyst, which is quite unsTable although it must be recognised that the RCM of **66** can be achieved with

$Mo(NAr)(CHCMe_2Ph)(O^tBu)_2$.[12] In contrast, when RCM reactions were attempted with diallyl ether **65**, in a sealed NMR tube ,and the reaction again monitored by ^1H NMR spectroscopy, a new set of resonances was clearly apparent in the NMR spectrum as shown in Figure **8**. The signals at 4.5 ppm are those of the CH_2 of the resulting 2,5-dihydro-furan **67** which is comparable to the data on the same product available commercially from Aldrich.[14] The resonance at 5.32 ppm correspond to the formation of ethylene. Peaks corresponding to the double bond of the resulting furan **67** were hidden under the signals corresponding to those of the starting dialkene and were therefore difficult to identify with precision, but integration was indeed consistent with the formation of **67**.

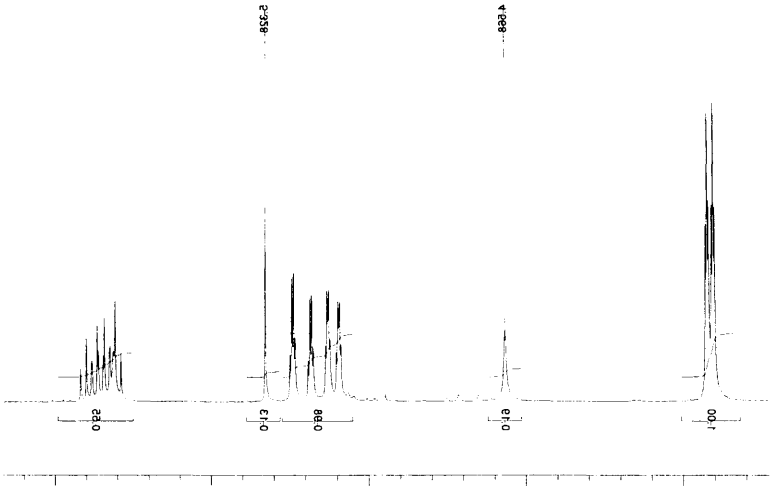


Figure 8 ^1H NMR spectrum of the reaction of 60 with diallylether to give 67

Although the conversion is very modest (15.2% by integration), this experiment clearly demonstrates the activity of the new Schrock-type complex **60** for RCM. Thus, it is therefore not unreasonable to suppose that a related initiator immobilised on a resin may also be active for olefin metathesis.

*III.3.2 RCM Catalysis with complex **59***

Schrock-type metal alkylidene complex **59** was engaged in RCM reactions with N,N-diallyl-4-methyl-benzenesulfonamide **66** and diallylether **65**, in a seal NMR tube using conditions described in Scheme **22**. The results of these experiments are described in Table **4**.

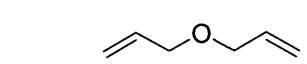
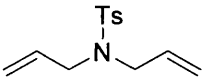
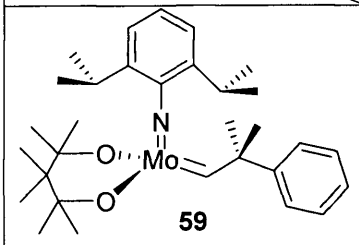
Initiator \ Dialkenes		
 59	 RCM product **67** Conversion 15.9%	No reaction

Table 4 Catalytic tests for 59

Sadly, no product resulting from RCM were observed with the N,N-diallyl-4-methyl-benzenesulfonamide. In contrast, on following the reaction of **59** with **65,** the formation of **67** was again clearly apparent, according to ^{1}H NMR spectroscopy[14], together with the expected formation of ethylene (Figure **9**).

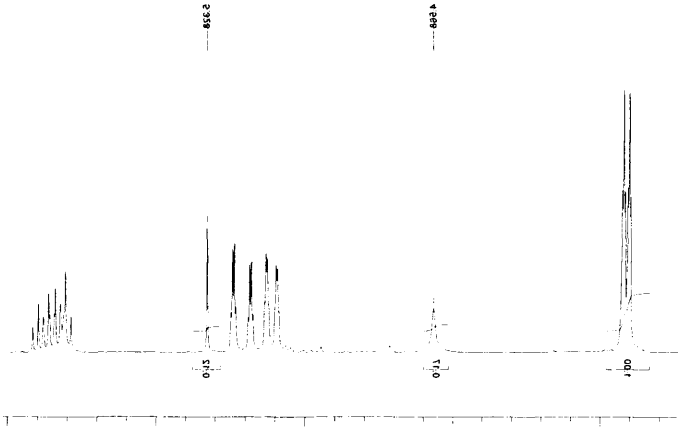


Figure 9 ^{1}H NMR spectrum of the reaction of 59 with diallylether to give 67

As before, the double bond of compound **67** resulting RCM could not be identified with precision, as its resonance was coincident with the unreacted starting material **66.** Again the conversion is very modest (15.9% by integration), but the fact that **67** is observed still demonstrates the activity of the complex **59** for metathesis.

III.3.3 RCM Catalysis with complex 64

Finally, RCM test reactions were performed with complex **64.** Again, the experimental conditions employed were those outlined in Scheme **22** the reaction being performed in a sealed NMR tube. The results of the experiments are summarised in Table **5.** Here, with this particular combination of RCM substrate and alkylidene complex catalytic results were a bit

more promising, as the desired products from RCM have been formed with two different substrates affording RCM products **67** and **68**.

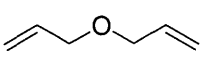
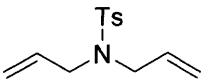
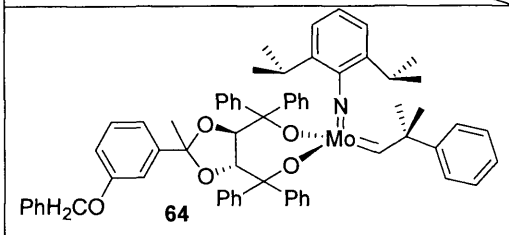
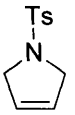
Dialkenes / Initiator		
 **64**	 RCM product **67** Conversion 14.5%	 RCM product **68** Conversion 9.5%

Table 5 Catalytic tests for 64

The reaction of **64** with diallylether performed in a sealed NMR tube gave rise to both ethylene and alkene **67**.[14] The NMR spectrum of the reaction mixture is presented Figure **10** below.

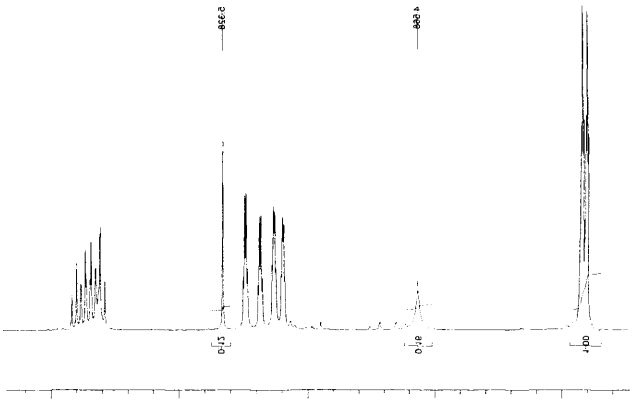


Figure 10 ^{1}H NMR spectrum of the reaction of 64 with diallylether to give 67

Similarly, complex **64** was tested for its ability to catalyse the RCM of N,N-diallyl-4-methyl-benzenesulfonamide in a sealed NMR tube, ^{1}H NMR spectroscopy clearly revealed the desired product 1-(toluene-4-sulfonyl)-2,5-dihydro-1H-pyrrole **68** had formed together with an equimolar quantity of ethylene (Figure **11**). Resonances at 4.00 ppm corresponded to the CH_2 have been observed and correspond to ^{1}H NMR data described in the literature[15]. Although the unambiguous assignment of resonances the newly formed double bond and aromatic ring could not be made as their chemical shifts are similar to those of the starting material, but their presence was inferred from integration. Again, the conversions are very modest, 9 to 15%, but

the activity of the new Schrock-type catalyst **64** for RCM has been demonstrated without doubt.

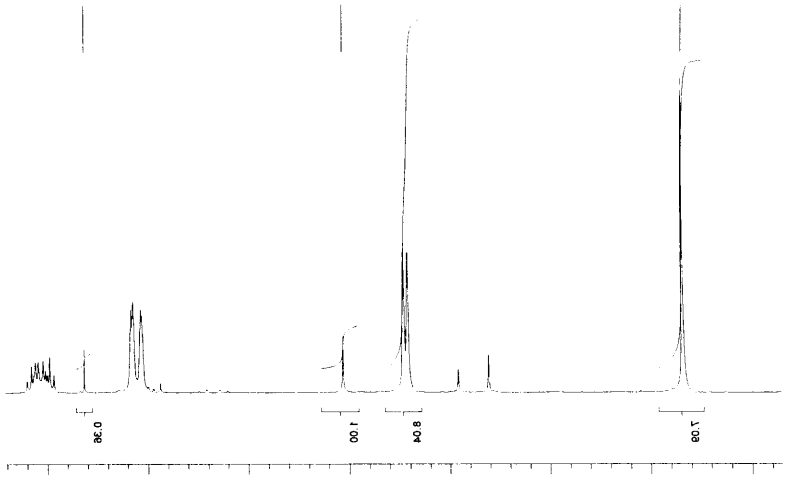


Figure 11 ^{1}H NMR spectrum of the reaction of 24 with N,N-Diallyl-4-methyl-benzenesulfonamide to give 68

Complex **64** has shown some RCM activity in the reaction involving the N,N-diallyl-4-methyl-benzenesulfonamide **68** substrate. Taking the results together it would seem that the TADDOL ligand which is the most hindered of the chelating dialkoxides, studied is the most effective in RCM reactions. Thus, the enhanced steric bulk of the TADDOLate ligand in catalyst **64** may confer greater stability and hence longer catalytic lifetimes to the system and therefore allow it to not only initiate the RCM of **66**, but also the more bulky substrate **65**.

*III.3.4 Catalysis with complex **69***

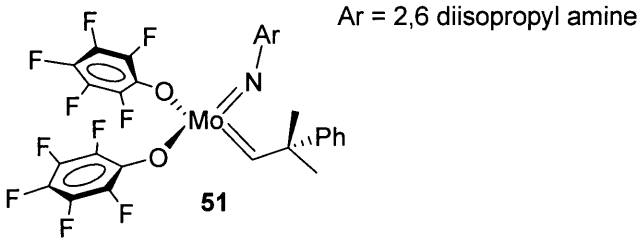
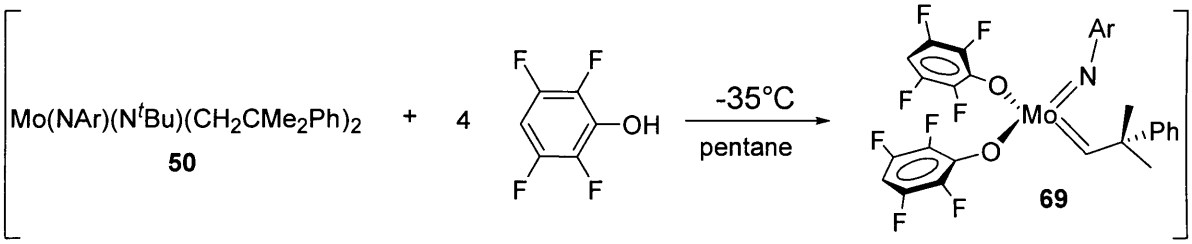


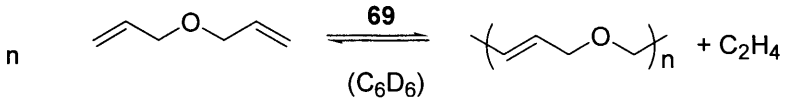
Figure 12 Pentafluorophenol-based complex

Complex **51** has been reported by Gibson *et al.* and has proven active for the ROMP of alkenes such as norbornene.[3] During this thesis a very related complex **52** was synthesised using similar methods to those described by Gibson, namely the reaction of the molybdenum compound **50** with tetrafluorophenol at -35°C. This was undertaken in order to provide a

homogeneous model of a polymer immobilised variant of this initiator that will be described later in this thesis (chapter **4** section **IV.2**).



Ar = 2,6 diisopropyl amine



Scheme 22

In order to probe the utility of complexes such as **69** for RCM, this new variant of a Schrock-type complex was used in a reaction aiming to initiate RCM of diallyl ether **66**. This was achieved by reacting a pentane solution of bis(imido)complex **50** (10mol %) with diallyl ether in a Schlenk. After stirring at room temperature for two days, the reaction vessel was opened to the atmosphere and the mixture passed through a short plug of silica to remove metal containing species. Subsequently, all volatile components were removed on a rotary evaporator at water pump pressure at 40°C. The oil obtained was dissolved in $CDCl_3$, and examined by ^{1}H NMR spectroscopy (Figure **13**). An identical reaction and work-up was performed with Gibson bis (pentaflurophenoxide) **51** and an identical ^{1}H NMR spectrum was obtained.

Unfortunately, the data were complex and did not readily allow for straightforward interpretation. By ^{1}H NMR spectroscopy four distinct regions were apparent (m 6.1-5.7; broad m, 5.3-5.1; m 5.05-4.90; broad m 4.00-3.90). Comparison with ^{1}H NMR spectrum of diallylether (peaks) reveals that the new non-volatile products contain the constituents of diallylether, but are clearly not diallylether (easily removed *in vacuo*). The broadness of the peaks suggests that one of the products is polymeric in nature. Indeed analysis of the crude mixture by GC-MS was attempted, but proved uninformative since none of the components of the mixture proved volatile.

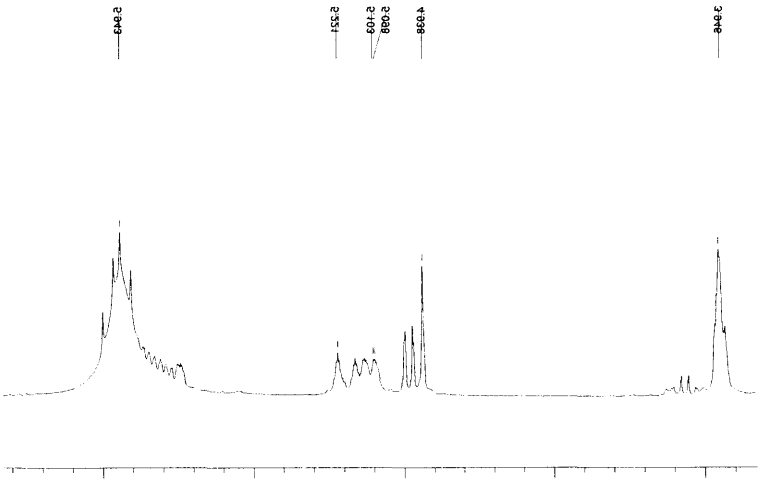
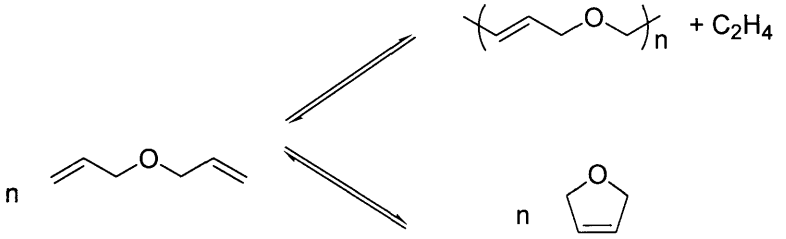


Figure 13 ^{1}H NMR data underlining ADMET polymerisation of 66

One explanation for the formation of a polymeric product could be a related process Acyclic Diene Metathesis (ADMET) had occurred in part as illustrated in Scheme **23**..

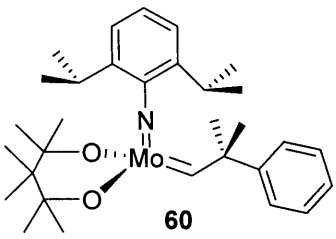


Scheme 23

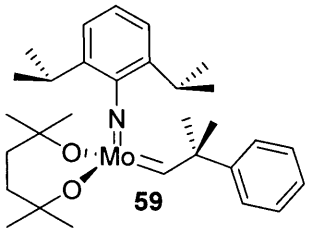
RCM and ADMET processes are competitive reactions, as they are similar in their mechanism.[16] Whether a product results from RCM or ADMET is controlled by the relative kinetics of the two processes, which are dependant upon factors such as the concentration of the starting material, the nature of the substrate and the nature of the catalyst.[13] Another important factor which could contribute to the formation of the ADMET product is the use of tetrafluorophenol ligands as Schrock-type complexes based on fluorinated alcohols seem to favour ROMP and ADMET reactions rather than RCM.[5] In this particularly case, it is possible that a mixture of ADMET and RCM products were obtained, but the RCM product was not observed due to the volatile nature of the 2,5 dihydrofuran.

III.4 Summary and Conclusions

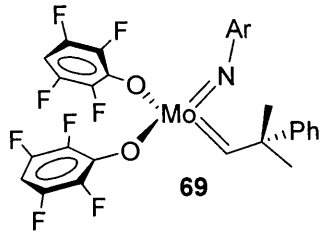
The *in situ* synthesis of new homogenous Schrock metal-alkylidene complexes **59**, **60**, and **64** has been performed. VT-NMR experiments have underlined the appearance of alkylidene resonances (both *syn* and *anti* rotamers) that are characteristic of such species. Catalytic metathesis tests have been undertaken and have shown that moderate-low RCM activity can be recorded for these species. Synthesis of tetraflurophenol-based Schrock-type complex **69** has also been carried out and ^{1}H NMR spectroscopy has highlighted its preference for ADMET reactions rather than RCM with the substrates probed.



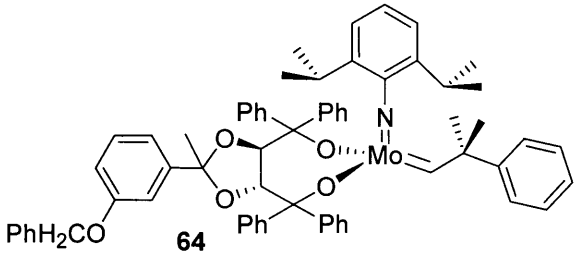
60



59



69



64

III.5. References

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Chapter 4

Synthesis of Polymer-supported Schrock-type Alkylidene Complexes

IV Synthesis of polymer-supported Schrock-type alkylidene complexes

In chapter two the syntheses of potentially-chelating diol TADDOL **8**; 2,3,3,4-tetramethyl pentane-2,4-diol **12** and their polymer supported analogues **15, 17, 40** (Figure 1), in addition to polymer-bound tetrafluorophenol **38** have been reported, with a view to synthesising novel homogenous Schrock-type imido alkylidene complexes and their polymer-supported counterparts.

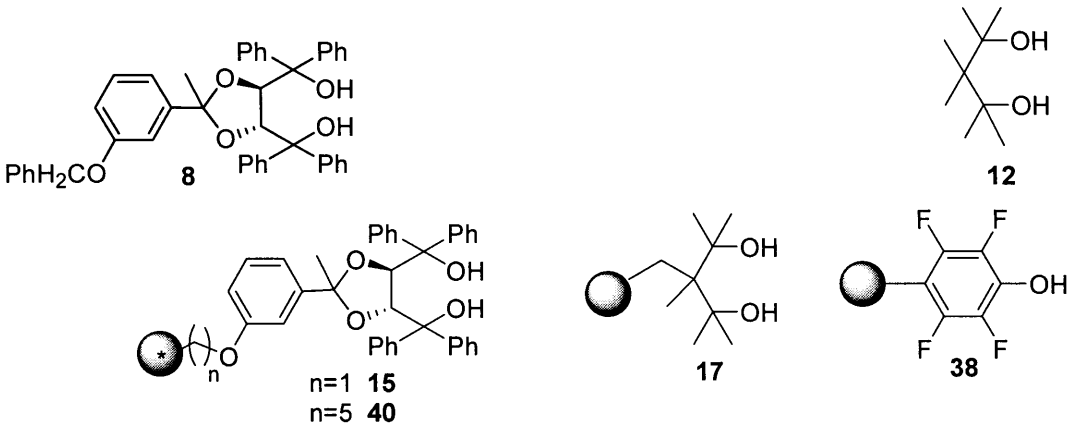


Figure 1 Chelating diols and polymer-supported diols

In the third chapter of this thesis, the syntheses of soluble Schrock-type alkylidene complexes **59, 60, 64** have been described and their ability to induce olefin metathesis, albeit in a modest way, demonstrated. This latter observation, underlined that the synthesis of their immobilised equivalents could lead to active metathesis initiators and may provide systems with greater stability as a result of site isolation and stabilisation phenomena possible on-resin. Hence, the preparation of such polymer-supported dialkoxide initiators will be investigated. The ideal precursor for their preparation is the bis(triflate) derivative $Mo(NAr)(CHCMe_2Ph)(OSO_2CF_3)_2DME$ **48**.

In addition, a reaction analogous to that used by Gibson *et al.*, for the formation of an imido alkylidene complex,[1] namely the reaction of pentafluorophenol with a mixed alkyl molybdenum bis(imido) complex will be probed with the polymer-bound variant of tetrafluorophenol **38**. Additionally, a potential alternative synthesis "on-bead" of a supported Schrock-type metal-alkylidene derivative will be discussed.

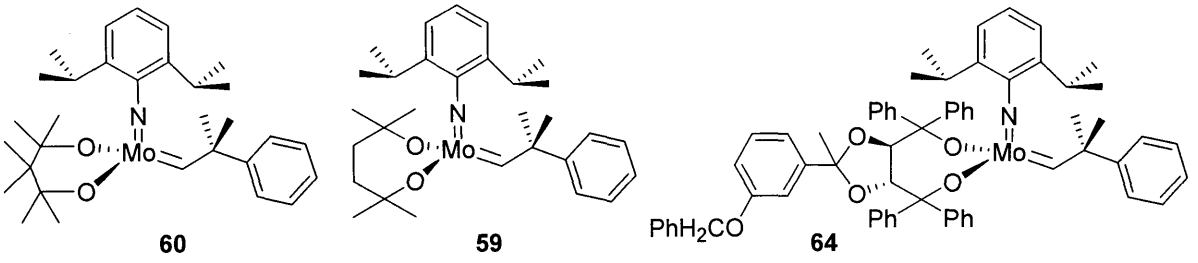
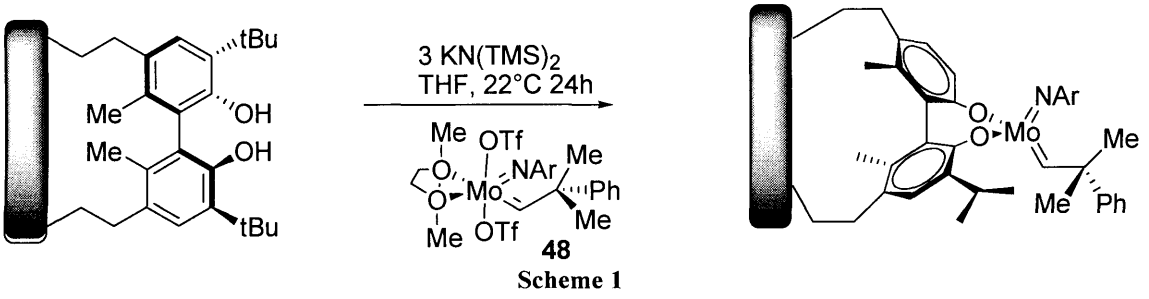


Figure 2 New Schrock-type initiator

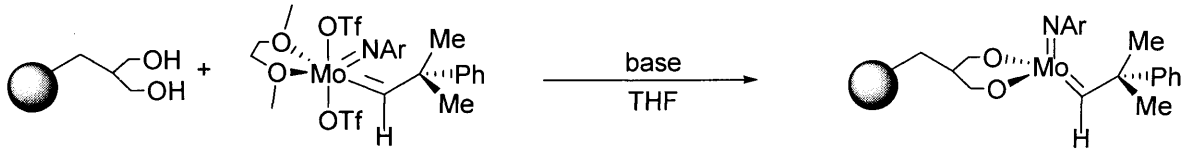
IV.1 Synthesis of polymer supported-diol-based Schrock-type complexes

Since the start of the work described in this thesis, three methods have been described in the literature for the heterogenisation of Schrock-type metal alkylidene complexes,[2-34] each of which has been described in chapter 1 section IV.3. Notably, Schrock and co-workers described and designed a strategy that involved the initial synthesis of a vinyl-functionalised BINOL, its polymerisation to give a BINOL-functionalised resin, deprotonation by excess $KN(TMS)_2$, and lastly reaction with bis(triflate) complex **48** to afford a new immobilised Schrock-type metal complex (Scheme **1**).



Scheme 1

The intention at the outset of this thesis was to exploit an extremely similar methodology for the heterogenisation of such molybdenum species on diol-functionalised Merrifield resins. Indeed, during this thesis, the deprotonation of diol-functionalised resins **15**, **17** and **40** (Scheme **2**) using a number of interrelated bases, namely $KN(TMS)_2$, $NaN(TMS)_2$, and $PhCH_2K$, was explored. $NaN(TMS)_2$ was also employed since it is similar in basicity and structure to $KN(TMS)_2$, but somewhat easier to prepare. These deprotonation reactions were performed by treating samples of **15, 40** and **17** with these bases at room temperature for periods of 12h. Subsequently, the polymers were washed several times to remove any excess base, before being reacted with the initiator precursor **48** for 24h at room temperature (Scheme **2**).

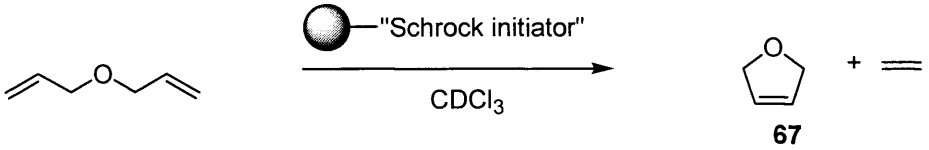


15, 40, 17 **9** **70, 71a, 71b**

base = $KN(TMS)_2$, $NaN(TMS)_2$ and $PhCH_2K$

Scheme 2

The observation and characterisation of immobilized species such as **70, 71a** and **71b** is not easy. One way to demonstrate the formation of the desired supported initiators **70** and **71** is to perform a catalytic test. Therefore, RCM reactions were performed with supported initiators **70**, **71a** and **71b** swollen in $CDCl_3$ using diallylether at room temperature for 48h (Scheme **3**, Table **1**), in a Schlenk and was probed by ^1H NMR spectroscopy. Attempts were made to induce RCM of diallylether using *ca.* 10 mol % of molybdenum assuming that the loading of the metal centre was at the maximum capacity of the polymer, which was calculated to be at 0.75 mmol/g.



67

Scheme 3

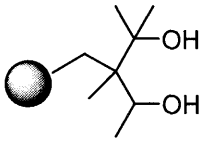
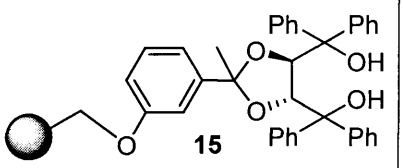
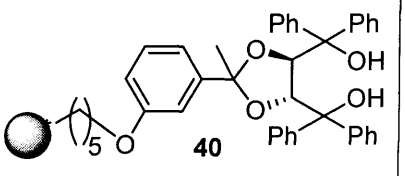
Supported diol / Base	 **17**	 **15**	 **40**
$NaN(TMS)_2$	No RCM	No RCM	No RCM
$KN(TMS)_2$	No RCM	No RCM	No RCM
$PhCH_2K$	No RCM	No RCM	No RCM

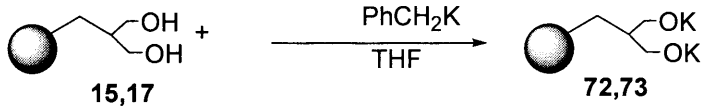
Table 1 Synthesis and RCM tests of supported Schrock complexes

Despite the variation in base used, no products resulting from RCM could be detected by ^1H NMR spectroscopy. Apparently, the pseudo-high dilution environment and the protection provided by the polystyrene matrix (see Chapter one) is not sufficient to stabilise the resulting supported complex. Alternatively, it is possible that the deprotonation of the supported-diols **15, 17** and **40** did not occur hence, none of the described complex had in fact formed although this seems unlikely as the base used are powerful and used with success by

Schrock. However, it is reasonable to suggest that according to the data obtained for the homogenous versions of these systems described in Chapter 3 (Section III.2.4), had the desired complex been formed then it would most likely have adopted the *anti* rotamer, which is known not to be the favoured rotamer, and as result, may not be sTable even on-resin. Therefore, other reactions have been undertaken with a view to synthesising supported initiators **15, 17** and **40** using the same conditions as used for the VT-NMR spectroscopic experiments described in chapter three section III.2.4.

Once formed, the new complexes were subject to RCM reactions with diallylether, in order to try and observe some catalytic activity, which would underline the formation of immobilised metal alkylidenes **15, 17** and **40**.

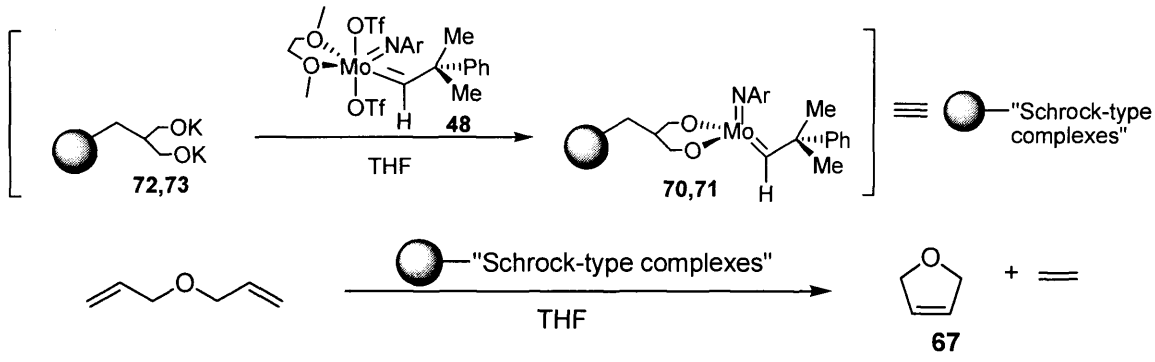
Thus, polymer supported diols **15** and **17** were reacted with potassium benzyl for 48h in order to form the resulting supported alkoxides **15** and **17** (Scheme **4**). Potassium benzyl was chosen as the base for all these reactions, as this is the base that has been used successfully by Schrock previously for the generation of Schrock-type metal-alkylidene initiators in solution.[2] Furthermore, these conditions are near-identical to those used for the deprotonation of related supported diol ligands on Merrifield resins in order to support Lewis acid.[5]



15,17 **72,73**

Scheme 4

Following formation of the supported dialkoxides by deprotonation and followed by several washings with THF and subsequent drying *in vacuo*, the initiator precursor **48** was added at -20°C in toluene d_8 and a quantity of diallyl ether calculated in a manner such that the reaction would be carried out using *ca.* 10% of the supported metal complex (Scheme **5**) introduced. The course of these reactions was followed by NMR spectroscopy by examining the fate of the substrate and the formation of any new compounds in solution, and the results presented in Table **2**.



Scheme 5

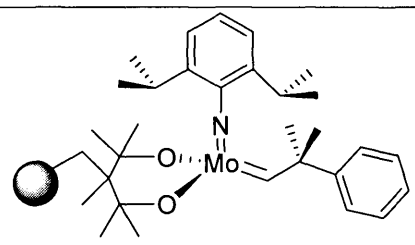
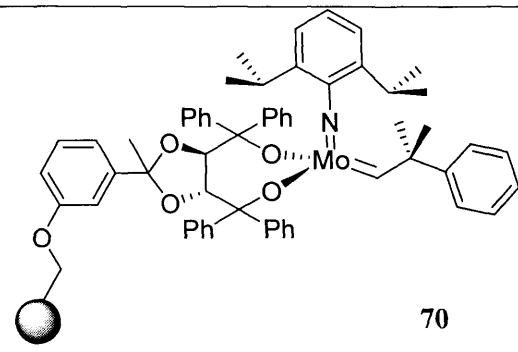
Proposed structures of supported initiators	 71	 70
Catalytic Activity	None	RCM 

Table 2 Diallylether RCM activity of the new supported complexes

Using this modified procedure, the outcome of the desired RCM reactions were more encouraging for the supported TADDOL-based initiator **70**, as ^{1}H NMR spectroscopy of the solution phase clearly revealed the formation of 2,5-dihydrofuran, the product resulting from RCM of diallyl ether (Figure **3**). The NMR spectrum clearly reveals a peak at 4.58 ppm corresponding to the ring methylene protons (*cf.* δ = 4.00 ppm in diallyl ether). Again the activity is very modest, compared to what was observed for the homogeneous version of the initiator with a conversion (by integration) of 14% being observed.

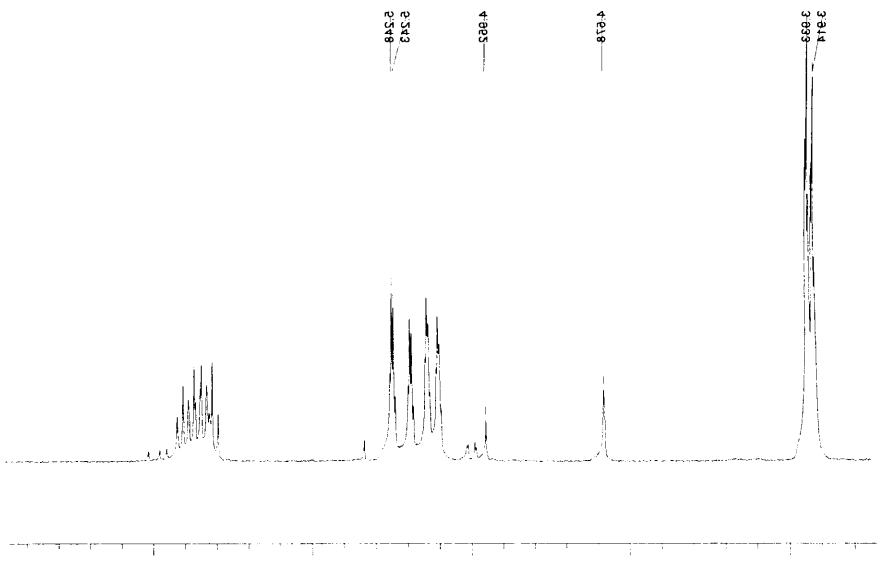


Figure 3 ^{1}H NMR spectrum of the RCM product generated by the supported complexes 70

Unfortunately, use of the polymer supported pentanediol ligand **17**, and its coordination to molybdenum led to no catalytic activity for RCM, for the resulting supported initiator **71**, no new products being observed by NMR. According to the results of ^{1}H NMR VT spectroscopic experiments (Chapter 3, Section 2), this is not totally surprising as only TADDOL-based initiators appeared to be active, possibly because this ligand is much more sterically demanding than **70**. Polymer-bound TADDOL-based initiator **71** could also be more active than polymer-supported initiator **70** since the metal binding site of the TADDOL motif, which holds the necessary molybdenum species, is held away from the polymer matrix, therefore acting as a spacer and as a result more closely mimicking homogenous reaction conditions. With this in mind, future work that investigates the effect of various of spacers between the polymer matrix and the active molybdenum centre would be of some interest, especially with the polymer **40,** to investigate and to obtain a clear view of the effectiveness of a spacer.

Attempts have been made to determine precisely the loading of the metal complexes on the polymers **70** and **71**. In the literature, Sherrington has reported the synthesis of supported molybdenum species on polymer beads and established the loading of metal centre by heating and destroying the polymer by acid digestion followed by ICP-AES of the resulting solutions.[6] In our case, we chose a less destructive and less time consuming option. Molybdenum loadings were determined indirectly by analysing polymer washings and measuring the amount of metal that was not anchored on the solid supports. To do this, following

deprotonation reactions with **48** and filtration, the resulting polymer beads were washed several times with THF, in order to remove any residual starting material **48** and leached initiator, and the resulting combined filtrate and washings were concentrated and dissolved in *aqua regia* in order to obtain an aqueous molybdenum-containing solution. This was subjected to ICP-AES analysis.

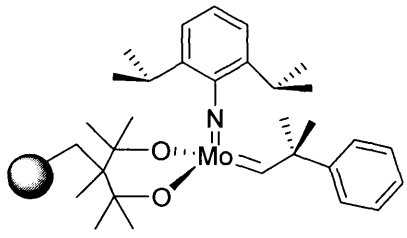
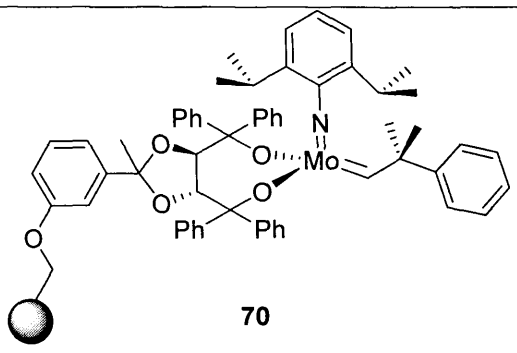
Resin	 **71**	 **70**
Mo loading (mmol/g)	0.44	0.35

Table 3 Loading of metal centers on polymers 70 and 71

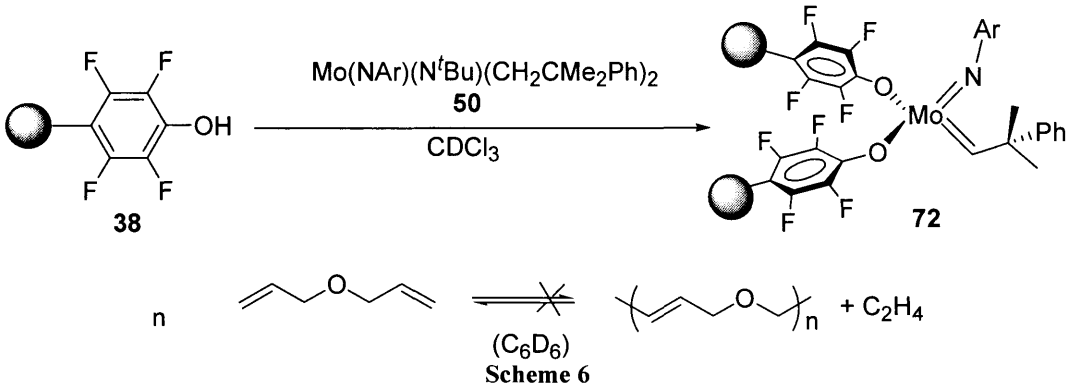
These loadings compare well with the loadings described in the literature by Schrock for similar types of supported molybdenum complex,[2] despite using a different tool (ICP-MS), which allow to quantify directly determine the metal loading. Unfortunately, this technique was not available to us.

IV.2 Synthesis of supported-tetrafluorophenoxide-based Schrock-type complexes

In chapter three, a discussion of the activity of pentafluorophenoxide-based initiators for RCM was presented. Here, the potential for preparing supported initiators based on the use of the resin **38** will be investigated (Scheme **6**). This resin provides an immobilised variant of the strongly acidic alcohol pentafluorophenol, used by Gibson and co-workers.

Attempts were made to prepare the supported imido alkylidene complex *in situ* by the reaction of immobilised tetrafluorophenol **38** with the mixed imido complex **50**. Once prepared, the quantity of diallylether necessary for a 10 mol % catalytic reaction was determined and added. Since it has been shown that the homogenous initiator could be generated at -35°C, the attempted synthesis of the polymer-supported analogue and its catalytic test was undertaken at -20°C for 48h. Undertaking these types of reaction at low

temperatures is essential, since initiator degradation occurs at high temperatures (see Chapter three) in solution.



Scheme 6

In contrast to the homogeneous reaction in Chapter 3, no new products could be isolated. It is important to note that during the initiator test the resin **72** did not appear to swell very well. This could be due to the creation of cross-linking when **50** is coordinating to the supported fluorophenol **5**, as two coordinations are possible as illustrated in Figure **4**. If the cross-linked coordination **B** is favoured then it will result in a loss of activity of the metal centre, since it is less accessible.

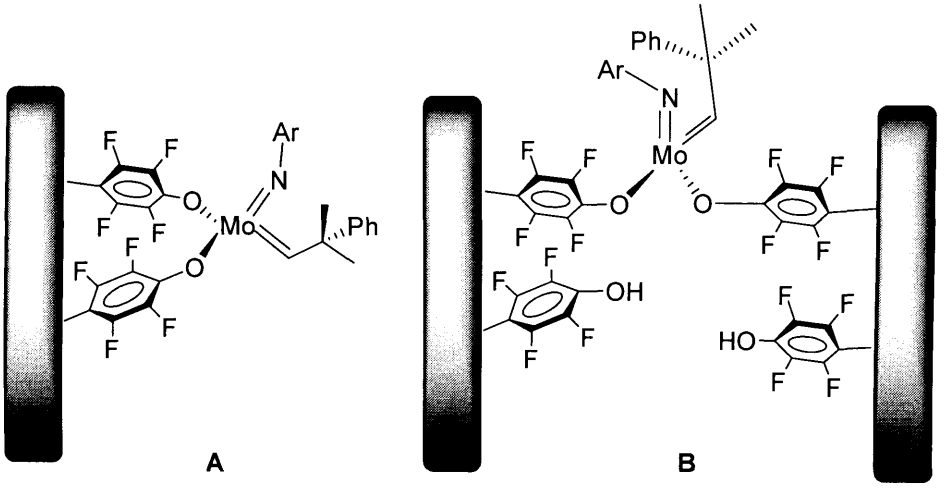


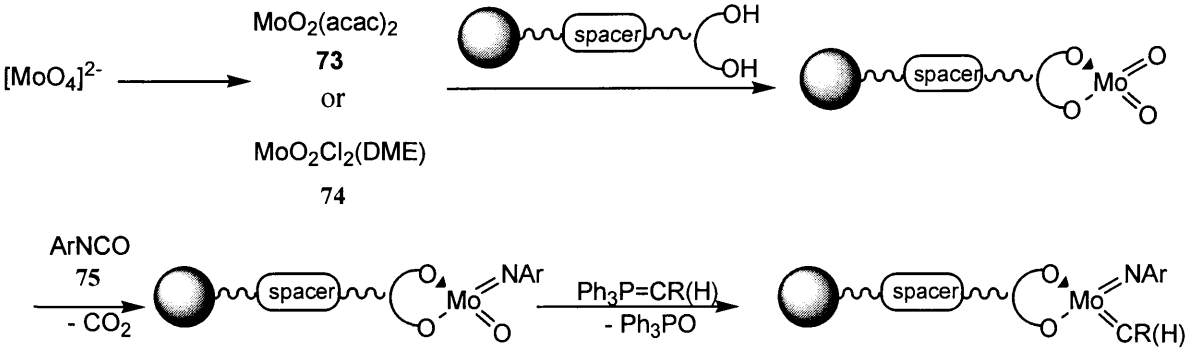
Figure 4 Competing coordination of the molybdenum metal centre by supported tetrafluorophenol

IV.3 Towards an "on-resin" synthesis of a supported Schrock-type initiator

So far all the attempts to synthesise supported Schrock-type initiators, have involved the initial synthesis of a supported diol (**15** and **17**) or alcohol ligands (**38**), followed by the reaction/immobilisation of an initiator precursor complex in order to generate the supported

initiators **70, 71** and **72**. There are disadvantages to this approach as the synthesis of the Schrock precursor (**48, 50**) used to immobilise the metal centre is not straightforward, and is time-consuming and costly. With this in mind, an alternative approach was sought, namely to synthesise the desired supported Schrock initiator "on-resin" using simple, high yielding transformations. Indeed, it is for exactly this type of approach that Merrifield resins were first synthesised, namely for the preparation of polypeptides.[7] Investigations into the feasibility of this new approach to a supported Schrock initiator will be discussed below.

A reasonable strategy for the preparation of a Schrock-type initiator using a minimal number of reactions is the following (Scheme 7): firstly the synthesis of molybdenum compounds **73** and **74**, will be formed followed by their immobilisation on a supported diol that would ideally bear a spacer in order to hold the complex away from the polymer matrix and hence, emulate a homogenous-like environment, followed by reaction with the isocyanate compound **75** to afford a mixed oxo-imido complex. Finally, in order to synthesise the alkylidene function, a simple Wittig reaction could be employed. The key step in this strategy is the reaction involving the isocyanate **75**. In the literature a few examples of such a transformation have been described and have been applied successfully with metal-oxo complexes with metals such as vanadium, tungsten, titanium, zirconium and molybdenum.[8, 9, 10]

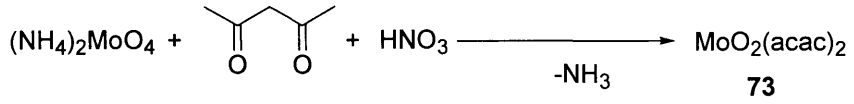


Scheme 7

In order to demonstrate the feasibility of this method, this alternative synthesis of a supported Schrock-type initiator was initially probed in solution to aid characterisation, since direct analysis of polymer-bound species is not straightforward.

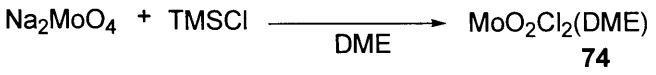
Firstly, the molybdenum compound **73** was synthesized according to a literature procedure by the reaction of ammonium molybdate (VI) tetrahydrate with aqueous ammonia, 2,4-pentandione, and nitric acid.[11] The resulting aqueous solution was stirred for 30 minutes

then placed at -20°C in the freezer for 18h. The resulting yellow precipitate that formed was collected by filtration and washed several times with cold water and ethanol prior to drying *in vacuo* (Scheme **8**) 91% .



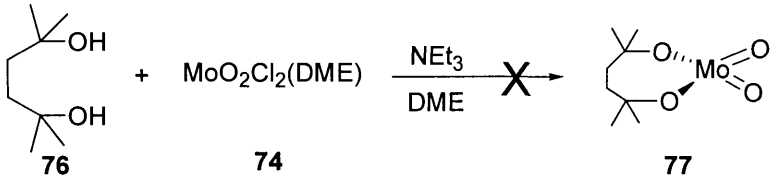
Scheme 8

The alternative molybdenum starting compound **74** was also prepared by following a literature procedure: a DME solution of sodium molybdate was reacted with trimethyl silyl chloride and was stirred for 18h at 85°C.[12] Finally, the solvent and volatile components were removed under vacuum to afford **74** as a white solid in yield 87%(Scheme **9**).



Scheme 9

In order to mimic the polymer-bound diol necessary for the procedure described in Figure **4**, but for ease of analysis a model reaction was undertaken off-bead. Thus, molybdenum compound **74** was reacted with diol **76** in DME (Scheme **10**). Sadly, the desired chelated dialkoxide complex **77** was not isolated, as the mixture become blue on application of vacuum, a sign that the product polymerised when the DME was removed, probably forming a polymer of the type of Mo_xO_y.[13] A possible explanation for this polymerisation is the use of a dialkoxide that is not sterically demanding enough to prevent the polymerisation when the DME is removed under vaccum.



Scheme 10

In order to probe this hypothesis, the same reaction was attempted under very similar conditions, but this time in the presence of trimethylphosphine in order to coordinate the metal centre and hopefully stabilise the desired monomeric product **77** as an adduct with trimethylphosphine. The reaction was followed by ^{31}P NMR spectroscopy. Unfortunately, the ^{31}P NMR data suggested that the tris(phosphine) product **78** (Scheme **11**) had formed in place

of the desired complex **77**, as two resonances at 8.32 ppm (d) and -1.61 ppm (t) were observed. These are very similar to those described in the literature for a similar molybdenum phosphine complex (Figure **5**).[14]

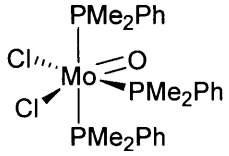
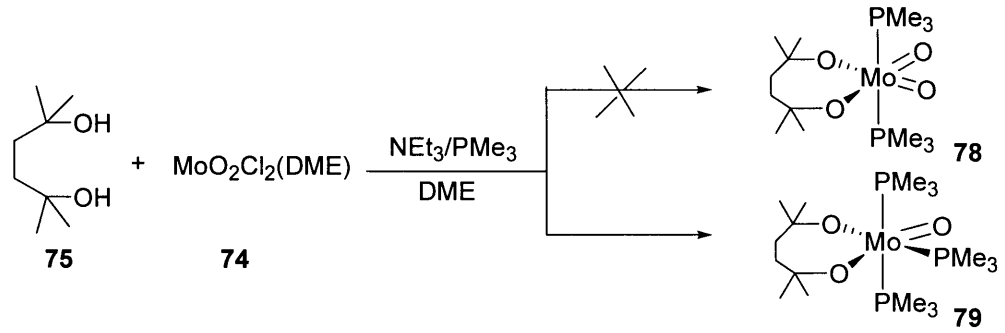


Figure 5 Example of $MoOCl_2(PMe_2Ph)_3$ described in the literature

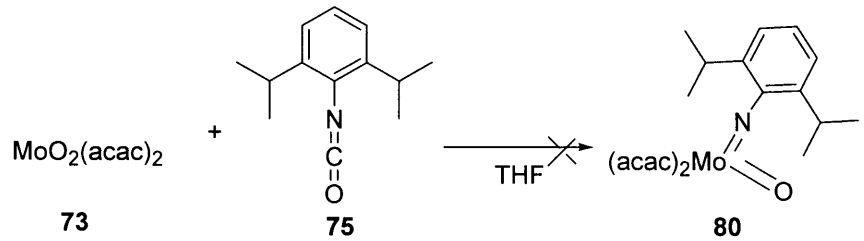
Nevertheless, the reactions still demonstrate that compounds such as **77** are reactive and have to be isolated as base adducts to prevent their decomposition to be observable (Scheme **11**).



Scheme 11

The target reaction for the synthesis of a supported equivalent to oxo compounds **77** will involve a polymer-supported diol, which brings the benefits of organic supports namely a pseudo-high dilution environment. This feature could prevent the polymerisation of complexes analogous to compound **77**.

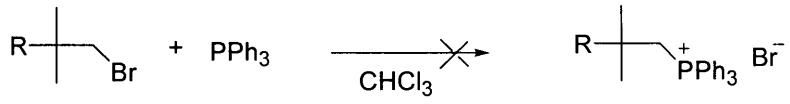
To further probe the viability of this "on-bead", approach the step involving the isocyanate **75** in order to introduce the imido group on the metal centre, has also been tested with molybdenum-based complex **73**, in THF at room temperature and at 40°C (Scheme **12**). Unfortunately, no reaction was observed, only a mixture of starting materials **73** and **75** were revealed by ^1H NMR and IR spectroscopies.



Scheme 12

The Wittig reaction described in Scheme **7** has also been explored with a view to generating an ylide of relevance to the synthesis of analogues of the Schrock-type initiators, namely those bearing neopentyl or neophyl groups. Firstly, synthesis of the phosphino salts has been carried out. Our attempts included the synthesis of phosphonium salt **82** by the reaction of the halogen compound **81** with triphenylphosphine (Scheme **13**). Unfortunately, no reaction was observed to occur even on prolonged heating at reflux in $CHCl_3$. Similarly, no reaction occurred on heating neat **81** with triphenyl phosphine. Other attempts have been done with $P(OEt_3)$ without any better success.

Since neophyl bromide **81** proved not very reactive, attempts were made to prepare the desired, corresponding phosphonium salt with neopentyl bromide **83** using similar experimental conditions (Scheme **13**). Once again, no reaction was observed to take place, even with $P(OEt_3)$.



R=Ph **81**
R=Me **83**

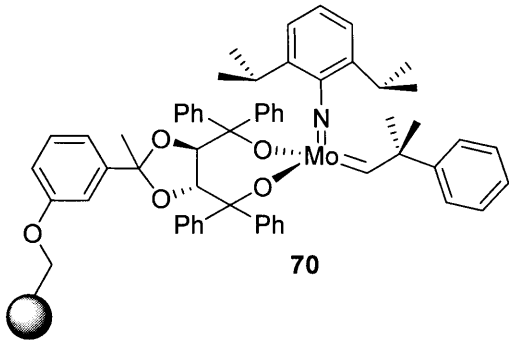
R=Ph **82**
R=Me **84**

Scheme 13

Attempts to synthesise branched phosphonium salts **27** and **29** did not work. It is sensible to think that instead of using branched halide, it would be easier to synthesise linear phosphonium salts. Only that branched phoshonium salts are necessary, to prevent decomposition of the supported Schrock that could result from the alkylidene generated by the corresponding ylide in the Wittig reaction step as it was exposed in Scheme **7**.

IV.4 Summary and Conclusions

In conclusion, this Chapter has clearly demonstrated the formation of new supported Schrock-type alkylidene complexes and their ability to catalyze the RCM of diallylether (**10**) although their activity is still very modest (Figure **5**). Despite the similarity in structure and the synthesis between the supported Schrock-type initiator described in this thesis and those described in the literature and reported in Chapter one there are differences in their activity for RCM. This tends to imply that the nature and the structure of the resin is extremely important



70

Figure 5 New Supported Schrock-types complexes

In addition, an ambitious way to obtain supported Schrock-type initiators "on-beads" has been probed which is still under investigation although it proved not as simple as expected, but still deserves attention.

IV.5 References

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Chapter 5

Experimental

V Experimental:

All operations were conducted under an atmosphere of dry nitrogen using standard Schlenk and cannula techniques, or in a nitrogen-filled glove box, unless stated otherwise. All NMR scale reactions were conducted using Young's tap valve NMR tubes. Solvents were freshly distilled under nitrogen from sodium/benzophenone (diethyl ether, toluene, THF and DME), from sodium (hexane, pentane), from calcium hydride (acetonitrile, DCM, MeOH and petroleum ether 40-60) or from P_2O_5 ($CDCl_3$, C_6D_6, toluene-d_8) and deoxygenated prior to use. Sonication was achieved by suspending the desired reaction vessel in a water-filled Grant Ultrasonic Bath XB2.

All solid reagents were used as received. Where appropriate, liquid reagents were dried, distilled and deoxygenated prior to use. Chloromethylated polystyrene (Merrifield resin, 1 mmol g^{-1} Cl) used was supplied by Avecia and prepared by copolymerisation of styrene, DVB (2%) and 4-vinylbenzyl chloride according to a proprietary procedure. (Chloromethylphenylpentyl)-polystyrene (2 % cross-linked, 1 mmol g^{-1}) was obtained from Aldrich. Otherwise all chemicals were bought from Aldrich.

Laboratory coat, safety spectacles and gloves were worn at all times, and all experiments conducted in an efficient fume-hood, following completion of appropriate COSHH assessments. Solvents were disposed of in the appropriate waste solvent receptacles (chlorinated/non-chlorinated), metal containing or organic waste in the appropriate residue vessels.

Routine NMR spectra were collected on a Bruker AM250 or AMX300 at ambient probe temperatures (~290 K) unless stated otherwise. Chemical shifts were referenced to residual protio impurities in the deuterated solvent (^1H), ^{13}C shift of the solvent (^{13}C), external $CFCl_3$ (^{19}F) or to external aqueous 85% H_3PO_4 (^{31}P). Solvent proton shifts (ppm): $CDCl_3$, 7.27 (s); C_6D_6, 7.16 (s), DMSO-d_6, 2.49 (quint), toluene-d_8 2.30 (s), 7.19 (m); Solvent carbon shifts (ppm): $CDCl_3$, 77.23 (t); C_6D_6, 128.39 (t); DMSO-d_6, 39.7 (sept), toluene d_8 137.5 (s), 128.9 (t) 125.2 (t) 20.4 (sept). Gel-phase ^{13}C NMR spectra of polystyrene resins were obtained on a Bruker ARX 300 machine following a modified literature procedure.[1] Approximately 80 mg of resin was placed in a 5mm NMR tube and 0.6 ml of solvent (carbon tetrachloride/benzene-d6 (4:1) or $CDCl_3$). The resin was given time to swell (10 mins) prior to obtaining spectra. NMR spectra obtained under CP MAS NMR were acquired by Dr. D. Apperley of the EPSRC Solid State NMR Service (University of Durham) using an Varian UNITY*Inova* spectrometer.

GC-MS were performed using a Perkin-Elmer Autosystem XL GC machine (PE-5MS 30 m coil, internal diameter = 0.25 mm, film thickness = 0.25 μm) coupled to a Perkin-Elmer Turbomass mass spectrometer in order to control the purity of solid compounds.

Elemental analyses (for isolated compounds only) were performed by the University of North London, Butterworths and Warwick Analytic Service. Infrared spectra were collected on a Perkin Elmer Spectrum One spectrophotometer using an ATR apparatus.

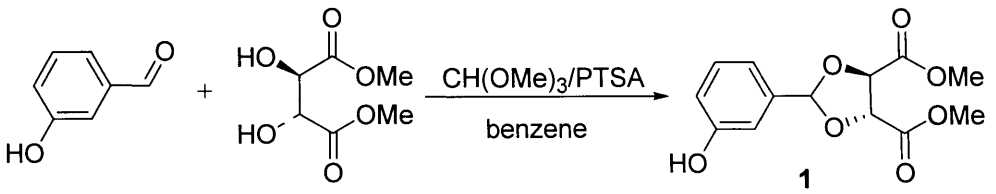
Loading were determined by observing the loss of chlorine or Br, by elemental analysis. Calculated loading were performed by assuming that the chemical transformations on the supported species have gone to completion.

Microwave reactions were performed using a Personal Chemistry oven or a CEM Discoverer oven.

Chapter II Synthesis of ligands and supports

Synthesis of compounds **1-8**[2], **9**[3], **12**[4], **13-17**[2], **40**[2], **41**[5] were performed according to literature procedures and their identity was confirmed by ^{1}H NMR spectroscopy, which were all in accordance with literature data.

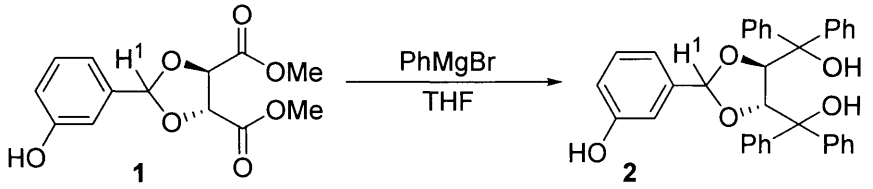
2-(3-Benzyloxy-phenyl)-2-methyl-[1,3]dioxolane-4,5-dicarboxylic acid dimethyl ester **1**



Trimethylorthoformate (2.6 ml 20 mmol), was added at 0°C, to a solution of 3-hydroxybenzaldehyde (2.48 g 20 mmol) in benzene (30 ml) containing a small amount of PTSA. The mixture was stirred for 30 minutes and then the dimethyl tartrate (3.3 g 20 mmol) was added. Distillation of the toluene /MeOH azeotrope was then carried at 60°C. Finally NEt_3 (10 ml) was added to neutralize the PTSA. The product was purified by column chromatography using Hexane/ethyl acetate as the eluent (60/40) rf 0.4 to afford **1** as a yellow oil in 15% yield (785 mg).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 3.72 (s, 3H, *Me*), 3.76 (s, 3H, *Me*), 4.78 (d, ^{3}J=5.7 Hz, 2H, C*H*), 4.92 (d, $^3J_{H\text{-}H}$=5.7 Hz, 2H, C*H*), 5.98 (s, 1H, *H*), 6.76-7.20 (m, 4H, aromatic).

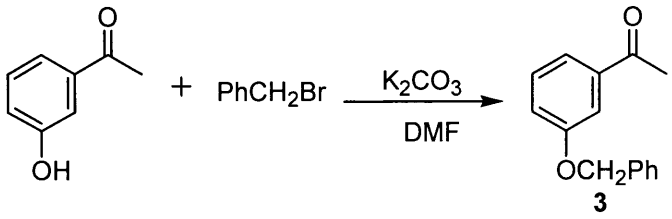
3-[4,5-bis-(Hydroxy-diphenyl-methyl)-[1,3]dioxolan-2-yl]-phenol **2**



PhMgBr (50 ml, 33 mmol) was added to ketal **1** (0.785 mg 3 mmol) in dry THF (20 ml). When addition was complete, the mixture was heated at reflux for 16h. After cooling, a saturated aqueous solution of NH_4Cl was added (30 ml). The resulting organic phase was dried over magnesium sulphate and vacuum evaporated. The oil obtained was crystallised from DCM, to give **2** as a white powder in 30% yield (442 mg). **2** was found to be 99% pure by GC-MS.

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 2.60 (s, 2H, *OH*), 5.06 (d, $^3J_{H\text{-}H}$=5.5 Hz, 2H, C*H*), 5.24 (d, $^3J_{H\text{-}H}$=5.5 Hz, 2H, C*H*), 5.98 (s, 1H, *H*), 6.68-7.50 (m, 24H, aromatic).

1-(3-Benzyloxy-phenyl)-ethanone **3**

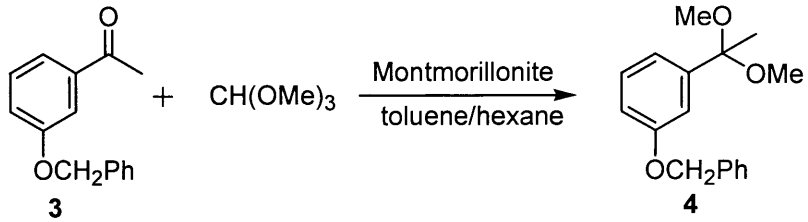


3

A 500 ml flask was charged with 3-hydroxyacetophenone (8 g, 58.7 mmol) and potassium carbonate (30 g, 217 mmol), along with dry DMF (250 ml). Then benzylbromide (10 g, 58.7 mmol) was added. The mixture was stirred overnight at room temperature. Finally the mixture was poured into DCM (250 ml), washed three times with water (500 ml), then dried over magnesium sulphate, and the solvent evaporated under vacuum to afford 1-(3-benzyloxy-phenyl)-ethanone **3** in 97% yield (13.3 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 2.56 (s, 3H, *CH_3*), 5.03 (s, 2H, *CH_2*), 7.08-7.56 (m, 9H, aromatic).

Benzyloxy-3-(1,1-dimethoxy-ethyl)-benzene **4**

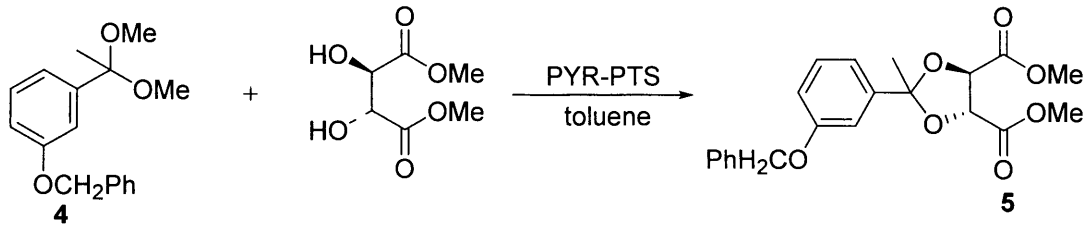


3 **4**

A mixture of K10 Montmorillonite (15 g) and trimethylorthoformate (20 ml, 154 mmol) was stirred for 1h at room temperature. Then a solution of **1** (5 g, 22 mmol) in hexane/toluene (100 ml, 1/1) was added and the mixture stirred overnight. The solvent was removed under vacuum to afford diketal **2** as a yellow oil in 95% yield (5.7 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.43 (s, 3H, *CH_3*), 3.08 (s, 6H, *Me*), 4.96 (s, 2H, *CH_2*), 6.79-7.35 (m, 9H, aromatic).

2-(3-Hydroxy-phenyl)-2-methyl-[1,3]dioxolane-4,5-dicarboxylic acid dimethyl ester **5**



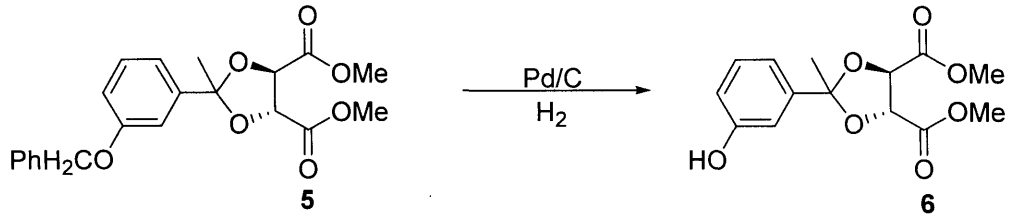
4 **5**

A mixture of the diketal **4** (6 g, 22 mmol), tartrate (3.92 g 22 mmol), and a catalytic amount of PPTS in toluene (200 ml) was heated under reflux using Dean-Stark conditions

until the distillation of the toluene methanol azeotrope was completed. Then the solution was allowed to cool, washed with a saturated sodium hydrogen carbonate solution (70 ml), dried over magnesium sulphate, and the solvent evaporated. The crude product was purified by chromatography (SiO_2, hexane/ethyl acetate, 10/1 then 4/1). A yellow oil was obtained in 80% yield (6.8 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.76 (s, 3H, *CH_3*), 3.54 (s, 3H, *Me*), 3.82 (s, 3H, *Me*), 4.77 (d, $^3J_{H\text{-}H}$=5.7 Hz, 1H, C*H*), 4.89 (d, $^3J_{H\text{-}H}$ =5.7 Hz, 1H, C*H*), 5.04 (s, 2H, *CH_2*), 6.82-7.44 (m, 9H aromatic).

2-(3-Hydroxy-phenyl)-2-methyl-[1,3]dioxolane-4,5-dicarboxylic acid dimethyl ester **6**

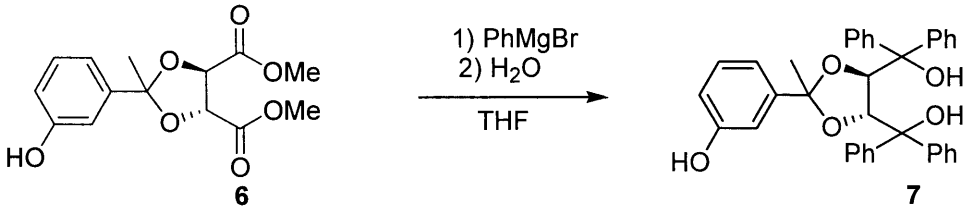


5 **6**

A suspension of just over 10% Pd/C (2 g) in ethyl acetate (20 ml) was connected to a source of hydrogen at atmospheric pressure. Once the catalyst was saturated (overnight), a solution of **3** (6.8 g, 17.6 mmol) in ethyl acetate (50 ml) was added dropwise. When the theoretical volume of hydrogen was consumed, the system was opened to the air, the suspension filtered through Celite and the solvent evaporated under vacuum. Compound **6** was isolated as a white solid in 95% yield (5.0 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.72 (s, 3H, *CH_3*), 3.32 (s, 3H, *Me*), 3.80 (s, 3H, *Me*), 4.76 (d, $^3J_{H\text{-}H}$=5.7 Hz, 1H, C*H*), 4.88 (d, $^3J_{H\text{-}H}$ =5.7 Hz, 1H, C*H*), 7.18-7.75 (m, 4H, aromatic).

5-bis-(Hydroxy-diphenyl-methyl)-2-methyl-[1,3]dioxolan-2-yl]-phenol **7**



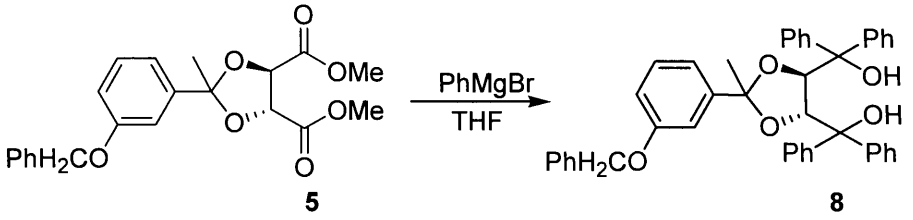
6 **7**

A solution of **5** (4.95 g, 16.72 mmol) in dry THF (40 ml) was added dropwise to a solution of phenyl magnesium bromide (58.5 ml, 2M, 117.00 mmol) in dry THF (70 ml) at 0°C. The reaction mixture was stirred at room temperature overnight. A saturated aqueous solution of NH_4Cl (50 ml) was added, the organic materials extracted three times with ethyl acetate (3 x 100 ml), and dried over magnesium sulphate. The solvent was evaporated

under vacuum and the product **7** was obtained as a foam in 79% yield (7.19 g). It was found to be 99% by GC-MS.

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.96 (s, 3H, *CH_3*), 2.34 (s, 1H, *OH*), 2.54 (s, 1H, *OH*), 5.01 d, $^3J_{H\text{-}H}$=5.7 Hz, 2H, C*H*), 5.08 (d, $^3J_{H\text{-}H}$=5.7 Hz, 2H, C*H*), 5.24 (s, 1H, *OH*), 6.52-7.48 (m, 24H aromatic).

[2-(3-Benzyloxy-phenyl)-5-(hydroxy-diphenyl-methyl)-2-methyl-[1,3]dioxolan-4-yl]-diphenyl-methanol **8**

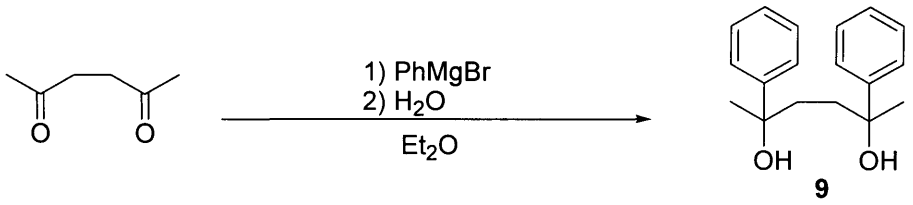


5 **8**

A solution of **5** (3 g, 7.76 mmol) in dry THF (30 ml) was added dropwise to a solution of phenyl magnesium bromide (17 ml, 2M, 27.16 mmol) in dry THF (70 ml) at 0°C. The reaction mixture was stirred at room temperature overnight. A saturated aqueous solution of NH_4Cl was added (40 ml), the organic materials extracted three times with ethyl acetate (3 x 100 ml), and dried over magnesium sulphate. The solvent was evaporated under vacuum and the product was obtained as a white powder in 74% yield (3.3 g). **8** was found to be 99% pure by GC-MS.

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.39 (s, 3H, *Me*), 4.76 (d, ^{3}J=11.6 Hz, 1H, C*H*), 4.83 (d, ^{3}J=11.6 Hz, 1H, C*H*), 5.18 (d, ^{2}J=5.1 Hz, 1H, CH_2), 5.25 (d, ^{2}J=5.1 Hz, 1H, CH_2), 6.82-7.59 (m, 29H aromatic).

2,5-Diphenyl-hexane-2,5-diol **9**

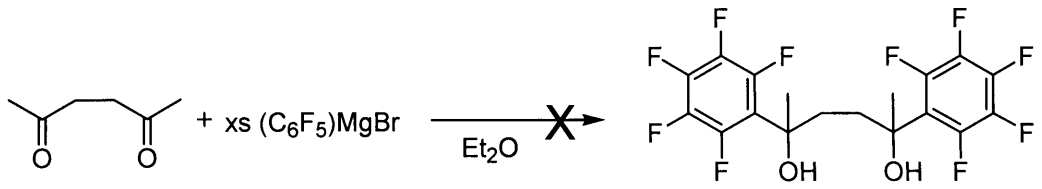


9

A solution of hexane-2,5-dione (4 g, 35 mmol) in dry diethylether (50 ml) was added dropwise to a solution of phenyl magnesium bromide (70 ml, 2M, 140 mmol) in dry diethyl ether (70 ml) at 0°C. The reaction mixture was stirred at room temperature overnight. A solution of HCl (1M, 100 ml) was added, the organic materials were extracted three times with diethylether (3 x 100 ml) and dried over magnesium sulphate. The solvent was evaporated under vacuum and the crude product was recrystallised from DCM and pentane. The product **9** was obtained as a white powder in 74% yield (6.93 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.36 (s, 3H, *CH_3*), 1.44 (s, 3H, *CH_3*), 1.63(m, 4H, *CH_2*), 2.32 (s, 2H, *OH*), 6.90-7.40 (m, 10H, aromatic).

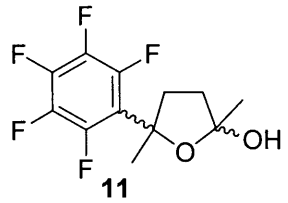
Attempted synthesis of 2,5-bis-pentafluorophenyl-hexane-2,5-diol **10**



10

Hexane-2,5-dione (1 g, 8.76 mmol) was treated with C_6F_5MgBr[6] (9.5 g, 35.04 mmol) in a similar manner to that used for the preparation of diol **9**, however none of the desired product, 2,5-bis-pentafluorophenyl-hexane-2,5-diol, was obtained. 1H NMR spectroscopic and GC-MS analysis indicated only the presence of the diketone.

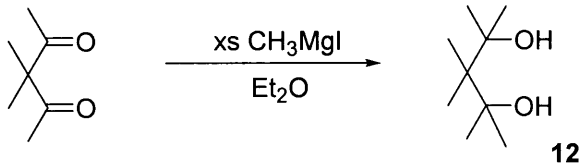
In contrast, a reaction undertaken with C_6F_5Li[7] (0.68 g 3.90 mmol) and hexane dione (0.22 g, 1.95 mmol) in similar conditions as described above proved unsuccessful, but this time yielded the cyclic product **11** as a brown oil in 64% yield (0.35 g).



11

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.54-1.62(m, 3H, *CH_3*), 1.62-1.67 (m, 3H, *CH_3*), 1.70-1.89- (m, 2H, *CH_2*), 1.92-2.08 (m, 2H, *CH_2*), 3.12 (s, 1H OH).

2,3,3,4-Tetramethyl-pentane-2,4-diol **12**

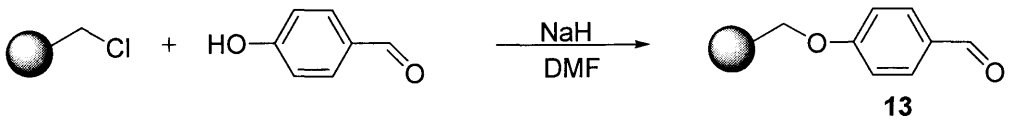


12

A solution of 3,3-dimethyl-pentane-2,4-dione (3.00 g, 23.4 mmol), in dry diethylether (50 ml) was added dropwise to a diethyl ether solution of phenyl magnesium bromide (2.4M, 120 ml, 288 mmol) at 0°C. The reaction mixture was stirred at room temperature overnight. An aqueous solution of HCl (1M, 100 ml) was added, and the organic materials were extracted three times with diethylether (3 x 100 ml), and dried over magnesium sulphate. The solvent was removed *in vacuo*, to leave the product **10** as a white powder in 62% yield (3.75 g). **12** was found to be 99% pure by GC-MS.

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 0.86 (s, 6H, *CH_3*), 1.24 (s, 12H, *CH_3*).

Immobilised ketone **13**



13

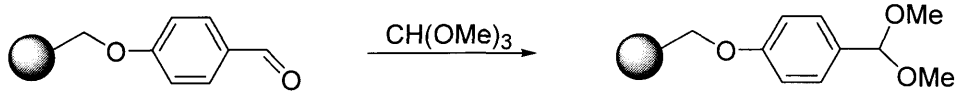
A solution of NaH, (0.58 g, 24 mmol) and *p*-hydroxy benzadehyde (2.93 g, 24 mmol) in DMF (50ml) were stirred at room temperature for 1h. Then Merrifield resin was added (6g, 1 mmol/g Cl) and the mixture was heated at 75°C for 48h. Subsequently, after hydrolysis, the resulting resin was washed with THF, DMF, Et_2O, and water. Finally the resin **13** was dried *in vacuo*. 6.37g of **13** were recovered.

Gel phase ^{13}**C** (75 MHz, 298K, C_6D_6) δ ppm: 122.73 (CH_2O), 196.75 (C=O).

IR 1628 cm^{-1} (C=O)

Elemental analysis expected Cl 0%, found : Cl< 0.3% loading: 0.92mmol/g

Immobilised ketal **14**

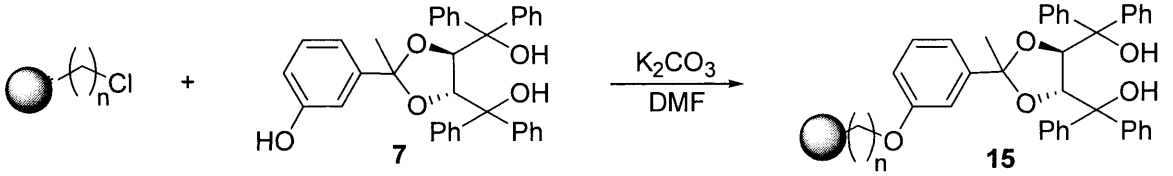


13 **14**

Resin **13** (4 g 0.92 mmol/g) was stirred at room temperature for 48h in $CH(OMe)_3$ (25 ml, 228 mmol) and then analysed. The ^{13}C NMR data show the disappearance of the C=O peak, something that was confirmed by the IR spectroscopy. 3.92g of **14** were recovered.

Gel phase ^{13}**C** (75 MHz, 298K,C_6D_6) δ ppm: 64.39 (O*Me*).

Supported 3-[4,5-Bis-(hydroxy-diphenyl-methyl)-2-methyl-[1,3]dioxolan-2-yl]-phenol (TADDOL) general procedure (**15**, **40**)



7 **15**

Merrifield resin (1 mmol/g), TADDOL **7** and potassium carbonate (25g) were introduced into a three necked flask fitted with a reflux condenser where the polymer was swelled in dry DMF. The reaction was stirred with an overhead stirrer for 5 days at 80°C. Finally, the resin was isolated by filtration and washed with toluene, water, acetone, THF and DCM (table **1**).

	Resin (g)	TADDOL (g, mmol)	K_2CO_3 (g, mmol)	Loading (mmol/g)	Mass recovered (g)
n=1 **15**	1	2.72, 5	25, 180	0.66 1.47	1.22
n=5 **40**	1	2.72, 5	25, 180	0.54 1.38	1.13

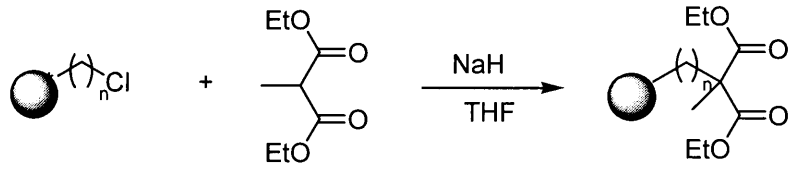
Table 1 Synthesis of Supported Taddol resins

Elemental analysis 15 expected Cl 0% Found 0%

40 expected Cl 0% found 0.88%

IR cm^{-1} (OH) **15**, 3372, **40**, 3221.4

Supported 2-Methyl-malonic acid diethyl ester: general procedure **16. 41**



16, 41

A three-neck flask fitted with a reflux condenser, an overhead-stirrer and charged with NaH. Then methyl-malonic acid diethyl ester was added, and the reaction stirred for 1h. Subsequently, Merrifield resin was added at 0°C, before the reaction was heated at reflux for 3 days. The functionalised Merrifield resin was isolated by filtration and washed with THF, water, methanol, acetone, and DCM (table **2**).

	Resin (g)	Ester (g, mmol)	NaH (g, mmol)	Loading (mmol/g)	Mass recovered (g)
n=1 **16**	6	2.78, 19	0.8, 33	0.88	6.23g
n=5 **41**	1	0.46, 3.1	0.14, 5.8	0.42	0.94g

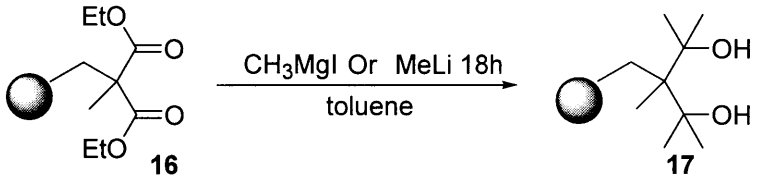
Table 2 Synthesis of supported 2-Methyl-malonic acid diethyl ester

Elemental analysis 16 expected Cl 0% found 0%

41 expected Cl 0% found 1.93%

IR cm^{-1} (C=O) **16** 1733.9, **41** 1713.2

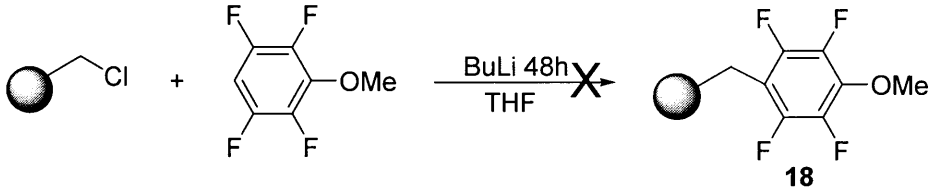
Supported 2,3,4-Trimethyl-pentane-2,4-diol **17**



Supported 2-methyl-malonic acid diethyl ester **16** (4.20 g, 0.88 mmol/g) was introduced into a three-necked flask fitted with a reflux condenser and was swelled in dry toluene (100 ml). Methyl magnesium iodide or MeLi (5.24 ml, 3.5 M, 18.52 mmol) in a toluene solution was added to the mixture and the reaction was stirred (overhead stirrer) at 80°C for three days. Finally, the resin was isolated by filtration and washed with toluene, water, acetone, THF and DCM. 3.93g of **13** were recovered.

IR: 3391.29 cm^{-1} (OH) loading (calculated) 0.90 mmol/g

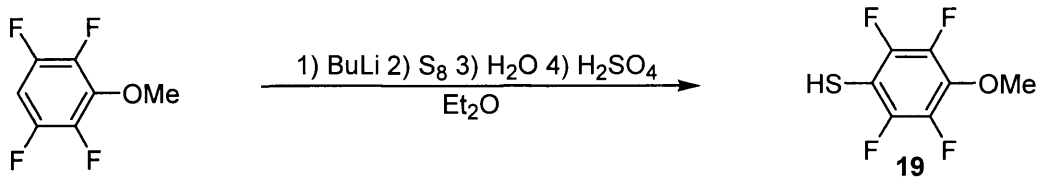
Attempted synthesis of supported tetraflouoroanisole **18**



1,2,4,5-Tetrafluoro-3-methoxy-benzene (2.16 g, 12 mmol) was dissolved in THF (40 ml) in a 250 ml Schlenk. With a syringe butyl lithium was added (7.47 ml, 1.6M, 12 mmol) and the reaction stirred for 4h. Finally the mixture was added to the Merrifield (12 g 1 mmol/g) resin swollen in THF at -78°C in three-necked flask fitted with a reflux condenser. The reaction was allowed to warm to room temperature, and was stirred with an overhead stirrer at 50°C for 48h. The resulting polymer was washed three times with THF, water, and a mixture of water and THF, and was dried under vacuum. Elemental analyses were obtained to determine the loading of the resin, something which underlined the failure of this attempt as the level of chlorine in the polymer was nearly identical to the level of chlorine in the starting Merrifield Resin (3.54%). 12g.of starting Merrifield resin were recovered.

Elemental analysis expected Cl: 0% Found 3.4%

2,3,5,6-Tetrafluoro-4-methoxy-benzenethiol **19**[8]

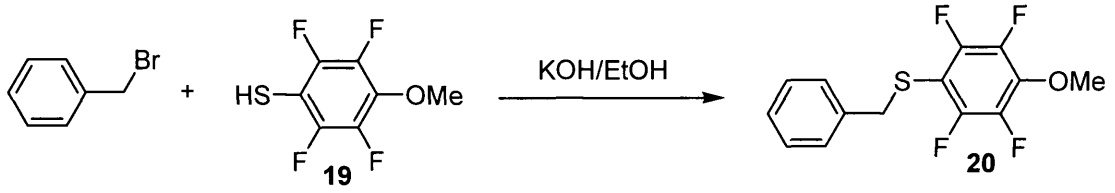


1,2,4,5-Tetrafluoro-3-methoxy-benzene (7 g, 38.9 mmol) was dissolved in dry diethylether (30 ml) in a 250 ml Schlenk. With a syringe, butyl lithium .(24.3 ml, 1.6M, 38.9 mmol) was added at -78°C. The reaction mixture was stirred at -78°C for 5h and then allowed to warm to -60°C. Sulphur (9.97 g, 38.9 mmol) was added to the reaction and the mixture turned yellow and was stirred for one hour. Finally the reaction was quenched by addition of sulphuric acid (1M, 20 ml) and water at room temperature. The organic layer was washed with water, the solution dried over magnesium sulphate and volatiles removed under vacuum to leave the product as a yellow oil in 61% yield (5.03 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 3.44 (s, 1H, *SH*), 3.96 (s, 1H, *CH_3*)

^{19}F (250 MHz, 298K, $CDCl_3$) δ ppm:-157.4 (s, 2F), -139.08 (s, 2F).

1-Benzylsulfanyl-2,3,5,6-tetrafluoro-4-methoxy-benzene **20**



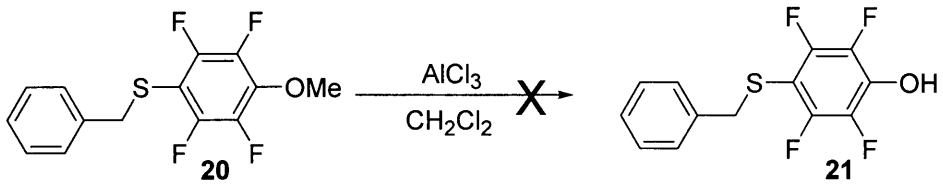
Tetrafluoro-4-methoxy-benzenethiol **19** (1 g, 4.71 mmol) was dissolved in ethanol (125 ml) together with potassium hydroxide (0.26 g, 4.71 mmol) in a flask. One equivalent of benzyl bromide (0.81 g, 4.71 mmol) was added to the reaction *via* a syringe and then the reaction was stirred at room temperature for 3 hours. The resulting KBr was removed by filtration, and the filtrate was evaporated to afford crude **20**, which was dissolved in diethylether (50 ml). The organic layer was washed three times with water (3x 50 ml), dried over magnesium sulphate and volatile components removed *in vacuo*. Derivative **20** was isolated as a brown solid 80% yield (1.14 g).

^{1}H (250 MHz, 298K, $CDCl_3$) δ ppm: 4.02 (s, 2H, *CH_2*), 4.06 (s, 3H, *CH_3*), 7.18-7.24 (m, 5H, *Ar*).

^{19}F (235 MHz, 298K, $CDCl_3$):-157.9 (2F), -134.7 (2F).

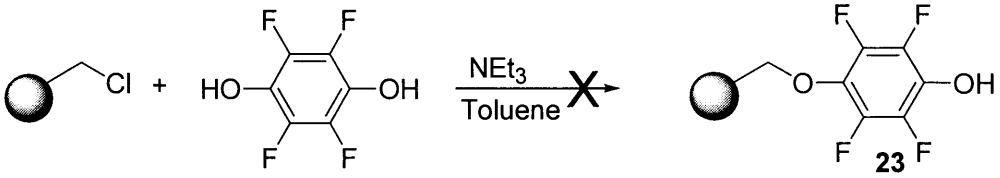
^{13}C (250 MHz) 39.1 (*CH_2*), 61.9 (*CH_3*), 105.7 (*C-S*), 126.3 (*C-H*), 128.4 (*C-H*), 128.6 (*C-H*), 138.9 (*C-CH_2* + *C-OMe*), 140.5 (d, $^1J_{C\text{-}F}$=265 Hz *C-F*), 147.68 (d, $^1J_{C\text{-}F}$=265 Hz *C-F*).

Attempted synthesis of 4-benzylsulfanyl-2,3,5,6-tetrafluoro-phenol



1-Benzylsulfanyl-2,3,5,6-tetrafluoro-4-methoxy-benzene (0.67 g, 2.22 mmol) was dissolved in DCM (15 ml). Aluminium trichloride (0.44 g, 3.3 mmol) was added, and the reaction was stirred for 48h, washed with water, then dried over magnesium sulphate. The product was not isolated, but a complex mixture of products including starting material and a small amount of **21** were identified as being present by GC-MS.

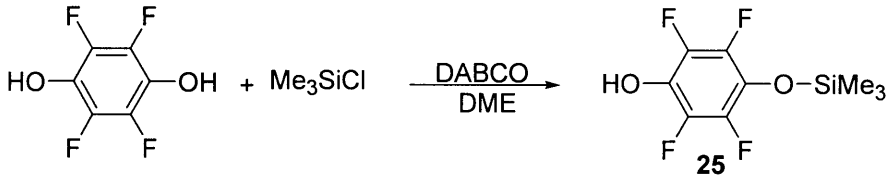
Attempted synthesis of supported tetrafluoro hydroxyquinone **23**



To a three-neck flask fitted with an overhead stirrer and a condenser, 2,3,5,6-tetrafluoro-benzene-1,4-diol (1.98 g, 10.89 mmol), in a minimum of diethyl ether (10 ml) was added. Then Merrifield resin (3.63 g, 1 mmol/g), together with toluene (110 ml) as a swelling agent and triethylamine (1.52 ml, 10.89 mmol) were added. The reaction was stirred and heated at 50°C for 3 days. Finally, the resin was isolated by filtration and washed with toluene, water, acetone, THF and DCM. Elemental analyses have shown a fluorine content, which is consistent with a cross linked polymer.

Elemental analysis expected Cl 0% found 1.95%, expected F 16.11%, found, 11.51%.

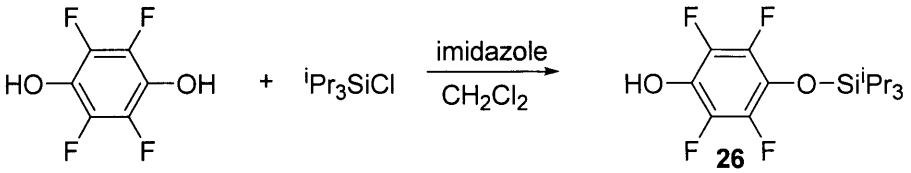
Attempted synthesis of 2,3,5,6-Tetrafluoro-4-trimethylsilanyloxy-phenol **25**



A 100 ml three-necked flask fitted with a reflux condenser was charged with 2,3,5,6-tetrafluoro-benzene-1,4-diol (3 g, 16.57 mmol), and suspended in dry DCM (50 ml). DABCO (3.01 g, 8.28 mmol) and trimethylsilane (0.19 g, 2.75 mmol) were added, before the reaction was then heated at reflux for 48h. After filtration, the solvent was removed

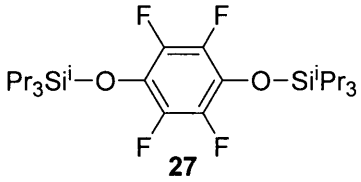
under vacuum. ^{1}H NMR spectroscopic analysis of the solid revealed a mixture of starting materials with only a trace of the desired product **25**.

Attempted synthesis of 2,3,5,6-Tetrafluoro-4-tri-tert-butylsilanyloxy-phenol **26**



26

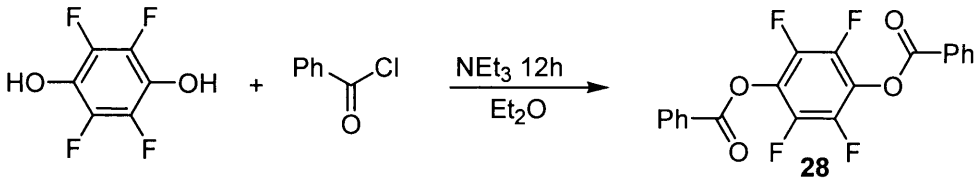
A 100 ml 3-necked flask fitted with a reflux condenser was charged with 2,3,5,6-tetrafluoro-benzene-1,4-diol (500 mg, 2.75 mmol), and suspended in dry DCM (50 ml). Tri-isopropyl chloro-silane (0.65 g, 2.75 mmol) and a catalytic amount of imidazole (0.19 g, 0.28 mmol) were added, before the reaction was then heated at reflux for one hour. GC-MS analysis of the crude reaction mixture revealed the presence of a mixture of three compounds, which seemed to be starting material with compound **26** and another compound whose mass spectrum was consistent with the diprotected quinine **27**.



27

m/z : 494 (M^+) 236 (-2 S^{i}IPr$_3$) 148 (-2 OSi). Retention time: 24.18

Benzoic acid 2,3,5,6-tetrafluoro-1.4-di-phenyl ester **28**



28

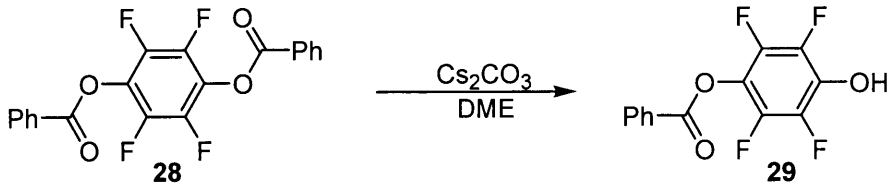
A solution of hydroxyquinone (1.71 g, 9.36 mmol), NEt_3 (2.63 ml, 18.72 mmol) and of benzoyl chloride (2.71 ml 18.72 mmol) in diethylether (50 ml) were stirred overnight in a flask. The resulting salt was removed by filtration and the filtrate was vacuum evaporated to afford the product, **28** as a white powder in 95% yield (3.66 g).

^{13}C (75 MHz, 298K, $CDCl_3$) δ ppm: 127.5 (*-C-O-C=O*), 131.0 (*C-H*), 131.16 (*C-H*), 134.94 (*C-H*), 135.57 (*-C-C=O*) 141.69 (d, $^1J_{C\text{-}F}$=181.53 Hz, *C-F*), 162.99 (C=O).

^{19}F (235 MHz, 298K, $CDCl_3$) δ ppm: -153.6 (4F).

Elemental analysis: C expected: 61.55%, found: 61.69%. H expected: 2.58%, found 2.61%.

Benzoic acid 2,3,5,6-tetrafluoro-4-hydroxy-phenyl ester **29**



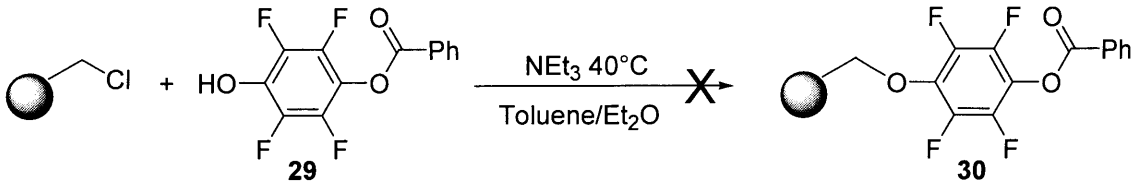
A three-necked flask fitted with a reflux condenser was charged with di-benzoic acid 2,3,5,6-tetrafluoro-1.4-di-phenyl ester (7 g, 17.9 mmol) and caesium carbonate (5.84 g 17.9 mmol). The mixture was suspended in dry DME (125 ml) and stirred for 48h at reflux temperature. Then a solution of aqueous HCl (1M, 25 ml) was added, the organic layer washed three times with water (50 ml), before being dried over magnesium sulphate. The solvent was removed *in vacuo* and finally the resulting product **29** was recrystalised from DCM and petroleum ether (60/40). The product **29** was isolated as a white crystalline solid in 45% yield (2.36 g).

^{1}H (250 MHz, 298K, d^{6}-DMSO) δ ppm: 3.35 (s, 1H, *OH*), 6.89-8.23 (m, 5H, *Ar*).

^{19}F (235 MHz, 298K, d^{6}-DMSO) δ ppm:-156.8 (2F), -133.092 (2F).

^{13}C (75 MHz, 298K, d^{6}-DMSO): 119.1 (*C-OH*), 125.7 (*C-O-C=O*), 129.3 (*C-H*), 130.2 (*C-H*), 134.6 (*-CH*), 135.59 (*-C-C=O*) 137.04 (d $^{1}J_{C\text{-}F}$=186 Hz, *C-F*), 141.04 (d, ^{1}J=180 Hz *C-F*), 162.82 (C=O).

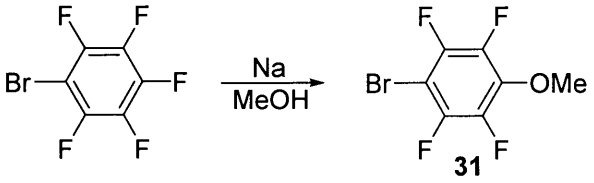
Attempted synthesis of supported benzoic acid 2,3,5,6-tetrafluoro-4-hydroxy-phenyl ester **30**



To a three-neck flask fitted with an overhead stirrer and a condenser, charged with benzoic acid 2,3,5,6-tetrafluoro-4-hydroxy-phenyl ester (1.61 g, 5.64 mmol) and a minimum of diethyl ether (10 ml), was added Merrifield resin (1.9 g, 1 mmol/g), together with toluene (110 ml) as a swelling agent, and triethylamine (0.78 ml, 5.64 mmol) . The reaction was stirred and heated at 50°C for 5 days. Finally, the resin was isolated by filtration and washed with toluene, water, acetone, THF and DCM. Elemental analysis has shown only a trace of fluorine, therefore little or no reaction was assumed to have occurred.

Elemental analysis expected Cl 0% found 3.37 expected F 16.11%, found 0.46%.

1-Bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene **31**



31

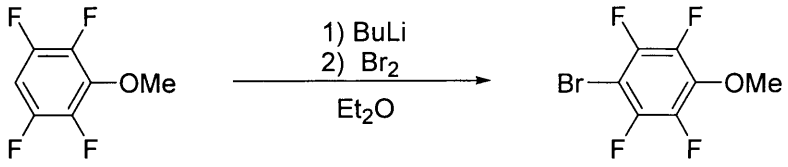
A three-necked flask, fitted with a reflux condenser was charged with 1-bromo-2,3,4,5,6-pentafluoro-benzene (4.4 g, 17.7 mmol), sodium methoxide (1 g, 17.7mmol), and the mixture was suspended in of dry methanol (125 ml) and stirred for 18h at reflux. Then water was added, the organic layers extracted with diethyl ether (2 x 50 ml) and dried over magnesium sulphate, before the solvent was removed under vacuum. The product **16** was isolated as a yellow oil in 89% yield (4.08 g), as a mixture of *ortho* and *meta* isomers.

^{1}**H** (major isomer) (250 MHz, 298K, $CDCl_3$) δ ppm: 3.95 (s, 3H, CH_3).

^{19}**F** (major isomer) (235 MHz, 298K, $CDCl_3$) δ ppm:-156.5 (2F), -134.5 (2F).

^{13}**C** (major isomer) (250 MHz, 298K, $CDCl_3$) δ ppm: 62.52 (OMe), 92.35 (C-Br), 138.33 (*C-OMe*), 141.5 (d, $^{1}J_{C\text{-}F}$=245.7 Hz, *C-F*), 145.8 (d, $^{1}J_{C\text{-}F}$=245.7 Hz, *C-F*).

1-Bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene (optimisation) **31**



31

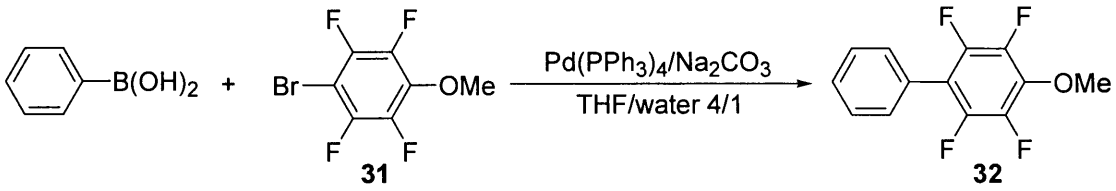
1,2,4,5-Tetrafluoro-3-methoxy-benzene (6g, 24 mmol) was dissolved in dry diethylether (60 ml) in a Schlenk. With a syringe, butyl lithium (15.18 ml, 24 mmol) was added at -78°C The reaction mixture was stirred at -78°C for 3h, then bromine (7.67 g, 24 mmol) was added to the reaction, the mixture turning yellow before being allowed to stir for two hours. Finally, the reaction was quenched by addition of aqueous HCl (1M, 100 ml) at room temperature and a saturated aqueous solution of sodium thiosulphate. The organic layer was washed with water before being dried over magnesium sulphate; volatile components were then removed under vacuum. The product **31** was isolated as a yellow oil in 76% yield (4.72 g).

^{1}**H** (250 MHz, 298K, $CDCl_3$) δ ppm: 3.95 (s, 3H, CH_3).

^{19}**F** (235 MHz, 298K, $CDCl_3$) δ ppm:-156.5 (2F), -134.5 (2F).

^{13}**C** (250 MHz, 298K, $CDCl_3$) δ ppm: 62.52 (OMe), 92.35 (C-Br), 138.33 (*C-OMe*), 141.5 (d, $^1J_{C\text{-}F}$=245.7 Hz, *C-F*), 145.8 (d, $^1J_{C\text{-}F}$=245.7 Hz, *C-F*).

2,3,5,6-Tetrafluoro-4-methoxy-biphenyl **32**



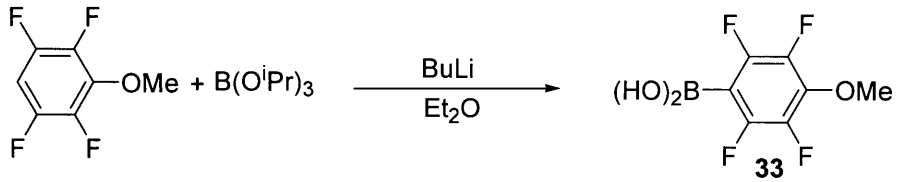
Phenyl boronic acid (0.24 g, 1.9 mmol), 1-bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene **31** (0.50 g, 1.9 mmol), sodium carbonate (0.41 g, 3.86 mmol) and palladium tetrakis triphenylphosphine (0.22 g, 0.19 mmol) were dissolved in a mixture of THF/water (4/1, 20 ml) in a 250 ml Schlenk. The reaction was stirred at 75°C for 48h. The mixture was allowed to cool to room temperature and a small quantity of H_2O_2 (3 ml) was added to neutralise any boronic acid remains. The organic layer was extracted with diethylether (3 x 25 ml), then passed through Celite in order to remove the palladium and triphenyl phosphine residues. Finally the organic layer was dried over magnesium phosphate and volatile components removed under vacuum to afford the product **32** as a brown powder in 89% yield (0.44 g).

^{1}**H** (250 MHz, 298K, $CDCl_3$) δ ppm: 4.05 (s, 3H, CH_3), 7.37-7.42 (m 5H *Ar*).

^{19}**F** (235 MHz, 298K, $CDCl_3$) δ ppm:-158.07 (2F), -145.60 (2F).

Elemental analysis: C expected 60.95%, found 61.05%, H expected 3.15%, Found: 3.21%.

Synthesis of 1,2,4,5-tetrafluoro-3-methoxy-phenyl boronic acid

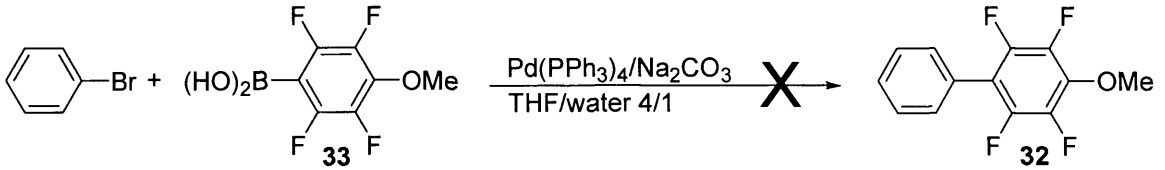


1,2,4,5-Tetrafluoro-3-methoxy-benzene (3.4 g, 18.8 mmol) was dissolved in dry diethylether (30 ml) in a Schlenk. With a syringe, butyl lithium (11.8 ml, 1.6M, 18.8 mmol) was added at -78°C The reaction mixture was stirred at -78°C for 3h, then triisopropylborate (11.76 ml, 24 mmol) was added. The mixture was stirred for two hour before being allowed to warm to room temperature. The reaction was quenched by addition of aqueous HCl (1M, 30 ml). The organic layer was separated, dried over magnesium

sulphate, and volatile components were removed under vacuum. The product **33** was isolated as a brown solid in 61% yield (2.56 g).

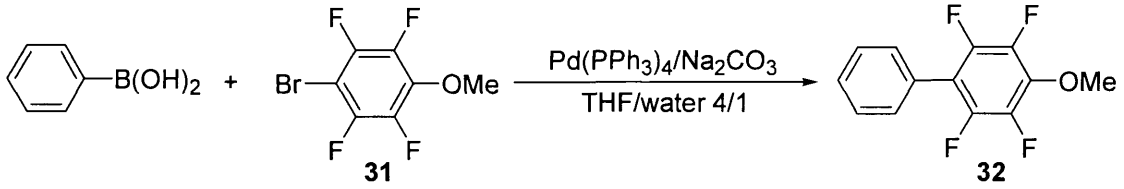
m/z :224 (M^+), 209 (-Me), 193 (-OMe), 181 (-$B(OH)_2$, 162 (-F).

Attempted synthesis of 2,3,5,6-tetrafluoro-4-methoxy-biphenyl **32**



1,2,4,5-Tetrafluoro-3-methoxy-phenyl boronic acid **33** (1 g 4.81 mmol), bromobenzene (0.75g, 4.88 mmol), sodium carbonate (1.03 g, 9.76 mmol) and palladium tetrakis triphenylphosphine (0.56 g, 0.49 mmol) were dissolved in a mixture of THF/water (4/1, 30 ml) in a 250 ml Schlenk. The reaction was stirred at 75°C for 48h. The mixture was allowed to cool to room temperature, and a small quantity of H_2O_2 was added to neutralise any boronic acid remaining. The organic layer was extracted with diethylether (2 x 30 ml), then passed through Celite in order to remove any palladium and triphenyl phosphine residues. Finally the organic layer was dried over magnesium phosphate and volatile components removed under vacuum. According to ^{1}H NMR spectroscopic analysis of the crude product, no reaction seemed to have occurred.

2,3,5,6-Tetrafluoro-4-methoxy-biphenyl (personal chemistry microwave reaction) **32**

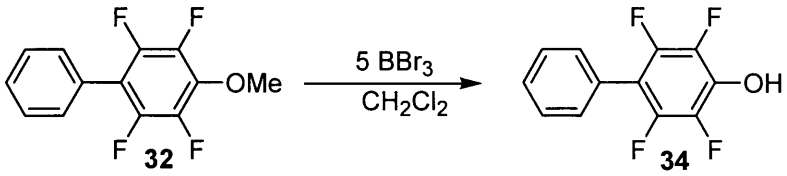


Phenyl boronic acid (0.12 g 0.95mmol), 1-bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene **32** (0.25 g, 0.95 mmol), sodium carbonate (0.21 g, 1.9 mmol) and palladium tetrakis triphenylphosphine (110 mg, 0.01 mmol) were dissolved in a mixture of THF/water (4/1, 5 ml) in a sample vial. The sealed reaction was stirred at a constant 120°C for 25 min, before the mixture was allowed to cool to room temperature, and then a small quantity of H_2O_2 was added to neutralise any remaining boronic acid. The organic layer was extracted with diethylether (2 x 15 ml), and then passed through Celite to remove any residual palladium and triphenyl phosphine. Finally the organic layer was dried over magnesium phosphate and volatile components removed under vacuum to afford the product **32** as a brown powder in 95% yield (0.47 g).

^{1}**H** (250 MHz 298K, $CDCl_3$) δ ppm: 4.05 (s, 3H, CH_3), 7.38-7.42 (m, 5H, *Ar*).

^{19}**F** (235 MHz 298K, $CDCl_3$) δ ppm:-158.07 (2F), -145.60 (2F).

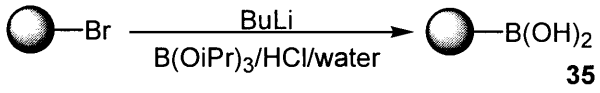
2,3,5,6-Tetrafluoro-biphenyl-4-ol **34**



2,3,5,6-Tetrafluoro-4-methoxy-biphenyl (0.215 g, 0.83 mmol), **32** was dissolved in DCM (25 ml) in a Schlenk. Tribromoborane (1.05 g, 4.2 mmol) was added *via* a syringe, and the reaction was stirred for 18h at room temperature. Water was added, then the organic layer was extracted with DCM (10 ml) and dried over magnesium sulphate and vacuum evaporated to afford 34 as a brown powder in 76% yield (0.15 g).

m/z :242,(M^+), 222(-*HF*), 193 (-*C-OH*) 174 (-*F*).

Supported boronic acid **35**[9]

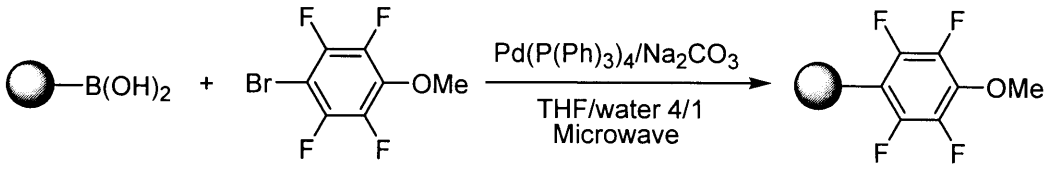


35

A nitrogen-filled three neck flask fitted with a reflux condenser and was charged with bromo-polystyrene (5 g, 4 mmol/g). The polymer was suspended in dry toluene (125 ml), then BuLi (21 ml, 1.6M, 36 mmol) was added, and the reaction was stirred at 70°C for 5 hours. The solvent was removed *via* a canula and the beads were washed 3 times with toluene (3 x 50 ml). Then the resin was suspended in dry THF (120 ml) and triisopropyl borate was added (16 ml, 69 mmol), and the reaction was stirred for 18h at room temperature. A mixture of dioxane/water/6M HCl (14/1/4) was added (100 ml) and the reaction was stirred for 2h at 65°C, after which time the beads were isolated by filtration and washed by using a Soxhlet apparatus charged with a mixture of dioxane/water (1/1). Finally, the polymer was dried under vacuum. 3.54g of **35** were recovered.

Elemental analysis: Br expected 0%, found 4.39%. Loading: 3.95 mmol/g.

Supported 1,2,4,5-Tetrafluoro-3-methoxy-benzene **36**



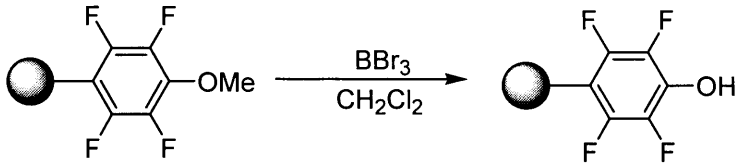
36

In a sample tube, supported boronic acid **35**, (0.240 g, 3.95 mmol/g), 1-bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene **31** (0.25 g, 0.95 mmol), palladium tetrakis triphenylphosphine (110 mg 0.01 mmol) and sodium carbonate (0.2 g, 1.9 mmol), and mixed with THF/water 4/1 (5 ml). The reaction was stirred and heated at 170°C for 100 minutes (CEM discoverer microwave). The polymer was isolated by filtration and washed with THF (15 ml) and water (15 ml). 0.32 g of **36** were recovered.

CP MAS ^{19}F (235 MHz, 298K, C_6D_6) δ ppm: -158.17 -144.89

Elemental analysis: F expected 21.2%, found 8.25%. Loading: 1.1mmol/g

Supported Tetrafluorophenol **38**

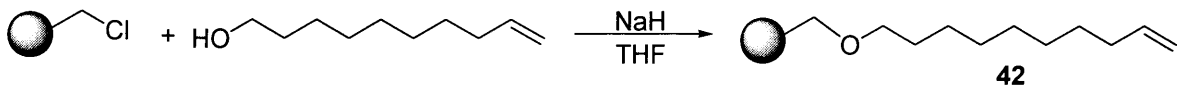


38

Supported tetrafluoroanisole **40** (0.5 g 1.1 mmol/g) and tribromoborane (1.6 g, 6.6 mmol) were stirred at room temperature in DCM (15 ml) for 48h in a Schlenk. Water was added (15 ml), the polymer isolated by filtration and was washed sequentially with water (30 ml), a mixture of water and DCM (1/1, 30 ml)) and DCM (30ml). 0.42 g of **38** were recovered.

IR: 3478 cm^{-1}(OH). Loading (calculated): 0.96 mmol/g

supported decen-1-ol **42**[10]



42

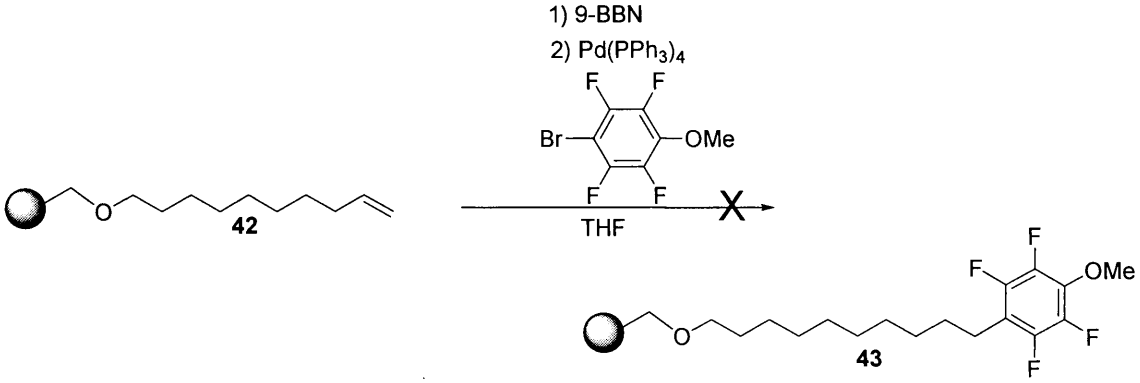
In a 100 ml, three-neck round bottom flask, fitted with a reflux condenser and an overhead stirrer, NaH (60 % dispersion in mineral oil, 0.70 g, 8.1 mmol) was washed with hexane (3 x 20 ml). Following removal of all liquids using a cannula filter, THF (50 ml) was added followed by undecen-1-ol (1.36 g, 8 mmol) and 18-crown-6 (0.35 g, 1.3 mmol). After stirring at room temperature for 30 minutes, chloromethylated polystyrene (4 g, 1mmol g^{-1} Cl) was added and the mixture was heated at reflux for 72h, with the mixture turning pale pink after 24h. The polymer beads were recovered by filtration, then washed with H_2O, H_2O:THF (1:1), THF (50 mL of each, 3 cycles) then acetone (2 x 50 mL) and finally dried at 70°C for 18 h under vacuum. 4.24 g of **42** were recovered.

Gel-phase ^{13}C (75 MHz, 298K, $CDCl_3$) δ ppm: 139.1 (CH=CH_2), 114.1 (CH=CH_2), 72.8 ($C_6H_4CH_2O$), 70.3 (OCH_2CH_2), 33.8 (CH_2CH=CH_2), 29.8, 29.5, 29.3, 29.1, 28.9, 26.3 (all CH_2; specific assignment not possible).

Elemental analysis: Expected Cl 0 %; Found Cl 0.46 % Loading: 0.86 mmol/g

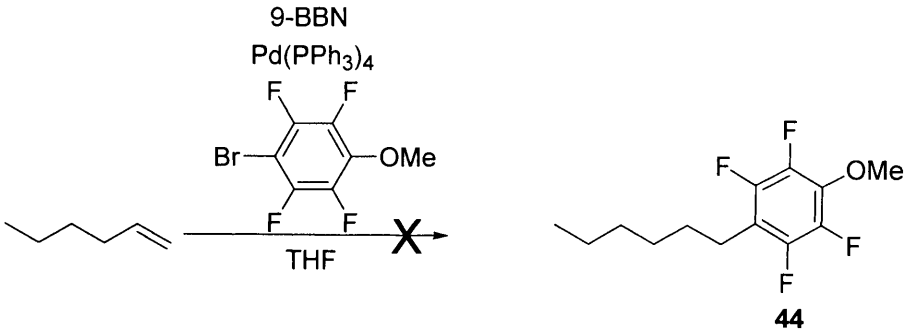
Attempted synthesis of supported 10-(2,3,5,6-Tetrafluoro-4-methoxy-phenyl)-decan-1-ol **43** [11]

Attempted synthesis of supported 10-(2,3,5,6-Tetrafluoro-4-methoxy-phenyl)-decan-1-ol **43** [11]



To a three-necked flask fitted with a reflux condenser flask was added supported decen-1-ol **42** (2 g 0.86 mmol/g), and THF (30 ml) as swelling agent. The reaction was cooled to 0°C, and 9-BBN was added *via* a syringe (17.2 ml, 0.5M THF, 1.72 mmol). The reaction was allowed to warm to room temperature and was stirred for 12h. The solvent was removed *via* a cannula, and the resulting beads were washed 3 times with THF (30 ml). The beads were re-swollen in THF (30 ml), and bromotetrafluoroanisole (2.20 g, 8.5 mmol) together with palladium tetrakis triphenylphosphine (0.97g 0.851 mmol) and sodium carbonate (1.80g, 17 mmol) added to the reaction mixture. The reaction was stirred for 48h at reflux temperature. After cooling, the resin was isolated by filtration and washed 3 times with THF (30 ml), THF/water (1/1, 30 ml) and water (30 ml). Elemental analysis were undertaken, and revealed only traces of fluorine, therefore the formation of **43** was deemed to have not been successful.

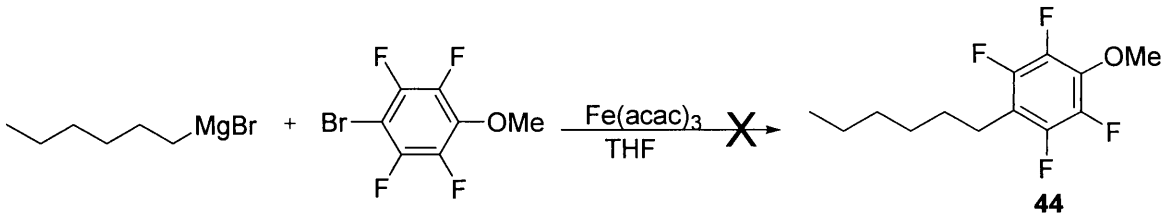
Attempted synthesis of 1,2,4,5-tetrafluoro-3-hexyl-6-methoxy-benzene **44**



In a Schlenk, hexene (0.159 g 1.9 mmol) was dissolved in THF (10 ml) and was cooled to 0°C. 9-BBN (3.8 ml, 0.5M THF, 1.9 mmol) was added *via* a syringe to the mixture, and the

reaction was stirred for 8h at room temperature. 1-Bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene **32** (0.50 g, 1.9 mmol), sodium carbonate (0.409 g, 3.8 mmol) and palladium tetrakis triphenylphosphine (223 mg, 0.19 mmol) were added. The reaction was stirred at 70°C for 48h, before the mixture was allowed to cool to room temperature, and then a small quantity of H_2O_2 was added to neutralise any boronic acid residues. The organic layer was extracted with diethylether (15 ml), and then passed through celite to remove the palladium and triphenyl phosphine. Analysis by GC-MS revealed a mixture of starting materials.

Attempted synthesis of 1,2,4,5-tetrafluoro-3-hexyl-6-methoxy-benzene **44**[12]



44

In a Schlenk hexyl magnesium bromide (0.73 g, 3.8 mmol), 1-bromo-2,3,5,6-tetrafluoro-4-methoxy-benzene **32** (1.0 g, 3.8 mmol), iron triacetylacetonate (110 mg, 0.01 mmol), and a 10 mol % solution of TMP in THF were dissolved in THF (20 ml). The reaction was stirred at room temperature for 2 hours. The reaction was re-taken in diethylether (30 ml) and was subsequently washed with aqueous HCl (1M, 20 ml) and with water (25 ml). The organic fraction was dried over magnesium sulphate and the solvent was removed under vacuum. The resulting oil was analysed by GC-MS, which revealed a mixture of starting materials and tetrafluoroanisole.

Chapter III: Synthesis of Novel Soluble Schrock-type Initiators:

The compounds **45** to **58**[13] were synthesised according to literature procedures and their identity was confirmed by ^{1}H NMR spectroscopy, and were all found to be in accordance with literature data.

Mo(NAr)$_2$Cl$_2$DME **45**

$$Na_2MoO_4 + 2\,ArNH_2 + 8\,TMSCl + 4\,NEt_3 \xrightarrow[DME]{70°C} Mo(NAr)_2Cl_2(DME) + 2\,NaCl + 4\,TMS_2O + 4\,HNEt_3Cl$$

Ar = 2,6 diisopropylamine

45

A three-necked flask, fitted with a reflux condenser was charged with Na_2MoO_4 (15 g, 72.8 mmol) suspended in dry DME (200 ml). Then a solution of degassed triethylamine (40.6 ml, 291 mmol) in dry DME (25 ml), followed by a solution of TMSCl (101.7 ml, 801 mmol) in DME (20 ml), and finally 2.6-di-isopropylphenylamine ($ArNH_2$) (27.5 ml, 145 mmol) in DME (25 ml) were added. The reaction was heated at 70°C overnight, the colour changing from yellow to blood red. The reaction was allowed to cool to room temperature and the solution was filtered *via* a canula. The resulting solid was washed several times with hexanes. All the liquid fractions were combined and dried under vacuum to give **45** as a red solid in 89% yield (39 g).

^{1}H (300 MHz, 298K, C_6D_6) δ ppm: 1.12 (d, $^3J_{H\text{-}H}$=6.85 Hz, 24H, CH(CH_3)$_2$), 3.08 (s, 4H, CH_2OMe), 3.32 (s, 6H, CH_2O*Me*), 4.15 (sept, $^2J_{H\text{-}H}$=6.85 Hz, 4H CH(CH$_3$)$_2$), 6.66-7.08 (m 6 Aromatic).

Neophyl Grignard reagent .**46**

$$PHCMe_2Cl \xrightarrow[Et_2O]{Mg} PHCMe_2MgCl$$

A three-necked flask was fitted with a dropping funnel and a reflux condenser, and was charged with Mg turning (3.78 g, 155 mmol) and enough dry diethyl ether to just cover the magnesium. Three drops of dibromoethane were added to activate the magnesium. Neophyl chloride (22.9 ml, 141 mmol) was then added over 10 minutes. This addition was repeated until an exothermic reaction commenced, at which point the mixture was heated at reflux for 3h. The Grignard reagent was transferred in a Schlenk *via* a canula filter. The

neophyl magnesium chloride was titrated with a 0.1M HCl solution using bromothymol blue as indicator. The concentration was calculated to be 0.79 mol L^{-1}.

Mo(NAr)$_2$(CH$_2$CMe$_2$Ph)$_2$ **47**

$$\underset{\mathbf{45}}{Mo(NAr)_2Cl_2(DME)} + 2\ \underset{\mathbf{46}}{PhCMe_2CH_2MgCl} \xrightarrow[Et_2O]{} \underset{\mathbf{47}}{Mo(NAr)_2(CH_2CMe_2Ph)_2} + 2\ MgCl_2$$

Mo(NAr)$_2$Cl$_2$(DME) **45** (39 g 64 mmol) was dissolved in dry diethyl ether (110 ml) in a Schlenk. With a syringe, the Grignard reagent **46** was added at -30°C (179 ml, 141 mmol). The colour changed from red to orange and $MgCl_2$ precipitated. The reaction mixture was allowed to warm to room temperature and was stirred for 3 hours. All the liquid phases were transferred to a second Schlenk *via* a canula filter. The resulting solid was washed three times with diethylether (3 x 50 ml). All the liquid fractions were combined in a Schlenk and concentrated *in vacuo* before being kept at -30°C, something which gave **47** in several crops as an orange crystal in 80% yield (36.7 g).

^{1}H (300 MHz, 298K, C_6D_6) δ ppm: 1.27 (d, ^{3}J=7.0 Hz, 12H, *CH*(CH$_3$)$_2$), 1.71 (s, 6H, C*Me$_2$*Ph), 1.95 (s, 2H, *CH$_2$*CMe$_2$Ph), 3.87 (sept, ^{3}J=7.0 Hz, 4H, *CH*(CH$_3$)$_2$), 7.19-7.69(m, 16H, Ar).

Mo(NAr)(CHCMe$_2$Ph)(OSO$_3$CF$_3$)2(DME) **48**

$$\underset{\mathbf{47}}{Mo(NAr)_2(CH_2CMe_2Ph)_2} + 3\ CF_3SO_3H \xrightarrow[DME]{} \underset{\mathbf{48}}{Mo(NAr)(CHCMe_2Ph)(OSO_2CF_3)_2(DME)} + ArNH_3OSO_3CF_3 + PhMe_2CCH_3$$

At -78°C, previously distilled triflic acid (2.7 ml, 29.37 mmol), was added carefully *via* a canula to a cooled solution of Mo(NAr)$_2$(CH$_2$CMe$_2$Ph)$_2$ (7.7 g, 9.79 mmol) **47**, in DME (150 ml), in a 3-necked flask. When the addition was complete, the reaction was allowed to warm to room temperature, and left overnight. The dark solution became orange. Subsequently, all the solvent was removed under vacuum. The resulting solid was extracted with toluene (50 ml) at 0°C. The toluene was then removed *in vacuo* and the solid dried under vacuum for 2 days. The resulting product was then recrystallized from pentane to give a green solid in 75% yield (5.9 g).

^{1}H (300 MHz, 298K, C_6D_6) δ ppm: 1.24 (d, $^3J_{H\text{-}H}$=6.8 Hz, 6H, CH(*CH$_3$*)$_2$), 1.40 (d, $^3J_{H\text{-}H}$=6.8 Hz, 6H CH(*CH$_3$*)$_2$), 1.84 (s, 6H, CHC*Me$_2$*Ph), 2.68 (s, 5H, *CH$_3$*O*CH$_2$*), 3.08 (m, 2H, O*CH$_2$*), 3.64 (s, 3H, O*CH$_3$*), 3.76 (sept, $^3J_{H\text{-}H}$=6.9 Hz, 2H, *CH*(CH$_3$)$_2$), 6.76-7.80 (m, 8H, aromatic), 14.15(s, 1H, *CH*CMe$_2$Ph).

Mo(NAr)(NtBu)Cl_2(DME) **49**

$$Na_2MoO_4 + {}^tBuNH_2 + ArNH_2 + 8\ TMSCl + 4\ NEt_3 \xrightarrow[70°C]{DME} Mo(NAr)(N^tBu)Cl_2(DME) + 2\ NaCl + 4\ TMS_2O + 4\ HNEt_3Cl$$

49

The title complex was prepared in the same manner as $Mo(NAr)_2Cl_2(DME)$, using, Na_2MoO_4 (12 g, 58.24 mmol), NEt_3 (32.5 ml, 321 mmol), TMSCl (81.4 ml, 641 mmol), $ArNH_2$ (11 ml, 58.24 mmol), followed by the addition of $^tBuNH_2$ (27 g, 58.24 mmol), to afford **49** in 87% yield (26.11 g) as a red solid following workup.

^{1}H (300 MHz, 298K, C_6D_6) δ: 1.38 (s, 9H NC*(CH$_3$)$_3$*), 1.54 (d, $^3J_{H\text{-}H}$=6.9 Hz, 12H, CH(*CH$_3$*)$_2$), 3.32 (s, 4H, *CH$_2$*OMe), 3.51 (s, 6H, CH_2O*Me*), 4.44 (sept, $^3J_{H\text{-}H}$=6.9 Hz, 2H, *CH*(CH_3)$_2$), 7.04-7.27 (m, 3H, aromatic).

Mo(NAr)(NtBu)(CH_2CMe_2Ph)2 **50**

$$Mo(NAr)(N^tBu)Cl_2(DME) + 2\ PhCMe_2CH_2MgCl \xrightarrow{Et_2O} Mo(NAr)(N^tBu)(CH_2CMe_2Ph)_2 + 2\ MgCl_2$$

49 **46** **50**

The title complex was prepared in the same manner as for $Mo(NAr)_2(CH_2CMe_2Ph)_2$ **47**, using **49** (5 g, 9.66 mmol), **46** (18.5 ml, 21.25 mmol), to afford **50** as a brown oil in 53% yield (3.11 g).

^{1}H (300 MHz, 298K, C_6D_6) δ ppm: 0.91 (s, 2H, *CH$_2$*CMe_2Ph), 0.96 (s, 2H, *CH$_2$*CMe_2Ph), 1.04 (s, 9H NC*(CH$_3$)$_3$*), 1.23 (d, $^3J_{H\text{-}H}$=7.0 Hz, 12H, CH(*CH$_3$*)$_2$), 2.93 (s, 6H, CH_2C*Me$_2$*Ph), 2.98 (s, 6H, CH_2C*Me$_2$*Ph), 3.69 (sept $^3J_{H\text{-}H}$=7.0 Hz, 2H *CH*(CH_3)$_2$), 6.91-7.35 (m, 13H, aromatic).

Synthesis of lithium salts: general procedure

$$BuLi + ROH \xrightarrow{hexane} LiOR + Bu$$

8

To a solution of alcohol in dry hexane (40 ml) was slowly added butyl lithium at -60°C. The reaction was allowed to warm to room temperature and stirred overnight. The solution was concentrated, the desired products precipitating on cooling as a white powder (table **3**).

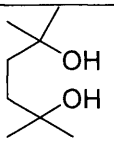
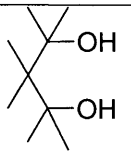
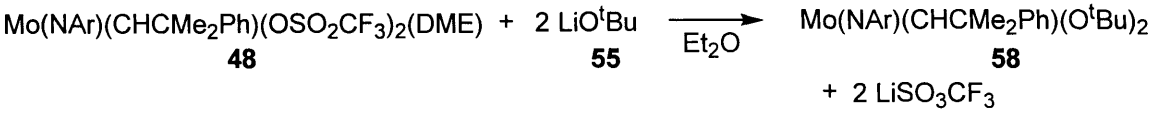
Alcohol ROH G, mmol	^{t}BuOH 5, 68	 5, 34.2	 1, 6.24
Butyl lithium ml, mmol	43, 68.4	42.75, 68.4	7.8 ml, 12.4
Yield, **product**	61%, **55**	74%, **56**	76%, **57**

Table 3 synthesis of Lithium salts

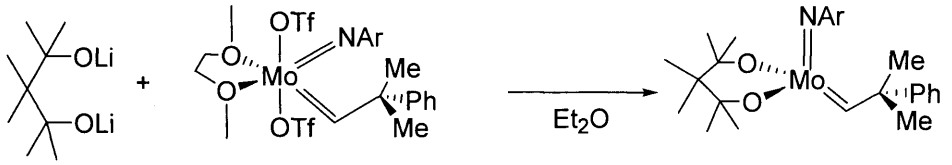
Mo(NAr)(CHCMe$_2$Ph)(OtBu)$_2$ **58**



A diethylether solution (25 ml) of Mo(NAr)(CHCMe$_2$Ph)(OSO$_3$CF$_3$)$_2$(DME) **48** (3 g, 3.78 mmol) was placed in a Schlenk, and cooled to -30°C. A diethyl ether (10 ml) solution of lithium *tert*-butoxide was added (7.56 mmol, 604 mg). When the addition was complete, the reaction was allowed to warm to room temperature, and stirred for 1h. The solvent was removed under vacuum, and the resulting material extracted three times with pentane (3 x 25 ml). The filtrate was evaporated *in vacuo* before a minimum of pentane (15 ml) was added and the product recrystallised at -30°C to give **58** as a brown solid in 74% yield (5.4 g).

^{1}H (300 MHz, 298K, C_6D_6) δ ppm : 1.51 (d, 12H, $^3J_{H\text{-}H}$=6.9 Hz, CH(*CH$_3$*)$_2$), 1.58 (s, 18H C*Me$_3$*), 1.57 (s, 3H, CHC*Me$_2$*Ph), 2.63 (s, 3H CHC*Me$_2$*Ph), 4.33 (sept, 2H $^3J_{H\text{-}H}$=6.9 Hz, *CH*(CH$_3$)$_2$), 7.41-7.8 (m, 8H aromatic), 11.73 (s, 1H, C*H*CMe$_2$Ph).

Attempted synthesis of Mo(2,3,3,4-tetramethyl-pentane-2,4-dioxo)(NAr)(CHCMe$_2$Ph) **59**

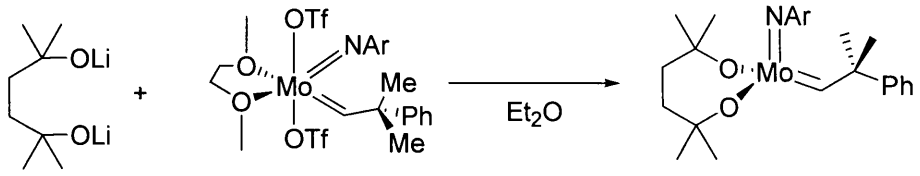


56 **48** **59**

A diethylether solution (15 ml) of 2,3,3,4-tetramethyl-pentane-2,4-diol (0.17 g, 1.10 mmol) was placed in a Schlenk, and cooled to -30°C. A diethyl ether solution (10 ml) of Mo(NAr)(CHCMe$_2$Ph)(OSO$_3$CF$_3$)$_2$(DME) **48** (0.8 g. 1.10 mmol) was added. When the addition was complete, the reaction was allowed to warm to room temperature and then stirred for 1h. The volatile components were removed *in vacuo* and the resulting solid extracted three times with pentane (3 x 10 ml). The filtrate was vacuum evaporated and a

minimum of pentane (5 ml) was added for the recrystallisation. Despite prolonged cooling and repeated attempts at purification, no crystals could be isolated. The ^{1}H NMR spectrum of the crude material revealed a very complex mixture of unidentifiable products.

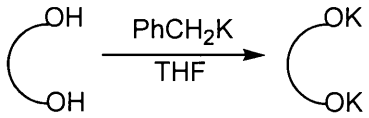
Attempted synthesis of Mo(2,5-dimethyl-hexane-2,5-dioxo)(NAr)(CHCMe$_2$Ph) **60**



57 **48** **60**

A diethylether solution (5 ml) of 2,2,5-dimethyl-hexane-2,5-diol (44.0 mg, 0.28 mmol) was placed in a Schlenk, and cooled to -30°C. A diethyl ether solution (10 ml) of Mo(NAr)(CHCMe$_2$Ph)(OSO$_3$CF$_3$)$_2$(DME) **48** (0.2 g, 0.28 mmol) was added. When the addition was complete, the reaction was allowed to warm to room temperature and then stirred for 1h. The volatile components were removed under vacuum and the resulting solid extracted three times with pentane (3 x 10 ml). The filtrate was vacuum evaporated and a minimum of pentane was added in an attempt to obtain crystals of the desired product **60**. Despite repeated efforts using a variety of conditions, no crystals have been isolated. The ^{1}H NMR spectrum of the crude material revealed a very complex mixture of unidentifiable products.

Synthesis of potassium salts: general procedure



The appropriate diol and benzyl potassium were dissolved in THF (25 ml). The reaction was stirred overnight, before the solvent was removed *in vacuo* and the resulting solid dried under vacuum (table **4**).

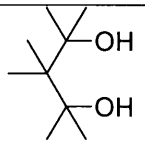
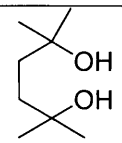
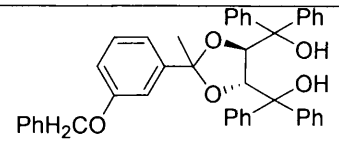
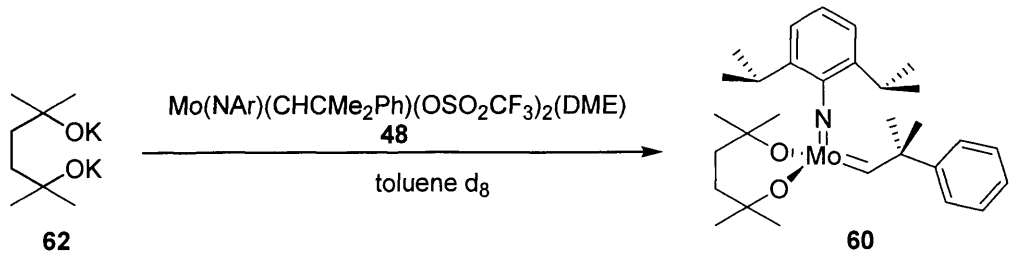
Diol g, mmol	 1.00, 6.24	 1.00, 6.83	 0.25, 0.39
Benzyl potassium g, mmol	1.62, 12.48	1.78, 13.67	0.10, 0.78
Yield, **identity**	91%, **61**	88%, **62**	89%, **63**

Table 4 synthesis of potassium salts

Synthesis of Mo(2,5-dimethyl-hexane-2,5-dioxo)(NAr)(CHCMe$_2$Ph): VT-NMR experiment **60**

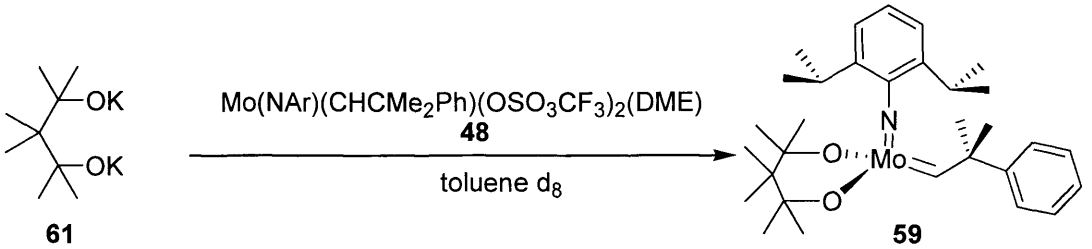


62 **60**

The potassium salt was dissolved in toluene-d$_8$ (10 mg, 0.044 mmol) and added to a toluene-d$_8$ solution of **48** (36 mg, 0.044 mmol) in a Young's tap NMR tube *via* a canula at -78°C. The reaction was then monitored by VT-NMR over the temperature range from -20°C to room temperature, a new alkylidene peak being observed to grow in.

Selected ^{1}**H** (400 MHz, 273K, toluene d$_8$) δ ppm: 1.08-1-86 (bm, 28H, *CH*$_3$, *CH*$_2$, *CH*$_3$CH), 2.31 (s, 6H, CMe$_2$) 4,18-4.21 (m, 2H, *CH*CH$_3$), 7.024-7.63 (m, 8H, Ar) 13.54 (s, 1H, =*CH*-CMe$_2$Ph).

Synthesis of Mo(2,3,3,4-tetramethyl-pentane-2,4-dioxo)(NAr)(CHCMe$_2$Ph): VT-NMR experiment **59**

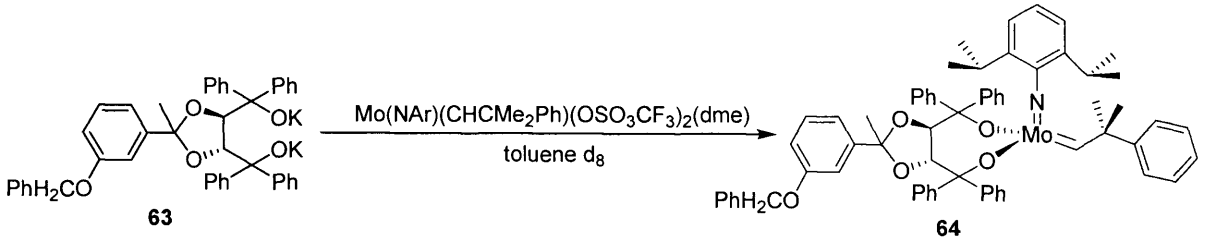


61 **59**

The potassium salt **61** was dissolved in toluene-d$_8$ (10 mg, 0.042 mmol) and added to a toluene-d$_8$ solution of **48** (34 mg 0.042 mmol) in a Young's tap NMR tube *via* a canula at -78°C. The reaction was then monitored by VT-NMR from -20°C to room temperature, and new alkylidene peaks being observed to grow in.

Selected ^{1}**H** (400 MHz, 273K, toluene d$_8$) δ ppm: 2.22 (bs, 6H, CMe$_2$), 4.16 (bs, 2H, *CH*CH$_3$), 13.05 (s, 1H, =*CH*-CMe$_2$Ph), 13.57 (s, 1H =*CH*-CMe$_2$Ph).

Synthesis of Mo(TADDOlate)(NAr)(CHCMe$_2$Ph): VT-NMR experiment **64**



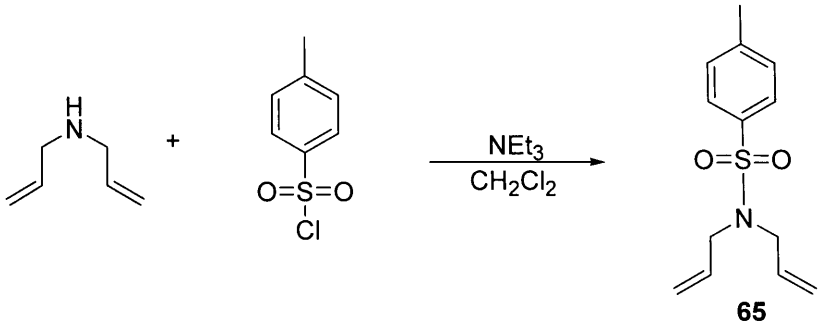
63 **64**

The potassium salt **63** was dissolved in toluene-d$_8$ (20 mg, 0.028 mmol) and added to a

toluene-d_8 solution of **48** (22 mg, 0.028 mmol) in a Young's tap NMR tube *via* a canula at -78°C. The reaction was then monitored by VT-NMR from -20°C to room temperature, and new alkylidene peaks being observed to grow in.

Selected **^{1}H** (400 MHz, 273K, toluene-d_8) δ ppm: 4,13 (bs, 2H, $CHCH_3$) 4.63-4.66 (m 1H, *CH*), 4.76-4.80 (m, 1H, *CH*) 5.20-5.29 (m, 2H, PhCH_2), 13.56 (s, 1H, =*CH*-CMe_2Ph).

para-Toluene sulfonic di allyl amine 43[14]

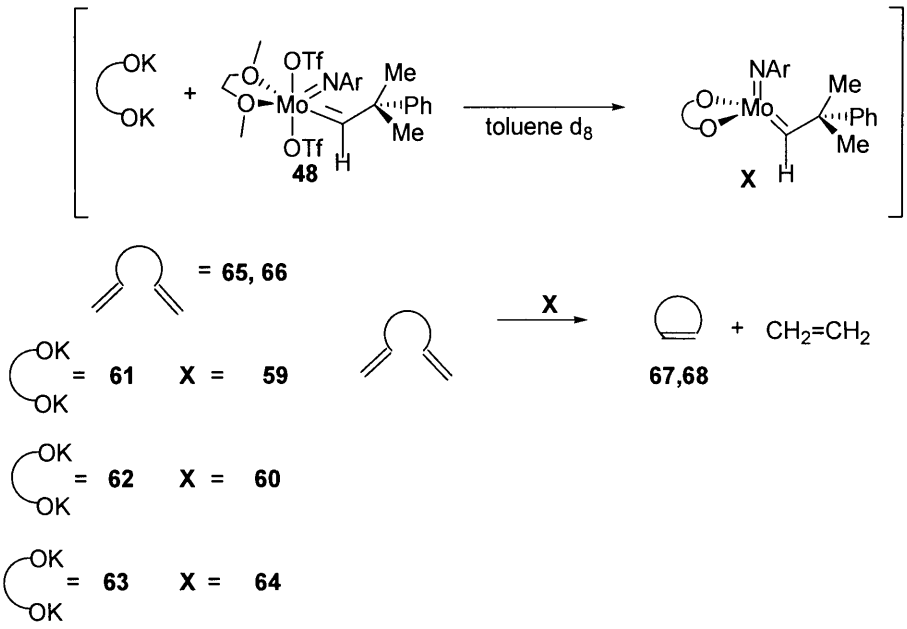


65

In a three-necked flask fitted with a condenser and dropping funnel NEt_3 (5.12 ml, 37 mmol) was added to a 0°C DCM solution (40 ml) of diallyl amine (3.5 g, 36 mmol), and was stirred for 30 min. Subsequently, *para*-toluene sulfonic chloride (6.5 g, 34 mmol) was added dropwise over 15 minutes, finally the reaction was allowed to reach room temperature and stirred for 12h. Then, water was added (30 ml), the organic layer was washed with brine, dried over magnesium sulphate and the DCM removed under vacuum to afford **43** as a colourless oil in 85% yield (7.69 g).

^{1}H (250 MHz, 298K, $CDCl_3$): 2.35 (s, 3H, *CH_3*), 367-3.80 (m, 4H, *CH_2*), 5.05-5.10 (m, 4H, =*CH_2*), 5.47-564 (m, 2H =*CH*), 7.22 (d 2H ^{3}J = 6.7Hz *CH*), 7.63 (d, 2H, ^{3}J = 6.7Hz *CH*).

Metathesis reaction with soluble Schrock initiators: general procedure



The potassium salts **X-Y** were dissolved in toluene-d_8 and added to a toluene-d_8 solution of **48** in a Young's tap NMR tube *via* a canula at -78°C. the amount of potassium salts were calculated in order to produce a catalytic reaction with a 10% mol of metal centre. Finally, the diene was added and the reaction was left at -5°C. The reaction was then monitored by ^{1}H NMR spectroscopy (table **5**).

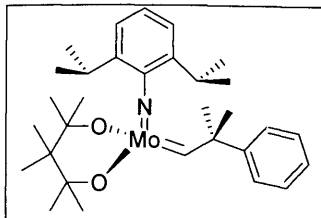
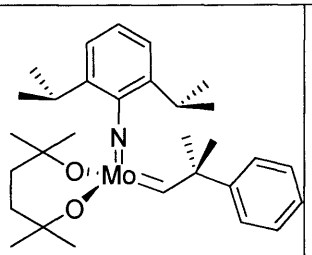
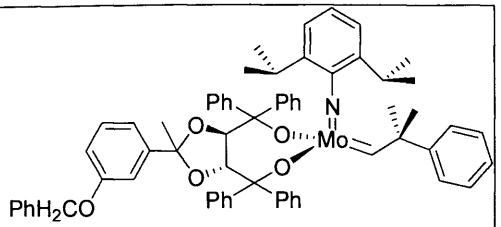
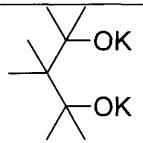
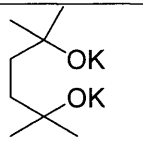
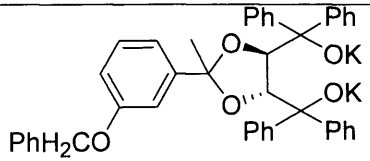
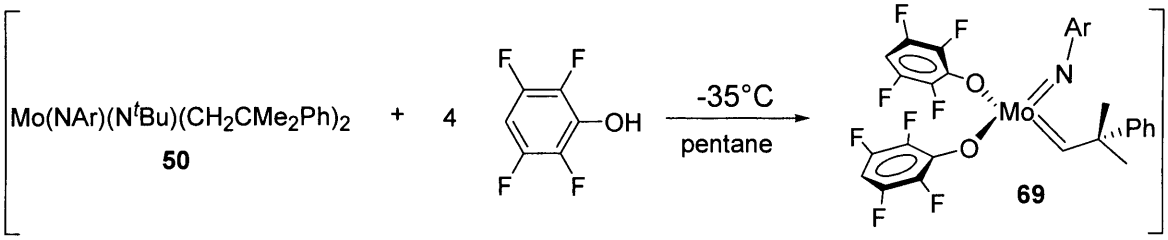
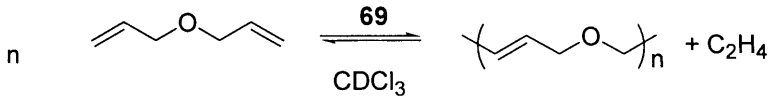
			
salt, (mg, mmol)	 10, 0.043	 10, 0.045	 20, 0.028
Bis triflate (mg, mmol)	34, 0.043	36, 0.045	22, 0.028
Reaction **A** conversion %	RCM 15.9%	RCM 15.2%	RCM 14.5%
Reaction **B** conversion %	No reaction	No reaction	RCM 9.5%

Table 5 Catalytic testing of the novel soluble Schrock initiator

Metathesis reactions with tetrafluorophenol-type ligands[15]





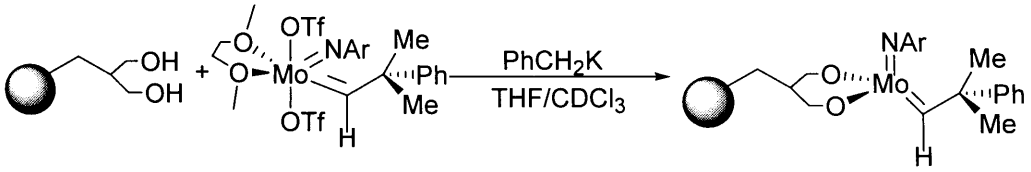
A pentane solution (10 ml) of tetrafluorophenol (0.110 mg, 0.66 mmol) was added at -35°C to a solution of Mo(NAr)(N^{T}Bu)(CH$_2$CMe$_2$Ph)$_2$ (90.1mg, 0.17 mmol) in pentane (10 ml). The reaction was then stirred at -35°C for 30 minutes. The solvent was removed under vacuum and then the mixture was dissolved in $CDCl_3$ (10 ml) and allyl ether (0.65 g 6.6 mmol) added; the mixture was then stirred for 12h. The mixture was passed through Celite and the solvent was removed under vacuum. Formation of the polymer was observed 0.225g.

^{1}H (250 MHz, 298K, $CDCl_3$): 3.90-4.00 (broad m), 4.90-5.05 (m), 5.1-5.3 (broad m), 5.7-6.1,(broad m).

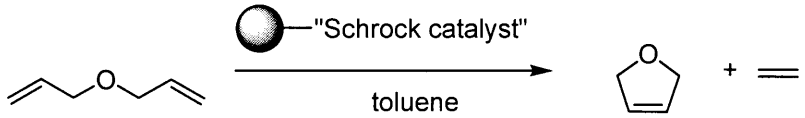
Chapter IV: Synthesis of polymer-supported Schrock-type alkylidene complexes

Compounds **73** and **74** were synthesised according to literature preparations,[16,17] their formation were monitored by ^{1}H NMR, with all data obtained being in accordance with that reported in the literature.

Metahesis reactions on solid supports: general procedure



The appropriate supported diol and $PhCH_2K$ were introduced into a Schlenk and dry THF added. The reaction was stirred for three days then the solvent was removed *via* a canula, and the resulting polymer was washed three times with THF. Then solutions of $Mo(NAr)(CHCMe_2Ph)(OSO_3CF_3)_2(DME)$ and diallylether in d_8-toluene, were added and the mixture stirred for 3 days at -20°C (table **6**). The conversion were determined by integration of the ^{1}H NMR of the solution phase (chapter 4 Figure 3).



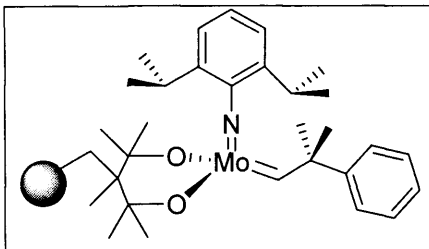
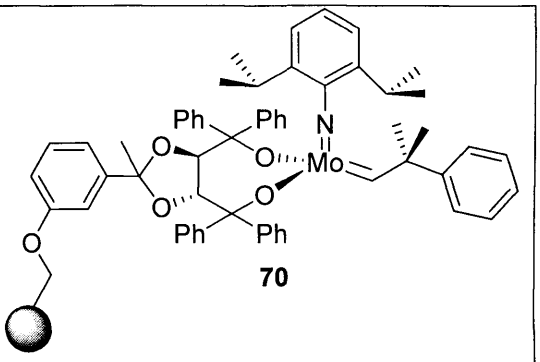
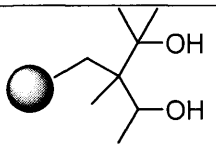
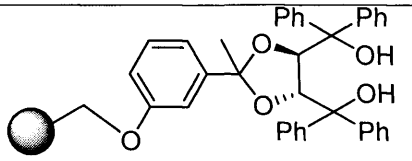
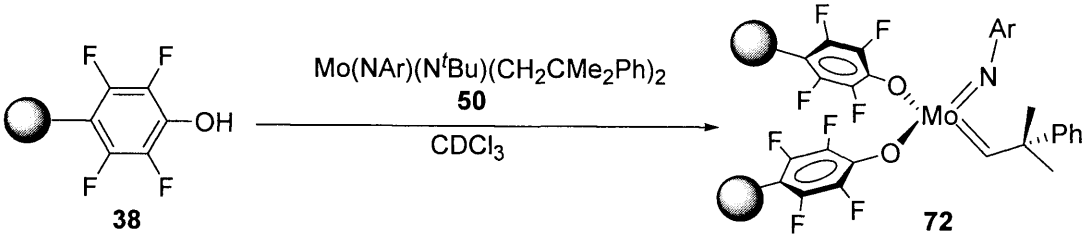
	 71	 70
Quantity of supported diol (mg)	 100	 100
$PhCH_2K$ (mg)	65	81
Bistriflate (mg)	79	52
Metathesis conversion	No reaction	RCM 14%

Table 6 catalytic testing of supported Schrock initiator

Preparation of solutions for ICP-AE analysis

Combined volatile components from the preparation of the various polymer-supported Schrock initiators were removed under reduced pressure before the residue being shaken with *aqua regia*. The resulting solution was washed into a 25 ml volumetric flask with conc. nitric acid (30 %, 2 x 5 ml) and then H_2O was added to make a 25 ml solution. The solutions were submitted for ICP-AE analysis that were subsequently obtained by E. Mansley (Department of Geology, University of Leicester).

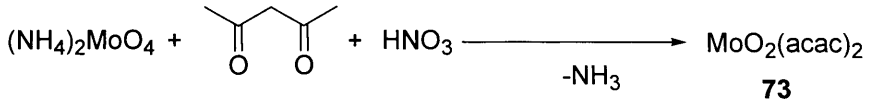
Metathesis reactions with supported tetrafluorophenol-type ligands **72**



38 **72**

A $CDCl_3$ solution (10 ml) of $Mo(NAr)(N^tBu)(CH_2CMe_2Ph)_2$ (32 mg, 0.05 mmol) and diallylether (51 mg, 0.52 mmol) was added at -35°C to the supported tetrafluorophenol **38** (80 mg 1.1 mmol/g), which was swollen in $CDCl_3$. The reaction was then stirred at -35°C for 3 days, and was followed by ^1H NMR spectroscopy. No reaction seemed to occur, as only unreacted diallylether was observed.

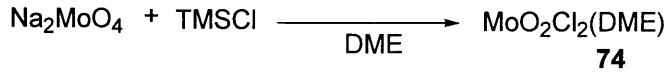
$MoO_2(acac)_2$ **73**[16]



Ammonium molybdate (VI) tetrahydrate (3.03 g, 15.46 mmol) was dissolved in aqueous ammonia (6 ml) by stirring. 2,4-Pentandione (7.0 ml, 6.8 mmol) was added before 16M nitric acid (5 ml) was added dropwise, at which point the solution turned green then yellow, followed by the formation of a yellow precipitate. The solution was vigorously stirred for 30 mins then placed in the freezer for 18h. The yellow precipitate was collected by suction filtration then washed with cold water (15 ml), followed by cold ethanol (15 ml) giving **73** as a yellow solid in 91% yield (4.41 g).

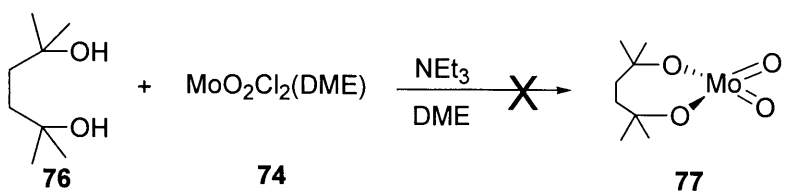
^1H (250 MHz, 298K, $CDCl_3$) δ ppm: 1.54 (s, 3H, *CH_3*), 1.70 (s, 3H, *CH_3*), 5.15(s, 1H, *CH*).

$MoO_2Cl_2(DME)$ **74**[17]



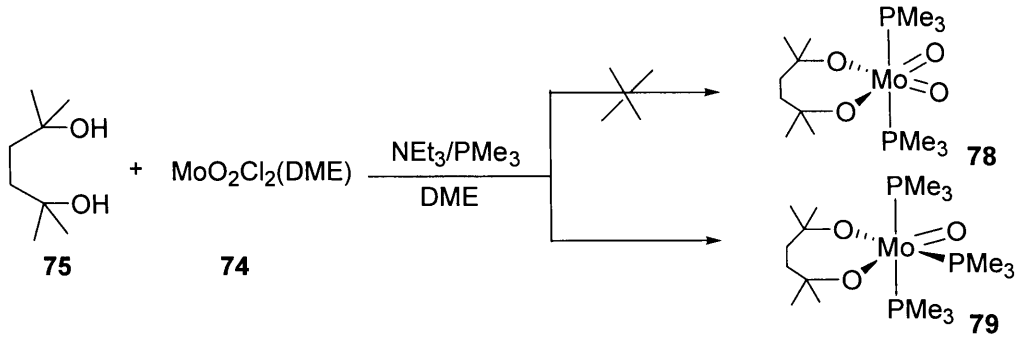
A DME solution (25 ml) of sodium molybdate (4 g, 19.42 mmol) was placed in a Schlenk and a DME solution (35 ml) of trimethylsilyl chloride (8.44 g, 77.69 mmol) was added. When the addition was complete, the reaction was stirred for 18h at 85°C. Finally the solvent was removed under vacuum to afford the desired product **74** as a white solid in 87% yield (5.61g).

Attempted synthesis of $MoO_2(dhd)$ **77**



A Schlenk was charged with a solution $MoO_2Cl_2(DME)$ (1.00 g. 3.57 mmol) **74** in DME (10 ml). A DME solution (10 ml) of 2,5-dimethyl-hexane-2,5-diol (0.52 g, 3.57 mmol) and NEt_3 (0.721 g 9.7 mmol) was added *via* a canula at –78°C, then the reaction was stirred at room temperature for 48h. The reaction was filtered using a canula. As the solvent was removed, the colourless solution starts to become blue, and a blue solid appeared, which was insoluble in all common organic solvents tested and is probably a polymeric compound Mo_xO_y.

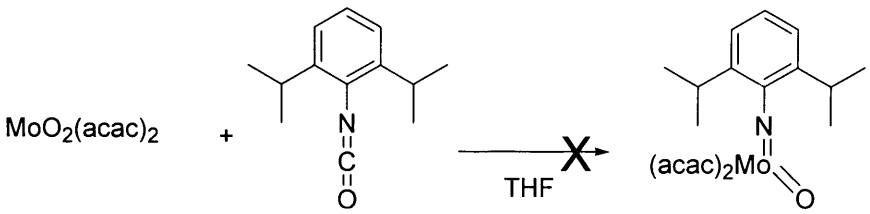
Attempted synthesis of $MoO_2(PMe_3)_2$ (dhd) **78**



A Schlenk was charged with a solution $MoO_2Cl_2(DME)$ (1.40 g 4.84 mmol) **74** in DME (15 ml). A DME solution (10 ml) of 2,5-dimethyl-hexane-2,5-diol (0.71 g, 4.85 mmol) and NEt_3 (0.98 g 9.7 mmol) was added *via* a canula at –78°C, then the reaction was stirred at room temperature for 48h. The reaction was filtered using a canula and the reaction was frozen, and was kept under vaccum. Finally PMe_3 (0.74 g, 9.7 mmol) was added by vacuum transfer, before leaving it to stir for 18h at room temperature. The solution which was yellow at the start became dark orange. Monitoring the progress of the reaction by ^{31}P NMR spectroscopy confirmed the formation of the product **79**.[18]

^{31}P (100 MHz, 298K, C_6D_6) δ ppm:-8.32 (d, $^2J_{P\text{-}P}$=21 Hz, 2P, *PMe_3*), -1.61 (t, $^2J_{P\text{-}P}$=21 Hz, 1P, *PMe_3*).

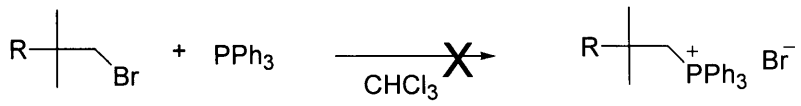
Attempted synthesis of $Mo(NAr)(O)(acac)_2$



$MoO_2(acac)_2$ **21** (1 g 3.07 mmol) was dissolved in THF. The tri-isopropyl phenyl isocyanate (0.65 ml, 3.07 mmol) was then added to the reaction. The reaction was stirred

for 24h at 40°C. ^{1}H NMR and IR spectroscopy revealed only a mixture of the starting materials.

Attempted synthesis of tert-butyl phosphonium salts



R=Ph **81**
R=Me **83**

R=Ph **82**
R=Me **84**

1-Bromo-dimethyl propane (5.00 g, 33.10 mmol) and triphenylphosphine (8.68 g, 33.10 mmol) were dissolved in a minimum of $CHCl_3$ (20 ml). The reaction was stirred and heated at reflux overnight. The solvent was subsequently removed under vacuum. None of the desired product was obtained, only a mixture of the starting materials were observed, according to ^{31}P NMR spectroscopy. The reaction was also tried with (2-bromo-1,1-dimethyl-ethyl)-benzene, without any success.

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Chapter 6

Appendices

VI Appendices

VI.1. CH501: Postgraduate Research Techniques

This is a compulsory module for all first year postgraduates.

Semester	Lecture Title	Lecturer	Attendance
1	Safety/Security	Mr. Acton	✓
1	Introduction to key techniques and equipment	Mr. Lee, Dr. Fawcett Dr. Eaton, Dr. Griffith	✓
1	NMR techniques I: 1D NMR	Dr. Griffith	✓
1	NMR techniques II: 2D NMR	Dr. Griffith	✓
2	NMR techniques III: the nOe effect	Dr. Griffith	✓
2	Advanced interpretation of spectra and presentation of spectra	Dr. Griffith	✓
2	ChemDraw/molecular modelling	Prof. Cullis	✓
2	Use of the library and computer based searches	Dr. Lloyd Dr. Solan	✓
2	Applications of 'Endnote'	Dr. Davies	✓
2	Advanced scientific writing	Dr. Malpass	✓
2	A course for demonstrators	Dr. Beasley	✓

VI.2. Additional Modules Studied

Taken in the first year, as part of Postgraduate Training.

Code	*Module title*	*Grade*
Credits	*Convenor*	
CH309	Strategies of Organic Synthesis	57%
(10 credits)	Dr P. Jenkins, Dr S. Handa	
CH316	Catalysis	
(10 credits)	Dr P. Dyer, Dr D. Davies	57%

VI.3. External Conferences Attended

RSC Catalysis symposium	Attended
30/04/01 Leicester University	
RSC Dalton division –	Attended
New vistas in organometallic and materials chemistry	
30/11/01 Imperial College	
RSC Catalysis symposium	Attended
04/11/02 Leicester University	
226thACS national meeting	Presented poster
07-10/11/03 New York City, U.S.A	

VI.4. Inorganic Colloquia Attended

All the speakers were resident at Leicester University unless otherwise stated.

09/10/00	Dr. A. Sarkar (NCL Pune, India)	Conformation and reactivity of Fischer carbene complexes.
16/10/00	Dr. G. A. Solan Dr. P. W. Dyer	Literature session.
23/10/00	Mr. M. Hanton Ms. N. Patel	Literature session.
30/10/00	Workshop	Techniques, strategies and challenges in chemistry.
11/12/00	Dr. R. Villar-Compte (Imperial College)	Anions as templating agents in co-ordination chemistry.
29/01/01	Dr. J. Iggo (University of Liverpool)	If you can see it, it's not the catalyst – or is it? NMR for monitoring catalytic reactions.
05/01/01	Prof. R. Mulvey (University of Strathclyde)	Inverse crown ether complexes and related mixed metal macrocycles of the *s*-block. (RSC lecture).
07/01/01	Dr. S. Bennett (Open University)	Widening the appeal: the role of independent learning in chemistry. (RSC annual education lecture).
12/01/01	Mr. A. West Ms. R. Chagger Mr. R Chester.	Literature session.

26/01/01	Mr. C Davies Ms. S. Kandola Mr. T Reeve **Mr. S. Suhard**	1st year outlines.
21/03/01	Prof. L. D. Hall (University of Cambridge)	1st Tim Norwood memorial lecture.
14/05/01	Prof. S. Doherty (Queen's University Belfast)	Zirconacylces in phosphine synthesis: coordination chemistry and applications in platinum group-catalysed carboxylation of olefins and ethylene polymerisation.
04/06/01	Mr. T. Reeve Ms. S. Kandola	Literature session.
11/06/01	Mr. M. Hanton Mr. B. Croxtall	2nd year progress.
18/06/01	Mr. J. Sherrington Ms. N. Patel	2nd year progress.
25/06/01	Mr. D. Wood	3rd year progress.
04/10/01	Dr. P. O'Brien (University of York)	Basic instinct: new synthetic adventures with chiral bases.
10/10/01	Dr. D. Bourrisou (Université Paul Sabatier)	Stable carbenes and diradicals: new stabilization and bonding modes.
22/10/01	Dr. A. Hooper (Institute of Arable Crops Research, Rothamstead)	Sex and bugs and rock and roll.

29/10/01	Mr. M. Hanton Ms. N. Patel	Literature session.
05/11/01	Mr. P. Griffith Mr. D. Harding	Literature session.
26/11/01	Mr. G. Barth Mr. M. Dix Mr. M. Giardiello	Literature session.
03/12/01	Dr. P. Dyer Dr. G. Solan	Organometallic synthesis at Leicester.
04/02/02	Ms. A. Hickman Ms. K. Sharpe Mr. J. Pelletier	1st year outlines.
11/02/02	Dr. R. Bedford (University of Exeter)	High activity catalysts for C-C bond formation.
18/02/02	Mr. A. West Ms. R. Chaggar Mr. O. Duaij	1st year outlines.
04/03/02	Dr. H. Braunschweig (Imperial College)	Compounds with novel boron-containing ligands: transition metal complexes of boron and [1]borametallocenophanes.
06/03/02	Dr. R. Schutt (ExxonMobile)	Supercritical phase behaviour in ethene polymerisation and polymer separation.
11/03/02	Mr. B. Croxtall Ms. S. Kandola Mr. T. Reeve	Literature session.

25/03/02	Mr. C. Davies Mr. J. Sherrington **Mr. S. Suhard**	Literature session.
29/04/02	Ms. A. Hickman Mr. J. Pelletier Mr. A. West	Literature session.
08/05/02	Dr. N. Long (Imperial College)	Ferrocene ligand design.
20/05/02	Dr. M. Coles (University of Sussex)	Anionic and neutral guanidine ligands.
27/05/02	Mr. M. Hanton	3rd year talk.
27/05/02	Mr. B. Croxtall Mr. J. Sherrington	3rd year talks.
07/10/02	Ms. K. Sharp Ms. R. Chaggar Mr. A. West	Literature session.
14/10/02	Mr. J. Pelletier Mr. O. Duaij Ms. A. Hickman	Literature session.
21/10/02	Prof. P. R. Raithby (University of Bath)	Adventures in organometallic polymer chemistry.
28/10/02	Dr. C. Metcalf	Transition metal complexes and their interaction with DNA.

11/11/02	Ms. E. Carrington-Smith Mr. J. Bennett Mr. R. Buckby Mr. N. Abboyi *Chair*: Mr T. Reeve	Literature session.
18/11/02	Dr. M. Turner (University of Sheffield)	Synthesis of conjugated polymers for EL/electronics.
02/12/02	Ms. N. Dinsdale Ms. E. Filali Mr. R. Forster Ms. R. Muir	Literature session.
09/12/03	Prof. T. Marder (University of Durham)	The role of transition metal boryl complexes in catalysed borylations including rhodium catalysed C-H bond functionalisation.
20/01/03	Prof. V. McKee (University of Loughborough)	Manipulating metal arrays within macrocycles.
02/06/03	Dr. Sarah Heath (University of Manchester)	Shedding light on biological systems: the development of dinuclear lanthanide probes.