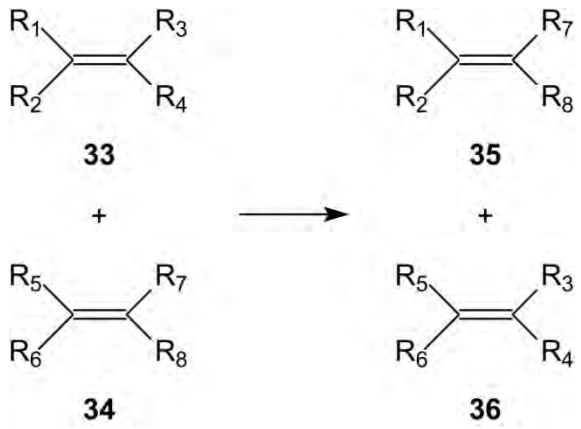
2. Literature Study

2.1 Alkene metathesis

The IUPAC definition of metathesis is “a bimolecular reaction involving the exchange of a bond (or bonds) between two interacting chemical compounds to form products with similar or identical bonding affiliations to those in the reactants”.[1] For example, two chemical compounds AB and CD react to give the products AD and CB. The chemical compounds can be ionic or covalent. Alkene metathesis is a reaction between two compounds containing double bonds.[2] The double bonds of the carbon atoms are broken and rearranged between the two compounds to give two new compounds that contain double bonds (**Scheme 2.1**).[2,3] The coordination of the compounds to the catalyst as well as the steric properties of the functional groups on the double bond of the newly formed compound determine whether the *cis*- or *trans*-isomer will form. The precatalysts developed by Richard R. Schrock and Robert H. Grubbs are effective for this reaction.[2,3]



Scheme 2.1 The alkene metathesis of **33** and **34** to produce **35** and **36**.

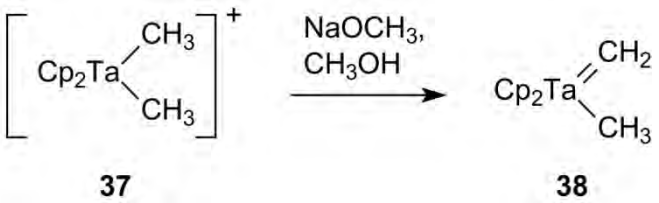
The alkene metathesis reaction was observed for the first time in the 1950s.[4,5] In 1971, Chauvin and Hérisson proposed that the reaction is initiated by a metal carbene, which then reacts with an alkene to produce a new alkene and a new metal carbene.[4,5] With improvements in the activation of the metal carbene, the reaction became more widely used. Schrock and Grubbs were leaders in the development of precatalysts that expanded the use of alkene metathesis.[5] Schrock’s molybdenum precatalysts and Grubbs’ ruthenium precatalysts made the use of alkene metathesis easier for chemists, since these precatalysts are so easy to handle. The contribution of Yves Chauvin, Richard R. Schrock and Robert H. Grubbs to alkene metathesis was recognised in 2005 when they were awarded the Nobel Prize in Chemistry.[5]

2.2 Catalysts

Heterogeneous catalysis refers to catalysis where the catalyst is in a different phase (gas, solid or liquid) than the reagents.[6] Homogeneous catalysis refers to catalysis where the catalyst is in the same phase as the reagents.[6] Two immiscible liquids are in separate phases. For example, the petrochemical alkylation process is an example of heterogeneous catalysis even though the catalyst (acid) and the reagents (hydrocarbons) are both liquids.[6] The hydrolysis of esters is an example of homogeneous catalysis; the catalyst and reagents are dissolved in water: $CH_3CO_2CH_3(aq) + H_2O(\ell) \leftrightarrow CH_3CO_2H(aq) + CH_3OH(aq)$ – with H^+ as the catalyst. Hydroformylation, Ziegler-Natta polymerisation, hydrogen transfer catalysis, hydrogenation and C-H activation are just a few examples of homogeneous catalysis where a metal complex is used as the catalyst.[6] Homogeneous catalysts can be divided into two main groups, namely poorly defined catalysts (Ziegler-Natta) and well defined precatalysts (Schrock and Grubbs).

A Ziegler-Natta catalyst is a reagent used in the production of unbranched, stereoregular vinyl polymers.[7] Ziegler-Natta catalysts are typically based on titanium chlorides and organometallic trialkyl aluminium compounds, for example $(CH_3)_6Al_2$.[8] Ziegler-Natta catalysts are used to polymerise terminal alkenes, $nRCH{=}CH_2 \rightarrow -[RCH\text{-}CH_2]_n-$. In 1963, the Nobel Prize in Chemistry was awarded to Karl Ziegler for his discovery of the titanium-based catalyst, and Giulio Natta for using the catalyst to prepare stereoregular polymers.[8]

The first nucleophillic carbene complex was prepared by Schrock in an attempt to synthesise homoleptic-tantalum(V)alkyne.[9] Schrock carbene complexes are usually characterised by an early transition metal in a high oxidation state with strong donor and weak π-acceptor ligands (**Scheme 2.2**). Schrock tungsten and molybdenum carbene complexes are well known for their activity in alkene metathesis[10-12] and their ability to act as replacements for phosphorous ylides during the Wittig reaction.[13] Schrock carbene complexes act as nucleophiles as a result of the partial negative charge on the carbene carbon, due to the polarisation of the electrons being shared by the electropositive metal and a more electronegative carbon atom.[15]



37 **38**

Scheme 2.2 Synthesis of a typical Schrock carbene complex (**38**).

During metathesis, a Schrock carbene catalyst is very reactive when compared to other alkene metathesis precatalysts.[10,11,14] Schrock developed several catalysts, but the most important are the arylimido complexes (the imido ligands are also referred to as imides or nitrenes) of molybdenum with the general formula $(Ar'N)(RO)_2Mo=CHR'$, where Ar' typically is 2,6-diisopropylphenyl, R' is a variety of ligands and R is neopentyl (Np) or neophyl ($C_6H_5C(CH_3)_2CH_2$) (**Figure 2.1**). These catalysts are very effective and perform metathesis on more than 1 000 equivalents *cis*-2-pentene per equivalent catalyst. Another advantage of these catalysts is that their reactivity can be adjusted by changing the nature of the alkoxide ligands.[10,11,14]

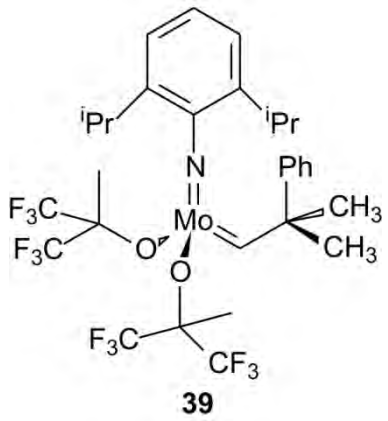


Figure 2.1 Commercially available Schrock carbene complex (**39**).

Schrock[14] and Grubbs'[16] precatalysts are stable towards a wide range of functional groups, but the ease with which Grubbs' precatalysts can be handled in air makes them more convenient for chemists. Homogeneous catalysis will therefore be further investigated by looking more closely at the Grubbs-type precatalysts.

2.3 Grubbs precatalysts

2.3.1 Structure and synthesis

The Grubbs 1 (**A1**) precatalyst is a transition metal carbene complex named after the chemist who first synthesised it, Robert H. Grubbs. The Ru-alkylidene moiety is not as nucleophillic as the alkylidenes in Schrock-type complexes.[2] The five coordinate, 16-electron metal centre is very stable towards water, acid and a wide range of functional groups. The two generations of the precatalyst are depicted in **Figure 2.2**.[2,3] Grubbs' precatalysts tolerate functional groups on the alkenes and are compatible with a wide range of solvents when compared to other alkene metathesis catalysts.[17] This contributes to the versatility of Grubbs' precatalysts. In organic synthesis, **A1** is regularly used to accomplish alkene cross metathesis (CM), ring opening metathesis polymerisation (ROMP) and ring closing metathesis (RCM). It is easily prepared from

$RuCl_2(PPh_3)_3$, phenyl-diazomethane and tricyclohexylphosphine in a one pot synthesis.[16,18] The relative air stability of **A1** makes it very easy to handle.

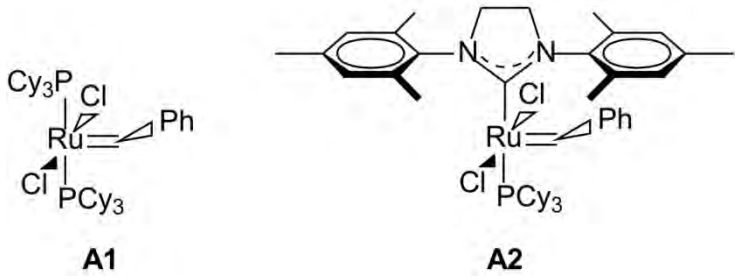


Figure 2.2 The Grubbs 1 (**A1**) and Grubbs 2 (**A2**) precatalysts.

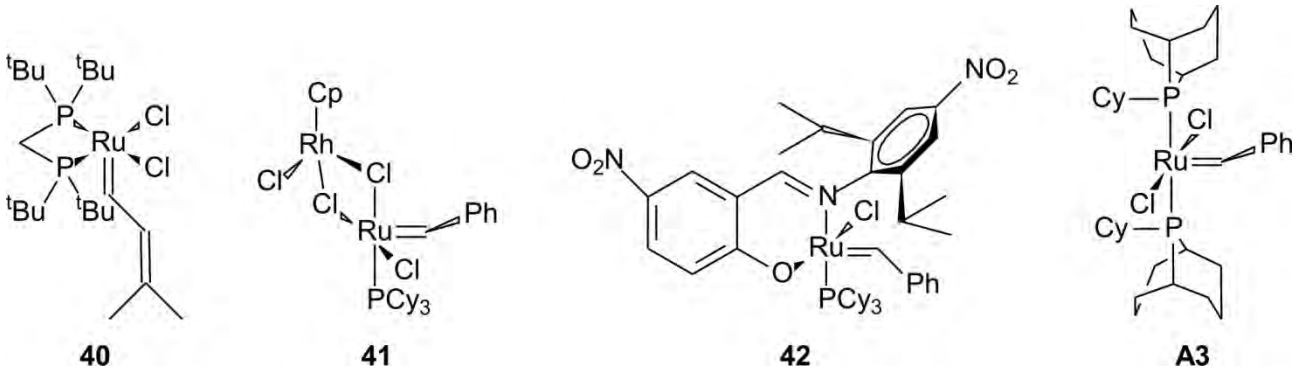
Grubbs 2 (**A2**) has the same uses in organic synthesis as **A1**, but with higher activity.[2,3] This precatalyst is also air stable and is easily prepared from **A1** and alkoxy-protected 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene.[18] The ligand is an N-heterocyclic carbene (NHC) and the ruthenium is now coordinated to two carbene groups. Both generation precatalysts are commercially available.

A variety of derivatives of **A1** containing monodentate and/or chelating N-, O-, P- and Cl-donating ligands have been prepared and investigated as catalysts for alkene metathesis reactions.[2] In many cases, these complexes have better properties (higher catalytic activity, higher thermal stability, higher functional group tolerance etc.) when compared to **A1**. None of these complexes have replaced **A1** in terms of general availability and versatility.[2]

A first class of these modified Grubbs alkene metathesis precatalysts contains the chelated bis-phosphine ligand, bis(di-tert-butylphosphanyl)methane (dtbpm) (represented by **40** in **Figure 2.3**).[2] The composition of these complexes is similar to that of **A1**, both contain sterically large and electron donating phosphines and two chloride ligands. The *cis*-orientation and the chelating nature of the dtbpm-ligand are believed to be responsible for a drastic reduction in metathesis activity.[2]

A next class of modified Grubbs alkene metathesis precatalysts is the chlorine-bridged bimetal complex **41** (**Figure 2.3**). Complex **41** and its derivatives, containing (*p*-cimene)$RuCl_2$ and (*p*-cimene)$OsCl_2$ bridge units, from the reaction of **A1** with a 0.5 equivalent of $[(L)MCl_x]_2$ (where L = *p*-cimene, M = Rh, Os or Ru).[2] These complexes show high reactivity towards cyclic and acyclic alkene substrates and perform ring opening metathesis polymerisation of cyclooctadiene up to 80 times faster than **A1**. Alkene metathesis reactivity increases as the bridge metal is changed from Ru to Rh. The observed trend of activity (k_{obs} (ROMP) Ru ~ Os < Rh) correlates with the increasing

electron negativity of the metals and is attributed to electron density withdrawal from the bridged chlorine atoms by the secondary metal centre.[2]



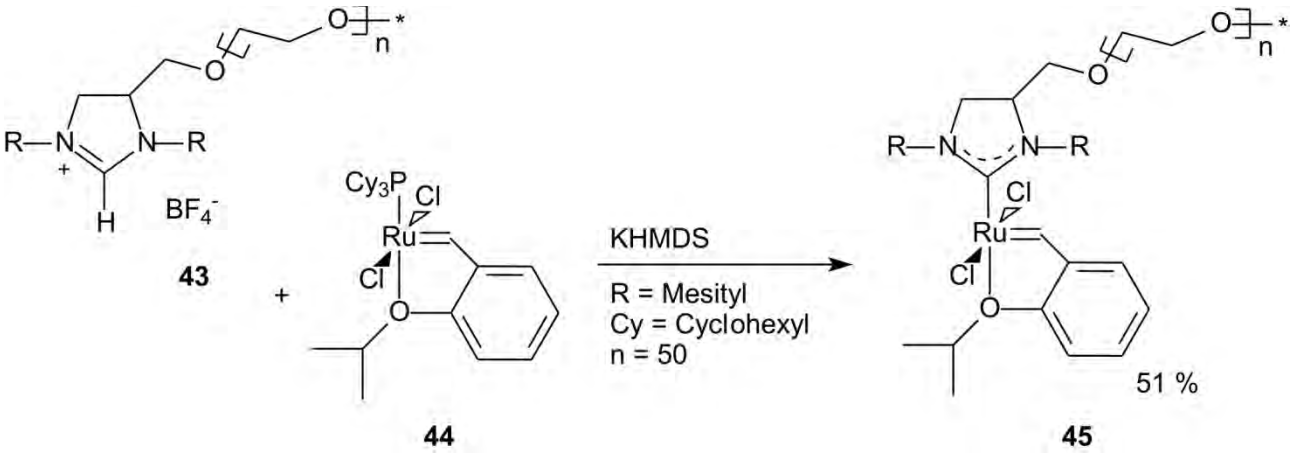
40 **41** **42** **A3**

Figure 2.3 Modified Grubbs alkene metathesis precatalysts.

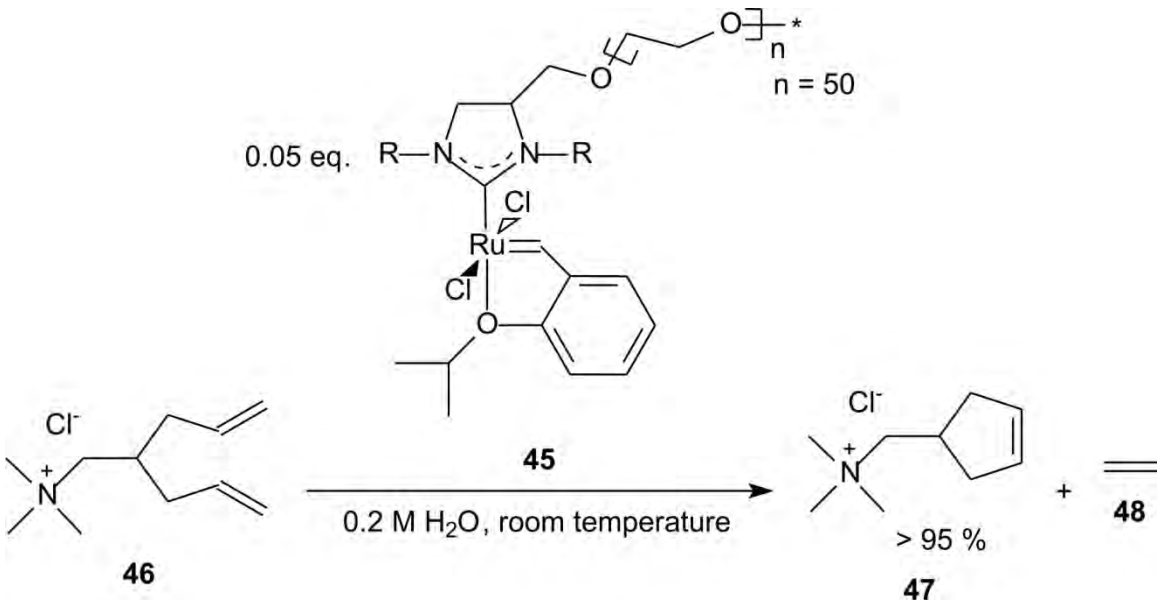
A third class of modified Grubbs alkene metathesis precatalysts is illustrated by the bidentate Schiff-base ruthenium adduct **42** (**Figure 2.3**). Complex **42** and its derivatives are easily prepared from **A1** with the thallium salt of the Schiff-base ligand.[2] The most remarkable property of these ruthenium salt adducts is their high stability towards air/moisture and thermolysis.[2] Although **42** and its derivatives are generally not as reactive towards alkene metathesis at room temperature, their reactivity increases dramatically with an increase in temperature.

In 2004, Forman *et al*.[19] reported complex **A3** (**Figure 2.3**) as a new derivative of **A1**.[16,20] According to Forman *et al*.,[19] during several metathesis reactions at higher temperatures, **A3** was more stable than **A1**. At these high temperature conditions, **A3** showed higher activity and better selectivity than **A1**.[19]

In the first generation Hoveyda-Grubbs precatalyst (**44**), one of the phosphine ligands was replaced with an isopropyloxy group bonded to the benzene ring (**Scheme 2.3**).[2,3] These complexes have the benefit of forming the same active species – $(PCy_3)(Cl_2)Ru=CHR'$ – as precatalyst **A1**, while they have a much higher stability towards moisture and air.[2] Initiation of **44** is almost 30 times slower than **A1**. The slower initiation is most likely a result of the unfavourable dissociation of the ether ligand due to chelating effects.[2] In one study, a water soluble Grubbs-type precatalyst (**45**) was prepared by bonding a polyethylene glycol chain to the imidazole group (**Scheme 2.3**).[21] The water soluble precatalyst is used to perform ring closing metathesis on a diene (**46**) in a watery medium (**Scheme 2.4**).[21]



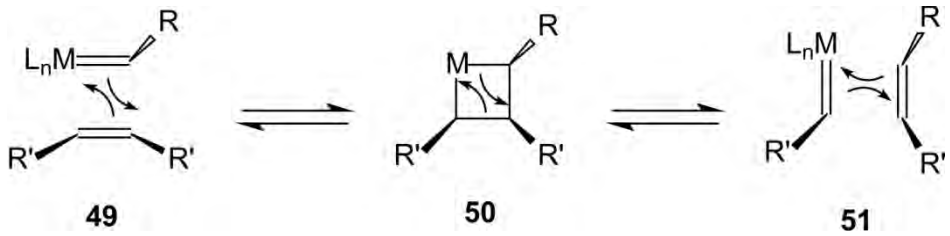
Scheme 2.3 Preparation of a water soluble Grubbs-type precatalyst (**45**).



Scheme 2.4 The ring closing metathesis of a water soluble ammonium carrying diene salt.

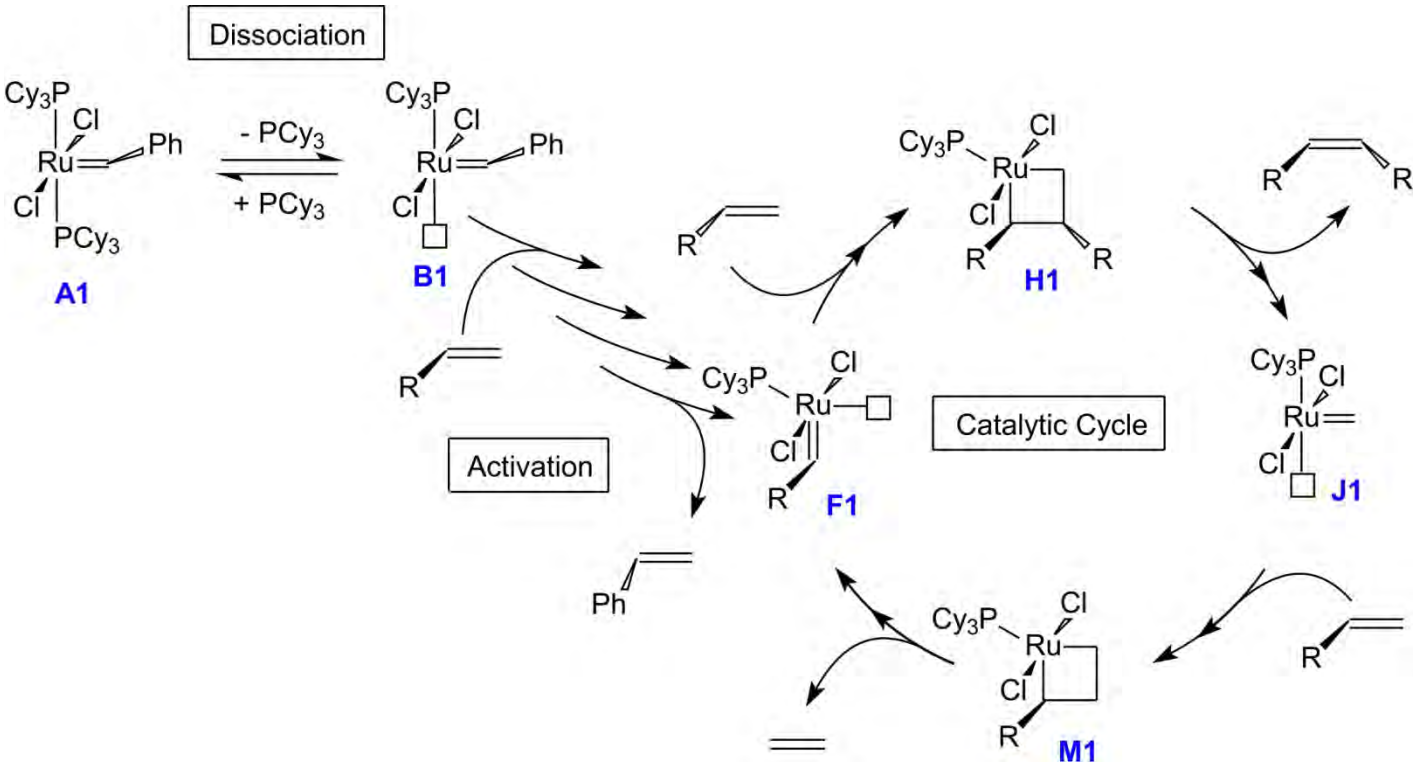
2.3.2 Mechanism

The generally accepted mechanism for the alkene metathesis reaction was proposed by Chauvin and consists of a [2 + 2]-cycloaddition reaction between a transition metal alkylidene complex and the alkene to form the intermediate metallacyclobutane ring (**Scheme 2.5**).[22,23] This is followed by a [2 + 2]-cycloreversion to form a new alkylidene and a new alkene. If the reaction is repeated enough times, an equilibrium solution of alkenes will form.[22,23] Such cycloaddition reactions are symmetry forbidden in the ground state and only take place photochemically.[24] The presence of d-orbitals on the metal alkylidene fragment breaks the symmetry and as a result of this the reaction easily takes place.[24]



Scheme 2.5 A [2 + 2]-cycloaddition between a transition metal akylidene complex and an alkene.

The general alkene cross metathesis catalytic cycle of **A1** is illustrated in **Scheme 2.6**. The first step, catalyst initiation, requires the dissociation of one PCy_3 ligand to form the very reactive intermediate **B1**.[2] During the activation phase, **B1** reacts with an alkene and forms a metallacyclobutane ring by going through a series of [2+2]-cycloaddition and cycloreversion steps to form the catalytically active species **F1**. The catalytically active species, **F1**, then enters the catalytic cycle wherein it is converted to the catalytically active methylidene species **J1** and back to **F1**, until the catalyst is deactivated or all the alkene is used up, by going through a series of [2+2]-cycloaddition and cycloreversion steps during which a series of metallacyclobutane rings (**H1** and **M1**) forms and dissociates.[2] The metallacyclobutane rings can dissociate to form new alkenes and new alkylidenes, or it can dissociate to form the original reagents.



Scheme 2.6 The general catalytic cycle of Grubbs 1 (**A1**).

2.4 Phosphine ligands

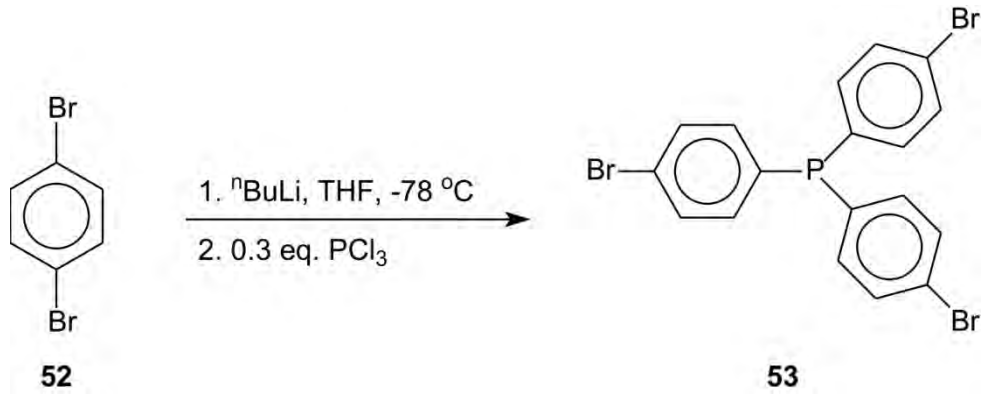
2.4.1 Introduction

In 1669, a businessman from Hamburg, Henning Brandt, was searching for gold in concentrated urine.[25] He observed a strange luminescence that we now know was a result of phosphorous being present. Three centuries after its discovery, phosphorous is used in all fields of Chemistry and Biochemistry.[25] In coordination chemistry, a ligand is described as a group that can donate or receive electrons.[26] Phosphines are widely used as ligands for transition metal complexes. Phosphines improve the solubility of metal complexes in a variety of organic solvents.[26] Most phosphines are not water soluble, although water soluble phosphines are found among the sulphonated phenylphosphines and piridylphosphines.[27-30] The ability of phosphines to stabilise the low oxidation states of metal atoms makes them useful in homogeneous catalysis.[26] An example is the design of asymmetrical phosphines for stereo selective catalysis.[26] Hydroformylation,[29-31] hydrogenation[27] and hydrocyanation[32] are some examples of reactions where phosphine metal complexes are used as catalysts. By keeping this in mind, some of the general synthesis methods for phosphine ligands will be discussed.

2.4.2 General synthesis methods

2.4.2.1 Halogenated phenyl compounds with phosphorous

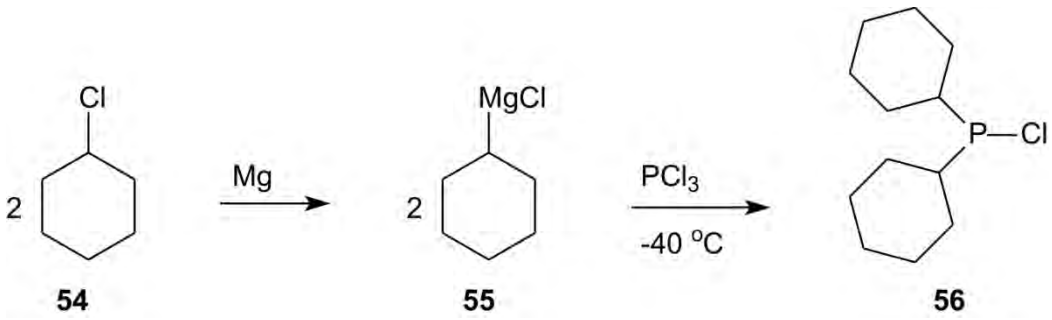
Ravindar *et al*.[33,34] reported a general synthesis method for the preparation of functionalised arylphosphines from 1,4-dibromobenzene, **52**, and trichlorophosphine (**Scheme 2.7**). This leads to the formation of triarylphosphines with halide functional groups on the aryl rings (**53**). This reaction is performed with a Grignard reagent of n-butyllithium (^{n}BuLi) to promote halogen exchange. ^{n}BuLi gave higher yields.[35]



Scheme 2.7 The synthesis of triarylphosphines (**53**) with halide functional groups on the aryl rings from **52**.

2.4.2.2 Grignard-type reactions with phosphorous

To avoid the hydrogenation of aromatic rings, which may cause problems, a synthesis route that uses cyclohexylphosphine dichloride and its derivatives can be used.[36] These phosphines are commercially available, but they are very expensive. Tomori *et al*.[36] provided a method for the synthesis of dicyclohexylphosphine chloride (**56**) via a Grignard reaction. Illustrated in **Scheme 2.8** is the synthesis of cyclohexyl magnesium chloride (**55**) from the corresponding halide and magnesium wire. The reaction of PCl_3 with **55** at 0 °C gave **56** as the product.



Scheme 2.8 The synthesis of dicyclohexylphosphine chloride (**56**) via a Grignard reaction.

2.4.2.3 Diels-Alder synthesis of cyclic phosphine compounds

An alternative to both preceding synthesis methods can be provided by Diels-Alder reactions. According to Kluger *et al*.,[37] 1-ethoxyphosphole-1-oxide (**57**) does not react readily with dienophiles, but it dimerises at a rate of 0.51 mol^{-1} second at 25 °C to give **58**. Kluger *et al*.[37] also reported the synthesis of 3,4-dimethyl-1-ethoxyphophole-1-oxide (**59**). An impure mixture of **59** reacts with maleic anhydride to give **60** after hydrolysis (**Figure 2.4**).[37]

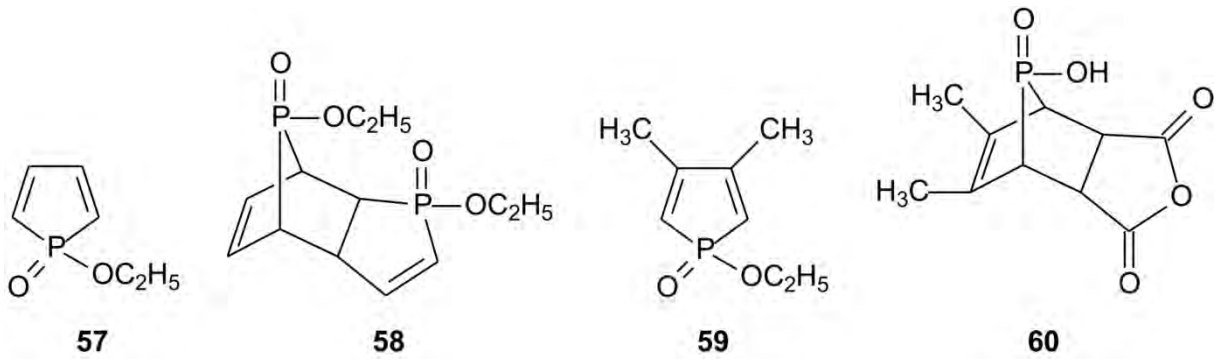
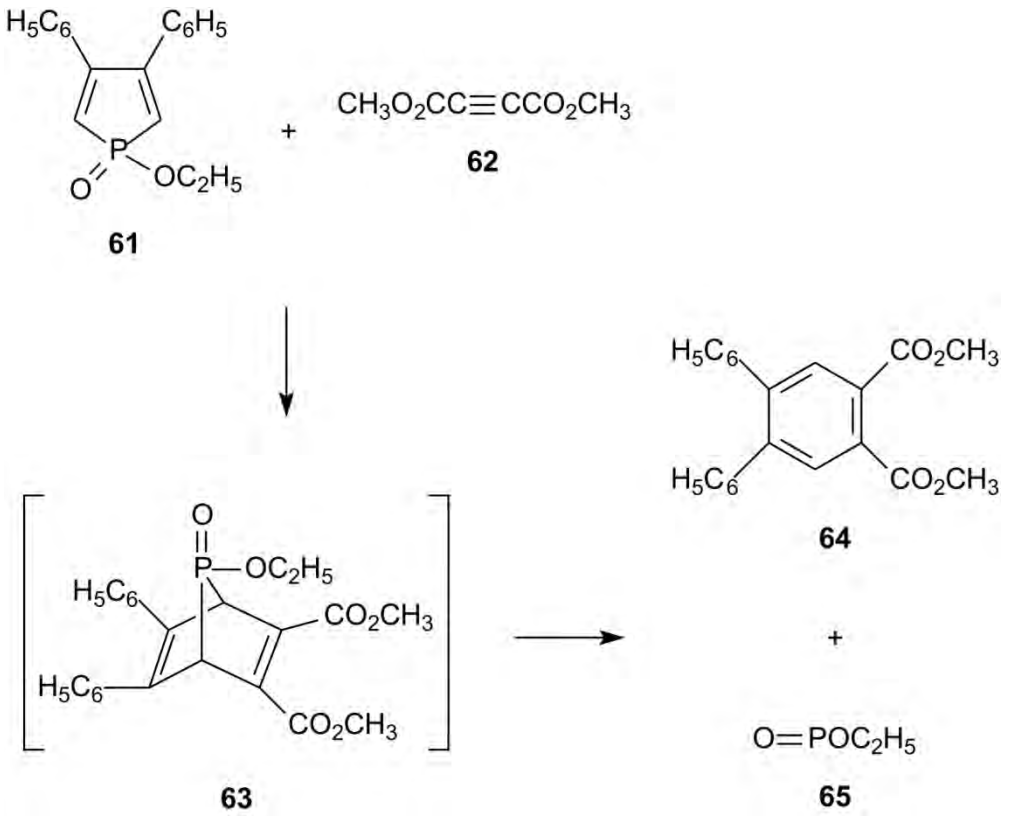


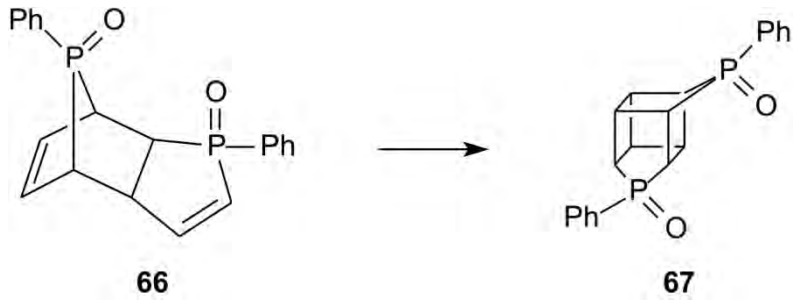
Figure 2.4 The Diels-Alder products (**58** and **60**) prepared from **57** and **59**.

According to Clarke and Westheimer,[38] compound **61**, which is structurally related to **59**, does not readily react with the most dienophiles, but it does react with dimethyl acetylenedicarboxylate to give dimethyl-4,5-diphenylphthalate (**64**) (**Scheme 2.9**).



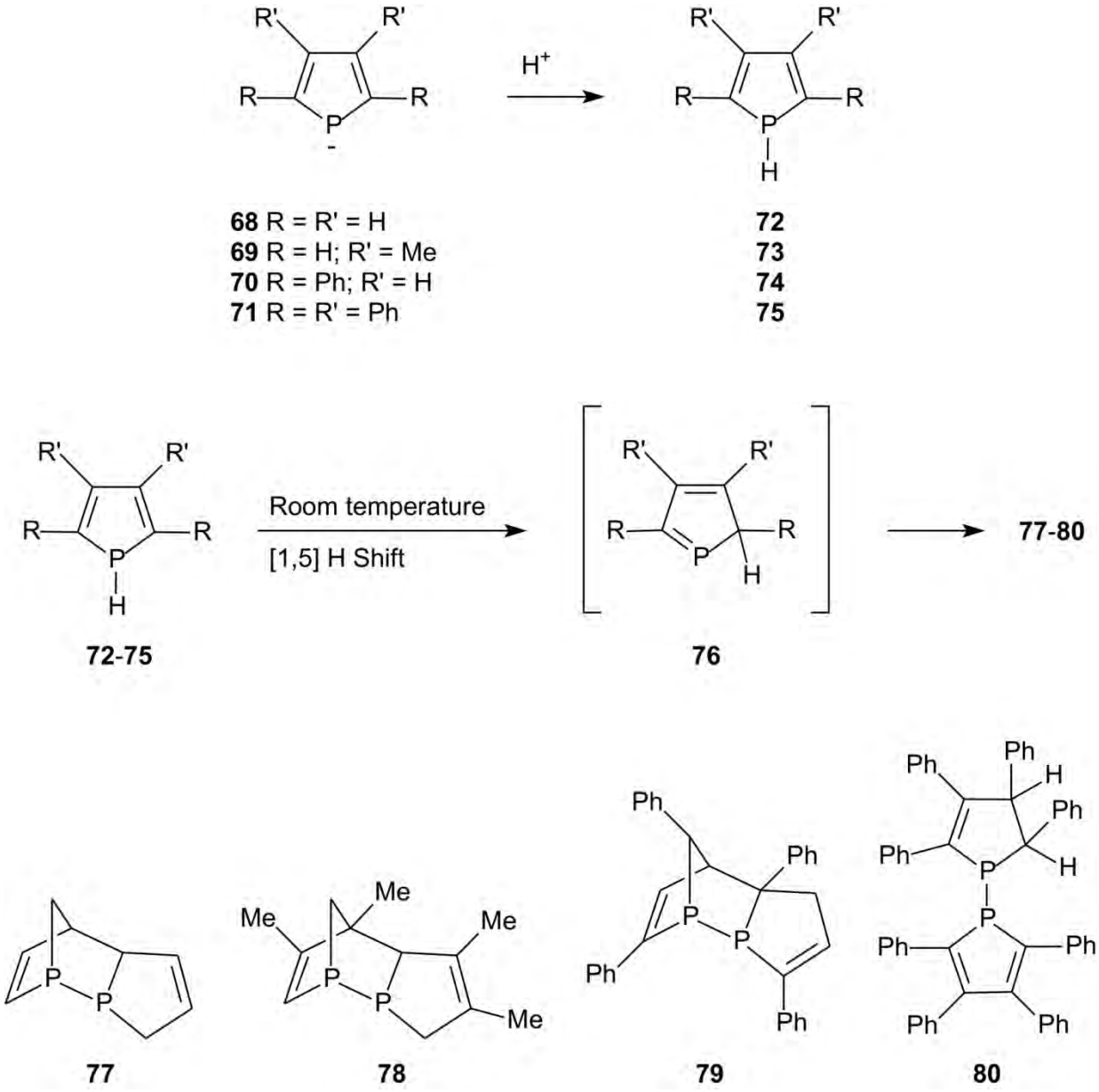
Scheme 2.9 The synthesis of dimethyl-4,5-diphenylphthalate, **64**, from 1-ethoxy-3,4-diphenylphosphole-1-oxide, **61**.

Tomioka *et al*.[39] reported the synthesis of the cage compound **67** from **66**. Compound **66** was irradiated with ultraviolet light in 1:3 acetone:benzene for two hours to give **67** in almost quantitative yield (**Scheme 2.10**).[39]



Scheme 2.10 The [2 + 2]-cycloaddition of **66** to give **67**.

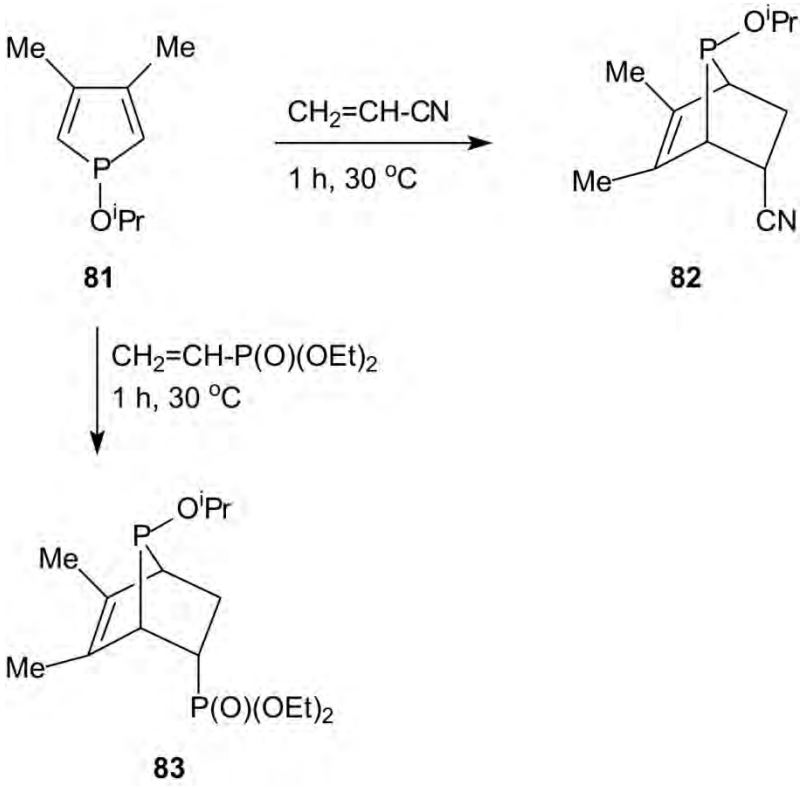
According to Carrier *et al*.,[40] the stability of phospha-alkenes is achieved through steric crowding or cyclic delocalisation. In both cases, the reactivity of the P=C double bond is decreased dramatically. There are few examples of Diels-Alder type reactions where these double bonds act as dienophiles. [4+2]-Dimers can be synthesised by protonation of the phospholyl anions.[40] Monomeric 2*H*-phospholes can be made by heating the dimers at moderate temperatures (~100 °C).[40] The obtained 2*H*-phospholes are not stabilised by steric crowding or cyclic delocalisation.[40] It seems as if these compounds are more reactive as dienes and dienophiles. The 1*H*-phosphole derivatives **72-75** are unstable at room temperature and they are converted to the 2*H*-phosphole dimers **77-80** (**Scheme 2.11**).[40]



Scheme 2.11 Synthesis of the 2*H*-phosphole dimers **77-80**.

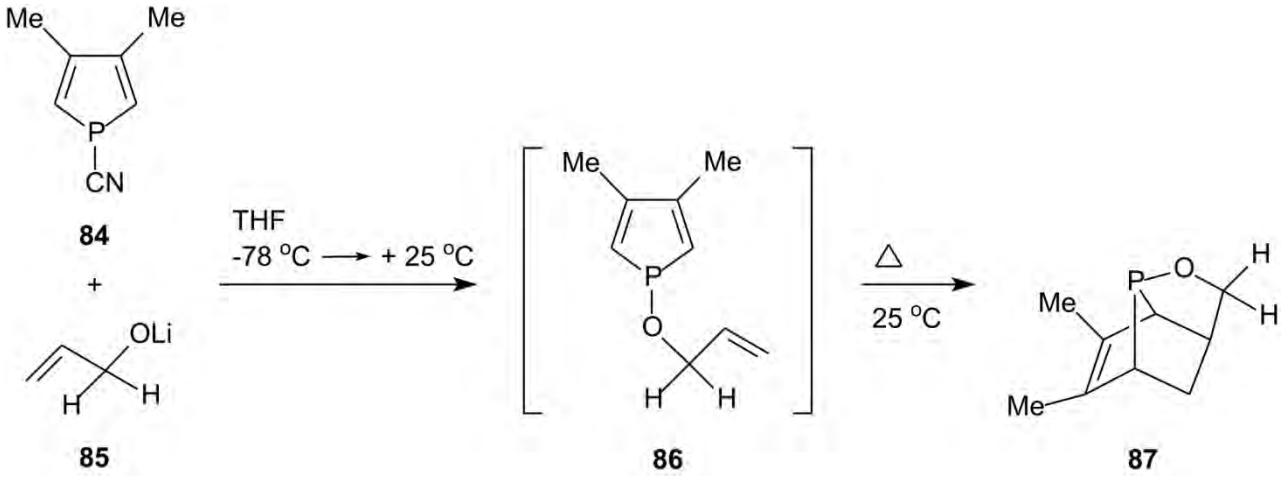
The coordination state of phosphorous determines the migratory ability of the functional groups; this ability decreases in the order pentacoordinate P >> tricoordinate P > tetracoordinate P.[40] Stabile 1*H*-phospholes can be synthesised if alkoxy derivatives are synthesised.[40] The migratory ability decreases in the order H >> Ph>> OR. The low migratory ability of the alkoxy group can be attributed to the strength of the P-O bond.[40]

Mattmann *et al*.[41] described Diels-Alder reactions where 1-isopropoxy-3,4-dimethylphosphole (**81**) is very reactive towards acrylonitrile as well as diethylvinylphosphonate (**Scheme 2.12**). These experiments demonstrate that it is possible to control the reactivity of phospholes by choosing the appropriate functional group on the phosphorous atom.

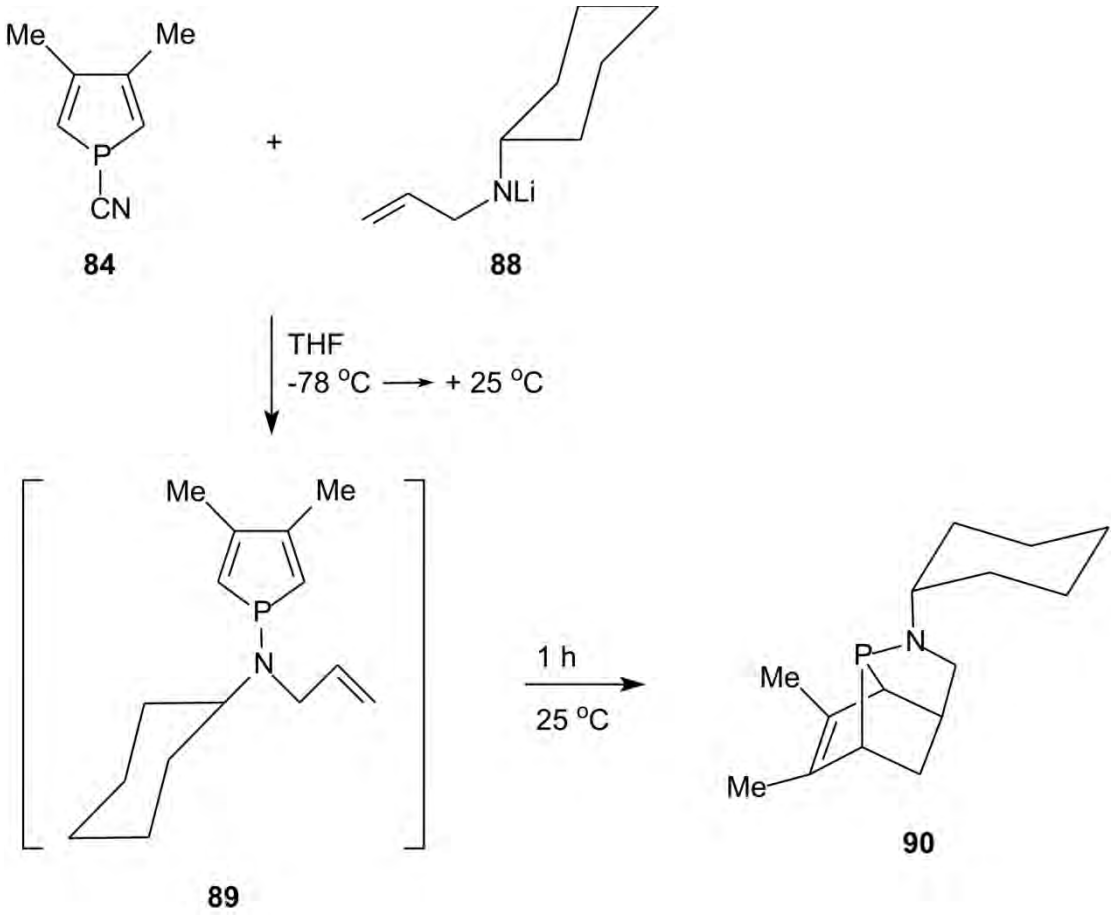


Scheme 2.12 The Diels-Alder reactions of **81** to give **82** and **83**.

In another publication, Mattmann *et al*.[42] described the intramolecular Diels-Alder cycloaddition of allyl-OLi (**85**) and 1-cyano-3,4-dimethylphosphole (**84**) to give compound **87** (**Scheme 2.13**). In compound **87**, the sum of the intracyclic angles at phosphor is 289.3°, which means a high coordination possibility for transition metals exist.[42] Lastly, Mattmann *et al*.[42] performed intramolecular Diels-Alder cycloaddition with the *N*,*N*-((allyl)-cyclohexyl)amino functional group (**88**) to give compound **90** (**Scheme 2.14**). This shows that amino groups can also have an activating effect on phospholes such as the alkoxy functional groups.



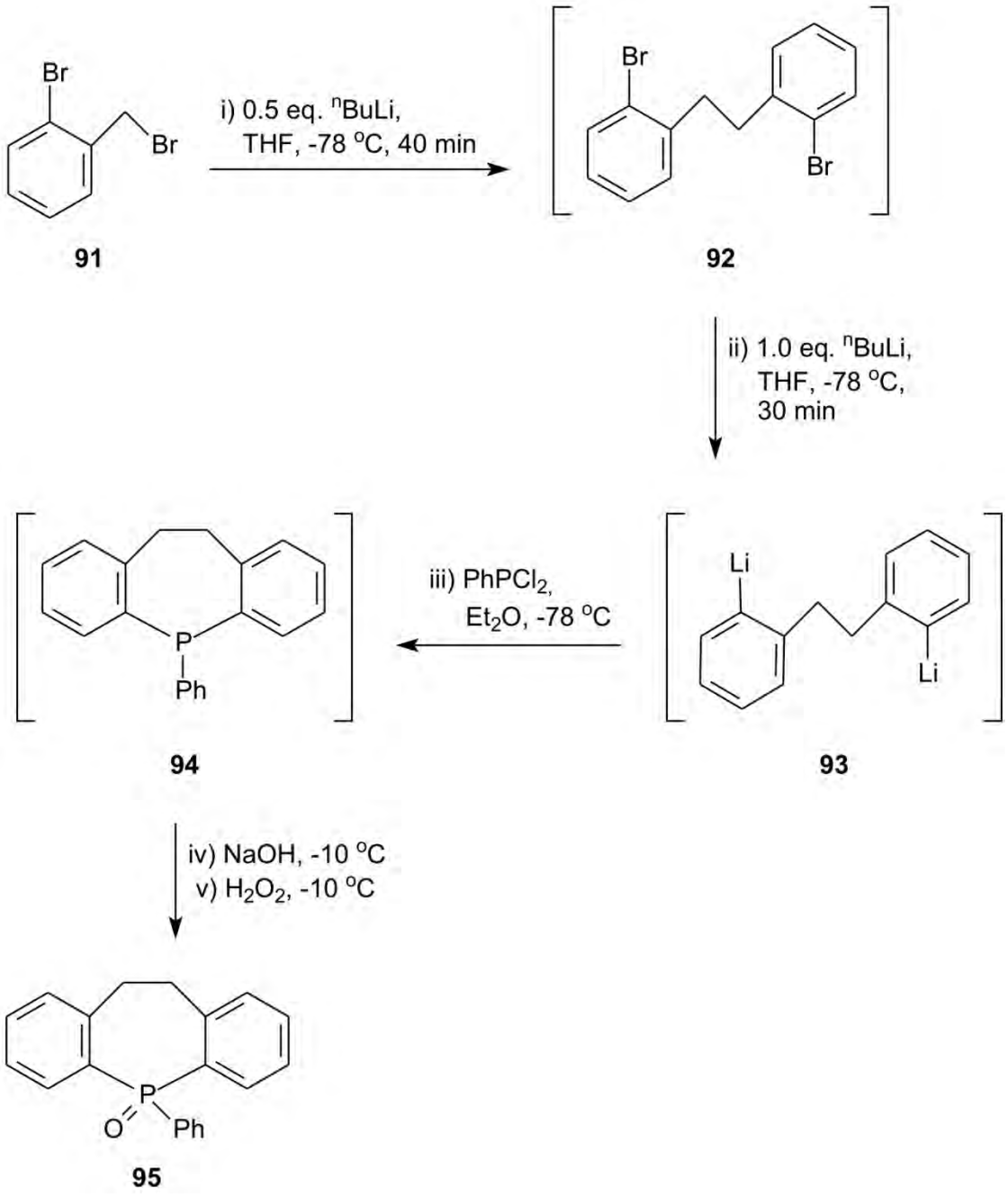
Scheme 2.13 The intramolecular Diels-Alder cycloaddition allyl-OLi (**85**) and 1-cyano-3,4-dimethylphosphole (**84**) to give **87**.



Scheme 2.14 The intramolecular Diels-Alder cycloaddition with the *N*,*N*-((allyl)-cyclohexyl)amino functional group (**88**) to give **90**.

2.4.2.4 Synthesis of phosphine compounds from lithium salts

In 1998, Warren and Wyatt[43] reported an improved synthesis for compound **95**. By combining the normal seven steps in a one pot synthesis, they could improve the overall yield dramatically. Treatment of **91** with 0.5 equivalents ^{n}BuLi in THF at -78 °C for 40 minutes gave **92**.[43] The solution was treated, without isolation, with a further 1.0 equivalent ^{n}BuLi in THF at -78 °C for 30 minutes to give 2,2'-dilithiumbisbenzyl (**93**). The solution was immediately quenched with $PhPCl_2$ to give the phosphine (**94**), thereafter it was immediately oxidised to the phosphine oxide (**95**) (**Scheme 2.15**). The previous best yield of 25% was improved to 75%.[43]



Scheme 2.15 The one pot synthesis of **95**.

This literature overview shows the diversity of the available phosphine compounds and their synthesis methods. The potential for the development of new transition metal catalysts is almost endless.

2.5 Steric and electronic ligand effects

According to Tolman, distinct changes can be observed in the properties of the phosphine ligands and their transition metal complexes by varying the functional groups on phosphine ligands.[44] Before 1970, this was mainly attributed to the electronic effects with a few references to steric effects.[44] Since then, several articles have appeared that show that steric effects are just as important as electronic effects and may in some cases dominate.[44]

To further explore this statement, a few of the current methods to investigate these effects will be discussed briefly in the underlying sections. In 2005, Küll[45] wrote a review of the various methods available. The reader can consult this article for a more in-depth discussion.

Organometallic chemists have been trying for more than 50 years to quantify the properties of transition-metal complexes in terms of the stereo-electronic properties of the ancillary ligands.[46-49] Such quantification would in principle be useful as a probe into the mechanism and to predict and control the reactivity, stereochemistry, and regiochemistry of stoichiometric and catalytic reactions involving phosphines, phosphine complexes, and other related ligands.[45] In order to investigate the electronic properties of ligands, a probe needs to be found that responds effectively and sensitively to changes in the electronic properties of the ligands.[45]

In the 1960s, Strohmeier *et al*.[50-55] investigated the σ-donor ability and the π-acceptor strength of various ligand classes. They wanted to establish a spectrochemical series for the ligand strength (a method to separate the σ-donor and the π-acceptor ability contribution of the M=L bond and a classification of transition metal fragments according to their π-donor ability).[51,56] They investigated the chemistry of transition metal carbonyl and nitrosyl complexes using N-, S-, O- and P-based ligand classes as standard donors. The fundamental principles necessary to quantify the electronic properties of a ligand were defined as follows:[45]

- The ligand contribution consists of a σ-donor and a π-acceptor part (the π-acceptor part can be virtually zero).
- The ligand changes the electron density on the central metal.
- The electron density on the metal determines the degree of back bonding.
- The CO ligand acts as a probe for the electron density on the central metal.

Two things were still missing, i.e. a better resolution to measure the influence of the rest of the functional groups, R, in the phosphine, and a way to quantify the results.[45] Strohmeier *et al*.[51]

developed better resolution to measure the influence of the functional groups with the sulfoxide family and later adopted it to the phosphines, whereas the quantification was Tolman's great achievement.[44,57] Tolman recognised the fact that the σ-donor ability and the π-acceptor strength of tertiary phosphines are the two main components of the net donating ability of phosphines.[45] They could be determined by measuring the A1-band in the IR-spectrum of any respective transition metal carbonyl complex.[45] These measurements were defined as the Tolman electronic parameter (TEP), which is the sum of the σ-donor and π-acceptor strength of a given tertiary phosphine.[45]

From the mid-1980s, Griering *et al*.[58] tried to quantify the net donating ability of phosphines (which is dependent on the σ-donor and π-acceptor properties of the ligand and influenced by steric factors) by means of a combination of regression and graphical analysis of the available experimental data.[45] These data include Tolman's electronic and steric parameters, χ and θ, respectively, as well as thermodynamic (H^0, S^0, and G^0), kinetic (reaction rates), and electrochemical (E^0) entities.[45] The method known as quantitative analysis of ligand effects (QALE) relies on experimental data of known ligands and provides the resolution of the net donating ability of a ligand into the four QALE parameters χ_d, λ, E_{ar} and π_p (χ_d is the corrected Tolman electronic parameter (TEP), λ denotes the steric switch based on Tolman's steric parameter θ, E_{ar} is the so-called aromatic effect and π_p represents the π-acidity).[45] According to Küll,[45] QALE is arguably the best method to describe the stereo-electronic properties of a ligand in great detail and to separate the individual effects. The drawback is QALE's reliance on very detailed experimental data for the ligands investigated, since regression and graphical analyses require equation systems based on experimental data that contain up to 20 to 30 independent equations.[45]

A competing system to the QALE system is the ECW system of Drago.[59-62] The name is derived from the contributing factors $E_{a/b}$ (electrostatic) and $C_{a/b}$ (covalent) and the constant W. According to Giering *et al.,*[63,64] the ECW system works well in cases where only χ and θ contribute, and fails where four parameters are required. Drago *et al.,*[59] in turn, argue that the QALE system treats steric effects as omnipresent and no explanation is provided for changes in covalency or softness of the acceptors. They further state that hard/soft, electrostatic/covalent, or charge/frontier are replaced with hard/steric, electrostatic/steric, or charge/steric.[59] They also state that in the ECW system the importance of covalency is found to vary with the acceptor, and that a linear steric contribution is not observed in most systems.[59]

What becomes apparent when looking at these different approaches is that understanding the factor or factors contributing to the properties of ligands is not easy to determine. Passing judgement on which method is best is beyond the scope of this study. A second point that also becomes very apparent is that both the above-mentioned methods rely on in-depth experimental

analysis. Küll[45] already mentioned that these methods are not applicable when trying to predict the properties of ligands that have not been synthesised yet.

As a potential theoretical approach, Suresh and Kolga[65] have claimed that the molecular electrostatic potential (MESP) expressed as V_{min} constitutes a method to calculate the carbonyl stretching frequency (*v*CO) value of transition metal carbonyl complexes using the V_{min} to quantify the nucleophillicity of the phosphorus centre.[45] They demonstrated that MESP can be used to calculate the p*K*a and therefore *v*CO of a nucleophillic ligand.[65] Giering *et al.*[66] claim that such a correlation is not permissible, since three families of phosphines can be distinguished (alkyl, aryl and phosphite) that correlate separately with the respective *v*CO band.[45] If the correlation with TEP is investigated, three closely-spaced parallel IR absorption lines representing the first three ligand classes described by Strohmeier are seen.[45] Küll[45] claims that the utility of MESP does therefore not lie in the replacement of existing methods based on available experimental data, but in the fast, easy and inexpensive method of collecting data for uncommon or unknown ligands. He also feels that the high correlation between TEP and MESP, despite the theoretical shortcomings, is acceptable.[45]

In a recent study, Slattery *et al.*[67] compared the donor properties of N-heterocyclic carbenes (NHC's) (**96**) and N-donors containing the 1H-pyridin-(2E)-ylidene (PYE) motif (**97**) (**Figure 2.5**).

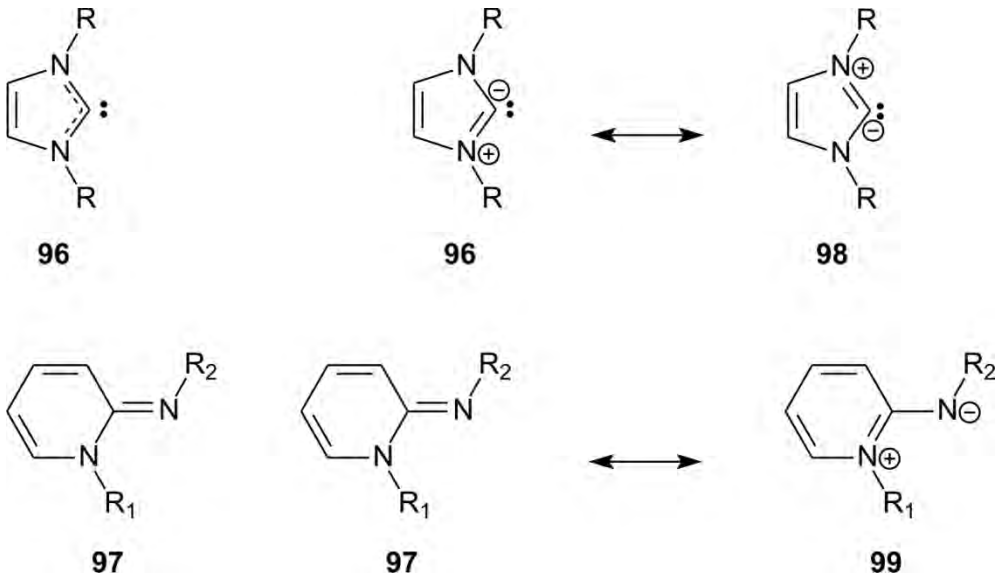


Figure 2.5 NHC (**96**) and PYE (**97**) ligands and their resonance structures.

They found that, according to spectroscopic and X-ray data, these two ligand classes have similar electronic properties with respect to their donor strength.[67] They found that density functional theory (DFT) clearly indicates a deficiency in using donor strength as an indicator of reactivity, when they compared palladium-catalysed coupling reactions.[67] They found that the small

difference in electronegativity between palladium and carbon in the Pd-NHC bond renders the bond almost entirely covalent and therefore resistant to electrophilic and nucleophillic attack.[67] The Pd-PYE bond has a more ionic character because of the greater difference in electronegativity between palladium and nitrogen and therefore is more susceptible to electrophilic and nucleophillic attack and therefore ligand substitution.[67] The metal-NHC bond is dominated by σ-donation, although several studies have demonstrated that both *π*-accepting and *π*-donating interactions can contribute to the overall bonding, which is dependent on ligand substitution, metal and d-electron count.[68-70] The PYE ligands are considered to be too strongly donating; this results in high activation energy for reductive elimination.[67] This study again confirms that understanding the ligand influence is no easy task.

In 2004, Otto and Roodt reported a potentially easy method to determine both steric and electronic effects.[71] They measured the IR-stretching frequencies in dichloromethane of the carbonyl ligand in a series of Rh(I) Vaska-type complexes $[RhCl(CO)L_2]$ and compared the data to that of $[Ni(CO)_3L]$ complexes.[71] They found a clear trend between the stretching frequencies of the Rh and Ni complexes. The rhodium Vaska-type complexes were used to establish the electronic parameters of various ligands in a similar fashion as the $[Ni(CO)_3L]$ complexes. The rhodium Vaska-type system provides easy accessibility to complexes that are safe to work with.[71] The number of available complexes is almost twice that of the available $[Ni(CO)_3L]$ complexes, making measurements more feasible. They used XRD-techniques to determine the cone angles of the various ligands. They implemented the effective cone angle principle, which takes the measured metal ligand bond distance into account when the cone angle is calculated.[39] Measuring steric effects using this method is once again dependent on the ability of the Rh(I) Vaska-type complexes to form usable crystals for XRD analysis.

A last investigation method that is worth mentioning is the one developed by Guzei and Wendt.[72] They stated that the steric effect of a ligand reflects not only its size, which can be measured by its volume, but also its shape and conformation that are dependent on the coordination centre and other ligands present in the system.[72] In 2006, Guzei and Wendt reported an improved algorithm to characterise ligand interactions in organometallic and coordination complexes in terms of the percentage of the metal coordination sphere shielded by a given ligand.[72] The ligand solid angle computations are performed numerically and employ introduced atomic radii that are larger than covalent radii, but smaller than van der Waals radii. They wrote a program “Solid-G” that numerically calculates ligand steric parameters in organometallic compounds in a reliable fashion.[72] The method based on ligand solid angle calculations describes each ligand by the percentage of the coordination sphere of the central atom shielded by the ligand. Since this program will be used in **Chapter 3** to investigate the steric effects of the various ligands it will be discussed in more detail there.

What becomes clear from this literature review is the variety of phosphine ligand synthesis methods that are available. Predicting which ligand will lead to a better catalyst without in-depth experimental analysis is no easy task. There is a need for a method to determine steric and electronic properties of potential ligands that satisfies all the requirements of in-depth experimental methods. Until such a method is found, it will remain an extremely difficult task to identify ligands that will be suitable for the Grubbs-type catalysts system. It is also apparent that a better understanding of the mechanism is necessary. If more and more ligands for the Grubbs-type systems are synthesised without a better understanding of the mechanism, the reliance on serendipity for the discovery of the next generation of highly active catalysts will continue.

2.6 Literature references

1. P. Muller, *Pure. Appl. Chem.*, 1994, **66**, 1077
2. R.H. Grubbs, *Handbook of Metathesis*, Wiley-VCH (Germany), 2003
3. S.I. Murahashi, *Ruthenium in Organic Synthesis*, Wiley-VCH (Germany), 2004
4. R.A. Grey, *J. Franklin Inst.*, 2000, **337**, 793
5. A.M. Rouhi, *Chem. Eng. News*, 2005, **83**, 8
6. C. Elschenbroich and A. Salzer, *Organometallics: A Concise Introduction*, Wiley-VCH (New York), 1992, p. 423-425
7. P. Corradini, G. Guerra and L. Cavallo, *Acc. Chem. Res.*, 2004, **37**, 231
8. T. Takahashi, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley & Sons (Chichester), 2001
9. R.R. Schrock*, Acc. Chem. Res.*,1979, **12**, 98
10. J.S. Murdzek and R.R. Schrock, *Organometallics*, 1987, **6**, 1373
11. R.R. Schrock, S.A. Krouse, K. Knoll, J. Feldman, J.S. Murdzek and D.C. Young, *J. Mol. Cat.*, 1988, **46**, 243
12. A. Fürstner, *Angew. Chem. Int. Ed. Eng.*, 2000, **39**, 3012
13. S.H. Pine, G.S. Shen and H. Hoang, *Synthesis*, 1991, 1615
14. R.R. Schrock, J.S. Murdzek, G.C. Bazan, J. Robbins, M. DiMare and M. O'Regan, *J. Am. Chem. Soc.*, 1990, **112**, 3875
15. R.R. Schrock, *J. Am. Chem. Soc.*, 1974, **96**, 6796
16. P. Schwab, R.H. Grubbs and J.W. Ziller, *J. Am. Chem. Soc.*, 1996, **118**, 100
17. T.M. Trnka and R.H. Grubbs, *Acc. Chem. Res.*, 2001, **34**, 18
18. M. Scholl, S. Ding, C.W. Lee and R.H. Grubbs, *Org. Lett.*, 1999, **1**, 953
19. G.S. Forman, A.E. McConnell, M.J. Hanton, A.M.Z. Slavin, R.P. Tooze, W. Janse van Rensburg, W.H. Meyer, C. Dwyer, M.M. Kirk and D.W. Serfontein, *Organometallics*, 2004, **23**, 4824

20. P. Schwab, M.B. France, J.W. Ziller and R.H. Grubbs, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2039; *Angew. Chem.*, 1995, **107**, 2179
21. S.H. Hong and R.H. Grubbs, *J. Am. Chem. Soc.*,2006, **128**, 3508
22. A.M. Rouhi, *Chem. Eng. News*, 2002, **80**, 29
23. K.J. Irvin and J.C. Mol, *Olefin Metathesis and Metathesis Polymerization*, Academic Press (London), 1997
24. A.M. Rouhi, *Chem. Eng. News*, 2002, **80**, 34
25. G. Bertrand, *Chem. Rev.*, 1994, **94**, 1161
26. F.A. Cotton and G. Wilkinson, *Advanced Inorganic Chemistry*, John Wiley & Sons (New York), 1988, p. 35-83
27. B. Cornils and E. Wiebus, *Chemtech*, 1995, **25**, 33
28. A.S.C. Chan, C.C. Chen, R. Cao, M.R. Lee, S.M. Peng and G.H. Lee, *Organometallics*, 1997, **16**, 3469
29. A. Buhling, P.C.J. Kamer and P.W.N.M. van Leeuwen, *J. Mol. Catal. A: Chem.*, 1995, **98**, 69
30. A. Buhling, P.C.J. Kamer, P.W.N.M. van Leeuwen and J.W. Elgersma, *J. Mol. Catal. A: Chem.*, 1997, **116**, 297
31. M. Tanaka, T. Hayashi and I. Ogata, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 2351
32. W. Goertz, W. Keim, D. Vogt, U. Englert, M.D.K. Boele, L.A. Van den Veen, P.C.J. Kamer and P.W.N.M. van Leeuwen, *J. Chem. Soc., Dalton Trans.*, 1998, 2981
33. V. Ravindar, H. Hemling, H. Schumann and J. Blom, *Synth. Commun*., 1992, **22**, 841
34. V. Ravindar, H. Hemling, H. Schumann and J. Blom, *Synth. Commun*., 1992, **22**, 1453
35. H. De Bod, *Synthesis and Application of Polar Phosphine Ligands*. Ph.D.-thesis, RAU, 2003, p. 35-170
36. H. Tomori, J.M. Fox, and S.L. Buchwald, *J. Org. Chem*., 2000, **65**, 5334
37. R. Kluger, F. Kerst, D.G. Lee and F.H. Westheimer, *J. Am. Chem. Soc.*, 1967, **89**, 3919
38. F.B. Clarke III and F.H. Westheimer, *J. Am. Chem. Soc.*, 1971, **93**, 4541
39. H. Tomioka, Y. Hirano and Y. Izawa, *Tetrahedron Lett.*, 1974, **51**, 4477
40. C. Carrier, H. Bonnard, G. De Lauzon and F. Mathey, *J. Am. Chem. Soc.*, 1983, **105**, 6871
41. E. Mattmann, D. Simonutti, L. Richard, F. Mercier and F. Mathey, *J. Org. Chem.*, 2001, **66**, 755
42. E. Mattmann, F. Mercier, L. Richard and F. Mathey, *J. Org. Chem.*, 2002, **67**, 5422
43. S. Warren and P. Wyatt, *J. Chem. Soc., Perkin Trans. 1*, 1998, 249
44. C.A. Tolman, *Chem. Rev.*, 1977, **77**, 313
45. O. Kühl, *Coord. Chem. Rev.*, 2005, **249**, 693
46. E.C. Alyea and D.W. Meek, *Advances in Chemistry*, American Chemical Society (Washington), 1982, p. 196
47. J.D. Atwood, M.J. Wovkulich and D.C. Sonnenberg, *Acc. Chem. Res.*, 1983, **16**, 350

48. C.D. Wood and P.E. Garrou, *Organometallics*, 1984, **3**, 170
49. L.H. Pignolet, *Homogeneous Catalysis with Phosphine Complexes*, Plenum (New York), 1983
50. W. Strohmeier and J.F. Guttenberger, *Chem. Ber.*, 1964, **97**, 1871
51. W. Strohmeier and F.-J. Müller, *Chem. Ber.*, 1967, **100**, 2812
52. W. Strohmeier and J.F. Guttenberger, *Chem. Ber.*, 1964, **97**, 1256
53. W. Strohmeier, J.F. Guttenberger and G. Popp, *Chem. Ber.*, 1965, **98**, 2248
54. W. Strohmeier, *Angew. Chem.*, 1964, **76**, 873
55. W. Strohmeier, G. Popp and J.F. Guttenberger, *Chem. Ber.*, 1966, **99**, 165
56. W.D. Horrocks Jr. and R.C. Taylor, *Inorg. Chem.*, 1963, **2**, 723
57. C.A. Tolman, *J. Am. Chem. Soc.*, 1970, **92**, 2953
58. J. Bartholomew, A.L. Fernandez, B.A. Lorsbach, M.R. Wilson, A. Prock and W.P. Giering, *Organometallics*, 1996, **15**, 295
59. S. Joerg, R.S. Drago and J. Sales, *Organometallics*, 1998, **17**, 589
60. R.S. Drago and S. Joerg, *J. Am. Chem. Soc.*, 1996, **118**, 2654
61. R.S. Drago, *Organometallics*, 1995, **14**, 3408
62. R.S. Drago, Applications *of Electrostatic-Covalent Models in Chemistry*, Surface Scientific Publishers, Gainesville, FL, 1994
63. A. Fernandez, C. Reyes, M.R. Wilson, D.C. Woska, A. Prock and W.P. Giering, *Organometallics*, 1997, **16**, 342
64. A.L. Fernandez, T.Y. Lee, C. Reyes, A. Prock and W.P. Giering, *Organometallics*, 1997, **17**, 3169
65. C.H. Suresh and N. Koga, *Inorg. Chem.*, 2002, **41**, 1573
66. W.P. Giering, A. Prock and A.L. Fernandez, *Inorg. Chem.*, 2003, **42**, 8033
67. J. Slattery, R.J. Thatcher, Q. Shi and R. Douthwaite, *Pure Appl. Chem.*, 2010, **82**, 1663
68. H. Jacobsen, A. Correa, C. Costabile and L. Cavallo, *J. Organomet. Chem.*, 2006, **691**, 4350
69. H. Jacobsen, A. Correa, A. Poater, C. Costabile and L. Cavallo, *Coord. Chem. Rev.*, 2009, **253**, 687
70. U. Radius and F. M. Bickelhaupt, *Coord. Chem. Rev.*, 2009, **253**, 678
71. S. Otto and A. Roodt, *Inorg. Chim. Acta.*, 2004, **357**, 1
72. I.A. Guzei and M. Went, *Dalton Trans.*, 2006, 3991