Chapter 1: A literature study on the advances and applications of the hydroformylation reaction as well as ligand modifications and their effects on catalytic activity

1.1 Introduction

Catalysis is one of the most important and most widely studied fields in chemistry. It is considered to be the key for the successful initiation and facilitation of a wide range of chemical reactions and in the selective production of valuable compounds. It plays a vital role in biological systems to ensure that an organism functions appropriately in response to demands and its environment, therefore ensuring its survival. In the industry today catalysis has a wide range of applications including the production of liquid fuels and bulk chemicals and is used in the production of many fine chemicals.

About 150 years ago Berzelius[1] discovered that certain species, which were referred to as "ferments", caused noticeable changes in substances when brought in contact with them and therefrom created the concept of catalysis. In 1895 Oswald designed a definition for the term catalysis, which is as follows: *A catalyst is a substance that changes the rate of a chemical reaction without itself appearing into the products.*[2] This definition was later modified to state that a catalyst increases the rate of a chemical reaction by lowering its activation energy, but does not become involved in the reaction itself.[2]

Catalysis is divided into two major classes namely homogeneous and heterogeneous catalysis. Homogenous catalysis involves a system where all of the components of a reaction, including the catalyst, exist in one phase, which in most cases is a liquid phase. Good examples include the hydroformylation reaction, Diels-Alder reactions catalysed by Lewis

acids and the hydrogenation reaction.[2] In heterogeneous catalysis, on the other hand, multiple phases are present, as in the case, for example, of the Fischer-Tropsch process which uses iron carbides as the catalyst.[3]

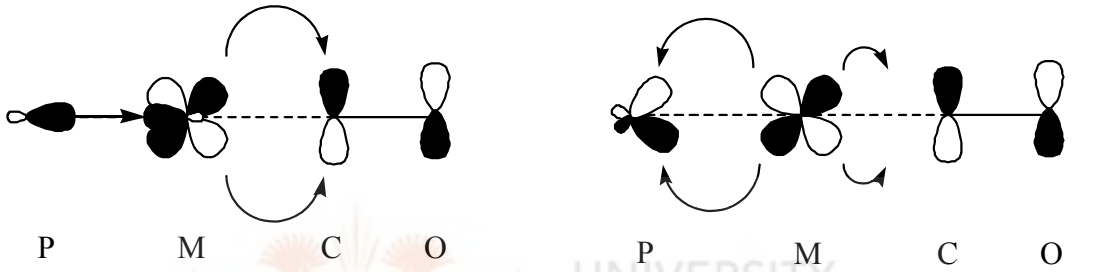
1.2 Organometallic catalysts and the importance of ligands on their activity

There are many types of catalysts but amongst them one of the most important classes includes organometallic catalysts. These catalysts involve a metal centre onto which organic ligands are co-ordinated. Research has shown not only that the type of metal centre determines the activity of a catalyst,[4] but also that the ligands play a vital role in determining the properties of the catalyst. In general, the ligands govern the efficiency and selectivity of the catalyst, which in turn is dependent on the type of ligand, its basicity (or electron density) and its size (steric properties).

1.2.1 Phosphine ligands and their basicity

Ligands exert individual electronic properties on catalysts, but since the present study involved mostly phosphine ligands the basicity of ligands will be discussed in terms of phosphine ligands. Phosphine ligands have a wide application in organometallic chemistry as well as in the industry.[2] The basicity of a phosphine ligand is determined by the types of groups that are bonded to the phosphorus atom. If alkyl groups are present on a phosphorus atom, the result will be the formation of strong bases, since the alkyl groups are found to be fairly electron donating.[5] These ligands therefore become good σ-donors and will donate electron density onto a metal centre. On the other hand, organophosphites are considered to be π-acceptors as they form stable complexes with electron-rich transition metals.[6]

This π-acidity and σ-basicity of phosphine ligands can be established on the basis of CO vibrational frequency changes using complexes such as $NiL(CO)_3$ or $CrL(CO)_5$ (where L = phosphine ligand).[7,8] As illustrated in Figure 1.1, an electron-rich ligand (Figure 1.1a) donates electron density onto the metal centre, increasing its electron density. This in turn causes a substantial amount of π-back donation to the CO ligands and as a result the IR vibrational frequency lowers in value. Strong π-acceptor ligands on the other hand (Figure 1.1b) remove electron density from the metal centre through back-donation, resulting in a much lower π-back donation onto the CO ligands. The consequence is that the vibrational frequency of CO increases in value.[9]



a: electron-rich P, low C-O stretch b: electron-poor P, high C-O stretch

Figure 1.1

Tolman[7] used vibrational spectra of $NiL(CO)_3$ with different ligands to define the electronic properties of phosphine ligands in terms of an electronic parameter χ. With L = $P(t\text{-}Bu)_3$ as a reference this parameter is defined as the difference between the vibrational frequencies of the reference complex and another complex. A few examples of the values of the electronic parameter that he obtained for a range of phosphine ligands are given in Table 1.1. From here it can be seen that there is a good correlation between the CO vibrational frequencies and the electronic character of the phosphine ligands, where a decrease in the basicity of the phosphine ligands causes an increase in the electronic parameter χ. When attempting to ascertain the contribution of only one substituent (χ_i-value) it is sufficiently accurate to simply use 1/3 of the χ-value for the 'homo' compound (PR_3) and extrapolate an 'additive' figure/value into an 'hetero' compound (eg. R'_2PR).

Table 1.1 Phosphine ligands and their χ-values.[7]

Ligand PR_3: R =	χ -value	IR frequency of $NiL(CO)_3$ (cm^{-1})
t-Bu	0	2056
n-Bu	4	2060
Ph	13	2069
CH_3O	20	2076
PhO	29	2085
Cl	41	2097
F	55	2111
CF_3	59	2115

1.2.2 The effect of ligand basicity on catalytic activity

It is clear from the previous section that ligands having different electronic properties will alter the electronic properties of an organometallic catalyst, therefore altering its activity within a certain process. These properties frequently play a role in the kinetic aspects of a chemical transformation. All chemical reactions have an energy profile, where there is an activation barrier that must be reached in order for the reaction to proceed. It is generally accepted that catalysts lower the activation barrier or -energy, thereby enhancing the rate of the reaction. However, as van Leeuwen stated in his book *Homogeneous Catalysis*,[2] this statement is in many cases "an over simplification", as for example in cases where reagents are totally unreactive towards each other (methanol *vs.* CO). He provides a general

description namely that a catalyst provides a new and more attractive reaction pathway that includes a lower activation energy.

The rate of a catalytic reaction is not always trivial to calculate, as it depends on the mechanism of the specific reaction. Each process has its own type of mechanism and as a result the role a catalyst plays within that mechanism can differ from one to another. Yet, whatever the case may be, the modification of the electronic properties of a catalyst would be expected to alter its ability to catalyse chemical reactions, and therefore in turn might have an effect on the rate at which the products are formed.

For example, in the hydrogenation of alkenes where Wilkinson's catalyst ($RhCl(L)_3$) is utilised, the last step involves a reductive elimination step to form an alkane.[10] It would be expected that the use of more electron-withdrawing ligands would most likely increase the rate of this step, which is reflected in the results of, for example, the hydrogenation of cyclohexene with various ligands.[10] Another example includes the rate acceleration of the reductive elimination step in the hydrocyanation of alkenes by co-ordinating electron-withdrawing ligands onto the nickel catalyst, as found by McKinney and Roe.[11]

1.2.3 Phosphine ligands and their steric properties

The steric properties of phosphine ligands also play a large role in the activity of a catalyst. It is quite difficult to separate this parameter from the electronic parameter, as they are often closely related, but a few methods have been developed to describe the relative steric properties of phosphine ligands. As will be shown these methods are also different for monodentate ligands compared to bidentate ligands.

For monodentate ligands the most common method involves the use of Tolman's parameter Θ, defined as the cone angle of a phosphine ligand.[12] As depicted in Figure 1.2 it involves a cone constructed from the metal centre, set at a distance of 2.28 Å from the phosphorus atom, which then covers all the peripheral atoms of the substituents on the phosphorus atom. From this the effective cone angle Θ can then be determined. Crystal structure analysis gives better insight on the actual size of the cone angle, as it usually differs from the cone angles obtained from calculations, and therefore the calculated value is only an approximate value and does

not always accurately describe the steric properties. Some of the typical cone angle values calculated by Tolman are given in Table 1.2.

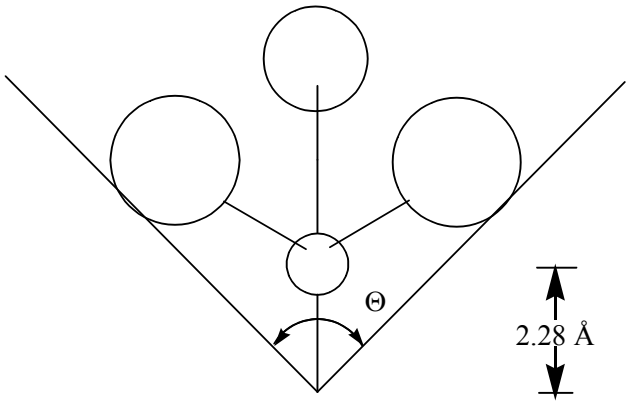


Figure 1.2

Table 1.2 Tolman cone angles for some phosphine ligands.[12]

Ligand PR_3: R =	**Θ-value (°)**
H	87
F	104
Br	131
CH_3	118
OCH_3	107
Ph	145
OPh	128
CF_3	137
C_6F_5	184
o-$C_6H_4CH_3$	194

Alternative methods include the measurement of complex dissociation constants for ligands, where the amount of dissociation correlates well with the steric parameter. Examples include the use of cobaloxime complexes[13] as well as molybdenum complexes of the type *cis*-$Mo(CO)_4L_2$.[14] Tolman also determined that the degree of substitution of $Ni(CO)_4$ with phosphine ligands correlates well with the steric parameter. [15] Other methods involve the use of thermochemistry where the heats of formation of metal-phosphine complexes can be

determined, which, if the electronic effects are small, is a measurement of the steric hindrance in these complexes.[16] It is found that an increase in the steric bulk of a ligand causes a decrease in the heats of formation.

For bidentate ligands the use of Tolman's parameter is quite complicated, and therefore another method has been developed which includes the concept of a bite angle. Rigid bidentate ligands contain what is known as a ligand backbone which keeps two phosphorus atoms at a constrained distance from each other. This distance is found to be very specific for each bidentate ligand and together with the flexibility of the backbone determines the bite angle that will result after complexing with a metal centre. This definition of a bite angle is depicted in Figure 1.3.[17]

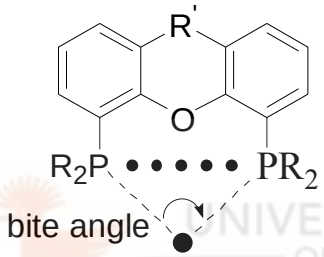


Figure 1.3

Although a wide variety of bidentate phosphines may be synthesised, not all of them have the correct conformations to co-ordinate onto a metal centre. The lone pairs of electrons on the phosphorus atoms need to point in the direction of the metal centre.[2] A few examples of common bidentate phosphines and their bite angles are given in Figure 1.4.

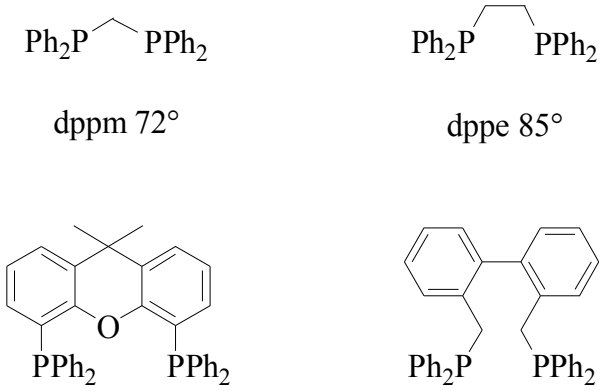


Figure 1.4

1.2.4 The effect of ligand steric properties on catalytic activity

In most cases the steric properties of the ligand influences the selectivity of a catalytic process, although there are cases where this parameter also influences the kinetics of a reaction. There are mainly four classes of selectivity that are present in catalytic processes, namely regioselectivity, enantioselectivity, diastereoselectivity and chemoselectivity. Steric effects have been observed mainly for the former case, while enantioselectivity and diastereoselectivity are mainly controlled by the presence of chiral ligands. Chemoselectivity is mainly influenced by kinetic control or electronic effects. Since regioselectivity was more important in the present study, attention will be given to this type of selectivity.

Regioselectivity involves the addition of one molecule or reactive intermediate to another that results in the formation of a compound where a certain atom or group can be positioned in one of two or more different places. For example in the Ni-catalysed hydrocyanation of butadiene to form adiponitrile, many different isomers are possible due to the fact that the cyanide can be added to either side of each double bond.[18] As can be seen in Figure 1.5 the first step involves the addition of a cyanide ion to one of the double bonds, which results in the formation of two isomers **a** and **b**. From **b** isomerisation takes place to form the isomers **c** and **d**, which in turn are converted into dinitrile isomers through the hydrocyanation process. As can be seen only compound **d** gives rise to the formation of adiponitrile **e**. The first two steps are mainly controlled by a retro-reaction[19] and by the kinetics of the reaction,[20] respectively, while the last step can be controlled by steric properties of the Ni-catalyst. It was found that steric bulk around the nickel complex results firstly in the co-ordination of 4-pentenenitrile **d** rather than 3-pentenenitrile **b**, and secondly in the formation of the linear compound adiponitrile **e** rather than the branched product **f**.[21] This steric effect has also been observed in the hydrocyanation of propene by Tolman *et al.*[22]

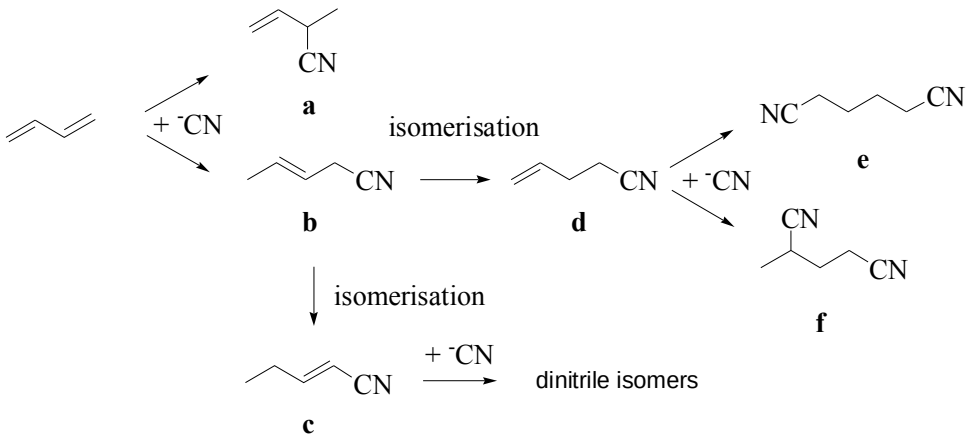


Figure 1.5

Regioselectivity is also important in most hydroformylation reactions and in Pd-catalysed cross-coupling reactions, which will be discussed later in this chapter.

1.3 The Rh- and Co-catalysed hydroformylation reaction

One of the most widely applied and most studied process is the hydroformylation reaction, which can be catalysed by either Co-based or Rh-based catalysts. This reaction was discovered by accident when Roelen was studying the Fischer-Tropsch process with a heterogeneous cobalt catalyst.[23] He showed that the reaction involved the conversion of alkenes to aldehydes and alcohols and that the reaction was not catalysed by the supported cobalt, but in truth by the complex $HCo(CO)_4$, which had formed in the liquid state. Later on it was discovered that rhodium could also be used as a catalyst, which in many cases has shown to be more efficient and that milder conditions could be used.[24] As depicted in Figure 1.6, this process leads to the formation of linear and branched aldehyde isomers.

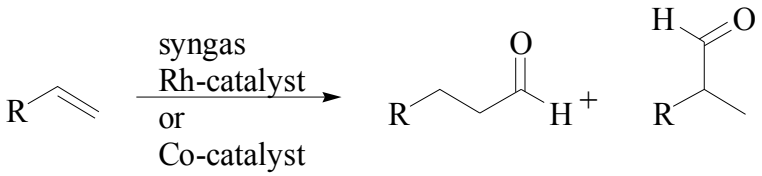


Figure 1.6

Even though this reaction seems very simple, it is somewhat challenging to control in order to get the preferable product from the alkene, as this reaction is influenced by many different variables. These variables include temperature, pressure, mass transfer, the catalyst and alkene concentrations, type and amount of ligand being used, and the solvent system. In the next few sections the accepted mechanisms proposed for both the Co- and Rh-catalysed hydroformylation reaction will be shown, after which a brief discussion will be given on how some of the variables mentioned influence the hydroformylation reaction. Attention will also be given to ligand modifications that have this far been developed, and how these ligands affect the hydroformylation reaction.

1.3.1 The Co-catalysed hydroformylation reaction

Even though $HCo(CO)_4$ proved to be a very efficient catalyst, it was found to be quite unstable and that it could perform the hydroformylation reaction only under extreme conditions. In the early sixties Slaugh from Shell Development reported the first cobalt catalyst modified with phosphine ligands.[25] It was found that the addition of a phosphine ligand increased the stability of the cobalt catalyst and also gave rise to better selectivity towards linear aldehydes. From this a wide range of phosphine-modified cobalt complexes have been reported, which will be expanded upon at a later stage.

The mechanism for the Co-catalysed hydroformylation reaction is not a trivial matter to elucidate, as a wide range of cobalt species have been reported to form under the syngas pressure. These species include multinuclear clusters, the formation of which depend strongly on the conditions used.[26,27] However, it was found that the dimeric products ($Co(CO)_8$, $Co(CO)_7PR_3$, etc.) are mostly produced, which forms an equilibrium with its monomeric counterpart. With this in mind the generally accepted mechanism as proposed by Mirbach[28] given in Figure 1.7. This mechanism is not meant to hold for each case, but rather to provide a general understanding of the process.

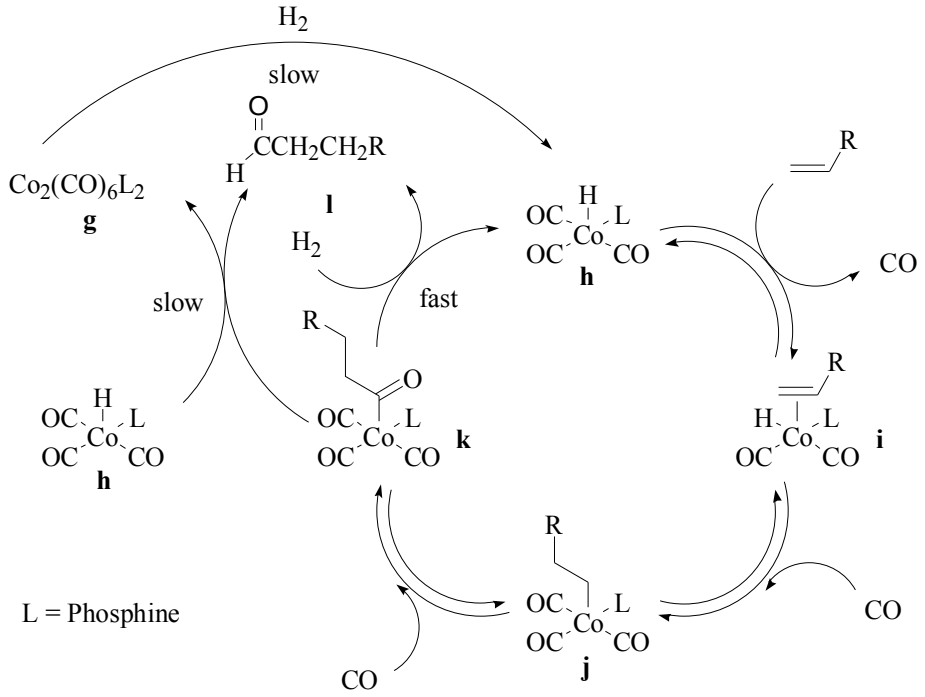


Figure 1.7

The first step of this process involves the dissociation of the dimeric **g** to the monomeric catalyst **h** under hydrogen gas pressure, a reaction that seems to be very slow. One of the carbon monoxide ligands then labilises to allow the incoming alkene to co-ordinate to the cobalt centre forming complex **i**. In the next step migratory insertion of the hydride into the alkene takes place, followed by the co-ordination of a carbon monoxide molecule onto the cobalt to form complex **j**. Migratory insertion of a carbon monoxide ligand into the alkane then occurs resulting in acyl complex **k**, after which the aldehyde **l** is released by reductive elimination either by the addition of a hydrogen molecule (which is a fast reaction) which reproduces the active catalyst **h** or by reaction of complex **k** with the catalyst **h** to reproduce the dimeric cluster **g** (which is a slow reaction).

1.3.2 The Rh-catalysed hydroformylation reaction

Soon after the discovery of the use of rhodium as a catalyst for the hydroformylation reaction, industrial applications of this process were being explored. It was shown by Wilkinson in the mid-sixties that arylphosphines proved to be the most efficient ligands to use with rhodium, providing very active catalysts at mild conditions,[24,29a,b] which is a great advantage above the cobalt system. With the rhodium catalysts the conditions needed are within the range of 1-25

atm and 90-110 °C, while with the cobalt catalysts much higher temperature and pressures are required (25-100 atm, 140-170 °C).[2]

The general mechanism for the Rh-catalysed hydroformylation reaction was first proposed by Heck,[30] and is given in Figure 1.8. As can be noted, this mechanism is dissociative, which corresponds with Wilkinson's work.[24,29a,b] Only the route for the linear aldehyde is shown; the route to the branched aldehyde is similar.

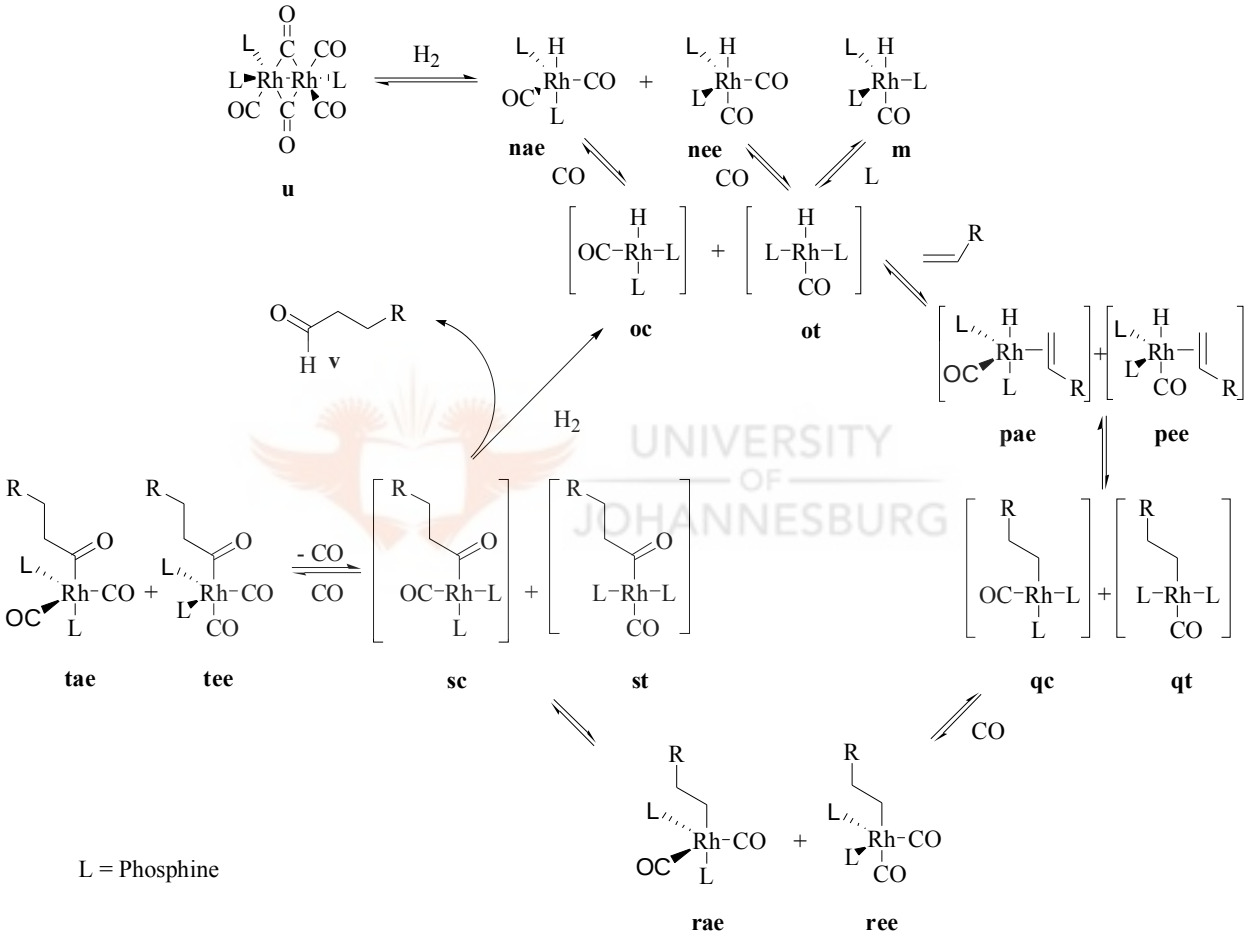


Figure 1.8

As illustrated in Figure 1.8, the mechanism can have several starting points. It has been discovered that at high rhodium concentrations and low hydrogen pressures the dirhodium complex **u** forms quite easily.[31] Dissociation of this complex under hydrogen gas pressure gives rise to complexes **nae** and **nee**, where the phosphine ligands are either in the axial-equitorial position (**ae**) or in the equatorial-equitorial position (**ee**).

For triphenylphosphine the common starting point is complex **m**, where three triphenylphosphine ligands are situated in equatorial positions. Under carbon monoxide gas pressure this complex can also form the various complexes **n**. Dissociation of an equatorial carbon monoxide from complexes **n** or an equatorial ligand from complex **m**, leads to the formation of the square planar intermediates **oc** and **ot**, where the phosphine ligands take on either the *cis* or the *trans* configuration, respectively. An alkene then co-ordinates to the rhodium centre in the equatorial position, to form two isomeric bipyramidal complexes **pae** and **pee**. In the next step migratory insertion of the hydride into the alkene takes place, forming *cis* and *trans* square planar intermediates **qc** and **qt**. Carbon monoxide co-ordinates to these complexes to form the bipyramidal complexes **r** which then undergo a second migratory insertion to form the acyl complexes **s**.

From complexes **s** is has been observed that two routes are possible: The first route involves a reaction with carbon monoxide to give the saturated acyl intermediates **t**, which has been observed by Brown and Kent,[32] and the second route involves a reaction with hydrogen gas resulting in the formation of the aldehyde **v** as well as the squar planar complexes **o**. The latter reaction presumably undergoes oxidative addition followed by reductive elimination, although so far no observations regarding this reaction have led to a definite conclusion.

1.3.3 The influence of different system variables on the hydroformylation reaction

One of the greatest difficulties when studying ligand effects is the sensitivity of the catalytic processes such as the hydroformylation reaction towards system variables including temperature, pressure, mass transfer, etc. In order to define and rationalise the outcome of a catalytic process with different ligands one needs to consider the system conditions under which the process should be performed and what probable consequences these may have on the study.

Two of these variables that play a significant role are temperature and pressure. In the Co-catalysed hydroformylation reaction high temperatures are required to perform the reaction. These high temperatures limit the use of certain types of ligands where, for example, arylphosphines cannot be used for this system as they usually decompose at high

temperatures. This was demonstrated by exposing some arylphosphines to a temperature of 190 °C, which led to phosphorus-carbon bond cleavage.[33] It was also found that cobalt catalysts are less active when using alkylphosphines and as a result even higher temperatures are required. The pressure applied affects not only the kinetics of the reaction, but can also modify the species present in the process. High-pressure *in situ* NMR spectroscopy showed that when high pressures of carbon monoxide are applied to a sample containing the complex $Co_2(CO)_6L_2$ (L = $P(n\text{-}C_4H_9)_3$), disproportionation of the catalyst takes place leading to the formation of a catalytically inactive cobalt salt $[Co(CO)_3L_2]^+[Co(CO)_4]^-$.[34]

With the Rh-catalysed hydroformylation reaction lower temperatures are required. It has been shown though that varying the temperature has a great influence on the rate of aldehyde formation, selectivity and solubility of the catalyst, amongst others. Reinius *et al.*[35] demonstrated that an increase in temperature enhances the butanal formation rate to a limit of 373 K, whereafter the rate started to drop. They also showed that an increase in temperature resulted in an increase in the selectivity towards isobutanal. It was demonstrated by Still *et al.*[36] that the solubility of 1-butene decreases with increasing temperature, while the solubility of both hydrogen and carbon monoxide gas increased with temperature.

With Rh-catalysed hydroformylation, low hydrogen pressures and high rhodium concentrations result in the formation of the inactive dirhodium complex **u** (Figure 1.8). It is expected that isomerisation of the alkene is favoured at low CO pressures, while at very low temperatures and higher CO pressures (> 10 atm) the migratory insertion reaction from complexes **p** to **q** (Figure 1.8) is found to be essentially irreversible.[2]

Another important variable is the ligand to metal ratio which normally determines the stability of the catalyst. For the Co-catalysed hydroformylation a study[37] was performed using different alkylphosphine ligands, in which the ligand to cobalt ratio was varied from 1:1 to 10:1. This resulted in an increase in selectivity towards linear products from about 60% to 90%. Reinius *et al.*[35] demonstrated this for the Rh-catalysed hydroformylation reaction, where an increase in the ligand to rhodium ratio (where arylphosphines were used as ligands) resulted in a decrease in the selectivity to isobutanal. They also demonstrated that at low ligand to rhodium ratios the butanal formation rate increased with the ratio, while at high ligand to rhodium ratios the rate started to stabilise. However, work done by Bergounhou *et*

al.[38] showed that applying different ligand to rhodium ratios using TPP (1,2,5-triphenylphosphole ligand) had virtually no influence on the activity or selectivity of the rhodium catalyst in the hydroformylation of styrene. With the hydroformylation of conjugated dienes, an accelerative effect was observed with triphenylphosphine as the ligand to rhodium ratio was increased.[39] In the hydroformylation of isoprene a remarkable increase in the conversion to aldehyde (10%, 45% and 100%, respectively) was observed, as the ligand to rhodium ratio was increased from 5 to 10 and 20. Thus ligand to catalyst ratios can have different effects in different reaction systems.

The type of solvent used in the catalytic process also plays a role in the outcome of the reaction. Important aspects here include the solubility of the reagents in the medium as well as the inertness of the solvent towards the reagents. Toluene and THF are usually the media of choice, but other systems have proved to be useful. Lin *et al.*[40] have demonstrated that ionic liquids can successfully be applied as a medium for the hydroformylation of higher olefins. The reaction was performed with water-soluble rhodium catalysts in 1-n-alkyl-3-methylimidazolium *p*-toluenesulfonate which gave excellent yields with good retention of the catalyst in the ionic liquid medium. CO_2-expanded liquids have shown to be favourable media for the hydroformylation of higher olefins under mild conditions.[41a,b] These liquids enhance the solubility of gaseous reagents (syngas) as well as the catalyst miscibility and provide higher turnover numbers. It was observed that the hydroformylation of 1-hexene in THF or toluene under forcing conditions (120 °C, pressures between 29-80 atm, 16 h reaction time), results in the formation of small amounts of alcohol together with the aldehydes.[42] However when ethanol is used as the solvent for this process, most of the aldehyde converts to alcohol under similar conditions with yields above 90%.

Mass transfer effects are also observed within the Rh-catalysed hydroformylation reaction, which is greatly influenced by the surface to volume ratio as well as stirring speed. It can be expected that increasing the surface to volume ratio should increase the transfer of the gaseous species into the medium. The effect of stirring speed on the process has been demonstrated by Guha *et al.*[43] first by performing the hydroformylation reaction in neat 1-octene as the solvent and substrate with different stirring speeds and secondly by determining the mass transfer coefficients for hydrogen and carbon monoxide gas in neat 1-octene. They discovered that an increase in the stirring speed enhanced the mass transfer coefficients of the

two gases. Furthermore induction periods were observed during the hydroformylation reaction, where an increase in the stirring speed decreased the duration of the induction period.

1.4 Ligand modifications and the resulting effects of varying stereo-electronic parameters on the hydroformylation reaction

1.4.1 Ligand effects in the Co-catalysed hydroformylation reaction

With the development of phosphine-based cobalt catalysts the first phosphine ligands that were applied were simple alkylphosphines that provided effective but less active catalysts. Slaugh[25] reported the order of activity for a range of phosphines at conditions of 195 °C and 36 atm of syngas, as follows: Ph_2EtP > $PhBu_2P$ > Bu_3P > Et_3P > $PhEt_2P$ > Cy_3P. At first glance the former phosphines seem to follow an order expected, where the most electron-poor phosphine (Ph_2EtP) showed the best activity in comparison to a very electron-rich phosphine (Bu_3P). However, the order thereof switches around with Et_3P and $PhEt_2P$ (being less electron-rich than Bu_3P) showing lower activity than Bu_3P. Here it is said that the rapid isomerisation of the alkene to less reactive internal alkenes should also be taken in consideration, which then can influence the outcome of the reaction.[2] Slaugh also reported the order for the linear to branched aldehyde ratio obtained for each ligand, as follows: Bu_3P > Et_3P ≈ $PhEt_2P$ ≈ Cy_3P ≈ $PhBu_2P$ > Ph_2EtP, which ranges from 5.5:1 to 3:1. Though it is clear that the type of ligand used has an effect on the linear to branched aldehyde ratio, there is no clear order in the steric influences. Later on Slaugh also used the diphosphine dppe (Figure 1.4) as a ligand for the cobalt catalysed process, which showed to have little effect on the on the activity and selectivity of the cobalt catalyst compared to tributylphosphine.[44]

A few years later it was discovered that phoban-based derivatives showed to be more effective ligands to use.[45] One of these ligands that was reported as an efficient ligand is 9-eicosyl-9-phosphabicyclononane which is given in Figure 1.9. The long C-20 chain provided a phosphine with a high boiling point and very stable cobalt catalysts.

Recently Sasol have developed a group of bicyclic aliphatic phosphines called Lim ligands, which are shown in Figure 1.9.[46] In these ligands the alkyl groups increase the electron density on the phosphorus atom, but the steric congestion caused by the ring system is expected to raise the χ-value of the ligands, which in turn makes them better π-acceptors. Electronic effects have been observed for these Lim ligands by performing the hydroformylation reaction using the ligands containing a different X group as shown in Figure 1.9. With the order of X = Me, OBz, Ph and CN an increase in the reaction rate was observed, while the selectivity towards the linear product decreased. Thus the better donor (Me) gave the highest linear to branched ratio, which was 4.9:1. However, NMR and IR studies showed that this was not an intrinsic ligand effect, as it was a measure of the amount of phosphine-free catalyst ($HCo(CO)_4$) that was present at equilibrium. The use of a less electron-rich ligand gave rise to formation of more of the phosphine-free catalyst, leading to a higher rate and a lower linear to branched aldehyde ratio.

Figure 1.9

In recent work done by Srivastava *et al.*,[47] arsine and stibine ligands were studied as alternatives to phosphine ligands, by comparing triphenylphosphine, triphenylarsine and triphenylantimony in the Co-, Rh- and Ru- catalysed hydroformylation reactions. The σ-donor abilities of these ligands follow the order of $SbPh_3 > PPh_3 > AsPh_3$.[48] In their results they observed that triphenylphosphine and triphenylarsine gave the same reaction rate in the cobalt-catalysed hydroformylation reaction of 1-hexene, while triphenylantimony caused a drop in the reaction rate. Thus it was clear from these results that a decrease in the σ-donor ability led to an increase in the hydroformylation reaction. The triphenylphosphine cobalt complex gave the highest selectivity (3.1:1) towards the linear product though, followed by triphenylantimony and triphenylarsine. The Rh-catalysed hydroformylation reaction provided similar results.

1.4.2 Ligand effects in the Rh-catalysed hydroformylation reaction

Significant research has been done on the Rh-catalysed hydroformylation reaction since the discovery of the use of rhodium catalysts in this process and in comparison to the cobalt system where ligand effects are not as clear or prominent, the Rh-catalysed hydroformylation reaction has showed to be quite sensitive towards the stereo-electronic properties of ligands. As will be shown ligand modification has led to the production of a large number of ligands that have different characteristics and play different roles within the Rh-catalysed hydroformylation reaction.

It was mentioned before that the rationalisation of ligand effects is not trivial as it is not only difficult to separate the electronic property from the steric property of a ligand, but is also determined by the specific system and conditions under which the reaction is being performed. Apart from the variables that have been discussed in the previous sections, two other aspects that play a role are the rate-determining step and the choice of alkene substrate. Numerous comments have been made as to which step might be the rate-determining step, but from an experimental point of view results do not always lead to a definite conclusion. It has been generally accepted that either alkene co-ordination or the migratory insertion of the alkene into the rhodium-hydride bond can be the rate-determining step depending on the reaction specifics.[2]

With triphenylphosphine as ligand the rate-determining step is allocated to the alkene co-ordination. This consequence was demonstrated by work done by van Rooy *et al.*[49] where they performed the hydroformylation reaction with a variety of alkene substrates using triphenylphosphine and tris(2-*tert*-butyl-4-methylphenyl)phosphite as ligands. In the case of triphenylphosphine the rate of the reaction dropped as more hindered alkenes were used. Furthermore they also showed that a higher selectivity towards the linear product was obtained with an increase in the number of substituents on the alkene. In the case of the use of the phosphite ligand the rate of the hydroformylation reaction proved to be independent of the alkene concentration, and the selectivity towards the linear aldehyde remained fairly constant amongst the various alkene substrates.

Density functional and QM/MM calculations were performed to determine the origin of stereo-induction of chiral aminophosphine phosphinite ligands in the hydroformylation reaction.[50] The results revealed that alkene insertion into the rhodium-hydride bond was the selectivity-determining step rather than alkene co-ordination.

Whatever the case may be there is a general trend that is observed for the stereo-electronic effects of ligands within the Rh-catalysed hydroformylation reaction as will be revealed within the next few sections.

1.4.2.1 Electronic effects in the Rh-catalysed hydroformylation reaction

Most authors agree that electron-rich phosphines give poor hydroformylation rates while electron-withdrawing phosphines give high hydroformylation rates. The explanation behind this observation is as was described before in this chapter when discussing the Vaska complexes, namely that the electron-donating ligands lead to increased back-donation to the carbon monoxide ligands, which in turn strengthens the bond between the rhodium centre and the carbon monoxide resulting in a decrease in the rate of formation of species **oc** and **ot** (Figure 1.8). This observation can be seen through a range of examples.

First the simple monodentate phosphines show a clear electronic effect. Tri-alkylphosphines are excellent σ-donors due to the fact that alkyl groups are electron-donating. These ligands reveal poor catalytic activity in the Rh-catalysed hydroformylation reaction.[51a,b] Arylphosphines on the other hand tend to be good π-acceptors, as the aromatic rings are electron-withdrawing. It was shown in the sixties that triphenylphosphine was a good ligand to use for the hydroformylation of alkenes and alkynes under mild conditions (70 °C and 100 atm syngas).[52]

A recent comparative study was performed where a range of combined alkylarylphosphines as given in Figure 1.10 was used in the hydroformylation of propene and 1-hexene.[53] The hydroformylation reaction was performed at 100 °C and a syngas pressure of 10 atm with a L/Rh ratio of 10, the results of which are given in Table 1.3. From these results it can be seen that all of these ligands are more electron-rich than triphenylphosphine in terms of their ^{31}P NMR signals. In the hydroformylation results it was observed that ligands **1-7** containing

alkyl groups gave poor yields of aldehyde, while the arylphosphines **8** and **9** gave moderate yields under the conditions mentioned. Triphenylphosphine being the most electron-poor ligand here gave an excellent yield of 98%. When hydroformylating 1-hexene conversions to aldehyde above 98% were observed for all these ligands as well as for the unmodified catalyst under the similar conditions with longer reaction times. The latter set of results unfortunately fail to highlight ligand effects. The steric effect will be dealt with at a later stage in this chapter.

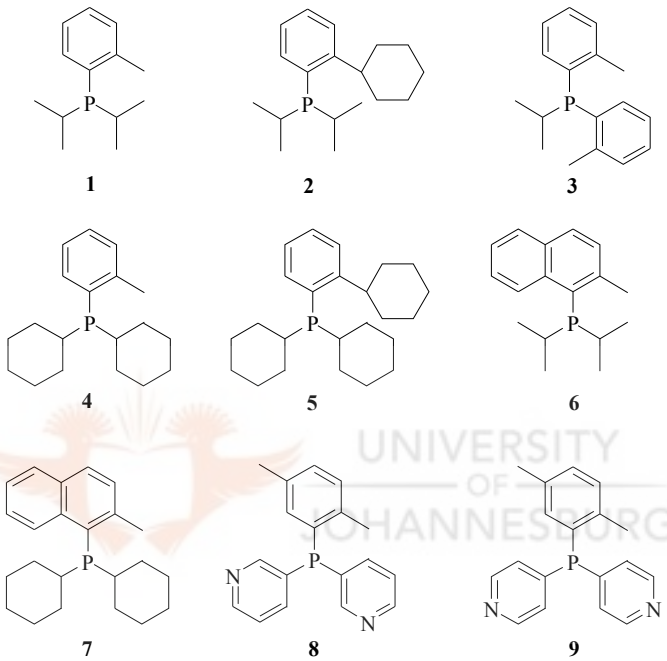
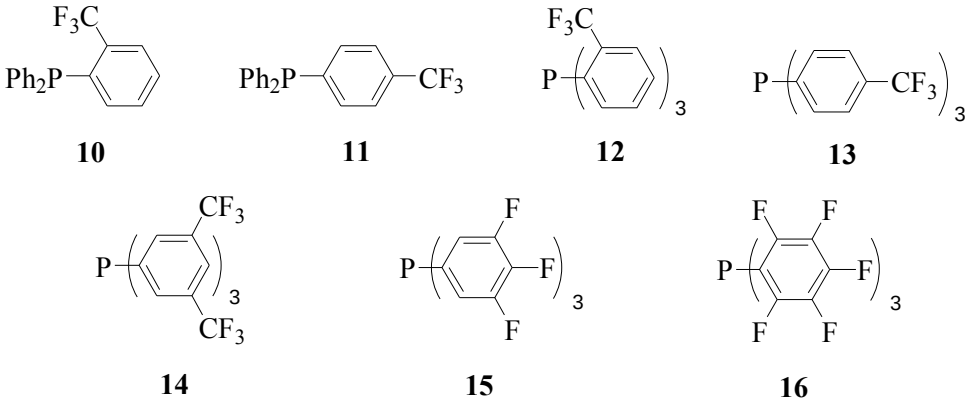


Figure 1.10

Table 1.3 Hydroformylation of propene with ligands in Figure 1.10.

Ligand	^{31}P NMR shift	Cone angle (°)	Conversion (%) after 2h	l:b
1	-4.8	165	52	1.1
2	-4.4	172	47	1.1
3	-22.3	198	22	0.9
4	-11.6	181	5	1.1
5	-14.6	211	35	1.0
6	-6.6	199	23	2.0
7	-8.1	185	22	2.0
8	-25.0	181	50	1.1
9	-15.7	-	53	1.1
PPh_3	-3.3	149	98	1.7

Fine tuning of arylphosphines by substituting different groups on the phenyl rings, has been shown to exert an influence on the electronic properties of the ligands. The use of electron-withdrawing groups on arylphosphines has shown to give faster reaction rates than observed for triphenylphosphine.[54a,b] Exceptions have been observed where fluorine and trifluoromethyl groups were used, as these groups reveal different behaviour than expected, which was also observed in the present study. In two recent studies[55a,b] where the ligands given in Figure 1.11 were used in the hydroformylation of propene, 1-hexene and 4-methoxystyrene, respectively, peculiar results were obtained. It was observed that ligands where the fluorine atom and trifluoromethyl groups were mainly in the *meta* and *para* position (**13**, **14**, and **15**) the electron-withdrawing nature of the fluoro groups resulted in electron-poor phosphines, which as a consequence gave rise to excellent yields of aldehyde in comparison with triphenylphosphine. An exception here was ligand **11** where the authors did not observe any conversion.[55a] The remainder of the ligands where the fluorine atom and trifluoromethyl groups were substituted on the *ortho* position, a positive electronic effect was observed where these ligands showed to have an electron-rich nature. When these ligands were applied within the hydroformylation reaction little to no conversions of aldehyde were obtained.



10 **11** **12** **13**

14 **15** **16**

Figure 1.11

On the other hand the substitution of electron-donating groups on the phenyl rings of arylphosphines give rise to more electron-rich ligands. Recent studies[56a,b] have shown that when alkyl groups such as methyl, ethyl, isopropyl and cyclohexyl groups were substituted onto the *ortho* position of the phenyl rings of tri-aryl phosphines, ligands were obtained that were more electron-rich than triphenylphosphine. This was observed first by ^{31}P NMR spectroscopy, where the value of the characteristic phosphorus signal shifted up-field with increasing electron density on the phosphorus atom, and secondly by the hydroformylation of propene where the conversion to aldehyde was found to decrease in a chronological order with the use of the substituted phosphine ligands in comparison with triphenylphosphine.

Phosphite ligands have been shown to give even more active catalysts than arylphosphines.[49,57] The R-O group on the phosphorus atom tends to withdraw electron density from the phosphorus atom to quite a large extent, thus giving an electron-poor ligand. Phosphite and amidophosphite ligands have been studied in the hydroformylation of styrene,[58,59] the structures of which are giving in Figure 1.12.

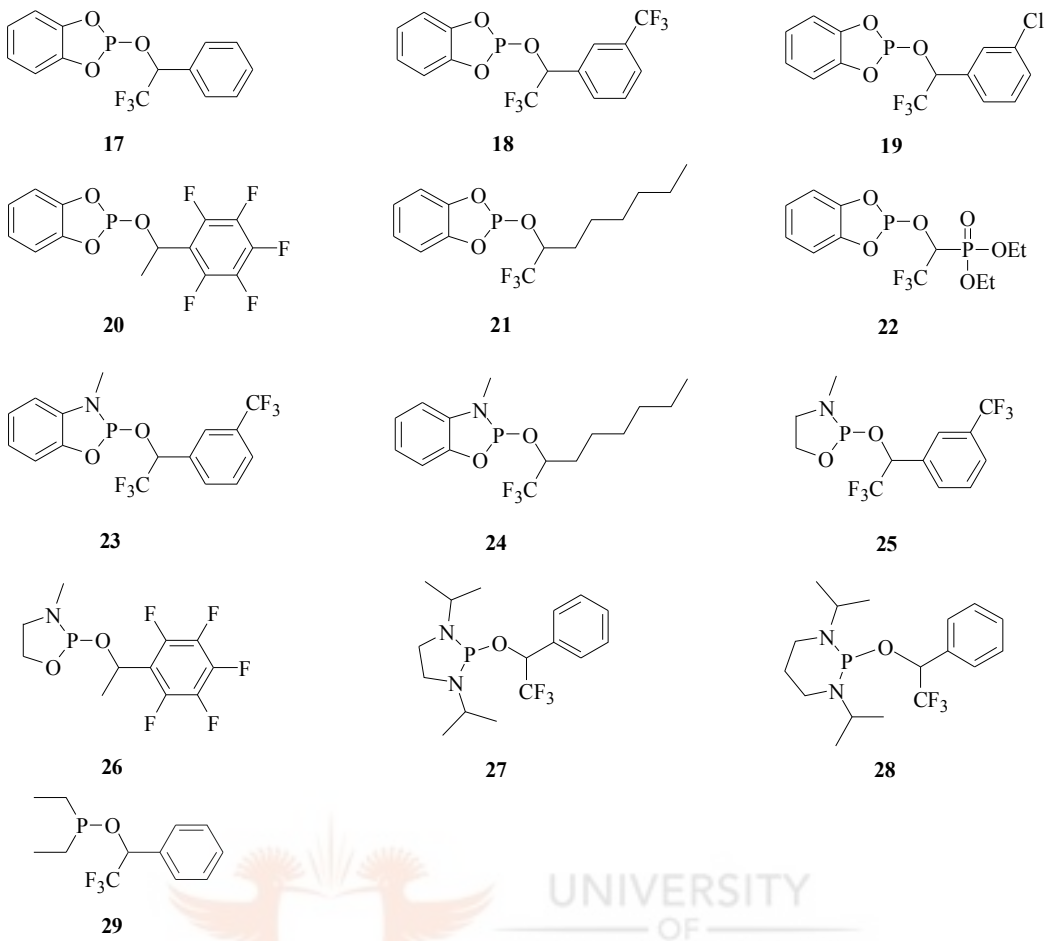
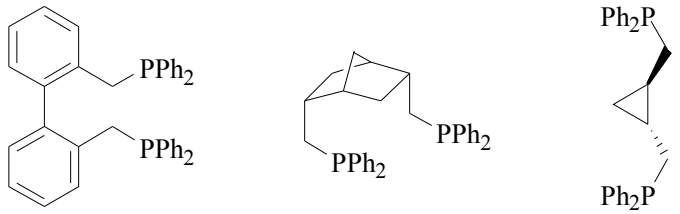


Figure 1.12

In the one study[58] the phosphite ligands **17-20** as well as the phosphinite ligand **29** gave excellent catalytic activities at 100 °C. In another study[59] the phosphite ligands **21** and **22** as well as the amidophosphite ligands **23-28** also gave excellent yields of aldehyde under mild conditions (70 °C, 100 atm syngas, 2 h). With ligands **25**, **27** and **28** slightly lower catalytic activities were observed, which therefore indicated that the replacement of the aromatic ring with alkyl chains gave rise to slightly more electron-rich phosphite ligand.

Bidentate ligands behave similarly to their monodentate counterparts with regards to electronic effects. However, an additional factor plays a role here, namely the 'bite angle'. This complicates matters as the efficiency of σ-donation from the phosphine ligand to the metal centre is dependent on the size of this bite angle. Generally it is accepted that the smaller the bite angle the better donors the pair of phosphines become.[2] This is shown for a range of diphosphine ligands, which will be given in the next few examples.

Diphosphines with simple alkyl chains in the backbone such as dppm and dppe (Figure 1.4), have generally small bite angles (around 90°) and as a result these ligands have shown to give low reaction rates within the hydroformylation reaction.[60] Other diphosphines with more extensive or rigid backbones such as ligands **30**, **31** and **32** (Figure 1.13) have larger bite angles (113°, 126° and 107°, respectively) and as such give higher reaction rates (factor of 5-6 times higher).[61a,b,c]



30 **31** **32**

Figure 1.13

One set of diphosphine ligands that provide the backbone for tuning bite angles is the xantphos ligands, which is based on xanthene.[62] A few of these xantphos ligands which have been studied by van Leeuwen *et al.*[63] are given in Figure 1.14. They performed the hydroformylation of 1-octene and styrene under mild conditions (80 °C, 20 atm syngas pressure and 120 °C, 10 atm syngas pressure, respectively), the results of which are shown in Table 1.4.

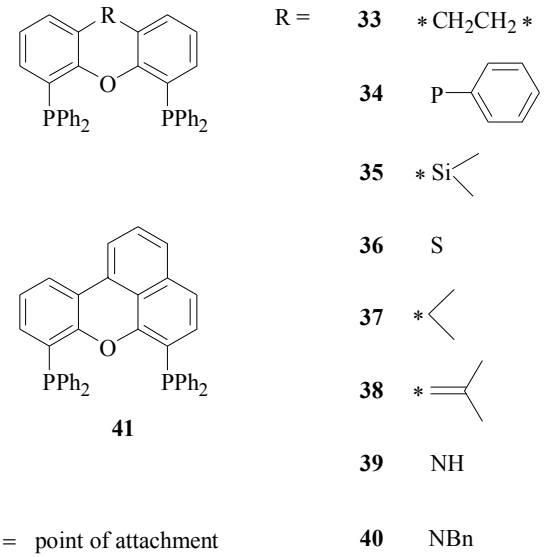


Figure 1.14

Table 1.4 Hydroformylation results with xantphos ligands.

		Hydroformylation of 1-octene		Hydroformylation of styrene	
Ligand	**Bite angle (°)**	**TOF ($mol.mol^{-1}.h^{-1}$)**	**l:b**	**TOF ($mol.mol^{-1}.h^{-1}$)**	**l:b**
33	102.0	36.9	8.5	5766	0.68
34	107.9	74.2	14.6	4960	1.13
35	108.5	76.5	34.3	4240	0.99
36	109.6	94.1	56.6	2735	1.22
37	111.4	187.0	52.2	6384	1.45
38	113.2	162.0	49.8	6010	1.45
39	114.1	154.0	50.6	7386	1.78
40	114.2	160.0	69.4	9148	2.04
41	120.6	343.0	50.2	14602	1.78

It is clear from this table that, with a few exceptions, the increase in the bite angle led to an increase in the reaction rate of both hydroformylation reactions. In the hydroformylation of styrene this effect on activity does not show a linear correlation for the first few ligands, but from ligand **36** onwards this effect is observed. The linear to branched ratio also generally increases along the series, which, as will be discussed later on, is probably due to larger steric effects. Similar observations are made with diphosphites.[64]

To establish the effect of changes in the diphosphines on the electronic character of the phosphorus atoms, van Leeuwen *et al.*[65] performed a study on thixantphos **36** by substituting different groups on the *para* position of the phenyl rings, as indicated in Figure 1.15, and then applying the resulting ligands in the hydroformylation of 1-octene using the same conditions as before. The results are given in Table 1.5.

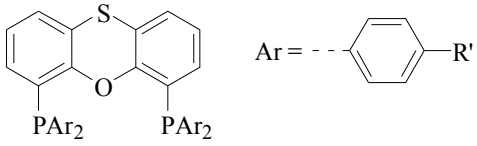


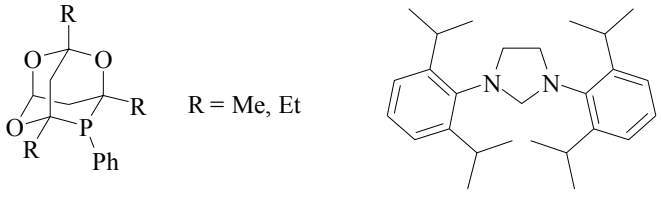
Figure 1.15

Table 1.5 Hydroformylation results of different thixantphos ligands

Ligand where R' =	ee:ea	l:b	TOF ($mol.mol^{-1}.h^{-1}$)
NMe_2	47:53	44.6	28
OMe	59:41	36.9	45
Me	66:34	44.4	78
H	72:28	50.0	110
F	79:21	51.5	75
Cl	85:15	67.5	66
CF_3	92:8	86.5	158

From Table 1.5 it was observed that subtle changes in the electronic properties of the phosphorus atom had an influence on the activity as well as selectivity of the Rh-catalyst in the hydroformylation reaction. As the basicity of the phosphine ligands decreased (in order from NMe_2 to CF_3), a general trend of increasing reaction rate was observed, with a few exceptions (F and Cl). This decrease in basicity of the ligands also led to an increase in the equatorial-equatorial co-ordination of the ligands on the rhodium centre, which in turn also increased the linear to branched aldehyde ratio.

A few examples of other type of ligands that have also been reported for their use in the hydroformylation reaction include the use of $AsPh_3$ and $SbPh_3$ which reveal different electronic properties from that of triphenylphosphine as was discussed before for the Co-catalysed hydroformylation reaction.[48] Ligands of the type **42** (Figure 1.16) have shown to form catalysts with similar activity to phosphite ligands in the hydroformylation reaction.[66] N-heterocyclic carbenes such as **43** have also been successfully utilised in the hydroformylation reaction. These carbenes are found to be quite electron-rich in nature and as a result high catalytic loadings and long reaction times are required for quantitative conversion of alkenes into aldehydes.[67,68]



42 **43**

Figure 1.16

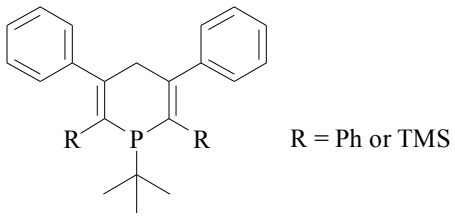
Diamine ligands have been found to form catalysts that can perform the hydroformylation reaction at room temperature with high activity and selectivity towards the branched aldehyde.[69] Bidentate ligands with P, E- moieties (E = O, S or Se) as well as Se, Se- moieties, have also shown to have different electronic properties and as a result have different effects on the activity and selectivity of the Rh-catalysed hydroformylation reaction.[70,71,72]

1.4.2.2 Steric effects in the Rh-catalysed hydroformylation reaction

Steric effects in the Rh-catalysed hydroformylation reaction are not easy to rationalise as so many different observations lead to different conclusions. To try and define what steric effects are and how and when it influences the hydroformylation reaction, a few aspects need to be kept in mind. Firstly, steric bulk is described in terms of Tolman's 'cone angle', as previously discussed, which is only a relative parameter that gives an estimate idea of the steric properties of ligands, but does not always reveal the true effects when applying these ligands in catalysis. Secondly, co-ordination onto a rhodium centre can take place either in an equatorial-equatorial or an equatorial-axial fashion and depending on the basicity of the phosphine ligand as well as the steric bulk the ee:ea ratio can vary to a great extent. Furthermore steric properties of ligands are found to mainly influence regioselectivity in the hydroformylation reaction. However, such characteristics can also have an influence on the reaction rate. In some cases the regioselectivity observed may actually be a result of electronic effects rather than steric effects. Some examples will be given in order to explain these statements.

With simple alkyl- and arylphosphines the Tolman cone angle can vary significantly with small differences in the structure as can be seen, for example, in Table 1.3. However, no significant steric effects have been observed for these class of ligands. In this example[53] it can be noted from Table 1.3 that there is no significant difference in the linear to branched aldehyde ratios for these ligands, with the exception that ligands **3** and **5** (having quite large cone angles of 198° and 211°, respectively) show a small selectivity towards the branched aldehyde. With the substitution of methyl and ethyl groups on the *ortho* position of the phenyl rings of tri-aryl phosphines, it was shown that the linear to branched aldehyde ratios obtained in the hydroformylation of propene with these ligands were all similar to those of

triphenylphosphine, despite significant differences in the Tolman cone angle.[56] However, bulky phosphine ligands such as **44** (Figure 1.17) have shown to give high selectivity towards branched aldehydes (93%) during the hydroformylation of styrene.[73]



44

Figure 1.17

Phosphite ligands exert significant influences on the activity and regioselectivity of rhodium catalysts.[2] When phosphite ligands with large steric bulk are applied to rhodium species, unstable rhodium complexes are formed, which may lead to the co-ordination of only one phosphite ligand on the rhodium centre. This has shown to be the case for tri-(*o-tert*-butylphenyl)phosphite, which has a cone angle of 180°.[74] A complex of the form $HRh(CO)_3L$ (L = phosphite ligand) was formed, which was found to be an electron-poor complex. As a result the hydroformylation of 1-alkenes with these kinds of bulky phosphite catalysts performed at turnover frequencies up to 170 000 $mol.mol^{-1}.h^{-1}$.[75] These ligands show a low selectivity towards the linear aldehyde, due to fast carbon monoxide consumption that leads to rapid isomerisation of the alkene.

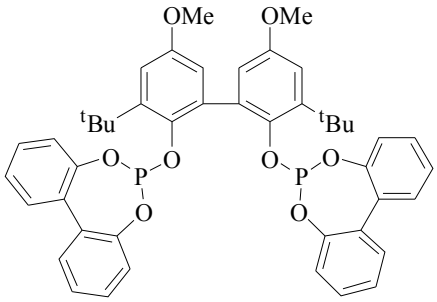
The phosphite and amidophosphite ligands in Figure 1.12 were also shown to enhance the selectivity of the rhodium catalyst towards the branched aldehyde product with values ranging from 77-91%.[59] Here it is said that the $HRh(CO)L_2$ complexes formed and thus the reasoning behind the effect observed for mono-ligated catalysts with bulky phosphites cannot be applied here. Even though it is not mentioned in the article, one might fairly anticipate that the relatively bulky nature of these ligands might result in a preference for equatorial-axial co-ordination of the ligands, as the steric bulk might be too large for an equatorial-equatorial co-ordination. This, together with the fairly electron-deficient nature of the complex, should lead to enhanced co-ordination of the alkene in the fashion that leads to the branched aldehyde.

In bidentate ligands the steric bulk as well as the bite angle determines the steric effects of these ligands. Firstly, the bite angle influences the ee:ea ratio of ligated catalysts. Since the equatorial axis is perpendicular to the axial axis, it can be expected that bidentate ligands with bite angles close to 90° would co-ordinate in an equatorial-axial fashion. Bite angles close to 120° will lead to equatorial-equatorial co-ordination as this is the angle of choice between ligands on the equatorial plane. Another way of explaining this includes the number of atoms that bridge the two phosphorus atoms.[2] When only a small number of atoms bridge the two donor atoms (≤ 4) equatorial-axial co-ordination of the resulting ligands takes place, while when a large number of atoms bridge the donor atoms (≥ 5) the co-ordination tends to be in an equatorial-equatorial fashion. A general trend that has been observed for equatorial-axial ligated complexes is that these complexes give low selectivity for the linear aldehyde. When high selectivity to linear aldehydes is obtained with certain complexes, these complexes were found to possess ligands that were co-ordinated in an equatorial-equatorial fashion. The reverse reasoning is not true, since there are many complexes having the bis-equatorial arrangement that give low selectivities.[2]

The hydroformylation results given in Table 1.4 for the xantphos ligands show that an increase in the bite angle causes an increase in the linear to branched aldehyde ratio, thus in some way supporting the theory above. However, when the ee:ea ratio for these ligands were determined,[63] no clear correlation between the ee:ea ratios and the regioselectivity could be observed. The ee:ea is therefore not the key parameter that controls the regioselectivity, but something else also plays a defining role. It is suggested that an expansion in the steric bulk around the bis-equatorial axis due to wider bite angles may lead to favoured co-ordination of the alkene having the least sterically hindered conformation. Thus the branched alkene are "forced" to undergo isomerisation instead to form the 1-alkene species.

For other diphosphines as well as diphosphites similar observations were made by various authors.[64,76] A very good example of a bis-equatorial ligated complex recently reported to provide excellent selectivity is that formed by $Rh(CO)_2(acac)$ and BIPHEPHOS (**45**, Figure 1.18).[77] High conversions with yields up to 86% of aldehyde were obtained where the linear to branched aldehyde ratio was 99:1. Another example is the pyrrole-based tetraphosphorus ligand **46** (Figure 1.18) with which the hydroformylation of 2-hexene and 2-octene gave

linear to branched aldehyde ratios of 80.6 and 51.7, respectively at 100 °C and 10 atm syngas pressure.[78]



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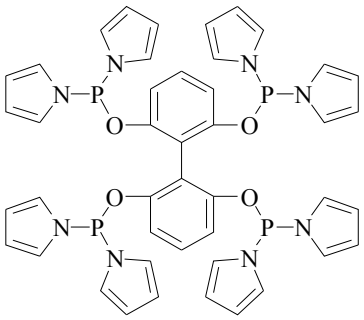


46

Figure 1.18

1.5 The effect of stereo-electronic properties of ligands on Pd-catalysed cross-coupling reactions

For comparison to the hydroformylation reaction, the stereo-electronic effects of ligands in the Pd-catalysed cross-coupling reaction and related reactions will briefly be discussed. Here in contrast to what was observed in the hydroformylation reaction, increasing ligand basicity leads to faster reactions. The cross-coupling reaction and related reactions such as the allylic alkylation reaction, Heck reaction and Suzuki reaction are important tools for the formation of carbon-carbon bonds. The common first step of these reactions involves an oxidative addition of an aryl- or alkylhalide onto the palladium catalyst, which in many cases has been found to be the rate-determining step in these reactions.

1.5.1 The generic mechanism of the Pd-catalysed cross-coupling reaction

The general mechanism involved in the Pd-catalysed cross-coupling reaction is outlined in Figure 1.19.[79] It starts with the oxidative addition of an alkyl- or arylhalide **b**' onto the zero-valent palladium catalyst **a**', resulting in the formation of complex **c**'. With the use of chlorides or bromides in **b**' this step is usually slow, and evidently becomes the rate determining step. With the use of iodides this is found to not be the case. The next step involves transmetallation of complex **c**' with an organometal **d**' which results in the

replacement of the halide with the alkyl or aryl group on the other metal to form complex **f'** and the metal salt **e'**. Various metals can be used in this process as indicated in Figure 1.19 and this step is usually fast irrespective of the metal. Complex **f'** undergoes reductive elimination to form the carbon-carbon bond between the alkyl or aryl groups forming the product **g'** and to reproduce the catalyst **a'**. The last step is also fairly slow and has been found that ligand modifications can influence this step as well.

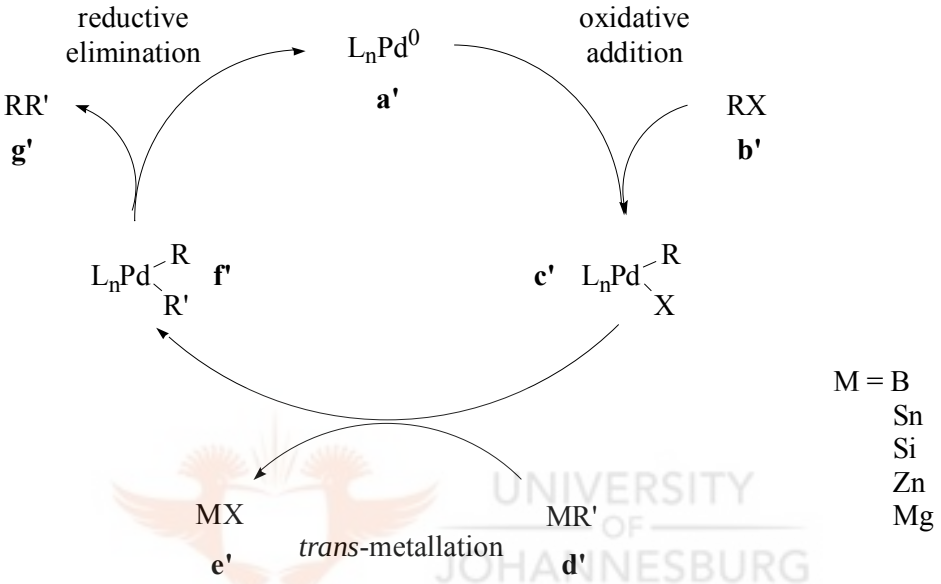


Figure 1.19

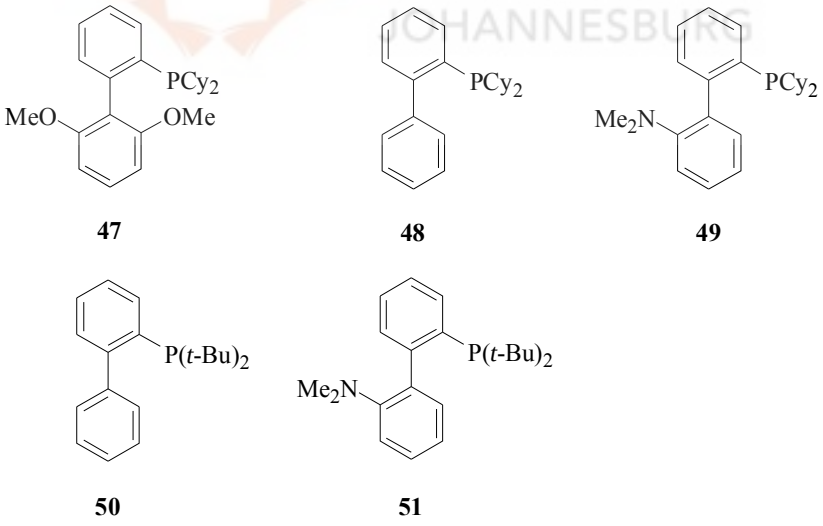
1.5.2 Ligand effects within the Pd-catalysed cross-coupling reaction

Electronic and steric properties both influence the outcome of the Pd-catalysed cross-coupling reaction by means of altering the reaction rate. In general electron-rich ligands lead to stabilisation of the palladium catalyst and as a consequence to an increased reaction rate.[80] It has been shown that alkylphosphines (having an electron-rich nature) in general increase the oxidative addition of aryl chlorides, which are typically unreactive.[81]

Buchwald *et al.*[82] designed *ortho-ortho*-disubstituted biaryl monophosphines, which to allow the cross-coupling of organozinc reagents with aryl chlorides. Ligands such as **47** (Figure 1.20) were found to be fairly electron-rich which stabilises the palladium catalyst through interaction of the aryl π-system with the empty *d*-orbitals on the metal. Cross-coupling

reactions at room temperature and low catalytic loading with these ligands give quantitative yields. The non-substituted biphenyl ligand **48**, however, gave little to no yields of the desired product, which was probably due to *ortho*-metallation that took place in the vacant space needed for oxidative addition, thus poisoning the catalyst.[83] Attempts to substitute electron-withdrawing groups instead of electron-donating groups resulted in diminished catalytic activity.[84] In the same paper attempts were also made to substitute strong electron-donating groups such as secondary amines on the biphenyl rings also resulted in diminished catalytic activity, the cause of which is believed to be preferable co-ordination to the organozinc reagent.

In the Suzuki reaction (where the transmetallation step involves a phenylboronic acid), the ligand **49**, which has a electron-donating group (NMe_2) substituted on only one *ortho* position of the biphenyl moiety, provided effective palladium catalysts for the cross-coupling of electron-rich and electron-deficient aryl chlorides at room temperature.[85] Further studies with **48**, **50** and **51**, where the cyclohexyl groups were replaced by *tert*-butyl groups, showed that ligand **50** was more efficient to use in the Pd-catalysed Suzuki reaction than ligand **49**.[86,87]



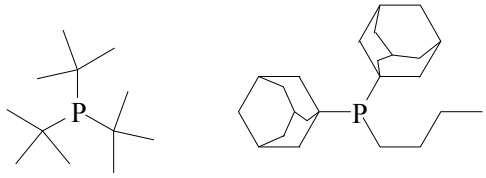
47 **48** **49**

50 **51**

Figure 1.20

The idea behind using bulkier phosphines was driven by the expectation that the bulkier the phosphines becomes, the easier the ligand can dissociate from the palladium centre and as a result the rate of oxidative addition increases. It was found that the larger the cone angle becomes as a result of a bulkier phosphine, the more sp^2 character is forced onto the

phosphorus lone pairs, which raises them in energy.[88] This in turn implies that bulkier phosphines become better σ-donors. Fu and Littke[89] showed that the use of bulky tri-*tert*-butyl phosphine **52** (Figure 1.21) with $Pd_2(dba)_3$ as the palladium source in the cross-coupling of hindered and deactivated aryl chlorides provided yields up to 92% of the desired product. An even bulkier phosphine di(1-adamantyl)-n-butylphosphine **53** (Figure 1.21) also performed the Pd-catalysed cross-coupling reaction of aryl chlorides with high activity providing yields up to 87%.[90]



52 **53**

Figure 1.21

The ligand tricyclohexylphosphine, which is fairly bulky and also quite electron-rich, has shown to provide an efficient catalyst $Pd(PCy_3)_2Cl_2$ for the Suzuki cross-coupling of a range of electron-deficient aryl chlorides, which provided yields between 83% to 98% at 100 °C.[91]

1.6 Conclusion

Homogeneous catalysis is an essential process in many industrial applications. This process mostly involves the use of organometallic catalysts, which are transition metals co-ordinated by organic ligands. The type of ligand plays a significant role in determining the properties of a catalyst.

The electronic property or basicity of a ligand can be defined in terms of changes in the CO vibrational frequencies of complexes such as $Ni(CO)_3L$ (L = ligand). σ-Donor ligands lead to lower vibrational frequencies, while π acceptor ligands cause the vibrational frequency to increase in value. The basicity of a ligand is found to alter the activity of the catalyst, which in turn alters the kinetics of a reaction.

The steric property or bulkiness of a monodentate ligand can be described by Tolman's cone angle. The bulkier the ligand the larger the cone angle becomes. For bidentate ligands the steric properties are described by the bite angle (E-M-E, E = donor atom). The steric properties of ligands mostly influence the ability of a catalyst to selectively allow the formation of one product over another. There are cases where steric effects also influence the reaction rate.

The hydroformylation reaction is an important industrial process which is catalysed by either Co- or Rh-catalysts. Both systems are sensitive to the stereo-electronic properties of ligands. The catalysts for these processes are usually modified by phosphine ligands, although other ligands such as carbenes and amines have been reported for their use in the hydroformylation reaction. Increasing the basicity of these ligands results in a reduction in the reaction rate of these processes mostly because of the increase in the metal-CO bond strength due to more π-back donation onto the carbonyl ligand, which therefore labilises at a slower rate.

An increase in steric bulk around the ligand can have several outcomes. First it can cause an increase in the linear to branched aldehyde ratio due to the increase in steric hindrance around the equatorial plane of the catalyst towards the incoming alkene, which would preferably co-ordinate in a linear fashion. Alternatively the ligand can also become so bulky that either only one of these ligands can co-ordinate or that two ligands would co-ordinate in an equatorial-axial fashion. In either case the co-ordination of the alkene is less hindered by the steric bulk and as a result more of the branched alkene species can co-ordinate onto the metal leading to a decrease in the linear to branched aldehyde ratio.

In the Pd-catalysed cross-coupling reaction the electronic properties of ligands cause the opposite effect to that in the hydroformylation reaction, where an increase in the basicity of the ligand causes an increase in the reaction rate. Here the electron-rich ligand stabilises the palladium catalyst enhancing its ability to undergo oxidative addition with aryl halides. It was also seen that bulkier ligands led to increased reaction rates.

1.7 Aim of present study

From the literature it is clear that ligands with different stereo-electronic properties exert different effects in the hydroformylation reaction. However, no systematic study has been performed on the effects of substitution of various groups on phosphine ligands on the hydroformylation reaction. Most authors agree as to the evidence that electron-poor ligands enhance the reaction rate of the hydroformylation reaction, while bulky ligands alter the linear to branched aldehyde ratio significantly compared to small ligands. However, no definite conclusion can be made from their work as to how manipulations on the ligands affect the hydroformylation reaction, since different authors use different reaction conditions and rhodium catalysts to perform the hydroformylation reaction. Accordingly, an aim of the present study's aim is to synthesise a series of ligands with systematic changes in their electronic and steric properties and to analyse their effects on the Rh-catalysed hydroformylation reaction under an uniform set of reaction conditions. In this way the only variable that would play a role in the reaction is the use of a different ligand and thus any changes in the outcome of the hydroformylation reaction would be directly correlated to ligand effects.

Another aspect of the study is to determine whether phosphine-borane complexes may be employed directly in the hydroformylation reaction without prior deprotection. Normally phosphines are protected with borane due to their sensitivity towards oxidation. In order to utilise the ligand the phosphine-borane complex first needs to be deprotected before the ligand can be applied to a catalytic process. This involves another step in the whole procedure and the phosphine ligand is still at risk as it can be oxidised in the process. The possibility of applying phosphine-borane complexes in CO-based reactions such as the hydroformylation reaction in which the *in situ* deprotection of the phosphine-borane adduct and subsequent formation of the ligand-modified catalyst is anticipated to proceed forms the second major aim of this study.

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