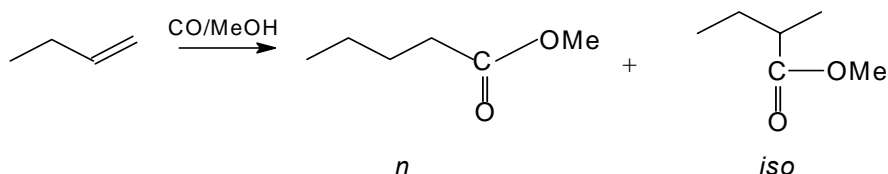


2 LITERATURE OVERVIEW

2.1. INTRODUCTION

The hydroesterification of an alkene with carbon monoxide (CO) in the presence of a palladium catalyst is known to form a carboxylic acid and/or ester in the presence of water (H₂O) or an alcohol, respectively. Carboxylic acids and esters are important chemicals used in the manufacture of products such as solvents, flavourings and perfumes.¹ Many articles and patents have been published and filed on the subject of hydroesterification and various types of alkenes was studied, such as cyclohexene,¹ ethylene (C₂H₄),^{2,3,4,5,6} propene,⁷ styrene,⁸ etc. The key of this study is to find an effective and economical route to produce the ester, methyl propionate (MePr) and the most attractive route is the Pd catalyzed methoxycarbonylation of ethylene (C₂H₄). The study is thus concerned with the hydroesterification of C₂H₄ with CO to produce MePr. Methoxycarbonylation is the hydroesterification process in which MeOH is used as the alcohol. The general reaction can be written as shown in Scheme 2.1.



Scheme 2.1. The hydroesterification of an alkene to form the corresponding ester.

For alkenes having more than two carbon atoms (propene and upwards), two possible products can form when it reacts with CO and MeOH, namely, the linear (*n*) and the branched (*iso*) product. C₂H₄ only forms the linear product (MePr). A range of possible products can be formed from the reaction of C₂H₄ and CO in MeOH as was illustrated in Scheme 1.1. The Pd catalyst usually consists of palladium acetate (Pd(OAc)₂), a phosphine ligand, as well as acid containing a weakly or non-coordinating anion. The metal cation therefore needs to have easily available coordination sites capable of activating the reacting C₂H₄ and CO molecules.

An overview of literature confirms the importance of this reaction and a recent book by Van Leeuwen,⁹ as well as important review articles by Robertson¹⁰ and Drent^{11,12} give important summations on the development of the Pd catalyzed reaction of C₂H₄, CO and MeOH. The key points of the reaction are summarised in the following paragraphs.

2.2. BRIEF OVERVIEW: METHOXYCARBONYLATION PROCESS

C₂H₄ and CO copolymerisation was first achieved *via* radical polymerisations.¹³ High pressures were required and the polymers had low weights. Also, the incorporation of CO was usually lower than required for a perfect alteration of C₂H₄ and CO. Reppe,¹⁴ employing nickel cyanide catalysts, discovered coordination polymerisation. In addition to the low molecular weight polymers, diethylketone and propanoic acid were also produced. Gough used the first Pd catalyst¹⁵ in obtaining the alternating copolymerisation of C₂H₄ and CO and reported it in 1967. Severe reaction conditions (temperatures up to 250 °C and pressures of 2000 bar) were used in the process and low rates and yields were obtained. The catalyst systems employed were PdCl₂(PR₃)₂ complexes (R = tertiary group). In the early 1980's Sen and co-workers¹⁶ published work in which tertiary phosphine Pd complexes were employed as catalysts, with tetrafluoroborate as the weakly coordinating anion. The reaction, where polyketone formed as product, was done in dichloromethane and although very mild conditions were used, the reaction rates, as well as yields, were still low. The use of weakly coordinating anions and phosphines together with Pd gave much more stable and active catalysts for the formation of the polyketone.

The major breakthrough came from work done by Shell Research in Amsterdam¹⁷ where similar Pd catalysts were used as those studied by Sen. In these reactions MeOH was used as solvent, resulting in the methoxycarbonylation of C₂H₄ to form MePr. Good initial results were obtained using a catalyst system containing Pd^{II}, PPh₃ and a strong acid (*e.g.* MsOH). The disadvantage of this system, however, is that, in the presence of strong acids phosphonium salts are formed, which leads to deactivation of the catalyst. Addition of weaker acids such as CF₃COOH inhibits this side reaction to some extent, but also leads to lower activity. When bidentate tertiary phosphine ligands were used in the processes no MePr formed; the product was perfectly alternating polymers with high molecular weight at very high rates (~ 6000 g/g of Pd/h). Also, mild reaction conditions was used (90 °C, 45 bar) in these processes. Two bidentate phosphines, 1,3-bis(*di-tert*-butylphosphino)propane (dtbpp)¹⁸ and a similar ligand, namely 1,2-bis(*di-tert*-butylphosphino)-*o*-xylene (dtbpx),¹⁹ are exceptions to the rule, see Figure 2.1.

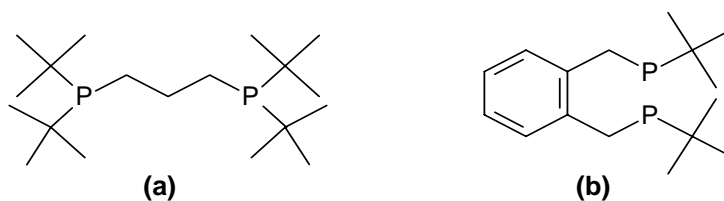


Figure 2.1. a) 1,3-bis(di-*tert*-butylphosphino)propane and b) 1,2-bis(di-*tert*-butylphosphino)-*o*-xylene.

Both gave MePr as main product with activities of up to 17000 mol MePr/mol Pd/h for 1,3-bis(di-*tert*-butylphosphino)propane and an even higher activity of 50 000 mol MePr/mol Pd/h for 1,2-bis(di-*tert*-butylphosphino)-*o*-xylene, which also gave excellent selectivities (99 % MePr). The disadvantage of these ligands is that they are very expensive. Although the monophosphine catalysts are several orders of magnitude slower than the bidentate catalysts, a cheaper alternative might be PPh_3 . Proper understanding of the catalyst system is needed to help in the development of an efficient catalyst system.

2.3. ELEMENTARY REACTIONS⁹

The elementary reactions are the same for MePr and polyketone formation: formation of an initiating species, propagation (insertion of C_2H_4 and CO), and a termination reaction.

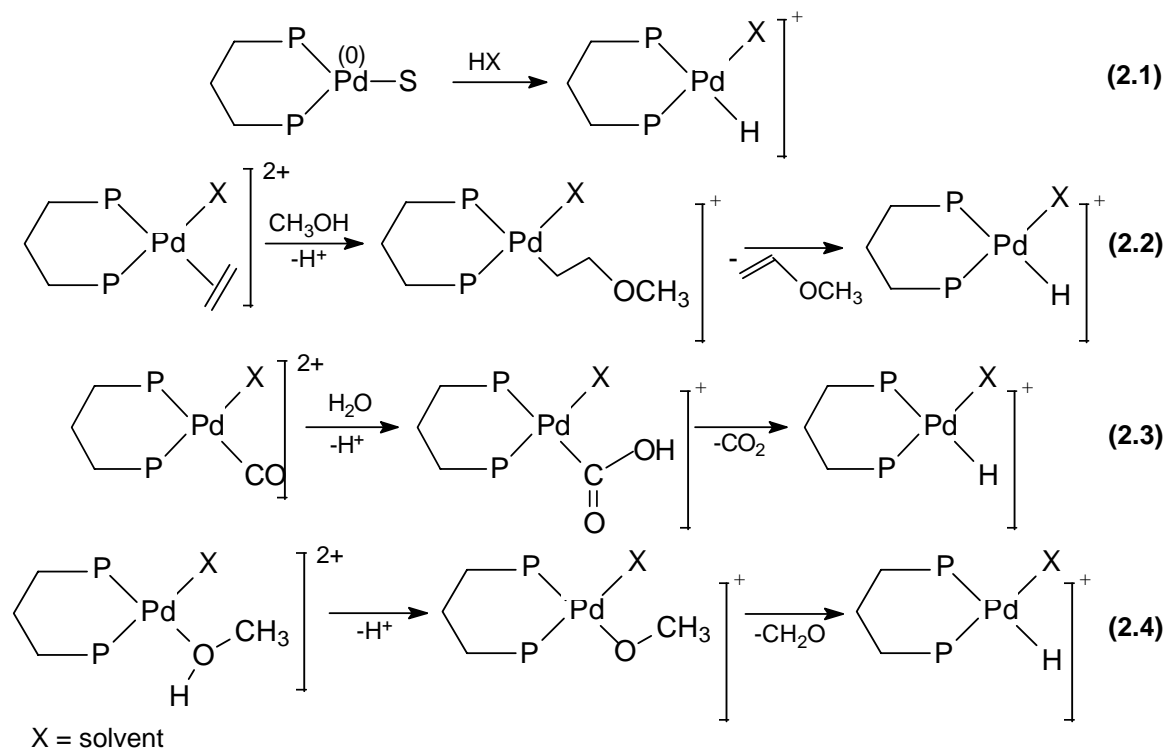
2.3.1. Initiation

The catalysts are cationic Pd phosphine systems that are prepared from $\text{Pd}(\text{OAc})_2$, an excess of monodentate phosphine (e.g. PPh_3) or a stoichiometric amount of a bidentate phosphine (e.g. dppe, dppp, dppb) and a Brønsted acid of a weakly or non-coordinating anion (e.g. MsO^- , TfO^-). The catalyst is made *in situ* by dissolving the reactants in MeOH. A Pd-alkyl initiator is needed to create the active catalyst when MeOH is not used as solvent, e.g. methylation of Pd with $\text{Sn}(\text{CH}_3)_4$.²⁰ Insertion of C_2H_4 and CO can occur *via* two possible mechanisms - the hydride or/and carbomethoxy mechanism.

The hydride mechanism

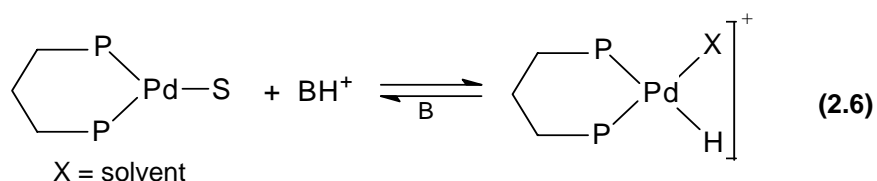
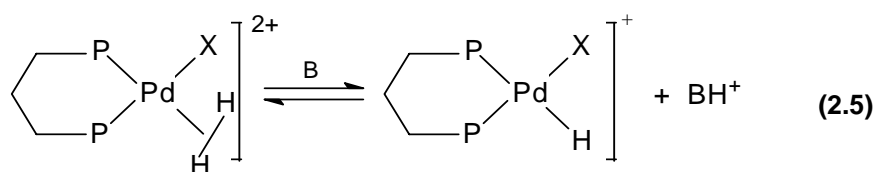
For the reaction in MeOH, without H_2 present, at least four possible routes can be presented in which hydride formation can occur. Equation 2.1 in Scheme 2.2 is the oxidative addition of the acid to a Pd^0 species, resulting in a Pd^{II} hydride complex. A

Wacker type of reaction which forms the hydride is shown in Equation 2.2. Equation 2.3 shows water that attacks at coordinated carbon monoxide, forming the hydride and carbon dioxide. Equation 2.4 shows how a proton is eliminated from a methoxy complex, forming the hydride and formaldehyde.



Scheme 2.2. Four possible routes showing the formation of the Pd-hydride species.

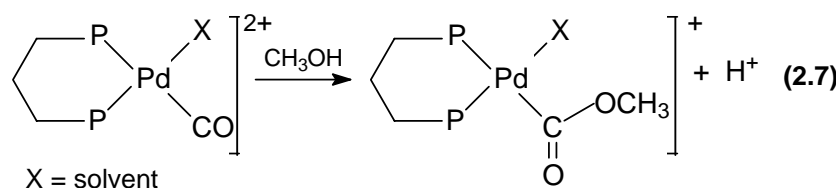
H_2 can also generate the Pd-hydride species as shown in Scheme 2.3. The reaction involves the heterolytic cleavage of H_2 with Pd and a base (Equation 2.5). The hydride is generated by the oxidative addition of acid to a Pd^0 species (Equation 2.6). The hydride species can again be converted back to Pd^0 as shown by the equilibria in Equation 2.5 and 2.6. Therefore, in too basic solution the base would react with the cationic Pd-hydride by abstracting a proton and forming the Pd^0 , which is inactive in polymerization reactions.



Scheme 2.3. The formation of the Pd-hydride species from hydrogen gas as proton source.

The carbomethoxy mechanism

The carbomethoxy species is formed when CO is bubbled through a MeOH solution containing the Pd catalyst, as shown in Equation 2.7 (Scheme 2.4). It can then undergo insertion of alkene that will lead to the formation of products. Exclusion of water is a prerequisite for clean formation of the carbomethoxy species, since the presence of water would give rise to the Pd-hydride complex.



Scheme 2.4. Formation of the Pd-carbomethoxy species.

2.3.2. Migration reactions

The propagation steps in the copolymerization of CO with alkenes and in the alkoxy carbonylation of alkenes catalyzed by Pd diphosphine complexes have been extensively studied and are well understood.²¹ Alkene insertions follow a migratory mechanism in the Pd and Pt square planar complexes with diphosphine ligands and many insertion products have been isolated.²² Alkene insertions with diphosphine ligands are much more complicated than CO insertion reactions.²³ Attempts to insert an alkene on Pd-acetyl complex would result in failure, since decarbonylation would occur. Under a CO pressure, however, insertion does occur and the observed rate of the alkene insertion depended on the CO pressure, due to the competition between CO and C₂H₄ coordination. Also, after C₂H₄ insertion did occur into the acetyl species β -hydrogen elimination occurred, except when norbornene or norbornadiene was used as alkenes. With these alkenes *syn* addition takes place and in the strained skeleton

no β -hydrogen elimination can take place.^{24,25} Therefore, most studies on alkene insertion and isolation of the intermediates employed these alkenes.

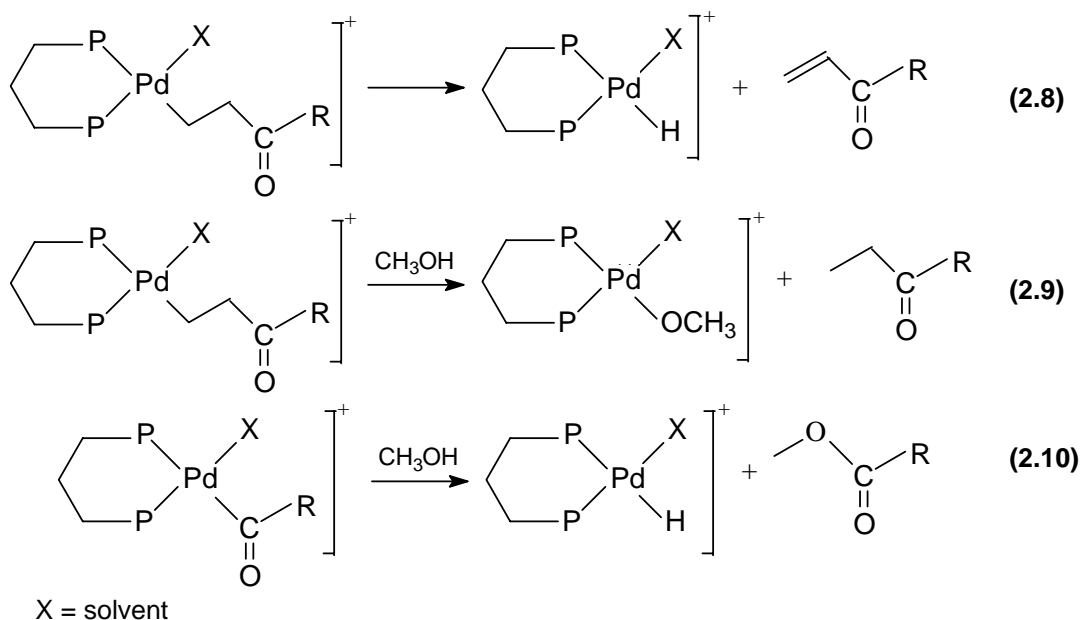
Strain and steric properties of the alkenes determine the rate of insertion.⁹ The insertion of C_2H_4 into the carbomethoxy complex $[Pd(dppp)((CO)(OCH_3))]^+$ is less reactive than the corresponding acetyl complex, $[Pd(dppp)((CO)(CH_3))]^+$, which is ascribed to the higher nucleophilicity of the acetyl group compared to the carbomethoxy group. Brookhart and co-workers succeeded in measuring the barrier for C_2H_4 insertion into $[Pd(dppp)((CO)(CH_3))]^+$, at 160 K ($\Delta G^\ddagger = 51.4$ kJ/mol).²⁵ The conclusion was that C_2H_4 inserts faster than CO in an ionic Pd-alkyl complex. The insertion of C_2H_4 into a Pd-methyl or -ethyl species, however, is more difficult, since the barrier of insertion for C_2H_4 was higher ($\Delta G^\ddagger = 67$ kJ/mol at ~ 233 K). At higher temperature the overall barrier will be higher, because alkene coordination will be disfavoured by entropy and competition with CO and solvent. Formation of CO complexes will also be less favourable at higher temperatures.

Stepwise mechanistic studies have been on alternating insertions.^{26,27,28,29,30} For the copolymerisation of an alkene and CO, the reaction proceeds *via* a perfectly alternating sequence of alkene and CO. This is surprising, since alkene insertion has a thermodynamic advantage over CO insertion. The CO insertion is in many cases thermodynamically unfavourable. The thermodynamically most favourable product in hydroformylation and carbonylation reactions is always the formation of low or high-molecular weight alkanes or alkenes, if chain termination occurs *via* β -hydride elimination. The insertion of CO is therefore always kinetically controlled. When a Pd-alkyl species has formed, a CO molecule will coordinate in the vacant site. CO coordinates more strongly to Pd than C_2H_4 , even when the Pd-centre is cationic. The reason for this is probably steric in nature, since the cone angle of C_2H_4 is much larger than that of CO and therefore the steric hindrance for the C_2H_4 complex is much larger. If the barriers of activation for the insertion of C_2H_4 and CO are of the same order of magnitude, insertion of CO will take place. For CO this insertion may be reversible and only after insertion of C_2H_4 has taken place will the CO insertion lead to chain growth. The Pd-acyl complex will then also preferentially coordinate to CO instead of C_2H_4 . Double insertions of CO do not occur because this is thermodynamically even more unfavourable, and in addition the migration of more electronegative groups to CO is usually slower. An "occasional" co-ordination of C_2H_4 now leads to insertion of C_2H_4 and thus a perfect alternation of the two monomers occurs. After insertion of C_2H_4 a

stable intermediate is formed as a result of the intermolecular coordination of the ketone group

2.3.3. Chain termination and chain transfer

The termination steps of the reaction have mostly been studied by the end group analysis of the polymer chains.³¹ Studies were also done where some, or all, of the intermediate species involved in chain transfer by alcoholysis of the acyl and alkyl chain, were identified.^{20,28} The common chain termination reactions comprise β -hydrogen elimination (Equation 2.8), protonation of a Pd-alkyl complex (Equation 2.9) and nucleophilic attack at Pd-acyl complex (Equation 2.10), as shown in Scheme 2.5.

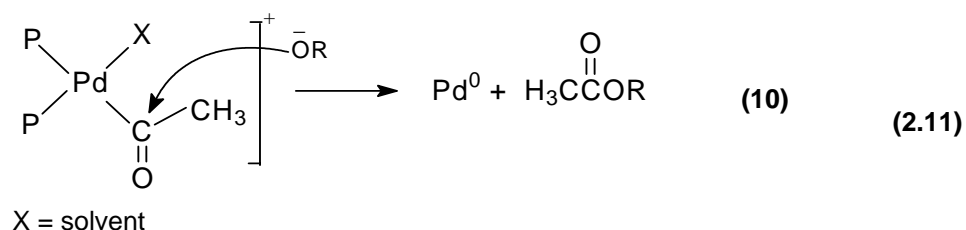


Scheme 2.5. Possible chain termination reactions.

The resulting hydride and methoxy complexes start a new chain *via* insertion of a molecule of C_2H_4 or CO, respectively. MeOH is actually the chain transfer reagent in the last two reactions. Other chain transfer reagents may also be used but will lead to different end groups.

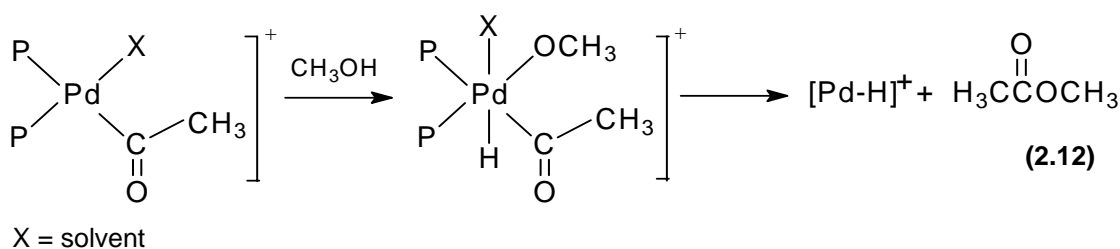
When the chain transfer is fast, the reaction observed is the alkoxy carbonylation of C_2H_4 , which is nothing but a perfect chain transfer after insertion of just two monomers. Three possible mechanisms that describe ester formation are given below.

The first mechanism is the direct, outer-sphere attack of an alcohol or alkoxide at the acyl carbon atom. This reaction is possible for both *cis* and *trans* diphosphine complexes as shown in Equation 2.11 (Scheme 2.6).



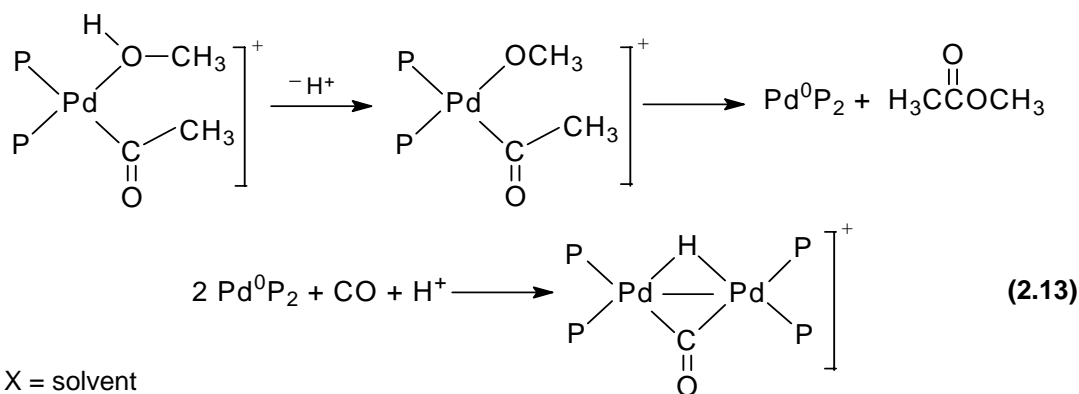
Scheme 2.6. Ester formation by direct attack of an alcohol.

The second mechanism involves the oxidative addition of MeOH to the divalent Pd-acyl complex. The only advantage of this reaction is that the new Pd-hydride initiator is formed in one step, but it is an unlikely reaction. Oxidative addition of alcohols is only known for electron rich Pd⁰ complexes, Scheme 2.7, Equation 2.12.³²



Scheme 2.7. Oxidative addition of an alcohol (MeOH) that leads to ester formation.

The last possibility for ester formation is a reductive elimination step from a Pd-acyl-alkoxy species, formed by deprotonation of the alcohol adducts. It requires *cis* coordination of the alkoxide and the acyl fragment. This mechanism is, however, also very unlikely for monodentate phosphines, since they prefer a *trans* orientation. After the reaction has taken place a Pd⁰ complex remains that has to undergo oxidative addition with the acid to regenerate an active hydride species. Pd⁰ complexes can undergo dimerisation. Oxidative addition of one proton per dimer will form very stable dimers of the type shown in Equation 2.13 (Scheme 2.8).



Scheme 2.8. Ester formation via reductive elimination.

Cis coordination is a prerequisite for ester formation. A *trans* complex therefore, has to rearrange to a *cis* complex, which will undergo reductive elimination. In a *trans* complex neither insertion reactions nor termination reactions will take place.

2.4. LIGAND EFFECTS ON CHAIN LENGTH⁹

Numerous ligands have been tested in polyketone/MePr catalysis, but what the actual relationship between the structure of the ligand and the influence on reaction rates and molecular weight is, is not that clear. Initially it was thought that fast polymerisation catalysts required bidentate ligands with a wide cone angle and a 1,3-propanediyl bridge, and that carbomethoxylation was favoured using monodentate ligands. However, it turned out that neither the bite angle nor the flexibility of the ligand bridge determines the rate of the growth process, but the steric bulk of the ligand. Furthermore, in MeOH as solvent the reaction is also much slower and the molecular weight is much lower. The termination state is thus relatively accelerated by MeOH. This suggests that ester formation is the dominant chain termination mechanism in MeOH as solvent.

The results obtained with the ligands in Figure 2.1 were therefore quite surprising, and the idea that only monodentate phosphine ligands would result in ester formation had to be revised. It was thought then that these bulky ligands easily lead to the formation of *trans*-coordinated, diphosphine complexes, which would explain the results. Another possibility also was that one of the phosphine moieties might dissociate from the Pd centre. Since the catalyst systems and conditions for polymer and propionate formation are very similar, it has to be the ligand that is responsible for the change in growth *versus* termination. For *cis*-bidentate ligands with very large cone-angles the product is an ester rather than polymer. Initially, increasing the steric bulk leads to

faster polymerisation, but at some point it is overtaken by the termination reaction giving propionate.

It is shown in Scheme 2.8 that a prerequisite in order to have ester formation an alcohol group and acyl group must occupy a *cis* orientation. Deprotonation of the alcohol and a migratory reductive elimination leads to ester formation. It is known from many stoichiometric reactions that the reductive elimination of the ester from the Pd-acyl-alkoxide species occurs nearly without an energy barrier.³³ If the termination process then is described as a reductive elimination step, it has important consequences for the impact of steric factors, since reductive elimination is strongly favoured by increasing the steric bulk of the ligand environment. In a study³⁴ on the influence of the bite angle on the reductive elimination of alkyl cyanide from [Pd(diphosphine)R(CN)], it was found that the reductive elimination for these complexes increased by orders of magnitude when the bite angle was increased. All the ligands used contained diphenylphosphino groups, the bite angle in this study is equivalent to the cone angle, or steric bulk of the ligand. The effect of reductive elimination is therefore much more pronounced than effects found on the rates of polymerisation.

The attack of the alcohol at the Pd-acyl complex is considered the rate-determining step for propionate catalysts; therefore the resting state of the catalysts may well be an acyl complex. The conclusion is that fast equilibria exist between the acyl complex and other complexes en route to it, and that the highest barrier is formed by the reaction of an alcohol with a Pd-acyl complex. The precise course of the reaction is not known, however, but it is likely that deprotonation of the coordinating alcohol and the migratory elimination are concerted processes that are accelerated by the steric bulk of the bidentate ligand. It was shown that the reaction of an Pd-acetyl complex and sodium methoxide is very fast and it occurs already at low temperature to give methyl acetate and a Pd^I-hydride dimer.³⁵

Upon changing the reaction medium of the copolymerisation reaction from MeOH to higher alcohols (ethanol, *t*-butanol) the molecular weight of the copolymer produced increased.^{16a-b,24a-b} For styrene-CO-copolymerisation the molecular weight also increased when 2,2,2-trifluoroethanol was used instead of MeOH.³⁶ Therefore, the alcohol also has a distinct effects on the termination reaction, at least relative to the rate of propagation. In stoichiometric reactions of Pd-acetyl complexes the order of decreasing reactivity of alcohols is³⁷:



It can be concluded therefore, that for Pd-complexes containing very bulky bidentate ligands, in the presence of an alkene and CO, will form esters, and those with relatively small ligands give polymer. There is thus competition between chain growth and chain termination. Not surprising then is the fact that the group of ligands with intermediate steric bulk will form oligomers. A few ligands that forms polymer, oligomer, ester or gives no reaction, are shown in Figure 2.2.

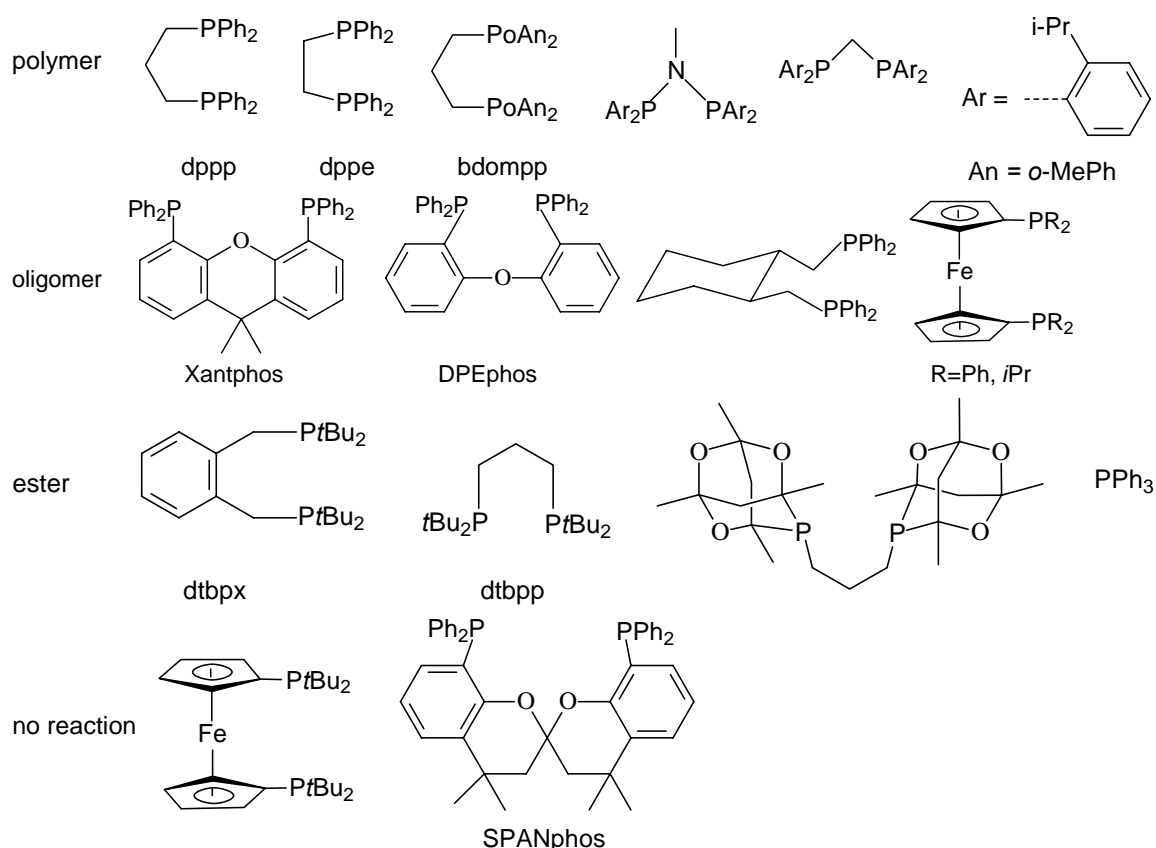


Figure 2.2. Ligands effects in the reaction of C_2H_4 and CO, in MeOH, in the presence of Pd catalysts.

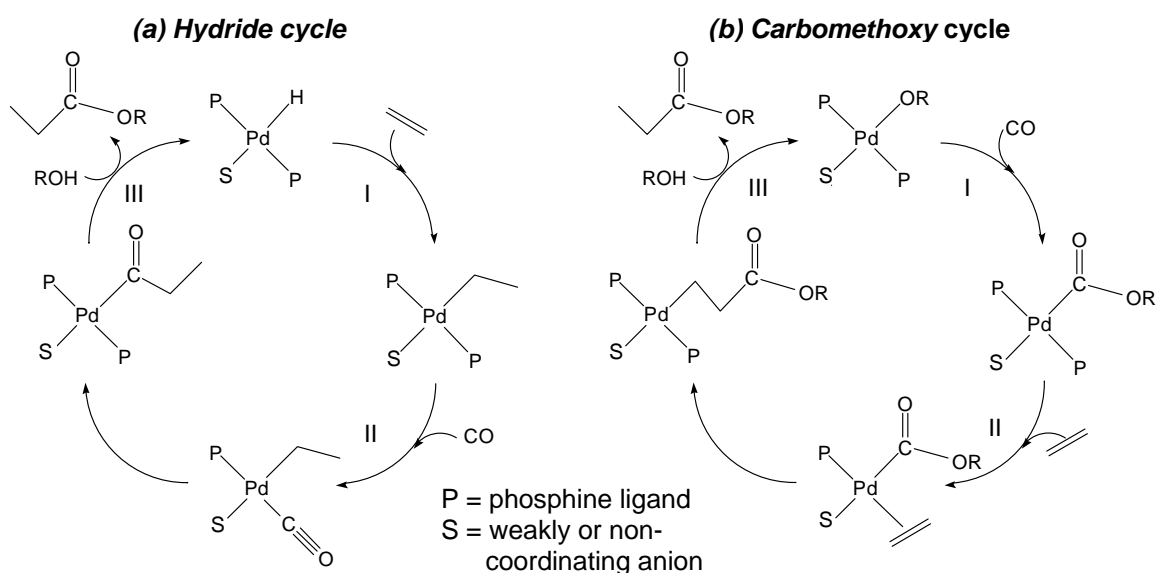
The regular *cis* bidentate ligands would normally form oligomers, but ligands such as Xantphos and DPEphos need to be discussed further. All three these ligands form both *cis* and *trans* complexes, and the rates of reaction are considerably slower than those of the *cis* bidentate ligands. Since *cis* coordination is needed the insertion rates are low and as a result only the proportion that occurs in the *cis* isomer would undergo reactions. The *cis* complexes, however, have relatively large cone angles and therefore, ester formation from the acyl intermediates will be fast and low molecular weight material should form.

Replacing the *t*-butyl groups in dtbpp or dtbpx by the smaller *i*-propyl groups give oligomers instead of the ester, MePr, at high rates. Replacing the 1,3-propanediyl bridge in dtbpp with a 1,2-ethanediyl bridge resulted in the formation of 3-pentanone for the reaction of C₂H₄, CO and H₂ in MeOH. The 3-pentanone was formed at extremely high rates instead of MePr, the product of the more bulky ligand.³⁸ Tris-sulfonated triphenylphosphine, tppts, forms MePr as product, since the resting state of the catalyst has a *trans* orientation.³⁹ *Trans* ligands, such as SPANphos and bis(*di-t*-butylphosphino)ferrocene give no reaction at all, demonstrating that they are strictly *trans*-coordinating ligands. These complexes undergo neither insertion nor termination reactions.

The conclusion can be made that very subtle changes in steric and electronic properties of the ligands can influence the rate of the insertion and chain transfer reaction.

2.5. THE CATALYTIC CYCLES

Two main catalytic routes have been proposed for the methoxycarbonylation process, namely the Pd-hydride route and the carbomethoxy cycle, as illustrated in Scheme 2.9. Up to now evidence for both cycles has been found and described in literature.^{6,22-33}



Scheme 2.9. The two possible routes for the methoxycarbonylation of C₂H₄ and CO in an alcohol to form methyl propionate: a) the hydride and b) carbomethoxy mechanism.

After the hydride species formed, as shown in Scheme 2.9, a C_2H_4 molecule will coordinate and insert into the Pd-hydride bond to form a Pd-ethyl species (step I). Coordination and insertion of CO (step II) leads to the formation of a Pd-acyl complex. Nucleophilic attack of an alcohol on the acyl species allows the release of the alkyl propanoate (step III) and it probably is the rate-determining step. This cycle is believed to be operative in the methoxycarbonylation of C_2H_4 and CO catalyzed by $Pd-PPh_3$ ²⁹ or $Pd-1,2-bis[(di-tertbutyl)phosphinemethyl]-benzene$ ^{2,3} complexes. In a study²⁹ using a $Pd-PPh_3$ complex, the analysis of the phosphorus containing by-products from the catalytic methoxycarbonylation of C_2H_4 with a combination of High Performance Liquid Chromatography (HPLC) and Mass Spectrometry (MS) indicated increasing levels of phosphonium salts through the course of the reaction. The major ones was characterized as methyltriphenylphosphonium (Me^+PPh_3), ethyltriphenylphosphonium (Et^+PPh_3) and 3-oxopentyltriphenylphosphonium ($CH_3CH_2C(O)CH_2CH_2^+PPh_3$) cations, which were isolated as the sulfonate salts. The latter were shown to be produced by metal mediated pathways and are indicative of the operation of the Pd-hydride mechanism. In a deuterium labelling study^{2,3} evidence for a hydride mechanism was obtained in the formation of MePr from CO, C_2H_4 and MeOH, catalyzed by a $Pd-1,2-bis[(di-tertbutyl)-phosphinemethyl]benzene$ complex. The reaction was carried out in CH_3OD using multinuclear NMR and all the possible intermediates were identified. The C_2H_4 and CO copolymerization process^{7,10,11} has also been shown to operate *via* the hydride mechanism. The hydride cycle is also active in the sequential insertion of C_2H_4 and CO into a rhodium complex of PEt_3 used to synthesize 3-pentanone *via* the formation of a Rh-hydride.³⁰ It is believed that hydrogen, water and the acid employed, which can act as Pd-hydride source, have a promoting effect on the catalyst system, while *p*-benzoquinone, that favours the formation of the carbomethoxy species, has an inhibiting effect.⁵

For the carbomethoxy mechanism to be operative in the catalytic cycle the requirement is the initial formation of a carbomethoxy species (step I). It is either formed by migratory insertion of CO into a Pd-methoxy bond or by nucleophilic attack of MeOH on coordinated CO. Coordination and insertion of C_2H_4 into the Pd-carbomethoxy species forms the Pd-EtCOOMe species (step II). Methanolysis (step III) allows for the formation of MePr. This mechanism has been confirmed for the stoichiometric formation of MePr with $Pd-1,3-bis(diphenylphosphino)propane$ complexes. Under catalytic conditions, confirmation of the carbomethoxy mechanism has also been obtained for the formation of poly- and oligo ketones.⁴⁰ It is believed that the carbomethoxy mechanism operates for propyne carbonylation to methyl methacrylate catalysed by Pd complexes of PPh_2py ,⁴¹ as well as in copolymerisation of CO and

C_2H_4 .^{7,10,11} It is also operative in the formation of MePr and methyl propenoate from CO, C_2H_4 and MeOH catalyzed by rhodium complexes containing electron donating β -ketophosphine and related ligands.⁴² All the intermediates in the carbomethoxy cycle have been characterized for the carboalkoxylation of C_2H_4 and CO by a Pd/diphosphine catalyst.²

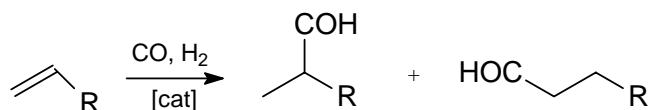
Crossover between the two mechanisms is also possible.¹⁰ Methanolysis of the acyl intermediates when starting with the carbomethoxy cycle leads to the formation of diesters and also to an active Pd-hydride species. Protonation of the alkyl intermediate in the hydride cycle allows crossover to the carbomethoxy cycle, in which keto-esters and diketones will result.

From the above mentioned examples it is clear that evidence for both the hydride and the carbomethoxy cycle exist. To develop an even better understanding of the above mentioned methoxycarbonylation reaction it is also essential to evaluate the fundamental steps and components associated with carbonylation catalysis.

2.6. CARBONYLATION CATALYSIS⁴³

Carbonylation chemistry forms the key in the formation of these important products. Since the discovery of one of the most important carbonylation processes hydroformylation, by Otto Roelen⁴⁴ in 1938, catalytic applications have paved the way of the use of organometallic compounds in industry. Bulk and fine chemicals and even natural products are being produced *via* homogeneous organometallic catalysis.

Hydroformylation is typically the reaction between the double bond of an alkene molecule and the mixture of hydrogen (H_2) and CO (synthesis gas), which leads to the formation of linear and branched aldehydes, Scheme 2.10.



Scheme 2.10. Hydroformylation of an alkene with hydrogen and carbon monoxide gas for the formation of linear and branched aldehydes.

Other important carbonylation processes include hydrocarboxylations, hydroamidations and hydroesterifications. Minor changes in the catalyst system as well as in the reaction conditions can lead to simple carboxylic acids, diacids, polyketones or unsaturated acids as products.

2.6.1. Carbon monoxide

The simple carbonyl group is one of the most versatile functionalities available in chemistry. Not only does its importance stem from its own inherent reactivity, *i.e.* being susceptible to both nucleophilic attack at the carbon and electrophilic attack at the oxygen, but also from the polarizing effect it has on neighbouring atoms and functional groups. It has the ability to stabilize a molecule by stabilizing an adjacent carbanion by charge delocalization into the C=O double bond.

Two possible canonical forms are given for CO, one where a double bond links the divalent carbon and oxygen atoms (“carbenelike” structure, C=O) and the other one where both the atoms has a lone pair of electrons and are linked by a triple bond (“dinitrogenlike” form, C≡O). Formal charges, C(+) and O(-), are present for the more important C≡O form, see Figure 2.3.

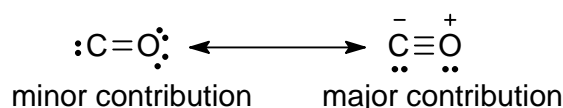


Figure 2.3. Valence bond description of carbon monoxide.

CO is not particularly a reactive molecule, despite having a formally divalent carbon atom. This is largely a kinetic rather than a thermodynamic phenomenon, reflecting the low polarity, high ionization potential and the low electron affinity of the molecule. CO can be regarded as a building block for the synthesis of many organic carbonyl compounds, such as aldehydes, ketones, carboxylic acids, acid halides, anhydrides, esters, amides, imides, ureas, carbonates, carbamates, isocyanates, as well as a wide variety of cyclic compounds. This is because the “incipient carbonyl group” can be introduced directly into a number of different sites in an organic molecule.

Converting a C≡O triple bond to a double bond does not require exceptionally high energy - it can be generated by formation of two additional bonds to carbon. Interestingly, the reaction of CO with Cl₂ involves breaking a Cl-Cl bond (+ 244 kJ mol⁻¹), converting C≡O to C=O (+ 272 kJ mol⁻¹) and forming two C-Cl bonds (-660 kJ mol⁻¹). In bond enthalpy terms the formation of COCl₂ is therefore favoured by about 144 kJ mol⁻¹, and even though an unfavourable entropy term reduces the free energy change somewhat, the experimentally determined value is still a substantial - 73 kJ mol⁻¹. However, the reaction is extremely slow in the absence of photolysis or catalysis. The relative kinetic inertness of CO means that much of its chemistry

depends on the use of extreme conditions, energetic reagents or some form of catalysis.

The simplest examples of such catalysis are the reactions of CO with protic reagents such as alcohols or secondary amines to form esters or amides of formic acid. Alkoxide $[\text{RO}]^-$ or amide $[\text{R}_2\text{N}]^-$ anions catalyze these reactions and the key step is the nucleophilic attack on CO by the catalyst. Organolithium reagents also reacts with CO at low temperatures ($-100\text{ }^\circ\text{C}$) *via* nucleophilic attack to give acyl lithium species. These can then react with trapping agents such as alkyl or silyl halides.

Another type of reaction involves the one-electron transfer to CO from alkali metals in liquid ammonia or ether solvents. Heating the products in air forms a fascinating series of delocalised oxocarbon dianions $[\text{C}_n\text{O}_n]^{2-}$ ($n = 2-6$).

Powerful electrophilic reagents, such as carbenium ions and diborane, attack CO at the carbon atom and form the acylium ions $[\text{R}_3\text{CCO}]^+$ and borane carbonyl $\text{H}_3\text{B}\cdot\text{CO}$, respectively. CO, however, is an extremely weak σ -donor and does not form stable complexes with more conventional Lewis acids such as BF_3 or aluminum chloride.

Transition metals, in contrast to main-group Lewis acids, form a range of complexes containing coordinated CO. The acute toxicity of CO, for example, is because of the ability of CO to complex to iron centres of hemoglobin, and thereby blocking the oxygen-binding sites.

The bond between a transition metal and CO arises when the CO donates electron density from the weakly antibonding $5\sigma^*$ orbital and accepts electrons into its strongly antibonding $2\pi^*$ orbitals, Figure 2.4.

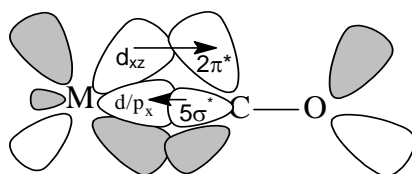


Figure 2.4. Bonding model for coordination of carbon monoxide to a transition metal.

As a result the $\text{C}=\text{O}$ becomes longer, *i.e.* double bond character ($\text{C}=\text{O}$) and a shift in the $\text{C}-\text{O}$ stretching frequency from the value in free $\text{C}\equiv\text{O}$ (2155 cm^{-1}) towards lower wave number is observed. This shift increases in magnitude with increasing negative charge on the metal. The isoelectronic complexes $\text{Ni}(\text{CO})_4$, $[\text{Co}(\text{CO})_4]^-$, $[\text{Fe}(\text{CO})_4]^{2-}$ and $[\text{Mn}(\text{CO})_4]^{3-}$ thus show infrared $\text{C}-\text{O}$ stretching frequencies at 2046, 1890, 1730

and 1670 cm^{-1} , respectively, consistent with increasing occupancy of the antibonding $2\pi^*$ orbitals of the carbonyl ligand as the charge on the metal increases. CO, therefore, has the ability to behave as a strong π -acid and thus stabilise the unusually low oxidation states in transition metal carbonyl complexes (0 to -3), since the build-up of electron density at the metal centre, produced by conventional ligand-to-metal σ -donation, is more than offset by metal-to-ligand electron transfer *via* the π -system.

2.6.2. The chemistry of coordinated carbon monoxide

The reactivity on coordination of $\text{C}\equiv\text{O}$ to a transition metal varies considerably with the type of metal centre involved. A metal in a high formal oxidation state and/or with strong π -acid coligands acts as a strong σ -acceptor but only a weak π -donor. This promotes nucleophilic attack on coordinated CO, as opposed to the behaviour of a metal in a low oxidation state having strongly electron-donating coligands. Although CO itself is already somewhat susceptible to nucleophilic attack, coordination to a metal can greatly increase this susceptibility. The main reason for this is that the negative charge resulting from addition of a nucleophile to coordinated CO is no longer centred solely at the carbonyl carbon, but is delocalised onto the metal and therefore, to any other π -acid ligands that is present. Reactions are known in which the mildest of nucleophiles (water, alcohols, *etc.*) add directly to a carbonyl ligand, under strictly neutral conditions. As expected, the most electrophilic carbonyl ligands are found in cationic, high oxidation state complexes, although even neutral metal carbonyls can react readily with strong nucleophiles, such as dialkylamides, alkoxides and carbanions.

The most characteristic reaction of coordinated CO, perhaps, is the insertion process, in which a carbonyl ligand undergoes concerted intermolecular attack by another ligand, typically an alkyl, aryl, or other 1-electron ligands. The importance of the insertion reaction in CO-based synthetic organic chemistry and in catalytic carbonylation reactions relies on the insertion of CO.

A mechanistic pattern can be rationalised in order to liberate the organic carbonyl product formed in homogeneous, transition metal catalysed carbonylation reactions. This involves the formation of a metal-carbon bond, followed by insertion of $\text{C}\equiv\text{O}$ to give an acyl-metal intermediate, which eventually goes on and regenerate the catalyst in its original form. The variety of products that can form from the different types of

catalytic carbonylation reactions (aldehydes, ketones, acids, esters, amides, anhydrides, *etc.*) arise from variations in the method of forming the initial M-R bond and of decomposing the post-insertion metallo-acyl complex.

2.6.3. Organometallic Chemistry

Organic molecules, together with CO can form interesting new complexes in the presence of a catalyst. Transition metal catalysts play a very important role to facilitate these reactions in the field called organometallic chemistry.

2.6.3.1. Elementary Steps in Organometallic Chemistry

A number of elementary reactions can be used to rationalise the elementary steps of a catalytic cycle (or cycles). These steps can include: oxidative addition, nucleophilic attack by the metal, reductive elimination, insertion, α - and β -eliminations, nucleophilic addition to a ligand, reductive displacement and ligand dissociation and replacement. These elementary reactions can combine to generate different types of catalytic processes and the steps are discussed below in more detail.

i. Oxidative addition

The ability of a transition metal to exist in a number of different oxidation states is one of its most pronounced characteristics. It can thus accept electrons from, or supply electrons, to its environment under relatively mild conditions. Such an environment can be a σ -antibonding orbital of an approaching molecule. Transfer of electron density to this σ -antibonding orbital from a metal orbital of matching symmetry - with some degree of electron transfer from the corresponding σ -bonding orbital to the metal - can result in the formation of an three-centre metal-ligand bond. The result is complete dissociation of the original ligand σ -bond and formation of two new bonds, Figure 2.5.

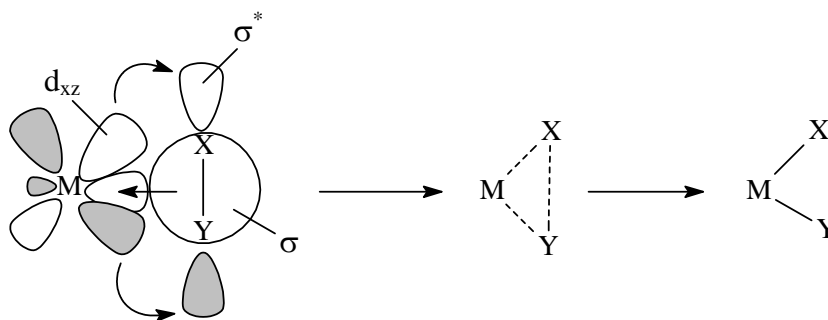
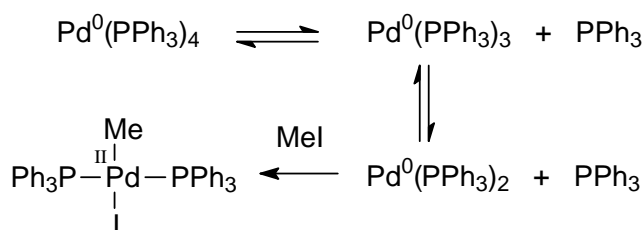


Figure 2.5. Oxidative addition of a ligand to a transition metal in which two new bonds are formed.

The metal has also increased its formal oxidation state by two units since the two previously nonbonding electrons are now involved in bonding. The overall reaction is called oxidative addition.

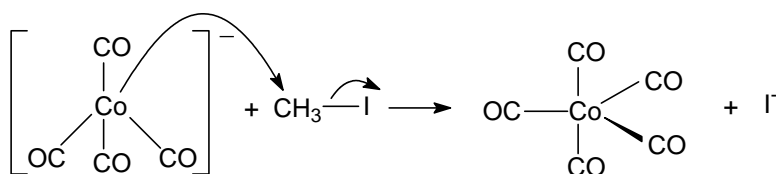
Many catalytic carbonylation reactions are initiated by oxidative addition of a C-X or H₂ bond to a Pd⁰ or RhI complex. Interestingly, the 18-electron, 4-coordinate Pd⁰ complex, Pd(PPh₃)₄, although “saturated”, can undergo dissociation of the phosphine ligands in solution to form “unsaturated” 16- or 14-electron complexes. Although not possible to isolate, the 14-electron complex, Pd(PPh₃)₂, is highly susceptible to oxidative addition, Scheme 2.11.



Scheme 2.11. Oxidative addition of methyl iodide (MeI) to a Pd⁰ complex.

ii. Nucleophilic attack by the metal

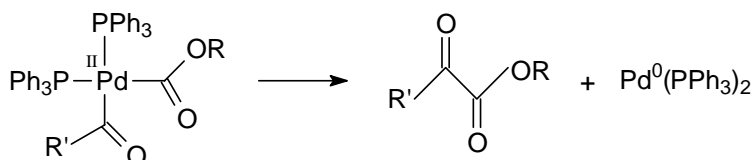
Both the coordination number and electron configuration of the metal increases when oxidative addition occurs - the formal oxidation state by two units, as well as the number of electrons associated with the metal by the same number. Therefore, oxidative addition cannot occur for electronically and/or coordinatively saturated complexes. If the complexes are electronically saturated, but not coordinatively saturated, the metal centre can act as a nucleophile towards alkyl halides and other species containing electrophilic centres, Scheme 2.12.



Scheme 2.12. Nucleophilic attack of Co on methyl iodide (MeI).

iii. Reductive elimination

Reductive elimination is the reverse of oxidative addition, since it involves the loss of two “one-electron ligands” from the metal centre and the two ligands combine to give a single elimination product. The combining ligands usually occupy a *cis* orientation with respect to each other in the metal molecule. Since it is the reverse of oxidative addition it also implies that in the product the coordination number and oxidation state of the metal are both reduced by two units. Reductive elimination can be seen as a decomposition pathway for carbonylation chemistry, since the products are released in this step of the catalytic cycle and the metal complex goes back to its initial state. An example is the alkene hydroformylation with Co^{III} in which decomposition of an acyl hydrido complex leads to the product aldehyde. Another example is the double-carbonylation of aryl halides to keto esters that depends on the reductive elimination of the OC-CO bond from a Pd^{II} complex, see Scheme 2.13.

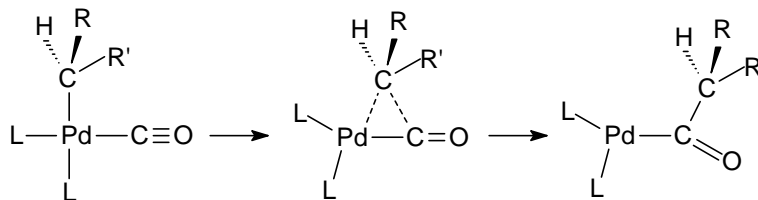


Scheme 2.13. Reductive elimination.

iv. Insertion

The insertion of CO into a metal-carbon bond is the key step for carbonylation reactions. In hydroformylation and hydroesterification migration of hydride to a coordinated alkene forms an alkyl and this one electron ligand migrates from the metal to the unsaturated, coordinated CO and subsequently inserts to form an acyl ligand. Vinyl ligands for example, which form when alkyne ligands insert into both M-H and M-C bonds, can migrate to coordinated alkenes, alkynes or CO. Acyls ligands too can migrate from the metal to coordinated alkenes forming keto-alkyl ligands. Therefore, many different types of organic molecules can form *via* sequences of different insertion reactions.

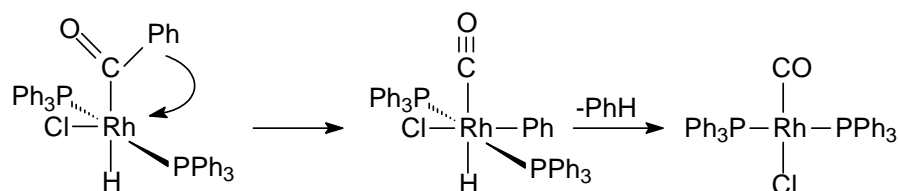
For ligand migration to occur a *cis* configuration of the combining ligands is required and this is normally highly stereospecific. Insertion of CO in particular has been shown to proceed with complete retention of configuration at the migrating carbon atom, which is consistent with the “front-side” attack implied by concerted migration, Scheme 2.14.



Scheme 2.14. Insertion of carbon monoxide into a Pd-CH₃ bond.

v. α - and β -Eliminations

These elementary reactions are simply the reversal of the CO insertion reactions, that is, ligand-to-metal migrations and ‘ α ’ and ‘ β ’ refers to the number of carbon atoms from the metal at which ligand fragmentation occurs. It involves the migration of an alkyl or aryl ligand from the α -carbon to the metal and is therefore α -elimination, Scheme 2.15.



Scheme 2.15. α -elimination of Ph from the α -carbon.

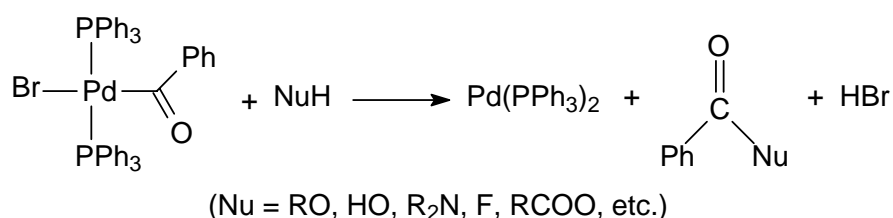
An example of β -elimination is the reversal of an alkene-hydride insertion reaction where the alkyl ligand is cleaved at the β -carbon. Coordinatively saturated complexes which are kinetically stable are not susceptible to this type of process, since for both α - and β -eliminations there is an increase in the coordination number of the metal by one. Strongly bound ligands such as phosphines and CO in coordinatively saturated complexes can completely inhibit β -elimination of hydride from alkyl ligands. To obtain stable transition alkyls the use of ligands that have β -hydrogens can be avoided and ligands such as benzyl or methyl can be used. α -hydride elimination (generating a hydrido carbene complex) does not seem to play a significant role in carbonylation chemistry.

vi. Nucleophilic Addition to a Ligand

Coordinated CO is susceptible towards nucleophilic attack (as compared to the free molecule), but many unsaturated ligands, such as alkenes, alkynes and arenes have the ability to delocalize charge over both the metal and ligands which result in enhanced reactivity to nucleophilic attack.

vii. Reductive Displacement

Reductive displacement is often the product-forming step of a catalytic cycle like reductive elimination and β -hydride elimination. This reaction is especially characteristic of metal-acyl complexes under basic conditions where there is reductive cleavage of a metal-ligand bond. Carboxylic acids, esters, amides, anhydrides and acyl fluorides can form from this type of reaction, Scheme 2.16.

**Scheme 2.16. Reductive elimination of a Pd-acyl complex under basic conditions.**

The detailed mechanism of reductive displacement varies from system to system. For example, for some Rh-catalyzed carbonylations, reductive elimination of acyl halide first takes place and then it is followed by the hydrolysis or alcoholysis step. For certain Pd based syntheses alcoholysis occurs at the metal before reductive elimination takes place.

viii. Ligand Dissociation and Displacement

A fundamental step in any catalytic cycle is the very simple replacement of one ligand by another, even if it is only a solvent molecule. A prerequisite for effective homogeneous catalysis is the facile exchange of neutral ligands such as phosphines, alkenes and CO at a kinetically labile metal centre and its occurrence in any catalytically active system can almost be taken for granted.

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