

1

Elementary Steps

1.1 Introduction

Catalyst performance plays a central role in the literature on catalysis and is expressed in terms of selectivity, activity and turnover number. Most often catalyst stability is not addressed directly by studying why catalysts perform poorly, but by varying conditions, ligands, additives, and metal, in order to find a better catalyst. One approach to finding a suitable catalyst concerns the screening of ligands, or libraries of ligands [1] using robotics; especially, supramolecular catalysis [2–4] allows the fast generation of many new catalyst systems. Another approach is to study the decomposition mechanism or the state the catalyst precursor is in and why it is not forming an active species. For several important reactions such studies have been conducted, but they are low in number. As stated in the preface, in homogeneous catalysis there has always been less attention given to catalyst stability [5] than there is in heterogeneous catalysis [6]. We favor a combined approach of understanding and exploration, without claiming that this is more efficient. In the long term this approach may be the winner for a reaction that we have got to know in much detail. For reactions, catalysts, or substrates that are relatively novel a screening approach is much more efficient, as shown by many examples during the last decade; we are not able to study all catalysts in the detail required to arrive at a level at which our knowledge will allow us to make predictions. We can reduce the huge number of potential catalysts (ligands, metals, co-catalysts) for a desired reaction by taking into account what we know about the decomposition reactions of our coordination or organometallic complexes and their ligands. Free phosphines can be easily oxidized and phosphites can be hydrolyzed and thus these simple combinations of ligands and conditions can be excluded from our broad screening program. In addition we can make sophisticated guesses as to what else might happen in the reaction with catalysts that we are about to test and we can reduce our screening effort further. To obtain a better understanding we usually break down the catalytic reaction under study into elementary steps, which we often know in detail from (model) organometallic or organic chemistry. As many books do, we can collect elementary steps and reverse the process and try to design new catalytic cycles. We can do the same for decomposition

processes and first look at their elementary steps [7]; the process may be a single step or more complex, and even autocatalytic. In this chapter we will summarize the elementary reactions leading to the decomposition of the metal complexes and the ligands, limiting ourselves to the catalysis that will be dealt with in the chapters that follow.

1.2

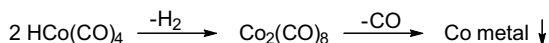
Metal Deposition

Formation of a metallic precipitate is the simplest and most common mechanism for decomposition of a homogeneous catalyst. This is not surprising, since reducing agents such as dihydrogen, metal alkyls, alkenes, and carbon monoxide are the reagents often used. A zerovalent metal may occur as one of the intermediates of the catalytic cycle, which might precipitate as metal unless stabilizing ligands are present. Precipitation of the metal may be preceded by ligand decomposition.

1.2.1

Ligand Loss

A typical example is the loss of carbon monoxide and dihydrogen from a cobalt hydrido carbonyl, the classic hydroformylation catalyst (Scheme 1.1).



Scheme 1.1 Precipitation of cobalt metal.

The resting state of the catalyst is either $\text{HCo}(\text{CO})_4$ or $\text{RC}(\text{O})\text{Co}(\text{CO})_4$, and both must lose one molecule of CO before further reaction can take place. Thus, loss of CO is an intricate part of the catalytic cycle, which includes the danger of complete loss of the ligands giving precipitation of the cobalt metal. Addition of a phosphine ligand stabilizes the cobalt carbonyl species forming $\text{HCo}(\text{CO})_3(\text{PR}_3)$ and, consequently, higher temperatures and lower pressures are required for this catalyst in the hydroformylation reaction.

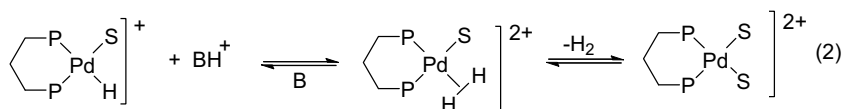
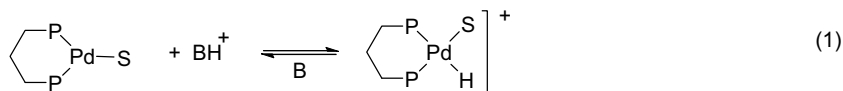
A well-known example of metal precipitation in the laboratory is the formation of “palladium black”, during cross coupling or carbonylation catalysis with the use of palladium complexes. Usually phosphorus-based ligands are used to stabilize palladium(0) and to prevent this reaction.

1.2.2

Loss of H^+ , Reductive Elimination of HX

The loss of protons from a cationic metal species, formally a reductive elimination, is a common way to form zerovalent metal species, which, in the absence of stabilizing

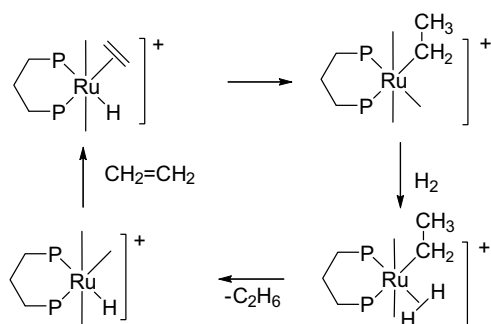
ligands, will lead to metal deposition. Such reactions have been described for metals such as Ru, Ni, Pd, and Pt (Scheme 1.2). The reverse reaction is a common way to regenerate a metal hydride of the late transition metals and clearly the position of this equilibrium will depend on the acidity of the system.



Scheme 1.2 Reactions involving protons and metal hydrides.

Too strongly acidic media may also lead to decomposition of the active hydride species via formation of dihydrogen and a di-positively charged metal complex (reaction (2), Scheme 1.2). All these reactions are reversible and their course depends on the conditions.

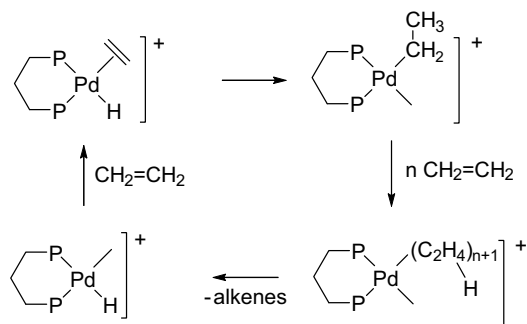
As shown in the reaction schemes for certain alkene hydrogenation reactions and most alkene oligomerization reactions (Schemes 1.3 and 1.4), the metal maintains the divalent state throughout, and the reductive elimination is not an indissoluble part of the reaction sequence.



Scheme 1.3 Simplified scheme for heterolytic hydrogenation.

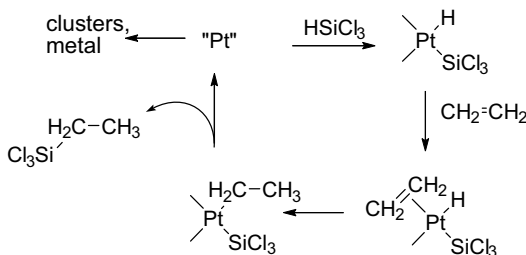
The species $L_n\text{MH}^+$ are stabilized by phosphine donor ligands, as in the Shell Higher Olefins Process ($M=\text{Ni}$) [8] and in palladium-catalyzed carbonylation reactions [9].

We mention two types of reactions for which the equilibrium, shown in Scheme 1.2, between MH^+ and $\text{M} + \text{H}^+$ is part of the reaction sequence, the addition of HX to a double bond and the Wacker reaction. As an example of an HX addition we will take hydrosilylation, as for HCN addition the major decomposition



Scheme 1.4 Alkene oligomerization.

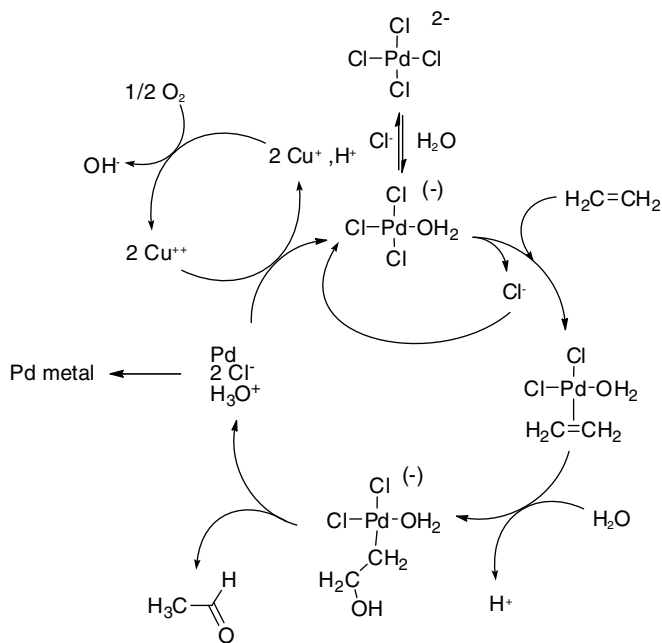
reaction is a different one, as we will see later. The hydrosilylation reaction is shown in Scheme 1.5 [10].



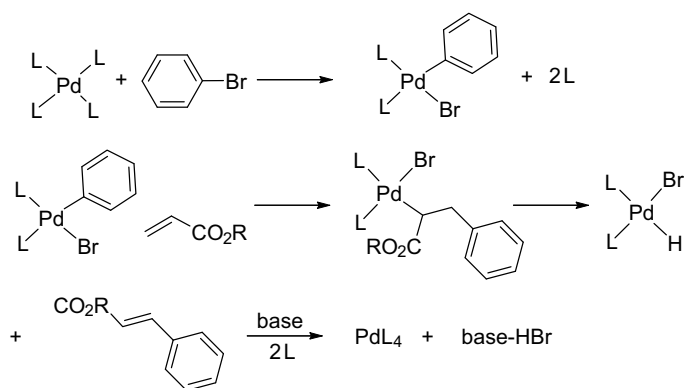
Scheme 1.5 Simplified mechanism for hydrosilylation.

In the Wacker reaction, elimination of HCl from “PdHCl” leads to formation of palladium zero [11] and the precipitation of palladium metal is often observed in the Wacker reaction or related reactions [12]. In the Wacker process palladium(II) oxidizes ethene to ethanal (Scheme 1.6) and, since the re-oxidation of palladium by molecular oxygen is too slow, copper(II) is used as the oxidizing agent. Phosphine ligands cannot be added as stabilizers for palladium zero, because they would be oxidized. In addition, phosphine ligands would make palladium less electrophilic, an important property of palladium in the Wacker reaction.

In the palladium-catalyzed Heck reaction (Scheme 1.7), as in other cross coupling reactions, the palladium zero intermediate should undergo oxidative addition before precipitation of the metal can occur. Alternatively, Pd(0) can be “protected” by ligands present, as in the example of Scheme 1.7, but this requires another dissociation step before oxidative addition can occur. Both effective ligand-free systems [13] and ligand-containing systems have been reported [14]. A polar medium accelerates the oxidative addition. The second approach involves the use of bulky ligands, which give rise to low coordination numbers and hence electronic unsaturation and more reactive species. Turnover numbers of millions have been reported [15].



Scheme 1.6 Ethanal formation from ethene via a Wacker oxidation reaction.



Scheme 1.7 The mechanism of the Heck reaction using excess phosphine.

1.2.3

Reductive Elimination of C-, N-, O-Donor Fragments

Many cross-coupling reactions have been reported in the last decades. The palladium and nickel-catalyzed formation of C–C, C–N, C–O, and C–P bonds has become an important tool for organic syntheses [16]. The general mechanism for C–C bond

Pd-catalyzed allylic alkylation of racemic substrates [31]. Modification of surfaces with chiral molecules has been known for several decades to give rise to enantioselective catalysis [32], but the similarity of ligands used in homogeneous and MNP-based enantioselective catalysis seems suspect. Evidence is growing that the latter reactions are catalyzed by homogeneous complexes [28, 33].

In the pyridine-palladium acetate catalyzed oxidation of alcohols the formation of PdNPs was observed by transmission electron microscopy (TEM) measurements [34], but, by using dendritic pyridine ligands containing a 2,3,4,5-tetraphenylphenyl substituent at the 3-position of the pyridine ring, this was suppressed successfully by Tsuji and coworkers [35].

A key issue for homogeneous catalysis is that MNPs can form in a reversible manner, while the formation of larger metal particles is usually irreversible, both thermodynamically and/or kinetically. MNPs still hold promise for new reactions to be discovered and as precursors for molecular catalysts they have shown advantages, but the control of their size during catalysis seems an intrinsic problem not to be solved easily.

1.3

Ligand Decomposition by Oxidation

1.3.1

General

The main tool for catalyst modification in homogeneous, catalytic processes is modification of the ligands. By changing the ligand properties we try to obtain better selectivity and activity. Decomposition of the ligands and their complexes has a large influence on the performance of the system. Catalysts based on late transition metals often contain phosphites and phosphines as modifying ligands. The decomposition routes of these ligands have received a great deal of attention. They are sensitive to many reactions as we will see. Nitrogen-based ligands, such as amines, imines and pyridines, are much more robust in general, but they are much less effective as ligands for low-valent late transition metals, such as rhodium(I) in rhodium-catalyzed hydroformylation. In ionic complexes though, we have seen an enormous increase in the use of nitrogen donor ligands in catalytic reactions that have become highly efficient and selective.

1.3.2

Oxidation

1.3.2.1 Catalysis Using O₂

Homogeneous catalysts for oxidation reactions using O₂ do not contain modifying soft ligands, but they are ionic species solvated by water, acetic acid, and the like. Examples include the Wacker process for making ethanal (palladium in water) and the oxidation of *p*-xylene to terephthalic acid (cobalt in acetic acid) [36].

Ligands based on nitrogen donor atoms are the ligands of choice; they stabilize high-valent metal ions and are not as sensitive to oxidation as phosphorus- or sulfur-based ligands. For example, phenanthroline ligands were used for the palladium-catalyzed oxidation of alcohols to ketones or aldehydes [37], and diamines are effective ligands for the copper-catalyzed oxidative coupling of phenols in the synthesis of polyphenylene ether [38]. We are not aware of commercial processes utilizing polydentate nitrogen ligands yet, although many interesting new oxidation catalysts have been reported in recent years [39]. Oxidation of the ligand backbone may be a concern as even porphyrins should be used in halogenated form in order to enhance their stability in oxidation reactions [40].

1.3.2.2 Catalysis Using Hydroperoxides

The commercial processes using hydroperoxides (*t*-butyl hydroperoxide and 1-phenylethyl hydroperoxide) for the epoxidation of propene involve “ligand-free” metals such as titanium alkoxides and ligand oxidation is not an issue for these processes [41]. For the asymmetric epoxidation using Sharpless’ catalyst, ligand oxidation is also not a major issue [42].

Phosphorus ligands are very prone to oxidation. Therefore, oxygen and hydroperoxides have to be thoroughly removed from our reagents and solvents before starting our catalysis. In spite of this common knowledge, oxidation of phosphine ligands has frequently obscured the catalytic results.

When phosphines are bonded strongly to a transition metal such that no or little dissociation occurs, their oxidation by hydroperoxides will not take place. This is the case for the platinum-catalyzed epoxidation reaction of alkenes by hydrogen peroxide developed by Strukul [43]. The bidentate phosphine ligands “survive” the hydroperoxidic conditions and asymmetric and regioselective epoxidations have been achieved, proving that the chiral ligands remain intact and coordinated to platinum. Typically, turnover numbers are 50 to 100, and while the use of hydrogen peroxide is attractive from a green chemistry point of view, these modest numbers have so far not led to industrial applications. Clearly, from a cost point of view, the Sharpless catalyst seems more attractive.

1.4

Phosphines

1.4.1

Introduction

Phosphines and diphosphines are widely used as the ligand component in homogeneous catalysts. Large-scale processes include rhodium-catalyzed hydroformylation for propene, butene, and heptene, ethene oligomerization, cobalt-catalyzed hydroformylation for internal higher alkenes, and butadiene dimerization. Small-scale operations include asymmetric hydrogenation of enamides and substituted acrylic acids, asymmetric isomerization to make menthol, alkoxyacylation

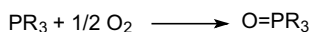
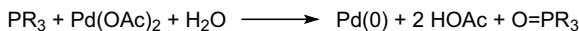
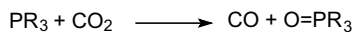
(ibuprofen), and Group 10 metal-catalyzed C–C bond formation (Heck reaction, Suzuki reaction). Future possibilities may comprise selective trimerization and tetramerization of ethene [44], more alkoxy-carbonylations (large-scale methyl methacrylate, more pharmaceuticals), hydroxycarbonylations, a large variety of new C–C [45] and C–N coupling reactions, asymmetric alkene dimerizations, alkene metathesis, and new hydroformylation reactions.

Garrou [46] reviewed the decomposition of phosphorus ligands in relation to homogeneous catalysis many years ago. Many interesting studies on phosphorus ligand decomposition have appeared since, but Garrou's review is still a useful collection of highly relevant reactions. At the time, the formation of phosphido species seemed to be the most common fate of our phosphine-containing catalysts, but in the last two decades many more reaction types have been added, as we reviewed in 2001 [7]. In a recent review Parkins discusses reactions taking place in the ligand in the coordination sphere, a large number of them being examples of phosphines [47]. The reactions in Parkins' review are ordered by metal. Exchange of substituents at phosphorus in metal complexes has been reviewed by Macgregor recently and his review shows that many new reactions have been discovered since the review by Garrou was published [48].

1.4.2

Oxidation of Phosphines

Oxidation of free phosphines was mentioned above (Section 1.3.2.2) as a reaction leading to phosphine loss. Phosphines are used extensively in a large number of organic synthetic reactions in which they usually end up as the phosphine oxide, that is, they are used as reducing agents. Well known examples are the Mitsunobu reaction to generate esters from alcohols and carboxylic acids under very mild conditions, and the Appel reaction to convert alcohols into alkyl halides, and the Wittig reaction. Therefore it is not surprising that, in catalysis, oxidation of phosphines is a common way to deactivate catalytic systems. Common oxidizing agents are dioxygen and hydroperoxides. High-valent metals may also function as the oxidizing agent. Sometimes this reaction is utilized on purpose and the reducing function of phosphines is used to activate the catalyst; for example palladium(II) acetate can be reduced by an excess of phosphine ligand (see Scheme 1.9, third reaction).



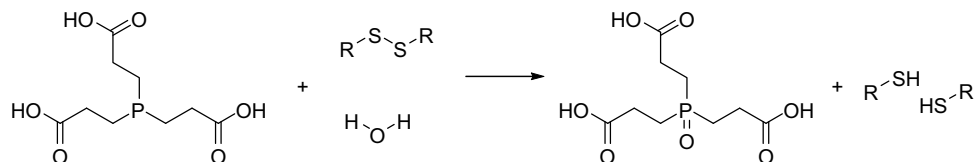
Scheme 1.9 Examples for oxidation of phosphines.

For instance, in cross coupling chemistry a palladium(II) precursor is reduced *in situ* by phosphine to generate Pd(0), the “active” species (the oxygen atom is provided by water). Molybdenum(VI), tungsten(VI) and water have been reported as oxidizing agents of phosphines [49]. Rh(III) carbonate oxidizes triphenylphosphine forming CO₂ and Rh(I) [50]. Rh(III) in water was found to oxidize tppts yielding tppts-O and Rh(I) [51]. Thermodynamics show that even water and carbon dioxide may oxidize phosphines to the corresponding oxides. These reactions may be catalyzed by the transition metal in the system, for example, Rh for CO₂ [52]. Water oxidizes phosphines using palladium as a catalyst and palladium has to be thoroughly removed after its use in a P–C cross coupling synthesis [53]. It should be mentioned, however, that, in view of the many successful applications of water and sCO₂ as solvents in homogeneous catalysis, these oxidation reactions are relatively rare.

Oxidation, or partial oxidation of phosphine can also be turned into a useful reaction if an excess of phosphine retards the catalytic reaction. Above we have mentioned that phosphine-free palladium compounds may be very active catalysts for cross coupling reactions, and, thus, intentional or accidental ingress of oxygen may be advantageous for the catalysis. Another example is the oxidation of one of the phosphine molecules in the Grubbs I metathesis catalyst.

Nitro and nitroso compounds are strongly oxidizing agents and, for instance, they have been reported to oxidize PH₃ [54]. Thus, nitrobenzene and phosphine give azoxybenzene and phosphorus acids under harsh conditions. In the palladium-catalyzed reductive carbonylation of nitrobenzene it was found that phosphine ligands are not suitable as they are oxidized to phosphine oxides [55]. Nitrosobenzene and isocyanate complexes of zerovalent Group 10 metals will transfer oxygen to triphenylphosphine and also form azoxybenzene [56]. Nitrosobenzene is much more reactive than nitrobenzene towards phosphines as it will oxidize arylphosphines in the absence of metal catalysts, forming azoxybenzenes at ambient temperature in the presence of base [57].

Many sulfur-containing compounds will also oxidize phosphines, and either form phosphine sulfide or, when water is present, phosphine oxides. This reaction has been known since 1935 [58] and, especially with water-soluble tris(2-carboxyethyl) phosphine (TCEP), it is of interest in biochemical systems [59]. It has been studied a couple of times over the years, but only in the last decade has it become extremely popular in biochemistry and molecular biology to reduce protein disulfide bonds (Scheme 1.10), for example in labeling studies, and as a preparatory step for gel electrophoresis [60].



Scheme 1.10 Reduction of disulfides by TCEP.

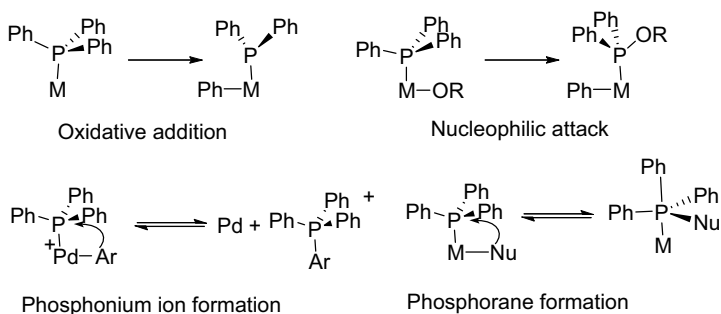
TCEP has also been employed for the reduction of sulfoxides, sulfonylchlorides, *N*-oxides, and azides (Staudinger reaction), thus showing that these compounds also present a potential hazard for phosphines in catalytic systems [61].

1.4.3

Oxidative Addition of a P–C Bond to a Low-Valent Metal

In the next four sections we will discuss four additional ways of phosphine decomposition: oxidative addition of phosphines to low-valent metal complexes, nucleophilic attack on coordinated phosphines, aryl exchange via phosphonium species, and substituent exchange via metallophosphorane formation. Interestingly, in all cases the metal serves as the catalyst for the decomposition reaction!

In his review [46a] Garrou emphasizes the first mechanism, oxidative addition of the phosphorus–carbon bond to low-valent metal complexes (or reductive cleavage of P–C bonds) and formation of phosphido species. In the last two decades experimental support for the other three mechanisms has been reported (Sections 1.4.4–1.4.6). In Scheme 1.11 the four mechanisms are briefly outlined.



Scheme 1.11 Four mechanisms for phosphine decomposition leading to P–C bond cleavage.

Reductive cleavage of the phosphorus–carbon bond in triaryl- or diarylalkylphosphines is an important tool for making new phosphines [62]. Metals used to this end in the laboratory are lithium, sodium (or sodium naphthalide), and potassium. Cleavage of triphenylphosphine with sodium in liquid ammonia to give Ph_2P^- , benzene, and NaNH_2 is carried out on an industrial scale for the synthesis of the ligand of the SHOP process, obtained via reaction of sodium diphenylphosphide with *o*-chlorobenzoic acid [63]. The cleavage reaction works well for phenyl groups and methyl and several methoxy-substituted phenyl groups; most other substitution patterns lead to a Birch reaction or cleavage of the functional group [62b]. It is not surprising, therefore, that low-valent transition metals will also show reductive cleavage of the P–C bond, although mechanistically it involves interaction of the metal with the carbon and phosphorus atoms rather than an initial electron transfer as is the case for the alkali metals. The reaction with transition metals is usually referred to as an oxidative addition of the $\text{R}'\text{-PR}_2$ molecule to the metal complex.

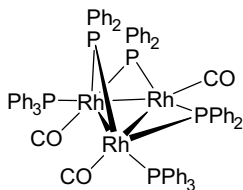
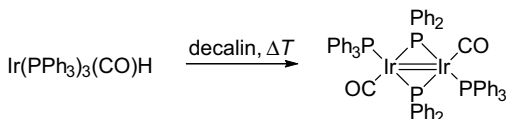


Figure 1.1 Rhodium cluster that may form in hydroformylation mixture work-up.

Oxidative addition of C–Br or C–Cl bonds is an important reaction in cross-coupling type catalysis, and the reaction of a P–C bond is very similar, although the breaking of carbon–phosphorus bonds is not a useful reaction in homogeneous catalysis. It is an undesirable side-reaction that occurs in systems containing transition metals and phosphine ligands, leading to deactivation of the catalysts. Indeed, the oxidative addition of a phosphine to a low valent transition metal can be most easily understood by comparing the $\text{Ph}_2\text{P}-$ fragment with a chloro- or bromo-substituent at the phenyl ring; electronically they are very akin, see Hammett parameters and the like. The phosphido anion formed during this reaction will usually lead to bridged bimetallic structures, which are extremely stable. The decomposition of ligands during hydroformylation, which has been reported both for rhodium and cobalt catalysts [64] may serve as an example.

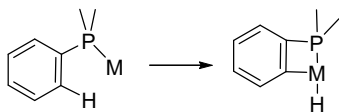
Thermal decomposition of $\text{RhH}(\text{CO})(\text{PPh}_3)_3$, the well known hydroformylation catalyst, in the absence of H_2 and CO leads to a stable cluster, shown in Figure 1.1, containing $\mu_2\text{-PPh}_2$ fragments, as was studied by Pruett's group at Union Carbide (now Dow Chemical) [65]. It is not known whether P–C cleavage takes place on a cluster or whether it starts with a monometallic species (see the reactions below taking place in clusters).

After heating, the corresponding iridium compound led to the formation of a dimer containing two bridging phosphido bridges. The phenyl group has been eliminated (as benzene or diphenyl), see Scheme 1.12. In view of the short Ir–Ir bond the authors suggested a double bond [66].



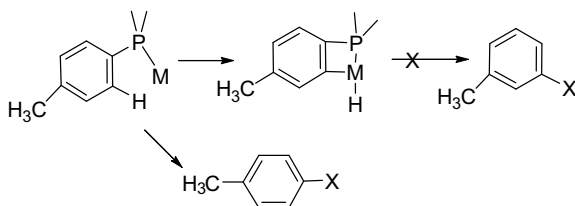
Scheme 1.12 Iridium dimer that forms in the absence of syn gas.

Several authors have proposed a mechanism involving orthometallation as a first step in the degradation of phosphine ligands, especially in the older literature. Orthometallation does take place, as can be inferred from deuteration studies, but it remains uncertain whether this is a reaction necessarily preceding the oxidative addition (Scheme 1.13).



Scheme 1.13 Orthometallation of a phosphine.

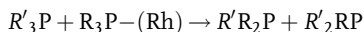
Subsequently the phosphorus–carbon bond is broken and the benzyne intermediate inserts into the metal hydride bond. Although this mechanism has been popular with many chemists there are many experiments that contradict it. A simple para-substitution of the phenyl group answers the question whether orthometallation was involved, as is shown in Scheme 1.14.



Scheme 1.14 Disproving of orthometallation as a decomposition pathway.

Decomposition products of *p*-tolylphosphines should contain methyl substituents in the meta position if the orthometallation mechanism were operative. For palladium-catalyzed decomposition of triarylphosphines this was found not to be the case [67]. Using rhodium-containing solutions of tri-*o*-, tri-*m*-, and tri-*p*-tolylphosphines Abatjoglou *et al.* found that only one isomeric tolualdehyde is formed from each phosphine [68]. Thus, the tolualdehydes produced are those resulting from intermediates formed by direct carbon–phosphorus bond cleavage. Likewise Co, and Ru hydroformylation catalysts give aryl derivatives not involving the earlier proposed ortho-metalation mechanism [69].

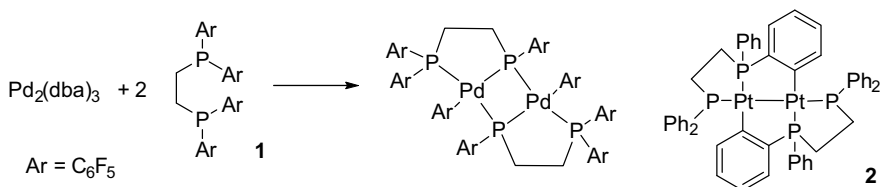
Several rhodium complexes catalyze the exchange of aryl substituents of triarylphosphines at elevated temperatures (130 °C) [68]:



Abatjoglou *et al.* proposed as the mechanism for this reaction a reversible oxidative addition of the aryl–phosphido fragments to a low valent rhodium species. A facile aryl exchange has been described for complexes Pd(PPh₃)₂(C₆H₄CH₃) I [70]. These authors also suggested a pathway involving oxidative additions and reductive eliminations. The mechanisms outlined below in the following sections, however, can also explain the results of these two studies.

Phosphido formation has been observed for many transition metal phosphine complexes [43]. Upon prolonged heating, and under an atmosphere of CO and/or H₂, palladium and platinum also tend to give stable phosphido-bridged dimers or clusters [71].

A “prototype” of an oxidative addition with concomitant P–C bond cleavage is the reaction of **1** (Scheme 1.15) with $\text{Pd}_2(\text{dba})_3$, which gives the addition of an aryl group to palladium and formation of phosphido bridges [72]. The interesting feature of this example is that the aryl group is a pentafluorophenyl group, for which only very few examples of this reaction have been reported. Hydrogen analogs dppe and dppp in their reaction with low valent metals, for example, $\text{Pt}(0)$ give metalation instead of P–C bond-cleavage (**2**, Scheme 1.15) [73].



Scheme 1.15 Reactions of diphosphines with zerovalent palladium and platinum complexes.

Bridging diphosphine metal complexes have been characterized that may be “en route” to P–C cleavage, such as shown in Figure 1.2 [74].

During the studies of the isomerization of butenyl cyanides, relevant to the hydrocyanation of butadiene to give adiponitrile, the intermediate $(\text{TRIPHOS})\text{Ni}(\text{CN})\text{H}$ complexes were found to decompose to benzene and highly stable μ -phosphido-bridged dimers (only one isomer shown) that deactivate the catalytic process. Oxidative addition as the mechanism would invoke $\text{Ni}(\text{IV})$ and therefore one of the mechanisms to be discussed later, nucleophilic attack or phosphorane intermediates, may be operative (Scheme 1.16).

Cluster or bimetallic reactions have also been proposed in addition to monometallic oxidative addition reactions. For instance, trishydridoruthenium dimers will cleave P–C bonds in aryl and alkyl phosphines to give phosphido-bridged hydrides. Alkylphosphines give alkenes as the co-product, but phenylphosphines give benzene. For phenylphosphines the intermediate containing a bridging phenyl group has been observed, thus showing that that the reaction is an oxidative addition of the P–C bond along the ruthenium dimer, and not a nucleophilic attack of a hydride at a phosphorus atom. The alkene products of the alkylphosphines are in accord with this mechanism, as they are formed via β -elimination of the intermediate alkylruthenium groups (Scheme 1.17) [75].

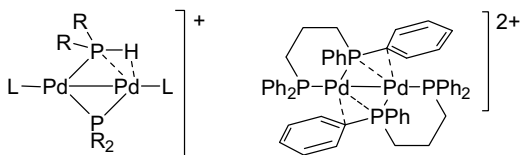
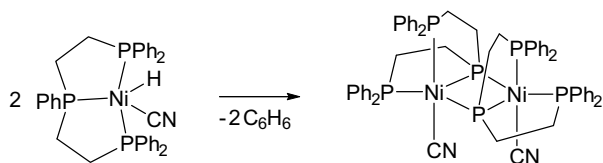
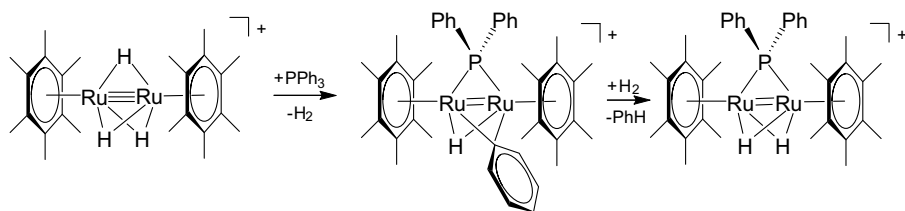


Figure 1.2 Interactions en route to P–C cleavage.



Scheme 1.16 P–C cleavage in a hydrocyanation catalyst.

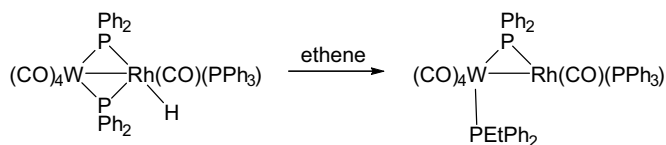


Scheme 1.17 P–C cleavage in a ruthenium dimer.

It has been known for a long time that clusters cleave P–C bonds. Nyholm and coworkers showed that $\text{Ru}_3(\text{CO})_{12}$ and $\text{Os}_3(\text{CO})_{12}$ react with PPh_3 to give, for example, $\text{Os}_3(\text{CO})_7(\mu_2\text{-PPh}_2)_2(\mu_3\text{-C}_6\text{H}_4)$ [76]. Similar reactions have been reported for 1,8-bis(diphenylphosphino)naphthalene and $\text{Ru}_3(\text{CO})_{12}$ [77].

As an illustration that rather complicated clusters may initiate the P–C cleavage reactions we mention that iridium-iron-monocarborane clusters have been reported containing $\mu_2\text{-PPh}_2$ groups and phenyl groups resulting from PPh_3 cleavage [78].

As in monometallic species, the reverse reaction can also be observed in dimers and clusters. An interesting example is shown in Scheme 1.18, which involves an insertion of ethene into a rhodium hydride bond when, subsequently, the ethyl formed migrates (or reductively eliminates) to the neighboring μ -phosphido group, forming a phosphine under very mild conditions [79].



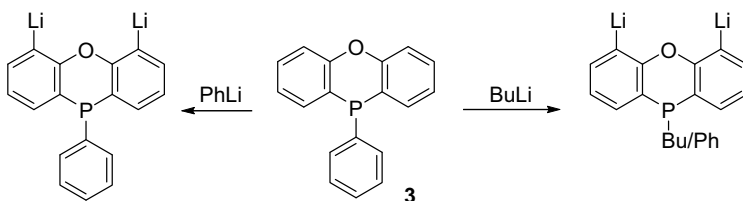
Scheme 1.18 P–C bond formation in a heterodimeric complex.

Most studies focus on unsubstituted phenyl groups, but, as in reductive cleavage with Group 1 metals, the substitution of the aryl groups will influence the rate of P–C cleavage and substituted aryls can perhaps be used to our advantage, to avoid transition metal catalyzed cleavage. In summary, a lot more studies are required to understand and suppress undesired cleavage of phosphorus–carbon bonds.

1.4.4

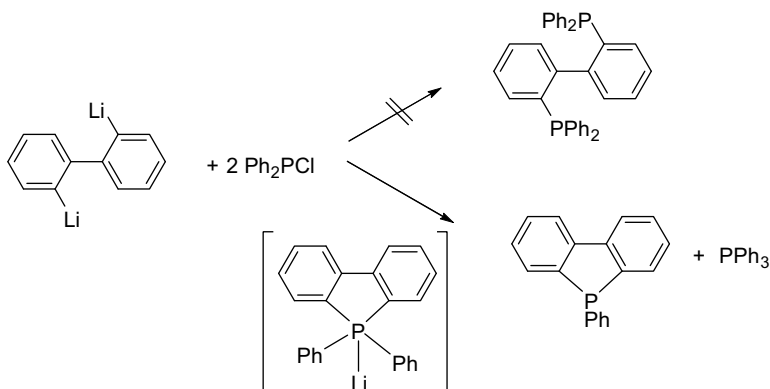
Nucleophilic Attack at Phosphorus

Here we are concerned with the metal-catalyzed or metal-aided nucleophilic attack at phosphorus in phosphines, but there are examples of butyllithium and Grignard reagents replacing hydrocarbyl substituents at phosphorus (halide and alkoxide replacement by hydrocarbyl anions is an ubiquitous reaction!). We mention three examples, but surely there are more reports in the literature. Pentafluorophenyl in $(\text{C}_6\text{F}_5)_3\text{P}$ was found to be replaced by ethylmagnesium bromide to give $\text{Et}(\text{C}_6\text{F}_5)_2\text{P}$ and $(\text{C}_6\text{F}_5)\text{Et}_2\text{P}$ [80]. The phenyl group in **3** (Scheme 1.19) is replaced by a methyl or butyl group upon reaction with methyllithium or butyllithium. Therefore, lithiation of the hydrogens ortho to oxygen should be done with phenyllithium to avoid side-product formation [81].



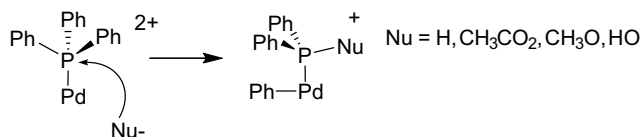
Scheme 1.19 Nucleophilic displacement at phosphorus.

Hypervalent phosphoranes have been invoked as possible intermediates or transition states for these exchange reactions [82]. Theoretical studies show that lithiophosphoranes may be transition states in these exchange reactions, rather than intermediates [83]. Another example of nucleophilic attack at phosphorus by carbon nucleophiles is the reaction of 2,2'-biphenyldilithio with $\text{Ph}_2\text{P}\text{Cl}$, which gives 9-phenyldibenzophosphole and triphenylphosphine quantitatively, rather than the expected diphosphine [84]. Schlosser proposed a lithiophosphorane intermediate for this reaction (Scheme 1.20) [85].



Scheme 1.20 Nucleophilic displacement leading to dibenzophosphole.

For a long time the literature underestimated the importance of nucleophilic attack as a mechanism for the catalytic decomposition of phosphines coordinated to metals, especially with nucleophiles such as acetate, methoxy, hydroxy and hydride (Scheme 1.21). For examples of nucleophilic attack at coordinated phosphorus see Refs [71, 86]. A very facile decomposition of alkylphosphines and triphenylphosphine (using palladium acetate, one bar of hydrogen and room temperature) has been reported [71a]. Acetate was suggested as the nucleophile, but hydride as the nucleophile cannot be excluded.



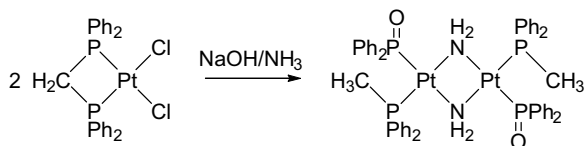
Scheme 1.21 Phosphine decomposition via nucleophilic attack.

A detailed reaction proving the nucleophilic attack was shown for platinum complexes [86d]. The alkoxide coordinated to platinum attacks phosphorus while the carbon atom coordinated to phosphorus migrates to platinum. Thermodynamically the result seems more favorable, but mechanistically this “shuffle” remains mysterious. See Scheme 1.25. Coordination to platinum makes the phosphorus atom more susceptible to nucleophilic attack, and the harder (P and O) and softer (C and Pt) atoms recombine as one might expect. The same mechanism was proposed by Matsuda [86a] for the decomposition of triphenylphosphine by palladium(II) acetate. In this study the aryl phosphines are used as a source of aryl groups that are converted into stilbenes via a Heck reaction. Even alkyl phosphines underwent P–C bond cleavage via palladium acetate.

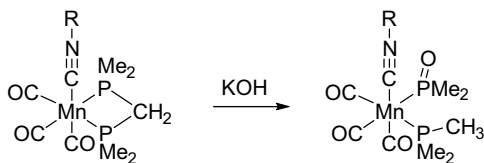
It is surprising indeed that phosphines can be effective ligands in cross-coupling reactions under basic conditions, for instance phenoxide will react with triphenylphosphine in palladium chloride complexes at 0 °C giving PdCl(Ph)(PPh₃)₂ together with phenyl phosphites, phosphonites and phosphates [87]. It was concluded that the intermediate PdCl(OAr)(PPh₃)₂ is highly labile. The mechanism most likely is a nucleophilic attack of the phenoxide at the phosphorus atom of the coordinated triphenylphosphine.

There are several examples of nucleophilic attack of hydroxide on coordinated dppm (bisdiphenylphosphinomethane) and its methyl analog. The P–C bond cleaved is the one with the methylene unit, which apparently is not very stable. For instance (dppm)PtCl₂ will react with NaOH in liquid ammonia to give Ph₂MeP and an SPO (diphenylphosphine oxide) both coordinated to platinum, involved in amide bridges with a second platinum unit (Scheme 1.22) [88]. The intermediate methylene anion formed has been protonated by ammonia.

Dmpm undergoes the same reaction when coordinated to manganese, Scheme 1.23 [89].

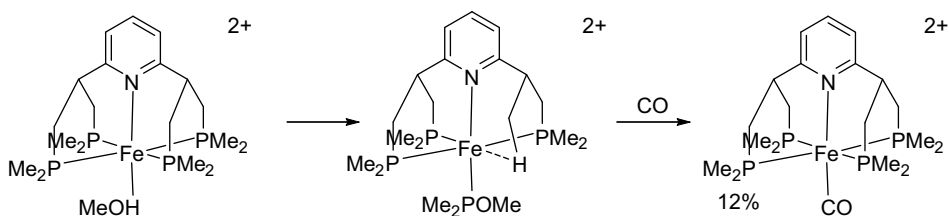


Scheme 1.22 Dppm decomposition via nucleophilic attack.



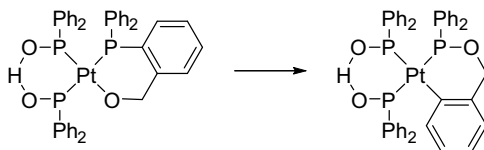
Scheme 1.23 Dppm decomposition via nucleophilic attack.

The pentadentate ligand with NP4 donor set in Scheme 1.24 undergoes a P–C cleavage reaction with methanol giving a phosphinite complex, while the methyl group formed by protonation of the methylene anion shows an agostic interaction with iron [90]. Surprisingly, when 10 bar of CO is applied, the reaction is reversed and the intact NP4 ligand is regenerated.



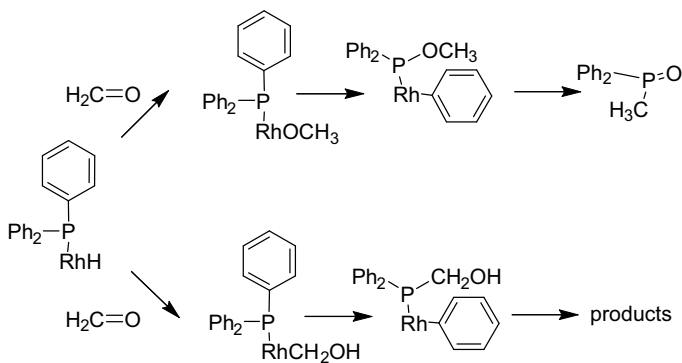
Scheme 1.24 NP4 decomposition via nucleophilic attack.

Ruthenium aryloxide complexes containing trimethylphosphine also showed an intramolecular nucleophilic attack, leading to methyl–phosphorus bond breaking and formation of a phosphinite ligand [91a]. In Section 1.4.6 we will discuss metallophosphoranes as intermediates in similar exchange reactions and it may well be that transition states or intermediates of this type occur in exchange reactions which we have presented here as nucleophilic mechanisms, or a metal–O/phosphorus–C “shuffle” reaction (Scheme 1.25) [86d].



Scheme 1.25 Metal-O/phosphorus-C “shuffle” reaction via nucleophilic attack.

A catalytic decomposition of triphenylphosphine has been reported [92] in a reaction involving rhodium carbonyls, formaldehyde, water, and carbon monoxide. Several hundreds of moles of phosphine can be decomposed this way per mole of rhodium per hour! The following reactions may be involved (Scheme 1.26).



Scheme 1.26 Catalytic decomposition of triphenylphosphine with formaldehyde and rhodium.

Related to this chemistry is the hydroformylation of formaldehyde to give glycolaldehyde, which would be an attractive route from syn-gas to ethylene glycol. The reaction can indeed be accomplished and is catalyzed by rhodium arylphosphine complexes [93], but clearly phosphine decomposition is one of the major problems to be solved before formaldehyde hydroformylation can be applied commercially.

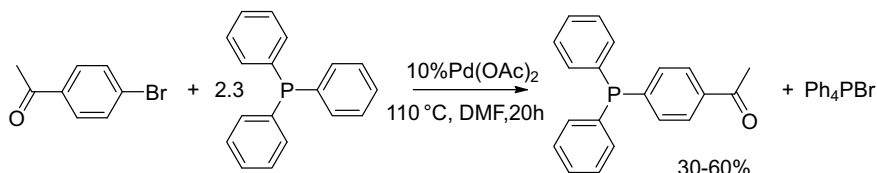
1.4.5

Aryl Exchange Via Phosponium Intermediates

Phosponium salts frequently occur in palladium and nickel chemistry, as reactant, intermediate, or as product. Decomposition of $(PPh_3)_2PdPhI$ gives Ph_4PI as was reported by Yamamoto [94]. Grushin studied the decomposition of a range of these complexes and found that iodides are more reactive than bromides and chlorides, and also that excess of phosphine and halides strongly influences the rate of decomposition (for aryl fluorides see Section 1.4.6) [95]. He suggests that exchange reactions during catalysis (*vide infra*) can best be avoided by using excesses of phosphines and halides. The latter are present anyway in cross coupling chemistry and there is no choice either, once we have decided on the substrate. Excess of phosphines may retard the reaction.

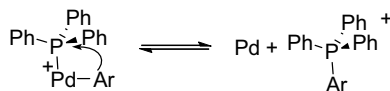
Aryl (pseudo)halides can be reacted with triphenylphosphine to give phosponium salts, and metals such as nickel and palladium catalyze this reaction. Nickel works well for only a few substrates and high quantities are required [96], but palladium acetate is an active precursor and shows a wide scope for this reaction [97]. Phosponium salts can be used as an aryl halide replacement in cross coupling reactions and thus phosponium salts add oxidatively to palladium(0) producing

a triarylphosphine as one of the products [94]. Addition of aryl halide to phosphine and exchange of the aryl groups has been used as a synthetic tool for making phosphines by Chan and coworkers (Scheme 1.27) [98]. As more or less statistical mixtures are obtained, the yields do not exceed 60%, but the method is highly tolerant of functional groups and avoids the use of sensitive and expensive reagents.



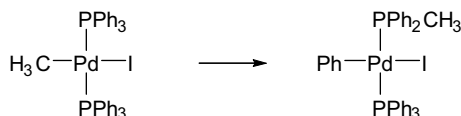
Scheme 1.27 Catalytic transfer of aryl groups in triphenylphosphine.

The interest in cross coupling reactions in the last decade has led to a large number of reports dealing with the involvement of the phosphine ligands in these reactions [99]. The mechanism has not been elucidated for all cases. The oxidative addition and nucleophilic attack discussed above may explain some of these results but, especially since the work of Novak, phosphonium intermediates have been considered as intermediates [99c]. Formally the mechanism also involves nucleophilic attack of a hydrocarbyl group at coordinated phosphines, but after the nucleophilic attack the phosphorus moiety dissociates from the metal as a phosphonium salt. Effectively, this is a reductive elimination. To obtain a catalytic cycle the phosphonium salt re-adds oxidatively to the zerovalent palladium complex (see Scheme 1.28), in accord with the findings of Yamamoto [94].

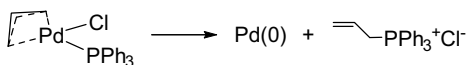


Scheme 1.28 Substituent exchange via phosphonium intermediates.

For the exchange of a palladium bonded methyl group and a phenyl group at phosphorus, Norton *et al.* [99a] proposed an intramolecular phenyl migration to palladium followed by reductive elimination of MePh_2P . They excluded the intermediacy of phosphonium species as deuterated phosphonium salts of the same composition did not participate in the reaction (Scheme 1.29). A metallophosphorane intermediate or transition state (Section 1.4.6) would also nicely explain the



Scheme 1.29 Intramolecular phenyl migration to palladium [99a].



Scheme 1.30 π -Allylpalladium phosphine complex giving a phosphonium salt.

intramolecular character, and would not invoke the occurrence of tetravalent palladium intermediates.

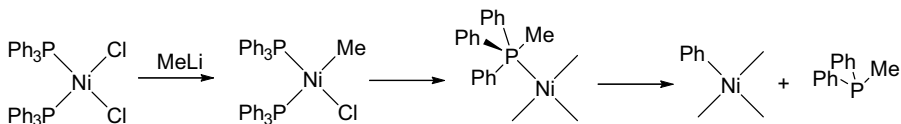
Aryl exchange has a deleterious effect on the yield and selectivity of the palladium-mediated coupling of aryl halides with alkenes (Heck reaction) or hydrocarbyl metals (Mg, B, Sn) [99, 100]. Polymerizations toward high molecular weight suffer especially from this side-reaction [101]; arylphosphines will be incorporated in the growing chain and the chain growth may stop there.

Formation of phosphonium species can also lead to catalyst deactivation in other systems. For example, the reductive elimination of allylphosphonium salts from cationic allyl palladium species (Scheme 1.30) may lead to “ligand consumption” and thus reduce (enantio)selectivity or activity of the catalyst.

1.4.6

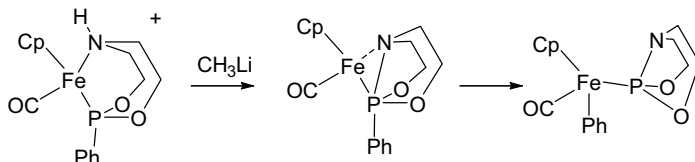
Aryl Exchange Via Metallophosphoranes

Metallophosphoranes and phosphoranes as intermediates in the reactions studied here are closely related mechanistically with the routes presented in Sections 1.4.4 (nucleophilic attack) and 1.4.5 (phosphonium salt formation). Already as early as 1971 Green and coworkers proposed the intermediacy of metallophosphoranes in the smooth, room-temperature exchange of methyl groups in methyl lithium and phenyl groups in PPh₃ coordinated to NiCl₂ [102]. Among other products the formation of free PMe₂Ph and PPhMe₂ was observed. Full details of the intermediates are not at hand and a schematic mechanism is outlined in Scheme 1.31.



Scheme 1.31 Hydrocarbyl exchange via a metallophosphorane.

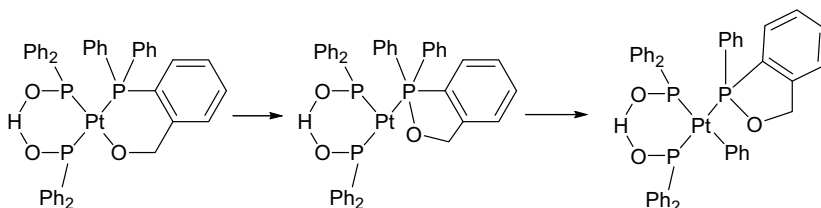
The decomposition of CoMe(PPh₃)₃ also leads to scrambled methyl/phenylphosphines [103]. In Scheme 1.32 a typical example is shown of a deprotonation of



Scheme 1.32 Exchange of nucleophiles via a metallophosphorane.

a coordinated amine, followed by a nucleophilic attack of the amide at the coordinated phosphonite, forming a metallophosphorane [104]. Upon warming to room temperature the phosphorane rearranges by migration of the phenyl group to iron. Addition of HCl to the latter gives back the starting material, thus showing that nucleophilic attack and its reverse are facile processes in the coordination sphere.

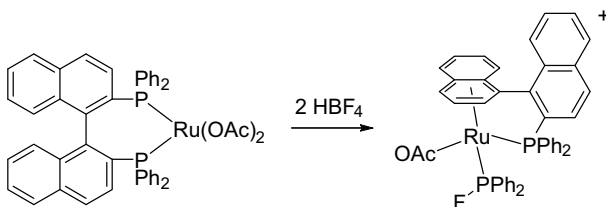
Several nucleophilic attacks described in Section 1.4.4 actually might proceed via a metallophosphorane, for instance the example in Scheme 1.25 would now read as shown in Scheme 1.33. As mentioned in Section 1.4.4 hydrocarbyl exchange in pyridylphosphines seems to involve lithiophosphoranes as transition states rather than as intermediates, as was indicated by DFT calculations [83]. This may also be true for some of the examples shown here.



Scheme 1.33 Exchange of nucleophiles via a metallophosphorane.

Grushin, in addition to the arylphosphines complexes of palladium halides, also studied the fluoride complexes of palladium and rhodium, in particular the aryl exchange reactions and their decomposition [95]. Heating of $\text{RhF}(\text{PPh}_3)_3$ in benzene led to an exchange of phenyl and fluoride groups to give $\text{RhPh}(\text{PFPh}_2)(\text{PPh}_3)_2$, while in chlorobenzene *trans*- $\text{RhCl}(\text{PFPh}_2)(\text{PPh}_3)_2$ was found as the product, together with biphenyl. DFT calculations showed that the most likely pathway is the formation of a metallofluorophosphorane as an intermediate [105]. In the decomposition of $(\text{PPh}_3)_2\text{PdPhF}$ Grushin found that Ph_3PF_2 was formed, thus, especially with fluorine atoms, the formation of phosphorane compounds is highly likely [95]. BINAP(O) palladium compounds show the same propensity for fluorophosphorane formation [106].

The findings by Pregosin on BINAP, ruthenium and tetrafluoroborate are highly relevant to catalysis. The use of inert anions such as BF_4^- would not arouse much suspicion, but his work shows that fluorodiphenylphosphines may form in such catalysts even at very low temperatures (Scheme 1.34) [107]. Water and acetate may

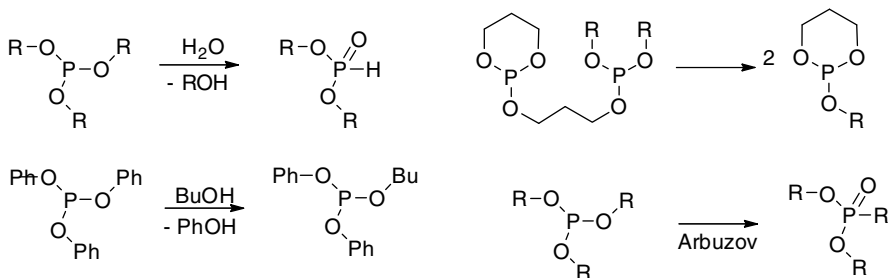


Scheme 1.34 F–C exchange in BINAP.

also function as the nucleophile. This is mentioned here because it might well involve phosphorane intermediates, as observed in the work reported by Grushin. Metallaphosphoranes were reviewed by Goodman and Macgregor in 2010 [108].

1.5 Phosphites

Phosphites are easier to synthesize and less prone to oxidation than phosphines. They are much cheaper than most phosphines and a wide variety of structures can be obtained. Disadvantages of the use of phosphites as ligands include several side-reactions: hydrolysis, alcoholysis, trans-esterification, Arbuzov rearrangement, O–C bond cleavage, P–O bond cleavage. Scheme 1.35 gives an overview of these reactions. In hydroformylation systems at least two more reactions may occur, namely nucleophilic attack on aldehydes and oxidative cyclizations with aldehydes. Lewis acids catalyze the Arbuzov reaction at room temperature [109].



Scheme 1.35 Various decomposition pathways for phosphite ligands.

Phosphites are the preferred ligands for the nickel-catalyzed hydrocyanation of butadiene to make adiponitrile [110]. Ligand decomposition studies for this system are lacking in the literature. Later, we will discuss a side-reaction in this system leading to catalyst deactivation.

Phosphites have been extensively studied for their use as ligands in rhodium-catalyzed hydroformylation. The first publication on the use of phosphites was from Pruett and Smith at Union Carbide [111]. The first exploitation of bulky *monophosphites* was reported by van Leeuwen and Roobeek [112]. Diphosphites came into focus after the discovery of Bryant and coworkers at Union Carbide Corporation that certain bulky diphosphites lead to high selectivities in the rhodium-catalyzed hydroformylation of terminal and internal alkenes (see Figure 1.3) [113].

It should be noted that all phosphites reported are *aryl* phosphites (sometimes the backbones may be aliphatic) and that the favored ones often contain bulky substituents. One of the reasons that aliphatic phosphites are used only sparingly is that they are susceptible to the Arbuzov rearrangement while the aryl phosphites are not. Acids, carbenium ions, and metals catalyze the Arbuzov rearrangement. Many

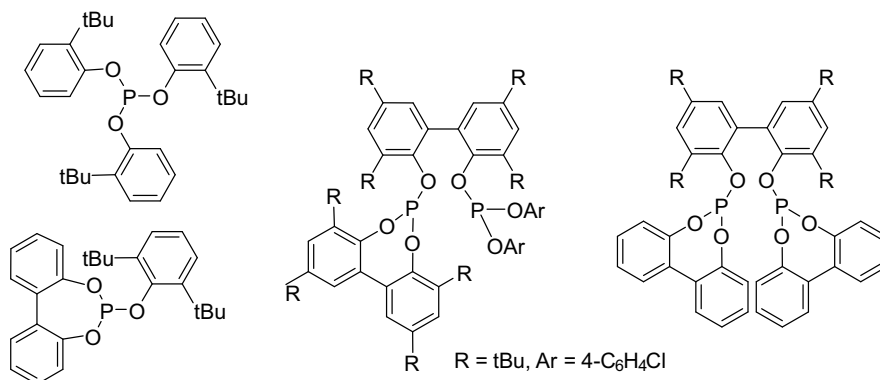
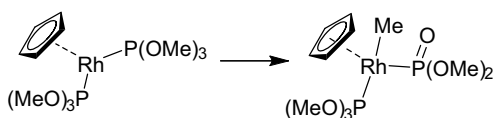


Figure 1.3 Typical bulky monophosphites and diphosphites.

examples of metal-catalyzed decomposition reactions have been reported (see Scheme 1.36) [114].

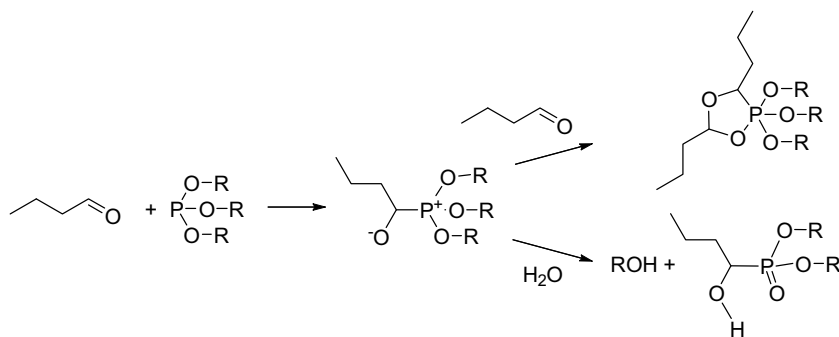


Scheme 1.36 Metal-catalyzed Arbusov reaction leading to phosphite decomposition.

Thorough exclusion of moisture can easily prevent hydrolysis of phosphites in the laboratory reactor. In a continuous operation under severe conditions traces of water may form via aldol condensation of the aldehyde product. Weak and strong acids and strong bases catalyze the reaction. The reactivity for individual phosphites spans many orders of magnitude. When purifying phosphites over silica columns in the laboratory one usually adds some triethylamine to avoid hydrolysis on the column.

Bryant and coworkers have extensively studied the decomposition of phosphites [115]. Stability involves thermal stability, hydrolysis, alcoholysis, and stability toward aldehydes. The precise structure has an enormous influence on the stability. Surprisingly, it is the reactivity toward aldehydes that received most attention. Older literature mentions [116] several reactions between phosphites and aldehydes of which we show only two in Scheme 1.37.

The addition of a phosphite to an aldehyde to give a phosphonate is the most important reaction [115]. The reaction is catalyzed by acid and, since the product is acidic, the reaction is autocatalytic. Furthermore, acids catalyze hydrolysis and alcoholysis and, therefore, the remedy proposed is continuous removal of the phosphonate over a basic resin (Amberlyst A-21). The examples in the patents illustrate that very stable systems can be obtained when the acidic decomposition products are continuously removed. The thermal decomposition of phosphites with aldehydes is illustrated in Figure 1.4.



Scheme 1.37 Reactions of phosphites and aldehydes.

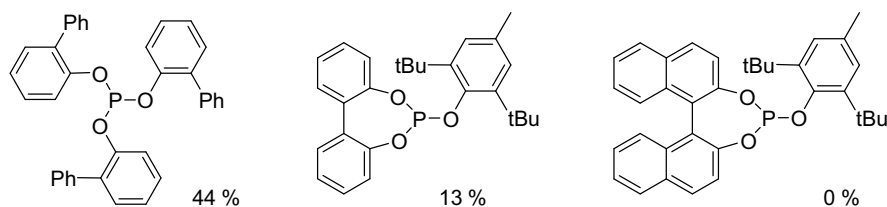
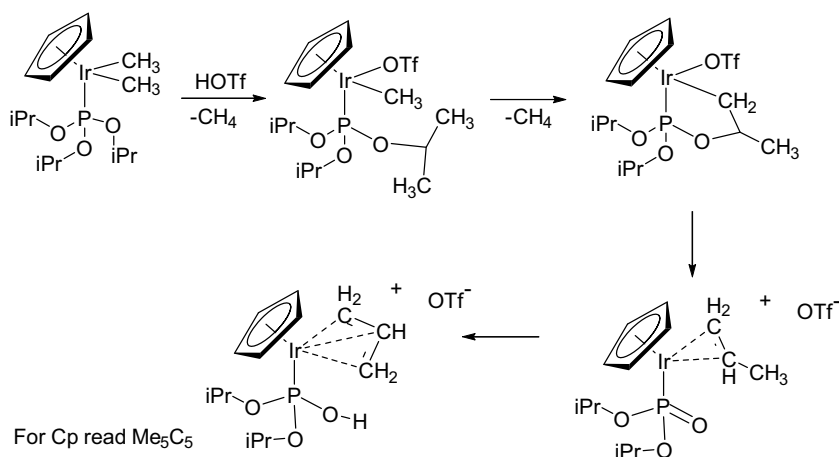


Figure 1.4 Reactivity of various phosphites toward C5-aldehyde [115]. Percentage decomposition after 23 h at 160 °C.

A decomposition reaction that looks like an Arbuzov reaction but actually is not was reported by Simpson [117]. The decomposition of an iridium triisopropyl phosphite complex involves a metallation of one of the propyl groups before an apparent Arbuzov reaction takes place. It is a nice example of the complexity of the decomposition pathways one can encounter (Scheme 1.38). The final complex contains a π -allyl group and a diisopropyl phosphite ligand.



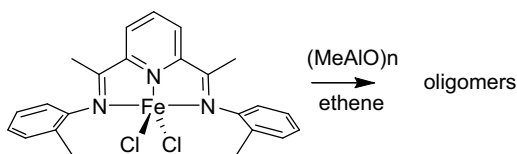
Scheme 1.38 Phosphite metallation followed by Arbuzov-like reaction.

Dealkylation of trimethyl phosphite in complexes of ruthenium is an acid-catalyzed reaction; the resulting phosphite is $\text{MeOP}(\text{OH})_2$ [118]. Metallation of phosphites will be discussed in Section 1.9.3.

1.6 Imines and Pyridines

Intrinsically, pyridines and imines are less susceptible to decomposition reactions than phosphorus ligands. They are less suitable for the stabilization of low-valent metal complexes and, at first sight, they may not be the ligands of choice for cross-coupling type chemistry [119], although even enantioselective Heck reactions have been reported for chiral bisoxazolines [120], and Suzuki–Miyaura reactions are catalyzed by palladium complexes containing nitrogen donor ligands [121], and, while these reactions may proceed without ligand (Sections 1.2.2–1.2.4), the occurrence of enantioselective reactions using nickel proves that the nitrogen bidentate donor remains coordinated during the process [122]. In the last decade nitrogen ligands have received a great deal of attention in copolymerization reactions [123] and oligomerization reactions [124]. No industrial applications have been reported so far, but for ethene oligomerization the activity and selectivity of the new imine-based catalysts is very promising.

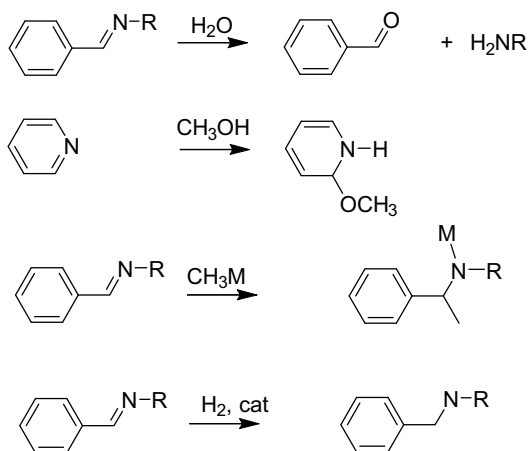
The latter development comprises the use of iron- and cobalt-containing pyridine-imine ligands. Extremely fast catalysts were reported simultaneously by the groups of Brookhart and Gibson [124]. Turnover frequencies as high as several millions per hour were recorded! Catalyst activities are very high and a separation of catalyst and product in a two-phase system as in SHOP may not be needed. The molecular weight distribution though will still require the isomerization/metathesis sequence as in the SHOP process. An example of such a catalyst is depicted in Scheme 1.39.



Scheme 1.39 Pyridine-imine-iron-based ethene oligomerization catalyst.

Activation of the chloride precursor involves alkylation with methyl aluminoxane and thus side-reactions such as those occurring in early-transition-metal catalyzed polymerization may occur (*vide infra*). No detailed studies about ligand stability have been published and ligand decomposition may not be an issue at all in this instance. A few reactions that may lead to decomposition of imines and pyridines are collected in Scheme 1.40.

We confine ourselves to the following reactions of imines:



Scheme 1.40 Decomposition reaction of imines and pyridines.

- Hydrolysis of imines leads to aldehydes and amines, the reverse reaction of the most frequent synthesis.
- Addition of water and methanol is catalyzed by metal ions. Like the former reaction it can be avoided if the catalytic reaction does not involve these reagents.
- Addition of metal alkyls leads to metal amides. The chemistry is complex and several reactions may occur [125].
- Catalytic hydrogenation to give amines may occur if the catalyst is accidentally active for this reaction and when hydrogen is present [126].

1.7

Carbenes

1.7.1

Introduction to NHCs as Ligands

Both the Fischer carbenes and the Schrock carbenes play an important role in catalysis, the former as ligands and the latter as initiator or substrate fragments. The discussion on carbenes as ligands will be limited to N-heterocyclic carbenes, as the older, different hetero-atom-containing Fischer carbenes have hardly been exploited in catalysis. The use of NHCs (N-heterocyclic carbenes) as ligands in complexes and catalysis [127] has enormously increased in the last decade. They are highly effective ligands in metathesis [128], cross coupling reactions [129], butadiene dimerization [130], polymerization [131], and, in this chemistry, results have been spectacular in terms of rate, selectivity, and turn-over numbers. Meanwhile NHCs have been found to be suitable ligands in hydrosilylation [132], carbonylation [133], gold C–C bond formation catalysis [134], hydrogen transfer [135], conjugate addition [136], hydroarylation of alkynes [137], oxidation [138], azide-alkyne click reactions [139],

nickel-catalyzed ring closure reactions [140], ethene oligomerization [141], and so on. Their stability and reactivity have been reviewed by Crudden and Allen [142].

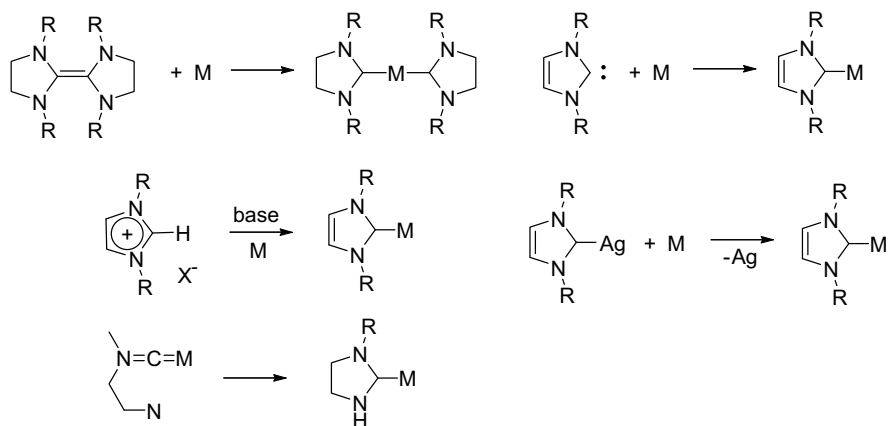
NHCs have been known since 1962 and many complexes have been synthesized by the Lappert group since the 70s [143]. The interactions of the orbitals on the nitrogen atoms and the carbon atom make the NHCs highly stable [144]. Especially since the introduction of steric bulk at the nitrogen atoms by Arduengo, which rendered them even higher in stability, they have become very useful and versatile ligands [145]. NHCs are strong σ donors and larger alkyl substituents on the nitrogen atoms increase their basicity further [146]. In many metal complexes NHCs can replace phosphines, bringing about drastic changes in the properties of the complexes, including the catalytic properties. The electronic and steric properties of NHCs have been reviewed by Nolan [147]. The development of the field of NHC ligands has been extremely rapid in the last decade, and one might say that the knowledge already gained in phosphine ligand chemistry has been transferred to carbene chemistry at high speed, giving birth to a plethora of metal complexes containing monodentate NHCs, but also bis-, tris-, tetra-, hexa-dentate and pincer-shaped NHCs [148]. NHCs are highly basic and form a strong σ -bond with the transition metals, which is much stronger than that of phosphines. Thus, while at low catalyst concentrations (10^{-3} M or less) an excess of phosphine is required, especially, for example, when carbon monoxide is a competing ligand (and substrate!), it was thought that NHCs could perhaps be used in stoichiometric amounts. In several instances this seems to be the case, not counting yet possible decomposition routes, which will be discussed below. In Section 1.7.2 the main side-reactions of NHCs will be mentioned and in Section 1.7.3 we will present a few decomposition routes for Schrock carbenes, which feature as substrate fragments in catalysis rather than as modifying ligands.

1.7.2

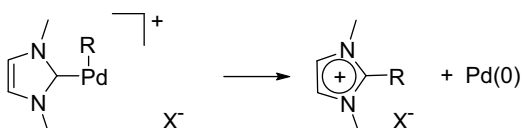
Reductive Elimination of NHCs

The introduction of NHC ligands in metal complexes is somewhat trickier than the introduction of phosphine and phosphite ligands, or, if one wishes, the chemistry at hand for NHCs is richer, as phosphorus ligands are rarely generated *in situ*! NHCs can be introduced by way of “electron-rich alkenes” (Lappert) [149], free carbenes (Arduengo) [145], as their imidazolium salts and base, by transfer from other metal complexes such as silver, or by *in situ* ring closure on the metal of amine isocyanides (see Scheme 1.41; in line with most literature we have drawn the metal–NHC bond as a single one) [150].

One of the most prominent decomposition reactions of NHC complexes is the reductive elimination discovered by McGuinness and Cavell [151] and we owe most of the information to the Cavell group [152]. Above we have seen that phosphines are susceptible to a number of decomposition reactions in their complexes, the present reaction is akin to the elimination of phosphonium salts from hydrocarbyl metal phosphine complexes (metal = e.g., Ni, Pd). The first reaction discovered was the elimination of trimethylimidazolium tetrafluoroborate from $[\text{PdMe}(\text{dmly})(\text{cod})]\text{BF}_4$ (dmly) 1,3-dimethylimidazolin-2-ylidene), presented schematically in Scheme 1.42.



Scheme 1.41 Synthesis of NHC complexes.



Scheme 1.42 Reductive elimination of an NHC-alkyl salt.

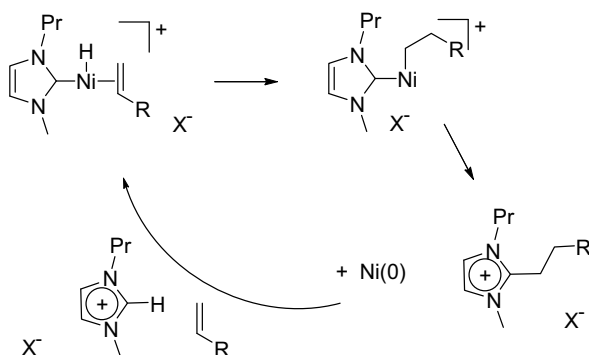
Cationic complexes react faster than neutral complexes. During the Heck reaction with NHC-modified palladium catalysts reductive elimination products were also found, containing either the aryl group or the phenylethyl group in the imidazolium salt. During carbonylation studies acetylimidazolium elimination products were identified [152c] and 2-alkylsubstituted imidazolium salts were also obtained during the NHC-Ni-catalyzed olefin dimerization reaction [141b, 153]. Subsequent reports have also shown the formation of 2-arylimidazolium salts from NHC-Pd-Aryl complexes [154].

DFT studies show that the mechanism of the reaction is a concerted reductive elimination and not a migration of the hydrocarbyl group to the carbene [155]. Most likely it can be compared with a migratory reductive elimination, as described for cross coupling reactions [156], but a detailed comparison for the geometries of the transition states of the two reactions has not been carried out. Other DFT studies indicated that electron-donating groups at the nitrogen atoms will slow down reductive elimination and, thus, *t*-butyl groups combining steric bulk and strong donor capacity should give the best results [157]. These results also show that the reductive elimination is very similar to the migratory reductive elimination in cross coupling, because in those reactions indeed electron-withdrawing substituents on the aryl group receiving the migrating hydrocarbyl group will enhance reductive elimination [158].

In spite of their facile elimination reactions NHC palladium complexes give highly active Heck catalysts [151], which the authors explain by competing reactions of

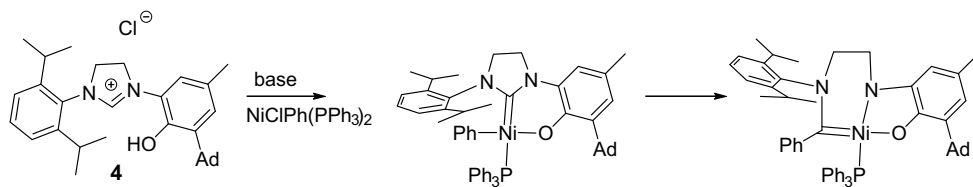
decomposition and catalysis (alkene insertion and β -elimination); as long as substrate is present the catalytic process is faster than the reductive elimination and catalysis continues (at higher temperatures). Several suggestions were put forward as to how to prevent reductive elimination, such as the use of oligodentate NHCs or bulky NHCs. Indeed, bulky NHCs were found to be the best ligands in Suzuki coupling chemistry [159]. Another effective approach to limit reductive elimination of NHC–R is the use of an excess of imidazolium salts as an ionic liquid solvent, which requires that oxidative addition of the salt to palladium(0) occurs, but this was suggested to be the case. In addition, the ionic medium will stabilize palladium(II) species and may facilitate separation of product and catalyst. Heck reactions under such conditions have been successfully carried out by Seddon and co-workers [160]. Examples of the oxidative addition of imidazolium salts to zerovalent nickel and palladium complexes leading to M(II) hydrides have been published meanwhile [161].

As in the case of the reversible oxidative addition and reductive elimination of phosphonium salts the imidazolium reactions can also be used to our advantage. In this instance the new substituent is introduced as an alkene, which inserts, effectively in the overall scheme, in the C–H bond of the imidazolium salt with the use of a nickel catalyst (Scheme 1.43, spectator phosphines or NHCs omitted on Ni) [162].



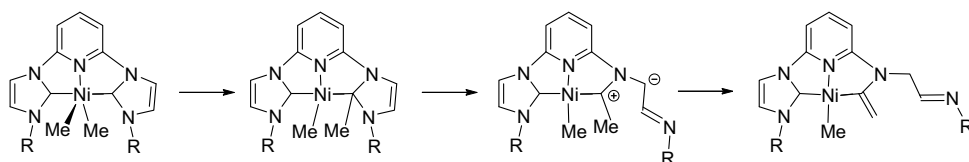
Scheme 1.43 Synthesis of alkyl imidazolium salts.

Grubbs and coworkers reported on a decomposition reaction of NHCs in nickel complexes that we will mention here in an attempt to collect reactions of potential interest, although its importance for catalysis was not yet known at the time of publication [163]. The reaction is shown in Scheme 1.44 and, most likely in an attempt to make a SHOP-type catalyst based on a phenol-NHC ligand instead of a phosphinophenolate, complex **4** was reacted with base and the phenylnickel precursor shown. We have drawn a likely intermediate that undergoes the reaction shown to yield the reported product (at room temperature in 60% yield). The authors point out the relationship with the NHC alkylation reactions reported by the Cavell group (*vide supra*), but the relation with phosphine chemistry can be stretched even further, because the reaction shown is a nucleophilic substitution at the carbene



Scheme 1.44 Nucleophilic attack on NHC followed by ring opening.

central atom. The mechanisms proposed for nucleophilic substitution in phosphorus ligands are presented in Sections 1.4.4–1.4.6 and Schemes 1.19–1.26. The difference with phosphine chemistry is that in phosphorus chemistry the harder anion ends up at the phosphorus atom and the softer carbon atom at platinum or palladium. Another ring expansion of an NHC has been reported, but in this case the reaction most likely proceeds via the alkene dimer of the NHC [163b].



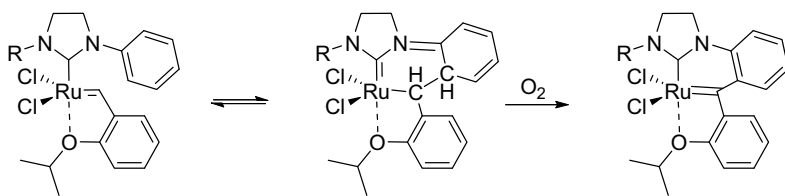
Scheme 1.45 Nucleophilic attack on NHC followed by ring opening.

An unusual ring opening [164] was reported by Danopoulos and coworkers in a reaction between the TMEDA dimethylnickel complex and a pyridine bisNHC pincer ligand (Scheme 1.45). At first sight this may seem a new reaction, but the mechanism proposed involves a nucleophilic displacement of the nitrogen atom at the carbene donor atom and a proton transfer completes the reaction. The proton transfer may be aided by the TMEDA present. The carbene carbon atom ends up as a vinyl (anion) bound to nickel. For the last compound we are not aware of a phosphorus analog, as this would be a nickelaphosphormethylene complex (a “Wittig” reagent), but would probably rearrange to a phosphinomethylnickel moiety (R_2PCH_2Ni).

1.7.3

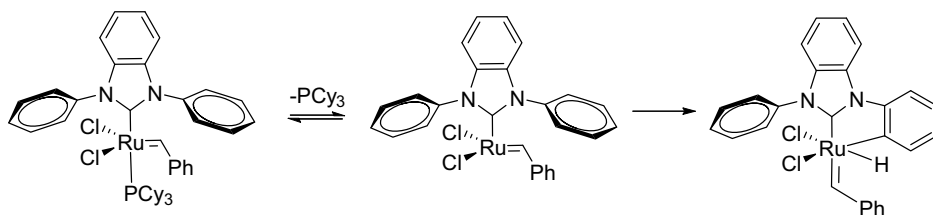
Carbene Decomposition in Metathesis Catalysts

The first decomposition reaction shown comprises a reaction between the NHC ligand and the carbene fragment involved in the metathesis reaction; the reaction is very specific for the precursor and ligand, but it presents a transition from the previous paragraph to this one! Blechert and coworkers found that the Hoveyda–Grubbs catalyst undergoes a reversible cyclization, as shown in Scheme 1.46, which, after oxidation of the ruthenacycle, renders the compound inactive. The oxidation with oxygen re-establishes the aromatic ring and a carbene–ruthenium bond not suitable for catalysis [165]. The compound was obtained in low yield and most likely the reaction can be prevented by an appropriate substitution pattern on the aryl ring.



Scheme 1.46 Reversible cyclization involving ligand and carbene in Hoveyda–Grubbs catalyst.

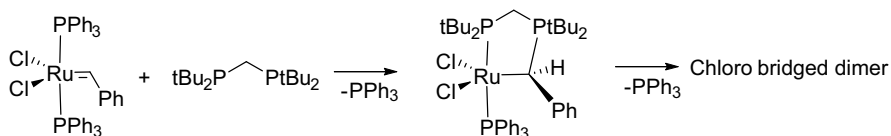
Another deactivation reaction involving both the NHC ligand and the reactant carbene was discovered by Grubbs for complexes containing non-substituted phenyl groups on the NHC nitrogen atoms [166]. The authors propose that it may involve a double C–H activation and only the first step is shown in Scheme 1.47 while the remaining part will be discussed later. In the absence of polar compounds C–H activation is an important starting point for decomposition reactions. It can be reduced effectively by choosing the proper substitution pattern on the aromatic rings [167].



Scheme 1.47 C–H activation in NHC metathesis catalyst.

In early studies Grubbs has shown that methylenidene ruthenium catalysts decompose in a monomolecular reaction, while alkylidene ruthenium catalysts show a bimolecular decomposition pathway involving phosphine dissociation; the inorganic products were not identified at the time [168]. The methylene ruthenium species features in many catalytic reactions and it was concluded that this decomposition reaction is the reason why high catalyst loadings are often needed.

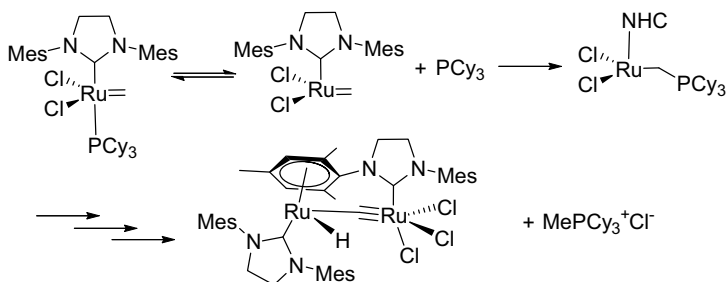
In the same year (1999) Hofmann and coworkers described the attack of electron-rich phosphines on the alkylidene coordinated to a Grubbs 1 catalyst; in this instance the phosphine is a bidentate and the attack may be aided by the intramolecular character [169]. They suggested that this reaction might be of importance in catalyst decomposition, as in many cases dissociation of phosphine from the ruthenium precursor is required to start catalysis. The reaction is shown in Scheme 1.48. After



Scheme 1.48 Nucleophilic attack of phosphine on carbene.

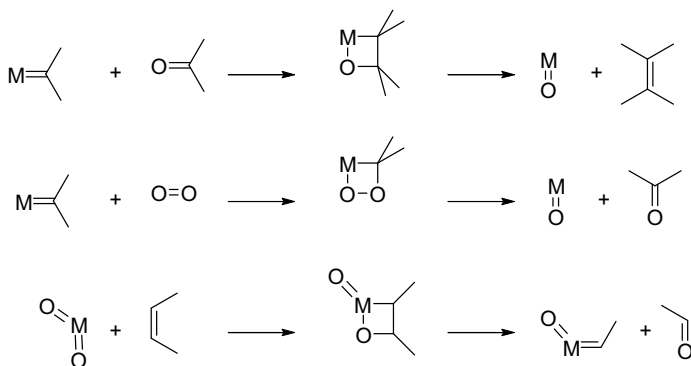
formation of the ylid triphenylphosphine dissociation takes place and the complex dimerizes (not shown).

The decomposition pathways of the most sensitive catalyst intermediate, the ruthenium methylenide species, were further studied by Grubbs and coworkers and they reported that nucleophilic attack of PCy_3 on the methylenide fragment was the initiating step of the process [170]. The highly basic phosphorus ylid formed abstracts a proton from another ruthenium methylenide and methyltricyclohexylphosphonium chloride, one of the products observed earlier, is formed. The resulting alkylidyne ruthenium complex reacts with the other, coordinatively unsaturated ruthenium species with formation of the dimer shown in Scheme 1.49.



Scheme 1.49 Grubbs catalyst undergoing nucleophilic attack at carbene by C_3P .

The sensitivity of metathesis catalysts for oxygenates changes drastically when we move in the periodic table from titanium to ruthenium. This has been noticed in both heterogeneous and homogeneous metathesis catalysis [171] and a simple metathesis reaction of the intermediate carbene metal complexes can be envisaged, and in some cases has been observed, that will convert metallocarbenes to metal oxide and the corresponding organic product. Clearly, reactions with oxygenates occur more frequently with molybdenum catalysts than with ruthenium catalysts. A few schematic reactions have been depicted in Scheme 1.50. It can be imagined that carboxylic



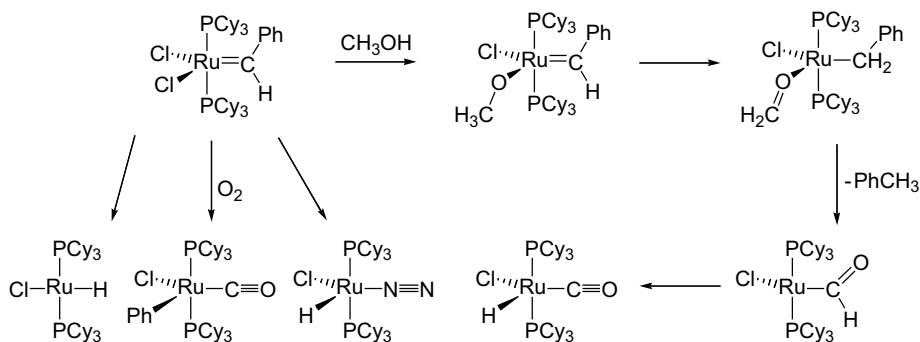
Scheme 1.50 Reactions of metal-carbenes with oxygenates and oxides.

acids and esters, aldehydes, imines, and so on will lead to similar reactions, in particular where early transition metals are concerned.

A Schrock molybdenum catalyst reacts cleanly with benzaldehyde according to Scheme 1.50 to give the expected products. In this instance ethyl acetate did not react with the catalyst [172]. Carbene–oxo transfer between metals (in this case tantalum and tungsten) has also been reported [173]. The reaction of metal oxides and alkenes gives the alkylidene species (reaction 3, Scheme 1.50) and aldehyde, but by the same token the reverse reaction could lead to catalyst deactivation [174].

Ruthenium catalysts are much more resistant to oxygenates than early transition metal catalysts, as has been known since 1965 [175], but the TONs of ruthenium catalysts for functionalized molecules are also much lower than those for purified, purely hydrocarbon alkenes. In the case of oxygenates 1% of catalyst is often used, while turnover numbers for the alkene substrates may be as high as one million. As in many other catalyzed reactions using alkenes as substrates, the removal of hydroperoxides is important in order to achieve high turnover numbers [176]. Note, however, that Me₄Sn-activated tungsten catalysts will also convert up to 500 molecules of oleate substrates [177]!

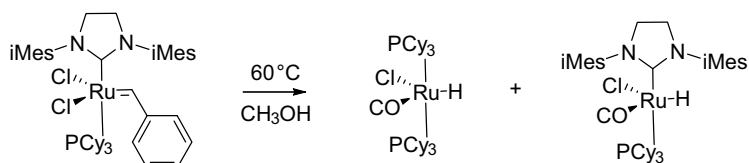
The degradation of the first-generation Grubbs metathesis catalyst with primary alcohols, water, and oxygen, and the formation and catalytic activity of ruthenium(II) monocarbonyl species has been studied by several groups [178]. For several reactions they reported RuHCl(CO)L₂ as the final product. A potential mechanism as proposed by Dinger and Mol [178a] is shown in Scheme 1.51.



Scheme 1.51 Grubbs 1 catalyst decomposition with alcohols and dioxygen.

The Grubbs 2 catalyst (Scheme 1.52) reacted faster with methanol under basic conditions than the Grubbs 1 catalyst and gave a mixture of products, including a ligand disproportionation reaction giving the same hydride that results from Grubbs 1; the mechanism was proposed to be the same as that shown in Scheme 1.51 [179].

The hydrides formed are highly active isomerization or hydrogenation catalysts, and thus their formation could drastically influence the selectivity of the metathesis reaction. The metathesis reaction is still faster than the methanolysis and thus

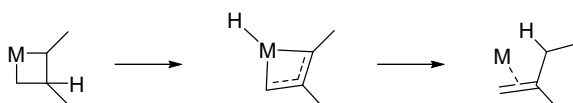


Scheme 1.52 Grubbs II catalyst decomposition with alcohols and dioxygen.

carrying out the reaction in alcohols has only a small effect on the outcome. Alternatively, the alkylidene catalysts were transformed on purpose into hydride species in order to carry out a tandem metathesis/hydrogenation reaction, as shown by Fogg and coworkers [178d]. Dinger achieved TOFs as high as $160\,000\text{ m m}^{-1}\text{ h}^{-1}$ for octene-1 hydrogenation at $100\text{ }^\circ\text{C}$ and 4 bar of hydrogen [179].

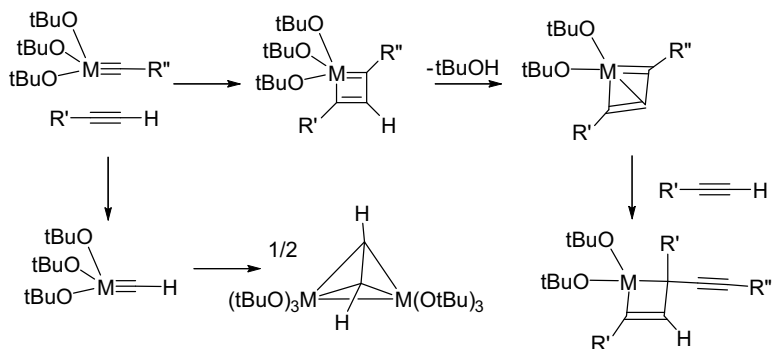
The reaction of the Grubbs 2 catalyst converted into a cationic triflate complex with water under slightly acidic conditions and acetonitrile gave benzaldehyde and a solvent ligated NHC-Ru complex [180]. The reaction starts most likely with a nucleophilic attack of water on the carbene carbon atom coordinated to a cationic ruthenium ion. It might be compared with the formation of phosphine oxides from phosphines coordinated to divalent palladium and water (Sections 1.4.2 and 1.4.4).

Decomposition of the intermediate metallacyclobutane complex is a reaction that has been mentioned many times, but for which not all that much solid evidence has been presented [181] (the by-products formed via this route are always present in only tiny amounts, and often the products can be accounted for by metathesis reactions). One such reaction is β -H elimination of the metallacyclobutane complex, especially in heterogeneous catalysis. For immobilized rhenium complexes the reaction has been proven [182] and DFT calculations show that also for ruthenium catalysts this reaction should have a low activation barrier (Scheme 1.53) [183]. The allyl metal hydride species can react in various ways, for example giving a metal alkene complex. The reverse reaction is also mentioned as a way to make the catalyst initiator from a metal complex and alkene [184].



Scheme 1.53 Metallacyclobutane decomposition to metal alkene complex.

A Schrock catalyst [185] for metathesis of alkynes can also undergo hydrogen loss from the intermediate, in this instance a metallacyclobutadiene generated from terminal alkynes (Scheme 1.54) [186]. Terminal alkynes can react in various ways with metal complexes and metathesis is not a common reaction. Mortreux found as one of the products of the decomposition reaction complex (top right, Scheme 1.54) and *t*-BuOH. This complex is highly active as a polymerization catalyst of alkynes and therefore it could not be identified when an excess of alkyne was present. The other complex, (bottom left, Scheme 1.54), can also be formed directly from



Scheme 1.54 Schrock alkyne metathesis catalyst decomposition pathways.

metal-alkylidyne complexes and their dimerization has already been mentioned by Schrock as a potential deactivation mechanism [187].

1.8

Reactions of Metal–Carbon and Metal–Hydride Bonds

1.8.1

Reactions with Protic Reagents

The simplest reactions of organometallic compounds are those of the early transition metal alkyls and hydrides with water, acids and alcohols. Oxophilic metal ions such as titanium, zirconium, and vanadium (but also main group metals such as lithium, magnesium, aluminum, zinc, to name a few) react very rapidly with water and if no care is taken to exclude protic reagents thoroughly this presents the most common pathway for their decomposition. Exclusion of such species, including oxygen, is common practice in “Ziegler” catalysis. Usually the aluminum alkylating agent is used in excess so as to remove the last traces of compounds that may decompose the catalysts. Pretreatment of reagents and solvents has been extensively studied and can be found in the appropriate literature [188]. Metal hydrides may undergo similar reactions.

For late transition metal alkyl compounds the situation is more complex and many are resistant to such reactions with water. Perhaps this was somewhat unexpected and it has retarded the development of transition metal chemistry and catalysis in water [189]. Since the 1970s we have learned that many transition metal alkyl species are stable in water and main group metal alkyl species have been known to be stable in water. Examples of main group metals include toxic alkyl heavy metal species such as methylmercury derivatives (a product of aquatic anaerobic organisms!), tetraethyllead and/or alkyltin derivatives (that require a copper catalyst for their decomposition in acidic water), and so on. Dimethylpalladium complexes react readily with weak acids, but monoalkyl species of palladium react very slowly, even at 100°C with strong

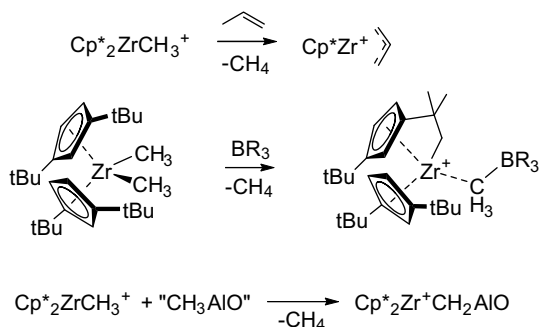
acids, thus enabling the copolymerization of ethene and carbon monoxide in methanol in the presence of acids [190, 191]. Likewise, the SHOP process [192], involving nickel alkyl species, can be carried out in 1,4-butanediol. The Ruhrchemie–Rhône Poulenc process for the hydroformylation of propene in water involves rhodium hydride and propyl species which are not decomposed by water at neutral pH.

Hydrocyanation of alkenes using nickel phosphite [193] or phosphine [194] catalysts involves nickel hydride intermediates which may react with HCN to give dihydrogen and nickel dicyanides. This reaction is irreversible and leads to catalyst decomposition. In the carbonylation reaction of methanol the Rh(III) methyl intermediate survives the strongly acidic conditions and rhodium methyl or acetyl species react with protons only as a side-reaction. This leads to trivalent rhodium halides, which have to be reduced before they can restart the catalytic cycle as Rh(I) undergoing oxidative addition of methyl iodide.

1.8.2

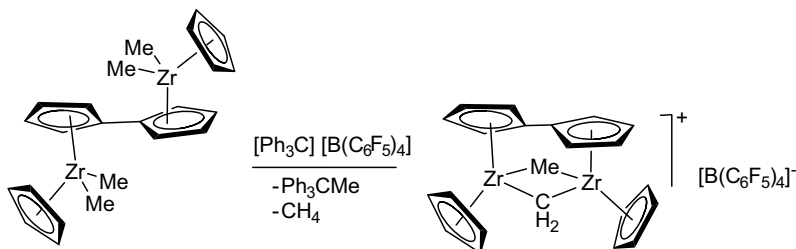
Reactions of Zirconium and Titanium Alkyl Catalysts

In addition to the obvious reactions of reactive metal alkyls with protic reagents a few reactions have been reported for zirconium and titanium alkyl compounds that may be relevant to the decomposition of these catalysts. Teuben reported that zirconium alkyl compounds react with propene to give an alkane and a π -allyl zirconium species [195]. The latter is inactive in alkene polymerization and thus stops the polymerization reaction (see Scheme 1.55). In ethene polymerization this reaction is less likely as it can only occur with products formed by β -hydride elimination and not with the substrate, ethene. Conceptually this reaction might be compared to the reaction of Pd(II) salts, especially acetates, with alkenes to give π -allyl palladium complexes and acid. Aluminoxanes and methylzirconium compounds lead to methane formation and bridging methylene species, as was reported by Kamisky [196].



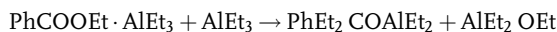
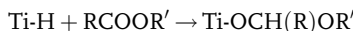
Scheme 1.55 Deactivation of zirconium catalysts.

Another example of catalyst deactivation via the formation of bridging methylene species, reported by Marks, is illustrated in Scheme 1.56 [197].



Scheme 1.56 Catalyst deactivation via $\mu\text{-CH}_2$ complex formation.

Hydride intermediates formed in chain transfer with hydrogen during olefin polymerization may also lead to deactivation reactions. For example, the presence of ester modifying agents in propene polymerization with Ziegler–Natta catalysts can lead to the formation of inactive titanium alkoxides [198]. The esters can also be reduced to alkoxides by reaction with excess aluminum alkyl [199].



1.9

Reactions Blocking the Active Sites

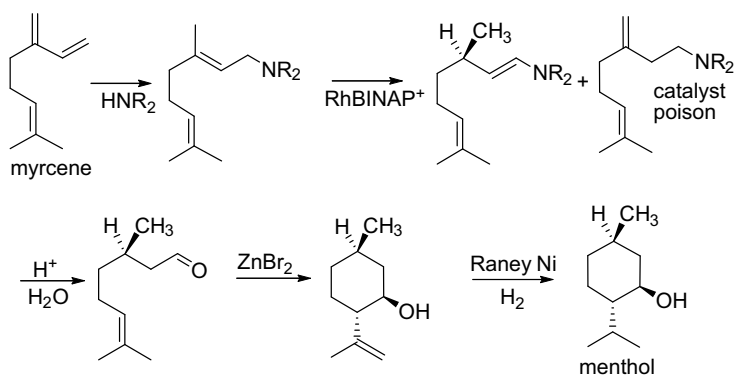
Impurities in the feed or alternative reactions of substrates can cause the formation of inactive species. For instance when alkenes are the substrate one can imagine that hydroperoxides, dienes, alkynes, enones, and so on can react with the catalyst to give inactive species. Sometimes this may be temporary and the catalyst activity can be restored, in which case one might say that “dormant” sites are formed. These reactions are highly specific and most of them will be treated in the chapters that follow. Dormant sites are well-known in propene polymerization catalysis and in hydroformylation catalysis. In metallocene-catalyzed olefin polymerization, coordination of AlMe_3 to $[\text{Cp}_2\text{ZrR}]^+$ can lead to dormant, alkyl-bridged species of type $[\text{Cp}_2\text{Zr}(\mu\text{-R})(\mu\text{-Me})\text{AlMe}_2]^+$.

1.9.1

Polar Impurities

Ligands competing with the substrate for the open coordination sites are an obvious cause for the slowing down of a reaction. Undoubtedly, hundreds of examples could be collected. We will mention only one that has been of practical importance, namely

in the asymmetric isomerization of the allylamine precursor for menthol, a process operated by Takasago [200]. The synthesis of menthol is given in Scheme 1.57. The key reaction is the enantioselective isomerization of the allylamine to the asymmetric enamine. The amine by-product blocks the cationic catalyst in this case.



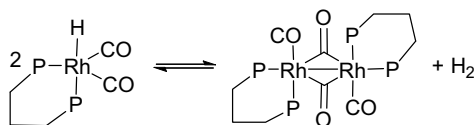
Scheme 1.57 Preparation of menthol according to Takasago.

1.9.2

Dimer Formation

Active, monomeric catalyst species may be involved in the formation of inactive dimers. When this equilibrium is reversible it only leads to a reduction in the amount of catalyst available and does not bring the catalysis to a full stop.

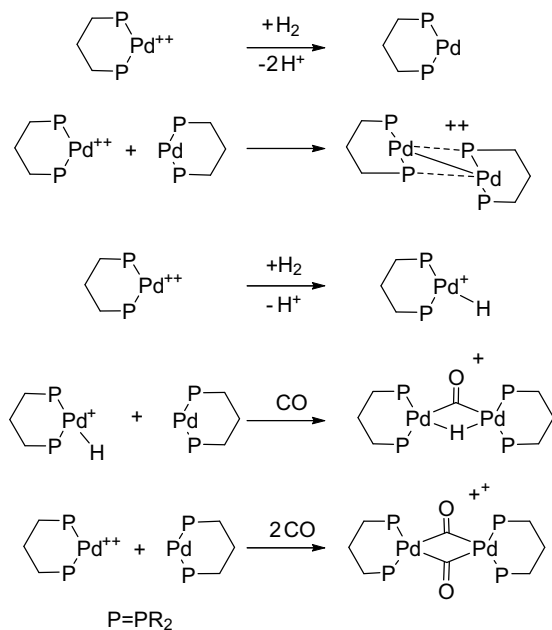
A well-known example is the formation of the so-called orange dimer from $\text{HRh}(\text{PPh}_3)_3\text{CO}$, already reported by Wilkinson [201]. This will occur at low pressures of hydrogen and high rhodium concentrations (see Scheme 1.58) [202]. The reaction is reversible.



Scheme 1.58 Rhodium dimer formation in rhodium catalysis.

Formation of zerovalent palladium species during carbonylation reactions catalyzed by divalent palladium leads to the formation of formally monovalent palladium [203]. A few types that have been observed are shown in Scheme 1.59.

When dimer formation becomes dominant, one might attempt to destabilize the dimer relative to the monomer. For instance, by making the ligand very bulky one might prevent dimer formation. Another approach is so-called “site isolation” by immobilization of the catalyst, as was described by Grubbs [204], or by encapsulation



Scheme 1.59 Formation of palladium(I) dimers in carbonylation catalysts.

in a dendrimer [205]. Grubbs's well-known example concerns a titanocene catalyst that is used as a hydrogenation catalyst. The intermediate titanium hydride is converted almost completely to a dimer rendering the catalyst to be of low activity. Immobilization of the catalyst on a resin support prevents dimerization and an active catalyst is obtained. In oxidation catalysis involving metal porphyrins or metal phthalocyanines dimer formation is a common phenomenon, for instance for Mn(III) phthalocyanine as shown in Figure 1.5 [206].

1.9.3

Ligand Metallation

In Scheme 1.55 we have shown an example of metallation of the ligand that led to an inactive zirconium catalyst. In late transition metal chemistry the same reactions

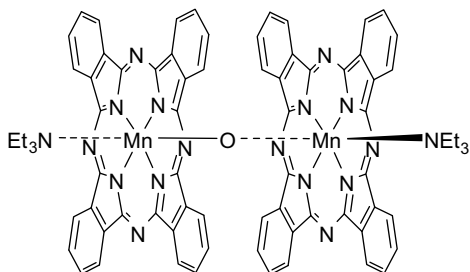
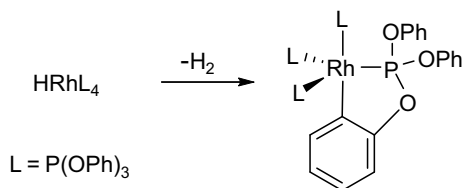
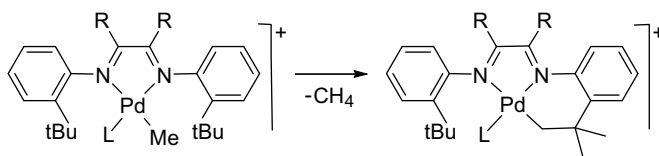


Figure 1.5 Manganese(III) phthalocyanine dimerization via an oxygen bridge.

occur, but now the complexes formed represent a dormant site and catalyst activity can often be restored. Work-up of rhodium-phosphite catalyst solutions after hydroformylation often shows the partial formation of metallated species, especially when bulky phosphites are used [207]. Dihydrogen elimination or alkane elimination may lead to the metallated complex. The reaction is reversible for rhodium and thus the metallated species could function as a stabilized form of rhodium during a catalyst recycle. Many metallated phosphite complexes have been reported, but we mention only two, one for triphenyl phosphite and rhodium [208] (see Scheme 1.60) and one for a bulky diimine and palladium (Scheme 1.61) [209].



Scheme 1.60 A metallated rhodium phosphite complex.



Scheme 1.61 Intramolecular C–H activation in a cationic palladium α -diimine complex.

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