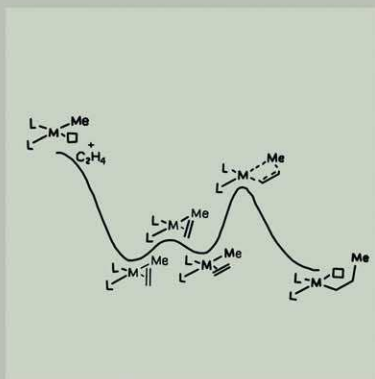


Current Methods in Inorganic Chemistry; Volume 3

Fundamentals of Molecular Catalysis



Hideo Kurosawa
Akio Yamamoto
(Editors)



Fundamentals of Molecular Catalysis

Current Methods in Inorganic Chemistry

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Current Methods in Inorganic Chemistry Volume 3

Fundamentals of Molecular Catalysis

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Preface

The past half-century has witnessed tremendous advances in homogeneous catalysis. A variety of new synthetic methodologies has been developed and applied to industrial processes as well as to laboratory syntheses. It is now hard to find a multi-step synthesis of complex organic molecules where transition metal-catalyzed processes are not employed. The remarkable progress in homogeneous catalysis stems from in-depth understanding of the mechanisms of the known homogeneous catalytic processes and from developments based on the new information derived in studying the behavior of organotransition metal complexes.

The effect of understanding the elementary processes is not limited to organic synthesis. Polymer synthesis has been profoundly influenced by development of single-site polymerization of olefins by complexes of early transition metals where the coordination and insertion modes of monomers are precisely controlled by proper ligand design. The vistas of polymer synthesis have also been broadened by discoveries of olefin polymerization and copolymerization by late transition metal catalysts. Ring opening metathesis polymerization that developed from the basic studies of metal carbene type complexes has opened up a new horizon in polymer synthesis, whereas ring-closing metathesis has provided a new methodology for synthesis of medium to large size ring compounds. We can further expect that some of the methodologies gained through studies on the elementary processes will be successfully applied to prepare materials of unique properties for various uses.

The rapid growth in organotransition metal chemistry and in homogeneous catalysis started in the early fifties with the advent of ferrocene, Ziegler catalyst, and the Hoechst–Wacker process. They spurred the rapid growth of organotransition metal chemistry, resulting in a tremendous increase in the number and variety of organotransition metal complexes showing novel chemical features that are applicable to catalysis. Many of the newly found reactions had not been known previously and they led to the realization of new synthetic methodologies performed under mild conditions with high specificity.

A distinct advantage of homogeneous catalysis over conventional heterogeneous catalysis is that it allows detailed clarification of the reaction mechanisms at the molecular level by catalytic cycles consisting of elementary processes. Thus the term molecular catalysis aptly describes the characteristics of homogeneous catalysis. The recent impressive advancement in catalytic asymmetric synthesis

demonstrates the utility of homogeneous catalysis where fine-tuning of properties of catalytic species can be achieved by modifying the environment around the central transition metal through proper design of chiral ligands. Upon understanding the basic concepts in catalysis further applications of the concepts can be accomplished to develop transition metal catalysts supported on the solid surface. One can thus create catalyst systems where the catalytic processes can be understood at the molecular level while the benefit of heterogeneous systems in separation is maintained.

Another effect of the progress in molecular catalysis can be found in green chemistry where development of atom-efficient synthesis through new synthetic routes is sought to minimize waste. Greener routes with less unfavorable impact on the environment may be provided by designing proper synthetic methodologies from the outset, based on the information of elementary processes in molecular catalysis

We felt that a book dealing with the fundamental reaction processes behind catalysis would be beneficial for both organometallic chemists and synthetic organic chemists.

Various elementary processes such as oxidative addition, reductive elimination, olefin and CO insertion into the metal-to-carbon bond have found extensive applications in organic synthesis. Other processes such as attack of nucleophiles on metal-bound CO and olefins, unique reactions of metal carbene complexes, and σ -bond metatheses are among the topics of special interest to organometallic chemists as well as to synthetic organic chemists. Our aim is to provide the reader with detailed accounts of elementary processes with the hope that the information provided here is used for further development of molecular catalysis.

We are very pleased to have authoritative reviews on elementary processes from experts working at the forefront of organometallic chemistry in the book. It is our pleasure to acknowledge their contributions to the present volume with appreciation for their time and effort. We would also like to acknowledge the assistance of the reviewers who served in checking the content of each chapter to minimize errors and enhance the value of the book. The project of publishing the book in its present form started with an invitation from Elsevier Science to contribute to the series "Current Methods in Inorganic Chemistry". We would like to acknowledge the initiative of Fred Fenter and the cooperation of Sandra Migchielsen and Derek Coleman in bringing this book to fruition.

Akio Yamamoto and Hideo Kurosawa
July 2002

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General Introduction

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1.1 INTRODUCTION

The chemistry of organotransition metal complexes [1] has progressed in step with the development of homogeneous catalysis [2], each influencing the other. In certain cases, study of chemistry of such complexes has been motivated by the wish to understand the mechanisms of important catalytic processes that were already developed and to improve their performance. On the other hand, examination of the chemical properties of a particular type of organotransition metal complex has sometimes led to discoveries of hitherto unknown fundamental reactions. Combination of the concept of a newly found elementary process with a known process will continue to lead to discoveries of novel catalytic processes and enrich the scope of organic synthesis

Much of homogeneous catalysis can be regarded as being constituted of one or more catalytic cycles, where the cycle is in turn composed of multi-step elementary processes. The performance of a catalyst system is assessed by measuring the number of moles of product formed per mol of the catalyst both in overall, giving the turnover number (TON), and per unit time, giving the turnover frequency (TOF). The turnover number of a catalyst depends both on the activity as well as the stability of the catalyst. By identifying the turnover-limiting step in the catalytic cycle and by enhancing the rate of this specific elementary process one can often increase the turnover frequency. Likewise, by identifying the decomposition path one can increase the lifetime and TON of a catalyst.

Since increasing catalyst activity of a catalyst species often comes from understanding the behavior of the organometallic species involved and by manipulating experimental conditions to influence a key fundamental step, an in-depth understanding of each elementary step will help developing new catalytic systems of high utility.

In the introductory part, attention is first focussed on describing catalytic systems as constructed of elementary processes. It is not intended to provide a

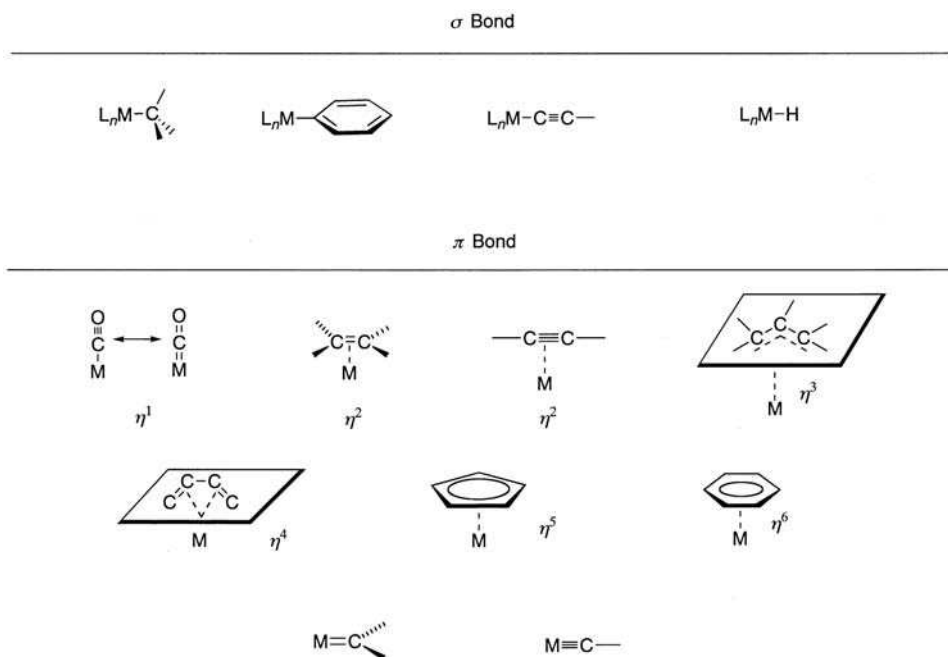
comprehensive summary of the many existing homogeneous catalytic systems, but rather to provide the reader with basic ways of understanding the mechanisms of homogeneous catalyst systems.

For readers who are not familiar with organotransition metal chemistry, an introductory account of the fundamentals of organotransition metal chemistry is given below as a guide, but several introductory monographs are available on this topic.

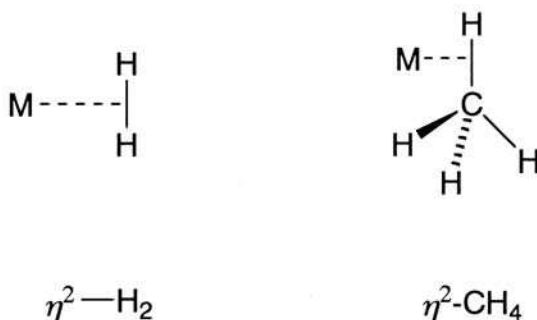
1.1.1 Bonding modes

Organotransition metal complexes can be broadly classified into two types, one with metal–carbon σ bonds and the other with metal–carbon π bonds between the central metal atom and a coordinated unsaturated ligand. A transition metal atom and an alkyl group [3] form a σ bond that is often reactive and the transition metal alkyl complex may play an important role in catalytic processes. Because of the importance of metal alkyls and hydrides in homogeneous catalysis, hydride complexes are also included in our discussion.

The nature of metal–ligand bonding can be described as a combination of two bonding modes, (a) ligand-to-metal electron donation and (b) metal-to-ligand back-donation. Scheme 1.1 illustrates representative examples of the σ and π



Scheme 1.1. Representative examples of σ -bonded and π -bonded complexes.

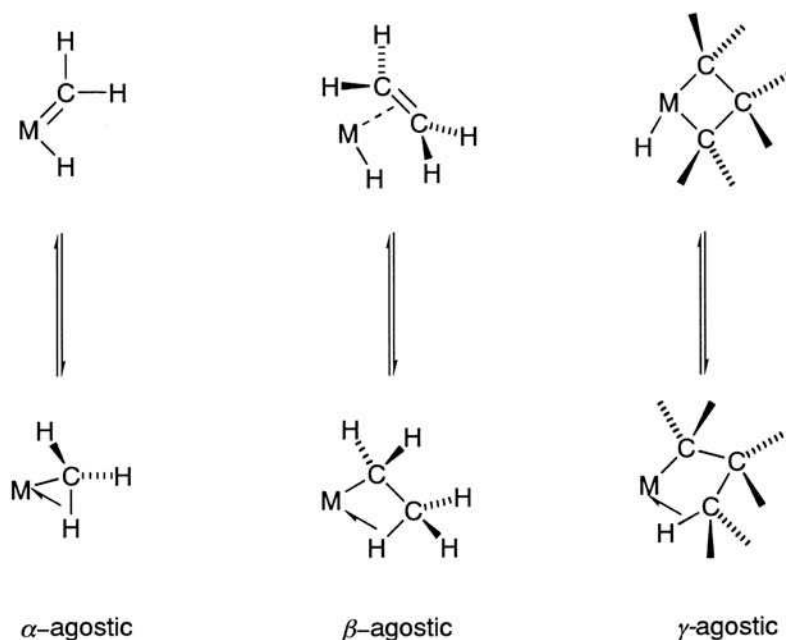
Scheme 1.2. Two types of side-on (η^2) bondings.

bonding types. The symbol η^n is used to indicate the connectivity of the metal with the ligand. The superscript indicates the number of ligating carbon atoms that interact with the metal. Thus the η^2 notation means that the metal is bonded to two carbons of an olefin bound to the metal in a side-on manner. When the ligating atoms are not carbons, the symbol κ^n is employed for describing the connectivity of the central metal [4]. Scheme 1.1 shows examples of (1) σ -bonded complexes with sp^3 , sp^2 , and sp carbons and hydride, and (2) π complexes with alkene, alkyne, allyl, diene, cyclopentadienyl, and arene ligands bonded with the metal through two to six carbon atoms. Carbon monoxide also forms a π bond with a transition metal.

Besides the usual π bonding, there are special types of bonding: metal-to-carbon double and triple bonds known in metal alkylidene and alkylidyne complexes and these are included in Scheme 1.1.

Recently, the existence of other types of σ -bond complexes was recognized [5] in which side-on coordination of a σ bond with a transition metal occurs in a ligand like H_2 ($\text{H}-\text{H}$) or an alkane ($\text{C}-\text{H}$). The bonding between H_2 and the transition metal can be accounted for by ligand to metal σ donation via electron transfer from the $\text{H}-\text{H}$ σ bonding orbital to the vacant metal d orbital accompanied by back donation from the filled metal d_π orbital into the H_2 antibonding σ^* orbital. The side-on bonding is described as η^2 using the notation discussed for olefin-metal π bonding. This type of bond may be involved in the activation of molecular hydrogen on interaction with a transition metal before the $\text{H}-\text{H}$ bond is cleaved to form a metal dihydride. The $\text{C}-\text{H}$ bond in methane may act in a similar way to the $\eta^2\text{-H}_2$ bond on interaction with a transition metal as the first step in cleavage of a $\text{C}-\text{H}$ bond in methane in a process that forms a transition metal complex having a methyl and a hydride ligands.

When an alkyl group is bound to a transition metal, some of the $\text{C}-\text{H}$ bonds in the alkyl ligand may interact with the metal. The interaction between the metal and the $\text{C}-\text{H}$ bond at the α carbon in the alkyl group is called an α agostic interaction [6], and that between the $\text{C}-\text{H}$ bond at the β carbon is named a β



Scheme 1.3. Agostic interactions.

agostic interaction. Furthermore the γ agostic interaction is also known. The agostic interaction is often indicated by a half arrow from the C–H bond to the metal. The α agostic interaction may be involved in a process to abstract the α hydrogen from a metal–alkyl complex to form a metal–alkylidene complex. The β agostic interaction may play a role in a process causing the abstraction of a β hydrogen in the alkyl ligand to afford an alkene and a metal hydride. The γ agostic interaction may precede the hydrogen abstraction in a process to form a metallacycle having the four-membered ring, a metallacyclobutane.

1.2 ELUCIDATION OF CATALYTIC MECHANISMS AS CYCLES COMPOSED OF ELEMENTARY STEPS

With our deeper understanding of the elementary processes of organotransition metal complexes and consequent advancement in clarification of mechanisms in homogeneous catalysis, we can now describe most such reactions in terms of catalytic cycles consisting of known elementary processes. The term molecular catalysis is appropriate to describe such catalysis.

The understanding of the following elementary processes that has gradually emerged with the progress of organotransition metal chemistry allows us to describe most catalytic cycles as combinations of such processes.

- (1) Ligand dissociation and coordination
- (2) Oxidative addition and reductive elimination.
- (3) Insertion and deinsertion (extrusion) of unsaturated compounds such as olefin, CO and isocyanide.
- (4) Transmetallation, i. e., transfer of an alkyl group from one metal to the other to form a new type of a metal alkyl complex.
- (5) Attack of a nucleophile or electrophile on a ligand coordinated to a transition metal center.
- (6) σ -Bond metathesis.
- (7) Reactions of metal alkylidene and alkylidyne complexes with olefins and alkynes.

Elementary processes (1) to (5) are most common but in certain cases processes (6) and (7) also operate.

In the following account we attempt to describe the catalytic cycles in terms of these elementary processes.

1.3 COMMENTS ON ELEMENTARY PROCESSES INVOLVED IN METAL-CATALYZED ORGANIC SYNTHESIS

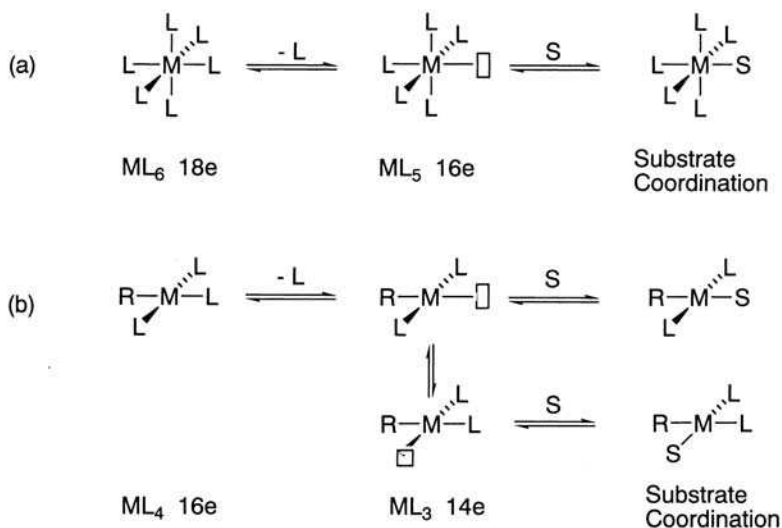
1.3.1 *Ligand dissociation and coordination processes*

In order for a substrate to be activated by a transition metal in homogeneous catalysis, prior interaction of the substrate with the transition metal catalyst is required. When the complex is coordinatively saturated with an 18 electron configuration [1,7], coordinative unsaturation is usually created by dissociation of all or part of a bound ligand from the complex thus allowing the resulting coordinatively unsaturated transition metal fragment to enter the catalytic cycle (Scheme 1.4).

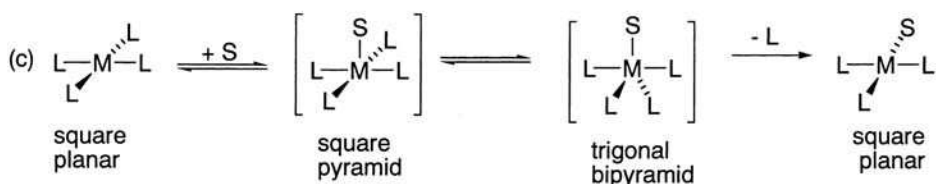
The binding of a substrate may proceed through a dissociative or associative process. The dissociation of a ligand in the dissociative process can be promoted thermally or photochemically. Such ligand dissociation is commonly observed in coordinatively saturated octahedral complexes (Scheme 1.4a) but certain types of transition metal complex having a square planar configuration also demonstrate such ligand dissociation affording T-shaped three-coordinate intermediates (Scheme 1.4b). For a complex to enter a process involving insertion processes with substrates such as carbon monoxide and olefin (*vide infra*) creation of a coordination site adjacent to the alkyl (R) group is required. The generation of the vacant site adjacent to the alkyl ligand may be performed by isomerization of a T-shaped '*trans*' isomer to the other T-shaped '*cis*' isomer. A kinetic study is helpful in shedding light on the detailed mechanism. When ligand dissociation is involved, addition of a ligand to the system may hinder the catalytic process, suggesting that dissociation of a ligand is involved at some point in the catalytic cycle.

When an associative process involves a square planar complex, the substrate (S)

Dissociative route



Associative route



Scheme 1.4. Dissociative and associative routes for binding of a substrate with the metal center.

may approach from top (or bottom) of the square plane to form a square pyramidal configuration. The intermediate is transformed through a trigonal bipyramidal configuration to the square planar configuration in replacement of a ligand by the substrate as shown in Scheme 1.4c. The coordinated substrate may enter subsequent reactions in a catalytic process to produce a product, which should be liberated from the metal center to allow the turnover of the catalytic cycle. It is often necessary to postulate *cis-trans* isomerization of a square planar complex [8] in the catalytic process.

1.3.2 Oxidative addition and reductive elimination

Since transition metal alkyls and hydrides are quintessential organometallic species that undergo various elementary processes in catalytic reactions, information on appropriate methods for their generation is quite important. Oxidative

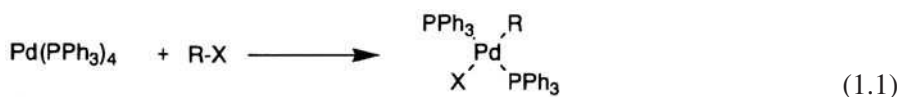
addition and transmetallation provide two important routes, among others, to generate such an organometallic complex [9].

(a) *Cleavage of polar bonds*

Oxidative addition of organic compounds having carbon–X bond (X = heteroatom) to a low valent transition metal complex such as Pd(0) or Rh(I) with cleavage of the C–X bond often yields reactive organotransition metal complexes. Cleavage of non-polar bonds will be discussed in Chapter 2, while cleavage of polar bonds will be dealt with in Chapter 3.

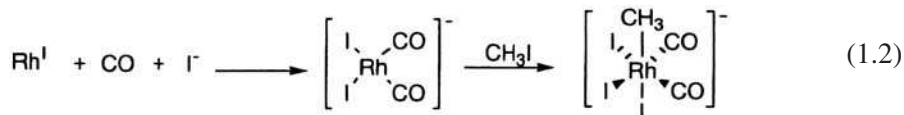
Catalytic processes utilizing carbon–halogen bond cleavage. Because of the ease of preparation of organic halides and their tendency to undergo ready C–halogen bond cleavage, organic halides have been extensively employed in organic synthetic applications of catalysis.

The oxidative addition of an aryl iodide to a zerovalent complex such as $[\text{Pd}(\text{PPh}_3)_4]$ gives *trans*- $[\text{Pd}(\text{Ar})\text{I}(\text{PPh}_3)_2]$ having a palladium–aryl and a palladium–iodide bond; indeed, this is one of the oldest examples of oxidative addition of aryl iodide to Pd(0) complex (Eq. 1.1) [10].

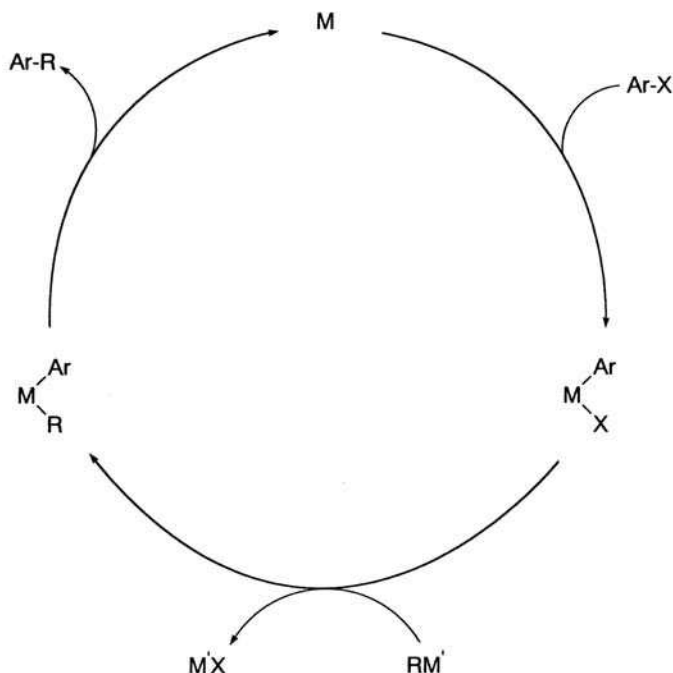


The process is preceded by dissociation of two triphenylphosphine ligands from the zerovalent palladium complex, $[\text{Pd}(\text{PPh}_3)_4]$, and gives a divalent organopalladium halide complex. In the *trans* isomer obtained in Eq. 1.1, the R ligand exerts *trans influence* and weakens the Pd–X bond situated at the position *trans* to R making the X ligand in *trans*- $[\text{Pd}(\text{Ar})\text{X}(\text{PPh}_3)_2]$ susceptible to substitution such as transmetallation. The enhancement of the substitution rate of the ligand at the *trans* position is called the *trans effect*.

Oxidative addition of methyl iodide to a Rh(I) complex coordinated with iodide and carbonyl ligands affords methylrhodium(III) type complex where the methyl and the iodide ligands are situated in mutually *trans* positions (Eq. 1.2).



The former type of oxidative addition can be coupled with other subsequent processes such as transmetallation to give diorganotransition metal complexes. Since reductive elimination often follows the transmetallation to liberate a product where the two organic moieties are coupled, a quite useful process catalyzed by



Scheme 1.5. Mechanism of transition metal-catalyzed cross-coupling of an aryl halide with a metal alkyl.

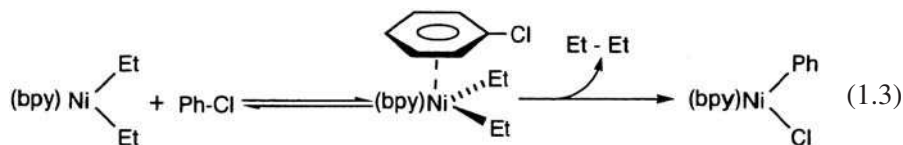
nickel or palladium complexes can be constructed to cause aryl–alkyl or alkenyl–alkyl coupling processes. The transmetalation will be discussed in Chapter 5 and reductive elimination will be dealt with in Chapter 9.

Scheme 1.5 illustrates a schematic catalytic cycle for the cross coupling process composed of (a) oxidative addition of an aryl halide, (b) transmetalation of an alkyl group to replace the X ligand to afford a diorganometal complex, and (c) reductive elimination with coupling of the aryl and alkyl groups.

The first successful application of the cross-coupling was reported independently by Tamao and Kumada's group [11,12] and by Corriu's group [13] using alkyl magnesium halide as the alkylating agent. The scope of Scheme 1.5 was later expanded by using other organometallic compounds RM' of tin, zinc, silicon, aluminum, lithium, zirconium, and boron for realizing useful coupling processes. By proper choice of the alkylating agents that are tolerant of functional groups, such as a carbonyl group attached to the alkyl group, the utility of the catalytic methods has been greatly enhanced. The cross-coupling methods using organotin reagents and organoboron reagents catalyzed by palladium complexes have been very much welcomed by synthetic organic chemists. Of these two methodologies, the cross-coupling method using organoboron compounds is often preferred because of their less toxic nature [14].

For the sake of simplicity the ligand is omitted in Scheme 1.5. When a monodentate tertiary phosphine is used as a supporting ligand, there arises the possibility of the existence of *trans* and *cis* isomers as the intermediates thus making the situation complicated. Oxidative addition of aryl halide to a palladium(0) complex usually gives a *trans* isomer but the initial species formed as a kinetic product may have a *cis* form which may be later isomerized into a *trans* form [15]. If the subsequent transmetallation takes place from the *trans* isomer with retention of the *trans* configuration, it would give the *trans*-diorganopalladium complex. Since the *trans*-diorgano complex is not suitable for undergoing direct reductive elimination, *trans* to *cis* isomerization may be required to bring the alkyl and aryl groups into mutually adjacent positions for liberating the reductive elimination product [16,17]. However, evidence supporting transmetallation through a bimetallic mechanism to provide a *cis*-diorganopalladium intermediate was presented recently, when phenyl iodide having fluorine and chlorine substituents was used [15]. Thus the apparently simple mechanism shown in Scheme 1.5 can be complicated depending on the substrates and other conditions.

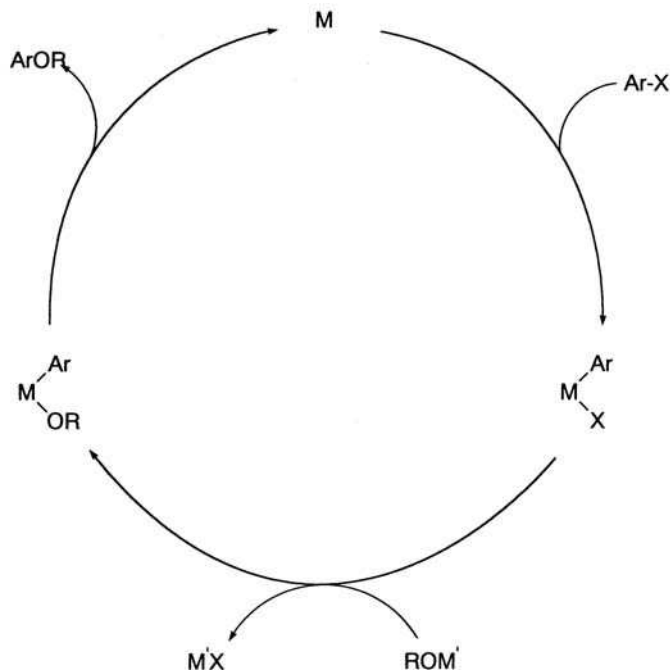
Further complications may be involved in the reductive elimination process in catalytic cross-coupling. Although Scheme 1.5 represents a conceptual mechanism consisting of three elementary processes, the actual mechanism may be somewhat different from that shown in Scheme 1.5. In coupling of the two alkyl groups of thermally stable $\text{NiEt}_2(\text{bpy})$ on treatment with chlorobenzene, interaction of chlorobenzene with $\text{NiEt}_2(\text{bpy})$ accelerates the production of butane (Eq. 1.3).



These results suggest that interaction of the diorganometal complex with the phenyl group in a haloarene may be involved in the actual catalytic cycle as well to facilitate the coupling of the two organo groups concomitant with the carbon-halogen bond cleavage without going through prior reductive elimination [18].

A very bulky monotertiary phosphine ligand has a higher tendency to dissociate from the metal center than less bulky ones and in certain cases catalytic processes may proceed with an active center where only one tertiary phosphine is coordinated. Extensive examination of the roles of various tertiary phosphine ligands, sometimes aided by combinatorial methods, has revealed usefulness of very bulky and electron-donating ligands such as tri(tertiarybutyl)phosphine $\text{P}(t\text{-Bu})_3$ and tri(*ortho*-tolyl)phosphine, $\text{P}(o\text{-tolyl})_3$, which serve as excellent ligands having high bulk and strong electron-donating abilities [19,20].

Ditertiary phosphine ligands coordinate to the metal with two donor atoms and fix the configuration of a chelated structure. Fixing the *cis* structures in this way sometimes lowers catalyst activity but can increase it by limiting the number of possible configurations of the active species.

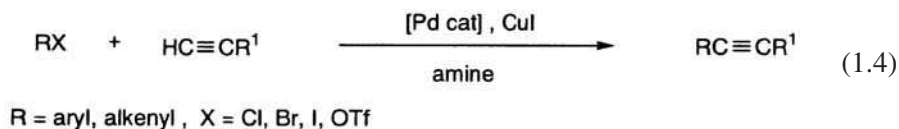


Scheme 1.6. Palladium-catalyzed synthesis of ether by cross-coupling of an aryl halide with a metal alkoxide.

Other type of applications have been made to prepare amines, ethers and sulfides by utilizing the reactivity of organopalladium complexes in association with replacement of the halide ligand by amide [19,20], alkoxide [19,20], and sulfide anions [21].

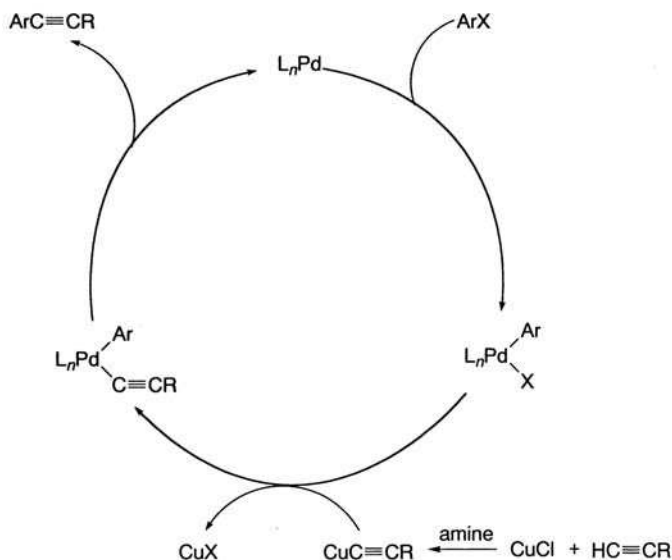
As a typical example, a catalytic cycle for ether formation from aryl halide and alkali metal alkoxide catalyzed by palladium catalyst is shown in Scheme 1.6.

Another application of the concept of transition metal-catalyzed cross-coupling is coupling of aryl or alkenyl halides with alkynes, named Sonogashira coupling (Eq. 1.4) [22].



The advantage of the process is that prior preparation of alkynylcopper compounds is not required but use of copper halide in the presence of an amine suffices for driving the catalytic process. The catalytic cycle is shown in Scheme 1.7.

In the scheme the oxidative addition of aryl halide to a Pd(0) species gives an arylpalladium halide and the halide ligand is then replaced by an alkynyl group in the alkynyl-copper intermediate generated by interaction of the alkyne with cop-



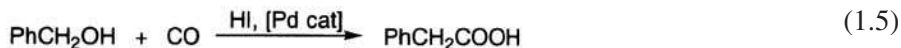
Scheme 1.7. Mechanism of cross-coupling of an aryl halide with an alkyne.

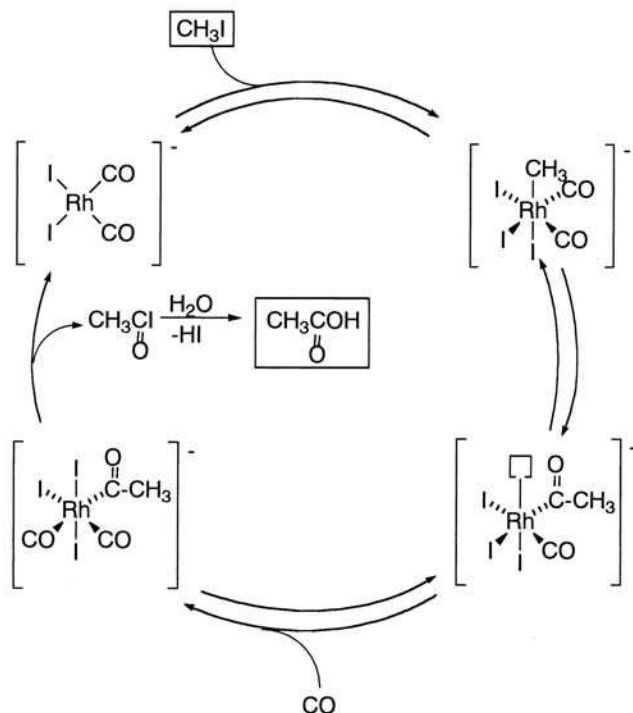
per halide in the presence of an amine [23]. The resulting alkynyl–arylpalladium species reductively eliminates the arylated alkyne. The transmetalation process, which plays an important role in the catalysis, will be discussed in Chapter 5.

Another important process involving oxidative addition of alkyl halide is found in the first step in Monsanto process, an important industrial process to convert methanol into acetic acid with carbon monoxide at 150–200°C under 30–60 bar of CO [24]. In the Monsanto process methyl iodide is formed first from methanol and hydrogen iodide, added as the promoter to the catalytic system. The subsequent reaction of methyl iodide with a rhodium(I) species forms a methylrhodium(III) iodide species by oxidative addition (Eq. 1.2).

The reactive methylrhodium(III) complex thus formed then undergoes CO insertion to give an acetylrhodium species as shown in Scheme 1.8. Reductive elimination of the acetyl and iodide ligands liberates acetyl iodide, which is hydrolyzed to produce acetic acid. The hydrolysis generates HI, which is recycled on reaction with methanol regenerating methyl iodide. The important elementary processes of CO insertion will be discussed in Chapter 7.

This type of oxidative addition involving the carbon–halogen bond cleavage may be involved in other catalytic processes using alcohols in the presence of hydrogen halide. For example, in the carbonylation of benzyl alcohol in the presence of HI, phenylacetic acid can be catalytically produced in the presence of a Pd(0) complex (Eq. 1.5) [25].

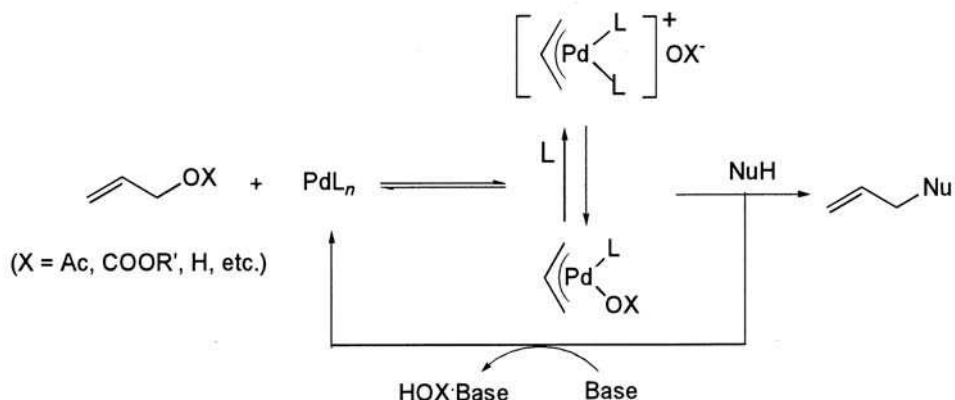




Scheme 1.8. Mechanism of catalytic carbonylation of methanol to acetic acid.

In the catalytic process, benzyl alcohol is converted into benzyl iodide on interaction with HI and the benzyl iodide formed oxidatively adds to Pd(0) species to generate benzylpalladium species. Insertion of CO into the benzyl–palladium bond gives a phenylacetyl–palladium iodide species, which on the subsequent reductive elimination releases phenylacetic iodide. In a similar way as we described in Scheme 1.8 in the catalytic conversion of methanol into acetic acid, phenylacetyl iodide is converted into phenylacetic acid on hydrolysis.

Catalytic processes involving cleavage of C–O bond. Among other oxidative addition processes involving cleavage of polar bonds, cleavage of allyl–oxygen bond in allylic acetates and carbonates has been extensively utilized in organic synthesis, notably by Tsuji [26] and Trost [27]. The allyl–O bond cleavage promoted by a palladium(0) complex gives electrophilic η^3 -allyl palladium(II) complexes that may be coordinated with one or two auxiliary ligand(s). The attack of a soft nucleophile on the terminal carbon in the η^3 -allyl palladium complex gives allylation product of the nucleophile and regenerates the Pd(0) species to drive a catalytic cycle for allylation of nucleophiles. When carbon nucleophiles such as active methylene compounds like malonic esters are used, the reaction provides an important means of C–C bond formation (Scheme 1.9).



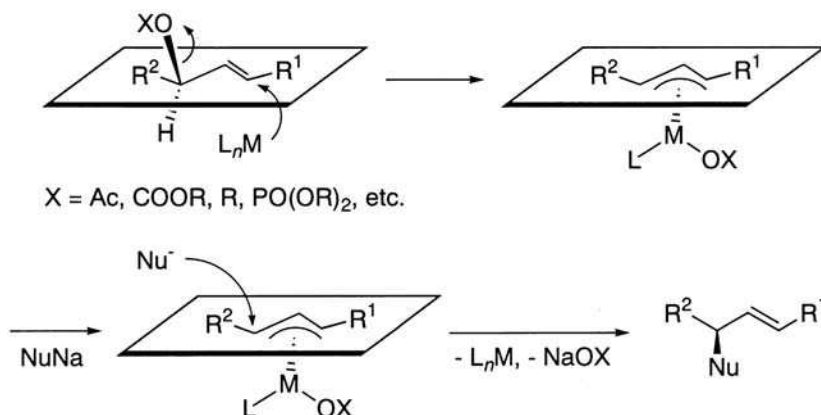
Scheme 1.9. Oxidative addition of an allylic compound to Pd(0) complex and nucleophilic attack on the η^3 -allyl ligand.

As will be discussed in Chapter 8, the attack of external reagents on an η^3 -allyl palladium complex also takes place on the central carbon allowing the other types of reaction to proceed.

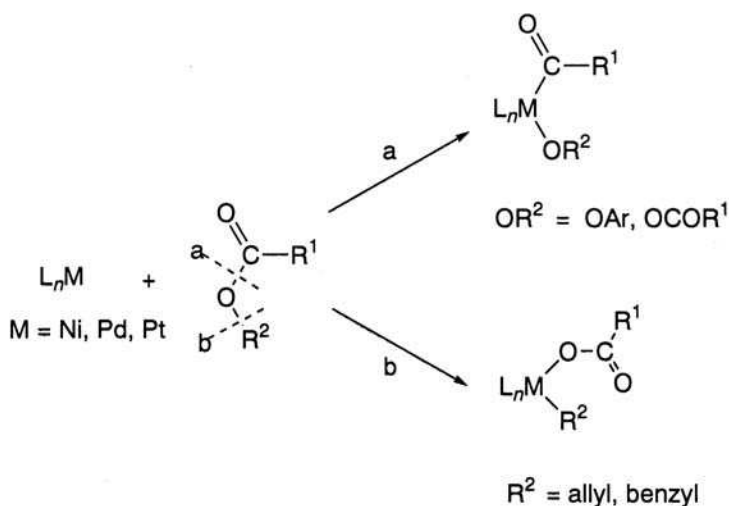
Although cleavage of the allyl–O bond in Scheme 1.9 to give η^3 -allyl palladium complexes is formally regarded as oxidative addition, the mechanism of the allyl–O bond cleavage is different from oxidative addition of alkyl halides, which has been established to proceed by an $\text{S}_{\text{N}}2$ mechanism as confirmed in oxidative addition of deuterated benzyl iodide [28]. An $\text{S}_{\text{N}}2'$ type mechanism involving the initial interaction of the central metal with the olefinic double bond in the allylic entity seems to be operative. In the oxidative addition of allylic acetate to a palladium complex the stereochemistry of the oxidative addition was established to proceed as shown in Scheme 1.10 with inversion of the stereochemistry with *anti*-elimination of the acetato group [29]. *Anti*-attack of a nucleophile on the η^3 -allyl ligand coordinated to the metal gives allylation product of the nucleophile with inversion of stereochemistry. Thus the overall process of catalytic allylation reaction proceeds with retention of the stereochemistry.

Beside oxidative addition involving allyl–O bond cleavage in allylic carboxylates, carbonates and ethers, other types of oxidative addition involving the cleavage of acyl–O bond in carboxylic esters and anhydrides have been studied for clarifying the factors causing the C–O bond cleavage. Oxidative addition of aryl carboxylates to a Ni(0) complex was found to proceed faster when the ligand attached to Ni(0) is more electron donating and the aryl group in the aryl carboxylate has more electron-withdrawing substituent. The results suggest that the nucleophilic attack of nickel on the electrophilic carbonyl group is involved in the oxidative addition process [30].

Recently, the acyl–O bond cleavage on reaction with low valent transition metal complexes has found application in preparation of carbonyl-containing compounds such as aldehydes and ketones by using palladium catalysts [31,32].



Scheme 1.10. Stereochemistry of oxidative addition of allylic compounds to L_nM to give η^3 allyl complexes and nucleophilic attack on the η^3 -allyl ligand.

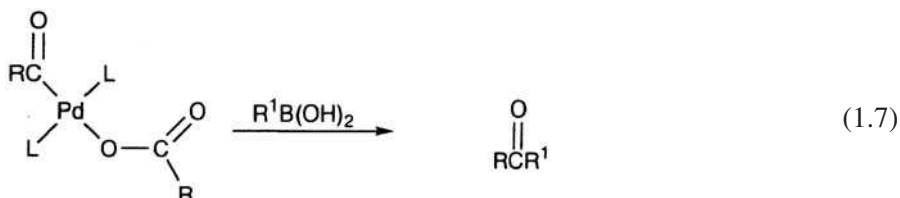
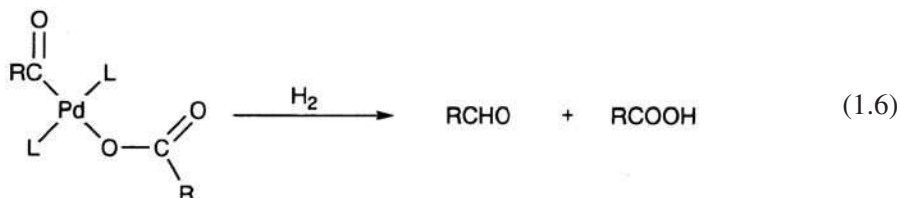


Scheme 1.11. Two types of C-O bond cleavage in carboxylic esters and anhydrides.

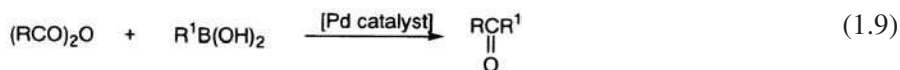
The methodology is based on the findings that the acyl-O bond in carboxylic esters and anhydrides can be readily cleaved on interaction with $Pd(0)$ complexes to give acylpalladium carboxylate or aryloxide type complexes [33] (Scheme 1.11).

Treatment of the acylpalladium carboxylate complex with H_2 liberates aldehyde and carboxylic acid (Eq. 1.6), whereas the reaction of the acylpalladium carboxylate with organoboron compounds affords ketones by transmetallation

followed by reductive elimination (Eq. 1.7) [34].



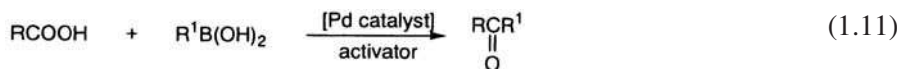
On the basis of the finding in Eq. 1.6 catalytic conversion of carboxylic anhydrides to aldehydes and carboxylic acids under hydrogen pressure has been developed (Eq. 1.8) [35]. The finding in Eq. 1.7 on the other hand, could be applied to catalytic conversion of carboxylic anhydrides with organoboronic acids into ketone synthesis [36] (Eq. 1.9).



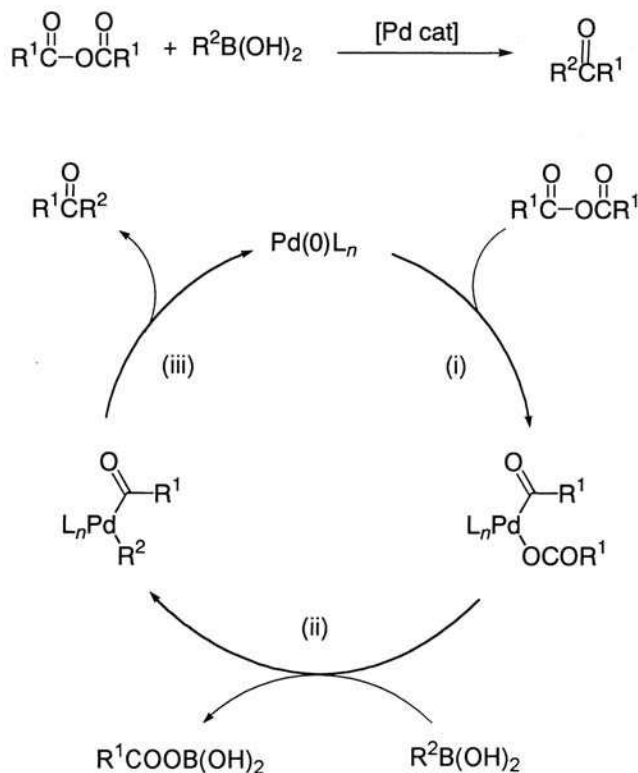
Mechanism of the palladium-catalyzed ketone synthesis, comprising oxidative addition of carboxylic anhydride, transmetalation with organoboronic acid, and reductive elimination, is shown in Scheme 1.12.

A related study utilizing cleavage of the acyl-S bond in thiol esters also showed the applicability of the acyl-S bond cleavage to ketone synthesis by using alkyl boronic acid [37].

Further application of the processes in Eqs. 1.8 and 1.9 led to syntheses of various aldehydes and ketones directly from carboxylic acids with use of an activator such as pivalic anhydride and dimethyl dicarbonate (Eqs. 1.10 and 1.11) [35,38].



These results illustrate some examples how fundamental processes found in organometallic chemistry can be applied to useful organic synthesis by combining them with other known elementary processes.

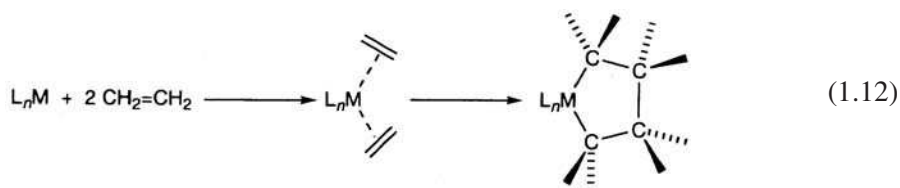


Scheme 1.12. Catalytic cycle for the formation of ketones from carboxylic anhydrides and organoboronic acids.

Other types of oxidative addition involving the cleavage of carbon–heteroatom bond will be discussed in Chapter 3.

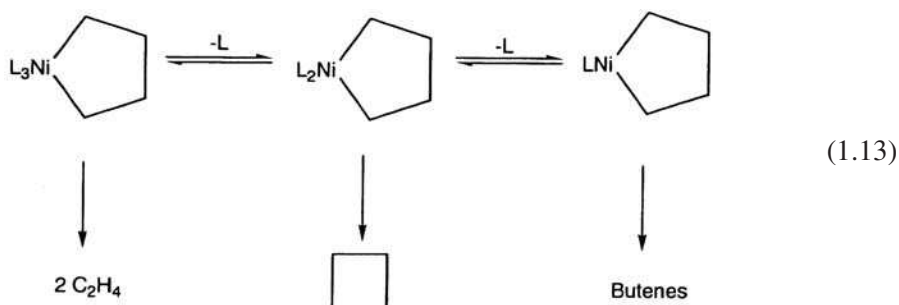
(b) Catalytic processes involving oxidative addition with C–C bond coupling

A special type of oxidative addition with C–C bond formation rather than bond cleavage as shown below is observed in certain types of synthetic processes (Eq. 1.12).



Two ethylene ligands coordinate to a low valent transition metal complex and couple with each other to form a five-membered ring called a metallacycle, in this case a metallacyclopentane. The metallacycles sometimes show particular

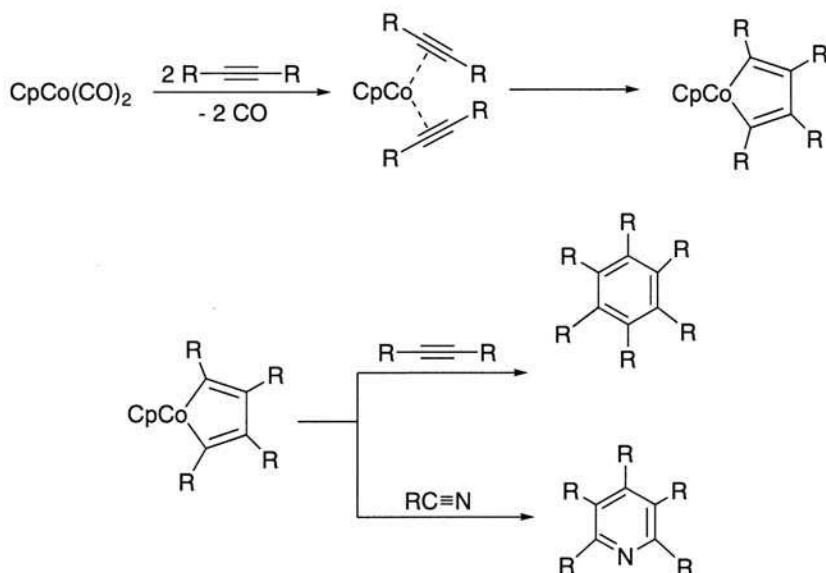
chemical behavior depending on the number of ligands attached to the metallacycle. For example, thermolysis of nickellacyclopentane having different numbers of ligands (L_n) releases different products. (a) Two ethylene molecules are liberated with reductive cleavage of the C–C bond in the metallacyclopentane (when $n = 3$), (b) cyclobutane is formed as reductive elimination product ($n = 2$), and (c) butene-1 is generated by another type of β -hydrogen elimination route (when $n = 1$) (Eq. 1.13). Utilization of the different behavior of the nickellacyclopentane leads to catalytic formation of cyclobutane from ethylene by controlling the ligand number [39].



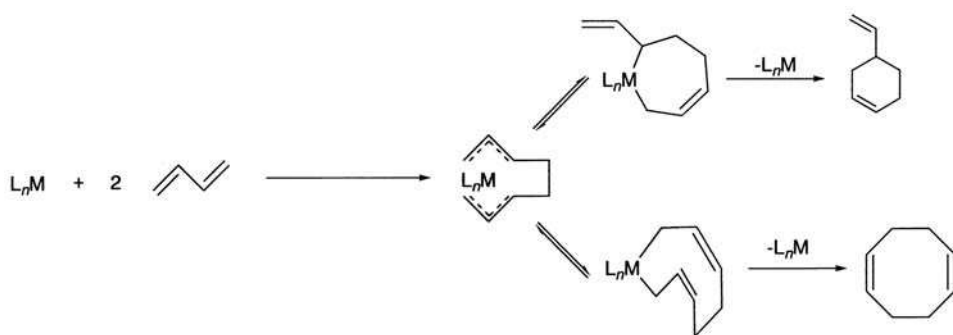
Likewise when two alkyne molecules coordinate to a transition metal such as Co(I) with subsequent coupling of the C–C bond, oxidative cyclization takes place to give a metallacyclopentadiene. Further reaction of another alkyne molecule with the metallacyclopentadiene followed by reductive elimination liberates benzene derivatives. Thus cyclotrimerization of three alkyne molecules catalyzed by a cobalt complex [40,41] can be performed. If a nitrile is used as the second component, pyridine derivatives are obtained catalytically as shown in Scheme 1.13 [42]. The catalytic cyclotrimerization and cyclodimerization of alkynes and conjugated enynes have found extensive applications in synthesis of complex cyclic compounds such as steroid derivatives [43].

When two 1,3-butadiene molecules coordinate to a low valent transition metal such as nickel or iron, the coordinated butadiene units may react with each other giving a cyclic intermediate, which on reductive elimination gives 1,5-cyclooctadiene or 4-vinylcyclohexene. The isolation of complexes having the bis η^3 -allylic structure provided an important concept in elucidating the butadiene cyclodimerization process catalyzed by a nickel complex in the early stage of development of homogeneous catalysis as pioneered by Wilke's group in Germany (Scheme 1.14) [44].

Recently the oxidative coupling of olefins and alkynes, not only with late transition metal complexes, but also with low valent early transition metal complexes to give metallacyclopentane or metallacyclopentadiene complexes is attracting increasing attention. For example, titanium(II) and zirconium(II) complexes react with olefins and form metallacycles. Various stoichiometric processes to produce useful compounds that are otherwise unavailable can be produced by exploit-



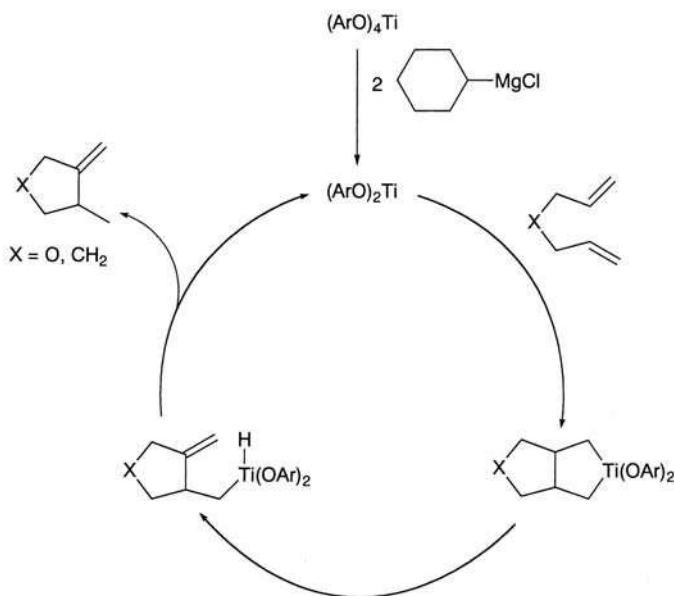
Scheme 1.13. Oxidative coupling of alkyne and nitrile molecules to produce benzene and pyridine derivatives.



Scheme 1.14. Catalytic cyclization of 1,3-butadiene.

ing the behavior of the metallacycles [45]. Application of the behavior of the early transition metal complexes in combination with other processes such as β -hydrogen elimination and the subsequent reductive elimination of the alkyl and hydrido ligands provided new methodology of catalytic production of cyclization products (Scheme 1.15).

Titanium(IV) complexes such as titanium tetraaryloxides and Cp_2TiCl_2 can be used as catalyst precursors. They are reduced in situ by treatment with Grignard reagents to generate reactive $d^2\text{Ti(II)}$ species. Oxidative coupling of the two double bond moieties with Ti(II) gives a metallacyclopentane that undergoes



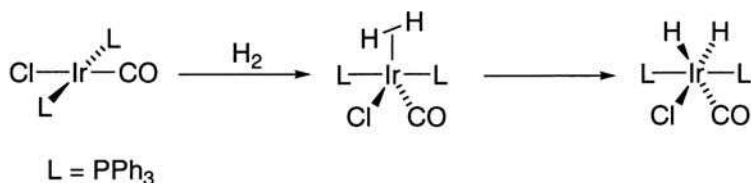
Scheme 1.15. Titanium-catalyzed cyclization of terminal dienes.

internal β -hydrogen elimination and transfer of the hydrogen to the other alkyl group to liberate the methylenecyclopentane type products. The Ti(II) species regenerated further carries the catalytic cycle.

The tendency of the early transition metal complexes to form metallacycles allows combination of the elementary step with other processes such as σ -bond metathesis as will be described later. Novel types of catalytic processes are developing in this area, particularly in tandem type organic synthesis enabling construction of complex molecules with short routes.

(c) Cleavage of non-polar bonds

On interaction with transition metal complexes some compounds with non-polar bonds undergo cleavage reactions. The cleavage reaction represents another type of important elementary process that can be utilized in organic synthesis. One of the most important processes is activation of molecular hydrogen to give transition metal hydrides. The process probably proceeds through initial side-on coordination of H_2 molecule to the metal to form an $\eta^2\text{-H}_2$ bond which can be regarded as a half activated state of H_2 before it is completely cleaved to form a dihydride (Scheme 1.2) [46]. Electron back donation from the metal d orbital to the anti-bonding σ^* orbital of H_2 leads to weakening of the H-H bond. The H-H bond having the bond dissociation energy of as big as 436 kJ/mol is weakened on interaction with a transition metal to be cleaved even at room temperature. Similar weakening of the σ bonds such as C-C , C-H , Si-Si , Si-H and others is known to



Scheme 1.16. Cis addition of H_2 to $trans-[IrCl(CO)(PPh_3)_2]$.

lead to cleavage of these bonds [47]. In certain cases η^2 type complexes with these bonds have been established as well. These issues will be dealt with in Chapter 2.

The activation and the subsequent cleavage of the H–H bond on interaction with a transition metal leads to formation of a transition metal dihydride [48]. Oxidative addition of H_2 to $trans-[IrCl(CO)(PPh_3)_2]$, the so-called Vaska's complex, gives $cis-[IrH_2Cl(CO)(PPh_3)_2]$ where the Cl and CO ligands are bent back (Scheme 1.16) with the two hydride ligands occupying the cis positions [49].

In oxidative addition, a dihydrogen molecule approaches the square planar Ir(I) complex causing bending back of the Cl and CO ligands forming a trigonal bipyramidal intermediate with H_2 in the equatorial plane and two L's in apical positions. On completion of the oxidative addition with cleavage of the H–H bond an octahedral Ir(III) dihydride complex $[IrH_2Cl(CO)L_2]$ is formed. Further discussion of the oxidative addition of H_2 and other non-polar substrates will be made in Chapter 2.

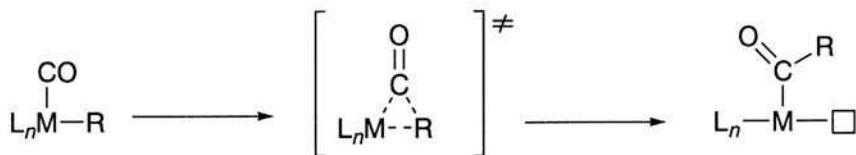
The transition metal hydride complexes thus produced can react further with various unsaturated compounds such as alkenes and alkynes to undergo insertion reactions giving transition metal alkyl and alkenyl compounds.

1.3.3 Insertion and deinsertion (extrusion) processes

Once a reactive organotransition metal complex is formed, it can react further with other substrates to undergo the succeeding reactions of synthetic utility such as insertions of olefins or carbon monoxide into the metal–carbon bond to give new alkyl- or acyl transition-metal compounds. Important insertion processes are 1,1-insertion and 1,2-insertions and their reverse processes.

(a) 1,1-Insertion

The process involves insertion of carbon monoxide and its isoelectronic analog, organic isocyanides into a transition metal–carbon bond. Of particular importance is the 1,1-insertion of CO into transition metal alkyls [50]. The insertion affords acyltransition metal complexes that are susceptible to further reactions with nucleophiles. Mechanistically, in most established cases the insertion of CO into the metal alkyl proceeds by a process involving migration of the alkyl ligand onto the coordinated CO ligand. The alkyl ligand attached to a transition metal is



Scheme 1.17. Migratory CO insertion into M-R bond.

activated by coordination of the CO ligand and the CO ligand itself is activated on its coordination to the transition metal to accept the migration of the alkyl ligand onto the CO ligand. Thus the term migratory insertion is often used. (Scheme 1.17)

For migratory insertion to take place a coordination site adjacent to the alkyl ligand should be available for the CO ligand to coordinate. In certain cases prior isomerization is necessary for creating a coordination site adjacent to the alkyl ligand. Since CO insertion coupled with other fundamental processes provides a convenient means to increase the carbon number of a substrate by one unit, carbonylation is a particularly important methodology in organic syntheses.

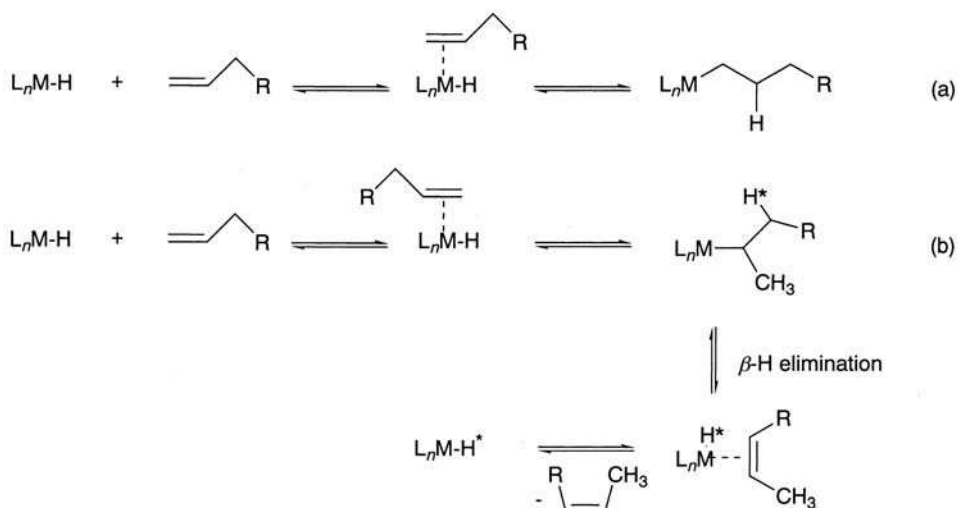
For electron-poor early transition metal complexes there are examples where the acyl group is bound with the transition metal in a side-on manner forming an η^2 acyl ligand through σ and π bonds. This allows more stabilization of the acyl product, but the stabilization of the acyl ligand makes the acyl complex less reactive for subsequent processes such as coupling of the C-C bond by reductive elimination.

Decarbonylation also provides a useful means of removing a carbonyl group in organic compounds, for example in conversion of aldehydes into alkanes [51] or acyl halides into alkyl halides [52]. Also in this case a coordination site *cis* to the acyl ligand is required for the alkyl group to migrate on the transition metal.

In contrast to the case of CO insertion that usually allows insertion of only one CO unit into a metal-carbon bond, isocyanides undergo multiple insertions sometimes leading to polyisocyanides [53,54]. Since the inserted isocyanide units may be regarded as imines derived from carbonyl groups, the insertion products can be regarded as polycarbonyl compounds where CO units are multiply inserted into the metal carbon bonds. The multiple insertion products of isocyanides have found applications both in organic synthesis and polymer synthesis [55].

The combination of CO insertion into a metal alkyl bond with other elementary processes leads to catalytic processes that produce useful compounds containing carbonyl groups. The most widely utilized of these processes are olefin hydroformylation and Heck carbonylation to prepare carboxylic acids and their derivatives.

Hydroformylation of olefins. Hydroformylation (oxo process) is the oldest homogeneous catalysis of industrial importance. Whereas the combination of an olefin with H_2 gives hydrogenation products, a mixture of H_2 and CO, called synthesis gas, instead gives various products including hydrocarbons, methanol, ethylene



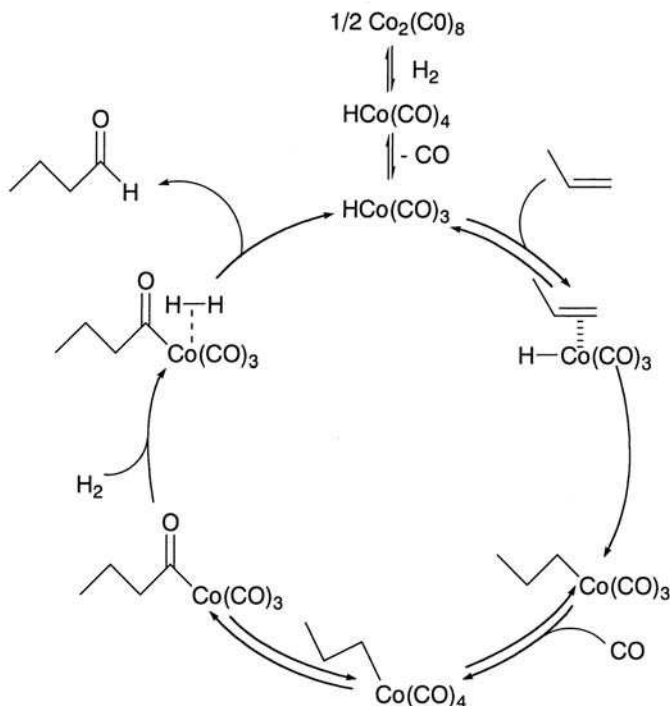
Scheme 1.18. Olefin insertion modes into M-H bond and β -H elimination.

glycol, and formaldehyde. When all three components, olefin, CO and H_2 , are treated with cobalt or rhodium carbonyls, they mainly yield aldehydes as products of catalytic hydroformylation of olefins.

The hydroformylation of propylene provides two types of products, *n*- and isobutyraldehydes depending on the insertion modes of propylene into the M-H bond. As shown in Scheme 1.18a and b, where $R = H$, the anti-Markovnikov type addition of M-H to the double bond in (a) gives the linear propyl, whereas the Markovnikov type addition gives the isopropyl group bound with the metal. Further insertion of CO yields the linear and branched acyl groups.

The catalytic cycle of the hydroformylation using the catalyst precursor $Co_2(CO)_8$ for giving a linear isomer is depicted in Scheme 1.19.

Oxidative addition of H_2 to the dimeric dicobalt octacarbonyl causes cleavage of the Co-Co bond to form $CoH(CO)_4$. After dissociation of a CO ligand to produce a vacant site for further reactions, the insertion of propylene gives a propylcobalt species. Insertion of CO into the Co-H bond is energetically unfavorable and CO insertion takes place only after the olefin insertion into the Co-H bond giving the propylcobalt species. There are a few possible courses for the acylcobalt complex to liberate aldehyde via reaction with H_2 . One is oxidative addition of H_2 to give an acyl(dihydrido)cobalt(III) species that reductively eliminates the aldehyde. The other is heterolytic cleavage of H_2 to add to the Co-acyl bond to liberate the aldehyde regenerating the Co-H species. A similar cleavage reaction of the cobalt acyl bond can take place by a concerted process called σ -bond metathesis, which will be discussed later. The third course is a bimolecular coupling of the cobalt acyl complex with a cobalt hydride complex to liberate aldehyde with generation of a Co(0) species. Evidence supporting the second and third possibilities has been

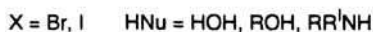
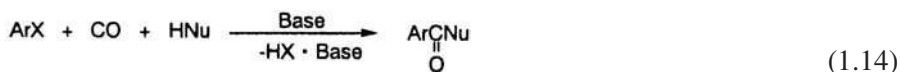


Scheme 1.19. Catalytic cycle accounting for the hydroformylation of propylene. The mechanism affording the branched aldehyde is omitted for clarity.

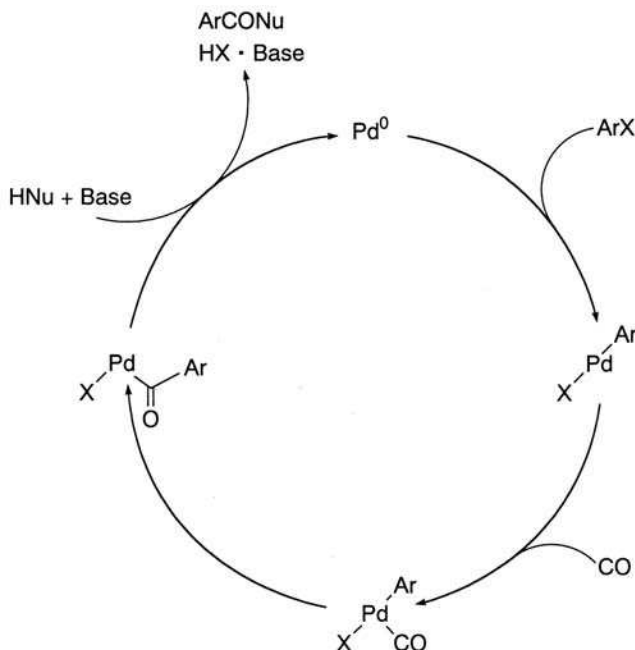
presented [56]. Since the catalysis is carried out under high-pressure conditions, establishment of the mechanism in systems under operating conditions is difficult.

Selective production of either a linear or branched aldehyde in hydroformylation is quite important in affecting the further utility of the aldehyde. Linear aldehydes can be converted into linear alcohols useful as detergents, after an aldol reaction followed by hydrogenolysis. Branched aldehydes afford important materials for pharmaceutical use, particularly when asymmetric synthesis of the branched aldehyde can be achieved [57].

Heck carbonylation. Another important process involving insertion of CO into an $\text{M}-\text{R}$ bond is catalytic conversion of aryl halides into carboxylic acid derivatives (Eq. 1.14), called the Heck carbonylation reaction, which has been utilized in laboratory organic synthesis and in industry [58].



The process comprises (a) oxidative addition of an aryl halide to $\text{Pd}(0)$ complex

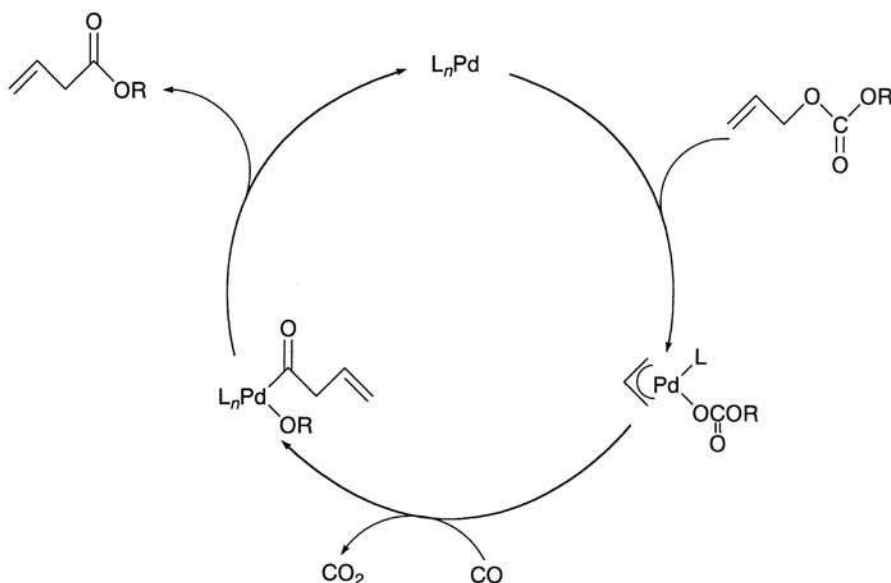


Scheme 1.20. Mechanism of Heck carbonylation of aryl halide.

to give an arylpalladium halide, (b) CO coordination and insertion to generate an acylpalladium halide species, (c) conversion of the acylpalladium species into carboxylic acid, ester or amide by reactions with water, alcohol, or amine in the presence of a base with generation of the $\text{Pd}(0)$ species that carries the catalytic cycle (Scheme 1.20).

There are two possibilities for formation of the products from the acylpalladium species. One is the direct attack of the nucleophile on the acyl ligand and the other involves coordination of the NuH to the palladium center. The palladium-bound NuH ligand, such as alcohol, is deprotonated by a base to give an acylpalladium alkoxide, which releases the ester as the reductive elimination product. Recent studies on model complexes provided some evidence supporting a route via reductive elimination [59].

Heck carbonylation involving the oxidative addition of aryl halides is not applicable to aliphatic halides, since alkyl halides react directly with nucleophiles. Tsuji developed a process of carbonylating allyl carbonates to form carboxylic esters by palladium-catalyzed carbonylation that is applicable to aliphatic substrates [60]. The process probably involves (a) the oxidative addition of allyl carbonates to $\text{Pd}(0)$ species to form η^3 -allyl palladium species, (b) CO insertion into the allyl-Pd bond to give acylpalladium species, (c) decarboxylation of the carbonate ligand to give alkoxide, and (d) liberation of butenoate esters by combination with the alkoxides as shown in Scheme 1.21.



Scheme 1.21. Catalytic carbonylation of allyl carbonate.

Although examples are still limited, there are some studies indicating the feasibility of the CO insertion into the allyl–palladium bond.

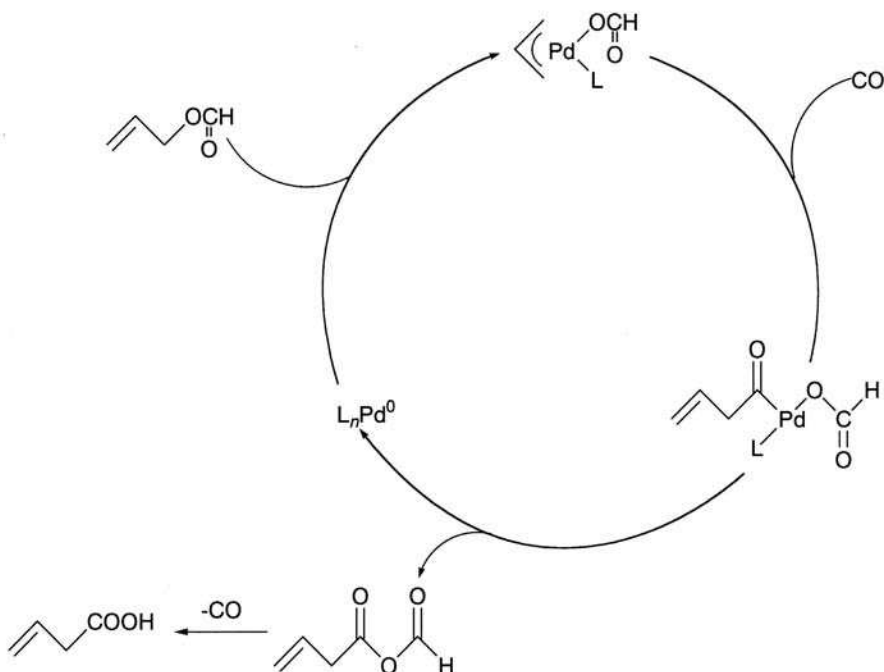
Another example utilizing the CO insertion into the allyl–palladium bond is palladium-catalyzed conversion of allyl formate into 2-butenic acid. The catalytic cycle involved is shown in Scheme 1.22.

In the palladium-catalyzed carbonylation process, allyl formate, prepared by the reaction of allyl alcohol with formic acid, oxidatively adds to Pd(0) species with the C–O bond cleavage to give allyl palladium formate. The CO insertion into the allylpalladium bond produces butenoyl palladium formate, which reductively eliminates butenoic formic anhydride with regeneration of the catalytically active Pd(0) species. Spontaneous decarbonylation of the mixed anhydride yields 3-butenic acid, which isomerizes to 2-butenic acid [61]. The process to give the butenoic acid proceeds only under CO pressure, suggesting that the CO insertion into the allyl–Pd bond is favored under CO pressure. When the reaction is carried out under normal pressure of CO, decarboxylation of the formate to give palladium hydride takes place. Reductive elimination of the allylpalladium hydride yields hydrogenation product of the allyl moiety [62].

Details of the insertion processes will be discussed in Chapter 7.

(b) 1,2-Insertion and β -elimination

When a transition metal alkyl or hydride is coordinated by an alkene or alkyne through a π bond, the metal–carbon bond or metal–hydride bond as well as the coordinated alkene or alkyne ligand are activated. The process leads to



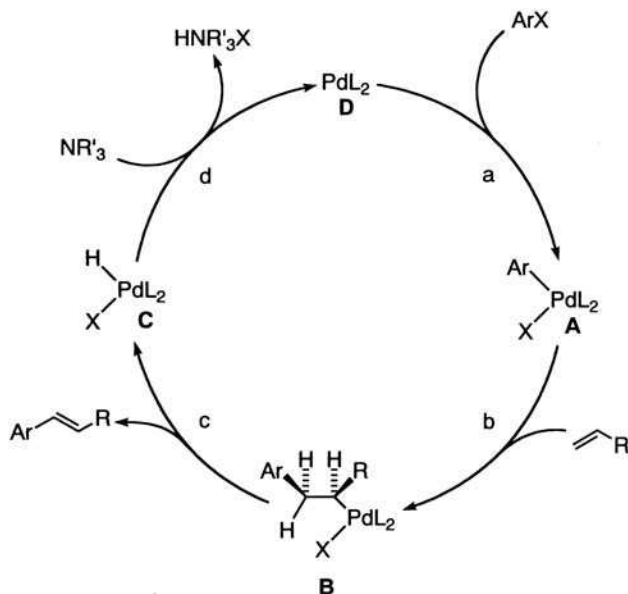
Scheme 1.22. Catalytic conversion of allyl formate into 3-butenic acid.

insertion of the alkene or alkyne into the M–C or M–H bond. Conversely when the inserted alkyl bond has hydrogen atoms at the β carbon, the hydrogen atom can be abstracted by the transition metal to form a metal hydride and an olefin. In limited cases a group containing carbon, halogen, oxygen and sulfur atoms may be abstracted by the transition metal. The 1,2-insertion and β -elimination are very important elementary processes that are involved in many transition metal catalyzed processes as will be discussed in detail in Chapter 6.

Combination of the oxidative addition of aryl halide with olefin insertion followed by β -hydrogen elimination provides a useful olefin arylation process catalyzed by a palladium complex (Mizoroki–Heck reaction) [63–65]. The essential part of the catalytic cycle is shown in Scheme 1.23.

In the Mizoroki–Heck process, aryl and alkenyl halides are converted on reaction with olefins in the presence of a base into arylated or alkenylated olefins. The arylation case is shown in the scheme but it is applicable also to the alkenylation process.

The relevant fundamental processes include: (a) oxidative addition of aryl (or alkenyl) halide to a Pd(0) complex to give arylpalladium(II) halide (**A**), (b) olefin coordination and insertion into the aryl–Pd bond to give arylated alkylpalladium species (**B**), (c) β -hydrogen elimination to liberate the arylated olefin generating a hydridopalladium halide $PdH(X)L_2$ (**C**), (d) removal of hydrogen halide from



Scheme 1.23. Mechanism of palladium-catalyzed arylation of olefins (Mizoroki–Heck reaction).

PdH(X)L_2 with aid of a base to regenerate the Pd(0) species (**D**), which further carries the catalytic cycle. Olefin insertion and β -elimination processes will be discussed later in Chapter 6 but some comments of the elementary processes pertinent to the mechanism will be given here.

It should be pointed out that a coordination site adjacent to the aryl ligand in the arylpalladium intermediate is required if the olefin insertion takes place through a dissociative mechanism under the constraint of square planar geometry. In most cases the oxidative addition of aryl halide to a tertiary phosphine-coordinated Pd(0) complex gives the *trans* isomer, but there also exists a certain possibility that the *trans* isomer is the thermodynamic product produced by isomerization of a kinetic *cis* isomer [66]. If the catalytic process does not proceed fast, it is likely that the olefin insertion into the aryl–palladium bond takes place with the *trans* isomer, *trans*- $[\text{PdAr(X)L}_2]$ produced by oxidative addition of ArX to a Pd(0) complex (see Eq. 1.1). The coordination site for the incoming olefin may be created by dissociation of a ligand L or X from *trans*- $[\text{PdAr(X)L}_2]$. Acceleration of the reaction rate by addition of a silver salt [67] has been noticed and the effect was utilized to facilitate the catalytic processes. The rate enhancement can be accounted for by removal of the halide ligand from the intermediate arylpalladium halide complex to create a cationic arylpalladium complex, a proposal derived on the basis of fundamental kinetic studies of the behavior of aryl and alkyl palladium halide complexes coordinated with tertiary phosphine ligands [68]. The removal of the halide ligand *trans* to the aryl ligand may also facilitate the *trans*–*cis*

isomerization of $trans\text{-}[\text{PdAr}(\text{solvent})\text{L}_2]^+$ to generate a coordination site *cis* to the aryl ligand to accommodate the incoming olefin ligand.

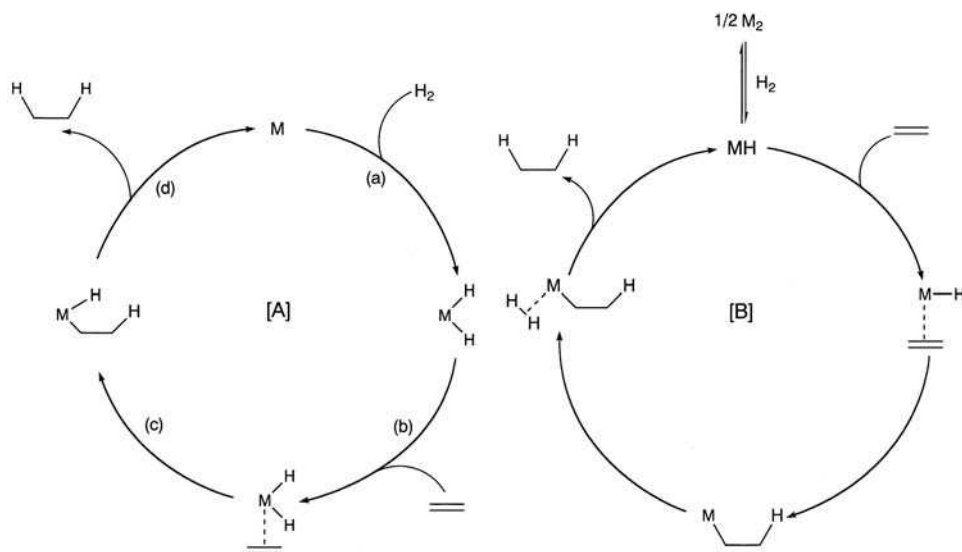
The presence of a vacant coordination site is also required for the β -hydrogen elimination to take place from arylated alkylpalladium intermediate. The hydrogen atom at the β -carbon should approach the metal atom after the rotation of the C–C bond to bring the hydrogen closer to the metal in the M–C–C–H plane to be abstracted in a *syn* fashion. It was also confirmed that isolated trialkylphosphine-coordinated $trans\text{-}[\text{Pd}(\text{H})\text{X}(\text{PR}_3)_2]$ species are thermally considerably stable and addition of a base such as triethylamine is required to induce the reductive elimination of $trans\text{-}[\text{Pd}(\text{H})\text{Cl}(\text{PR}_3)_2]$ by removing hydrogen chloride [69]. These studies on reactions of isolated neutral and cationic monoorganopalladium complexes provide relevant information in considering the reaction course of the catalytic processes as shown in Scheme 1.23.

Because various important industrial organic processes utilize olefins, convenient methods to convert olefins into various products are vital. Transition metal catalysts with proper ligands have proved most useful in controlling the course of these reactions. Transition metal complexes catalyze skeletal isomerization, double bond isomerization, polymerization, and other processes. Insertion of a terminal olefin into a transition metal hydride bond by 1,2-insertion or 2,1-insertion produces either a linear (a) or a branched (b) metal alkyl as we have briefly discussed (Scheme 1.18). The transition metal abstracts a hydrogen atom at the β -carbon to yield an olefin-coordinated transition metal hydride in a process termed as β -hydrogen or β -hydride elimination. Because abstraction of the β -hydrogen occurs most frequently, the term β -elimination usually means abstraction of the hydrogen. However, it should be noted that there are examples of abstraction of other substituents at the β -carbon such as alkyl, halogen, thiolate, and carboxylate.

Olefin insertion into the M–H bond and its reverse process can cause the skeletal isomerization of the metal alkyl, where the influence of an auxiliary ligand controls the linear to branched ratio (*n* to *i* ratio). Use of sterically demanding tertiary phosphines is known to favor the linear alkyl.

When the β -hydrogen elimination takes place from a β -carbon different from the original one, as marked by H* in Scheme 1.18b, an olefin with internal double bond is produced. By replacement of the coordinated olefin with an incoming olefin, catalytic double bond isomerization from terminal to internal position takes place. In some catalytic isomerization processes there is also the possibility of double bond isomerization involving abstraction of an allylic hydrogen by metal followed by 1,3-hydrogen transfer process [70]

The transition metal alkyl can undergo further insertion of olefins or carbon monoxide. By combination of these fundamental processes various catalytic processes such as hydrogenation, oligomerization, polymerization, and hydroformylation of olefins can be performed.



Scheme 1.24. Catalytic hydrogenation of olefin.

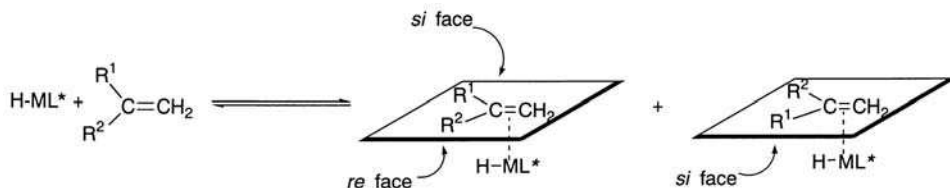
(c) Catalytic hydrogenation

Scheme 1.24 shows the simplified mechanisms of hydrogenation of an olefin to give an alkane.

Scheme 1.24A comprises elementary steps of (a) oxidative addition of H_2 to produce a metal dihydride, (b) olefin coordination, (c) insertion of the coordinated olefin to afford a metal alkyl hydride, and (d) reductive elimination of the alkyl and the hydrido ligands to liberate alkane. Some of the elementary steps in Scheme 1.24A such as oxidative addition of H_2 , olefin coordination, and insertion may be reversible depending on the transition metal, olefin, and experimental conditions. In certain cases olefin coordination may take place preceding the dihydrogen oxidative addition. Since oxidative addition of H_2 produces a *cis* dihydrido complex as the kinetic product, the relative positions of the hydrido and coordinated olefin should be considered for explanation of the catalytic reaction course. If the alkyl ligand formed by olefin insertion is situated *trans* to the remaining hydrido ligand, isomerization to bring the hydrido and alkyl ligands to mutually *cis* positions is required to cause the subsequent reductive elimination of the alkyl and hydrido ligands.

Scheme 1.24B shows the other possibility of catalytic hydrogenation of olefin driven by a transition metal monohydride. The monohydride can be sometimes obtained by cleavage of dinuclear transition metal complexes such as $\text{Co}_2(\text{CO})_8$ on treatment with dihydrogen or it can be generated by protonation of an electron rich metal complex [71]. Insertion of an olefin into the M-H bond to form an alkyl may proceed similarly to Scheme 1.24A.

Heterolytic cleavage or σ bond metathesis of the metal alkyl by interaction with



Scheme 1.25. Control of coordination of enantio faces in prochiral olefins to a transition metal coordinated with chiral ligand.

H₂ (to be discussed later) can also liberate the alkyl group from the metal alkyl as alkane with generation of a metal hydride as shown in Scheme 1.24B. Although examples of such cleavage processes demonstrated unequivocally are still limited [72,73], Scheme 1.24B should be considered as a possible reaction route in certain types of olefin hydrogenation.

Beside the regiochemistry in affording the linear or branched alkyls (Scheme 1.18a or b), choice of the enantioface in substituted olefins on coordination to a transition metal center is very important in determining the effectiveness of asymmetric synthesis and in stereoregular polymerization.

The mode of coordination of a substituted olefin to a transition metal complex can be controlled by using an appropriate chiral ligand that favors one mode of coordination over another by influence of the chiral ligand arising mainly from steric origin. The prochiral olefin has two enantiofaces, *re* face and *si* face, through which the olefin coordination to metal takes place (Scheme 1.25).

When insertion of the coordinated prochiral olefin to a metal alkyl or a metal hydride takes place, the stereochemistry of the substituted carbon atom is determined as either *R* or *S* enantiomer. When the chiral alkyl group is reductively eliminated with the hydrido ligand, asymmetric hydrogenation of an olefin producing enantiomeric excess of one of the optical isomers can be achieved.

Various asymmetric hydrogenation of olefins have been achieved by designing proper chiral ligands containing P, N, O, and S donors [74,75]. Most chiral ligands designed by various researchers are bidentate ones that are easier to fix the stereochemical conformations around the central metal atom. In certain cases, use of a specially designed optically active monodentate phosphine ligand such as MOP (2'-diphenylphosphino-2'-methoxy-1,1'-binaphthyl) is preferred since the two active sites on the complex are not occupied in the monotertiary phosphine ligand [76].

Following the development of successful catalytic hydrogenation of olefins, recent attention is directed to catalytic hydrogenation and transfer hydrogenation of ketones and imines [77]. Because of requirement of production of various pharmaceutical compounds of importance, further development is expected in asymmetric catalytic hydrogenation.

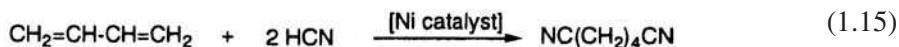
Asymmetric synthesis using homogeneous catalysts with well-designed chiral

ligands has shown the great advantage of homogeneous catalysis using transition metal complexes over heterogeneous catalysts that suffer from the difficulty of precisely controlling the environment of the catalytic site.

The selection of the enantioface of an olefin will be discussed later in association with the stereospecific olefin polymerization.

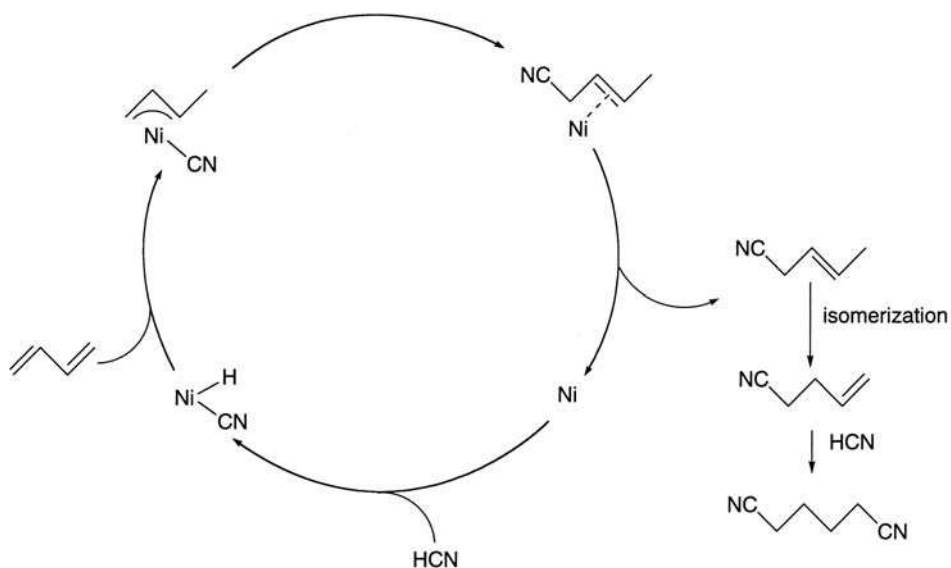
(d) *Diene insertion*

Insertion of dienes into M–H bond or M–alkyl bond affords η^3 -allylic complexes or its η^2 -alken- η^1 -yl resonance form. The allylic complex may further undergo insertion of other unsaturated compounds such as alkene or diene into the unsubstituted or substituted terminal of the allylic ligand. If successive butadiene insertion takes place, polymers with internal unsaturated bonds are produced as will be described later. A nickel-catalyzed reaction of butadiene with 2 mol of HCN affords adiponitrile, an important feedstock in polymer synthesis (Eq. 1.15).



Scheme 1.26 shows a simplified catalytic cycle to account for production of adiponitrile by a nickel catalyst [78,79].

The cycle contains elementary steps comprised of (a) addition of HCN to a Ni(0) species to give nickel hydride cyanide, (b) 1,4-insertion of butadiene to give η^3 -methallyl intermediate, (c) reductive elimination to liberate 1-cyano-2-butene. The liberated cyanoolefin having the internal double bond is further isomerized



Scheme 1.26. Catalytic formation of adiponitrile from butadiene and HCN using a nickel catalyst.

by the nickel catalyst to the terminal olefin, which undergoes another addition of HCN to give adiponitrile.

(e) Olefin polymerization

Here we deal with addition polymerization of unsaturated compounds initiated by transition metal complexes. Other issues concerning polymerization are not discussed here. In polymer synthesis, there are several complicating factors that are not encountered in preparation of low molecular weight compounds. Problems to be considered include control of molecular weight, molecular weight distribution, copolymerization, and stereoregularity of the polymers. For understanding these factors one needs to understand the modes of initiation, chain growth, chain transfer, and chain termination.

When a transition metal alkyl or a metal hydride reacts with olefin molecules to undergo successive insertions, chain growth of a polymer attached to the transition metal takes place. If β -hydrogen elimination occurs from the polymer chain, a transition metal hydride coordinated with the olefin derived from the polymer chain will be produced. By displacement of the coordinated olefin from the transition metal by the other monomer olefin, the polymer with an unsaturated terminal bond is liberated with generation of a transition metal hydride coordinated with the olefin. New chain growth will follow from the hydride, with the net result of control of the molecular weight without termination of the polymerization process. The process is in fact a chain transfer process.

The relative rate of the monomer insertion versus the rate of β hydrogen elimination is one of the most important factors in determining the molecular weight. The other possibility of termination of polymerization, beside the decomposition process of the growing polymer chain by impurities such as oxygen and water, is reductive elimination. The reductive elimination may take place by combination of the growing polymer chain and the other alkyl or a transition metal hydride generated by the β -hydrogen elimination.

In the polymerization of ethylene initiated by a transition metal hydride, for example, insertion of an ethylene molecule gives a metal ethyl. Successive insertion of two ethylene molecules into the metal hydride gives a metal butyl, from which β -hydrogen elimination liberates 1-butene and a metal hydride. Repetition of the insertion process leads to catalytic dimerization of ethylene. If one can modify the rates of olefin insertion and of β -hydrogen abstraction at will, one should be able to achieve, in principle, the production of high molecular weight polymer or of oligomers of a specific chain length as planned.

Since the advent of the Ziegler catalyst, enormous effort has gone into clarifying the polymerization mechanism. The progress of mechanistic studies, however, was hindered by heterogeneity of the catalyst systems and unavailability of transition metal alkyls suitable for the mechanistic studies. Understanding of the polymerization process has been recently much improved by examining homogeneous systems as described below. We can now state that most of the features

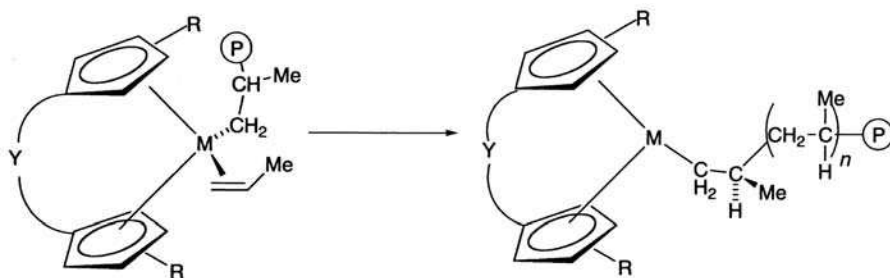


Scheme 1.27. Mechanism of coordination polymerization of olefins.

of the coordination polymerization can be accounted for by a polymerization mode consisting of successive insertions of olefins into a transition metal alkyl as depicted in Scheme 1.27.

Catalyst systems composed of the mixture of bis(η^5 -cyclopentadienyl)MCl₂ (M = Ti, Zr, Hf) and aluminoxane, an oligomer of composition $(-\text{O}-\text{AlMe}-)_n$ prepared by partial hydrolysis of trimethylaluminum, provide excellent catalyst systems for performing homogeneous type polymerization [80]. By modifying the substituents attached to the cyclopentadienyl (Cp) ligands or η^5 -indenyl ligand, various well-defined catalyst precursors are obtained that control the environment around the central metal. A particular success was developed by connecting two substituted cyclopentadienyl or indenyl ligands with connecting linker groups, thus limiting the rotation of the cyclopentadienyl rings and controlling the environment around the metal center. Creation of C₂ symmetries with the two substituted Cp rings afforded the environment to control the coordination of a substituted olefin, for example, propylene. If the propylene molecule binds the metal center with *re* face or *si* face and olefin insertion (or mechanistically, alkyl migration to the propylene plane) takes place, the configuration of the prochiral propylene is fixed as *R* or *S*. Successive propylene insertions with the same mode of coordination and insertion would lead to production of polymers having the sequence of *R, R, R*-... or *S, S, S*-... giving isotactic polypropylene. On the other hand, if coordination and insertion take place on the alternate faces, syndiotactic polypropylene would be produced. Quite a variety of ligands have been designed to control the monomer coordination and successfully applied to production of polymers of designed structures. Catalysts using the cyclopentadienyl type ligands, called metallocene catalysts, are now used in industry. They are called single site catalysts because of the homogeneous nature of the catalysts in production of high molecular weight polyethylene or polypropylene of narrow molecular weight distribution.

The role of aluminoxane in polymerization with transition metal complexes has not been completely clarified. It certainly serves as the alkylating reagent of the transition metal halides to produce metal dialkyls. Methylaluminoxane, having Lewis acidity, can abstract one of the two alkyl groups at the metal center and creates a cationic metal alkyl species with a readily accessible coordination site for the incoming olefin molecules. As described previously, a cationic monoalkyl complex having a vacant coordination site for the monomer is suitable in accepting the monomer and initiate the polymerization. Abstraction of one of the methyl



Y = SiMe₂, -(CH₂CH₂)-,

M = Ti, Zr, Hf, lanthanoid metal

Scheme 1.28. Polymerization of propylene with Kaminsky-Brintzinger type catalyst.

groups in Cp₂ZrMe₂ with B(C₆F₅)₃ having a Lewis acid character to generate a cationic methylzirconium species was demonstrated and gave high activity for ethylene polymerization [81]. Computational chemistry has helped in providing in-depth understanding of the polymerization mechanisms [82].

Since the discovery of Ziegler catalyst control of the molecular weight of the polyolefins has remained as one of the most important problems to be solved. A catalyst system containing the early transition metals such as titanium and zirconium usually give high molecular weight polymers, whereas use of late transition metal catalysts had been thought to give oligomers at most. Control of olefin polymerization can be performed, in principle, by adjusting the rate of growth by olefin insertion vs the rate of chain termination. An industrial process for producing linear ethylene oligomers using nickel-based catalyst employing *P,O*-coordinating chelate ligand, called Shell Higher Olefin Process (SHOP), has been developed by Keim et al. [83].

It was recently found that late transition metal alkyls such as nickel and palladium produce high polymers by using suitable ligands to control the chain transfer process [84,85]. It was also found that iron and cobalt compounds in the presence of aluminoxane compounds gave high molecular weight polyethylene [86,87]. Brookhart recently showed that putting steric hindrance around the diimine type ligand attached to a nickel or palladium catalyst center gave highly branched polyethylene suitable for production of soft films. He proposed that the branching of the polymer chain is caused by β -hydrogen elimination, rotation of the coordinated olefin produced by the β -hydrogen elimination around the bond connecting the metal and the C=C bond, followed by reinsertion giving the branching (cf. Scheme 1.18). Repetition of this process involving β -hydrogen elimination from the internal CH₂ and re-insertion into the metal-H bond would lead to generation of branched polymers [88]. Further discussion on the polymer

growth or chain transfer issue will be made in Chapter 6.

Another important issue in olefin polymerization is copolymerization of different types of monomers. If one can freely produce copolymers of non-polar and polar monomers, which are difficult to copolymerize with conventional initiators, it would provide useful polymer materials. The Ziegler type catalysts using trialkylaluminum is not suitable for polymerizing polar monomers, whereas late transition metal catalysts are more tolerant of polar monomers. Recently catalysts using late transition metal catalysts have been intensively studied [89]. Because of the obvious importance of these polymeric materials in industrial use, further studies are expected on the applicability of late transition metal complexes for polymerization.

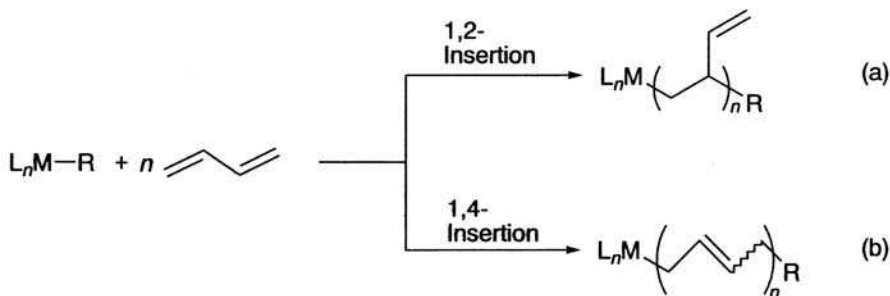
(f) *Diene polymerization*

1,3-Dienes such as butadiene and isoprene are important feedstock for production of polymer materials as well as low molecular weight compounds. Of particular synthetic importance is manufacturing synthetic rubbers using transition metal catalysts. Diene polymers can be prepared by successive insertions of dienes into transition metal alkyls or metal hydrides.

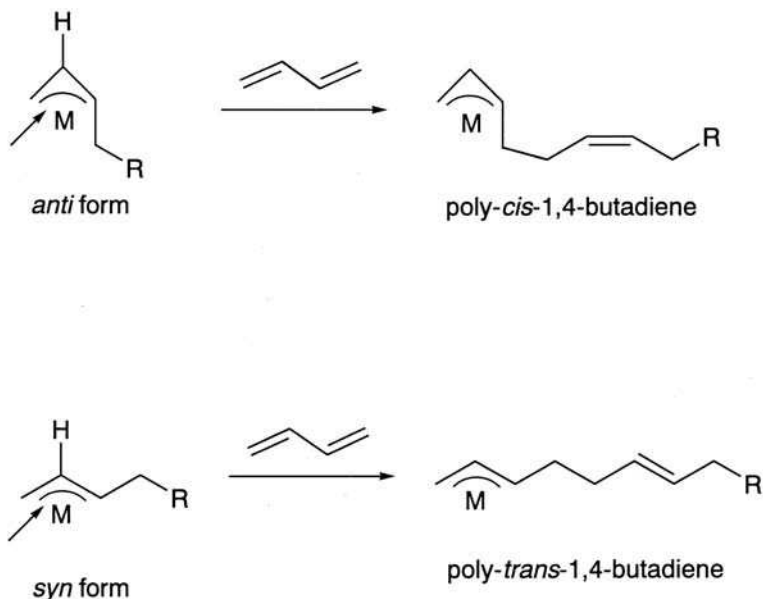
Scheme 1.29 illustrates the 1,3-butadiene insertion processes to give complexes with linear or branched chain attached to the metal.

Butadiene may insert into the M–R bond by 1,2-insertion or 1,4-insertion mode. The latter mode giving the poly-*cis*-1,4-butadiene is particularly important for producing materials for synthetic rubber tires. For isoprene polymerization the situation is further complicated because of the presence of the methyl substituent. Since the physical properties of poly-*cis*-1,4-isoprene are quite similar with those of natural rubber, knowing the means to control the polymerization behavior is of particular industrial importance.

The diene insertion may take place into the σ -allyl-metal bond or into η^3 -allyl-metal bond. In the latter case, after the first insertion of the diene into M–R bond to give a substituted η^3 -allylic complex, there are two possible sites for the further insertion of butadiene, one into the substituted site to give the 1,2-insertion



Scheme 1.29. Two modes of 1,3-butadiene insertions into M–R bond.

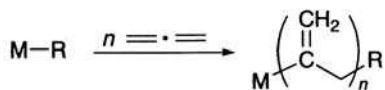


Scheme 1.30. Possible routes to give poly-*cis*-1,4-butadiene and poly-*trans*-1,4-butadiene by insertion into the *syn* or *anti* η^3 -allyl complex.

products and the other into the unsubstituted site to give 1,4-insertion product. If 1,2-insertion takes place with restriction of the coordination site for 1,3-butadiene, branched products will be obtained. On the other hand, a possible explanation for the formation of poly-*trans*-1,4-butadiene or poly-*cis*-1,4-butadiene can be found by considering the *syn* and *anti*-configurations of the substituted η^3 -allyl complexes. The *anti* and *syn* forms are defined by the configuration of the η^3 -allyl complex having the substituent attached to the η^3 -allyl ligand at the side opposite to or at the side same as the proton bonded at the central methine carbon. The diene insertion into the less hindered site of the η^3 -allyl ligand with the *anti* form would give the poly-*cis*-1,4-butadiene, whereas into the η^3 -allyl complex with the *syn* form would provide the poly-*trans*-1,4-butadiene (Scheme 1.30).

Insertion of 1,2-propadiene, allene, into the transition metal-carbon bond gives methylene-substituted polymers (Scheme 1.31) [90].

Beside polymer synthesis, there are a variety of synthetic applications using the specific properties of the diene [91].



Scheme 1.31. Polymerization of 1,2-propadiene (allene).

(g) *Copolymerization of olefin and CO*

Another step forward recently accomplished is copolymerization of ethylene and carbon monoxide. The two substrates having totally different properties can be introduced into a polymer chain alternately to make a new type of copolymers [92]. Other olefins such as propylene, styrene, and propadiene [93] can be also copolymerized with CO.

To understand the reasons for the alternating copolymerization of ethylene and CO, we need to understand why the successive insertion of ethylene does not occur and why only a single insertion of CO takes place into the palladium–alkyl bond. To provide answers to these questions it is necessary to have fundamental information regarding the relative energy levels before and after insertions, for transition states in insertions of CO and ethylene, and the extent of stabilization arising from the α - and β -agostic interactions. Recent progress in computational chemistry enables the assessment of relative energies and activation barriers to help understand why one reaction course is preferred over another [94]. The details of the insertion processes involving 1,2- and 1,1-insertion of unsaturated substrates will be dealt with in Chapters 6 and 7.

1.3.4 Transmetallation

Transmetallation transfers a hydrocarbyl or hydrido ligand from one metal to another. Since the transmetallation generates a new transition metal alkyl, it constitutes one of the most important elementary processes in molecular catalysis.

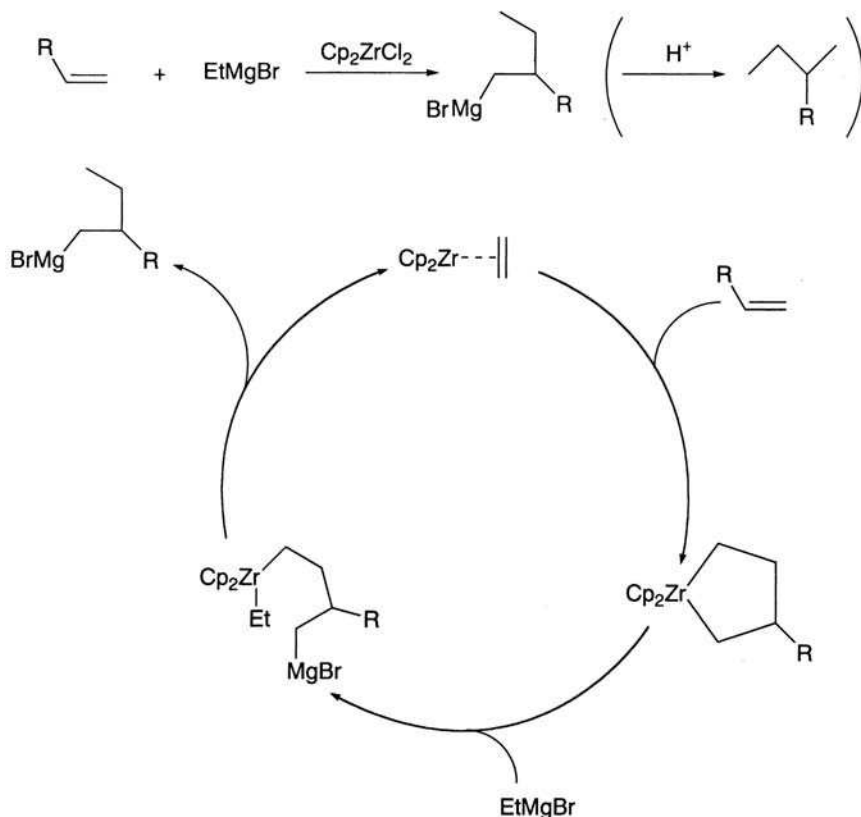
Details of the transmetallation processes will be discussed in Chapter 5 but it is appropriate here to point out some examples of transmetallation in catalysis.

(1) We have already seen in elucidation of catalytic cycles for cross-coupling of aryl halides and alkylmagnesium compounds that diorganotransition metal species are formed by transmetallation from a non-transition metal alkyl to a transition metal compound. In designing the catalytic cycle of the catalytic cross-coupling process, conceiving the idea of alkylating the phenylnickel chloride complex obtained in Eq. 1.3 with a Grignard agent was crucial for successful construction of the catalytic cycle as shown in Scheme 1.5 [11].

(2) Transmetallation is important in forming a transition metal catalyst such as titanium alkyl by alkylating the titanium chloride with alkylaluminum compound in Ziegler type catalysts.

(3) Early transition metal complexes differ from late transition metal complexes, such as palladium complexes, in their behavior particularly in the reductive elimination. For example, Cp_2TiEt_2 does not give butane thermally as the coupling product but releases ethane and gives ethylene-coordinated Cp_2Ti complex through a β -hydrogen elimination process. For utilizing the titanium compounds as catalysts to perform the C–C bond coupling a special strategy utilizing transmetallation has been devised.

One useful method is the reaction of two olefin or alkyne molecules to form five-



Scheme 1.32. Zr-catalyzed coupling of an olefin with ethylmagnesium bromide.

membered metallacycles and their subsequent transmetalation to non-transition metal compounds such as magnesium, zinc, and aluminum. Scheme 1.32 illustrates an example of catalytic combination of the ethyl group in $EtMgBr$ and an olefin catalyzed by Cp_2ZrCl_2 . The catalyst precursor Cp_2ZrCl_2 reacts with $EtMgBr$ to give Cp_2ZrEt_2 , which is reduced to $Cp_2Zr(ethylene)$ with liberation of ethane. Another olefin interacts with the ethylene-coordinated Zr(II) species to form a zirconacyclopentane as an oxidative addition product. Transmetalation between the zirconacyclopentane and $EtMgBr$ gives the zirconium complex having the ethyl and magnesium-containing alkyl groups. β -Elimination followed by hydrogen transfer produces magnesium-containing compound with regeneration of the ethylene coordinated zirconium(II) species. Protonolysis of the alkylmagnesium compound liberates the alkane derived from the olefin and ethylmagnesium compound [95].

Titanium analog, Cp_2TiCl_2 and its alkoxide analog serve also as catalyst to cause hydrometallation of an alkyne and olefin. For example, Cp_2TiH produced by thermolysis of $Cp_2Ti(propyl)_2$ reacts with an alkyne to undergo its insertion to give a vinyltitanium complex. Transmetalation with isopropylmagnesium chloride

produces vinylmagnesium bromide with regeneration of Cp_2TiH produced by β -hydrogen elimination. Thus the catalytic cycle to give hydromagnesation product of the alkyne can be constructed [96]. Various methods to cause carbometallation reactions have been developed [97]

Various variation of these methods is possible with use of alkynes. Employment of terminal dienes and diynes in reactions with $\text{Cp}_2\text{Zr}(\text{olefin})$, generated in situ by the reaction of Cp_2ZrCl_2 with alkylmagnesium halide, gives a ring-bearing metallacycle, which can be applied to synthesis of a variety of cyclic products [98]. We have seen in Scheme 1.15 the ring-forming process promoted by $\text{Ti}(\text{II})$ species. Combination of the intermediate formed in the process with transmetallation process can give a variety of products. With combinations of alkynes in the presence of CuCl a process of synthesizing various arenes has been developed [99].

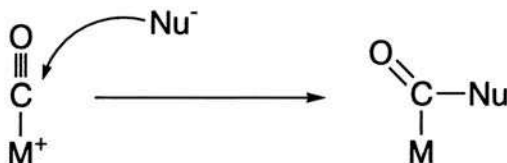
Another approach of using transmetallation process is to transfer the organic moiety bound with early transition metal complexes to late transition metal complexes such as nickel to utilize the reactivity of the diorganonickel complexes to undergo reductive elimination. Various benzene and pyridine derivatives have been prepared by the methodology [100].

1.3.5 External attack on coordinated substrates

The nature of an unsaturated compound is modified by formation of a π bond with a transition metal. Since catalytic processes in organic synthesis are often associated with conversion of unsaturated substrates, alteration of the character of free unsaturated compounds by binding to a transition metal affords a quite useful means in designing the strategy of organic synthesis. For example, the usually electron-rich and nucleophilic properties of unsaturated compounds such as alkenes are modified by formation of a π bond with an electrophilic metal center such as $\text{Pd}(\text{II})$.

Arenes usually having electron-rich character become electrophilic by modification of their character on coordination to a transition metal carbonyl, where the carbonyl groups act as electron withdrawing ligands. Thus the benzene ligand in $\text{Cr}(\text{C}_6\text{H}_6)(\text{CO})_3$, which can be derived by displacement of CO with benzene from $\text{Cr}(\text{CO})_6$, is electrophilic in nature and reacts with nucleophiles. By utilizing the alteration of the original properties of these unsaturated compounds such as olefins and arenes on coordination to transition metal complexes, various synthetic pathways can be furnished.

Attack of nucleophiles on η^1 -, η^2 -, and η^3 -bonded ligands has found extensive use in catalytic processes. Catalytic processes using the attack on η^4 -, η^5 -, and η^6 -ligands have been less developed, although some stoichiometric synthetic applications using the reactivities of these π -complexes with external nucleophiles have been reported [101]. Details of the additions to coordinated unsaturated ligands are dealt with in Chapter 8.



Scheme 1.33. External attack of a nucleophile on the coordinated CO ligand.

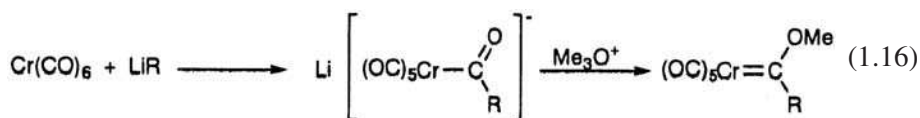
(a) *Catalytic processes involving the external attack on the coordinated CO ligand*

Because of the anticipated dwindling supply of petroleum, exploitation of alternative resources such as natural gas and coal will have increasing importance. Thus development of suitable methods for utilizing carbon monoxide will have ever-increasing demand in chemical industry.

There are two principal routes for utilizing carbon monoxide catalytically. One is insertion of the coordinated CO into the M–R bond (Scheme 1.17). The other is external attack of a nucleophile on the CO ligand coordinated to a transition metal complex (Scheme 1.33).

Beside nucleophiles that attack the electrophilic carbon atom on the coordinated carbonyl ligand, electrophiles such as oxophilic silyl compounds can attack the oxygen atom in the carbonyl ligand.

Furthermore, nucleophilic attack of alkyllithium coupled with the subsequent addition of electrophiles gives Fischer type (heteroatom stabilized) carbene complexes (Eq. 1.16) [102].

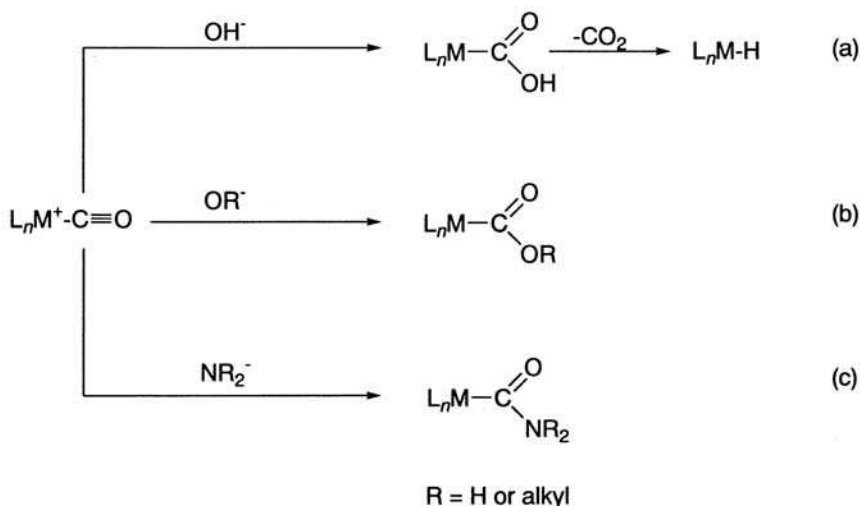


Representative routes for the nucleophilic attack on the coordinated CO relevant to catalysis are shown in Scheme 1.34.

Although the processes to give the acyl type complexes (a) to (c) are formally represented as attack of external nucleophiles on the coordinated CO, it is possible that the NuH such as H₂O, ROH, or R₂NH initially binds the metal atom and then attack the adjacent CO ligand. In that case the proton attached to the nucleophile is abstracted by a base including the substrate such as amine itself.

The hydroxycarbonyl complex generated by the attack of OH[−] on the coordinated CO (Scheme 1.34a) is susceptible to decarboxylation affording a metal hydride, which may react with a proton to produce H₂. The process is considered to be involved in catalytic conversion of CO and H₂O into CO₂ and H₂ (the water gas shift reaction) as shown in Eq. 1.17.





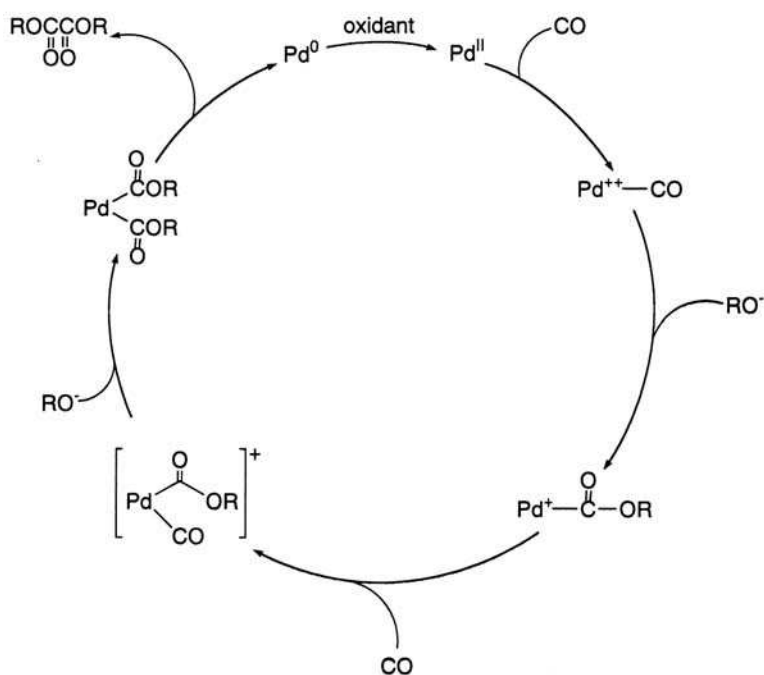
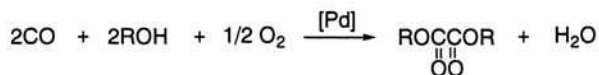
Scheme 1.34. Nucleophilic attack of OH^- , OR^- , and NHR^- on coordinated CO.

Although the water gas shift reaction is accomplished with heterogeneous catalysts, useful information regarding the reaction mechanism was obtained in organometallic chemistry [103].

The attack of amine and alcohol in combination with a base on the coordinated CO affords alkoxy carbonyl and carbamoyl-metal species, respectively (Scheme 1.34b and c). Factors controlling the nucleophilic attack on the CO ligand coordinated to Pd(II) species have been reasonably well clarified [104]. The reaction can be coupled with other elementary processes such as reductive elimination to realize useful synthetic processes. When a Pd(0) species is formed by the reductive elimination, for example, it should be re-oxidized to Pd(II) for letting it enter the catalytic cycle to undergo the subsequent processes involving the nucleophilic attack of the coordinated CO ligand. Thus finding of a suitable oxidizing agent presents a crucial issue for realizing a catalytic process. Various oxidizing agents have been tried in attempts to accomplish the smooth re-oxidation process, including Cu(II) as will be discussed in conversion of ethylene to acetaldehyde.

A successful industrial process for synthesizing oxalic ester from CO and alcohol with O_2 as an oxidant with the aid of alkyl nitrite (Scheme 1.35) was commercialized (Ube process).

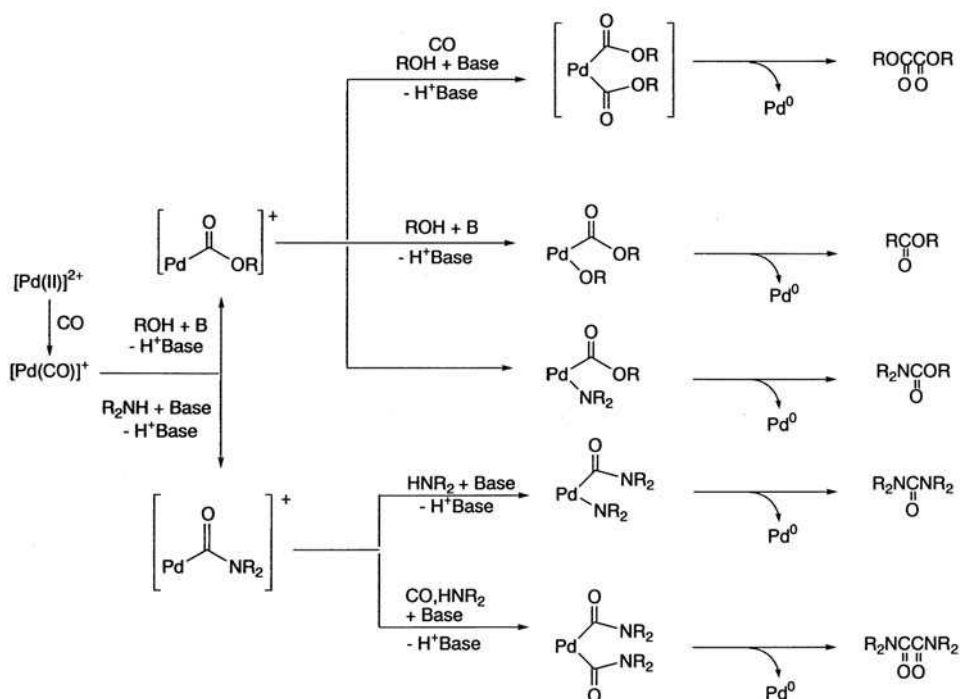
The precise mechanism in the catalytic oxalate synthesis has not been established, but it is likely that the catalytic process proceeds as shown in Scheme 1.35. The catalytic cycle is comprised of nucleophilic attack of RO^- on the CO coordinated to Pd(II) to give an alkoxy carbonylpalladium(II) species, which further undergoes the similar CO coordination followed by external RO^- attack to give bis(alkoxy carbonyl)palladium(II) complex [105,106]. Reductive elimination of the two alkoxy carbonyl ligands to generate a Pd(0) species and its re-oxidation are



Scheme 1.35. Catalytic cycle for oxalate synthesis using alkyl nitrite.

the crucial processes in the catalytic process. In the Ube process, the oxidation of Pd(0) species is smoothly performed with the aid of alkyl nitrite. Model complexes having two methoxycarbonyl ligands bound to Pd(II) coordinated with bipyridine and phenanthroline ligands have been isolated and characterized [107]. It should be possible, in principle, to construct catalytic cycles by combining fundamental processes to produce carbonyl-containing compounds such as alkyl and aryl carbonate, oxamide, urea, and carbamate as shown in Scheme 1.36 by incorporating the external attack of oxygen- and nitrogen-nucleophiles on the CO coordinated to electrophilic Pd(II) center.

Oxamide can be catalytically produced from CO and a secondary amine in the presence of 1,4-dichloro-*trans*-2-butene as the oxidant [108]. It was con-



Scheme 1.36. Reaction courses giving carbonyl-containing products in combination with O- and N-nucleophiles.

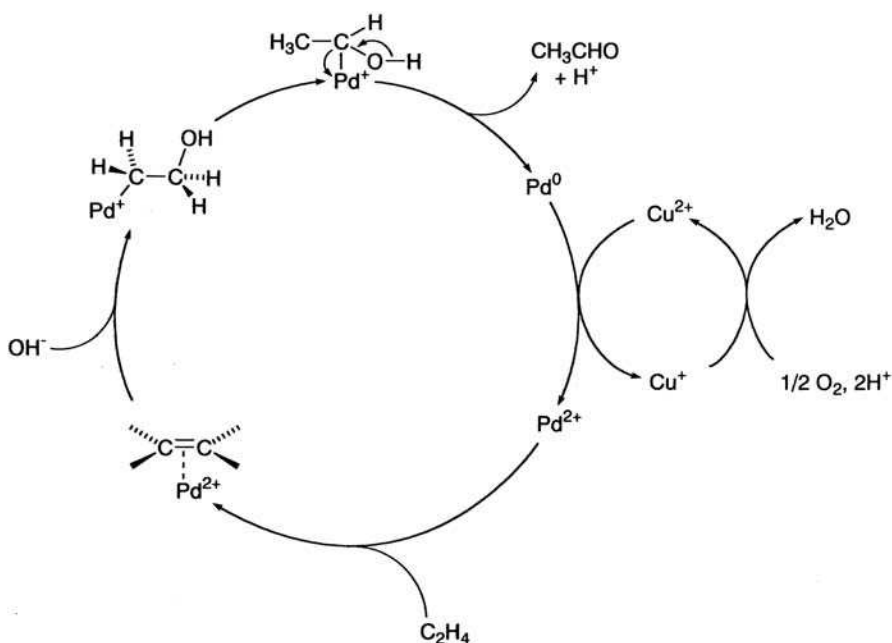
firmed that $[\text{Pd}(\text{PPh}_3)_4]$ species could be readily converted to $[\text{PdCl}_2(\text{PPh}_3)_2]$ by 1,4-dichloro-trans-2-butene with liberation of 1,3-butadiene. The palladium chloride $[\text{PdCl}_2(\text{PPh}_3)_2]$ is transformed into $[\text{PdCl}(\text{CONEt}_2)(\text{PPh}_3)_2]$ by attack of diethylamine on the coordinated CO ligand bound to Pd(II) species. Thus it is probable that the oxalate and oxamide are produced by reductive elimination of bis(alkoxycarbonyl)palladium(II) and bis(carbamoyl)palladium(II) species [109]. The exact mechanisms for catalytic synthesis of carbonates, carbamates, and urea derivatives are yet to be established. However, on the basis of various indirect pieces of evidence and of model studies, the reaction routes shown in Scheme 1.36 provide plausible courses. Currently, most of the industrial processes to produce these industrially important feedstocks depend on conventional stoichiometric methods using environmentally unfavorable methodologies. Thus invention of more atom efficient and environmentally benign processes is required and fundamental studies on the reactions of the CO-coordinated complexes are expected to provide important information to realize the green processes. For example, conventional processes for production of polycarbonate, an important engineering plastic, employ phosgene in combination with sodium salt of bis-phenol to accomplish the polycondensation process by removal of NaCl. The polycarbonate

can be produced by exchange process of bis-phenol and diphenyl carbonate and the route for obtaining diphenyl carbonate or dimethyl carbonate is under active investigation. Although the turnover number and turnover frequency are still low, a new route involving the reductive elimination of the alkoxycarbonyl and alkoxide ligands may be eventually realized [110].

(b) External attack of nucleophiles on alkene coordinated to electrophilic metal complexes

Electron withdrawal from the coordinated alkene to an electrophilic metal center makes the coordinated alkene susceptible to attack by an external nucleophilic agent or by a ligand coordinated to the metal. A classic example using modification of the chemical nature of ethylene coordinated to a cationic metal center can be seen in palladium-catalyzed Hoechst–Wacker process [111]. The catalytic cycle can be represented by Scheme 1.37, which is comprised of the main cycle to convert the ethylene coordinated to Pd(II) into acetaldehyde and auxiliary cycles to re-oxidize the Pd(0) species to Pd(II) with Cu(I). The Cu(I) produced in the process is oxidized in turn to Cu(II) with oxygen.

In the first step in the main catalytic cycle, a π type coordination of ethylene to Pd^{2+} catalyst center takes place to give a π -bonded ethylene complex of palladium(II). Attack of an OH⁻ anion on the coordinated ethylene molecule

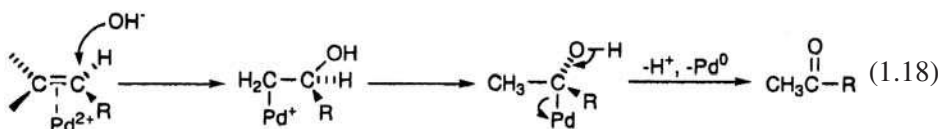


Scheme 1.37. Mechanism of conversion of ethylene into acetaldehyde catalyzed by Pd(II) and Cu(II).

to form a π -hydroxyethylpalladium species then follows where the π -bonded complex is transformed into the σ -type complex. Model studies regarding the attack of the nucleophile indicated that the nucleophilic addition takes place in a trans mode with approach of the OH^- nucleophile from the *anti*-side of the ethylene coordinated to the Pd center [112].

The β -hydroxyethylpalladium species is subsequently transformed into α -hydroxyethylpalladium species by skeletal isomerization involving β -hydrogen abstraction and transfer of the hydride ligand to the methylene carbon of vinyl alcohol formed. The α -hydroxyethylpalladium liberates acetaldehyde as shown in the scheme with generation of Pd(0). The key of success in realizing the catalytic process was to re-oxidize the Pd(0) species produced to Pd(II) with Cu(II), which is reduced in the auxiliary redox process to Cu(I) that is in turn re-oxidized by oxygen to Cu(II).

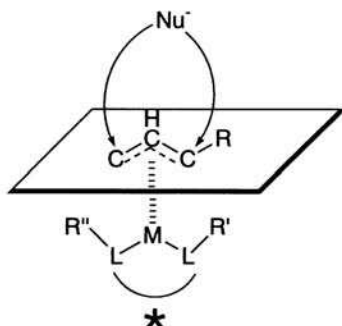
When α -olefins such as propylene are employed, 2-ketones are catalytically produced [113]. The process involves the nucleophilic attack at the substituted carbon in the terminal double bond. Skeletal isomerization through β -hydrogen elimination and re-addition of the hydrido ligand on the terminal methylene provides a branched metal alkyl with CH_3 and OH substituents. Ketone can be liberated from the Pd(II) complex with release of Pd(0) (Eq. 1.18).



External attack of an acetate anion on the ethylene molecule coordinated to Pd(II) is operative in industrial production of vinyl acetate, first reported by Moiseev et al. [114] and later commercialized by Kuraray in Japan after modification of the process. In certain cases the process of attack by an external nucleophile is reversible and the nucleophile bonded may dissociate to convert the σ -bonded complex back into the π complex.

(c) *External attack of a nucleophile on η^3 -allyl transition-metal complexes*

In contrast to the processes based on the external attack of a nucleophile on the coordinated CO or olefin ligands on Pd(II) species, where re-oxidation of the Pd(0) produced to reactive Pd(II) presents a considerable problem, no such problem is involved in reaction of a Pd(0) complex with allylic substrates. As we have already discussed in Schemes 1.9 and 1.10, allylic compounds such as allylic acetates or carbonates readily oxidatively add to Pd(0) species to form η^3 -allyl palladium(II) complexes that are susceptible to nucleophilic attack. The catalytic process converting allylic substrates to produce allylation products of nucleophiles has found extensive uses in organic synthesis, notably in the work of Tsuji and Trost. Employment of a chiral ligand in the catalytic allylation of nucleophiles allows catalytic asymmetric synthesis of allylation



Scheme 1.38. Control of the external attack of a nucleophile on the coordinated allyl ligand.

products [115–117]. Scheme 1.38 shows the concept of the influence of chiral ligand in controlling the external attack of a nucleophile.

In certain cases decrease in the optical activity in the catalytic allylation products is observed with increase of the catalyst. The cause can be ascribed to the intervention of a bimolecular process involving attack of the coordinated η^3 -allyl ligand by a Pd(0) species from the opposite side of the allyl plane [118].

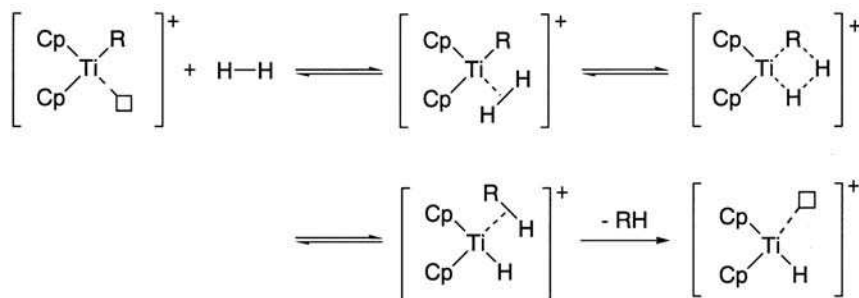
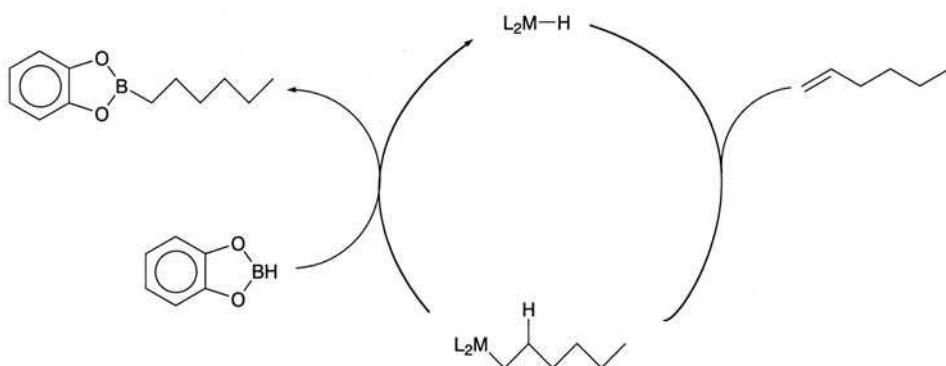
1.3.6 σ -Bond metathesis

The mechanisms of most of catalytic processes discussed so far can be accounted for by a combination of the well-established elementary processes in a relatively straightforward manner, but some cannot be so accommodated (Sections 1.3.1–1.3.5).

Electron-poor early transition metal complexes, particularly those of lanthanoid(III) and Group 4 metals of Ti(IV), Zr(IV), and Hf(IV) that have no d electrons cannot undergo oxidative addition because of a lack of d electrons. Thus the reaction shown in Scheme 1.39 involving the Ti-alkyl bond cleavage on the reaction of $[\text{Cp}_2\text{TiR}]^+$ type complex with H_2 cannot be explained in terms of oxidative addition and the subsequent reductive elimination. A concerted process involving four center-four electron bond rearrangement as shown in Scheme 1.39 is invoked instead to account for the process.

Such a process is operative in the chain transfer in coordination polymerization initiated by a titanium alkyl. The molecular weight of the polymer with a Ziegler type catalyst having a metal-alkyl growing chain can be controlled by addition of H_2 . The growing polymer chain R is liberated into solution on reaction with H_2 as R-H by coupling of the polymer chain with a hydrogen atom with generation of a Ti-H species. The titanium hydride produced is capable of resuming the olefin insertion process, thus performing the chain transfer process.

Examples of processes involving σ -bond metathesis are recently increasing [119]. Hydroboration of terminal olefins is catalyzed by lanthanoid hydride or

Scheme 1.39. σ -Bond metathesis.

Scheme 1.40. Hydroboration of an olefin catalyzed by a lanthanoid complex.

its precursor, lanthanoid alkyl. The cycle shown in Scheme 1.40 comprising insertion of the olefin into the metal–hydride bond and the subsequent σ -bond metathesis accounts for the catalysis. In the σ -bond metathesis process the metal–alkyl bond formed by olefin insertion is cleaved on interaction with the B–H bond in catecholborane to release the alkylated borane with regeneration of the catalytically active metal hydride [120].

Involvement of σ -bond metathesis may be operative not only with early transition metal complexes but also with late transition metal complexes, [121].

The reactions of late transition metal complexes with H_2 are usually explained by oxidative addition of H_2 giving dihydride. However, in certain reactions of transition metal alkyls or acyls with H_2 or boranes, involvement of σ -bond metathesis better accounts for the results.

σ -Bond metathesis of metal alkyls with H_2 can be also considered as heterolytic cleavage of H_2 with the anionic alkyl ligand. Some $\eta^2\text{-H}_2$ complexes are known to show acidic character and tend to undergo proton loss [122]. Experimental evidence to differentiate these possibilities is hard to obtain and one would need the help of computational chemistry to have a reasonable theoretical explanation.

1.3.7 Reactions of metal-alkylidene and alkylidyne complexes

Alkylidene and alkylidyne complexes having metal to carbon multiple bonds are unique to organometallic complexes [123]. Although free carbene and carbyne molecules are quite unstable chemical species, they are stabilized on coordination to transition metal complexes forming metal-carbon double bond and triple bond. When a carbene ligand bound with a metal is substituted with a heteroatom, the carbene complex is called Fischer type carbene complex whereas an alkylidene-metal complex having no heteroatom substituent is called Schrock type complex. They show chemical properties particularly unique to transition metal complexes. Important catalytic processes involving the metal-carbon multiple bond include olefin metathesis, ring-opening metathesis polymerization, and ring-closing metathesis. Quite remarkable progress has been made quite recently.

There was a long controversy regarding the mechanism of the olefin metathesis, but now the process has been established to proceed through involvement of a transition metal alkylidene species that forms a metallacyclobutane reversibly on interaction with an olefin [124]. Elementary processes in typical catalytic processes involving metal alkylidene complexes are illustrated in Scheme 1.41.

(a) Olefin metathesis

Interaction of a metal alkylidene complex with an olefin forms a metallacyclobutane. Cleavage of the metallacyclobutane complex at bonds different from the original ones leads to liberation of a new olefin and formation of a new metal carbene complex (Scheme 1.41a). This type of transformation is operative in a catalytic cycle of olefin metathesis as shown in Scheme 1.42 [125].

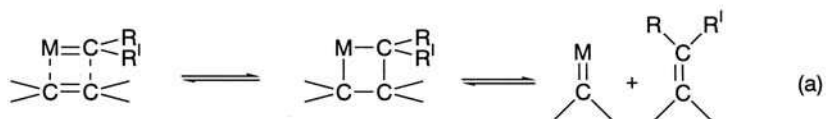
Alkyne metathesis can be also carried out with transition metal complexes as shown in Scheme 1.43. Complexes corresponding to the intermediates in the catalysis having metallacyclobutadiene structures have been isolated in the reaction of alkylidyne complexes with alkynes [126]

The carbonyl group in ketones and carboxylic esters also can be converted into olefins by a similar mechanism involving the cyclooxabutane formation and the subsequent cleavage. The process offers considerable utility in organic synthesis in preparation of olefins from carbonyl compounds as in Wittig reactions. However, because of the stable nature of the formed early transition metal oxide, the process has not been made catalytic [127].

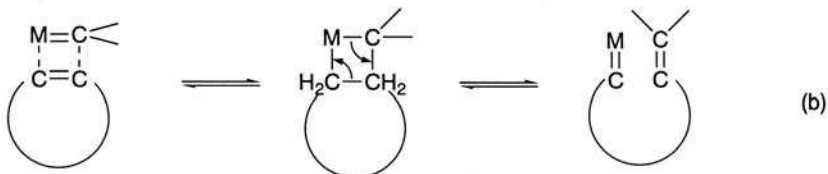
(b) Ring-opening metathesis polymerization

When a cyclic olefin of a suitable ring size is employed as a substrate to interact with a metal alkylidene complex, ring-opening metathesis polymerization is initiated (Scheme 1.41b). Natta first discovered ring opening polymerization of cyclic olefins by combined systems of Group 6 transition metal complexes with organoaluminum compounds [128]. It was established much later that the mechanism of the process differs from the coordination polymerization of the

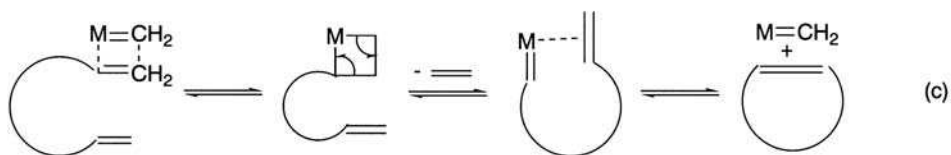
(a) Olefin metathesis



(b) Ring Opening Metathesis Polymerization



(c) Ring closing metathesis

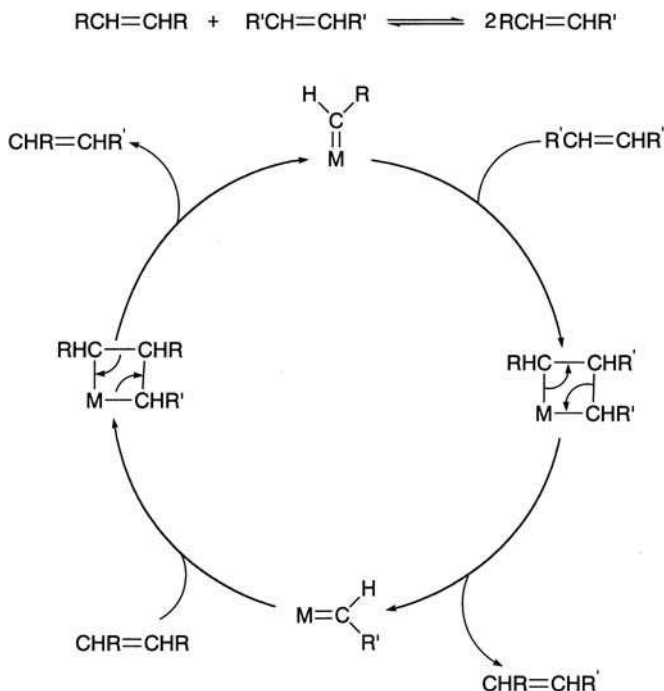


Scheme 1.41. Carbene complexes and their behavior in catalyzing the olefin metathesis (a), ring-opening metathesis polymerization (b), and ring-closing olefin metathesis (c).

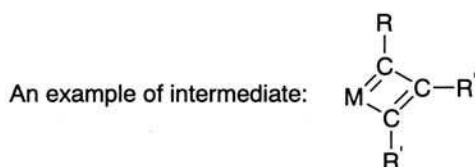
Cossee type. The mechanism comprised of olefin metathesis type elementary processes involving a metal carbene complex and a metallacyclobutane was established only recently after the development of the chemistry of metal-carbene complexes [129]. Understanding of the novel kind of reaction mechanism opened a new horizon in polymerization. Various new types of polymerization of cyclic monomers have been realized by ROMP. An advantage of the process is that the processes are tolerant to polar reactants and solvents enabling ready incorporation of polar substituents into polymers. Another advantage is that the ROMP is living in nature and polymers of narrow molecular weight distributions are available by the method.

(c) Ring-closing metathesis

Utilizing the concept of olefin metathesis involving a metallacycle formation between two terminal olefin groups, one can design a ring-closing process as shown in Scheme 1.41c. Such ring-closing metathesis has found an extensive use in synthesis of medium- to large-size ring compounds, which are often found among naturally occurring products of biological activities. Synthesis of these



Scheme 1.42. Catalytic cycle of olefin metathesis.



Scheme 1.43. Alkyne metathesis catalyzed by an alkylidyne complex.

medium ring size compounds presents a formidable task by conventional means but the advent of ring-closing metathesis provided efficient short-cuts. Olefin metathesis is composed of equilibrium processes as shown in Scheme 1.41a. In ring-opening olefin metathesis the reaction is driven to polymerization, since it is a downhill process that way. In ring closing metathesis, on the other hand, release of ethylene from the system drives the process to the cyclic products.

Further treatment of the elementary processes involving metal alkylidene and alkylidyne complexes will be given in Chapter 4.

1.4 CATALYTIC CYCLES CONSTITUTED OF MULTIPLE COMPONENTS OF ELEMENTARY PROCESSES

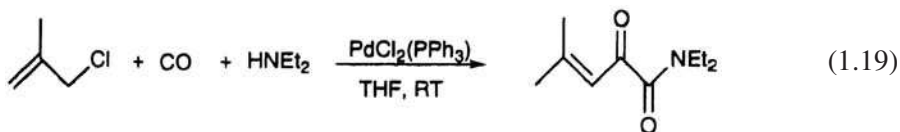
The catalytic processes so far described contained catalytic cycles comprised of a few elementary processes and elucidation of the mechanisms was relatively straightforward. By combination of multiple elementary processes the scope of the catalysis can be further expanded. We have already dealt with hydroformylation of olefins, which uses three types of substrates and the catalytic process consists of at least three elementary processes. For obtaining the aldehydes in good selectivity, the catalysis must proceed by combination of proper sequence of elementary processes. In the following examples, we shall deal with other types of catalytic processes composed of multiple steps of elementary processes.

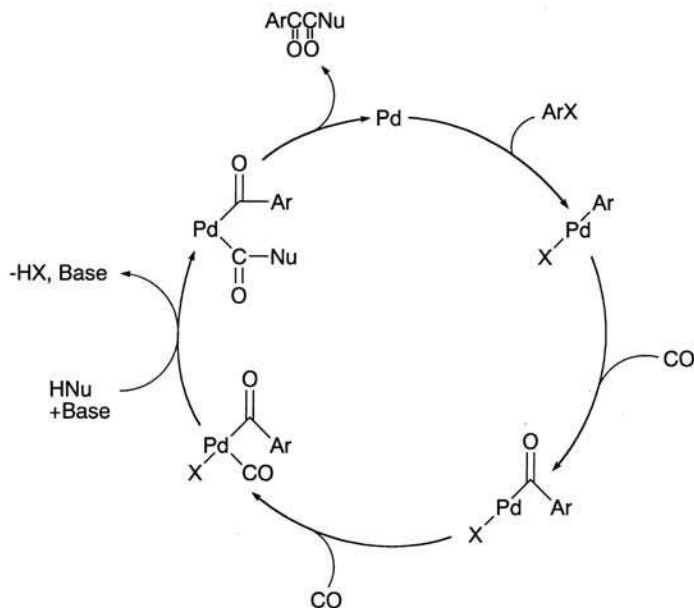
1.4.1 Double carbonylation of aryl halides to α -keto acid derivatives

Incorporation of aryl groups, CO and nucleophiles to give carboxylic acid derivatives has been accomplished by Garrou and Heck [130]. As we have already discussed, the process can be accounted for by combination of the oxidative addition of aryl halide, CO insertion and attack of alcohol on the palladium catalyst center in the presence of a base, and reductive elimination of the acyl and alkoxide groups. Combination of the process to give the acylpalladium intermediate with attack of an amine on a coordinated CO ligand to form a carbamoyl ligand, as discussed previously regarding the nucleophilic attack of amine on the CO ligand (Scheme 1.34c), can lead to realization of double carbonylation process. Scheme 1.44 shows the catalytic cycle involving reductive elimination of the two types of the acyl ligands.

The catalytic cycle is common with the single carbonylation of aryl halides in the steps of oxidative addition of aryl halide to a Pd(0) species and the subsequent CO insertion process. Since successive CO insertion into the acylpalladium bond is not thermodynamically favorable, incorporation of another CO molecule takes the route of coordination of the CO molecule to the acylpalladium(II) intermediate. Attack by a nucleophile such as secondary amine, alcohol, and water in the presence of an appropriate base, including the amine itself, gives bis acyl type intermediate which reductively eliminates α -keto acid derivatives [131].

Although the scope of catalytic double carbonylation was considered to be limited to aryl and vinyl halides and the process was not applicable to aliphatic halides because of ready direct reaction of alkyl halides with amines, later examination revealed that allyl halides could be double carbonylated when the reaction was carried out in the presence of a limited amount of an amine under CO pressure (Eq. 1.19).





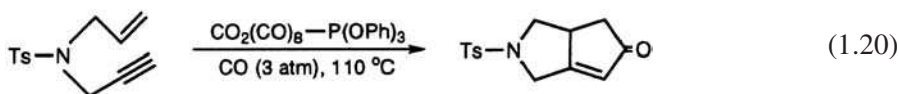
Scheme 1.44. Mechanism of double carbonylation to convert aryl halides, CO, and nucleophiles into α -keto acid derivatives.

The influence of the amount of amine can be elucidated by mechanistic considerations of the double carbonylation. An allyl halide readily forms an η^3 -allylpalladium halide by oxidative addition to Pd(0) species and the amine can attack the allyl ligand to generate allylamine. However, the nucleophilic attack is a reversible process and CO insertion into the allylpalladium species can take place in the presence of a small amount of amine to allow the formation of the acylpalladium species. Attack of the amine on the coordinated CO giving the carbamoylpalladium species followed by reductive elimination by coupling with another alkenoyl ligand produces the α -keto amide [132].

As further application of the double carbonylation a one-pot synthesis of α -amino amides has been achieved by using primary amines [133]

1.4.2 Pauson–Khand reaction

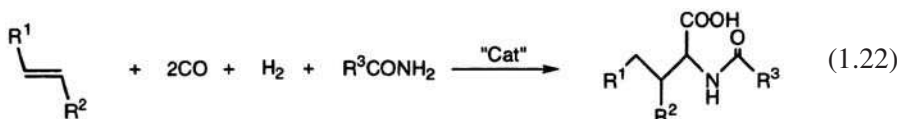
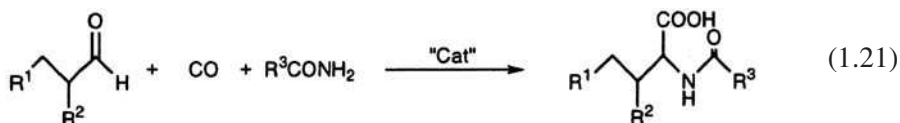
Combination of three unsaturated compounds, i.e., alkyne, alkene, and CO provides a convenient means of catalytically synthesizing useful products such as cyclic unsaturated ketones in a one-pot process. On the basis of fundamental studies of the reactions of alkyne-coordinated cobalt carbonyl complex with olefins, a catalytic process to synthesize cyclic ketones has been developed (Eq. 1.20) [134].



Although the mechanistic details remain to be established, it is likely that the catalytic process is comprised of alkyne coordination and multiple insertions of alkene and CO followed by reductive elimination.

1.4.3 Other processes comprised of multi-component elementary steps

Beside the above-mentioned processes there exist a variety of processes involving multi-component elementary processes. For example, amidocarbonylation converts olefins, CO, H₂, and amides into *N*-acyl α -aminoacids (Eqs. 1.21 and 1.22) [135].



As the number of substrates participating in the catalytic process is increased, the variety of catalytic products increases, whereas establishment of the mechanism will become increasingly difficult. In-depth understanding of the elementary processes discussed in later chapters will help understanding the mechanisms and further designing the novel catalytic processes.

1.5 OTHER RELEVANT ASPECTS

1.5.1 Cooperative action of multimetallic systems in promotion of certain types of organic reactions

We have focused our attention so far on the behavior of single metal complexes in catalyzing various organic processes. A variety of catalytic processes could be developed by combination of the elementary processes of these relatively simple transition metal complexes. Combination of different transition metal(s) with a transition metal complex acting as the catalyst center may cause modification of the behavior of the principal transition metal complex. Thus by 'fine tuning' the property of the principal transition metal complex by a ligated auxiliary complex of another metal an enhanced catalytic activity that may not be achieved by the single metal complex may be developed [136]. In certain cases the modification of the properties of the main transition metal complex may alter the originally observed properties and induce quite unexpected properties. Examples of substrate activation with heteropolynuclear complexes have been reported [137].

Using multi-metal center systems can increase the diversity in reactivities of metal complexes, since we can anticipate different types of activation of substrates on their interaction with di-, tri-, and polymetallic systems. Until recently, chemistry of metal cluster complexes had been confined mostly to synthesis and determination of metal cluster complexes, particularly with carbonyl ligands. However, the metal clusters having carbonyl ligands suffer some limitations in their reactivities due to the electron-withdrawing character of the coordinated CO ligands acting as π acid, rendering the metal centers less electron rich and less amenable to reactions unique to low valent transition metal complexes such as oxidative addition reactions. The recent progress on the interaction of multimetallic transition metal complexes having pentamethylcyclopentadienyl or cyclopentadienyl ligands indicates that special types of activation of a particular bond, e.g., C–H and C–C bonds in hydrocarbons can be achieved by the action of multi-nuclear systems [138]. Details of the activation of non-polar bonds in organic compounds by multi-metallic centers will be discussed in Chapter 2.

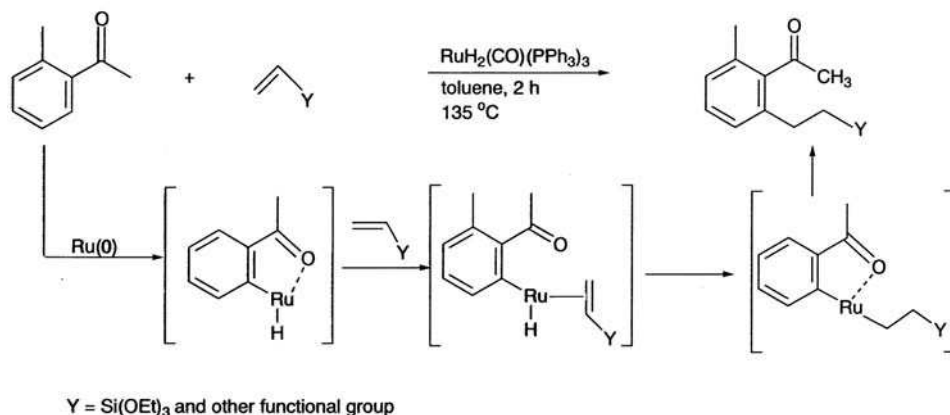
1.5.2 Toward development of environmentally benign processes

The recent demand for making synthetic processes more environmentally benign and atom efficient enhances the requirement for replacing the conventional stoichiometric systems with catalytic ones. Even when a catalytic process can be realized, it is desirable to develop a system where wastes are not released.

The processes so far developed depend on established elementary processes such as oxidative addition of organic halides for forming reactive organometallic complexes having a metal to carbon bond. Although organic halides often provide inexpensive and reactive starting materials, the halide part must eventually appear as an inorganic salt, typically after reaction with a base. It is therefore desirable to develop a better process with higher atom efficiency [139]. To circumvent organic halides as starting materials, other types of substrate should be developed that are amenable to ready bond cleavage on interaction with transition metal complexes for generating reactive organotransition metal complexes. Thus the importance of developing processes involving cleavage of C–H, C–C, C–O, C–S, and C–N bonds will increase [140].

Among these bond cleavage processes C–H bond cleavage promoted by transition metal complexes recently attracted the wide attention [141]. Previously, conversion of benzene and ethylene in the presence of $\text{Pd}(\text{OAc})_2$ into styrene and stilbene was reported and the reaction was considered to proceed through the formation of a phenylpalladium intermediate [142]. Recently, various attempts to activate C–H bonds in aliphatic and aromatic compounds have been reported [143]. We shall see more examples of catalytic C–H bond activation with the progress of organometallic chemistry and further examples of performing efficient catalyses utilizing the C–H bond activation.

When an organic substrate has a functional group to interact with a transition



Scheme 1.45. Ruthenium-catalyzed functionalization of acetylarenes.

metal complex, the C–H bond can be brought into proximity of the transition metal center assisted by interaction of the functional group. A recently developed route utilizing the C–H bond activation by a ruthenium complex provides an example of a halide-free catalytic process (Scheme 1.45) [144].

Interaction of an acetyl arene with ruthenium is assisted by binding of the carbonyl group, which brings the ortho hydrogen close to ruthenium and leads to the oxidative addition with the C–H bond cleavage. The process is followed by olefin insertion and reductive elimination to liberate the product.

Various attempts have been made to make these catalytic processes more environmentally benign. Processes that can be practiced in aqueous media [145], biphasic system [146] or ionic liquid [147] have attracted increasing attention and will gain further importance.

1.5.3 Tandem processes

In synthesis of complex molecules, well-designed synthetic strategies involving transition metal catalyzed intra- or intermolecular processes can lead to short cuts to target molecules by so-called tandem or domino reactions [148]. Further progress is expected in the field to accomplish efficient synthesis.

1.6 FURTHER PROSPECTS

Although the mechanisms of catalytic systems are much better understood in homogeneous systems than in heterogeneous ones, heterogeneous systems have a distinct advantage over the homogeneous ones in ease of separation of the catalyst used from the products and reusability of the heterogeneous catalysts

for further reactions. Thus various approaches have been developed to support the catalyst systems on solid or on polymer supports for providing the ease of manipulation, while still keeping the fundamental information gained in the studies of homogeneous systems [2g,149]. The use of these transition metal catalysts supported on polymers such as polystyrene allows development of catalytic systems with the advantage of the ease of separation and still keeping the character of the transition metal unaltered. The polymer supported catalyst systems also allow their application for combinatorial synthesis [150,151].

Another recent development is the utilization of solid catalyst systems such as nickel or palladium deposited on carbon in the presence or absence of ligands such as tertiary phosphines. Treatment of heterogeneous catalyst systems such as palladium supported on carbon by addition of ligands can modify the nature of the heterogeneous catalysts [152,153]. On the other hand, addition of tertiary phosphine ligands may sometimes have an adverse effect on the catalysis. Recent finding suggests that treatment of the surface palladium atoms with organic halides causes oxidative addition of the halide and renders leaching of the surface species into solution [154].

Further development of utility of the concepts gained in studies of homogeneous catalysis to heterogeneous systems is expected.

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Activation of Substrates with Non-Polar Single Bonds

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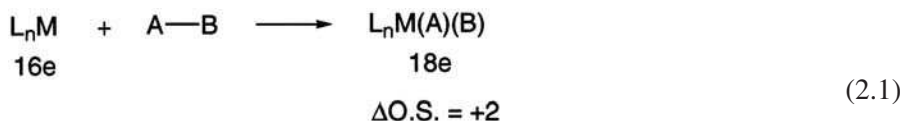
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2.1 SIGNIFICANCE OF THE AREA

The use of transition metals as homogeneous catalysts for organic reactions has transformed industrial and organic synthesis over the last 40 years. In 1960, such syntheses were almost always carried out by traditional procedures and among organometallic reagents, one normally encountered only Grignard and organolithium reagents. In the 1970s and 80s, a wide variety of organometallic catalysts and reagents were introduced, but growing environmental sensitivity led to considerations of atom economy (waste minimization) causing organometallic reagents to be deemphasized in favor of catalysts. Practically every synthesis of any complexity now reported includes one and often many steps involving homogeneous catalysis [1,2]. At the same time, an increasing number of commercial syntheses have incorporated such catalysts. Within the last 10 years, asymmetric synthesis of optically active molecules using an optically active catalyst has become a major subfield [3].

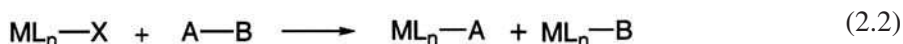
2.2 ACTIVATION PATHWAYS

Most of these catalytic reactions rely on activation steps by which one of the substrates interacts with the metal via Eq. 2.1, in which one of the substrate's covalent bonds is cleaved. This often happens by oxidative addition, one of the key reactions of organometallic chemistry [1]. Oxidative addition mechanisms tend to depend on the polarity of the bond being cleaved, leading to the division of the topic between non-polar bonds in this chapter and polar ones in the next (Chapter 3).



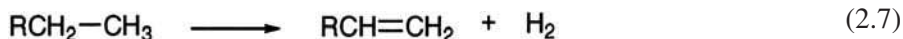
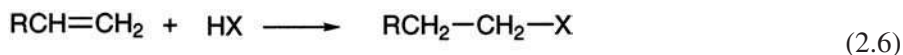
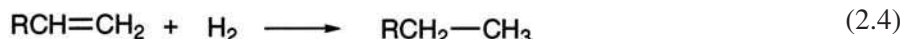
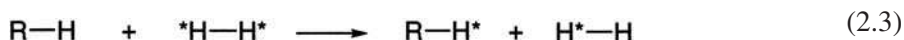
(L_nM = metal and associated ligands)

Other activation mechanisms, notably σ -bond metathesis (Eq. 2.2), are discussed in detail below, but once again, the net result is that a covalent bond in the substrate is broken and one or more substrate-derived groups are transferred to the metal.



Electrophilic and radical activation pathways are also known, but these are much more rarely involved in catalytic cycles; some examples are discussed in later sections. Radical pathways involve bond homolysis and are therefore governed by bond energy considerations. For example a typical series showing increasing C–H reactivity towards radicals is: $\text{C}_6\text{H}_6 < \text{CH}_4 < \text{CH}_3\text{Me} < \text{CH}_2\text{Me}_2 < \text{CHMe}_3 < \text{HSiMe}_3$; this is also the order of decreasing X–H bond strength ($\text{X} = \text{C}, \text{Si}$). Electrophilic pathways are favored where the intermediate species is stabilized by delocalization of the charge, as in classical organic chemistry. Electron-rich arenes, such as $\text{C}_6\text{H}_5\text{OMe}$, are therefore extremely reactive and give ortho and para substitution, unless the electrophile is bulky, in which case para substitution can dominate. Catalytic applications of these pathways are rare.

A number of substrates with non-polar single bonds play a key role in homogeneous catalysis. In view of its fundamental importance and key role in so many catalytic cycles, perhaps the most important example is the H–H bond in dihydrogen, a substrate in isotope exchange (Eq. 2.3, $\text{H}^* = \text{D}$ or T), and in hydrogenation (Eq. 2.4) and hydroformylation of unsaturated organic substrates (Eq. 2.5). The Si–H and B–H bonds in silanes and boranes are the next most important and are associated with catalytic hydrosilation and hydroboration of unsaturated organic substrates (Eq. 2.6). Somewhat rarer is cleavage of a C–H bond, implicated in alkane dehydrogenation (Eq. 2.7). C–C, Si–Si and B–B cleavage processes are still relatively rare.



Normally, an activation step is followed by other steps that lead to functionalization or other transformation of the substrate. These include topics covered in the later chapters of the book: binding and activation of substrates with multiple bonds (Chapter 4); transmetalation of alkyl groups (Chapter 5); 1,2-insertion and

β -elimination (Chapter 6); 1,1-insertion and α -elimination (Chapter 7); addition to an unsaturated ligand (Chapter 8); and reductive elimination (Chapter 9).

2.2.1 Oxidative addition

In the oxidative addition of an A–B bond to a metal, new M–A and M–B bonds are formed as the A–B bond is cleaved (Eq. 2.1). The reverse reaction, reductive elimination, leads to the extrusion of an A–B molecule from a precursor M(A)(B) complex; this is often the product forming step in a catalytic reaction. In the oxidative direction, we break the A–B bond and form an M–A and an M–B. Since A and B are always considered as 1e X-type (anionic) ligands, the oxidation state, the electron count, and coordination number of the metal all increase by two units during the reaction. The change of +2 in the formal oxidation state gives the reaction the name oxidative addition. These terms as well as the conceptual basis of organometallic chemistry are discussed in a previous work [4].

(a) Concerted mechanism

Oxidative additions in general proceed by a great variety of mechanisms, but the situation for non-polar bonds is much more simple in that concerted reaction is very often seen. The fact that the electron count increases by two units in Eq. 2.1 means that a vacant 2e site is always required on the metal. We can either start with a 16e complex, or a two electron vacant site can be opened up in an 18e complex by the prior loss of a two-electron ligand, such as PPh₃. The change of +2 in the oxidation state means that a metal complex of a given oxidation state must also have a stable oxidation state two units higher to undergo oxidative addition (and vice versa for reductive elimination). This is the case for Ni(0), Pd(0), Pt(0), Ni(II), Pd(II), Pt(II), Co(I), Rh(I), Ir(I), Fe(II), Ru(II), Os(II).

Whatever the mechanism, there is a net transfer of a pair of electrons from the metal into the σ^* orbital of the A–B bond, and of the A–B σ electrons to the metal. This cleaves A–B and makes M–A and M–B bonds. Because the metal acts as a reductant, the reaction normally involves a low oxidation state metal; metals are therefore often in an oxidation state no higher than +2. In contrast, a more highly oxidized metal is more likely to undergo reductive elimination.

(b) Binuclear oxidative addition

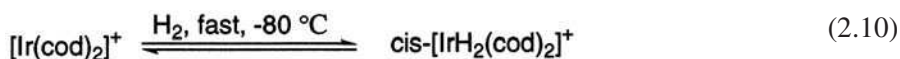
Some metals prefer to change oxidation state, electron count, and coordination number by one unit instead of two. Eq. 2.8 shows an example of binuclear oxidative addition, a reaction that brings about these changes and therefore can be favored by such metals. This typically occurs for a paramagnetic first row 17e transition metal complex or an 18e M–M bonded dimer that can dissociate to give

a 17e radical. Co(II) and Cr(II) are the chief metals that give this binuclear variant (Eq. 2.9) [5].



(c) *Oxidative addition versus reductive elimination*

These are in principle reversible, but because the position of equilibrium obeys the overall thermodynamics, in practice the reactions often tend to go in the oxidative or reductive direction only, depending on the case. Which is seen depends on the relative stabilities of the oxidation states or, more quantitatively, on the A–B versus M–A and M–B bond strengths. Alkyl hydride complexes commonly eliminate alkane, but only rarely do alkanes oxidatively add to a metal. Third row elements, which tend to have stronger metal–ligand bonds tend to give oxidative addition more easily. Occasionally, an equilibrium is established in which both the forward and back reactions are observed. It is typical for the two hydrogens to end up cis to one another in the product in Eq. 2.10 [6].

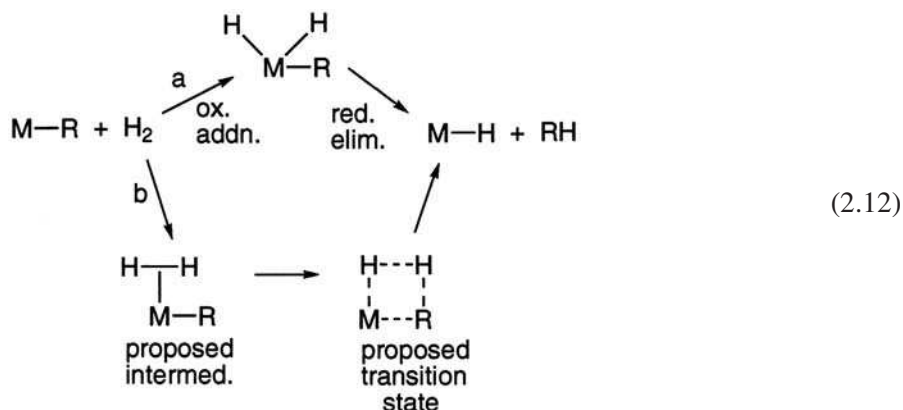


Oxidative addition is usually favored by strongly donor ligands because these stabilize the higher oxidation state.

2.2.2 σ Bond metathesis

Pathways that seem to be oxidative addition followed by reductive elimination can in fact be σ -bond metathesis reactions [7]. These are unambiguously recognizable for d^0 early metal complexes, such as Cp_2ZrRCl or WMe_6 because oxidative addition is forbidden in such cases because the oxidative addition product would unambiguously exceed the maximum permitted oxidation state for the metal. In a reaction of such a complex with H_2 (Eq. 2.11), the metal therefore cannot follow the path a of Eq. 2.12. Instead a concerted process (path b of Eq. 2.12) is believed to operate. Path b may go via formation of an intermediate H_2 complex which is permitted even for d^0 species. In any case, the complex needs a vacant site; this is equivalent to the metal complex having less than 16 valence electrons or a labile ligand that can dissociate to create a 16e intermediate. The strong proton donor character of $M(H_2)$ species may encourage proton transfer to the R group.

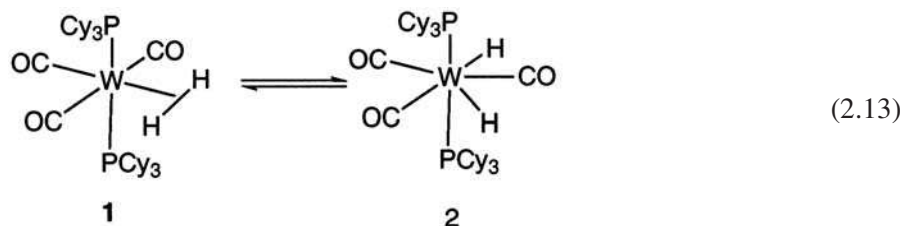




For a σ -bond metathesis pathway to be fast, the substrate usually needs to have at least one H, so for example H_2 and C-H bonds can react in this way. Other cases may be possible but can go more slowly (e.g., Si-Si).

2.3 σ BOND COMPLEXES

It is very often the case that the initial interaction between the metal and the σ bond is the formation of a sigma complex [8]. Unlike more familiar σ -donor complexes such as $\text{M}-\text{NH}_3$, where the lone pair of electrons on the N atom is bound to the transition metal atom, in a σ complex an X-H bond such as C-H, H-H, and Si-H binds to a metal center, acting as a 2e donor. In doing so, we have the addition (because the electron count increases by two electrons) but not the oxidative part of the overall reaction (because the oxidation state is unchanged). This adduct can be stable (even isolable in condensed phase in some cases) or go on to give oxidative addition or heterolytic splitting depending on the situation. Sometimes the adduct is in equilibrium with the oxidative addition product, as in Eq. 2.13 [9]. Binding in this way requires a 2e vacant site at the metal but it does not cause a change in oxidation state, so it is available even to d^0 metals (e.g., Ti(IV), W(VI)) that cannot undergo oxidation.



In general, the bonding in a σ interaction is best described in terms of two important interaction: a σ -type interaction between a suitable empty d_σ orbital on the metal (Fig. 2.1 a) and the σ electrons in the X-H in the ligand and a π

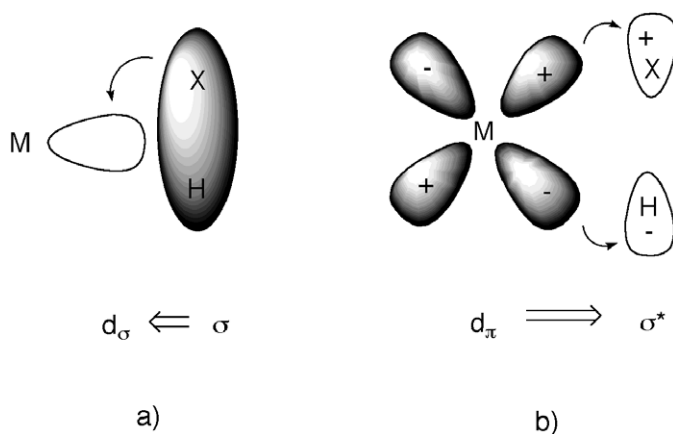


Fig. 2.1. The bonding picture for a σ complex.

back-donation of electron density from the $M(d_{\pi})$ orbitals to the X-H σ^* orbitals (Fig. 2.1 b). In complexes with weak backbonding, the length of X-H bond is similar to that in free X-H. If the metal is electron rich and donates strongly to the ligand, the X-H bond can rupture, giving both an M-X and a M-H bond by oxidative addition. When oxidative addition is incomplete, σ complexes with elongated X-H bonds are observed.

The strength of the M-(HX) interaction is affected by the energy of the X-H σ and σ^* orbitals. As X becomes more basic (e.g., Si), the energy of the X-H σ orbital increases, and the extent of electron transfer to metal also increases, leading to enhanced σ donation. Weaker X-H bonds such as metal-hydrogen bonds have lower energy σ^* orbitals, leading to enhanced π back-donation. As expected from this analysis, M-H-M (hydride bridged) and Si-H-M (agostic silane) complexes are almost always strongly bound, and the X-H bond ($X = M, Si$) is substantially stretched relative to the free state.

2.3.1 Dihydrogen complexes

The first σ dihydrogen ($\eta^2\text{-H}_2$) complex was isolated by Kubas in 1984 [10], and since then many isolable dihydrogen complexes have been prepared. Complexes with H-H bonds are frequently called non-classical hydrides, as opposed to classical hydrido complexes, which have terminal M-H bonds only. There are a number of reviews that adequately cover the literature [11-14]. The formation of the celebrated Kubas complex, **1**, was proved by NMR spectroscopy and neutron diffraction methods; its slow reversible equilibration (Eq. 2.13) with complex **2**, the product of oxidative addition, was studied by NMR spectroscopy.

If complex **1** is best regarded as being derived from $\text{W}(\text{CO})_3(\text{PCy}_3)_2$ and undissociated H-H, then it must be considered a σ complex. This is appropriate

because the H–H distance of 0.82 Å in **1** measured by neutron diffraction is not very different from its value in free H₂ (0.74 Å). We can also look at σ complexes as being derived from the classical adduct [L_nM(X)(H)] in which an attractive interaction between X and H causes these two ligands to approach one another. This description is more appropriate for ‘stretched’ σ complexes in which the X–H distance is substantially longer than in the free XH molecule. Such stretched complexes with H₂ ligands are known but are most common with Si–H ligands. Jackson and Eisenstein [15] have shown how hydrido ligands even in classical dihydrides of type, [L_nMH₂] have a mutually attractive interaction not present in CH₄.

A variety of spectroscopic techniques has been applied for structural determination of dihydrogen complexes. X-ray structure analysis may not be the best tool for precisely locating the positions of hydrogen atoms. Neutron diffraction is much more appropriate, although the necessity of large high-quality crystals has so far limited this method to only a few complexes. In most of the neutron diffraction data H₂ appears bonded to metals in a side-on fashion with d(H–H) of ca. 0.82 Å. Brammer et al. [16] found that in [ReH₇{P(*p*-C₆H₄CH₃)₃}₂] one H₂ unit has an unprecedented *r*(H–H) of 1.357 Å. This distance was much longer than those in the previously reported H₂ complexes and supported the existence of an intermediate group between classical hydrides and ‘normal’ H₂ complexes: stretched H₂ complexes. Morris [17] suggested a *r*(H–H) range of 1.1–1.6 Å as appropriate for stretched H₂ complexes. A few structurally characterized stretched dihydrogen complexes are now known with a wide range of H–H distances. *cis*-[Ir(H₂)HCl₂(P^{*i*}Pr₃)₂] (1.11 Å) [18], [Os(H₂)(en)₂(OAc)]PF₆ (1.34 Å) [19], [Ru(H₂)(C₅Me₅)(dppm)](BF₄) (1.10 Å) [20], [Os(H₂)Cl(dppe)₂](PF₆) (1.22 Å) [21].

Upon binding to a metal, the H–H stretching band (ν (H–H)) in the IR spectrum red-shifts from the 4300 cm^{–1} in free hydrogen. A range of 2300 to 3100 cm^{–1} has been observed for H₂ complexes but it is not always seen. The appearance of ν (H–D) stretch approximately halfway between the H₂ and D₂ bands has been taken as convincing evidence of presence of a σ -dihydrogen complex. Raman studies on H₂ complexes have not been successful because the complexes decomposed under laser irradiation even when exceptional precautions were taken.

The H₂ resonance in dihydrogen complexes usually appears in the range 0 to –10 δ in the ¹H NMR, and is often broad. The presence of a H–(H,D) bond is shown by the ¹*J*(H,D) coupling constant of 20–34 Hz in the ¹H NMR spectrum of the H–D analogue. This compares with a value of 43 Hz for free HD and approximately 1 Hz for the classical H–M–D species. Quantum chemical studies have shown that in free H₂, the coupling constant initially increases with H–H distance while it decays to zero in the limit of complete dissociation [22]. The suggested reason for that was that the lengthening of the H–H bond causes the nuclear magnetic moments to perturb the electronic wave function, resulting in

an initial increase in the coupling constants. However an inverse relationship between $^1J(\text{H,D})$ and the H–H distance has been experimentally observed in dihydrogen complexes and it seems more reasonable that the coupling between the two nuclei is reduced as the H–H bond is lengthened by coordination to the metal. A recent quantum chemical calculation of $^1J(\text{H,D})$ coupling constant using density functional theory (DFT) suggested that the reduced $^1J(\text{H,D})$ value in elongated dihydrogen complex is due to the increasing M–H₂ bond strength [23]. Maltby et al. proposed a linear empirical correlation between $^1J(\text{H,D})$ coupling constants and H–H distances shown below for a series of dihydrogen complexes, whose structures have been determined by X-ray diffraction, neutron diffraction or solid-state NMR techniques [24].

$$r(\text{H-H}, \text{\AA}) = 1.42 - 0.0167^1J(\text{H,D}, \text{Hz})$$

An unusual temperature dependence of $^1J(\text{H,D})$ has been discovered in several stretched dihydrogen complexes [20,21,25]. To account for the reduced $^1J(\text{H,D})$ at higher temperature, Klooster et al. [20] proposed the thermal population of the vibrational excited states of the H₂ units, where the higher energy states have longer H–H distances. DFT calculation, combined with quantum nuclear motion calculation, has strengthened this hypothesis and predicted an isotope effect on the H–H distance [26]. Very recently, direct experimental evidence for this proposal was reported by Law et al. [27].

It was proposed that non-classical hydrogen complexes and classical dihydrides could be distinguished by an application of $T_1(\text{min})$ measurement. Two protons that are very close together can relax one another very rapidly by the so-called dipole–dipole mechanism. The rate of relaxation ($1/T_1$) depends on r^{-6} (r = internuclear distance) and is thus very sensitive to the H–H distance r . A non-classical hydrogen complex, where the distance is about 0.85 Å, might therefore show unusually rapid relaxation in view of the very short value of r appropriate to an H₂ complex. However, T_1 values are different at different magnetic fields, and thus the values should be adjusted when comparing data obtained from different experiments. In classical dihydrides, the internuclear distance between the two hydrides is generally longer than ~ 1.6 Å, leading to a relaxation time on the order of half second. In unstretched molecular hydrogen complex the relaxation time is tens of milliseconds at -80°C . Values of T_1 between 6 and 90 ms at 200 MHz have been taken to indicate stretched H₂ complexes [17]. Although estimation of $r(\text{H-H})$ in a dihydrogen complex by T_1 measurement has been proven to be useful, some precautions need to be taken. The rapid rotation of the dihydrogen ligand about the M-(H₂) bond reduces the relaxation rate, and ortho hydrogen atoms of adjacent arylphosphine ligands can make a substantial contribution to the relaxation. Certain metals having a high magnetogyric ratio (γ) such as Re, Nb, V, Mn, Co, Ta cause a significant dipole–dipole relaxation of attached protons [28a]. The $T_1(\text{min})$ is the minimum T_1 value as the temperature is varied.

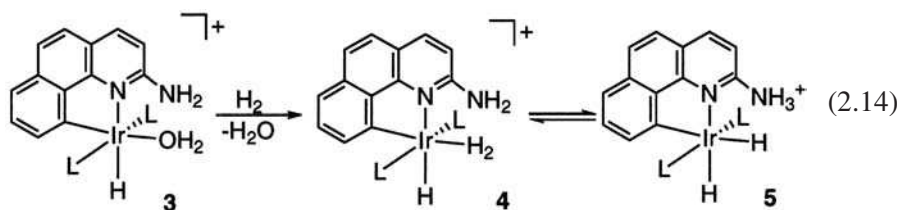
While electronic properties of the metal center have only small effects on T_1 (min) or $^1J(\text{H,D})$ for unstretched H_2 , it was found that stretched H_2 complexes are much more sensitive to the ligand environment. The T_1 (min) values for a series of $[\text{Re}(\text{H}_2)\text{H}_5\{\text{P}(p\text{-XC}_6\text{H}_4)_3\}_2]$ complexes vary with the electron donor/acceptor properties of X in a way that suggests that the strongest donor group, OMe, leads to a lengthening of $r(\text{H}\cdots\text{H})$ to 1.42 Å and the strongest acceptor group, CF_3 , causes a shortening to 1.24 Å [28b].

(a) *Reactivity of metal-bound dihydrogen*

A coordinated dihydrogen can be easily displaced to generate a two electron vacant site on the metal center, which allows a ligand such as the substrate for a catalytic reaction to bind. A wide range of lability of the H_2 is seen for a variety of complexes. Some cationic complexes bind hydrogen so strongly that for instance, $[\text{CpRu}(\text{dmpe})\text{H}_2]^+$ does not lose H_2 appreciably in the solid state in vacuo and is even stable in acetonitrile solution at ambient temperature [29]. In contrast some H_2 complexes are so labile that a substantial pressure of H_2 is required for their preparation. The Cr analogue of **1**, is so labile in solution that it can only be detected under 60 atm H_2 pressure. The activation energy for the elimination of hydrogen from $(\eta^2\text{-H}_2)\text{Cr}(\text{CO})_3[\text{P}(\text{C}_6\text{H}_{11})_3]_2$ was estimated to be 12.7 kcal/mol [30]. Since the H–H bonds in most H_2 complexes are not stretched, it is not surprising that the activation energy for loss of H_2 (more generally XH) is not usually large. Facile loss of XH can be important in applications to catalysis, for example, because the resulting coordinatively unsaturated intermediates may be very reactive. The complexes $[\text{MH}_4\text{L}_3]$ (M = Fe, Ru, Os; L = tertiary phosphine) all have the same stoichiometry, but the Fe and Ru complexes are very much more labile and more catalytically active for a variety of reactions, including alkane activation. The T_1 data suggested that the Fe and Ru complexes have H_2 ligands, while the Os complex is a classical hydride [31].

Heterolytic hydrogen activation of H_2 by a transition metal to give a proton and a hydride is one of the important chemical processes. It has been suggested that heterolytic H_2 activation is involved in the sequential proton–electron transfer steps in the catalytic cycles of some enzymes such as hydrogenase and nitrogenases [32]. Free H_2 is so weak an acid that it cannot readily be deprotonated even by very strong bases; $\text{p}K_{\text{a}} = 35$ in THF [33]. The acidity of H_2 is greatly enhanced by coordination to a metal, particularly an electrophilic cationic metal. Deprotonation of a dihydrogen complex by an external base has been demonstrated in several studies [34]. In $[\text{IrH}(\text{H}_2)(\text{bq})(\text{PPh}_3)_2]^+$ (bq = 7,8-benzoquinolinato), the H_2 ligand is kinetically deprotonated by alkyl lithium reagents in preference to the hydride ligand, although since they share the same conjugate base they must have the same $\text{p}K_{\text{a}}$ [35]. Crabtree and co-workers have compared the reactivity of $[\text{IrH}(\text{H}_2)(\text{bq})(\text{PPh}_3)_2]^+$ with a series of bq- NH_2 complexes, which have an appended NH_2 group at the 2-position of 7,8-benzoquinoline [36]. H_2 displaces water from complex **3** (L = PPh_3) to give **5**, a species in which the dihydrogen

has been split heterolytically, hydride remaining on the metal and a proton being abstracted by the pendant amino group (Eq. 2.14).



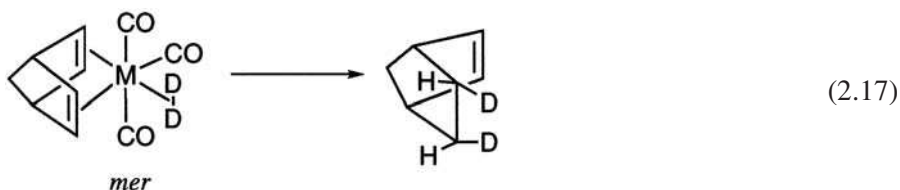
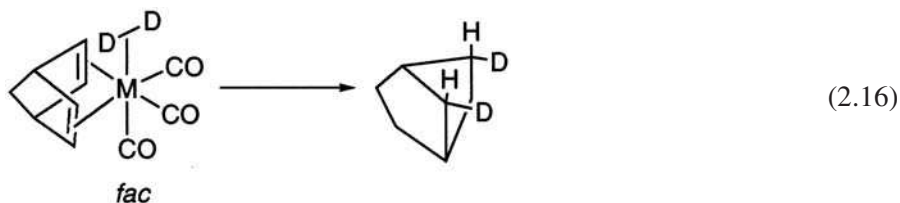
DFT calculations on a model system with $L = \text{PH}_3$ suggested that the dihydrogen complex, **4**, should be slightly more stable than **5**. This disagreement between theory and experiment suggested that tautomer **4** might be directly observable with a sufficiently electron-donor L . The authors wondered if more basic alkyl phosphines than PPh_3 would be useful and therefore moved to PBu_3^n , with the result that the dihydrogen complex (**4**, $L = \text{PBu}_3^n$) is now the stable form. Similar results were obtained with other basic phosphines, PET_2Ph and PMePh_2 . This implies that the basicity of the Ir–H bond is affected strongly by the nature of the phosphine, a result that was consistent with DFT calculation using the series PH_3 , PFH_2 , PHF_2 , and PF_3 . Other factors than electronic may also play a role, however. The acidities of ligands like H_2O that are bound via a lone pair are slightly affected by small differences in the ligand set. In contrast, the acidity of σ -complexes like $\text{M}(\text{H}_2)$ are very sensitive to the ligand environment.

Chinn and Heinekey [37] also demonstrated that the bound H_2 in $[\text{CpRu}(\text{dmpe})(\text{H}_2)]^+$ can be deprotonated by the mild base triethylamine in acetonitrile. The observed $\text{p}K_a$ is 17.6 (acetonitrile). In this system, the dihydrogen complex is present in equilibrium with the dihydride complex, but the thermodynamically less acidic dihydrogen is found by spin saturation transfer experiments to be deprotonated more rapidly than the dihydride. Therefore, the kinetic product of the reverse reaction, protonation of the neutral hydride, must be a dihydrogen complex by microscopic reversibility, which is consistent with experimental results. Morris investigated the effect of the R group on the $\text{p}K_a$ values for a series of ruthenium complexes of the type $[\text{CpRu}(\text{R}_2\text{PCH}_2\text{CH}_2\text{PR}_2)_2(\text{H}_2)]^+$ in THF and reported the expected correlation of the $\text{p}K_a$ of these H_2 complexes with the basicities of the ligands. For instance, the change from $\text{R} = p\text{-C}_6\text{H}_4\text{CF}_3$ to $\text{R} = \text{Me}$ causes the $\text{p}K_a$ to increase from 4.5 to 10 [38].

Several dihydrogen complexes of Ru and Ir appeared to have catalytic activity in D_2/H^+ exchange. Collman and co-workers [39] have observed that deprotonation of bound H_2 in $[\text{Ru}(\text{H}_2)(\text{oep})(\text{thf})]$ was a key step in catalytic isotope exchange between water and hydrogen. In $[\text{IrH}(\text{H}_2)(\text{bq})(\text{PPh}_3)_2]^+$, M-D_2 appears to exchange with the cis M-H and binding of ROH is followed by exchange with the cis M-D (Eq. 2.15) [40].



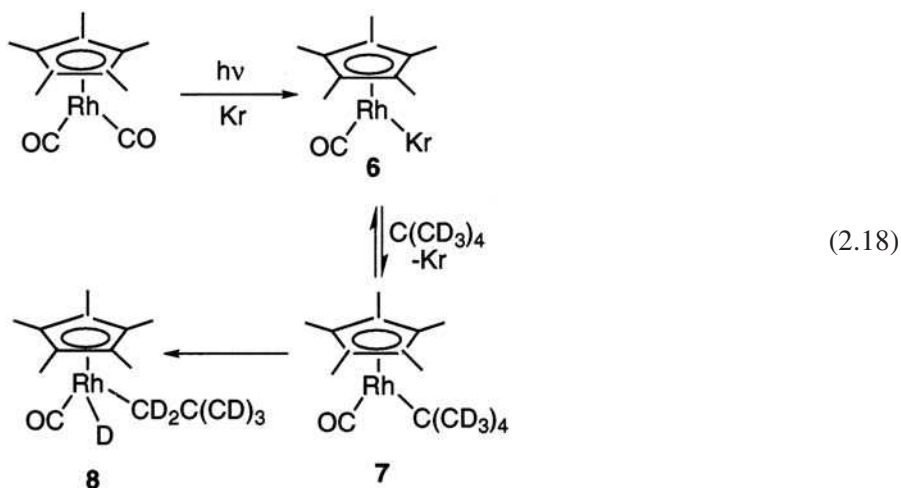
Bianchini and his co-workers [41] have demonstrated H_2 transfer to an alkene such as dimethyl maleate with $[Rh(P(CH_2CH_2PPh_2)_3)H_2]$. Jackson et al. [42] have reported that *fac*-(nbd) $M(CO)_3(H_2)$ ($M = Cr, Mo, \text{ or } W$, nbd = norbornadiene), which is generated by photolysis of (nbd) $M(CO)_4$ in liquid Xe in the presence of H_2/D_2 , undergoes hydrogenation of NBD to yield *endo* deuterated nortricyclene upon warming (Eq. 2.16). On the other hand, H_2/D_2 transfer to the diene in *mer*-(nbd) $M(CO)_3(H_2)$ leads to formation of the *endo* deuterated norbornene (Eq. 2.17). This observed stereospecificity of the catalytic hydrogenation is consistent with the intramolecular transfer of H_2 to the bound NBD.



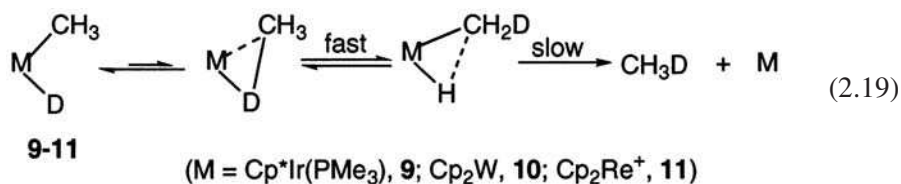
2.3.2 Alkane complexes and agostic C–H–M complexes

In contrast to H_2 complexes that are commonly isolable, complexes of methane or other alkanes are rare and remain an important object of organometallic chemistry [43]. The reason that the C–H bond is more weakly bound than H_2 is perhaps because the C–H bond is slightly less basic and much more hindered than the H–H bond in dihydrogen ligands. However, the presence of a C–H σ bond has been experimentally observed in a number of transition complexes in matrix-isolated, solution, or gas phases. Perutz [44] generated an alkane complex from the photochemical reaction of $M(CO)_6$ ($M = Cr, Mo, W$) using low temperature matrices such as an alkane or alkane/rare gas. Although no C–H activation was observed in these complexes, an estimation of the M–alkane bond of 10 kcal/mol suggested the viability of alkane C–H bond as σ donor. Bergman and Moore [45] have explored the photochemistry of $[Cp^*Rh(CO)_2]$ with perdeuterated neopentane ($C(CD_3)_4$) in liquefied krypton solution by using low-temperature time resolved infrared spectroscopy. Photolysis of $Cp^*Rh(CO)_2$ yields $[Cp^*Rh(CO)(Kr)]$ complex **6** initially which then reacts rapidly with perdeuterated neopentane to give a transient alkane complex $[Cp^*Rh(CO)(C(CD_3)_4)]$ **7** (Eq. 2.18). The alkane complex then proceeds to form a C–H activation product $[Cp^*Rh(CO)(D)(CD_2C(CD_3)_3)]$ **8**. Both complexes **6**

and **7** could be resolved spectroscopically by the difference in their ν_{CO} stretching bands.



Other alkanes such as cyclohexane were also found to form σ complexes in earlier studies by the same research group [45a,b]. Recently, George et al. [46] have characterized an *n*-alkane complex, $\text{CpRe}(\text{CO})_2(n\text{-heptane})$, which was said to be the least reactive of all the reported organometallic alkane complexes yet seen. The existence of transient σ alkane complexes has been confirmed indirectly by observation of hydrogen exchange between the hydride and the alkyl ligands in alkyl hydride complexes. Bergman et al. [47], Norton et al. [48], and Gould and Heinekey [49] all reported on complexes (**9–11**) in which intramolecular deuterium scrambling between $\alpha\text{-C-H}$ and M-H occurs faster than reductive elimination of alkane. Complexes **9** and **11** show an inverse kinetic isotope effect ($k_{\text{H}}/k_{\text{D}} = 0.5$ (**9**), 0.8 (**11**)) for reductive elimination, which is also consistent with a fast pre-equilibrium involving an alkane σ complex before the rate determining loss of alkane (Eq. 2.19). The alkane complex is sufficiently long lived so the metal atom can coordinate interchangeably to different C–H bonds and reversibly undergo oxidative addition.



Related studies by Jones et al. [50] with $[\text{Tp}'\text{Rh}(\text{CNCH}_2\text{CMe}_3)(\text{CH}_3)\text{D}]$ ($\text{Tp}' = \text{tris-3,5-dimethylpyrazolylborate}$) and $[\text{Tp}'\text{Rh}(\text{CNCH}_2\text{CMe}_3)(\text{CD}_3)\text{H}]$ provided both kinetic and equilibrium data for the isomerization. Gross and Girolami [51] have also described the hydrogen exchange between the hydride and CH_3 in $[(\text{C}_5\text{Me}_5)\text{Os}(\text{dmpm})(\text{CH}_3)\text{H}]^+$. This complex undergoes the exchange at a rate

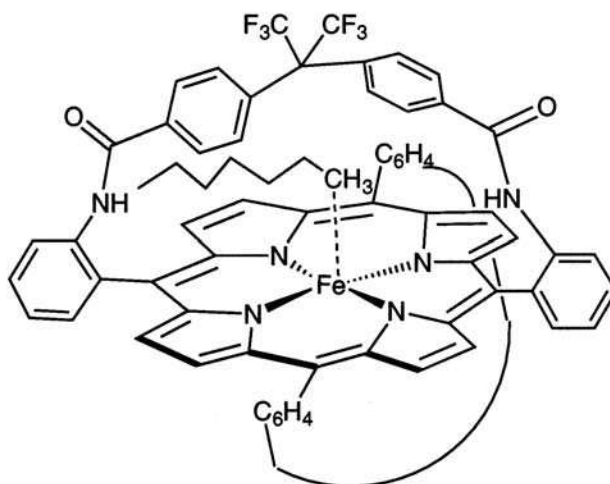
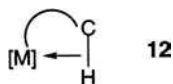


Fig. 2.2. Structure of an A-frame porphyrin–heptane complex.

high enough to be dynamic on the NMR time scale and the results indicate reversible alkane complex formation from the methyl/hydride complex at a rate of over 100 s^{-1} at 100°C . In 1997, Evans et al. [52] reported the first X-ray structure showing an interaction between a transition metal and an alkane. In this structure, a disordered *n*-heptane is located in a hydrophobic binding cavity created by an A-frame porphyrin (Fig. 2.2). The iron atom lies $0.26 \text{ \AA}$ out of the porphyrin plane because of the heptane coordination and the Fe–C distances of 2.5 and $2.8 \text{ \AA}$ are in the range typically observed in moderate or weak C–H agostic interactions.

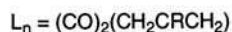
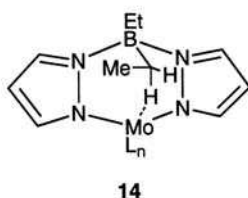
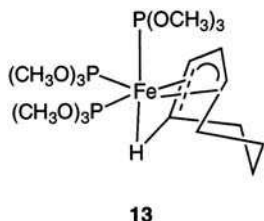
(a) Agostic C–H complexes

Some C–H bonds of transition metal ligands are found to have an agostic interaction of type **12**, where a C–H bond is oriented in a manner to intramolecularly bind to the metal.

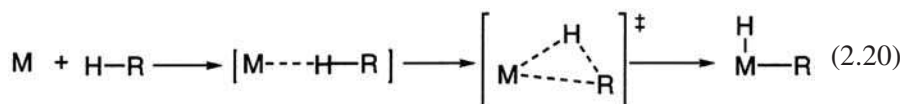


Trofimenko [53] was the first to observe unusual high field signals for ethyl hydrogens in the ^1H NMR spectrum of $\text{Ni}[\text{Et}_2\text{B}(\text{pz})_2]_2$ ($\text{pz} = 1\text{-pyrazolyl}$). Later a C–H–M interaction in the Mo analogue of $\text{Ni}[\text{Et}_2\text{B}(\text{pz})_2]_2$ was proposed based on the high field ^1H NMR signal and reduced C–H IR stretching frequencies [54]. Subsequently Cotton et al. [55] confirmed a short CH–Mo distance of $2.2 \text{ \AA}$ in the Mo complex from X-ray crystallographic analysis and proposed the current three-center/two-electron ($3\text{c-}2\text{e}$) bonding model. More direct evidence

of the agostic C–H–M interaction came from neutron diffraction studies with $[\text{Fe}(\text{P}(\text{OCH}_3)_3)(\eta^3\text{-C}_8\text{H}_{13})]^+$ **13** where a very short Fe–H distance of 1.87 Å and a stretched aliphatic C–H bond of 1.16 Å were found [56]. The term ‘agostic,’ introduced by Brookhart and Green and their influential 1983 review, has since become widely used [57]. Neutron diffraction studies show that the C–H bond is not greatly elongated (bound, 1.13–1.19 Å; unbound, 1.1 Å) by the interaction. In early work on complexes with weak agostic interactions, it was not clear whether the C–H bond just happened to be close to the metal atom or whether there was a genuine attraction. Complex **14** was the first to show a very short metal–HC separation and therefore an unambiguously attractive interaction.



A previous comparison of a series of structures of complexes containing the C–H–M group helped elucidate the kinetic pathway for the approach of a C–H bond to a metal center by Bürgi and Dunitz’s method [58]. It was found that the C–H bond approaches the metal atom with an M–H–C angle of 130°, and the C–H bond then turns, bringing the carbon atom close to the metal center, preparing the bond for oxidative addition (Eq. 2.20) [59].

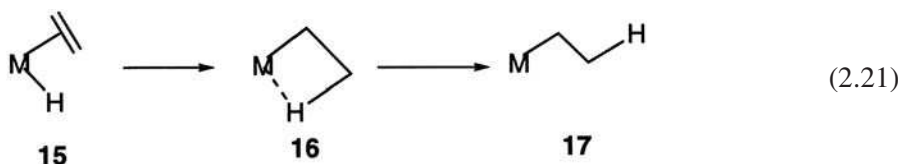


A kinetic pathway for $[\text{IrH}(\text{PH}_3)_2] + \text{H}_3\text{C}-\text{H}$ based on theoretical work by Cundari [60] closely resembles the experimental results, at least up to the transition state, after which no experimental data could be collected.

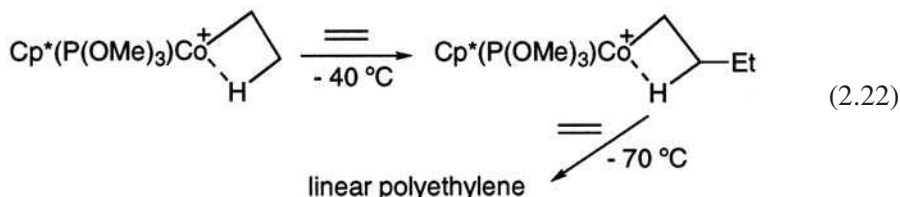
The existence of agostic C–H–M interaction can be deduced from several physical parameters. ^1H NMR chemical shifts of C–H protons involving an agostic bond are normally upfield of TMS ($\delta = -5$ to -15 ppm), and in this respect resemble complexes containing terminal hydrides. The 3c–2e interaction in an agostic complex is also revealed in reduced $J(^{13}\text{C},\text{H})$ coupling constants. In free C–H ligand, these are generally around 125 Hz, and in the C–H–M bridges $J(^{13}\text{C},\text{H})$ values are generally found in the range 60 to 120 Hz. Unfortunately, interpretation of the NMR spectrum is often complicated by dynamic processes. For example, an agostic CH_3 group will normally rotate so rapidly that each proton is in the bridging site for one-third of the time. From the value of the resulting averaged $J(^{13}\text{C},\text{H})$ coupling constant an agostic methyl group cannot be securely distinguished from an unbound methyl group; the upfield shift of the

agostic CH_3 group is also reduced by two-thirds. The isotopic perturbation of resonance (IPR) technique can be a powerful tool in such a case [61]. The IPR experiment involves taking the ^1H NMR spectrum of a mixture of isotopomers of the partially deuterated methyl, i.e., CD_2H and CH_2D . The difference in the zero-point energies of the two C-H(D) bonds leads to favoring the lighter H atoms being in the bridging site in the isotopomers. This is because the H/D zero-point energy difference is greater for the terminal C(H,D) than for the weaker bridging C(H,D) bond and so there is an energy advantage for a H to be in the bridging site. If bridging and terminal ligands have a significant chemical shift difference, as is usually the case, the averaged resonance for the isotopomers will show temperature-dependent and separate signals displaced from the CH_3 signal. In addition to NMR data, IR spectroscopy has also been used as diagnostic for agostic interactions, although the stretching frequencies of agostic C-H-M bonds have been reported for relatively few complexes. The ν_{CH} values of those agostic complexes are found at lower frequencies ($2700\text{--}2300\text{ cm}^{-1}$) than for free sp^3 C-H bonds.

Formation of a β -agostic intermediate has been implicated for hydride-olefin insertion (Eq. 2.21) [62].

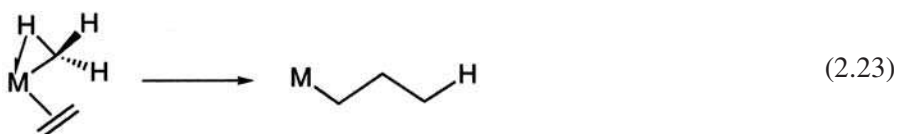


Sometimes the agostic complex can even be the most stable state, as in the case of $[\text{Cp}^*\text{Co}(\text{C}_2\text{H}_4)(\text{CH}_2\text{CH}_2\text{-H})]^+$ [63]. It seems that the agostic structure **16** is favorable over the ethylene-hydride structure **15** if the metal center is electrophilic. Many stable agostic compounds are either cationic, or have π -acid ligands, or have early transition metals in high oxidation states [57]. Brookhart and co-workers [64] studied $[\text{Cp}^*\text{Co}\{\text{P}(\text{OMe})_3\}(\text{CH}_2\text{CH}_2\text{-H})]^+$ that, for a later transition metal, had unusual catalytic reactivity for alkene insertion into a metal-alkyl bond (Eq. 2.22), a rare reaction at that time. They proposed that complexes having an agostic ground state have a lower energy barrier for such an insertion compared to those with an alkene-hydride ground state.

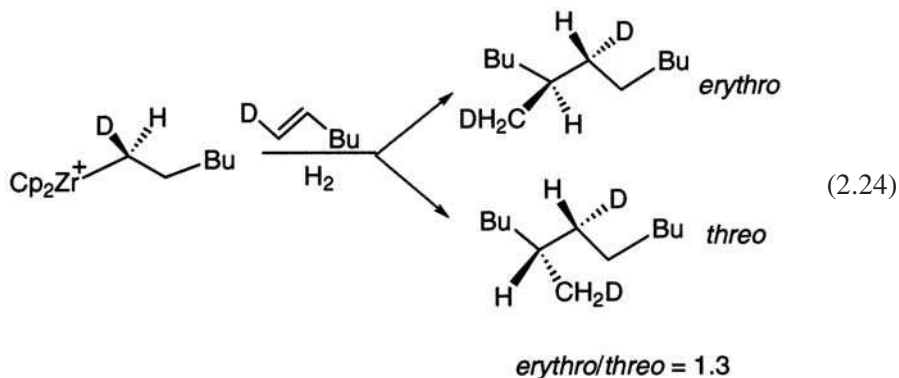


There are also many reports of α -agostic C-H-M interactions that are of particular interest since they are thought to play an important role in olefin

polymerization by Ziegler–Natta catalysts [57,65]. Such binding might lower the activation barrier to olefin insertion and control the stereospecificity of the olefin insertion [66]. The first α -agostic interaction to be fully characterized crystallographically was the titanium complex $[\text{Ti}(\eta^2\text{-Me})\text{Cl}_3(\text{dmpe})]$ [67]. The neutron diffraction structure has shown that the methyl group is tilted toward the titanium metal such that one of the hydrogens approaches the metal giving a $\text{C-H}_\alpha\text{-Ti}$ angle of 93.5° . The structure of $[\text{TiMeCl}_3]$ showed an interesting symmetrical distortion of the methyl group, having the Ti-C-H angle of 101° rather than the 109.5° of the normal sp^3 atom [68]. This flattening is thought to be due to donation of C-H bonding electrons to the empty d orbitals of Ti. The presence of α -agostic C-H-M interactions in some catalytic systems was probed through elegant isotopic labeling studies, developed by Grubbs, Brintzinger, and Bercaw [69]. Where olefin insertion proceeds with α -agostic assistance, the agostic binding may serve to rotate the methyl group towards the alkene and so prepare it for insertion (Eq. 2.23)

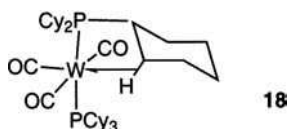


In the isotope experiment, the stereochemistry of the insertion is different, depending on whether $\alpha\text{-H}$ or $\alpha\text{-D}$ agostic interaction is involved. If an isotope effect is found, agostic transition states are indicated. For example, Krauledat and Brintzinger [69a,b] have shown that in hydrodimerization of deuterated 1-hexene with methylaluminumoxane (MAO)-activated zirconocene dichloride (Cp_2ZrCl_2) the product distribution is consistent with an α -agostic assisted insertion (Eq. 2.24).

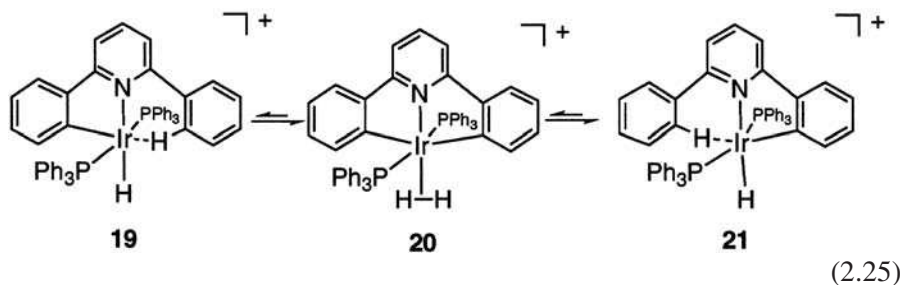


Agostic C-H-M interactions are often present between a metal and a C-H bond located in a relatively remote position on the ligand from the point of the attachment of the ligand to the metal. Kubas et al. [70] characterized agostic

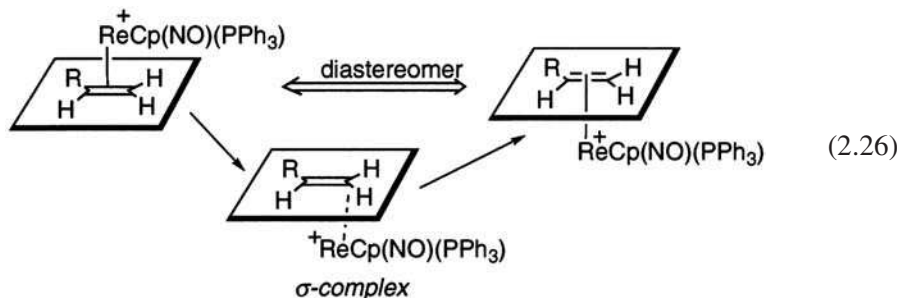
interactions in $[\text{W}(\text{CO})_3(\text{PCy}_3)_2]$ **18**, which is also capable of binding H_2 as a σ complex.



The crystal structure of the 2,6-diphenyl pyridine complex **19** shows a σ interaction between the C–H bond and the coordination site trans to Ir–C (Eq. 2.25) [71]. Rapid conversion between C–Ir/H–C **19** and C–H/Ir–C **21** is observed, a reaction that involves oxidative addition of the agostic C–H bond and reductive elimination of the aryl hydride. This is a rare example of reversible metalation of an agostic group under mild conditions. The tautomeric equilibration was suggested to go via the doubly metalated species **20** having a non-classical hydride but an Ir(V) dihydride could not be excluded.

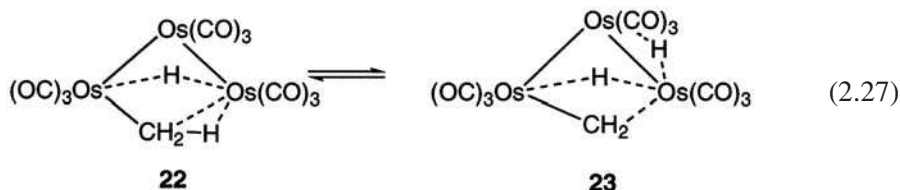


Peng and Gladysz [72] reported an unusual interconversion of diastereomers in $[\text{CpRe}(\text{NO})(\text{PPh}_3)(\text{H}_2\text{C}=\text{CHR})]$ system in which the Re moves from one enantioface to the other. Since the isomerization occurs without ligand dissociation and also without stereochemical or isotope scrambling of alkene, an agostic C–H–Re interaction was invoked as the most likely intermediate (Eq. 2.26).



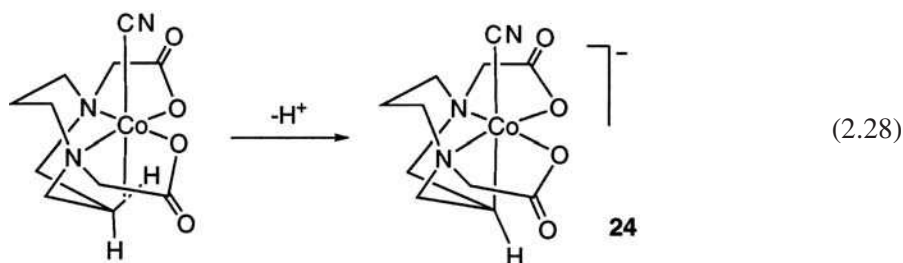
Calvert and Shapley [73] identified the first agostic interaction in a polynuclear system, in which an isomeric equilibrium was observed between an agostic complex **22** and its hydrido-methylene tautomer **23** (Eq. 2.27). It had been shown by neutron diffraction that only one isomer (**22**) exists in the solid state. This paper

also introduced the powerful IPR method (see above) into inorganic chemistry for the first time.



Weak C–H–M attractions were identified by Albinati et al. in a number of late transition metal complexes [74,75]. The H–M distances are in the range 2.3–2.5 Å. In the ^1H NMR spectra of these complexes the resonances are not shifted upfield and the $^1J(^{13}\text{C},\text{H})$ values are not reduced as in complexes with normal agostic interactions. Since the square-planar coordination geometry of the d^8 metal is almost undistorted by the approach of the C–H bond perpendicular to this plane, these complexes must represent a very early stage of C–H–M bridge formation.

Since the metal centers in the agostic C–H–M system are essentially electrophilic, the C–H bond becomes more acidic. A wide range of pK_a values are observed and in some cases strong bases are necessary to deprotonate the C–H bonds. A unique Co(III)–alkyl complex **24** was prepared by facile deprotonation of an agostic bond by methoxide ion (Eq. 2.28) [76].



Reactivity and selectivity for metal bound alkane is further discussed in the later section.

2.3.3 Si–H–M complexes

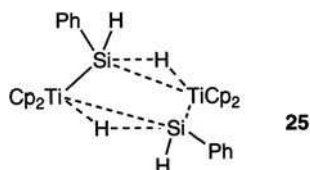
Since the first recognized Si–H σ complexes were reported by Jetz and Graham [77] for the product from the reaction of $\text{Re}_2(\text{CO})_{10}$ with R_2SiH_2 ($\text{R} = \text{Me}, \text{Ph}$), many examples have been found. Schubert [78] and Crabtree [79] reviewed earlier work on η^2 -coordinated H–Si bonds and recently Corey and Braddock-Wilking [80] have reviewed transition metal chemistry of hydrosilation. By comparison with other σ complexes, the structures of silane complexes more closely resemble those of oxidative addition products rather than those of simple σ complexes with an unstretched X–H bond. This is maybe because the Si–H bond has a much greater basicity than other σ donor ligands like H–H and C–H and thus acts as a

better σ donor. In addition, the Si–H bond is weaker than H–H and C–H bonds, so the Si–H has lower energy σ^* orbitals, making it a better π acceptor. Both types of interactions elongate the Si–H bond. It is quite common to find Si–H–M complexes with Si–H bonds stretched to a distance of 1.8 Å, that is about 20% longer than the Si–H distance in a free silane. Schubert [78] considers that a Si–H distance of 2.0 Å is the limiting one indicating the presence of σ interaction. As another piece of evidence showing the Si–H–M agostic complex behaves rather like an oxidative addition product, the magnitude of $^1J(\text{Si}, \text{H})$ coupling constant is reduced far more than $J(\text{H}, \text{D})$ or $J(\text{H}, \text{C})$ for $\text{M}(\text{H}_2)$ or C–H–M complexes. For instance, while $^1J(\text{Si}, \text{H})$ coupling constants in free silanes are generally found between 150 and 200 Hz, $^1J(\text{Si}, \text{H})$ values in σ Si–H complexes usually fall in the range of 20 to 100 Hz. Although the coupling constant is dependent on the electronic properties of metal and ligands, $^1J(\text{Si}, \text{H})$ of 20 Hz or less suggests little Si–H σ interaction is retained in the complex.

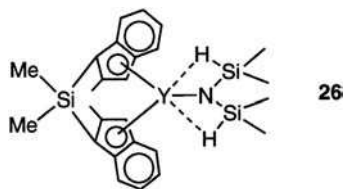
The σ interaction can readily be tuned by changing substituents at both the metal center and the silicon. Any build-up of negative charge on metal atom or positive charge on the Si atom due to ligand on the metal or substituents on Si leads to back-donation to the Si–H σ^* orbital being enhanced so that the extent of oxidative addition increases. The best measures of the extent of oxidative addition are physical parameters such as $^1J(\text{Si}, \text{H})$ coupling constants in the NMR spectrum, the Mn–Si bond distances, and $\Delta H^\ddagger$ for the reductive elimination of silane, as demonstrated in detailed studies of a series of $[\text{CpMn}(\text{CO})_2(\text{H–SiR}_3)]$ complexes differing by SiR_3 ($\text{SiR}_3 = \text{SiHET}_2, \text{SiPh}_3, \text{SiCl}_3$) [81]. As the R group of the SiR_3 becomes more electronegative, the magnitude of $\Delta H^\ddagger$ increases in the order of $\text{SiHET}_2 < \text{SiPh}_3 \ll \text{SiCl}_3$, the $^1J(\text{Si}, \text{H})$ coupling constant decreases, and the Mn–Si distance decreases. The data clearly demonstrate that electron-withdrawing groups on the silicon center lead to stronger binding to the metal and ultimately to Si–H cleavage. However, it was argued that there was no case where the Si–H bond in $\text{CpMnL}_2(\text{HSiR}_3)$ was fully broken and that the metal in the product was said to have the same formal oxidation as in the reactant. A similar tuning of σ interaction by varying substituents on a metal center was observed in the series of complexes of type $\text{Cp}(\text{CO})\text{LMn}(\text{H–SiR}_3)$ with different L ligands ($\text{L} = \text{CO}, \text{CN}(t\text{-Bu}), \text{P}(\text{OPh})_3, \text{P}(\text{p-ClC}_6\text{H}_4)_3, \text{PPh}_3, \text{P}(\text{p-MeC}_6\text{H}_4)_3, \text{PMe}_3$), while the silane group is kept constant [81,82].

Careful analysis of the crystal structures of type of $\text{Cp}(\text{CO})_2\text{Mn}(\text{H–SiR}_3)$ complexes indicates that the Mn–Si distance becomes considerably longer as the oxidative addition proceeds while the Mn–H distance becomes a little longer and $r(\text{Si–H})$ remains about same [81]. Based on the structural analysis a reaction trajectory for oxidative addition of silane to a metal was proposed. The H atom of the Si–H unit approaches Mn, and the Si–H unit then pivots, increasing the Mn–Si interaction. This is similar to the trajectory for the interaction of an agostic C–H bond with a metal atom, as mentioned earlier in this chapter, and is consistent with theoretical work [83].

While the majority of η^2 -silane complexes characterized to date are mononuclear species, there are several dinuclear or polynuclear metal complexes with bridging M–H–Si interaction. A Si–H–M interaction was unambiguously identified in compound **25** by X-ray structure determination, showing the Si–H bond distance of 1.58 Å. This is 7% longer than in free silane and represents a rare case of unstretched silane σ complex [84]. The unique unstretched silane σ bond is further documented in the tetrahedral geometry around the silicon atom, which is largely retained, as opposed to the more distorted geometry at the Si atom in the extensively studied mononuclear Mn complexes.

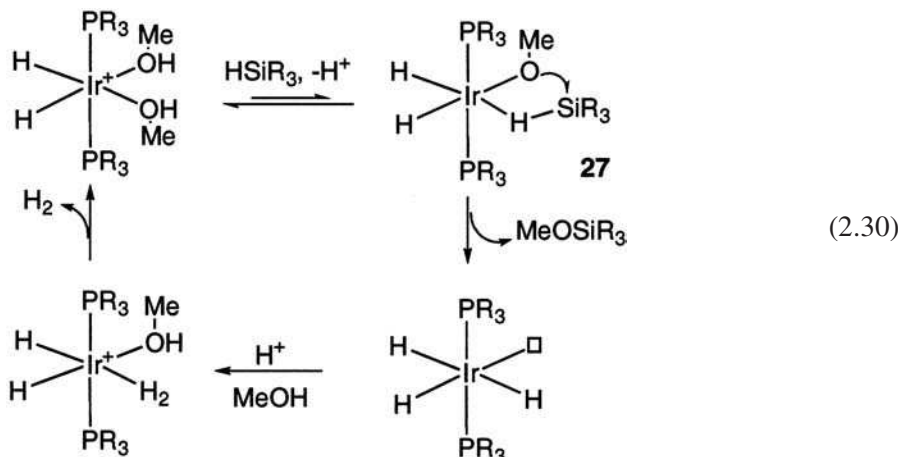


Recently, several complexes with an agostic Si–H–M have appeared in the literature [85]. The majority of them has at least one SiMe₂ bridging ligand. Yttrium complex **26** exhibits unusual multiple Si–H–M agostic interactions, which were characterized by X-ray structural determination and other spectroscopic methods [86]. The bond angle of the sp² type Si–N–Si bond in the bis(dimethylsilyl)amide fragment is found to be strongly opened to 153°, well above the Si–N–Si angles so far reported (121–133°); the Y–N–Si angle of 103° is also abnormally reduced. The geometric distortions of the ligands are attributable to the presence of two Si–H–Y agostic interactions. The Y–Si distances of 3.0 Å and the H–Y distance of 2.54 Å are in the range of those seen for σ interactions in related complexes. The presence of an unusual σ agostic interaction was very recently confirmed by DFT calculation on a Ln model complex, showing that the interaction is dominated by electrostatic effects and by electron donation from the Si–H bond to vacant d orbitals, not to f orbitals [87].



The importance of a Si–H–M interaction in reaction intermediates was demonstrated in the studies of silane alcoholysis by an Ir complex (Eq. 2.29) [88]. Kinetic and mechanistic studies of silane alcoholysis catalyzed by [IrH₂S₂(PPh₃)₂]SbF₆ (S = solvent) suggest that an unstretched silane **27** is an active intermediate. In this system the Ir(III) center carries a positive charge making the metal electrophilic. A Si–H bond coordinated to the electrophilic metal center would be activated without oxidative addition. The result is enhanced sensitivity to nucleophilic attack by

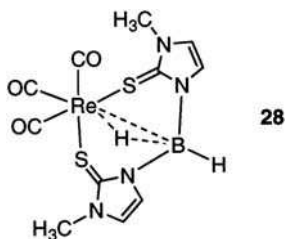
alcohol at the Si atom. Spectroscopic and mechanistic studies were consistent with the sequence shown in Eq. 2.30.



Si-H-M intermediates have also been assumed to be the immediate precursors to the four-center transition state proposed in σ bond metathesis reactions [89].

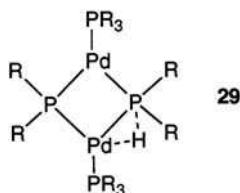
2.3.4 Other non-polar X-H-M complexes

B-H-M complexes have been known for a long time and M-H-BH₃⁻ σ complexes are particularly stable, as shown in [Ti(HBH₃)₂(H₂BH₂)(PMe₃)], [Cp₂Zr(H₂BH₂)₂], and [Hf(H₃BH)₄] [55,88]. Analogous AlH₄⁻ complexes are also known [90]. Garcia et al. [91] reported a rhenium complex **28** containing a strong B-H-M agostic interaction, which can be cleaved only by addition of excess amount of a base such as imidazole, triphenylphosphine and *tert*-butylisonitrile.



A distinctive Sn-H-M interaction has been characterized in several metal complexes such as [(η^5 -MeC₅H₄)(CO)₂Mn(H-SnPh₃)] [92], [η^6 -C₆H₄(OCH₃)₂Cr(CO)₂(HSnPh₃)] [93] and [η^6 -Mes)Cr(CO)₂(HSnPh₃)] [94]. In these complexes the ¹J(Sn, H) coupling constants are found in the range of 150–300 Hz, which is much lower than that found in tetrahedral alkyltin hydrides

(1500–2000 Hz). A σ complex **29** with an agostic P–H bond was reported by Albinati et al. [95] as the protonation product of the corresponding neutral bis(μ -phosphanide)dipalladium complex. The 2e–3c interaction was suggested on the basis of $J(\text{P,H})$ coupling constant of 151 Hz; in comparison the values for the terminal P–H bond are 322–324 Hz.

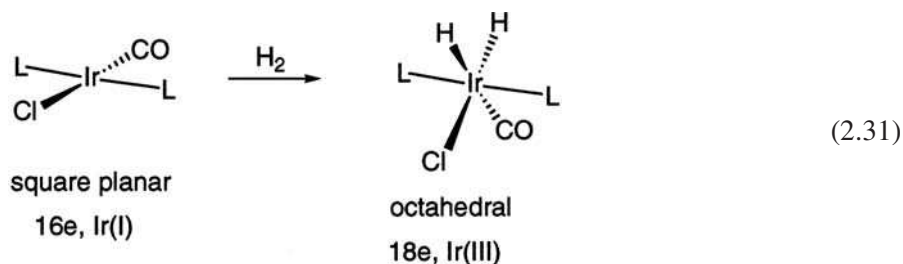


$[(\text{PhS})\text{Fe}(\text{CO})_3(\text{PET}_3)]^-$ is protonated at -80°C to give as the kinetic adduct a complex assigned as $[(\eta^2\text{-PhS-H})\text{Fe}(\text{CO})_3(\text{PET}_3)]$, a σ complex with an S–H bond [96].

2.4 NON-POLAR σ BOND ACTIVATION

2.4.1 Dihydrogen activation

The best studied oxidative addition is that of H_2 to the 16e square planar d^8 species, $\text{IrCl}(\text{CO})(\text{PPh}_3)_2$, known as Vaska's complex [97]. This gives an 18e d^6 octahedral Ir(III) dihydride complex (Eq. 2.31). In a concerted addition of this sort, two mutually trans ligands in the starting Ir(I) complex fold back with the result that the cis dihydride isomer is formed, at least initially. Subsequent rearrangement may also occur.

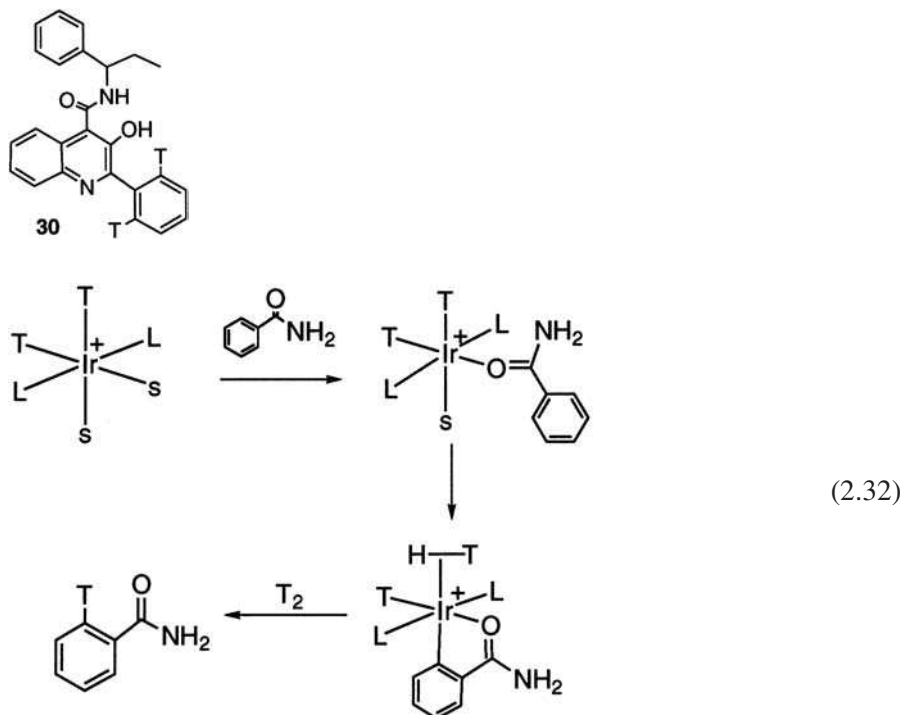


In Vaska's complex, either the pair of trans phosphines or the trans X/CO pair of ligands can fold back, depending on the situation [98]. Occasionally both isomers are formed. The LUMO in a d^8 square planar complex has $d_{x^2-y^2}$ character, and so tends to lie in the plane of the ligands. Folding back two of the mutually trans ligands directs an empty orbital in the direction of the incoming H_2 ligand. The transition state presumably resembles a stretched dihydrogen complex, i.e., an H_2 complex with an elongated H–H bond.

The reactions are usually second order and show negative entropies of activation (ca. -20 eu) consistent with an ordered transition state like σ -bonded H_2 complex. They are little affected by the polarity of the solvent, but may be accelerated to some extent by electron releasing phosphines.

(a) *Dihydrogen activation in catalysis*

Isotope exchange. The simplest reaction involving hydrogen activation is isotope exchange. This is relevant to the significant practical problem of tritium labeling of pharmaceuticals, normally used in radiotracer studies for subsequent determination of the fate of a given compound in chemical and biochemical systems. Incorporation of the isotope by exchange with gaseous T_2 is currently carried out with one of the following closely related homogeneous catalysts: $[IrH_2(Me_2CO)_2L_2]BF_4$, $[(cod)IrL_2]BF_4$, or $[Ir(cod)(PCy_3)(py)]BF_4$ (cod = 1,5-cyclooctadiene; L = PPh_3 ; Cy = cyclohexyl; py = pyridine.) [99]. An advantage of these catalysts is the selectivity of incorporation of the isotope, a feature that clearly arises from the selectivity of the cyclometalation step, and the tolerance of functional groups; an example is shown as **30** below. Incorporation of the radio-label in the final step in this way avoids the involvement of synthetic steps using radioactive materials. The mechanism (Eq. 2.32) proposed relies on cyclometalation giving CH activation of the substrate, followed by exchange with the hydrides on the metal, that are able to exchange with free H_2 (D_2 or T_2) in a subsequent step. Intermediates relevant to this cycle have been directly observed [59].



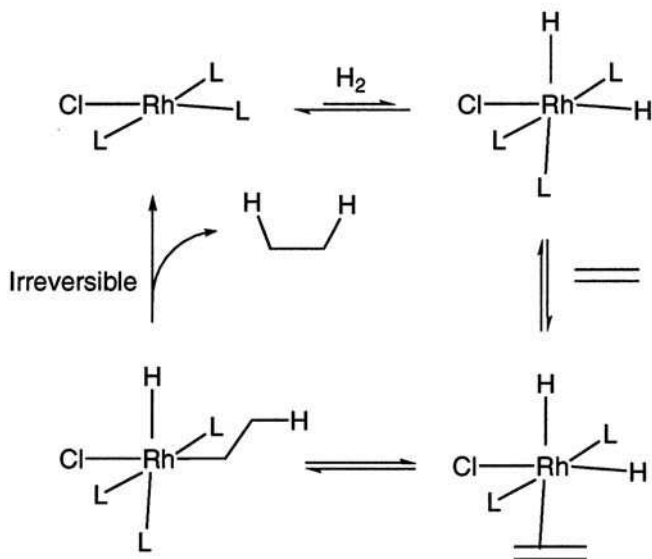


Fig. 2.3. A mechanism for the hydrogenation for alkenes by Wilkinson's catalyst. (Reproduced from ref. [4] with permission.)

Hydrogenation of unsaturated substrates. Hydrogenation of alkenes and alkynes is one of the most widely useful reactions involving dihydrogen activation. The mechanism of Wilkinson's complex offers a good example of the process (Fig. 2.3) [100]. The cycle shown is just one of several that operate in the real system, depending on the exact conditions. It serves to show a key point, that the activation step is the first step in the cycle. As in the Vaska case, the ligands fold back so that the *cis*-dihydride is formed. An early ^{31}P NMR experiment (Fig. 2.4) went far to establish the H_2 activation and subsequent steps in the pathway [100d]. At low temperature the H_2 adduct is stable but at room temperature, the phosphine that is *trans* to a hydride dissociates, as shown by the loss of coupling to this nucleus. There is no significant formation of free phosphine that would have appeared at the location indicated by the arrow. Sweeping the sample with N_2 removes the coordinated H_2 showing the reversibility of the oxidative addition in this case.

The corresponding Ir compound forms an H_2 adduct that is stable. Phosphine does not dissociate, thanks to the stronger M–L bonds in the third row, and so the Ir analogue of Wilkinson's catalyst is inactive. If we were to start with an Ir compound with only two phosphines it is evident that dissociation would no longer be needed. Schrock and Osborn [101] had shown that $[(\text{cod})\text{RhL}_2]\text{BF}_4$ is an effective hydrogenation catalyst via COD loss by hydrogenation to COA (COA = cyclooctane; L = a variety of phosphines), so it was logical to look at $[(\text{cod})\text{IrL}_2]\text{BF}_4$. This proved to be a highly active catalyst and the related

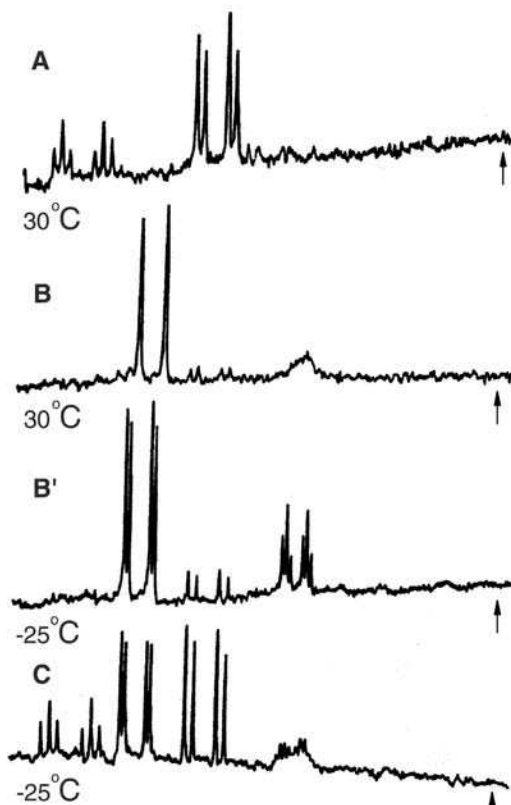


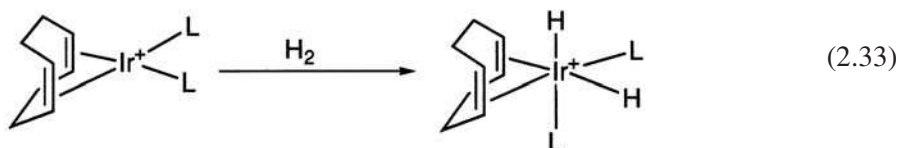
Fig. 2.4. Proton decoupled ^{31}P NMR data for $\text{RhCl}(\text{PPh}_3)_3$: (A) dissolved in CH_2Cl_2 ; (B) after addition of H_2 at 30°C ; (B') after addition of H_2 and cooling to -25°C ; (C) after sweeping solution B with nitrogen. The different P nuclei in the complex are seen, together with coupling to Rh (large) and couplings to other phosphines (small). In spectrum B, the loss of coupling to Rh and P for one of the two P resonances indicates that this ligand is reversibly dissociating. The most intense peaks are assigned to the pair of equivalent trans phosphines. Free PPh_3 (arrow) is absent. (Reproduced from ref. [4] with permission.)

$[(\text{cod})\text{Ir}(\text{py})(\text{PCy}_3)](\text{BF}_4)$ was even better, being highly active for hindered alkenes [102]. A non-coordinating solvent such as CH_2Cl_2 proved essential, however, to avoid solvent binding to the metal.

The relevance of the Ir system to the oxidative addition problem is that the H_2 adducts are much more stable in this system than for Rh. This is a common trend. Third row elements give oxidative addition most readily, followed by second and then first row transition metals. The reason seems to be the decrease in M–L bond strength across the series, favoring reductive elimination for the lighter elements.

Hydrogen addition to the $[(\text{cod})\text{IrL}_2]\text{BF}_4$ series occurs in time of mixing even at -80°C , so the kinetic barriers are very small for H_2 . Once again, the

cis-dihydride is formed (Eq. 2.33). This stereochemistry allows insertion and subsequent hydrogenation of the COD to occur easily.



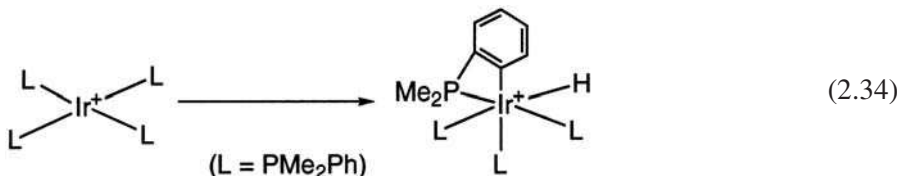
Binuclear oxidative addition can occur in suitable cases, the first example being Iguchi's $\text{Co}(\text{CN})_5^{3-}$ system [103]. Two $\text{Co}(\text{II})$ precursors cooperate to homolyze H_2 to give two moles of the $\text{Co}(\text{III})$ hydrides, $[\text{HCo}(\text{CN})_5]^{3-}$. This allows the system to hydrogenate activated olefins, such as acrylic acid.

Dihydrogen can cleave d^0 alkyls like WMe_6 to give methane and the overall pathway looks at first sight like an oxidative addition of H_2 followed by a reductive elimination of MeH [104]. Metals like $\text{W}(\text{VI})$ with a d^0 configuration cannot give oxidative addition, however, because they cannot be oxidized further: $\text{W}(\text{H})_2\text{Me}_6$ would be $\text{Mo}(\text{VIII})$. Dihydrogen binding in the form of an H_2 complex, as in $\text{W}(\text{H}_2)\text{Me}_6$, is still allowed, however, and proton transfer from the bound H_2 can give methane, so an alternative path is available. Such a path could also operate in non- d^0 systems where a high oxidation state or other mitigating factor disfavors oxidative addition.

2.4.2 Alkane C–H bond activation

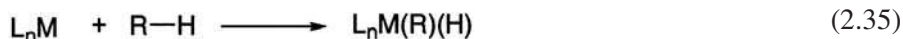
A topic that has attracted considerable attention in the last 20 years is alkane activation [105]. The activation product is of interest in itself and is the first subject of this section but the ultimate goal is functionalization of the alkane to give alcohol or alkene.

The earliest examples involved cyclometalation, where a CH bond, often of an arene, is held in the vicinity of the metal. Creation of a 2e vacancy at the metal often results in the formation of the cyclometalation product, a reaction that may be reversible or not. Eq. 2.34 shows a typical cyclometalation.

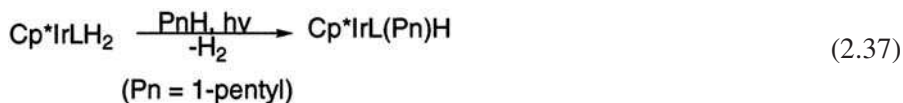
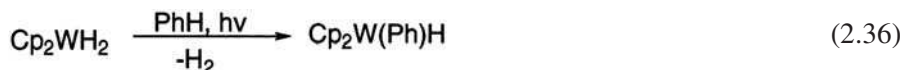


For the intermolecular activation of a C–H bond, a number of different situations can arise. Most often, the reaction of Eq. 2.35 is thermodynamically uphill. The oxidative addition of RH is in general less favorable than that of H_2 because of the rather weak $\text{M}–\text{R}$ bond formed from an alkane. In contrast, arenes are much easier to activate in this way, the $\text{M}–\text{Ar}$ bond being much stronger; this is true even

after accounting for the stronger Ar–H bond in the starting arene.



One way to encourage the oxidative addition for alkanes is to start from a highly unstable metal fragment. These can be formed by photoextrusion of H₂ from a starting dihydride, as in the examples shown in Eqs. 2.36 and 2.37. Cp₂WH₂ gives the unstable tungstenocene in this way but this is only capable of activating arenes, such as benzene (Eq. 2.36) [106]. In a key experiment, Bergman and co-workers [107] photoextruded H₂ from an Ir(III) dihydride to give oxidative addition of a wide range of alkanes. Once the alkyl hydride is in hand, thermal routes are possible; for example, heating the pentyl hydride in the presence of methane leads to reductive elimination of pentane (Eq. 2.38) and oxidative addition of methane.



The selectivities of such reactions are very different from those found for traditional electrophilic and radical pathways, both of which are highly selective for tertiary over secondary CH bonds, with primary bonds being unreactive. In oxidative addition, in contrast, both primary and secondary CH bonds react and tertiary CH bonds do not. Depending on the system, the selectivity may favor primary or secondary bonds, depending on the intrinsic reactivity and steric encumbrance of the system.

Among catalytic alkane conversions, the most important is the Shilov system and its descendants [108]. Discovered around 1970, these involve Pt(II) salts in aqueous solvents. Initially, the reaction studied was H/D exchange with D₂O, where polydeuteration of alkanes was seen. The selectivity for attack at the terminal methyl groups of long chain alkanes made it clear that one was not dealing with classical electrophilic chemistry. The intervention of colloidal Pt was also excluded.

A later variant involved incorporation of an oxidant, Pt(IV), which led to formation of functionalized species, RX, from alkane, RH. In the typical chloride-rich Shilov systems, X is commonly Cl and OH. The Pt(IV) oxidant is reduced to Pt(II) during the reaction, but it has proved hard to replace this expensive oxidant by a cheaper one while retaining activity. A remarkable system of this type discovered by Periana [109] uses conc. H₂SO₄ as both oxidant and solvent and a Pt(II) 2,2'-bipyrimidine complex as catalyst with the result that CH₃OSO₃H, a methanol derivative, is formed from methane.

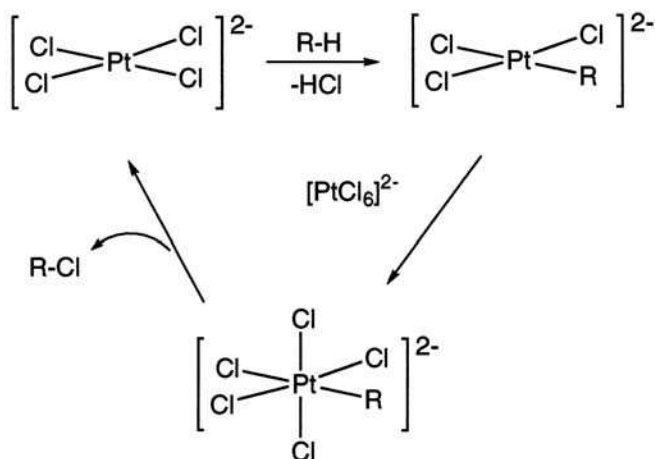


Fig. 2.5. C–H bond activation mechanism by Pt(II) complex proposed by Shilov.

Stahl et al. [110] have gone furthest in elucidating the mechanism of these reactions (Fig. 2.5). Starting with $[\text{PtCl}_4]^{2-}$, reaction with RH leads to the formation of a Pt(II) alkyl and HCl. It is not yet clear exactly how this step takes place. Certainly one possibility is oxidative addition of RH followed by reductive elimination of HCl. Loss of Cl^- , binding of an alkane as a σ complex in analogy with H_2 binding in Kubas' complex, and loss of a proton from the bound alkane is a plausible alternative. Oxidation by Pt(IV), an electron transfer, not an alkyl transfer, leads to the Pt(IV) alkyl. Since $[\text{PtCl}_4]^{2-}$ is such a good leaving group, nucleophilic attack at the alkyl by Cl^- , H_2O or HSO_3^- , depending on the exact conditions, gives the RX product (Fig. 2.5).

The other main catalytic alkane functionalization reaction is alkane dehydrogenation to give alkene. This is a reverse hydrogenation, so is normally thermodynamically uphill. There are three main methods to get round this problem. In the first, a sacrificial hydrogen acceptor is added, commonly *tert*-BuCH=CH₂ (TBE). Cyclooctane conversion to cyclooctene (COE) is a convenient system for study [111]. The TBE has an unusually high heat of hydrogenation and COE has an unusually low one, so the driving force of the overall reaction is significant. The second strategy is to drive the system with light [112]. Finally, the H_2 can be expelled from the system in a reflux apparatus (acceptor free conditions), which also provides a suitable driving force [113].

One complex, $[\text{IrH}_2(\text{PPh}_3)_2(\text{tfa})]$ ($\text{tfa} = \text{CF}_3\text{COO}^-$), carries out all three reactions [114]. This has been studied mechanistically with the result that the pathway of Fig. 2.6 seems most likely.

One limitation of this catalyst is degradation via P–C bond cleavage. When $(p\text{-FC}_6\text{H}_4)_3\text{P}$ was used as phosphine, PhF formation was found to be associated with catalyst deactivation. An important step forward was therefore a move to

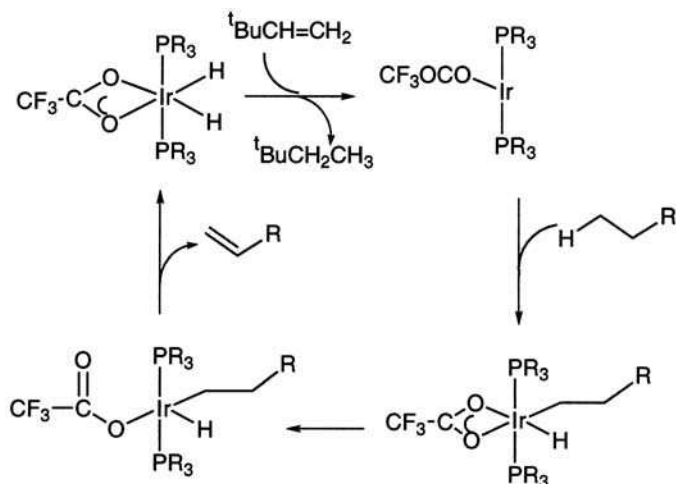


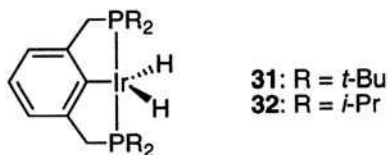
Fig. 2.6. The catalytic cycle proposed for the dehydrogenation of alkane RCH_2CH_3 to give the alkene $RCH=CH_2$ by an iridium complex.

PMe_3 , a ligand with a far lower tendency to undergo P–C bond cleavage. Using this strategy, $RhCl(PMe_3)_2(CO)$, was found to be an excellent catalyst capable of executing thousands of turnovers. Maguire et al. [115] reported photocatalyzed dehydrogenation of alkanes using $RhCl(PMe_3)_2(CO)$ with unprecedented efficiency; quantum yield up to 0.10 and turnover number as high as 5000. This reaction proceeds without sacrificial hydrogen acceptors. It was shown that the photolysis of $RhCl(PMe_3)_2(CO)$ results in loss of CO, which is considered as the sole driving force needed for this thermodynamically unfavorable reaction. In related studies the Goldman group developed the first efficient thermochemical alkane dehydrogenation system using sacrificial hydrogen acceptors and $RhCl(PMe_3)_2(CO)$ as catalysts under high pressure H_2 atmosphere [116]. At $100^\circ C$ under 1000 psi H_2 pressure, cyclooctane is rapidly dehydrogenated to yield cyclooctene (900 turnover) accompanied by H_2 transfer to norbornene, a sacrificial H_2 acceptor. A mechanism that involves addition of H_2 , loss of CO, transfer of H_2 to a sacrificial acceptor, and then generation of catalytically active $Rh(CO)_2Cl$ species was proposed to explain the counter-intuitive role of dihydrogen gas.

The first example of thermochemical catalytic system for acceptorless alkane dehydrogenation was reported by Fujii and Saito [117]. Their approach was to purge the reactor continuously with an inert gas in order to prevent the reversible hydrogenation of alkenes by the evolving H_2 . Unfortunately, these thermochemical catalytic systems are limited by low catalytic activities and catalyst instability.

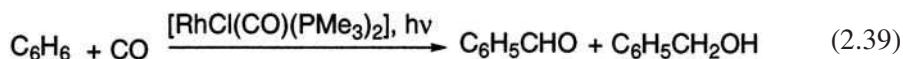
Pincer (mer, tridentate) phosphines have proved resistant to degradation and useful in alkane dehydrogenation catalysis. Recently, Xu et al. [118] found that a dihydrido Ir complex containing a tridentate monoanionic aryl bis(phosphino) (PCP) pincer, **31** ($R = \text{tert-butyl}$), is highly active catalyst for dehydrogenation

of cyclooctane to cyclooctene, the catalyst having long term stability at the high temperatures needed. More recently, an even higher catalytic reactivity of up to 1000 turnovers/h was observed by employing the PCP analog **32** [119]. Possibly the reaction intermediates in the dehydrogenation cycle, such as alkyl hydrides, are sterically disfavored by the bulky *tert*-butyl groups, facilitating turnover.



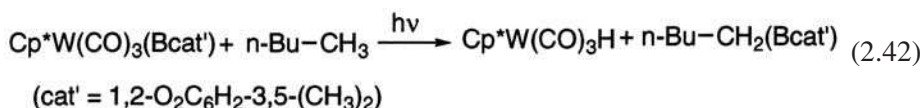
The two main types of catalytic alkane functionalization reaction known for late transition metals, Shilov chemistry and alkane dehydrogenation, have now been discussed. Both involve alkyl-metal intermediates, R–M, formed from an alkane, R–H, yet paradoxically, the alkyls behave quite differently in the two cases. In Shilov chemistry, the R–M intermediate selectively undergoes an S_N2 attack by X[–] (Cl[–] or OH[–]) to give R–X as the final product (a step sometimes called ‘reductive elimination’). In alkane dehydrogenation, the alkyl group β-eliminates to give alkene as the final product. The difference in behavior seems to lie in the much better ability of Pt(II) to act as a leaving group [120]. This facilitates both loss of H⁺ from the methane oxidative addition product [Pt(Me)(H)Cl₃][–] and nucleophilic attack of X[–] on [(Me)PtCl₄][–] in the product-forming step.

Alkane carbonylation has also proved possible with RhCl(PMe₃)₂(CO), an endothermic process driven by light absorption (Eq. 2.39) [121].

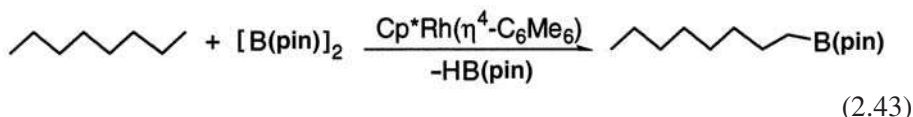


In the case of *n*-decane (Eq. 2.40), there was high selectivity for terminal attack (1, 86%; 2, 5%; 3, 4%; 4, 2%; 5, 3%) [122]. The reaction is thought to involve the 14e [RhCl(PMe₃)₂] fragment formed by photoextrusion of CO. Isonitriles can also insert in the same way to give imines as the final product.

Very recently, a promising new reaction has been discovered, alkane borylation, illustrated by Eq. 2.41 [123]. This can be driven by light, or, being exothermic, it can be carried out as a thermal process. Photoextrusion of CO from the tungsten carbonyl precursor is believed to be followed by oxidative addition of the alkane CH bond, followed by reductive elimination of the R–BR₂ product (Eq. 2.42) [123a].

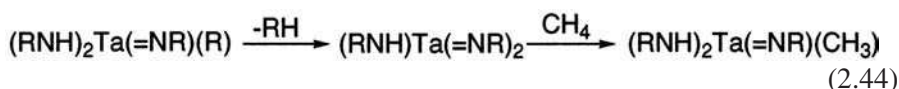


Important work by Chen et al. [123b] has shown how borylation of alkanes can be achieved both photochemically and thermally from diboron reagents to give alkylboranes (Eq. 2.43). The best catalysts, $[\text{CpRh}(\text{ethylene})_2]$ and $[\text{Cp}^*\text{Rh}(\eta^4\text{-C}_6\text{Me}_6)]$, are active at 150°C . The B–B bond oxidatively adds to the metal probably followed by CH oxidative addition. Reductive elimination gives rise to a new B–C bond being formed. Functionalization occurs at the terminal position of a linear alkane as in the alkane chemistry described above. Since C–B bonds are in principle precursors to a wide variety of functional groups, this reaction has great promise for future development.

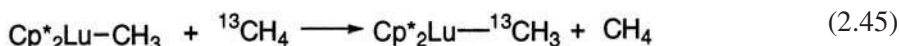


Methane and ethane have attracted special attention because of the potential importance of natural gas liquefaction. Conversion of methane to a transportable liquid such as methanol would make many remote gas sources economically viable. Sen [124] has reported a number of unusual reactions of methane, such as the conversion of methane, CO and oxygen to acetic acid with RhCl_3 as catalyst and of methane, trifluoroacetic anhydride and H_2O_2 to the methyl esters with $\text{Pd}(\text{II})$ as catalyst.

Alkane activation by addition across a $\text{M}=\text{N}$ multiple bond has been shown in some cases. For example, Schaller et al. [125] finds that methane can add across a Ta imide (Eq. 2.44).

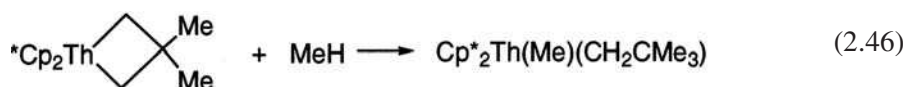


The d^0 metals can also carry out alkane activation. In the classic example from Watson [126], exchange occurs at 70°C and is detected by isotope labeling. No reaction with the cyclohexane solvent occurs (Eq. 2.45).



Analogous chemistry occurs with $\text{Cp}^*_2\text{Sc}-\text{CH}_3$ [127].

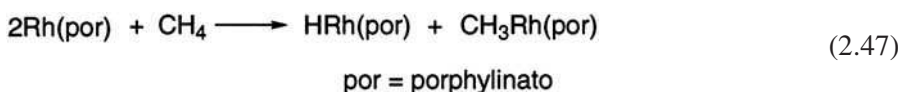
Marks and Fendrick [128] was able to drive a similar reaction using a thorium metallacycle (Eq. 2.46).



Mercury photosensitization has been shown to go via interaction between the $^3\text{P}_1$ excited state, Hg^* , and the alkane, RH , ultimately to liberate free radicals, R

and H. This chemistry has been put to synthetic use by trapping the radicals in various ways to form alcohols, amines, carboxylic acids and other functionalized derivatives, all on a multigram scale [129].

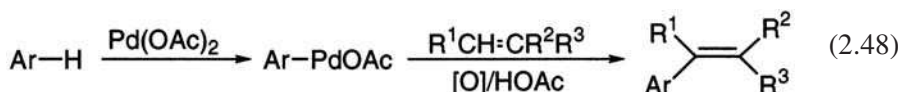
Another case of homolytic alkane activation was reported by Sherry and Wayland [130], who found that a pair of Rh(II)porphyrin radicals can cleave methane via a binuclear oxidative addition following termolecular kinetics (Eq. 2.47).



Electrophilic arene CH activation is classic for metals such as Hg(II), Au(I) and Rh(III). For example, $[\text{Rh}(\text{oep})]^+$ reacts with $\text{C}_6\text{H}_5\text{OMe}$ to give the $[(p\text{-MeOC}_6\text{H}_4)\text{Rh}(\text{OEP})]^+$ [131]. The reagent, being very bulky, avoids ortho substitution.

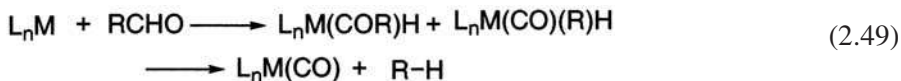
In the case of arene activation, Jones [132] has shown how the initial interaction with the metal can give an η^2 -arene complex prior to CH activation. This is the case for the $[\text{Cp}^*\text{Rh}(\text{PMe}_3)]$ fragment, formed by photoextrusion of H_2 .

In Fujiwara's interesting arene activation chemistry, oxidative addition of an arene CH bond to Pd, specially fast for electron-rich arenes, is followed by a Heck-like insertion of an alkene to give a vinylated arene as product. Arenes undergo unexpected selective trans hydroarylation with both terminal and internal $\text{C}=\text{C}$ double bonds, both inter- and intramolecularly, with turnover numbers up to 4500, giving the thermodynamically less favorable cis-alkenes. The simplicity, generality, and efficiency of this process could be very attractive for possible industrial application (Eq. 2.48) [133].



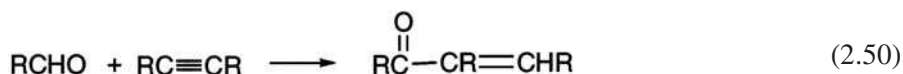
(a) *Catalytic reactions involving C–H activation*

Aldehyde CH bonds are reactive in oxidative addition, so it is not unexpected to find that aldehydes readily undergo catalytic reactions involving this oxidative addition. Several catalysts decarbonylate aldehydes as a result of the acyl hydride formed after the C–H addition undergoing deinsertion of CO, followed by reductive elimination of the alkane product (Eq. 2.49). The hard step in the process is the thermally induced dissociation of the resulting tightly bound CO. One such catalyst is $[\text{Rh}(\text{triphos})\text{Cl}]$ (triphos = $\text{PhP}(\text{CH}_2\text{CH}_2\text{PPh}_2)_2$) [134].



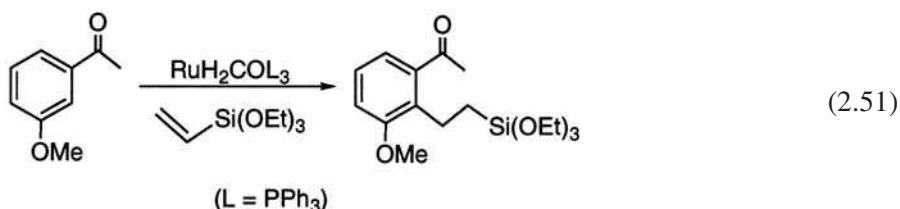
The acyl derived from the aldehyde can also be intercepted by an alkyne, with

the formation of an α, β -unsaturated ketone (Eq. 2.50).

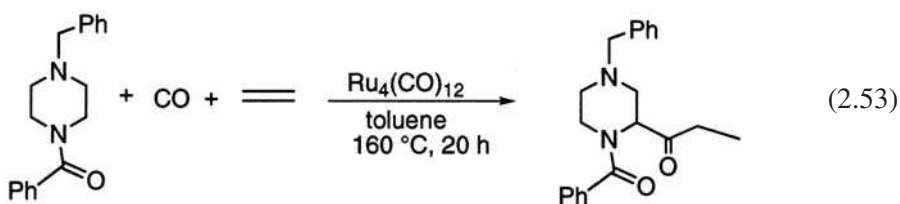
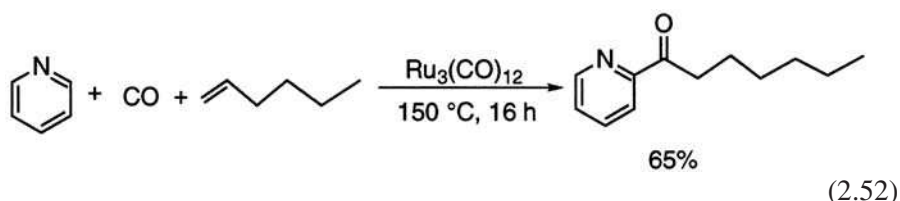


Excellent catalysts in this case are $\text{Ni}(\text{cod})_2/\text{P}(\text{C}_8\text{H}_{17})_3$, [135a] and $[\text{Rh}(\text{cod})\text{Cl}]_2/\text{dppf}$ [135 b] {dppf = 1,1'-(diphenylphosphino)ferrocene}. In the latter case, propargyl substituents are tolerated even though these could, in principle, give CH bond cleavage rather easily.

An important catalytic process that relies on cyclometalation is the Murai reaction [136]. This involves heteroatom directed cyclometalation of an arene followed by insertion of an alkene and reductive elimination to give a net alkylation of the arene. The most common catalyst is $\text{RuH}_2(\text{CO})(\text{PPh}_3)_3$. An example of transformation brought about by this catalyst is shown in Eq. 2.51.



In a somewhat related process, pyridine, CO and an alkene give an acyl pyridine with $\text{Ru}_3(\text{CO})_{12}$ as catalyst (Eq. 2.52) [137]. Related transformation is also possible (Eq. 2.53) [138].



(b) Biomimetic systems

In addition to organometallic alkane conversion, a number of enzymes also carry out these reactions with air as oxidant. The key step is still under discussion but appears to be an H atom abstraction from the R–H bond by a metal oxo group, followed by a ‘rebound’ step in which the resulting R radical abstracts OH from

the metal (Eq. 2.54). This seems to be possible for a variety of Fe(V)=O groups.



The specific spin state adopted by the oxo species involved is believed to play a role in the process by requiring the rebound step to occur with or without intersystem crossing [139]. Methane monooxygenase, for example, converts methane to methanol by such a route. This might seem an advantageous basis on which to model a biomimetic system using coordination chemistry. In fact, all the enzyme reactions of alkanes using air involve a monooxygenase pathway, which implies the presence of a stoichiometric 2e reductant to activate the dioxygen substrate. This renders the overall process economically problematic. As an alternative to a monooxygenase pathway, one can imagine using a 2e reduced form of O_2 , such as H_2O_2 , as oxidant. The cost rises for such a substitution but at least such systems provide a possible route to a viable system. We do not enter into the details of this chemistry here because it has been extensively reviewed elsewhere [140] and it does not fall within the organometallic focus of this book.

2.4.3 Alkane C–C bond activation

C–C bond breaking in alkanes is of great interest because this reaction can lead to skeletal rearrangement or cracking. Such processes play an important role in petroleum industry, for example, because branched alkanes are more useful fuels than are linear ones. While X–H activations are often fast, X–Y activations (where neither X nor Y is H) are commonly slow. This is ascribed to the omnidirectional character of the $\text{H}(1s)$ orbital allowing it to form strong bonds in the transition state, as well as to the lesser steric hindrance in the X–H case. Although C–C cleavage reactions are much rarer than those involving C–H bonds, a number of examples are now known. The most recent review of the field is that of Murakami and Ito [141].

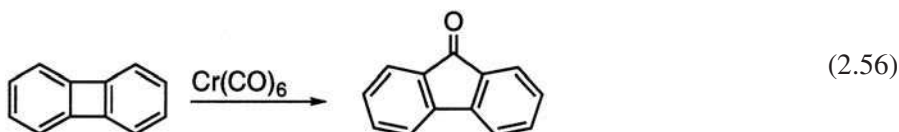
The longest established example, the opening of cyclopropane by Pt(II) to give a metallacyclobutane relies on ring strain to overcome the normally large barrier for such reactions. The resulting platinacyclobutane further reacts with several nitrogen donor ligands ($\text{L} = \text{pyridine}$, 2-, 3-, and 4-methylpyridine, 2,6-dimethylpyridine, 2,2'-bipyridine, and ethylenediamine) to yield the corresponding platina(IV)cyclobutane derivative (Eq. 2.55) [142].



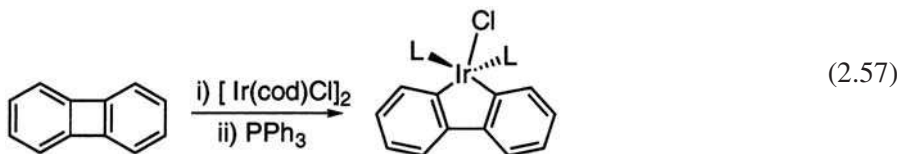
Adams et al. [143] later unambiguously determined the structure of the product using NMR and IR spectroscopic studies on the bis(pyridine) adduct. In addition to the relief of ring strain, the high reactivity of cyclopropane is attributed to the fact that the C–C bond HOMO and LUMO in cyclopropane have more p

orbital character than in unstrained alkanes and thus allows better interaction with both the metal d_σ and d_π orbitals. Mechanistic studies by Bergman et al with $\text{Cp}^*\text{Rh}(\text{PMe}_3)$ complex revealed that cyclopropane undergoes C–H activation prior to a subsequent rearrangement in which a C–C bond is cleaved [144]. The C–C bond of cubane, another very strained hydrocarbon, is also very readily opened [145].

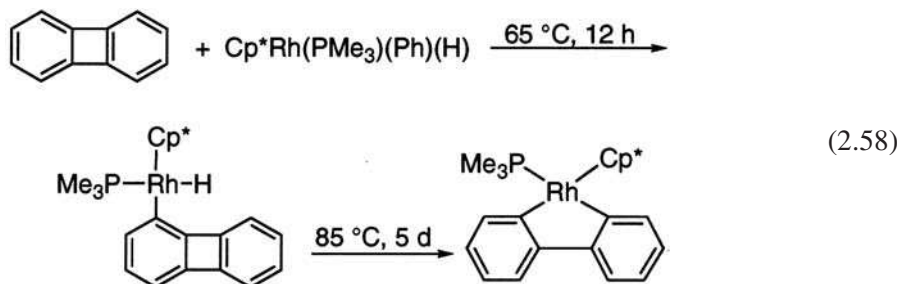
More activated are C–C bonds between sp^2 carbons. While an aryl–aryl C–C bond is quite strong, diphenylene, with its 4-membered ring and possibility for out-of-plane attack by the metal, is in a very good position to give C–C bond cleavage (Eq. 2.56) [146]. Although even in this favorable case, temperatures well in excess of 100°C are often required. For example, $\text{Cr}(\text{CO})_6$ was shown to give fluorenone at 225°C [147].



A number of unusual 5-coordinate complexes with a structure intermediate between T- and Y-shaped were prepared by opening diphenylene; part of the reason for the low coordination number may be the high trans effect of the phenylene rings (Eq. 2.57) [148].

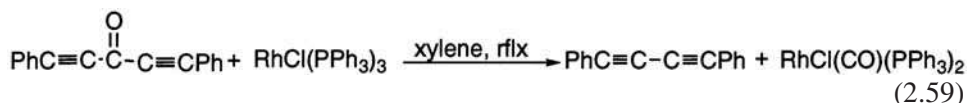


$\text{Cp}^*\text{Rh}(\text{PMe}_3)\text{PhH}$ shows initial insertion into an arene CH bond (65°C , 12 h) followed by C–C cleavage (85°C , 5 d) (Eq. 2.58) [149].

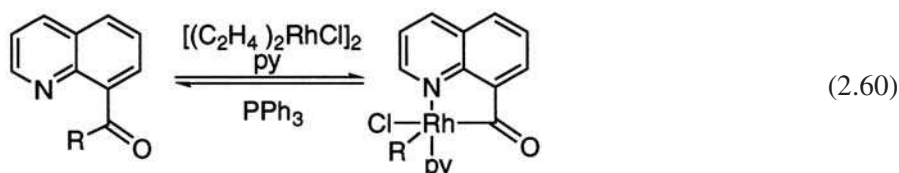


C–C bonds between carbonyls and other sp^2 carbon centers are more activated still, and opening is possible even below room temperature in strained cases, for example of cyclopropenone by $\text{Pt}(\text{II})$ at -35°C [150]. Likewise, cleavage of a bond between a carbonyl and an sp carbon is possible, as in the decarbonylation

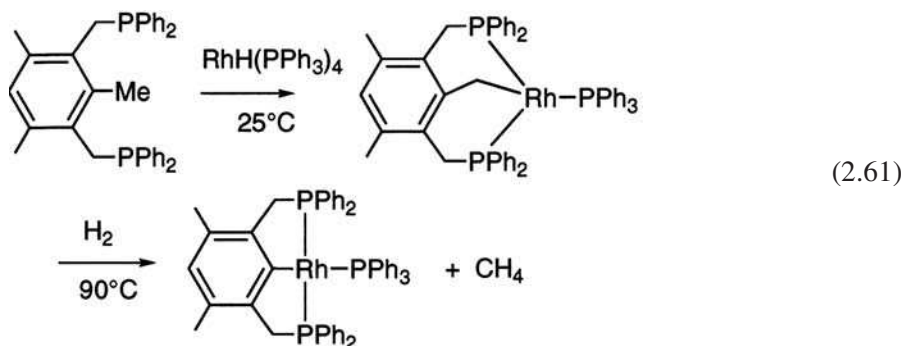
of a dialkynylketone (Eq. 2.59) [151].



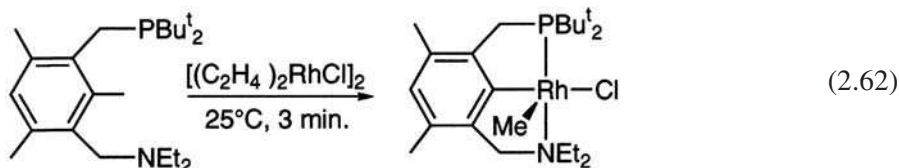
In a series of interesting investigations, Suggs and Jun [152] have shown ready C–C cleavage by directed attack in quinoline-derived ketones where the metal binds in such a way as to bring it into close proximity with the bond to be cleaved (Eq. 2.60; R = CH₂Ph, Et; py = pyridine). Addition of PPh₃ causes reductive elimination back to the starting ketone. Intermolecular versions of this reaction were also observed [153].



Other forms of kinetic encouragement have been applied to the problem. For example, pincer phosphines with an endo-directed C–C bond undergo first C–H and then C–C cleavage with Rh(I) (Eq. 2.61) [154].

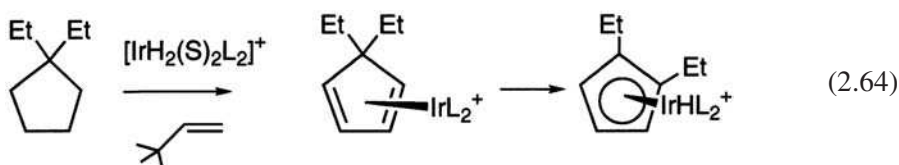
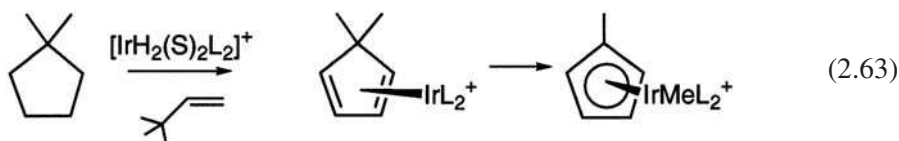


Milstein and co-workers have also shown a very unusual and highly selective case where C–C activation was the only reaction observed, as in the example shown in Eq. 2.62 [155]

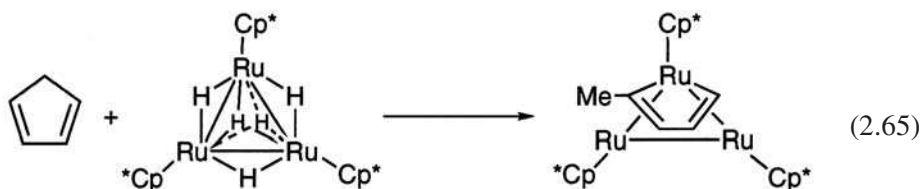


Aromatization of a cyclopentadiene to a cyclopentadienyl can occur with C–C bond breaking. Benfield and Green [156] reported an interesting reversible migration of an ethyl group from a cyclopentadienyl ring to a Mo metal, resulting in

aromatization of the ring. The energy gain from the formation of the aromatic Cp must add 25 kcal/mol of stability to the product. A similar aromatization can even be effected in alkanes. For instance, Crabtree et al. [157] have achieved indirect C–C activation in 1,1-dimethylcyclopentane by combining alkane dehydrogenation to the diene, followed by alkyl migration, whose net effect is aromatization of the alkane (Eq. 2.63). Such reactions can be reversible, as in the case of Eq. 2.64 where the ethyl group first migrates to the metal and then back to the ring producing diethylcyclopentadienyl complexes; only the 1,2-diethyl isomer is shown in Eq. 2.64 but the 1,3-species is also formed.



Suzuki et al. [158] has pioneered the study of the triruthenium cluster of Eq. 2.65, which is exceptionally reactive thanks to its hydride ligands. In the case shown here, a C–C bond of the cyclopentadiene undergoes oxidative addition to the cluster resulting in a ring opened product. This kind of reaction is no doubt facilitated by the polymetallic center, which can bind the diene at one metal to bring the C–C bond into proximity with a second metal that cleaves the C–C bond.

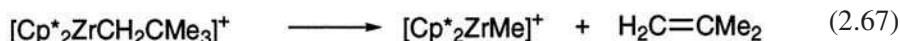


Bridging hydrogens omitted

One of the more remarkable cases of C–C bond cleavage occurs in β -alkyl elimination (Eq. 2.66). This occurs for lanthanides and related systems where the M–C bond energy greatly exceeds the M–H energy, the reverse of the situation with the late transition metals. In the lanthanides there is no limitation of coordination by electron count, only of steric saturation [159].

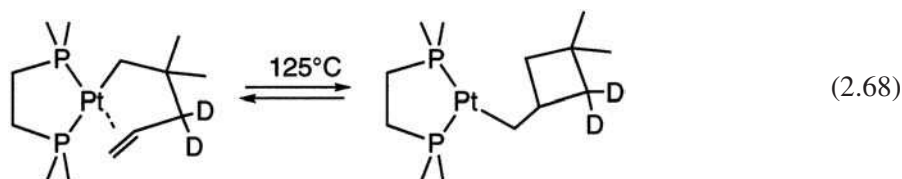


A similar reaction is seen in a cationic Zr(IV) species (Eq. 2.67) [160]

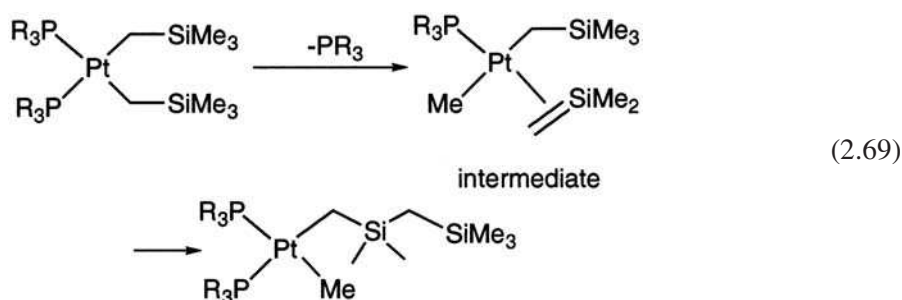


This type of β -alkyl elimination is recognized as an important chain transfer step in Ziegler–Natta and metallocene polymerization catalysis [161]. When it occurs the polymer chain terminates in a C=C bond and in certain systems can undergo insertion and get back into the polymer growth cycle.

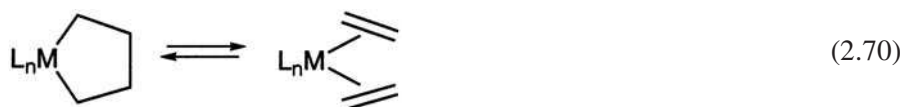
In a number of cases, a β -alkyl elimination can occur for the late transition metals where a strained ring is properly oriented relative to the metal. Eq. 2.68 shows a reversible case [162].



The greater reactivity of Si–C over C–C bonds is illustrated by the β -alkyl elimination of Eq. 2.69, where no ring strain or other inducement is necessary for the reaction to take place [163].



Oxidative coupling and its reverse, reductive cleavage, are relatively common reactions in organometallic chemistry that illustrate what is essentially a double β -alkyl elimination (Eq. 2.70).



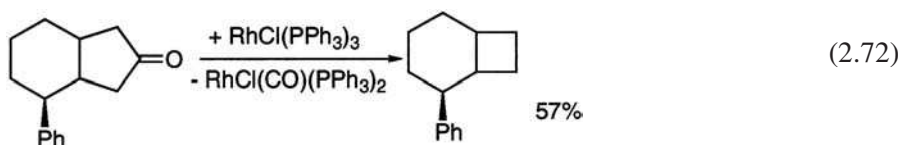
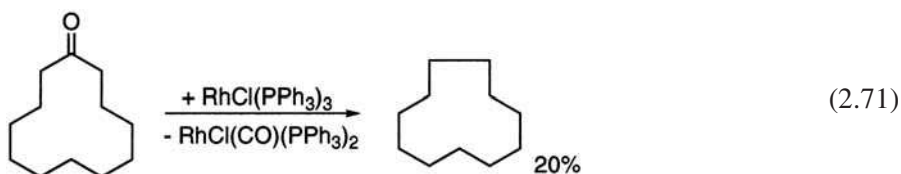
A rare example of a radical C–C cleavage occurs with the paramagnetic Rh(II) species, Rh(tmp) {tmp = tetramesityl porphyrin}; it proceeds slowly at 70°C to give MeRh(tmp), but the substrate, the TEMPO {TEMPO = 2,2,6,6-tetramethyl-1-piperidinyloxy} radical, is a loaded case that is particularly prone to transfer Me [164].

On the other hand, it has proved possible to activate a C–C bond by using bare ('naked') transition metal ions, generated by various ionization methods in the gas phase [165]. Using an ion-beam instrument, for example, Armentrout and Beauchamp [166] were able to show that the reaction of Co^+ with *n*-butane gives CoC_2H_4^+ . An exothermic and quite facile C–C insertion by the metal is thought

to be followed by β -hydrogen elimination and reductive elimination of ethane. In this case, the corresponding Co–C bond strengths are much higher than in the case of a metal complex and the reagent, Co^+ , is extremely unhindered [167].

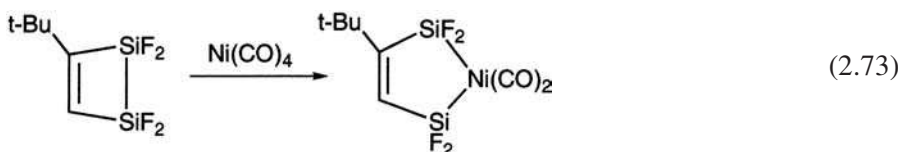
A number of catalytic reactions involve C–C bond cleavage, often driven by strain. For example, biphenylene can be converted to tetraphenylene with $\text{Ni}(\text{cod})(\text{PMe}_3)_2$ at 100°C or $\text{Pt}(\text{PR}_3)_3$ at 120°C [168]. In the Pt case, a series of intermediates could be isolated that suggest a pathway involving double oxidative addition of the biphenylene C–C bond, as in the stoichiometric reactions previously discussed, followed by double reductive elimination to give the product.

Eqs. 2.71 and 2.72 show unusual cases where a catalytic C–C cleavage occurs with little or no acceleration via relief of strain, but the reactions are very slow and go in low yield [169].

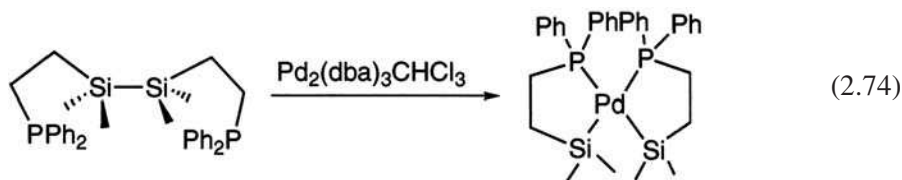


2.4.4 Si–Si activation

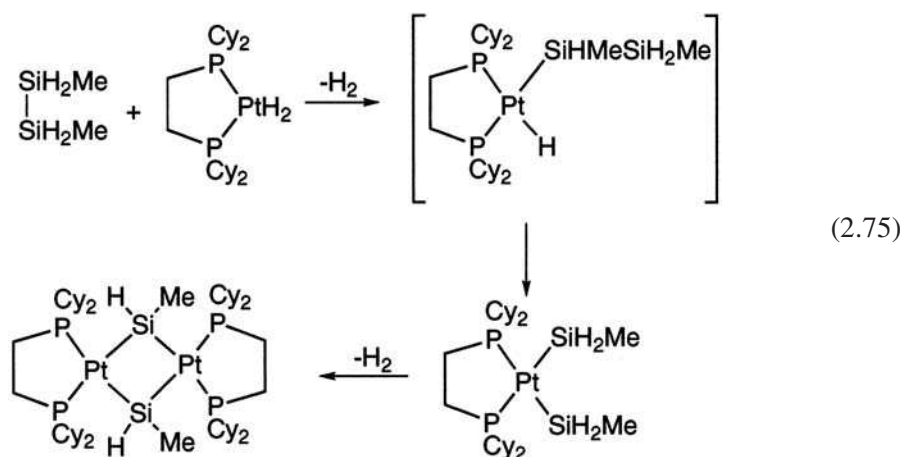
Since oxidative addition of the Si–Si bond to transition metals can produce many different types of M–Si compounds, such as bis(silyls), silylenes, and disilenes, a range of potential catalytic processes is possible. Although the Si–Si bond energy is smaller than that of Si–H, the activation barrier for bond cleavage is much higher. This is because unlike the Si–H σ bond, the σ orbital of silicon–silicon bond possesses high directionality along the bond axis and steric hindrance prevents the approach of a metal. The reactivity of Si–Si bonds is often enhanced by introduction of strong electron-withdrawing groups on silicon. It is perhaps no surprise that most examples of stable bis(silyl) complexes were derived from oxidative addition of halogenated disilanes to metals. For example tetrafluorodisilacyclobutene has been shown to be highly reactive toward $[\text{Ni}(\text{CO})_4]$ to give a Ni(II) complex with a 5-membered ring (Eq. 2.73) [170].



Isonitrile ligands bound to palladium turn out to be very efficient in promoting the bis-silylation of alkenes [171]. Another possibility to make oxidative addition of Si-Si bond easier is the introduction of potentially chelating functionality such as phosphino groups in the disilane (Eq. 2.74) [172].

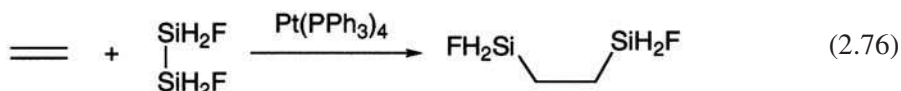


Some Si-Si activation involves initial Si-H activation followed by silylene migration. An example is the reaction between tetrahydrodimethyldisilane and a cis-platinum dihydride that gives $[(dcpe)Pt]_2(\mu-SiHMe)_2$ ($dcpe = 1,2$ -bis(dicyclohexylphosphino)ethane) via the intermediacy of a disilanylplatinum hydride (Eq. 2.75) [173]. The transformation of a disilanylplatinum hydride to bis(silyl)platinum complex seems to proceed via an intramolecular α -silylene migration.

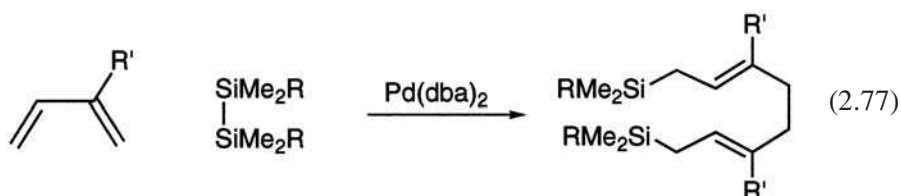


Transition metal catalyzed bis-silylation of unsaturated hydrocarbons is a convenient synthetic tool for obtaining organosilicon compounds. Some excellent reviews on this subject are available [174]. A variety of stereo- and regioselective bis-silylation reactions of $C\equiv C$ bonds has been achieved by using many different Pd complexes. In the presence of $Pd(PEt_3)_2$ the reaction between $HMe_2Si-SiMe_2H$ and $PhC\equiv CH$ results in addition of the Si-Si bond to the alkyne in moderate yield. As expected, the yield is increased with use of activated disilanes, which contain electronegative substituents such as fluorine, chlorine, and alkoxide [175]. Tert-alkyl isonitriles [176] and bicyclic phosphates as ligands [177] efficiently catalyze the bis-silylation of alkynes with otherwise unreactive disilanes such as hexamethyldisilane and 1,1,2,2-tetramethyl-1,2-diphenyldisilane.

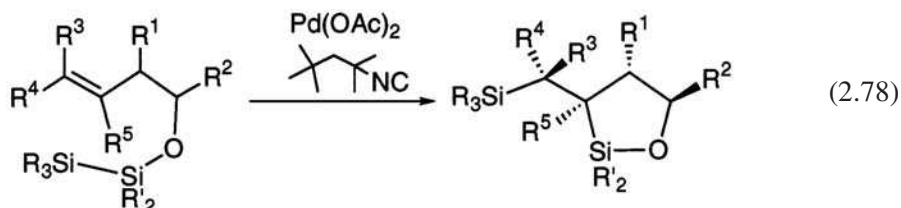
Bis-silylation of simple olefins is scarce. Tanaka et al. have shown successful bis-silylation of ethylene and norbornene by using platinum phosphine catalysts (Eq. 2.76) [178]. Bis-silylation of terminal alkenes such as 1-octene and styrene are also known [179].



Reactions of 1,3-dienes with disilanes have been known to yield either 1:1 or 1:2 addition products, depending on the choice of catalysts and disilanes. For example, $\text{NiCl}_2(\text{PEt}_3)_2$ catalyzes 1,4-addition of the Si-Si bond to 1,3-diene to produce 1,4-disilyl-2,3-butenes [180], while the use of $\text{Pd}(\text{dba})_2$ as catalysts afford bis-silylative dimerization products with high regio- and stereoselectivity (Eq. 2.77) [181].



Ito and his co-workers [182] reported a very interesting example of intramolecular bis-silation of C=C bonds catalyzed by palladium acetate/*tert*-alkyl isocyanide, which leads to formation of a cyclic bis-silation product (Eq. 2.78). Subsequent oxidation of the two carbon-silicon bonds can introduce two hydroxyl groups leading to the stereo- and regiospecific synthesis of 1,2,4-triols. Stereospecific dihydroxylation of olefins is currently of particular interest in organic synthesis.



2.4.5 Activation of other non-polar single bonds

Of the many other bonds that have been shown to undergo oxidative addition, the only really significant case is the P-C bond of phosphines. Hundreds of examples of this reaction are known, specially for aryl groups, as discussed in the exhaustive review by Garrou [183]. Typically a metal complex of PR_3 liberates RH on heating, where the R group arises from the phosphine and the H comes from a hydride ligand initially present, or formed by some process such as

cyclometallation. This reaction can lead to catalyst deactivation if the PR_2 group that results from the P–C bond cleavage bridges with another metal and gives an inactive cluster species or other decomposition product. A modified version of the reaction occurs when the metal has an aryl or alkyl group R' , different from the R group of the PR_3 . In this case R/R' exchange can occur and $\text{R}_3\text{P–M–R}'$ can be transformed into $\text{R}'\text{R}_2\text{P–M–R}$. This can lead to the wrong R group being incorporated into the phosphine, modifying the properties of the catalyst, and to the wrong R group being incorporated into the product of the catalytic reaction with the result that the catalytic reaction itself is compromised. This reaction probably occurs quite commonly but may not always be recognized because it may only result at a low level of contamination with impurities of the desired product.

2.4.6 Theoretical work

The very rapid recent advances in quantum chemistry thanks to the introduction of DFT and of hybrid quantum mechanical/molecular mechanics methods [184–189] have allowed chemically useful accuracy to be obtained in modeling both electronic and steric effects in transition metal compounds, including specific accounting of steric effects in large ligands. These methods are now taking their place along with traditional experimental work in solving problems of mechanism and structure. Some of these results have been incorporated into the above discussions but we can expect a flowering of such work in future increasingly to shape our thinking in this developing area.

2.5 CONCLUSION

The activation of non-polar bonds by transition metals has been of major interest in the last quarter century. With H_2 , we have the simplest case possible and therefore the one that has been most extensively treated by theoretical methods. Reactions of H_2 also tend to be the fastest among all the substrates considered in this chapter. The structures of polyhydrides formed on H_2 addition include classical and non-classical forms, a topic that has excited much controversy because of the difficulty of structural characterization. Hydrides, whether formed by H_2 or XH addition, are also involved in a wide variety of useful catalytic reactions from isotope exchange to alkane functionalization. The activation of XH bonds also allows formation of a wide variety of M–X bonds that, apart from their intrinsic interest, are also key intermediates in a very large number of catalytic reactions, such as hydrogenation, hydrosilation and various carbonylation reactions. The activation of X–X bonds, where neither group is a hydrogen atom is much more difficult, and except for cases where these bonds are either weak (e.g., Si–Si) or strained (biphenylene) there has been little work done. However,

recent successes with unstrained B–B and C–C bonds suggest that this area may be capable of further useful development in the near future. Perhaps the greatest challenge in the area is finding methods to catalyze practical functionalization reactions of C–H bonds in organic compounds that are not activated by the presence of an adjacent functional group and to do so with tunable and predictable selectivity.

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Activation of Substrates with Polar Single Bonds

Sanshiro Komiya and Masafumi Hirano

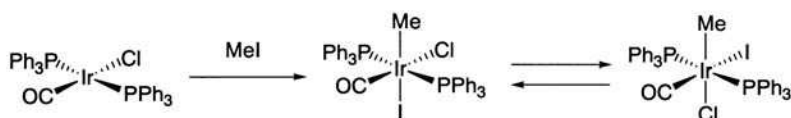
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3.1 INTRODUCTION

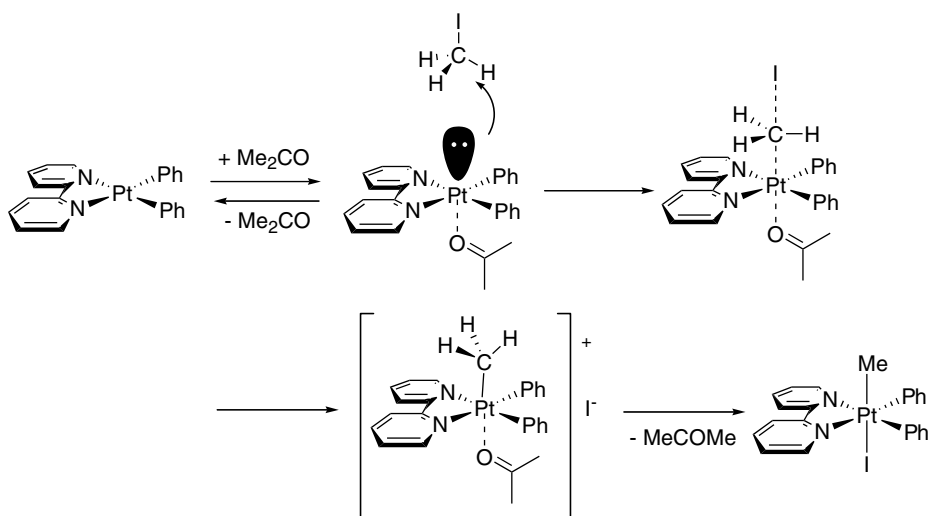
Cleavage of polarized chemical bonds is the most utilized inlet toward organic chemical transformations in organic synthesis, since such bonds are susceptible to nucleophilic or electrophilic activation. Recent development of organometallic chemistry reveals that the use of transition metals in these bond cleavages provides us with highly selective and efficient chemical processes such as cross coupling reactions with Grignard reagents, Suzuki–Miyaura coupling reactions, Mizoroki–Heck reactions, palladium promoted allylic alkylations, ruthenium catalyzed aldol type and Michael reactions etc. In these reactions, hetero atom–carbon or polar carbon–hydrogen bond formally oxidatively adds to a transition metal to give reactive organotransition metal intermediates, to which substrates selectively react leading to new C–C bond formation. Among them, carbon–halogen bond activation is the most extensively investigated in the past half century and generally three types of mechanisms are known; ionic, radical and concerted mechanisms. In contrast, systematic studies concerning cleavages of other bonds by transition metal complexes are still far less documented to date, although many examples of C–O, C–S and C–N bond cleavage frequently appear in transition metal mediated organic chemical transformations. In this chapter, fundamental concepts and reactions including recent advances on activation of polar chemical bonds by transition metal complexes are described in the order of carbon–halogen, carbon–oxygen, carbon–sulfur and other polar single bond activations. Cleavages of polar bonds except for carbon–halogen bond are mentioned in a relatively enumerative way, due to lack of their systematic studies.

3.2 CARBON–HALOGEN BOND CLEAVAGE REACTIONS

The cleavage reaction of carbon–halogen bond is one of the most well studied reactions from the early stage of development of organometallic chemistry. For



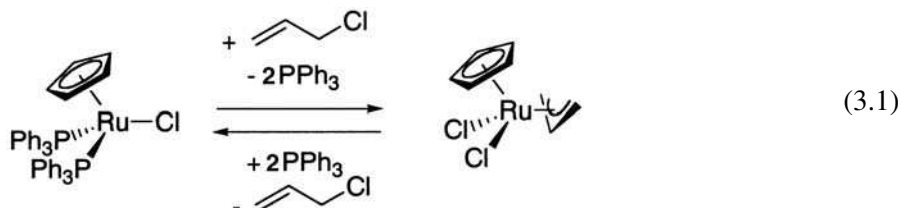
Scheme 3.1.



Scheme 3.2.

example, dialkylzinc and Grignard reagents are prepared by the reactions of organic halides with main group metals such as zinc and magnesium, which are now classified as oxidative addition. Such carbon–halogen bond cleavage reactions also take place with many low-valent transition metal complexes giving organotransition metal complexes as typically documented in reactions of Vaska's complex $\text{IrCl}(\text{CO})\text{L}_2$ (Scheme 3.1) [1].

However, transition metal complexes with higher metal valency can also display oxidative addition in some cases. For example, platinum(II) or ruthenium(II) complexes give tetra-valent organometallic complexes as shown in Scheme 3.2 and Eq. 3.1 [2–4]. In these reactions, prior coordination of a Lewis base is considered to increase nucleophilicity of the metal for oxidative addition.

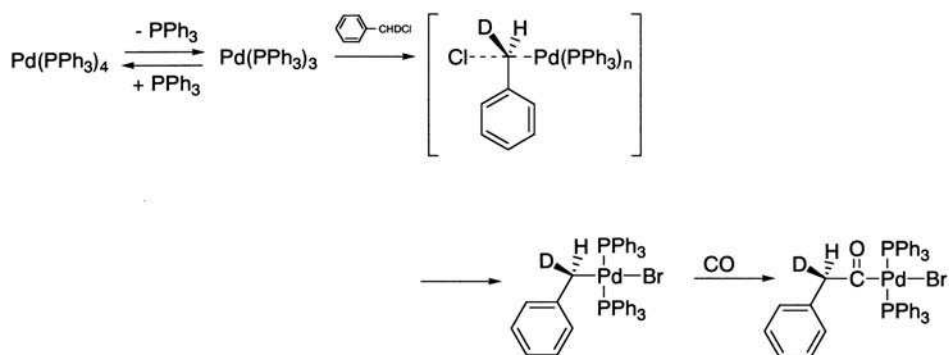


(3.1)

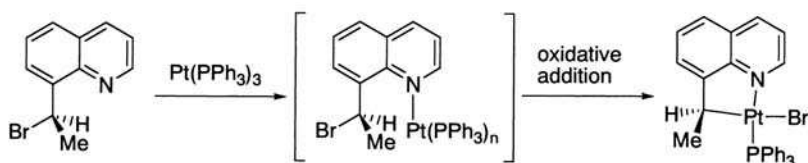
Oxidative addition of carbon–halogen bond to low-valent group 10 metal complexes is one of the most well defined reactions from the mechanistic point of view [5]. Mechanisms for the carbon–halogen bond oxidative addition are generally divided into 3 mechanisms, namely ionic, radical, and concerted processes. Mechanisms for the oxidative addition are known to vary depending on the metal, organic halide, supporting ligand, and reaction conditions. Thus, it is normally difficult to predict the operating mechanism for these bond cleavage reactions without detailed mechanistic studies. Particularly, complete discrimination between single electron transfer and ionic nucleophilic mechanisms in the carbon–halogen bond oxidative addition is a very difficult task without detailed experimental evidence, because reactivity trends in single electron transfer reaction from organic halide to the metal giving a cation radical and the nucleophilic attack of the metal to the carbon should be the same in general. In addition carbon–halogen bonds can interact with the metal in a concerted manner as in the case of oxidative addition of non-polar chemical bonds such as C–H and C–C. Three types of the reaction mechanisms for carbon–halogen bond oxidative addition are summarized below.

3.2.1 Ionic S_N2 type mechanism

Highly reduced late transition metal complex is basically regarded as a Lewis base and therefore acts as a nucleophile. Such a complex attacks the alkyl carbon releasing free halogen anion by the associative bimolecular process. The anion then adds to the metal to give the product. Therefore, the reactivity trends in this oxidative addition are quite similar to those observed in conventional S_N2 reaction in organic chemistry [6]. For example, this oxidative addition is significantly affected by the steric congestion at carbon, and thus the reactivity of alkyl halides decreases as follows: Me > primary > secondary $\gg$ tertiary. Regardless of steric hindrance, the organic and halogen groups in the resulting product are normally mutually *trans* (*vide infra*). The reaction is also enhanced by increase of nucleophilicity of the metal center. Third row transition metal complexes are generally more active toward oxidative addition of organic halides than first row complexes because the former have stronger M–X bonds than the first row counterparts. Because S_N2 mechanism involves associative transition state giving an ionic intermediate, the reaction is greatly accelerated by use of polar solvent and the entropy of activation usually shows large negative values ($\Delta S^\ddagger = -40$ to -50 eu). Contrary to the radical mechanism (*vide infra*), tosylate normally reacts much faster than halides because tosylate is one of the best anionic leaving groups. The reactivity toward oxidative addition of alkyl tosylate/halide thus obeys the following order: ROTs > RI > RBr > RCl $\gg$ RF. Another notable feature of this mechanism is inversion of configuration at the α -carbon of the organic halide. As a typical example, treatment of benzyl chloride (*S*)-Ph(D)(H)CCl with Pd(PPh₃)₄ under CO atmosphere gives an acyl complex (*R*)-



Scheme 3.3.



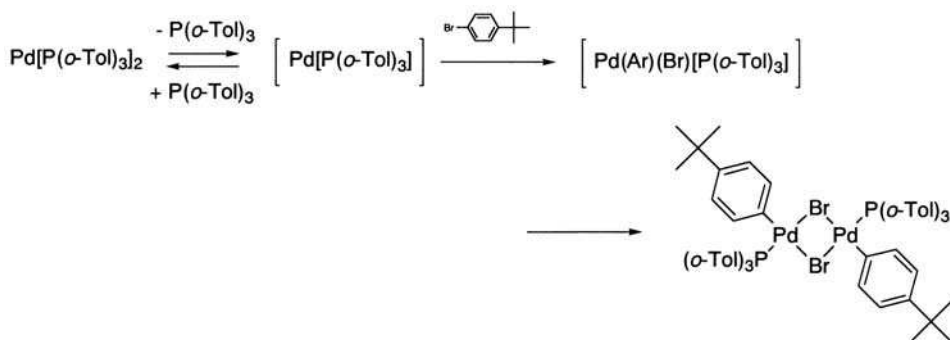
Scheme 3.4.

trans- $\text{Pd}[\text{COC}(\text{Ph})(\text{H})(\text{D})]\text{Cl}(\text{PPh}_3)_2$ (Scheme 3.3) [6]. In this reaction oxidative addition of C–Cl bond to a zero-valent palladium complex takes place with complete inversion of configuration followed by insertion of CO into the resulting Pd–C bond to give the final acyl product.

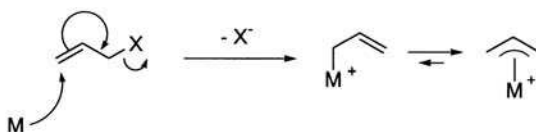
Another explicit example for the stereochemistry in the $\text{S}_{\text{N}}2$ type oxidative addition is the reaction of Pt(0) complex with an optically active substituted quinoline. (Scheme 3.4) The reaction can be guided by the prior coordination of the nitrogen atom to bring the carbon–bromine bond near the metal atom and the stereochemistry is inversion of configuration at carbon [7].

Coordinative unsaturation of the metal is also an important factor for oxidative addition for effective $\text{S}_{\text{N}}2$ type interaction. This usually provides enough space for incoming electrophilic carbon. In some cases, 14e species may form prior to the oxidative addition. Intriguingly, oxidative addition of aryl bromide to even a two-coordinate palladium(0) complex $\text{Pd}[\text{P}(o\text{-Tol})_3]_2$ also involves prior dissociation of a phosphine ligand giving a 12e complex ' $\text{Pd}[\text{P}(o\text{-Tol})_3]$ ' (Scheme 3.5) [8,9].

Although allylic carbon–halogen bond cleavage reactions by organic nucleophiles are accepted to proceed *via* $\text{S}_{\text{N}}2'$ mechanism [10], as exemplified by reaction of PhLi with labeled allylic chloride which preferentially gives terminally labeled product (Eq. 3.2) [11], those by transition metal complexes are a matter of discussion. In the past half century, a great progress has been made in the transition metal mediated catalytic allylations of organic substrates. The allylic

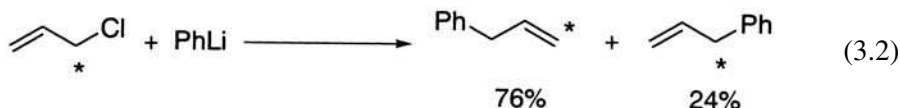


Scheme 3.5.



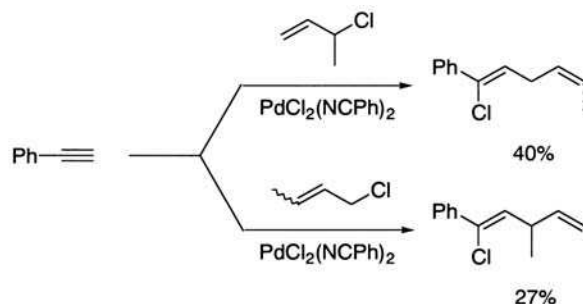
Scheme 3.6.

electrophiles are sometimes considered to be attacked by metal nucleophiles from the *exo* face with inversion of configuration at the γ -carbon. Thus, an $\text{S}_{\text{N}}2'$ mechanism is proposed, where a transition metal complex attacks γ -carbon of the allylic group leading to ejection of the halogen anion at the α -carbon (Scheme 3.6) [12]. A superficial $\text{S}_{\text{N}}2'$ -like C–C bond formation occurs in Pd(II)-catalyzed coupling reaction between phenylacetylene and allylic chlorides (Scheme 3.7) [13]. However, a proposed mechanism involved insertion of C=C bond of allylic chloride into 2-chlorovinyl–Pd bond which is formed by chloropalladation of acetylene, followed by β -Cl elimination.

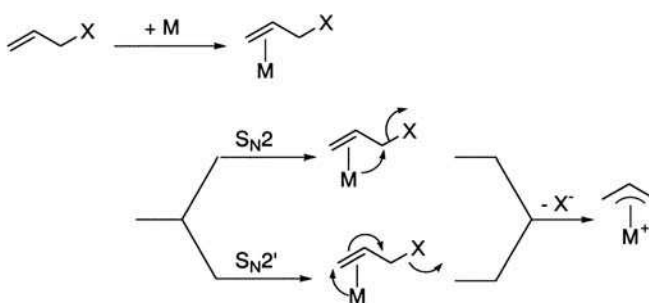


Another important mechanism for the allylic carbon–halogen bond cleavage involves prior η^2 -coordination of the C=C double bond to the transition metal followed by $\text{S}_{\text{N}}2$ - or $\text{S}_{\text{N}}2'$ -type nucleophilic addition (Scheme 3.8).

Though the stereochemistry for oxidative addition of allylic halide had been rather ambiguous until 1990s, it was found to vary depending on the reaction conditions. Cyclic allylic carboxylates were mainly employed to obtain the stereochemical information for the oxidative addition of allylic electrophiles in general (cf. Section 3.3). As shown in Eq. 3.3 the oxidative addition of the *trans* allylic chloride to $\text{Pd}_2(\text{dba})_3$ in a polar solvent such as acetonitrile or DMSO dominantly gives the *cis* product (*trans/cis* = 3/97 in DMSO), suggesting conventional $\text{S}_{\text{N}}2'$

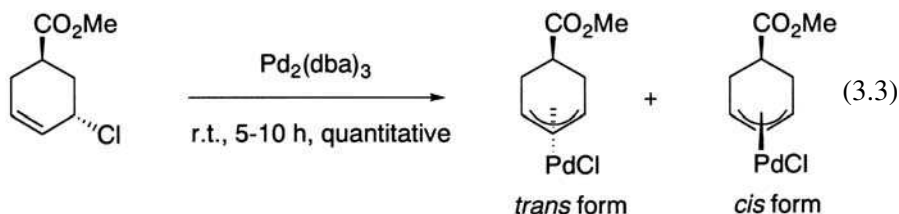


Scheme 3.7.



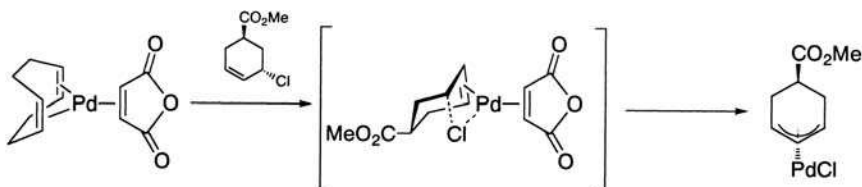
Scheme 3.8.

mechanism or modified $\text{S}_{\text{N}}2$ mechanism in Scheme 3.8 [14]. Since such oxidative addition involves an ionic intermediate, a polar solvent such as DMSO accelerates the reaction.

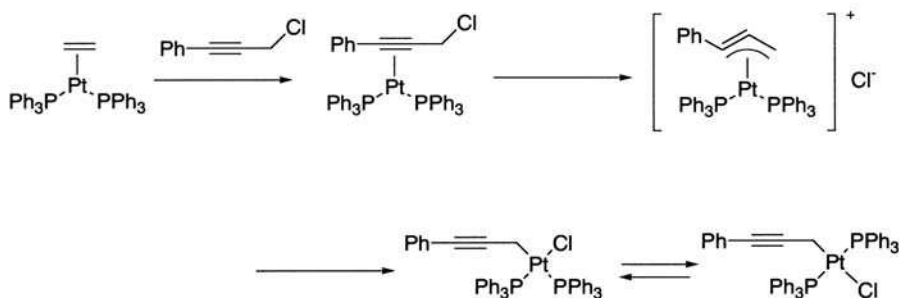


On the other hand, the oxidative addition in a non-polar solvent such as benzene gives the *trans* product. This oxidative addition is considered to occur by prior coordination of allylic halide to $\text{Pd}(0)$ from the *syn* face and the chelation by the chlorine atom and $\text{C}=\text{C}$ bond allows *syn* elimination of the chloro moiety (Scheme 3.9). The addition of π -acceptor such as electron deficient olefins in a non-polar solvent also facilitates the *syn* oxidative addition [14].

The prior η^2 -coordination is also proposed for oxidative addition of phenylpropargyl halides to zero-valent platinum complex $\text{Pt}(\text{PPh}_3)_4$, where $\text{Pt}(\text{PPh}_3)_2$ and $\text{Pt}(\text{PPh}_3)_3$ are active species for the oxidative addition. Kinetic study reveals slow formation of $\text{Pt}(\eta^2\text{-PhC}\equiv\text{CCH}_2\text{X})(\text{PPh}_3)_n$ ($n = 2, 3$), from which



Scheme 3.9.



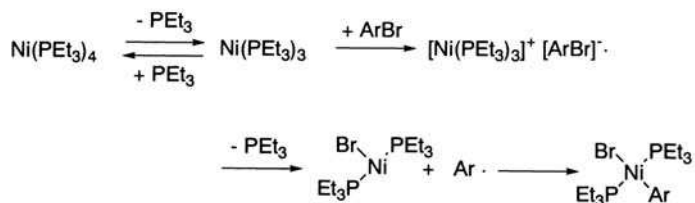
Scheme 3.10.

the C–X bond is rapidly cleaved to form cationic propargyl complex $[\text{Pt}(\eta^3\text{-PhCCCH}_2)(\text{PPh}_3)_n]^+\text{X}^-$ without dissociation of PPh_3 , followed by conversion to a propargyl complex *cis*- $\text{Pt}(\eta^1\text{-CH}_2\text{C}\equiv\text{CPh})(\text{X})(\text{PPh}_3)_2$ [15,16].

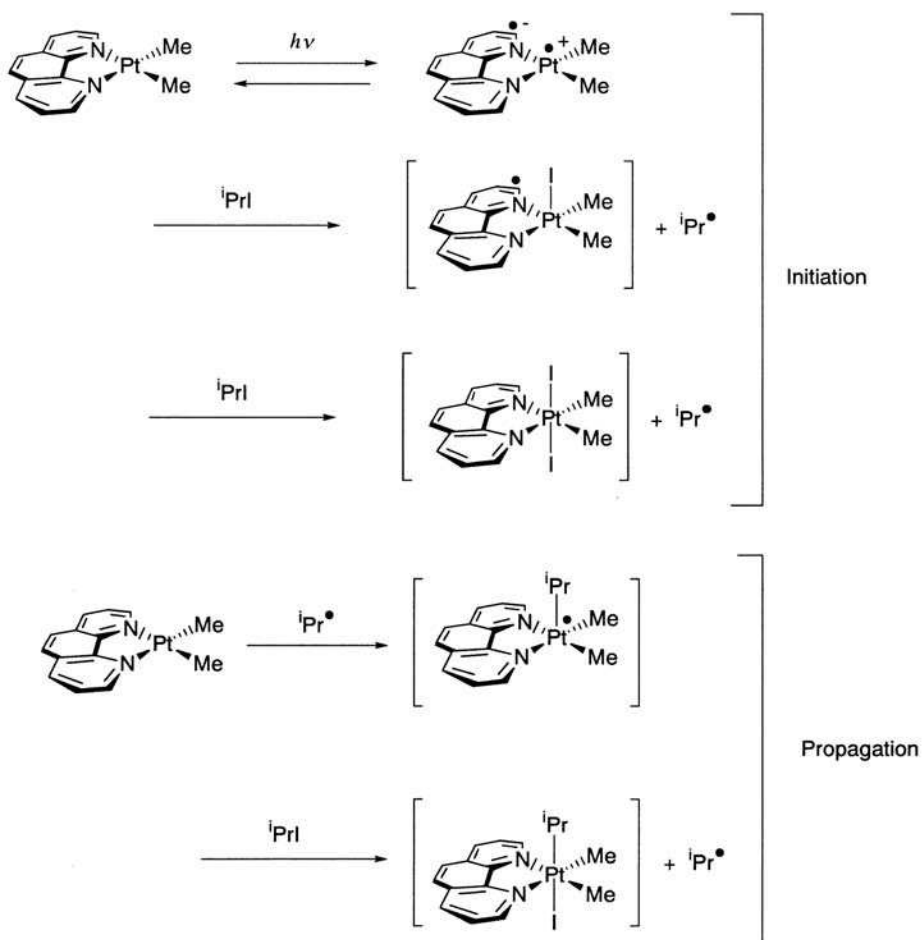
3.2.2 Radical process-single electron transfer

Oxidative addition of many organic halides to zero-valent group 10 metals is believed to involve single electron transfer process affording radical intermediates. For example, aryl halide is known to interact with a zero-valent coordinatively saturated complex $\text{Ni}(\text{PET}_3)_4$, leading to one electron transfer from nickel(0) to the aryl halide accompanied by halogen transfer to Ni (Scheme 3.11) [17]. Thus formed aryl radical couples with the nickel(I) species $\text{NiX}(\text{PET}_3)_2$ to give oxidative addition product $\text{NiArX}(\text{PET}_3)_2$. The electron transfer process from metal to the aryl halide is considered to be rate-determining step for the oxidative addition. Radical ion pair consisting of Ni(I) species and Ar radical is considered to stay in the solvent cage during the reaction.

Since the total reaction is basically initiated by generation of an organic radical, the reaction rate is closely related to the stability of the resulting radical. This type of oxidative addition therefore takes place rapidly for tertiary alkyl halides and quite slowly for tosylate regardless of steric repulsion. The stereochemistry of the α -carbon is completely lost. When the radical ion pair is not stable enough in the cage, the radical escapes to the solution leading to radical chain process

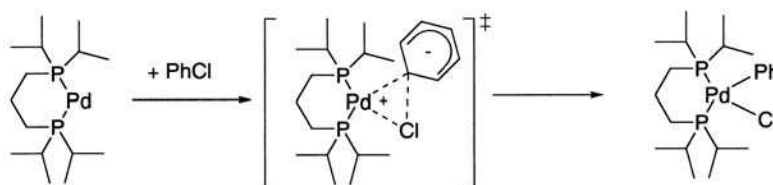


Scheme 3.11.



Scheme 3.12.

of oxidative addition. For example, both thermally and photochemically initiated oxidative additions of isopropyl iodide to $\text{PtMe}_2(\text{phen})$ give tetra-valent platinum complex *cis,trans*- $\text{PtMe}_2^i\text{PrI}(\text{phen})$, where isopropyl radical acts as a chain carrier (Scheme 3.12) [18].

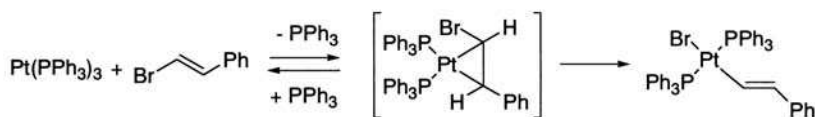


Scheme 3.13.

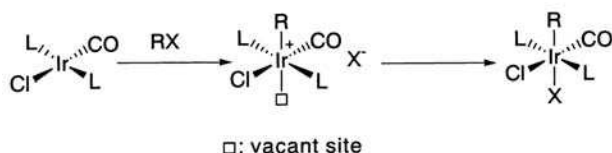
3.2.3 Concerted mechanism

Concerted mechanism of the oxidative addition is regarded as a reverse reaction of reductive elimination where effective overlapping between the filled d_{π} orbital of the metal and the unoccupied σ^* orbital leads to cleavage of the bond. Since this mechanism involves an associative intermediate or transition state, the reaction is normally second order with negative entropies of activation ($\Delta S^{\ddagger} \approx -20$ eu). The stereochemistry at the carbon is normally retained. This is neither ionic nor radical process, and usually applied to the less polar bond such as H–H, Si–H, C–H, or even C–C bond. However, in spite of intrinsic high polarity of carbon–halogen bond, such a three-center concerted process is often found in the oxidative addition of aryl halide to electron rich palladium(0) complexes. For example, a highly basic 14e palladium(0) complex, Pd(dippp) [dippp = 1,3-bis(diisopropylphosphino)propane] reacts with phenyl chloride to give *cis*-Pd(Cl)(Ph)(dippp) (Scheme 3.13) [19]. In this reaction, pseudo first-order rate constants for the reaction of Pd(dippp) with $\text{RC}_6\text{H}_4\text{Cl}$ show good correlation with Hammett's σ^- values, indicating nucleophilic nature of the reaction. However, the rates of the oxidative addition are found to increase in the order $\text{ArCl} < \text{ArBr} < \text{ArI}$, which is opposite order to the typical organic $\text{S}_{\text{N}}\text{Ar}$ mechanism. This may be attributable to their bond dissociation energy difference. Thus, this oxidative addition is proposed as $\text{S}_{\text{N}}\text{Ar}$ reaction involving three-center Meisenheimer transition state.

Such three-center concerted process is also proposed for the oxidative addition of alkenyl halide (Scheme 3.14) [20,21]. Reaction of $\text{Pt}(\text{PPh}_3)_3$ with (*E*)- β -bromostyrene gives *trans*-[PtBr{(E)- β -styryl}(PPh₃)₂], where C–Br bond oxidative addition proceeds *via* prior π -coordination of alkenyl group resulting in retention of configuration at carbon.



Scheme 3.14.



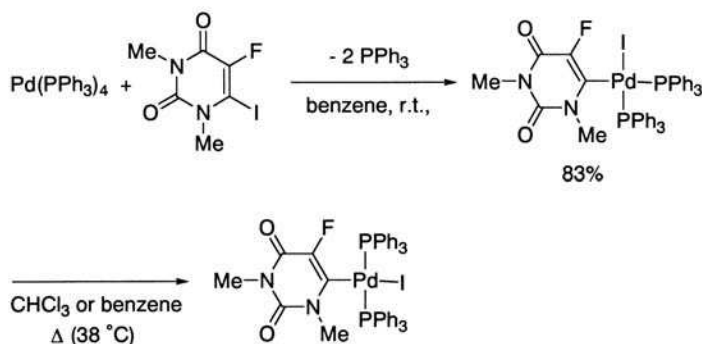
Scheme 3.15.

3.2.4 Stereochemistry of the resulting complex in oxidative addition of organic halides

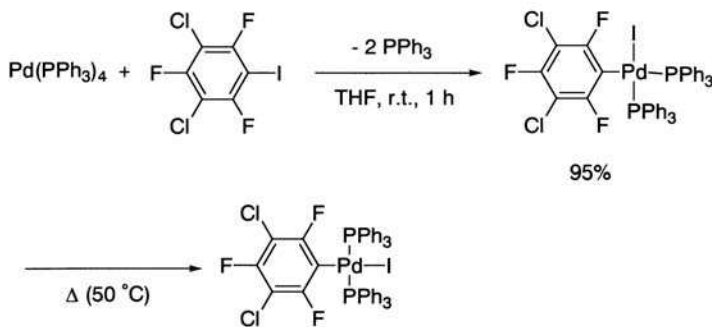
Stereochemistry of the organic and halogen ligands about the metal in the final resulting complex is normally mutually *trans*. If oxidative addition of an organic halide to Vaska's square planar complex proceeds via S_N2 (or S_N2') mechanism, the *trans* configuration of the product is reasonable because resulting halogeno anion would occupy the vacant site *trans* to the alkyl ligand in the 16e square pyramidal intermediate (Scheme 3.15).

However, formation of *cis*-isomer is sometimes observed depending on the substrates and/or complexes. Stereochemistry of the reaction of alkenyl halide with $Pt(PPh_3)_3$ giving exclusively the *trans* product as shown in Scheme 3.14 needs interpretation, because the *cis* product is a logical outcome from the proposed 3-center mechanism. Scheme 3.14 may be the result of *cis*–*trans* isomerization of the product. In fact, initial formation of a *cis* isomer has been demonstrated in the alkenyl carbon-iodine oxidative addition of iodouraciles to $Pd(PPh_3)_4$ (Scheme 3.16) [22].

Another interesting example of oxidative addition giving *cis* configuration is the reaction of $Pd(PPh_3)_4$ with $C_6Cl_2F_3I$ in THF giving *cis*- $Pd(C_6Cl_2F_3)(I)(PPh_3)_2$, which is isolable but spontaneously isomerizes to the more stable *trans*- $Pd(C_6Cl_2F_3)(I)(PPh_3)_2$ under ambient conditions (Scheme 3.17) [23]. This is



Scheme 3.16.



Scheme 3.17.

believed to be a part of proof of the oxidative addition *via* concerted mechanism.

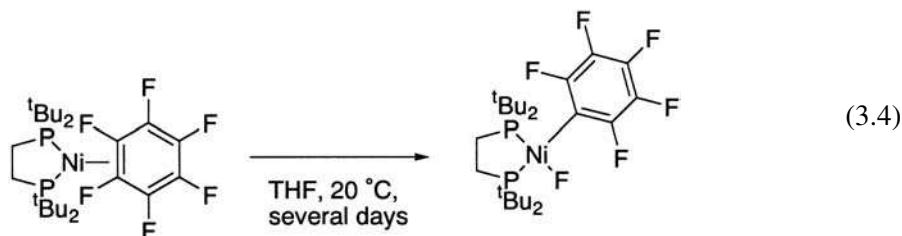
The kinetic study for the reaction outlined in Scheme 3.17 has demonstrated that the isomerization from *cis* to *trans* is significantly retarded by the addition of a small amount of PPh_3 , implying prior dissociation of the coordinated PPh_3 , but the rate constant reaches a constant value at a certain concentration of PPh_3 , suggesting involvement of a concomitant process independent of PPh_3 concentration. Although this isomerization proceeds *via* several different routes, Eyring plot of the total isomerization rate constants gives apparent kinetic parameters with negative entropy of activation ($\Delta S_{\text{iso}}^\ddagger = -21 \text{ J K}^{-1} \text{ mol}^{-1}$), in which a mechanism involving an associative process *via* a four-coordinated μ -iodopalladium dimer $(\text{Ph}_3\text{P})(\text{Ar})(\text{I})\text{Pd}(\mu\text{-I})\text{PdL}_n$ and Berry's pseudo rotations in the penta-coordinated species such as μ -iodopalladium dimer $(\text{Ph}_3\text{P})_2(\text{Ar})(\text{I})\text{Pd}(\mu\text{-I})\text{PdL}_n$ or $\text{Pd}(\text{I})(\text{Ar})(\text{PPh}_3)_2(\text{solvent})$ has been proposed.

As a rare example, oxidative addition *via* ionic mechanism to give the *cis* product is also known [16,17,24]. Oxidative addition of propargyl halides to a zero-valent platinum complex results in *cis*-(halogeno)(η^1 -propargyl)platinum(II) complex as a kinetic product (Scheme 3.10).

3.2.5 Recent topics on carbon–halogen bond cleavage

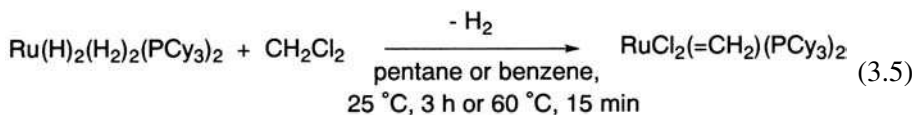
Among carbon–halogen bonds, carbon–fluorine bond is generally regarded as the least reactive bond because of its high bond dissociation energy (for examples, Me-F : 453 kJ/mol, Me-Cl : 350 kJ/mol, Me-Br : 293 kJ/mol, Me-I : 235 kJ/mol [25]). Nevertheless, C–F bond activation currently attracts interests due to possible applications toward the synthesis of fluorinated compounds for MOCVD, the synthesis of ligands for catalysts used in fluorine-based ionic fluids, and the synthesis of biologically inert materials. The oxidative addition of C_6F_6 to $\text{Ni}(\text{cod})(\text{PEt}_3)_2$ with gentle warming ($30\text{--}35^\circ\text{C}$) leads to the formation of *trans*- $\text{NiF}(\text{C}_6\text{F}_5)(\text{PEt}_3)_2$, though the yield is poor (7%) [26]. In these reactions, prior

coordination of η^2 -C₆F₆ species is considered to be a key step for the C–F bond cleavage reaction (Eq. 3.4) [27].



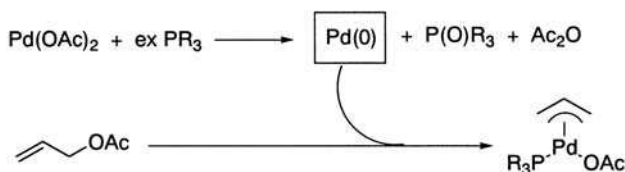
NiEt₂(bpy) is also active toward C–F bond cleavage of C₆F₆, where pre-coordination of electron deficient C₆F₆ to Ni(II) promotes reductive elimination of the ethyl groups to give Ni(0) complex evolving butane, and successive C–F bond oxidative addition gives Ni(F)(C₆F₅)(bpy) followed by disproportionation to afford Ni(C₆F₅)₂(bpy) in 35% yield [28]. Photochemical reactions of group 9 metal complexes such as Cp^{*}Rh(C₂H₄)(PMe₃) and Cp^{*}IrH₂(PMe₃) with C₆F₆ also give Cp^{*}M(F)(C₆F₅)(PMe₃) [29] *via* coordinatively unsaturated ‘Cp^{*}M(PMe₃)’ species. On the other hand, thermal reaction of Cp^{*}RhH₂(PMe₃) with C₆F₆ in pyridine gives Cp^{*}Rh(H)(C₆F₅)(PMe₃). This complex is probably formed by the initial deprotonation by pyridine to give [Cp^{*}Rh(H)(PMe₃)][–], whose nucleophilic attack to the electron deficient C₆F₆ affords Cp^{*}Rh(H)(C₆F₅)(PMe₃) [30]. One of the problems for the C–F bond cleavage of partially fluorinated organic compound is the concomitant C–H bond cleavage. Very recently, facile orthometallation reaction of *ortho*-C–F bond over *ortho*-C–H bond in aromatic ketones such as fluorinated benzophenones has been shown experimentally as well as by DFT calculations [31]. This may arise from thermodynamic stability of the product.

Another recent topic in carbon–halogen bond cleavage is double oxidative addition of C–Cl bond to a single metal center. Although it is well known that *gem*-dihalogen compound acts as a synthon of carbene, double oxidative addition of these compounds to transition metal complexes has been less explored. The double oxidative addition of C–Cl bonds in CH₂Cl₂ to Ru(H)₂(H₂)₂(PCy₃)₂ affords RuCl₂(=CH₂)(PCy₃)₂, which is known to act as an efficient metathesis polymerization catalyst (Eq. 3.5) [32].



3.3 CARBON–OXYGEN BOND CLEAVAGE REACTIONS

Carbon–oxygen bond cleavages are particularly attractive in relation to development of environmentally benign halogen-free processes and are frequently



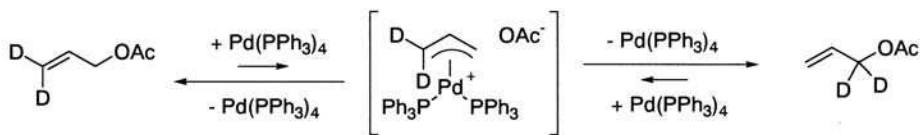
Scheme 3.18.

encountered in palladium-catalyzed organic reactions [33–36]. Allylic alkylation, allylation of nucleophiles, and carbonylation of allylic compounds are typical examples of this type. In many cases, it is assumed that η^3 -allylpalladium(II) complex is formed by oxidative addition of the allylic ester to the putative zero-valent palladium species formed *in situ* from Pd(II) (Scheme 3.18).

Although formation of zero-valent palladium complexes has been unequivocally established in the reaction of Pd(II) such as Pd(OAc)₂ with tertiary phosphine [5] or electron deficient olefins [37], the studies on oxidative addition of oxygen-containing compounds such as carboxylate, carbonates, carboxylic anhydrides, ethers, epoxides, acetals, and alcohols are still relatively less explored to date. This section deals with the C–O bond cleavage reactions promoted by transition metal complexes. Some organic reactions involving carbon–oxygen bond cleavage are also described.

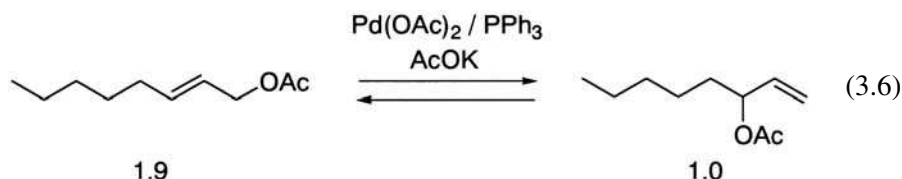
3.3.1 C–O bond oxidative addition of allyl carboxylates

Carbon–oxygen bond oxidative addition of allylic esters has been frequently assumed in the Pd-catalyzed allylation processes. However, the explicit examples of such oxidative addition were not known until the 1980s. One of main reasons for this may arise from the fact that no apparent reaction occurs between zero-valent palladium complexes such as Pd(PPh₃)₄ or Pd(CH₂=CH₂)(PPh₃)₂ and allyl carboxylates even at 80°C, although allyl carboxylates are usually used as reagents in these catalytic reactions. However, when CD₂=CHCH₂OAc is treated with Pd(PPh₃)₄, equal amounts of CD₂=CHCH₂OAc and CH₂=CHCD₂OAc are produced at room temperature, suggesting that fast C–O bond cleavage and formation are actually taking place under the reaction conditions (Scheme 3.19) [38].

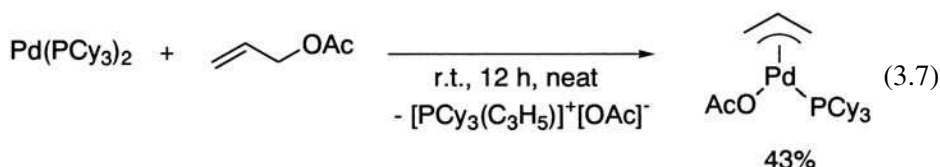


Scheme 3.19.

Similar 1,3-acetato shift reaction had also been known by $\text{Pd}(\text{OAc})_2/\text{PPh}_3$ system as shown in Eq. 3.6 [39].

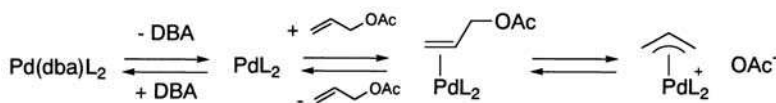


The first example of C–O bond oxidative addition has been observed by use of a coordinatively unsaturated palladium(0) complex having basic bulky phosphine ligands, $\text{Pd}(\text{PCy}_3)_2$ at room temperature to give $\text{Pd}(\eta^3\text{-allyl})(\text{PCy}_3)(\text{OAc})$ accompanied by formation of a phosphonium salt, $\text{Cy}_3\text{P}(\text{CH}=\text{CHMe})^+(\text{OAc})^-$ (Eq. 3.7) [38]. Thus a series of $\eta^3\text{-allyl}$ palladium(II) complexes are isolated by the reactions of $\text{Pd}(\text{PCy}_3)_2$ with various allylic acetates.

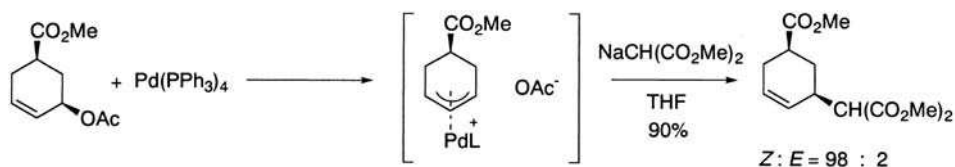


Oxidative addition of allylic ester is considered to proceed *via* $\text{S}_{\text{N}}2'$ mechanism including *anti* side attack to the allyl moiety as described in the carbon halogen bond oxidative addition [33,34]. However, detailed mechanistic investigation by UV and electric conductivity for the reaction of allyl acetate with a zero-valent palladium complex $\text{Pd}(\text{dba})_2$ (dba = dibenzylideneacetone) in the presence of tertiary phosphines reveals presence of a neutral short-lived intermediate ($t_{1/2} = 8\text{--}25$ s) [40]. This finding may suggest prior coordination of allyl acetate to the coordinatively unsaturated 14e species PdL_2 , giving a zero-valent complex $\text{Pd}(\eta^2\text{-CH}_2=\text{CHCH}_2\text{OAc})\text{L}_2$ followed by the C–O bond cleavage. As shown in Scheme 3.20, these successive reactions are in equilibrium, in which the cationic $\eta^3\text{-allyl}$ palladium(II) complex is more favored in the following order: $\text{L}_2 = \text{DPPB} > \text{DPPF} > (\text{PPh}_3)_2$. [DPPB = 1,4-bis(diphenylphosphino)butane, DPPF = 1,1'-bis(diphenylphosphino)ferrocene.]

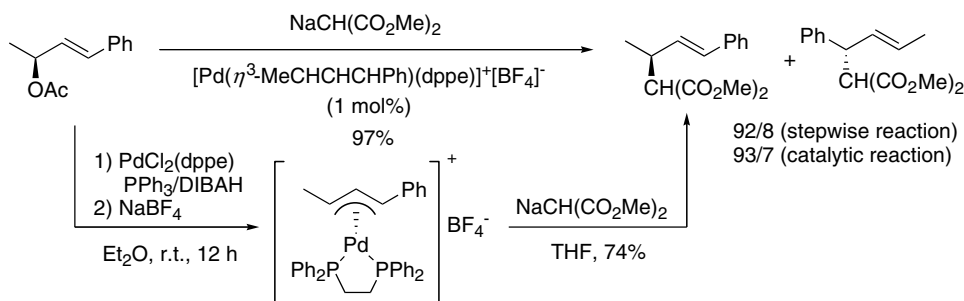
Stereochemistry of the C–O bond cleavage has been initially elucidated indirectly by the following experiments. Catalytic C–C bond formation reaction of (*Z*)-3-acetoxy-5-carbomethoxycyclohexene with sodium dimethyl malonate



Scheme 3.20.



Scheme 3.21.



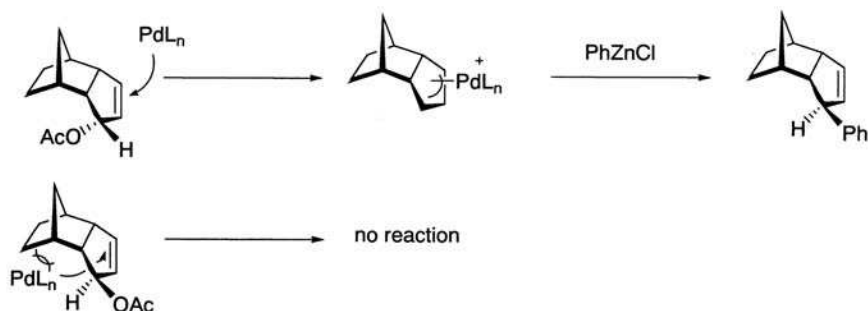
Scheme 3.22.

promoted by $\text{Pd}(\text{PPh}_3)_4$ in the presence of PPh_3 dominantly yields the *Z*-product. The net retention of configuration is interpreted by the formation of η^3 -allylpalladium(II) complex with inversion of configuration, followed by the nucleophilic attack by malonate from the *exo*-face (Scheme 3.21) [41].

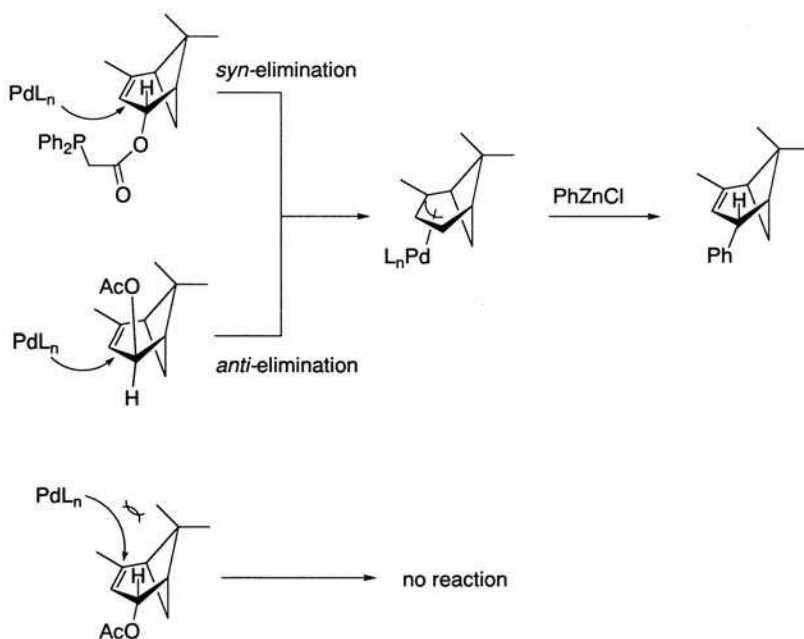
Stereochemistry of oxidative addition of allylic acetate to a $\text{Pd}(0)$ complex was unequivocally confirmed by using optically active substrate (Scheme 3.22) [42]. The oxidative addition resulted in the formation of enantiomerically pure η^3 -allylpalladium(II) complex showing inversion of configuration. Further treatment of the isolated η^3 -allylpalladium(II) complex with sodium dimethyl malonate led to the alkylation with inversion of configuration. Consistently, the catalytic reaction gave net retention product. This is a direct evidence for the stereochemistry of oxidative addition and alkylation.

Another indirect evidence for the *anti* elimination of the leaving group is obtained by use of a sterically regulated allylic compound as shown in Scheme 3.23. While the *endo*-acetate reacts with zero-valent palladium complex to give the *exo*-product via η^3 -allylpalladium intermediate after the treatment with PhZnCl , the *exo*-acetate remains intact because of the steric congestion of the substrate at the reaction site [43]. It is known that PhZnCl attacks the η^3 -allylpalladium from the palladium side (*syn* addition). This fact also suggests the importance of prior coordination of the $\text{C}=\text{C}$ bond to palladium(0) from the opposite face of the leaving group.

As shown above, the *anti*-elimination is normally the lower energy process for the allylic C–O bond cleavage by low-valent palladium complexes. However, if



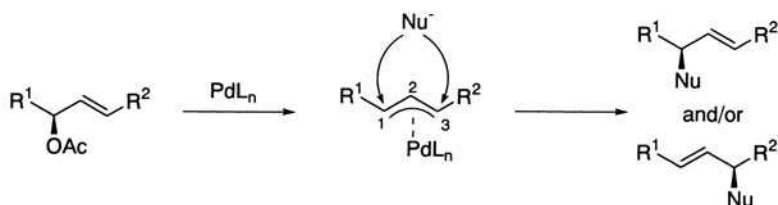
Scheme 3.23.



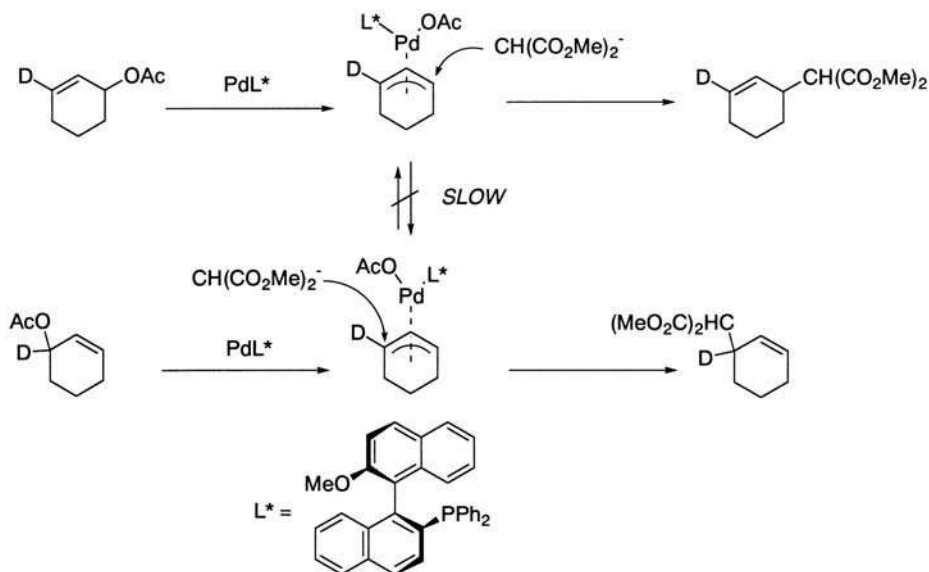
Scheme 3.24.

the incoming palladium complex is forced to approach the allylic moiety from the leaving group side (*syn*-face), *syn*-elimination for the C–O bond cleavage also takes place. Phosphinoacetate $\text{PPh}_2\text{CH}_2\text{CO}_2$ guides the direction for the attack of the palladium complex from the *syn*-face by facile coordination of the phosphorus atom, and thus promotes the *syn*-elimination of the leaving group (Scheme 3.24) [44].

Once oxidative addition of allylic carboxylate occurs to form η^3 -allyl-palladium(II) complex, both α - and γ -carbons of the allylic moiety are susceptible to attack of various nucleophiles to give products, where allylation usually takes place at the less-hindered side of the η^3 -allylic ligand (Scheme 3.25).



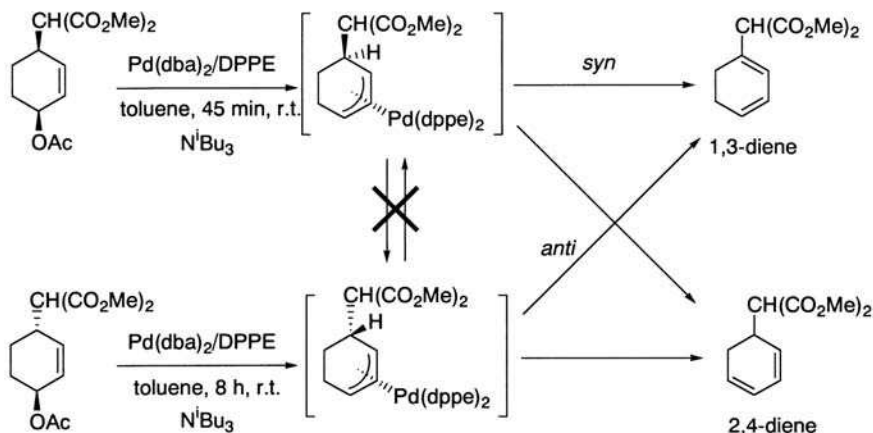
Scheme 3.25.



Scheme 3.26.

Regioselectivity of the product can be controlled by the use of bulky monodentate ligand such as 2-(diphenylphosphino)-2'-methoxy-1,1'-binaphthyl (MeO-MOP) as shown in Scheme 3.26 [45]. The key steps in this reaction are selective *anti*-elimination of the acetate, to form η^3 -allylic complex, which is attacked by the carbanion at the site *trans* to the phosphine ligand from the *exo*-face. The observed regioselectivity may be due to the enhanced positive charge at the carbon *trans* to the phosphine [46]. More details on the regiochemical control of nucleophilic attack of η^3 -allyl complexes are given in Chapter 8.

In the case of C–O bond cleavage of allylic carboxylate, the resulting η^3 -allylic complex sometimes gives the conjugated diene by subsequent elimination of a hydrogen at the homoallylic position. The following study suggests the formation mechanism of the conjugated diene [47,48]. As shown in Scheme 3.27, treatment of *cis*-cyclic acetate with Pd(0) and successive elimination of acetic acid gives a mixture of 2,4-diene and 1,3-diene in 88:12 ratio both *via syn* H-elimination, respectively. On the other hand, similar treatment with the *trans*-allylic acetate



Scheme 3.27.

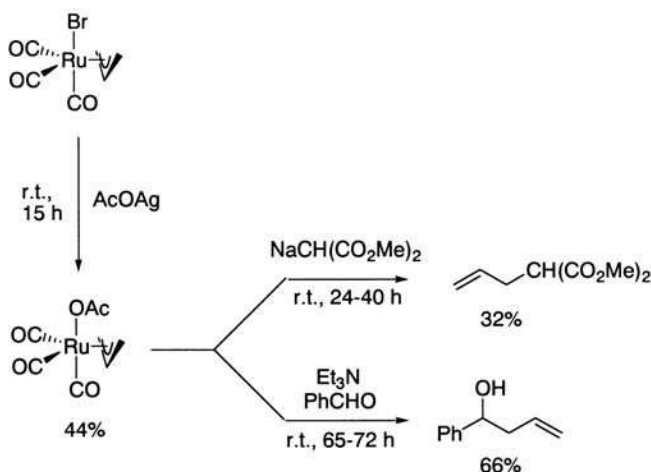
also gives an analogous mixture in 62 : 38. In the case of reaction of the *trans*-allylic acetate, the resulting η^3 -allylpalladium has the malonate group in the *endo*-face. Although the normal *cis*- β -hydrogen elimination should give only 2,4-diene [49], the observed result shows occurrence of *trans*-elimination process to give a significant amount of the 1,3-diene. Since no interconversion of the (η^3 -allyl)palladium intermediates is observed under these conditions, involvement of base-assisted *anti*-elimination mechanism has been proposed [50,51].

Ruthenium complexes attract recent interest as new promising candidates for efficient, specific and environmentally benign allylation catalysts. It is noticeable that some η^3 -allylruthenium(II) complexes have an ambiphilic property in catalysis involving the C–O bond activation [52]. When allyl carboxylates or carbonates are treated with nucleophilic 1,3-dicarboxylates or electrophilic aldehyde in the presence of Ru complexes, catalytic allylations of nucleophiles or electrophiles take place [53]. In both reactions, η^3 -allylruthenium complexes are assumed to be intermediates. Independent synthesis and reactions of the model compounds support this observation (Scheme 3.28). This ambiphilicity of the allylruthenium(II) may arise from the different reactivity of η^1 and η^3 forms in the allylic moiety [54].

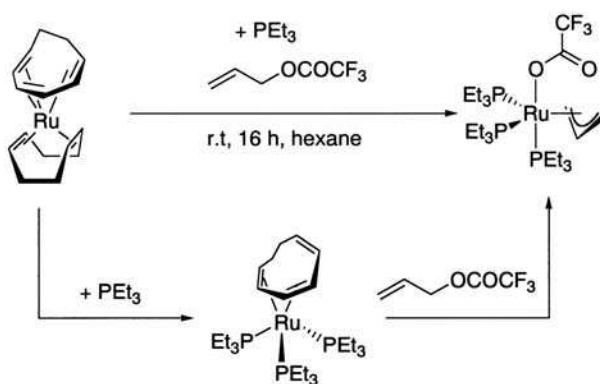
Direct evidence for the oxidative addition of allyl carboxylates to a zero-valent ruthenium complex with the allyl–O bond cleavage, has been obtained by the reaction of Ru(cod)(cot) ($\text{cot} = 1,3,5\text{-cyclooctatriene}$) with allyl carboxylates in the presence of tertiary phosphine under ambient conditions to give $\text{Ru(OCOR)(}\eta^3\text{-C}_3\text{H}_5\text{)}\text{L}_3$ [55], where $\text{Ru}(\eta^4\text{-C}_8\text{H}_{10})\text{L}_3$ acts as an intermediate for the reaction (Scheme 3.29) [56].

3.3.2 C–O bond oxidative addition of vinyl carboxylates

Oxidative addition of vinyl carboxylates with the vinyl–O bond cleavage is much less explored to date than that of allyl carboxylates. Reaction of vinyl

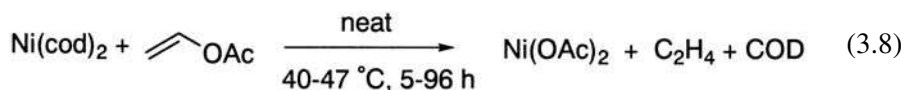


Scheme 3.28.

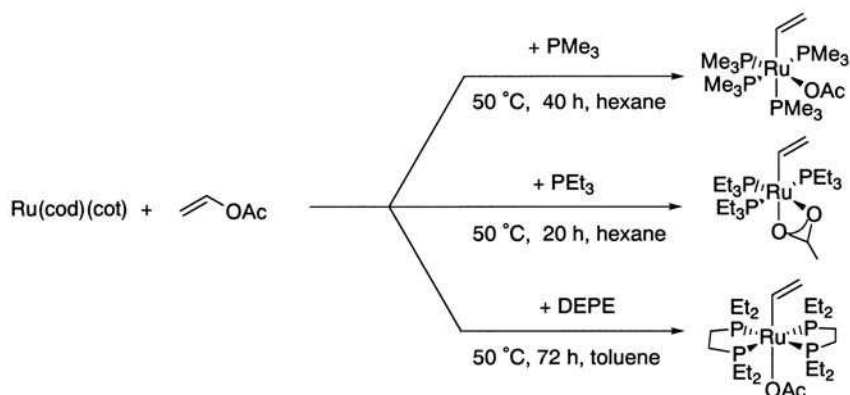


Scheme 3.29.

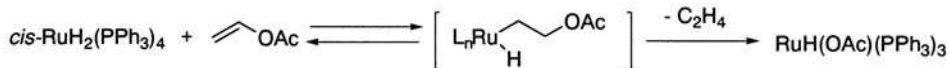
acetate with $\text{Ni}(\text{cod})_2$ in the presence or absence of tertiary phosphine liberates ethylene with formation of $\text{Ni}(\text{OAc})_2$ (Eq. 3.8) [57].



Although no vinylnickel species is detected at all in this C–O bond cleavage, oxidative addition of vinyl acetate is proposed to be an initial step of the reaction. An explicit example of C–O bond oxidative addition of vinyl acetate is observed in the reaction of $\text{Ru}(\text{cod})(\text{cot})$ in the presence of tertiary phosphines such as PMe_3 , PEt_3 and DEPE to give *cis*- $\text{Ru}(\text{C}_2\text{H}_5)(\kappa^1\text{-OAc})(\text{PMe}_3)_4$, *mer*- $\text{Ru}(\text{C}_2\text{H}_5)(\kappa^2\text{-OAc})(\text{PEt}_3)_3$ and *trans*- $\text{Ru}(\text{C}_2\text{H}_5)(\kappa^1\text{-OAc})(\text{depe})_2$, respectively (Scheme 3.30) [58,59].



Scheme 3.30.



Scheme 3.31.

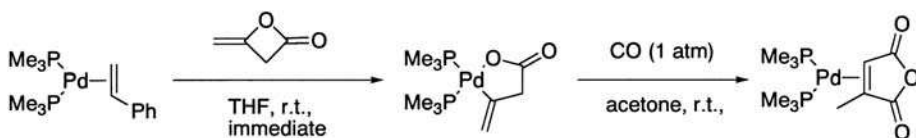
C–O bond cleavage of alkenyl carboxylates such as vinyl and allyl carboxylates can also be achieved by transition metal hydrides. For example, a divalent ruthenium dihydride complex $\text{cis-RuH}_2(\text{PPh}_3)_4$ reacts with vinyl acetate to give $\text{cis-Ru}(\text{H})(\text{OAc})(\text{PPh}_3)_4$ accompanied by evolution of ethylene (Scheme 3.31) [60]. This reaction is proposed to involve insertion of the $\text{C}=\text{C}$ bond into the $\text{Ru}-\text{H}$ to give a β -acetoxyethylruthenium(II) intermediate (1,2-addition) followed by the β -acetato elimination to yield the products. C–O bond oxidative addition of vinyl acetate to give hydrido(vinyl)ruthenium(IV) followed by reductive elimination of ethylene is also a possible alternative mechanism.

Unexpected 2,1-addition of $\text{Ru}-\text{H}$ bond across the $\text{C}=\text{C}$ bonds of ethyl vinyl ether [61], vinyl acetate [62] and vinyl chloride [63] followed by α -hydrido, α -acetato and α -chloro eliminations, respectively, to give carbene complexes has been also known.

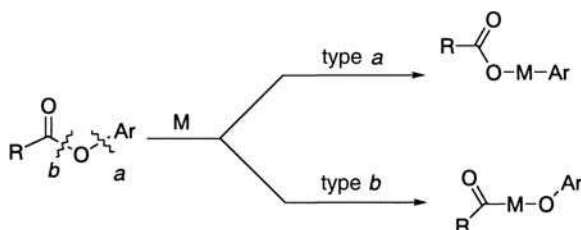
Palladium(0) complex is known to cleave the C–O bond of diketene to form palladalactone complex (Scheme 3.32). Interestingly, exposure of the palladalactone to atmospheric CO leads to successive CO insertion into the $\text{Pd}-\text{C}$ bond and proton migration to form a zero-valent maleic anhydride complex [64].

3.3.3 C–O bond cleavage of aryl and benzyl carboxylates

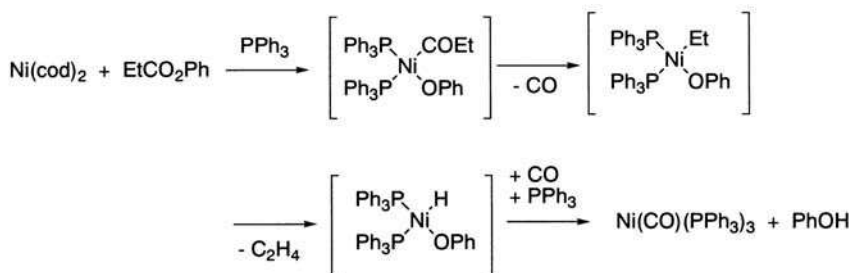
As shown above, C–O bonds in carboxylates such as allylic or vinylic esters are dominantly cleaved at the $\text{RC}(\text{O})\text{O}-\text{R}'$ bond by low-valent transition metal



Scheme 3.32.



Scheme 3.33.



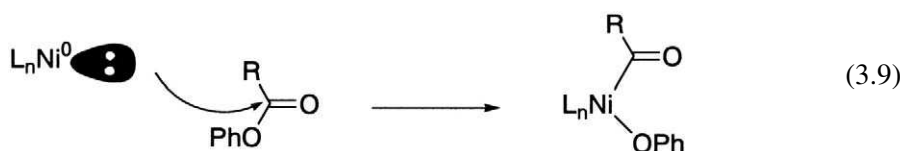
Scheme 3.34.

complexes giving (carboxylato)(organo)metal complex (type a in Scheme 3.33). However, the cleavage of $\text{RC}(\text{O})-\text{OR}'$ bond is rather popular for aryl carboxylates leading to (acyl)(aryloxo)metal complex (type b).

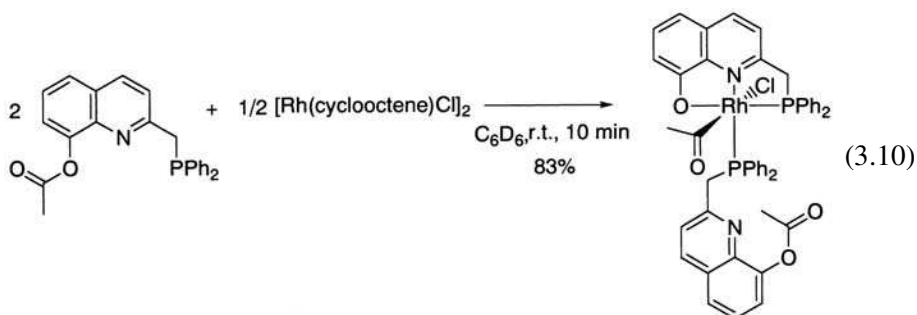
For example, the acyl-aryloxo bond cleavage (type b) is shown by the reaction of $\text{Ni}(\text{cod})_2$ with phenyl propionate in the presence of PPh_3 (Scheme 3.34) or 2,2'-bipyridine [65]. The reaction products are ethylene, phenol, and (carbonyl)nickel complex. Formation of these products is conveniently understood by initial oxidative addition of $\text{EtC}(\text{O})-\text{OPh}$ followed by decarbonylation, β -hydrogen elimination and reductive elimination, though (acyl)(aryloxo)nickel(II) intermediate is not isolated. However, such an intermediate is isolated by the selective insertion of CO into the (alkyl)(aryloxo)nickel (or palladium) complexes, which smoothly affords esters by reductive elimination promoted by electron deficient olefins. The results suggest that the oxidative addition involving C-O bond cleavage is essentially reversible.

The kinetic studies reveal that the oxidative addition of $\text{RC}(\text{O})-\text{OAr}$ bond

is well understood as the nucleophilic attack of the zero-valent nickel to the carboxylic carbon (Eq. 3.9).

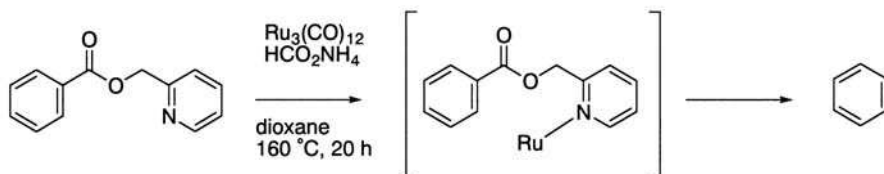


Recently, use of an electron donating and rigid PN ligand with a pendant carboxylate made possible to isolate the (acyl)(aryloxo)rhodium(III) complex by oxidative addition (Eq. 3.10) [66]. This reaction probably occurs *via* prior coordination to the Rh(I) center by the P and N atoms, by which the adjacent carboxylate is forced to approach the Rh(I) center. This reaction proceeds quite quickly to be completed within 10 min at room temperature.

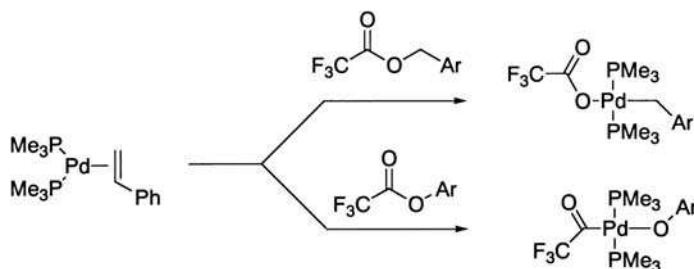


Contrary to aryl carboxylates, benzyl carboxylates generally undergo type a scission. However, the pyridinomethyl esters also effectively guide the bond cleavage of type b probably *via* intramolecular coordination (Scheme 3.35) [67]. Since decarbonylation from the resulting acyl group rapidly occurs in this system, catalytic decarboxylation takes place in the presence of ammonium formate as a hydride source.

Trifluoroacetates also oxidatively add to Pd(0) complex (Scheme 3.36) [68]. A zero-valent Pd complex Pd(styrene)(PMe₃)₂ cleaves the RC(O)O–R bond of benzyl trifluoroacetate to give (trifluoroacetato)(benzyl)palladium(II) complex, whereas the RC(O)–OAr bond of aryl trifluoroacetate is cleaved under the same conditions leading to (aryloxo)(trifluoroacyl)palladium(II) complex. Thus, nature



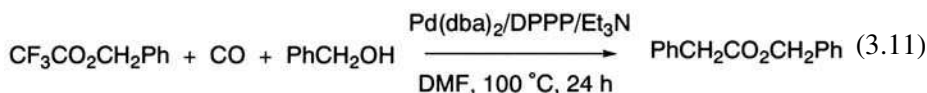
Scheme 3.35.



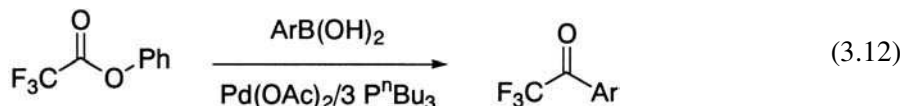
Scheme 3.36.

of the ester group is considered to control the selectivity of type a and b bond cleavages.

Catalytic applications of these C–O bond cleavage reactions are relatively well documented. Carbonylation of benzyl trifluoroacetate gives benzyl phenyl acetate by $\text{Pd}(\text{dba})_2/\text{DPPP}$ [DPPP = 1,2-bis(diphenylphosphino)propane] in the presence of NEt_3 (Eq. 3.11) [68]. This reaction is considered to proceed by initial carboxylato–benzyl $[\text{RC}(\text{O})\text{O}-\text{R}]$ bond cleavage to give (trifluoroacetato)(benzyl)palladium(II) complex, followed by CO insertion into the Pd–benzyl bond and then nucleophilic attack by benzyl alcohol to give the product.



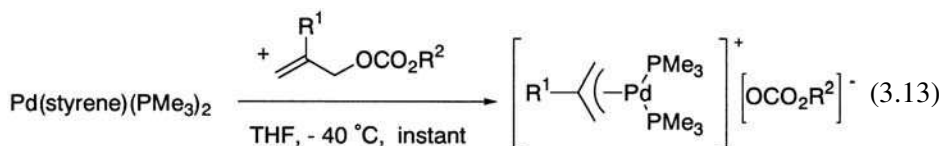
Catalytic synthesis of aryl trifluoromethyl ketone *via* $\text{RC}(\text{O})-\text{OAr}$ bond cleavage is also known. Combination of $\text{Pd}(\text{OAc})_2$ with 3 equiv of P^nBu_3 catalyzes the formation of aryl trifluoromethyl ketone from phenyl trifluoroacetate and arylborane (Eq. 3.12) [69]. This reaction is interpreted by $\text{RC}(\text{O})-\text{OPh}$ bond oxidative addition to give (acyl)(phenoxo)palladium(II) complex, followed by metathesis (transmetallation) of phenoxopalladium species with arylborane and reductive elimination of acyl and aryl carbons to form the product.



3.3.4 C–O bond cleavage of allyl carbonates

Transition metal catalyzed allylation by using allylic carbonates is one of the most versatile allylation methods. The Pd-catalyzed reaction is believed to proceed by the following mechanism. First of all, oxidative addition of the C–O bond to Pd(0) gives $(\eta^3\text{-allyl})(\text{carbonato})\text{palladium}(\text{II})$ complex, which undergoes decarboxylation to give the alkoxo complex [70]. The resulting $(\eta^3\text{-allyl})(\text{alkoxo})\text{palladium}(\text{II})$ complex immediately reacts with nucleophiles (HNu)

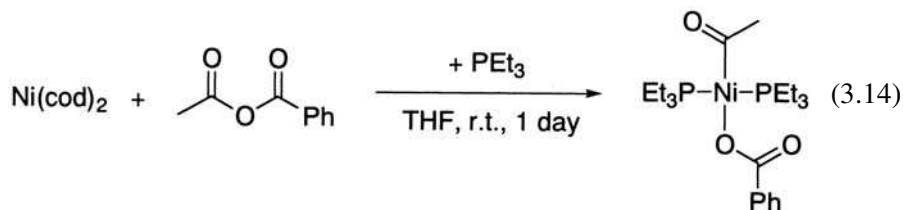
or CO to give the corresponding products (allyl–Nu or allyl–CO₂R) under catalytic conditions. However, isolation of the oxidative addition product was relatively difficult due to facile succeeding reactions. The unambiguous example for the oxidative addition of allyl carbonate has been demonstrated by using electron donating and compact PMe₃ ligand (Eq. 3.13) [71].



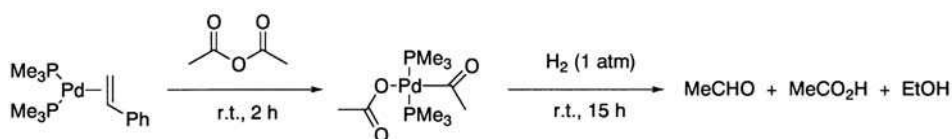
In this reaction, the oxidative addition of the C–O bond of allyl carbonate gave a cationic η^3 -allylpalladium(II) complex with carbonate anion. The resulting carbonate anion is extremely nucleophilic, so that the carbonate anion is easily replaced by chloride in the chlorinated solvent such as CH₂Cl₂ or CHCl₃.

3.3.5 C–O bond cleavage of carboxylic anhydride

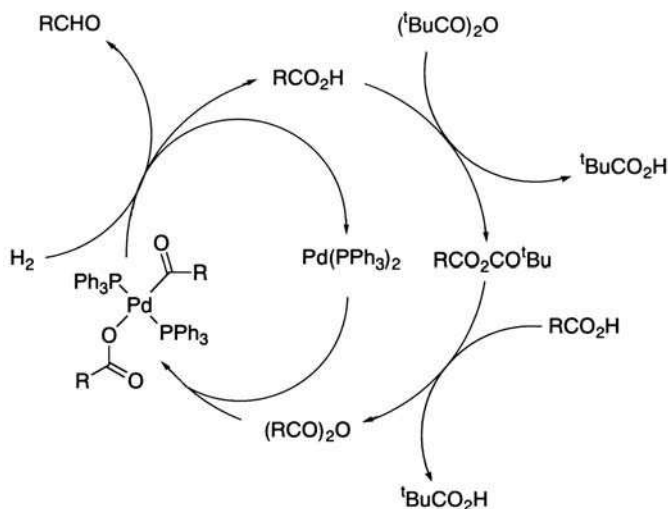
Carboxylic anhydrides also oxidatively add to zero-valent group 10 metal complexes. Reaction of Ni(cod)₂ with MeCO₂COPh in the presence of PEt₃ results in the regioselective oxidative addition of the MeCO–OC(O)Ph bond to give *trans*-Ni(COME)(OCOPh)(PEt₃)₂ (Eq. 3.14) [72].



Such oxidative addition of carboxylic anhydride also takes place to electron rich Pd(0) complexes, and hydrogenolysis of the resulting complex gives corresponding aldehyde and carboxylic acid. For example, reaction of Pd(styrene)(PMe₃)₂ with acetic anhydride leads to oxidative addition of the C–O bond to give (acetyl)(acetato)palladium(II) complex, which reacts with atmospheric H₂ to give acetaldehyde, acetic acid, and ethanol (Scheme 3.37) [73]. Ethanol may be produced by reduction of acetaldehyde.



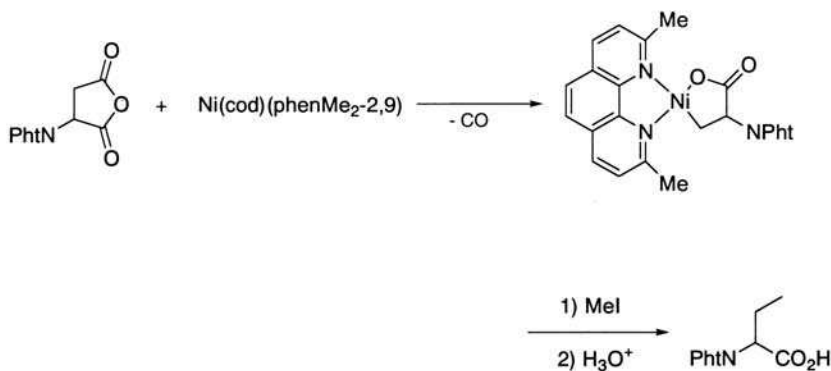
Scheme 3.37.



Scheme 3.38.

This reaction is applied to catalytic conversion of carboxylic acids to aldehydes in the presence of pivalic anhydride under H_2 (3 MPa) (Scheme 3.38) [74]. In this system, bulky pivalic anhydride is slow to react with $\text{Pd}(0)$ complex for kinetic reasons, but it is used to reproduce carboxylic anhydride from the generated acid.

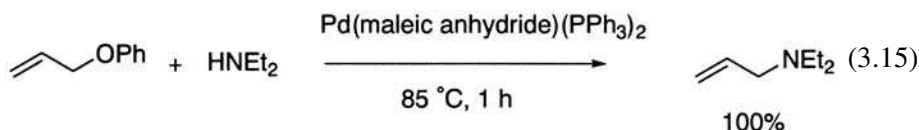
The oxidative addition of cyclic carboxylic anhydride with C–O bond cleavage is also well documented. For example, reaction of *N*-phthaloylaspartic anhydride with $\text{Ni}(\text{cod})(\text{Me}_2\text{phen-2,9})$ at room temperature results in the formation of nickelalactone in high yield, where regioselective oxidative addition of the acid anhydride takes place, and the decarbonylation gives the product (Scheme 3.39) [75]. Treatment of the nickelalactone with organic halides gives *N*-phthaloylamino acids.



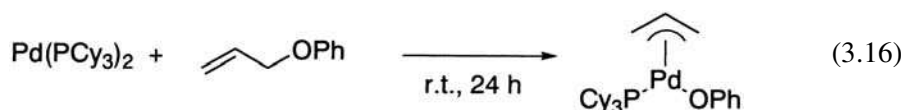
Scheme 3.39.

3.3.6 C–O bond cleavage of ethers

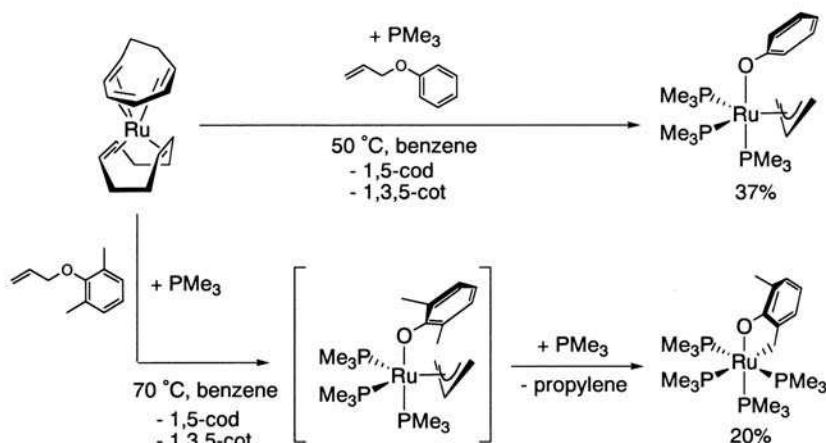
Similar to carboxylates and carbonates, the C–O bond cleavage of allylic ethers with low-valent metal complexes relatively is well documented (Eq. 3.15). Typical example is demonstrated in the reaction of group 10 metal complexes such as Pd or Ni resulting in the clean allyl–O bond cleavage [76].



Although oxidative addition of allyl phenyl ether smoothly takes place by Pd(PCy₃)₂ (Eq. 3.16), alkyl allyl ether is unreactive [38]. This sharp contrast may be due to the difference of stability in the resulting phenoxo- and alkoxo-complexes.



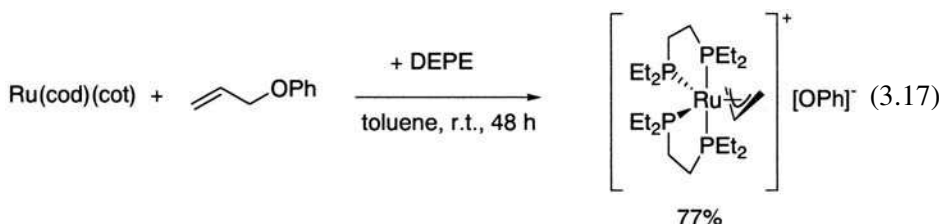
Oxidative addition of allyl and vinyl ethers to zero-valent ruthenium complex also takes place under mild conditions. The reaction of Ru(cod)(cot) [cod = 1,5-cyclooctadiene, cot = 1,3,5-cyclooctatriene] with allyl phenyl ether or phenyl *ortho*-tolyl ether in the presence of PMe₃ results in cleavage of the C–O bond to give a (η³-allyl)(aryloxo)ruthenium(II) complex, Ru(OAr)(η³-C₃H₅)(PMe₃)₃ (Scheme 3.40) [77]. When allyl 2,6-xylyl ether is employed in this reaction, further C–H bond activation takes place to give an oxaruthenacycle



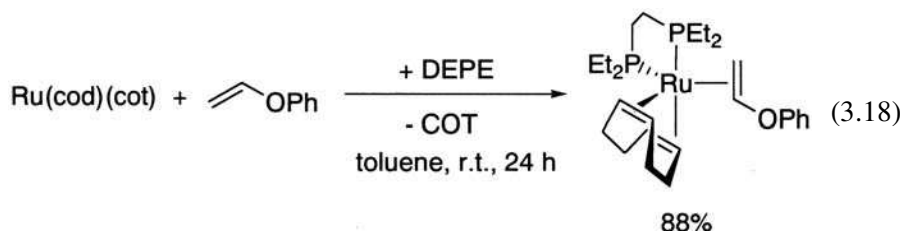
Scheme 3.40.

complex $cis\text{-Ru}[\overline{\text{OC}_6\text{H}_3(2\text{-CH}_2)(6\text{-Me})}](\text{PMe}_3)_4$ with concomitant evolution of propylene.

When a bidentate phosphine such as DEPE [DEPE = 1,2-bis(diethylphosphino)ethane] is employed in the reaction with allyl ether, cationic complex $[\text{Ru}(\eta^3\text{-C}_3\text{H}_5)(\text{depe})]^+[\text{Oph}]^-$ is obtained (Eq. 3.17) [55b].

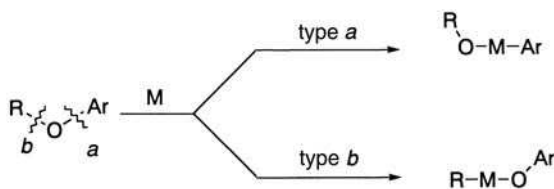


Contrary to the allyl phenyl ether, phenyl vinyl ether reacts with $\text{Ru}(\text{cod})(\text{cot})$ in the presence of PMe_3 to give a cationic dinuclear tri- μ -hydroxo complex $[(\text{Me}_3\text{P})_3\text{Ru}(\mu\text{-OH})_3\text{Ru}(\text{PMe}_3)_3]^+[\text{H}(\text{Oph})_2]^-$ with evolution of ethylene. Formation of ethylene- d_1 in the presence of D_2O suggests the formation of vinylruthenium species in this reaction [78]. On the other hand, similar treatment with a bidentate phosphine DEPE does not cause the C–O bond cleavage but gives a zero-valent complex $\text{Ru}(\eta^2\text{-C}_2\text{H}_3\text{OPh})(\text{cod})(\text{depe})$ (Eq. 3.18) [79].

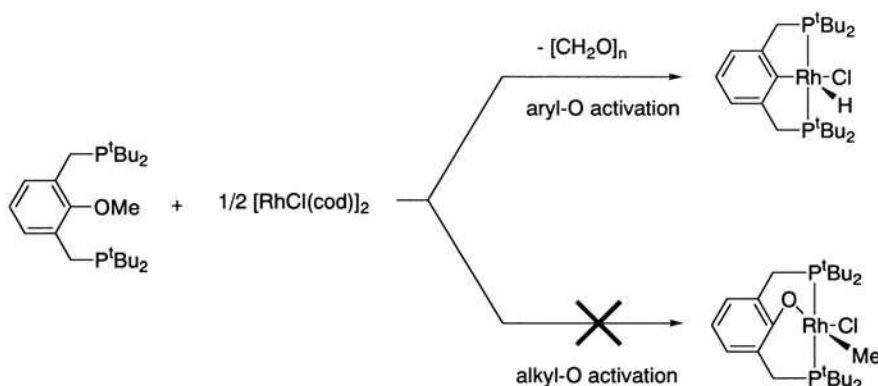


C–O bond in alkyl aryl ethers is more resistant toward cleavage than that in allyl or vinyl ethers. In alkyl aryl ethers such as anisole, activation of RO–Ar bond (type a in Scheme 3.41) is difficult in comparison with that of R–OAr bond (type b), probably because the relatively stronger bond dissociation energy of the aryl–O bond than that of alkyl–O bond due to aromatic conjugation as well as higher stability of aryloxo-metal products.

For example, treatment of $\text{FeH}(2\text{-naphthyl})(\text{dmpe})_2$ with anisole leads to the

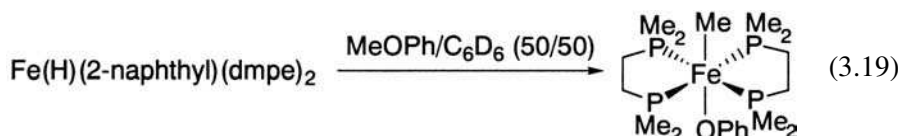


Scheme 3.41.



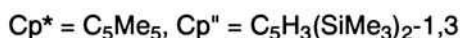
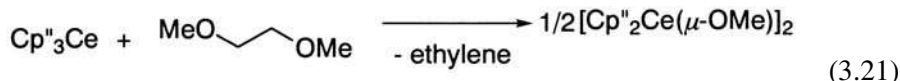
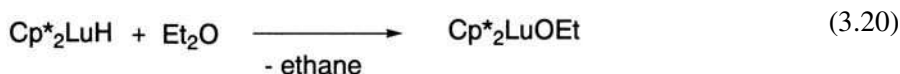
Scheme 3.42.

Me–OPh cleavage giving *trans*-FeMe(OPh)(dmpe)₂ as a thermodynamic product, indicating type b scission (Eq. 3.19) [80].

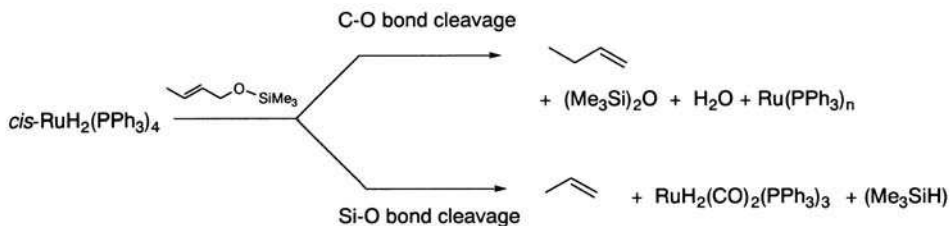


When the bond is forced to be placed proximately to Rh center as shown in Scheme 3.42, exclusive cleavage of the aryl–O bond (type a) takes place [81]. The reaction mechanism for the aryl–O bond cleavage by Rh(I) is proposed as follows: the Rh(I) inserts into the aryl–O bond *via* η^2 -arene intermediate, followed by 1,2-migration of the methoxy group from aryl carbon to the Rh center, and then β -hydrogen is smoothly eliminated.

The C–O bond cleavage of dialkyl ethers is much more difficult than that of alkyl aryl ethers. Nevertheless some lanthanoid complexes are known to cleave C–O bond of diethyl ether (Eq. 3.20) or dimethoxyethane (Eq. 3.21) to give ethoxide complexes [82,83].



The C–O bond cleavage of alkenyl silyl ethers is known to take place at room temperature by transition metal hydride such as *cis*-RuH₂(PPh₃)₄, CoH(N₂)(PPh₃)₃ and RhH(PPh₃)₄ [84]. Since the isomerization of allyl silyl

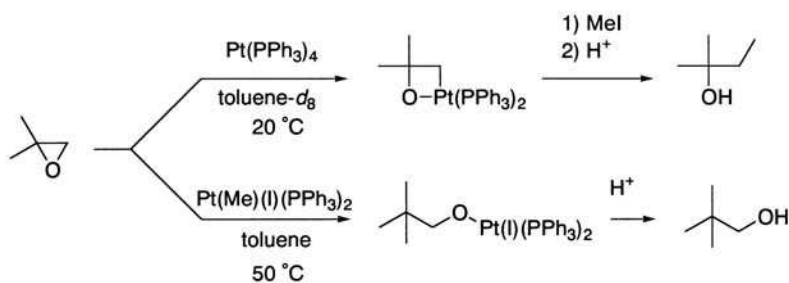


Scheme 3.43.

ethers to alkenyl silyl ethers takes place by these hydride complexes [85], the C–O bond is probably cleaved by the prior insertion of the C=C bond into the metal–hydride bond followed by β -siloxo elimination to give olefins (Scheme 3.43). Interestingly, when PPh₃ is added to the reaction system, the C–O bond cleavage path is blocked, and instead the Si–O bond is cleaved to give organosilane and carbonyl complex, which is probably formed by subsequent β -hydrogen elimination from alkoxo complex releasing aldehyde, followed by formation of acyl complex, via oxidative addition of aldehyde, and decarbonylation. This dramatic change in the C–O/Si–O bond cleavage is explained by difference of the mechanism, where the Si–O bond cleavage occurs by direct sigma bond metathesis reaction, while the prior coordination is prerequisite for the C–O bond cleavage.

3.3.7 C–O bond cleavage of epoxides

Although the C–O bond cleavage of epoxides takes place by simple bases and acids, transition metal mediated C–O bond cleavage has also been studied in relation to catalytic and stoichiometric reactions such as polymerization, isomerization, the C–C bond formation, deoxygenation and ring expansion reactions. For unsymmetrical epoxides, the regioselectivity of the C–O bond cleavage is of particular interest. Simple organic nucleophiles are known to attack the less substituted carbon atom of the epoxide in neutral or basic media as anticipated for a normal S_N2 process and the more substituted carbon tends to react in acidic media because of the higher stability of the carbocation product by prior protonation [86]. For transition metal mediated C–O bond cleavage of epoxides, the regioselectivity is found to be affected by the metal valency. A zero-valent group 10 metal complexes such as Ni(PPh₃)₄ and Pt(PPh₃)₄ cleave the less substituted C–O bond of the epoxide to form tertiary alcohol or ketone *via* oxametallacycle complex (Scheme 3.44). In contrast, di-valent group 10 complexes such as PtMeI(PPh₃)₂ cleave the more substituted C–O bond of the epoxide to form primary alcohol or alkoxide [87]. These reactions can be understood by preferential attack of highly basic zero-valent metal complexes to the less substituted carbon giving an oxametallacycle, but the di-valent group 10 metal complexes attack the oxygen atom as a Lewis acid so as to afford more stable highly substituted

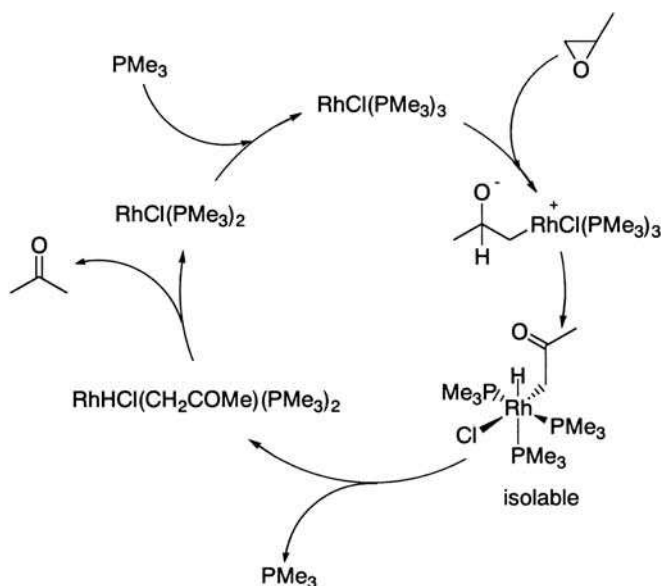


Scheme 3.44.

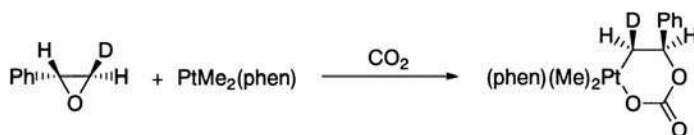
carbocation followed by methyl migration. Thus, it is presumed that zero-valent complex behaves as a Lewis base and di-valent complex acts as a Lewis acid in this system.

Reaction of mono-valent rhodium complex, $\text{RhCl}(\text{PMe}_3)_3$ with propylene oxide gives analytically pure tri-valent *cis*-hydridoalkylrhodium(III) complex, *cis-mer*- $\text{RhHCl}(\text{CH}_2\text{COME})(\text{PMe}_3)_3$, indicating that cleavage of the less hindered C–O bond takes place [88]. This complex catalyzes selective transformation of propylene oxide to acetone in high yield as shown in Scheme 3.45. Similar reactions with $\text{IrCl}(\text{cyclooctene})(\text{PMe}_3)_3$ also give related (acyl-methyl)(hydrido)(chloro)iridium(III) complexes [89].

It is notable that certain complexes react with epoxides and CO_2 to give met-



Scheme 3.45.

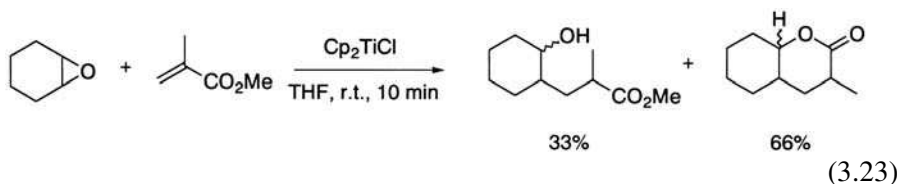
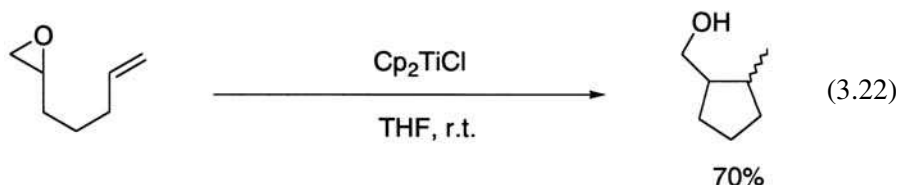


Scheme 3.46.

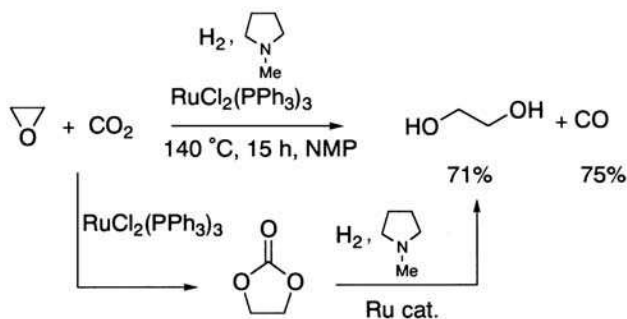
allacarboxylates. For example, treatment of $\text{PtMe}_2(\text{phen})$ with styrene oxide in the presence of CO_2 gives platinacarboxylate complex with inversion of configuration (Scheme 3.46) [90]. Probably, the di-valent starting platinum complex having an electron donating 1,10-phenanthroline has enough Lewis basicity to undergo $\text{S}_{\text{N}}2$ addition leading to the C–O bond cleavage at the less substituted carbon with inversion of configuration. The subsequent CO_2 insertion into the Pt–O bond gives the metallacarboxylate complex.

Catalytic formation of carbonate by coupling reaction of epoxide with CO_2 has been achieved by $\text{RuCl}_2(\text{PPh}_3)_3$ (Scheme 3.47) [91]. When this reaction is carried out in the presence of hydrogen gas with a base such as *N*-methylpyrrolidine, the ruthenium complex catalyzes further hydrogenolysis and decarbonylation of ethylene carbonate to form ethylene glycol.

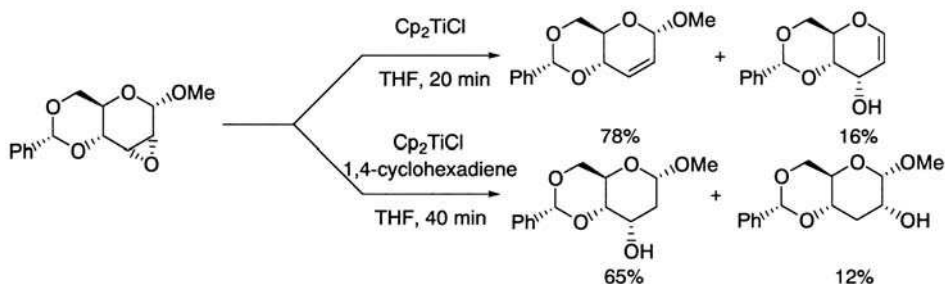
One electron reduction of epoxides by tri-valent titanocene monochloride Cp_2TiCl is reported [92]. This reaction has versatile applications in chemical transformation of epoxides for deoxygenation, isomerization, intramolecular cyclization and coupling reaction with olefins (Scheme 3.48 and Eqs. 3.22 and 3.23).



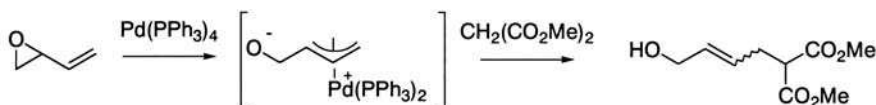
Catalytic transformation of vinyl epoxides is notable in view of organic synthesis. The C–O bond cleavage reaction of vinyl epoxides at the allylic position by a transition metal complex gives η^3 -allyl complexes having an oxoanion moiety. Since the oxoanion moiety in the η^3 -allyl complex can abstract an acidic hydrogen of substrates, the resulting carbanion can attack the η^3 -allyl complex as a nucleophile leading to a formal 1,4-addition reaction as shown in Scheme 3.49 [93]. It



Scheme 3.47.



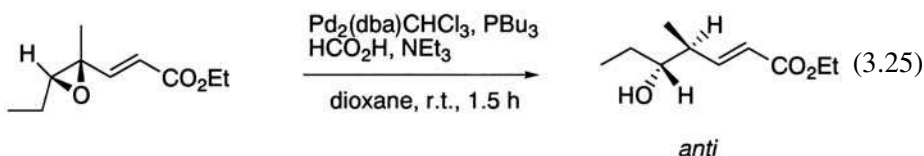
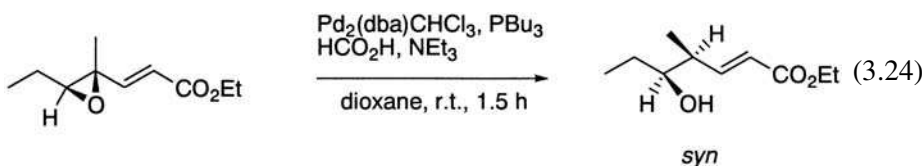
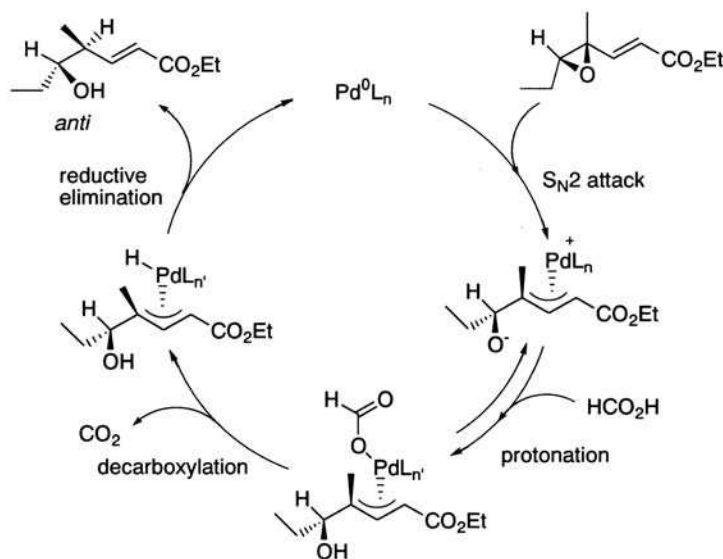
Scheme 3.48.



Scheme 3.49.

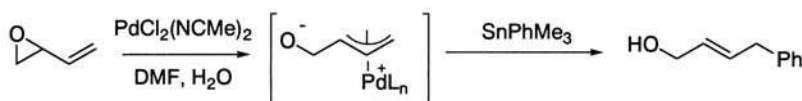
is worth noting that neutral active hydrogen containing compounds can be used as nucleophiles in this allylation.

In the C–O bond cleavage reaction of vinyl epoxides by a palladium complex, formic acid acts as a good proton and hydride donor evolving CO_2 (Eqs. 3.24 and 3.25). Zero-valent palladium complex favors the attack at an allylic carbon in an $\text{S}_{\text{N}}2$ manner to give η^3 -allylpalladium(II) complex with inversion of configuration, and formate anion coordinates to the palladium center (Scheme 3.50). Then, decarboxylation of the formate affords palladium hydride, which attacks the η^3 -allyl moiety from the *endo* side. Thus, 1,2-addition of hydrogen atoms takes place regioselectively with inversion at the allylic carbon [94].



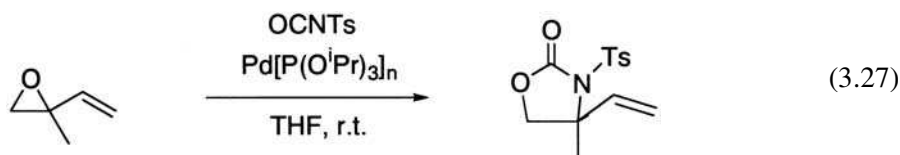
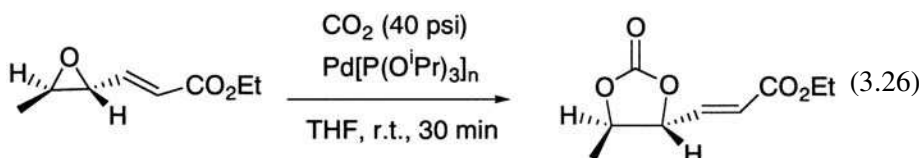
Similarly, 1,4-addition reactions of organostannanes to vinyl epoxides took place in a polar solvent such as DMF giving allyl alcohols (Scheme 3.51) [95]. Addition of water enhanced this 1,4-addition, implying importance of protonation.

When such C–O bond activation reaction of vinyl epoxide is carried out in the presence of CO_2 [96] or isocyanates [97], nucleophilic attack of the η^3 -allyloxooanion at the electron deficient carbons takes place to give carbonates and oxazolidine with retention of configuration (Eqs. 3.26 and 3.27). Palladium



Scheme 3.51.

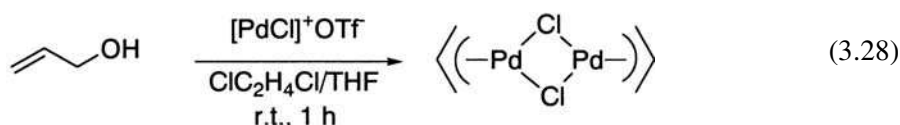
phosphite complex derived from $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ and $\text{P}(\text{O}^i\text{Pr})_3$ acts as highly efficient catalyst.



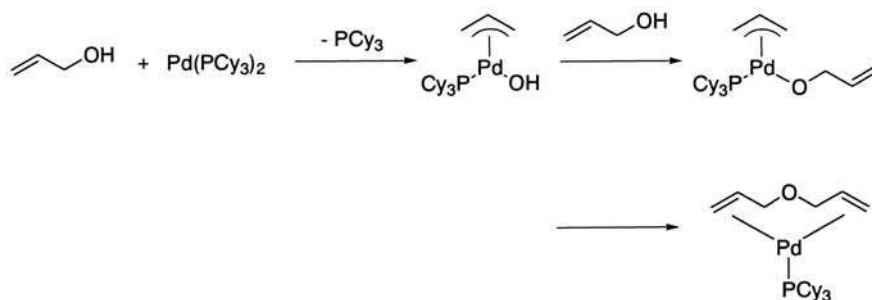
3.3.8 C–O bond cleavages of alcohols and acetals

The C–O bond of allylic alcohols is known to be cleaved by zero-valent palladium complex such as $\text{Pd}(\text{PCy}_3)_2$ (Scheme 3.52) [38]. In this reaction, because the resulting hydroxo ligand is basic enough to react with the proton of another allyl alcohol, $(\eta^3\text{-allyl})(\text{allyloxo})\text{palladium(II)}$ complex is initially formed, and then reductive elimination of the $\eta^3\text{-allyl}$ and allyloxo fragments takes place to yield mainly zero-valent palladium complex having diallyl ether as a ligand.

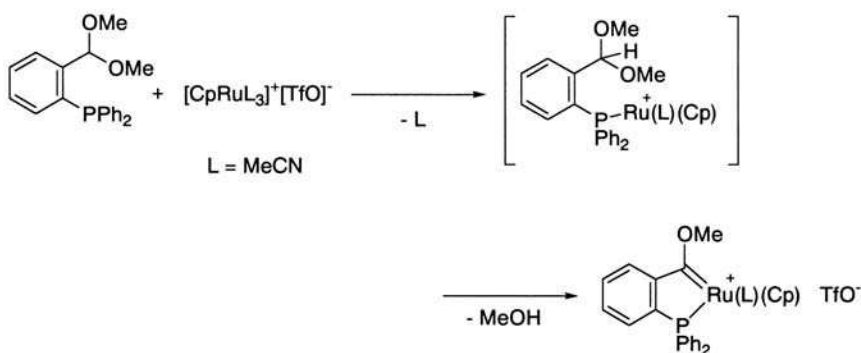
When phosphine-free di-valent complexes such as PdCl_2 [98] or $[\text{PdCl}]^+\text{OTf}^-$ [99] are employed for the reaction with allyl alcohol, dimeric $(\eta^3\text{-allyl})\text{palladium(II)}$ complex is formed in good yield (Eq. 3.28).



C–O bond in acetals is also cleaved by a cationic Ru complex to give an alkoxy carbene complex. This reaction is explained by the initial coordination of



Scheme 3.52.



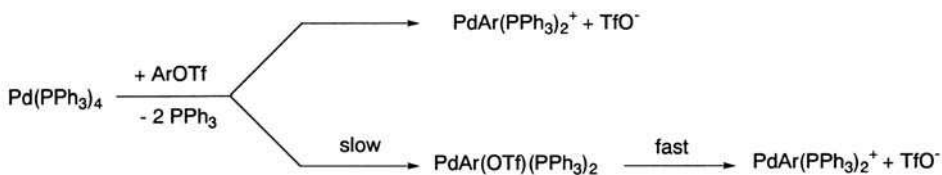
Scheme 3.53.

the phosphorus atom followed by the release of methanol to form alkoxy-carbene complex as shown in Scheme 3.53 [100].

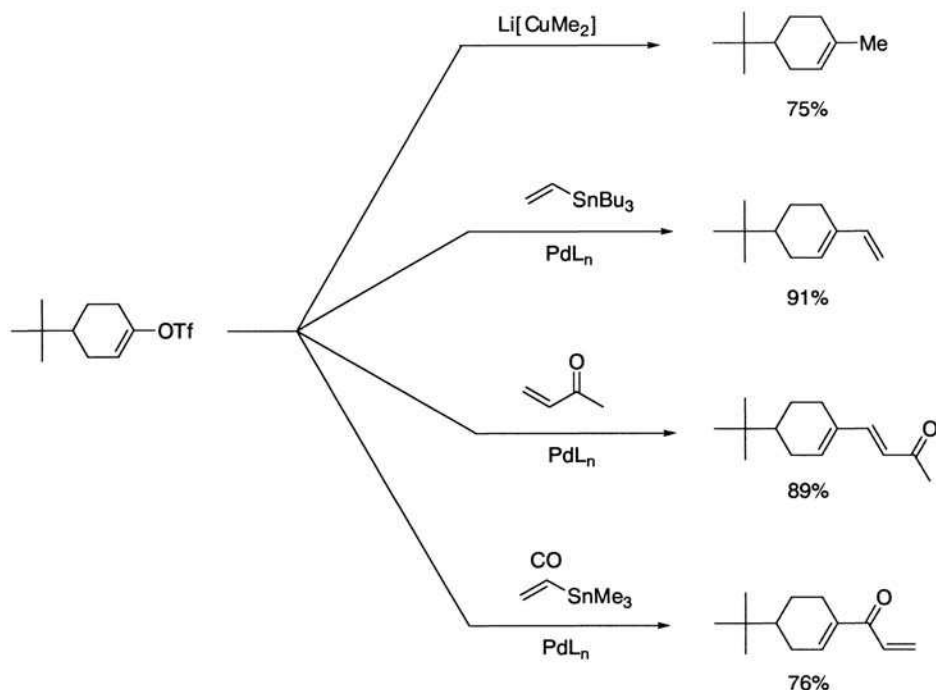
3.3.9 Other C–O bond cleavage

C–O bond cleavage of aryl triflates or tosylates is also studied in relation to Mizoroki–Heck type reactions [101]. Oxidative addition of PhOTf to $\text{Pd}(\text{PPh}_3)_4$ is 10^4 times slower than that of PhI . Since similar trend is observed for the catalytic Mizoroki–Heck reaction, the oxidative addition of aryl compound is considered to be the rate-determining step in the overall catalytic process. This feature suggests that the C–O bond cleavage of aryl triflate proceeds by the concerted $\text{S}_{\text{N}}\text{Ar}$ mechanism. However, since the triflate normally acts as a non-coordinating anion, thermally unstable cationic arylpalladium(II) complexes are formed in this reaction (Scheme 3.54).

Compared with allylation reactions, alkenylations involving carbon–oxygen bond cleavage have been less explored. However, enol triflates and tosylates are employed for catalytic alkenylation by Group 10 complexes in the presence of Gilman or Grignard reagents as well as organostannanes (Scheme 3.55) [102–104]. Such cross coupling reactions provide useful alkenylation method in high yields.



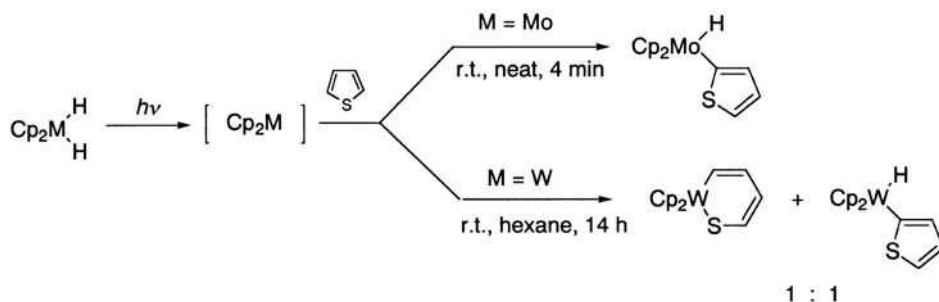
Scheme 3.54.



Scheme 3.55.

3.4 CARBON–SULFUR BOND CLEAVAGE REACTIONS

Carbon–sulfur bond cleavages are extensively studied not only for synthetic applications but also for interests in catalytic desulfurization mechanism of the industrial hydrodesulfurization (HDS) process of naphtha, petroleum and lubricants [105]. Aromatic organosulfur compounds such as thiophenes, benzothiophenes and dibenzothiophenes are frequently contained in fossil oil and their sulfur atoms are generally difficult to remove in HDS process [106]. In the industrial HDS process, Mo/Co/S or Ni/Mo/S heterogeneous catalysts supported on alumina are widely employed. In order to obtain ideas to develop more efficient catalysts as well as to shed some light on their mechanisms at a molecular level, transition metal complex-mediated cleavages of C–S bond are extensively studied. On the other hand, thiiranes and thietanes are frequently employed for preparation of transition metal sulfides, in which their C–S bonds are smoothly cleaved. In this section, the C–S bond cleavages of thiophene derivatives, thiiranes, thietanes, vinylic sulfides, allylic sulfides, thiols and dithioacetals are overviewed.



Scheme 3.56.

3.4.1 C–S bond cleavages of thiophenes, benzothiophenes, and dibenzothiophenes

One of the common methods for the C–S bond cleavage of thiophene is the oxidative addition to low-valent coordinatively unsaturated complexes. However, one may encounter the concomitant cleavage of the C–H bond by the metal complexes. The development of preferential cleavage of the C–S bond over the competitive C–H bond is a topic of this reaction.

Coordinatively unsaturated ‘Cp₂M’ (M = Mo, W) species, which is generated by UV photolysis or thermolysis of Cp₂MH₂ or Cp₂M(H)(R), can cleave the C–S bond of thiophene by oxidative addition. While reaction of ‘Cp₂Mo’ with thiophene exclusively yields (hydrido)(thienyl)molybdenum(IV) complex, that of ‘Cp₂W’ with thiophene gives a mixture of thiametallacycle and (hydrido)(thienyl)tungsten(IV) complexes (Scheme 3.56) [107]. In the latter case, insertion of the metallocene fragment into the C–S bond was found to be kinetically favored, since the prolonged reactions give the hydrido(thienyl)tungsten(II) complex as a major product.

Similar competitive C–S and C–H bond cleavage reaction is known for coordinatively unsaturated rhodium complex. While heating Cp*Rh(H)(Ph)(PMe₃) in the presence of thiophene exclusively gives the C–S bond cleavage product Cp*Rh(SCH=CHCH=CH)(PMe₃) [108], exposure of Cp*Rh(H)₂(PMe₃) to UV light with thiophene gives a mixture of the C–S and the C–H bond cleavage products in 3:1 ratio [109]. Since the ratio of C–S and C–H bond cleavage products is always 3:1 throughout the photolysis, they are considered to be formed by the parallel reaction rather than the sequential reactions, though the C–H bond cleavage product can be converted to the C–S bond cleavage product at high temperature. Thus, these bond cleavage reactions would take place *via* different intermediates. Since the photolysis of Cp*Rh(H)₂(PMe₃) with arene is known to form η²-arene complex, the C–H bond cleavage likely proceeds *via* the η²-thiophene complex. Heating of alternatively prepared Cp*Rh(D)(2-thienyl)(PMe₃) gives a 1:1 mixture of Cp*Rh(SCD=CHCH=CH)(PMe₃) and

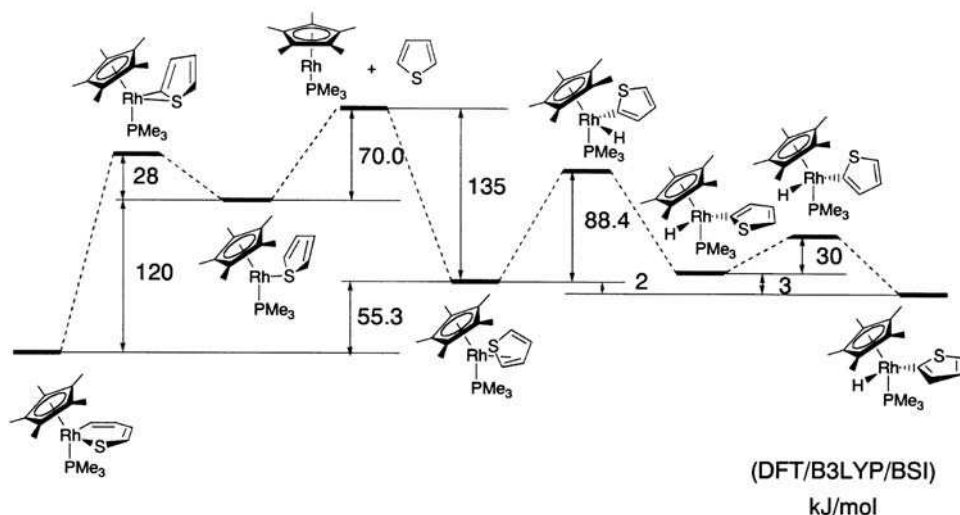


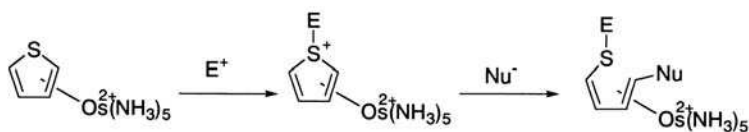
Fig. 3.1. Energy diagram for competitive C–S and C–H bond cleavage by $\text{Cp}^*\text{Rh}(\text{PMe}_3)$ species.

$\text{Cp}^*\text{Rh}(\overline{\text{SCH}=\text{CHCH}=\text{CD}})(\text{PMe}_3)$, and the $\Delta S^\ddagger$ value for this reaction is found to be 3.0 eu. These facts suggest that the reaction is an intramolecular process and the C–S bond cleavage takes place *via* a symmetrical intermediate such as η^1 -S-coordinated thiophene. The mechanism is also supported by exclusive formation of an S-coordinated complex in the thermal reaction of $\text{Cp}^*\text{Rh}(\text{H})(\text{Ph})(\text{PMe}_3)$ with 2,3,4,5-pentamethylthiophene. As shown in Fig. 3.1, DFT calculations for the reaction of $\text{Cp}^*\text{Rh}(\text{PMe}_3)$ with thiophene suggest the initial κ^1 -S coordination of thiophene followed by the C–S bond cleavage, whereas the C–H bond cleavage proceeds *via* η^2 -C=C coordination of thiophene [110]. Although the former η^1 -S intermediate is less stable than the latter η^2 -C=C intermediate, the former η^1 -S intermediate readily gives an η^2 -C–S species, where the overlap between the LUMO of thiophene and the HOMO of the metal fragment is maximized to facilitate the cleavage of the C–S bond.

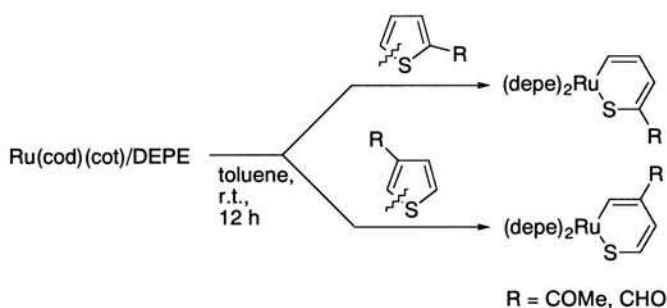
Similar parallel reactions with benzothiophene are also observed in thermal [111] or photochemical reaction of iron(0) complexes [112].

π -Coordinated thiophenes are susceptible to the reaction at the carbon adjacent to S by nucleophiles leading to the C–S bond cleavage. For example, cationic osmium(II) complex forms η^2 -thiophene and -benzothiophene complexes (Scheme 3.57) [113], and treatment with carbon electrophiles such as MeOTf gives S-alkylated complex, in which C–S bond remains intact. Further reactions of the S-alkylated complex with nucleophiles such as hydride, cyanide, pyridine, and PPh_3 lead to the C–S bond cleavage.

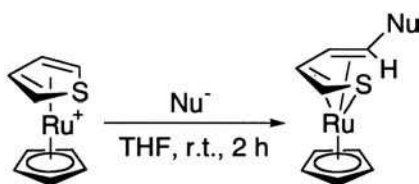
Similarly, $[\text{RuCp}(\eta^5\text{-thiophene})]^+[\text{PF}_6]^-$ reacts with a variety of nucleophiles such as H^- , OMe^- , SMe^- and $\text{CH}(\text{CO}_2\text{Me})_2^-$ to cleave the C–S bond giving neutral complexes [114].



Scheme 3.57.



Scheme 3.58.

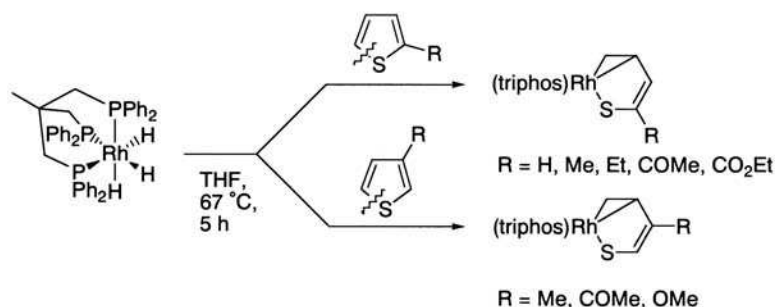


(3.29)

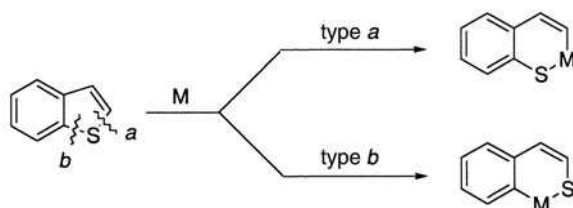
Unsymmetrically substituted thiophenes have two C–S bonds of different nature. Regioselectivity of the C–S bond cleavage promoted by ruthenium(0) complex is controlled by both steric and electronic factors as described in Scheme 3.58 [115]. While the reaction of $\text{Ru}(\text{cod})(\text{cot})/\text{DEPE}$ with thiophene bearing a substituent at 2-position causes selective insertion of $\text{Ru}(0)$ into the less substituted C–S bond (1,5-insertion) to avoid the steric repulsion, the reaction with thiophene bearing a substituent at 3-position exclusively leads to 1,2-insertion of the ruthenium(0) into the C–S bond due to electronic reasons. This regioselectivity can be explained by the preferential attack of the Ru to the low-lying LUMO (C–S anti-bonding orbital), whereas steric effect becomes more important in the reaction of 2-substituted thiophene.

Rhodium complex is less sensitive to such electronic factors in the C–S bond cleavage reaction of thiophenes. Similar treatment of either 2- or 3-substituted thiophene by $\text{RhH}_3[(\text{PPh}_2\text{CH}_2)_3\text{CMe}]$ exclusively results in 1,5-insertion of the rhodium complex, where rhodium center also constitutes 3-membered ring in the metallacycle (Scheme 3.59) [116].

For benzothiophenes two types of C–S bond cleavages are known (Scheme 3.60).



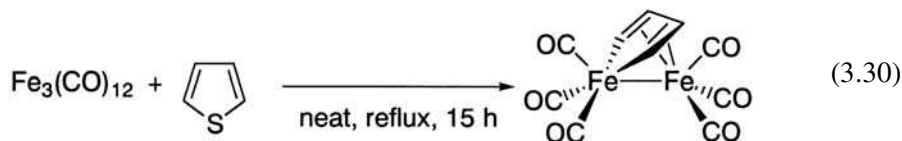
Scheme 3.59.



Scheme 3.60.

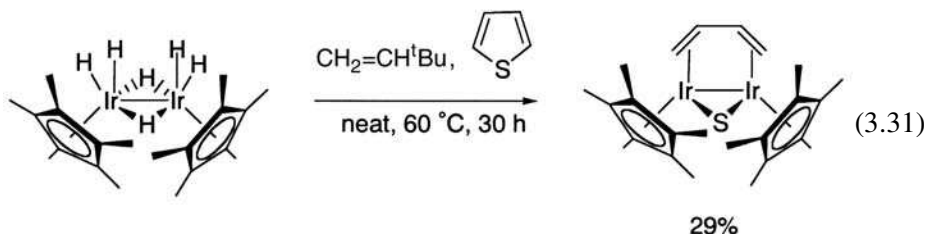
Transition metal complexes usually favor insertion into the carbon–sulfur bond adjacent to C(alkenyl)–S bond (type a), but some complexes insert into the C(aryl)–S bond (type b) [117]. *Ab initio* calculations suggest that the most important controlling factor for determining selectivity in the C–S bond cleavage of benzothiophene is the thermodynamic stability of the resulting metal–carbon bond [118].

C–S bond cleavage reactions by multinuclear complexes are also interesting for the following reasons. As noted above, the ring opening reactions of thiophenes and benzothiophenes have been achieved by mono-nuclear low-valent transition metal complexes under mild conditions. Although the second C–S bond cleavage is indispensable to remove the sulfur atom from these organosulfur compounds, it is generally difficult to cleave the second C–S bond by the mono-nuclear complexes. Multinuclear complexes seem to be effective for removal of sulfur atom from the organosulfur compounds. Indeed, the first double C–S bond cleavage reaction of thiophene has been achieved by $\text{Fe}_3(\text{CO})_{12}$ in 1960s (Eq. 3.30) [119].



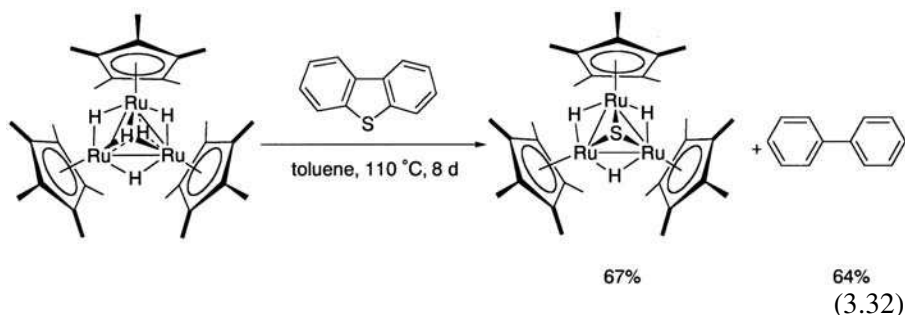
Reaction of dinuclear polyhydrido-iridium complex $[\text{Cp}^*\text{Ir}(\text{H})_2(\mu\text{-H})_2]_2$ with

thiophene in the presence of *t*-butylethylene as a hydrogen acceptor leads to formation of a $\mu\text{-}\eta^2, \eta^2$ -butadiene complex (Eq. 3.31) [120,121].



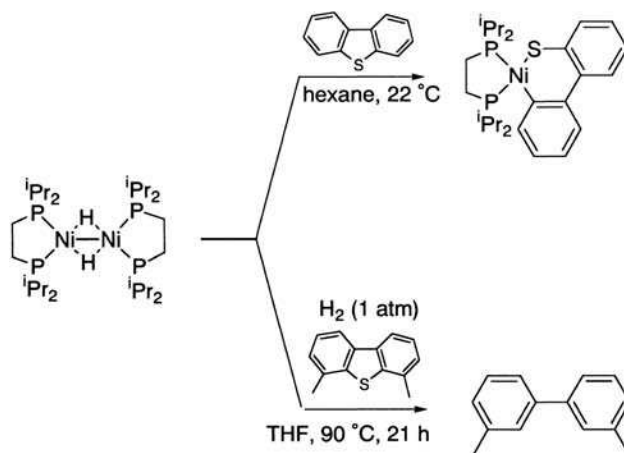
A dinuclear hydridonickel complex $[\text{Ni}(\mu\text{-H})(\text{dippe})]_2$ [dippe = 1,2-bis(diisopropylphosphino)ethane] has high reactivity toward thiophene, benzothiophene, and dibenzothiophene under ambient conditions to give thianickellacycle complex (Scheme 3.61) [122]. Moreover, smooth desulfurization of 4,6-dimethyldibenzothiophene can be achieved to give 3,3'-dimethylbiphenyl at 90°C under atmospheric hydrogen.

Trinuclear hydridoruthenium cluster is also effective for the desulfurization of dibenzothiophene, though the reaction proceeds quite slowly (Eq. 3.32) [123].

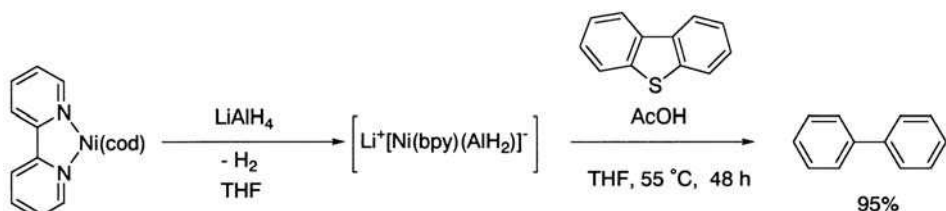


In relation to the industrial HDS process, reactions of thiophene families with hydride sources are of interest. A combination of $\text{Ni}(\text{OAc})_2$, RONa , and NaH is an excellent reagent for complete desulfurization of dibenzothiophene and 4,6-dimethyldibenzothiophene under ambient conditions (65°C) [124]. Reaction of $\text{Ni}(\text{cod})(\text{bpy})$ with LiAlH_4 gives $\text{Li}^+[\text{Ni}(\text{bpy})(\text{AlH}_2)]^-(\text{thf})_n$, which also removes sulfur atom from dibenzothiophene in the presence of proton source such as acetic acid (Scheme 3.62) [125]. A single electron transfer mechanism from the nickel ate complex to dibenzothiophene is proposed in this system.

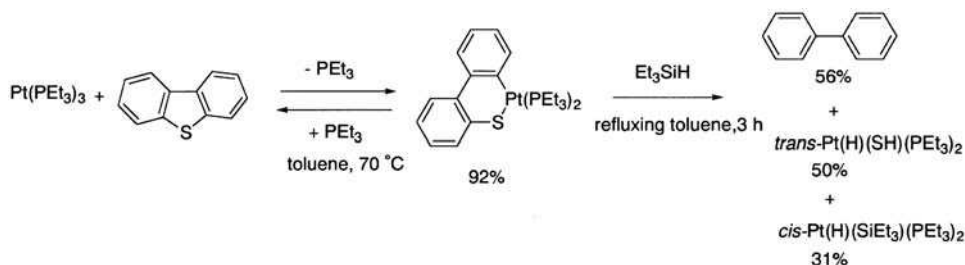
A zero-valent platinum complex reversibly reacts with dibenzothiophene to give a thiaplitanacycle complex [126], which further reacts with the hydride such as Et_3SiH to produce biphenyl and a mixture of *cis*- $\text{Pt}(\text{H})(\text{SH})(\text{PEt}_3)_2$ and *trans*- $\text{Pt}(\text{H})(\text{SiEt}_3)(\text{PEt}_3)_2$, although the reaction of thiaplitanacycle complex with hydrogen does not give hydrogenolysis products (Scheme 3.63).



Scheme 3.61.



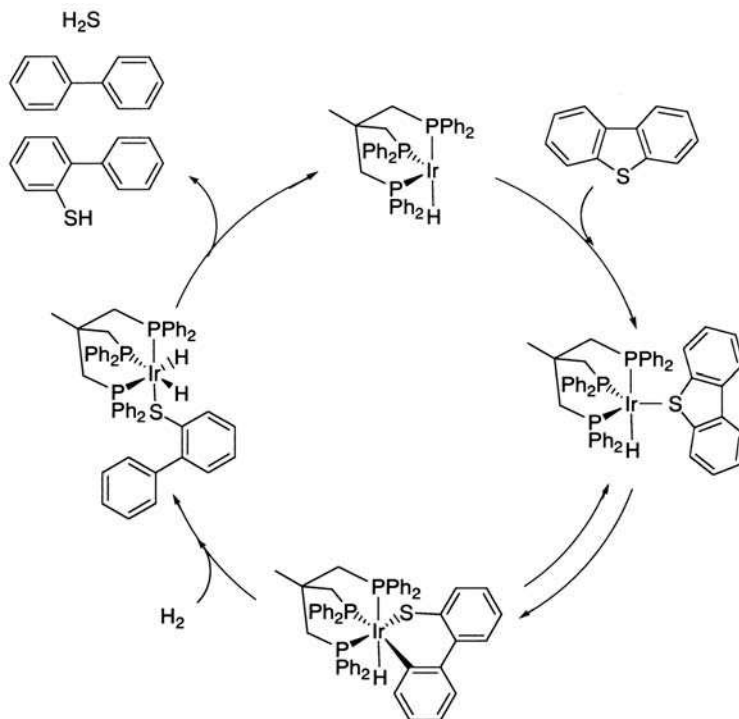
Scheme 3.62.



Scheme 3.63.

Despite many efforts in this field, homogeneous catalytic desulfurization by transition metal complexes is still very limited to date. One of rare examples is the catalytic conversion of benzothiophene to a mixture of biphenyl, H_2S , and 2-phenylthiophenol by a 16e complex of iridium(I) under H_2 (Scheme 3.64) [127].

Water/organic solvent biphasic catalysis is also applied for the removal of organosulfur compounds. In this system, benzothiophene is easily converted into 2-ethylbenzenethiol, which is removable to a basic aqueous layer. Thus, the

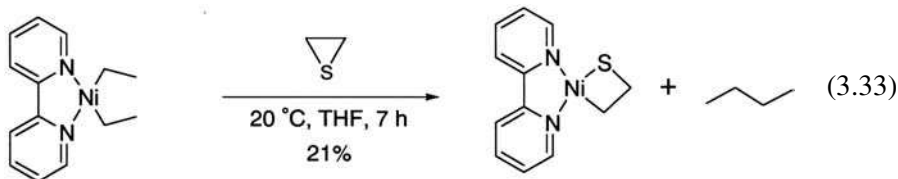


Scheme 3.64.

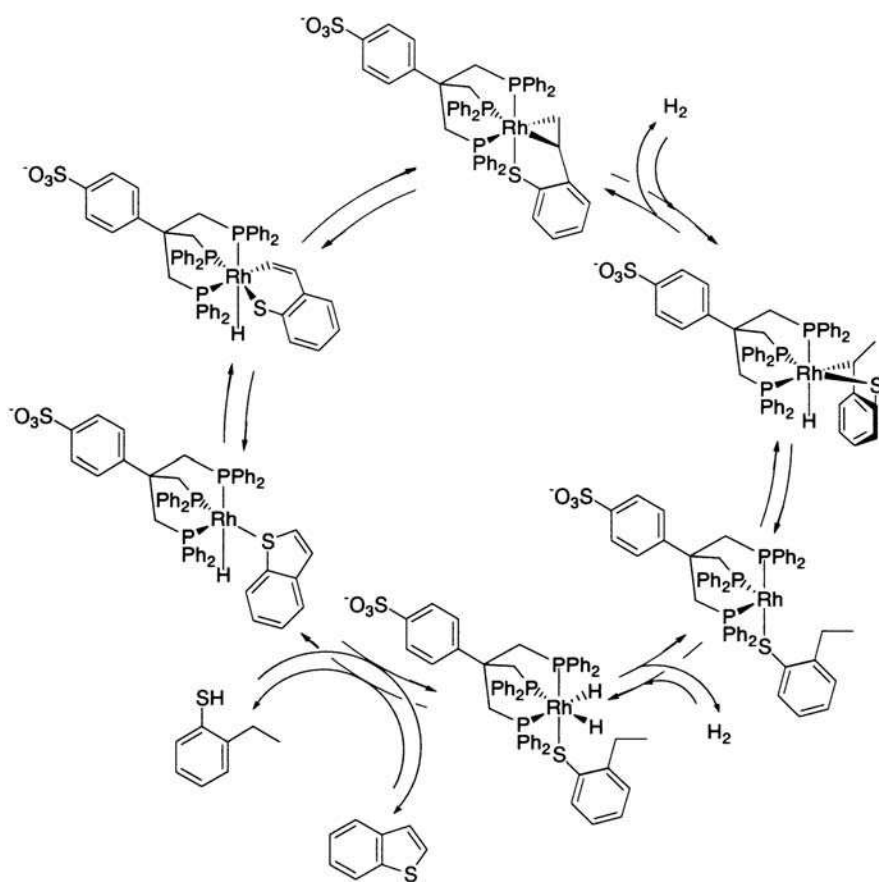
catalyst and sulfur compounds can be separated from the hydrophobic layer by the simple phase separation (Scheme 3.65) [128].

3.4.2 C–S bond cleavage of thiiranes and thietanes

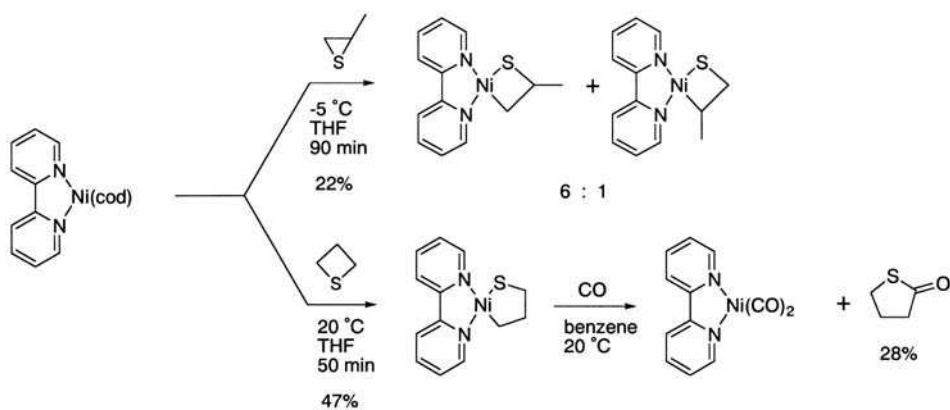
Although the C–S bond of thiiranes is cleaved by both acids and bases [129], such bond cleavage reactions by transition metal complexes have been extensively studied from both mechanistic and synthetic points of view. For example, oxidative addition of thiiranes or thietane to NiEt₂(bpy) (Eq. 3.33) or Ni(cod)(bpy) (Scheme 3.66) gives thianickellacycle complex [130]. Exposure of the thianickellacyclopentane to the atmospheric CO gives γ -thiobutyrolactone.



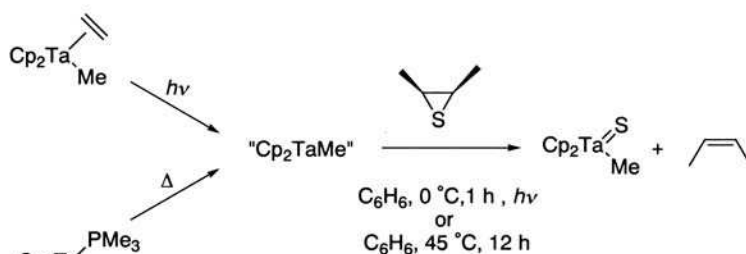
Tri-valent methyltantalocene complex Cp₂TaMe generated by the photolysis of Cp₂Ta(Me)(C₂H₄) or thermolysis of Cp₂Ta(Me)(PMe₃) has high reactivity



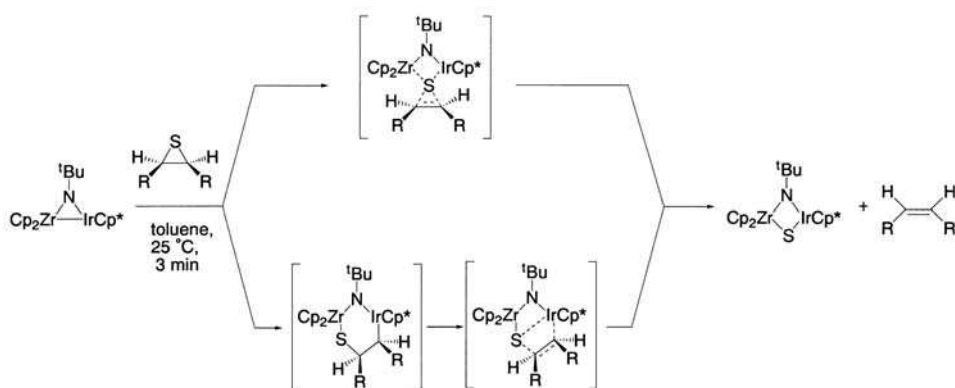
Scheme 3.65.



Scheme 3.66.



Scheme 3.67.

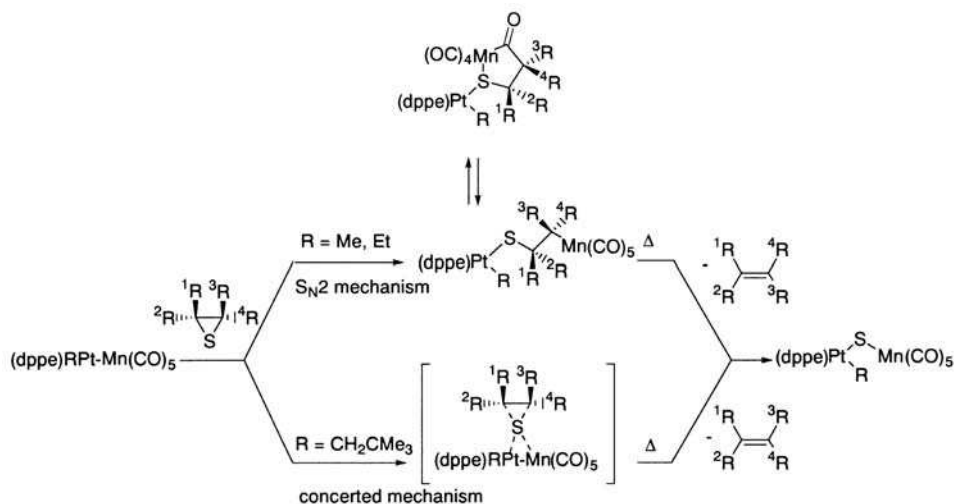


Scheme 3.68.

toward abstraction of the sulfur atom from *cis*-2-butene sulfide (Scheme 3.67) [131]. Since the overall stereochemistry about the olefin in the overall reaction is retention to give *cis*-2-butene, a three-center concerted mechanism is proposed for this reaction.

Rapid desulfurization of thiiranes by heterodinuclear complexes is achieved by using an early–late dinuclear transition-metal complex. $\text{Cp}_2\text{Zr}(\mu\text{-N}^t\text{Bu})\text{IrCp}^*$ reacts with thiiranes in almost diffusion controlled rates to give μ -sulfido complex and corresponding olefin with retention of configuration at the alkenyl carbon center (Scheme 3.68) [132]. Two mechanisms such as completely concerted sulfur transfer reaction and insertion of the C–S bond into the Zr–Ir bond followed by concerted four-center elimination are proposed.

A series of heterodinuclear late organotransition metal complexes $(\text{dppe})\text{RPt-M}(\text{CO})_4$ ($\text{M} = \text{Mn, Re}$) show the unexpected regio- and stereoselective desulfurization of thiiranes controlled by the ancillary alkyl ligand (Scheme 3.69) [133]. Reaction of the methyl complex, $(\text{dppe})\text{MePt-M}(\text{CO})_4$ with *cis*- and *trans*-2-butene sulfide results in the insertion of the thiirane into the Pt–M bond followed by the CO insertion into the carbon–M bond and coordination of the S atom to the

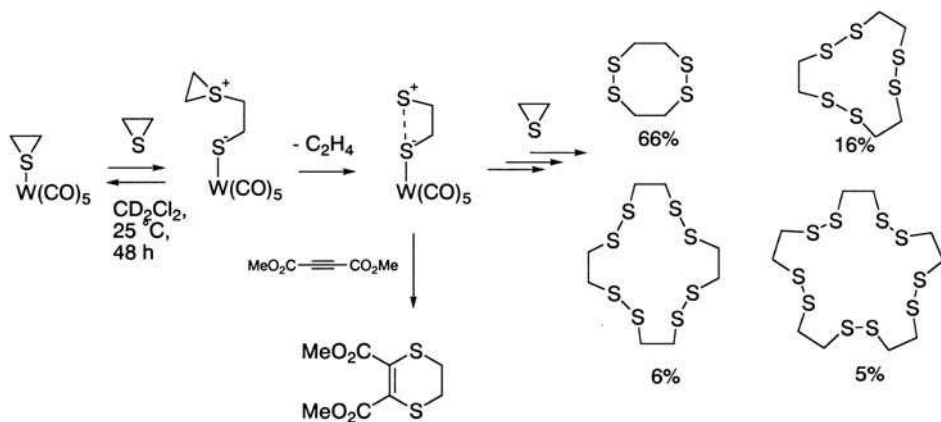


M to give a platinum complex having thiametallacycle moiety. The stereochemistry of the thiametallacycle reveals inversion of configuration at the methylene carbon, suggesting an S_N2 mechanism. Thermolyses of the *anti* and *syn* complexes give $(dppe)MePt(\mu-S)Mn(CO)_4$ and *trans*- and *cis*-2-butene, respectively. In sharp contrast, the reaction of the neopentyl analogue, $(dppe)(Me_3C)Pt-Mn(CO)_4$ with 2-butene sulfide directly produces $(dppe)MePt(\mu-S)Mn(CO)_4$ and 2-butene, where the overall stereochemistry is retention of configuration, suggesting a concerted mechanism. It is notable that the ancillary alkyl group on the platinum center controls the delicate difference of reaction process of the desulfurization. Since the reaction of SMe_2 with methylplatinum-manganese complex causes ionization to give $[(dppe)MePt(SMe_2)]^+ [Mn(CO)_4]^-$ but the neopentylplatinum-manganese complex remains unreacted, initial ionization is a decisive process for the stereoselectivity.

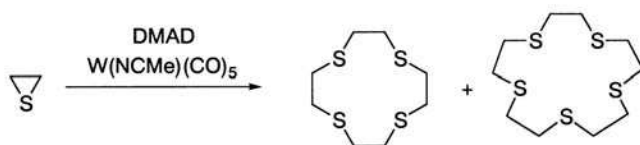
Metal carbonyl complexes show rich reactivities toward thiiranes and thietanes [134]. Reaction of $W(CO)_5(NCMe)$ with thiirane results in the ligand exchange reaction to give $W(thiirane)(CO)_5$ (Scheme 3.70) [135]. This complex catalyzes formation of cyclic polydisulfides with olefin elimination (Scheme 3.71).

This catalysis involves (1,2-ethanedithiolato)tungsten intermediate, which can be trapped by the addition of dimethyl acetylenedicarboxylate (DMAD). Interestingly, in the presence of DMAD, the formation of cyclic polydisulfides is greatly suppressed, and the cyclic polythioethers (thiacrowns) are mainly formed (Scheme 3.72).

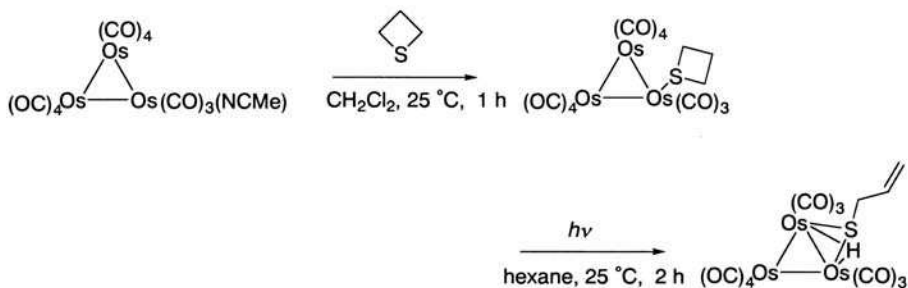
Similarly, thietane also displaces the coordinated acetonitrile on the electron poor metal center in $Os_3(CO)_{11}(NCMe)$ to give $Os_3(CO)_{11}[S(CH_2)_3]$ (Scheme 3.72) [136,137]. Photo-irradiation of the resulting complex leads to



Scheme 3.70.



Scheme 3.71.

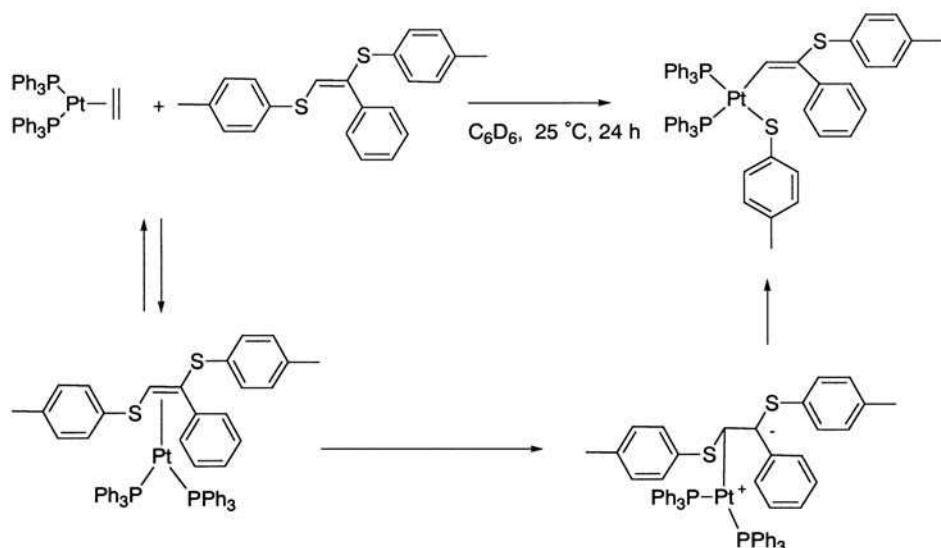


Scheme 3.72.

successive C–S and C–H bond cleavages of the coordinated thietane giving (μ -hydrido)(propylenethiolato)triosmium cluster. Radical mechanism for these bond cleavage reactions under photo-irradiation conditions is proposed [138].

3.4.3 C–S bond cleavages of vinylic sulfides

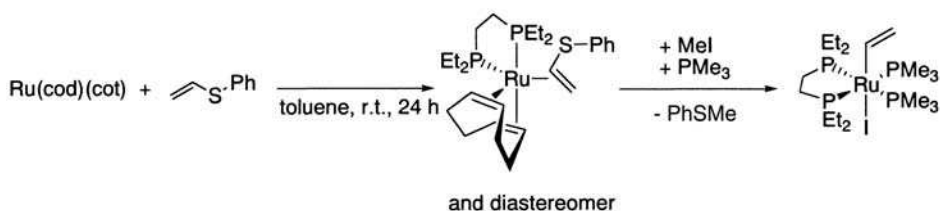
Oxidative addition of vinylic C–S bond to zero-valent platinum complex has recently been investigated in detail [139]. The reaction of $\text{Pt}(\text{C}_2\text{H}_4)(\text{PPh}_3)_2$ with



Scheme 3.73.

phenyl vinyl sulfide gives only η^2 -coordinated complex and the C–S bond cleavage reaction does not occur even at 50°C at all. However, the C–S bond of the vinyl sulfide with electron-withdrawing substituents is cleaved smoothly (Scheme 3.73). The reaction of $\text{Pt}(\text{C}_2\text{H}_4)(\text{PPh}_3)_2$ with substituted vinyl sulfides gives an equilibrium mixture between $\text{Pt}(\text{C}_2\text{H}_4)(\text{PPh}_3)_2$ and $\text{Pt}(\eta^2\text{-vinyl sulfide})(\text{PPh}_3)_2$ at the initial stage of the reaction, and then the Pt(0) attacks the less substituted carbon to form a zwitterionic intermediate, from which the thiolato anion migrates to the cationic Pt(II) to give vinylplatinum(II) complex.

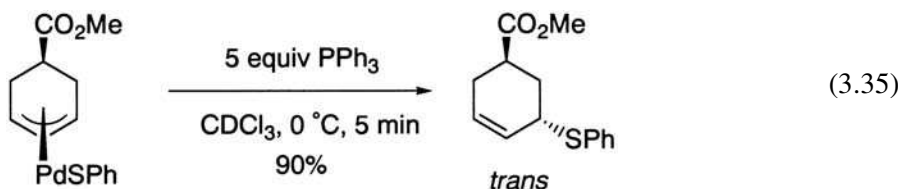
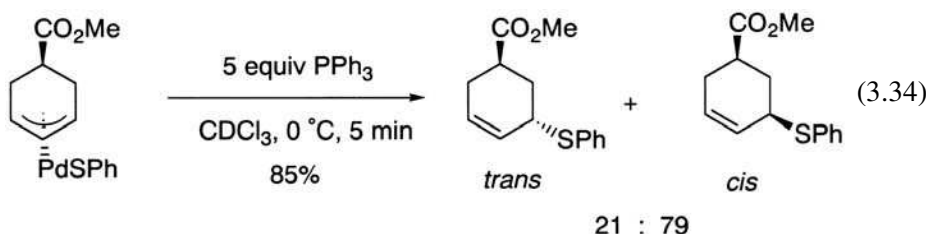
Similar treatment of $\text{Ru}(\text{cod})(\text{cot})/\text{DEPE}$ with phenyl vinyl sulfide also gives a zero-valent η^2 -coordinated complex $\text{Ru}(\eta^2\text{-C}_2\text{H}_3\text{SPh})(\text{cod})(\text{depe})$ (Scheme 3.74) [79]. Treatment of this complex with an electrophile such as MeI in the presence of PMe_3 causes cleavage of the C–S bond to form $\text{Ru(I)}(\text{C}_2\text{H}_3)(\text{depe})(\text{PMe}_3)_2$ and MeSPh . Probably, electrophilic attack of the methyl to the sulfur atom on the coordinated phenyl vinyl sulfide is a major driving force in this reaction.



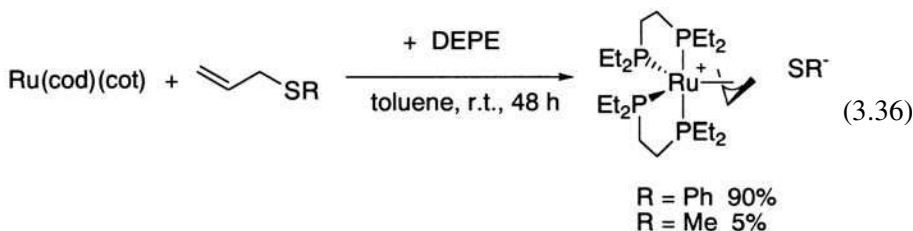
Scheme 3.74.

3.4.4 C–S bond cleavages of allylic sulfides

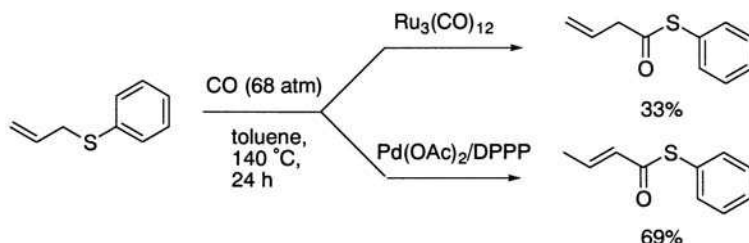
C–S bond cleavage of allylic sulfides has a similarity to that of allyl ether from a mechanistic point of view. While no apparent oxidative addition of allyl phenyl sulfide to zero-valent palladium is observed for $\text{Pd}(\text{PPh}_3)_4$, similar treatment with $\text{Pd}(\text{PCy}_3)_2$ [38,140] or $\text{Pd}(\text{styrene})(\text{PMe}_3)_2$ [141] results in the formation of dinuclear bridged (η^3 -allyl)palladium(II) complexes $\text{Pd}_2(\mu\text{-}\eta^3\text{-C}_3\text{H}_5)(\mu\text{-SPh})(\text{PR}_3)_2$. Oxidative addition of C–S bond occurs smoothly in the reaction of phosphine-free complexes such as $\text{Pd}_2(\text{dba})_3$ and $\text{Pd}(\text{maleic anhydride})(\text{cod})$ with allyl phenyl sulfide to give $[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)(\text{SPh})]_2$. Addition of PPh_3 to $[\text{Pd}(\eta^3\text{-C}_3\text{H}_5)(\text{SPh})]_2$ leads to reductive elimination to give allyl phenyl sulfide [142], suggesting reversibility of the oxidative addition of allyl sulfide. Analysis of the stereochemistry of the reductive elimination of $\text{Pd}(\eta^3\text{-MeOCOC}_6\text{H}_8)(\text{SPh})$ is shown in Eqs. 3.34 and 3.35, suggesting involvement of attack of the sulfido anion from the *exo* face.



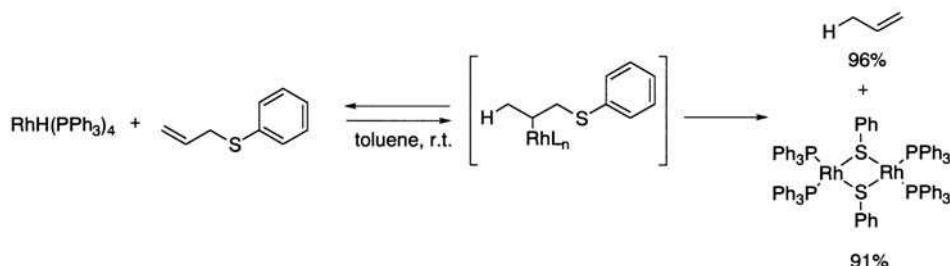
Allyl sulfides react with $\text{Ru}(\text{cod})(\text{cot})/\text{DEPE}$ to give cationic η^3 -allyl-ruthenium(II) complexes (Eq. 3.36) [143]. Allyl phenyl sulfide gives a much higher yield of the η^3 -allyl complex than allyl methyl sulfide.



Catalytic carbonylation of allyl phenyl sulfide is achieved by $\text{Ru}_3(\text{CO})_{12}$ under CO atmosphere to give $\text{CH}_2=\text{CHCH}_2\text{COSPh}$ (Scheme 3.75) [144]. The reaction proceeds by the C–S bond cleavage, CO insertion into Ru–C or Ru–S bond, followed by reductive elimination. It is interesting to note that $\text{Pd}(\text{OAc})_2/\text{DPPP}$



Scheme 3.75.



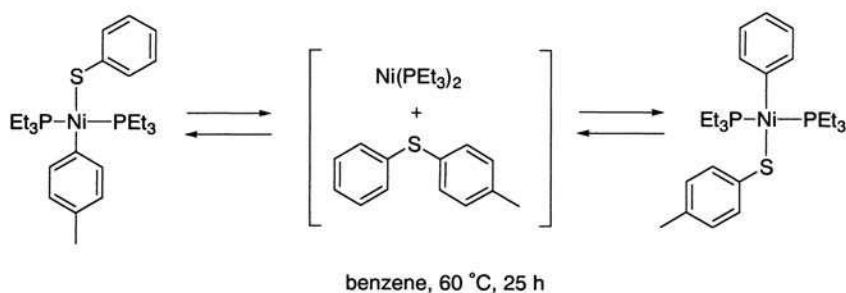
Scheme 3.76.

can also act as a catalyst of this reaction, but the product is isomerized to $\text{MeCH}=\text{CHCOSPh}$.

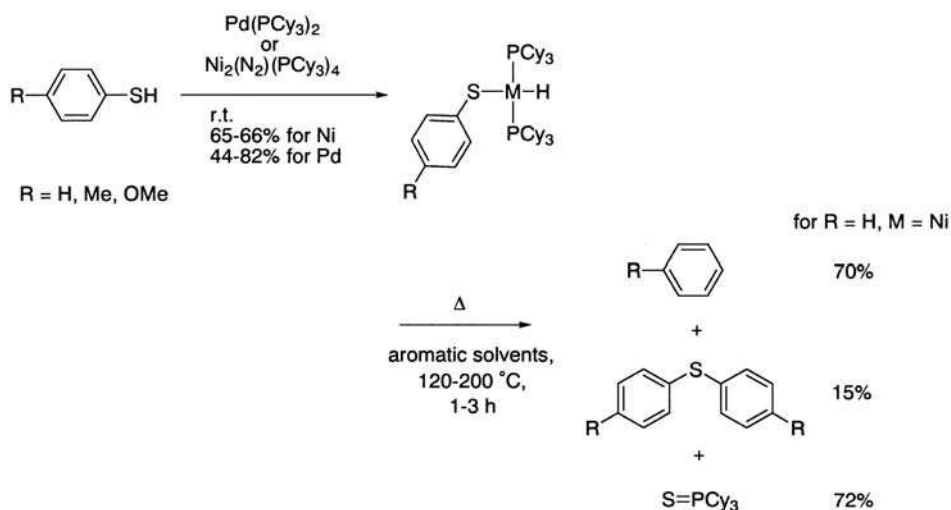
C–S bonds in allylic sulfides are cleaved not only by oxidative addition but also by β -sulfido elimination mechanism. The C–S bond cleavage by β -sulfido elimination usually occurs by the reaction of allyl sulfide with transition-metal hydride such as $\text{RhH}(\text{PPh}_3)_4$, $\text{RhH}(\text{CO})(\text{PPh}_3)_3$, $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$, and $\text{RuH}_2(\text{PPh}_3)_4$ to give corresponding olefins and μ -sulfido complexes (Scheme 3.76) [145]. The reaction of $\text{RhD}[\text{P}(\text{Ph}-d_5)_3]_4$ with allyl phenyl sulfide liberates propylene- d_0 , $-d_1$, $-d_2$, and $-d_3$ in 33:57:9:1 molar ratio, and the remaining allylic sulfide also contains deuterium atom. The results suggest that the allylic sulfide undergoes a facile H–D exchange reaction by $\text{C}=\text{C}$ insertion into the Rh–D bond followed by β -elimination to regenerate the sulfide prior to the C–S bond cleavage.

3.4.5 C–S bond cleavages of other sulfides, thiols and dithioacetals

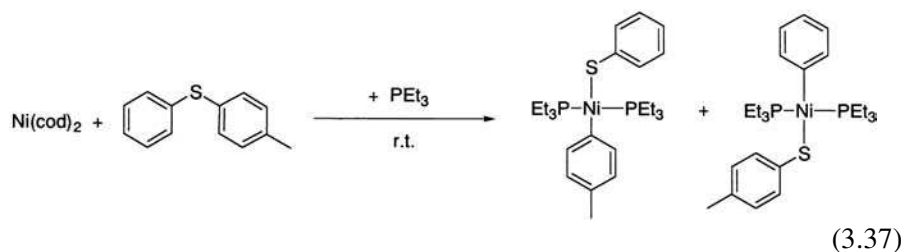
Reversible C–S bond cleavage of diaryl sulfide is known. Treatment of $\text{Ni}(\text{cod})_2$ with phenyl *p*-tolyl sulfide in the presence of PEt_3 results in the C–S bond cleavage at room temperature, giving a mixture of *trans*-(benzenethiolato)(*p*-tolyl)nickel(II) and *trans*-(phenyl)(*p*-toluenethiolato)nickel(II) (Eq. 3.37) [146]. Heating of the reaction mixture leads to the equilibration suggesting reversible oxidative addition/reductive elimination (Scheme 3.77).



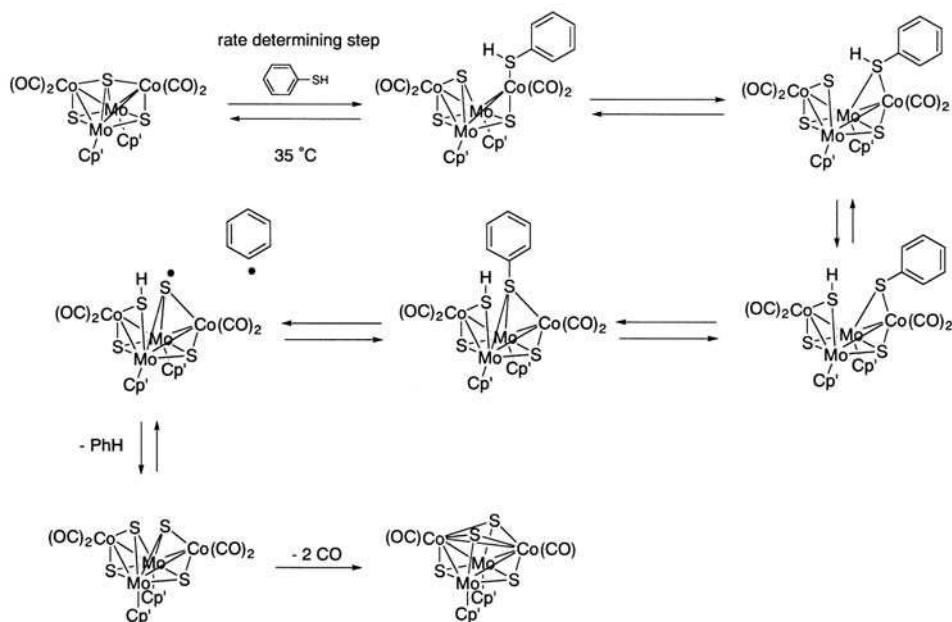
Scheme 3.77.



Scheme 3.78.



Reactions of arenethiols with Ni(0) or Pd(0) phosphine complexes lead to the formation of *trans*-(arenethiolato)(hydrido)metal(II) complexes (Scheme 3.78) [147]. Thermolysis of these complexes does not induce simple reductive elimination of the arenethiolato and hydrido ligands, but gives a mixture of arene, aryl sulfide, and phosphine sulfide.

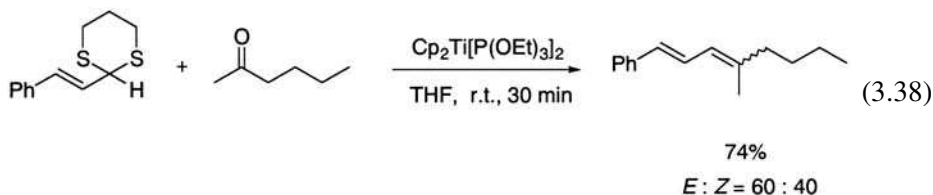


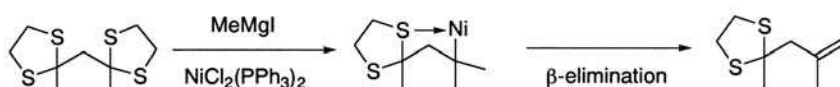
Scheme 3.79.

In relation to HDS catalysis, C–S bond cleavage of thiols has also been extensively investigated. Co/Mo/S cluster shown in Scheme 3.79 reacts with benzenethiol to give a new μ -sulfido cluster by releasing benzene. Such reactions are also regarded as one of the model reactions of heterogeneous HDS catalyst [148]. In this system, a radical mechanism is proposed for the C–S bond cleavage and the activation enthalpy $\Delta H^\ddagger$ for the Ph–S bond cleavage is estimated to be only 110 kJ/mol, in spite of the high Ph–S BDE (350 kJ/mol) [149]. This may be due to the stabilization effect by μ_3 -S coordination as well as by delocalization of the unpaired electrons of the arenethiolato ligand.

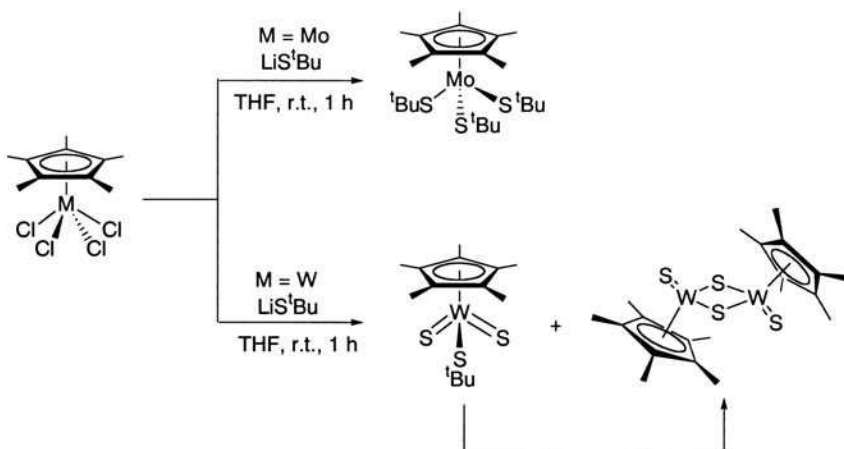
The same cluster also cleaves the C–S bond of thiiranes to give corresponding olefins with retention of configuration [150] and cleaves the C=S double bond in thioisocyanates to give isocyanide [151].

Dithioacetals are recently employed as a carbene synthon. Titanium carbenes prepared *in situ* by reduction of Cp_2TiCl_2 with Mg in the presence of $\text{P}(\text{OEt})_3$ followed by addition of dithioacetals are effective reagents for olefination of carbonyl compounds (Eq. 3.38) [152].





Scheme 3.80.



Scheme 3.81.

Dithioacetals are also considered as dication syntons. For example, bisdithioacetals are employed for the nickel catalyzed cross coupling reaction with Grignard reagents to give homoallylic dithioacetals (Scheme 3.80) [153]. In this reaction, only one of the dithioacetal moieties is the reactive site and a chelate intermediate is proposed.

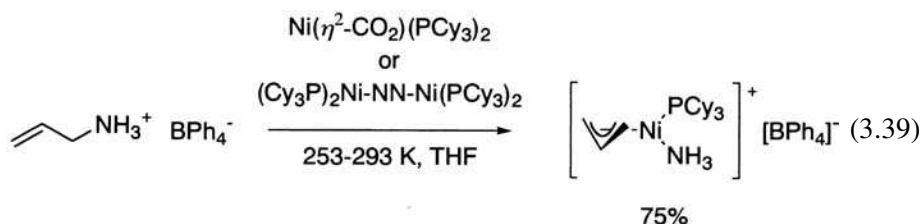
One of other interesting reactions involving C–S bond cleavage is performed on a high-valent group 6 metal center (Scheme 3.81) [154,155]. While the reaction of Cp^*MoCl_4 with LiS^tBu gives a trithiolate complex $\text{Cp}^*\text{Mo}(\text{S}^t\text{Bu})_3$, Cp^*WCl_4 yields $\text{Cp}^*\text{W}(\text{S})_2(\text{S}^t\text{Bu})$ via C–S bond cleavage. The latter reaction is followed by further C–S bond cleavage to give a dinuclear μ -sulfide complex $[\text{Cp}^*\text{W}(\text{S})(\mu\text{-S})]_2$. Similar C–S bond cleavage on high-valent complex is also performed by the reaction of Cp^*TaCl_4 with LiSCPh_3 giving $\text{Cp}^*\text{Ta}(\text{S})(\text{Cl})(\text{SCPh}_3)$.

3.5 RECENT DEVELOPMENTS ON OTHER POLAR SINGLE BOND CLEAVAGE

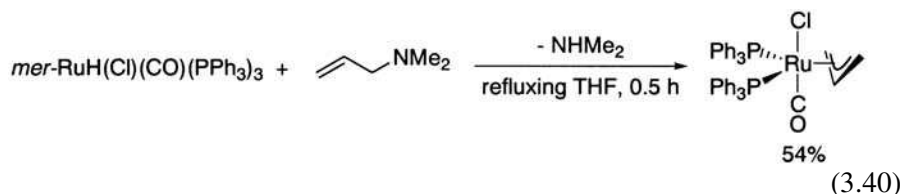
3.5.1 C–N bond cleavage

Though carbon–nitrogen bond cleavage reaction is less explored, allylic C–N bond can be cleaved by low valent late transition metal complexes. Treatment of (μ -dinitrogen or carbon dioxide)nickel(0) complexes with allylammonium

tetraphenylborate results in the oxidative addition of the C–N bond to give a cationic η^3 -allylnickel(II) complex (Eq. 3.39) [156].



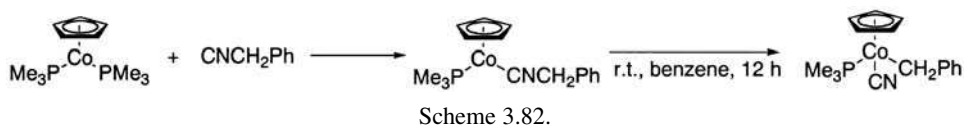
Similar C–N bond cleavage of allylamine by hydridoruthenium(II) is also reported to give an η^3 -allylruthenium(II) complex (Eq. 3.40) [157].

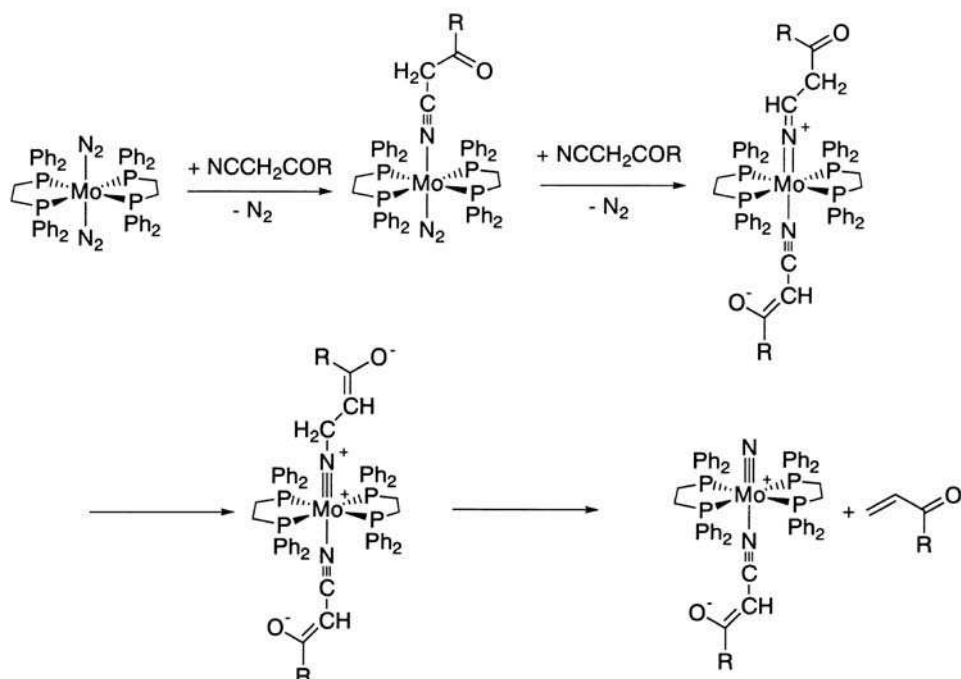


The major driving force for these reactions is likely to be thermodynamic stability of the η^3 -allylmethyl complexes.

Oxidative addition involving the C–N single bond cleavage of isonitrile to electron-rich $\text{CpCo}(\text{PMe}_3)_2$ is known (Scheme 3.82) [158]. One equiv of CNCH_2Ph replaces one of the PMe_3 ligands in $\text{CpCo}(\text{PMe}_3)_2$ to give $\text{CoCp}(\text{PMe}_3)(\text{CNCH}_2\text{Ph})$, in which the C–N single bond oxidatively adds to the Co(I) to give $\text{CoCp}(\text{CH}_2\text{Ph})(\text{CN})(\text{PMe}_3)$ at 25°C . The use of more electron donating pentamethylcyclopentadienyl ligand enhances the C–N bond oxidative addition.

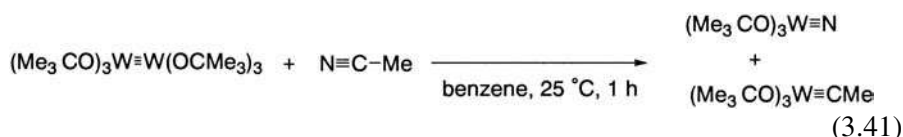
The $\text{C}\equiv\text{N}$ triple bond in nitrile is also cleaved by a molybdenum(0) complex by a sequence shown in Scheme 3.83 [159]. Thus, reaction of bis(dinitrogen)molybdenum complex, *trans*- $\text{Mo}(\text{N}_2)(\text{dppe})_2$, with nitriles such as $\text{NCC}(\text{HRCOR})'$ gives a zwitterionic enolatomolybdenum complex with a nitride ligand. Both dinitrogen ligands in *trans*- $\text{Mo}(\text{N}_2)(\text{dppe})_2$ are replaced by nitriles followed by the formation of zwitterionic enolate complex by disproportionation. The subsequent 1,2-proton migration in the enolate ligand forms the $\text{Mo}\equiv\text{N}$ triple bond. The cleavage of the resulting C–N single bond gives zwitterionic enolate complex with a nitride ligand.





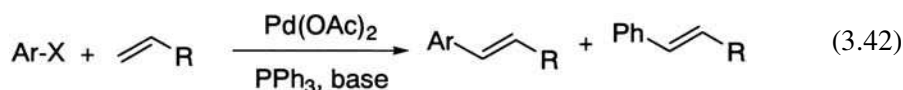
Scheme 3.83.

Interestingly, C≡N triple bond in nitriles can be cleaved by the metathesis reaction with tungsten–tungsten triple bond. Thus, as shown in Eq. 3.41, reaction of (Me₃CO)₃W≡W(OCMe₃)₃ with acetonitrile or benzonitrile gives corresponding alkylidyne and nitride complexes in quantitative yields [160].

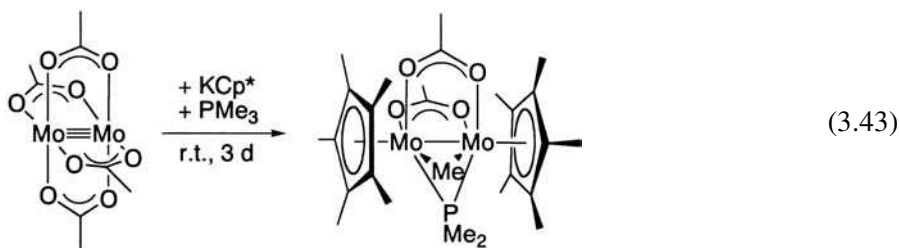


3.5.2 P–C, P–H and P–Se bond cleavages

Attention has been paid to P–C bond cleavage of organophosphorus compounds not only for synthetic application but also for understanding of a deactivation process in Mizoroki–Heck reaction [161], Migita–Kosugi–Stille coupling [162], or hydroformylation [163]. Simultaneous arylation originated from triarylphosphine is sometimes involved (Eq. 3.42).

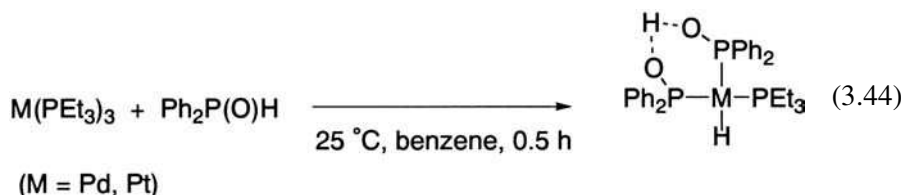


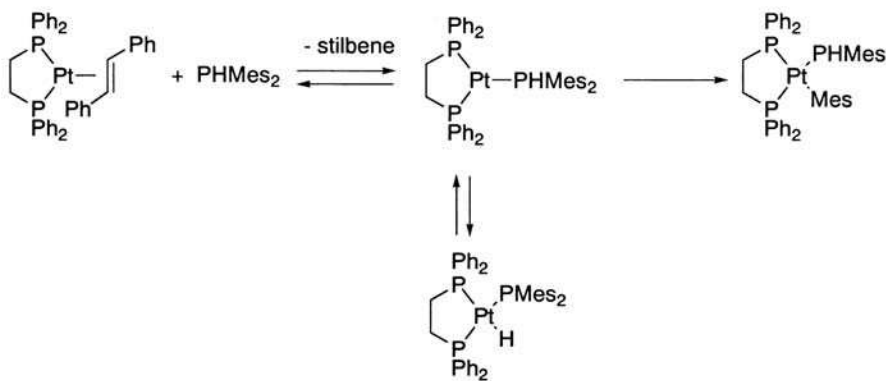
Such a side-reaction is considered to be initiated by P–C bond cleavage *via* aromatic electrophilic substitution of P by Pd or a 1,2-shift of aryl group from P to Pd [164]. An alternative route for the P–C bond cleavage is that from quarternary tetraarylphosphonium salts given by the prior reaction of triarylphosphine with aryl halide [165]. The aryl transfer commonly takes place in the triaryl compounds of group 15 elements and the yield for the phenyl transfer is found to increase in the order $\text{BiPh}_3 \ll \text{SbPh}_3 < \text{AsPh}_3$, but decrease $\text{AsPh}_3 > \text{PPh}_3 \gg \text{NPh}_3$, suggesting importance of both BDE of group 15–carbon bond ($\text{Bi–C} < \text{Sb–C} < \text{As–C} < \text{P–C} < \text{N–C}$) and donor ability of group 15 element ($\text{BiPh}_3 \ll \text{SbPh}_3 < \text{AsPh}_3 < \text{PPh}_3 < \text{NPh}_3$). It is worth noting that P–C bond cleavage is normally observed for aryl–phosphorus bond in arylphosphine or (alkyl)(aryl)phosphine, but a few examples of olefinic or aliphatic P–C bond cleavage in quarternary tetraorganophosphonium salts [5] or methyl group from PMe_3 [166] are also known. Such alkyl migration from alkylphosphine sometimes takes place in dinuclear or cluster complexes to give μ -phosphido complexes (Eq. 3.43) [167].



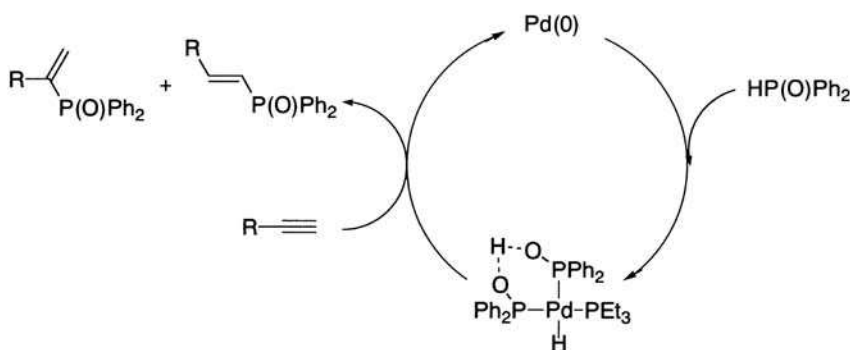
Secondary phosphines are more reactive toward zero-valent complexes. When zero-valent platinum $\text{Pt}(\text{trans-stilbene})(\text{dppe})$ reacts with PHMes_2 (Mes = mesityl), competitive oxidative addition of P–H and P–C bonds takes place *via* a three-coordinate $\text{Pt}(\text{dppe})\text{PHMes}_2$ common intermediate (Scheme 3.84) [168]. Since the P–H bond cleavage product is converted to the P–C bond cleavage product, the former is regarded as a kinetic product and the latter is a thermodynamic one.

Oxidative addition of $\text{Ph}_2\text{P}(\text{O})\text{H}$ to $\text{M}(\text{PEt}_3)_3$ ($\text{M} = \text{Pd}, \text{Pt}$) takes place under ambient conditions (Eq. 3.44) [169]. In this reaction, the P–H bond initially oxidatively adds to the zero-valent group 10 metal complex to give a (hydrido)metallacycle complex stabilized by an internal hydrogen bond. As shown in Scheme 3.85, the reaction is applied to catalytic hydrophosphinylation of terminal alkynes promoted by zero-valent palladium complexes.



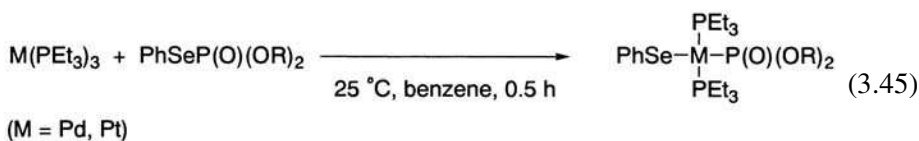


Scheme 3.84.



Scheme 3.85.

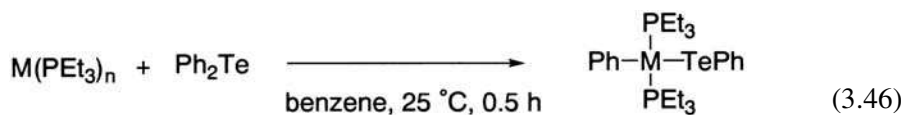
P–Se bond oxidatively adds to zero-valent palladium and platinum complexes [170]. Treatment of $\text{M}(\text{PEt}_3)_3$ ($\text{M} = \text{Pd}, \text{Pt}$) with $\text{PhSeP}(\text{O})(\text{OR})_2$ results in oxidative addition to give *trans*- $\text{M}(\text{SePh})[\text{P}(\text{O})(\text{OR})_2](\text{PEt}_3)_2$ (Eq. 3.45). Catalytic addition of selenophosphates $\text{PhSeP}(\text{O})(\text{OPh})_2$ to terminal alkynes $\text{RC}\equiv\text{CH}$ giving $\text{R}(\text{SePh})\text{C}=\text{CHP}(\text{O})(\text{OPh})_2$ is also performed by $\text{Pd}(\text{PPh}_3)_4$ via similar mechanism shown in Scheme 3.85.



3.5.3 C–Se and C–Te bond cleavage

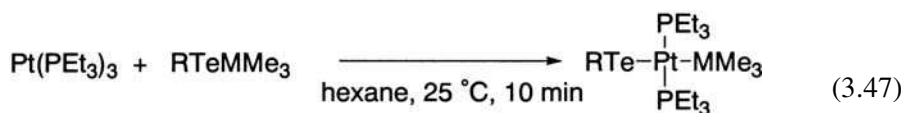
C–Se and C–Te bonds also oxidatively add to zero-valent group 10 complexes. Reaction of $\text{M}(\text{PEt}_3)_n$ ($\text{M} = \text{Ni}, \text{Pd}, \text{Pt}$, $n = 3, 4$) with Ph_2Te gives *trans*-

M(TePh)(Ph)(PEt₃)₂ under mild conditions (25°C, 30 min) (Eq. 3.46) [171]. Ph₂Se reacts with Pt(PEt₃)₃ more easily at 50°C in 5 h to give *trans*-Pt(SePh)(Ph)(PEt₃)₂ in 90% yield. Ph₂S does not react with Pt(PEt₃)_n at room temperature even after 1 day, but heating at 50°C gives only *trans*-Pt(SPh)(Ph)(PEt₃)₂ in less than 3% yield in 1 day. These results show that the ease of oxidative addition of a carbon–chalcogen bond to Pt(PEt₃)₃ decreases in the order C–Te > C–Se > C–S, which is the reverse order of their bond strengths.



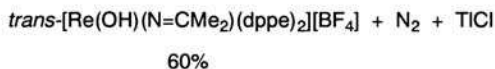
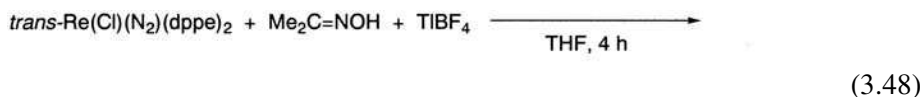
3.5.4 Te group 14 element bond cleavage

Oxidative addition of other group 14 atom–tellurium bonds (Si–Te, Ge–Te, and Sn–Te) is also achieved (Eq. 3.47) [172]. Reactions of zero-valent platinum complex Pt(PEt₃)₃ with RTeMMe₃ (M = Se, Ge, Sn) at 25°C result in the formation of the *trans*-Pt(TeR)(MMe₂)(PEt₃)₂ within 10 min.



3.5.5 N–O bond cleavage

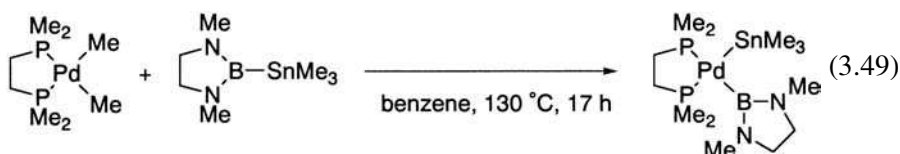
N–O bond in oxime Me₂C=NOH can also be cleaved by reaction with *trans*-Re(Cl)(N₂)(dppe)₂ in the presence of TIBF₄ to give *trans*-[Re(OH)(N=CMe₂)(dppe)₂][BF₄] (Eq. 3.48) [173]. The π-accepting ability of the N=CMe₂ moiety may stabilize the product.



3.5.6 B–Sn bond cleavage

Reaction of PdMe₂(dmpe) with (NMeC₂H₄NMe)B–SnMe₃ gives Pd(SnMe₃)[B(NMeC₂H₄NMe)](dmpe), where oxidative addition of the B–Sn bond to the palladium(0) species is involved (Eq. 3.49) [174]. Thus, Pd catalyzed

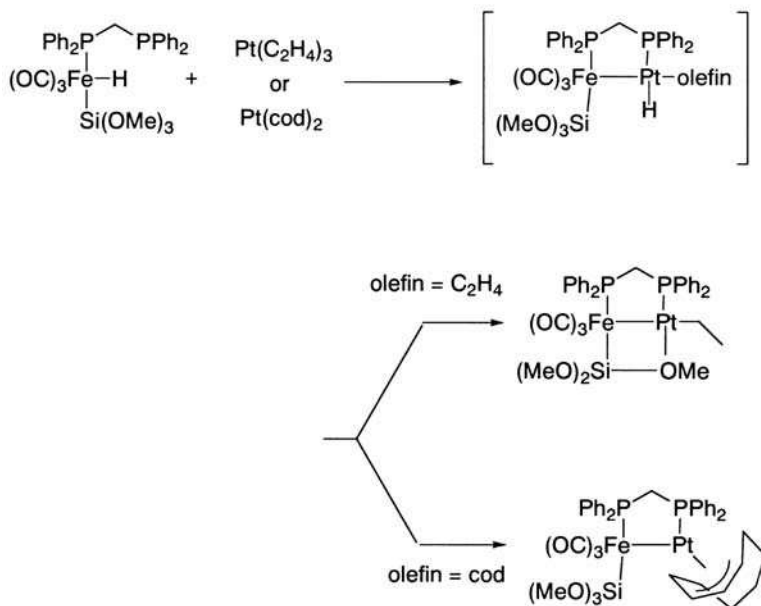
borylstannation of internal alkynes is successfully achieved at room temperature quantitatively, in a manner similar to Scheme 3.85.



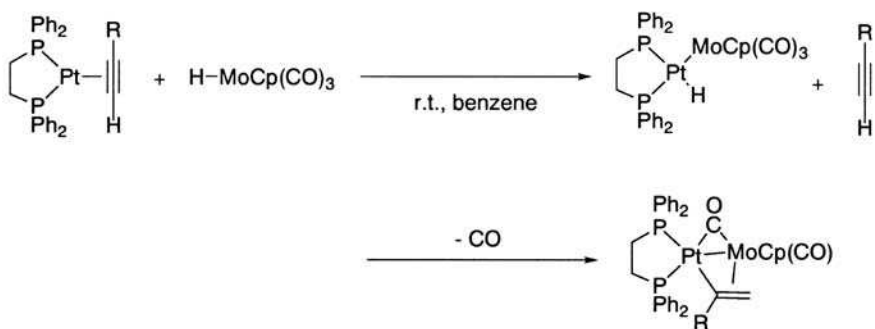
3.5.7 M–H and M–C bond cleavages

Oxidative addition of transition metal–hydride and transition metal–carbon bonds to zero-valent transition metal complexes provides convenient method for preparation of homo- and heterodinuclear organometallic complexes. Oxidative addition of iron–hydride to zero-valent platinum complex giving Fe–Pt heterodinuclear complexes was demonstrated by the reaction of $\text{HFe}[\text{Si}(\text{OMe})_3](\text{CO})_3(\kappa^1\text{-dppe})$ with zero-valent platinum complex such as $\text{Pt}(\text{C}_2\text{H}_4)_3$ or $\text{Pt}(1,5\text{-cod})_2$ giving eventually heterodinuclear ethyl or cyclooctenyl complex (Scheme 3.86) [175]. The resulting heterodinuclear structure is stabilized by the bridging dppe ligand and the siloxo moiety.

Oxidative addition of molybdenum–hydride bond in $\text{HMoCp}(\text{CO})_3$ to $\text{Pt}(\text{terminal alkyne})(\text{dppe})$ complex also takes place to give an alkenylplatinum complex under mild conditions (Scheme 3.87) [176]. In this reaction, subse-



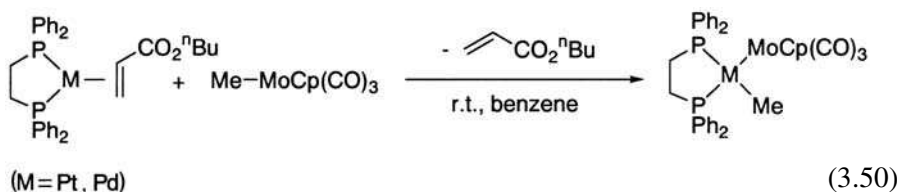
Scheme 3.86.



Scheme 3.87.

quent Markovnikov addition of the H–Pt bond to the liberated terminal alkyne to give $(\text{dppe})(\text{CH}_2=\text{CR})\text{Pt}-\text{MoCp}(\text{CO})_3$, followed by decarbonylation of a carbonyl ligand, leads to the formation of μ -alkenyl complex $(\text{dppe})\text{Pt}[(\mu-\text{CH}_2=\text{CR})(\mu-\text{CO})\text{MoCp}(\text{CO})_2]$ as a final product.

Further unequivocal examples for oxidative addition of organometallic M–C bond to a zero-valent complex were obtained by the reactions of $\text{Me}-\text{MoCp}(\text{CO})_3$ and $\text{AcCo}(\text{CO})_4$ with palladium(0) and platinum(0) complexes giving $(\text{dppe})\text{RM}-\text{M}'\text{L}_n$ ($\text{M} = \text{Pt}, \text{Pd}$, $\text{M}' = \text{Mo}, \text{Co}$) in high yields (Eq. 3.50) [177]. Such oxidative addition reaction is considered to be reversible, since the organic group in $\text{L}_2\text{RM}-\text{M}'\text{Cp}(\text{CO})_3$ transfers to M' to give $\text{RM}'\text{Cp}(\text{CO})_3$ by reductive elimination at M [178].

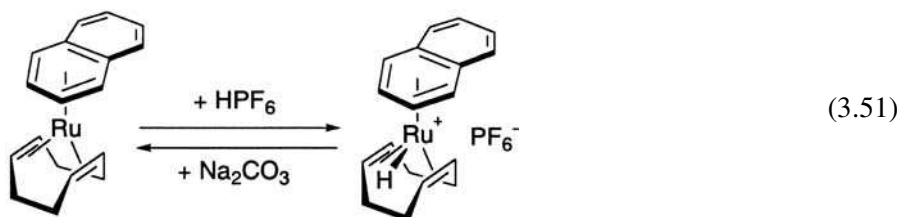


3.5.8 Brønsted acids and related compounds

Though C–H bond activation currently attracts intensive attention because of potential utilization in organic synthesis, polar heteroatom–hydrogen cleavage reactions by transition metals are also interesting, since they could provide new methodologies for organic, organometallic and inorganic syntheses.

Although the Brønsted acid has strong ionic bonding character, it can oxidatively add to low-valent transition metal complexes to give hydride complexes. In these reactions, the proton is formally converted to the hydride by virtue of oxidation of transition metals. When Brønsted acids having a non-coordinating

anion are employed in this reaction, cationic hydride complex can be isolated (Eq. 3.51) [179].



Treatment of $\text{Pd}(\text{PCy}_3)_2$ with HCl gives (hydrido)(chloro)palladium(II) complex (Eq. 3.52) [180], where protonation is considered to occur first, followed by the addition of halide anion.

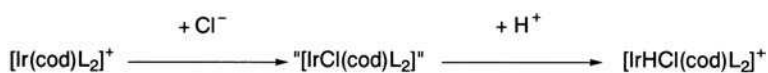


On the other hand, in reaction of cationic complex such as $[\text{Ir}(\text{cod})(\text{PMe}_2\text{Ph})_2]^+$ with HCl , halide anion attacks the cationic metal center initially, and then addition of the proton gives $[\text{IrHCl}(\text{cod})(\text{PMe}_2\text{Ph})_2]^+$ (Scheme 3.88) [181].

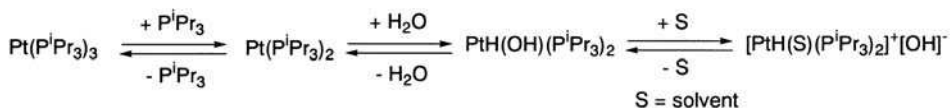
Bond cleavage reactions of O–H, S–H and N–H bonds by late transition metal complexes are also known to provide alkoxo-, aryloxo-, thiolato- and amidometal complexes.

Oxidative addition of water to platinum(0) complex is known to occur via two-coordinate platinum(0) complex (Scheme 3.89) [182]. The resulting (hydrido)(hydroxo)platinum(II) rapidly liberates hydroxo anion by the addition of organic solvent such as THF or pyridine to give a cationic platinum(II) complex.

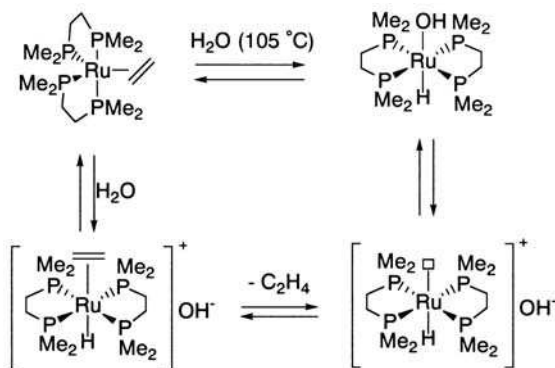
It is interesting to note that dimethyl maleate stereoselectively inserts into the Pt–OH bond of some hydroxoplatinum(II) complex giving the *erythro* product, indicating *cis*-insertion (Eq. 3.53) [183].



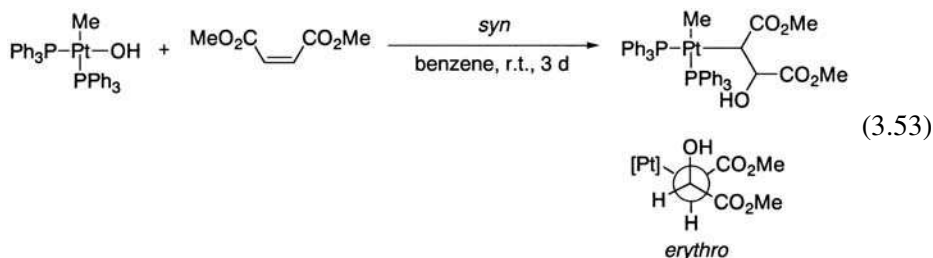
Scheme 3.88.



Scheme 3.89.



Scheme 3.90.



This reaction may be regarded as a possible model reaction of Wacker reaction, although the mechanism involving *exo* attack of a free water on the coordinated olefin is generally accepted [184].

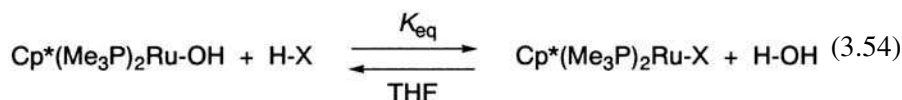
Oxidative addition of water to iridium(I) has also been known [185]. In this reaction, reaction of $[\text{Ir}(\text{PMe}_3)_4]^+[\text{PF}_6]^-$ with water in THF gave a rare mononuclear hydroxo complex *cis*- $[\text{Ir}(\text{H})(\text{OH})(\text{PMe}_3)_4]^+[\text{PF}_6]^-$ in high yield. A neutral iridium(I) complex $\text{IrCl}(\text{dmsO})_3$ is recently reported to show high activity toward oxidative addition of water [186].

Oxidative addition of water to ruthenium(0) has also been known (Scheme 3.90) [187]. Treatment of ethylene complex $\text{Ru}(\text{C}_2\text{H}_4)(\text{dmpe})_2$ with water results in the formation of (hydrido)(hydroxo)ruthenium(II) complex. This product is probably formed by protonation of the metal followed by liberation of ethylene and addition of hydroxo anion.

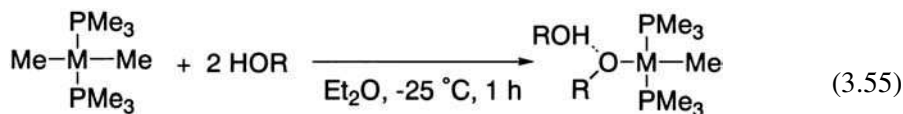
These late transition metal hydroxides usually act as strong base. For example, Scheme 3.91 shows that hydroxopalladium(II) complex reacts with amines and thiol to give amido- and thiolatopalladium(I) complexes [188]. It is worth noting that alkali metal hydroxides do not react with these reagents at all.

By using Eq. 3.54, relative bond strengths of M–H, M–O, M–N, and M–C are estimated for $\text{Cp}^*\text{RuX}(\text{PMe}_3)_2$ and $\text{PtX}(\text{Me})(\text{dppe})$, and show good correlation with the H–X bond dissociation energy ($\text{M}-\text{C}\equiv\text{CPh} > \text{M}-\text{OH} > \text{M}-\text{Ph} > \text{M}-\text{H}$

> M-OMe > M-R > M-NHPh > M-NPh₂) [189].

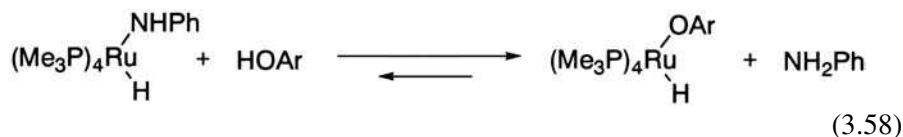
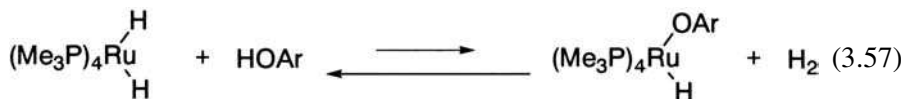


O-H bond of alcohols such as phenols or fluorinated alcohols is cleaved by dialkylmetal(II) complexes to give (alkyl)(aryloxo)- or (alkyl)(alkoxo)nickel(II) and palladium(II) complexes with evolution of alkane (Eq. 3.55) [190]. Some aryloxo and alkoxometal complexes have enough basicity to have strong hydrogen bonding with free alcohol both in solid state and in solution.



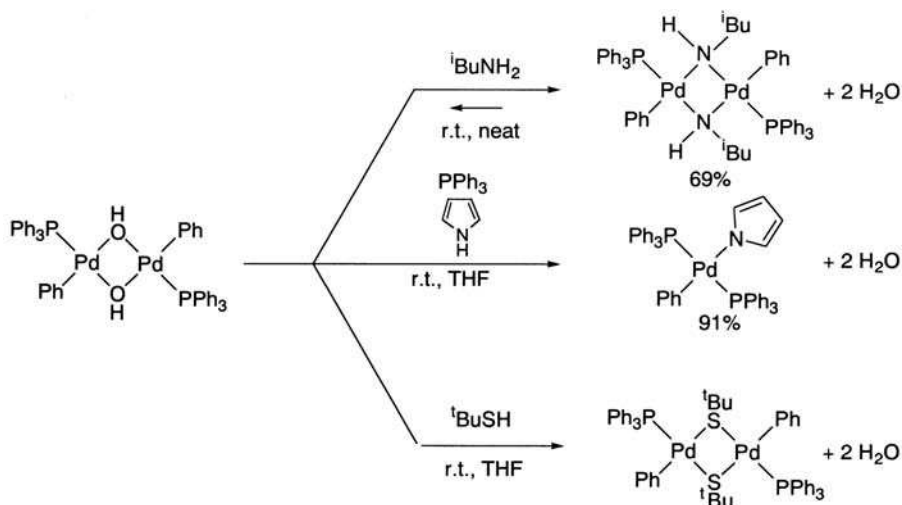
M = Ni, Pd

Phenols rapidly react with *cis*-RuH(CH₂Ph)(PMe₃)₄, *cis*-RuH₂(PMe₃)₄, and *cis*-RuH(NHPh)(PMe₃)₃ to give *cis*-RuH(OPh)(PMe₃)₄ (Eqs. 3.56–3.58) [191, 192]. These reactions are triggered by protonation of the coordinatively saturated complexes by phenols to form cationic hydride complexes.

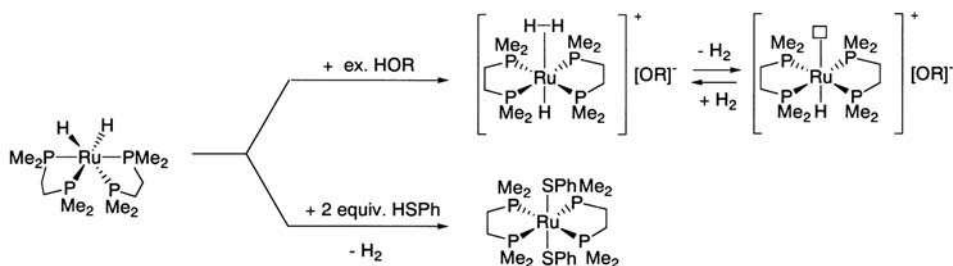


Protonation of hydridoruthenium(II) complex *cis*-RuH₂(dmpe)₂ by less protic alcohols such as methanol and ethanol takes place if the reactions are carried out in the presence of an excess reagent (Scheme 3.92) [193]. Cationic dihydrogen complexes *trans*-[RuH(H₂)(dmpe)₂]⁺[OR][−] are obtained as an equilibrium mixture with [RuH(dmpe)₂]⁺[OR][−] and molecular hydrogen. When *cis*-RuH₂(dmpe)₂ reacts with benzenethiol, further reaction proceeds to give dithiolatoruthenium(II) complex with evolution of molecular hydrogen.

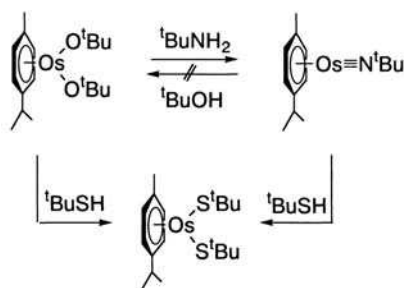
Treatment of dialkoxoosmium(II) shown in Scheme 3.93 with *t*BuNH₂ results in the successive N-H bond cleavages to give imidoosmium(II) complex



Scheme 3.91.



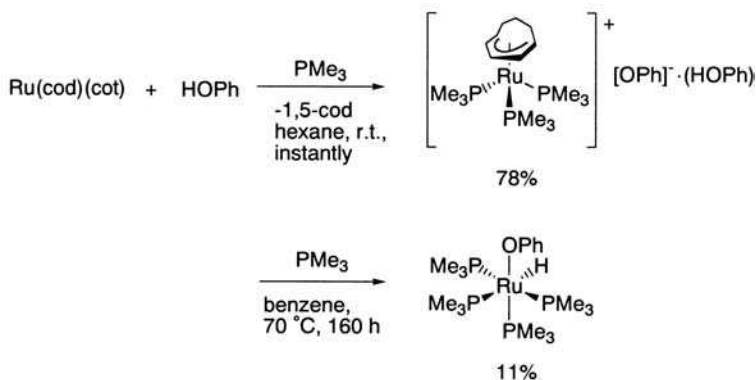
Scheme 3.92.



Scheme 3.93.

irreversibly [194]. The reaction of imidoosmium(II) or dialkoxoosmium(II) with $t\text{-BuSH}$ leads to the formation of dithiolatoosmium(II) complex.

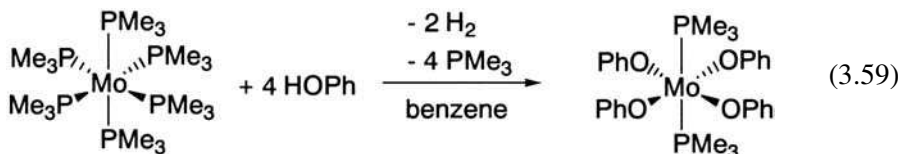
Reaction of phenols with zerovalent ruthenium complex, $\text{Ru}(\text{cod})(\text{cot})$



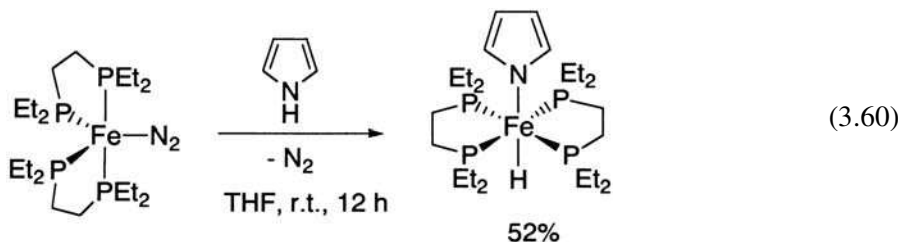
Scheme 3.94.

in the presence of PMe_3 yields a formal oxidative addition products *cis*-(hydrido)(phenoxo)ruthenium(II) complex (Scheme 3.94). In reality, however, protonation at the cot ligand is taking place as an initial step giving a cationic η^5 -cyclooctadienyl complex $[\text{Ru}(\eta^5\text{-C}_8\text{H}_{11})(\text{PMe}_3)_3]^+[\text{OPh}]^-(\text{HOPh})_n$ from which (hydrido)(phenoxo)ruthenium(II) is produced [195].

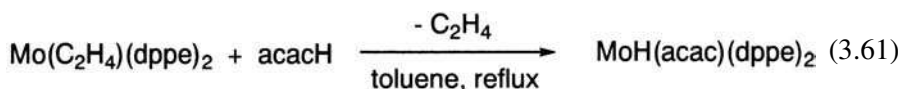
Reaction of a molybdenum(0) complex $\text{Mo}(\text{PMe}_3)_6$ with an excess amount of phenol gives tetraphenoxomolybdenum(IV) complex accompanied by evolution of molecular hydrogen (Eq. 3.59) [196].



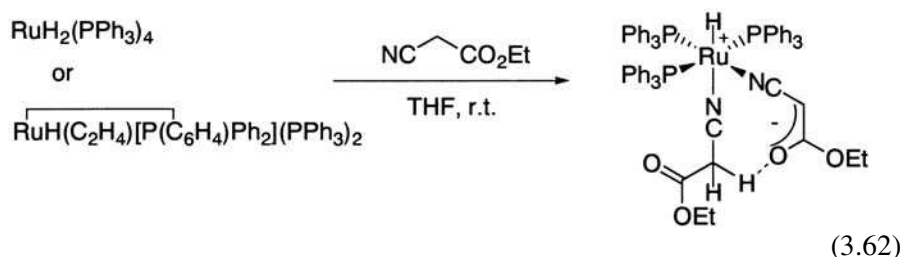
Oxidative addition of N–H bond is also known as shown in Eq. 3.60 [108].



C–H bond in active methylene compounds is acidic and can also oxidatively add to low-valent transition metal complexes giving transition metal enolates. For example, acetylacetonone oxidatively adds to low-valent Mo complexes giving hydrido(acetylacetonato)metal complexes [197].



When cyanoacetate is employed as a reactant, zwitterionic enolatoruthenium(II) complex is formed due to strong coordination ability of the cyano group to Ru, producing high nucleophilicity on the enolate carbon (Eq. 3.62) [198]. Thus, the zwitterionic enolatoruthenium(II) complex smoothly reacts with electrophiles such as Michael acceptors and aldehydes.



Because of this increased nucleophilicity of the enolate, catalytic reactions with high atom economy such as chemoselective aldol, Knöevenagel and Michael reactions catalyzed by Re, Fe, Ru, Rh and Ir complexes are achieved under neutral and mild conditions [199–202].

3.6 SUMMARY

In this chapter, cleavage reactions of carbon–halogen, carbon–oxygen, carbon–sulfur, and other polar single bonds were described. As described, these bond cleavage reactions are extensively studied to provide new inlets toward organic syntheses and catalyses. Since most of these accomplishments appear from organic synthetic points of view, important activation steps are frequently described as speculation. Nevertheless, such reactions giving ideas concerning cleavages of polar chemical bonds are described as the pages allow. Therefore, in some parts rather enumerative expressions were employed in this chapter. For further comprehensive understanding concerning cleavages of polar bonds such as carbon–halogen and carbon–oxygen bond cleavages, the following concise reviews are recommended reading [6,33–36].

3.7 REFERENCES

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Transition Metal–Carbene Complexes in Olefin Metathesis and Related Reactions

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4.1 SCOPE

During the past few decades, a wide variety of molecules with transition metal–carbon multiple bonds have been studied. The chemistry of doubly bonded species – carbenes – is particularly interesting because it leads to several synthetically important transformations, and for this reason, metal carbenes are the main subject of this chapter. Our discussion begins with a classification of metal–carbene complexes based on electronic structure, which provides a way to understand their reactivity patterns. Next, we summarize the mechanistic highlights of three metal–carbene-mediated reactions: carbonyl olefination, olefin cyclopropanation, and olefin metathesis. Throughout the second half of the chapter, we focus mainly on ruthenium–carbene olefin metathesis catalysts, in part because of widespread interest in the applications of these catalysts, and in part because of our expertise in this area. We conclude with some perspectives on the chemistry of metal carbenes and on future developments in catalysis.

4.2 CLASSIFICATION OF TRANSITION METAL–CARBENE COMPLEXES

Carbenes are defined as species containing divalent carbon [1], and they may display either electrophilic or nucleophilic reactivity depending on whether the two unshared electrons on the carbon center are unpaired (triplet carbene) or paired (singlet carbene). Metal–carbene complexes can be classified in a similar way based on their reactivity toward electrophiles and nucleophiles. The resonance forms shown in Fig. 4.1 define the limiting structures, and the formal charge on the carbene carbon indicates the preferred reactivity. Those that are nucleophilic at carbon are called Schrock-type complexes or alkylidenes, and they generally

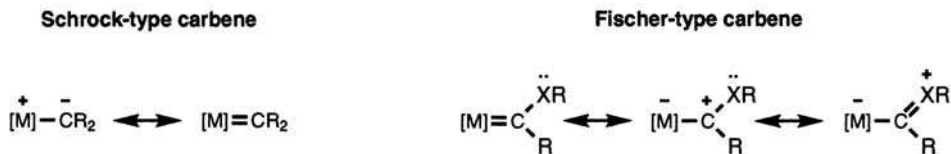
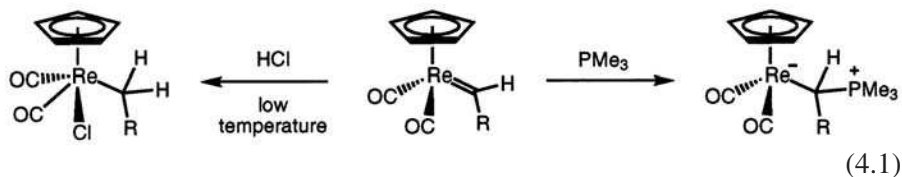


Fig. 4.1. Metal–carbene resonance forms; R = alkyl or aryl, X = π -donor heteroatom.

contain alkyl- or aryl-substituted carbene fragments [2]. Schrock reported the first example of such a complex in 1974 [3]. In these cases, the metal–carbene bond can be represented by two resonance forms, one with a formal $M=C$ double bond and the other with charge separation, by analogy to ylides.

At the other extreme, metal carbenes that are electrophilic at carbon are called Fischer-type complexes, and they generally contain π -donating heteroatom substituents [4]. Fischer reported the first example in 1964 [5]. In these cases, the metal–carbene interaction can be represented by three resonance structures, the first with a formal $M=C$ double bond, the second with a $M-C$ single bond and charge separation, and the third with additional multiple bond character between the carbon and the heteroatom substituent.

The nucleophilic–electrophilic/Schrock–Fischer distinctions have been extremely useful throughout the development of metal–carbene chemistry because they provide a way to categorize metal carbenes and rationalize their reactivity patterns [6]. Yet, as an increasing variety of complexes are studied, it is becoming clear that these classifications represent only the prototypical complexes that were initially discovered. We now know of many examples with intermediate characteristics and reactivity profiles, such as electrophilic species that lack heteroatom stabilization and even complexes like $(Cp)(CO)_2Re=CHR$ that display ambiphilic reactivity, meaning that this rhenium carbene reacts with both nucleophiles and electrophiles (Eq. 4.1) [7].



For these reasons, defining every metal–carbene complex as absolutely either Schrock- or Fischer-type can be misleading. An alternative view considers the wide-ranging variations in metal–carbene structure and reactivity as points along a continuum. The extremes of this continuum differ in the electronic ground states of both the carbene and metal fragments (triplet or singlet), as described by Hall [8], Goddard [9], and Gordon [10,11]. In Fig. 4.2, we summarize the properties of four representative metal–carbene cases: a traditional Schrock-type complex,

	1	2	3	4
Category:	traditional Schrock-type carbene (alkylidene)	halocarbene	traditional Fischer-type carbene	Wanzlick-Lappert-Arduengo carbene
Example:				
Ground state of free carbene:	triplet	singlet	singlet	singlet
Typical metal centers:	higher oxidation state, earlier transition metals	lower oxidation state, later transition metals		variable
Typical ancillary ligands on M:	Cl, Cp, alkyl	good π -acceptors, e.g. CO		variable
Typical carbene substituents:	alkyl, aryl, H	F, Cl	good π -donors, e.g. OR, NR ₂	
Character of metal-bound carbene carbon:	nucleophilic	variable	electrophilic	electrophilic or unreactive
Metal–carbon bond order:	2	1-2	1-2	~1
Bonding interactions:	M–C covalent σ + M–C covalent π	C→M dative σ + M→C π -backbonding	C→M dative σ + M→C π -backbonding + heteroatom→C π -donation	C→M dative σ + heteroatom→C π -donation
Illustration of bonding interactions:				
Trends:	metal→carbon π-backbonding decreases bond order decreases reactivity of carbene carbon changes from nucleophilic to electrophilic			

Fig. 4.2. Characteristics of representative metal–carbene complexes.

a halocarbene complex, a traditional Fischer-type complex, and a Wanzlick–Lappert–Arduengo carbene complex. The rows include, from top to bottom: examples of each type of metal carbene, the ground states of the carbene and metal fragments, typical metal centers and ancillary ligands, typical substituents on the carbene carbon, the reactivity of the carbene center, the metal–carbon bond orders,

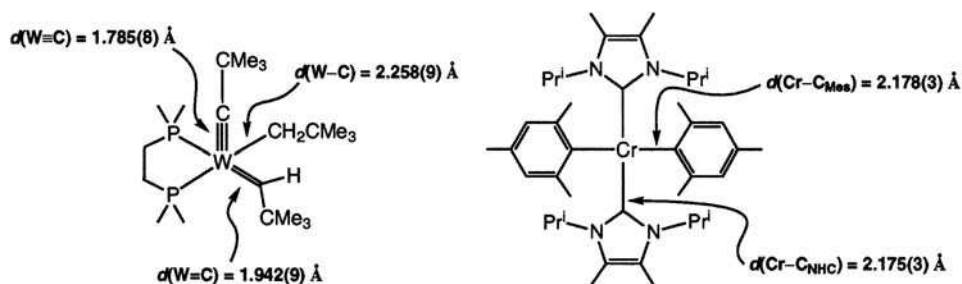


Fig. 4.3. Examples of the relationship between metal–carbon bond distance and bond order.

and the main bonding interactions. Trends in these properties across the four cases are illustrated below the table.

The traditional Schrock-type category corresponds to the first column in Fig. 4.2. The metal–carbene bonding in these complexes can be considered as the interaction of a triplet metal center with a triplet carbene fragment to form a covalent metal–carbon double bond. This bonding scheme is similar to that in carbon–carbon double bonds (e.g., ethylene). The bond order in these metal carbenes is clearly equal to two and is reflected by bond lengths obtained from X-ray diffraction studies. This relationship between bond distance and bond order is illustrated by the famous tungsten complex $(\text{dmpe})\text{W}(\text{CH}_2\text{CH}_3)(\text{CHCMe}_3)(\text{CCMe}_3)$, which contains an alkyl, an alkylidene, and an alkylidyne ligand, all coordinated to a single metal center (Fig. 4.3) [12]. There is a substantial decrease of 0.32 Å in going from the tungsten–carbon single to double bond, and a further decrease of 0.16 Å in going from the double to triple bond.

The traditional Fischer-type category corresponds to the third column in Fig. 4.2. In these carbene complexes, the bonding interaction can be described as a combination of three components: (i) donation of the lone pair from the singlet carbene fragment into an empty metal orbital, (ii) π -backbonding from a filled metal d orbital into the unoccupied carbon p orbital, and (iii) additional stabilization through π -donation from the heteroatom substituent to the carbon p orbital. This description is similar to the Dewar–Chatt–Duncanson bonding model for metal–alkene interactions (as well as the bonding model for metal carbonyls), in that they each involve an electronic donor–acceptor synergism [13]. It also accounts for the partially unoccupied p orbital on the carbene carbon, which leaves it subject to nucleophilic attack and explains the intermediate metal–carbon bond order (between one and two).

The second column consists of halide-substituted carbene complexes [14]. In these cases, the bonding scheme is similar to Fischer carbenes in that the singlet halocarbene fragments interact with singlet metal centers, but the halide substituents do not contribute as much electron density into the carbon p orbital as the more strongly π -donating alkoxide substituents. Presumably, this electronic deficit

is offset by greater π -backbonding from the metal center to the halocarbene. The extent of the backbonding, and thus the reactivity of the carbene carbon, is highly dependent on the electronic effects of the ligands on the metal center. For example, the carbene in $[(\text{Cp})(\text{CO})_2\text{Fe}=\text{CF}_2]^+$ is electrophilic, whereas the carbene in $(\text{PPh}_3)_2(\text{NO})(\text{Cl})\text{Ru}=\text{CF}_2$, which contains more electron-donating PPh_3 ligands and hence can engage in more metal $\rightarrow$ carbon π -backbonding, is nucleophilic [14,15].

The fourth column consists of metal complexes with Wanzlick–Lappert–Arduengo carbenes [16,17]. These carbenes are usually characterized by the presence of two strongly π -donating substituents, and the most common are *N*-heterocyclic carbenes (NHCs), also known as diaminocarbenes or nucleophilic carbenes (because of the reactivity of the *free* carbenes). These ligands are an extreme case of the traditional Fischer-type complexes because the π -donation from the nitrogen lone pairs into the carbon p orbital is so extensive that many free NHCs are stable without metal coordination. Wanzlick–Lappert–Arduengo carbenes coordinate to metals predominantly by strong σ -donation through the carbon lone pair, and they typically behave as unreactive ancillary ligands similar to phosphines (PR_3). As illustrated by the bond lengths of the chromium complex in Fig. 4.3, there is no formal metal–carbon multiple bond: the chromium–aryl and chromium–NHC distances are identical within experimental limits [18]. As a result, the metal–carbene interaction is usually represented as a single or a dative ($\text{C}:\rightarrow\text{M}$) bond.

All of the factors included in Fig. 4.2 contribute to the preference of a metal center and a carbene fragment to exist in triplet or singlet states, so there is *no single criterion* that can be used to classify carbene complexes. A good example is provided by ruthenium carbene complexes like $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$, which we will discuss at length later in this chapter. The metal center is formally a lower oxidation state, later transition metal center $[\text{Ru}(\text{II})]$, which is more common for Fischer-type complexes. At the same time, however, the ruthenium carbene has a phenyl substituent and the complex does not contain any good π -acceptor ligands, both characteristics of Schrock-type carbenes. Perhaps the best overall assessment of this situation is that the electron-donating PCy_3 ligands likely favor a metal triplet ground state, and the aryl substituent on the carbene carbon likely stabilizes the carbene triplet ground state.

Fig. 4.4 illustrates the four types of metal–carbene complexes that we have described as points along the metal–carbene continuum. This relationship can be considered a continuum in the sense that the orbitals on the carbene carbon can be involved in varying degrees of overlap with adjacent metal and substituent orbitals. Moving from left to right, the interaction between the metal and the carbene changes from a covalent-type double bond to a dative-type single bond. Although the bonding in metal carbenes is more involved than we have described here, the metal–carbene continuum is a useful qualitative model because it provides a unified way to think about the full range of these complexes.

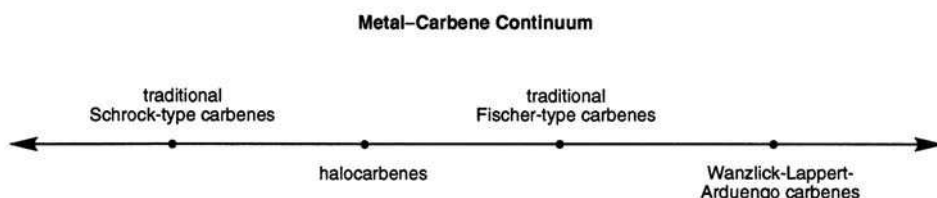


Fig. 4.4. Four categories that range across the metal–carbene continuum.

4.3 REACTIVITY OF TRANSITION METAL–CARBENE COMPLEXES

4.3.1 Introduction

As a site of unsaturation, the metal–carbene bond is a potential locus for reactivity. The three transformations that we have selected to discuss in this chapter are shown in Fig. 4.5. Pathway (a) illustrates metal–carbene mediated carbonyl olefination, in which an alkylidene complex reacts stoichiometrically with an organic carbonyl-containing compound, to afford an olefin in place of the carbonyl and a metal–oxo complex. This overall transformation of a carbonyl to an olefin is conceptually the same as the Wittig reaction with phosphorus ylides, although the mechanism is different. Pathway (b) illustrates the olefin cyclopropanation reaction, in which single bonds are formed between the metal-bound carbene and each of the two carbon atoms of an olefin to yield a cyclopropane ring. And in pathway (c), the olefin metathesis reaction converts starting olefins into new olefins by the metal–carbene catalyzed cleavage and reassembly of carbon–carbon double bonds.

Olefin cyclopropanation and carbonyl olefination are generally mediated by tra-

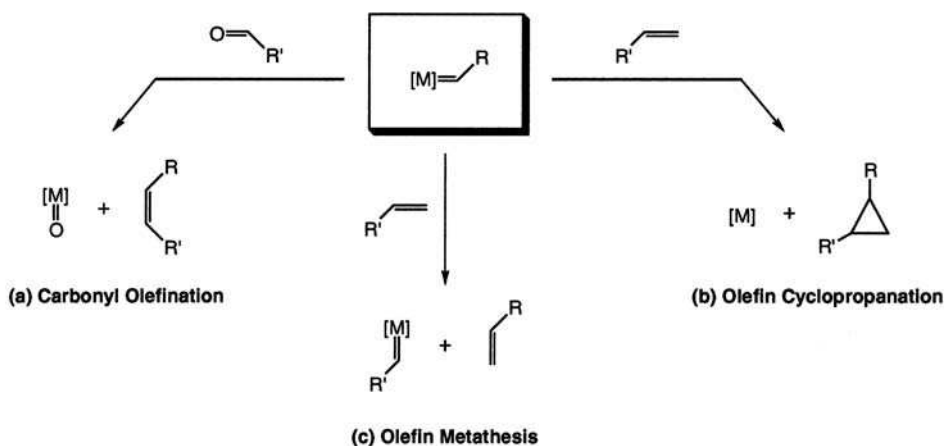


Fig. 4.5. Three synthetically useful reactions mediated by metal–carbene complexes.

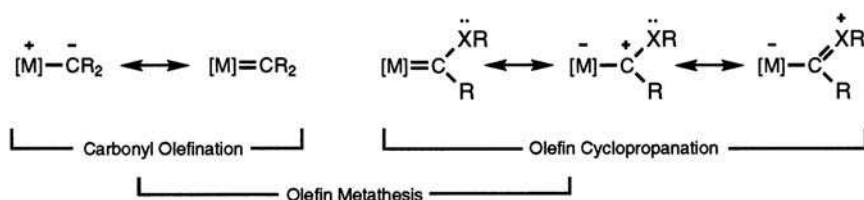


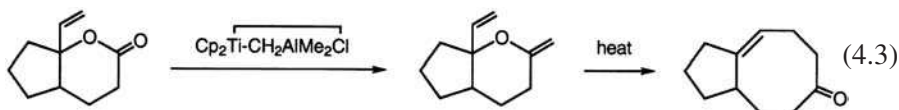
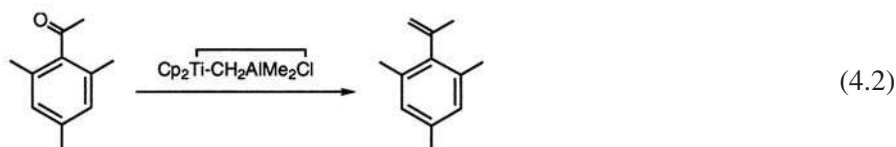
Fig. 4.6. The reactivity patterns of the various formal representations of metal–carbene polarization.

ditional Fischer- and Schrock-type complexes, respectively, whereas the carbene complexes active for olefin metathesis often exhibit intermediate characteristics (Fig. 4.6). As one would expect from the metal–carbene continuum model, there is some overlap in these reactivity patterns.

Transition metal–carbene complexes undergo many more reactions in addition to these three and have been widely applied to the synthesis of organic molecules. Because this material is outside the scope of the chapter, we direct the interested reader to reviews on other carbene-mediated transformations [19–21].

4.3.2 Carbonyl olefination

In 1978, Tebbe reported that a complex prepared by reaction of titanocene dichloride with trimethylaluminum could transform esters into the corresponding vinyl ethers in moderate yields [22,23]. The use of the “Tebbe reagent,” $Cp_2Ti(\mu-CH_2)(\mu-Cl)AlMe_2$, became the first reliable method for this transformation and a general way to convert carbonyl groups into β -substituted methylenes. This titanium complex exhibits activity for carbonyl olefination that distinguishes it from phosphorus-based ylides [24]. In particular, the Tebbe reagent can methylenate less electrophilic carbonyl groups and more sterically hindered ketones in good yields, it is not sufficiently basic to enolize ketones, and it is reactive with a broader range of carbonyl compounds, including esters and amides [25]. These properties make the Tebbe reagent synthetically useful, as illustrated by the examples in Eqs. 4.2 and 4.3.



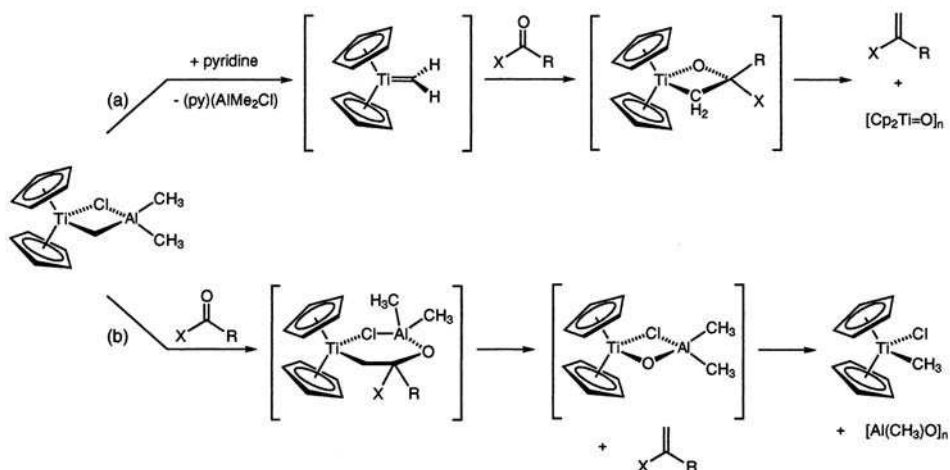


Fig. 4.7. Proposed mechanisms of the Tebbe reagent for the olefination of carbonyls in the presence of base (pathway a) and the absence of base (pathway b).

Under standard reaction conditions, a Lewis base (e.g., pyridine) coordinates to the aluminum and activates the complex, releasing the titanium methylene $[\text{Cp}_2\text{Ti}=\text{CH}_2]$ (Fig. 4.7, pathway a) [26]. This metal carbene undergoes $[2+2]$ cycloaddition with the carbonyl compound to form an oxometallacyclobutane, which then fragments to yield the desired olefin and a titanium–oxo species. The driving force for this process is the formation of the strong titanium–oxo bond, but this also renders the oxo species catalytically inactive and the reaction irreversible, so stoichiometric amounts of the Tebbe reagent are required in olefination reactions. In the absence of base, the proposed mechanism involves formation of a six-membered metallacyclic intermediate rather than the oxometallacyclobutane (Fig. 4.7, pathway b), and ultimately the oxygen of the original carbonyl group becomes part of an aluminum–oxo polymer [26,27].

The usual representation of Schrock-type nucleophilic carbenes as electron rich at carbon can be especially misleading in the case of the Tebbe reagent and related complexes. These high oxidation state complexes are electron-deficient and electrophilic at the metal center, and it is unlikely for polarization of the metal–carbon bond to remove even more electron density from the metal under these circumstances. Thus, the reactivity of the Tebbe reagent is more closely related to the electrophilicity and oxophilicity of the metal center than to the nucleophilicity of a polarized carbene carbon; that is, the reactivity is due to carbonyl polarization upon complexation, not attack of the alkylidene carbon on an unactivated, electrophilic carbonyl carbon.

Since the discovery of the Tebbe reagent, related systems have been developed that offer advantages in cases where alkylaluminum chloride-free conditions are necessary [27]. One example is the “Petasis reagent,” Cp_2TiMe_2 , synthesized

by the reaction of Cp_2TiCl_2 with MeLi . These derivatives react as though they generate $[\text{Cp}_2\text{Ti}=\text{CH}_2]$, but their mode of action is probably more similar to that of the Tebbe reagent in the absence of base (Fig. 4.7, pathway b). Because titanocene-based reagents generally cannot transfer alkylidenes other than methyldiene, alternative reagents also have been developed for this purpose, such as the Takai–Oshima–Lombardo $\text{CX}_2\text{R}_2/\text{Zn}/\text{TiCl}_4$ protocols [27].

4.3.3 Olefin cyclopropanation

Metal–carbene mediated cyclopropanation offers a practical way to convert olefins into strained, three-membered rings that are difficult to prepare by other methods. Although the majority of carbene complexes utilized for cyclopropanation are generated *in situ* because of their instability [21,28], one isolated example is the pentacarbonyl tungsten benzyldiene $(\text{CO})_5\text{W}=\text{CHPh}$. This complex reacts with a wide variety of alkyl- and aryl-substituted olefins at low temperatures to yield cyclopropane derivatives. Carbonyl dissociation is unlikely at low temperatures, which precludes the formation of a tungsten–carbene–olefin intermediate, and the evidence suggests that direct reaction of the carbene with the olefin occurs as shown in Fig. 4.8. The proposed mechanism involves electrophilic addition of the carbene carbon atom to the olefin, followed by ring closure via electrophilic attack of the second carbon atom of the olefin on the carbene carbon atom [21,28]. Because this process permanently transfers the carbene to the olefin and leaves the metal complex without a carbene ligand, the metal carbene must be regenerated in a separate step to make the cyclopropanation catalytic. For example, in one of the most widely used protocols, diazo compounds are added to copper precursors. Recent studies have confirmed that the active species is a Cu(I) carbene complex, and an alkoxycarbonylcarbene derivative coordinated with the sterically bulky iminophosphoramidate ligand has been characterized by NMR at low temperature [29].

The direct carbene insertion scheme in Fig. 4.8 is thought to be the most common cyclopropanation mechanism, but in some cases the reaction may occur in a stepwise fashion through a metallacyclobutane intermediate. Once formed by

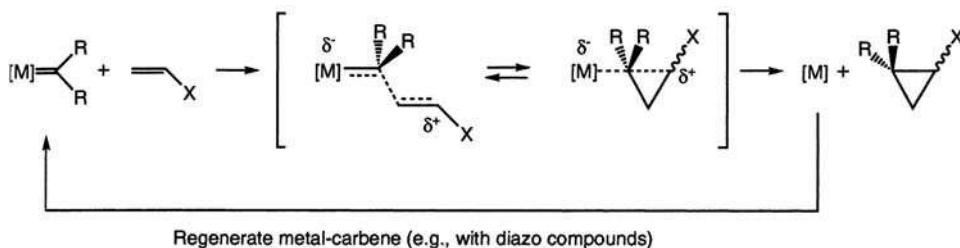


Fig. 4.8. Proposed mechanism for olefin cyclopropanation.

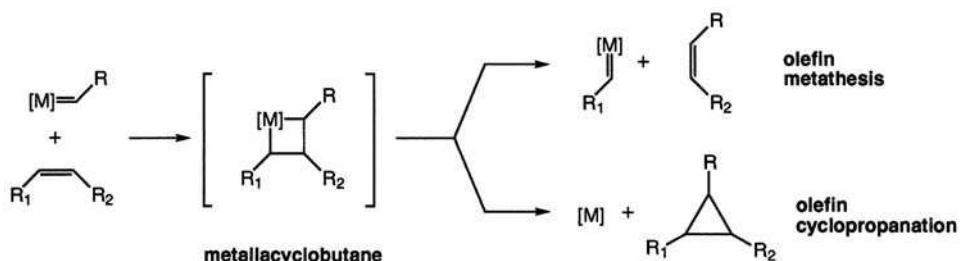


Fig. 4.9. Olefin metathesis and cyclopropanation pathways for a metallacyclobutane intermediate.

[2 + 2] cycloaddition of an olefin to a metal carbene, the metallacyclobutane can undergo either reductive elimination to yield a cyclopropane or retrocycloaddition to yield metathesis products (Fig. 4.9) [28,30].

The factors that direct a metallacyclobutane intermediate along one of these pathways are only partially understood. For example, in the case shown in Fig. 4.10, both metathesis and cyclopropanation are mediated by the same tungsten–carbene complex when the reaction is performed in a non-coordinating solvent [31]. These conditions are consistent with reaction via a metallacyclobutane because they allow the olefin to coordinate to the metal center, a prerequisite for [2 + 2] cycloaddition. In contrast, only cyclopropanation occurs when the reaction is performed in a coordinating solvent, presumably because formation of a metal–solvent adduct prevents olefin coordination and leaves only a direct carbene transfer mechanism available.

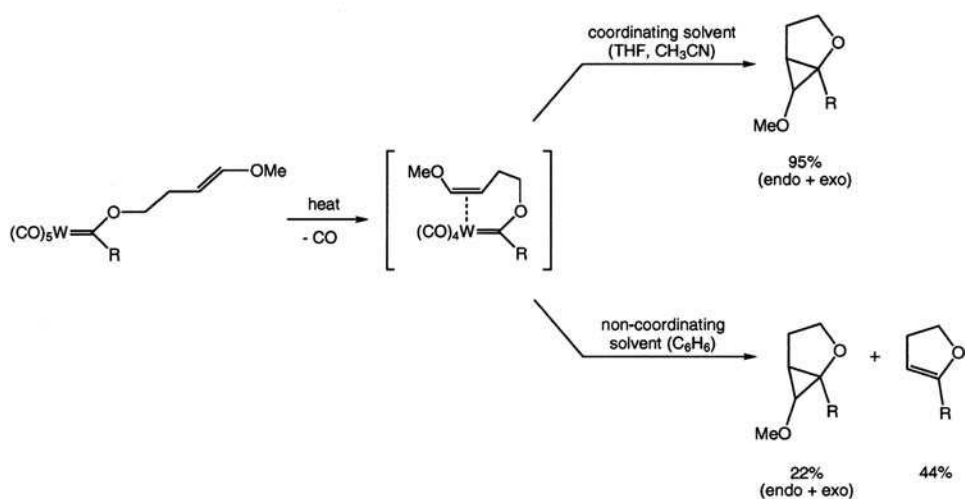


Fig. 4.10. A tungsten–carbene complex that mediates both olefin cyclopropanation and metathesis.

4.4 OLEFIN METATHESIS

4.4.1 Introduction

The reaction of a metal–carbene complex with an olefin may lead to either cyclopropane or metathesis products, depending on the metal center and its ancillary ligands. In the case of olefin metathesis, the reaction may occur in variations that have enormous numbers of synthetic applications. Although these products are diverse in structure, they are all related by the same basic metal–carbene-mediated mechanism of formation. Because we provide only an overview of applications in this section and do not specify the particular catalyst used in each case, we direct the reader to the extensive reviews that are available for more information [32].

Perhaps the most basic form of the olefin metathesis reaction is the cross metathesis (CM) of acyclic olefins to yield new acyclic olefins (Fig. 4.11). The ratio of CM products may be controlled by steric and electronic factors to provide one product preferentially, rather than a statistical mixture, which is key to the synthetic utility of this reaction. For example, various functionalized olefins, dimers with bioactive substituents, and trisubstituted olefins have all been made by CM [33], and one of the industrial applications is the synthesis of insect pheromones [34].

Dienes can be cyclized in the ring-closing metathesis (RCM) reaction with concomitant formation of volatile olefin side products (usually ethylene) (Fig. 4.12). RCM has been used to make small- and medium-sized rings, including carbocyclic

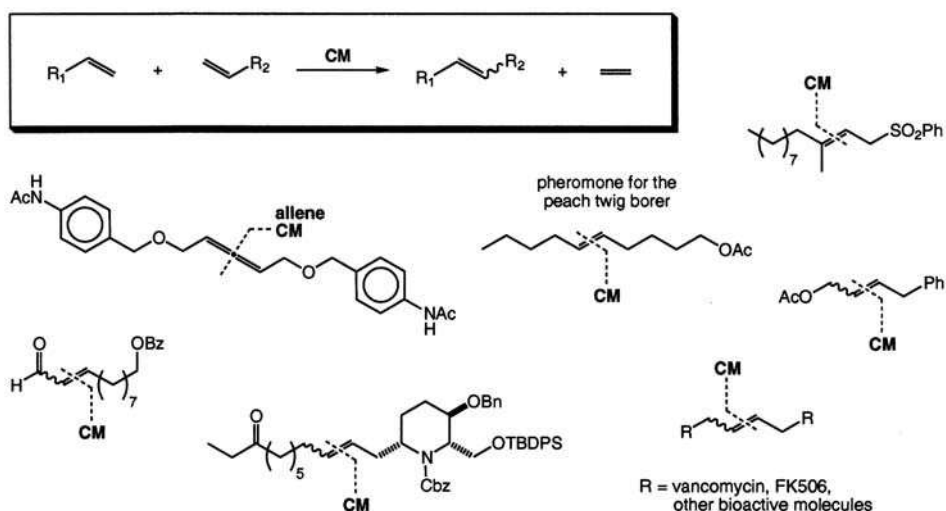


Fig. 4.11. A variation of the olefin metathesis reaction: cross metathesis (CM).

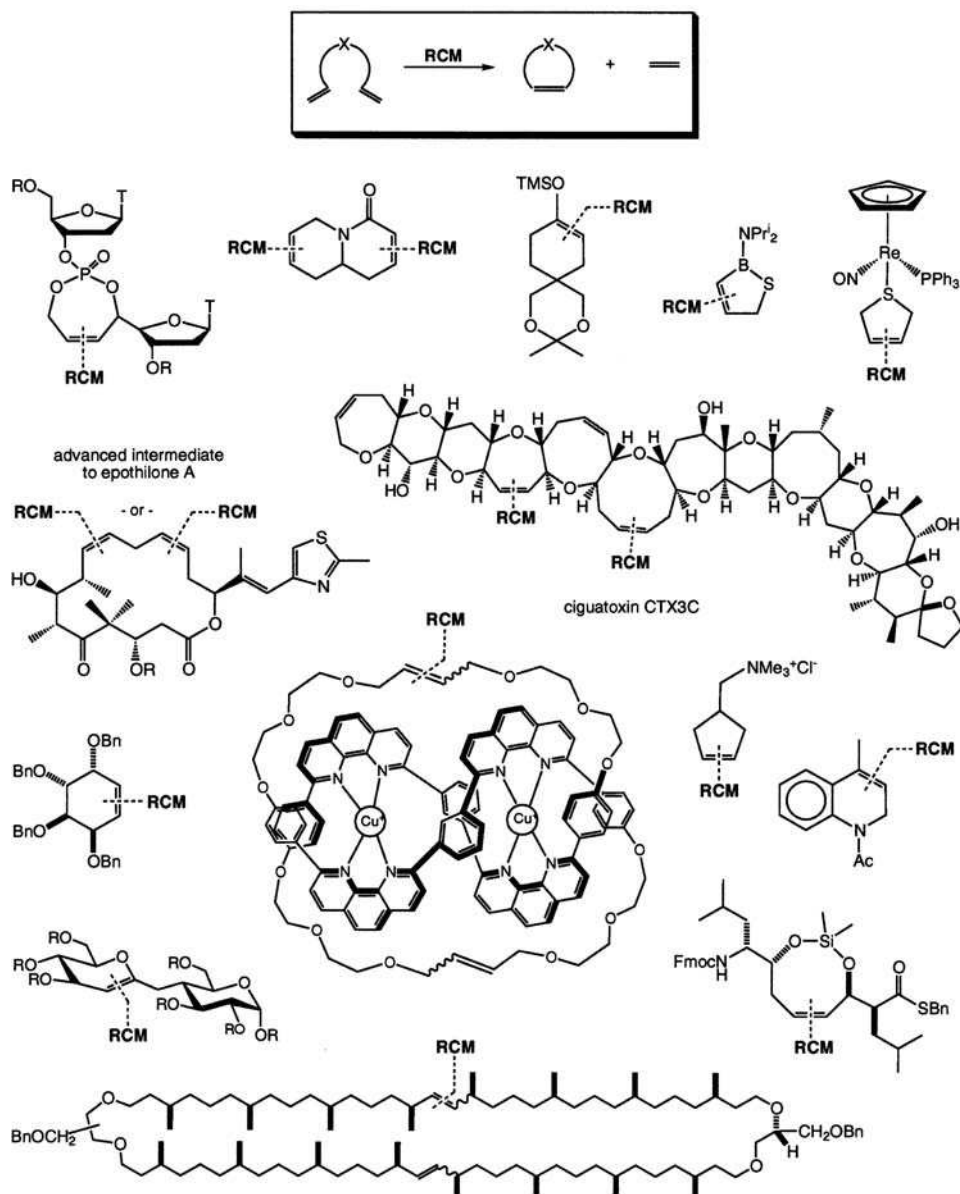


Fig. 4.12. Another variation of the olefin metathesis reaction: ring-closing metathesis (RCM).

cles with pendant functionalities and rings that contain potentially coordinating heteroatoms like boron and sulfur [35]. RCM can also lead to large rings, such as the 72-membered ring that is a precursor to archaeal membrane lipids [36]. Other representative applications include the synthesis of highly functionalized disaccharides and dinucleotides [37], RCM to “tie” a “molecular knot” [38], and

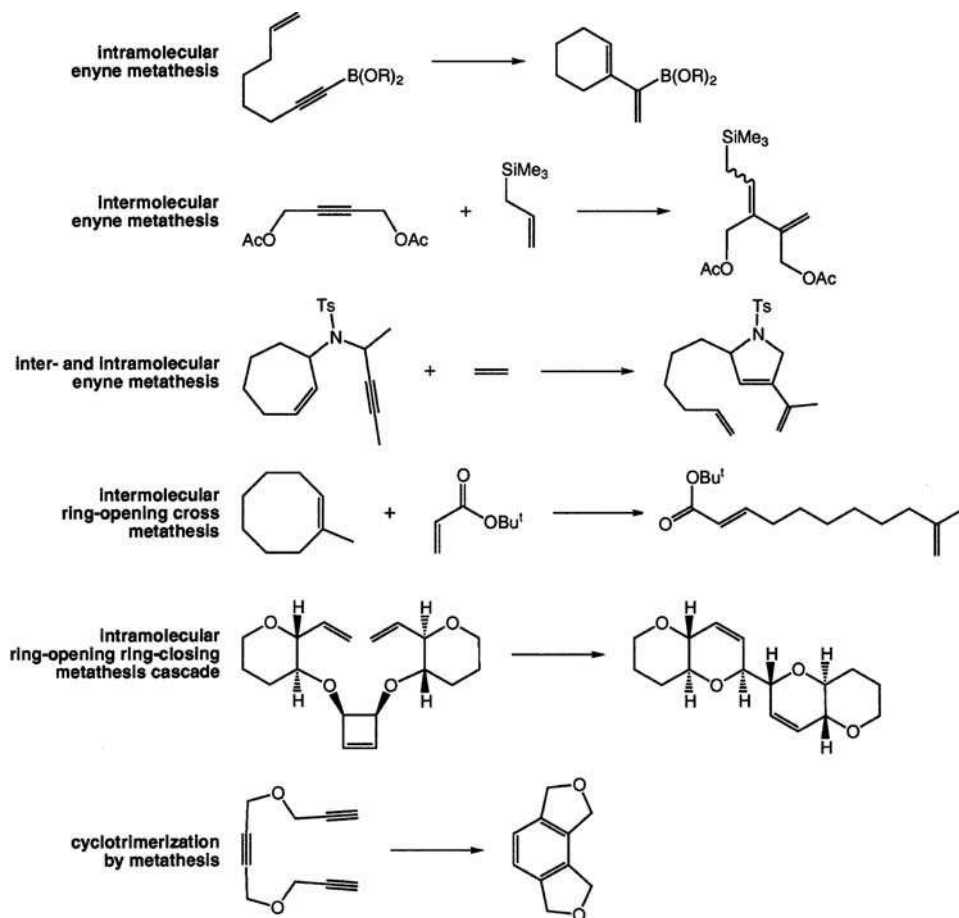


Fig. 4.13. Examples of enyne metathesis reactions, ring opening-cross metathesis cascades, and other metathesis sequences.

a large number of uses in natural product synthesis, such as of epothilone A [39] and polycyclic ethers like the ciguatoxins [40].

More complex small molecules can also be made by metathesis cascades and tandem reaction sequences involving olefin metathesis components [41]. The examples illustrated in Fig. 4.13 include inter- and intramolecular enyne metathesis between an olefin and an alkyne [42], ring-opening cross metathesis to form new substituted acyclic olefins [43], ring-opening ring-closing sequences [44], and the cyclotrimerization of alkynes [45].

A large number of applications involve the synthesis of polymers by either ring-opening metathesis polymerization (ROMP), which transforms cyclic olefins into unsaturated polymers (Fig. 4.14) [46,47], or acyclic diene metathesis polymerization (ADMET), which converts acyclic olefins into polymers (Fig. 4.15)

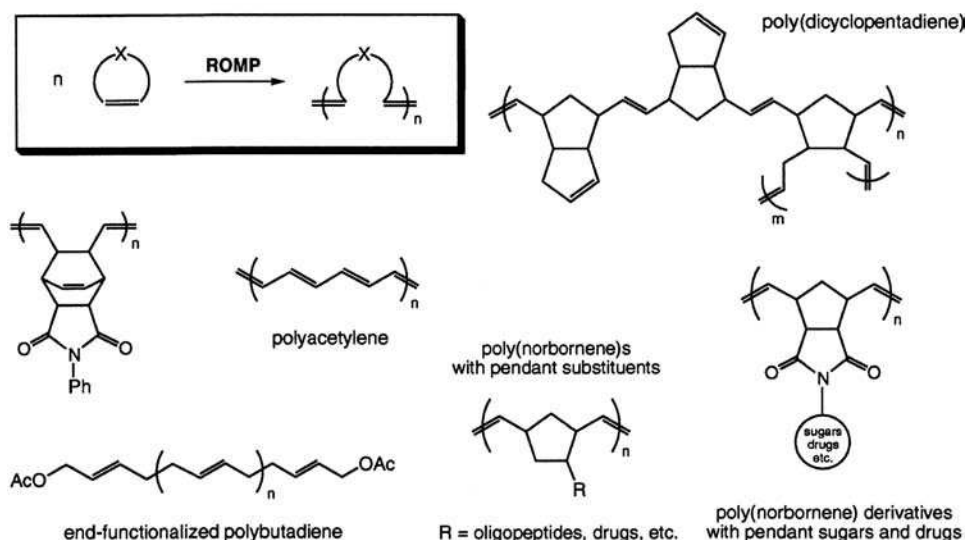


Fig. 4.14. The synthesis of polymers by olefin metathesis: ring-opening metathesis polymerization (ROMP).

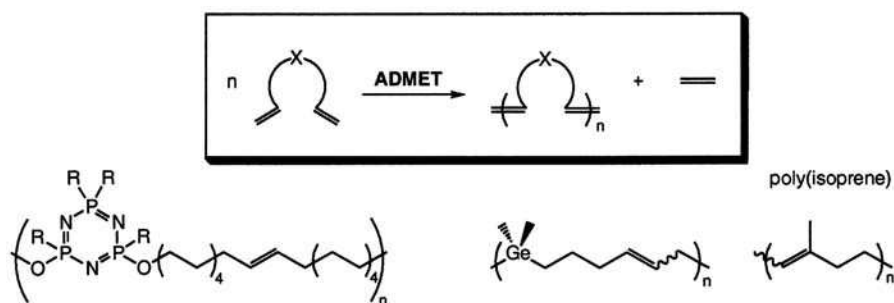


Fig. 4.15. Representative products of acyclic diene metathesis (ADMET) polymerization.

[48]. These reactions differ in that the driving force for ROMP is the relief of ring strain in the monomer, whereas ADMET is similar to CM in the release of volatile olefin byproducts. A variety of norbornene-derived polymers with pendant sugars, drugs and oligopeptide sequences [49] have been made by ROMP, as well as polyacetylenes (e.g., from cyclooctatetraene) [50], and the commercially important poly(dicyclopentadiene). Poly(isoprene) and many polymers with heteroatom functionalities, such as phosphazene and alkylgermanium species, have been synthesized by ADMET [51]. The reverse process, ADMET depolymerization, can be used to degrade unsaturated materials [52].

4.4.2 History and mechanism

Olefin metathesis was discovered as a side reaction during the Ziegler–Natta polymerization of olefins [47a,53]. At DuPont, researchers observed that norbornenes polymerized by a ring-opening process to yield unsaturated polymers rather than by the expected addition polymerization (Fig. 4.16). Others also observed that heterogeneous catalysts that were intended to polymerize propylene sometimes generated butenes and a copolymer of propylene and ethylene instead. Phillips Petroleum developed the latter reaction into the triolefin process, which is used to convert propylene into ethylene and 2-butene, and ultimately produce a variety of specialty olefins [47a]. Many groups at the time developed routes to new polymers by ROMP, but Calderon and co-workers at Goodyear were among the first to investigate new catalyst systems and thus demonstrate the power and breadth of the olefin metathesis reaction [53].

The initially proposed mechanism involved the pairwise $[2 + 2]$ addition of two olefins in the coordination sphere of a metal to form a metal-coordinated cyclobutane, followed by cycloreversion [54]. As illustrated in Fig. 4.17, this process would exchange the halves of the original olefins to yield two new olefins. However, unexpected results during chain transfer polymerization reactions, in which an acyclic olefin is added to a cyclic olefin to control the molecular weight, suggested that the fragments of the olefins scrambled faster than allowed by the pairwise $[2 + 2]$ mechanism [55]. These results led Chauvin to propose an alternative mechanism that involved the exchange of one-carbon fragments – carbenes – on the metal center, and later refinements included metallacyclic intermediates.

The currently accepted mechanism consists of (i) coordination of an olefin to the metal center, (ii) $[2 + 2]$ cycloaddition between the metal carbene and the

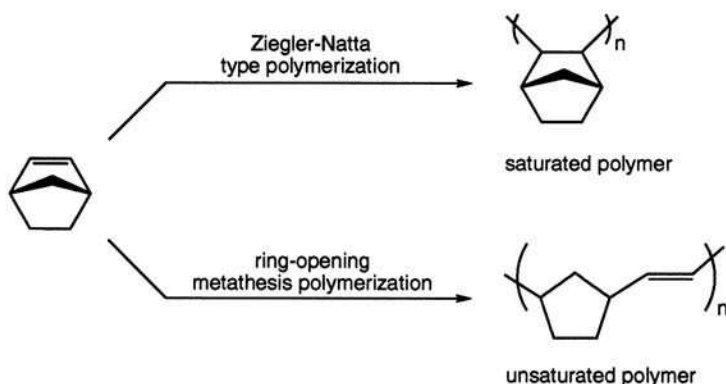


Fig. 4.16. Saturated versus unsaturated products from the Ziegler–Natta type polymerization and the ring-opening metathesis polymerization of norbornene.

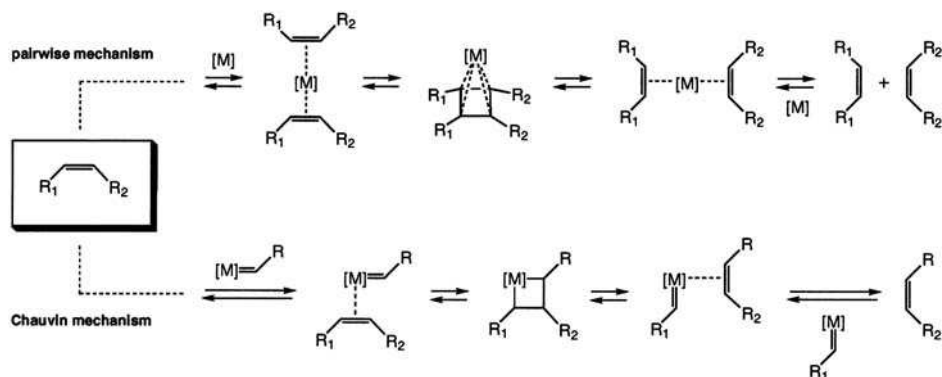
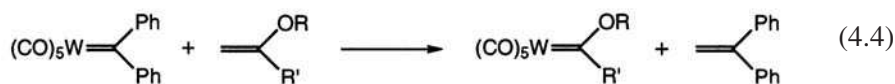


Fig. 4.17. The pairwise [2 + 2] mechanism and the Chauvin mechanism for olefin metathesis.

olefin to form a metallacyclobutane, (iii) rupture of the metallacyclobutane to regenerate a carbene and an olefin, and (iv) displacement of the coordinated olefin with a new olefin to begin the cycle again (Fig. 4.17) [54]. The metallacyclobutane can eliminate an olefin from either side of the ring, leading to degenerate metathesis, in which the starting olefin and carbene are reformed, or productive metathesis, in which new olefins and carbenes are produced. As the catalytic cycle continues, an equilibrium mixture of olefins is produced, and the ultimate product ratio is determined by thermodynamic parameters. For instance, if one of the olefins is volatile, it can be removed from the system to drive the equilibrium toward the desired products. The overall process is analogous to that of $[Cp_2Ti=CH_2]$ in the carbonyl olefination reaction, except that all the steps are reversible.

The Casey and Fischer groups first demonstrated the ability of a well-defined metal–carbene species to undergo carbene exchange with an olefin, by showing that the reaction of $(CO)_5W=CPh_2$ with a vinyl ether produced a new alkoxy-carbene and a new olefin (Eq. 4.4) [54]. Although this particular tungsten carbene does not catalyze further cross metathesis, similar complexes can be used to initiate the metathesis polymerization of strained hydrocarbon rings [56].



The source of the one-carbon metal fragment was not addressed in the original Chauvin papers. However, groundbreaking work by Schrock showed that alkylidene complexes could be synthesized by treating tantalum precursors with alkyllithium reagents (Eq. 4.5) [3,57]. This tantalum alkylidene complex also does not catalyze olefin metathesis, but the synthesis and isolation of the first alkylidene complex was an important milestone in the development of well-defined olefin metathesis catalysts.

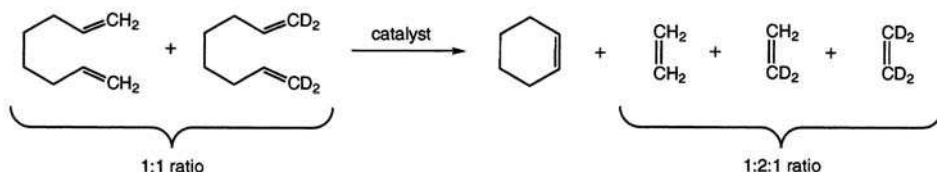
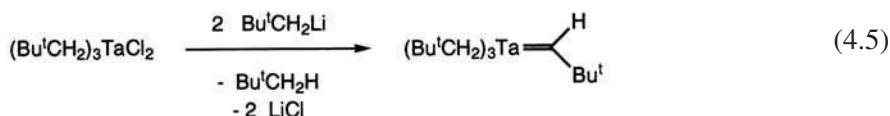


Fig. 4.18. Labeling experiment to confirm the Chauvin mechanism of olefin metathesis.

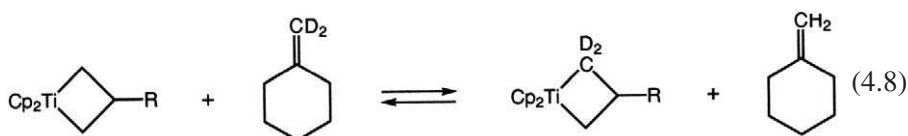
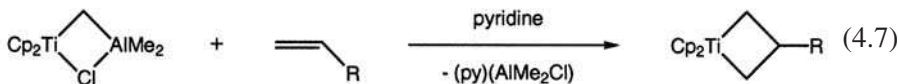
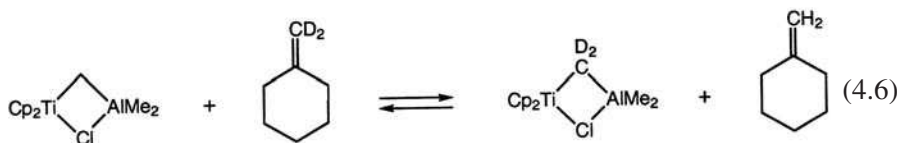


Further mechanistic studies ruled out the original pairwise [2 + 2] mechanism and provided additional support for the Chauvin mechanism. Labeling studies, such as the experiment in Fig. 4.18, revealed that the kinetic product (the product at low conversion) of the metathesis of 1,7-octadiene derivatives is a statistical distribution (1 : 2 : 1) of d_0 -, d_2 -, and d_4 -labeled ethylene [58]. This is inconsistent with the pairwise [2 + 2] mechanism, which would have produced a non-statistical distribution (1 : 1.6 : 1) of labeled ethylene.

With experimental support for the metal–carbene-mediated mechanism of olefin metathesis, a number of groups initiated studies with isolated metal–carbene and metallacyclobutane complexes. Early work by Chauvin and Katz on the polymerization of strained olefins using Fischer-type carbenes demonstrated the success of such an approach [56]. The introduction of high oxidation state alkylidene complexes led to well-defined catalyst in which the propagating species could be observed and studied, such as the tungsten-based systems developed by Osborn, Schrock, and Basset [59,60]. The best-studied and useful of these have been the Schrock arylimido alkylidene complexes, and we will return to these later in this chapter.

Tebbe found that titanocene complexes promoted olefin metathesis in addition to carbonyl olefination. Despite the fact that these complexes have low activity, they proved to be excellent model systems. For example, the Tebbe complex exchanges methylene units with a labeled terminal methylene at a slow rate that can be easily monitored (Eq. 4.6) [54]. This exchange is the essential transformation of olefin metathesis. When reactions with olefins are performed in the presence of a Lewis base, the intermediate titanium metallacycle can be isolated and even structurally characterized (Eq. 4.7) [61]. These derivatives were not only the first metathesis-active metallacyclobutane complexes ever isolated, but they were also the first metallacyclobutanes isolated from the cycloaddition of a metal–carbene complex with an olefin. These metallacycles participate in all the reactions expected of olefin metathesis catalysts, especially exchange with olefins

(Eq. 4.8) and ROMP (Fig. 4.19).



The corresponding metallacyclobutane can be isolated when the Tebbe complex reacts with one equivalent of norbornene (Fig. 4.19) [62]. This metallacycle continues to react with excess norbornene to generate poly(norbornene), and then carbene transfer to acetone can be used to remove the propagating metal species and end-cap the polymer chain. Subsequent studies established that these systems are living polymerizations. The experimental proof for living character includes the observations that (i) the propagating species can be observed for extended periods, (ii) the propagating species remains active for extended periods, (iii)

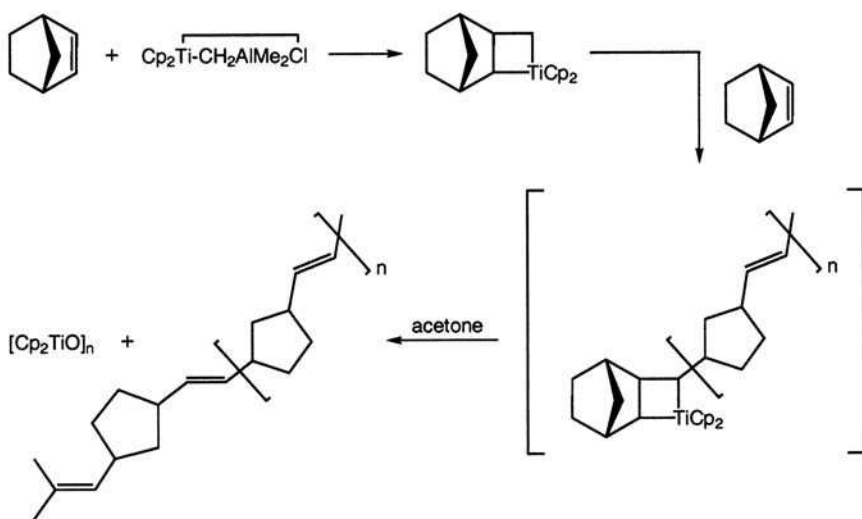


Fig. 4.19. ROMP of norbornene with the Tebbe reagent.

there is a linear relationship between molecular weight and conversion, (iv) the polymers exhibit narrow molecular weight distributions, and (v) block copolymers can be made by sequential addition of different monomers [63].

Since the living nature of titanium-catalyzed ROMP was first demonstrated, researchers have found that the ROMP of highly strained olefins by many metal carbenes are living polymerizations. In these cases, propagation is much faster than termination or chain transfer reactions, and with the appropriate catalyst tuning, initiation can be made fast relative to propagation. Consequently, it is possible to prepare well-defined polymers with narrow polydispersities, as well as block copolymers with controlled block lengths using ROMP [63].

4.4.3 Related reactions with alkynes

A reaction closely related to olefin metathesis is alkyne polymerization, which occurs between a metal carbene and an alkyne [64]. After initial alkyne coordination to the metal center, [2 + 2] cycloaddition leads to a metallacyclobutene complex instead of the metallacyclobutane formed in olefin metathesis (Fig. 4.20) [65]. Rupture of this ring and continuation of the cycle results in a growing polymer chain. This reaction can be used to synthesize conjugated polymers, which have unique physical properties [64].

By analogy to olefin metathesis, *alkyne* metathesis occurs between a complex containing a metal–carbon triple bond – a metal carbyne (or alkylidyne) – and an alkyne substrate [66]. As illustrated in Fig. 4.21, this mechanism parallels the Chauvin mechanism for olefin metathesis: after alkyne coordination to the metal center, [2 + 2] cycloaddition between the metal carbyne and the alkyne yields a metallacyclobutadiene, which rearranges and fragments productively to afford a new carbyne and a new alkyne (Fig. 4.21) [54].

Recent developments in catalyst design have produced efficient new molybde-

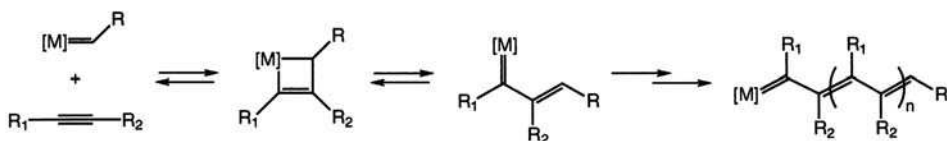


Fig. 4.20. The mechanism of alkyne polymerization.

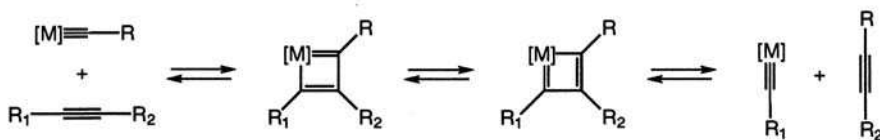


Fig. 4.21. The mechanism of alkyne metathesis.

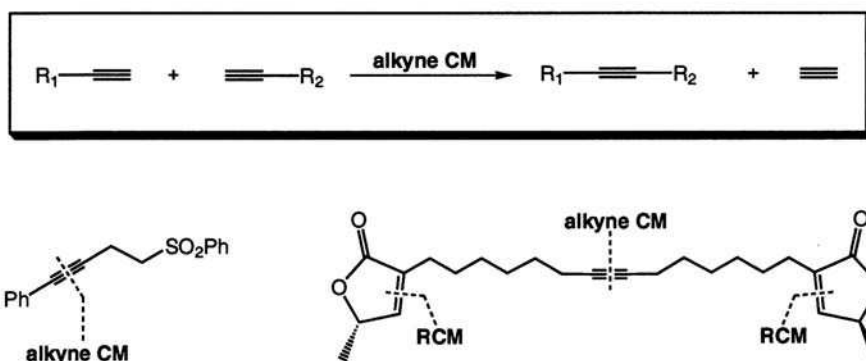


Fig. 4.22. Products of alkyne cross metathesis (alkyne CM).

num and tungsten catalysts for the alkyne versions of various olefin metathesis reactions [67]. For example, alkyne cross metathesis has been used to synthesize new disubstituted alkynes (Fig. 4.22), which can be partially reduced to obtain olefins instead [68]. Likewise, ring-closing alkyne metathesis (RCAM) is a particularly flexible reaction because the cyclic alkyne product can be partially reduced to yield the E or Z cyclic olefin with complete selectivity [69]. This approach has been applied in syntheses of the prostaglandins and the epothilones (Fig. 4.23) [70].

The ROMP of cyclic alkynes like cyclooctyne may be used to make alkyne-containing polymers in a reaction similar to olefin ROMP (Fig. 4.24) [71]. Additionally, Bunz and co-workers have pioneered the application of acyclic

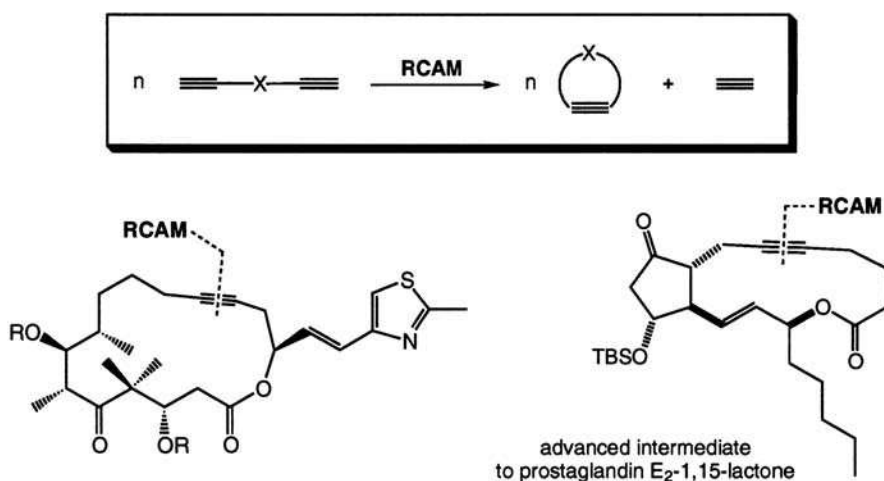


Fig. 4.23. A variation of the alkyne metathesis reaction: ring-closing alkyne metathesis (RCAM).

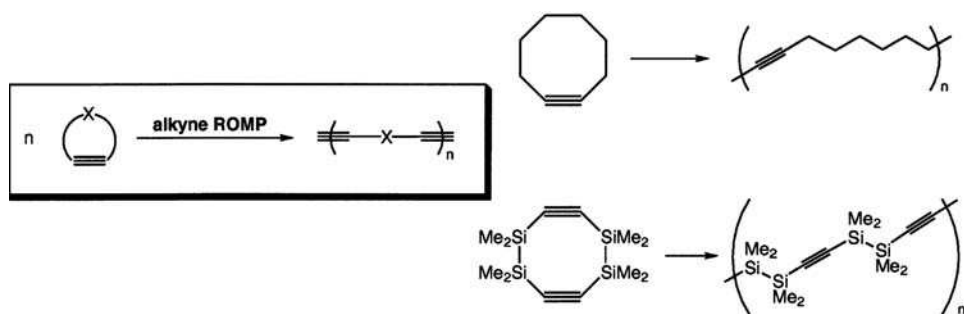


Fig. 4.24. Another variation of the alkyne metathesis reaction: alkyne ring-opening metathesis polymerization (alkyne ROMP).

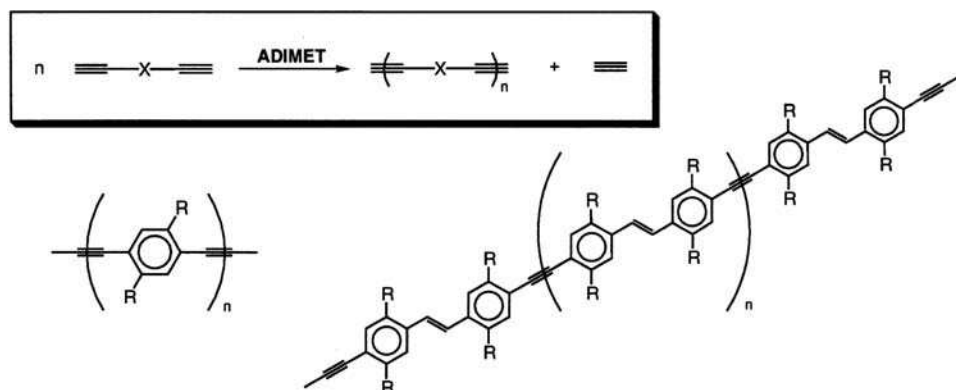


Fig. 4.25. Products of acyclic diene metathesis (ADIMET) polymerization.

diene metathesis polymerization (ADIMET) in the synthesis of highly conjugated poly(aryleneethynylene) materials (Fig. 4.25) [72].

4.5 CATALYSTS FOR OLEFIN METATHESIS

4.5.1 Introduction

The first catalysts for the olefin metathesis reaction were ill-defined, multi-component initiators consisting of transition metal halides or oxides with alkylating co-catalysts, such as $\text{WCl}_6\text{--SnMe}_4$ or $\text{MoCl}_5\text{--EtAlCl}_2$ [47a]. There is substantial evidence that small amounts of the highly active metal–carbene species is generated *in situ*, but the utility of these catalyst systems in organic synthesis is limited by the harsh alkylating conditions. Other ill-defined initiators, such as $\text{RuCl}_3\text{--H}_2\text{O}$ and $\text{IrCl}_3\text{--EtOH}$, are active without co-catalysts, and there is also ev-

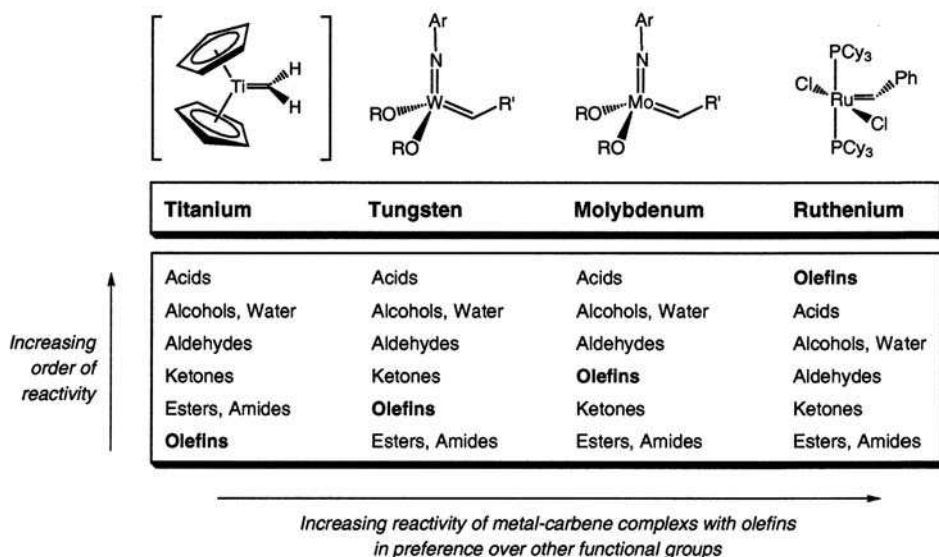


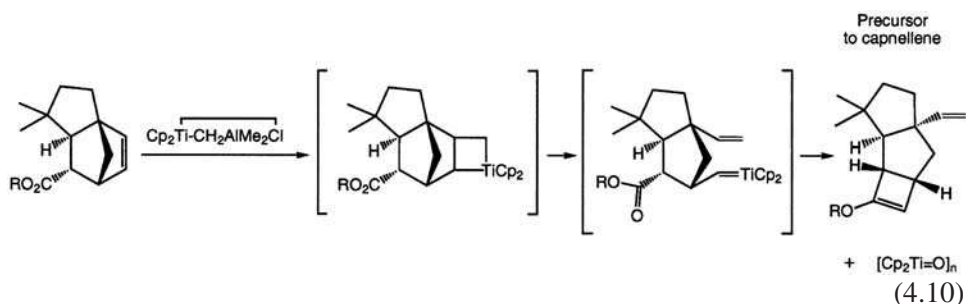
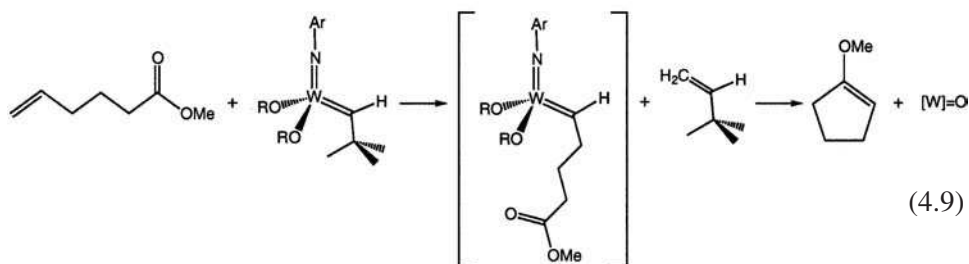
Fig. 4.26. The reactivity of early and late transition metal olefin metathesis catalysts with various functional groups.

idence for formation of metal–carbene species in these systems by rearrangement of metal–olefin adducts.

Two of the important advantages of well-defined, single-component catalysts over ill-defined initiators is that they provide control over reaction initiation and functional group compatibility. For example, the variability of metal–carbene reactivity is illustrated in Fig. 4.26, where the reactivity of four carbene complexes toward olefins is compared to other organic functional groups [73,74]. All of these complexes catalyze the olefin metathesis reaction, but there is a gradual change in relative reactivities as the metal center is varied from an early transition metal to a more electron rich, later transition metal. The more oxophilic metals to the left side of the periodic table react preferentially with carbonyl functionalized compounds: for instance, the titanium methylidene and the tungsten neopentylidene complexes both olefinate ketones. In comparison, the molybdenum neopentylidene complex reacts preferentially with olefins in the presence of ketones but is deactivated by other polar and protic functional groups, such as alcohols and water. And furthest to the right, the ruthenium benzylidene complex displays the greatest functional group tolerance and reacts preferentially with olefins in the presence of all the other functionalities listed.

Although the reactions of metal–carbene complexes with various functional groups can lead to catalyst–substrate compatibility problems, these same reactivity profiles can be used in tandem reaction sequences. In the following two examples, a tungsten–carbene complex (Eq. 4.9) and a titanium complex (Eq. 4.10) are

used to generate metal alkylidenes, which then react intramolecularly with ester carbonyl groups. In each of these cases, relative reaction rates have been tuned to favor a two step metathesis–olefination sequence.



4.5.2 Molybdenum imido alkylidene catalysts

The molybdenum and tungsten carbene complexes that have been developed by Schrock and co-workers are among the most highly active single-component olefin metathesis catalysts, and they have been studied in great detail [60,75]. As illustrated in Fig. 4.27, these complexes are composed of a sterically bulky alkylidene (e.g., $R' = \text{CMe}_2\text{Ph}$), a bulky arylimido ligand (e.g., $\text{Ar} = 2,6\text{-Pr}_2\text{C}_6\text{H}_3$), and two bulky alkoxide ligands [e.g., $\text{R} = \text{CMe}_3$, $\text{CMe}(\text{CF}_3)_2$], all of which help stabilize the four-coordinate, formally 14-electron metal center. The alkylidene ligand can adopt two major conformations, *syn* and *anti*, with the *syn* form more stable in most cases. The rates of interconversion are affected by the electronic character of the alkoxides and the substitution pattern on the imido aryl group. Most significantly, Schrock also found that there was a dramatic activity difference between the *syn* and *anti* isomers. For some catalyst derivatives, the *anti* isomer is more reactive toward olefin substrates by several orders of magnitude, and the *syn*–*anti* interconversion appears to be the rate limiting step in the catalytic cycle. The electronic character of the alkoxide ligands is also directly linked to catalyst activity, because more electron withdrawing alkoxides increase the electrophilicity of the metal center and thus increase the rate of olefin metathesis.

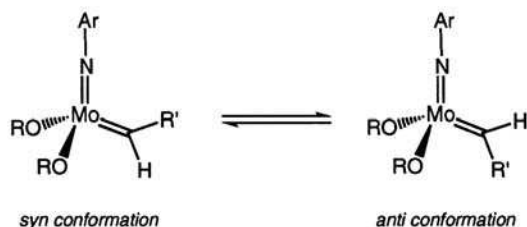


Fig. 4.27. Molybdenum arylimido alkylidene catalysts in *syn-anti* conversion.

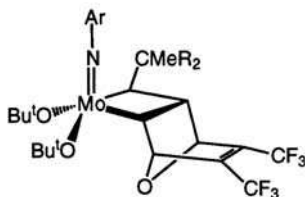


Fig. 4.28. Molybdenum metallacyclobutane intermediate.

Evidence indicates that the stereodetermining step in the catalytic cycle is metallacyclobutane formation and that the stereochemistry of the metallacycle is transferred to the product (Fig. 4.28). Consequently, *trans* metallacyclobutanes rearrange to yield *trans* olefins, and *cis* metallacyclobutanes yield *cis* olefins. The synthesis of five-coordinate adducts of the general formula $(\text{NAr})(\text{OR})(\text{L})\text{M}=\text{CH}(\text{Bu}')$ (e.g., $\text{L} = \text{PMe}_3$), which are not metathesis active, demonstrated that binding of a donor ligand (in a substrate, for example) was detrimental to catalytic activity, and also confirmed the reactivity patterns of different alkylidene conformations.

4.5.3 Ruthenium alkylidene catalysts

The two most widely used ruthenium olefin metathesis catalysts are the first generation bis(phosphine) catalyst $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**1**) and the second generation *N*-heterocyclic carbene catalyst $(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**2**) (Fig. 4.29). Both of these catalysts operate under extremely mild conditions and in the presence of most common functional groups, and as a result, they are largely responsible for placing olefin metathesis in the repertoire of standard carbon-carbon bond forming reactions used by synthetic chemists. This section provides a historical account of the development of ruthenium olefin metathesis catalysts, from early efforts in this area to the current state-of-the-art in ruthenium catalyst technology. Particular emphasis is placed on mechanistic work because these studies have played an important role in the design of new catalyst systems.

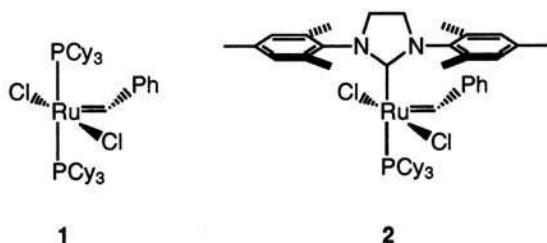


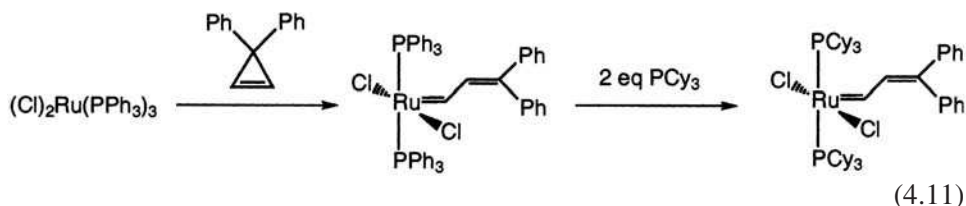
Fig. 4.29. The two most widely used ruthenium-based olefin metathesis catalysts: $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**1**) and $(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**2**).

4.5.4 Development of first generation ruthenium catalysts

Although most of the original metathesis catalyst systems were based on the early transition metals, there were sporadic reports of ROMP reactions initiated by group VIII metal salts [47a]. These catalyst systems showed relatively low metathesis activity (that is, they reacted slowly with acyclic olefins after activation with a strained olefin), but one particular ruthenium(II)–olefin complex stood out as an attractive catalyst precursor, as it showed remarkable functional group tolerance and efficiently polymerized a wide variety of functionalized norbornenes in aqueous solution [76]. These early studies provided several insights that led to the development of well-defined ruthenium-based olefin metathesis catalysts. First, they suggested that ruthenium carbene complexes would be good targets for the development of functional group tolerant catalysts. There was some independent evidence that a ruthenium carbene moiety was generated in the multi-component catalyst systems, but none of the isolated ruthenium carbene complexes known at the time were active for olefin metathesis. Second, they indicated that viable catalysts should possess a 2^+ oxidation state, because Ru(II) precursors were known to both initiate olefin metathesis reactions and form stable carbene adducts. Third, they also suggested that the desired compounds should have a 16-electron configuration at the metal center. Unlike their 18-electron analogues, 16-electron ruthenium complexes would be expected to contain electrophilic, coordinatively unsaturated metal centers that could bind olefins directly. Finally, this early work showed that strained cyclic olefins could serve as carbene precursors when coordinated to Ru(II) centers.

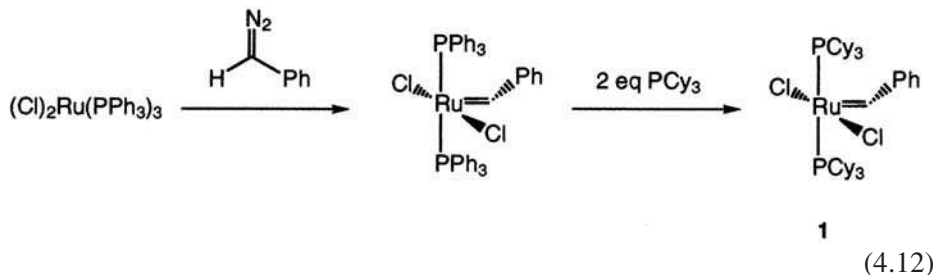
Based on these considerations, reactions of Ru(II) precursors with diphenylcyclopropene were screened for alkylidene formation; diphenylcyclopropene is a highly strained, cyclic olefin that can be used to prepare other metal–carbene complexes [77]. As shown in Eq. 4.11, $(\text{Cl})_2\text{Ru}(\text{PPh}_3)_3$ reacts cleanly and quantitatively with the cyclopropene to yield $(\text{PPh}_3)_2(\text{Cl})_2\text{Ru}=\text{CHCH}=\text{C}(\text{Ph})_2$ [78]. This 16-electron ruthenium(II) carbene complex was the first homogeneous, single-component ruthenium-based olefin metathesis catalyst. Although it could only polymerize highly strained olefin substrates, this complex demonstrated an unprecedented tolerance for functional groups and protic solvents (see Fig. 4.26).

The general structure of $(L)_2(X)_2Ru=CHR$ has continued to serve as the basis for subsequent generations of ruthenium-based catalysts [79].

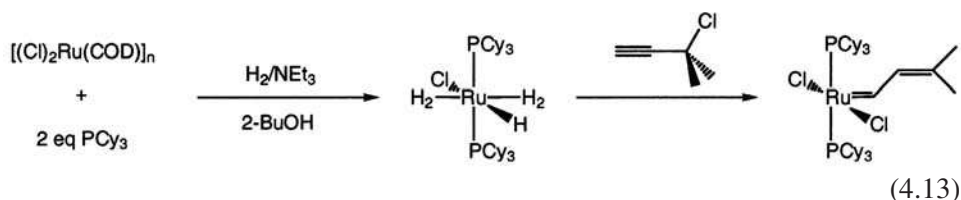


The low activity of $(PPh_3)_2(Cl)_2Ru=CHCH=C(Ph)_2$ prompted ligand modifications aimed at increasing both reaction rates and substrate scope. Earlier studies of Mo(VI)- and W(VI)-based catalysts had shown that increasing the electrophilicity of the metal center in turn increased olefin metathesis activity [60]. However, substitution of the phosphines and chlorides of $(PPh_3)_2(Cl)_2Ru=CHCH=C(Ph)_2$ with more electron withdrawing ligands had only minimal effects [80]. In contrast, catalytic activity increased dramatically when the PPh_3 ligands were replaced with larger and more electron-donating phosphines [81]. The new catalysts were prepared by a simple phosphine exchange procedure (Eq. 4.11), and the highest activity was obtained using tricyclohexylphosphine (PCy_3). This new complex, $(PCy_3)_2(Cl)_2Ru=CHCH=C(Ph)_2$, reacted with a wide variety of terminal and cyclic olefins and could readily promote ROMP, RCM, and CM reactions.

The high activity and functional group tolerance of $(PCy_3)_2(Cl)_2Ru=CHCH=C(Ph)_2$ opened the door for widespread application of olefin metathesis in organic and polymer chemistry. To improve the synthesis of the catalyst, diazoalkanes were used as more readily available alkylidene precursors [82]. As illustrated in Eq. 4.12, phenyldiazomethane reacts rapidly with $(Cl)_2Ru(PPh_3)_3$ at $-78^\circ C$ to liberate N_2 and produce the ruthenium benzylidene complex $(PPh_3)_2(Cl)_2Ru=CHPh$ [83]. Subsequent phosphine exchange with PCy_3 produces the bis(tricyclohexylphosphine) benzylidene catalyst $(PCy_3)_2(Cl)_2Ru=CHPh$ (**1**) in high yield (>90%) and purity (>95%). This methodology is amenable to scale-up procedures and has been used to produce kilogram quantities of catalyst **1**. The ease of synthesis, high reactivity, and high functional group tolerance of **1** have made it the work-horse catalyst for the synthesis of polymeric materials and organic molecules by olefin metathesis.

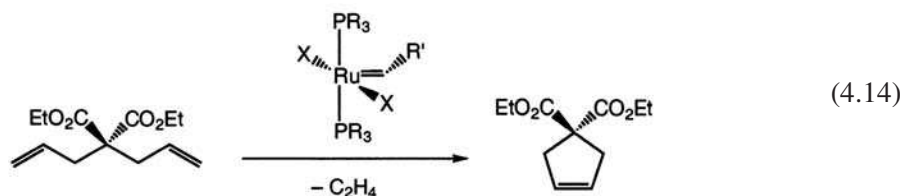


New synthetic methodology based on the rearrangement of vinyl halides provided an additional route to ruthenium alkylidene complexes [84]. As shown in Eq. 4.13, this procedure utilizes simple alkynes as carbene precursors and introduces the PCy_3 ligands directly in the first step. These advances eliminated the use of potentially explosive diazo compounds and the extra phosphine exchange procedures required in earlier syntheses [85]. This procedure is currently carried out on the multi-kilogram scale and produces the dimethylvinylcarbene catalyst that is predominantly used in commercial applications of ruthenium metathesis technology.



4.5.5 Mechanism of first generation catalysts

In order to design superior catalyst systems and expand the applications of these first generation catalysts, it was necessary to understand the fundamental mechanism of ruthenium-catalyzed olefin metathesis reactions. Initial investigations focused on the activity of **1** and its derivatives for the catalytic RCM of diethyl diallylmalonate (Eq. 4.14) [86]. These studies revealed that, in all cases, the overall catalytic activity was inhibited by the addition of free phosphine, and that the turnover rate was inversely proportional to the concentration of added phosphine. This indicated that phosphine dissociation was required for catalytic activity, and further suggested that olefin metathesis may be initiated by the substitution of a phosphine ligand with an olefin substrate.



These initial mechanistic studies with bis(phosphine) catalysts were able to distinguish between overall associative and dissociative possibilities [86]. As shown in pathway (a) of Fig. 4.30, an associative mechanism involves coordination of an olefin directly to the 16-electron pre-catalyst, to form an 18-electron olefin complex that then undergoes [2 + 2] cycloaddition. In contrast, pathways (b) and (c) illustrate mechanisms in which the dissociation of a ligand occurs prior to [2 + 2] cycloaddition. Pathway (b) involves formation of the same 18-electron

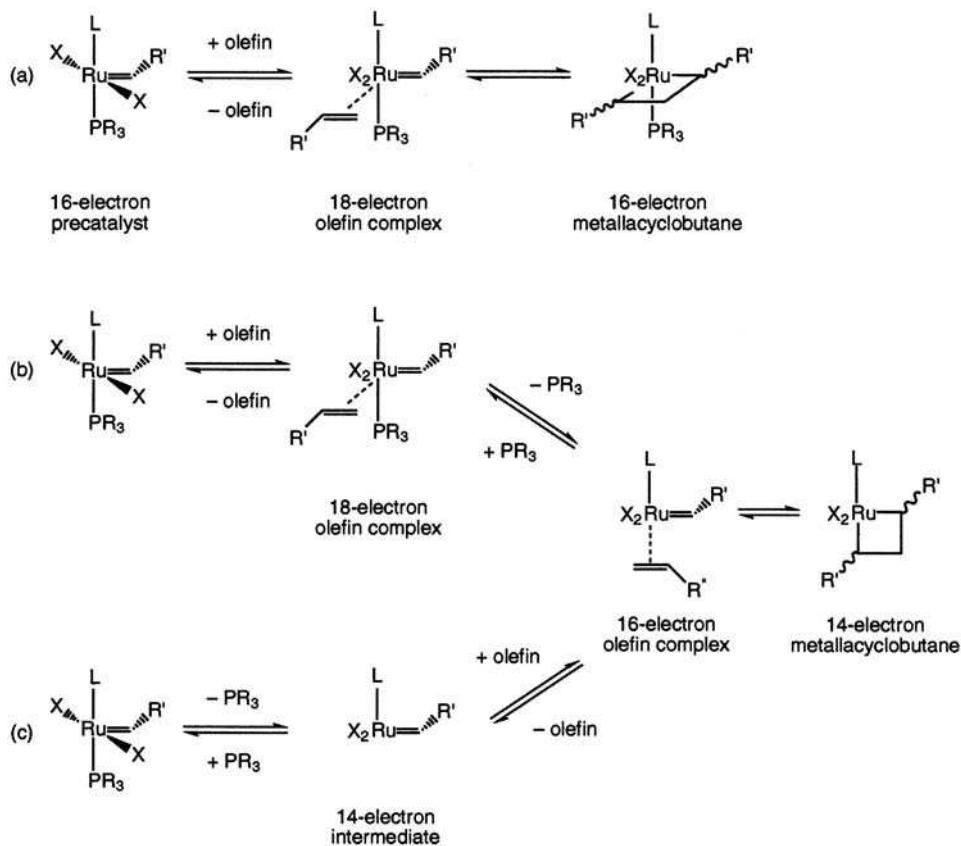


Fig. 4.30. Three ways for $(L)(\text{PR}_3)(\text{X})_2\text{Ru}=\text{CHR}'$ catalysts to enter the catalytic cycle.

olefin complex as in pathway (a), followed by dissociation of a phosphine ligand, whereas pathway (c) begins with the initial dissociation of a phosphine ligand from the 16-electron pre-catalyst, prior to any olefin coordination.

More recent mechanistic studies have been able to distinguish between pathways (b) and (c), and all results indicate that (c) is operative [87]. The initial ligand dissociation and substitution steps have been studied using ^{31}P NMR magnetization transfer experiments, ^1H NMR and UV-vis kinetics, and mass spectrometry [87,88]. These investigations indicate that both phosphine/phosphine (Fig. 4.31a) and phosphine/olefin (Fig. 4.31b) substitution reactions in $(L)(\text{PR}_3)(\text{X})_2\text{Ru}=\text{CHR}'$ complexes proceed by a dissociative mechanism involving a 14-electron intermediate $(L)(\text{X})_2\text{Ru}=\text{CHR}'$ (A). Although this proposed intermediate has not been observed in solution, presumably due to its low concentration, it has been identified in the gas phase [88].

An overall catalytic cycle for olefin metathesis reactions catalyzed by $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$ (1) and its derivatives is summarized in Fig. 4.32. The first

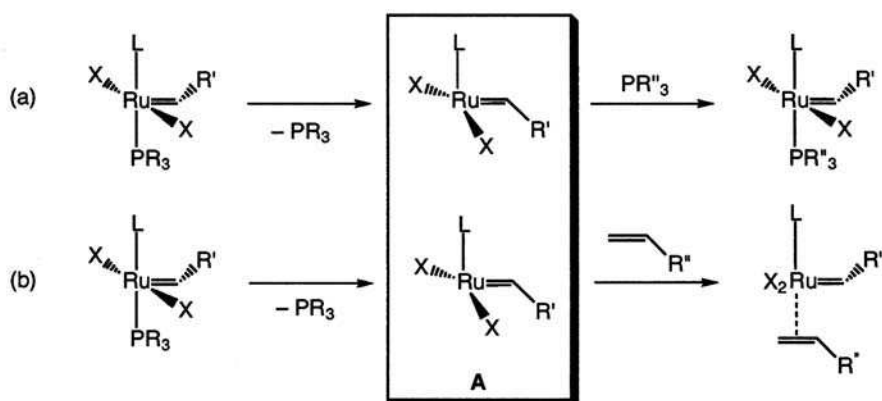


Fig. 4.31. Dissociative ligand substitution reactions of $(L)(PR_3)(X)_2Ru=CHR'$ ($L = PR_3$ or NHC): phosphine/phosphine and phosphine/olefin substitutions.

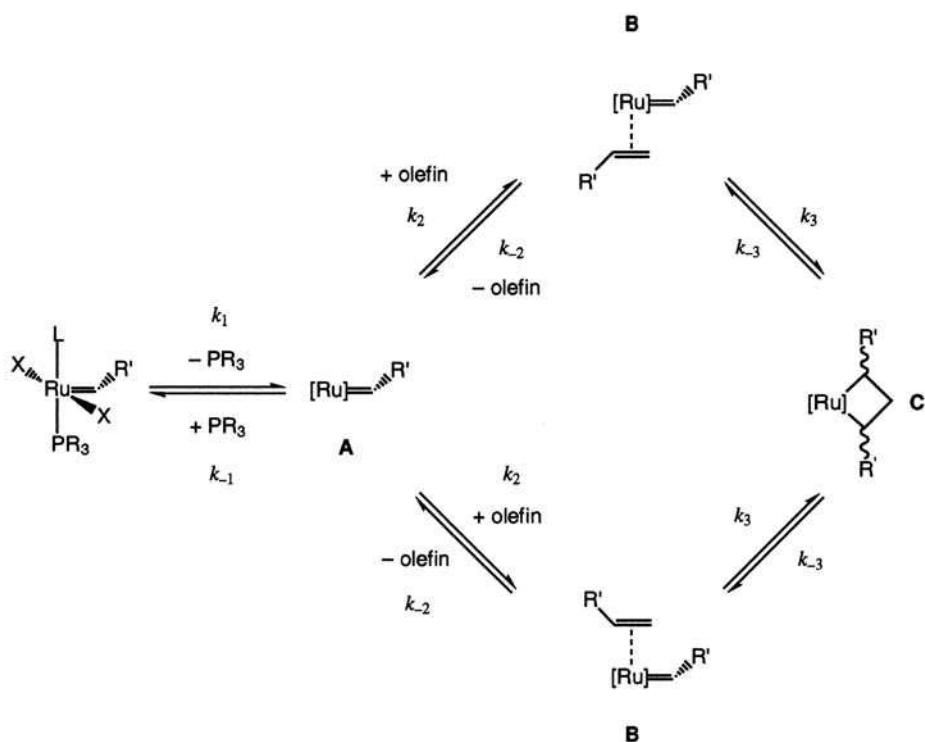


Fig. 4.32. The general mechanism of olefin metathesis catalyzed by $(L)(PR_3)(X)_2Ru=CHR'$ complexes; $Ru = (PCy_3)(X)_2Ru$ or $Ru = (IMesH_2)(X)_2Ru$. For simplicity, this illustration shows a degenerate metathesis reaction.

step, catalyst initiation, involves phosphine dissociation to produce the 14-electron intermediate $(L)(X)_2Ru=CHR'$ (**A** where $L = PCy_3$). This mono(phosphine) complex reacts with an olefin to generate a 16-electron alkylidene–olefin adduct (**B**). The carbon–carbon bond forming step involves the coupling of the coordinated alkene with the alkylidene moiety to generate a metallacyclobutane (**C**). Notably, metallacyclobutane intermediates have been postulated but never observed in ruthenium-catalyzed olefin metathesis reactions, so it is unclear whether the metallacycle (**C**) is a discrete intermediate or merely a transition state along the reaction coordinate [88]. Subsequent metallacycle cleavage regenerates the alkene adduct (**B**), and liberation of coordinated olefin regenerates the 14-electron species (**A**).

The cycle outlined in Fig. 4.32 indicates that the overall metathesis activity of the catalysts is determined by the relative magnitudes of several rate constants: (i) the rate constant for phosphine dissociation (k_1) dictates the rate at which the 16-electron pre-catalyst complex enters the catalytic cycle, (ii) the ratio of k_{-1} to k_2 controls the rate of catalyst deactivation (by re-coordination of phosphine) versus catalytic turnover (by coordination of olefinic substrate and subsequent steps), and (iii) the rate constant for metallacycle formation (k_3) determines the rate of the carbon-carbon bond formation. High olefin metathesis activity is expected when a ruthenium alkylidene catalyst exhibits fast initiation (a large value of k_1), high selectivity for binding olefins relative to phosphines (a small value of k_{-1}/k_2), and fast metallacyclobutane formation (a large value of k_3).

The effects of ligand variation on overall catalytic activity and on catalyst initiation rates have been studied extensively. The catalytic activity for the RCM of diethyl diallylmalonate for a series of ruthenium carbenes is summarized in Fig. 4.33 [86]. The complexes that contain larger and more basic phosphine ligands exhibit improved catalytic activity ($PCy_3 > PCy_2Ph > PCyPh_2 \gg PPh_3$). On the other hand, the complexes that contain larger and more electron donating halide ligands (X) show lower activity ($I < Br < Cl$). These results suggest that catalytic activity is increased by ligands that stabilize the metallacyclobutane intermediate (**C**). For instance, larger and more electron donating phosphines would be expected to stabilize the electron deficient, coordinatively unsaturated metallacyclobutane. Similarly, the smaller and harder chlorides would be expected

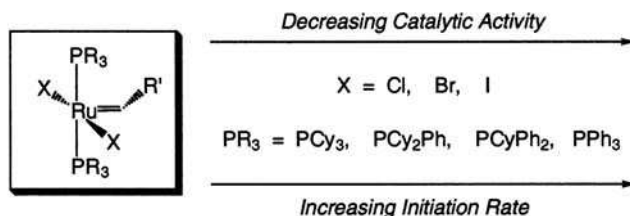


Fig. 4.33. Effects of ligand substitution on catalytic activity and catalyst initiation.

to serve as better ligands for this intermediate than the softer and more polarizable iodides.

In many cases, ancillary ligand substitution has the opposite effect on the rate of catalyst initiation. For example, complexes containing larger and more basic phosphines show lower initiation rates ($\text{PCy}_3 < \text{PPh}_3$) [89], whereas those containing larger and less electronegative halide ligands exhibit higher rates of initiation ($\text{Cl} < \text{Br} \ll \text{I}$). The halide effect is particularly dramatic, and the substitution of chlorides with iodides increases the initiation rate constant (k_1) by two orders of magnitude [87]. The effect of the phosphine ligands on catalyst initiation can be rationalized by increased labilization of less basic phosphines; that is, the lower basicity of PPh_3 (pK_a of $[\text{HPPH}_3]^+ = 2.7$) relative to PCy_3 (pK_a of $[\text{HPCy}_3]^+ = 9.7$) should lead to a lower barrier for phosphine dissociation. Likewise, increasing the size of the halide ligands from chloride to iodide should create unfavorable steric interactions between the PR_3 and X ligands and further promote phosphine dissociation. The electronic contribution of the X-type ligands to phosphine dissociation rates is expected to be negligible because cis electronic effects on dissociative substitution reactions are typically small.

Catalyst initiation and overall catalytic activity are not always opposing effects. For example, complexes that contain chelating ligands, such as bidentate phosphines [90], Schiff bases [91], and tris(pyrazolyl)borates [92], generally show both low rates of initiation and low overall olefin metathesis activity (Fig. 4.34). Both effects appear to result from slow rates of ligand dissociation from the starting complexes, which leads to low concentrations of the catalytically active 14-electron species in solution.

These mechanistic studies provide some guidelines for the design of improved olefin metathesis catalysts. For example, they indicate that a more labile L-type ligand is necessary for faster catalyst initiation. At the same time, they suggest that a more electron donating (and hence less labile) L-type ligand is essential to achieve faster turnover within the catalytic cycle. As we will describe in the next section, these seemingly contradictory requirements can be fulfilled by differentiating the L-type ligands in complexes of the general formula $(\text{L}^1)(\text{L}^2)(\text{X})_2\text{Ru}=\text{CHR}$.

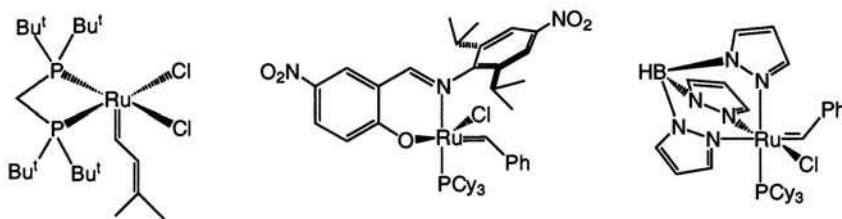


Fig. 4.34. Ruthenium alkylidene complexes that exhibit low initiation rates for olefin metathesis.

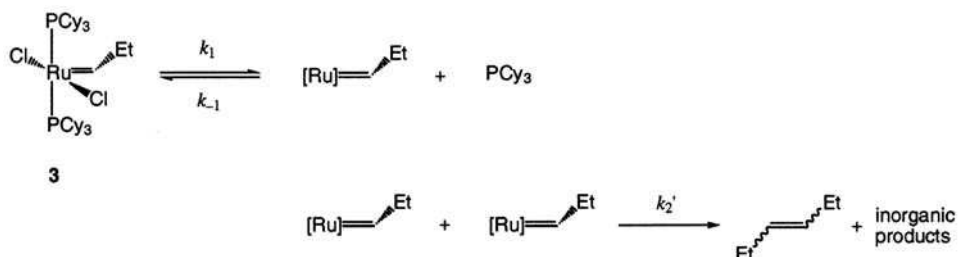


Fig. 4.35. Proposed mechanism of thermal decomposition of $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHtEt}$ (**3**); $[\text{Ru}] = (\text{PCy}_3)_2(\text{Cl})_2\text{Ru}$.

Another important mechanistic issue is the thermal decomposition of ruthenium alkylidene catalysts. To understand the decomposition pathways available in these systems, the thermolysis of two ruthenium alkylidene complexes, the propylidene $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHtEt}$ (**3**) and the methylidene $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CH}_2$ (**4**), was examined in detail [93]. These two compounds were chosen because a variety of alkylidenes [as modeled by the propylidene (**3**)] and the methylidene (**4**) are key intermediates in a range of olefin metathesis reactions with terminal alkenes. The studies revealed that the thermal decomposition of the propylidene (**3**) is a second order process that is inhibited by the addition of free PCy_3 . The organic products of this reaction are *trans*-3-hexene, the olefin resulting from dimerization of the alkylidene fragment, and free PCy_3 . The ruthenium products consist primarily of multiple ruthenium hydrides. These data strongly suggest that alkylidene decomposition involves phosphine dissociation followed by the bimolecular coupling of two equivalents of a 14-electron intermediate (Fig. 4.35). Notably, this mechanism implicates a common 14-electron intermediate (**A**) in both the catalytic cycle and the thermal decomposition of **3**.

In contrast to complex **3**, the methylidene $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CH}_2$ (**4**) decomposes according to first order kinetics, and its decomposition is not inhibited by the addition of free phosphine. The thermal decomposition products include free PCy_3 and a mixture of unidentified ruthenium products, but ethylene is not observed in the reaction mixture. Deuteration of the methylidene ligand leads to incorporation of deuterium into the PCy_3 ligand, which suggests that the decomposition of **4** proceeds by intramolecular phosphine activation [93].

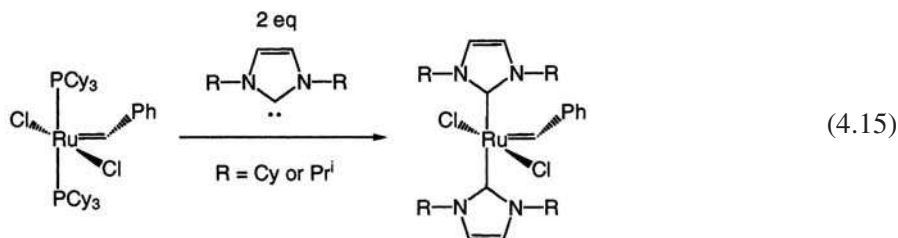
These results have significant implications for olefin metathesis reactions involving ruthenium methylidene versus substituted alkylidene complexes. First, the use of phosphine scavengers to increase the overall rate of metathesis results in a concomitant increase in the rate of catalyst decomposition. This effect is manifested in the high reactivity but limited longevity of catalysts in the presence of CuCl and HCl [86,93,94]. For instance, the half life of $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**1**) in the presence of CuCl is only 10 minutes at 55°C , compared to the half life of 8 days for **1** alone. Second, the short half life of the methylidene $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CH}_2$ (**4**) is consistent with the proposed mechanism.

CH₂ (**4**) (40 minutes at 55°C under standard reaction conditions) relative to that of the propylidene (**3**) (8 hours at 55°C) or benzyldiene (**1**) (8 days at 55°C) derivatives suggests that the first order decay of **4** contributes significantly to catalyst decomposition during RCM and CM reactions. For these reasons, ligands that increase the rate of metathesis and decrease the decomposition rates of the alkylidene and methyldiene intermediates are highly desirable.

Because phosphine dissociation contributes to decomposition, a number of chelating ligand systems, such as Schiff bases and tris(pyrazolyl)borates (Fig. 4.34), were designed to address this problem. As anticipated, these complexes are quite thermally stable, but they also have dramatically reduced catalytic activity.

4.5.6 Second generation ruthenium catalysts: *N*-heterocyclic carbene ligands

In 1998, Herrmann and co-workers prepared a series of bis(*N*-heterocyclic carbene) complexes (NHC)₂(Cl)₂Ru=CHPh by the reaction of **1** with a variety of free *N*-heterocyclic carbenes (Eq. 4.15) [95]. Previous mechanistic studies suggested that these compounds would have very low olefin metathesis activities due to the high activation barriers for ligand dissociation. As described earlier in this chapter in the context of carbene classification, NHC ligands are phosphine-like in their electronic characteristics, but they are also stronger σ -donors and do not readily dissociate from transition metal centers. Experimental and theoretical studies indicate that the ligand dissociation energy of an NHC can be 20 to 40 kcal mol⁻¹ higher than that of a tri(alkyl)phosphine [96,97]. Surprisingly, however, the bis(NHC) complexes were found to be good catalysts for the polymerization of cyclooctadiene and cyclooctene [95,97]. Assuming a mechanism similar to that outlined in Fig. 4.32, this activity suggested that catalytic turnover was extremely efficient once an NHC ligand dissociated from ruthenium. In terms of rate constants, the NHC ligands serve to dramatically decrease the ratio of k_{-1} to k_2 and/or to increase the magnitude of k_3 .



Several groups reported the reactions of catalyst **1** with a variety of NHC ligands [96–99]. The use of derivatives containing relatively small *N*-substituents (cyclohexyl, isopropyl) led to the formation of both the mono and bis(NHC) ruthenium products (Fig. 4.36a) [97]. However, the reaction of an excess of 1,3-

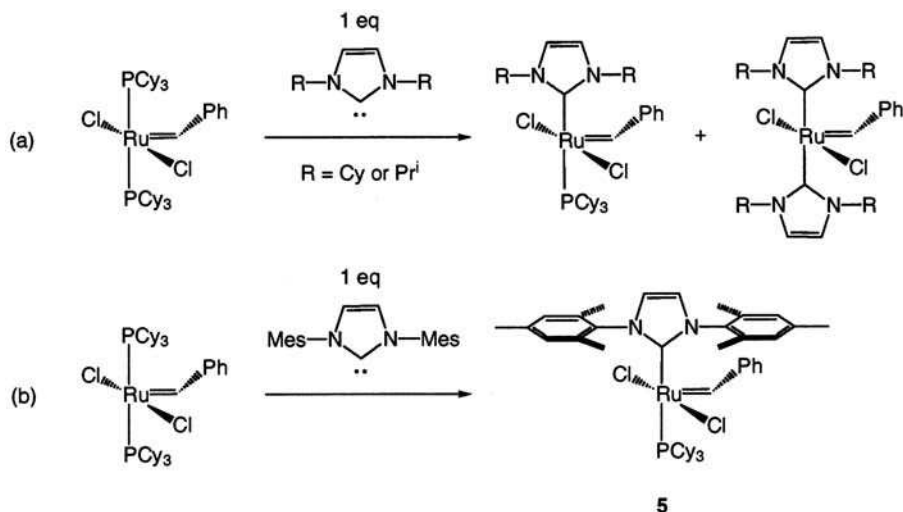
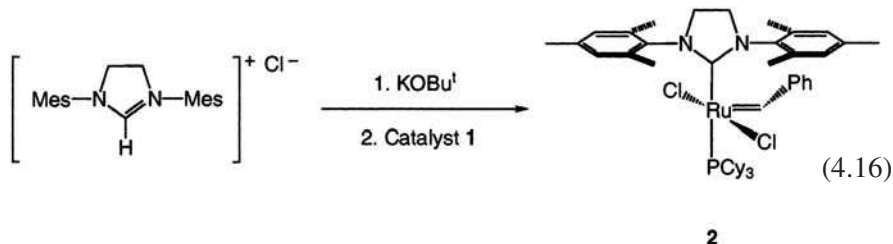


Fig. 4.36. Synthesis of mixed NHC–phosphine ruthenium alkylidene complexes.

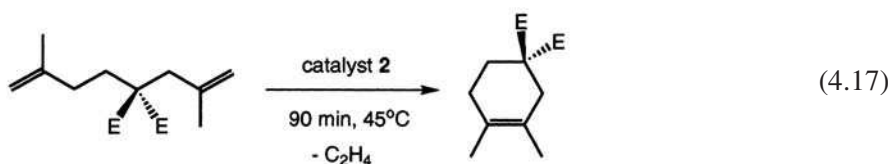
dimesityl-imidazoline-2-ylidene (IMes) with **1** produced only the mixed NHC–phosphine species (IMes)(PCy₃)(Cl)₂Ru=CHPh (**5**) (Fig. 4.36b) [96,98]. This catalyst combines a highly electron donating ligand of relatively low lability (the NHC) with a ligand that can more readily dissociate from the ruthenium center (the phosphine). The combination of these two features provides catalysts with high rates of catalytic activity and low rates of decomposition.

To introduce further steric and electronic perturbations, the saturated analog of IMes was examined, 1,3-dimesityl-imidazolidine-2-ylidene (IMesH₂) [100]. This derivative is thought to be more basic than the unsaturated IMes, and it was expected to lead to further improvements in olefin metathesis activity [16]. As shown in Eq. 4.16, a one pot synthesis of (IMesH₂)(PCy₃)(Cl)₂Ru=CHPh (**2**) was developed that involves reaction of the imidazolium salt with potassium-*tert*-butoxide, followed by alcohol elimination in the presence of (PCy₃)₂(Cl)₂Ru=CHPh (**1**) to generate **2** in good yield [100].



Catalysts **2** and **5** are the “second generation” in ruthenium catalyst development, and they show superior activity for olefin metathesis reactions relative to the parent catalyst **1**. In general, **2** is a better catalyst than **5**, although their relative activities depend somewhat on the particular substrate. Both complexes complete simple metathesis reactions, such as the RCM of diethyl diallylmalonate [100] and the ROMP of cyclooctadiene [101], at rates that are approximately 2–3 orders of magnitude higher than with catalyst **1**. In fact, catalyst **2** shows higher activity for the polymerization of cyclooctadiene than molybdenum-based catalysts. The high activity of **2** is maintained even at catalyst loadings as low as 0.0001 mol% (monomer : catalyst = 1,000,000 : 1).

The NHC-coordinated catalysts **2** and **5** also exhibit dramatically improved substrate scope relative to bis(phosphine) catalysts. For example, whereas catalyst **1** is unreactive toward sterically congested substrates and cannot form tetra-substituted RCM products, catalysts **2** and **5** readily form tetra-substituted olefins in five- and six-membered rings systems (Eq. 4.17; E = CO₂Et) [98,100]. They also mediate CM between terminal olefins and 2,2-disubstituted olefins to form new trisubstituted double bonds [102]. Previously, these transformations could only be accomplished using molybdenum-based catalysts.



Furthermore, these second generation catalysts have opened up new classes of substrates for use in olefin metathesis reactions, such as CM between electron deficient olefins and alkyl olefins [103] and the self-metathesis of electron deficient olefins [104]. The example in Fig. 4.37 illustrates the high yields of cross products that can be obtained by using catalyst **2** in reactions of alkyl olefins with α,β -unsaturated carbonyl compounds.

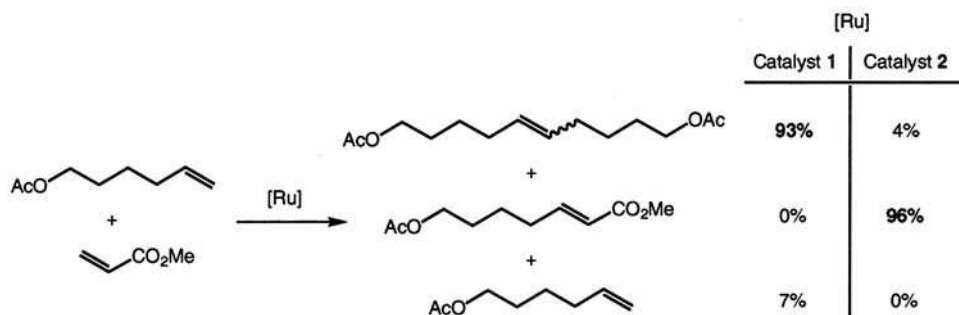


Fig. 4.37. Comparison of CM with α,β -unsaturated olefins and catalysts **1** and **2**.

4.5.7 General mechanism of second generation catalysts

Mechanistic studies show that these second generation catalysts mediate olefin metathesis by a mechanism similar to the first generation bis(phosphine) systems [87]. In both cases, catalytic turnover is inhibited by the addition of free phosphine and increased by the addition of phosphine scavengers. Ligand substitution reactions (phosphine/phosphine and phosphine/olefin) of complex **2** are also dissociative and involve a 14-electron intermediate [87]. Surprisingly, however, the differences in activity between first and second generation catalysts does not originate from initiation effects, as originally anticipated. The NHC ligand was expected to labilize the trans-coordinated phosphine by its large trans effect, but in fact, the initiation rate of catalyst **2** is two orders of magnitude *slower* than of **1** (Table 4.1, entries 1 and 2).

Instead, the high catalytic activity of **2** is a direct consequence of the reactivity of intermediate **A** (where $L = \text{IMesH}_2$). This 14-electron complex can bind olefins at a rate proportional to k_2 , or it can be deactivated by re-coordination of phosphine with a rate proportional to k_{-1} . The ratios of these critical rate constants for a variety of olefins reveals that k_{-1}/k_2 for $(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**1**) is four orders of magnitude *larger* than that for $(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CHPh}$ (**2**) [87,89]. The relative magnitudes of k_1 (10^2 smaller) and k_{-1}/k_2 (10^4 larger) for **2** relative to **1** translate into the observed 10^2 – 10^3 higher rate of overall catalytic activity shown by the NHC-coordinated catalyst in olefin metathesis reactions (Table 4.1, entries 1 and 2) [105].

In other words, the first generation bis(phosphine) catalysts display excellent initiation properties, and conversion of the pre-catalyst $(\text{PR}_3)_2(\text{X})_2\text{Ru}=\text{CHR}'$ to the phosphine-dissociated active species $(\text{PR}_3)(\text{X})_2\text{Ru}=\text{CHR}'$ (**A** where $L = \text{PR}_3$) occurs readily. Once **A** is generated, it binds olefin and undergoes $[2 + 2]$

TABLE 4.1

Ligand substitution effects in first and second generation ruthenium olefin metathesis catalysts ^a

Entry	Complex	k_1 (relative)	k_{-1}/k_2 (relative) ^b	k_{ROMP} (relative) ^c
1	$(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CHPh}$ (2)	1	1	1
2	$(\text{PCy}_3)_2(\text{Cl})_2\text{Ru}=\text{CHPh}$ (1)	150	10,000	~ 0.01 – 0.001 ^d
3	$(\text{IMesH}_2)(\text{PCy}_3)(\text{I})_2\text{Ru}=\text{CHPh}$	220	360	1.4
4	$(\text{IMesH}_2)(\text{PPh}_3)(\text{Cl})_2\text{Ru}=\text{CHPh}$	60	1.6	50
5	$(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CH}_2$	~ 0.001	–	~ 0.0001

^a All data from reference [87].^b k_{-1}/k_2 values are for reaction with ethyl vinyl ether. As described in reference [87], k_{-1}/k_2 (unlike k_1) is an olefin dependent term. Electron-rich olefins, such as ethyl vinyl ether, provide close to a lower limit for this ratio.^c k_{ROMP} values are for the ROMP of 1,5-cyclooctadiene.^d Value estimated from ref. [101].

cycloaddition and cycloreversion at a given rate. In comparison, the second generation NHC-coordinated catalysts display slower phosphine dissociation and hence slower initiation, and less of the active species **A** (where L = NHC) is formed. However, once **A** forms, it has a 10,000-fold increased selectivity for binding olefins with respect to the PCy₃-coordinated derivative (PCy₃)(X)₂Ru=CHR', and thus turnover in the catalytic cycle occurs much more rapidly with second generation catalysts.

All ligand substitutions have a significant influence on k_1 , k_{-1}/k_2 , and the overall catalytic activity in NHC-based catalyst systems [87]. These effects are currently under investigation, and some of the important initial results are included in Table 4.1. In general, the relative values of k_1 and k_{-1}/k_2 show excellent correlation with the overall metathesis activity of these complexes. Changing the halide ligand of **2** from chloride to iodide (entries 1 and 3), for example, results in a 100-fold increase in the initiation rate constant (k_1) and a concomitant 100-fold increase in k_{-1}/k_2 . Consequently, the overall catalytic activities of the dichloride and diiodide catalysts are almost identical. In contrast, changing the phosphine ligand from PCy₃ to PPh₃ (entries 1 and 4) increases the rate of phosphine dissociation (k_1) without significantly affecting k_{-1}/k_2 . The increased initiation rate of the PPh₃ catalyst is likely due to the lower basicity of PPh₃ relative to PCy₃, and it translates into 60-fold higher activity of the former for the ROMP of cyclooctadiene. Substitution of the PCy₃ ligand with more electron-poor PPh₃ derivatives [e.g., (P(*p*-CF₃C₆H₄))₃] results in additional increases in both initiation rates and catalytic activity [106].

Another significant ligand effect in these complexes is substitution on the metal–carbene moiety (Ru=CHR'). When the benzylidene of **2** is substituted with a methylidene (Table 4.1, entries 1 and 5), the rate of COD polymerization decreases by approximately four orders of magnitude [107]. This effect appears to reflect predominantly the low initiation rate of the methylidene complex. Although the origin of this effect is poorly understood at this time, the data clearly indicate that methylidene formation can slow catalysis in these systems. Substrate design, particularly substitution of terminal olefins with alkyl or aryl groups, may be used to prevent the generation of methylidene intermediates during metathesis reactions [108].

The utility of the NHC-based catalysts is derived not only from their high catalytic activity but also from their robustness with respect to thermal decomposition. Nolan has described the inertness of (IMes)(PCy₃)(Cl)₂Ru=CHPh (**5**), which shows no degradation after one hour in refluxing toluene (120°C) or after 10 minutes in refluxing diglyme (165°C) [96b]. (IMesH₂)(PCy₃)(Cl)₂Ru=CHPh (**2**) has similar thermal stability in a wide variety of solvent systems [109]. Preliminary studies show that the decomposition of **2** is strongly inhibited by the addition of free phosphine, and this suggests that thermal degradation may involve phosphine dissociation followed by bimolecular reactions of intermediate **A** [94]. These observations also indicate that the high thermal stability of **2** results from

the relatively low rates of phosphine dissociation (k_1) in this complex, as well as steric and electronic stabilization of **A** by the NHC ligand. Interestingly, decomposition of the methyldiene $(\text{IMesH}_2)(\text{PCy}_3)(\text{Cl})_2\text{Ru}=\text{CH}_2$ is not affected by the addition of phosphine, which implies that this process involves an alternative mechanism like C–H activation at the electron-rich ruthenium center.

4.5.8 Perspectives on catalyst development

Due in large part to the development of ruthenium catalysts, olefin metathesis reactions can now be carried out on a diverse array of functionalized electron-rich and electron-poor olefins. As we have described, mechanistic analysis was instrumental in the design of more highly active second generation catalysts with expanded substrate scope, which was achieved by proper differentiation of the two L-type ligands within the $(\text{L})_2(\text{X})_2\text{Ru}=\text{CHR}'$ framework. Further investigations have revealed that these new catalysts display several unexpected features, and mechanistic analysis continues to be an invaluable tool for understanding reactivity patterns and for the development of new catalyst systems.

Recently, significant advances have been made in the area of asymmetric olefin metathesis reactions, such as the kinetic resolution of olefins containing remote stereogenic centers and the enantioselective desymmetrization of prochiral olefin substrates [110]. For example, Schrock and Hoveyda have developed state-of-the-art chiral molybdenum-based catalysts with biphenolate and dinaphtholate ligands (Fig. 4.38) [111]. Ruthenium-based catalysts coordinated with enantiomerically pure *N*-heterocyclic carbene ligands have also been made (Fig. 4.38), and the increased functional group tolerance of ruthenium compared to molybdenum should provide access to an even greater variety of functionalized substrates for enantioselective olefin metathesis [112].

The biggest challenge that remains in the field is control over the stereoselective formation of *cis* or *trans* olefins. Further experimental and theoretical mechanistic studies are needed to identify the stereodetermining steps of the reaction, and to discern the structures of important intermediates, such as the olefin complex **B** and

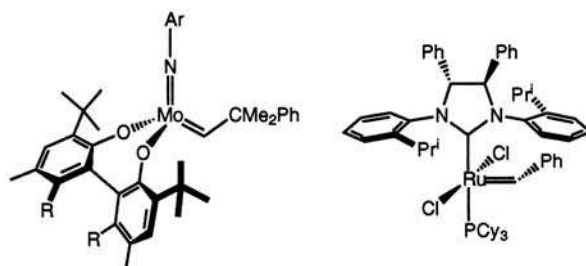


Fig. 4.38. Molybdenum and ruthenium catalysts for asymmetric olefin metathesis reactions.

the metallacyclobutane **C** in the case of ruthenium alkylidene catalysts (Fig. 4.32). The geometries of these intermediates will provide valuable information about the steric and electronic factors that influence stereoselectivity.

4.6 CONCLUSIONS

In this chapter, we have outlined the reactivity patterns and mechanisms that characterize a variety of metal–carbene complexes, with particular emphasis on carbonyl olefination, olefin cyclopropanation, and olefin metathesis. The main theme that ties together our discussion is the basic understanding of metal–carbene bonding and its relationship to mechanism and reactivity. Although the overall reactivity of any particular carbene complex depends on the nature of the metal center and the specific ligand array, it is preferable to think about the properties of metal carbenes in a cohesive way with the continuum model. Importantly, the reactivity of the metal–carbene unit can be modified by subtle ligand effects. On the one hand, this sensitivity results in many situations where reactivity becomes unpredictable, but on the other hand, it also leads to useful variations, as illustrated by a wide range of olefin metathesis catalysts that differ in efficiency and functional group compatibility. The study of reaction mechanisms is essential to help clarify these structure–activity relationships and ultimately contribute to an increasingly refined understanding of metal–carbene bonding.

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Transmetalation

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5.1 INTRODUCTION

The transmetalation of organometallic compounds, which means the transfer of σ -bonded alkyl, aryl, and alkynyl ligands and π -allyl ligands from one metal to another, activates a metal–carbon bond and forms a new metal–carbon bond [1–6]. It provides common and useful methods for preparing various organometallic compounds. Intermolecular alkyl and aryl group transfer from a main group element to a transition metal is involved in many synthetic organic reactions catalyzed by transition metal complexes, i.e., cross-coupling reactions of organic halides with alkyl, aryl, and alkynyl metal compounds, carbometalation of unsaturated molecules, and coordination polymerization of alkenes. In spite of the long history and abundance of stoichiometric and catalytic reactions involving transmetalation, the number of reports on the detailed study of transmetalation is much smaller than that in the fundamental reactions of organotransition metal complexes described in other chapters of this book. Transmetalation of organometallic compounds mostly involves bimetallic intermediate or transition state, which is distinct from the other unimolecular reactions of organometallic compounds.

Scheme 5.1 summarizes typical transmetalation reactions that are classified into three categories based on the reaction mechanisms. The first reaction (i) (redox type) is intermolecular organic ligand transfer accompanied by oxidation and reduction of metal centers. The reaction pattern resembles the inner-sphere oxidation and reduction of non-organometallic transition metal complexes, which causes the transfer of OH or a halogeno ligand between two metal centers via an intermediate having the bridged anionic ligand [7]. Relative stability of metal–carbon bonds of the starting and produced organometallic compounds influences thermodynamics of the transmetalation directly. The dissociation energies of metal–carbon bonds of several homoleptic alkyl compounds were estimated by calorimetric measurement of this type of transmetalation [8,9].

The second type of transmetalation (Scheme 5.1 (ii), metal exchange type) is a

(i) redox type



(ii) metal exchange type



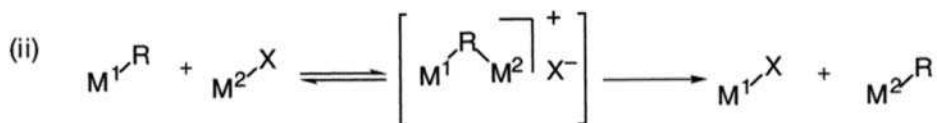
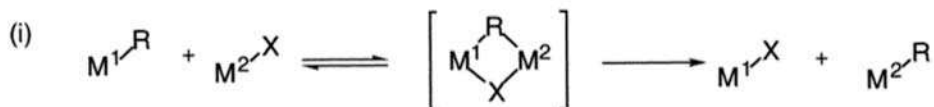
(iii) ate complex formation type



Scheme 5.1.

metal–ligand exchange between organometallic compounds and metal complexes with a halogeno or pseudo-halogeno ligand. It is the most common among the three types of reactions. The intermolecular exchange of alkyl or aryl ligands between two organometallic compounds ($X = R'$ in Scheme 5.1 (ii)) falls under this category. Since the pre-dissociation of the carbon-bonded ligand does not occur easily, the transmetalation reactions take place via associative intermediates with bridging alkyl, aryl, alkynyl or allyl ligand. The dinuclear intermediate complexes are often stabilized further by a bridging halogeno or pseudo-halogeno ligand, as shown in Scheme 5.2 (i), although an alternative cationic intermediate in Scheme 5.2 (ii) is considered in several reactions.

The formation of the dinuclear intermediate and its dissociation to two metal complexes in a concerted pathway suggest a reversible intermolecular exchange of the two ligands. Most of the transmetalation reactions, however, occur smoothly

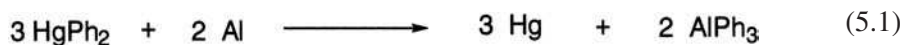


Scheme 5.2.

and irreversibly. Typically, alkyl compounds of Li and Mg readily undergo transmetalation with halogeno complexes of transition metals and of group 13 and 14 elements such as B, Si, Al, and Sn. Transmetalation in the reverse direction is quite rare. Two rationales, kinetic and thermodynamic, are possible to account for the irreversible reactions. Lower nucleophilic nature of alkyl compounds of B, Al, Si and transition metals than alkyllithium and alkylmagnesium compounds makes the transmetalation in the reverse direction more difficult to occur than the forward transmetalation. This kinetic rationalization for the direction of the transmetalation was mentioned in several previous books [3,5]. The relative stabilities of two metal–carbon bonds and two metal–X (X = halogeno or pseudo-halogeno) bonds involved in the reaction determine the thermodynamics of the transmetalation. The coordination of an alkyl group to an electropositive metal and that of a halogeno anion to a less-electropositive metal in the starting complexes of the above reactions are a driving force of the apparently irreversible transmetalation. The mismatch in the coordination bonds will be relieved by the transmetalation, which produces LiX or MgX₂ and organometallic compounds of less-electropositive metals. This thermodynamic aspect of transmetalation provides general explanation or prediction of the transmetalation, although it does not correlate directly with the relative thermodynamic stability of M–C and M–X bonds of the starting complexes and products.

The reaction (iii) in Scheme 5.1 (ate complex formation type) means alkyl (or other organic) ligand transfer from one metal to the other to produce a pair of metal cation and anionic organometallic complex. It transports the organic ligand only, while the reaction in Scheme 5.1 (ii) causes simultaneous intermolecular transfer of σ -bonded organic and halogeno (or pseudo-halogeno) ligands. The valence of the metal centers remains unchanged during this type of transmetalation. The reactions forming anionic transition metal complexes (ate complexes) are of significant interest in organic and organometallic chemistry and are described in the following section.

The reactions in Eqs. 5.1 and 5.2 show two contrasting preparative reactions of triorganoaluminum. They are classified into redox type and metal exchange type in Scheme 5.1, respectively. Diphenylmercury reacts with metallic aluminum to induce the transfer of the phenyl group from Hg to Al, producing AlPh₃ and Hg (Eq. 5.1) [10].



The latter reaction is the alkylation of AlCl₃ with organometallic compounds such as a Grignard reagent and alkyllithium, which has been used in the preparation of a number of organoaluminum compounds (Eq. 5.2) [11].

The combination of the metals involved in the reaction leads to another classification of transmetalation into three categories: (1) organic ligand transfer between

main group element and transition metal complex, (2) that between transition metal complexes, and (3) the reaction between main group metal compounds. The reactions in (1) were used as the preparative method of alkyl transition metal complexes. The discovery of olefin polymerization and oligomerization, started from the nickel effect found by Ziegler, brought about the attention to the transmetalation between organometallic compounds of main group elements and transition metal complexes. The transmetalation between transition metal complexes in category (2) is newer and less common than the reactions in (1). The reactions in category (3) were already known early in the previous century and then have been used as important synthetic tools of organometallic compounds of main group elements.

The studies of details of transmetalation for the last few decades seem to have reinforced importance of transmetalation in organometallic chemistry and its contribution to this and related fields. Chemical Abstracts has added transmetalation to the keyword list in 1995. In this chapter, the author describes the transmetalation of organometallic compounds, both of main group metals and of transition metals, as well as its mechanism and relevance to transition metal complex-catalyzed reactions.

5.2 ORGANIC LIGAND TRANSFER FROM MAIN GROUP METAL TO TRANSITION METAL

5.2.1 Preparation of organotransition metal complexes

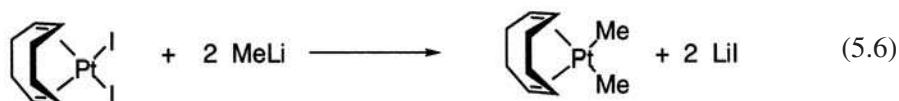
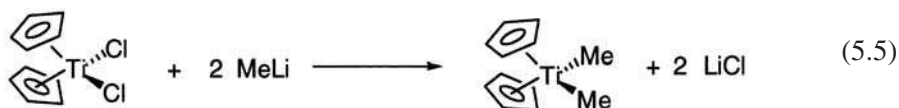
Various alkyl, aryl, and alkynyl complexes of transition metals are prepared from the reaction of organometallic compounds of main group elements with halogeno or pseudo-halogeno complexes of transition metals. A suitable combination of the two starting materials can be selected from a number of organometallic compounds of main group elements and transition metal complexes to obtain the desired organotransition metal complex. Alkyl and aryl compounds of not only main group metals such as Li, Mg, Al, B, and Sn but also transition and post-transition metals such as Cu, Hg, and Zn are employed for alkylation (or arylation) of halogeno complexes of transition metals.

Grignard reagent, RMgX , is a common alkylating reagent and is used in the preparation of organotransition metal complexes such as $\text{Ti}(\text{CH}_2\text{SiMe}_3)_4$, $\text{Ni}(\text{C}_3\text{H}_5)_2$, $\text{NiMe}(\text{Cp})(\text{PPh}_3)$, PtIme_3 , $\text{PtPh}_2(\text{PEt}_3)_2$, and $\text{VMe}(\text{C}_5\text{H}_5)_2$ [12–16]. Representative reactions are shown in equations 5.3 and 5.4.

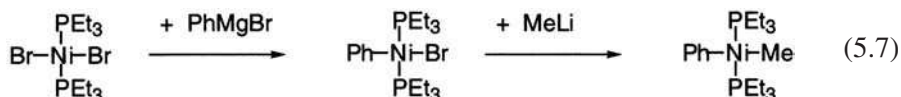


The transmetalation causes partial or total replacement of halogeno ligands in the starting transition metal complexes with organic ligands.

Alkylolithium is used to alkylate halogeno complexes of many organotransition metal complexes, giving the corresponding alkyl complexes. The reactions of methylolithium with halogeno complexes of transition metals produce the corresponding methyl complexes such as Cp_2TiMe_2 , WMe_6 , $\text{PtMe}_2(\text{cod})$, and CrMe_4 (Eqs. 5.5 and 5.6) [17–20].



Other alkylolithium and aryllithium also cause peralkylation or perarylation of di- or trihalogeno complexes of transition metals. The role of organolithium as alkylating reagent in the above transmetalation is similar to that of organomagnesium reagents, but the reactivity of organolithium reagent is higher. Methylolithium reacts with Cp_2TiCl_2 , having an electropositive Ti(IV) center, to produce the dimethyltitanocene smoothly, whereas dimethylation of the complex occurs less efficiently by using the corresponding methylmagnesium reagents. The higher reactivity of organolithium than organomagnesium reagent may be attributed to higher nucleophilicity of the organolithium or to the different polarity between the Li–C and Mg–C bonds as mentioned in the previous section. A combination of organomagnesium and organolithium reagents enabled the successive introduction of two different organic ligands to a metal center, as shown in Eq. 5.7.



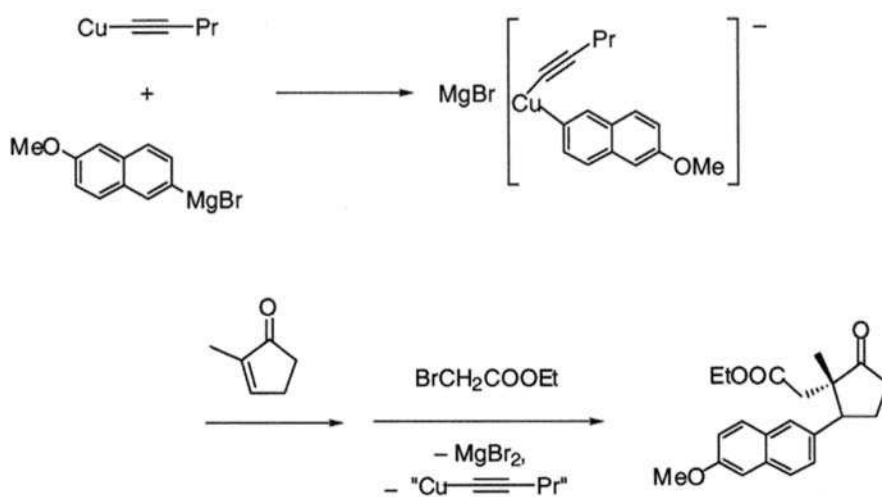
An aryl(bromo)nickel complex with PEt_3 ligands, *trans*- $\text{NiAr}(\text{Br})(\text{PEt}_3)_2$, obtained from the reaction of arylmagnesium bromide with $\text{NiBr}_2(\text{PEt}_3)_2$, reacts with methylolithium to cause substitution of the remaining bromo ligand with the Me group [21].

The high reactivity of alkylolithium in the transmetalation often causes multiple alkylation of halogeno complexes of transition metals to produce anionic polyalkyl complexes (ate complexes). The reaction is classified into transmetalation in Scheme 5.1(iii). The most common and important ate complexes in organic and organometallic chemistry are organocuprates [22–24] (Eq 5.8).

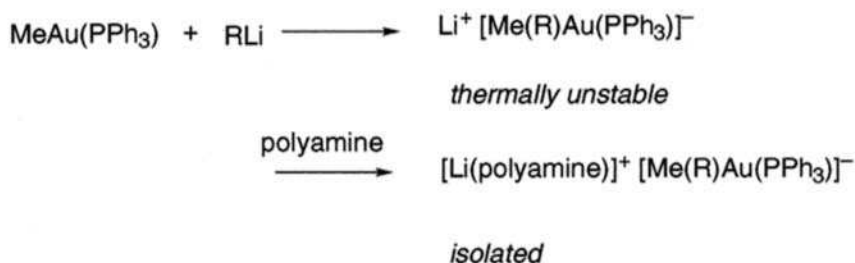


CuI reacts with an excess amount of MeLi to produce the corresponding cuprate, LiCuMe_2 . Many other organocuprates have been prepared and characterized. Structural studies of organocuprates in the solid state revealed a typical dimer form, $[\text{Li}_2\text{Cu}_2\text{R}_4]$, which is composed of an eight-membered ring containing two Li, two Cu, and four bridging alkyl ligands [25]. Organocuprates with other structures and compositions, including higher ordered cuprates, were also characterized by crystallography. A theoretical investigation was recently carried out to determine the detailed reaction pathways in the addition of organocuprates to alkynes and α,β -unsaturated carbonyl compounds. It was revealed that the dimer cuprate, $[\text{Li}_2\text{Cu}_2\text{Me}_4]$, and the dimer of a higher ordered cuprate, LiClLiCuMe_2 , are more favorable intermediates than the monomeric organocopper reagent [26]. The dimer organocuprates, characterized by the structural study in the solid state, exist in solution and act as the active species of the C–C bond forming reaction.

Synthetically useful heterocuprates, $[\text{CuRR}']^-$, which contain a sacrificial ligand, were prepared from the easily obtained Cu salts such as alkynylcopper and CuCN. The alkynyl and CN group is commonly used as a sacrificial ligand because it shows much lower reactivity toward an electrophilic reagent than the co-existing alkyl ligand. Structural studies of the heterocuprates are scarce. A recent study revealed the polymeric structure of $\text{Li}_2[\text{CuAr}_2(\text{CN})]$ in the solid state [27]. Scheme 5.3 depicts the formation of the heterocuprate prepared from alkynylcopper and organomagnesium reagent and its reaction with cyclopentenone, leading to 1,2-bisalkylation [28]. The 1,4-addition of organocuprates to the cyclic α,β -unsaturated ketones is a common method to introduce alkyl substituents at the β -position and has been used in synthesis of the natural products that contain the cyclic ketone part.



Scheme 5.3.



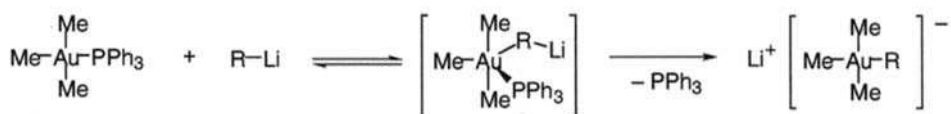
Scheme 5.4.

Alkyl or aryl group-bonded ate complexes of other transition metals, such as Pt, Rh, and Au, are also obtained by the reactions of excess alkyllithium or aryllithium with halogeno complexes of these metals. Methylgold(I) with a phosphine ligand reacts with alkyllithium to produce three-coordinated dialkylaurate(I) complex (Scheme 5.4) [29,30]. These dialkylaurates with phosphine ligand are in equilibrium with neutral alkylgold complexes via reversible substitution reactions of an alkyl ligand of the aurate with phosphine and of a phosphine ligand of the neutral complex with the alkyl group. The addition of diglyme or polyamine to the above mixture induces coordination of the additive to Li cation and makes isolation of the ate complex possible [31].

Tetraalkylaurate(III) complexes were prepared by alkylation of neutral alkylgold(III) complexes by alkyllithium (Eq. 5.9) [32–34].

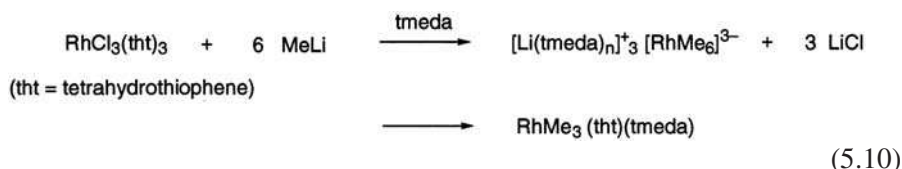


The reaction leads to selective substitution of the phosphine with a new alkyl ligand, keeping the geometry of the three alkyl ligands of the starting complex in a square-planar coordination. The reaction of trimethylgold(III) complex with various alkyl lithium reagents obeys first-order kinetics in concentration of the Au(III) complex. These results indicated an associative pathway, as shown in Scheme 5.5. The nucleophilic attack of alkyllithium at an apical coordination site of the square-planar Au(III) center forms an intermediate having a penta-coordinated Au center and a bridging coordination of the alkyl group to Au and Li.



Scheme 5.5.

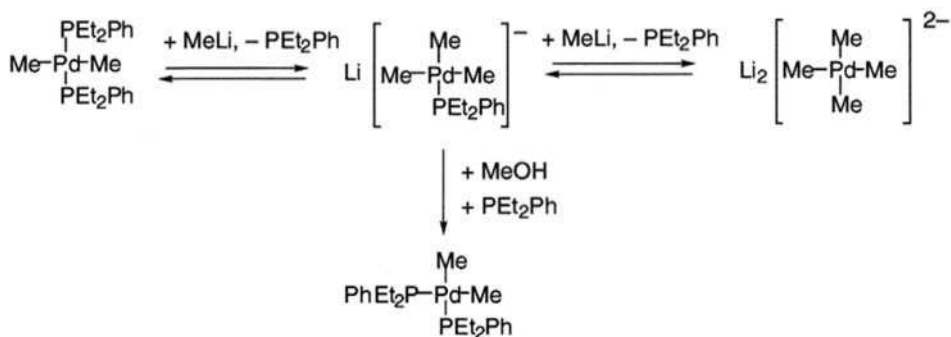
An anionic pentamethylplatinate(IV) complex, $\text{Li}[\text{PtMe}_5(\text{PPh}_3)]$, and homoleptic hexamethylplatinate(IV), $\text{Li}_2[\text{PtMe}_6]$, were prepared analogously by stepwise methylation of the neutral methylplatinum complexes [35,36]. Eq. 5.10 shows the preparation of the hexamethylrhodate(III) complex, $\text{Li}_3[\text{RhMe}_6]$ [37].



$[\text{RhMe}_6]^{3-}$, formed from the reaction of RhCl_3 with $\text{MeLi}(\text{tmeda})$ ($\text{tmeda} = N,N,N',N'$ -tetramethylethylenediamine) is stable at low temperature in solution and is converted, upon raising the temperature, into a neutral trimethylrhodium(III) complex with auxiliary tmeda and tht (tetrahydrothiophene) ligands. The ate complexes of groups 9 and 10 transition metals prefer mononuclear structures rather than di- or multi-nuclear structures with bridging ligands, while the bridging coordination of alkyl or aryl ligands stabilizes the dinuclear or multinuclear structures of organocuprates.

Dimethylpalladium(II) complex with PEt_2Ph ligand undergoes alkylation by MeLi or PhLi to afford palladate complexes which are characterized by NMR spectra of the solution. Detailed NMR studies of mixtures of the complex and MeLi or PhLi in various ratios revealed stepwise conversion of the neutral dimethyl complex into monoanionic palladate and then into homoleptic dianionic tetraorganopalladate complexes [38] (Scheme 5.6).

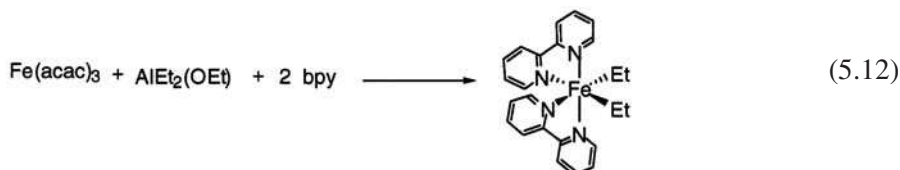
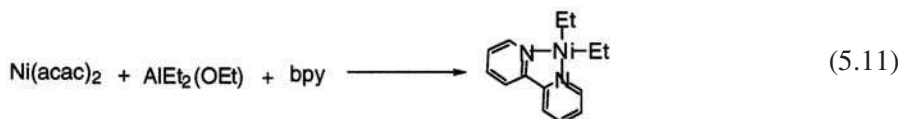
Quenching of the formed $[\text{PdMe}_3(\text{PEt}_2\text{Ph})]^-$ by MeOH in the presence of PEt_2Ph results in the formation of $\text{cis-PdMe}_2(\text{PEt}_2\text{Ph})_2$, which is thermodynamically less stable than the *trans* isomer. The formation of the *cis* isomer is rationalized by easier protonolysis of the methyl ligand at the *trans* position to a methyl ligand than the methyl ligand *trans* to the phosphine ligand. The T-shaped



Scheme 5.6.

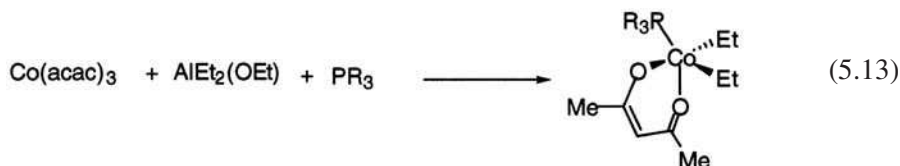
coordinatively unsaturated intermediate 'PdMe₂(PEt₂Ph)', formed via the above protonation of the methyl ligand, has two methyl ligands at cis positions and undergoes rapid ligation of phosphine to the vacant coordination site.

The reaction of acetylacetonato compounds of transition metals with alkylaluminum is a useful tool for synthesizing alkyl complexes of many transition metals. As shown in equations 5.11 and 5.12, acetylacetonato compounds of Ni, Fe, and Co are converted cleanly into the corresponding methyl or ethyl complexes with auxiliary bpy and tertiary phosphine ligands by using Me₂Al(OEt) or Et₂Al(OEt) as the alkylating reagents [39–43].



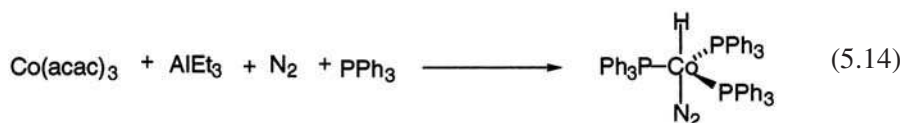
R₂Al(OEt) (or R_nAl(OEt)_{3-n}) was chosen as the alkylating reagent because it causes the transmetalation more smoothly than triorganoaluminum, AlR₃. The starting acetylacetonato complexes, sparingly soluble in Et₂O, react with R_nAl(OEt)_{3-n} with gradual dissolution and are converted into the alkyl complexes which crystallize from the solution owing to their limited solubility in the solvent. The produced alkyltransition metal complexes can be easily separated as the crystalline products from the Al-containing by-products that dissolve in the Et₂O solution. Workup and purification of the products are free from hydrolysis of the alkylating reagent or dissolution of inorganic salt in water to remove it from the product. This contrasts with the reactions of alkyllithium or alkylmagnesium with halogeno complexes of transition metals, which often requires hydrolysis of the remaining alkylating reagent.

The reactions of acetylacetonato compounds of transition metals, such as Ni, Fe, Mo, Pt and Co, with R_nAl(OEt)_{3-n} cause partial alkylation and give the product with both alkyl and acetylacetonato ligands [44–49] (Eq. 5.13).

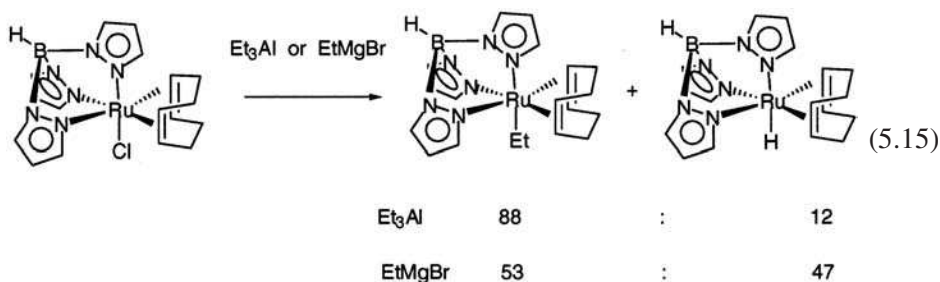


The complexes formed via the above reactions can be regarded as an intermediate of peralkylation of di- or trivalent transition metal acetylacetonato compounds.

Several reactions of $\text{Et}_2\text{Al}(\text{OEt})$ with transition metal complexes afforded hydrido complexes rather than the expected ethyl complexes (Eq. 5.14).



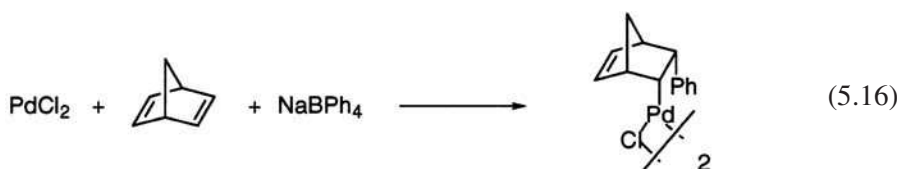
$\text{Et}_2\text{Al}(\text{OEt})$ reacts with $\text{Co}(\text{acac})_3$ and with $\text{RuCl}_3 \cdot n\text{-H}_2\text{O}$ in the presence of PPh_3 to result in the formation of $\text{CoH}(\text{N}_2)(\text{PPh}_3)_3$ and $\text{RuH}_2(\text{PPh}_3)_4$, respectively [50,51]. Ethyl complexes of these metals with the phosphine ligands are formed as the initial product and are converted into the hydrido complexes via rapid β -hydrogen elimination of the ethyl ligands. On the other hand, the reaction of $\text{Et}_2\text{Al}(\text{OEt})$ with $\text{Co}(\text{acac})_3$ in the presence of 2,2'-bipyridine produces the ethylcobalt complex. Rate of the β -hydrogen elimination of alkyl ligand during preparation of the complex is influenced not only by the auxiliary ligands but also by the alkylating reagent used. The alkylation of chlororuthenium complex with a hydrotrispyrazolylborato ligand by ethyl aluminum and magnesium compounds was reported recently. The reaction produces ethylruthenium and/or hydridoruthenium complexes, whose ratio varies depending on the alkylating reagents (Eq. 5.15) [52].



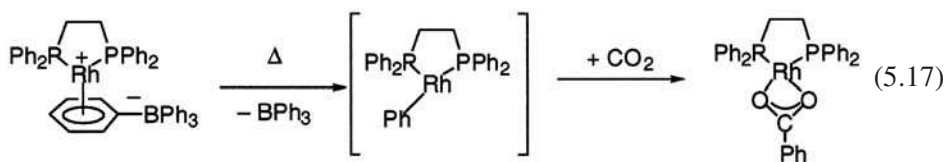
The transmetalation of organometallic compounds of B, Si, and Sn with transition metal complexes, leading to the isolation of organotransition metal complexes, is much less common than the reactions using organolithium, magnesium, and aluminum compounds described above. Accordingly, these reactions have little significance as preparative methods of organotransition metal complexes. On the other hand, many synthetic organic reactions by transition metal catalysis convert these organometallic compounds to organic products via transmetalation of organoboronic acids, fluorosilicates and organostannanes. The transmetalation of organotin compounds with halogeno palladium complexes will be presented in the next section, along with relevance of the transmetalation to the mechanism of cross-coupling reactions of organic halides with organotin compounds; most studies of the transmetalation of organotin compounds with transition metals concern the Pd complex-catalyzed cross-coupling reaction. Several transmetalation reactions of organoboron and organosilicon compounds with transition

metal halogeno complexes, which forms the organotransition metal complexes, are mentioned below.

The B–C bonds of tetraorganoborate, BR_4^- , and organoboronic acid, $\text{RB}(\text{OH})_2$, are more reactive toward transmetalation than that of triorganoborane, BR_3 . Phenyl group transfer from BPh_4^- to transition metals takes place under mild conditions. The reaction of PdCl_2 with NaBPh_4 in the presence of norbornadiene produces a Pd complex with a phenylnorbornenyl ligand (Eq. 5.16) [53].



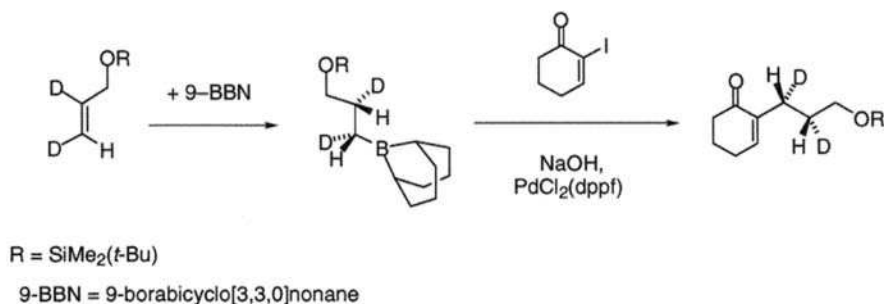
The reaction can be explained by the transmetalation of the borate with PdCl_2 giving phenylpalladium intermediate and the subsequent insertion of a C=C double bond of norbornadiene into the Pd–Ph bond. Cationic π -allyl–palladium(II) and –rhodium(I) complexes having a BPh_4^- counter anion induce phenyl group migration from B to the transition metals at elevated temperature to form phenyl complexes [54,55] (Eq. 5.17).



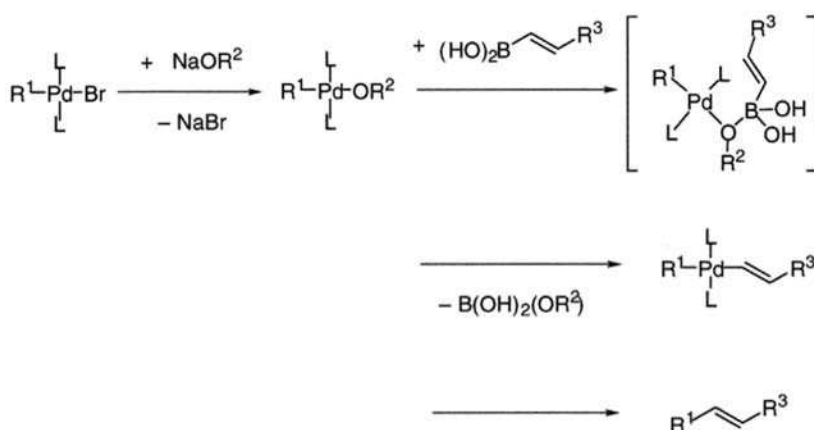
The BPh_4^- anion, whose aromatic ring is π -coordinated to the metal center, undergoes phenyl group migration to the transition metal with liberation of BPh_3 .

The transmetalation of tetraalkyl borate to transition metal complex is included in the proposed mechanism for Ni catalyzed cross-coupling of the borate with organic halides [56]. The stereochemistry of Pd-catalyzed cross-coupling of alkylborane with alkenyl iodide was studied by using deuterium-labeled organoborane. Selectively labeled alkyl borane, prepared from the addition of 9-BBN to allyl ether, reacts with 2-iodocyclohexene in the presence of a Pd(II) complex catalyst and a base to afford 2-alkylcyclohexenone, as shown in Scheme 5.7 [57]. This reaction probably involves the initial formation of a borate anion from the starting alkyl borane and added OH^- . The resultant borate undergoes subsequent cross-coupling with iodocyclohexenone. The absolute configuration of the starting alkylborane is retained in the coupling product, indicating that the transmetalation took place with retention of stereochemistry.

Arylboronic and alkenylboronic acids undergo transition metal complex-catalyzed synthetic organic reactions such as cross-coupling with organic halides [58–60], 1,4-addition to α,β -unsaturated ketones [61–63], and ring-opening addition to vinyl oxirane [64]. Scheme 5.8 depicts the mechanism proposed for the

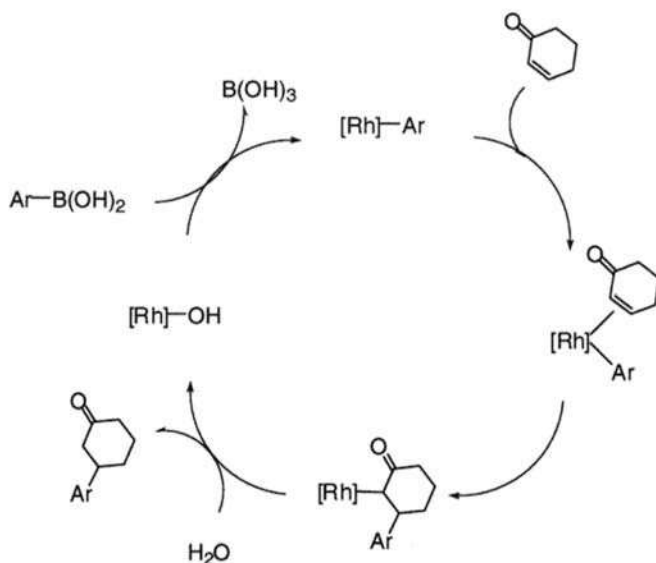


Scheme 5.7.



Scheme 5.8.

Pd complex-catalyzed cross-coupling reaction of alkenyl bromide with alkenyl boronic acid. The transmetalation does not take place directly between the intermediate bromopalladium complex and the boronic acid. Base-promoted displacement of the halogeno ligand at the Pd center with the alkoxide group is followed by its reaction with the alkenyl boronic acid to form alkenylpalladium intermediate. The latter step of the reaction is facilitated by the high affinity between boron and oxygen atoms and by labile nature of the Pd–O bond. This ligand exchange was proposed to involve a dinuclear intermediate having a bridging alkoxo ligand bonded to the Pd and B centers. Since organoboronic acids are stable in the presence of protic solvents and miscible with water, the cross-coupling reaction using organoboronic acid can be carried out in water or water-containing solvents. The isolation of diorganopalladium complex from the transmetalation of organoboronic acid with organopalladium halide has not been achieved, probably due to the faster reductive elimination of the cross-coupling product than the transmetalation. Analysis of a mixture of arylboronic acid and arylpalladium complex by mass spectrometry using the electrospray technique revealed the existence

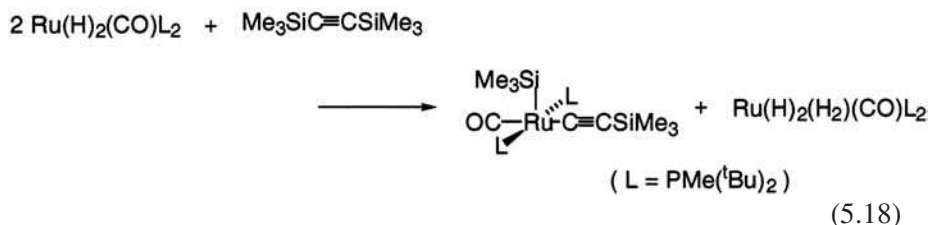


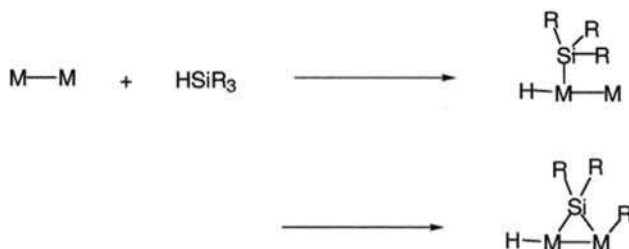
Scheme 5.9.

of a diarylpalladium complex, $\text{Pd}(\text{Ar})(\text{Ar}')(\text{PR}_3)_2$, in addition to the starting Pd complex [65].

A recent study of the mechanism of Rh complex catalyzed 1,4-addition of arylboronic acid to enones showed the presence of the intermediates of the reaction, arylrhodium complex, hydroxorhodium complex, and enolatorhodium complexes, which were found in the NMR spectra of the reaction mixture using BINAP as the ligand (Scheme 5.9) [66]. The reaction involves insertion of the C–C double bond of the substrate into the Rh(I)–Ar bond and hydrolysis of the resultant enolatorhodium complex to form the arylated ketone as the reaction product. The hydroxorhodium species undergoes transmetalation of arylboronic acid to regenerate the arylrhodium intermediate.

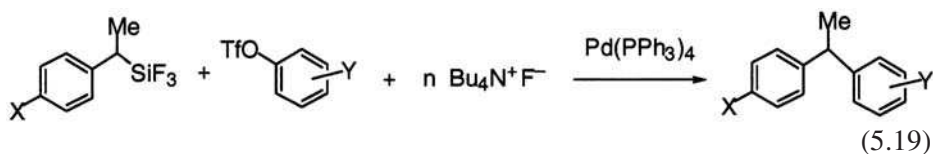
The transmetalation of organosilanes, SiR_4 , with transition metal complexes is uncommon due to the stable and non-polar Si–C bond [67]. Although Si–C bond activation of tetraorganosilanes promoted by transition metal complexes is known, the intermolecular (Eq. 5.18) [68–71] and intramolecular (Scheme 5.10) [72–78] reactions are classified into oxidative addition more appropriately than transmetalation.



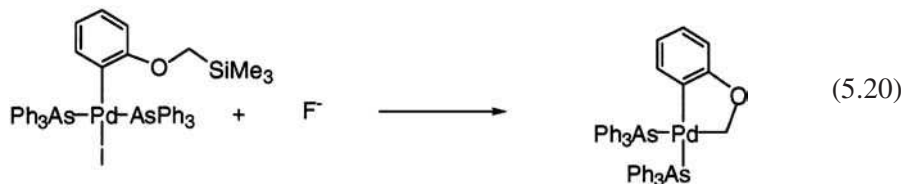


Scheme 5.10.

Organofluorosilicates, $\text{RSiF}_n(\text{X})_{5-n}^-$, have a more polar and reactive Si-C bond than tetraorganosilanes. Fluorosilicates containing penta- and hexa-coordinated Si centers are obtained from the reaction of chlorosilanes with fluoro anion [79,80] and undergo oxidative cleavage of the Si-C bond by Br_2 or Cu(II) . On the other hand, alkyltrifluorosilane undergoes Pd catalyzed cross-coupling with aryltriflates in the presence of added fluoride ion, as shown in Eq. 5.19 [81,82].



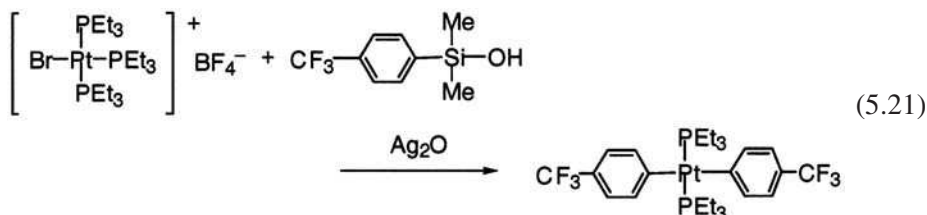
The use of a chiral auxiliary ligand results in enantioselective cross-coupling reaction whose stereoselectivity varies to a large extent depending on the reaction conditions. Since fluoride addition is indispensable to the smooth coupling reaction, the reaction probably involves the initial conversion of the fluorosilane, RSiF_3 , into fluorosilicate, RSiF_4^- . The mechanism proposed for this reaction involves alkyl ligand transfer of the resultant fluorosilicate to the arylpalladium complex, giving an aryl(alkyl)palladium intermediate. The palladium complex, which has the aryl ligand with a silylated substituent at the ortho position, undergoes fluoride induced intramolecular C-Si bond activation to produce five-membered palladacycles, as shown in Eq. 5.20 [83].



The effect of added fluoride is said to promote the formation of fluorosilicate and enhance the transmetalation. Detailed studies on the transmetalation via direct reaction of fluorosilicate with Pd complexes have not been reported.

Si-C bond activation of silanol promoted by Ag_2O has also been employed as a key step of cross-coupling of the reagent catalyzed by transition metal complexes

[84–87]. The reaction of arylsilanol with bromoplatinum(II) complexes in the presence of Ag_2O leads to arylplatinum complexes via transmetalation from Si to Pt, as shown in Eq. 5.21 [88].

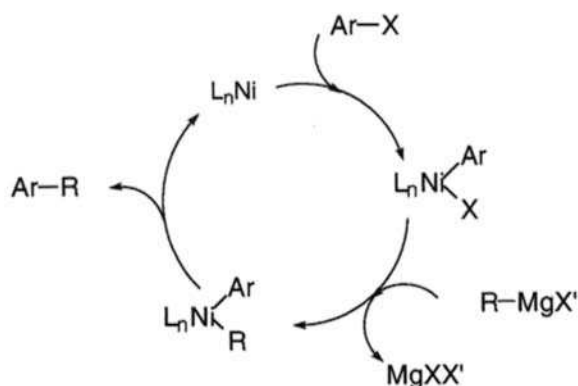


The added Ag_2O in this aryl group transfer from Si to Pt is considered to play a dual role of activating both Pt–Br bond and Si–C bond.

5.2.2 Relevance to cross-coupling reactions catalyzed by transition metal complexes

A number of cross-coupling reactions of organic halides and triflates with alkyl, aryl, and alkenyl main group metal compounds have been reported since 1972 when the Ni catalyzed cross-coupling reaction of haloarene with Grignard reagent was reported [2,89–92]. The Pd version of the cross-coupling using organomagnesium reagent was reported three years later [93]. Cross-coupling of Grignard reagent with haloalkenes and haloalkanes was achieved by using Fe(III) and Co(II) catalysts [94,95]. A mechanism involving the transmetalation of organomagnesium reagent with halogeno transition metal complexes was proposed to account for the results of the reactions, as shown in Scheme 5.11.

The catalytic cycle involves the oxidative addition of aryl halide to Ni(0) precursor, the transmetalation of organomagnesium reagent to the resulting aryl(halogeno)nickel complex giving an aryl(alkyl)nickel(II) intermediate, and



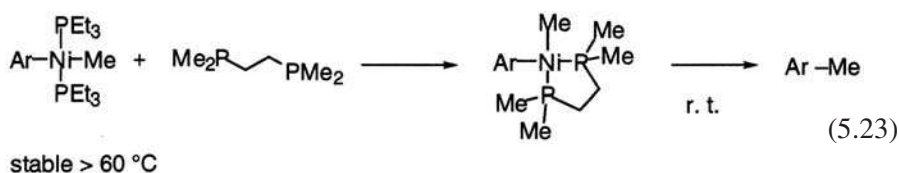
Scheme 5.11.

the reductive elimination of the cross-coupling product to regenerate the Ni(0) species. This mechanism is reasonable except for the issue of the configuration of the aryl(alkyl)nickel intermediate in the reaction using monodentate phosphine ligand.

Diorganonickel-phosphine complexes with *trans* geometry are more stable than the *cis* isomer and are isolated as the sole product in common preparative reactions (Eqs. 5.7 and 5.22) [21,96].

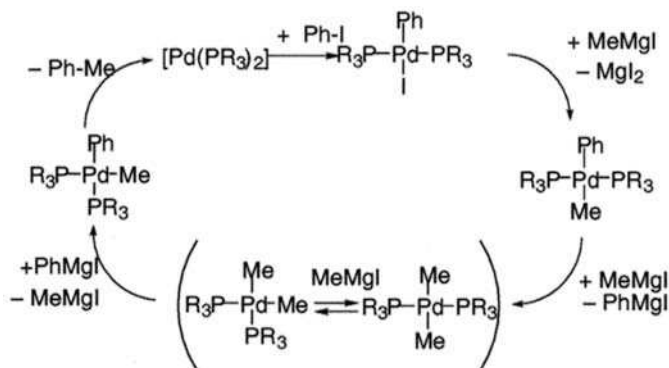


These complexes do not undergo direct coupling of the organic ligands via concerted reductive elimination. Actually, *trans*-NiMe(Ar)(PEt₃)₂ is stable and does not cause reductive elimination of the coupling product. Upon change of the geometry by replacing the monophosphine ligand with chelating dmpe (1,2-bis(dimethylphosphino)ethane), the resulting *cis*-NiMe(Ar)(dmpe) releases the coupling product easily [97] (Eq. 5.23).



The *cis*–*trans* isomerization of diorganonickel complex via dissociative or associative intermediates was investigated in detail from both experimental and theoretical aspects [98]. All these results suggest that the stable *trans* diorganonickel intermediate of the cross-coupling reaction may be converted into the reactive *cis* isomer during the reaction. Further details are not clear at present in the Ni-catalyzed system.

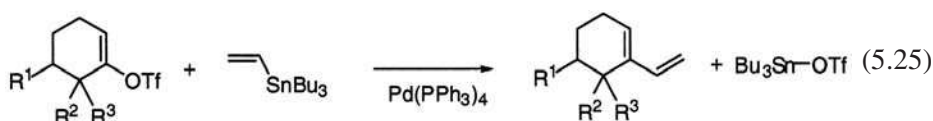
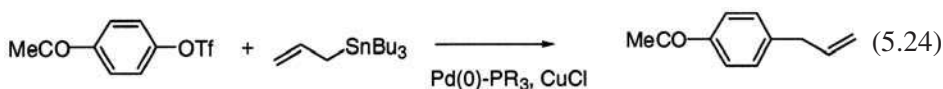
The mechanism of cross-coupling catalyzed by Pd complexes faces the same issue on the intermediate structure; *trans*-aryl(alkyl)palladium(II) complex, which is more stable than the *cis* isomer, does not undergo direct reductive elimination of alkylarene. The reaction of MeMgI with arylpalladium complexes revealed rapid and reversible conversion promoted by methylmagnesium reagents [99]. Scheme 5.12 depicts the catalytic cycle proposed based on the results of this study. The reaction of the arylpalladium complex, *trans*-PdI(Ph)(PR₃)₂, with MeMgI leads to the formation of *trans*-PdMe(Ph)(PR₃)₂, which is thermodynamically more stable than the *cis* isomer. The *trans* complex formed does not undergo spontaneous *trans*–*cis* isomerization but undergoes ligand exchange with MeMgI to give PdMe₂(PR₃)₂ as a *cis* and *trans* mixture. Further exchange of the ligand with PhMgI in the reaction mixture leads to the formation of *cis*-PdMe(Ph)(PR₃)₂ which induces facile reductive elimination of the cross-coupling product. The



Scheme 5.12.

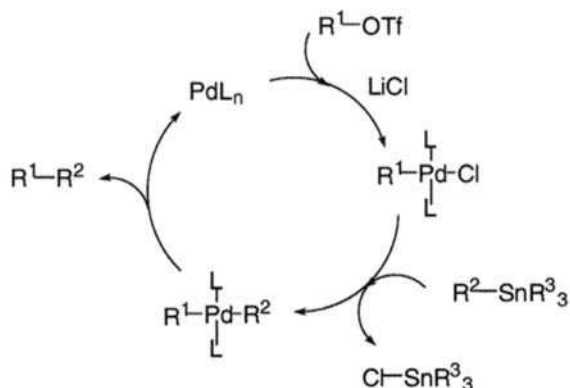
transmetalation between organomagnesium reagent and Pd complexes serves not only to transport methyl ligand from Mg to Pd but also to regulate the concentration of the trans and cis methyl(aryl)palladium intermediates in the reaction mixture and to promote selective reductive elimination of the cross-coupling product.

Pd-catalyzed coupling of aryl or alkenyl halides and triflates with organotin compounds also takes place smoothly to produce the coupling products, which was discovered by Stille and Kosugi independently and developed by a number of research groups (Eqs. 5.24 and 25) [100–103].



Allyl, aryl, alkynyl, and alkenyl ligands in organotin compounds undergo the coupling reaction much more easily than methyl or butyl ligands. A large difference in the reactivity among the ligands results in selective coupling of the unsaturated ligand in SnRBU_3 and SnRMe_3 (R = alkenyl, aryl, alkynyl, etc.) with organic triflates. The methyl and butyl groups attached to Sn act as spectator ligands during the reaction. Stille and his coworkers started mechanistic studies soon after their discovery of the reaction and proposed a catalytic cycle of the reaction, as depicted in Scheme 5.13 [104,105].

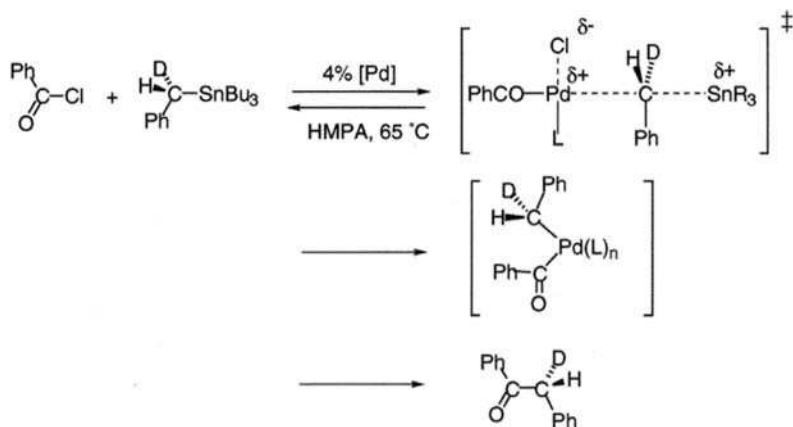
The oxidative addition of aryl or alkenyl halides to Pd(0), followed by transmetalation of organotin to Pd(II) complex, causes activation of the Sn–C bond and the formation of a new Pd–C bond. For aryl or alkenyl triflates the reaction needs often to be promoted by the addition of Cl^- , which was thought to



Scheme 5.13.

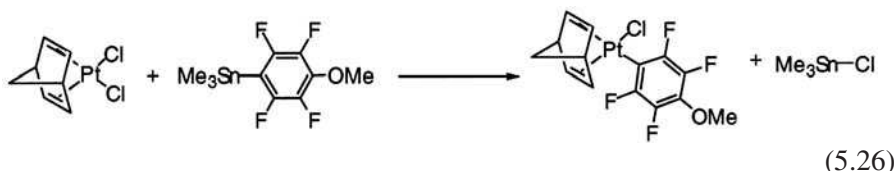
accelerate the otherwise inefficient transmetalation by coordination to the Pd(II) center of the organopalladium intermediate. The reactions of an optically active $\text{Me}_3\text{Sn}(\text{CDHPh})$ with acyl halides in the presence of a stoichiometric amount of arylpalladium halogeno complex or of a catalytic amount of the Pd complex produced the corresponding coupling product in polar solvents such as HMPA and MeCN. Detailed analyses of the reaction revealed that the transmetalation of benzylic ligand from Sn to Pd proceeds with inversion of stereochemistry. Based on the results, an associative intermediate was proposed which contains a penta-coordinated carbon analogous to the intermediate in $\text{S}_{\text{E}}2$ reactions of organic substrates (Scheme 5.14).

The reaction of organostannane with halogenoplatinum complexes was reported to form organoplatinum complex via transmetalation between Sn and Pt



Scheme 5.14.

(Eq. 5.26) [106,107].



A similar associative intermediate having a hypervalent carbon center was also proposed to account for the reaction of the Pt complex. The intramolecular transmetalation of Pd complex with a stannyl group containing organic ligand was also observed (Eq. 5.27) [108].

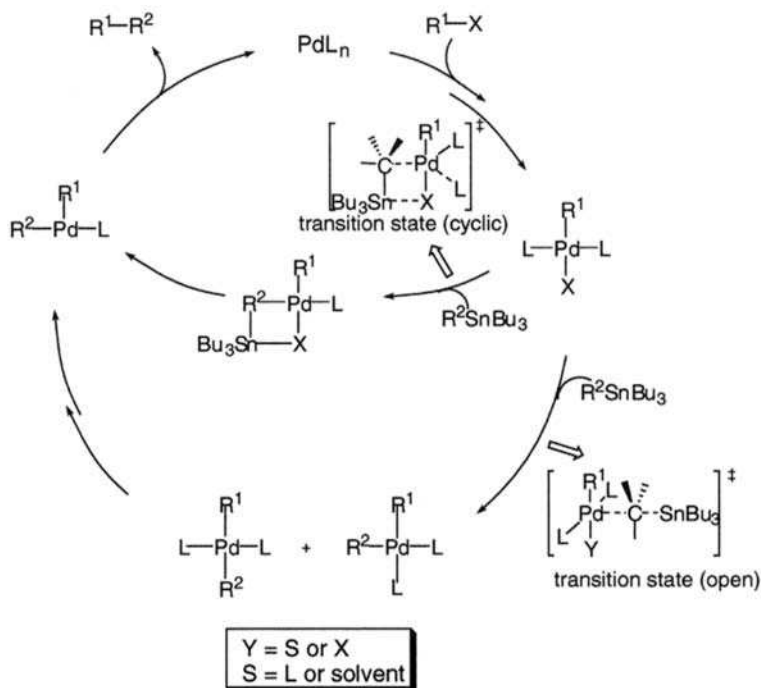


Recent comprehensive studies by Espinet et al. on the Stille reaction and related transmetalation reactions revealed the mechanistic features of transmetalation of organostannanes with Pd complexes, which is a key step in the Pd-catalyzed coupling of organic halides or triflates with organostannanes [109,110]. The reaction can follow two basically different pathways involving a cyclic or an open transition state in the transmetalation step (Scheme 5.15).

The oxidative addition of organic halides to PdL_n gives initially *cis*- $[\text{PdR}^1\text{XL}_2]$, which quickly isomerizes to *trans*- $[\text{PdR}^1\text{XL}_2]$. The oxidative addition of organic triflates to PdL_n requires addition of halide for some weaker ligands ($\text{L} = \text{AsPh}_3$) but not in other cases ($\text{L} = \text{PPh}_3$). The transmetalation rate for *trans*- $[\text{PdR}^1\text{XL}_2]$ complexes increases in the order $\text{X} = \text{I} < \text{Br} < \text{Cl} < \text{OTf}$, and $\text{L} = \text{PPh}_3 < \text{AsPh}_3$. Thus the need of adding chloride in some cases to obtain an efficient catalysis is not connected to the transmetalation step but to the oxidative addition step.

The species on which transmetalation occurs is strongly dependent on the nature of X and the solvent, and is determinant of the subsequent pathway of the reaction. In case of $\text{X} = \text{halide}$ and solvents such as chloroform, THT, or *N*-methyl-2-pyrrolidinone (NMP) the species in solution is actually *trans*- $[\text{PdR}^1\text{XL}_2]$, and the transmetalation goes via a cyclic transition state (upper cycle in Scheme 5.15), producing the associative substitution of one L by the α -carbon of the group to be transferred from the stannane. Splitting of the bimetallic complex formed completes the transfer of R^2 and produces a three-coordinate palladium complex, which undergoes very fast reductive elimination to give the coupling product.

For $\text{X} = \text{OTf}$ in NMP or hexamethylphosphoramide (HMPA), or for $\text{X} = \text{halide}$ in HMPA, the actual complex in solution is the ionic *trans*- $[\text{PdR}^1(\text{S})\text{L}_2]^+\text{X}^-$ ($\text{S} = \text{NMP, HMPA}$). Since the cationic complex lacks a good bridging ligand such as a halide, a cyclic transition state is not possible and the transmetalation goes via

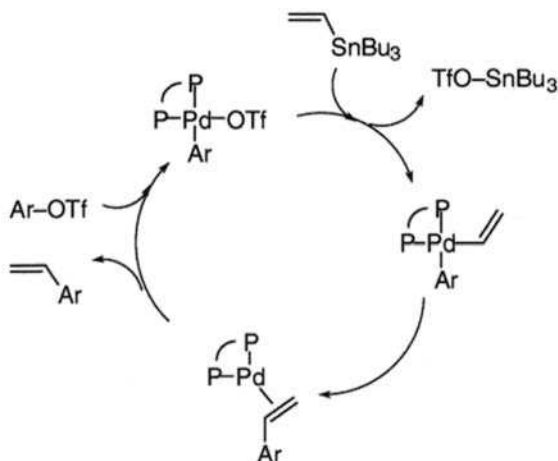


Scheme 5.15.

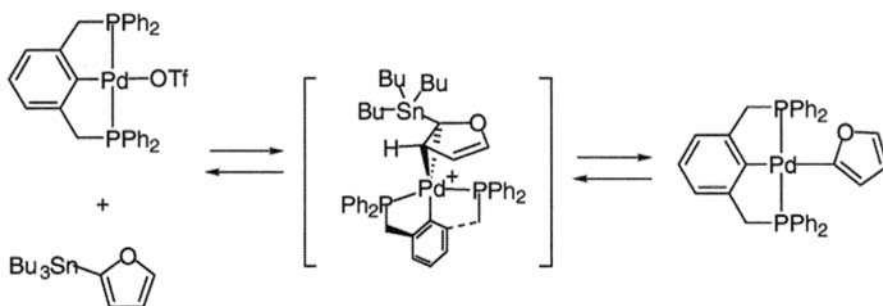
an open transition state (lower cycle in Scheme 5.15). This pathway also operates for $X = \text{OTf}$ in THF, where the solution contains *trans*-[PdR¹L₃]OTf and *trans*-[PdR¹(OTf)L₂] as an equilibrated mixture. In this pathway the transmetalation produces competitively *cis*-[PdR¹R²L₂] and *trans*-[PdR¹R²L₂]. The former complex gives the coupling product very rapidly, but the latter requires isomerization prior to coupling. The fact that one of the two pathways is taken depending on the reaction conditions including the kinds of solvent and anionic ligand has stereochemical implications at the transmetalated carbon. The stereochemical outcome of the reactions via the cyclic and open transition states corresponds to retention [111] and inversion [105], respectively.

Most of the intermediates of the reaction of [Pd(Ar)(OTf)(dppe)] (Ar = 3,5-dichlorotrifluorophenyl, dppe = 1,2-bis(diphenylphosphino)ethane) with $\text{CH}_2=\text{CHSnBu}_3$ can be observed by NMR monitoring of the reaction. The chelating ligand makes impossible the cyclic mechanism (which should require decoordination of one arm of the strong chelating ligand), and retards the coupling in [PdR¹R²(P-P)], making the observation of this intermediate possible (Scheme 5.16) [112].

A study of the reaction of furyl(tributyl)tin with a Pd-OTf complex with a pincer ligand revealed the selective cleavage of the Sn-furyl bond over the Sn-butyl bond (Scheme 5.17) [113]. Transmetalation takes place to give the furylpalladium



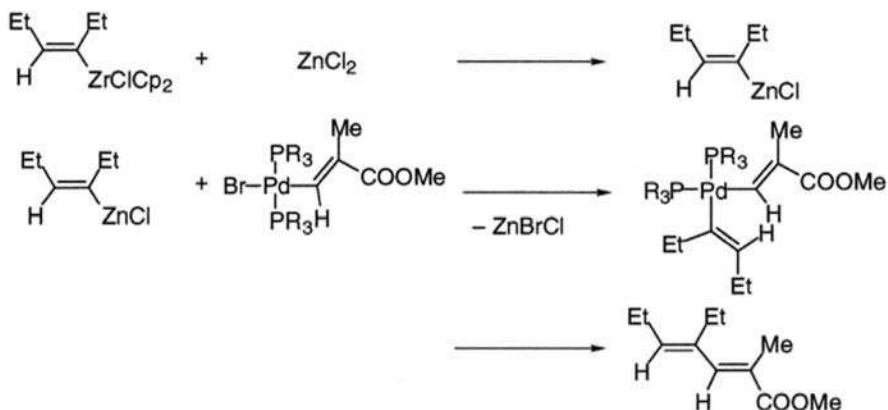
Scheme 5.16.



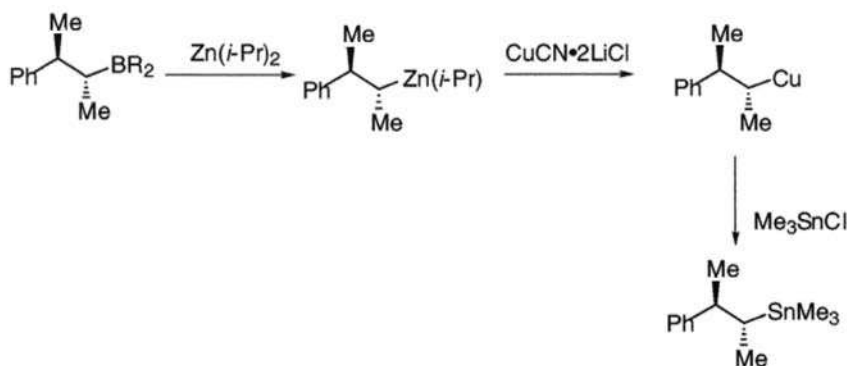
Scheme 5.17.

complex, which is preceded by the coordination of 2-tributylstannylfuran to the metal center via the tin-substituted C=C double bond. In the reaction, the electrophilic palladium center prefers to cleave the Sn-furyl bond via coordination of the C=C double bond. Transfer of the thiolato ligand of Sn-SR compound with a neutral Pd complex was also studied [114]. The arylpalladium thiolato complexes formed undergo thermally induced reductive elimination of sulfides [115]. The reactions of palladium complexes with organotin compounds caused the experimental results which indicate transfer of the methyl ligand from Sn to Pd [105,113]. Related transmetalations between alkyltransition metal complexes with main group metal compounds are mentioned in 5.2.4.

Several coupling reactions catalyzed by transition metal complexes were reported to involve multistep intermolecular transfer of organic ligand in the transmetalation procedure. The Pd complex catalyzed cross-coupling of methyl bro-



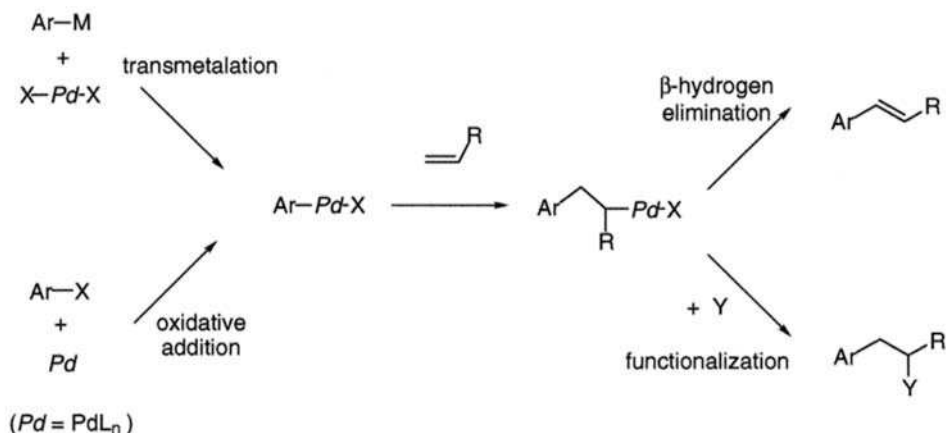
Scheme 5.18.



Scheme 5.19.

momethacrylate with an alkenylzirconium compound in the presence of ZnCl_2 provides 1,3-dienes with high stereoselectivity. Transmetalation of the vinyl ligand from Zr to Zn, and then to Pd is postulated to account for the smooth and selective cross-coupling reaction (Scheme 5.18) [116].

Alkylborane reacts with dialkylzinc and then with CuCN to cause the formation of alkylstannanes as shown in Scheme 5.19 [117]. This reaction was postulated to involve three-step intermolecular alkyl ligand transfer. Ligand exchange between the alkyl borane and diisopropylzinc gives a new alkylzinc compound. It causes alkylation of CuCN to produce an alkylcopper species. Further reaction with Me_3SnCl forms organotin compounds having the alkyl ligand derived from the starting alkyl borane. Each reaction in these multi-step transmetalations changes the reactivity of the alkyl or vinyl ligand by altering the coordinating metal centers.

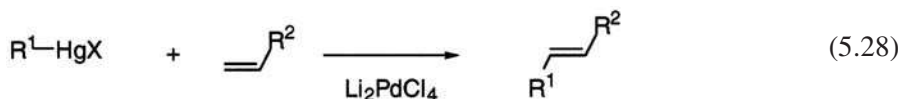


Scheme 5.20.

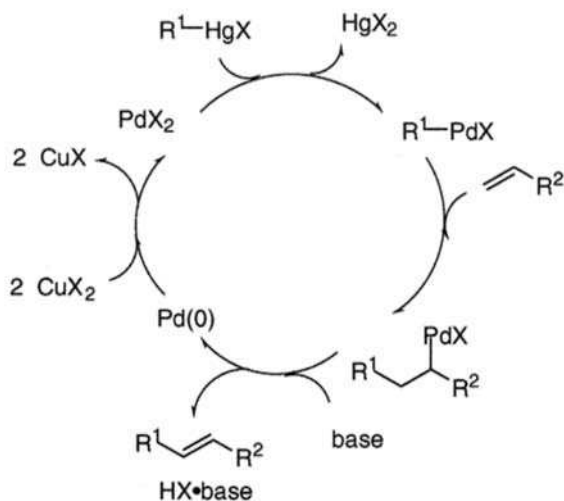
5.2.3 Relevance to carbometalation of alkenes

The 1,2-insertion of alkenes into transition metal–carbon σ -bond leads to C–C bond formation under mild conditions, as described in Chapter 6. This reaction is considered to be a crucial step in the coordination polymerization and carbometalation of alkenes catalyzed by transition metal complexes. A common and important carbometalation is the Heck-type arylation or vinylation of alkene catalyzed by Pd complexes [118]. The arylation of alkene, most typically, involves the formation of arylpalladium species and insertion of alkene into the Pd–aryl bond as shown in Scheme 5.20. The arylpalladium species is formed by the oxidative addition of aryl halides to Pd(0) complexes or the transmetalation of aryl compounds of main group metals with Pd(II) complexes. Insertion of alkene into the Pd–aryl bond produces 2-arylalkylpalladium species whose β -hydrogen elimination leads to the arylalkene. Oxidative chlorination of the 2-arylalkylpalladium intermediate forms chloroalkanes as the product.

Arylmercury(II) is a typical soft organometallic reagent whose metal–carbon bond is reactive due to the labile d^{10} metal center [119,120]. The reaction of ArHgX ($\text{X} = \text{Cl}, \text{OAc}$) with alkene catalyzed by Li_2PdCl_4 leads to the arylation of alkene (Eq. 5.28).

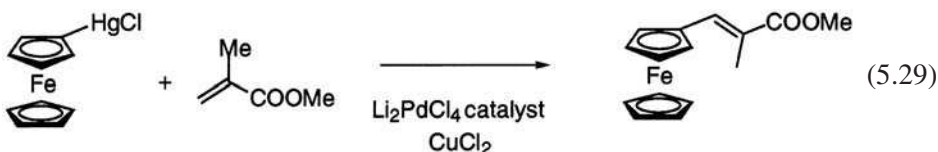


Scheme 5.21 illustrates the mechanism of the Pd-complex-catalyzed reaction of ArHgCl with the alkenes [121]. The catalysis involves aryl ligand transfer from Hg to Pd and subsequent insertion of the alkene into Pd–C bond and β -hydrogen elimination of the resultant alkylpalladium species. Elimination of HX

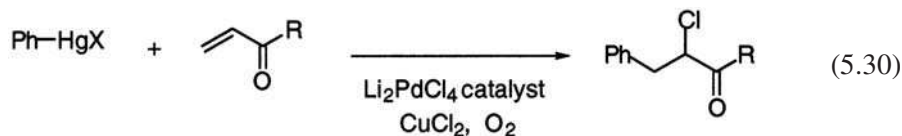


(X = halogen) from Pd(II) intermediate is enhanced by the base that is added to the reaction mixture. CuX_2 oxidizes Pd(0) to Pd(II), similarly to many other Pd-complex-catalyzed synthetic organic reactions.

This reaction is applied to a wide range of alkenes such as acrylic esters, styrene, ethylene, 1-alkene, 1,3-dienes, allyl chloride, allyl acetate, and vinyl ethers [122]. Tolerance of the arylmercury compounds to polar functional groups in the substrate renders the reaction applicable to the synthesis of many functionalized styrene derivatives. A ferrocenyl mercury compound undergoes addition to alkene via the Heck type reaction of methyl methacrylate (Eq. 5.29) [123].

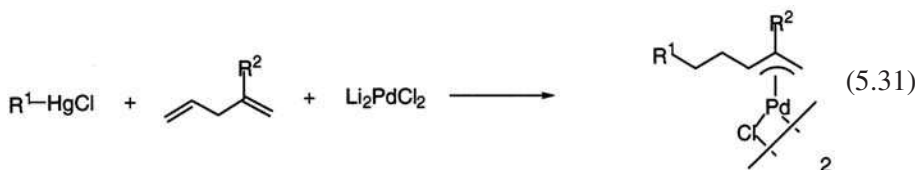


Eq. 5.30 shows the reaction of organomercury with α,β -unsaturated ketone to produce chlorinated compounds rather than β -hydrogen elimination [121].

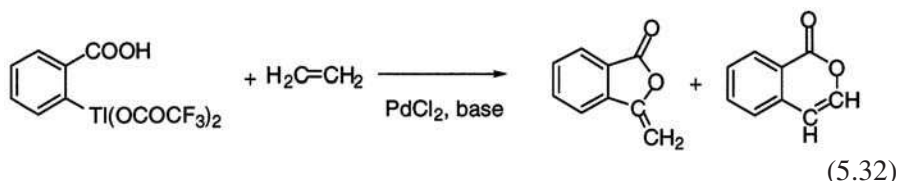


Stoichiometric arylation of dienes by ArHgCl is also known. The reaction of 1,4-diene with ArHgCl and Li_2PdCl_4 forms the isolable π -allylpalladium complex via arylation of a less sterically hindered $\text{C}=\text{C}$ double bond and migration of the

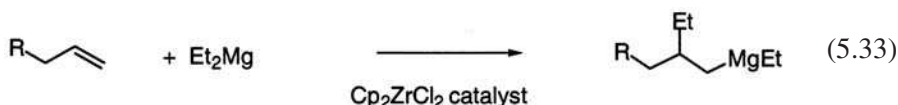
Pd center along the ligand (Eq. 5.31) [124,125].



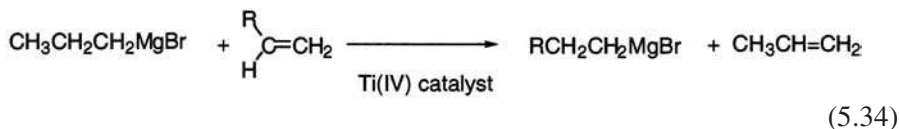
1,3- and 1,5-dienes also react under similar conditions to afford the corresponding π -allylpalladium complexes. The Pd-complex-catalyzed arylation of alkenes by using aryl compounds of other main group metals such as B, Tl, and Si were reported. The Tl version of this chemistry is applied to the synthesis of aromatic lactone from arylthallium compounds having functionalized groups such as COOH and amide groups at the ortho position (Eq. 5.32) [126,127].



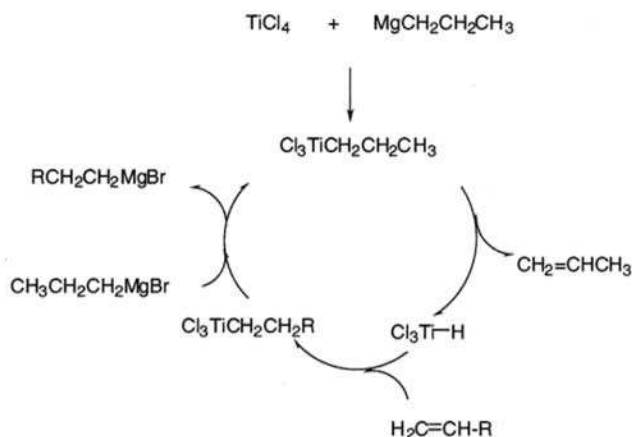
Titanocene- and zirconocene-catalyzed alkene polymerization involves initial alkyl group transfer from alkylaluminum cocatalyst to Ti or Zr centers and subsequent multiple insertion of monomer into the metal-carbon bond. Zr complex catalyzed carbomagnesation shown in Eq. 5.33 [128–136] also involves alkyl ligand transfer between the main group metal and Zr.



The reactions show high regioselectivity. Details of the mechanism are illustrated in Chapter 1, Scheme 1.32. Ti(IV) compound-catalyzed hydromagnesation of alkenes (Eq. 5.34) by using propyl Grignard reagent involves transmetalation of alkyl group between Mg and Ti compounds (Scheme 5.22) [137,138].



The catalytic cycle in Scheme 5.22 involves β -hydrogen elimination of alkyltitanium intermediate to form a hydridotitanium species that catalyzes hydromagnesation. Exchange of the alkyl group takes place rapidly between the alkylmagnesium and -titanium compounds during the reaction.



Scheme 5.22.

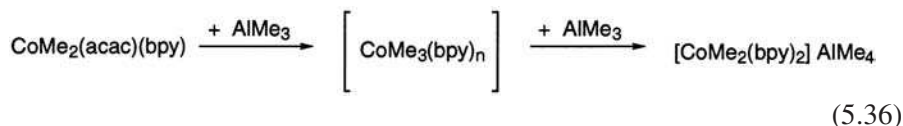
5.2.4 Organic ligand transfer from transition metals to main group element

Most of transmetalation between main group metal compounds and transition metal complexes leads to the formation of a transition metal–carbon bond. The reaction which causes alkyl or aryl ligand transfer from transition metal to main group element is much less common. Olefin polymerization catalyzed by a metallocene catalyst is sometimes accompanied by chain transfer caused by the transfer of the growing polymer end from Ti or Zr to an Al compound that is used as the cocatalyst (Scheme 5.23) [139,140].

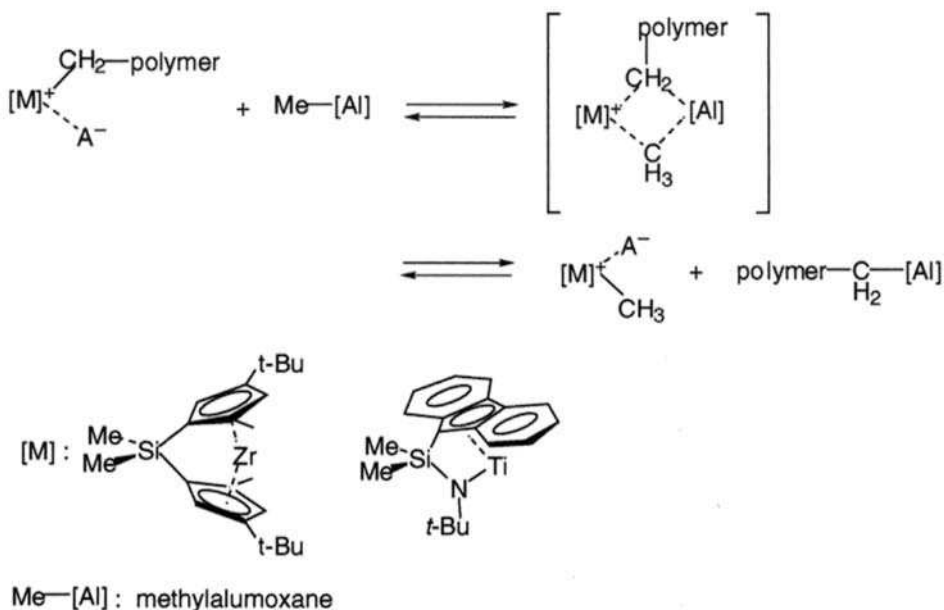
The growing alkyl polymer bonded to Ti or Zr undergoes alkyl ligand exchange with a methyl aluminum cocatalyst via a four-membered cyclic intermediate. This chain transfer to the cocatalyst is less significant to polymer growth than that by β -hydrogen elimination. An analogous organic ligand transfer from transition metal to Al center was observed in the reaction of AlCl_3 with $\text{Cp}_2\text{ZrCl(R)}$ to give alkylaluminum species which was trapped by acyl halides (Eq. 5.35) [141].



Alkylation of the Co complex by means of trimethylaluminum produces a cationic methylcobalt complex with an AlMe_4^- counter ion (Eq. 5.36) [142].



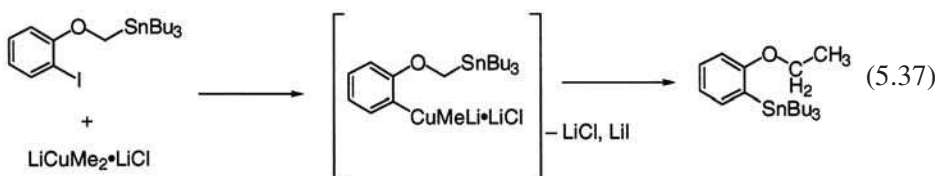
The above reaction, which involves conversion of AlMe_3 into AlMe_4^- , is attributed



Scheme 5.23.

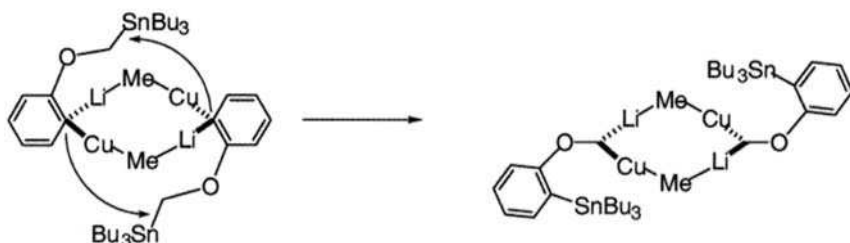
to the initial formation of neutral methylcobalt complexes, followed by methyl group transfer from Co to Al to give the product.

The organic ligand transfer from transition metal to main group metal is involved in stoichiometric and catalytic reactions shown below. A cuprate containing 2-(tributylstannyl)methoxyphenyl ligand is easily converted into 2-ethoxy-1-tributylstannylbenzene (Eq. 5.37) [143].



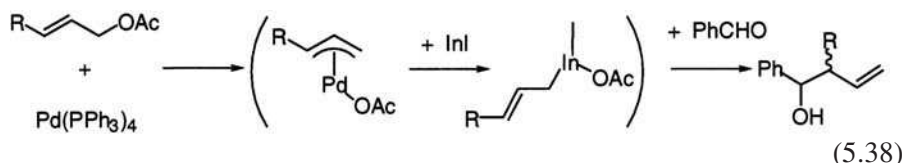
This reaction proceeds via a dinuclear intermediate, as shown in Scheme 5.24. The SnBu_3 group of the ortho substituent of the phenyl ligand is able to approach the Cu-Ph bond of another cuprate unit in the eight-membered cyclic dimer structure. Alkyl and phenyl ligand exchange between Sn and Cu centers in both cuprates leads to the introduction of a phenyl group to the Sn center.

The reactions of allylic compounds with aldehydes catalyzed by the Pd complex in the presence of main group metal compounds lead to allylation of the



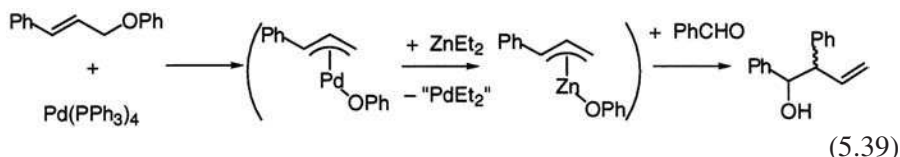
Scheme 5.24.

aldehydes, as shown in Eq. 5.38 [144].

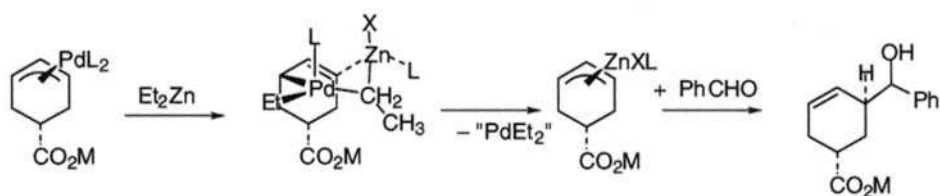


The π -allyl ligand bonded to Pd(II) usually acts as an electrophile and does not react with aldehyde directly. The transmetalation of the allyl ligand from Pd to In produces an allylindium intermediate that is responsible for the C–C bond forming reaction.

In the reaction using ZnEt_2 , exchange of the allyl and ethyl ligands occurs between Pd and Zn, affording π -allylzinc and ethylpalladium intermediates. The former compound reacts with aldehyde to induce its allylation, while the latter is converted into a Pd(0) complex via β -hydrogen elimination of the ethyl ligand (Eq. 5.39) [145,146].

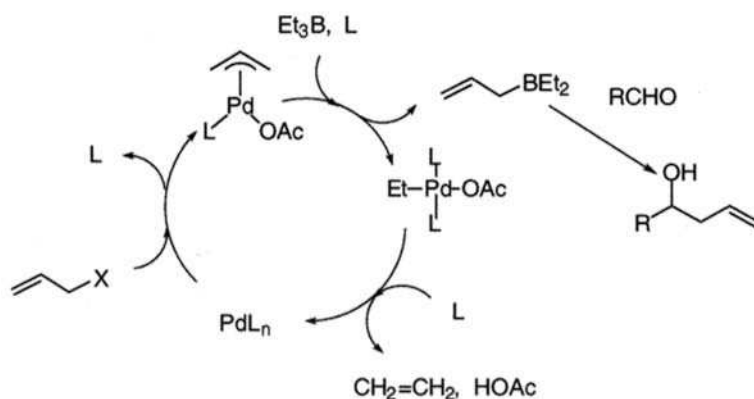


Scheme 5.25 shows the mechanism of the transmetalation proposed based on the stereochemical outcome of the allylation reaction. Ethyl ligand transfer from Zn to Pd takes place via an intermediate with a bridging ethyl ligand. This intermediate leads to the coordination of π -allylic ligand by Zn on the same side of the Pd center. The rearrangement of the π -allyl ligand bonded to Pd to σ -allyl is coupled with the ligation of the allyl group to the Zn center. Although the liberation of the diethylpalladium species by transmetalation was proposed in Scheme 5.25, the actual Pd-containing product was not identified. Analogous allyl and ethyl ligand exchange between Pd and B was proposed in the 1,2-addition of allylic ether to aldehyde in the presence of Pd(0) complex and BEt_3 (Scheme 5.26) [147,148].



$\text{X} = \text{OR}$ or OCOC_6H_7
 (The original report did not mention the kind of X in detail)

Scheme 5.25.



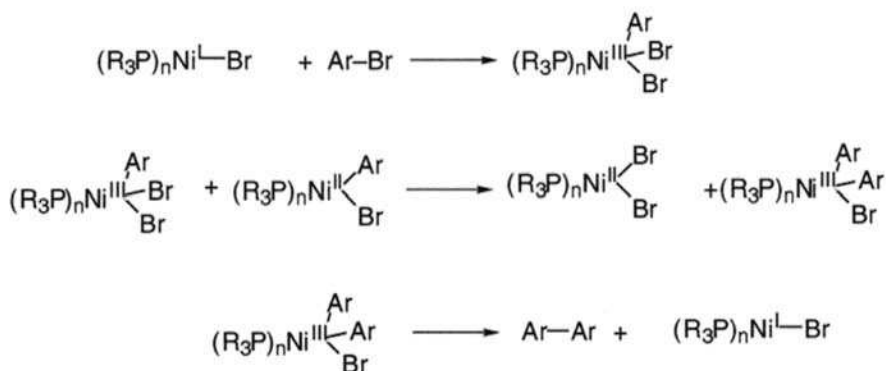
Scheme 5.26.

These reactions enabled addition of the allylic electrophiles to the carbonyl group of aldehydes via oxidative addition of the allylic compounds to $\text{Pd}(0)$ and transfer of the allyl group from $\text{Pd}(\text{II})$ to main group elements.

5.3 ORGANIC LIGAND TRANSFER BETWEEN TRANSITION METALS

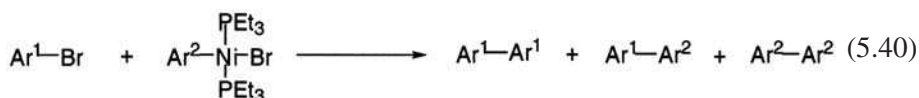
5.3.1 Intermolecular aryl ligand transfer

Studies of intermolecular aryl ligand transfer of nickel complexes [149] started almost at the same time as the first preparation of the arylnickel complexes because they were regarded to be involved in Ni complex promoted intermolecular coupling of aryl halides to give biaryls. Kochi reported the reaction of bromoarene with $\text{NiBr}(\text{Ar})(\text{PEt}_3)_2$ at elevated temperature in THF to produce biaryl as the



Scheme 5.27.

coupling product via intermolecular aryl ligand transfer (Eq. 5.40).

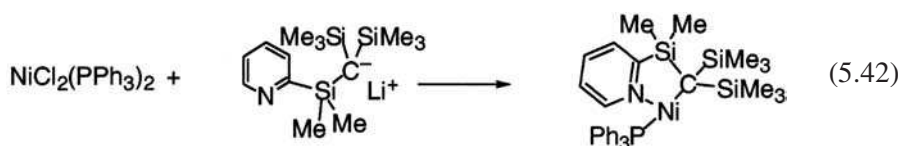


The reaction of bromoarene with the arylnickel complex with a different aryl group gives three possible biaryls, indicating rapid scrambling of the aryl groups between bromoarene and Ni complexes during the reaction. They proposed a unique mechanism involving Ni(I) and Ni(III) intermediates based on results of the detailed kinetic studies, cross-over experiments, and detection of the paramagnetic intermediates (Scheme 5.27) [150]. The Ni(I) complex formed in the reaction mixture undergoes oxidative addition of bromoarene to produce $\text{NiBr}_2(\text{Ar})(\text{PEt}_3)_n$. The dibromoarylnickel(III) complex undergoes intermolecular ligand exchange with $\text{NiBr}(\text{Ar})(\text{PEt}_3)_2$ giving the bromodiarlylnickel(III) complex, $\text{NiBr}(\text{Ar})_2(\text{PEt}_3)_n$, which is responsible for the reductive elimination of biaryl. Small amounts of Ni(I) and Ni(III) intermediates formed in the reaction mixture trigger the coupling reaction which involves the aryl ligand transfer of the intermediate Ni complexes. Electron transfer between bromoarene and the nickel(II) complex probably causes initial formation of Ni(III) species, which is proposed based on results of the reactions of organic halides with transition metal complexes giving the metal-containing radicals [151].

Monoarylnickel(III) complexes were obtained from the reaction of NBS (*N*-bromosuccinic imide) with arylnickel(II) complex (Eq. 5.41) or its electrochemical oxidation [152,153].



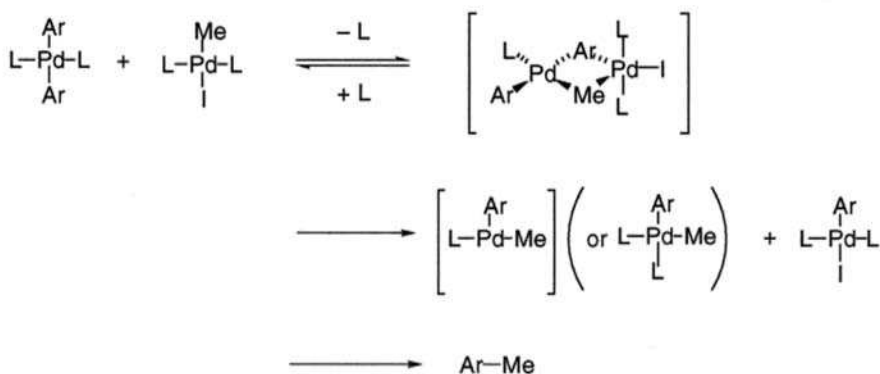
Although the above reaction pathway involves arynickel(I) intermediates also, the isolated Ni(I) complexes having Ni–C σ -bond are quite rare. $\text{NiCl}_2(\text{PPh}_3)_2$ reacts with a bulky alkyl lithium, $\text{C}_5\text{H}_4\text{N}-\text{SiMe}_2-\text{C}(\text{SiMe}_3)_2\text{Li}$, to afford $\text{Ni}(\text{C}(\text{SiMe}_3)_2-\text{SiMe}_2-\text{C}_5\text{H}_4\text{N})(\text{PPh}_3)$ (Eq. 5.42) [154].



The complex exhibits unique properties originating from the Ni(I) center, such as a T-shaped three coordination structure, longer Ni–N (2.007(3) Å) and Ni–C (2.205(3) Å) bonds than those of organonickel(II) complexes, and paramagnetism confirmed by ESR measurement.

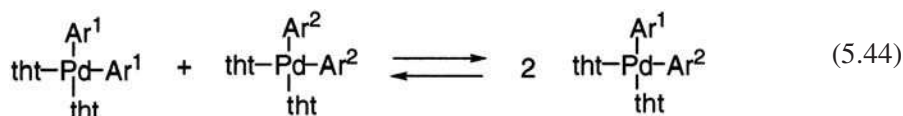
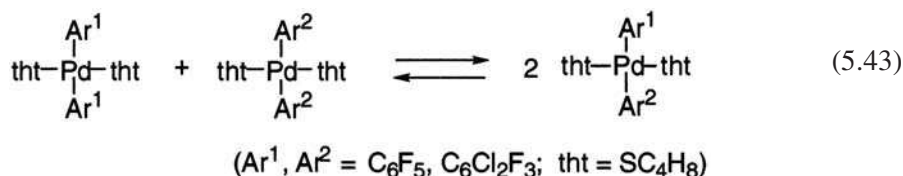
Arylpalladium(II) complexes were reported to undergo intermolecular exchange of the aryl ligands without oxidation or reduction of the metal centers. Ozawa reported thermal reaction of a mixture of *trans*- $\text{PdAr}_2(\text{PEt}_2\text{Ph})_2$ and *trans*- $\text{PdI}(\text{Me})(\text{PEt}_2\text{Ph})_2$ to liberate Ar–Me and proposed the bimolecular mechanism shown in Scheme 5.28 to account for kinetic results of the reaction [155]. The two different organopalladium complexes undergo exchange of the aryl and methyl ligands via a dinuclear intermediate with bridging ligands. The resultant methyl(aryl)palladium complex undergoes reductive elimination of the product. This intermolecular exchange of organic ligands is triggered by dissociation of a phosphine ligand of the diarylpalladium(II) complex. It forms the three-coordinated Pd intermediate, which is readily trapped by the tetracoordinated iodo(methyl)palladium complex to give a dinuclear intermediate having two bridging organic ligands.

Pd(II) complexes with perhalogenated aryl ligands, $\text{C}_6\text{F}_2\text{Cl}_3$ and C_6F_5 , have stable Pd–C bonds and do not cause coupling reactions even when the two

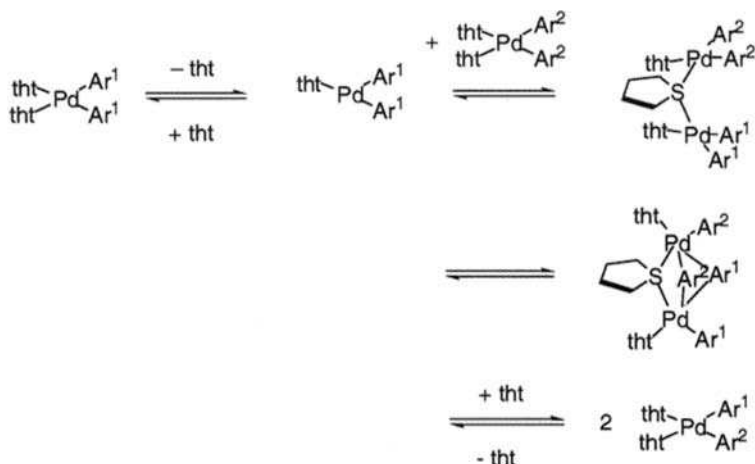


Scheme 5.28.

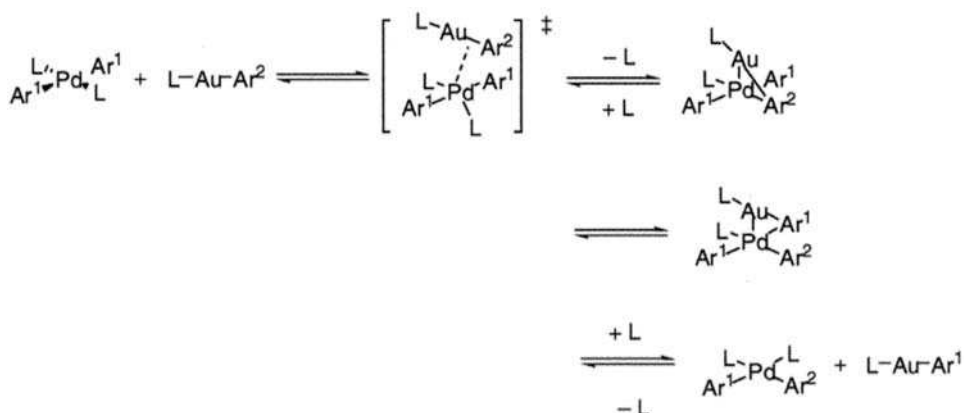
aryl ligands are bonded at cis positions. Espinet investigated details of intermolecular migration of the ligands by using a combination of the aryl ligands and auxiliary tetrahydrothiophene (tht) or SMe_2 ligands that coordinate to Pd weakly and leave the metal center easily [156]. An equimolar mixture of $\text{trans-Pd}(\text{C}_6\text{Cl}_2\text{F}_3)_2(\text{tht})_2$ and $\text{trans-Pd}(\text{C}_6\text{F}_5)_2(\text{tht})_2$ causes their partial conversion into $\text{trans-Pd}(\text{C}_6\text{Cl}_2\text{F}_3)(\text{C}_6\text{F}_5)(\text{tht})_2$ to give a mixture of these three complexes in a statistical molar ratio (Eq. 5.43). Analogous conproportionation type reaction of a mixture of $\text{cis-Pd}(\text{C}_6\text{Cl}_2\text{F}_3)_2(\text{tht})_2$ and $\text{cis-Pd}(\text{C}_6\text{F}_5)_2(\text{tht})_2$ affords $\text{cis-Pd}(\text{C}_6\text{Cl}_2\text{F}_3)(\text{C}_6\text{F}_5)(\text{tht})_2$ (Eq. 5.44).



Both reactions are reversible and do not occur for diarylpalladium complexes with the ligands unsuited to make bridges, such as PPh_3 or py. The mechanism involving a dinuclear intermediate accounts for results of the above reactions (Scheme 5.29). A T shaped complex $\text{Pd}(\text{Ar}^1)_2(\text{tht})$, formed via dissociation of a tht ligand, is quickly captured by $\text{Pd}(\text{Ar}^2)_2(\text{tht})_2$ giving the dinuclear intermediate with a bridging tht ligand. Aryl ligand exchange between the two Pd centers leads to the conproportionation, giving the mononuclear product with different



Scheme 5.29.

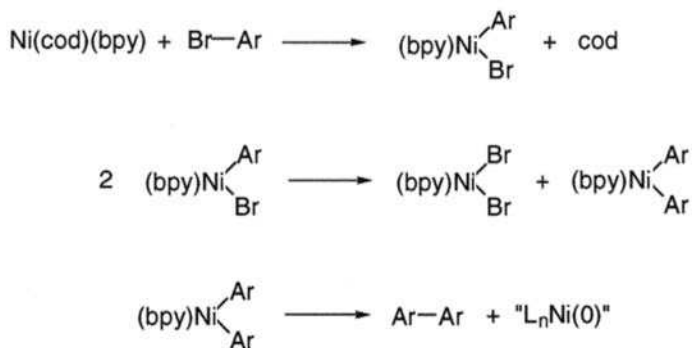


Scheme 5.30.

aryl ligands at the Pd center. Cis–trans isomerization of the above diarylpalladium complexes is much slower than the intermolecular aryl ligand transfer. Retention of the coordination geometry of the complexes throughout the reaction is consistent with the above mechanism in which the bridging coordination of the intermediate is kept during the transmetalation.

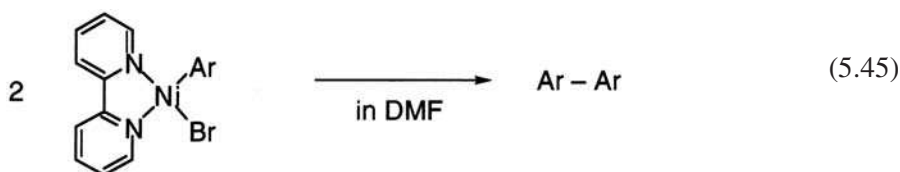
Addition of a catalytic amount of arylgold(I) complex, $\text{AuAr}(\text{tht})$, to the Pd complexes causes more rapid intermolecular aryl ligand transfer accompanied by cis–trans isomerization [157]. This reaction takes place by reversible aryl ligand transfer between Au(I) and Pd(II) (Scheme 5.30), which is much faster than the aryl ligand transfer between Pd(II) complexes. An associative intermediate having Au–Pd bond was proposed based on kinetic results of the reaction. The structure of the intermediate is similar to a hydrido bridged heterobimetallic complex, $[(\text{PEt}_3)_2(\text{C}_6\text{F}_5)\text{Pt}(\mu\text{-H})\text{Au}(\text{PPh}_3)]^+$, with a metal–metal bond [158]. Formation of the intermediate occurs directly from the reaction of four-coordinated Pd(II) complex with two-coordinated Au(I) complex rather than the reaction of a three-coordinated Pd(II) complex. Switching of the Au–Ar bond takes place very easily in the dinuclear intermediate to cause the total aryl ligand exchange between Pd and Au.

Several monoaryl complexes of group 10 metals formulated as $\text{MX}(\text{Ar})(\text{L})_2$ or $[\text{MAr}(\text{solv})(\text{L})_2]^+$ (X = anionic ligand, L = neutral ligand, solv = solvent) undergo disproportionation type aryl ligand transfer. Heating of $\text{PtMe}(\text{OCOCF}_3)(\text{dmpe})$ (dmpe = 1,2-bis(dimethylphosphino)ethane) in benzene or aromatic solvents causes activation of an aromatic C–H bond to produce arylplatinum complex $\text{PtAr}(\text{OCOCF}_3)(\text{dmpe})$ which undergoes disproportionation, giving $\text{PtAr}_2(\text{dmpe})$ and $\text{Pt}(\text{OCOCF}_3)_2(\text{dmpe})$. The reaction using pentafluorobenzene leads to smooth aryl ligand transfer and subsequent disproportionation, giving a mixture of the di- and mono-arylplatinum complexes and bis(trifluoroacetate)platinum complex in a statistical 1 : 2 : 1 molar ratio (Scheme 5.31) [159].



Scheme 5.33.

Neutral arylnickel(II) complexes, NiBr(Ar)(bpy) ($\text{Ar} = \text{Ph}, \text{C}_6\text{H}_4\text{Me}, \text{C}_6\text{H}_4\text{OMe}, \text{etc.}$), form biaryls when they are dissolved in DMF at room temperature [161,162] (Eq 5.45).



The reaction mechanism, which is different from that in Scheme 5.27, was proposed from results of the kinetic study of the reaction. The reaction of bromoarene with NiBr(Ar)(bpy) , generated in situ from oxidative addition of bromoarene to Ni(cod)_2 ($\text{cod} = 1,5\text{-cyclooctadiene}$) in the presence of bpy , forms biaryl in DMF. Rate of the reaction obeys second-order kinetics in the Ni complex and is influenced by concentration of bromoarene to a minor extent. Scheme 5.33 depicts a plausible pathway of the reaction.

The bromoarylnickel(II) complex undergoes disproportionation to give dibromo- and diarylnickel complexes. The latter complex undergoes facile coupling of two aryl ligands because reductive elimination of the two aryl ligands at cis coordination sites takes place very easily [163,164]. The rate-determining step of the total coupling reaction in DMF resides in the disproportionation. A calorimetric study showed that dihalogenonickel(II) complex with bipyridine ligands, in DMF, undergoes dissociation of the halogeno ligand and exists as the cationic species in the solvent [165]. Bromo(aryl)nickel complex is also considered to dissociate the bromo ligand easily in DMF to generate a cationic complex, $[\text{Ni(Ar)(DMF)(bpy)}]^+\text{Br}^-$. The reaction of bromoarene with NiBr(Ar)(bpy) in THF does not give any coupling products at room temperature, and forms biaryl, at the elevated temperature, which proceeds via Ni(I) and Ni(III) intermediates. Consequently, NiBr(Ar)(bpy) undergoes coupling reaction of the aryl groups via two distinct pathways depending on the solvent used; one path involves dispro-

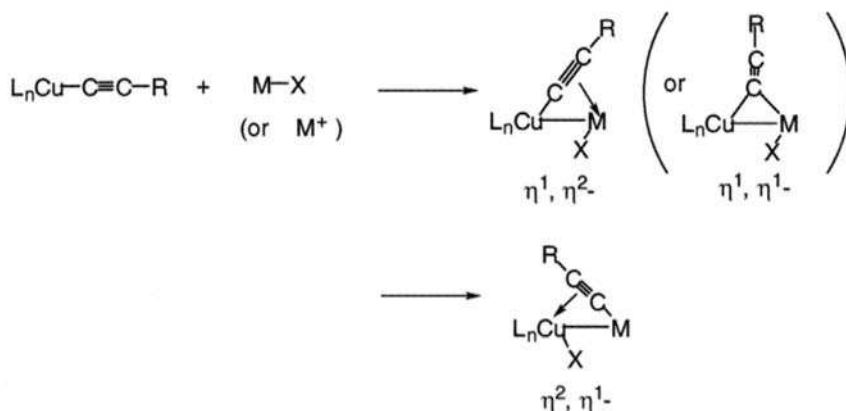
portionation of the monoarylnickel species followed by reductive elimination of biaryl from diarylnickel(II), and the other involves formation of Ni(I) and Ni(III) species, and coupling of two aryl ligands of diarylnickel(III) intermediate. Dehalogenative condensation of haloarene by Ni(0) complexes in polar solvents such as DMF and MeCN is well-known as a preparation method of biaryl [166–170]. These reactions were conducted under various conditions and with various additives and ligands, whose mechanisms differ from each other depending on these parameters of the reactions.

5.3.2 Intermolecular alkynyl ligand transfer

Intermolecular alkynyl ligand transfer of transition metal complexes is more common than the aryl and alkyl ligand transfer. Alkynyl compounds of Cu(I) and Hg(II) transport the ligand to other transition metals, giving various alkynyl transition metal complexes. $[\text{Cu}(\text{C}\equiv\text{CR})]_n$ [171], isolated or generated in situ from the reaction of alkyne, CuI, and base, was employed in preparation of a number of alkynyl complexes of group 5–10 transition metals. The alkynyl ligand transfer is depicted schematically in Eq. 5.46 [172–175].



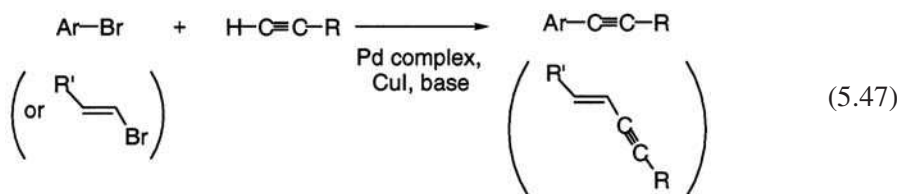
The reaction of halogeno transition metal complexes with $[\text{Cu}(\text{C}\equiv\text{CR})]_n$ produces heterobimetallic complexes that have a bridging alkynyl ligand bonded to Cu in η^2 -fashion and to the other transition metal in η^1 -fashion (Scheme 5.34) [176–178]. The structure of the products suggests initial coordination of alkynyl ligand to transition metal to form the intermediate dinuclear complex with a η^1, η^2 - or η^1, η^1 -coordinated alkynyl ligand. It is soon transformed into the product



Scheme 5.34.

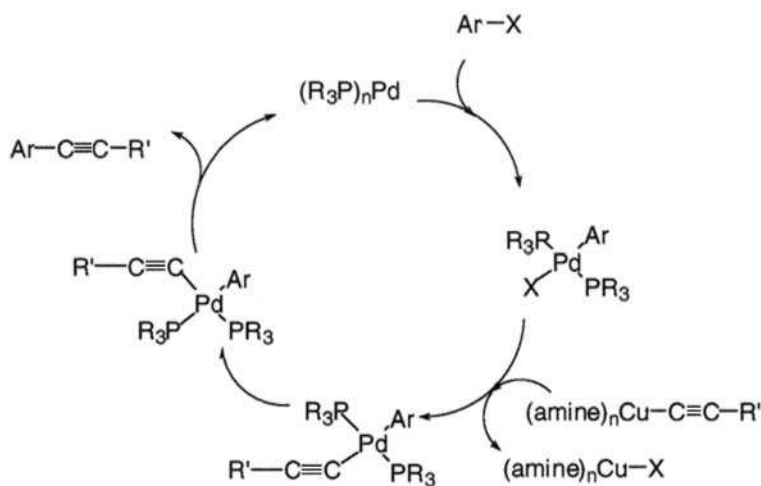
having a η^2, η^1 -bond via switching of the coordination bond. Elimination of halogenocopper from this dinuclear compounds leads to alkynyl complexes of the transition metals.

Among such reactions, the alkynyl ligand transfer from Cu to group 10 metals is of greater interest in relevance to synthetic organic reactions promoted by these metal complexes. Pd complex catalyzed cross-coupling of haloarene or haloalkene with terminal alkyne in the presence of Cu(I), found by Sonogashira, Takahashi, and Hagihara, provides an efficient tool to prepare arylacetylenes and enynes (Eq. 5.47) [179–181].



The C(sp)–C(sp²) bond forming reactions have only a few alternative methods for a quarter century since its discovery. The mechanism proposed for the selective cross-coupling is shown in Scheme 5.35.

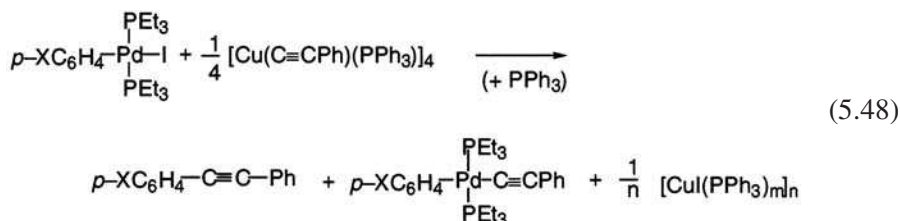
Oxidative addition of aryl (or vinyl) halide to Pd(0) precursor forms the monoarylpalladium complex that is the common intermediate in the catalytic cross-coupling reactions of haloarene with organometallic compounds of main group elements such as Mg, Si, and Sn. Alkynylcopper, formed from alkyne, Cu(I) salt and base in the reaction mixture, transfers the ligand to the above Pd complex, giving an intermediate complex with aryl (or vinyl) and alkynyl ligands bonded to Pd. Reductive elimination of arylacetylene (or enyne) occurs



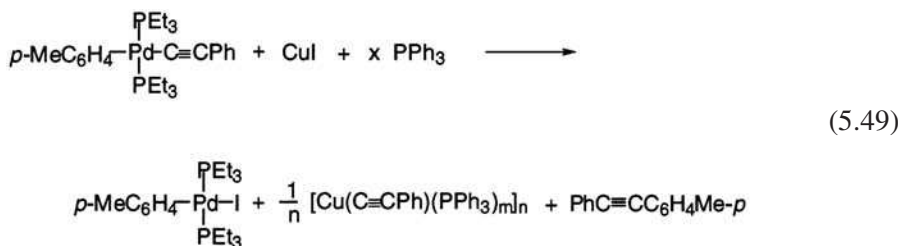
Scheme 5.35.

from the intermediate Pd complex containing the two organic ligands at *cis* positions.

Aryl(alkynyl)palladium complexes have not been studied until recently. *cis*-Pd(C₆F₅)(C≡CR)(L)₂ (L = chelating diphosphine), prepared from the reaction of bromo(aryl)palladium complex with silver acetylide, does not undergo coupling of the aryl and alkynyl ligands at *cis* positions due to too stable Pd–aryl bond [182]. *Trans*-PdI(Ar)(PEt₃)₂ reacts with the phenylethynyl copper complex [Cu(C≡CPh)(PPh₃)₄] to cause transmetalation of the alkynyl ligand and/or subsequent reductive elimination of arylalkyne (Eq. 5.48) [183].



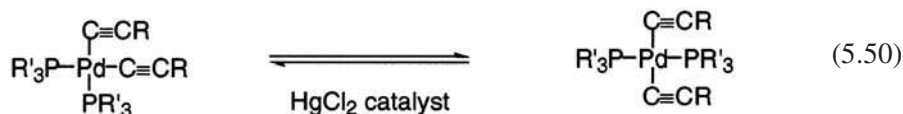
The reaction of aryl(alkynyl)palladium complex with CuI in the presence or absence of PPh₃ ligand causes formation of alkynylcopper and aryl(iodo)palladium complexes via transmetalation of the alkynyl ligand from Pd to Cu (Eq. 5.49).



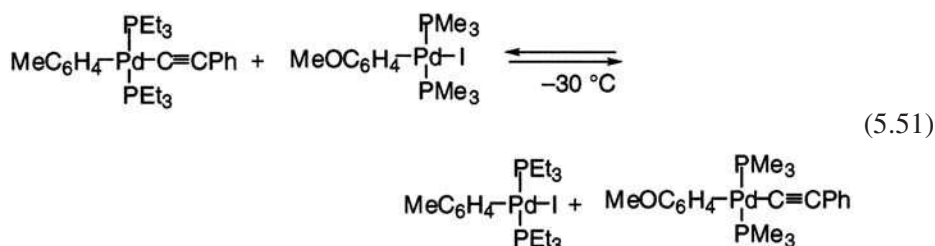
The relative ratios of the alkynylcopper and aryl(alkynyl)palladium complexes in equilibration vary depending on the amount of added PPh₃. The presence of excess added PPh₃ tends to destabilize alkynylcopper species (or stabilize iodocopper species) and shifts the equilibrium of the transmetalation to formation of Cu–I bond *via* transmetalation of the alkynyl ligand from Cu(I) to Pd(II) [184]. The alkynyl ligand transfer between Cu and Pd complexes is associated with coupling of the aryl and phenylethynyl groups to give ArC≡CPh. Although *trans*-PdAr(C≡CPh)(PEt₃)₂ does not give the coupling product spontaneously, addition of CuI causes coupling of the ligands under mild conditions. CuI seems to induce *trans*–*cis* isomerization of the Pd complex via rapid and reversible transmetalation of the alkynyl ligands between Pd and Cu or via PEt₃ transfer from Pd to Cu giving isomerizable three-coordinate Pd intermediate.

Isomerization of *cis*- to *trans*-Pt(C≡CPh)₂(PR₃)₂ promoted by CuI or HgCl₂ was reported to take place via reversible alkynyl transfer between the metal centers

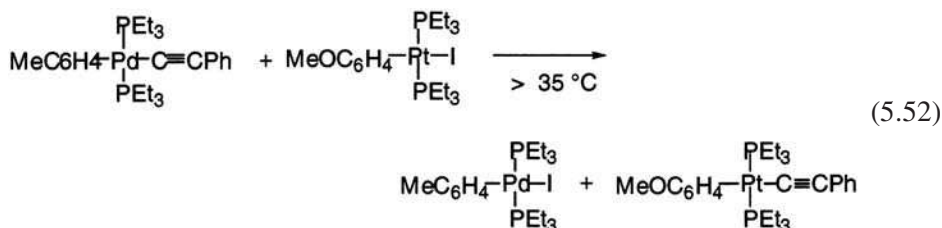
(Eq. 5.50) [185–187].



The alkynyl and iodo ligands of the aryl(iodo)palladium and aryl(alkynyl)-palladium complexes undergo mutual exchange at -30°C (Eq. 5.51) [183].



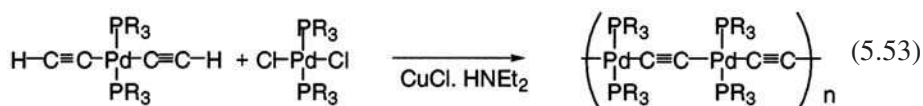
Exchange reactions of aryl and iodo ligands and of aryl and alkynyl ligands are not observed at all. Analogous alkynyl ligand transfer from aryl(alkynyl)palladium complexes to aryl(iodo)platinum complexes shown in Eq. 5.52 occurs above 35°C to cause complete alkynyl group transfer from Pd to Pt [183].



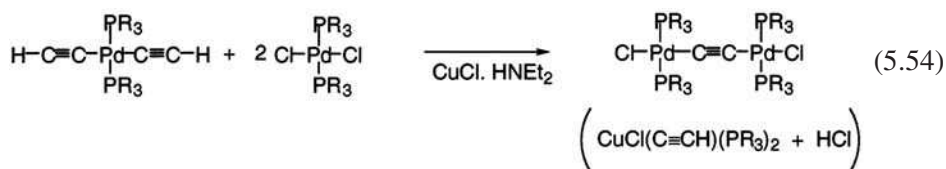
Kinetic results of the reaction suggest the associative pathway having a transition state containing bridging alkynyl ligand bonded to Pd and Pt centers. The reaction with addition of CuI proceeds much more rapidly via a stepwise transmetalation, including alkynyl ligand transfer from Pd to Cu and then Cu to Pt. Although the equilibrium between alkynylpalladium and alkynylcopper is significantly favored to the former complex, a rapid interconversion between these complexes contributes to transportation of the alkynyl ligand from Pd to Pt via alkynylcopper intermediate, which is faster than the direct alkynyl ligand transfer from Pd to Pt.

Alkynyl ligand transfer from Cu to group 10 metals is applied to synthesis of metal containing polyynes. An equimolar reaction of bis(ethynyl)palladium complex and dihalogenopalladium complex in the presence of base and CuI causes condensation to give the polymer having ethynediyl and Pd in an

alternating fashion (Eq. 5.53) [188–191].

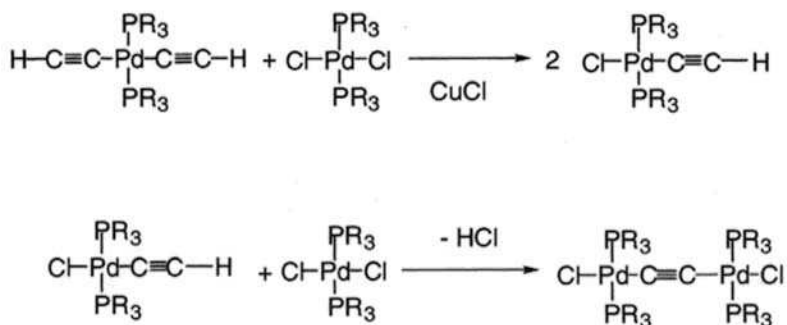


The reaction is employed to synthesize various organometallic polymers such as Pt containing polymers, polymers containing aryleneethynylene units, and metaladendrimer or hyperbranched polymers [188–193]. The initial product of the condensation of *trans*-Pd(C≡CH)₂(PR₃)₂ and *trans*-PdCl₂(PR₃)₂ in the presence of CuI and amines is a dinuclear Pd complex with a μ -ethynediyl ligand, Cl–Pd(PR₃)₂–C≡C–PdCl(PR₃)₂ (Eq. 5.54) [194,195].



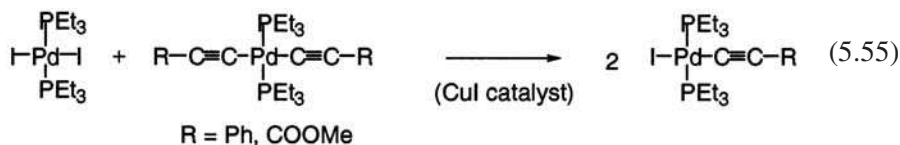
The reaction requires intermolecular exchange of the ethynyl and chloro ligands. Scheme 5.36 illustrates one of the possible mechanisms leading to the dimer complex. The pathway involves the initial conproportionation of the two starting complexes to afford *trans*-PdCl(C≡CH)(PR₃)₂ which reacts further with *trans*-PdCl₂(PR₃)₂ to afford the dinuclear product. Smooth polycondensation involving this intermediate indicates that the reaction proceeds via combination of condensation of monomer and oligomers and conproportionation type intermolecular alkynyl ligand transfer among them.

Equimolar reactions of *trans*-Pd(C≡CPh)₂(PEt₃)₂ with *trans*-PdI₂(PEt₃)₂ and of *trans*-Pd(C≡CCOOMe)₂(PEt₃)₂ with *trans*-PdI₂(PEt₃)₂ in the presence of CuI catalyst give the alkynyl ligand transfer reaction product *trans*-PdI(C≡CPh)(PEt₃)₂ or *trans*-PdI(C≡CCOOMe)(PEt₃)₂, respectively, in high

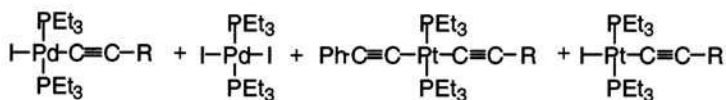
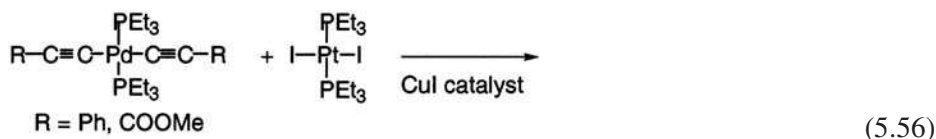


Scheme 5.36.

yields (Eq.5.55) [196].



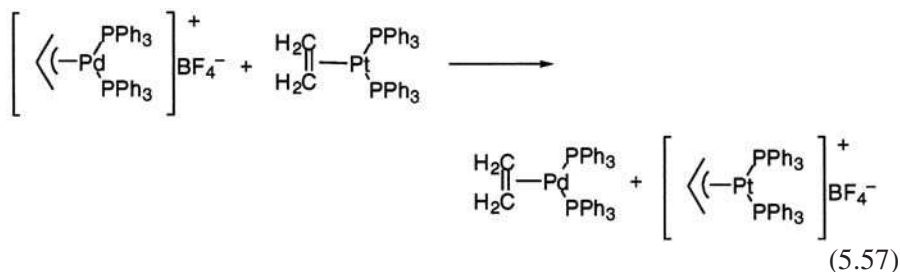
This conproportionation of dialkynylpalladium and diiodopalladium complexes, giving the complex with iodo and alkynyl ligands, appears to be thermodynamically favored due to higher stability of the product, *trans*-PdI(C≡CR)(PEt₃)₂, than the two starting complexes. The reaction without addition of CuI proceeds much more slowly than the above reactions and does not attain the equilibrium in a short period. Analogous intermolecular transfer of the alkynyl ligands between Pd and Pt complexes is also observed to form a mixture of several possible complexes as shown in Eq. 5.56.

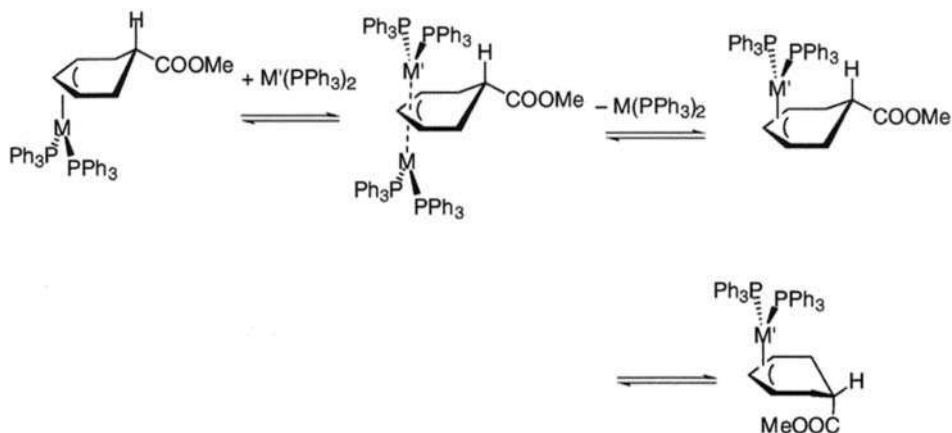


Trans-PdI(C≡CR)(PEt₃)₂ shows the highest stability among the Pd and Pt complexes with iodo and/or alkynyl ligands.

5.3.3 Intermolecular allyl, propargyl, and allenyl ligand transfer

Transmetalation of π -allyl transition metal complexes and of the complexes with related C3 ligands proceeds via unique pathways that are not found in the intermolecular transfer of η^1 -bonded organic ligands. Rich information about stereochemistry of unsymmetrically substituted π -allyl ligands of Pd complexes provides a useful probe to investigate details of the reaction mechanism. Cationic π -allylpalladium(II) complex reacts with ethylene-coordinated Pt(0) complex to afford the π -allylplatinum(II) complex and Pd(0) complex via transfer of the allyl ligand from Pd to Pt (Eq. 5.57).

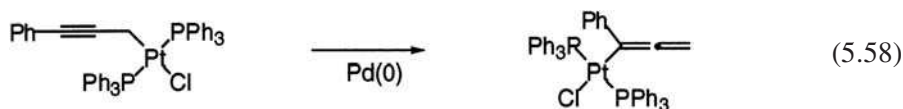




Scheme 5.37.

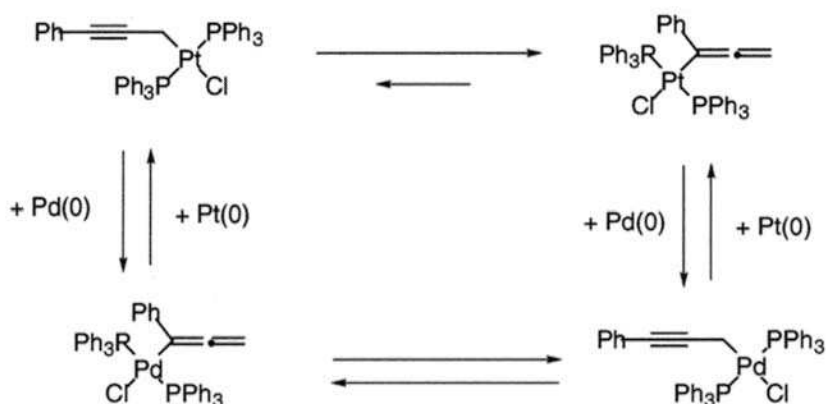
Transmetalation of neutral π -allylpalladium(II) complex, $\text{Pd}(\eta^3\text{-CH}_2\text{CMeCH}_2)\text{-Cl}(\text{PPh}_3)_2$, with $\text{Pt}(0)$ complex also occurs but at a slower reaction rate. The reactions are classified as the redox type in Scheme 5.1. The reaction of $\text{Pd}(\text{II})$ complex with six-membered cyclic π -allyl ligand having a COOMe group with $\text{Pt}(\text{C}_2\text{H}_4)(\text{PPh}_3)_2$ results in allyl ligand transfer to produce the cationic π -allylplatinum complex with the inversion stereochemistry [197–199]. Scheme 5.37 illustrates the mechanism to account for the smooth inversion transmetalation.

The π -allyl ligand bonded to cationic $\text{Pd}(\text{II})$ center tends to undergo nucleophilic substitution by organic nucleophiles from the opposite side of the metal center (Chapter 8). Attack of $\text{Pd}(0)$ or $\text{Pt}(0)$ complex in this fashion causes inversion of stereochemistry of the complex; repetition of the reactions results in epimerization. The allyl ligand transfer between Pd centers takes place much faster than that from Pd to Pt . Isomerization between the $\text{Pt}(\text{II})$ complexes with a propargyl ligand and that with an allenyl ligand is catalyzed by $\text{Pd}(0)$ complex (Eq. 5.58) [200,201].



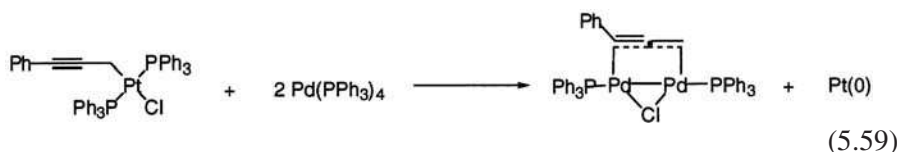
This reaction proceeds via the transmetalation of the ligand between the Pd and Pt complexes as shown in Scheme 5.38.

The propargylplatinum(II) complex reacts with $\text{Pd}(0)$ complex to form $\text{Pt}(0)$ complex and allenylpalladium(II) complex, the latter of which undergoes spontaneous and/or $\text{Pd}(0)$ -catalyzed rapid isomerization into the propargylpalladium(II) complex. The reaction of the produced $\text{Pt}(0)$ complex and propargylpalladium(II) complex leads to the formation of allenylplatinum complex. Each of the transmetalation reactions in the above procedure is accompanied by allenyl–propargyl

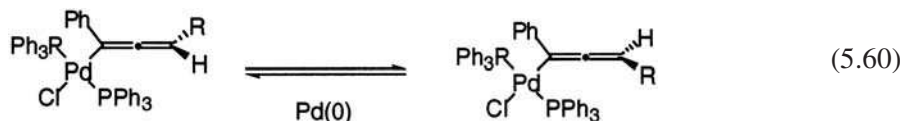


Scheme 5.38.

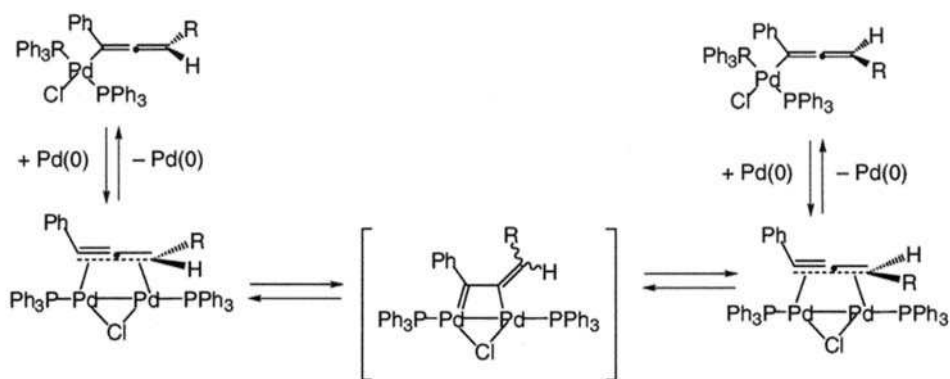
isomerization of the ligand via dinuclear intermediates with a μ -allenyl ligand. The reaction shown in Eq. 5.59 shows the formation of a dipalladium complex with a μ -allenyl ligand in the reaction mixture related to the above isomerization. It was separately confirmed that the dipalladium complex is readily formed from Pd(0) complex and η^1 -allenyl or -propargylpalladium(II) complex.



Recently, stereochemical aspect of the reversible transfer of allenyl ligands between Pd(0) and Pd(II) complexes was reported as shown in Eq. 5.60 [202].

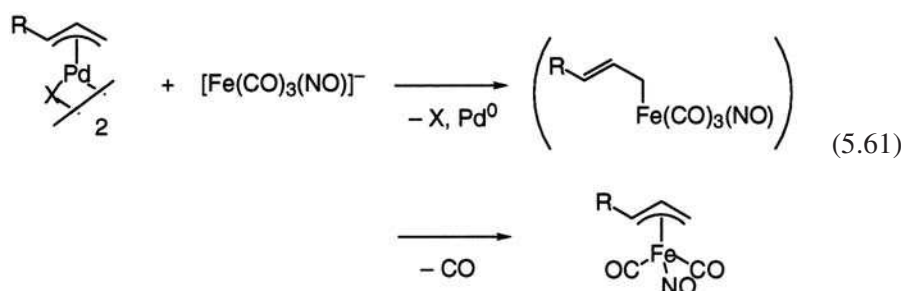


The optically active Pd complex with a chiral allenyl ligand undergoes epimerization in the presence of a catalytic amount of Pd(0) complex. This reaction does not involve the isomerization to the propargyl complex, but takes place via a dinuclear intermediate as depicted in Scheme 5.39. The μ -allenyl ligand in the dinuclear palladium intermediate may racemize via a vinyl-vinidene intermediate. This type of reaction is probably involved in a kinetic resolution of racemic propargyl alcohols promoted by chiral transition metal complex [203]. The intermolecular allyl ligand transfer from Pd to Fe complexes occurs under



Scheme 5.39.

mild conditions [204] (Eq. 5.61).

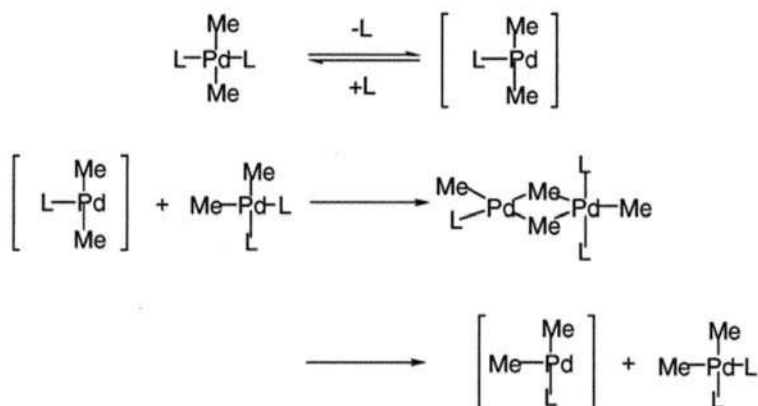


This transmetalation changes polarity of allyl ligand; the starting π -allylpalladium complex undergoes nucleophilic attack at the terminal carbons of the allyl ligand, while the produced Fe complex reacts with an electrophile to form a carbon-carbon bond.

5.3.4 Intermolecular transfer of the alkyl ligands

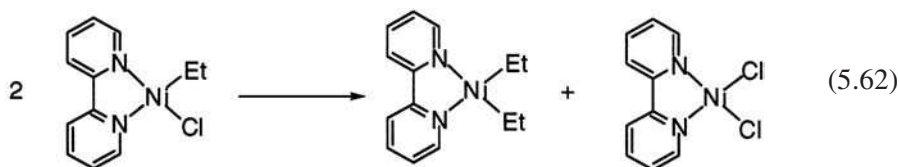
Scheme 5.40 depicts the plausible mechanism of the isomerization of trans-dimethylpalladium complex with phosphine ligands to its cis isomer [205]. The three-coordinated dimethylpalladium complex, which is formed via dissociation of a phosphine ligand, reacts with the four-coordinated complex to cause intramolecular methyl ligand exchange. The reaction of trans and cis complexes affords two cis complexes as shown in the above scheme. This promoting effect of the cis complex in the isomerization of trans to cis complex gives autocatalytic type kinetics of the reaction.

$\text{NiCl}(\text{Et})(\text{bpy})$ undergoes the disproportionation to produce an equimolar mixture of the dichloro and diethyl nickel complexes in THF at room temperature

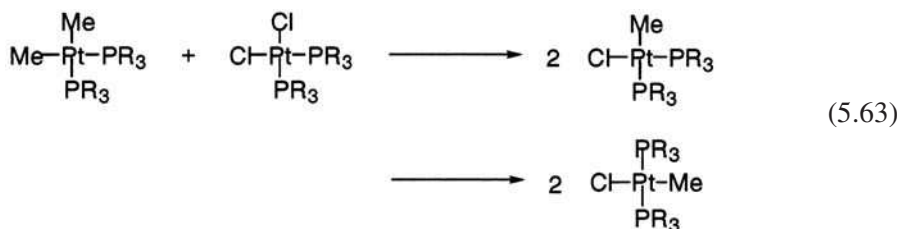


Scheme 5.40.

[206] (Eq. 5.62).



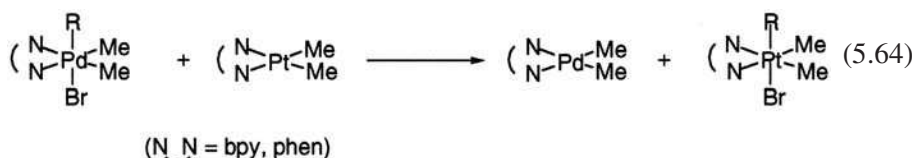
It is more facile than the reaction of $\text{NiBr}(\text{Ar})(\text{bpy})$, whose disproportionation via intermolecular aryl ligand transfer requires polar solvents to assist Ni-halogeno bond activation as mentioned in a previous section. Methylplatinum complexes with monodentate phosphine, arsine and thioether ligands cause methyl ligand transfer leading to disproportionation and *cis*–*trans* isomerization [207] (Eq. 5.63).



The reaction mixture contains dimethyl-, chloro(methyl)-, and dichloroplatinum complexes in a statistical molar ratio. *Cis*- $\text{PtCl}(\text{Me})(\text{PR}_3)_2$ isomerizes into the *trans* form during the reaction.

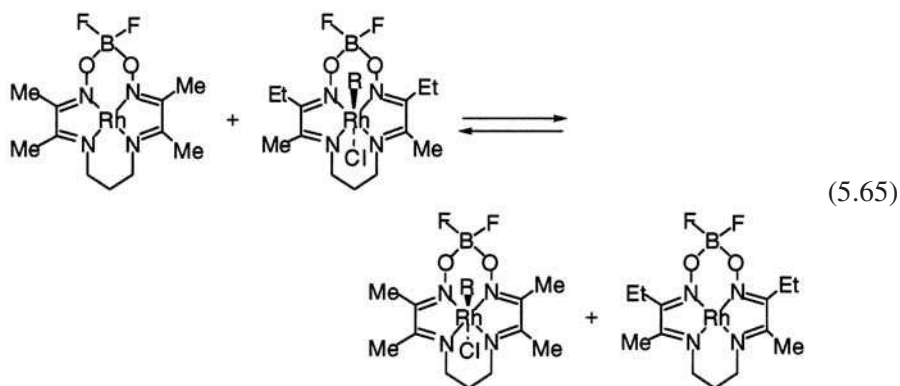
Halogeno(trialkyl)palladium(IV) complexes with bipyridine and phenanthroline ligand react with dimethylplatinum complex with the *N*-ligand to cause transfer of the halogeno and the apical alkyl ligands of the Pd complex to Pt as

shown in Eq. 5.64 [208,209].



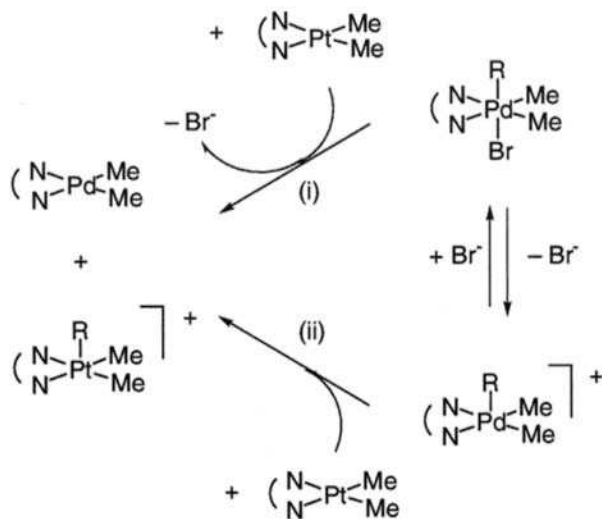
Kinetic studies of the reaction in acetone revealed the two reaction pathways shown in Scheme 5.41. Direct reaction of the octahedral Pd(IV) complex with the Pt(II) complex (path (i)) is observed but in a much lower reaction rate than the reaction involving initial halogen dissociation followed by the alkyl ligand transfer from the cationic Pd complex to the Pt complex (path (ii)).

Stepwise transfer of the halogeno and alkyl ligands between two metal centers is observed also in Rh and Co complexes with macrocyclic ligand. The Rh(I) complex with a macrocyclic tetraaza ligand undergoes oxidative addition of organic halides to produce the octahedral Rh(III) complex with alkyl and halogeno ligands at two apical coordination sites. This Rh(III) complex reacts with the square-planar Rh(I) complex to cause the intermolecular transfer of both ligands (Eq. 5.65) [210].

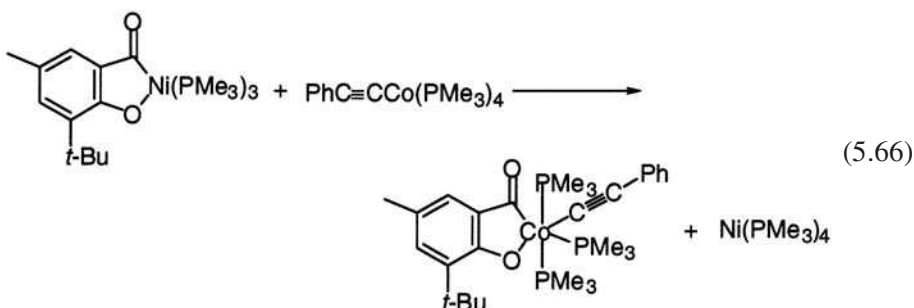


Kinetic studies revealed that the reaction proceeds via an intermediate containing the alkyl ligand bridging over the two Rh centers. Intermolecular alkyl ligand transfer between the cobaloxime ligand was also reported in detail [211]. These reactions accompany oxidation and reduction of the metal centers (redox type in Scheme 5.1). The complexes have rigid and stable square-planar coordination formed by auxiliary macrocyclic ligand, which minimizes the energy of the structural change caused by the transmetalation.

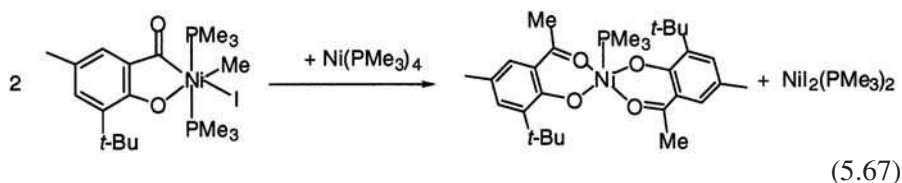
Ni(II) and Ni(IV) complexes with chelating 2-acylphenolato ligand undergo several unique reactions including the transmetalation as mentioned below. The nickel(II) complex with a 2-acylphenoxido ligand, $\text{Ni}\{\text{CO}-\text{C}_6\text{H}_2(\text{Me})(\text{t-Bu})-\text{O}\}(\text{PMe}_3)_3$, reacts with $\text{Co}(\text{C}\equiv\text{CPh})(\text{PMe}_3)_4$ to cause intermolecular transfer of the chelating ligand, giving the Co(III) complex with the phenolato and alkynyl



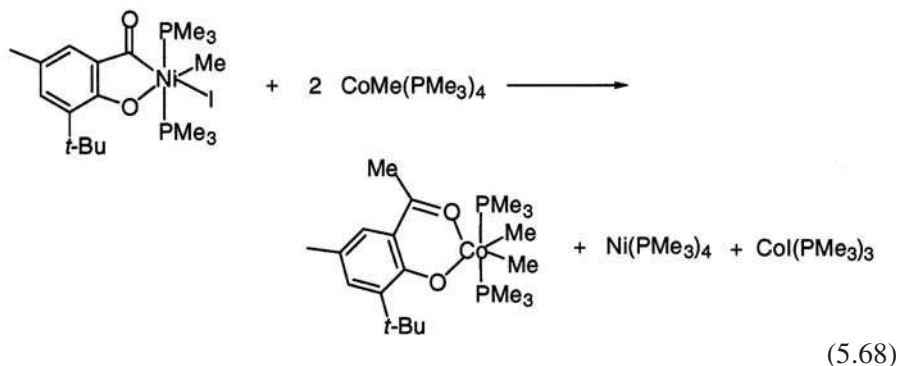
ligands (Eq. 5.66) [212].



This reaction forms Co(III) (d^6) and Ni(0) (d^{10}) complexes from Co(I) (d^8) and Ni(II) (d^8) complexes. High stability of the produced Co(III) complex enhances the intermolecular ligand transfer. Octahedral methyl(2-acetylphenoxido)nickel(IV) iodo complex, in the presence of a catalytic amount of $\text{Ni}(\text{PMe}_3)_4$, undergoes coupling of methyl and aryl ligands and subsequent transfer of the formed 2-acetylphenoxido ligand to give a mixture of $\text{NiI}_2(\text{PMe}_3)_2$ and $\text{Ni}\{\text{O}-\text{C}_6\text{H}_2(\text{Me})(t\text{-Bu})-\text{COMe}\}_2(\text{PMe}_3)$ with two chelating phenoxido ligands (Eq. 5.67) [213].

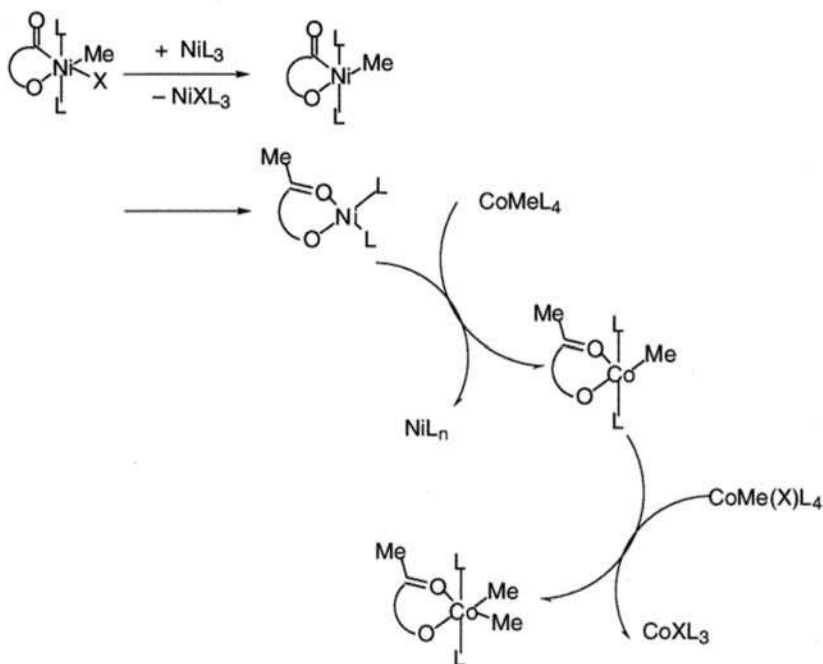


The 1 : 2 molar reaction of the Ni(IV) complex with $\text{CoMe}(\text{PMe}_3)_4$ produces the complexes formed through a complex reaction pathway involving transmetalation (Eq. 5.68) [214].



A produced Co(III) complex contains a 2-acetylphenoxido and two methyl ligands. Scheme 5.42 depicts the proposed mechanism to account for the reaction results.

The Ni(IV) complex is reduced by Ni(0) species in the reaction mixture to give a methyl(2-methylphenoxido)nickel(III) complex, which undergoes further



Scheme 5.42.

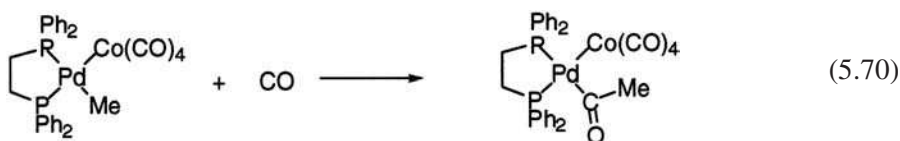
reductive coupling of the methyl and aryl ligands. The reaction of $\text{CoMe}(\text{PMe}_3)_3$ with the formed Ni(I) complex causes transfer of the phenoxido ligand from Ni(I) to Co(I), giving the Co(II) intermediate with a methyl and 2-acetylphenoxido ligands. Further reaction with $\text{CoMe}(\text{PMe}_3)_3$ affords the Co(III) product.

5.3.5 Intramolecular alkyl ligand transfer in dinuclear complexes

Intramolecular transfer of the organic ligand in dinuclear metal complexes is included in most of the intermolecular transmetalation reactions as shown in Scheme 5.2. Several dinuclear organotransition metal complexes were isolated and investigated to elucidate details of the organic ligand transfer involving activation and formation of the metal–carbon bond. Heterometallic dinuclear complexes with metal–metal bond undergo alkyl or aryl ligand transfer from one metal to the other. Thermal reaction of $\text{Pt}(\text{cod})\text{Me}-\text{WCp}(\text{CO})_3$ produces $\text{WMeCp}(\text{CO})_3$, which involves methyl ligand transfer from Pt to W and ensuing separation of the two metal centers due to the cleavage of metal–metal bond by the transmetalation (Eq. 5.69) [215].

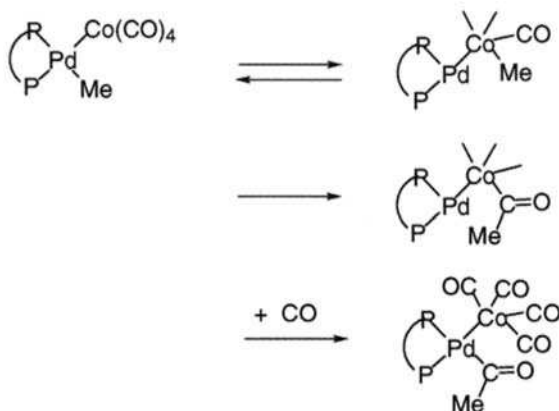


Similar reactions of Pt–Mo and Pt–Fe complexes also cause alkyl ligand transfer induced thermally or by addition of π -acid that enhances activation of the metal–carbon bond [216–218]. The reaction of Pd–Co complexes containing Pd–Me bond with CO leads to formal insertion of CO into the Pd–Me bond (Eq. 5.70) [219].



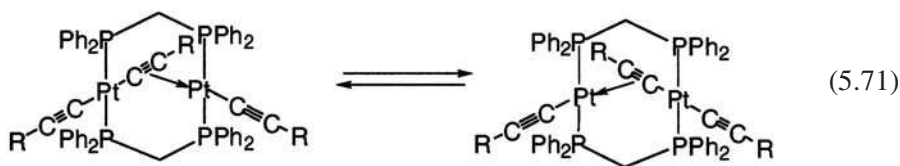
The detailed experimental and theoretical studies, however, elucidated the pathway involving transmetalation shown in Scheme 5.43. Initial methyl ligand migration leads to formation of the complex with Co–Me bond. The subsequent insertion of CO ligand into Co–Me bond takes place rapidly, and subsequent transfer of the acetyl ligand from Co to Pd affords the product.

The formation of the dinuclear complex with a bridging alkynyl ligand and its rapid switching from the $\mu\text{-}\eta^1\eta^2$ to the $\mu\text{-}\eta^2, \eta^1$ coordination mode provides the plausible mechanism of the intermolecular alkynyl ligand transfer [220]. Most typically, an A-frame dinuclear alkynyl-platinum complex with bridging diphosphine ligands undergoes rapid switching of coordination modes via Pt-

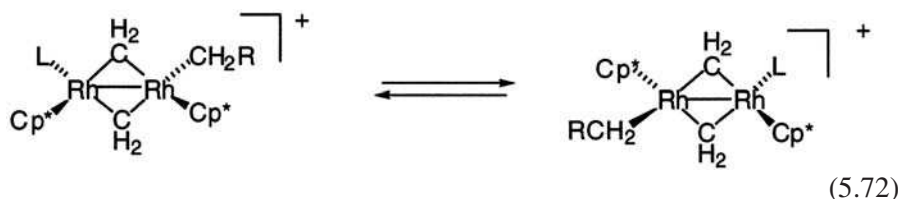


Scheme 5.43.

alkynyl σ -bond activation (Eq. 5.71) [221].



Reversible transfer of the alkyl group between the metal centers has been observed in dinuclear Rh complexes (Eq. 5.72) [222].



The above intramolecular reactions involve dinuclear intermediate with a symmetrically bridging alkyl, aryl, and alkynyl ligands.

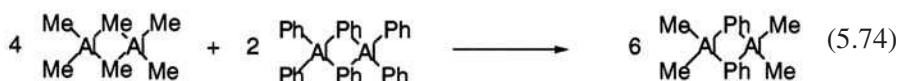
The aryl- and alkyl-transition metal bonds are thermodynamically less stable than the alkynyl-metal bond [223]. The number of intermolecular transmetalation reactions of alkynyl transition metal complexes, however, is much larger than those of alkyl and aryl complexes as shown above. The stable bridging coordination of alkynyl ligands of the intermediate dinuclear complexes with a σ, π -coordination probably makes the transmetalation, which involves activation of the thermodynamically stable metal-alkynyl bond, kinetically favorable.

5.4 TRANSMETALATION OF MAIN GROUP METAL COMPOUNDS

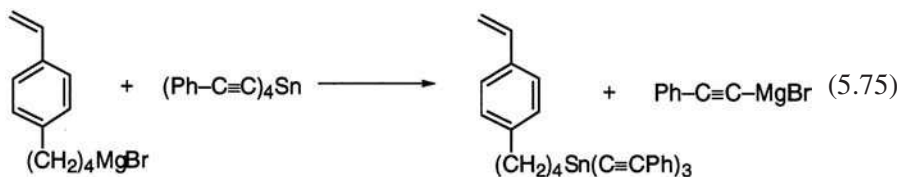
The transmetalation of main group metal complexes is common and useful as the preparative method of organometallic compounds of these metals. The studies of the reactions so far have emphasized application to synthetic organic reactions rather than elucidation of the detailed reaction mechanisms. This section surveys briefly the transmetalations of mechanistic interest or those involving uncommon transmetalation between main group elements. The metal exchange type transmetalation of the main group metal compounds in Scheme 5.1 (ii) involves the intermediate with a bridging alkyl or aryl ligand bonded to two different metal centers. Such binary compounds of Li and Mg or other combinations of metals with bridging organic ligands have been isolated and characterized [224]. Alkyl or aryl ligand exchange among Li, Mg, and Al, proceeds smoothly due to their tendency to accept the bridging coordination of the organic ligand. Trinaphtylborane reacts with triethylaluminum to cause transmetalation giving the completely metal-exchanged products (Eq. 5.73) [225].



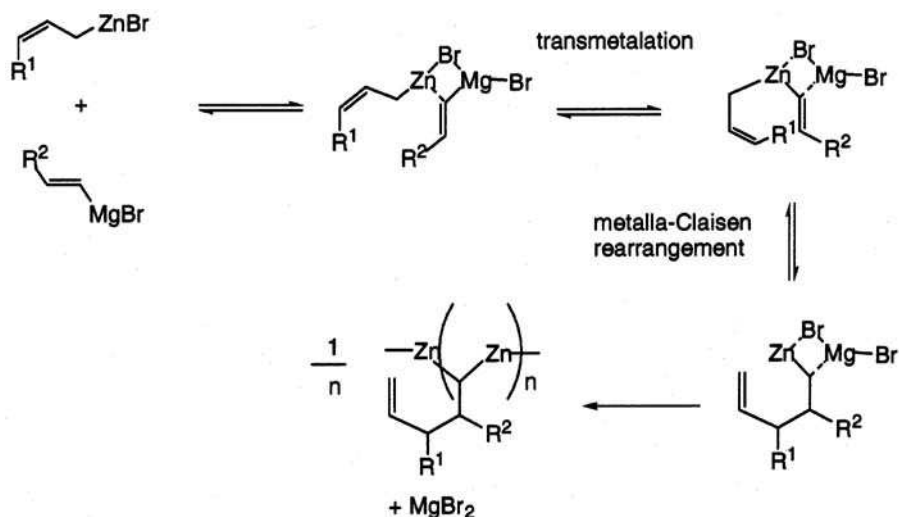
The 2 : 1 molar reactions of trimethylaluminum and triphenylaluminum occurs at room temperature to afford the dimethyl(phenyl)aluminum which is stabilized by bridging phenyl ligands bonded to two Al centers symmetrically (Eq. 5.74) [226].



Analogous organic ligand exchange is applied to transmetalation of alkylmagnesium bromide with tetrakis(alkynyl)tin to form the alkyltin compounds in which three alkynyl ligands on Sn act as a spectator ligand in the cross-coupling reaction (Eq. 5.75) [227].

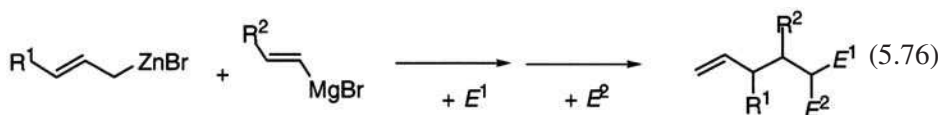


Theoretical and experimental studies on the reaction of allylzinc compounds with vinylmagnesium (or other organometallic compounds with vinyl-metal bond) revealed details of the reaction involving transmetalation. The reagents prepared from a combination of allylzinc and vinylmagnesium bromide are doubly trapped



Scheme 5.44.

by different electrophiles (Eq 5.76) [228–230].



The organometallic species formed in the reaction is an oligomeric alkylenedizinc compound as shown in Scheme 5.44. The initial transmetalation of vinylmagnesium reagent via Mg–Zn binary intermediate and subsequent metalla-Claisen rearrangement of the complex promoted by the Mg salt afford alkylenedizinc-magnesium compound. Further extrusion of MgBr_2 leads to the oligomeric organozinc compounds that are responsible for the reaction with electrophilic reagents.

5.5 SUMMARY

Transmetalation forms new metal–carbon bonds under mild conditions. It serves to alter the reactivity of the organometallic intermediates in the metal complex-promoted synthetic organic reactions. The recent studies of the transmetalation have replaced previously postulated and obscure mechanisms of several metal complex-promoted synthetic organic reactions with the more convincing mechanism based on the precise description of the transmetalation reactions. This chapter intended to concentrate on the activation and formation of metal–carbon σ -bond by transmetalation and skipped other topics such as intermolecular transfer of carbene [231] and Cp ligands. Since transmetalation would occur between the

two complexes with a number of different metal centers, organic ligands, and auxiliary ligands, this field has many remaining issues to be investigated.

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1,2-Insertion and β -Elimination

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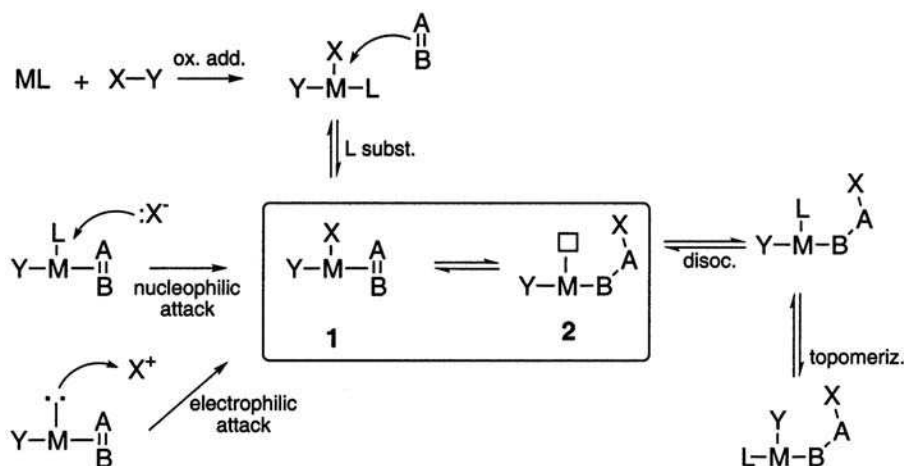
6.1 INTRODUCTION

The *cis-1,2-addition* of M–X bonds to unsaturated A=B bonds and its reverse, the β -*elimination* of X from M–B–A–X, are fundamental elementary steps of catalytic reactions such as hydrogenation, hydroformylation, oligomerization, polymerization, hydrosilation, hydrocyanation, or alkene isomerization processes, as well as the Heck reaction. Most of the reactions described in the literature involve M–H or M–C bonds, and alkenes or alkynes. Besides them there are processes where the unsaturated substrate is different from alkene or alkyne: This includes CO₂, CS₂, aldehydes and ketones, imine, or nitrile. Also, there are processes involving M–Si, M–Sn, M–B, M–N, M–P, or M–M bonds. The insertion of alkenes into M–carbene bonds is not essentially different in their intimate mechanism, but it is not discussed in this chapter.

The heart of the *cis-1,2-addition*, at a first level of approximation, is common to most of the processes to be considered. It consists of an orbital interaction in a four-center transition state (TS) from which the bond rearrangement occurs (Eq. 6.1). The result of the *cis-1,2-addition* can also be looked at as arising from insertion of the unsaturated group A=B into the M–X bond, and for this reason the reaction is also named *insertion*. Another way to describe the process is as an *endo attack* of X to the coordinated A=B reagent (often an alkene).



Depending on all the actors playing a role in Eq. 6.1, each particular case can show important variations in the details of the insertion. Thus, the kind of transition metal, its oxidation state, the nature of X and of A=B will produce dramatic changes in the kinetics and thermodynamics of this step. Some cases have been studied in detail and examples are discussed later.



Scheme 6.1.

Theoretical calculations, which allow an approximation to the intimate mechanism, usually start from a point (**1**) where the unsaturated species is already attached to the metal and *cis* to the M–X bond. In the reverse reaction, *β*-elimination of X, the metal has to provide a *cis* coordination vacant, which is represented by an empty square in (**2**) in Eq. 6.1 and throughout the chapter. In practice there are steps previous to the insertion or the *β*-elimination process which only very rarely are specified as separate from the insertion itself. It is important to be aware that these previous steps can have profound influence on the reaction rate even in cases when they are not rate determining, because they can control thermodynamically the concentration of the active species **1** or **2**. In the literature, the word ‘insertion’ is often applied to the whole process of transformation of some M–X entity and free A=B into **2**. The specific insertion step can be then referred to as the X-migration step.

Some of the possible processes leading to **1** or **2** from different precursors are depicted in Scheme 6.1 to illustrate the incidence of factors additional to what is, strictly speaking, the insertion or *β*-elimination step. For instance, the formation of **2** can require ligand dissociation, and perhaps topomerization. The origin of the M–X moiety in **1** can be diverse (e.g. oxidative addition, electrophilic or nucleophilic attack to the metal), and can be prior to or follow the coordination of A=B. The incorporation of the alkene can imply associative or dissociative pathways. Topomerization (maybe requiring previous dissociation) can be needed to reach a *cis* arrangement in **1** or **2**. This will be more clear in the pages that follow, where the most common cases of insertion are discussed.

The discussion of the most important catalytic processes as such will be avoided in this chapter, as they are easily found in the existing literature. However, mention will be made of less popular catalytic cycles involving insertion.

Since most of the important insertion/ β -elimination processes affect molecules where $A=B$ is a carbon–carbon double or triple bond, the discussion is organized considering first the different types of $M-X$ bond involved, and the insertion of alkenes or alkynes. Less abundant cases are discussed later. The reader should have in mind that sometimes the word ‘alkene’ is used in a more general way, meaning an unsaturated carbon–carbon bond not involved in aromaticity. Also the word ‘alkyl’ can be used in a more general context meaning hydrocarbyl.

Finally, the *exo attack* of nucleophiles to coordinated alkenes, studied in chapter 8 of this book, should be mentioned at this point. The *exo attack* is mechanistically and stereochemically different from the insertion (it produces a *trans-1,2-addition*), but when no chiral centers are formed, the result of an insertion and that of an *exo attack* are indistinguishable.

6.2 INSERTION OF ALKENES INTO $M-H$ OR $M-C$ BONDS

6.2.1 Theoretical studies and basic features of the insertion step

The advances in computational chemistry in the last decade have provided insight into the intimate details of processes that cannot be experimentally observed. Several methods at different levels of sophistication can be applied, and reviews on them have appeared. More detailed consideration of these aspects can be found in the reviews of Niu and Hall [1], and Koga and Morokuma [2], which contain numerous references. The insertion in real systems is the result of many subtle influences throughout the process. These can be better calculated independently on model systems which help us to analyze the experimental results. For this reason we consider first the modern theoretical results before discussing the real systems.

The insertion of alkenes into $M-R$ bonds (whether $M-H$ or $M-C$) is now considered as a migratory insertion process and requires a mutually *cis* arrangement of the alkene and the $M-H$ or $M-C$ bond. Since in many practical processes the alkene is an external ligand which needs to coordinate immediately prior to insertion, a few theoretical studies consider also the coordination step as part of the insertion process.

The orbital interaction leading to the fission of the $M-R$ bond and the formation of the new bonds is the typical synergetic interaction of transition metals with π -acceptor ligands. The $\sigma(M-R)$ and $\pi(\text{alkene})$ orbitals, which are occupied, interact in a four-centered transition state with the $\sigma^*(M-R)$ and $\pi^*(\text{alkene})$ orbitals, which are vacant. This interaction produces a mixing of the $\pi(\text{alkene})$ and $\pi^*(\text{alkene})$ orbitals that polarizes the alkene: Compared to the simple alkene coordination (Fig. 6.1, left), where the donor and acceptor alkene orbitals interact only with the metal orbitals (this is the classical Chatt–Dewar model), the interaction with $\sigma(M-R)$ and $\sigma^*(M-R)$ leading to insertion polarizes the donor alkene orbital towards C_α

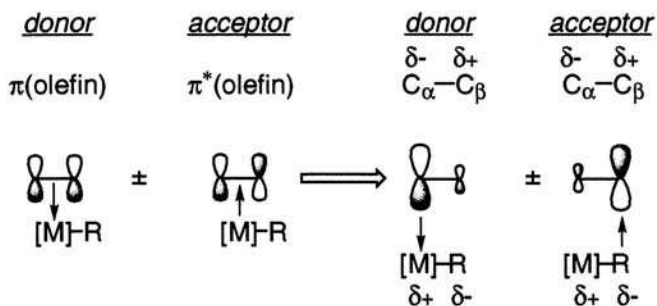
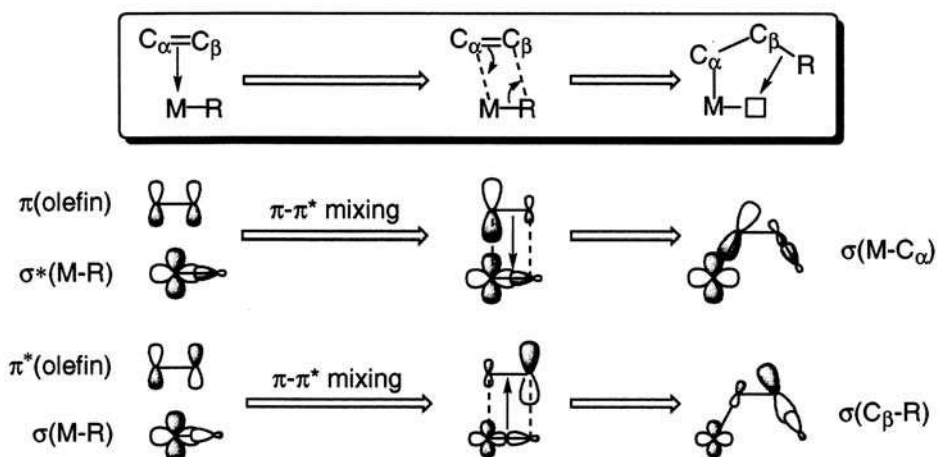


Fig. 6.1. Mixing of the alkene orbitals leading to insertion.



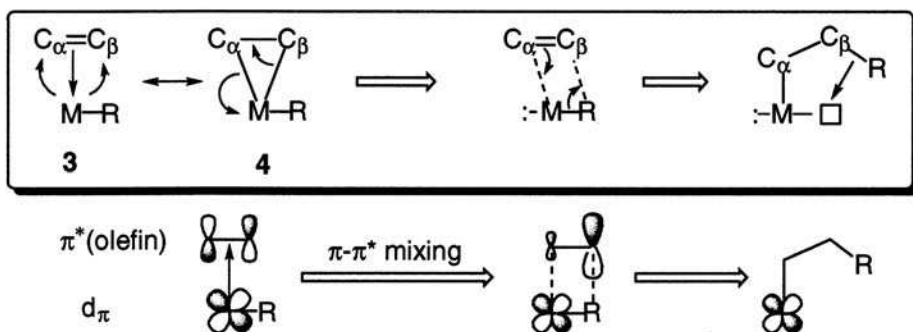


Fig. 6.3. Removal of $M \rightarrow L$ back donation in the insertion process.

orbital to the π^* (olefin) orbital, thus this additional interaction has to be considered (Fig. 6.3). Its importance depends on the relative stability of the d orbitals of the metal and the π^* orbitals of the alkene. The d orbitals become very stable for late transition metals, and for them π back-donation is modest, but it can be important for early transition metals. Low oxidation states, or alkenes with electron withdrawing substituents will also increase π back-donation. Depending on its importance, the metal-alkene bond is better represented by the Dewar–Chatt–Duncanson model (**3**, moderate back-donation) or by the metallacyclopropane model (**4**, important back-donation) [3]. The insertion process requires breaking of this extra back-bonding component of the metal–alkene bond, giving back the electron pair to the d_π metal orbital, which becomes essentially non-bonding in the inserted product.

This model allows us to discuss some features of the insertion step. A general reaction profile is represented in Fig. 6.4. The stability of the π -complex compared to the reactants can change dramatically for different cases, and the reaction medium is very influencing. If the reactant complex is very stable (for instance if it lacks a low-lying empty orbital because ligands or a coordinating solvent are filling the coordination sphere), the coordination of the alkene can be thermodynamically disfavored, thus reducing the concentration of π -complex (case (a)); moreover, the barrier to alkene coordination can become rate-determining. In the other extreme (case (b)), for a metal center with low lying empty orbitals in a solution in a weakly or non-bonding solvent, the coordination of the alkene should be exothermic, unless severe steric hindrance is involved. Many cases lie between these two extremes (case (c)). Of course the strength of the metal alkene interaction has an influence on the stability of the π -complex, which will be higher the stronger the π interaction. A strong M –alkene bond will favor the coordination of the alkene but it will increase the barrier to insertion, which can then become rate-determining. Ideally a sufficient alkene coordination with little or no back-bonding is desirable for easy insertion process.

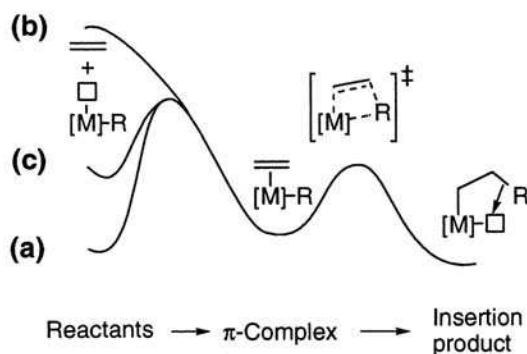


Fig. 6.4. General reaction profile for the insertion of alkenes into M–R bonds.

(a) *Influence of the d^n configuration*

If one looks at the R-migration step exclusively, the case most favorable for insertion is that of d^0 complexes where no M–alkene back-bonding exists, whereas d^n metal centers are expected to show higher insertion barriers. In agreement with this, early transition metal metallocenes, alkoxides, and other derivatives with d^0 configuration (group 4 cationic complexes and group 3 neutral complexes) are not easily isolated and are active catalysts for the polymerization of alkenes [4]; in contrast related lower valent d^n complexes of the same metals (Ti(II) or Zr(II) complexes) afford easily isolable alkene complexes which do not catalyze polymerization (although they can catalyze oligomerization reactions) [5].

Many theoretical studies of insertion concern the very important case of insertion of ethylene (or α -alkenes) into a growing polymer, following the Cossee–Arlman direct insertion mechanism (Scheme 6.2) [6]. In this particular case, the resting states of the catalyst before and after each propagation step are similar, and contain an M–alkyl bond stabilized by an agostic interaction. The interactions with the solvent or external ligands must be also rather similar for both resting states. Thus, the values calculated must correspond only to the coordination and insertion of the alkene.

For d^0 complexes the theoretical studies indicate that both ethylene association and ethylene insertion into M–Me bonds are exothermic, with a low barrier of

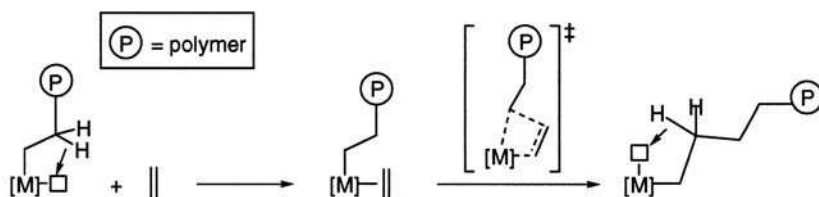


TABLE 6.1

Stabilizing energies for the ethylene π -complex, and insertion barriers into the M–Et bond for comparable d^0 to d^2 systems (kcal/mol) [9b]

Complex ^a	Electron configuration	π -complex	Insertion barrier
$L^1\text{Sc(III)C}_2\text{H}_5$	d^0	–10.8	3.1
$L^2\text{Ti(IV)C}_2\text{H}_5^+$	d^0	–24	4.8
$L^2\text{Ti(III)C}_2\text{H}_5$	d^1	–25	22.1
$L^1\text{Nb(III)C}_2\text{H}_5$	d^2	–49.7	47

^a $L^1 = \text{NH}(\text{CH}_2)\text{NH}_2^-$; $L^2 = 2\text{NH}_2^-$.

activation [7,8]. In sterically unencumbered $[\{L\}\text{M}(\text{Et})]^n$ fragments ($n = 0$ for Sc(III), Y(III), La(III); $n = 1$ for Ti(IV), Zr(IV), Hf(IV); $\{L\} = (\text{OH})_2$, Me_2 , $(\text{NH}_2)_2$) [9], the β -agostic bond strength follows the order $\text{Ti} \approx \text{Zr} > \text{Hf}$ and $\text{Sc} \approx \text{Y} \geq \text{La}$. The formation of the π -complex is exothermic by about 8–13 kcal/mol for group 3, and 20–27 kcal/mol for group 4. The insertion barriers follow the order $\text{Sc} < \text{Y} < \text{La}$ and $\text{Ti} < \text{Zr} < \text{Hf}$ and are lower for group 3 than for group 4 complexes.

For early transition d^1 and d^2 complexes higher association energies for the alkene complexes and consistently higher insertion barriers are expected according to the theoretical model. In fact the values calculated for the d^2 complex in Table 6.1 are noticeably higher than those for comparable d^0 or d^1 systems [9b]. Thus the stabilizing energy and the insertion barrier for the process $L^1\text{M(III)Et} + \text{C}_2\text{H}_4 \rightarrow L^1\text{M(III)(butyl)}$ are much larger in the Nb(III) d^2 complex than in the analogous Sc(III) d^0 complex. Similarly, the addition of one electron to the d^0 $L^2\text{Ti(IV)Et}$ raises the alkene insertion barrier from 4.8 to 22.1 kcal/mol. These changes make the insertion extremely difficult or virtually impossible.

A more subtle variation is seen in the ethylene complexation and insertion barriers of precursor monocationic complexes $[\text{M}(\text{NH}_2)_n(\text{NH}_3)_{2-n}\text{R}]^+$ having d^1 – d^4 electron configurations, for which the alkene stabilization is found to diminish almost linearly with an increasing number of electrons. For $\text{R} = \text{Me}$ the values (kcal/mol) fall in the range –30 (for d^1), –25 (for d^2), –15 (for d^3), and –12 (for d^4). Ethylene insertion barriers for $\text{R} = \text{Et}$ were calculated to be in the range 6–16 kcal/mol and are more affected by the type of transition metal or its oxidation state than by the number of d electrons [10]. In the same vein, calculations for d^3 complexes of type $[\text{CpLCrMe}]^+$ show that the insertion step is not a bottleneck in the propagation of ethylene polymerization, with activation barriers in the range 6–10 kcal/mol [11].

For late transition metals, the experimental results show that they can be active catalysts in polymerization reactions, as well as in other reactions involving insertion. This shows again that the increasing number of d electrons does not run parallel to more d_π electron availability from the metal and a higher stabilization

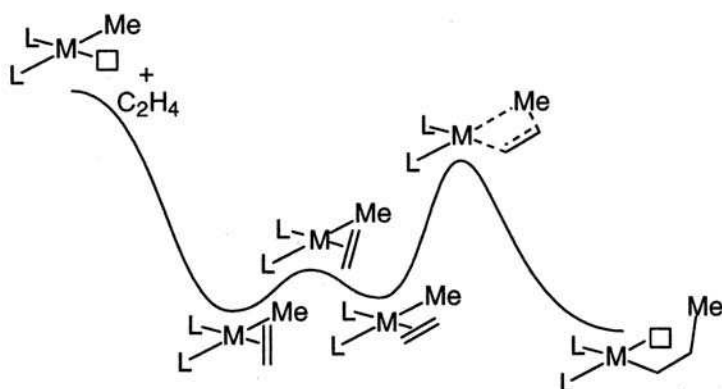
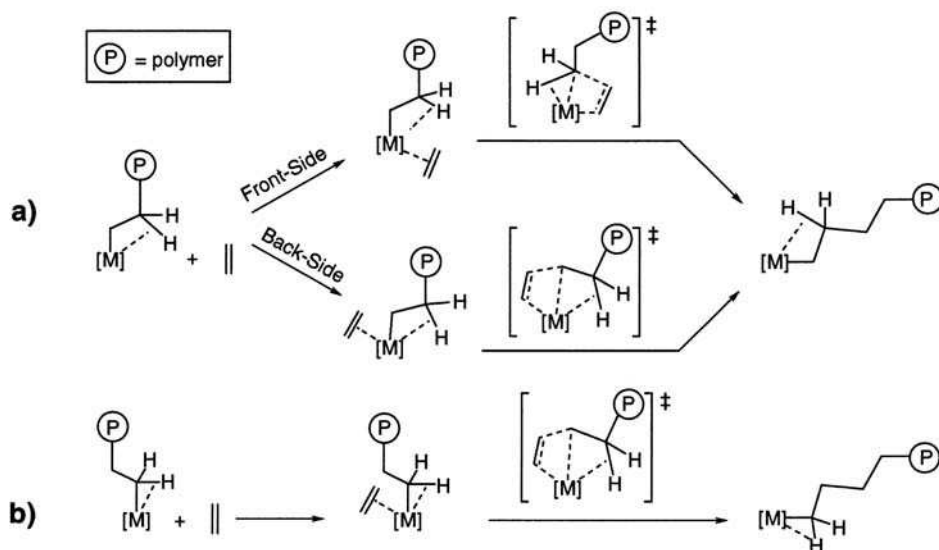


Fig. 6.5. Energy profile for the insertion process ($M = \text{Ni, Pd, Pt}$; all the complexes are monocations).

of the alkene complex. On the contrary, going away from the more electropositive early transition metals, the increasing stabilization of the d orbitals renders these electrons less available, and the back-bonding to the coordinated alkene can be very modest [9]. This has been shown experimentally by Brookhart *et al.* for the complexes $[\text{PdMe}(\text{phen})\text{L}]^+$ ($\text{L} = p$ -substituted styrenes), where the electron-rich styrenes bind tightest to Pd [12].

Theoretical studies on the insertion of ethylene into d^8 $[\text{MMeL}_2]^+$ ($M = \text{Ni, Pd, Pt}$) catalysts provide the relative potential energy plot in Fig. 6.5. The process consists of a coordination of the alkene perpendicular to the coordination square plane, followed by an easy alkene rotation to an in-plane coordination and a more difficult insertion. The rate-determining step of these reactions is the migratory insertion of the alkene and these calculations show that the stabilization of the system upon coordination of the alkene increases in the order $\text{Ni} < \text{Pd} < \text{Pt}$, whereas the insertion transition state changes very little. This explains the catalytic activity $\text{Ni} > \text{Pd} > \text{Pt}$ generally observed, which is associated to insertion barriers in the range of 10 kcal/mol for Ni, 16 kcal/mol for Pd, and 25 kcal/mol for Pt [1].

An interesting difference between early and late transition metals is not apparent from the picture we have used so far. The early transition metals in high oxidation states are highly electrophilic, more polarizing, and have low lying empty d orbitals. For these reasons they are able to retain agostic interactions throughout the insertion process [9], whereas in the late transition metals (e.g. 16-electron square planar π -alkene complexes) this interaction is suppressed almost completely in the transition state [13]. Thus, the insertion process in early transition metals is better represented by the more complex Scheme 6.3. Two additional aspects, which will not be discussed in detail, appear in the scheme: (i) The two possibilities of coordination of the alkene from the side of the α -carbon or from the side of the agostic interaction, which lead to somewhat different insertion



Scheme 6.3.

barriers [9]; and (ii) the participation of α -agostic interactions, that seem more common and important than it was initially believed, whether in the transition state (a) or stabilizing the alkyl complexes (b) [4,14]. The β -agostic interaction that has to be overcome for the insertion in late transition metals is estimated to be about 12 kcal/mol [13]. The immediate consequence is that, since successive alkene insertions in early metals work without breaking completely the agostic interaction, chain propagation should be faster for these polymerization catalysts.

(b) Influence of the ancillary ligands

At least three different types of influence are associated to the spectator ligands. The first one is related to steric effects. An excessive steric bulk of the ligands will be certainly detrimental to the insertion process if it impedes severely the approach of the incoming alkene. However, studies comparing moderately encumbered geometries, such as the very common metallocene complexes $\text{Cp}_2\text{MR}^{n+}$, $\{(\text{H}_2\text{Si})\text{Cp}_2\}\text{MR}^{n+}$, or $\{\text{HN}-(\text{H}_2\text{Si})\text{Cp}\}\text{MR}^{n+}$ with less crowded fragments $\{L\}\text{M}(\text{Et})^{n+}$ ($L = (\text{OH})_2, \text{Me}_2, (\text{NH}_2)_2$) show that appropriate steric bulk of the auxiliary ligands can produce a very noticeable lowering of the insertion barrier. The reason is that, prior to insertion, the alkyl chain is already forced into such a conformation that the deformation to attain the insertion transition state is minor [9]. This effect can favor the insertion process to the point that it can make it feasible in non- d^0 metal complexes. For example, the hypothetical Ti(III) d^1 complex $[(\text{MgCl}_3)_2\text{TiEt}(\text{C}_2\text{H}_4)]$ (which might be a model of Ti(III) species existing in Ziegler–Natta catalysts) shows an insertion barrier of

only 6.7 kcal/mol (compared with 22.1 kcal/mol for the unencumbered complex in Table 6.1) [15].

Another influence comes from the kind of ancillary ligands. Strong π -acceptors can sequester the electron density of d^n systems more efficiently than the coordinated alkene, also reducing the amount of undesired π -back-bonding and facilitating insertion. For instance, the d^2 Nb(III) and Ta(III) complexes $[\text{MCp}^*(\eta^4\text{-diene})\text{X}_2]$ ($\text{Cp}^* = \text{C}_5\text{Me}_5$) produce living alkene polymerization [16], and the Zr(II) complex $[\text{ZrCpEt}(\eta^4\text{-butadiene})(\text{dmpe})]$ ($\text{dmpe} = \text{Me}_2\text{PCH}_2\text{CH}_2\text{PMe}_2$) produces selective dimerization of ethylene to 1-butene [5a].

Finally, the *trans* influence of the ligand *trans* to R is an important factor in the insertion barrier. If it is high, the M–R bond will be polarized rendering R more nucleophilic. As can be seen in Fig. 6.1 this should facilitate the migratory insertion. In fact, in the pentacoordinated system $[\text{Pt}(\text{H})\text{X}(\text{PH}_3)_2(\text{C}_2\text{H}_4)]$ in which X is *trans* to the migrating H, the calculated barriers for insertion are 33.9 kcal/mol for X = Cl, but only 11.8 kcal/mol for X = SnCl_3 [17]. In the square-planar system $[\text{PtH}(\text{SiH}_3)(\text{PH}_3)(\text{C}_2\text{H}_4)]$ the calculated barrier for insertion into the Pt–H bond is 20.6 kcal/mol if PH_3 is *trans* to H, and drops to only 4.4 kcal/mol if SiH_3 is *trans* to H [18].

(c) Influence of the solvent

Although the number of theoretical studies simulating the solution phase is more scarce, those existing confirm the importance of solvation effects, which are different for the different steps throughout the insertion process. For instance, Fig. 6.6 plots the relative enthalpies (kcal/mol) and free energies in the gas phase and in toluene for the insertion process $\text{LZrCH}_3^+ + \text{ethylene}$ ($\text{L} = \text{CpCH}_2\text{Cp}$) [19]. Both the entropy and the solvation effects can be seen in this plot. The formation of the π -complex has a clearly negative ΔH but, because ΔS has a large negative value, ΔG in the gas phase has a smaller negative value. Overall the alkene coordination is, however, clearly exergonic. When the solvent toluene is taken into consideration, this balance is almost thermoneutral. The transition state is also affected although the insertion barrier is almost the same in this case for the gas phase or the toluene solution. Thus the insertion process would be disfavored in toluene compared to the gas phase because of the incidence of the not-so-favored alkene coordination step. Obviously more coordinating or polar solvents or counterions should be expected to produce larger effects than toluene.

(d) Influence of the migrating R group

For the d^6 systems $[\text{CpMR}(\text{PH}_3)(\text{CH}_2\text{CH}_2)]^+$ ($\text{R} = \text{H}, \text{CH}_3$; $\text{M} = \text{Co}, \text{Rh}, \text{Ir}$) the values in Table 6.2 have been calculated [20]. The insertion becomes thermodynamically and kinetically less favorable down a triad, as we have previously seen for other d^n systems.

Table 6.2 illustrates another point that is also of general application; according to the barriers calculated, the insertion is kinetically much more favorable for

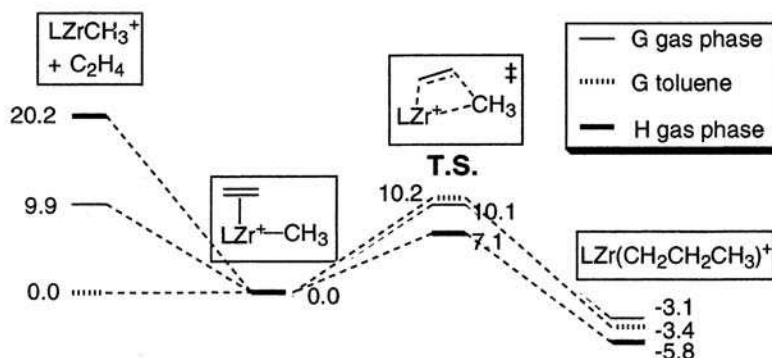


Fig. 6.6. Relative enthalpies (ΔH , kcal/mol) and free energies in the gas phase and in toluene for the insertion process $\text{LZrCH}_3^+ + \text{ethylene}$ ($\text{L} = \text{CpCH}_2\text{Cp}$)

TABLE 6.2

Insertion barriers (kcal/mol) and enthalpies relative to the π -complex $\text{CpMR}(\text{PH}_3)(\text{CH}_2\text{CH}_2)^+$ ($\text{R} = \text{H}, \text{CH}_3$; $\text{M} = \text{Co}, \text{Rh}, \text{Ir}$)

M	R	Insertion barrier	ΔH insertion
Co	H	0.3	-3.4
Rh	H	2.7	-1.0
Ir	H	6.1	+3.7
Co	CH_3	15.2	-12.7
Rh	CH_3	19.8	-8.5
Ir	CH_3	23.2	-5.3

hydride migration (alkene insertion into $\text{M}-\text{H}$) than for methyl migration (alkene insertion into $\text{M}-\text{CH}_3$). A comparative study of the alkene insertion into $\text{M}-\text{H}$ or $\text{M}-\text{CH}_3$ bonds for the entire second row of transition metals has shown that for most of them the insertion barrier is about 20 kcal/mol higher for $\text{M}-\text{CH}_3$ than for $\text{M}-\text{H}$ [21]. The orbital interactions for insertion are basically identical, whether in a $\text{M}-\text{C}$ or in a $\text{M}-\text{H}$ bond (see Fig. 6.7 and compare with Fig. 6.2), but the spherically symmetric $1s$ orbital, not needing rehybridization, is better able to stabilize the transition state than the more directional p orbital of the carbon atom involved in $\text{M}-\text{CH}_3$ bond. In other words, the hydride can continuously change the direction of its bond from the metal to the alkene, but for the CH_3 group a large part of the $\text{M}-\text{CH}_3$ bond has to be broken before the CH_3 can start to bind towards the alkene. In addition, the approximation of the alkene to the less encumbered $\text{M}-\text{H}$ finds less repulsion than with $\text{M}-\text{CH}_3$.

Different hydrocarbonyl groups also show differences between them. This can be illustrated with the data in Table 6.3, where some naked and ligand stabilized methyl and aryl Pd systems undergoing insertion (Scheme 6.4) are compared [13,22].

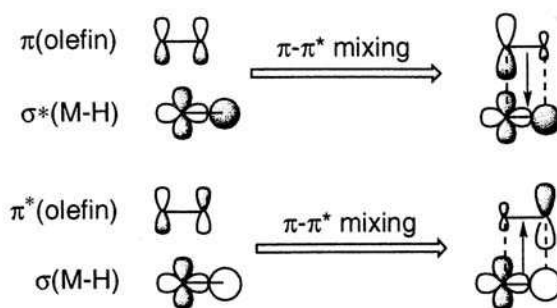
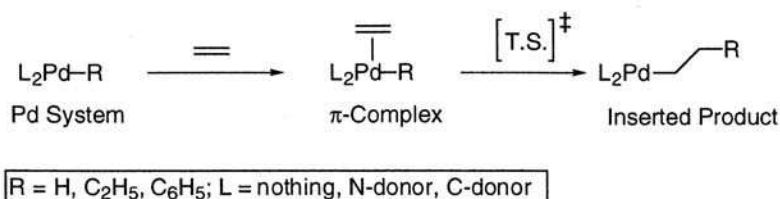


Fig. 6.7. Orbital interactions for insertion into M-H bonds.



Scheme 6.4.

TABLE 6.3

Energies (kcal/mol) for the reaction of ethylene with different Pd systems ^a

System	π -Complex	Transition state	Inserted product	Reference
$Pd(CH_3)^+$	-43.9	-25.6	-40.8	[13]
$Pd(C_2H_5)^+$	-36.0	-10.9	-25.7	[13]
$Pd(CH_3)(NH_3)_2^+$	-27.3	-9.3	-34.8	[13]
$Pd(C_2H_5)(NH_3)_2^+$	-14.9	+4.4	-22.5	[13]
$Pd(CH_3)(C_2N_2H_4)^+$	-29.8	-13.4	-36.8	[13]
$PdPh(C(NH_2)_2)_2^+$	-19.5	-11.2	-34.8	[22]

^a Values relative to zero for each system + C_2H_4 reactant pair.

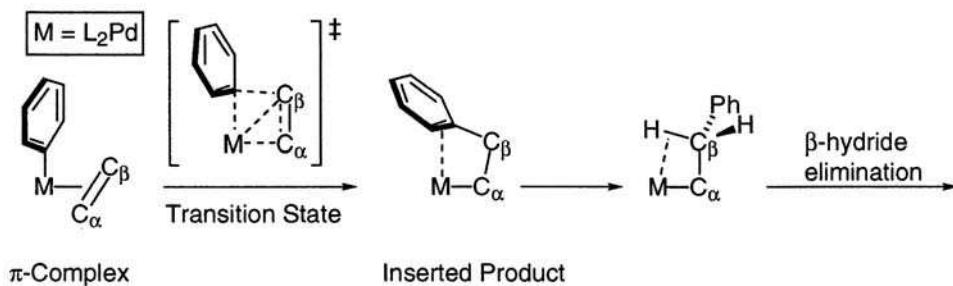
Several interesting points can be mentioned:

(1) The stabilization upon alkene coordination is clearly larger for the reaction of the naked formally 10-electron systems PdR^+ . This strong alkene bonding arises from a charge-induced dipole interaction from the polarizable ethylene ligand, which compensates for the reduced ability of a naked cationic Pd system to provide π back-donation. On looking at these features, these naked systems can be considered reasonable models of d^0 systems. The strength of the Pd-alkene bond is noticeably reduced in ethyl derivatives compared to similar methyl systems, due to partial delocalization of the positive charge onto the larger ethyl group. Both

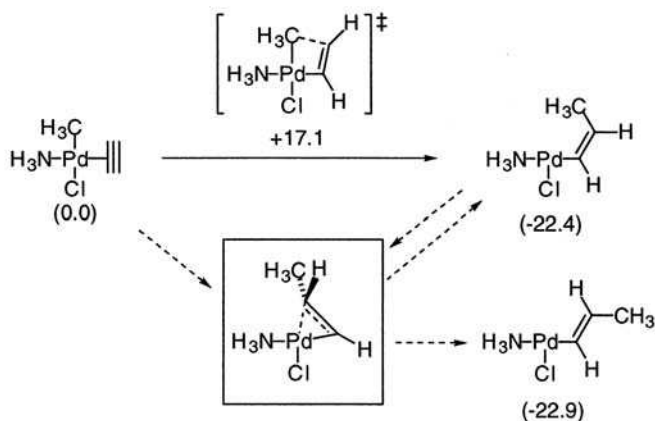
insertions are endothermic but that of the methyl derivative is less endothermic and has a lower barrier due to the creation of previously non-existent β -agostic interactions upon insertion, in the transition state and the final product, which stabilize these states.

(2) The binding alkene energy decreases very noticeably in the systems containing ancillary ligands, because these ligands also delocalize the positive charge. In fact the calculations show that, in the presence of ligands, the effect of the length of the R group on the charge is very much diminished. The data in Table 6.3 show that, the π -complexes of $\text{Pd}(\text{CH}_3)(\text{NH}_3)_2^+$ or $\text{Pd}(\text{CH}_3)(\text{C}_2\text{N}_2\text{H}_4)^+$ ($\text{C}_2\text{N}_2\text{H}_4 = \text{diimine}$) are more stabilized than that of the ethyl derivative $\text{Pd}(\text{C}_2\text{H}_5)(\text{NH}_3)_2^+$, and the difference in stability between the methyl and ethyl derivatives is larger than for the naked complexes. The main reason is that, upon coordination of the alkene, the β -agostic interaction existing in the otherwise 14-electron three-coordinated ethyl precursor is lost, whereas in the naked complexes with many vacant coordination sites the coordination of the alkene does not affect the Pd–Et bond. Once the alkene is coordinated, both complexes will gain β -agostic interaction in the transition state and in the inserted product, and the corresponding energy differences from their π -complexes are very similar. Thus the main difference between the methyl and larger alkyls in the presence of ligands is the ease of alkene coordination.

(3) The case of the phenyl derivative is interesting. Even accepting some variations due to the different ligand used, it seems clear that the addition of ethylene is much less favorable for the phenyl system than for methyl (phenyl delocalizes better the positive charge) and somewhat better than for ethyl (phenyl does not lose β -agostic interaction upon alkene coordination). The insertion barrier is much lower than for alkyl derivatives because of the ease of electron density rearrangement using the π -orbitals of phenyl (Scheme 6.5). Finally, the inserted product is very efficiently stabilized by the coordination of phenyl to the free coordination site on Pd. It is worth noting that this aromatic interaction is more favorable than the β -agostic interaction (through which β -hydride elimination will occur in a Heck reaction) by about 4.6 kcal/mol.



Scheme 6.5.



Scheme 6.6.

(e) Insertion of alkynes

While alkene and alkyne insertions proceed by similar mechanisms according to their similarity in electronic structure, they show different reactivity because the alkynes have occupied π orbitals lower in energy and unoccupied π^* orbitals higher in energy than alkenes, making an alkyne a worse donor and a worse acceptor. The computed binding energy of acetylene in $[\text{PdCl}(\text{CH}_3)(\text{C}_2\text{H}_2)(\text{NH}_3)]$ is only 5.8 kcal/mol [23]. The calculations favor an η^2 -in-plane coordination of acetylene, although the energy differences to η^2 -out-of-plane (2 kcal/mol) or σ (7.5 kcal/mol) coordinations are very small. The insertion pathway is shown in Scheme 6.6, along with estimated energy values. The insertion is quite exothermic and the insertion barrier is rather high. The transition state features an acetylene close to σ coordination. The great energy barrier may be ascribed to two factors: (i) the directionality of the methyl orbital, which cannot interact efficiently with both the metal d and acetylene π^* orbitals in the transition state; and (ii) the high energy of the π^* orbital of the acetylene. The latter is estimated as 3.23 eV, compared to 2.66 eV for the corresponding ethylene π^* orbital in $[\text{PdCl}(\text{CH}_3)(\text{C}_2\text{H}_4)(\text{NH}_3)]$. Electron withdrawing substituents in the alkyne will make the insertion easier because they lower the energy of the π^* orbital.

The outcome of the reaction from the T.S. should be a *cis* alkenyl, but it is not rare that *trans* alkenyls are formed. Interestingly, in the vicinity of the transition state (within a few kcal/mol) was found the skewed structure framed in the Scheme 6.6, which might become more stable than the planar transition state upon change of the alkyne or the complex. From this structure, which can be drawn also as an alkyl/carbene chelated ligand, either *cis* or *trans* alkenyl can be formed. This could explain satisfactorily the experimental results.

TABLE 6.4

Experimental [M]X bond energies (kcal/mol) for some organometallic systems

[M]	H	Me	C _n H _{2n-1}	Ph	Other (X)
(Cp*) ₂ (Bu'O)Th(IV)	93.0	83.4	78.9 (Et)	92.6	–
(Cp*)(PMe ₃) ₂ Ru(II)	40.0	34.0	29.0 (Et)	40.0	48.9 (OH)
(CO) ₅ Mn(I)	58.6	44.7	–	49.4	54.0 (I)
(Cp*)(PMe ₃)Hf(III)	74.0	56.0	52.0 (Bu)	82.0	64.0 (I)
(dppe)MePt(II)	25.0	26.0	21.0 (Et)	31.0	40.0 (OH)

6.2.2 Thermochemistry of the insertion into M–H and M–C bonds

Catalytic processes often proceed through thermodynamically unfavorable but feasible equilibria, and depend more on kinetic factors and the existence of an irreversible termination step (a thermodynamic sink). It is interesting, however, to know the thermochemistry of the processes. This can be estimated from the dissociation energies of the bonds to be broken and made in a reaction. A considerable effort has been put for obtaining these data, and a proposal of interpretation of organometallic bond dissociation energies has been offered [24]. The data gathered in Table 6.4 are only meant to reflect the complex dependence of these values on a number of factors that cannot be discussed in simple terms. Usually phenyls show somewhat larger bond energies and *n*-alkyls smaller energies than hydrogen or methyl. These can display very similar or very different values depending on the system involved, and extrapolation to different systems should be avoided.

For processes involving alkenes or alkynes, in addition to the organic C–H, C–C, or π -component of C–C multiple bonds, the data to be considered are the M–H, M–C and M–alkene (or alkyne) bond energies.

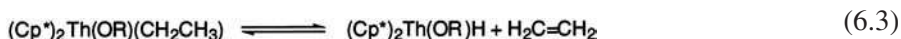
A comparison of the values of $D(\text{M–H})$ and $D(\text{M–C})$ bond dissociation energies is important in processes such as the β -H elimination, which is a termination process of polymerization reactions (Eq. 6.2). In general M–H bonds are stronger than M–C bonds. T. Marks et al. suggest a difference $D(\text{M–H}) - D(\text{M–C})$ for middle and late transition metals typically in the order of 30 kcal/mol, which (corrected for the organic bonds) affords for Eq. 6.2 $\Delta H_{\text{reac}} \approx +10$ kcal/mol, i.e. a slightly endothermic process [25], although it can still become spontaneous when entropic factors ($T\Delta S \approx 6$ to 12 kcal/mol per additional particle in the reaction, near room temperature) are considered [26]. In practice alkyls of middle and late transition metals often decompose via β -hydrogen elimination, and give dimerization or oligomerization rather than polymerization processes.



For early transition metals and for f-elements, β -hydrogen elimination is

more endothermic and the process is clearly spontaneous in the direction of insertion. For instance $D(\text{Th-H}) - D(\text{Th-alkyl})$ is about 20 kcal/mol, which affords $\Delta H_{\text{reac}} \approx +20$ kcal/mol for Eq 6.2, a quantity that will keep ΔG positive after correction for entropy. A similar result is found for U [27], Zr and Hf complexes [26]. This gives early transition elements, lanthanides and actinides a thermodynamic advantage as alkene polymerization catalysts, since the chain termination β -H elimination can be highly endothermic for them.

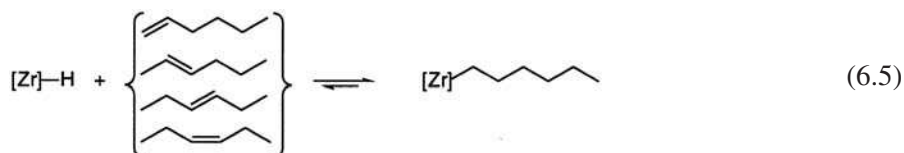
It has been suggested that the low $D(\text{M-H}) - D(\text{M-alkyl})$ values may be related to the high polarity of the M-X ($\text{X} = \text{H}$, alkyl) bonds with these electropositive metals, and the poor ability of the hydridic hydride ligand to stabilize the attendant negative charge, compared to a better ability to delocalize this charge in alkyl ligands. If π -donor ancillary ligands such as alkoxides are used, the extra electrons place additional negative charge on the hydrido ligand, further destabilizing the M-H compared to the M-alkyl interaction (Eq. 6.3, $\Delta H_{\text{reac}} \approx +35$ kcal/mol). This is consistent with the experimental observation of depression of chain termination by β -H elimination in soluble Ziegler–Natta catalysts containing alkoxide ligands [28].



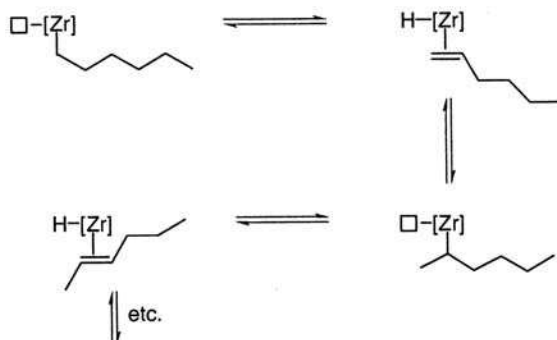
The reaction shown in Eq. 6.4 is exothermic ($\Delta H_{\text{reac}} \approx -13$ kcal/mol) in the direction of insertion. Interestingly, for the corresponding reaction with acetylene, where a weaker π C–C component is broken and a stronger Zr–alkenyl bond is formed, the exothermicity is much greater ($\Delta H_{\text{reac}} \approx -52$ kcal/mol) [26].



Assuming for Eq. 6.4 $T\Delta S \approx 9$ kcal/mol, the small value for $\Delta G_{\text{reac}} \approx -4$ kcal/mol permits facile reversibility of the alkene insertion, double bond migration (by successive β -H elimination/readdition, Scheme 6.7), and the easy thermodynamic manipulation to drive the reaction in either sense, in the so called hydrozirconation of alkenes (Eq. 6.5) [29].



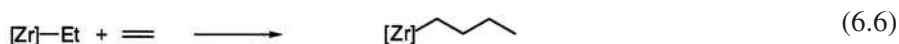
The energy difference between alkene–hydride and alkyl forms is often small, and the preferred structure is based on a subtle balance of electronic and steric factors. The Rh complexes $[(\text{C}_5\text{Me}_5)\text{RhH}(\text{CH}_2\text{CH}_2)\text{L}]^+$ ($\text{L} = \text{P}(\text{OMe})_3$, PMe_3), become $[(\text{C}_5\text{Me}_5)\text{Rh}(\text{CH}_2\text{CH}_2-\mu\text{-H})\text{L}]^+$ when $\text{L} = \text{CH}_2\text{CH}_3$ [30]. The alkene–hydride iron complex $(\text{C}_5\text{Me}_5)\text{FeH}(\text{CH}_2\text{CH}_2)(\text{PMe}_3)$ changes to the inserted form in the isoelectronic cobalt cation $[(\text{C}_5\text{Me}_5)\text{Co}(\text{CH}_2\text{CH}_3)(\text{PMe}_3)]^+$ [31]. These changes are associated to a decrease in electron density in the metal center,



Scheme 6.7.

but structural changes induced by the ancillary ligands can be also decisive. In the series of complexes $[\text{Pt}(\text{C}_2\text{H}_5)(\text{P}-\text{P})]^+$, the complexes with the diphosphines making a seven-membered (o -(Bu^tPCH_2) $_2\text{C}_6\text{H}_4$) or six-membered ($\text{Bu}^t\text{P}(\text{CH}_2)_3\text{PBu}^t$) metallacycle have the structure $[\text{Pt}(\text{C}_2\text{H}_5)(\text{P}-\text{P})]^+$, but if the diphosphine makes a five-membered metallacycle and has a smaller bite angle ($\text{Bu}^t\text{P}(\text{CH}_2)_2\text{PBu}^t$) the complex has the structure $[\text{PtH}(\text{C}_2\text{H}_4)(\text{P}-\text{P})]^+$ [32]. These observations are consistent with the seminal calculations by Thorn and Hoffmann on the model species $[\text{PtH}(\text{C}_2\text{H}_4)(\text{PH}_3)_2]^+$ suggesting a P–Pt–P angle of ca. 95° , increasing to 110° at the transition state [33]. In fact the X-ray structure of the agostic alkyl complex $[\text{Pt}(\text{C}_2\text{H}_5)(\text{Bu}^t_2\text{P}(\text{CH}_2)_3\text{PBu}^t_2)]^+$ resembles that proposed for the transition state of H migration.

The propagation step in a polymerization can be represented by Eq. 6.6 ($[\text{Zr}] = \text{Cp}^*\text{ZrEt}$), and is exothermic. The enthalpy change ($\Delta H_{\text{reac}} \approx -21$ kcal/mol) is essentially due to the breaking and making of C–C bonds, and renders the reaction spontaneous after correction for entropy. The insertion into a Zr–Me bond in Cp^*ZrMe_2 is less exothermic than into the Zr–Et bond ($\Delta H_{\text{reac}} \approx -6$ kcal/mol), due to a greater magnitude of $D(\text{Zr}-\text{Me})$. Larger interligand nonbonded repulsions for Et than for Me seem to be the reason of this difference [26].

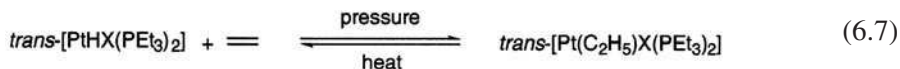


6.2.3 Mechanistic and kinetic studies of the insertion into M–H bonds and the reverse reaction

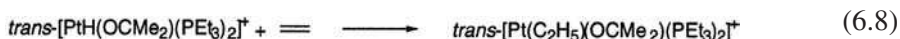
(a) Insertion of alkenes into M–H bonds

The need for insertion of alkenes into M–H bonds to explain alkene hydrogenation [34], hydroformylation [35], isomerization [36], and other processes was recognized in the early 1960s. The reversibility of the process was unambiguously confirmed on the system in Eq. 6.7, where both Pt complexes can be isolated and interconverted under adequate conditions [37]. Decomposition of the isotopi-

cally labeled $[\text{Pt}(\text{CD}_2\text{CH}_3)\text{Br}(\text{PEt}_3)_2]$ produces a mixture of differently deuterated ethylenes, and a mixture of $[\text{PtHBr}(\text{PEt}_3)_2]$ and $[\text{PtDBr}(\text{PEt}_3)_2]$, suggesting a reversible insertion/ β -elimination faster than final decoordination of ethylene [38].



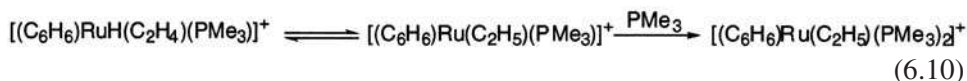
The insertion takes place more readily on a cationic platinum hydride, and an intermediate *trans*-hydrido-ethylene complex was isolated (Eq. 6.8) [39]. Although the *trans*-hydrido-ethylene complex, having the alkene *trans* to the high *trans* influence hydride ligand, is thermodynamically more stable, insertion requires the alkene and hydride ligands to be *cis*. This isomerization occurs more easily on the cationic acetone complex.



The conversion between alkene-hydrido complex and alkyl complex required for the insertion/deinsertion process is evidenced as an equilibrium (Eq. 6.9) in CD_3NO_2 solution for $[\text{CpRhH}(\text{C}_2\text{H}_4)(\text{PMe}_3)](\text{BF}_4)$ (which is obtained by protonation of $\text{CpRh}(\text{C}_2\text{H}_4)(\text{PMe}_3)$ with HBF_4) [40]. The NMR signals of the hydride and the ethylene hydrogens, which appear sharp at low temperature (corresponding to the predominant left side of the equilibrium), become broad humps at room temperature due to exchange. The equilibrium is further confirmed by deuteration experiments with D_2O , whereupon the signals of both Rh-H and C_2H_4 disappear.



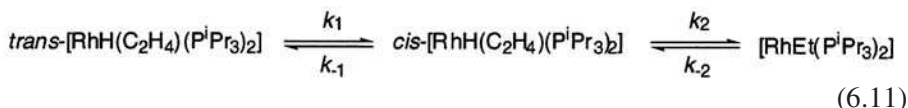
In a related Ru complex the equilibrium can be shifted to the ethyl complex by addition of a tertiary phosphine to block the empty coordination site produced by insertion (Eq. 6.10) [41].



The equilibrium also lies towards the alkyl complex when this is stabilized by the presence of electronegative substituents. Thus the insertion of perfluoroethylene in the corresponding hydride complexes produces *trans*- $[\text{Rh}(\text{CF}_2\text{CF}_2\text{H})(\text{CO})(\text{PPh}_3)_2]$ [42].

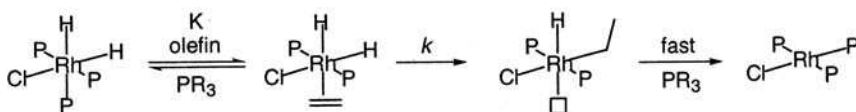
The advent and popularization of more sophisticated NMR experiments, such as magnetization transfer techniques [43], was a great asset for kinetic studies. Using these techniques the equilibrium involving insertion/deinsertion in the complex $[\text{RhH}(\text{C}_2\text{H}_4)(\text{PPr}_3)_2]$ has been studied in detail [44]. A hydride complex is the only species observed by ^1H NMR from -90 to 0°C . Its resonances

broaden above 0°C due to exchange, which is further supported by deuterium labeling experiments. IR spectra in solution, and low temperature ^{31}P NMR spectra reveal the existence of two isomeric hydrides in solution (*trans* : *cis* $\approx$ 3 : 1; ΔG^0 (25°C) $\approx$ 0.5 kcal/mol). Magnetization transfer is observed from coordinated ethylene to the hydride, but not to free ethylene if this is added. These results suggest that the insertion is intramolecular, with a rapid equilibrium between *cis* and *trans* species, and the mechanism in Eq. 6.11 has been proposed. The activation parameters for insertion from the *cis* alkene hydride, calculated from the exchange rates measured between -40 and 0°C, are $\Delta H^\ddagger = 13.0$ kcal/mol and $\Delta S^\ddagger = -2$ eu.

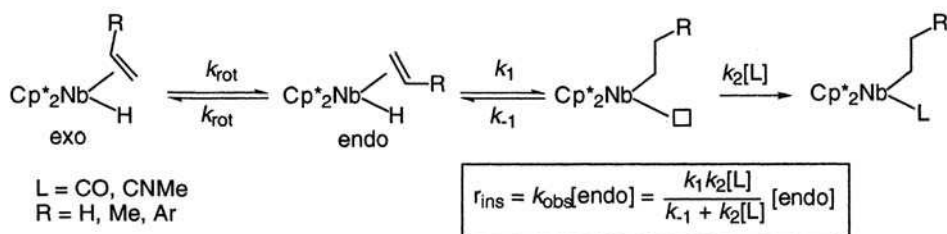


The influence of the electronic properties of the alkene on the insertion rate has been evaluated in the kinetic study of the reaction of a Rh(III) dihydrido complex and *para*-substituted styrenes (Scheme 6.8) [45]. The process is part of the proposed mechanism for the rhodium catalyzed hydrogenation of alkenes. Under pseudo-first order conditions (excess of PR_3 and alkene) in benzene the rate law is $-\text{d}[\text{RhH}_2\text{Cl}(\text{PR}_3)]/\text{d}t = k_{\text{obs}}[\text{RhH}_2\text{Cl}(\text{PR}_3)]$ with $k_{\text{obs}} = Kk[\text{alkene}]/\{[\text{PR}_3] + K[\text{alkene}]\}$. The values of K and k determined for different *para*-substituted styrenes show that more electron withdrawing substituents in the substituted styrene ring increase the value of K (better alkene coordination), but decrease k (slower insertion). These opposite trends tend to cancel each other and the overall rates of the process vary little for different styrenes. K values are in the range 0.3×10^{-3} to 2.5×10^{-3} , and k values in the range 0.1 to 0.5 s^{-1} for $\text{R} = \text{Ph}$. The dependence of k on the Hammett constant σ^+ of the *para*-substituents in the styrene correspond to $\rho^+ \approx -0.9$ and it is suggested that the higher stability of the alkene complex (ground state for the insertion step) is responsible for the lower insertion rates for styrenes with electron withdrawing groups.

The pentamethylcyclopentadienyl niobocene d^2 complexes $[\text{Cp}^*_2\text{NbH}(\text{CH}_2\text{CHR})]$, in which the alkene is coordinated to the metal center *cis* to the metal hydride, with a planar arrangement of the alkene carbon-carbon bond and the metal-hydrogen bond, are ideally suited for insertion without interference of the need for alkene rotation, and have been studied thoroughly [46]. In solution only the endo hydrido-alkene tautomer (Scheme 6.9) is observed by



Scheme 6.8.



Scheme 6.9.

^1H NMR, establishing a lower relative limit $k_{-1} \geq 100k_1$. For ethylene ($\text{R} = \text{H}$) the ethylenic endo hydrogens show magnetization transfer to the hydride but not to the CH_2 group exo, showing that alkene rotation in this case is very slow compared to insertion. Irreversible insertion is induced by addition of a trapping ligand (CO or CNMe), and the reaction kinetics are first order in $[\text{endo}]$ and $[\text{L}]$, in agreement with a rapid insertion/ β -elimination pre-equilibrium, followed by a slow rate-limiting bimolecular trapping.

The exchange rates measured by magnetization transfer and coalescence methods allow one to calculate the insertion rates for the different complexes. Some values are given in Table 6.5. The Arrhenius parameters calculated for the insertion were $\Delta H^\ddagger = 14.7$ kcal/mol and $\Delta S^\ddagger = -11.2$ eu for ethylene, and $\Delta H^\ddagger = 16.0$ kcal/mol and $\Delta S^\ddagger = -6.7$ eu for styrene.

On the other hand, the ground state energies of the alkene hydrido complexes were assessed from the equilibrium constants for competitive binding of ethylene, propene, or styrenes to the Nb center. These differences were minor and the effects on insertion rate observed can then be assigned mostly to the transition state. Although the insertion rate in this system is almost insensitive to the solvent polarity, it is observed that electron-donating groups on the β -carbon accelerate the rate of alkene insertion. This suggests that, although the insertion (and its microscopic reverse β -elimination) proceed through a relatively non-polar cyclic transition state, some fractional positive charge develops at the β -carbon in the

TABLE 6.5

Insertion rate constants for endo- $(\text{Cp}^*)_2\text{NbH}(\text{CH}_2\text{CHR})$ complexes

R	T ($^\circ\text{C}$)	k_1 (s^{-1})	Method
H	39	1.24	magnetization transfer
Me	-1	25.3	coalescence
Ph	48	2.81	magnetization transfer
Ph	59	5.79	magnetization transfer
Ph	70	21.1	magnetization transfer
Ph	83	29.5	coalescence

TABLE 6.6

Rate constants (s^{-1}) and free energies of activation (kcal/mol) for the dynamic processes I and II in Scheme 6.10

R, L	k_I (T , $^{\circ}\text{C}$)	$\Delta G_I^{\ddagger}$	k_{II} (T , $^{\circ}\text{C}$)	$\Delta G_{II}^{\ddagger}$
Me, P(OMe ₃)	6.6 (−84)	10.2	11 (−44)	12.2
Me, PMe ₃	47 (−49)	11.3	8.4 (−49)	12.1
H, P(OMe ₃)	168 (−109)	7.8	1.9 (−10)	15.0
H, PMe ₃	431 (−80)	8.8	0.3 (−23)	15.0

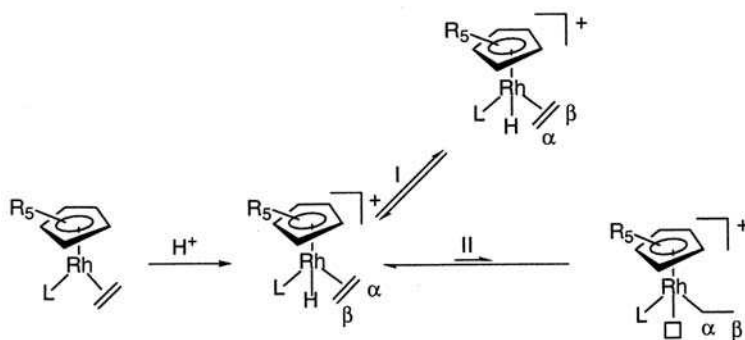
transition state, and the hydrogen migrates more nearly as H^- than as H^+ . This might be the usual case of insertion into hydridic M–H bonds with electropositive metals.

For the third-row analogs $[(\text{C}_5\text{R}_5)_2\text{TaH}(\text{CH}_2\text{CH}_2)]$ ($\text{R} = \text{H}, \text{Me}$) the insertion barriers are about 3 kcal/mol higher than for the Nb compounds [47]. For another d^2 system, $[\text{Cp}_2\text{WH}(\text{CH}_2\text{CHMe})]^+$, a barrier of 24 kcal/mol is found [48]. Interestingly, for the related d^0 complexes Cp^*ScH , where the coordination of the alkene should be less favorable and the Sc–H bond more hydridic, the insertion is too fast to be measured [49].

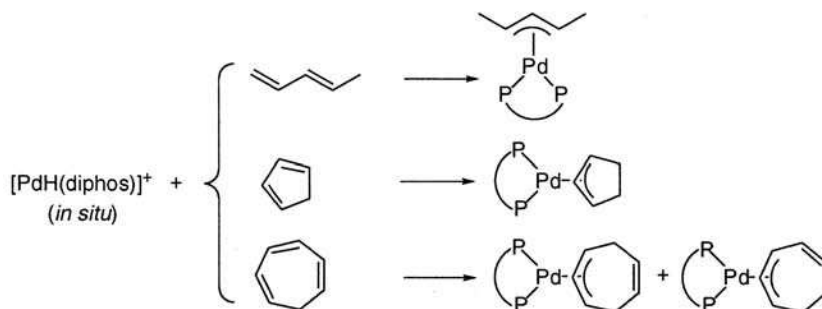
Olefin rotation (process I) and hydride migration (insertion step, process II) parameters have been measured for $[(\text{C}_5\text{R}_5)\text{RhH}(\text{CH}_2\text{CH}_2)\text{L}]^+$ complexes ($\text{R} = \text{H}, \text{Me}$; $\text{L} = \text{P}(\text{OMe})_3, \text{PMe}_3$), obtained by protonation of $[(\text{C}_5\text{R}_5)\text{RhL}(\text{CH}_2\text{CH}_2)]$ (Scheme 6.10), using ^1H and ^{13}C line shape analysis and magnetization transfer techniques [50]. The results are shown in Table 6.6. The Eyring plots for hydride migration afforded $\Delta S^{\ddagger} = 0$ within the experimental error, consistent with an intramolecular process; thus $\Delta G^{\ddagger} \approx \Delta H^{\ddagger}$ is temperature-independent. The rotational barriers are higher the higher the electron density on Rh. The barriers to insertion are insensitive to the ligand L, showing a negligible influence of ligands *cis* to the migrating H group. The influence of the *trans* ligand is higher and a decrease by ca. 3 kcal/mol is observed when Cp (*trans* to H in the pseudo-octahedral complex) is substituted by the more electron donating Cp^* . This may be a reflection of an increased negative charge on the H favoring its migration. Similar trends, with somewhat lower values for the free energies of activation, are observed in the Co analogs [51].

A study of the insertion of alkenes into the M–H bond of the d^0 complex $[\text{Cp}^*\text{ThH}(\text{OR})]$, where the alkene complex is not detected, affords the following order of reactivity: ethylene > 1-hexene > 4-methoxystyrene > styrene $\gg$ cyclohexene. The rates and activation parameters are for the full insertion process, including the insertion and the pre-equilibrium of coordination of the alkene [52].

The insertion of conjugated dienes into M–H bonds is usually irreversible since the product of the reaction is a stable allylic complex. Similarly, non-conjugated



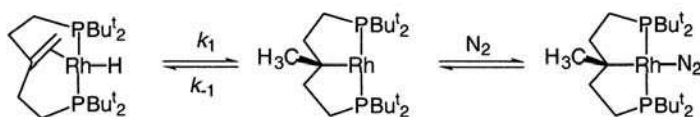
Scheme 6.10.



Scheme 6.11.

dienes provide allylic complexes if metal migration along the chain is permitted (Scheme 6.11) [53–55]. A related insertion into M–C bonds will be discussed in detail later in this chapter.

It is worth noting that, although all the insertion processes discussed imply a *cis* arrangement of the hydride and the alkene, in some special instances insertion from a *trans* arrangement seems feasible. In fact, *trans* insertion of an alkene into an M–H bond without prior isomerization into the *cis* complex has been observed in a rhodium complex geometrically constrained to *trans* geometry (Scheme 6.12) [56]. The X-ray structures of the hydride and the dinitrogen complexes have been determined. In the former the C=C double bond plane does not lie perpendicularly to the Rh–H bond; the C=C–Rh angle is about 73°, and a further shift of the hydride provides a ‘*cis* arrangement’ in the transition state at a reasonable energetic cost. The activation parameters for the hydride migration are $\Delta H^\ddagger = 7.1$ kcal/mol, $\Delta S^\ddagger = -39.3$ eu, and $\Delta G_{298}^\ddagger = 18.8$ kcal/mol, with $k_1 = 0.197$ s⁻¹ at 40°C. The less stable 14-electron intermediate was not directly observed, but its trapping by N₂ has a substantially higher barrier than that of the β -elimination process. Dissociation of N₂ from the dinitrogen complex

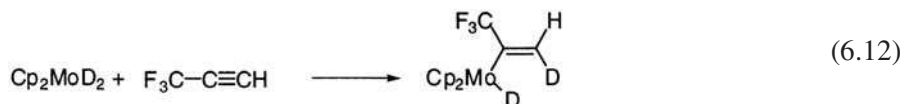


Scheme 6.12.

($\Delta G_{298}^{\ddagger} = 24.1$ kcal/mol) is the rate-determining step for its conversion in the hydrido-alkene species.

(b) *Insertion of alkynes into M–H bonds*

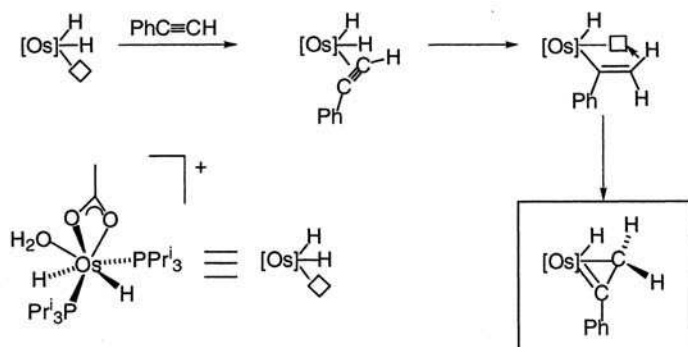
The insertion of alkynes to give alkenyl products is often irreversible. The insertion is usually *cis*, as expected from a four-center concerted mechanism (e.g. Eq. 6.12) [57,58]. Exceptions have been reported, generally for di- or mono-substituted alkynes with electron withdrawing substituents.



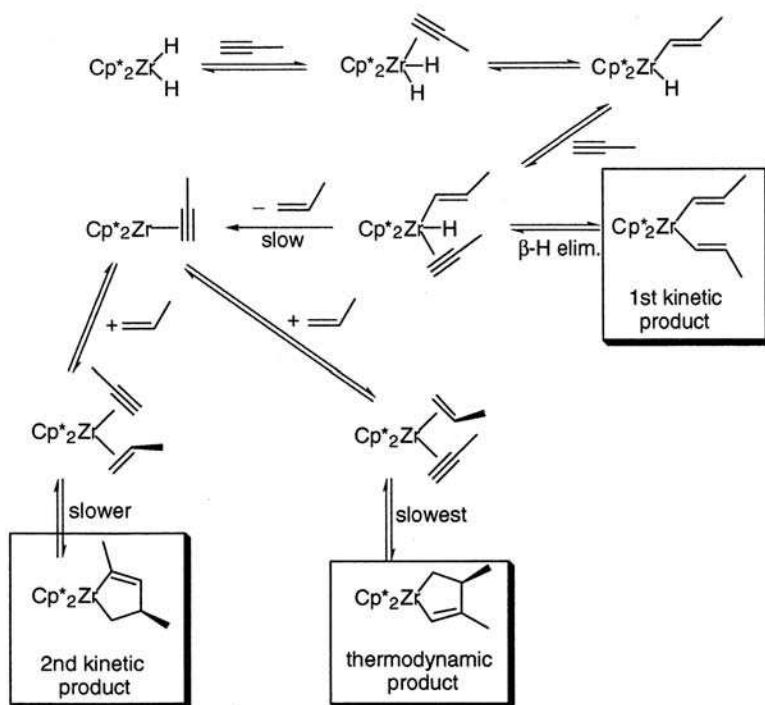
In some cases the *cis* product is observed first and then isomerization to the final *trans* product occurs [59], but sometimes the only product observed is the *trans* derivative. *Trans*-[PtHCl(PEt₃)₂] in polar solvents reacts with DMAD (MeO₂C≡CO₂Me) to give the *cis* alkenyl product, as expected from the four-center transition state [60], but in benzene it gives a mixture of *cis* and *trans* alkenyl, and in the presence of a catalytic amount of a free radical initiator only *trans*-alkenyl is formed, supporting that a radical chain mechanism could be operating also [61]. Further data on the insertion of alkynes containing electron withdrawing substituents in *trans*-[PtH₂L₂] complexes confirmed the participation of a radical pathway from ESR studies on the reaction mixtures [62].

A different way to obtain *trans*-alkenyls is the isomerization of the initial *cis*-alkenyl or its direct formation from a skewed intermediate such as that framed in Scheme 6.6. Interestingly, the insertion of phenyl acetylene into an Os–H bond affords a metallacyclopropene which has exactly that skewed structure, as determined by single crystal X-ray diffraction (Scheme 6.13). This unequivocally demonstrates the feasibility of that kind of structure as intermediates or transition states for the isomerization of transition metal alkenyls [63].

An example of reversible insertion of alkynes into M–H bonds has been reported in the context of the reactivity summarized in Scheme 6.14 [64]. The three products framed are successively formed. The formation of the two zirconacyclopentenes from the bispropenyl initial kinetic product requires β -H elimination followed by reductive elimination of propene, its coordination to give a propene-propyne complex, and finally oxidative coupling of the two unsaturated ligands.

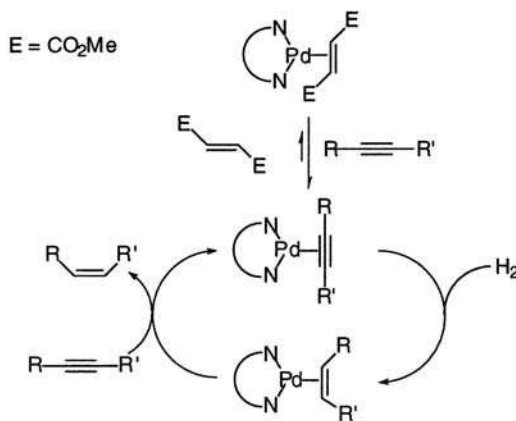


Scheme 6.13.



Scheme 6.14.

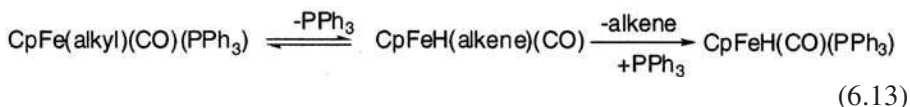
A method for the selective hydrogenation of alkynes to (Z) alkenes has been described using a $\text{Pd}(0)$ complex as catalyst (Scheme 6.15) [65]. The mechanism has not been elucidated, but the catalytic cycle probably involves the formation of an alkyne $\text{Pd}(0)$ complex, oxidative addition of H_2 , insertion, and reductive elimination of the hydride-alkenyl.



Scheme 6.15.

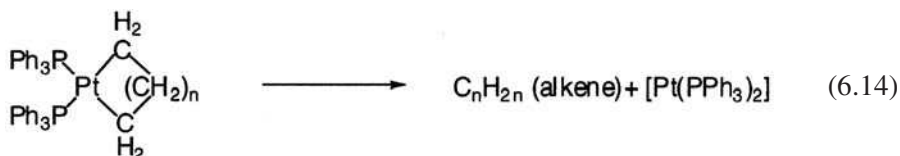
(c) β -H elimination from *M*-alkyl

During the discussion of the insertion reaction we have seen that very often the insertion process is reversible and very fast, as shown by the fast exchange of α -, β -, and hydride hydrogens. The β -H elimination process is a most important way of decomposition of transition metal alkyls, and many studies deal with their thermal decomposition. An available *cis* coordination site is required to get to the transition state, and this explains the kinetic stability of metal complexes coordinatively saturated with tightly bound ligands, which should in principle dissociate prior to β -H elimination. This is the picture provided by the kinetic studies on the thermolysis of $[\text{CpFe(alkyl)(CO)(PPh}_3)]$ complexes shown in Eq. 6.13., where the addition of PPh_3 blocks the reaction completely [66]. In this case, the lack of isotope effect using alkyls deuterated at the β position, and the observation of H-D scrambling and skeletal isomerization from branched to straight-chain alkyls, suggest that alkene dissociation is the rate-determining step for thermolysis.



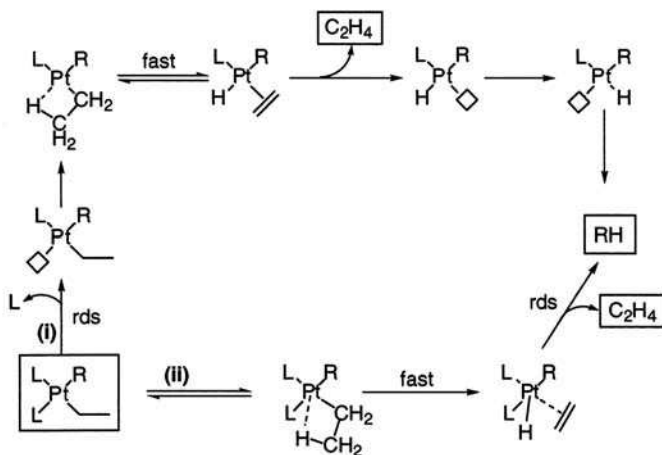
Still the most common picture for β -H elimination is this sequence: Creation of a vacant *cis* site, reversible β -H elimination via a planar four-center transition state, and displacement or loss of the coordinated alkene. If the lack of a vacant *cis* site explains the stability of many complexes, the inherent difficulty to produce a planar four-center transition state is probably responsible for the stability of metallacycles, as compared to simple alkyls. The decomposition rates of $\text{Pt}(\text{CH}_2)_n(\text{PPh}_3)_2$ (Eq. 6.14) illustrate this fact dramatically: The complexes with $n = 4, 5$ are 10^4 times more stable than the complex with $n = 6$, because the former are less flexible, and the corresponding planar four-center transition state

for β -H elimination is higher in energy. The seven-membered metallacycle can adopt this structure almost as easily as the freely rotating simple alkyls, and its decomposition rate to give alkenes is about two-thirds that of di-*n*-alkyls [67].

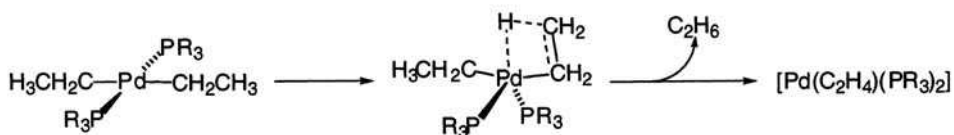


However, there are exceptions to this simple picture. The thermolysis of bis(alkyl) Pt and Pd complexes has been studied in detail, and displays a somewhat more complex behavior [68,69]. For complexes *cis*-[PtRR'(PPh₃)₂] with different alkyls, the thermolysis gives alkane and alkene in a 1 : 1 ratio, and the thermolysis rate is severely reduced by addition of PPh₃. If R and R' are different each one undergoes β -H elimination to the alkene statistically, according to the number of β -H atoms on each alkyl (for instance, for ethyl/propyl the ratios are ethane : ethylene = propylene : propane = 2 : 3). In the absence of added phosphine, using alkyls deuterated at the β -carbon no isotope effect was found, and H-D scrambling was observed in the alkene/hydride, but not in the R group giving rise to RH (or RD). This supports a decomposition path (i, Scheme 6.16) that starts by a rate determining dissociation of ligand to produce a 14-electron intermediate, which then undergoes fast and reversible β -H elimination followed by alkene dissociation, isomerization and reductive elimination of RH.

In the presence of added PPh₃ the dissociative pathway becomes very slow and the associative pathway (ii), through an 18-electron pentacoordinated intermediate or transition state, becomes dominant. H-D scrambling and no isotope effect are again observed in this case.



Scheme 6.16.

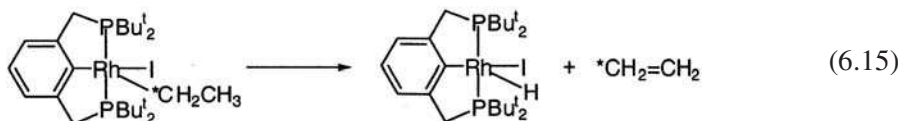


Scheme 6.17.

For the thermolysis of *trans*-[PdEt₂(PR₃)₂] the results are very different: The reactions are retarded only slightly by added phosphine, and no H–D scrambling occurs, suggesting that the β -H elimination is irreversible in this case. Thus the decomposition of *trans*-[Pd(CH₂CD₃)₂(PR₃)₂] evolved only a 1 : 1 mixture of CH₂=CD₂ and CD₃CH₂D, and showed a moderate isotope effect ($k_{\text{H}}/k_{\text{D}} = 1.4 \pm 0.1$) supporting that β -H elimination is rate-determining. Phosphines with larger cone angles produce increased thermolysis rates. The decomposition is suggested to occur through a transition state with an almost trigonal bipyramidal structure at which the β -H atom is transferred from one Et group to the other in an irreversible process (Scheme 6.17) [70].

A kinetic study on the β -H elimination from monoalkyl complexes *cis*-[PtRBr(PEt₃)₂] in acetone, in the presence of an excess of halide to prevent concurrent isomerizations, shows that the ethyl complex decomposes at a rate ten times slower than that of n-propyl or n-butyl analogues [71]. The activation parameters for R = Et are $\Delta H^\ddagger = 101 \pm 2$ kJ/mol, $\Delta S^\ddagger = +5 \pm 4$ J/K mol, and $\Delta G^\ddagger_{298} = 27.5$ kcal/mol. For *cis*-[Pt(*n*-C₄H₉)X(PEt₃)₂] the rates of decomposition increase in the order X = N₃ < NO₂ < Cl < NCS < Br < NCSe < I. A mechanism involving fast and reversible β -H elimination in a pre-rate-determining step, followed by slow alkene loss from a 5-coordinate [Pt(H)X(alkene)L₂] intermediate is proposed.

An irreversible β -H elimination is observed in the decomposition of PCP-based rhodium(III)–alkyl complexes (Eq. 6.15) [72]. Isotopic labeling with ¹³C proves that there is no incorporation of ¹³C in the methyl end of the ethyl ligand, discounting fast reversible β -H elimination. This occurs in an irreversible fashion. Deuterium labeling reveals a kinetic isotope effect of $k_{\text{H}}/k_{\text{D}} = 1.4$ for ethyl, supporting that β -H elimination is rate determining. The activation parameters in toluene were $\Delta H^\ddagger = 21.2$ kcal/mol, $\Delta S^\ddagger = -21.1$ eu, and $\Delta G^\ddagger_{298} = 27.5$ kcal/mol.



Rate-determining β -H elimination has been observed in other cases. The thermolysis of deuterium labeled [Ir(octyl)(CO)₂(PPh₃)] shows a kinetic isotope effect of $k_{\text{H}}/k_{\text{D}} = 2.28$ [73]. For [CoEt₂(acac)(PMe₂Ph)₂] a similar value of 2.30

is found, indicating that, again, the β -H elimination is rate determining in spite of the fact that, in the Co complex, ligand dissociation is needed [74].

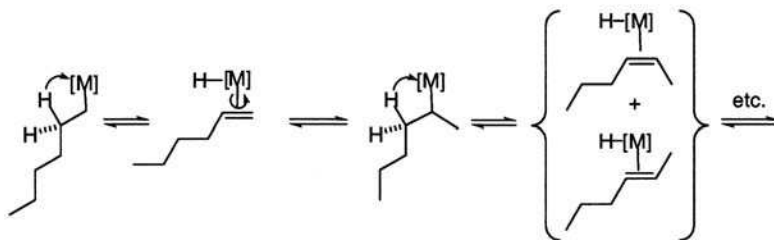
Coordinative unsaturation not necessarily provokes easy β -H elimination, and thermally stable unsaturated (Tp^{iPr})MEt complexes of Co and Fe ($\text{Tp}^{\text{iPr}} = \text{hydrotris}(3,5\text{-diisopropylpyrazolyl})\text{borate}$) have been reported [75]. These tetrahedral complexes are formally 14- and 15-electron species, respectively, and react with CO to give insertion and coordination, increasing its coordination number to 6 for Co, and 5 for Fe. However, they are resistant to β -H elimination and only small amounts of ethane or ethylene are formed upon heating in heptane several hours at 110°C . This is attributed to the fact that these species are high spin ($\mu = 5.0\mu_{\text{B}}$ for Co; $\mu = 4.2\mu_{\text{B}}$ for Fe) and all their non-bonding d orbitals are fully or half occupied. Thus, the coordinative unsaturation is deceptive and in fact the complexes lack low-lying empty d orbitals.

(d) Combining β -H elimination/insertion: metal migration (chain walking), alkyl isomerization, and alkene isomerization

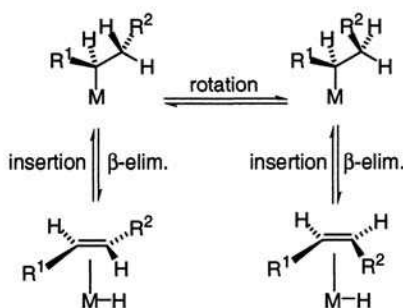
The effect of successive insertion and β -H elimination episodes on a coordinated alkene-hydride (or on a transition metal alkyl) is represented in Scheme 6.18. The metal can migrate along the alkyl chain, provided that: (a) the next β -carbon offers a hydrogen susceptible to β -H elimination; and (b) the rotation about the M-(alkene) bond is easy. The expression ‘chain walking’ (or ‘chain running’) is used to describe this migration [76].

If the initial and final products of the chain walking are alkyls, the process produces alkyl isomerization to the thermodynamically more stable alkyl complex. This can be the one with less steric requirement (the terminal one) as in the hydrozirconation reaction shown in Eq. 6.5, or an internal alkyl if an M-C(internal) bond is particularly strong. When the initial and final products are alkenes which can coordinate to and decoordinate from the metal (and this decoordination can be induced by the reaction conditions or by steric and electronic factors), the result of the process is an alkene isomerization.

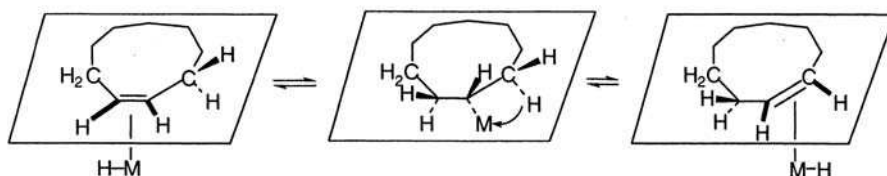
When the double bond is differently substituted there is the possibility of *cis* and *trans* (or *E* and *Z*) isomers. The alkyl intermediate in a simple alkyl chain can



Scheme 6.18.



Scheme 6.19.

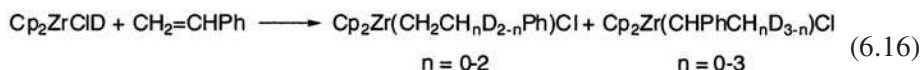


Scheme 6.20.

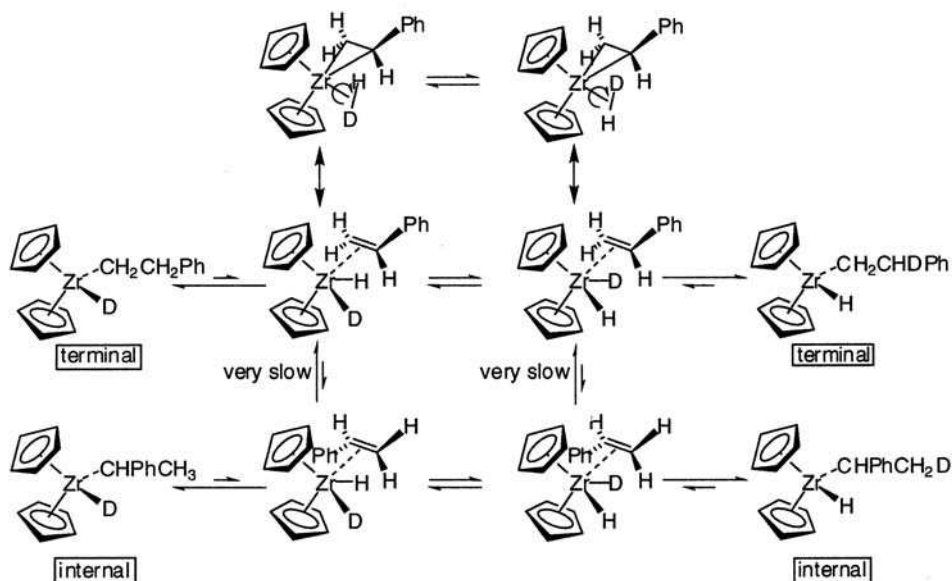
freely rotate about the $C_\alpha-C_\beta$ bond, changing the H that will be eliminated and the stereochemistry of the alkene produced (Scheme 6.19). Usually at least some selectivity will be observed towards the more stable alkene on steric grounds.

On the contrary, when the chain walking is operating in a cyclic system (Scheme 6.20), the rotation about the $C_\alpha-C_\beta$ bond is severely hindered (unless the carbocycle is extremely large and flexible) and the metal is confined to walk all the time on the same face of the cycle.

The alkyl isomerization associated to hydrozirconation leads usually to terminal alkenes, but in contrast to most alkenes, the hydrozirconation of styrene gives a mixture of terminal (85%) and internal (15%) isomers, a ratio that does not change on prolonged standing at room temperature. On the other hand, ^2H NMR studies on the products obtained using a zirconium deuteride (Eq. 6.16) show that, for each isomer, deuterium scrambling into the β positions is complete in minutes, whereas the scrambling into the α positions is less than 20% of statistical after one week [77]. The whole process is found to be catalyzed by a small amount of the hydrido alkyl complex $[\text{Cp}_2\text{ZrHR}]$ where the scrambling takes place. H for Cl exchange between the hydrido catalyst and the chloro complexes leads to the products in Eq. 6.16.



These results are well understood within the frame of Scheme 6.21, where the processes leading to exchange of one H for one D are shown. Considering the



Scheme 6.21.

terminal alkyl at the left of the Scheme, β -H elimination, H-for-D exchange at the coordination sphere (possibly via a transition state close to a H-D complex), and D readdition produces the fast scrambling observed for the β hydrogens. The same process holds for the internal alkyl complex. The scrambling between the α and β hydrogens usually observed in other systems occurs because the α and β carbons in the alkyl undergo fast exchange; in other words there is a fast metal migration from one to the other. This migration requires rotation of the coordinated alkene in such a way that the two carbons in turn get close to the migrating H (or D), and produces the isomerization between terminal and internal complexes. The fact that this is observed as a very slow process indicates that the alkene rotation has a very high activation barrier (perhaps corresponding to alkene dissociation), making the metal migration a high energy slow process.

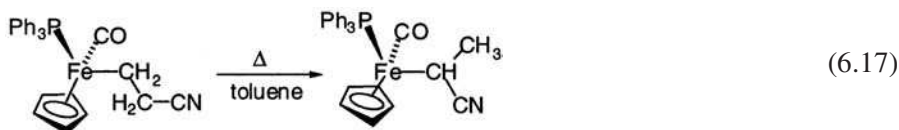
The evaluation of thermodynamic factors in the metal migration is better achieved in systems without severe kinetic influences. The isomerizations observed in alkyl complexes $[\text{Pd}(\text{alkyl})(\text{S}_2\text{CNMe}_2)(\text{PR}_3)]$ (prepared from the reaction of $[\text{PdCl}(\text{S}_2\text{CNMe}_2)(\text{PR}_3)]$ and the appropriate alkyl lithium or Grignard reagent) reveal a number of interesting points (Table 6.7) [78]. The terminal:internal ratio for different alkyls when the internal isomer bears a secondary alkyl, is always very close to 10:1 for different alkyls and ligands. This equilibrium corresponds to a free energy difference of 1.6 kcal/mol, which is believed to represent the difference in stabilization between M-C(primary) and M-C(secondary) in the absence of steric constraints or other factors. Tertiary

TABLE 6.7

Equilibria positions of alkyl isomerization reactions in $[\text{Pd}(\text{alkyl})(\text{S}_2\text{CNMe}_2)(\text{PR}_3)]$

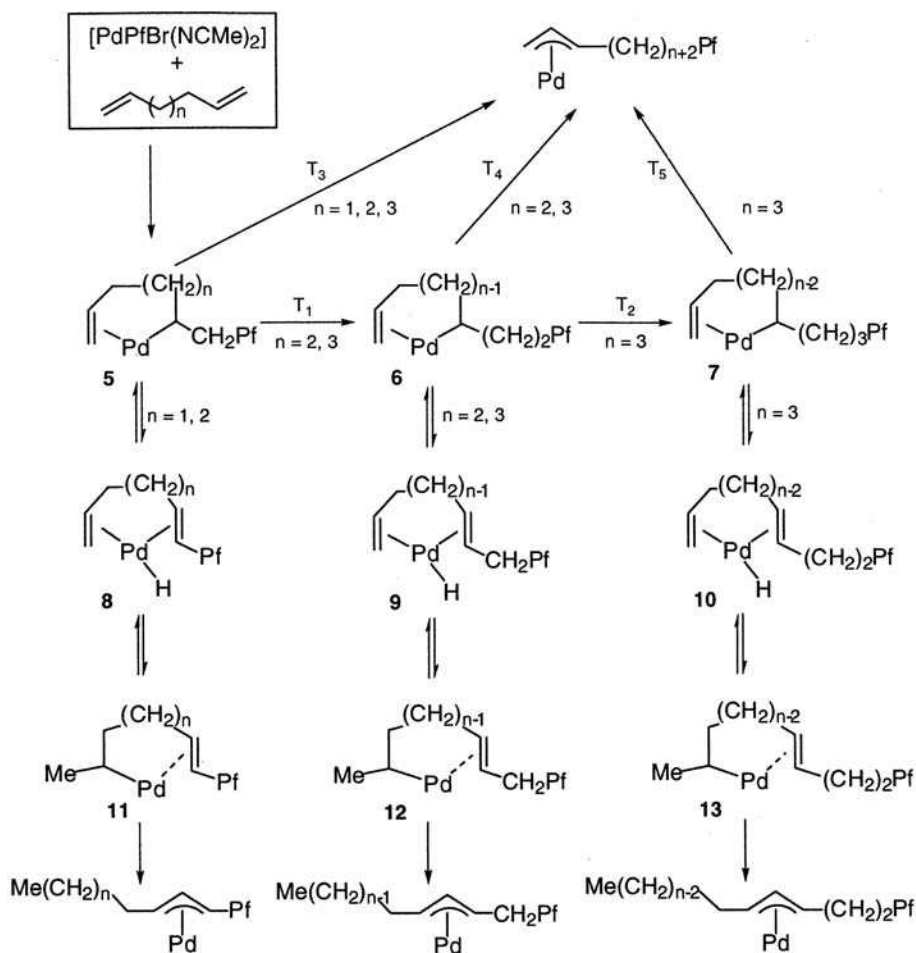
Terminal : internal alkyl ligand isomers	Isomer ratio
$-\text{CH}_2\text{CH}_2\text{CH}_3 : -\text{CH}(\text{CH}_3)_2$	10 : 1
$-\text{CH}_2\text{CH}(\text{CH}_3)_2 : -\text{C}(\text{CH}_3)_3$	'infinite'
$-\text{CH}_2\text{CH}_2\text{CN} : -\text{CH}(\text{CN})\text{CH}_3$	'zero'
$-\text{CH}_2\text{CH}_2\text{CF}_3 : -\text{CH}(\text{CF}_3)\text{CH}_3$	1 : 1

carbons are more disfavored and the isomerization to the primary isomer is complete. The presence of the electron-withdrawing substituent completely reverses the equilibrium in favor of the isomer having the metal on the secondary carbon bearing the CN group, a behavior also observed in Fe complexes (Eq. 6.17) [79]. In the case of the iron complex, the isomerization towards the internal alkyl had been explained considering that a carbon with electron-withdrawing substituents (which introduce a polar contribution in the M–C bond) should produce a stronger bond. However, the more thorough study in Pd shows that a substituent CF_3 , similar to CN in electron withdrawing ability, produces a 1 : 1 mixture of the two isomers. This change from the usual 10 : 1 to 1 : 1 must be the effect of polarity only in the M–C bond, and should be about the same for CF_3 and for CN. The superior stabilization in the case of CN is then attributed to π interactions of CN with metal orbitals, that are reflected in a 50 cm^{-1} shift of $\nu(\text{CN})$ to lower frequencies.



The thermodynamic sink of a metal in a chain walking process is often determined by the best position in the carbon chain to block efficiently the vacant position by the intervention of a heteroatom (leading to a chelated metallacycle), or a double bond (leading to an allyl). The ability of Pd to migrate along a chain even to remote positions can be seen in the formation of palladium allyls from Li_2PdCl_4 , organomercurials, and 1,4-, 1,5-, 1,6-, and 1,7-dienes. This involves arylation of Pd by the organomercurial RHgCl , insertion of one double bond into the Pd–R bond, and chain walking of Pd to form the allyl complex [80]. The formation of η^1 - η^2 -enyl palladium complexes that thermally migrate to allyl complexes has been proved, and X-ray structures of these intermediates have been studied [81,82].

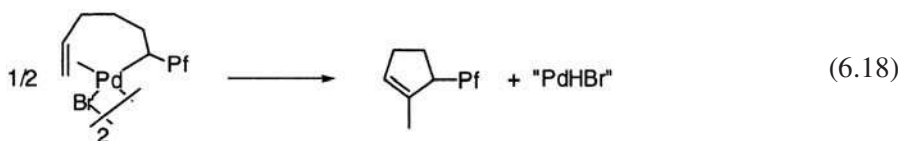
All possible processes associated to chain walking can be seen operating in the study of the reaction of $[\text{Pd}(\text{C}_6\text{F}_5)\text{Br}(\text{NCMe})_2]$ with linear dienes. The initial insertion is highly regioselective, with addition of the C_6F_5 group (Pf) to the terminal carbon. Nevertheless, a number of different products are observed. Mon-



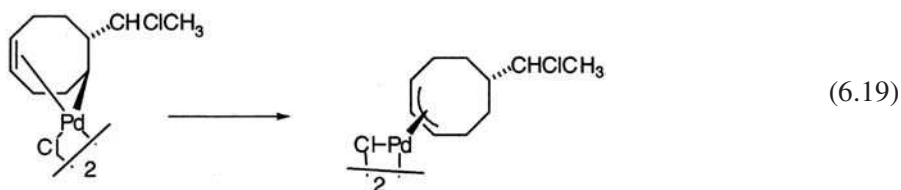
Scheme 6.22.

itoring by NMR the reaction with the stoichiometric amount of 1,5-hexadiene, 1,6-heptadiene or 1,7-octadiene, under temperature control, it was possible to detect at low temperature the formation of the $\eta^1\text{-}\eta^2$ -enyl palladium complexes **5–7** (Scheme 6.22) that isomerize sequentially at different temperatures depending on the ring size of the palladacycle ($T_{\text{isomerization}}$: 7.5- < 6.6- < 5.5-membered ring) [83]. These $\eta^1\text{-}\eta^2$ -enyl palladium derivatives are steps of the Pd-migration process, arrested by coordination of the unattacked double bond. The final products of their isomerization are several isomeric $\text{Pf-}\eta^3$ -allylpalladium complexes. Although the major allylic derivative in each case arises from Pd migration to the terminal double bond, minor amounts of η^3 -allylpalladium complexes formed

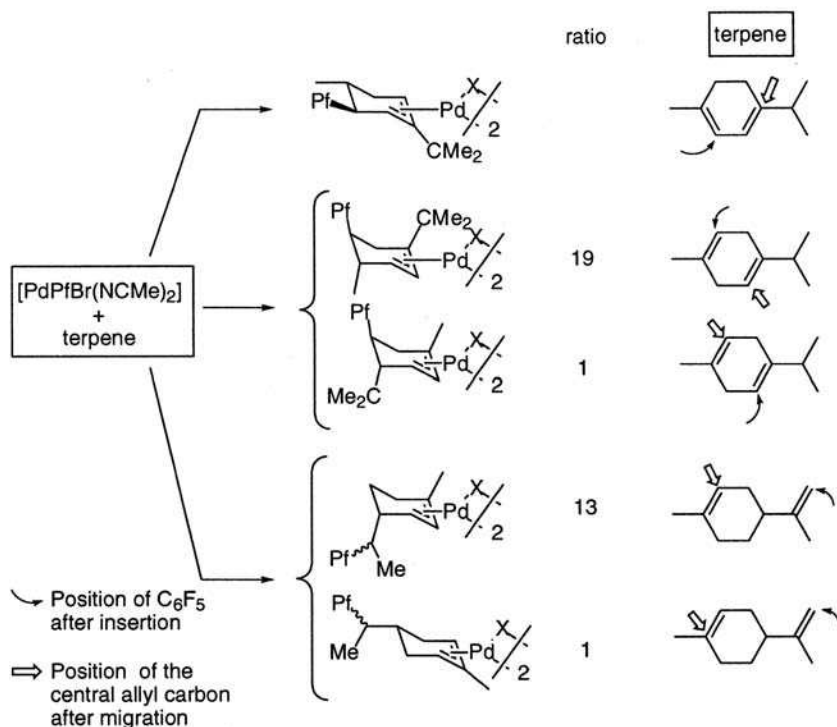
by double bond switch in the process of Pd migration are also seen. This occurs in non-observed 1,5- or 1,6-diene-hydrido-palladium intermediates **8–10**. A small amount of cyclic organic derivatives was detected in each case, coming from the cyclization of η^1 - η^2 -enyl palladium intermediates (Eq. 6.18). The use of excess diolefin gives rise to additional η^3 -allyl palladium complexes without the Pf group, and to the corresponding Pf-substituted linear dienes. These are formed via displacement of the Pf-dienes by the starting diolefin in a hydrido palladium intermediate during the Pd-migration process. Considering the number of ways of evolution of the system, with their corresponding activation barriers, this example shows that it is not surprising that the reaction conditions will play a decisive role in the outcome of reactions where metal migration is involved.



The metal migration along cyclic structures occurs with face retention (e.g. Eq. 6.19) and this has been unequivocally demonstrated with the aid of X-ray determinations [82,84].

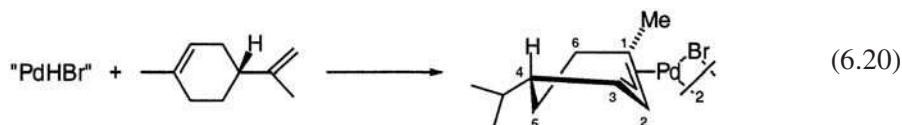


Metal chain walking in alkyl chains and face retention in cyclic systems can be combined for the diastereoselective preparation of cyclic allyl palladium systems. The reactions in Scheme 6.23 are illustrative (some very minor products can also form) [85]. For the cyclohexadienes the chemoselectivity towards insertion of the less hindered double bond is very high, and the regioselectivity (addition of the C_6F_5 group to the less substituted carbon) is excellent. For the two isomers of limonene the insertion of the exocyclic double bond occurs, and the migration of Pd to the cyclohexene moiety is controlled by the stereochemistry of the chiral carbon: the Pd atom can only 'enter the cycle' on the face of the H atom in this chiral carbon, and this forces the stereochemistry of the palladium allyl formed. From that carbon the chain walking in the cycle can take any of the two directions towards the double bond, and both allyls are found although in very different ratios. Due to the lack of stereoselectivity in the insertion reaction, the external chiral carbon produced can have any of the two conformations. Thus in an enantiomerically pure limonene, the stereochemistry of the allyl moiety is fixed by that of the original chiral carbon, but up to four diastereomers are formed due to the two stereochemically different allyls and the two conformations of the external chiral carbon.



Scheme 6.23.

Using a synthon of PdHBr, the insertion of the external double bond of limonene does not produce a new chiral carbon, and this source of stereoisomerism is removed. Then the ‘gated migration’ of Pd into the cyclohexene fragment affords enantioselectively a chiral Pd allyl complex (85% yield) along with other minor products (Eq. 6.20) [55].

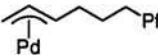
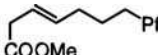
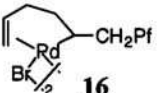
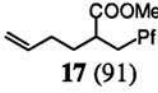
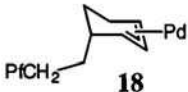
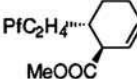
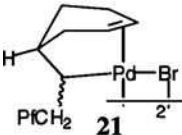
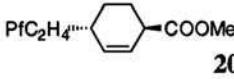
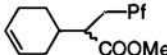
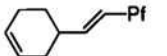


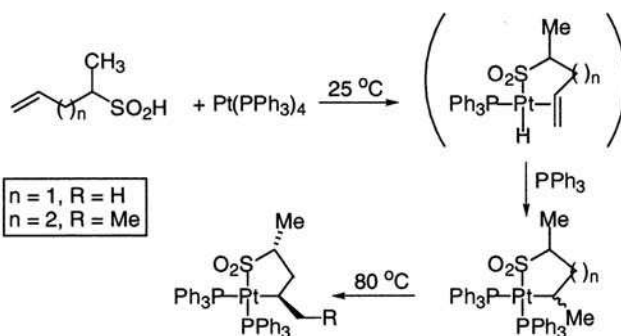
Temperature control of the chain walking has been applied with moderate success for synthesis of esters derived from thermodynamic η^3 -allyls or kinetic σ - η^2 -enyl palladium intermediates by carbonylation in methanol [86]. Some results are shown in Table 6.8.

Regioselective intramolecular hydroplatination of compounds obtained by oxidative addition of sulfinic acids, is followed by Pt migration (if needed to give a 5-membered metallacycle) and reversible dehydrometallation to afford a metallacycle with two chiral centers in a highly stereoselective way, as seen in Scheme 6.24 [87].

TABLE 6.8

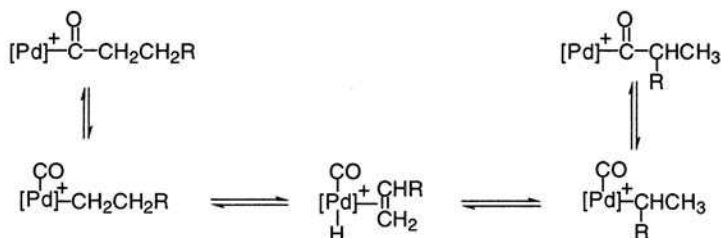
Ester formation from arrested migration intermediates

Diene	η^1 - η^2 -Enyl/ η^3 -allyl (ratio, %)	Product (ratio, %)
1,5-hexadiene	 14	 15
1,5-hexadiene	 16 / 14 (90/10)	 17 (91), 15 (9)
4-vinyl-1-cyclohexene	 18	 19 (48)
4-vinyl-1-cyclohexene	 21 / 18 (74/12)	 20 (48)
4-vinyl-1-cyclohexene		 22 (69)
		 23 (2)
		19 (6), 20 (6)

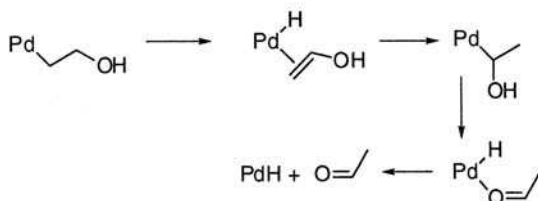


Scheme 6.24.

A nice example of reversibility of the insertion of both alkenes and CO is provided by the isomerization of the acyl complex $[\text{Pd}(\text{CO}'\text{Pr})(\text{PPh}_3)_2(\text{MeCN})]\text{BF}_4$, which takes place also with acyls with different alkyl chains [88]. The complexes isomerize to equilibrium mixtures with a different alkyl chain, where the more stable isomer is that having the least branching in the alkyl group. The isomerization is first order in metal complex and inverse first order in MeCN, and is inhibited by PPh_3 . It involves CO deinsertion followed by reversible H abstraction, and finally CO reinsertion as shown in Scheme 6.25.



Scheme 6.25.



Scheme 6.26.

A combination of β -H elimination reactions seems to be operating in the last steps of the Wacker process, once the coordinated ethylene has been transformed into a hydroxyethyl group (Scheme 6.26) [89].

Chain walking is a typical side reaction in the polymerization of alkenes, producing branching, and many examples can be found [76].

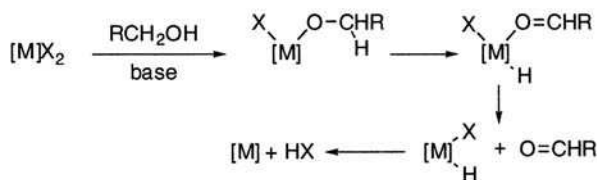
(e) β -H elimination from M -allyl and M -alkenyl

β -H elimination from allylic complexes leads to 1,3-dienes and this is the final step of some synthetically useful reactions such as the Pd-catalyzed elimination of acetic acid from allylic acetates to give 1,3-dienes. The β -H elimination is believed to be analogous to that in the alkyl complexes, by previous isomerization of the allyl moiety from η^3 to σ . However, recently some studies suggest that alternative mechanisms can be operating, sometimes simultaneously, such as direct deprotonation of the H in β position to the allyl group [90–92], or even, in some special cases, a cyclic mechanism outside the metal coordination sphere [93].

The reversible β -H elimination from alkenyl complexes, as a mechanism of isomerization of the alkenyl ligand has been discussed before (Scheme 6.14).

(f) β -H elimination from other M -E-CH groups

The chemistry of alkoxides, amides, and related groups has been reviewed [94,95].

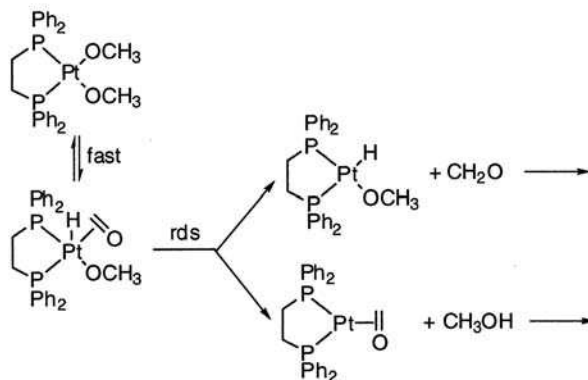


Scheme 6.27.

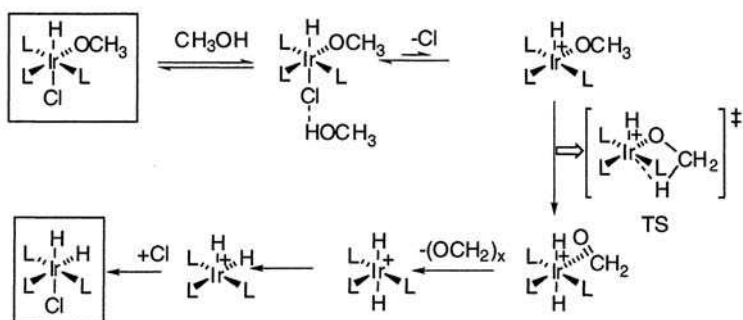
Alkoxides. β -H elimination from alkoxides is responsible for the reducing properties of alcohols towards some transition metal complexes, particularly in the presence of base. The formation of a metal alkoxide followed by β -H elimination affords a hydride. Decoordination of the aldehyde and HX elimination, if the hydride is unstable, will reduce the oxidation state of the complex in two units, often leading to decomposition products (Scheme 6.27).

Alkoxides of early transition metals (oxophilic metals) are well stabilized by π donation of the oxygen lone pairs to the metal, and β -elimination is disfavorable. On the contrary, the decomposition of late transition metal alkoxides to metal hydrides is easy although comparison of alkyls and alkoxides is not simple. The thermal decomposition of $[Pt(OCH_3)_2(dppe)]$ occurs at 25°C to give methanol and formaldehyde. $[Pt(OCd_3)_2(dppe)]$ shows no isotope effect. The activation parameters are inconsistent with a dissociative mechanism: $\Delta H^\ddagger = 15.4 \pm 0.5$ kcal/mol, $\Delta S^\ddagger = -24 \pm 5$ eu. A mechanism involving a fast reversible β -H elimination pre-equilibrium followed by rate-determining release of the organic products is proposed (Scheme 6.28) [96].

$[Pt(CH_2CH_3)_2(dppe)]$ requires temperatures over 150°C to give ethylene and ethane. Compared to the previous case it might appear that the alkoxo derivatives are thermodynamically less stable than the corresponding alkyls. However, in the mixed compound $[Pt(CH_2CH_3)(OCH_3)(dppe)]$, the β -elimination occurs at



Scheme 6.28.

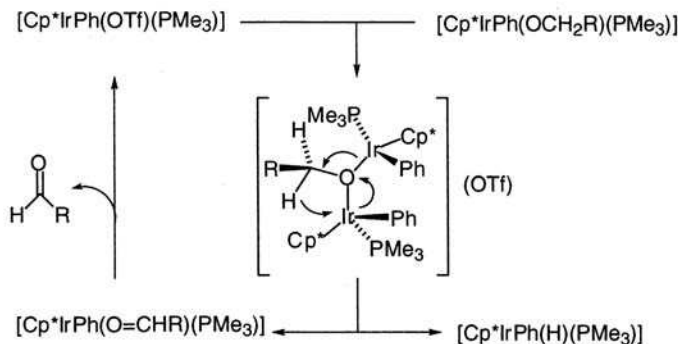


Scheme 6.29.

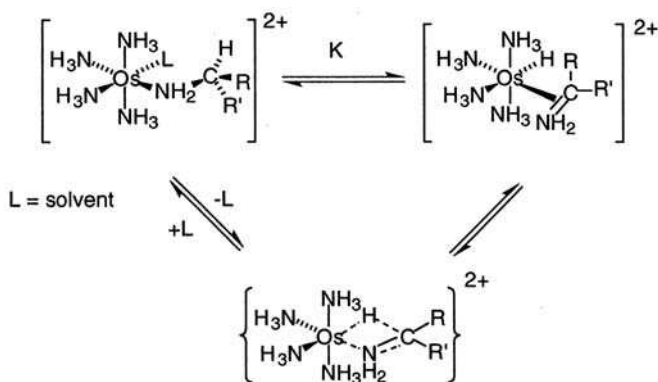
100°C, and gives a ratio ethane : ethylene = 2 : 3 meaning that it operates faster on the ethyl group than on the methoxide. It is suggested that the differences in rate are associated to the transition state (the presence of polar ligands like methoxide can accelerate β -elimination from both alkyl and alkoxo substituents), and not the ground state for the M–O and M–C bonds. The strengths of these bonds for group 8–10 metals are similar to each other [97]. In other words, the higher instability of alkoxo derivatives for late transition metals, as compared to alkyls, is kinetic in nature.

An elegant study of the decomposition of octahedral alkoxo complexes *mer-cis*-[IrH(OR)Cl(PR'₃)₃] (R = Me, Et, ⁱPr; H *trans* to Cl) in alcohol/benzene solution to give *mer-cis*-[IrH₂Cl(PR'₃)₃] and the corresponding aldehyde or ketone offers a different result. The mechanism starts by a pre-equilibrium of Cl dissociation which is induced by alcohol coordination to the halide. This is followed by irreversible rate-determining β -H elimination through the sterically favored transition state, facile irreversible dissociation of the carbonyl compound, ligand rearrangement, and reassociation of the chloride (Scheme 6.29) [98]. This proposal is supported by kinetic studies on the effect of complex concentration (first order), the alcohol, which serves as catalyst (1.33 order), the nature of the phosphine, and the reaction medium. The kinetic isotope effect (combined primary and secondary) for the decomposition of *mer-cis*-[IrD(OCD₃)Cl(PMe₃)₃] was $k_H/k_D = 2.45$, whereas the secondary kinetic isotope effect for *mer-cis*-[IrD(OCH₃)Cl(PMe₃)₃] was $k_H/k_D = 1.10$. The activation parameters observed were $\Delta H^\ddagger = 24.1 \pm 1.8$ kcal/mol, $\Delta S^\ddagger = -0.6 \pm 5.9$ eu.

A bimolecular mode of β -H elimination has been proposed for the coordinatively saturated complexes [Cp*IrPh(OCH₂R)(PMe₃)]. These complexes are stable but [Cp*IrPh(OTf)(PMe₃)] catalyzes the hydride formation following the mechanism in Scheme 6.30. This hydride transfer reaction can be used to selectively oxidize primary alcohols in the presence of secondary alcohols [99].



Scheme 6.30.

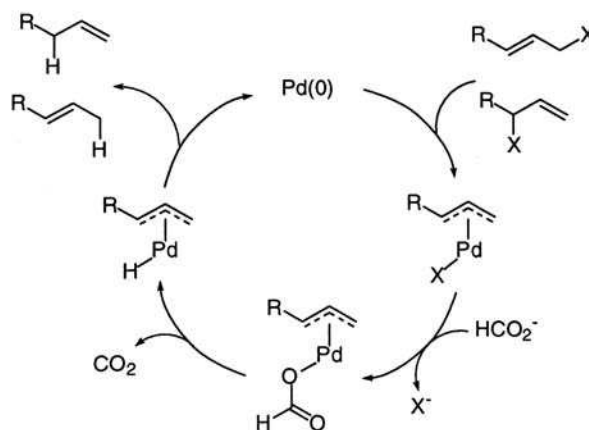


Scheme 6.31.

Thiolates. The thioaldehyde hydrido complexes $[(\text{C}_5\text{Me}_5)_2\text{Ta}(\text{H})(\eta^2-\text{S}=\text{CHR})]$ seem to be in rapid equilibrium with the corresponding 16-electron thiolate species $[(\text{C}_5\text{Me}_5)_2\text{Ta}(\text{SCH}_2\text{R})]$ through a β -H migratory insertion/elimination process [100]. The low concentration of the latter precludes its direct observation.

Amino complexes. The β -H elimination from a coordinated amine has been observed for $[\text{Os}(\text{NH}_3)_4\text{L}(\text{NH}_2^i\text{Pr})]^{2+}$ ($\text{L} = \text{CH}_3\text{CN}, \text{MeOH}$) to give the imine hydrido species $[\text{OsH}(\text{NH}_3)_4\{\eta^2-\text{NH}_2=\text{CH}(\text{CH}_2\text{CH}_3)\}]^{2+}$. The reverse reaction, insertion of the imine into the Os–H bond, is also observed and the equilibrium constant is estimated as $K = [\text{hydrido-imine}]/[\text{amino}] = 10^4$ at 25°C (Scheme 6.31) [101]. The structure of a related complex $[\text{Mo}(\text{H})(\eta^2-\text{Me}_2\text{C}=\text{NAr})(\text{N}^i\text{PrAr})_2]$ ($\text{Ar} = 3,5\text{-C}_6\text{H}_3\text{Me}_2$) has been crystallographically determined [102].

Amido complexes. β -H elimination from the monomeric iridium amido complex $[\text{Ir}(\text{NPhBz})(\text{CO})(\text{PPh}_3)_2]$ has been observed and the products are the hydrido complex $[\text{IrH}(\text{CO})(\text{PPh}_3)_2]$ and $\text{PhCH}=\text{NPh}$. Kinetic studies indicate that dissociation



Scheme 6.32.

of a PPh_3 occurs prior to the β -H elimination [103]. This kind of elimination has also been observed, in competition with reductive elimination, for the decomposition of some $[\text{Pd}(\text{amido})(\text{aryl})\text{L}_n]$ complexes, where the products arene + imine (from β -H elimination), and arylamine (from reductive elimination) are observed [104].

Formates. The decarboxylation reaction of metal formates is a fairly general route for the synthesis of metal hydrides and it has been applied to many transition metals. As an example, allyl palladium formates, which are believed to be intermediates in the catalytic reductive cleavage of allylic acetates and carbonates with formic acid to give monoolefins (Scheme 6.32), have been synthesized. In fact the complexes undergo decarboxylation and the reductive elimination of the allyl hydrido fragments, supporting the catalytic cycle proposed [105].

Enolates. The β -H elimination from enolates involves formal elimination of ketene, and has been recognized in the decomposition of $[\text{Ru}(\text{Me})\{\text{OC}(\text{CH}_2)\text{H}\}(\text{PMe}_3)_4]$ to $[\text{Ru}(\text{Me})(\text{H})(\text{PMe}_3)_4]$, upon warming it in solution to 65°C . When this thermolysis was run in the presence of tert-butyl alcohol as a trap, tert-butyl acetate was formed in 10–15% yield, consistent with the formation of ketene during the course of the reaction [106].

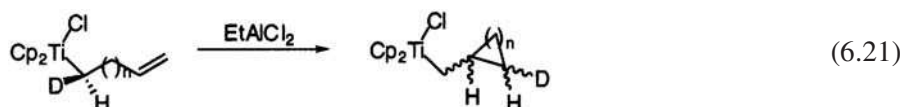
6.2.4 Mechanistic and kinetic studies of the insertion into M–C bonds and the reverse reaction

(a) Insertion of alkenes into M–C bonds

The insertion of alkenes into M–C bonds is a key step in the polymerization reaction by Ziegler–Natta type systems, in oligomerization reactions, and in the

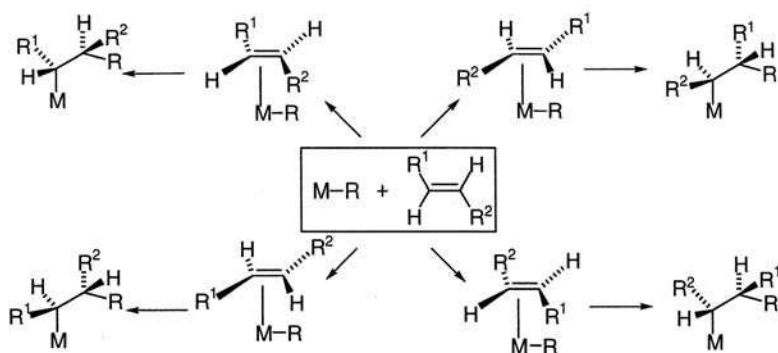
synthetically useful Heck reaction. As such it has been the subject of many mechanistic studies, and it is mostly on these that this section is focused. Although many studies in this section are in connection with polymerization reactions, a specific treatment of polymerization is beyond the scope of this book; the 'state of the art' of some aspects can be found in specific reviews [4,107].

The debate on the mechanism of polymerization, whether an insertion mechanism (Cossee–Arlman) [6], or a metathesis-type mechanism initiated by α -H elimination from the alkyl complex to give a hydrido–carbene intermediate (Green–Rooney) [108], was solved in favor of the former on the basis of the absence of isotope effect on the rates of insertion, and on the stereochemistry of alkene intramolecular insertion, when α -D alkyls were used in the cyclization reaction shown in Eq. 6.21 [109].

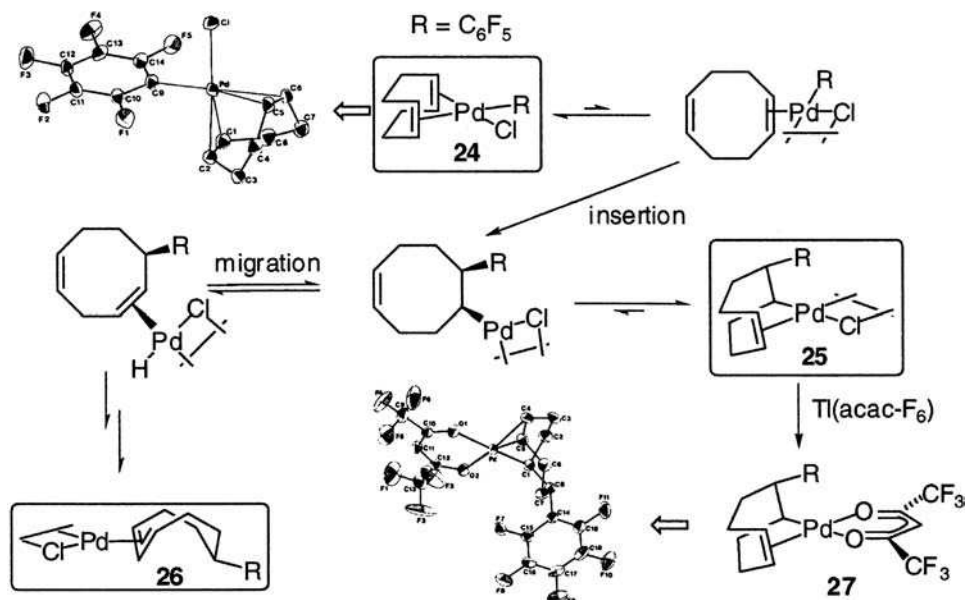


Since the insertion of alkenes into M–C bonds proceeds via a four-center transition state, some requirements have to be accomplished; namely: (1) the alkene and the hydrocarbonyl group have to take *cis* coordination sites; (2) the double bond and the M–C bond have to become coplanar; and (3) the 1,2-addition is *cis*, and this controls the relative stereochemistry at both carbons in case of prochiral alkenes (Scheme 6.33). The regio and stereoselectivity of this process controls the tacticity of polymers.

We saw earlier in this chapter that the alkyl migration step in the insertion of alkenes into M–alkyl bonds should be spontaneous, since the balance for breaking and making of C–C bonds usually compensates for the entropic contribution. In fact the number of complexes with M–C bonds *cis* to a coordinated alkene that can be isolated or detected, and then evolve to the inserted product, is small. Usually either the reaction is too fast (and the precursor is not observed) or too slow (and



Scheme 6.33.

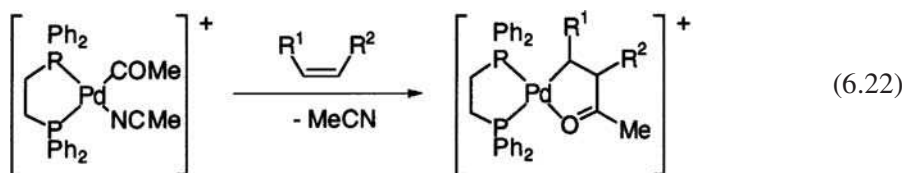


Scheme 6.34.

the insertion does not take place). The system in Scheme 6.34 is an uncommon example that demonstrates clearly the steps of the reaction [82]. Compound **24** is a stable *cis*-aryl-alkene complex which owes its stability to the impossibility of the *cis* double bond, involved in a chelating ligand, to become coplanar with the Pd–C bond unless the other double bond is decoordinated. Its X-ray structure features a longer distance Pd to midpoint of the *trans* double bond, reflecting the high *trans* influence of the R group and supporting easy decoordination of that *trans* double bond. This decoordination is rate determining for insertion, and when it occurs (smoothly at room temperature) the compound evolves fast and competitively to the kinetic **25** and the thermodynamic **26** products, via the putative intermediates shown in the Scheme. Both products have a *cis* stereochemistry for the R and Pd groups (by NOE for **26**; by X-ray diffraction of its direct derivative **27** for **25**) supporting the expected *cis* addition for the insertion. The competitive formation of **25** and **26** needs a common intermediate; **25** is not an intermediate, since its transformation into **26** is extremely slow (again rate determining decoordination of the double bond is needed). The Pd chain walking and the recoordination of the double bond from the common σ intermediate have comparable rates, and are very fast.

The need for a coordination site easily accessible to the alkene and *cis* to the M–C bond is already announced in the stability of the Ti complex in Eq. 6.21, which undergoes insertion only when a Lewis acid ($EtAlCl_2$), able to help in the temporary dissociation of the halide, is added [109]. The complex

$[\text{Pd}(\text{C}_6\text{F}_5)\text{Br}(\text{bipy})]$ is ineffective towards the insertion of dienes, but insertion takes place immediately when the blocking Br ligand is removed with AgClO_4 , to give allyl derivatives, after chain walking if necessary. Under the same conditions and in comparable times, *trans*- $[\text{Pd}(\text{C}_6\text{F}_5)\text{BrL}_2]$ ($\text{L} = \text{py}, \text{PPh}_3$) gives only *trans*- $[\text{Pd}(\text{C}_6\text{F}_5)(\text{OCIO}_3)\text{L}_2]$ [110]. Similarly, a number of simple alkenes insert into the Pd–acetyl bond of $[\text{Pd}(\text{COMe})(\text{NCMe})(\text{dppe})]^+$ thanks to the easy displacement of the weakly bound acetonitrile (Eq. 6.22) [111].



These examples suggest that, except for alkene complexes strongly stabilized by π back-donation, the alkyl insertions are fast once the prerequisites for *cis* coordination, and coplanar arrangement are accomplished. Although the alkyl migration (insertion into M–C bonds) has a higher activation barrier than the H migration (insertion into M–H bonds), the reason why alkyl–alkene complexes not undergoing easy insertion are observed more often than hydrido–alkene complexes is probably one or more of the steps preceding insertion, such as difficult alkene rotation, difficult *trans* to *cis* isomerization, or strongly bound ligands blocking the coordination positions. Except for these reasons the insertion is sufficiently fast, and only at low temperatures are the corresponding alkyl alkene complexes detected.

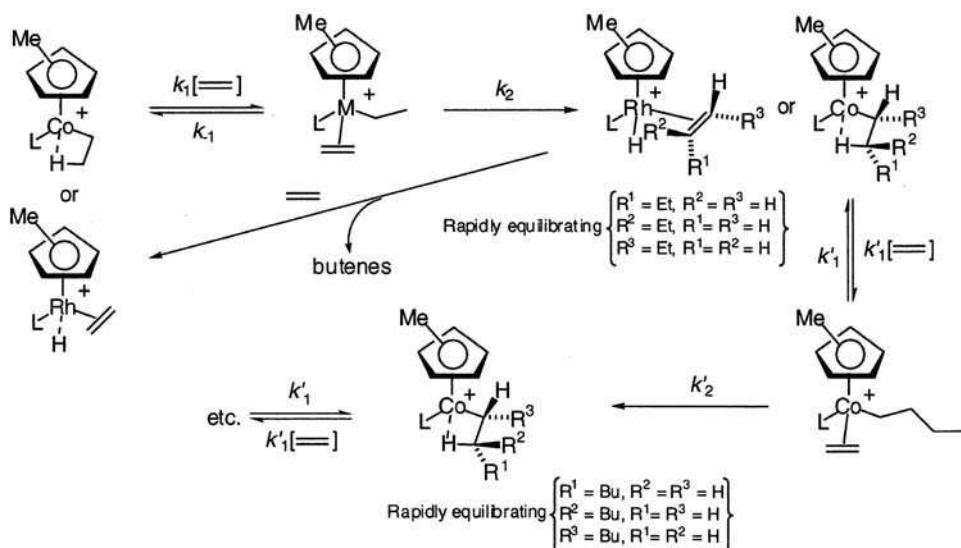
The Co(III) complex $[\text{Cp}^*\text{Co}(\text{Et})\{\text{P}(\text{OMe})_3\}](\text{BF}_4)$ has an agostic Et group and is active in ethylene polymerization. On the basis of low temperature ^1H and ^{13}C NMR studies, the mechanism in Scheme 6.35 was proposed. Initially the only species detected were the agostic alkyls, which are the resting state of the catalyst. The successive alkyl–alkene complexes were not seen [112]. However, working with high concentrations of doubly labeled ^{13}C ethylene at -80°C these elusive species could be detected [51]. The Rh homologue is a catalyst for the dimerization of ethylene [50]. For the Rh complex the hydrido alkene or alkyl alkene forms are slightly more stable than the agostic forms, the ethyl–ethylene complex is the resting state of the catalyst, and the ethyl migration is the turnover-limiting step in the catalytic cycle. Kinetic measurements for these and related systems (Cp in place of Cp^* ; PMe_3 in place of $\text{P}(\text{OMe})_3$) afforded barriers for the migration of H and Et. Some $\Delta G^\ddagger$ values are gathered in Table 6.9. $\Delta S^\ddagger$ values were close to 0, as expected for an intramolecular migration. Activation parameters for ethylene rotation were also determined. For the complexes studied, the differences in free energies of activation for the migratory insertion process, $\Delta G^\ddagger(\text{Et}) - \Delta G^\ddagger(\text{H})$, lie in the range 6–11 kcal/mol and correspond approximately to relative migratory insertion rates $k_{\text{H}}/k_{\text{Et}}$ of 10^6 – 10^8 at 23°C .

The activation parameters found for these Co and Rh complexes can be

TABLE 6.9

Comparison of parameters for R migration in complexes $[\text{Cp}^*\text{MR}(\text{C}_2\text{H}_4)\text{P}(\text{OMe})_3](\text{BF}_4)$ (kcal/mol)

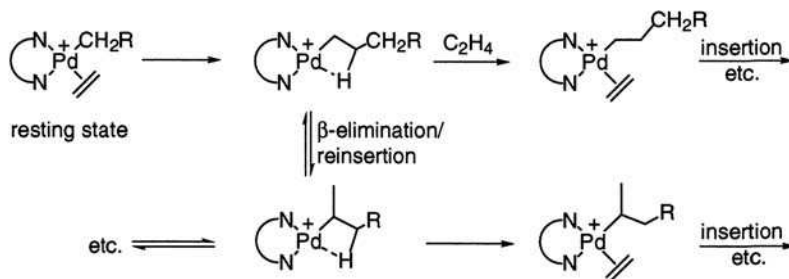
M	$\Delta G^\ddagger$ (H migration) R = H	$\Delta G^\ddagger$ (Et migration) R = Et	$\Delta\Delta G^\ddagger$
Co	6–8	14.3	8–6
Rh	12.2	22.4	10.2



Scheme 6.35.

compared with other values in the literature. The barrier for R-migratory insertion in $[\text{Cp}^*_2\text{Ta}(\text{R})(\text{C}_2\text{H}_4)]$ is 21.3 kcal/mol for R = H [47], whereas the migration is not observed for R = Me, even at high temperatures (as a consequence of the high barrier expected, about 30–35 kJ/mol). Similar values apply to $[\text{Cp}_2\text{W}(\text{R})(\text{CH}_2\text{CHMe})]^+$ [48]. These higher values for both migratory insertions reflect the important stabilization of the alkene by π back-donation in the d^2 complexes. On the other hand, the free energies of insertion increase going from first to second to third transition row.

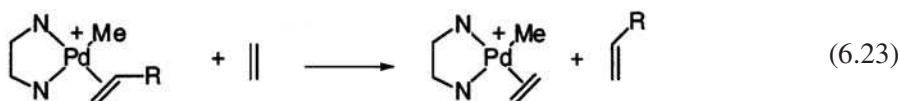
Complexes of the type $[\text{M}(\text{Me})(\text{L}-\text{L})(\text{OEt}_2)]^+$ (M = Ni, Pd, L–L = chelating N,N ligand with bulky substituents), generated in solution by protonation of the dimethyl precursors with $\text{H}(\text{OEt}_2)\text{BAR}_4$, are catalyst for the polymerization of ethylene and α -olefins [113], and have been studied in detail. For the Pd complexes the catalyst resting state is an alkyl–alkene complex $[\text{Pd}(\text{R})(\text{alkene})(\text{N}-\text{N})]^+$. The turnover determining step is the migratory alkyl insertion, with barriers in the



Scheme 6.36.

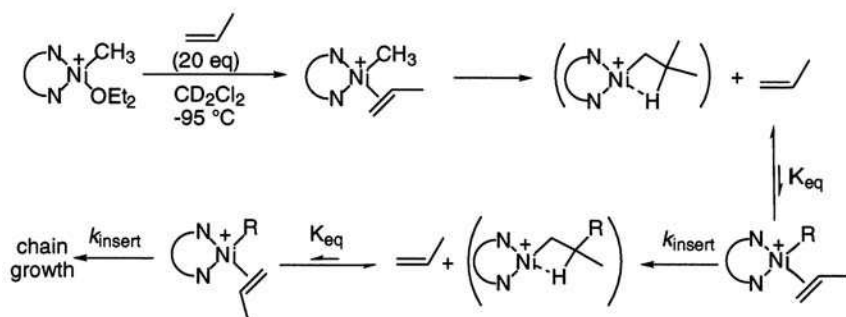
range 16.9–17.6 kcal/mol. Palladium migration along the chain (chain walking) in the $[\text{Pd}(\text{alkyl})(\text{N}-\text{N})]^+$ β -agostic species formed is rapid, producing branching (Scheme 6.36) [114,115]. Model studies using palladium-*n*-propyl and -isopropyl systems provide mechanistic details of this process.

The rate of associative exchange of free ethylene with bound ethylene (Eq. 6.23) in $[\text{Pd}(\text{CH}_3)(\text{C}_2\text{H}_4)(\text{N}-\text{N})]^+$ is retarded by bulky substituents. Thus, for the complex $[\text{Pd}(\text{CH}_3)(\text{C}_2\text{H}_4)(\text{phen})]^+$ with a N–N ligand lacking axial bulk, the ethylene exchange is too fast to be measured by NMR techniques, even at -100°C . Consistently, the system catalyzes the dimerization of ethylene, rather than polymerization, indicating that chain transfer by alkene displacement by the monomer is much faster than propagation.



For similar Ni complexes the catalyst resting state for the polymerization of ethylene is again an alkyl–alkene complex. The insertion for the Ni systems is faster than for the analogous Pd complexes, and the migratory alkyl insertion barriers for the first and subsequent insertions are very similar, all in the range 13.3–14.0 kcal/mol [116]. Thus, $\Delta\Delta G^\ddagger(\text{Pd}-\text{Ni})$ of 5 kcal/mol are not far from the differences found for the pair Rh–Co. For the insertion of propene, the resting state is an agostic alkyl complex (observed at -120°C), and the chain propagation is first order in propene (it was zero order for ethylene) due to a preequilibrium of alkene coordination (Scheme 6.37). Barriers for migratory insertion are similar for ethylene and propene.

Studies on the insertion of *para*-substituted styrenes into the Pd–Me bond of cationic $[\text{Pd}(\text{CH}_3)(p\text{-XC}_6\text{H}_4\text{CH}=\text{CH}_2)(\text{phen})]^+$ ($\text{X} = \text{CF}_3, \text{Cl}, \text{H}, \text{CH}_3, \text{OCH}_3$) reveal that the insertion is faster for electron withdrawing substituents in the styrene [12]. The electron rich styrenes bind tightest to Pd, and the kinetic and thermodynamic data indicate that both the ground and the transition states are stabilized by electron donor substituents, but the effect is greater in the ground states. These results are understood on the basis of a Pd–styrene bond dominated



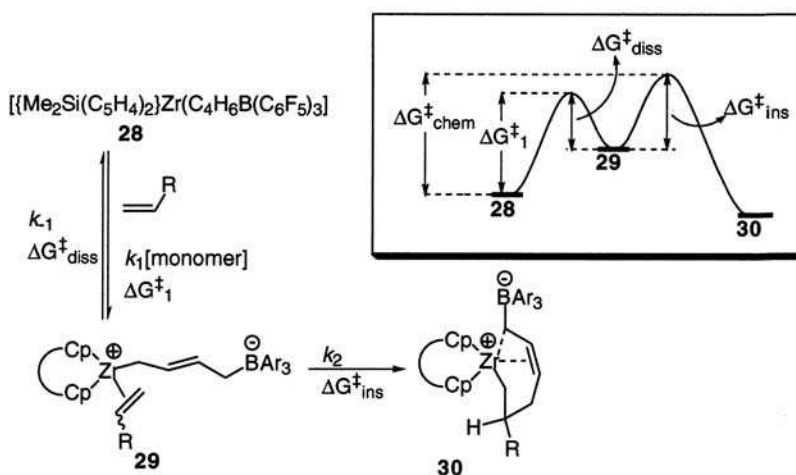
Scheme 6.37.

by donation from the π orbital of the alkene to the metal. In contrast, in the complexes $[\text{Cp}_2\text{Nb}(\text{H})(p\text{-XC}_6\text{H}_4\text{CH}=\text{CH}_2)(\text{phen})]$ it is the electron-withdrawing substituents that stabilize the alkene complex towards insertion, suggesting that the $d\pi \rightarrow p\pi^*$ donation dominates [47].

The rates of insertion of ethylene into Pd–alkyl and Pd–acyl bonds have been evaluated for this type of systems, in particular $[\text{Pd}(\text{R})(\text{C}_2\text{H}_4)(\text{L-L})]^+$ (R = alkyl, acyl; L-L = phen, 1,3-diphenylphosphinopropane) [117,118]. Lower activation barriers for the acyl complexes were consistently found with $\Delta\Delta G^\ddagger(\text{alkyl-acyl})$ about 2 kcal for the phen complexes and 4 kcal for the phosphino derivatives. Insertion barriers for CO insertion into the Pd–alkyl bond are even lower, making the alternating copolymerization of alkenes and CO possible and almost flawless (a perfect sequence of CO insertion into M–alkyl and alkene insertion into M–acyl with absence of alkene insertion into M–alkyl) [119].

Obtaining direct experimental evidence about the extremely fast homogeneous Ziegler–Natta catalysts is extremely difficult. It was generally assumed that the coordination of the alkene imposed the higher barrier to polymer growing. However, a very careful study on the *ansa*-metallocene $[\{\text{Me}_2\text{Si}(\text{C}_5\text{H}_4)_2\}\text{Zr}(\text{C}_4\text{H}_6\text{B}(\text{C}_6\text{F}_5)_3)]$ (**28**) with a number of α -olefins has revealed that the transition state for the actual insertion step is always somewhat higher than that for the coordination (Scheme 6.38) [120]. Values of $\Delta G_{\text{ins}}^\ddagger$ in the range 9–11 kcal/mol were estimated. The ratio between the rate of insertion and dissociation from **29**, k_{-1}/k_2 was in the range 30–200. Since the alkyl migration step is clearly rate determining, it seems that the interactions between the catalyst backbone, the growing polymer chain and the coordinated alkene in **29** must govern the features (chemoselectivity, regiochemistry, stereoselectivity) of the polymerization reaction with homogeneous Ziegler type polymers.

Metal allyl complexes are analogous to alkyls due to the generally easy $\eta^3\text{-}\sigma$ interconversion, and they insert alkenes as shown in the preceding example, and for a number of Pd–allyl complexes [121]. However, some formal insertions into M–allyl bonds do not proceed through the four-center transition state formed

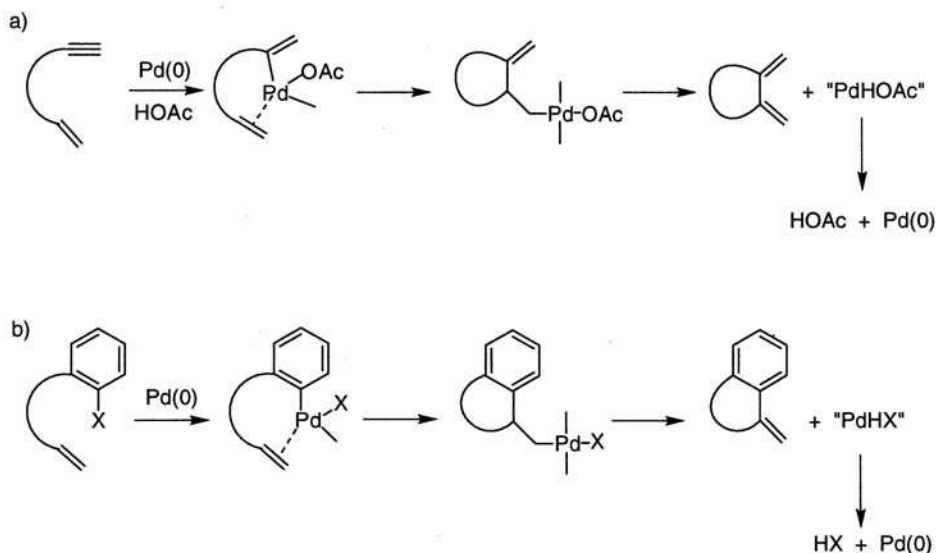
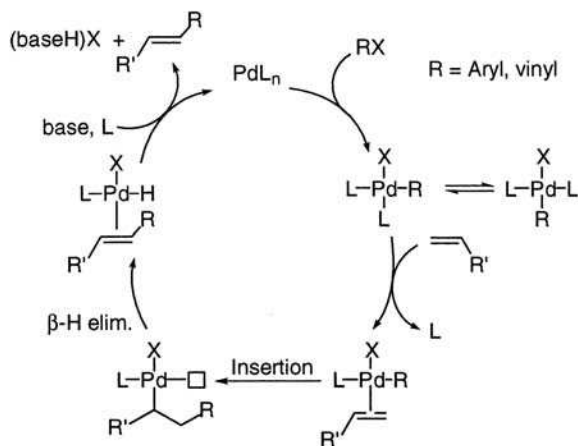


Scheme 6.38.

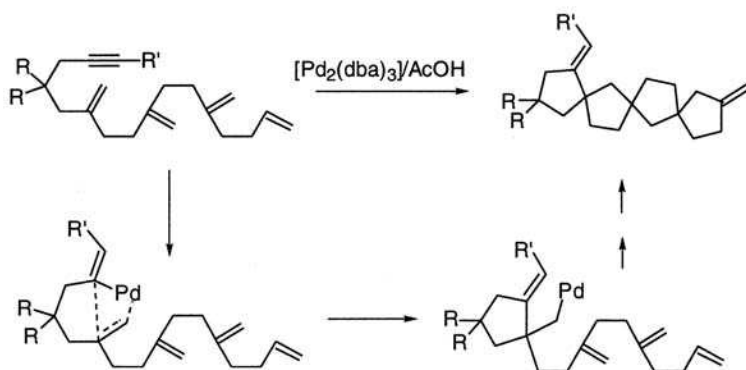
by the alkene and a metal σ -allyl intermediate, and an electrocyclic mechanism operates for the insertion of dienes into Pd-allyl bonds as has been shown by the regiochemistry of the final products [122]. Recently, theoretical studies have found a lower energy pathway for the direct insertion of alkenes into an η^3 -allyl metal bond [123].

Allenes also insert into M-C bonds and the new C-C bond is formed with the central atom of the allene leading to an allylic derivative. Insertion of allenes into M-alkyl [124], and Pd-allyl bonds [125] have been reported.

The ease of successive alkene insertions into M-C bonds and the competition of β -H elimination/alkene decooordination determine the ability of a complex to act as a polymerization (many and efficient insertions), oligomerization (just a few), or alkene substitution catalyst if insertion is immediately followed by β -H elimination. Electrophilic metal complexes, such as the early TM metallocenes (Ziegler-Natta type) and cationic group 10 derivatives are among the most active polymerization catalysts as it was mentioned before. Oligomerization catalysts can be found among early and also late transition metals [126]. For alkene substitution, the most used metal is palladium in the many versions of the aryl or vinyl substitution of alkenes (Heck reaction) [127]. The intermolecular Heck reaction (Scheme 6.39) involves a single insertion into an M-aryl (or M-vinyl) bond [128]. After insertion of the alkene, β -H elimination and decooordination of the substituted alkene follows, the unstable metal hydride eliminates HX and the Pd(0) complex re-enters the catalytic cycle. A base is used to neutralize the acid formed. In this process the metal switches between the Pd(0)/Pd(II) oxidation states and, although some alternative species (Pd(II)/Pd(IV)) have been proposed for certain catalytic systems [129], the former combination seems to be operative in most cases.



The intramolecular version of the Heck reaction leads to the formation of cyclic compounds (Scheme 6.40) [130]. In this case the C–C bond is generally formed at the most substituted position of the alkene (exo mode), in contrast with the intermolecular case where the opposite regiochemistry holds. The Baldwin rules for cyclization are usually operative. The Scheme 6.40 (a) depicts the general cyclization reaction of an enyne, where the vinylpalladium intermediate is formed by insertion of the alkyne fragment into a Pd–H bond formed by protonation of Pd(0) species; the first M–C bond can also be formed by oxidative addition of a



Scheme 6.41.

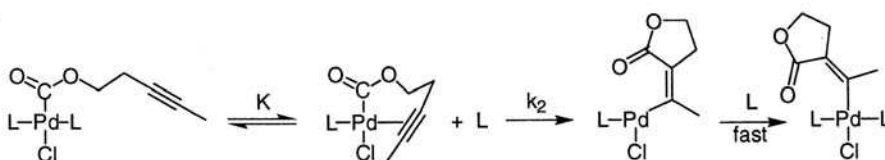
C–X bond in the organic substrate (b, Scheme 6.40), as in the intermolecular case. The intramolecular Heck reaction has developed enormously and opened up many new synthetic approaches to complex organic molecules.

The reaction has also been carried out in a cascade (or tandem) fashion which involves several insertion steps, as in the formation of the spiro derivative in Scheme 6.41 (a zipper reaction) [131]. It has also been combined with other processes such as carbonylation or nucleophilic attack [132].

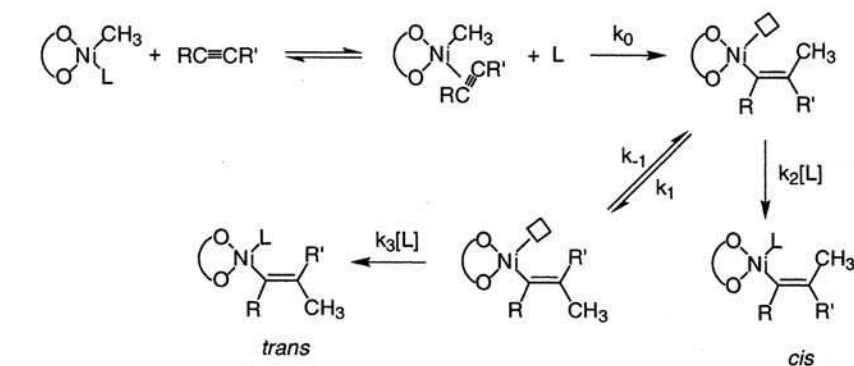
(b) *Insertion of alkynes into M–C bonds*

The intramolecular insertion of alkynes into a Pd–C bond has been observed and kinetically studied. The reaction involves a pre-equilibrium substitution of a phosphine ligand by the alkyne moiety, followed by rate determining insertion in a four-coordinate intermediate (Scheme 6.42). The longer the spacer chain (n) the more favorable ligand substitution ($K = 2.0(9)$ for $n = 2$ versus $K = 4.40(2)$ for $n = 3$) although the opposite is observed for the insertion step ($k_2 = 7(3)$ for $n = 2$ versus $k_2 = 0.301(2)$ for $n = 3$). It seems that the short chain alkyne intermediate ($n = 2$) is strained enough to deviate from the usual perpendicular arrangement and adopts a conformation that places the alkyne closer to coplanarity and to the insertion transition state [133].

Kinetics consistent with a ligand substitution preequilibrium have also been found for the reaction of $[\text{Ni}(\text{acac})(\text{CH}_3)(\text{PR}_3)]$ and substituted alkynes. Faster



Scheme 6.42.



R	R'	% product			
		Kinetic distr.		Thermod. distr.	
		<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>
Ph	Ph	0	100	25	75
Ph	CD ₃	65	35	50	50
^t Bu	H	30	70	100	0
Ph	H	65	35	100	0

Scheme 6.43.

reaction rates are observed for alkynes with electron withdrawing substituents as expected from a lower lying LUMO ($\text{RC}\equiv\text{CR}'$: $\text{R} = \text{R}' = \text{Ph}$, COOMe ; $\text{R} = \text{Ph}$, $\text{R}' = \text{Me}$, $\text{H} \gg \text{R} = {}^t\text{Bu}$, $\text{R}' = \text{H}$, Me ; $\text{R} = \text{Me}$, $\text{R}' = \text{Me}$, ${}^n\text{Bu}$, see Section 6.2.1 (e)). The stereochemistry of the insertion is *cis*, but isomerization (k_1) occurs as fast (or faster) as ligand coordination (k_2). As a result, the products of the reaction are a kinetic mixture of *cis* and *trans* isomers that further evolve to their equilibrium ratio (Scheme 6.43) [134]. This apparent lack of stereoselectivity in the insertion of alkynes due to easy isomerization is a general feature for this type of unsaturated substrates (see Section 6.2.3 (b)).

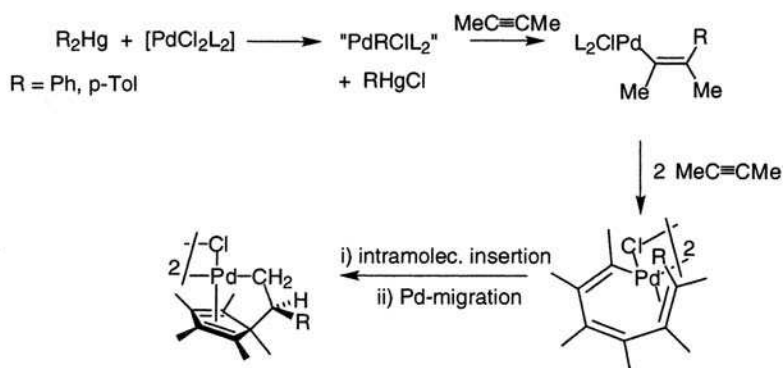
The regiochemistry of insertion is generally difficult to predict since it is strongly influenced by sterics and the auxiliary ligands coordinated to the metal play an important role. As an example, the insertion of 1-hexyne into the $\text{Pd}-\text{CH}_3$ bond of $[\text{Pd}(\text{CH}_3)(\text{N}-\text{N})(\text{MeCN})]^+$ gives 1,2- and 2,1-insertion products, the former being more abundant the bulkier the chelating ligand (Table 6.10) [135].

Sequential insertion of alkynes into the newly formed $\text{M}-\text{vinyl}$ bond after the first insertion leads to organometallic products with three alkyne units incorporated (Scheme 6.44) [136]. Although this is formally related to the alkyne cyclotrimerization process, the mechanism of this important catalytic reaction is not fully elucidated. Oligomerization of alkynes to give enynes [137], and polymerization of alkynes are applications of this sequential insertion of alkynes into $\text{M}-\text{vinyl}$ bonds [138]. The insertion of alkynes into the $\text{M}-\text{C}$ bond of group

TABLE 6.10

Regioselectivity of the insertion of 1-hexyne into Pd–Me bond of $[\text{Pd}(\text{CH}_3)(\text{N}-\text{N})(\text{MeCN})]^+$

	2,1-insertion	1,2-insertion
	71%	29%
	51%	49%
	30%	70%

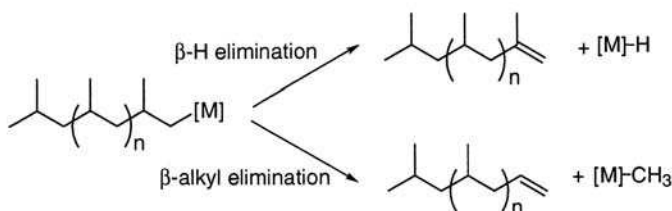


Scheme 6.44.

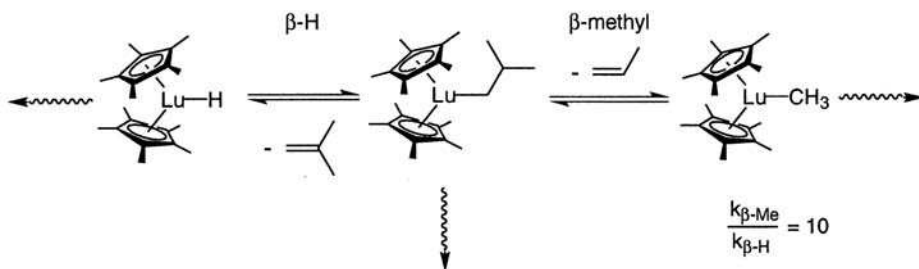
10 metallacycles has been applied to the synthesis of new organic derivatives [139].

(c) β -alkyl (aryl) elimination

Examples of β -alkyl elimination, often competing with β -H elimination, have been observed for both early and late transition metals. Looking at the thermodynamics of both processes, the difference between $\text{D}(\text{M}-\text{H})$ and $\text{D}(\text{M}-\text{C})$ is higher for late transition metals and generally makes β -H elimination less endothermic

Chain transfer pathways by β -elimination

Scheme 6.45.

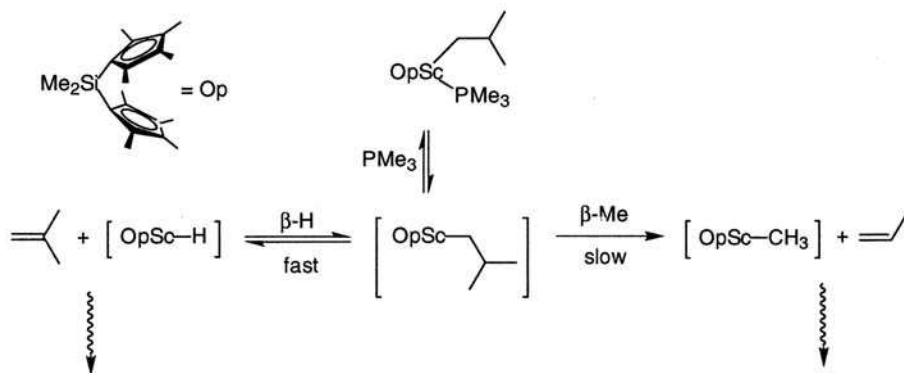


Scheme 6.46.

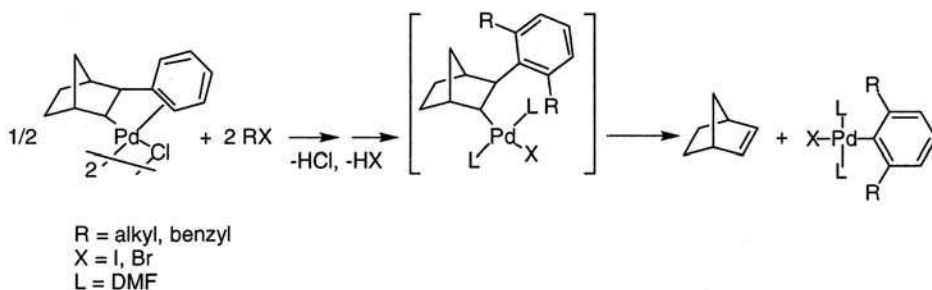
and preferred over β -alkyl elimination. For early transition metals a competition is feasible and more probable. In fact, β -alkyl elimination is an important chain transfer process for Ziegler–Natta type and related polymerization catalysts (Scheme 6.45) [4,107,140]. The pursued controlled degradation of polyolefin materials should be achieved by a reverse polymerization reaction (successive β -alkyl eliminations) and some attempts have been carried out with zirconium-based supported systems [141].

The relative rates found for β -H and β -alkyl elimination are very variable and dependent on the specific complex. Faster β -alkyl elimination by a factor of 10 was found for the manifold decomposition of $[\text{Lu}(\text{Cp}^*)_2(\text{CH}_2\text{CH}(\text{CH}_3)_2)]$ (Scheme 6.46) [142]. However the rate of β -H elimination is higher in the decomposition of a related scandium derivative (Scheme 6.47) [143].

Activation parameters for β -methyl elimination have been determined recently for the Zr and Hf metallocenium ion pairs depicted in Eq. 6.24. The activation free energies for the Zr and Hf complexes are almost the same, as the more favorable $\Delta H^\ddagger$ found for Hf (22.5 (0.9) kcal/mol for Zr and 17.3(0.9) kcal/mol for Hf) is partially offset by the negative entropy of activation (4.3 (3.3) cal/mol for Zr and -11.9 (3.4) cal/mol for Hf) [144]. However, small changes in the ancillary ligands have a stronger influence on the rates of elimination as shown by the stability of the three metallocenium complexes in Eq. 6.24 [144,145]. Steric factors play an important role since the less hindered cyclopentadienyl ligands lead to the more

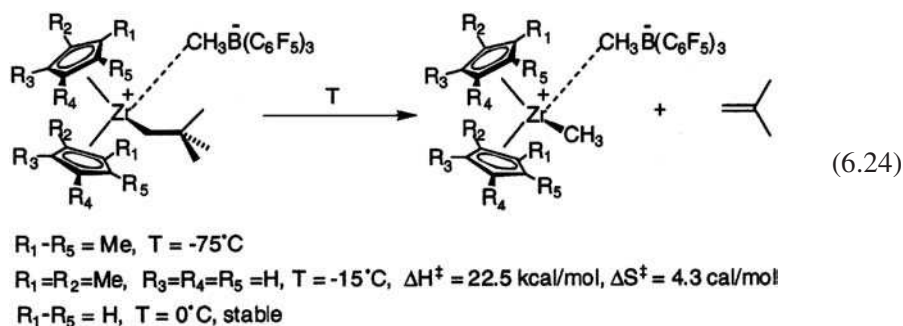


Scheme 6.47.

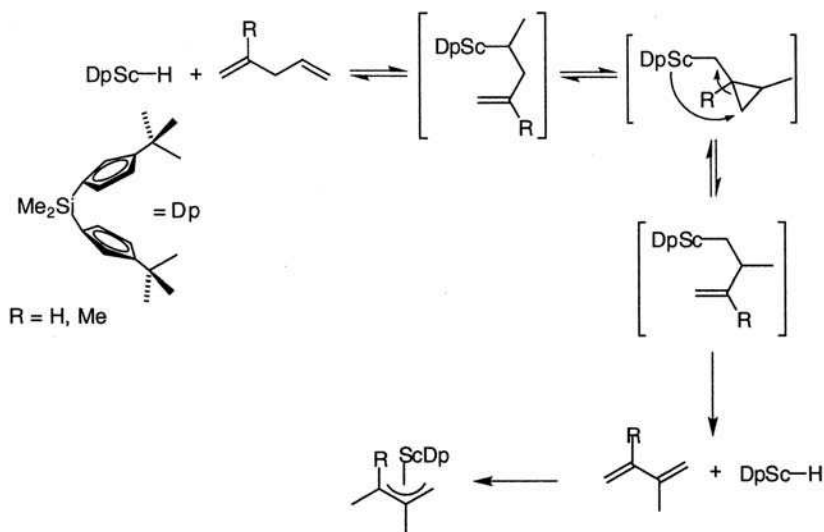


Scheme 6.48.

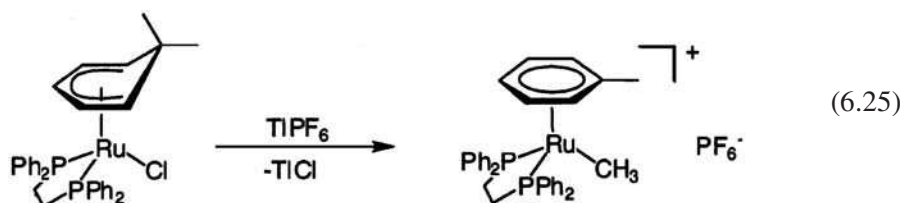
stable zirconium complex. In fact, the norbornyl palladium derivative shown in Scheme 6.48 only undergoes β -aryl elimination when the aryl is 2,6-disubstituted [146].



The thermodynamics of β -alkyl elimination can be favored when a small cycle is involved since the reaction relieves the ring strain. Thus, many ring opening processes such as cyclopropyl- or cyclobutylmethyl rearrangements or metal catalyzed methylenecyclopropane cleavage are facile. The aromatization

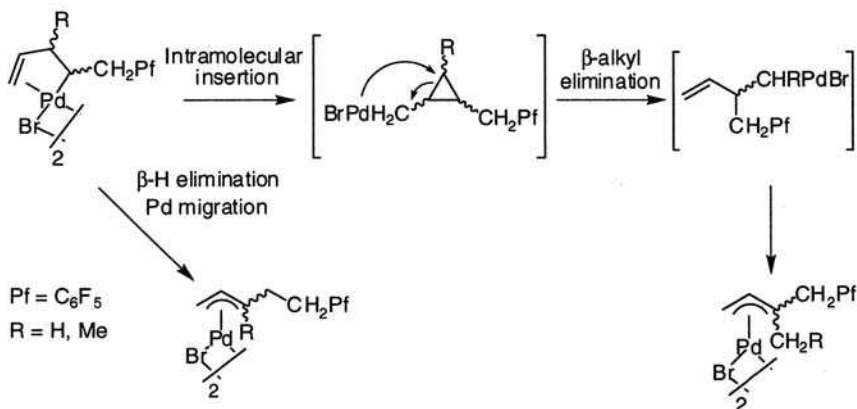


of the organometallic moiety can also provide an extra driving force for β -alkyl elimination (Eq. 6.25) [147].

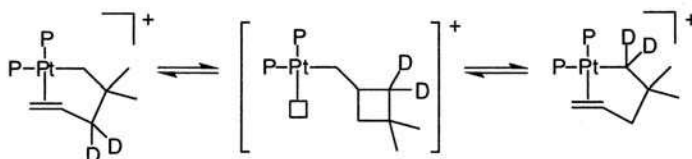


Combining intramolecular insertion into M–C bonds and β -alkyl elimination, leads to skeletal rearrangements. This is the case of the reaction of 1,4-pentadienes either with a scandium hydrido complex (Scheme 6.49) [148], or with a Pd–aryl derivative (Scheme 6.50) [149]. In both cases cyclopropylmethyl metal formation and ring cleavage by β -alkyl elimination leads to rearranged metal allyls. In the palladium case intramolecular insertion competes with β -H elimination (metal migration) and both rearranged and non-rearranged metal allyls are formed in a competitive way (Scheme 6.50). These examples show that β -alkyl elimination can be facile for both early and late transition metal complexes. This process should be considered as a source of unexpected products in some metal catalyzed organic transformations.

Deuterium labeling has been used to detect a cyclobutylmethylplatinum formation and ring cleavage by β -alkyl elimination that occurs in a reversible way for the platinum complex in Scheme 6.51 [150]. A similar degenerate rearrangement occurs for the pentenyl derivative $[Y(Cp^*)_2\{\eta^1\text{-}\eta^2\text{-CH}_2(\text{CH}_2)_2\text{CH=CH}_2\}]$ [151].

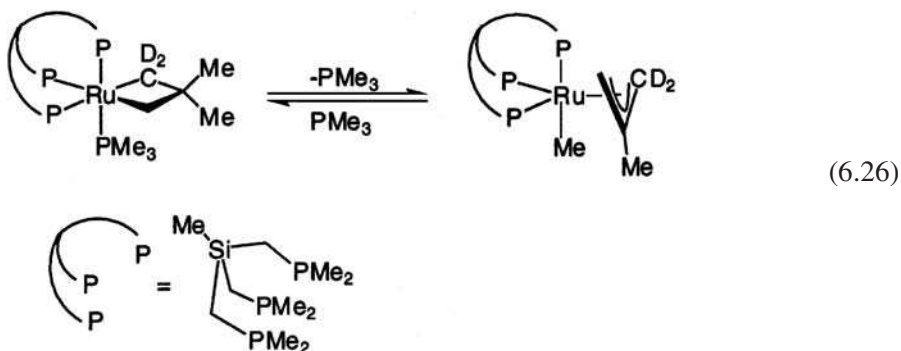


Scheme 6.50.

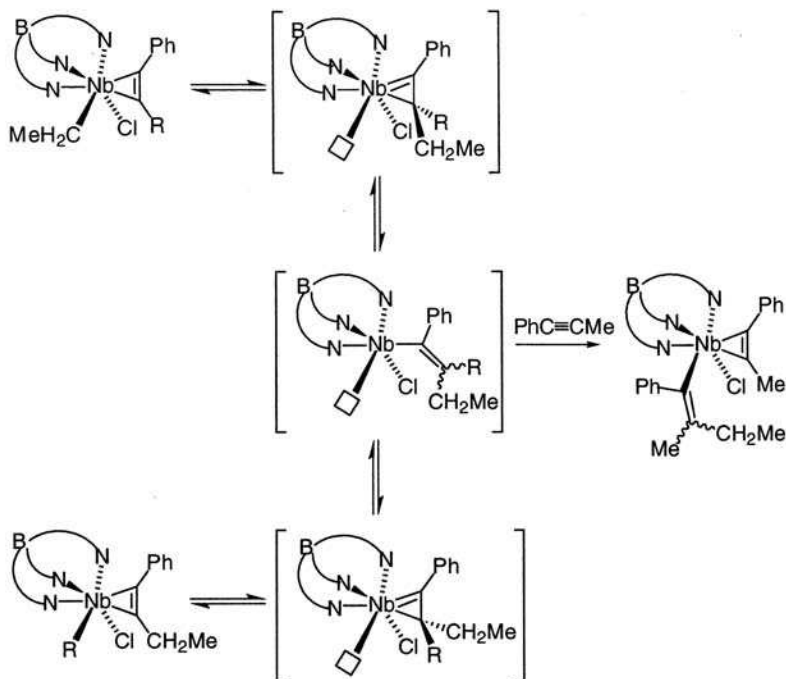


Scheme 6.51.

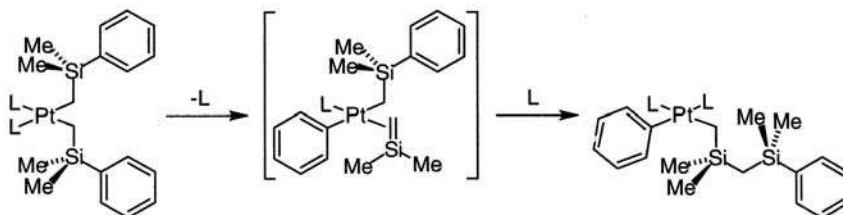
Other reversible β -alkyl eliminations cause the transformation of ruthenacyclobutanes to methyl allyl ruthenium derivatives (Eq. 6.26) [152], or alkyl exchange by a rare formal β -alkyl elimination in a metal alkenyl complex (Scheme 6.52) [153]. Reversible propene extrusion by β -alkyl elimination has also been described for some zirconium metallacycles [154].



Although β -alkyl eliminations are by far more common, β -elimination of aryl groups have also been reported as the reaction in Scheme 6.48. The example in Scheme 6.53 shows a β -C elimination process from a silyl substituted alkyl and competition experiments in this system have determined that phenyl elimination is preferred over methyl elimination [155].



Scheme 6.52.

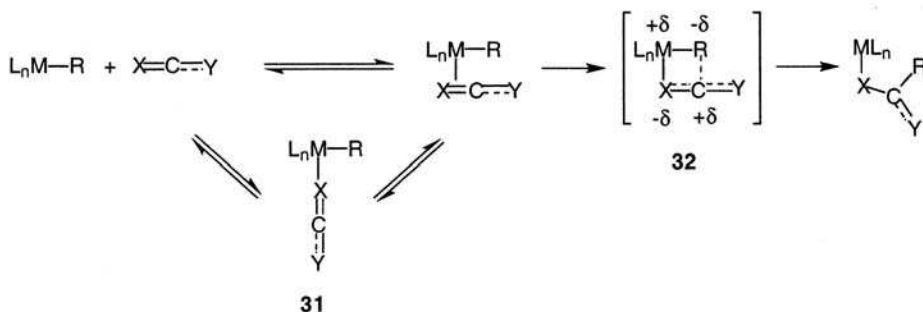


Scheme 6.53.

β -Alkyl eliminations from other substrates such as alkoxides and imines are also possible and have been proposed in the palladium catalyzed oxidative cleavage of cyclobutanols and cyclobutanone oximes. Both processes involve β -alkyl eliminations from cyclobutyl derivatives [156].

6.3 INSERTION OF OTHER SUBSTRATES INTO M-H AND M-C BONDS

Unsaturated substrates with a C-X multiple bond where X is a heteroatom, usually O or N, are susceptible to insertion into M-C and M-H bonds. The

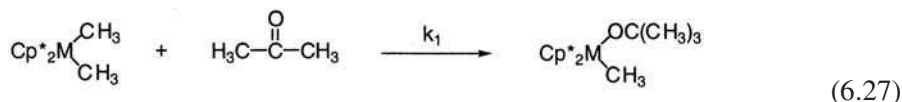


Scheme 6.54.

following compounds can give 1,2-insertion: C=O bonds in CO₂ [157–162], ketenes [163], ketones [164,165], and aldehydes [54,162], isocyanates [163,166]; C=S bonds in CS₂ [160,167,168], isothiocyanates [166,167]; C=N, C≡N bonds in imines [101,169], diimides [163,166], nitriles [160,170]. The resulting moiety usually coordinates to the metal to give a new complex.

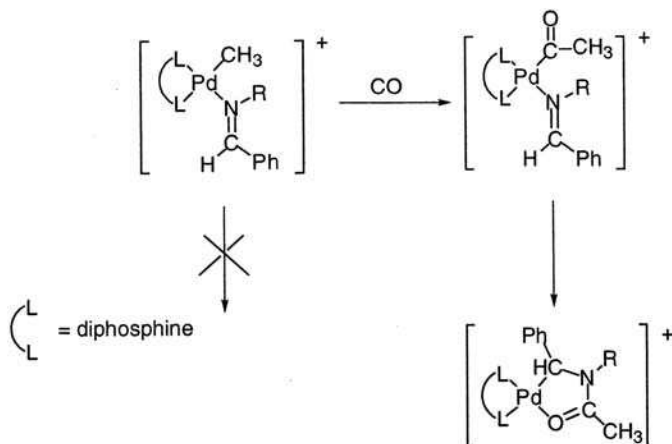
The C=X bond in these substrates is polar and the preferred transition state must be that depicted in Scheme 6.54 (**32**) with the negative X atom binding the metal, and leading to the formation of M–X and C–R bonds. Usually, the heteroatom X in the substrate has lone pairs and can also bind the metal as a monodentate ligand (**31**, Scheme 6.54). The attainment of the transition state for insertion requires the κ^2 -coordination of the substrate or at least a slippage that places the C atom close enough to interact with the M–R bond [171]. Then a high stability of complex **31**, can be a serious drawback for the observation of the insertion reaction in some substrates (e.g. imines) [169].

Mechanistic studies support the transition state drawn in Scheme 6.54. The insertion of CO₂ into the Re–H bond of [ReH(bipy)(CO)₃] shows a strong solvent dependence and second order rate law ($-d[\text{Re}]/dt = k_i[\text{Re}][\text{CO}_2]$) which leads to the proposal of a transition state with charge separation [158]. The kinetics for insertion of acetone in the M–CH₃ bond of thorium and uranium derivatives have been analyzed and k_1 measured for both derivatives (Eq. 6.27) [165]. The faster insertion observed for Th ($k_1(\text{Th}) = 30 k_1(\text{U})$) correlates with the greater polarity of the Th–Me bond, which favors the transition state in Scheme 6.54. The polarization of the unsaturated substrate accounts for the following reactivity order found for insertion of several CO₂-like molecules in the Zr–R bond (R = CH₃, CH₂Ph, Ph): Ph₂C=C=O > PhN=C=O > *p*-TolN=C=Np-Tol $\gg$ CO₂ [163].



Cp* = $\eta^5\text{-C}_5\text{Me}_5$

M = U, Th

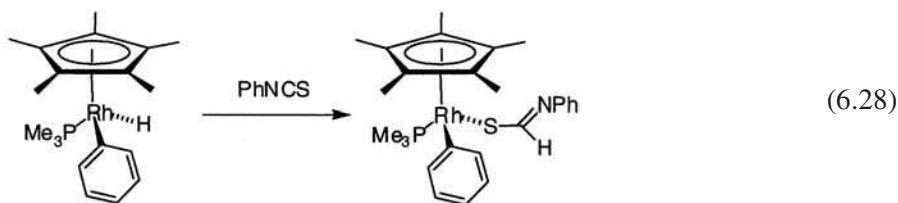


Scheme 6.55.

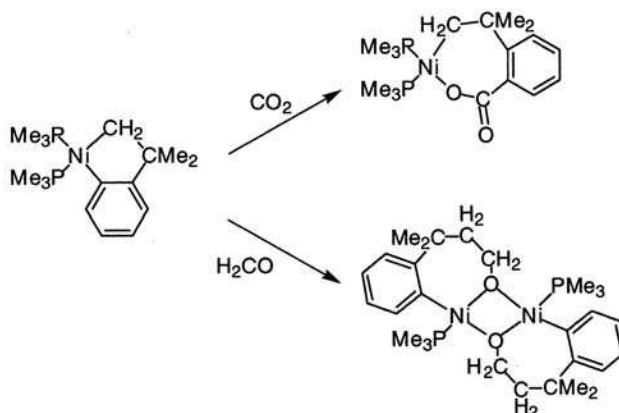
An exception to the regiochemistry described above (R binds to C) is shown in Scheme 6.55 [169]. The imine moiety does not insert into the Pd–alkyl bond but inserts into the Pd–acyl bond and the authors attribute this different behavior to the formation of a strong amide bond in the reaction with the acyl derivative. This thermodynamic driving force and the electrophilic character of the acyl carbon may explain the different regiochemistry observed.

The insertion of imine into an Os–H bond shows the usual regiochemistry (H binds the C atom). The process is reversible and the imino–hydrido and amino complexes are in equilibrium (see Section 6.2.3 (f)) [101].

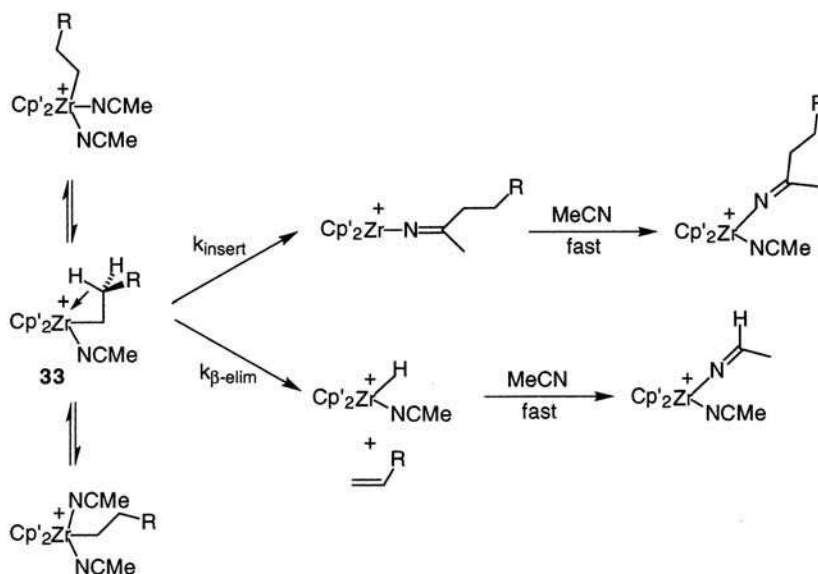
Besides M–H [101,166,167,170], insertion of unsaturated C–X bonds has been observed for many types of M–hydrocarbyl bonds where the C atom can be sp^3 (alkyl, benzyl, allyl, etc.) [54,161–163,170], sp^2 (aryl) [162], or sp (alkynyl) [168]. It is difficult to extract a trend regarding the ease of insertion of CX into M–R bonds for different R groups from the experimental results in the literature, since steric as well as electronic factors seem to be important. Insertion into Rh–H bond is preferred over Rh–phenyl in $[\text{Cp}^*\text{RhHPh}(\text{PMe}_3)]$ and both CS_2 and PhNCS insert only into the Rh–H bond (Eq. 6.28) [167]. Depending on the substrate, insertion of the C=O bond into the Ni–benzyl (H_2CO) or Ni–aryl bond (CO_2) occurs as shown in Scheme 6.56 [162].



Acetonitrile inserts into Zr–H and Zr–C bonds and this has been observed for



Scheme 6.56.

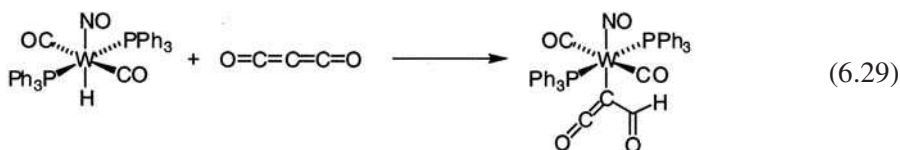


Scheme 6.57.

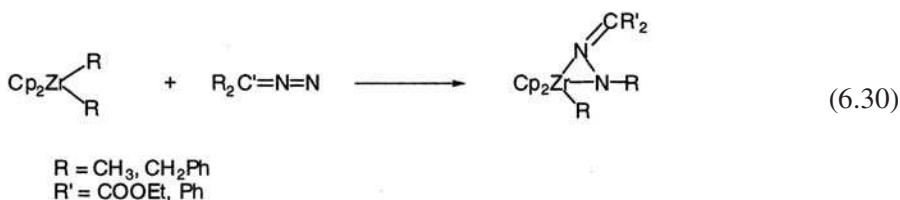
$[(\text{C}_5\text{H}_4\text{Me})_2\text{Zr}(\text{R}')(\text{NCMe})_2]^+$ ($\text{R}' = \text{CH}_2\text{CH}_2\text{R}$). Competitive insertion of MeCN into the $\text{Zr}-\text{R}'$ bond and β -H elimination followed by fast insertion of MeCN into the $\text{Zr}-\text{H}$ bond thus generated occurs (Scheme 6.57) [170]. Kinetic studies on this system reveal that both insertion and β -H elimination take place from a common complex (33) as the ratio of products does not depend on the concentration of acetonitrile but is inhibited by it. The rate constants obtained for $\text{R} = \text{H}$ show that insertion is faster than β -H elimination ($k_{\text{insert}} = 4.38 \times 10^{-4}$ and $k_{\beta\text{-elim}} = 8.20 \times 10^{-5}$) whereas the opposite holds for $\text{R} = \text{alkyl}, \text{Ph}$ ($k_{\text{insert}} \ll k_{\beta\text{-elim}}$) and

only the products of insertion of acetonitrile into the Zr–H bonds are observed. From these data the rate of insertion of acetonitrile decreases in the order $\text{H} > \text{Et} \gg {}^n\text{Pr}, {}^n\text{Bu}, \text{CH}_2\text{CH}_2\text{Ph}, \text{neohexyl}$.

Insertion of the C=C bond of carbon suboxide into M–H bonds ($\text{M} = \text{W}, \text{Re}$) in preference to the C=O bond (Eq. 6.29) has been observed [172].



Diazoalkanes also undergo insertion of the N=N bond into Zr–R bonds to give hydrazone complexes (Eq. 6.30) [173].



6.4 INSERTION INTO OTHER M–E BONDS

M–E bonds other than M–C or M–H also undergo 1,2-insertion. A convenient organization is to consider separately the M–E bonds to elements with an electronegativity not very dissimilar to that of H or C (Si, Sn, B) and then those clearly more electronegative (group 15, 16 and 17 donor atoms). M–M bonds are also susceptible to cleavage by 1,2-insertion of unsaturated substrates and some bimetallic complexes show a reactivity consistent with insertion of alkynes [174], or other C=X bonds [175], but this will not be further extended in this chapter.

6.4.1 Insertion into M–Si, M–Sn, M–B bonds

(a) Theoretical studies

The insertion of alkenes and alkynes into M–E ($\text{E} = \text{SiR}_3, \text{SnR}_3, \text{BR}_2$) is not substantially different from the insertion into M–H or M–C bonds. The same orbital considerations hold in these cases (see Section 6.2.1) and theoretical methods have been applied to analyze these processes, generally in the context of mechanistic studies of catalytic reactions where this may be an important step (hydrosilation, hydroboration, diboration, silylstannation, etc.). Table 6.11 contains some calculated activation energies for insertion of ethylene and alkynes into M–ER_n bonds of comparable systems. The balance of bond breaking/bond making is less favorable for M–Si than for M–C or M–H bonds. Moreover, the directionality of the $\sigma(\text{M}–\text{Si})$ bonds is detrimental for insertion as discussed when

TABLE 6.11

Calculated barriers of insertion (kcal/mol) for the process $cis\text{-}[\text{Pt}(\text{PH}_3)\text{R}(\text{R}')(\text{unsat})] \rightarrow [\text{Pt}(\text{PH}_3)\text{R}(\text{R}'\text{-unsat})]$

	R = SiH ₃ ; R' = H [18]	R = H R' = SiH ₃ [18]	R = SiH ₃ R' = SiH ₃ [176]	R = B(OH) ₂ R' = B(OH) ₂ [179]
M = Pt; H ₂ C=CH ₂	21	54	45	22.9
M = Pt; HC≡CH				9

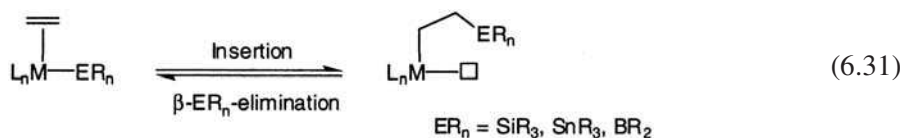
comparing M–H and M–C bonds. These two factors lead to the following order in the values of insertion barriers of ethylene: Pt–H < Pt–CH₃ < Pt–SiR₃ [18]. For the reaction mechanisms that involve insertion of an alkene into the M–SiR₃ bond, this is generally the rate determining step (e.g. disilation [176]). When alternative pathways are possible the one that involves insertion into the M–SiR₃ bond is disfavored (e.g. hydrosilation). However, in real systems, insertion into either M–H or M–SiR₃ bonds seem to occur (see Section 6.4.1 (c)).

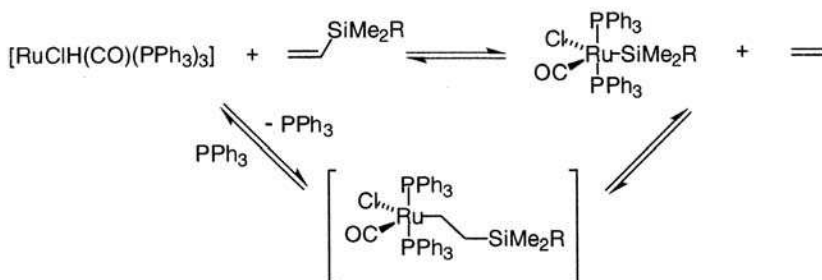
The electronegativity of the ER_n group when E = B, Si, Sn is close to that of the metal and the polarization of the corresponding σ and σ^* orbitals may be altered compared to the M–C case. Thus, keeping the same basic interactions in the transition state, a more electrophilic E group (E-centered σ^*) can give rise to a lower barrier for insertion. This has been invoked to explain the more favorable insertion of terminal alkynes into the Pd–SnH₃ bond (16.3–27.3 kcal/mol depending on the alkyne) versus the Pd–SiH₃ bond (18.3–29.3 kcal/mol) in [Pd(PH₃)(SnH₃)(SiH₃)(HC≡CR)] [177]. It is important, however, to bear in mind that the nature of the R substituents in the ER_n group can alter significantly the insertion barriers to the extent that insertion of ethylene into the Rh–E bond has been calculated to follow the order: B(OH)₂ < H < BH₂ [178].

The insertion of acetylene into a Pt–B(OH)₂ bond has a lower barrier than insertion of ethylene (see Table 6.11) [179]. This is important in some Pt-catalyzed diboration processes that are less efficient for alkenes (where insertion is rate determining and slow) but work well for alkynes.

(b) *Mechanistic studies and selected stoichiometric examples*

Fewer data are available regarding activation parameters and rates for insertion of alkenes or alkynes into M–ER_n bonds, compared to the information reported for insertions into M–C bonds. However there are good examples of insertion and β -ER_n elimination reactions (Eq. 6.31), most of them, but not all, involving M–Si bonds.



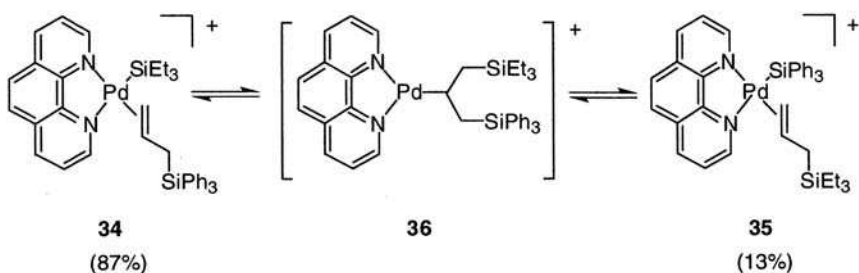


Scheme 6.58.

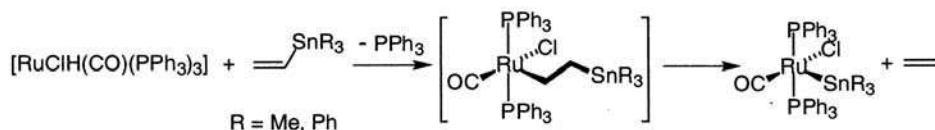
Clear cut examples of insertion of alkenes into $\text{M}-\text{SiR}_3$ bonds have been reported for complexes of Zr [180], Fe [181], Ru [182], Co [183], Pd [184] and some of these insertion processes are reversible [181,182,184]. Insertion of a vinyl silane into the $\text{Ru}-\text{H}$ bond of $[\text{RuCl}(\text{CO})\text{H}(\text{PPh}_3)_3]$ and $\beta\text{-SiR}_3$ elimination explains the formation of the ruthenium silyl. The reaction can be reversed in the presence of excess ethylene (Scheme 6.58) [182].

Brookhart et al. have demonstrated with an elegant crossover experiment that insertion of an alkene into a $\text{Pd}-\text{SiR}_3$ bond of an electrophilic cationic complex is fast and reversible at -60°C . Starting either from complex **34** or **35** generated at low temperature a rapid equilibration to the mixture represented in Scheme 6.59 occurred [184]. The insertion and $\beta\text{-SiR}_3$ elimination are fast and the inserted product (**36**) could not be detected (Scheme 6.59). The insertion of styrene in some of these systems is faster for $\text{R} = \text{SiEt}_3$ than for $\text{R} = \text{CH}_3$ [184].

Besides the reversible processes just mentioned, $\beta\text{-SiR}_3$ elimination from a silyl substituted metal alkyl or metallacycle is a well-documented process [185,186]. This reaction accounts for an easy loss of a silyl group that can be used to generate a $\text{M}-\text{SiR}_3$ moiety in catalytic processes such as dehydrogenative silylation reactions (see below). This reaction, and the analogous $\beta\text{-SnR}_3$ elimination, may also be involved in the loss of regioselectivity found for some $\text{C}-\text{C}$ coupling reactions of vinyl silanes or vinyl tin derivatives (*cine* substitution in Hiyama and Stille



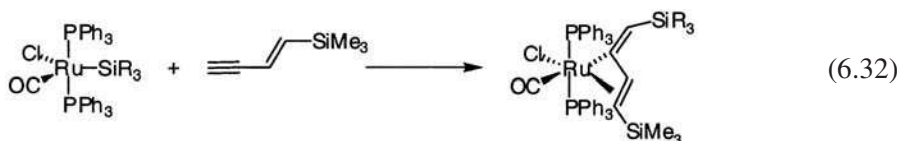
Scheme 6.59.



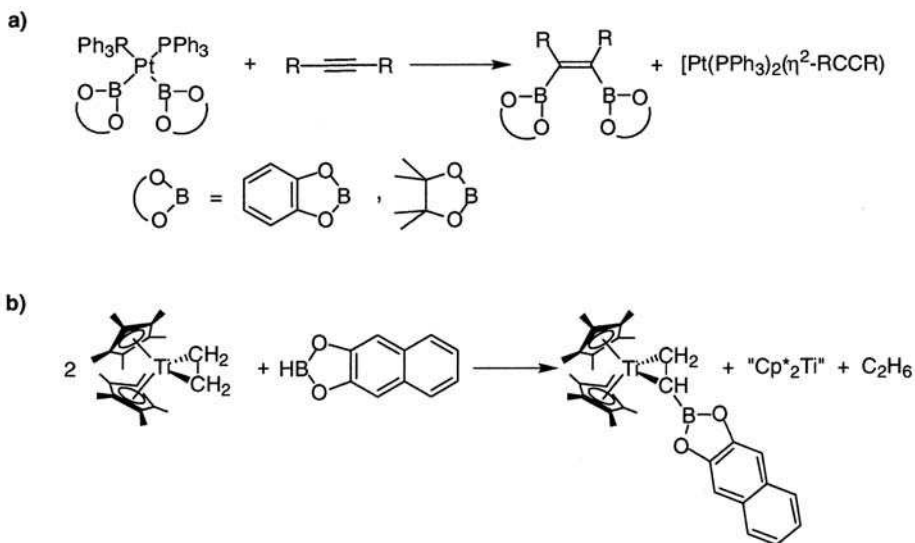
Scheme 6.60.

couplings) [187]. The generation of a trialkyl stannyl ruthenium derivative from a trialkylvinyltin via β - SnR_3 elimination has been reported (Scheme 6.60) [188].

The stoichiometric insertion of an alkyne into a $\text{Ru}-\text{SiR}_3$ bond has also been reported (Eq. 6.32) [189], and the reverse β - SiR_3 elimination from a nickel alkenyl derivative has recently been proposed [190].



1,2-Insertion into metal boryl bonds is represented by two examples described for a late and an early transition metal complexes. Platinum diboryl complexes react with alkynes to give the diborylated alkene (Scheme 6.61, a) [191]. A titanium(II) metallocene with a coordinated ethylene reacts with borane to give, via insertion of the alkene into a $\text{M}-\text{B}$ bond and subsequent β -H elimination, a complex with a coordinated vinylborane (Scheme 6.61, b) [192]. Both processes can be made catalytic.



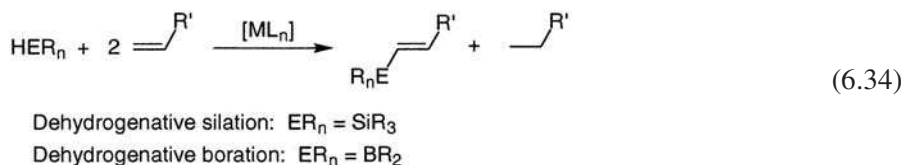
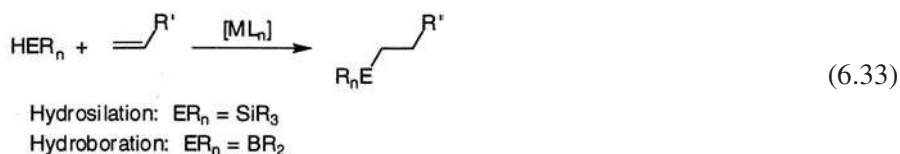
Scheme 6.61.

(c) *Catalytic applications*

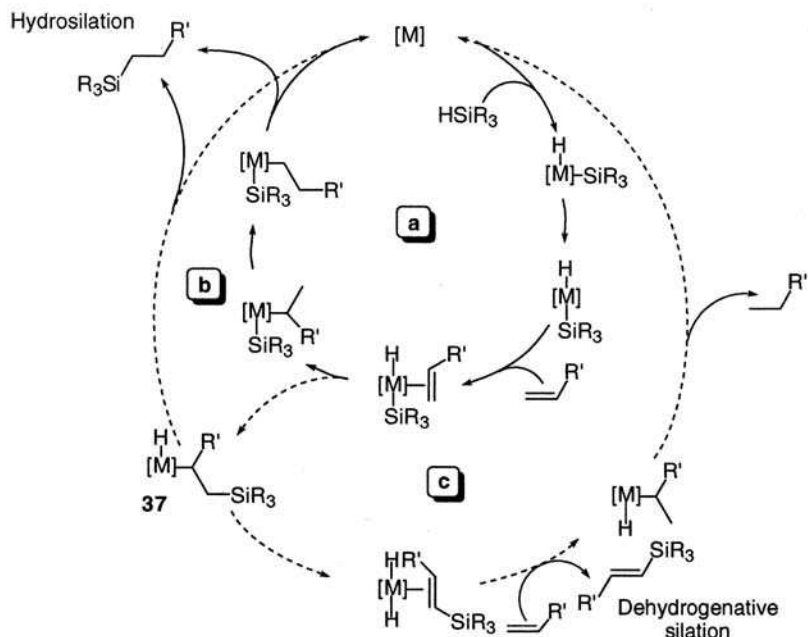
Several synthetically very useful processes involve the 1,2 insertion of unsaturated substrates into the M–SiR₃ bond (hydrosilation [193], dehydrogenative silation [193a,194], and disilation [176]) or the M–BR₂ bond (hydroboration [195], dehydrogenative boration [196], and diboration [191,195,197]) Catalytic reactions have been developed lately that comprise the 1,2 addition of two different ER_n groups to an alkene or alkyne (silylstannation [198], borylsilation [199], borylstannation [200]). Every possible combination is then available for functionalization of the unsaturated substrate [201].

The mechanism of the processes where the alkene or alkyne is functionalized by two ER_n groups necessarily involves the insertion of the substrate into one M–ER_n bond. The actual mechanism depends on the specific reaction, type of substrate, and catalyst. For diboration or disilation of alkenes, theoretical studies have found this step rate determining when the catalyst is a Pt complex [176,179]. The insertion of acetylene into Pt–BR₂ bonds is faster than the insertion of ethylene, and this step is not rate determining for diboration of alkynes [178,179]. As was pointed out before (see Section 6.4.1 (a)), insertion of an alkyne into the Pd–SnR₃ bond is preferred over insertion into the Pd–SiR₃ in the silylstannation of alkynes [177].

The hydrosilation and hydroboration of alkenes produce a saturated tetraalkyl silicon or boron derivative (Eq. 6.33). In addition dehydrogenative silation or boration derivatives are sometimes encountered as side products. These are substituted alkenes analogous to the Heck reaction products where a new C–Si (or C–B) bond is formed instead of a C–C bond (Eq. 6.34).



Two different mechanisms can be envisioned for these reactions that differ in the insertion step. Since both processes are very similar we will only discuss the silation process which have been more extensively studied. The so called Chalk–Harrod mechanism (Scheme 6.62, a) was first proposed for the hydrosilation of alkenes, and involves insertion of the alkene into the M–H bond formed by oxidative addition of the silane to the metal, followed by reductive elimination of a silyl alkyl. A competing route (the modified Chalk–Harrod mechanism, Scheme 6.62, b) derives from insertion of the alkene into the M–SiR₃ bond to

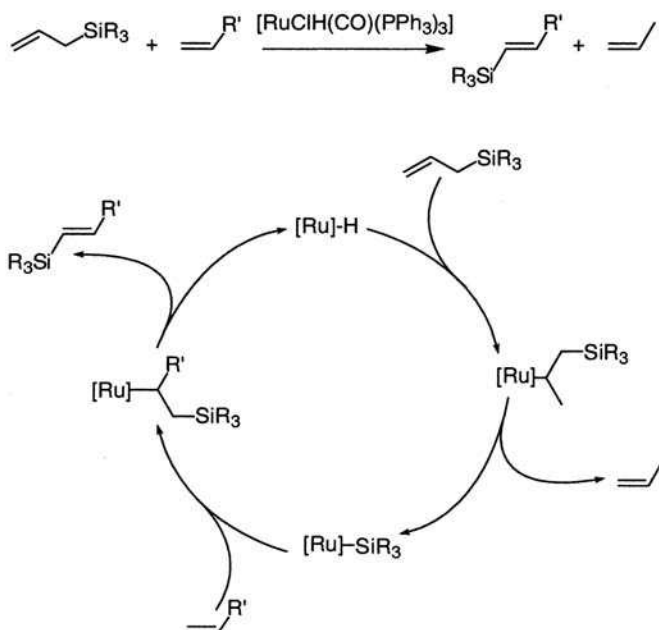


Scheme 6.62.

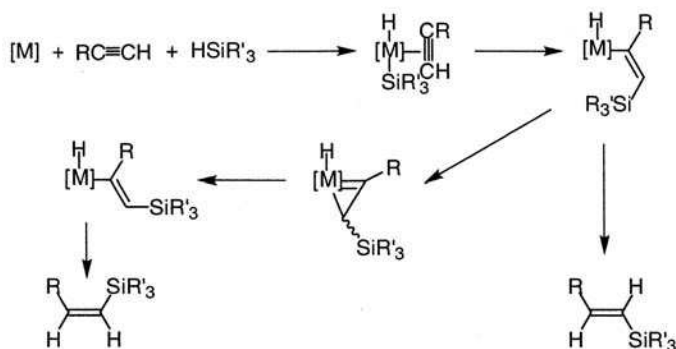
form a silyl substituted metal alkyl (**37**, Scheme 6.62) and reductive elimination of the silylalkyl and hydrido fragments. Theoretical studies on a platinum phosphine model calculate that insertion into the $M-H$ bond (route a) provides a mechanism with lower activation barriers than insertion into the $M-SiR_3$ bond [18]. However mechanistic studies on Pd and also Co systems favor route b (Scheme 6.62) [183,184]. The presence of the dehydrogenative silylation byproduct is a strong indication of insertion into the $M-SiR_3$ bond since it is formed by β -H elimination on intermediate **37** (Scheme 6.62, c).

Systems and conditions that proceed cleanly by route c (Scheme 6.62) are efficient for catalytic dehydrogenative silylation. A $M-SiR_3$ source is necessary and this can be a silane, with concomitant reduction of the alkene to give an alkane (Scheme 6.62, c). β - SiR_3 elimination has been artfully used to produce a $M-SiR_3$ moiety from vinylsilanes or allylsilanes. Scheme 6.63 depicts the use of allylsilanes described by Murai et al. to produce silyl substituted alkenes and propene as byproduct [194b].

The hydrosilylation of terminal alkynes involves the insertion of the alkyne into the $M-SiR_3$ bond, as has been determined for rhodium and iridium $[M(\text{triso})L_2]$ complexes (triso = $CH(P(O)Ph_2)_3$, $L = CO, C_2H_4, \text{cyclooctene}$) [202]. The β -vinylsilanes obtained are a mixture of *cis* and *trans* products and an isomerization of the initially formed *cis* silylvinyl metal complex, through an η^2 form, accounts for the stereochemistry found (Scheme 6.64). Competition of both Chalk-Harrod



Scheme 6.63.



Scheme 6.64.

and modified Chalk–Harrod mechanisms has been reported for the hydrosilylation of enynes catalyzed by ruthenium complexes [189].

6.4.2 Insertion into M–X bonds (X = N, P, O, S, Se, halogen)

(a) General considerations and theoretical studies

Unlike the H or ER_n cases (E = group 13, 14 element), X moieties, when the donor atom belongs to groups 15, 16 or 17, give stable or moderately stable

TABLE 6.12

Calculated energies of the HOMO Pd–X for PdX₂ fragments [203a]

Entry	X	$E_{\text{HOMO Pd-X}}$ (eV)	$E_{\text{LUMO } \pi^*} - E_{\text{HOMO Pd-X}}$ (eV) ^a
1	CH ₃	−7.97	3.97
2	H	−9.07	5.07
3	η^1 -C-acac	−10.05	6.06
4	Br	−10.99	6.99
5	Cl	−12.17	8.17
6	CN	−12.73	8.73
7	OCH ₃	−14.53	10.53
8	F	−14.97	10.97
9	κ^2 -O,O'-acac	−15.52	11.52
10	OH	−16.12	12.12

^a The authors take a constant value for $E_{\text{LUMO } \pi^*} = -4$ eV based on free ethylene on the assumption that the value will not change much on complexation to Pd(II).

free nucleophiles. This is the case of amines, phosphines, alkoxides, thiolates and halides, and less so for amido and phosphido groups. Even in an isolated complex with a preformed M–X bond a coordination/decoordination process may produce free X[−] which could attack the unsaturated substrate. Therefore apparent insertions into these M–X bonds should be looked at with caution (see Chapter 8).

Bäckvall, Siegbahn et al. have addressed, using theoretical methods, the feasibility of the insertion of alkenes into M–X bonds for neutral palladium complexes [203]. They have calculated the energy of the HOMO corresponding to the M–X bond which is the one interacting with the LUMO (alkene π^*) in the insertion transition state.

The corresponding HOMOs when X = F, OH, OMe, κ^2 -O,O'-acac are very low energy and the energy difference with the alkene centered LUMO is very big making the interaction unfavorable (entries 7–10, Table 6.12). On the contrary the HOMO–LUMO energy gap for H and CH₃ is smaller and insertion can proceed (entries 1, 2, Table 6.12). Thus, insertion is feasible for X groups with a high energy HOMO, which correlates with a soft character and an unstable free X. Table 6.12 shows a number of X groups with intermediate HOMO energies (entries 4–6), and their reactivity towards insertion is more difficult to predict. Since insertion is easier for the softer X groups (higher energy M–X HOMO), it can be anticipated that this pathway will be more favorable for amido than amino groups, and for phosphido than phosphine groups.

Competitive or preferential nucleophilic (*trans*) addition is specially important for late transition metals since, in general, they are good σ -acceptors and efficiently activate alkenes or alkynes upon coordination. Coordinated X groups that have lone pairs (X = amido, alkoxide, etc.) may give a 1,2-*cis* addition product by nucleophilic intramolecular attack, depending on the availability of this lone

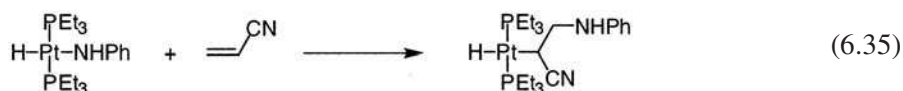
pair. Experimentally, this possibility is indistinguishable from an insertion process where the $\text{HOMO}_{\text{M-X}}$ orbital interacts with the alkene-centered LUMO as discussed above, since the same stereochemistry results; both possibilities will be considered hereupon as insertion processes.

Early transition metals in high oxidation states can act as σ - and π -acceptors when X bears lone pairs, so a coordinated X becomes a worse nucleophile, and this two component donation makes the M–X bonds very strong [26]. The thermodynamic balance for the insertion reactions may not be favorable nor even thermoneutral, as was calculated for the insertion of alkenes into Ln-NR_2 bonds (Ln = lanthanide), so if insertion reactions are to be accomplished in these systems they have to be coupled with other processes that provide extra driving force.

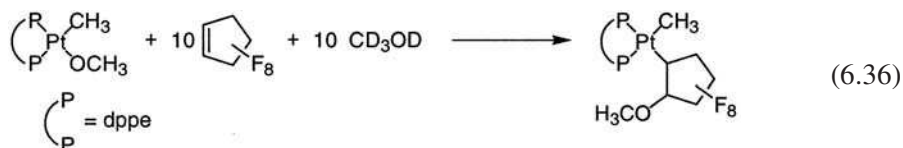
With this scenario, it is not surprising that true insertions into M–X bonds reported in the literature are not as abundant as for M–H and M–E (E = C, Si, B, etc.) bonds.

(b) Selected stoichiometric examples

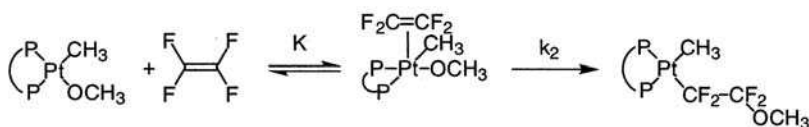
The chemistry of late transition metal amido and alkoxide complexes has been reviewed including the few insertion reactions that they undergo [94,204]. There are some interesting examples that are worth pointing out. Acrylonitrile inserts into the Pt–N bond of $[\text{PtH}(\text{NHPh})(\text{PEt}_3)_2]$ (Eq. 6.35). The involvement of nucleophilic attack on the alkene by a free amido anion has been ruled out by measuring the rate of amido exchange between Pt atoms in a crossover experiment between $[\text{PtH}(\text{NHPh})(\text{PEt}_3)_2]$ and $[\text{PtD}(^{15}\text{NHPh})(\text{PEt}_3)_2]$, which is much slower than the insertion process [205].



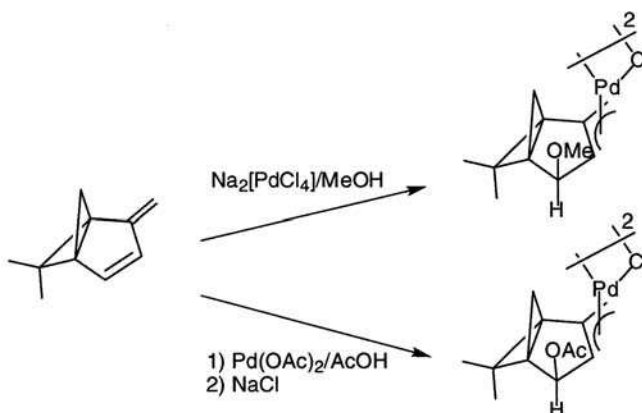
A closely related methoxide complex $[\text{Pt}(\text{Me})(\text{OMe})(\text{dppe})]$ (dppe = diphenylphosphinoethane) inserts perfluoroethylene into the Pt–OMe bond (Scheme 6.65). The mechanism of the reaction is consistent with coordination of the alkene in a rapid preequilibrium, followed by rate determining insertion. It does not involve dissociation of the methoxide ligand since exchange of this ligand with deuterated methanol is too slow to account for product formation, and the reaction of perfluorocyclopentene in deuterated methanol does not afford a deuterated product (Eq. 6.36) [206].



Casalnuovo, Calabrese and Milstein have described a good example of insertion of norbornene into the Ir–anilido bond of $[\text{IrCl}(\text{H})(\text{NHPh})(\text{PEt}_3)_2]$ in the course of



Scheme 6.65.



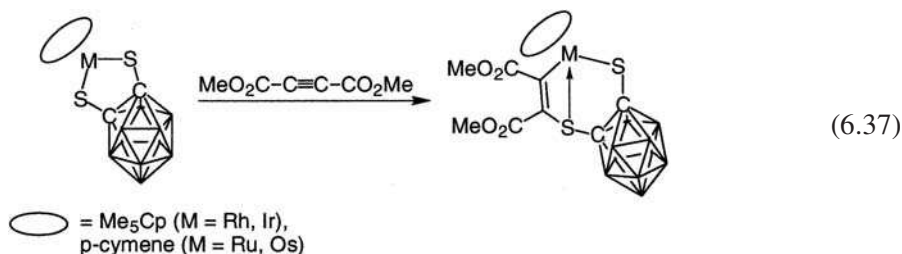
Scheme 6.66.

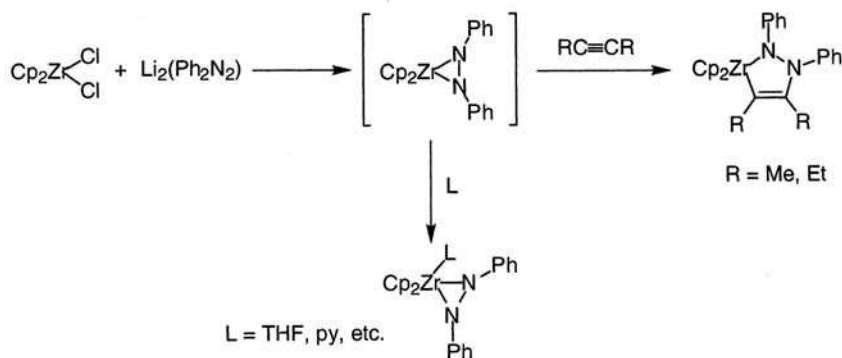
the catalytic hydroamination of that alkene (see below). The *cis* stereochemistry of the alkyl amino iridium complex formed supports the insertion process [207]. In these three examples insertion in the M–N bond is favored over insertion into the M–H or M–Me bonds.

Cis addition of acetate and methoxide has been observed for the reaction of Pd salts with a pinene derivative (Scheme 6.66). Although the corresponding complexes containing the Pd–OR moieties were not detected, the stereochemistry of the final complex is indicative of insertion [208].

Alkynes insert in the Zr–N bond of a chelating η^2 -hydrazido ligand to give a 2,3 diazametallacyclopentene. The strain of the three-membered hydrazido metallacycle clearly enhances its reactivity towards insertion (Scheme 6.67) [209].

Rh, Ir, Ru and Os M–S bonds of a chelating dithiolate ligand are susceptible to insertion of alkynes to give metallacyclic structures as the one shown in Eq. 6.37 [210].





Scheme 6.67.

Substrates that contain polarized C–Y unsaturated moieties (Y = heteroatom) have been observed to insert into M–X bonds to give new metal complexes. This is the case of CO₂, COS, and PhNCO, that insert in the Pt–N bond of [PtH(NHPh)(PEt₃)₂] [205], or CS₂ into the Pd–OR bond of [Pd(Me)(OR)(dppe)] to give [Pd(Me){κ¹-SC(S)OR}(dppe)] (R = CH(CF₃)Ph) [211].

The reverse insertion reaction, β-X elimination, has also been found for X = PR₂ [212], OR [185,213], SR [185,214], and halide [185,215].

(c) Catalytic applications

Synthetic applications that consist of metal catalyzed addition of X–X' to carbon–carbon unsaturated substrates, generally alkynes, have been described for X = X' = SR, SeR, TeR and X = SeR, X' = PR₂ as well as X = SR, X' = BR₂, SiR₃ [201]. These transformations generally involve oxidative addition of the X–X' reactant to the metal center followed by insertion of the alkyne, into the M–X bond. Reductive elimination leads to the final disubstituted alkene, which shows *cis* stereochemistry.

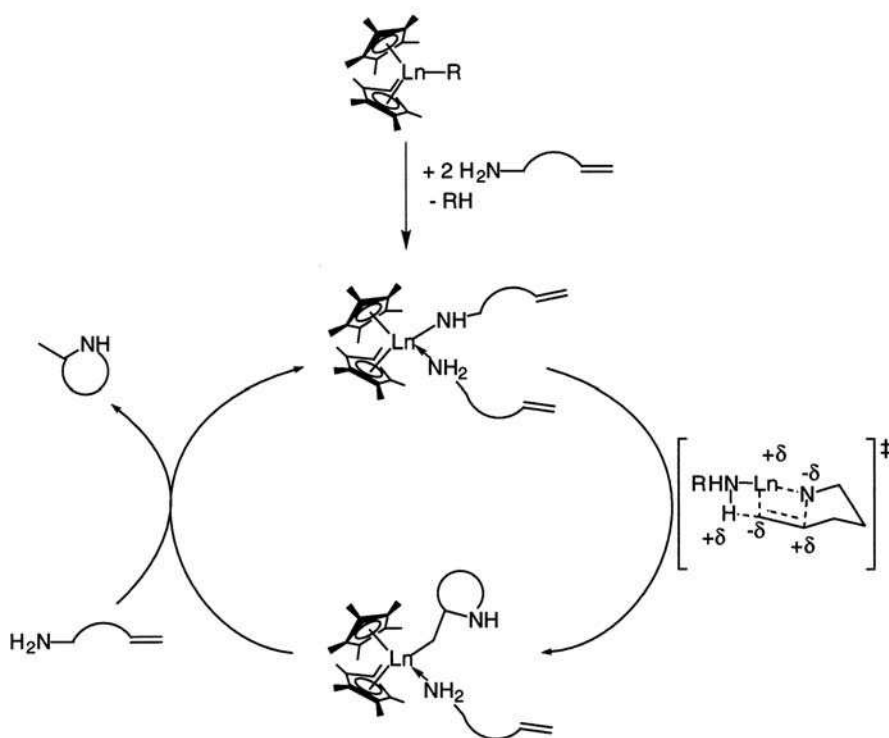
Metal mediated H–X addition to alkenes and alkynes is also a very interesting synthetic process that affords new phosphine derivatives (X = PR₂, hydrophosphination), sulfides (X = SR), and amines (X = NR₂) [201a]. Although several mechanistic pathways can be envisaged for these reactions, insertion into the M–X bond has been proposed in the course of the addition of the heavier X groups, i.e. hydrophosphination and addition of thiols [212,216]. More studies are needed, though, in some cases, to substantiate the insertion step.

When lighter and harder X groups are involved (X = NR₂ and OR), insertion is less favored (see Section 6.4.2 (a)) and other mechanistic pathways, particularly nucleophilic attack in the case of late transition metals, are prevalent. This is the case of an important catalytic process, the Wacker oxidation of alkenes that transforms ethylene to acetaldehyde or terminal alkenes in ketones. For a long time a controversy was on, regarding the nature of the step that leads to the new

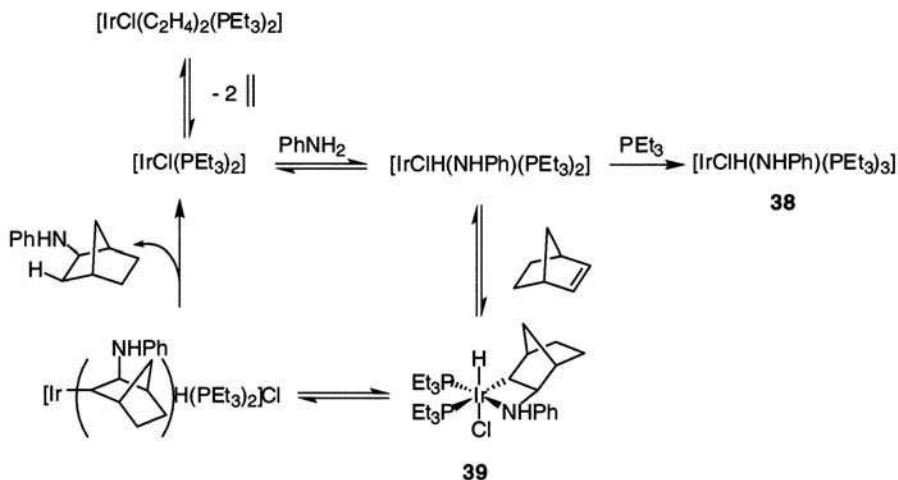
C–O bond (insertion of the alkene into the Pd–OH bond or nucleophilic attack of water on a Pd-coordinated alkene). The nucleophilic pathway (*trans* attack) is more generally accepted although some discordance still remains [217].

Several approaches have been taken to the development of efficient hydroamination processes and they have led to catalytic reactions that follow three main types of mechanisms: (a) nucleophilic attack on activated metal-coordinated alkenes (applied mainly to late transition metals) [218], (b) cycloaddition of an alkyne and a metal imido moiety [219], (c) insertion into an M–N(amido) bond [207,220]. The subject has been reviewed recently [221].

The insertion approach is very successful in the hydroamination of alkynes and alkenes catalyzed by lanthanide complexes developed by Marks et al. [220]. Thorough mechanistic studies have been undertaken for the intramolecular reaction (hydroamination–cyclization of aminoalkenes), although the intermolecular version of the process is also efficient [222]. The mechanism of the reaction can be represented in a simplified way by Scheme 6.68. The insertion step is almost thermoneutral, but the protonolysis of the M–aminoalkyl bond that follows is exothermic and provides the necessary driving force. The insertion of the alkene into the Ln–N bond is irreversible and rate determining and it goes through a



Scheme 6.68.



Scheme 6.69.

highly ordered transition state (represented for an aminopentene derivative in Scheme 6.68). The activation parameters found, specially the negative entropy value, support this activated complex ($\Delta H^\ddagger = 12.7$ kcal/mol, $\Delta S^\ddagger = -27$ eu). Some assistance by the other molecule of coordinated aminoalkene has been proposed on the basis of the high kinetic isotope effects found [220a].

By using late transition metals a catalytic hydroamination reaction based on insertion has been found by Milstein et al. [207]. It brings about the hydroamination of norbornene with aniline by using $[\text{IrCl}(\text{C}_2\text{H}_4)_2(\text{PEt}_3)_2]$ as catalyst precursor (Scheme 6.69). Labeling studies show that the H and NHPH moieties add in a *cis* fashion to the exo face of the alkene. Complex **38** and the intermediate **39** (Scheme 6.69) have been isolated, and **39** structurally characterized by X-ray crystal diffraction. The actual insertion (or *cis* M–NHR addition to the alkene) is interpreted by the authors as an intramolecular nucleophilic attack of the nitrogen lone pair of the coordinated amido group, since the electrophilic Ir(III) center is likely to activate the alkene towards nucleophilic attack.

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1,1-Insertion into Metal–Carbon Bond

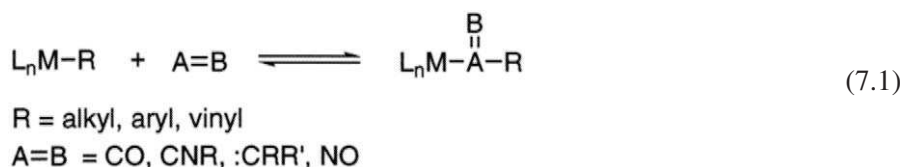
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7.1 INTRODUCTION

Among elementary processes involved in transition metal-catalyzed organic synthesis, 1,1-insertion and α -elimination constitute two fundamental processes quite important in transforming organic substrates. The 1,1-insertion can be expressed as a general form as given below (Eq. 7.1).



Various unsaturated compounds can be inserted into the metal alkyl, aryl, and alkenyl complexes to give new organometallic complexes having various functional groups. The insertions of carbon monoxide (CO) and isocyanide (CNR) into transition metal–carbon σ -bond are particularly important processes, since a carbon unit can be increased in the process and the acyl type complexes formed by the insertion processes can be subjected to further transformations to synthesize useful organic compounds. For example, the CO insertion constitutes a fundamental step in industrially important processes such as hydroformylation of olefins, acetic acid synthesis from methanol and CO, Fischer–Tropsch process, amidocarbonylation, olefin and CO copolymerization processes as well as in a variety of laboratory syntheses of carbonyl containing compounds.

Insertion processes are reversible in certain cases, subject to thermodynamic factors in Eq. 7.1. Particularly important among the deinsertion processes is the decarbonylation by which a compound with one less carbon unit is produced. Decarbonylation of acyl halides and aldehydes are utilized for removing a carbonyl

unit from the starting compounds to produce alkyl and aryl halides or alkanes, alkenes or arenes depending on the subsequent elementary processes.

Unsaturated compounds such as CO can be formally inserted into a metal–heteroatom bond such as hydroxide, alkoxide, amide, and sulfide. However, it presents a difficult problem to determine whether the overall insertion process proceeds through a migratory insertion process or by an alternative process. For example, the anionic ligand such as OH and alkoxides may dissociate first to provide a vacant coordination site for the CO ligand that is subsequently attacked by the anion to give the same product as that obtained by the migratory insertion of the anionic ligand on the coordinated CO.

7.2 CO INSERTION

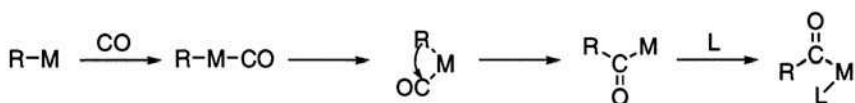
7.2.1 Fundamentals of CO insertion

Because of the importance of the CO insertion into a transition metal–carbon σ -bond in relation to the transition metal-catalyzed carbonylation, the mechanism of the CO insertion has attracted considerable attention [1,2]. Through fundamental studies on model complexes, the route of CO insertion has been established for most transition metal complexes to be the one through alkyl migration mechanism [3–8]. While CO insertion can occur with various metal–heteroatom σ -bonds, only insertion into metal alkyls (hydrocarbyls) will be discussed in this chapter.

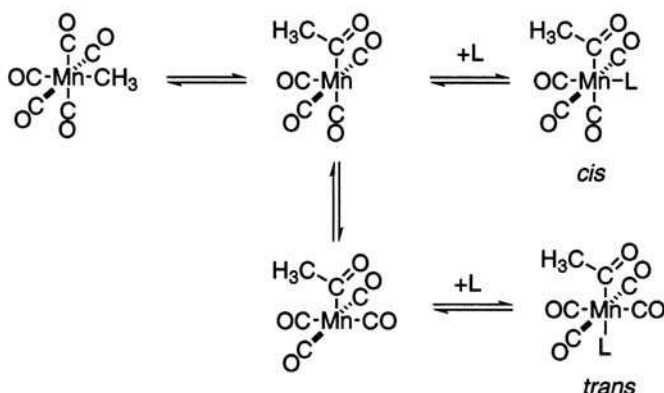
The generally accepted mechanism for CO insertion consists of the following steps: (a) coordination of CO to the metal center; (b) isomerization of the alkyl–carbonyl complex, if necessary, to bring the CO ligand adjacent to the alkyl ligand, (c) migration of the alkyl group to the CO ligand to give the acyl complex; (d) stabilization of the resulting coordinatively unsaturated acyl species by coordination of an appropriate ligand (Scheme 7.1).

The first convincing example of CO insertion into a metal–alkyl bond dates back to 1957, when Coffield demonstrated the reversible reaction of $\text{MnCH}_3(\text{CO})_5$ with CO to give $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_5$ [9]. This CO insertion mechanism, which has been extensively studied by kinetic and/or spectroscopic means since the 1960s, has been regarded as a prototype of other CO insertion systems [10–12]. The important conclusions derived through these studies are summarized below.

(1) The mechanism for CO insertion into $\text{R–Mn}(\text{CO})_5$ involves the formation of a coordinatively unsaturated acyl(tetracarbonyl)–manganese intermediate, $\text{RCO–Mn}(\text{CO})_4$.



Scheme 7.1.



Scheme 7.2.

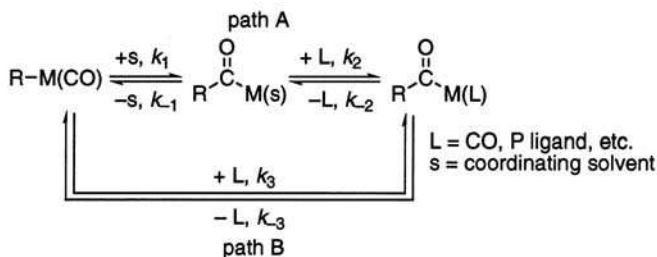
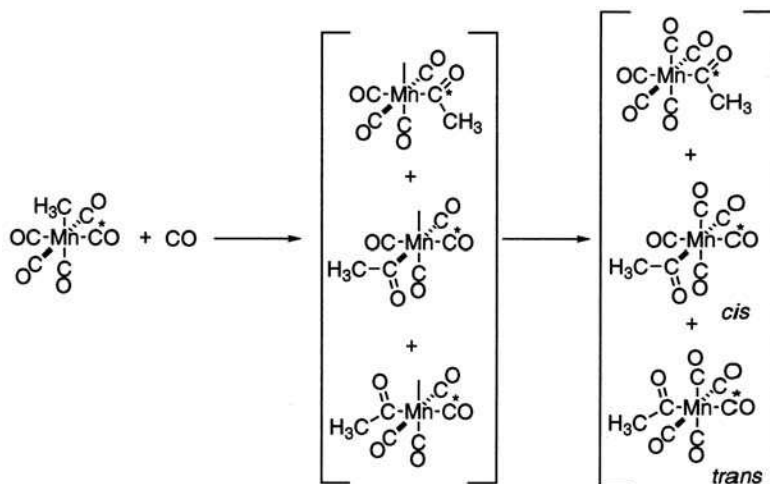
(2) The acyl intermediate is formed by an intramolecular 1,2-migration of the alkyl group onto one of the adjacent CO ligands. The resulting vacant site can be occupied by incoming CO or other ligand.

(3) The CO insertion takes place stereospecifically with retention of configuration of the alkyl group [13,14].

While the formation of the acyl moiety from the CO and the hydrocarbyl ligand is normally referred to as the 'CO (or carbonyl) insertion', most stereochemical studies have indicated that the migration of a hydrocarbyl group to an adjacent CO affords the acyl species. The stereochemistry of CO insertion has been demonstrated by using labeled CO. When the incoming ligand is ^{13}CO , the product contains only one labeled CO, which binds at a site *cis* to the newly formed acetyl group [15]. Analogously, by using a phosphorus ligand as the external nucleophile, it has been established that the *cis*- $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_4(\text{L})$ was initially formed as the kinetic product and the *cis* isomer was subsequently isomerized to the *trans* form (Scheme 7.2) [16,17].

The carbonylation from *cis*- $\text{MnCH}_3(^{13}\text{CO})(\text{CO})_4$ gave the acyl products, whose positional ratios of isotopic label on the basis of ^{13}C NMR were compatible with the methyl migration mechanism [18]. The mixture of the $\text{Mn}(*\text{COCH}_3)(\text{CO})$, *cis*, and *trans*- $\text{CH}_3\text{COMn}(*\text{CO})$ products (see Scheme 7.3) was obtained in a ratio of 1 : 2 : 1, whereas the carbonyl migration pathway would not have provided the *trans* isomer.

A great deal of effort has been made to identify the active intermediates in CO insertion. Interpretation of solvent effects is complicated by the fact that the insertion induced by CO, tertiary phosphines, and other 2e ligands, is a two-stage process in polar solvents (Scheme 7.4, path A). A solvent-independent pathway, involving the direct reaction between an alkyl complex and the incoming ligand, has been observed in nonpolar solvents [11] (Scheme 7.4, path B). In the alkyl migration step with the rate constant k_1 , a solvent molecule(s) acts as a



trigger and a solvent-coordinated acyl complex is formed. The subsequent ligand coordination step with k_2 involves the displacement of solvent by the incoming ligand, L. In a number of investigations, the rate constant, k_1 , has been found to increase with increasing polarity of the solvent. The solvent effect was ascribed to stabilization of the coordinatively unsaturated acyl species by direct solvent coordination to the vacant binding site to form $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_4(\text{solvent})$ as the intermediate [10,19]. However, it is difficult to understand why the attack of nucleophilic ligands to the solvent-coordinated species should not retard the k_2 step. A kinetic study regarding the CO insertion into $p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}_2\text{Mn}(\text{CO})_5$ provided the explanation that the solvent did not enhance the rate by stabilizing the intermediates, but rather by catalyzing the CO insertion process [20].

Recently, Ford et al. explored laser flash photolysis of the $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_5$ to give acyl intermediates relevant to carbonylation of $\text{MnCH}_3(\text{CO})_5$ [21]. The time resolved infrared (TRIR) and time resolved optical (TRO) spectra of the long-lived acyl intermediate indicated that a dihapto acyl complex $\text{Mn}(\eta^2\text{-$

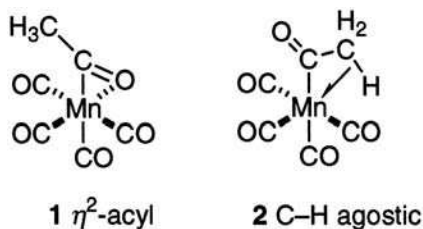


Fig. 7.1. Plausible acyl intermediates.

$\text{CH}_3\text{CO}(\text{CO})_4$ (**1** in Fig. 7.1) was formed in weakly coordinating solvents such as cyclohexane, whereas the solvento complex *cis*- $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_4(\text{thf})$ was observed in strongly coordinating THF. Although the photodecarbonylation of $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_5$ is not the precise microscopic reverse of the carbonylation of $\text{MnCH}_3(\text{CO})_5$, it was postulated that the nature of the intermediates in the decarbonylation process is relevant to the carbonylation mechanism.

For clarifying the factors influencing the ease of CO insertion and its reverse process, it is desirable to know the metal–carbon bond energies in the initial metal alkyl and the product metal acyl species. However, the presently available thermochemical data for the bond dissociation energies in acyl–transition metal complexes are not sufficient to allow us to advance a reasonable argument for the thermodynamic feasibilities of insertion and deinsertion processes [22–24].

Recently, however, the progress of the molecular orbital theory, notably of the density functional theory, has reached the stage of allowing us to estimate the energies of the initial metal alkyl and of the product metal acyl species and further delineate the reaction courses proceeding through transition states. Some of the results obtained by theoretical calculations regarding the energies of the initial and final stages as well as the activation barriers are in reasonably good agreement with the experimental results. Thus we can now present more consistent pictures of the reaction courses in the carbonylation reactions.

The following theoretical study using gradient corrected density functional methods revealed that the dihapto species, $\text{Mn}(\eta^2\text{-CH}_3\text{CO})(\text{CO})_4$ (**1** in Fig. 7.1), is a stable intermediate in the photodecarbonylation of $\text{Mn}(\text{CH}_3\text{CO})(\text{CO})_5$. Non-solvent-assisted thermal carbonylation of $\text{MnCH}_3(\text{CO})_5$ proceeds through a different acyl species (**2** in Fig. 7.1) stabilized by agostic interaction between a C–H bond in the acetyl group and the manganese [25].

The nature of the ligand into which the CO is to be inserted strongly influences the ease of CO insertion. The metal to hydride bond is known to be resistant to CO insertion, whereas deinsertion from the formyl to the hydride proceeds readily [26]. However, in certain cases the unfavored insertion into metal hydrido complexes takes place when a η^2 -formyl bond is formed, giving an extra stability to the product [27].

The CO insertion into trifluoromethyl complexes is difficult, whereas the dein-

sertion from the trifluoroacetyl ligand to the trifluoromethyl ligand readily takes place [28–30]. This is in contrast to the ease of CO insertion into phenyl–metal bond, which has about the same metal–C bond strength with the trifluoromethyl–metal bond. The difference in behavior of CO insertion may be accounted for by difference in the energy of the σ -lone pair orbital of R^- [31]. In other words, the electronegative trifluoromethyl group is not favored by the CO ligand, since the alkyl insertion is a process of migration of the alkyl group to the electrophilic carbonyl ligand. This is also reflected by the increase in the ionization potential (IP) of the R^- group. The effective IP clearly distinguishes the reactivity of different groups with similar metal–carbon bond strength.

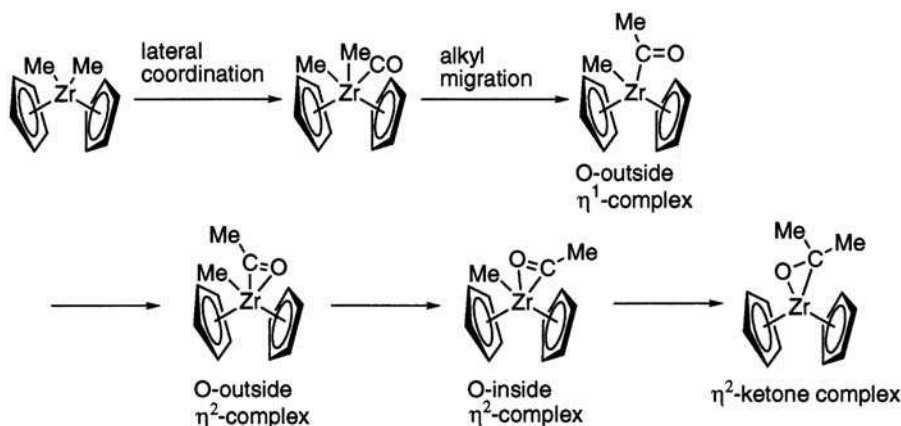
Another issue of interest is the feasibility of multiple CO insertions into the metal–carbon bond to provide an α -ketoacyl species. If multiple CO insertion is possible, one can expect various types of applications in preparation of organic compounds [32]. However, easy elimination of CO from $Mn(CH_3COCO)(CO)_5$, which can be prepared from $CH_3COCOCl$ with $Mn(CO)_5^-$, suggests that consecutive insertion of CO into the $Mn-CH_3$ bond is not feasible in agreement with the absence of the examples of double CO insertion into metal–carbon bond [33]. Although the dissociation energy of the $Mn-COCH_3$ bond is slightly less than that of $Mn-CH_3$ bond, the effective IP of the acyl anions is considerably higher than that of the alkyls, rendering the CO insertion into the Mn -acetyl bond less favored.

The behavior of early transition metal alkyls toward CO is somewhat different from that of late transition metal alkyls. Very little applications using early transition metal complexes for carbonylation processes have been reported in contrast to the abundant examples of applications of late transition metal complexes to carbonylation of organic substrates. However, fundamental studies on the chemistry of early transition metal alkyls toward CO insertion provide us with important information regarding the mechanisms of catalytic carbonylation processes. Thus we deal here with the chemistry of CO insertion into early transition metal alkyls and into late transition metal alkyls separately.

7.2.2 CO insertion into early transition metal alkyls

With the increase in the number of isolated examples of early transition metal alkyls, detailed fundamental studies on the CO insertion chemistry have also increased. The CO insertion chemistry into d-element and f-element metal alkyls has recently attracted considerable attention.

For a transition metal alkyl complex to undergo the CO insertion, initial coordination of the CO molecule to the metal center is required. The Group 4 transition metal alkyls in high oxidation states are electron poor and accept electrons from the CO ligand with little back-bonding from the metal d orbital to the π^* orbital of the CO. The subsequent alkyl migration to the CO ligand gives the coordinatively unsaturated transition metal acyl species. Because of the electrophilicity



Scheme 7.5.

of high valent early transition metal complexes, the acyltransition metal complexes produced by the CO insertion tend to form η^2 -acyl bonding, which gives higher stability to the product than the η^1 -acyl complexes by additional binding of the carbonyl oxygen with the metal [34,35]. Thus the formation of the η^2 -acyl complexes facilitates the CO insertion on thermodynamic grounds. Some of the methyl–acetyl complexes further undergo the transfer of the methyl group to the carbonyl carbon in the η^2 -acetyl ligand to form η^2 -ketone complexes as shown in Scheme 7.5. Complexes of this type have been isolated in Group 4, 5, 6, and 7 transition metals and their structures have been established [36–39].

Scheme 7.5 illustrates the theoretical results on the course of CO insertion into a dimethyl bis(cyclopentadienyl)zirconium complex [40]. The CO molecule approaches the zirconium center from the side position (lateral coordination) in the rate-limiting step in the insertion process. The methyl migration to the coordinated CO gives an η^1 -acetylzirconium complex which is further stabilized to the η^2 -acetyl complex having the carbonyl oxygen directed toward outside. After the outside to inside isomerization, reductive elimination of the acetyl and the methyl groups affords a zirconium complex where acetone is coordinated to the zirconium through η^2 -C=O bond. A nonplanar arrangement of the alkyl and acyl ligands with a dihedral angle of ca. 50° in the transition state allows the approach for the C–C coupling. Formation of η^2 -ketone complexes via alkyl(η^2 -acyl) species has been reported in carbonylation of several dialkylbis(cyclopentadienyl) complexes of early transition metals [41].

7.2.3 CO insertion into late transition metal alkyls

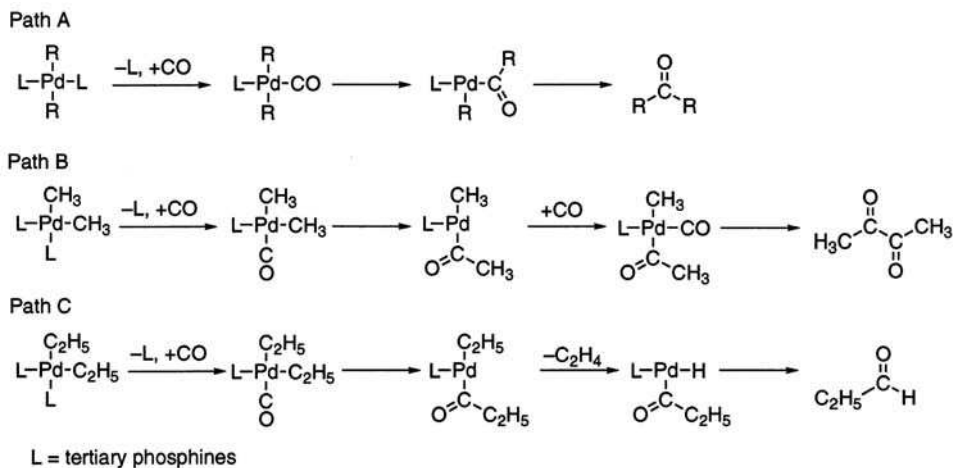
Most known processes utilizing carbon monoxide are catalyzed by late transition metal complexes. This is due to the ease of oxidative addition of substrates such as organic halides to low valent transition metal complexes and reductive

elimination processes yielding the product by C–C bond formation with regeneration of low valent species again. The notable examples of commercial and laboratory applications are conversion of methanol to acetic acid catalyzed by cobalt or rhodium complexes in the presence of HI (Chapter 1, Scheme 1.8), hydroformylation of olefins catalyzed by cobalt or rhodium complexes (Scheme 1.19), conversion of organic halides into carboxylic acids and derivatives catalyzed by palladium complexes (Scheme 1.20), and alternating copolymerization of an olefin and CO. In these CO utilizing catalytic processes, transition metal alkyl (including alkenyl and aryl) complexes are formed at certain stages in the catalytic process and the CO insertion into the metal alkyl bond gives acyl complexes. The chemistry of these organometallic complexes differs from each other depending on the transition metal in the periodic table.

In the chemistry of group 8 and 9 metal complexes, consideration of octahedral complexes is required, whereas with group 10 metal complexes, particularly in Pd(II) complexes with tertiary phosphine ligands, the reactions proceed mostly under the constraint of square planar geometry with possible involvement of unstable five coordinate species. Thus mechanistic considerations of the reaction courses are somewhat simpler.

(a) *Migration mode in CO insertion*

A most illustrative example showing the constraint of the square planar geometry can be seen in the carbonylation of square planar dialkyl palladium complexes having two tertiary phosphine ligands. The *cis* and *trans* dialkylpalladium complexes react with carbon monoxide at room temperature giving different products depending on the alkyl groups and the stereochemistry of the starting complexes (Scheme 7.6).



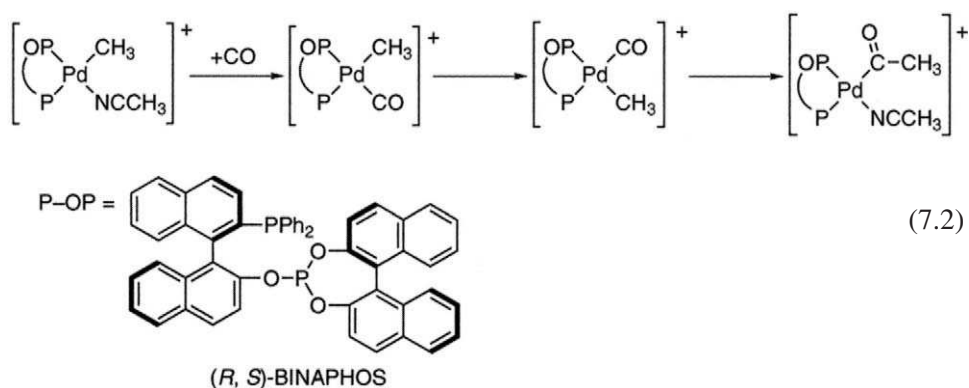
Scheme 7.6.

The reaction mechanisms can be accounted for consistently by assuming the occurrence of alkyl migration to the CO coordinated at the adjacent position in the square plane. In the reaction of the *trans* complexes, ketones can be obtained by the alkyl migration to the coordinated CO followed by facile reductive elimination of the alkyl and acyl ligands from T-shaped acyl(alkyl)palladium complexes (path A). However, the *cis* isomers upon alkyl migration to the coordinated CO afford T-shaped complexes bearing the alkyl and acyl groups in mutually *trans* positions, which are not appropriate for direct reductive elimination of ketones without *trans*–*cis* isomerization in the square planar geometry. Thus, the T-shaped intermediate derived from the *cis*-[Pd(CH₃)₂L₂] is susceptible to further coordination and insertion of CO to give a diketone (path B). The formation of propionaldehyde from *cis*-[Pd(C₂H₅)₂L₂] with CO is ascribable to β -hydrogen elimination of the T-shaped ethyl(propionyl)palladium intermediate and the following reductive elimination (path C) [42].

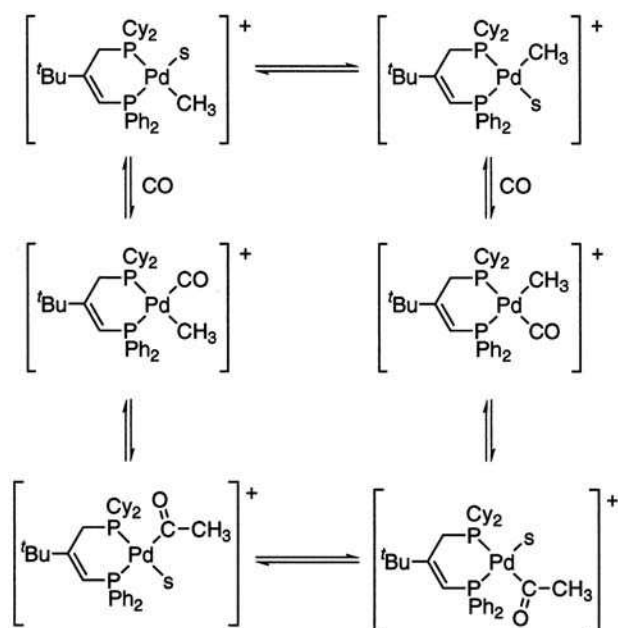
The mechanism of the methyl migration to the adjacent CO ligand giving the T-shaped acetyl palladium species is in agreement with the result of theoretical calculation [31b,43].

Although the CO insertion proceeds by the alkyl migration mechanism, especially for the group 10 transition metal alkyls, the acyl complex may undergo the subsequent isomerization, depending on the nature of the ligand situated at the site *trans* to the acyl ligand. The presence of the rapid equilibrium makes the clear-cut determination of the mechanism a difficult matter.

Evidence indicating the involvement of isomerization following the alkyl migration to the coordinated CO ligand was obtained in the CO insertion into a cationic methylpalladium complex coordinated with a chiral phosphine–phosphite ligand, (*R,S*)-BINAPHOS, as shown in Eq. 7.2 [44].



Detailed NMR studies on several monoalkylpalladium and platinum complexes bearing nonsymmetrical chelating phosphine ligands revealed that the CO insertion occurs via alkyl migration as shown in Scheme 7.7 [45,46].



Scheme 7.7.

An extended Hückel and *ab initio* Hartree–Fock calculations for the CO insertion into $[\text{Pt}(\text{CH}_3)(\text{CO})\text{F}(\text{PH}_3)]$ also indicated the methyl migration mode [47]. Notably, widening of the F–Pt–PH₃ bond angle was predicted to occur in the transition state for the migratory insertion. *Ab initio* calculations of CO insertion in $[\text{Pd}(\text{CH}_3)(\text{CO})(\text{PH}_3)_2]^+$ and $[\text{Pd}(\text{CH}_3)(\text{CO})(\text{P}-\text{P})]^+$ (P–P = H₂PCH=CHPH₂) showed that both the alkyl and CO ligands move cooperatively with opening of the P–Pd–P angle [48,49].

From experimental results of acceleration of CO insertion into cationic methylpalladium complexes $[\text{Pd}(\text{CH}_3)(\text{CH}_3\text{CN})(\text{P}-\text{P})]^+$ in the order of DPPE $\ll$ DPPF $<$ DPPP $\approx$ DPPB (DPPE = 1,2-bis(diphenylphosphino)ethane; DPPF = 1,1'-bis(diphenylphosphino)ferrocene; DPPP = 1,3-bis(diphenylphosphino)propane; DPPB = 1,4-bis(diphenylphosphino)butane) the kinetic barriers to migratory insertion in $[\text{Pd}(\text{CH}_3)(\text{CO})(\text{P}-\text{P})]^+$ were found to decrease with increase of the P–Pd–P angle as well as the steric bulk of the diphosphine ligand [50].

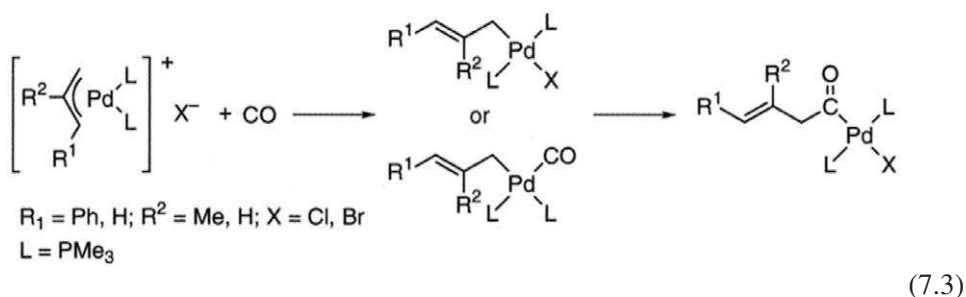
The kinetic data obtained in the CO insertion into cationic methylpalladium complexes having bidentate phosphines are listed in Table 7.1. The rigidity of the chelate ligand backbone was observed to have little or no effect on the CO insertion barriers by comparing the reactivities of five-membered DPPE, DPBZ, and DPPEE systems (DPBZ = 1,2-bis(diphenylphosphino)benzene; DPPEE = *cis*-1,2-bis(diphenylphosphino)ethylene), in contrast to the expectation that a ligand of higher flexibility may enhance the migration by promoting the conformational rearrangement [51].

TABLE 7.1

Kinetic data for CO insertion into the cationic methylpalladium complexes

Ligand	Temperature (K)	Rate constant (10^4 s^{-1})	$\Delta G^\ddagger$ (kcal/mol)
DMPE	248	3.2	18.4(2)
DPPEE	238	18	17.1(2)
DPBZ	232	4.23	17.1(2)
DPPE	226	1.9	17.1(1)
DPPP	191	0.45	14.8(1)
DIPPP	191	3.4	14.1(2)
DPPB	194	5.5	14.2(2)

Examples of CO insertion into η^3 -allyl transition metal complexes are quite limited. Eq. 7.3 shows that the CO insertion into the η^3 -allylpalladium proceeds to give isolable acylpalladium complexes depending on conditions [52]. The reluctance to the CO insertion may be caused by the stability of η^3 -allyl transition metal complexes. Another factor for the lower reactivity of the allylpalladium complex to provide the acylpalladium complex is the facile decarbonylation of the acyl complex produced by the CO insertion into the η^3 -allyl bond. In fact removal of the X ligand in the butenoylpalladium complex having the halide ligand X in Eq. 7.3 by addition of a silver salt causes rapid decarbonylation of the butenoyl entity giving the η^3 -allylpalladium complex.



The catalytic carbonylation of allyl carbonates under CO pressure to give butenoate esters can be accounted for by assuming the CO insertion into allyl–palladium bond [53,54].

(b) Intratriad trends

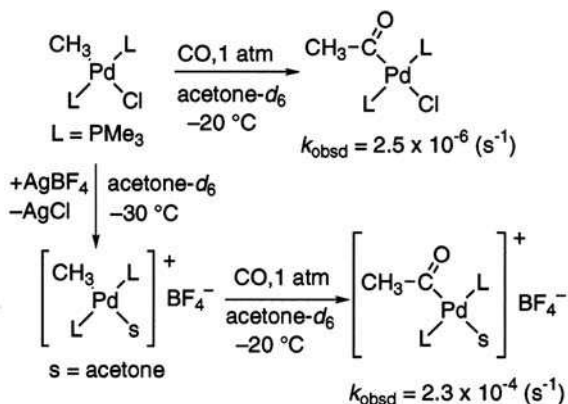
It is generally observed that 5d metals show lower reactivity toward CO insertion than the 3d and 4d metals in the same triad [8,55]. Since CO insertion takes place with breaking of the metal–carbon bond, the reactivity should be strongly influenced by the strength of this bond, which is generally represented by metal–carbon bond dissociation energies. Indeed, precedents of the CO insertion processes into monoorganoplatinum complexes generally having the stronger metal–carbon bond than Pd–C bond are relatively limited [56–59]. The results of these studies indicated that the CO insertion into the Pt–C bond is less favorable than that into the Pd–C bond.

The differences in the energetics of the palladium and platinum complexes for the CO insertion can be explained by taking relativistic effect into account as discussed by Koga and Morokuma [43]. Recent theoretical results on the cationic monomethyl–platinum and –palladium complexes clearly showed that the relativistic effect acts adversely to the CO insertion into the M–CH₃ bond [48]. Since the relativistic effect is much larger for platinum complexes than for the palladium complexes, the metal–carbon bonds in the platinum complexes should be stronger than in the palladium complexes. Cleavage of the strong platinum–carbon bond in the alkyl(carbonyl)platinum complex in the CO insertion process will require a larger activation energy.

(c) Promoting factors for CO insertion

In many palladium-catalyzed reactions, generation of cationic intermediates has been often found to enhance the catalytic activities [60]. A number of reports have demonstrated that the CO insertion into metal–carbon σ -bonds can be accelerated by formation of cationic complexes from neutral complexes [50,61–63].

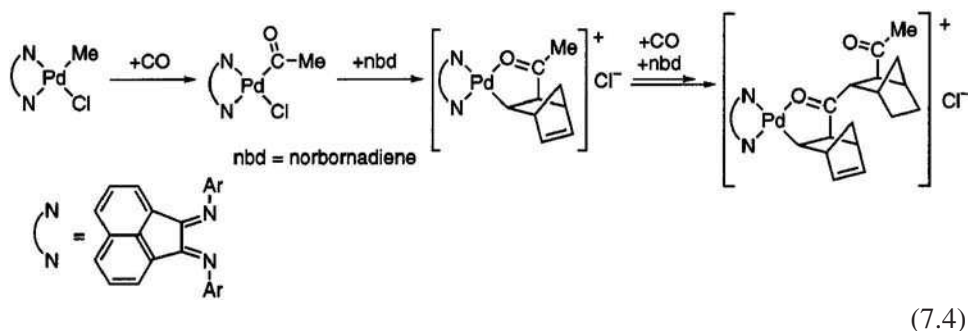
Scheme 7.8 illustrates that the first order rate constant of the CO insertion process into the neutral methyl(chloro)palladium complex was increased by 100



Scheme 7.8.

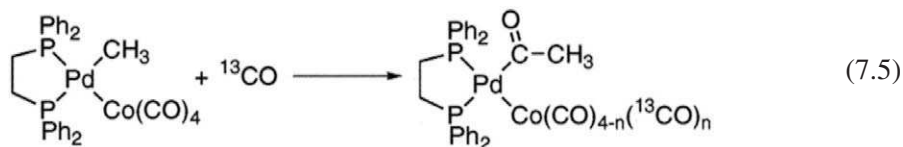
times by converting the neutral complex into the corresponding cationic solvent-coordinated complex by removal of the chloride ligand with AgBF_4 [61]. Similar trends can be seen from the results of CO insertion into monoalkyl complexes bearing chelating P–P and P–N ligands [64]. The CO insertion rates of methyl-palladium complexes of the type $[\text{PdCH}_3(\text{X})\text{L}_2]$ or $[\text{PdCH}_3(\text{L}')\text{L}_2]^+\text{X}^-$ (X = anions or anionic ligands; L and $\text{L}' = 2\text{e}$ ligands) were markedly dependent on the coordinating ability of ligands, anions, and solvents. Experimental results on promotion of the insertion by employing weakly coordinating ligands or anions suggested that the availability of a coordination site for the incoming CO is quite important for the insertion to proceed. For a monoorganopalladium complex having two monodentate tertiary phosphine ligands to undergo a concerted insertion process, the monoorganopalladium complex is required to possess a coordination site available adjacent to the hydrocarbonyl ligand for the incoming substrate. In fact, the reactivity of cationic organopalladium complexes having chelating phosphine ligands such as DMPE and DPPE toward CO insertion were greater than that of the cationic monoorganopalladium complexes having two trimethylphosphine ligands in mutually *trans* positions [61].

The stepwise alternating insertions of CO and an alkene into Pd–C bonds comprise important steps in living catalysts for the alternating copolymerization [65]. The olefin insertion into acyl complexes provides cationic alkyl species in which a carbonyl oxygen is coordinated to the palladium center as shown in Eq. 7.4 The chelating alkyl complexes, whose presence has been confirmed by several research groups, would give extra stabilization to prevent occurrence of β -elimination.

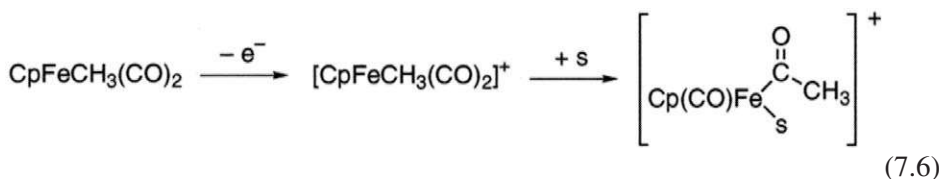


Modification of the behavior of a palladium methyl complex by coordination of a second transition metal complex was reported to enhance the CO insertion rate. The CO insertion into palladium–methyl bond in a Pd–Co heterodinuclear complex, $(\text{dppe})(\text{CH}_3)\text{Pd}-\text{Co}(\text{CO})_4$, proceeded with a higher reaction rate than into the mononuclear palladium complex, $\text{Pd}(\text{CH}_3)\text{Cl}(\text{dppe})$ (Eq. 7.5) [66]. The outcome of the reaction using ^{13}CO was consistent with the mechanism of the preferential insertion of the carbonyl on Co center into the Pd–C bond and the coordination of incoming CO to Co. Theoretical studies suggested that the

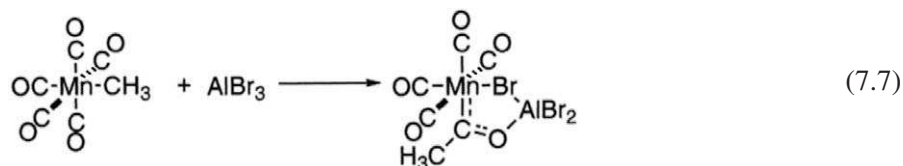
insertion consisted of the following four steps: methyl migration from Pd to Co, insertion of a carbonyl into the Co–CH₃ bond, coordination of incoming CO to the vacant site on Co, and migration of the acetyl ligand from Co to Pd.



The CO insertion can be promoted by 1e oxidation of metals. A partial positive charge on the CO carbon induced by increase of electrophilicity of the metal would facilitate the nucleophilic alkyl migration. The effect of electron deficiency is to promote incorporation of the solvent molecules that may assist the CO insertion [67]. For example, rate enhancement of CO insertion into CpFeCH₃(CO)₂ (Cp = η^5 -cyclopentadienyl) by treatment with Ce(IV) and trityl salts has been demonstrated (Eq. 7.6) [68].

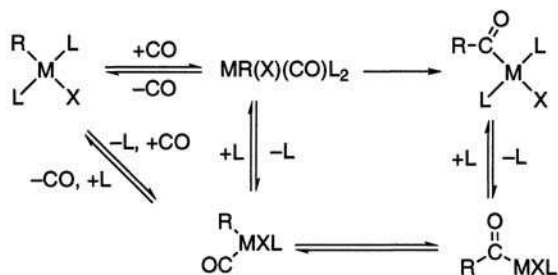


Promotion of CO insertion with the aid of Lewis acid is another example of enhancement of CO insertion by causing electron deficiency [69]. AlCl₃ and AlBr₃ can induce a rapid acyl formation giving Mn(RCO)(CO)₅ (R = CH₃, CH₂C₆H₅), CpFe(CH₃CO)(CO)₂, and CpMo(CH₃CO)(CO)₃ from the corresponding alkyl complexes. In the absence of CO the reaction of Mn(CH₃)(CO)₅ with AlBr₃ gave the acyl complex in which aluminum is coordinated to the acyl oxygen (Eq. 7.7). Along with increase in the electrophilicity of the coordinated CO, the Lewis acid should exert a strong stabilizing effect on coordinatively unsaturated acyl intermediates [70].



(d) *Four- vs. five-coordinated intermediates*

Group 10 metal alkyls having d⁸ electrons may undergo the CO insertion from a four- or five-coordinate intermediate [8]. In a detailed kinetic study concerning the carbonylation, Garrou and Heck proposed two possible insertion pathways via five-coordinate adducts, [MR(CO)(X)L₂] (M = Pt, Pd, Ni; R



Scheme 7.9.

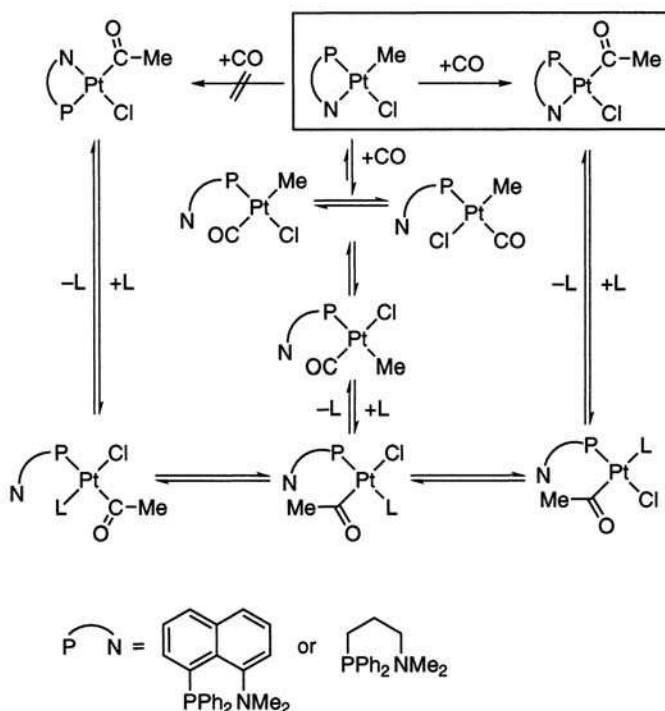
= alkyl; X = halides; L = tertiary phosphines) and four-coordinate species $[\text{MR}(\text{CO})(\text{X})\text{L}]$ [55] (Scheme 7.9). In a favored dissociative pathway, CO insertion takes place through the four-coordinate intermediate, $[\text{MR}(\text{CO})(\text{X})\text{L}]$, formed by release of a phosphine ligand from the bis(phosphine)palladium species. Another associative pathway involving direct insertion from the five-coordinate intermediate is dominant in the presence of sufficient ligand. These paths may occur depending on the nature of the complex and the reaction conditions.

For palladium systems the dissociative pathway is often preferred. Cationic four-coordinate methyl(carbonyl)palladium complexes, $[\text{PdCH}_3(\text{CO})\text{L}_2]^+$, have been observed by spectroscopic means [64,71] and sometimes isolated [65d,72] as key intermediates in the formation of the acyl complexes. The dissociative pathway has also been confirmed in the reaction of CO with neutral methylplatinum complexes having a bidentate P–N ligand from which CO-coordinated intermediates were formed with dissociation of N atom of the ligand (Scheme 7.10) [64,73]. The P–N ligand forms a chelate again after the reaction at ambient temperature to give the isolable acetylplatinum product.

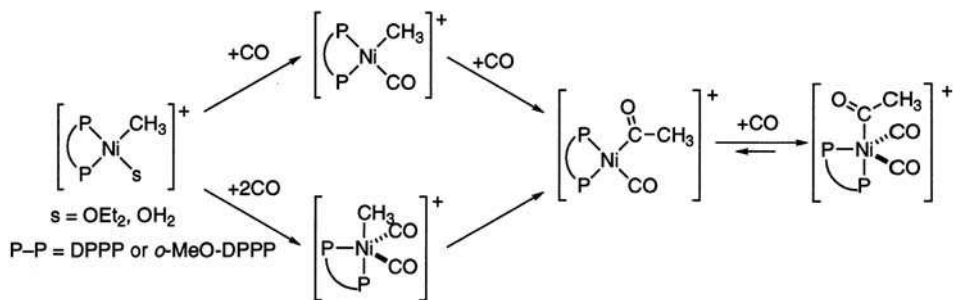
The intermediacy of the five-coordinate carbonyl complex in the carbonylation of neutral phenylpalladium complexes was not confirmed by the experiments using cylindrical Internal Reflectance Fourier Transform Infrared Spectroscopy (CIR-FTIR) [74]. For cationic hydrocarbylpalladium complexes bearing tridentate nitrogen donor ligands, CO insertion takes place giving square planar acylpalladium complexes. Theoretical studies suggest that the five-coordinate methylpalladium and –platinum intermediates having two PH_3 [48] or three NH_3 [75] ligands with square pyramidal and trigonal bipyramidal structures are not preferred during CO insertion, but involvement of a square pyramidal complex at the transition state was suggested.

On the contrary, reactions of nickel complexes often provide five-coordinate species [76]. It has been clarified that five-coordinate insertion pathway for carbonylation of cationic monomethylnickel derivatives is energetically favorable under reaction conditions of copolymerizing CO and ethylene (Scheme 7.11) [77].

Involvement of a five-coordinate species during CO insertion was suggested experimentally and theoretically in carbonylation of monoalkylpalladium com-



Scheme 7.10.



Scheme 7.11.

plexes with rigid bidentate [78] and tridentate [75,79] ligands, which will prevent the formation of a vacant coordination site and α -elimination of the generated acyl complexes by the ligand dissociation (Fig. 7.2).

(e) Considerations of the multiple insertion of CO

The nature of ligands in the reacting complex has a marked effect on the rate of reaction and the insertion pathway. Consequently, a detailed understanding of the

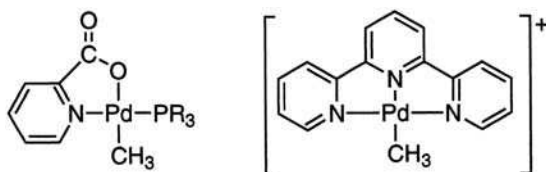


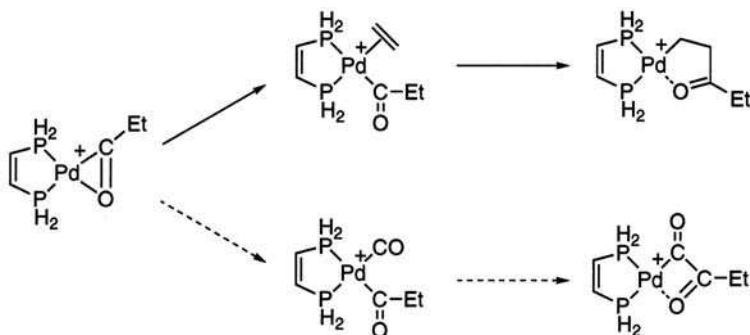
Fig. 7.2. Monomethylpalladium complexes having rigid bidentate and tridentate ligands.

insertion reaction and of the role of ligands in modifying the reaction is important for the rational development of catalyst systems.

The understanding concerning the CO insertion into the palladium–alkyl bond and olefin insertion into the palladium–acyl bond is important for elucidating the factors governing the alternating polymerization of olefin and CO [80]. In an attempt to clarify the mechanisms of the alternating copolymerization of ethylene and CO initiated by palladium complexes and to account for factors influencing the copolymerization, some theoretical studies with a model complex having a rigid bidentate ditertiary phosphine ligand have been made [81,82]. Important conclusions relevant to the reasons for enabling the alternating insertion of ethylene and CO were that the ethylene insertion into η^2 -propionylpalladium species was found to be exothermic by 129 kJ/mol, whereas the consecutive CO insertion into the η^2 -propionylpalladium species was endothermic by 2 kJ/mol (Scheme 7.12).

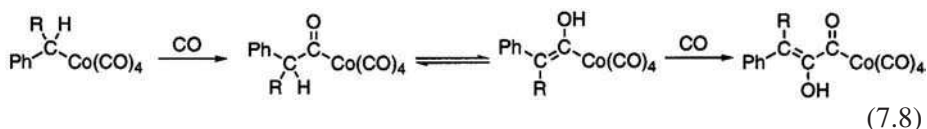
Although the consecutive CO insertion is energetically unfavorable, it is still possible to obtain α -ketoacid derivatives catalytically under certain experimental conditions. This was achieved by combination of the CO insertion into metal carbon bond with the attack of a nucleophile on the coordinated CO ligand followed by reductive elimination as we already discussed in the General Introduction (Chapter 1, Scheme 1.44) [83].

Another way to achieve introduction of two CO molecules is to convert the initial product of CO insertion into an enolic complex that can further



Scheme 7.12.

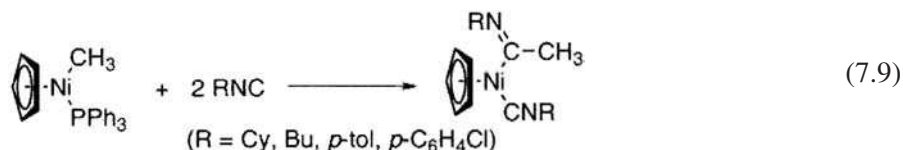
react with the incoming CO. It has been shown that the enolization of an acyl complex $\text{Co}(\text{PhCHRCO})(\text{CO})_4$ to $[\text{Co}\{\text{PhCR}=\text{C}(\text{OH})\}(\text{CO})_4]$ permits the second CO molecule to insert as shown in Eq. 7.8 [84].



7.3 ISOCYANIDE INSERTION

7.3.1 Stoichiometric reactions of isocyanides with metal alkyls

Isocyanides, having an isoelectronic structure with carbon monoxide, also strongly coordinate to transition metal center and insert into metal–carbon σ -bonds of complexes in a manner similar to the CO insertion [85]. Transformation of alkyl and aryl ligands into iminoacyl moiety generally takes place in both early and late transition metals. The first investigation of the insertion reaction of isocyanides was reported by Hagihara's group in 1968 [86]. As the 1,1-insertion products, iminoacylnickel complexes have been isolated by the reaction of methylnickel complex, $\text{CpNiMe}(\text{PPh}_3)$, with several alkyl and aryl isocyanides (Eq. 7.9). From the following studies on other metal alkyl or aryl systems it has been revealed that steric and electronic features of the complexes or the inserting isocyanides affect the ease of insertion [87].



Similarly to the CO insertion, it has been suggested that the mechanism of the isocyanide insertion involves alkyl migration to pre-coordinated isocyanide ligands. Generally, prior coordination of the isocyanide to the metal upon displacement of anionic ligand (dissociative pathway) is assumed rather than direct isocyanide coordination with increase of coordination number (associative pathway) [87,88]. For the reaction of isocyanides with neutral methylpalladium complexes bearing bidentate nitrogen ligands, formation of cationic methypalladium complexes via substitution of chloro ligand by isocyanides was strongly suggested by a dramatic increase of conductivity during the reaction and by the IR spectrum indicating σ -coordination of the isocyanides (Eq. 7.10) [89]. The rate-determining insertion reaction presumably proceeds with nucleophilic attack by the anionic ligand on the metal center to form a five-coordinate neutral species, which subsequently undergoes the alkyl migration. Indeed, it has been shown

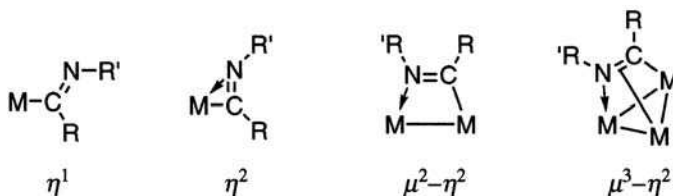
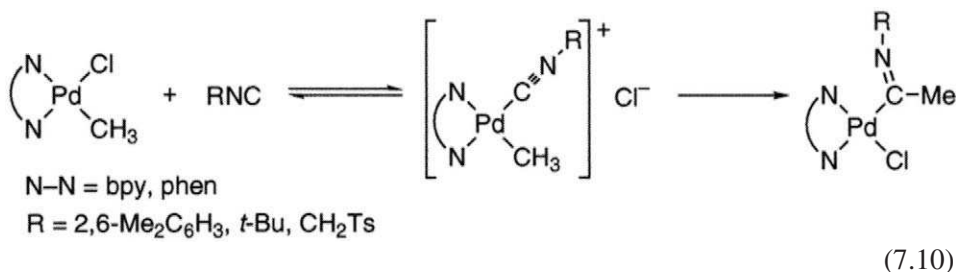
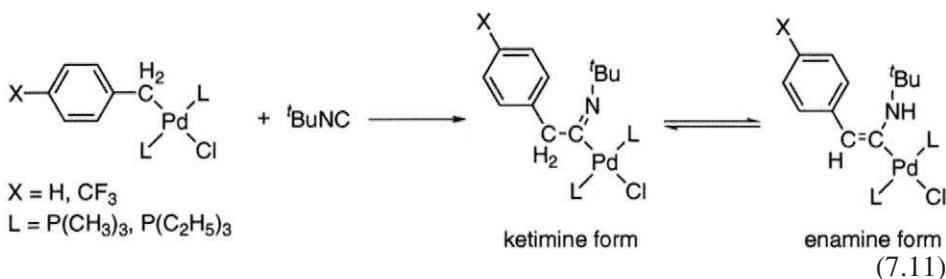


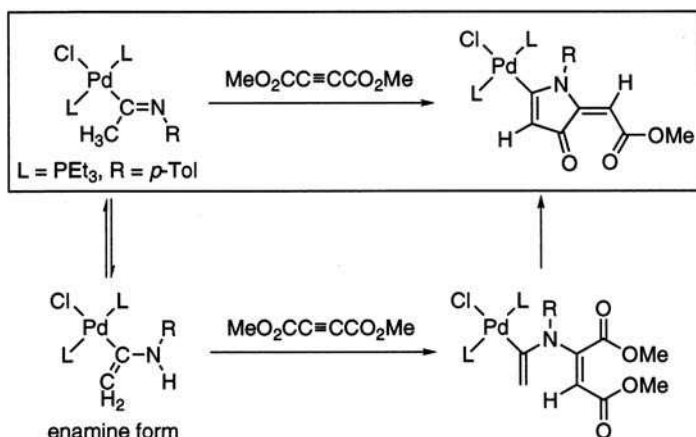
Fig. 7.3. The bonding modes of iminoacyl ligands.

that an increase in the coordinating ability of the anion promotes the isocyanide insertion into alkylplatinum and alkyliron complexes in the following order: $\text{Cl}^- \sim \text{Br}^- > \text{I}^- > \text{NO}_3^- \gg \text{ClO}_4^-$ [88a,90]. The postulated mechanism is consistent with the results that the insertion reaction is faster when isocyanides containing electron-withdrawing groups are employed [88b,89b,91].



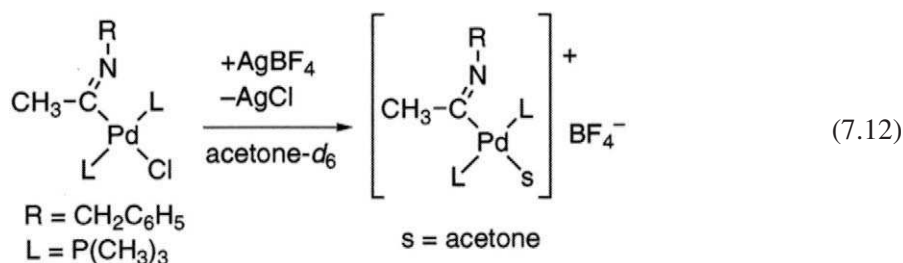
The iminoacyl complexes arising from the insertion of isocyanides exhibit interesting chemical and structural properties. A number of binding structures of iminoacyl ligand including η^1 , η^2 , $\mu^2\text{-}\eta^2$, or $\mu^3\text{-}\eta^2$ modes have been recognized as mono- and multi-nuclear insertion products as shown in Fig. 7.3. An equilibrium between the enamine–ketimine forms of the iminoacyl group has been directly confirmed by ^1H and ^{13}C NMR spectra of the products obtained from benzylpalladium complexes with *tert*-butyl isocyanide (Eq. 7.11) [92]. The prototropic tautomerism enables to explain the product of the reaction of the iminoacyl complex *trans*-[Pd{C(=NC₆H₄-*p*-Me)Me}Cl(PEt₃)₂] with MeO₂CC≡CCO₂Me as shown in Scheme 7.13 [93].



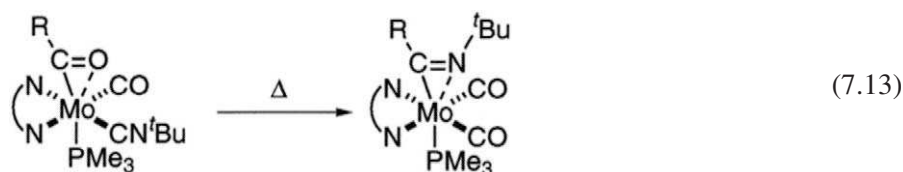


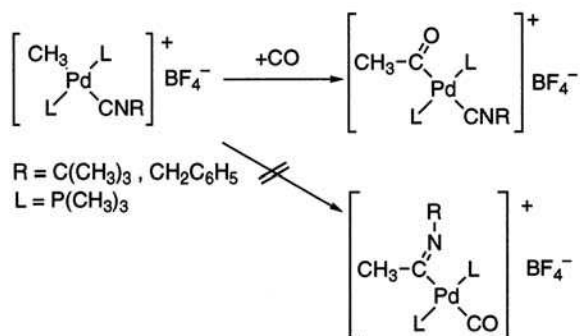
Scheme 7.13.

In general, the iminoacyl complexes are thermodynamically more stable than the acyl complexes, so that deinsertion of isocyanides from iminoacyl complexes has not been observed in contrast to the facile α -elimination of CO from acyl complexes. The removal of a halide ligand from a neutral iminoacylpalladium complex by treatment with AgBF_4 affords the corresponding cationic iminoacyl complex from which no deinsertion of the isocyanide proceeded (Eq. 7.12) [61b].



Relative susceptibility of isocyanide and carbonyl ligands to insertion depends on reaction systems. The greater thermodynamic stability of the iminoacyl complexes than the acyl complexes was demonstrated by thermal isomerization of acyl(isocyanide)molybdenum to iminoacyl(carbonyl)molybdenum complexes (Eq. 7.13) [94].





Scheme 7.14.

However, formation of stable iminoacyl complexes does not always prevail in the competition reaction systems involving CO and isocyanide. Cationic methylpalladium complexes bearing isocyanides react with CO under ambient conditions to give the corresponding acetyl palladium complexes through CO insertion and not the iminoacylpalladium complexes as shown in Scheme 7.14 [61b].

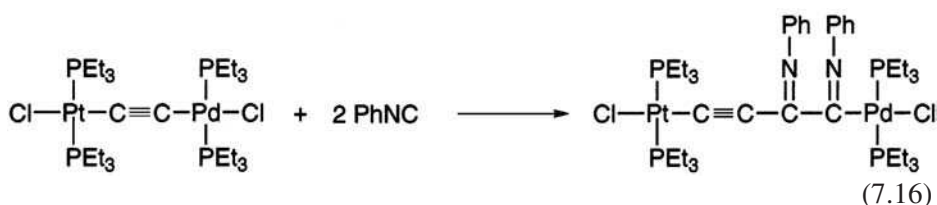
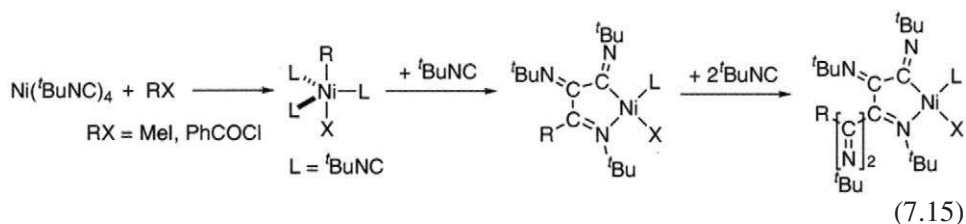
7.3.2 Polymerization of isocyanide by multiple insertion into metal–carbon bond

The insertion ability of isocyanides differs from that of CO. In contrast to the carbon monoxide, for which consecutive CO insertion is disfavored, isocyanides readily undergo the multiple insertion processes especially with more nucleophilic metals such as Ni and Pd (Eq. 7.14). The multiple insertion may lead to new types of organic compounds difficult to prepare by other synthetic methods.

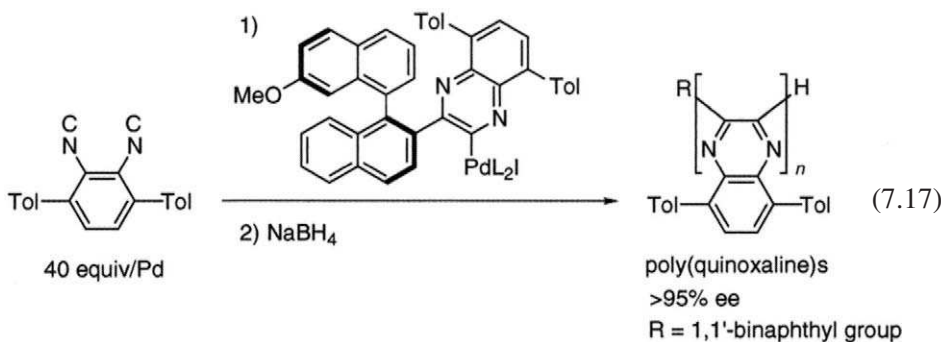


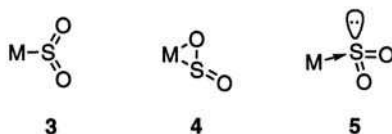
Complexes having η^2 -iminoacyl ligands obtained from multiple insertions usually contain the ligand bonded as four- or five-membered ring. Otsuka et al. reported that $\text{Ni}(\text{CN}^i\text{Bu})_4$ undergoes multiple successive insertion of isocyanides, when allowed to react with MeI or PhCOCl [95]. Sequential insertions of three isocyanide molecules into the nickel–methyl bond formed by oxidative addition of MeI to Ni(0) afford a five-membered product, from which isocyanide polymer can be obtained by further treatment with additional isocyanide (Eq. 7.15). Square planar organopalladium complexes are also effective for the multiple insertion of isocyanides [90a,96], whereas only single insertion of isocyanide is observed for platinum system [97]. Treatment of heterodinuclear μ -ethynediyl complexes $\text{Cl}(\text{R}_3\text{P})_2\text{PtC}\equiv\text{CPd}(\text{PR}_3)_2\text{Cl}$ with aryl isocyanides in the molar ratio 1 : 2 caused

the double insertion into Pd–C bond (Eq. 7.16) [98].

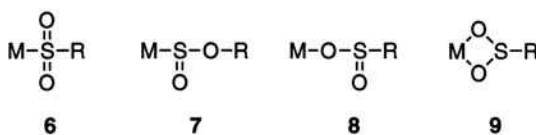


The poly(isocyanide)s obtained by multiple insertions of isocyanides show unique properties such as non-linear optical behavior, ion-channels, and optical activity arising from those single-handed helical structures [99]. When enantiomers of chiral isocyanides are polymerized, optically active polymers are obtained with predominantly one screw sense [100]. The selective synthesis of single-handed helical polymers of achiral isocyanide has been established by characterization of Ni(II) salts with an optically active additive [101]. Nickel complexes having chiral acetate ligands provided single handed helical poly(isocyanide)s, but the molecular weight of the resulting polymers is quite low [102]. The screw-sense selective polymerization of phenylene diisocyanide was achieved by use of optically active palladium complexes containing chiral 1,1'-binaphthyl groups as the initiators (Eq. 7.17) [103].





Scheme 7.15.



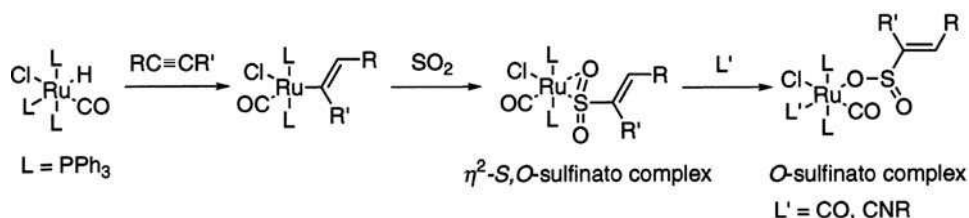
Scheme 7.16.

7.4 SO₂ INSERTION

7.4.1 Stoichiometric reaction of sulfur dioxide with transition metal complexes

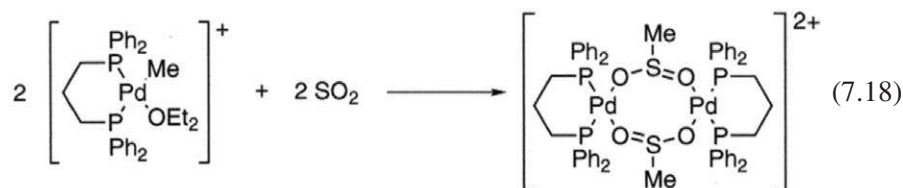
Insertion of sulfur dioxide (SO₂) into the metal–carbon bond of transition metal alkyl and aryl complexes has also been studied extensively. SO₂ shows several binding modes to transition metals as shown in Scheme 7.15 because it is amphoteric, behaving as a Lewis acid and a Lewis base. The Lewis base character of SO₂ provides the structural types η^1 -planar (**3**) or η^2 (S,O) (**4**) where SO₂ donates a pair of electrons to the metal accompanied by π back-bonding from filled d orbitals of the metal atom. The Lewis acid behavior of SO₂ as a ligand affords an η^1 -pyramidal bonding mode (**5**) where SO₂ accepts a pair of electrons from the metal. As η^2 ligands like olefins or carbon dioxide generally tend to prefer 1,2-insertion, *O*-alkyl-*S*-sulfoxylates (**7**), *O*-sulfinates (**8**), or *O,O'*-sulfinates (**9**) can be obtained by the insertion of SO₂ into alkyl complexes. However, usually the thermodynamically favored product is an *S*-sulfinato (**6**) produced through an apparent 1,1-insertion (Scheme 7.16).

Since Wojcicki et al. [104] reported that CpFeR(CO)₂ (R = alkyl or aryl group) reacts with SO₂ to give the corresponding sulfinato complexes, CpFe(SO₂R)(CO)₂, a number of transition metal alkyl complexes have been shown to undergo the 1,1-insertion. In case of oxophilic titanium or zirconium system, *O*-sulfinato complexes have been isolated as insertion products [105]. A vinylsulfinatoruthenium complex, [Ru(SO₂CR'=CHR)Cl(CO)(PPh₃)₂], prepared by the reaction of [RuCl(H)(CO)(PPh₃)₃] with alkyne in the presence of SO₂ showed a η^2 – S, O coordination structure containing a hemilabile dative interaction of one sulfoxide of an *S*-sulfinato ligand [106]. The resulting linkage can be converted into *O*-sulfinato by treatment with π -acids such as CO and isocyanides as shown in Scheme 7.17. Recently, a unique insertion product, *O,O'*-sulfinato bridged dimer, has been isolated by the reaction of a cationic monomethylpalla-



Scheme 7.17.

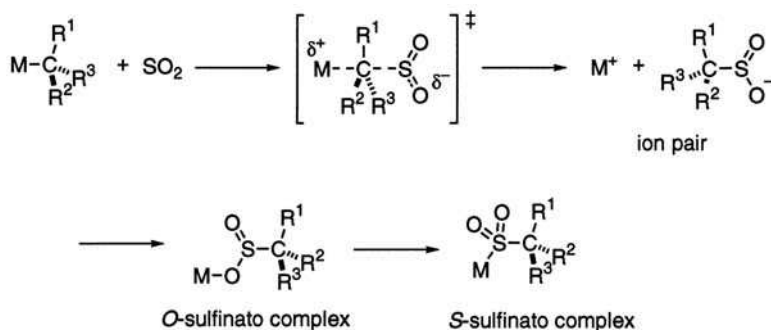
dium complex with SO_2 (Eq. 7.18) [107].



Although *S*-bound sulfinato complexes are formally 1,1-insertion products, detailed mechanistic studies with $\text{CpFeR}(\text{CO})_2$ and related complexes have suggested that the SO_2 insertion takes place via the species $\text{M}^+\text{O}_2\text{SR}^-$, most likely a contact ion pair, as shown in Scheme 7.18. Generation of *O*-sulfinato species in preference to the *S*-sulfinato complex has been confirmed by NMR and IR spectroscopy [108]. Moreover, the related kinetic results on the insertion into a series of $\text{CpFeR}(\text{CO})_2$ in liquid SO_2 or in organic solvents are consistent with the electrophilic substitution mechanism [109]. The results of the detailed studies on the insertion processes can be summarized as follows:

(1) The SO_2 insertion into $\text{CpFeR}(\text{CO})_2$ in organic solvents follows second-order kinetics, first order in both the alkyl complex and the SO_2 .

(2) A greater carbanionic character of the hydrocarbonyl ligand enhances the rate of SO_2 insertion, thus the alkyl complexes show higher reactivities than the aryl complexes. Acceleration of the reaction rate was also observed by replacing the



Scheme 7.18.

CO ligand with more basic P-donor ligands or by increasing the degree of methyl substitution on the η^5 -cyclopentadienyl ligand.

(3) The sterically hindered R group retards the insertion reaction.

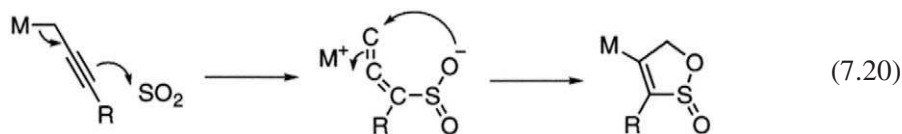
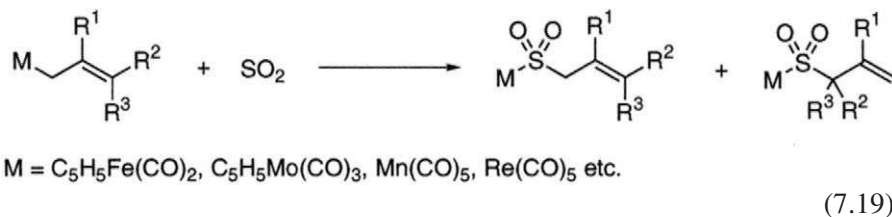
(4) Extremely large negative values of $\Delta S^\ddagger$ (ranging from -43 to -62 eu) for the SO_2 insertion have been observed.

Employment of an optically active alkyliron complex with an asymmetric α carbon atom revealed the nature of the transition state in insertion processes. The reaction of *threo*-[CpFeCHDCHDC(CH₃)₃(CO)₂] with SO_2 proceeds to give the corresponding *erythro*-*S*-sulfinato complex with inversion of configuration at α -carbon whereas the CO insertion reaction of the alkyl complex with PPh_3 occurs with retention of configuration [13]. The stereochemical inversion in the SO_2 insertion suggests a backside approach of SO_2 to the α -carbon of alkyl ligands at the transition state.

It can be concluded that strongly electrophilic character of SO_2 having a vacant orbital on sulfur enables to undergo the $\text{S}_{\text{E}}2$ backside attack on the α -carbon of the alkyl ligand prior to binding to the metal, which leads to formation of an alkyl sulfinato anion with inversion at the carbon. Formation of the kinetic product, *O*-bound sulfinato complex, is followed by rearrangement to the thermodynamic product, *S*-bound sulfinato complex.

The notable feature of the above mechanism is that the SO_2 can attack coordinatively saturated 18e complexes without coordination to the metal center. However, an intramolecular insertion mechanism can not be ruled out for square planar 16e complexes. The SO_2 insertion into *trans*-PtPh(Cl)(PEt₃)₂ complex containing a strong platinum–carbon bond may proceed via a five-coordinate intermediate PtPh(Cl)(SO₂)(PEt₃)₂ to give *trans*-PtSO₂Ph(Cl)(PEt₃)₂ [110]. On the other hand, a free radical chain process is suitable for a photochemical reaction of SO_2 with organocobaloximes to form the corresponding sulfinato complexes [111].

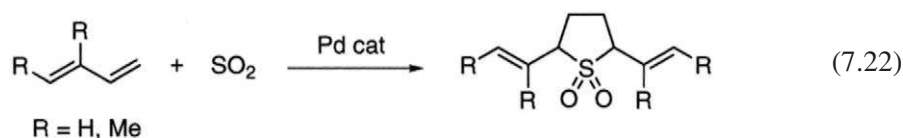
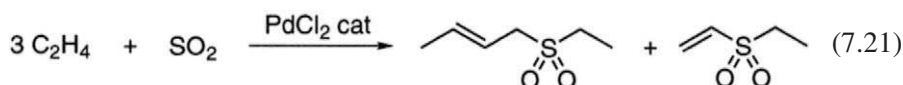
Reactions of transition metal σ -allyl complexes with SO_2 afford two types of *S*-sulfinato products according to Eq. 7.19 [112]. Similar incorporation of SO_2 with rearrangement and the subsequent cyclization have been observed in case of propargyl complexes as shown in Eq. 7.20 [113].



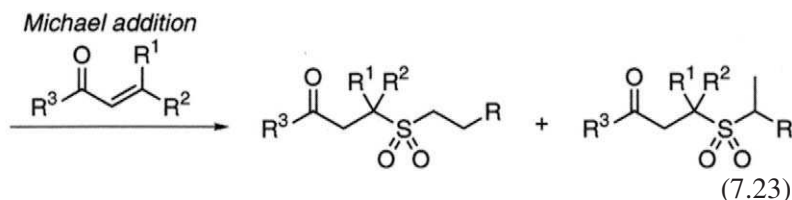
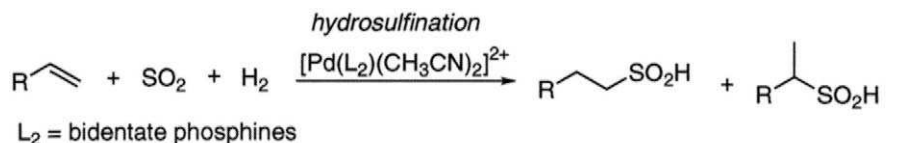
7.4.2 Transition metal-catalyzed reaction of sulfur dioxide

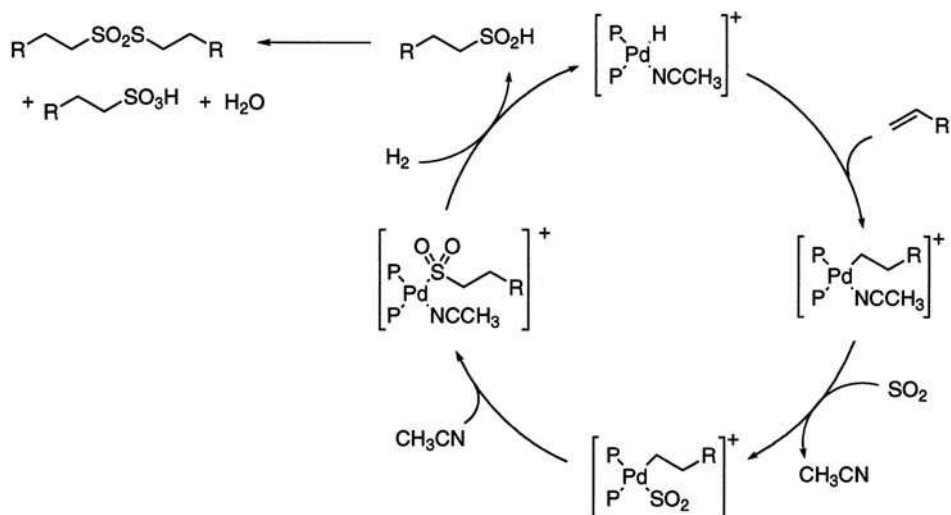
Although a potentially close similarity between CO and SO₂ toward insertion reaction has been recognized, the synthetic applications of catalyst system involving SO₂ insertion as a key step are limited. The reasons may be due to lower reactivity of SO₂ than CO and instability of sulfinic acids as representative products of SO₂ fixation.

The first catalytic transformation of SO₂ into organic sulfur compounds was reported in 1968 [114]. The reaction of ethylene and SO₂ in the presence of PdCl₂ provides a mixture of sulfones (Eq. 7.21). The result of a loss of the catalyst activity under dehydrative conditions is suggestive of the participation of a hydridopalladium species. A mixture of Pd(acac)₂, PPh₃, and AlEt₃ is an active catalyst for synthesis of cyclic sulfones (2,5-dialkenylsulfolane) which can be obtained from 1,3-dienes up to 75% yield (Eq. 7.22) [115].

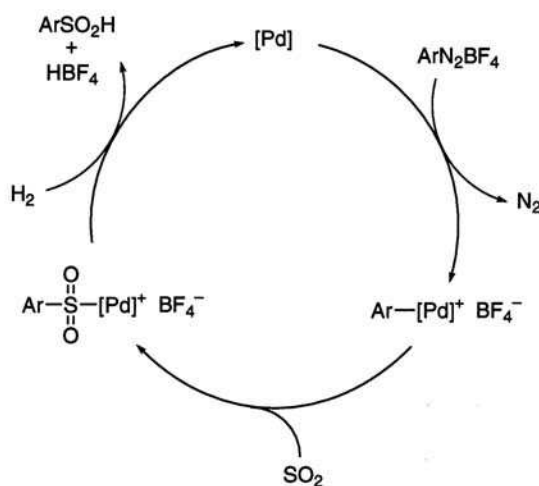


In analogy to hydroformylation, alkenes react with SO₂ and H₂ to give a so-called *hydrosulfonation* product, sulfinic acids [116]. Cationic Pd(II) and Pt(II) complexes bearing bidentate phosphine ligands are effective catalyst precursors. A plausible mechanism for the hydrosulfonation involves formation of alkyl intermediates by olefin insertion into metal hydrides, subsequent insertion of SO₂, and reformation of the hydrides with the release of sulfinic acids (Scheme 7.19). However, aliphatic sulfinic acids readily undergo disproportionation to give thiosulfinic acid esters, sulfonic acids, and water at the reaction temperature. The unstable sulfinic acids can be conveniently converted into γ -oxo sulfones by addition of α,β -unsaturated carbonyl compounds as Michael acceptors to the reaction mixture (Eq. 7.23) [117].





Scheme 7.19.

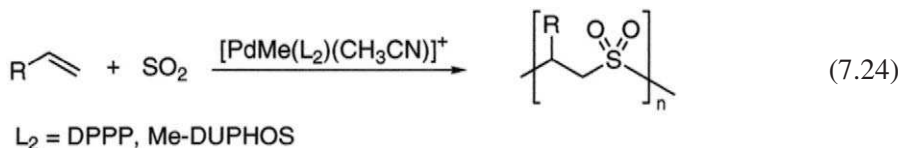


Scheme 7.20.

Aromatic sulfinic acids can be synthesized from aryldiazonium tetrafluoroborates by hydrogenative sulfination in the presence of palladium on activated charcoal [118]. As depicted in Scheme 7.20, the catalytic cycle consists of oxidative addition of the substrates to $Pd(0)$ to form cationic arylpalladium(II) intermediate, SO_2 insertion into palladium–carbon σ -bond, and the following hydrogenolysis of sulfinylpalladium intermediate. The key to success is the formation of the cationic

Pd(II) species countered by BF_4^- anion, which may enable liberation of HBF_4 without base regenerating catalytically active Pd(0) species.

Palladium catalysts also promote copolymerization of SO_2 with alkenes analogously to copolymerization of CO and alkenes (Eq. 7.24) [119]. The catalyst activities for the polysulfone synthesis are lower by an order of magnitude than those for the polyketone synthesis. Perfectly alternating copolymers can be obtained by use of cationic methylpalladium(II) complexes, $[\text{PdMe}(\text{CH}_3\text{CN})\text{L}_2]^+\text{BF}_4^-$ ($\text{L}_2 = 1,3\text{-bis}(\text{diphenylphosphino})\text{propane}$ and $1,2\text{-bis}(2,5\text{-dimethylphosphinolato})\text{benzene}$), in contrast to a lower degree of alternation provided by a radical polymerization [120].

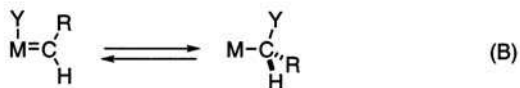
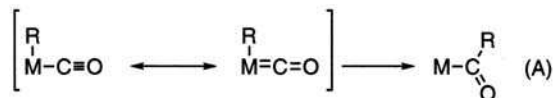


7.5 α -ELIMINATION AND 1,1-INSERTION INVOLVING ALKYLIDENE LIGANDS

The CO ligand can be considered as a carbene ligand with $\text{C}=\text{O}$ bound to the metal. Thus the reversible alkyl migration to the coordinated CO may be regarded as alkyl migration to the coordinated carbene ligand (Scheme 7.21A). In a similar sense alkyl migration to the coordinated carbene ligand gives a metal alkyl and its reverse process involving α -elimination of Y gives a metal carbene complex as shown in Scheme 7.21B.

When Y in Scheme 7.21B is hydrogen, the reverse process yielding a metal carbene-hydride complex is α -hydrogen elimination process. It provides an important route leading to decomposition of metal alkyls beside the more often encountered β -hydrogen elimination pathway giving metal hydride coordinated with an olefin.

Since transition metal carbene complexes serve as efficient catalysts for im-



Scheme 7.21.

portant catalytic processes such as olefin metathesis, ring-opening metathesis polymerization, and ring closing metathesis, the information concerning the α -elimination and its reverse process is important. Synthesis and reactivities of transition metal carbene complexes are dealt with in Chapter 4 and we discuss herein briefly other aspects of the α -elimination processes that are relevant to catalysis [121].

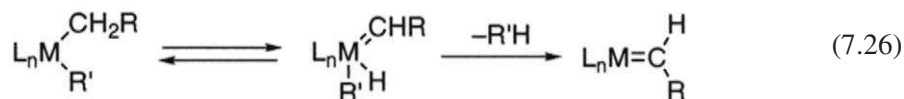
7.5.1 α -H elimination

Among possible α -elimination routes shown in Scheme 7.21B with $Y = H$, alkyl, or a heteroatom, α -hydrogen elimination is the most well documented and important process. Before the advent of single component carbene catalysts for metathesis type catalysis, notably molybdenum and ruthenium complexes prepared by the groups of Schrock and Grubbs, ill-defined olefin metathesis catalysts had been prepared and used by treating transition metal salts or oxides with alkylating reagents such as trialkylaluminum. The nature of the active catalyst centers for olefin metathesis was later proposed and eventually established as metal carbene species that interact reversibly with olefins forming metallacyclobutane complexes [122]. Although the single component carbene complexes can now be prepared as discussed in Chapter 4, a brief treatise of the route to give transition metal carbene complexes via α -hydrogen elimination is provided here to help in understanding the behavior of transition metal alkyls and metal–carbene complexes of catalytic activities.

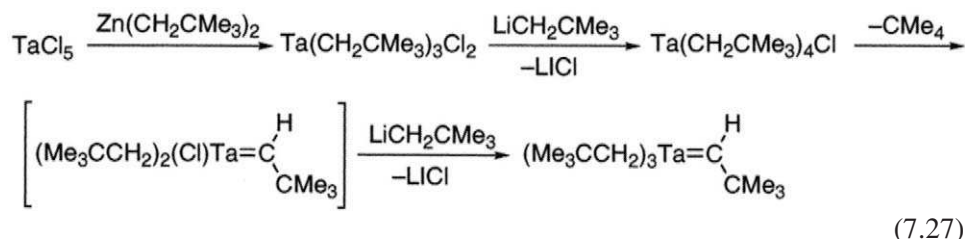
Transition metal alkyls having α -hydrogen(s) may undergo the α -hydrogen elimination process as shown in Eq. 7.25.



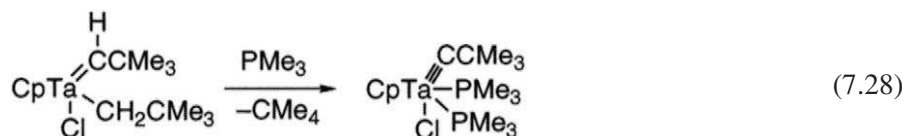
The process is reversible and the hydrido–alkylidene species may not be observed when the σ -alkyl species is thermodynamically more stable. However, when a route allowing the removal of the hydride, for example reductive elimination with another alkyl ligand as shown in Eq. 7.26, is provided, a stable alkylidene species can be isolated.



The alkylidene complex, called Schrock type carbene complex, was first isolated in an attempt of synthesis of pentakis(neopentyl)tantalum(V) (Eq. 7.27) [123].

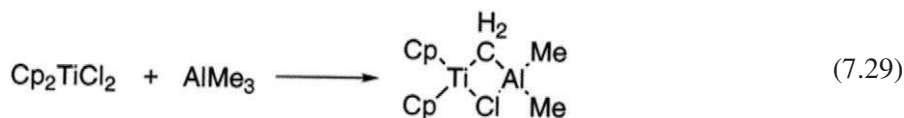


Further α -hydrogen elimination giving an alkylidyne complex was induced by addition of PMe_3 to an alkylidene complex (Eq. 7.28).



The propensity toward the α -hydrogen elimination from the alkylidene ligand was ascribed to the steric effect of the bulky neopentyl group pushing the α -hydrogen toward the metal to facilitate the α -hydrogen abstraction as revealed by neutron diffraction studies of the structure of an alkylidene complex, $\text{Ta}(\text{=CHBu}')\text{Cl}_3\text{PMe}_3$ [124].

Another aspect of the relevance of the carbene complex to catalysis is stabilization of the methylidene ligand by aluminum alkyls as observed in the formation of the Tebbe's complex as shown in Eq. 7.29 [125].



The utility of the Tebbe type complex in carbonyl olefination is discussed in Chapter 4. The bridged complex may be regarded as a special type of a carbene complex where the $\text{Cp}_2\text{Ti}=\text{CH}_2$ unit is masked by interaction with the AlMe_2Cl entity. Formation of the Tebbe's complex suggests the occurrence of α -hydrogen elimination in the preparation of the Ziegler–Natta and Kaminsky type olefin polymerization catalysts from titanium chlorides and methylaluminum compounds.

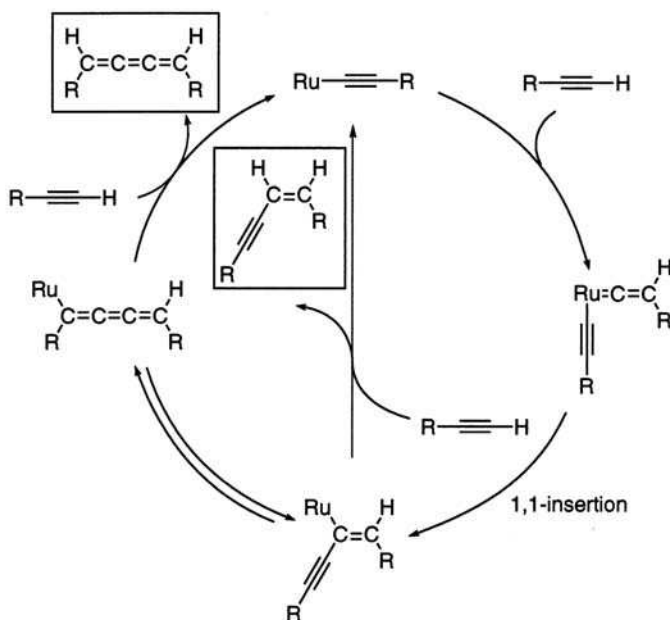
In discussion of the stability of transition metal alkyls, information on the relative ease of the α - vs. β -hydrogen elimination is important. The similar information is also essential in understanding the termination and chain transfer mechanisms in polymerization of olefins by transition metal alkyl complexes. The relative rates of the α -hydrogen elimination and β -hydrogen elimination have been measured [126,127]. Interestingly, the rate of α -hydrogen elimination was found to be much higher than the β -hydrogen elimination. It was concluded that the α -hydrogen elimination path is kinetically favored over the β -hydrogen elimination route, which gives a thermodynamically favored olefin–hydride product.

7.5.2 Alkynyl migration to carbene ligand

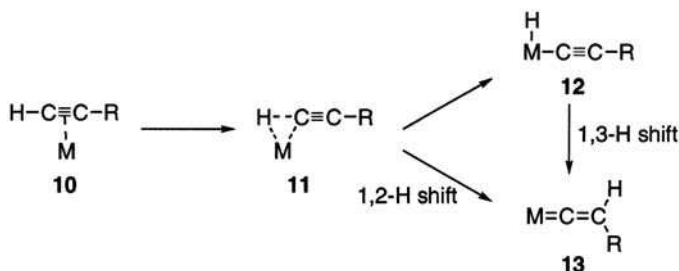
Another type of migration process of synthetic utility relevant to catalysis is alkynyl group migration to a carbene ligand ($Y = \text{alkynyl group}$ in Scheme 7.21B). The migration process as shown in Scheme 7.22 is believed to be involved in catalytic dimerization of terminal alkynes [128,129].

Several routes that lead to formation of alkenylidene type complexes are known [130]. A route involving the side-on coordination of an alkyne to a low valent transition metal complex (**10**) may lead to a hydrido alkynyl complex (**12**) through the activation of the C–H bond in the coordinated alkyne (**11**) as shown in Scheme 7.23. Proton 1,3-migration in the alkynyl–hydrido complex to the β alkynyl carbon in **12**, or the direct 1,2-transfer of the proton in **11** gives the alkenylidene complex **13** [131]. It is also possible that the alkenylidene complex is produced by protonation of the alkynyl complex.

The dimerization process in Scheme 7.22 involves migration of the alkynyl group to the alkenylidene ligand to give σ -enynyl–ruthenium complex. Its further reaction with the alkyne, possibly via σ -bond metathesis or protonation by the alkyne affords enyne with regeneration of an alkynyl–ruthenium complex that carries the catalysis. The σ -enynyl–ruthenium complex, on the other hand, may be isomerized to butatrienyl–ruthenium complex, which on further reaction with the alkyne liberates butatriene with regeneration of the alkynylruthenium species. Sto-



Scheme 7.22.



Scheme 7.23.

ichiometric carbon–carbon bond formation relevant to the catalytic dimerization of alkynes has been observed in reactions of several transition metal complexes with alkynes [132].

7.6 REFERENCES

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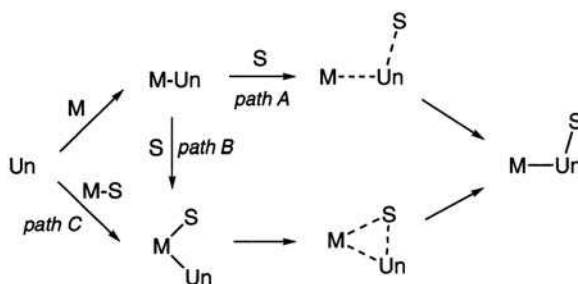
Addition to Unsaturated Ligands

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8.1 INTRODUCTION

The transition metal-catalyzed transformation of unsaturated organic substrates (Un) requires, as the first step in a catalytic cycle, formation of the coordinative bond between the metal and the substrate group [1]. As shown in Scheme 8.1, the substrate is activated, via coordination, for a new bond formation with another substrate group (S), which may directly attack Un (path A). In some cases the bond formation involving an externally added substrate actually proceeds via its coordination to the metal, as shown in path B. Namely the attack of S, which can be either a nucleophile or an electrophile, takes place initially at the metal center which can be electronically deficient or rich, respectively, to make a new metal–ligand bond. This step then is followed by the bond formation between the two ligands on the same metal coordination sphere. The order of the coordinative bond formation via path B may even be reversed as shown in path C. The bond formation in the metal coordination sphere after path B or C includes such fundamental elementary steps as migratory insertion and reductive elimination reactions, which are the topics of the other chapters in this book. It is the bond forming process between the metal-bound ligand and the metal-free substrate group that is treated in this chapter.



Scheme 8.1.

There are basically three types of substrate groups *S* that are capable of directly attacking the metal-bound ligand to make a new bond in path A. These include a nucleophile with an electron pair to be used for the new bond with an atom in the ligand, a radical group contributing only one electron to the new bond, and an electrophile which accepts an electron pair from the ligand. Although stoichiometric organometallic reactions involving each of the three substrate types have been fully characterized in literature, reactions involving the external nucleophile play a more crucial role than those of the other two in actual catalytic transformations. This chapter is divided according to the type of externally attacking substrate group, with more emphasis being laid on the reaction of the nucleophile. The literature citation is not necessarily comprehensive, but is intended to refer to those describing mechanistically fundamental aspects of the transformations involving the attack of the external substrate group at the metal-bound ligand.

8.2 NUCLEOPHILIC ATTACK AT COORDINATED LIGAND

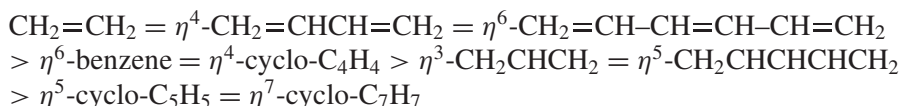
Those nucleophilic attacks which are of synthetic significance include attacks at carbonyl, alkene, alkyne, arene, and allylic ligands. These ligand groups are normally much less reactive toward nucleophiles when existing free from coordination. It should be pointed out that not all transition metal fragments provide coordinated unsaturated molecules with an enhanced susceptibility to nucleophiles. These molecules become more reactive when coordinated to the more electron-deficient metal fragment. Actually, the nucleophilic attack becomes more facile with the increase in the oxidation state of the metal, in the positive charge of complex, and in the electron-attracting ability of auxiliary ligands.

The new ligand groups generated by the nucleophilic attack show various reactivities useful for synthetic applications. For example, the acyl ligand produced by the attack of organolithium and Grignard reagents at the carbonyl ligand is easily treated for the bond formation with a number of electrophiles, while it is difficult to carry out a controlled manipulation of the acylmetal intermediate formed from the reaction between metal-free carbon monoxide and these organometallic reagents [2]. Reductive elimination and migratory insertion of the newly generated groups are among the transformations that are of great synthetic utility.

The metal-bound carbonyl ligand is readily subjected to the attack of not only carbanions but heteroatom nucleophiles such as alcohols and amines to form ligands useful for formation of compounds containing ester and amide functionalities. The ease with which the nucleophilic attack takes place at metal-coordinated alkenes and alkynes provides a basis for oxidation of these molecules in the presence of a transition metal complex catalyst [3,4a], as exemplified by the Wacker type alkene oxidation by the use of a Pd catalyst. Metal catalyzed addition of alcohols or amines to alkenes and alkynes also involve the analogous nucleophilic attack [4b–e]. The attack of carbanions and heteroatom nucleophiles

at the η^3 -allyl ligand bound to certain transition metals, most typically Pd, represents another key step in transition metal catalyzed organic synthesis [3,5a,b]. The reactive species is often a cationic η^3 -allyl complex formed by ionization of η^2 -alkene complex $M(\eta^2\text{-CR}_2=\text{CR}'\text{CR}''\text{X})$ and thus can be regarded as an allyl cation in which the reaction site is stereoselectively protected by the metal fragment. Indeed many of the nucleophilic attacks at the η^3 -allyl ligand are highly stereospecific. An analogous sequence involving complexation, ionization and stereospecific nucleophilic attack constitutes stereoselective substitution of propargyl electrophiles [5c,d].

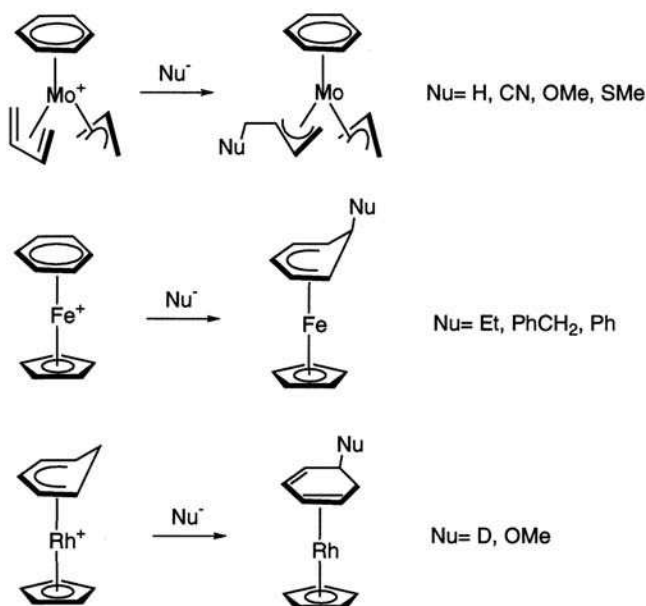
The order of reactivity of various unsaturated ligands with respect to the nucleophilic attack is one of key issues in designing both stoichiometric and catalytic transformations. This is particularly important for the chemoselectivity in the transformation of a class of complexes containing more than two different ligand groups. An empirical rule (Davies–Green–Mingos rule) has been proposed [6] for the relative susceptibility of unsaturated hydrocarbon ligands in cationic 18-electron complexes to nucleophiles:



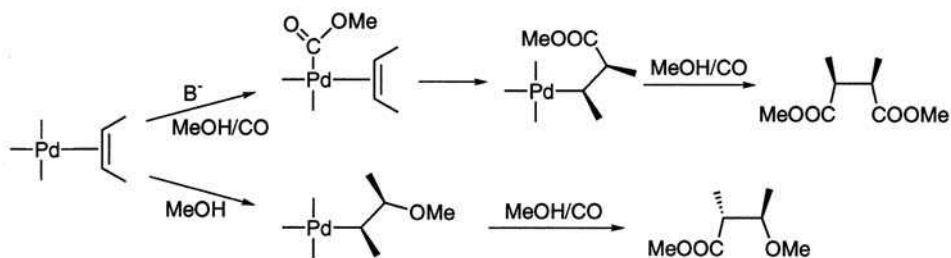
This is the order based on three features. First, even-numbered carbon ligands react faster than odd-numbered carbon ligands, as exemplified by the first and second reactions of Scheme 8.2.

Second, those which are cyclically conjugated (closed), e.g. benzene and cyclopentadienyl, are less reactive than the open counterparts, e.g. cycloheptatriene and cyclohexadienyl, respectively (Scheme 8.2, third reaction). Third, for even open ligands, a nucleophile attacks a terminal carbon (first reaction); while for odd open ligands, attack at a terminal carbon takes place in the case of a complex having strongly electron-withdrawing auxiliary ligand(s). The synthetically most important odd open ligand is allyl, which accepts the nucleophilic attack at both terminal and central carbons depending on the nature of the metal fragment. Details about this selectivity will be given in section 8.2.4. Notice that the reactivity orders shown above apply in the kinetically controlled reaction, while the nucleophilic attack at the unsaturated ligand is often a reversible process, as will be discussed later, so that there is a chance for the initial kinetic product to isomerize to the thermodynamic one.

Competition between carbonyl and hydrocarbon ligands, though difficult to predict, is another key issue in catalytic reactions. For example, the products of the Pd-catalyzed reaction of alkenes with carbon monoxide and alcohol with the aid of an oxidant depended on whether a base was present or not, where the base played a key role to determine the site of the initial nucleophilic attack of the alcohol as shown in Scheme 8.3 [7]. Thus, with some bases added, the first step of the catalysis was thought to be formation of Pd–COOR intermediate by the attack

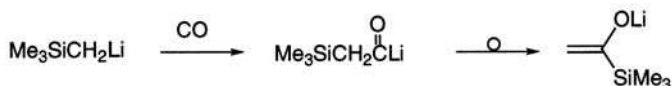


Scheme 8.2.

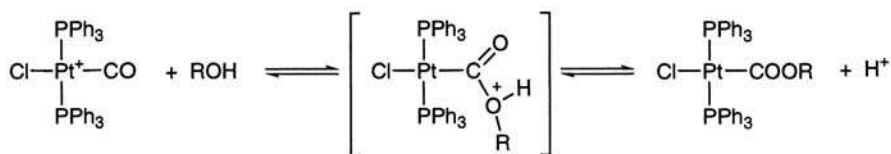


Scheme 8.3.

of the alcohol at Pd–CO species, followed by migratory insertion of alkene ligand into Pd–COOR bond. The final step would be incorporation of another molecule of carbon monoxide between Pd and the alkyl group, eventually affording 1,2-diester compounds. On the other hand, in the absence of the base, the first step was suggested to be nucleophilic attack of the alcohol at the coordinated alkene to give 2-alkoxyalkylpalladium species, followed by incorporation of only one carbon monoxide to give 2-alkoxy esters. To explain these results, it was postulated that the nucleophilic attack at the carbonyl ligand is accelerated by the addition of a base to a greater extent than that at the alkene ligand. Mechanistic aspects of the related stoichiometric nucleophilic attack of alcohols will be described in sections 8.2.1 and 8.2.3 in more detail.



Scheme 8.4.



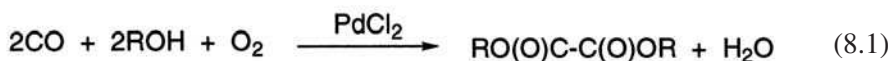
Scheme 8.5.

8.2.1 Reaction of carbonyl and related C1 ligands

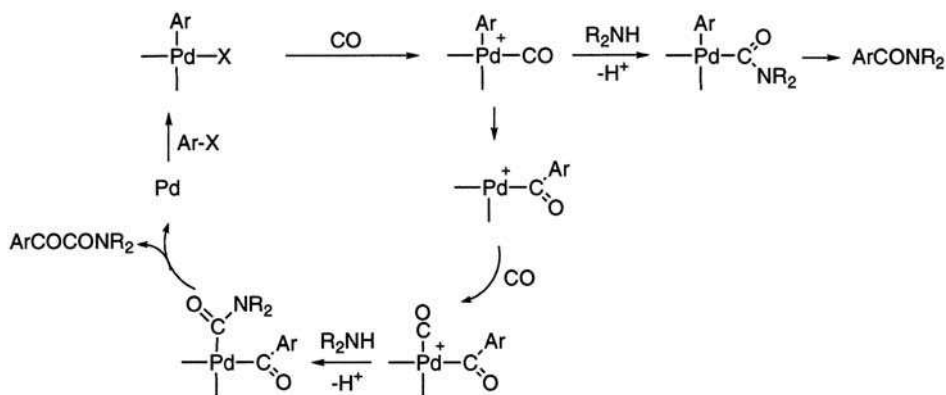
It is known that carbon monoxide is attacked by organolithium and Grignard reagents at the carbon to generate acylmetallic moieties [2a,b]. However, these are too reactive to be manipulated further for the practical synthetic use except for a few specially designed systems, e.g. Scheme 8.4 involving intramolecular silyl migration of silylacetyl lithium [2b].

When carbon monoxide is coordinated with a transition metal atom of the sufficiently electron deficient nature [8], it is expected that the susceptibility of the carbon atom to the nucleophilic attack is enhanced relative to that of free CO molecule; note, for example, the high sensitivity of CO ligand in $[\text{PtCl}(\text{PR}_3)_2(\text{CO})]^+$ to a neutral alcohol (Scheme 8.5), while free CO is inert to the alcohol.

Also, the type of nucleophiles capable of attacking the carbonyl ligand is widespread, ranging from carbon centered anions (e.g. Me^- , Ph^-) to hydride, and heteroatom anions (e.g. OH^- , OR^-) or neutral molecules (e.g. R_3N). Moreover, the new ligand group formed by such nucleophilic attack can be subjected to further organometallic transformations in a controllable manner (e.g. migratory insertion shown in Scheme 8.3, or reductive elimination), accomplishing efficient incorporation of carbon monoxide unit(s) into organic products [1]. Some other practically important homogeneous catalyses proceeding via the nucleophilic attack at the CO ligand include syntheses of α -ketoester or α -ketoamide from CO, organic halide and alcohol or amine (e.g. Scheme 8.6) [9], oxalate ester or amide from CO, alcohol or amine with the aid of oxidant (Eq. 8.1) [10a–f], and carbonates or carbamates from the same reagents [10f,g].



The success of the double carbonylation shown in Scheme 8.6 relies on the relative rate of the attack of amine at the Pd-bound CO vs. the insertion of CO into the Pd–Ar bond [9c]. If an amine of strong nucleophilicity and small steric



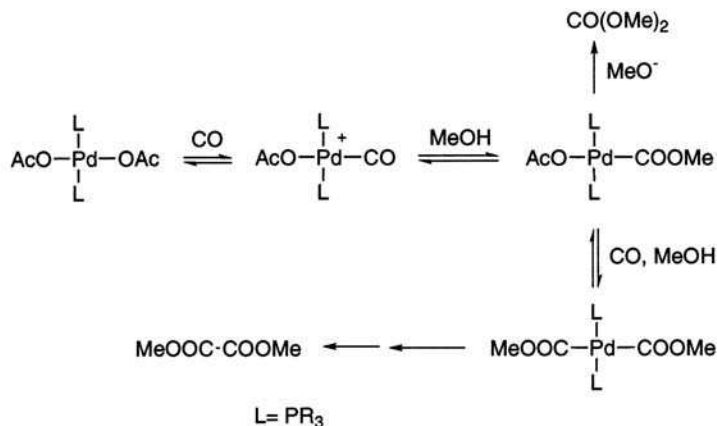
Scheme 8.6.

size is used, the nucleophilic attack at the carbonyl ligand to give carbamoyl-Pd intermediate is preferred, and thus the formation of single carbonylation product (amide) predominates. On the other hand, the use of a smaller amount of less nucleophilic amine results in the preferential CO insertion into the Pd-Ar bond to give benzoyl intermediate. Formation of this eventually leads to the double carbonylation, as shown in Scheme 8.6.

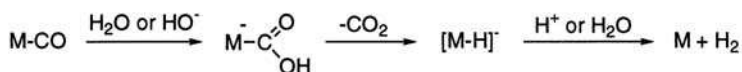
In the model reaction of the oxalate ester synthesis [10c], the efficiency and selectivity (oxalate vs. carbonate) of carbonylation of methanol with a stoichiometric amount of $\text{Pd}(\text{OAc})_2$ were examined as a function of added phosphine, base, and CO pressure. Without added phosphine, $\text{Pd}(\text{OAc})_2$ is very effective in forming dimethyl oxalate at room temperature. Use of PPh_3 slowed the formation of the oxalate, a reaction temperature of ca. 50°C being required. At room temperature $\text{Pd}(\text{COOMe})(\text{OAc})(\text{PPh}_3)_2$ was isolated. More basic phosphine, e.g. PBu_3 almost completely inhibited the oxalate formation. The formation of oxalate decreased and that of dimethyl carbonate increased by the use of low CO pressure and some bases (e.g. Et_3N). A reaction scheme accounting for these observations was presented (Scheme 8.7).

The attack of OH^- or H_2O at CO ligand to form an M-COOH moiety (Scheme 8.8) is also important in some catalyses such as water gas shift reaction and reduction of organic substrates such as nitrobenzene [11a-c]. The key transformation of M-COOH is decarboxylation to give a metal hydride, as exemplified by Scheme 8.8 with $\text{M} = [\text{trans-PtCl}(\text{PEt}_3)_2]^+$ [12] and $\text{M} = \text{Ru}_3(\text{CO})_{11}$ [11b]. The hydride complex $[\text{Ru}_3(\text{CO})_{11}\text{H}]^-$ further undergoes protonation by water to generate H_2 and $\text{Ru}_3(\text{CO})_{11}$. The polycarbonyl ruthenate, or an iron complex $[\text{Fe}_3(\text{CO})_{11}]^{2-}$ formed by deprotonation of $[\text{Fe}_3(\text{CO})_{11}\text{H}]^-$ [11e], served as a highly active reductant for nitrobenzenes to give anilines [11c,d].

From a mechanistic point of view, it is often difficult to classify the direct nucleophilic attack at the carbonyl carbon (Scheme 8.1, path A; $\text{Un} = \text{CO}$, $\text{S} =$



Scheme 8.7.



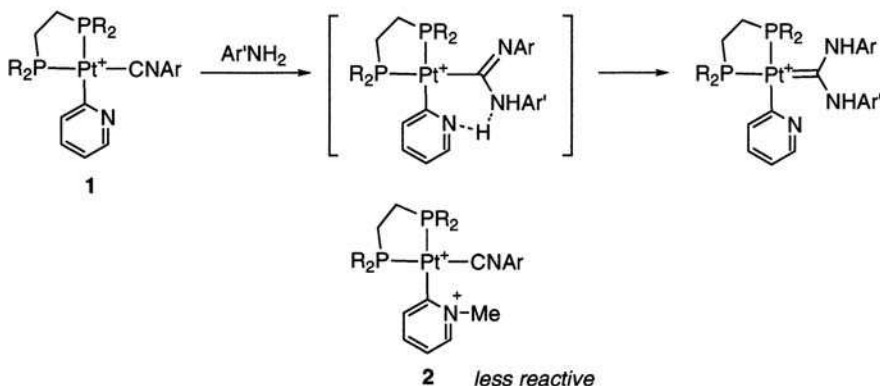
Scheme 8.8.

Nu) distinctively from a reaction sequence (path B) involving initial nucleophilic attack at the metal, which may or may not accompany loss of another ligand, and subsequent 1,1-migratory insertion involving the newly coordinated nucleophile group and CO ligand. The reaction between an alkene or alkyne ligand and the nucleophile can also take the analogous dual courses, but in principle a detailed stereochemical analysis of the adduct can help to distinguish between the direct and the stepwise courses. However, no such information is available in the case of the reaction of the carbonyl complexes.

(a) Reversibility of nucleophilic attack

As mentioned above, a variety of nucleophiles can form a bond with the carbon of the carbonyl ligand. One feature common to most of the reactions of various nucleophiles is that the bond formation between carbonyl carbon and nucleophile is more or less a reversible process. Alkoxycarbonyl or carbamoyl complexes formed from carbonyl complexes and alcohol or amine readily undergo the reversed course, namely $\text{C}(\text{O})-\text{OR}$ or $\text{C}(\text{O})-\text{NR}_2$ bond cleavage, either spontaneously or upon treatment with an acid (see e.g. Scheme 8.5). It is also noted that metallocarboxylic acids, $\text{M}-\text{COOH}$ (typically $\text{M} = \text{PtR}(\text{PR}'_3)_2$; $\text{R} = \text{Cl}, \text{Ph}$) tend to dissociate OH^- ion, rather than H^+ in solution [12,13].

The kinetics of formation of $\text{Pt}-\text{COOR}$ complexes from cationic carbonyl complex and alcohols (Scheme 8.5) was examined in the presence of a base [14]. The rate was first-order with respect to the concentrations of the carbonyl complex and alcohol, but independent of the concentration of the base, while the

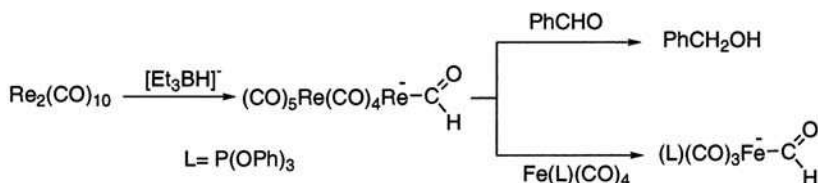


Scheme 8.9.

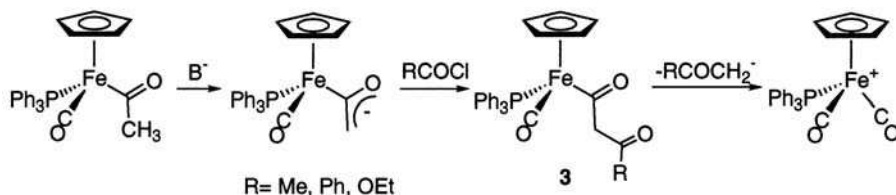
equilibrium constant did depend on $[\text{H}^+]$. The forward rate constant in Scheme 8.5 decreased in the order, $\text{R} = \text{Me} > \text{MeOCH}_2\text{CH}_2 > \text{Et} > {}^n\text{Pr} > \text{PhCH}_2 > {}^i\text{Pr} > {}^t\text{Bu}$. Thus, the electronic property of the substituent in alcohols affected the reaction rate to a lesser extent than the steric bulk of the substituent. It was proposed that the rate-determining step is the attack of the alcohol at the carbonyl carbon forming an oxonium intermediate, and subsequent rapid dissociation of H^+ occurs. On the other hand, the attack of a primary amine at the coordinated isocyanide ligand in cationic Pt complexes was shown to be faster in the presence of intramolecular proton acceptor (**1**) than the reaction of the reference complex **2** (Scheme 8.9) [15]. Note, however, that the overall transformation observable was the production of diaminocarbene ligand, instead of aminoimidoyl ligand $\text{Pt}-\text{C}(=\text{NR})(\text{NHR})$ which is equivalent to $\text{Pt}-\text{COOR}$ obtained in Scheme 8.5.

Of further note is that formylmetal complexes MCHO , usually formed by intermolecular reaction of metal carbonyl complexes with hydrides of other metals, underwent ready dissociation of H^- unit, which may be received by some external electrophilic reagents including ketones, organic halides, and even carbonyl ligand on other metal (Scheme 8.10) [16]. It was proposed that in these reactions a metal hydride is not formed as a transient species but direct transfer of H^- from CHO to the appropriate electrophilic center takes place. Even an acyl ligand underwent fragmentation into carbanion and metal-carbonyl moiety. For example, as shown in Scheme 8.11 β -ketoacyliron complex **3**, prepared from ferraenolato complex and an acyl electrophile, underwent spontaneous C-C bond cleavage, giving rise to an iron carbonyl complex and an enolate ion [17].

The nucleophilic attack at the carbonyl ligand is believed to induce the increase in the electron density at the metal and the oxygen atom. Such an increase would contribute to destabilization of the product complex. Therefore, the presence of more electron-withdrawing auxiliary ligand(s) is advantageous to delocalization of the electron density on the metal. A strategy to divert the charge on the

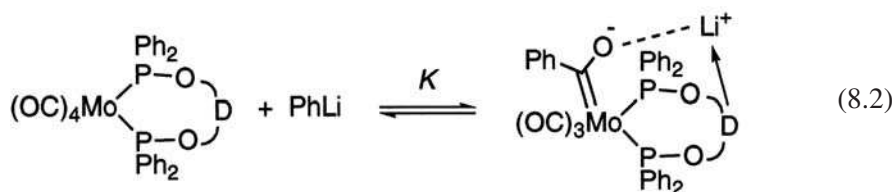


Scheme 8.10.



Scheme 8.11.

acyl oxygen has realized an otherwise difficult attack of RLi on a CO ligand in $\text{Mo}(\text{CO})_4[\text{PPh}_2(\text{OR})]_2$ as shown in Eq. 8.2 [18].



Thus, the $\text{Mo}(\text{CO})_4(\text{PPh}_2\text{OR})_2$ analogs in which the R group was modified in such a way as to locate the Li^+ ion, via coordination of D, at the suitable position for interaction with the oxygen of the acyl ligand underwent efficient alkylation with RLi. Moreover, the equilibrium constant of Eq. 8.2 increased as the acyl oxygen– Li^+ coordination was maintained more favorably by the crown ether auxiliary connected to the phosphinite ligand, as summarized in Table 8.1. The molecular structure of an isolable lithium acylate $(\text{CO})_3\text{Mo}(\text{PhCOLi})[\text{Ph}_2\text{P}(\text{OCH}_2\text{CH}_2)_3\text{OPPh}_2]$ is shown in Fig. 8.1.

TABLE 8.1

Equilibrium constants for Eq. 8.2 in THF and benzene at 25°C

Complex $\text{L}_2 =$	K	
	THF	Benzene
$\text{O}(\text{CH}_2\text{CH}_2\text{O})_2$	< 7	< 45
$\text{O}(\text{CH}_2\text{CH}_2\text{O})_3$	2700	> 100,000
$\text{OCH}_2\text{CH}_2\text{N}(\text{Me})\text{CH}_2\text{CH}_2\text{N}(\text{Me})\text{CH}_2\text{CH}_2\text{O}$	50,000	> 300,000

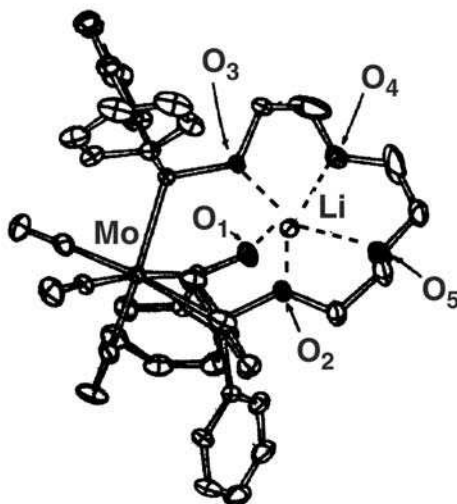
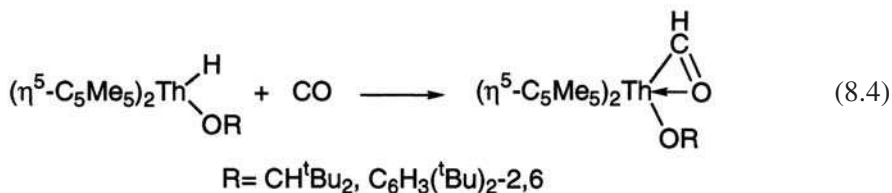
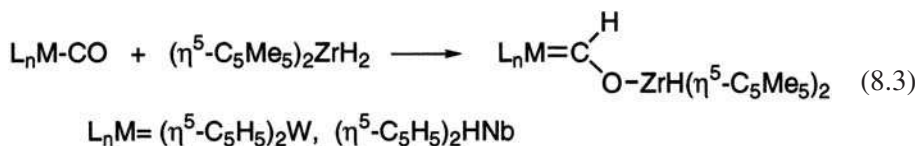
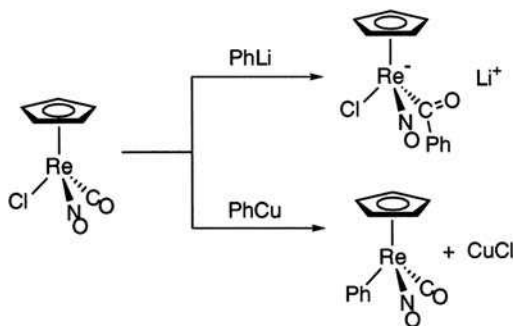


Fig. 8.1. Molecular structure of $(\text{CO})_3\text{Mo}(\text{PhCOLi})[\text{Ph}_2\text{P}(\text{OCH}_2\text{CH}_2)_3\text{OPPh}_2]$. Bond lengths ($\text{\AA}$): $\text{Li}-\text{O1} = 1.84$; $\text{Li}-\text{O2} = 2.09$; $\text{Li}-\text{O3} = 2.00$; $\text{Li}-\text{O4} = 2.20$; $\text{Li}-\text{O5} = 2.05$. Reproduced with permission from American Chemical Society.

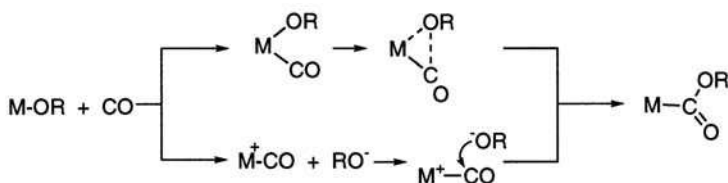
Similarly, thermodynamically unfavorable formyl ligand formation by the attack of hydride compounds at the coordinated carbonyl was often facilitated by intra- and intermolecular metal coordination with the oxygen of the CHO ligand, as exemplified in Eqs. 8.3 and 8.4 [16d,e,h].



It should also be mentioned that in certain cases another type of specific interaction between the $\text{C}(\text{O})\text{Nu}$ ligand and an electrophile triggers the $\text{C}-\text{Nu}$ bond cleavage. For example, the rate of the reverse reaction of Scheme 8.5 was dependent on the concentration of H^+ , suggesting rate-determining protonation of the alkoxy oxygen atom in the degradation of $\text{Pt}-\text{COOR}$ compounds.



Scheme 8.12.



Scheme 8.13.

(b) *The site of nucleophilic attack*

As mentioned before, the site of the initial attack in the reaction of nucleophiles with carbonyl complexes has duality (carbon or metal), and the clear distinction of the attack site is often difficult. The 18-electron carbonyl complex in Scheme 8.12 underwent attack of phenyllithium or phenyl Grignard reagents at the carbon to give benzoylmethyl complex, while the metal was the site of the attack by a phenylcopper reagent to give a phenylmetal complex [19].

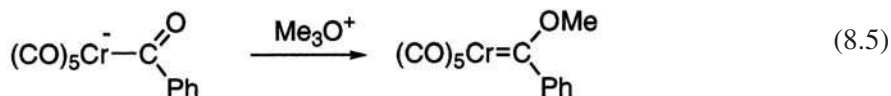
The reaction of 16-electron carbonyl complexes of Pd and Pt with alcohols and amines may presumably proceed without metal–alkoxy or metal–amide bond formation (cf. Scheme 8.5). The reaction of alkoxymetal complexes with carbon monoxide offers an interesting mechanistic diversity (Scheme 8.13).

Two paths, one proceeding via a migratory insertion of the carbonyl and alkoxy ligands in the coordination sphere and the other involving initial dissociation of RO^- anion which subsequently attacks the coordinated carbonyl, can be envisioned. In the course of the carbonylation of the Ir complex $\text{Ir(CO)}_2(\text{PPh}_3)_2(\text{OPh})$, spectroscopic evidence was obtained which substantiated the occurrence of an ion pair $[\text{Ir(CO)}_3(\text{PPh}_3)_2]^+ \text{OPh}^-$ prior to the C–O bond formation [20]. Similarly, reaction of CO with organopalladium alkoxide $\text{Pd}(\text{bdpp})(\text{Me})(\text{OMe})$ ($\text{bdpp} = 2,4\text{-bis(diphenylphosphino)pentane}$) was proposed to proceed via initial ligand substitution to generate an ionic species $[\text{Pd}(\text{bdpp})(\text{Me})(\text{CO})]^+ (\text{OMe})^-$, though no definite evidence for this route has been provided [21a]. The only fact which suggested the proposed path was that the fast dissociation of the methoxide anion

in a CD_3OD solution of the parent complex has been observed. In contrast to the Pd case, the analogous Pt complex $\text{Pt}(\text{dppe})(\text{Me})(\text{OMe})$ did not show evidence for occurrence of $\text{Pt}-\text{OMe}$ bond dissociation, even in the course of the carbonylation [21b]. For example, the carbonylation product $\text{Pt}(\text{dppe})(\text{Me})(\text{COOMe})$ obtained in the presence of CD_3OD contained less than 5% OCD_3 group. The proposed path is the migratory insertion of $\text{Pt}(\text{dppe})(\text{Me})(\text{CO})(\text{OMe})$ intermediate.

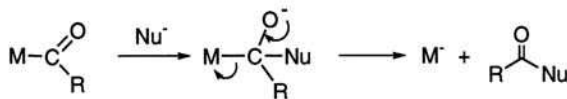
(c) *Further transformation of nucleophilic adduct*

The product from nucleophilic attack at the carbonyl carbon undergoes, besides the reverse course of the attack, some transformations useful for the purpose of utilizing the new ligand group. These include alkene insertion and reductive elimination, as in Schemes 8.3, 8.6 and 8.7. Decarboxylation of $\text{M}-\text{COOH}$ was also described (Scheme 8.8). The acyl complex reacts with carbon electrophile to give carbene complex (Eq. 8.5) [22].



The acyl, alkoxycarbonyl and carbamoyl ligands can accept the attack of nucleophiles at the carbonyl carbon (Scheme 8.14). The charge accumulated at oxygen by this attack may be brought to the metal atom upon $\text{M}-\text{C}$ bond cleavage, completing the nucleophilic substitution of the $\text{M}-\text{C}(\text{O})\text{R}$ bond. This transformation is believed to be key to the final step of a catalytic cycle for ester and amide synthesis starting from, e.g. alkenes and alcohols under CO pressure (see Scheme 8.3). However, a kinetic study on alcoholysis of benzoyl complex $\text{Pd}(\text{COPh})(\text{I})(\text{PPh}_3)_2$ to give benzoate esters suggested that the esters are formed by reductive elimination of alkoxy intermediates $\text{Pd}(\text{COPh})(\text{OR})(\text{PPh}_3)_2$, but not by a sequence similar to Scheme 8.14 [9d].

Nucleophilic attack of an azide ion at the carbonyl ligand, followed by elimination of N_2 , afforded a metal coordinated cyanate ligand (Scheme 8.15) [23]. The kinetic study of the reaction between $[\eta^5-\text{C}_5\text{H}_5\text{Fe}(\text{CO})_2\text{L}]^+$ and NaN_3 in



Scheme 8.14.



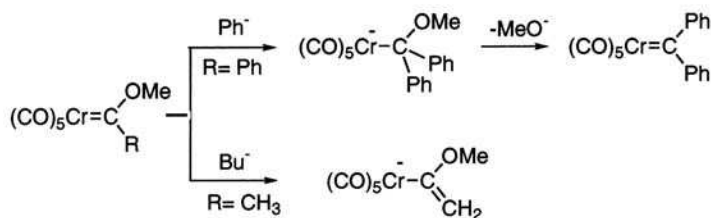
Scheme 8.15.

methanol showed the rate to have first-order dependency on both the complex and N_3^- , with rate constant for the attack of N_3^- decreasing in the order $L = CO > PPh_3 > C_2H_4$. The higher reactivity for $L = CO$ than $L = PPh_3$ is understandable in terms of both steric and electronic effects; the former complex should have the CO ligand of the more electron-deficient nature and the less crowded environment than the latter. The lower reactivity of the ethylene complex is more difficult to explain. There is a possibility that N_3^- attacks first the ethylene carbon atom to give β -azaethyliron intermediate, which rearranges slowly, via the reverse of the nucleophilic attack at ethylene, to the acylazido complex, and eventually to the cyanate. It was indeed known that other nucleophiles, $MeNH_2$ and MeO^- , attacked the ethylene of $[\eta^5-C_5H_5Fe(CO)_2(C_2H_4)]^+$ giving a substituted ethyliron complexes (see next section). Hydrazine also attacked the carbonyl carbon in $[\eta^5-C_5H_5Fe(CO)_3]^+$ to give an intermediate $[\eta^5-C_5H_5Fe(CO)_2(CONHNH_2)]$, which then lost ammonia to give the cyanate complex.

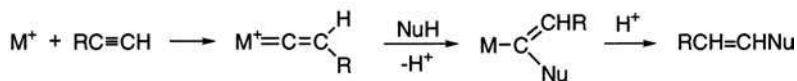
(d) *Reaction of isocyanide and carbene ligands*

The reactivity trend in the nucleophilic attack at metal-bound isocyanide ligand is similar, in general, to that at the carbonyl ligand. The nitrogen atom in the imido ligand thus formed may be somewhat more basic than the oxygen in the corresponding acyl ligand. It then follows that the hydrogen of alcohol and amine (primary, secondary) readily migrates, after the attack at the isocyanide carbon, to the nitrogen to lead to carbene ligand formation (cf. Scheme 8.9).

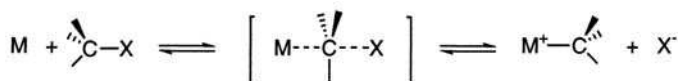
Fischer carbene ligands can also be attacked by nucleophiles because of a minor, if any, contribution of $d\pi-p\pi$ back-bonding to the metal-carbon bond. The attack may lead to formation of alkylmetal and new carbene complexes (Scheme 8.16). If there is a C-H bond next to the carbene carbon, deprotonation sometimes occurs upon attack of base to give vinylmetal complexes (Scheme 8.16) [24]. The reverse reaction will be discussed in section 8.3. An α -carbon of vinylidene ligand, generated from 1,2-hydrogen shift of terminal alkyne upon contact with coordinatively unsaturated metal fragment, is also susceptible to the nucleophilic attack (Scheme 8.17). This attack is believed to constitute a catalytic cycle for anti-Markownikov addition of NuH ($Nu = RO, RCOO$, etc.) to alkynes [4c]. Schrock carbenes are sensitive to electrophiles (see 8.3.1), but not to nucleophiles.



Scheme 8.16.



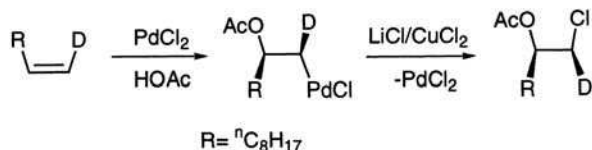
Scheme 8.17.



Scheme 8.18.

8.2.2 Reaction of alkyl ligands

Compared to the acyl and related ligands shown in Scheme 8.14, the alkyl ligand is less susceptible to nucleophilic attack. This attack corresponds to the reverse of one of the oxidative addition courses involving alkyl halides and related electrophiles. This is an S_N2 reaction with low valent metal complex fragment where the leaving group may be pushed out of the coordination sphere (Scheme 8.18). If the reverse of this step is traced starting from alkylmetal complexes combined with a highly donating group as a nucleophile, the coupling product may be formed, together with lower valent complex. The closely related direct nucleophilic attack at the alkyl ligand has been known in organothallium chemistry [25]. Alkyl complexes of Pt(IV) were shown to undergo attack of halide or alkoxide anion to give alkyl halides or ethers together with Pt(II) complexes [26]. In the case of alkyl complexes of other transition metals, the reverse course of Scheme 8.18 may not possess enough driving force to cause the nucleophilic substitution to be completed. Some unique device to stabilize a rather unstable low valent metal moiety could allow such substitution. A related nucleophilic attack may have probably been involved in Pd-catalyzed oxidation of alkenes by the use of auxiliary oxidants such as Pb(IV) and Cu(II) salts (e.g. Scheme 8.19) [27]. The auxiliary might have increased the oxidation state of Pd atom in oxypalladation intermediate (next section), thereby enhancing susceptibility of the alkyl ligand to the nucleophilic attack. The similar sequence has been proposed in the halogenolysis of alkyl complexes of Co and Fe [28,29]. Related discussions will be given in section 8.3 for electrophilic attack at alkylmetal complexes.

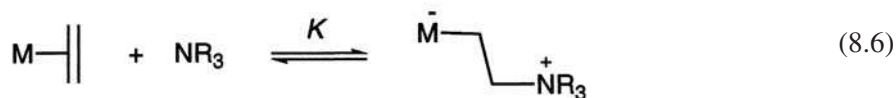


Scheme 8.19.

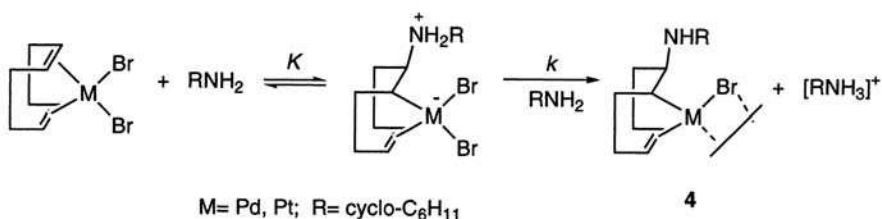
8.2.3 Reaction of alkene and alkyne ligands

Like the metal-bound carbonyl ligand, alkene and alkyne ligands coordinated to transition metals are susceptible to the attack of various nucleophiles to form new complexes containing alkyl or vinyl ligands with a substituent derived from the nucleophile bonded at the β -carbon. The range of nucleophiles is again widespread, spanning from hydride and carbanions to heteroatom anions and neutral molecules. However, not all of the existing alkene or alkyne complexes are capable of undergoing the attack of the nucleophile. For example, complexes having a metal–alkene or alkyne bond with significant contribution of π back-bonding (e.g. $\text{Ni}(\text{PPh}_3)_2(\text{olefin})$) do not react with nucleophiles, but rather with electrophiles, as will be described in the later section of this chapter. On the other hand, a few metal complexes such as those of $\text{Hg}(\text{II})$ and $\text{Tl}(\text{III})$ can give rise to alkylmetal complexes apparently derived from nucleophilic attack at the metal-bound alkene, which however is too short-lived to allow even spectroscopic detection.

In principle, the nucleophilic attack at alkene or alkyne ligand can be a reversible process, like the reaction of carbonyl ligand. The reversibility often has been confirmed in the reaction of heteroatom-based nucleophiles, but carbon nucleophiles rarely undergo the reversible attack at alkenes and alkynes [30]. Occurrence of an equilibrium reaction was observed between the combination of alkene–metal complex with amine on one hand, and zwitter ionic adduct made from the former combination on the other (Eq. 8.6) [31,32]. The isolation of the latter adduct was also realized in some cases as described later. It was demonstrated that this type of reversible adduct formation did not accompany E–Z isomerization of the alkene, meaning stereospecific nature of the C–N bond formation and its reverse. A closely related stereochemical analysis demonstrated that the attack of the amine at the coordinated alkene takes place from the side opposite to the metal atom, as will be discussed later in more detail.



The equilibrium constants for a series of zwitter ion formation represented by Eq. 8.6 ($\text{M} = \text{trans-PtCl}_2(\text{Y})$; $\text{Y} = \text{amine}$) provided insight into electronic and steric effects of nucleophiles. In Eq. 8.6, the K value for ${}^n\text{PrNH}_2$ was ca. 2 times as large as those for ${}^i\text{PrNH}_2$ and ${}^n\text{Pr}_2\text{NH}$, and more than 100 times as large as that for NEt_3 . Cyclic amines, e.g. piperidine and pyrrolidine gave quite stable σ -adducts. These trends indicate that the steric bulk of the attacking amine plays a more influential role than the electronic effect [32]. This is similar to the role of the alcohol substrate in its attack at the Pt-bound carbonyl ligand shown in Scheme 8.5.

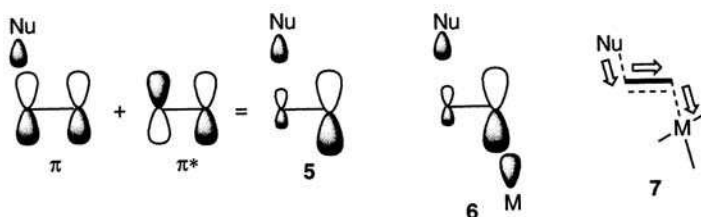


Scheme 8.20.

The reversibility of the zwitter ion adduct formation in Eq. 8.6 also affected the rate law of the formation of amino-substituted alkylmetal complexes. Thus, kinetic studies indicated [33] that the rate of the formation of β -aminoalkyl complex **4** in Scheme 8.20 was second-order with respect to the concentration of the amine, namely $\text{rate} = k[\text{amine}]^2[\text{complex}]$. This is consistent with a reaction sequence shown in Scheme 8.20 involving a reversible formation of the zwitter ionic intermediate, followed by the rate-determining deprotonation by the second amine molecule. The observed rate constant appeared to contain contributions from both the equilibrium constant of the first step and the rate constant of the second deprotonation, so that the direct comparison of the rate of the initial nucleophilic attack at the coordinated alkene between Pd and Pt complexes was not possible. However, the higher overall reactivity (ca. 70 times) of Pd complex than Pt complex was consistent with the higher ionization potential of Pd than Pt. This difference in the ionization potential then would lead to the weaker π basicity of Pd(II) than Pt(II) for π back-donation to alkene π^* orbital, and therefore facilitated the nucleophilic attack at the Pd–alkene complex more than that at the Pt complex.

(a) Role of metal in facilitating nucleophilic attack

As described above, more extensive π back-bonding from metal to unsaturated ligands appears to retard the nucleophilic attack. It is also known that the metal-free alkene and alkyne molecules without electron-withdrawing substituent are generally not reactive with nucleophiles. Some explanations based on molecular orbital calculations have been presented for the specific role of a certain class of transition metals in facilitating the nucleophilic attack at alkenes and alkynes [34]. The high barrier to the reaction between free ethylene and a nucleophile can be ascribed to increasing repulsion between electrons in ethylene π MO and the lone pair orbital (Nu) of the nucleophile with the increasing contact of the nucleophile with one ethylene carbon. Although mixing of ethylene π^* into the anti-phase combination of the two occupied fragment orbitals may take place as the nucleophile approaches ethylene (Scheme 8.21, **5**), a stabilization effect of the interaction between ethylene π^* and the lone pair orbital of the nucleophile would not be sufficiently large to compensate the destabilization caused by the repulsion between ethylene π and the lone pair orbital.



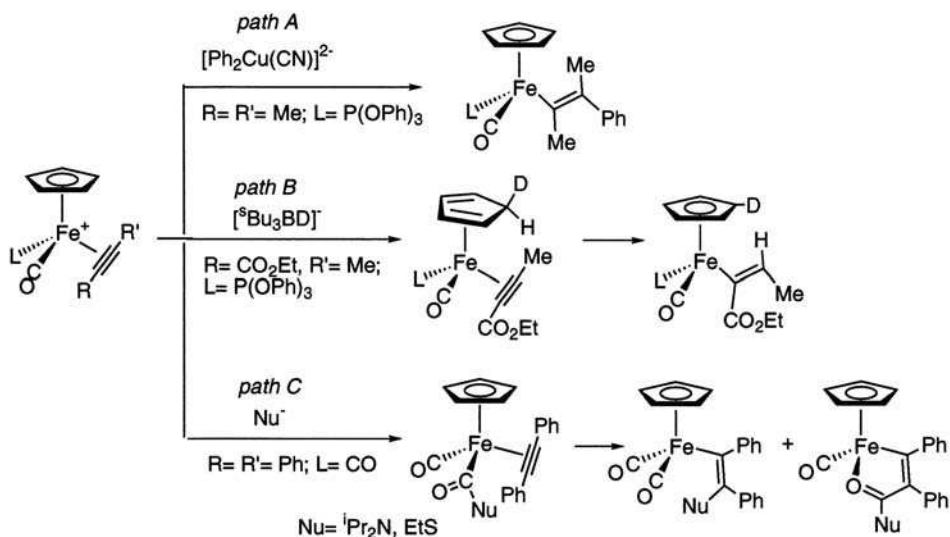
Scheme 8.21.

Coordination of ethylene to electrophilic metals (e.g. Pd(II)) may lower the π and π^* levels of ethylene and the more effective π^* -Nu interaction would contribute, to some extent, to the stabilization of the transition state. Another important role of the metal, in particular the one with the cationic charge [34f], in enhancing the nucleophilic attack is thought to be its ability to facilitate charge transfer from the nucleophile to the ethylene as well as to the metal by the use of its low lying acceptor orbital (Scheme 8.21, **6**). This charge transfer can stabilize the otherwise unstable combination of two occupied orbitals shown in **5**. It should be noted that not all metal cations coordinated with alkene are effective in accepting the electron flow. For example, Li^+ ion has a too-high acceptor orbital for this purpose [34d].

It was suggested that the charge transfer from the nucleophile to the alkene-metal fragment is greatly assisted by mixing of the π^* into the π orbitals of ethylene ligand where this mixing is coupled with a slippage of the ethylene ligand from a symmetrical η^2 -bonding toward an η^1 -bonding [34a]. This deformation may occur to a progressively increasing extent as the nucleophilic attack proceeds. There could be another case where the distortion takes place at the earlier stage of the nucleophilic attack. Overall, the enhanced nucleophilic attack at the metal-bound alkene ligand may involve three kinds of electron flow, namely charge transfer from Nu to ethylene, that from α -carbon to β -carbon, and that from β -carbon to metal, as schematically shown in **7** of Scheme 8.21.

(b) Stereochemistry of nucleophilic attack

Alkene and alkyne ligands susceptible to the nucleophilic attack are usually bound to a metal atom that is electrophilic in nature. Therefore, a reaction course might occur where a nucleophile attacks the metal atom first, instead of the carbon of the unsaturated ligand, with a concomitant dissociation of a ligand group other than the unsaturated ligand in the case of an 18-electron complex. The sacrificial ligand loss for the coordination of the nucleophile to metal does not necessarily occur in the case of a coordinatively unsaturated complex. The new ligand group made by such nucleophilic attack at the metal may then undergo migratory insertion with the unsaturated ligand to give a β -substituted alkyl or alkenyl ligand



Scheme 8.22.

which bears the same composition as, but the different stereochemistry from, that produced by the direct attack of the nucleophile at the unsaturated ligand. The stereochemical distinction can be made with considerable ease if the unsaturated ligand is an alkyne, or a kind of alkene capable of delivering a diastereochemical information.

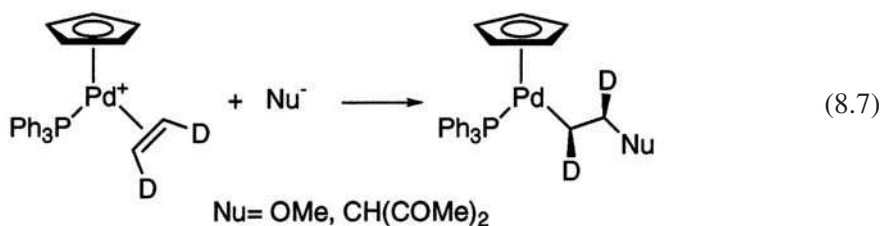
Stereochemistry of products from nucleophilic attack at alkyne and cyclic alkene ligands in 18-electron iron complexes $[(\eta^5\text{-C}_5\text{H}_5)(\text{CO})(\text{L})\text{Fe}(\text{Un})]^+$ has been extensively examined [35]. It was deduced that most nucleophiles including $(\text{MeOOC})_2\text{CH}^-$, Ph^- , RNH_2 and PhS^- attacked directly at the carbon of the unsaturated ligand from the side opposite to the iron metal (e.g. Scheme 8.22, path A).

There are two interesting exceptions to this trend. The reaction of hydride with alkyne complex $[(\eta^5\text{-C}_5\text{H}_5)(\text{CO})(\text{L})\text{Fe}(\text{EtOOC}\equiv\text{CCMe})]^+$ gave $(\eta^5\text{-C}_5\text{H}_5)(\text{CO})(\text{L})\text{Fe}(\text{EtOOC}\text{=CHMe})$ with Fe and H substituents positioned *cis* to each other (Scheme 8.22, path B) [36a]. Importantly, the use of $[\text{DBEt}_3]^-$ led to incorporation of deuterium in the C_5H_5 ligand, but not in the newly formed alkenyl ligand. This result, together with the stereochemistry of the product, led to a proposal that the overall reaction consisted of two steps: the first is the attack of the hydride at the $\eta^5\text{-C}_5\text{H}_5$ ligand from the side opposite to Fe, and the second is a transfer of an endo H atom of $\eta^4\text{-C}_5\text{H}_6$ ligand to the alkyne ligand. The latter unique step could involve participation of metal orbitals, or a formyl complex intermediate. It should also be noted that BD_4^- reacted with 16-electron alkyne complex $[(\eta^5\text{-C}_5\text{H}_5)(\text{P}(\text{OMe})_3)\text{Mo}(\text{HC}\equiv\text{C}'\text{Bu})]^+$ to give $[(\eta^5\text{-C}_5\text{H}_5)(\text{P}(\text{OMe})_3)\text{MoCH}=\text{CD}'\text{Bu}]$, with the stereochemistry of the addition of Mo

and D being *cis*, consistent with the initial attack of the hydride at the metal atom [37].

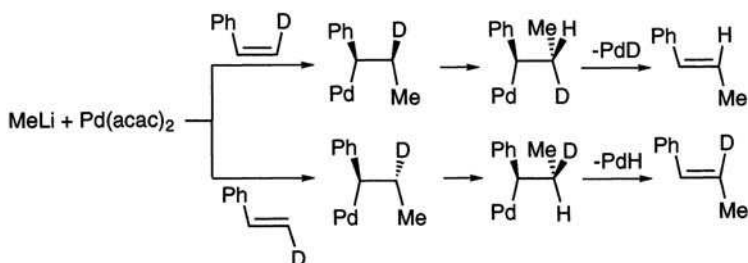
The second exception to the external nucleophilic attack at the coordinated alkynes is shown in Scheme 8.22, path C [36b]. In the reaction of $[(\eta^5\text{-C}_5\text{H}_5)(\text{CO})_2\text{Fe}(\text{PhC}\equiv\text{CPh})]^+$ with amines, alkoxides or thioalkoxides, the nucleophile attacks initially the CO ligand to give a CONu ligand, and then Nu migrates to the alkyne carbon to give the vinyl ligand having Fe and Nu located *cis* to each other. In some cases the CONu group undergoes the migratory insertion.

Upon treatment with oxygen and carbon nucleophiles, 18-electron ethylene- d_2 complex of Pd gave alkyl complexes whose ^1H NMR analysis revealed the *trans* stereochemistry of the nucleophilic attack (Eq. 8.7) [38]. In the case of the reaction of 16-electron alkene complexes of Pd and Pt, both *trans* and *cis* attacks occurred depending on the nature of the nucleophile as well as the auxiliary ligand. The *trans* attack appears to dominate in the reaction of cyclic dialkene ligands (e. g. cyclooctadiene, norbornadiene) chelating to the metal with some nucleophiles including oxygen, nitrogen (see, e.g., Scheme 8.20) and carbon nucleophiles such as $(\text{MeOOC})_2\text{CH}^-$ except for phenylmercury reagent [39].

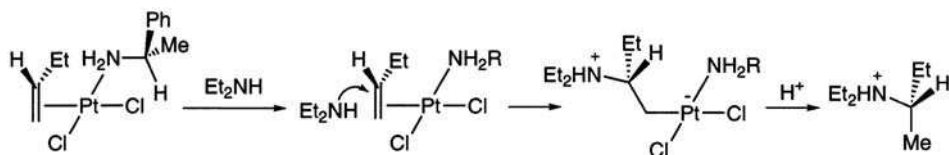


The stereochemistry of the reaction with simple monoalkene ligands in 16-electron complexes appears more diverse. In agreement with the *cis* stereochemistry in the reaction of the phenylmercurial, the reaction of methyl anion (from MeLi) with deuteriostyrene complex of Pd to give *E* - β -methylstyrene was interpreted in terms of *cis* stereochemistry of the carbopalladation step (Scheme 8.23) [40]. In the overall transformation which could model the Heck reaction, the *cis* addition of Pd and Me groups across the $\text{C}=\text{C}$ bond of styrene was followed by rotation about the $\text{C}-\text{C}$ single bond, originally $\text{C}=\text{C}$ bond, and the specific *cis*- β -H or -D elimination depending on the stereochemistry of the deuterated styrene used.

The aminometallation reaction is of special relevance to the key step involved in metal-catalyzed amination of alkenes and alkynes [4b,d,41]. The reversible attack of aliphatic amines at the monoalkene ligand shown in Eq. 8.6 may proceed in stereospecific *trans* addition and elimination [42]. For example, diethylamine was reacted with 1-butene, which coordinated to Pt using only one enantioface of the olefin ((*S*)-1-butene-Pt bond) (Scheme 8.24) [42a]. Alkylplatinum complex thus formed was subjected to acidic work-up to give optically active amine salt having the *S*-configuration at the asymmetric carbon. This result unambiguously demon-



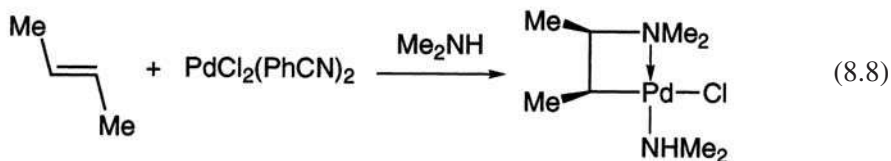
Scheme 8.23.



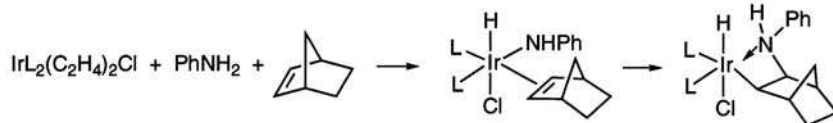
Scheme 8.24.

strated the *trans* attack of diethylamine. Ammonia underwent similar nucleophilic addition with the same stereochemistry.

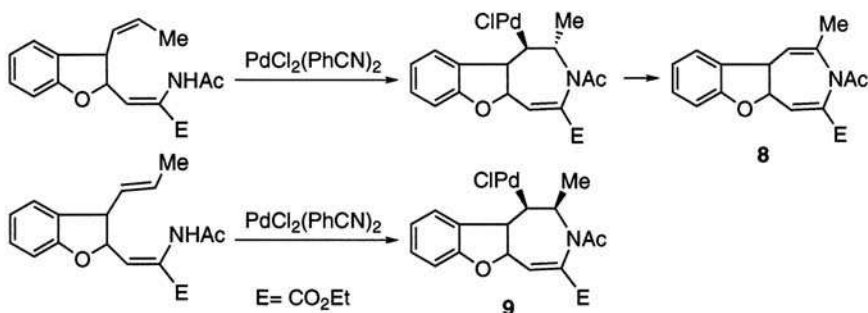
The reaction of *trans*-2-butene with dimethylamine in the presence of $\text{PdCl}_2(\text{PhCN})_2$ afforded chelated β -aminoalkylpalladium complex shown in Eq. 8.8 [42b]. The X-ray structure determination revealed the *cis* configuration of two methyl substituents on the metal-containing ring, demonstrating again the *trans* attack of the amine at *trans*-2-butene ligand, although no isolable alkene palladium complex was used as the substrate in this case.



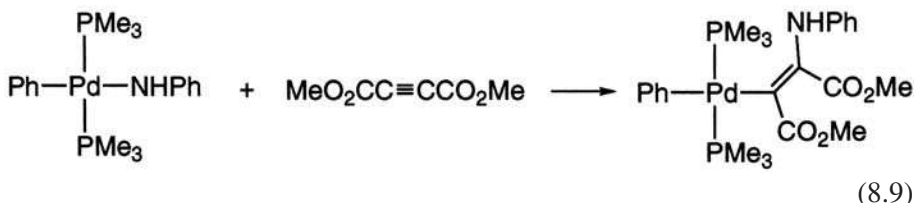
In contrast to the above results, *cis* addition of nitrogen and metal atoms to alkenes was suggested in Th-catalyzed intramolecular cyclization of α,ω -aminoalkenes [4b]. Some aminometallation reactions of alkenes or alkynes using aromatic amines also proceeded via *cis* addition [43,44]. Addition products in Scheme 8.25 and Eq. 8.9 were characterized by X-ray structure determination. The reaction may have proceeded via migratory insertion involving a metal-anilido intermediate, which was an actual starting material in Eq. 8.9. Notice that in this case the alkyne underwent migratory insertion into Pd–N bond, rather than to Pd–C bond.



Scheme 8.25.

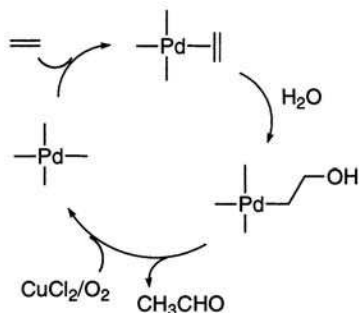


Scheme 8.26.

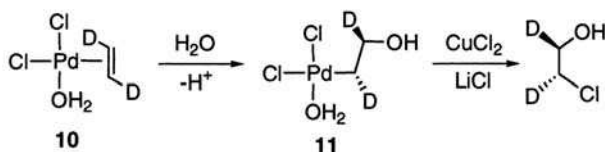


A more activated amine underwent intramolecular *cis* aminopalladation reaction as shown in Scheme 8.26 [45]. Thus, treatment of the amine bearing Z-alkene substructure with $\text{PdCl}_2(\text{PhCN})_2$ afforded unstable aminopalladated intermediate, which was prone to β -H elimination to give enamine **8**, while the similar treatment of the E-alkene counterpart afforded organopalladium complex **9**, which was remarkably inert with respect to the β -H elimination. The difference in the trend with respect to the β -H elimination was attributed to the different ease of the two organopalladium cyclic intermediates to take a configuration favorable for the β -H elimination (small dihedral angle about Pd-C-C-H). These results were consistent with the *cis* stereochemistry of the initial heterocycle formation.

Hydroxypalladation of ethylene with H_2O to give β -hydroxyethylpalladium intermediate is a key step involved in the Wacker process, an industrial oxidation of ethylene to acetaldehyde (Scheme 8.27). How the C-O bond formation takes place has been a matter of controversy for a long time. Occurrence of *trans* attack of water at the Pd-bound ethylene ligand was suggested by a stereochemical



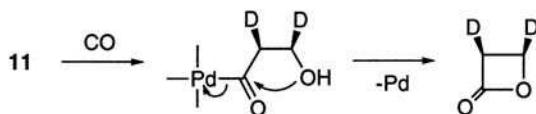
Scheme 8.27.



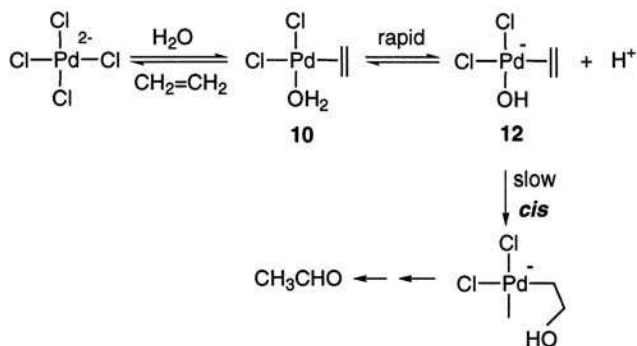
Scheme 8.28.

analysis of chlorohydrin- d_2 , a major product of oxidation of *E*-dideuterioethylene formed under the condition where the concentrations of Cl^- ($>5\text{ M}$) and CuCl_2 ($>3\text{ M}$) were considerably high compared to those employed in the Wacker reaction (Scheme 8.28) [46]. In this analysis the stereochemistry of the second step, namely CuCl_2 -assisted electrophilic chlorination of organopalladium(II) intermediate **11** was assumed as inversion based on results in similar transformations (e.g. Scheme 8.19). In another model reaction, *E*-dideuterioethylene complex was reacted with water under carbon monoxide pressure to give β -propiolactone whose ^1H NMR analysis indicated the *trans* hydroxypalladation (Scheme 8.29) [47]. Here again it was believed, and also evidenced experimentally, that carbonylation of the intermediate like **11** proceeded with retention of configuration at the α -carbon.

A reaction course contrary to the above model studies has been offered primarily based on kinetic aspects of the Wacker reaction [48]. Particular attention has frequently been paid to the fact that the actual Wacker condition is considerably different from those used in Schemes 8.28 and 8.29 (e.g. Cl^- concentration in



Scheme 8.29.



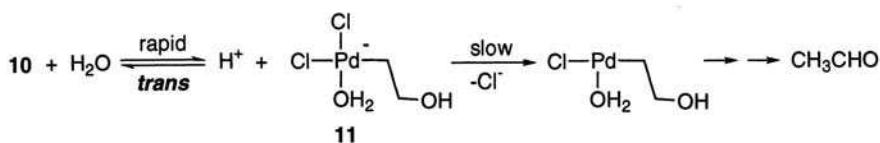
Scheme 8.30.

the Wacker reaction is lower than 1 M). Under the actual Wacker conditions the kinetic rate law of the overall process is Eq. 8.10, which exhibits inverse $[H^+]$ dependency. This behavior was proposed to be consistent with Scheme 8.30 involving slow migratory insertion (*cis* hydroxypalladation) in intermediate **12** which lies in equilibrium with aquo complex **10** and thus is suppressed by H^+ .

$$\text{rate} = k[\text{PdCl}_4^{2-}][\text{C}_2\text{H}_4] / [H^+][\text{Cl}^-]^2 \quad (8.10)$$

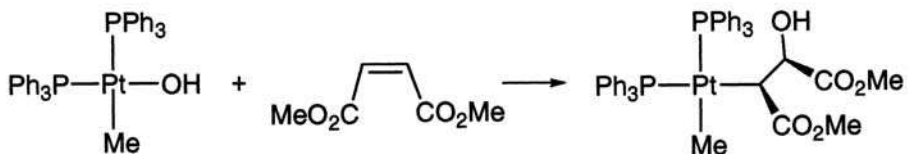
However, the rate law, Eq. 8.10 may also be consistent with the *trans* attack of water (Scheme 8.31) if the rate-determining step corresponded to a later step, e.g. decomposition, via Cl^- dissociation, of the β -hydroxyethylpalladium intermediate **11**. It was further assumed that **11** lies in rapid equilibrium with the η^2 -ethylene complex **10** so that the higher concentration of H^+ should lower the concentration of complex **11** to retard the overall rate. In any case, more effort needs to be made with regard to the stereochemical issue since no direct stereochemical proof has been available with regard to the hydroxypalladation step under the Wacker condition. It should also be noted that a recent analysis on correlation between rates of Wacker type oxidation vs. ionization potentials, HOMO and LUMO for a series of alkenes suggested that a rate-determining step of the oxidation corresponds to a transformation having characteristics of nucleophilic attack at alkenes [49]. In other words, this analysis appears to be more consistent with Scheme 8.30 involving the nucleophilic attack (hydroxypalladation) as a slow step than with Scheme 8.31 involving the similar attack as a fast step.

The *cis* hydroxymetallation was actually observed under certain conditions. Thus, Pt complex *cis*-Pt(Me)(OH)(PPh₃)₂ reacted with dimethyl maleate in benzene to give a high yield of β -hydroxyalkyl complex *cis*-Pt(Me)[CH(COOMe)CH(OH)(COOMe)](PPh₃)₂ of which X-ray structure determination unambiguously established occurrence of the *cis* addition of Pt and OH to the alkene (Eq. 8.11) [50]. Added free PPh₃ did not retard the insertion



Scheme 8.31.

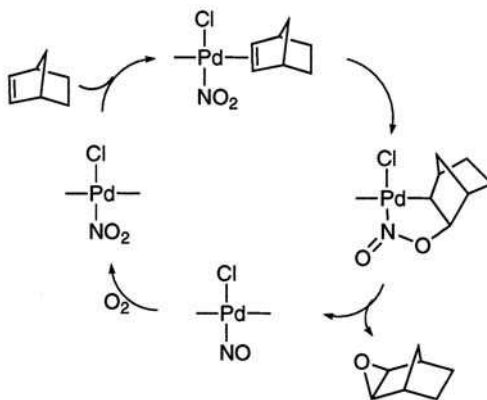
reaction. The reaction might have proceeded via migratory insertion of 18-electron intermediate $\text{Pt}(\text{Me})(\text{OH})(\text{alkene})(\text{PPh}_3)_2$.



(8.11)

Analogous reaction of $\text{Pt}(\text{Me})(\text{OMe})(\text{dppe})$ with $\text{CF}_2=\text{CF}_2$ in THF to give β -methoxytetrafluoroethyl complex was proposed to involve migratory insertion step, without dissociation of OMe^- ion, though no direct stereochemical evidence has been provided [51]. Apparent migratory insertion of alkenes to metal-hydroxo bond has also been observed in other metal complexes such as those of Ir [52].

Attack of the oxygen atom of NO_2^- anion at Pd-coordinated alkene ligand afforded metallacycle compounds (Scheme 8.32) [53]. The X-ray structure determination of the product from dicyclopentadiene complex of Pd(II) established the *cis* oxypalladation. The metallacycle thus formed can be regarded as an intermediate in Pd-catalyzed oxidation of alkenes to ketones or epoxides with the use of NO_2 ligand as a mediator and O_2 as an oxidant.



Scheme 8.32.

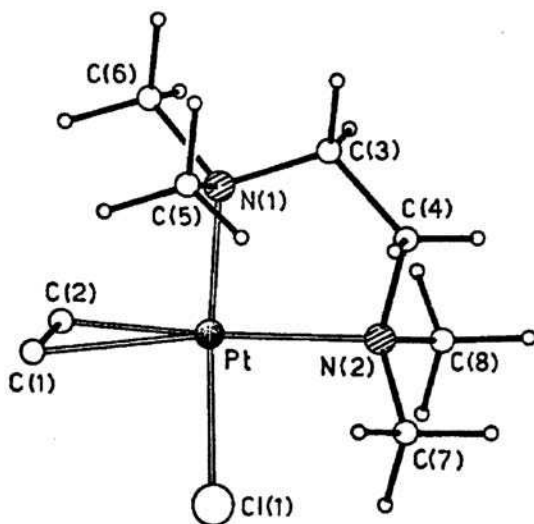
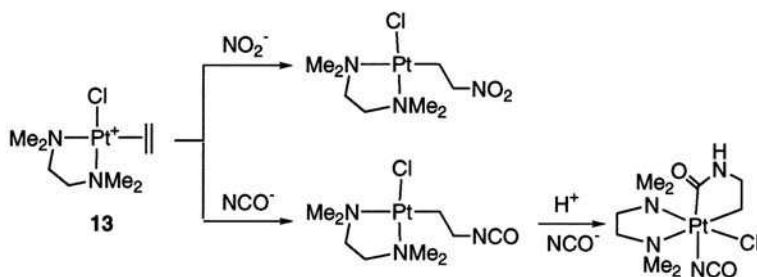


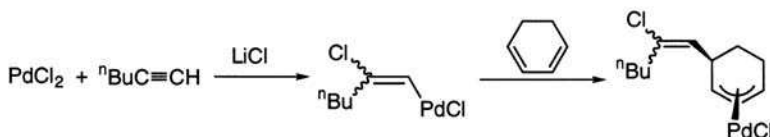
Fig. 8.2. Molecular structure of complex **13**. Bond lengths (Å): Pt–C1 = 2.176(9); Pt–C2 = 2.242(11); C1–C2 = 1.47(2); Pt–Cl = 2.287(2); Pt–N1 = 2.045(6); Pt–N2 = 2.128(6). Reproduced with permission from *Cryst. Structure Communication*.



Scheme 8.33.

The NO_2^- ion also attacked ethylene ligand of cationic Pt complex **13** of Scheme 8.33 [54]. The ethylene coordination geometry in **13** was much distorted, as shown in Fig. 8.2 [54a]; Pt–C2 length is 0.066 Å longer than Pt–C1 and C=C bond tilts from the axis orthogonal to the coordination plane by 10°. Though such distortion may partly be due to the crystal packing effect, the unsymmetrical ethylene coordination was thought [34a] to provide the ethylene ligand with unusually high susceptibility toward nucleophilic attack. Indeed, NCO^- and N_3^- ions, which normally attack directly at the metal, reacted with the ethylene carbon, with the adduct from NCO^- attack having been quenched by H^+ to furnish metallacycle compound of Pt(IV) shown in Scheme 8.33 which was structurally characterized by X-ray crystallography [55]. The CN^- ion, however, displaced ethylene ligand of **13**.

Halometallation reaction of alkenes and alkynes is believed to be involved in



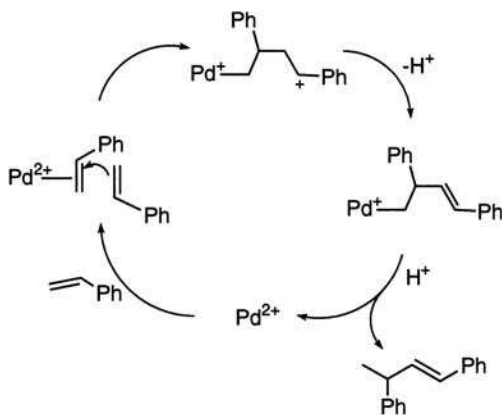
Scheme 8.34.

some catalytic transformations of these compounds with halide anions. Stereochemical examination of products derived from stoichiometric or catalytic transformation suggested that both *trans* and *cis* additions of metal and halogen atoms to unsaturated compounds occurred [56]. Scheme 8.34 shows attempts of trapping intermediate chloropalladation products with diene [56b]. The use of high halide ion concentration tended to favor *trans* halopalladation of alkynes, whereas low concentration favored *cis* addition.

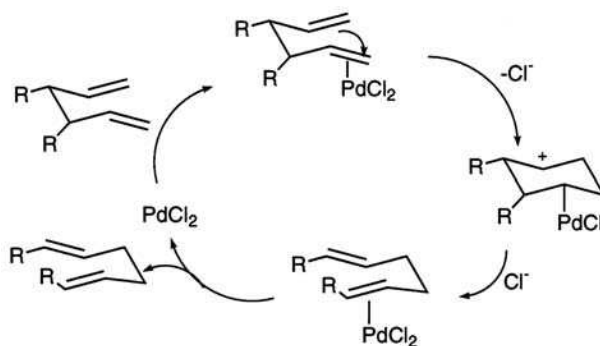
(c) *Nucleophilic attack by unsaturated carbon*

The coordinated alkene or alkyne ligand can be attacked by other alkene or alkyne molecule to accomplish some metal-catalyzed synthetically useful transformations. Typical examples include dimerization and polymerization of alkenes catalyzed by highly electrophilic cations $[\text{PdL}_2(\text{MeCN})_2]^{2+}$ ($\text{L} = \text{MeCN}, \text{PR}_3$) (e.g. Scheme 8.35) [57], and Cope rearrangement of 1,5-hexadiene derivatives catalyzed by PdCl_2 (Scheme 8.36) [58]. It was proposed that the key step in these reactions was the C–C bond formation via attack of the external alkene at the alkene carbon which was made highly electron-deficient by coordination to Pd(II) ion.

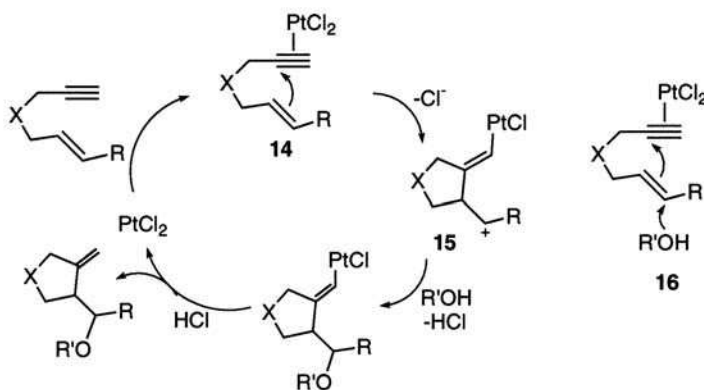
The similar step involving alkyne ligand coordinated with Pt(II) center and external alkene nucleophile was believed to induce formation of vinyl–platinum bond and carbonium ion center as shown in **14** and **15** of Scheme 8.37 [59]. The



Scheme 8.35.



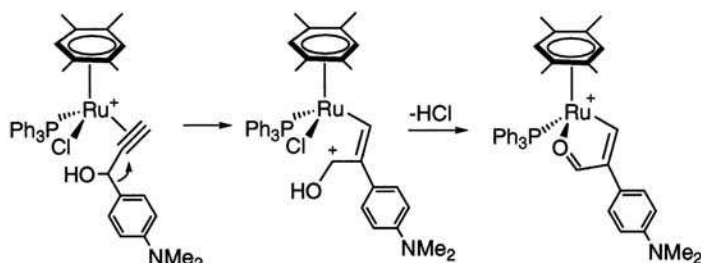
Scheme 8.36.



Scheme 8.37.

latter species was then trapped by alcohol or water to release H^+ , which finally replaced Pt(II) bonded to the vinyl ligand with retention of geometry with regard to the $\text{C}=\text{C}$ bond to furnish the cyclic product. Stereoselective incorporation of deuterium in the product in the reaction performed in CD_3OD demonstrated that the initial $\text{C}-\text{C}$ bond formation occurred at the side opposite to Pt atom with respect to the alkyne ligand as shown in **14**. This, together with the further analysis of the stereoselectivity at the alkene terminal strongly suggested a concerted, rather than stepwise, formation of the $\text{C}-\text{C}$ bond (alkyne-alkene) and $\text{C}-\text{O}$ bond (alkene-alcohol), with the stereochemistry of the addition with regard to the alkyne and alkene moiety being all *trans*. In other words, the $\text{Pt}-\text{C}$, $\text{C}-\text{C}$ and $\text{C}-\text{O}$ bond formation took place at the consecutively aligned two unsaturated molecules as in **16**.

Coordination of the $\text{C}-\text{C}$ triple bond of an aryl-substituted propargyl alcohol with an electron-deficient Ru(II) center caused 1,2-migration of the aryl group to the sp carbon center (Scheme 8.38) [60].



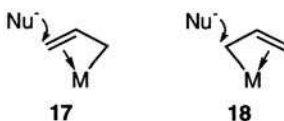
Scheme 8.38.

8.2.4 Reaction of allyl and propargyl ligands

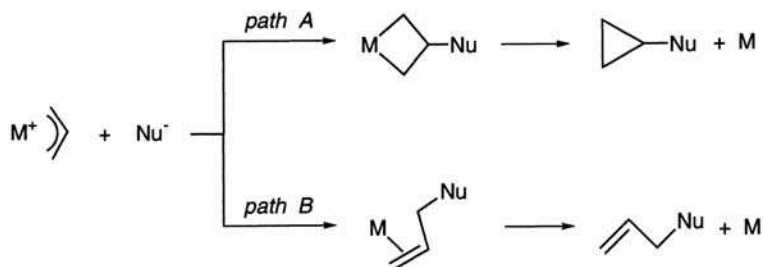
Reaction of transition metal complexes containing allyl ligand with nucleophiles is one of the most extensively studied transformations in organometallic chemistry. This is clearly due to the remarkable progress in highly selective organic synthesis which relies on the versatile role of the allyl complexes of several transition metals, especially Pd, either as an indispensable carrier of catalytic cycle, or a reagent for stoichiometric transformation. The kind of metal atom that furnishes the coordinated allyl ligand with high susceptibility to the nucleophile is widespread, spanning from early to late transition metal elements. The type of nucleophiles capable of attacking the η^3 -allyl ligand is again variable, as in the previously described reactions of the carbonyl and alkene/alkyne complexes.

The nucleophilic attack at the η^3 -allyl ligand may be formally written as either that at a coordinated alkene ligand (Scheme 8.39, **17**) or that at an alkyl-metal bond (**18**). In terms of one extreme formalism **17**, the C=C bond to be attacked would have the less electron density and therefore the greater sensitivity when this is coordinated (η^3 -form) than when free (η^1 -form) (cf. 8.2.3). Alternatively, in terms of another formalism **18**, the nucleophilic attack at the sp^3 carbon of the $\eta^1 : \eta^2$ -allyl form would be also easier than that at purely sp^3 carbon of η^1 -allyl form, possibly because of greater distortion toward sp^2 character of the carbon to be attacked in the former case. It should be pointed out that η^1 -allyl complexes are particularly susceptible to electrophiles, as will be discussed in the later section.

The propargyl ligand is electronically analogous to the allyl if both are bound to the metal via η^1 -coordination. If bound in the η^3 -form, the former may generate considerably higher strain compared to the η^3 -allyl system. The η^3 -propargyl ligand



Scheme 8.39.

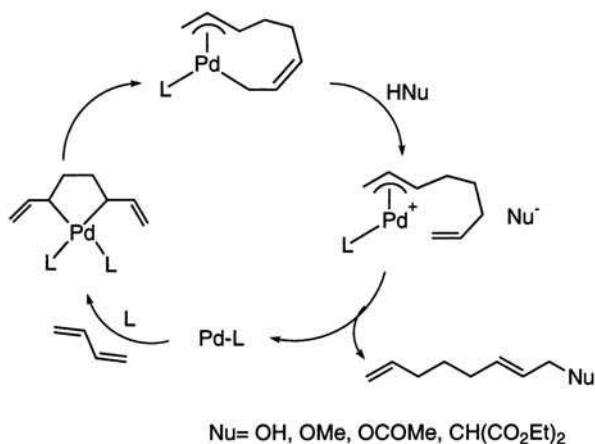


Scheme 8.40.

has been found to exhibit reactivities both analogous to and different from those of the η^3 -allyl ligand. The reactions of η^3 -propargyl complexes will be illustrated in the appropriate sections of which the primary concern is the η^3 -allyl ligand.

The η^3 -allyl ligand accepts the attack of the nucleophile both at the central and the terminal carbon, giving metallacyclobutane and η^2 -alkene complex, respectively (Scheme 8.40). Both paths A and B contribute to construction of a catalytic cycle [5a,b,61]. The former path A may be followed by reductive elimination of cyclopropane and oxidative addition of allylic electrophile to regenerate the η^3 -allyl complex, while the metal fragment from path B can be brought back to the starting complex more easily via ligand exchange and oxidative addition. Catalyzed allylic substitution with remarkable stereochemical features discussed later relies on the terminal nucleophilic attack. Analogous nucleophilic attack (path B) is believed to play a role also in Pd-catalyzed telomerization of dienes as in Scheme 8.41 [62].

When making bond with the allyl carbon, the nucleophile can approach it from both sides of the allyl plane (opposite to and same as the metal atom), with this dichotomy being analogous to that encountered in the reaction of alkene/alkyne



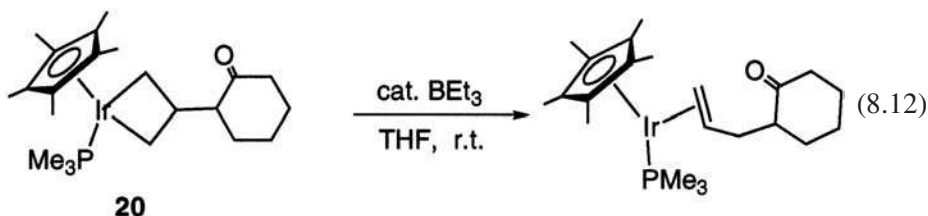
Scheme 8.41.

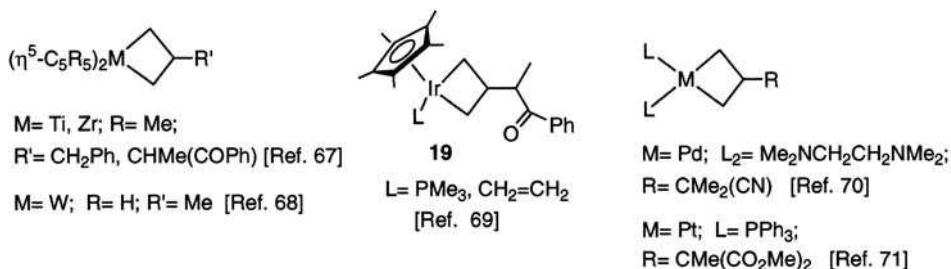
complexes. Factors affecting the site- and stereoselectivity in the nucleophilic attack will be discussed later. It should be pointed out here that the bond formation between the η^3 -allyl ligand and the nucleophile is more or less a reversible process, as was described in the corresponding reactions of carbonyl, alkene and alkyne ligands. It is this reversibility that has to be taken into account in explaining the selectivity of the overall reaction.

(a) *Site selectivity*

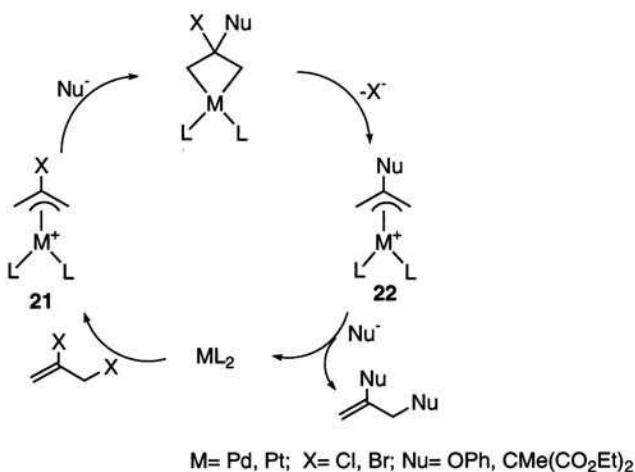
As shown in Scheme 8.40, there is no change of the formal metal oxidation state during the nucleophilic attack at the central carbon of the η^3 -allyl ligand, while the oxidation number of the metal is reduced by two as a result of the attack at the terminal carbon. The η^2 -alkene complex formation by the terminal attack has actually been confirmed in the reaction of η^3 -allyl complexes of middle transition metals having 18-electron configuration such as $[(\eta^5\text{-C}_5\text{H}_5)(\text{NO})(\text{CO})\text{Mo}(\eta^3\text{-allyl})]^+$ and $[(\eta^5\text{-C}_5\text{H}_5)(\text{NO})(\text{PPh}_3)\text{Re}(\eta^3\text{-allyl})]^{2+}$ [63,64], but not so often until recently in the reaction of Pd complexes which model key intermediates in catalytic allylic substitution reaction. The reaction of analogous Pt complex gave η^2 -alkene complex of Pt(0), $\text{Pt}\{\eta^2\text{-CH}_2=\text{CHCH}_2\text{CH}(\text{COMe})_2\}(\text{PPh}_3)_2$ stable enough to be detected by ^1H NMR spectroscopy [65]. Recently the detailed structure analysis of an analogous η^2 -alkene complex of Pd(0) has been made [66] in order to shed light on the origin of the highly enantioselective catalytic allylic alkylation (see later). Under the catalytic reaction condition, the alkene ligand made by the bond formation between allyl and nucleophile is then replaced by substrates such as allyl acetate to form a new alkene–Pd(0) complex, which is ready to undergo oxidative addition, or dissociation of the leaving group, regenerating the η^3 -allyl complex of Pd(II).

As is predicted by the Davies–Green–Mingos rule (see 8.2), the nucleophilic attack at the central carbon may occur in the reaction of η^3 -allyl ligand attached to a metal fragment which is not so electron-deficient in nature. Well-characterized, representative metallacyclobutane complexes formed by the central attack are shown in Scheme 8.42. Note that an Ir complex containing both alkene and allyl ligands underwent predominant attack at the allyl ligand to give **19** ($\text{L} = \text{CH}_2=\text{CH}_2$). Moreover, the irridacycle **20** in Eq. 8.12 obtained from the reaction of cyclohexanone enolate isomerized to η^2 -alkene complex via the reverse of the central attack and the eventual terminal attack [69].





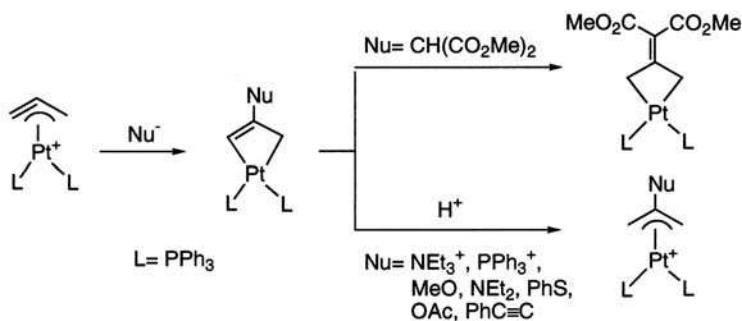
Scheme 8.42.



Scheme 8.43.

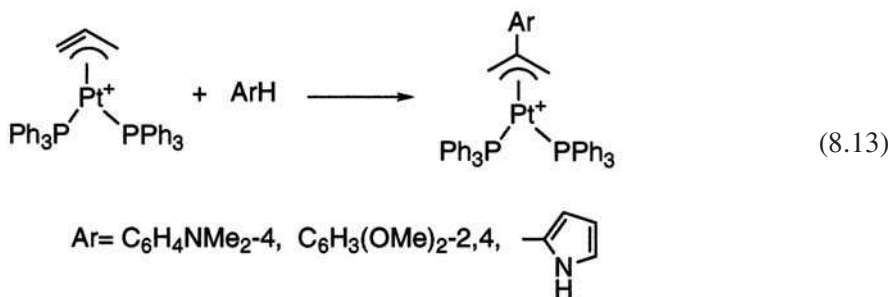
Facile reductive elimination of palladacyclobutane complex allowed cyclopropane synthesis (Scheme 8.40, path A) both in catalytic [61] and stoichiometric [72] transformations. Also, when the central carbon bore a substituent with high leaving ability as in **21** of Scheme 8.43, nucleophilic substitution at this carbon occurred with considerable ease so as to maintain the metal- η^3 -allyl bonding framework to give **22** [73]. The new η^3 -allyl complex **22** then underwent the attack of the second nucleophile at the terminal carbon to complete one cycle of the catalysis for double substitution of allylic compounds.

Compared to the η^3 -allyl complexes of Pd(II) and Pt(II), the η^3 -propargyl analogs were much more prone to accept the central attack of the nucleophile [74]. A metallacyclobutene complex formed then underwent either 1,3-hydrogen shift to give trimethylenemethane complex or further addition of proton to give substituted η^3 -allyl complexes (Scheme 8.44). The central carbon of η^3 -propargyl complex of Pt was more reactive to nucleophile than that of Pd [75]. This order of the reactivity at central carbon (Pt > Pd) is the same as that of the stability

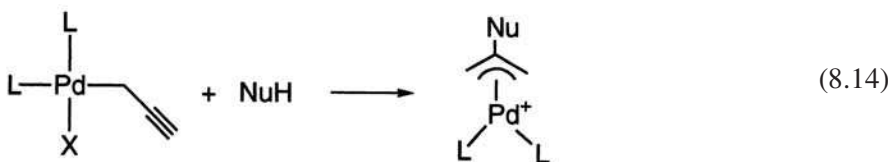


Scheme 8.44.

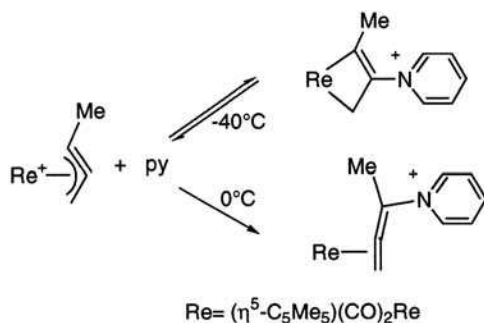
of the σ -alkyl complex of M(II) to which the metallacyclobutane belong [76a]. The very high electrophilicity of the Pt complex can also be illustrated by the aromatic substitution reaction shown in Eq. 8.13 [77]. It should be noted that the nucleophilic attack at the allyl terminus, which gave M(0) complex, occurred more easily for Pd complex than Pt complex [76b].



The central attack at η^3 -propargyl complexes of Pd may also have relevance to a reaction sequence involved in Pd catalyzed transformations of propargylic electrophiles [78]. Although initial reports proposed direct reaction of η^1 -propargyl complex of Pd with nucleophile (Eq. 8.14), participation of η^3 -counterpart appears more plausible in view of general trend of the reactivity of η^1 - and η^3 -types of complexes involving both propargyl and allyl ligands.



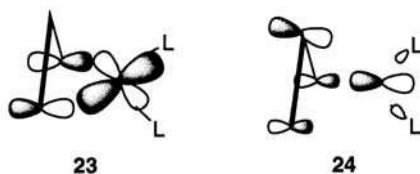
In many of the reported examples of nucleophilic attack at η^3 -allyl and -propargyl complexes, some ambiguity remained as to whether the observed site of the attack was a kinetic or thermodynamic origin. In several cases clear



Scheme 8.45.

evidence was available which indicated kinetic preference of the central attack, as exemplified by Eq. 8.12. Similarly, cationic η^3 -propargyl complexes of Re underwent attack of amines, phosphines and carbanions to give rhenacyclobutenes as a kinetic product, and η^2 -allene or η^2 -alkyne complexes as a thermodynamic product (e.g. Scheme 8.45) [79].

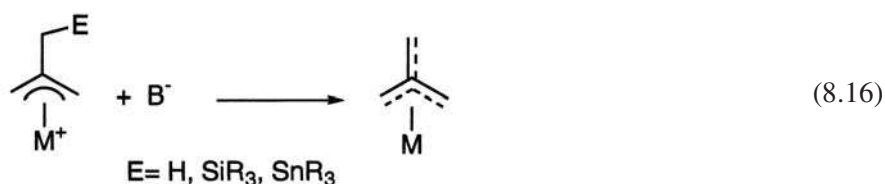
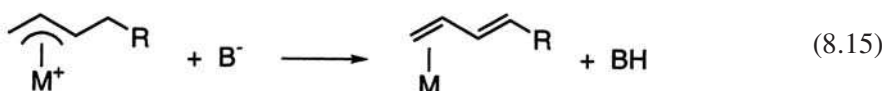
Molecular orbital calculations of η^3 -allyl and η^3 -propargyl anions coordinated with several metal fragments including PdCl_2 , $[\text{PdL}_2]^{2+}$ ($\text{L} = \text{PH}_3, \text{NH}_3$), and $[\text{Pt}(\text{PH}_3)_2]^{2+}$, suggested that the central carbon bears the greater positive charge than the terminal carbons irrespective of the nature of the metal fragment [80]. The observed preference of the central attack in the reaction of the η^3 -propargyl and some of η^3 -allyl complexes appears to be ascribable to a charge-controlled mechanism. It is not certain whether most of the reports describing the terminal attack in the reactions of the η^3 -allyl complexes have arisen from kinetic control. However, if this were the case, then the terminal attack must be due to frontier orbital control, since LUMO of η^3 -allyl complexes including $[\text{Pd}(\eta^3\text{-allyl})(\text{PH}_3)_2]^+$ consists of an anti-bonding combination of metal $d\pi$ and allyl $n\pi$ orbitals bearing big lobes at the terminal carbons but no contribution of the central carbon (Scheme 8.46, **23**) [80a]. However, the recent calculation showed [80c] that if PH_3 of the Pd complex was substituted by NH_3 , a less acidic and more donating ligand than PH_3 , LUMO was no more the $d\pi$ - $n\pi$ anti-bonding combination like **23** but a different MO (**24**), namely an anti-bonding combination of a p orbital of Pd and π^* MO of the allyl ligand. This new LUMO possessed the big lobe at the central



Scheme 8.46.

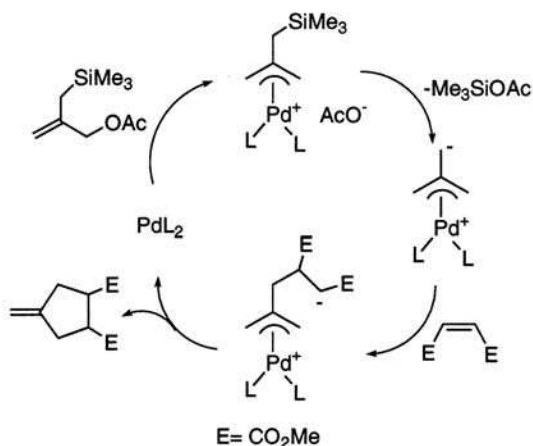
carbon, consistent with the fact that the nucleophilic substitution for chloride at the central carbon in $[\text{Pd}(\eta^3\text{-CH}_2\text{CClCH}_2)\text{L}_2]^+$ was easier in the case of $\text{L}_2 = \text{tetramethylethylenediamine}$ or $\text{L} = \text{pyridine}$ than $\text{L} = \text{PR}_3$ [73b].

Some η^3 -allyl complexes have two other sites which are attacked by nucleophiles; deprotonation or demetallation takes place at the α -carbon of substituent attached to either terminal or central allyl carbon, as shown in Eqs. 8.15 and 8.16. If B^- in Eq. 8.15 is a leaving group of allylic substrates such as allyl acetate and carbonate, the overall transformation is diene synthesis under mild condition [3]. Eq. 8.16 is also very useful in synthetic application such as [2 + 3] cycloaddition using $\text{CH}_2=\text{C}(\text{CH}_2\text{SiMe}_3)\text{CH}_2\text{OAc}$ as a trimethylenemethane precursor (Scheme 8.47) [81].



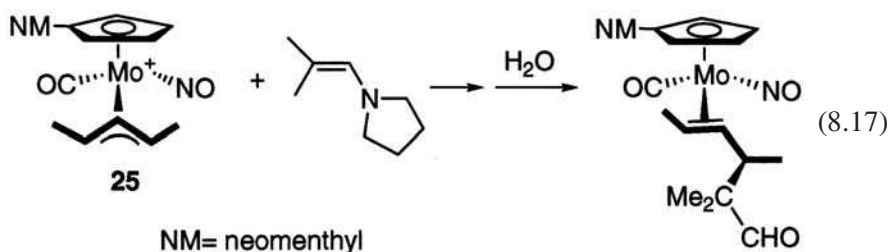
(b) Stereochemistry

In the reaction of most 18-electron η^3 -allyl complexes, the nucleophile approaches the η^3 -allyl ligand directly from the side opposite to the metal with



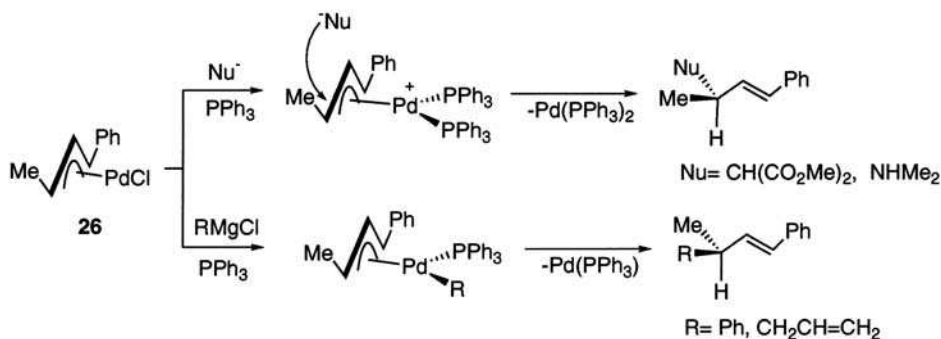
Scheme 8.47.

respect to the allyl plane, as is demonstrated by reaction of optically active complex **25** in Eq. 8.17 [82]. In Eq. 8.17 the nucleophilic attack was highly regioselective, too, as will be explained in more detail later, so that the coupling product was obtained in an almost enantioselective form. The same external attack of nucleophile occurred in the reaction of 16-electron η^3 -allyl complexes of Pd with a majority of nucleophiles such as stabilized carbanion and amine. On the other hand, some nucleophiles such as vinyl and phenyl anions attacked the Pd atom of coordinative unsaturation to form organo(η^3 -allyl)palladium intermediate, which subsequently underwent reductive elimination to give the allyl–nucleophile coupling product. The stereochemical duality of the reaction of the Pd complex was clearly demonstrated by the use of optically active complex **26** in Scheme 8.48 [83].

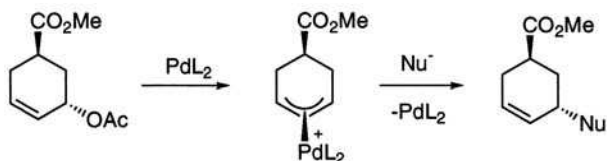


The external attack at the η^3 -allyl ligand has a very important implication in the stereochemical outcome of the catalytic allylic substitution. Since the allylic substrate (e.g. acetate, carbonate) and Pd(0) generate η^3 -allyl intermediate with inversion of configuration at the sp^3 carbon which bears leaving group, subsequent external nucleophilic attack makes the overall nucleophilic substitution a stereoretentive process (e.g. Scheme 8.49) [84].

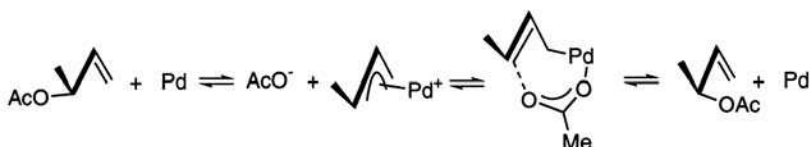
It seems somewhat puzzling to trace the recent remarkable success in attaining highly enantioselective Pd-catalyzed allylic substitution to the external nucleophilic attack as a key step. In other words, it appears a difficult task to control



Scheme 8.48.



Scheme 8.49.

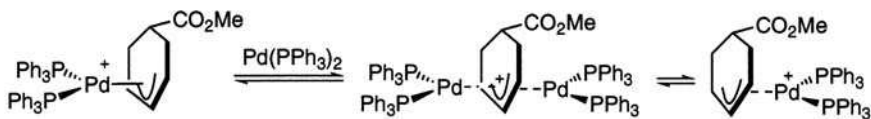


Scheme 8.50.

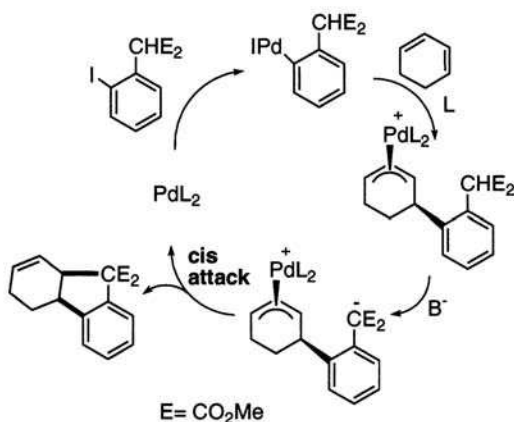
a stereochemistry of the bond formation taking place outside the coordination sphere distant from the chiral center of auxiliaries. How a such apparently difficult goal has been reached will be explained in a later section.

The degree of stereospecificity in the catalyzed substitution may be lowered by some mechanisms. For example, OAc^- anion, generated by oxidative addition of allylic acetate with inversion, is able to regenerate the allylic acetate with retention via C–O coupling on the coordination sphere as shown in Scheme 8.50 [85]. This may induce racemization or epimerization of the substrate (allylic acetate). Another mechanism affects the stereochemical outcome. That is, a $\text{Pd}(0)$ complex, which was supposed to exist during the catalysis, was demonstrated to play a role of a nucleophile undergoing the external attack at the η^3 -allylpalladium intermediate (Scheme 8.51) [86]. The net result of the attack was the transfer of the η^3 -allyl ligand with inversion of configuration between two Pd atoms, decreasing the stereospecificity of the overall allylic substitution. This mechanism might have some bearing with the origin of much improved degree of stereochemical retention in the nucleophilic substitution shown in Scheme 8.49 if a polymer-supported Pd catalyst having anchored PPh_2 donor was used instead of a soluble $\text{Pd}(\text{PPh}_3)_4$ [84]. Compared to the catalysis proceeding in a purely homogeneous solution phase, a chance of loss of stereochemical identity via Scheme 8.51 might be suppressed with the use of the supported catalyst working at a solid–solution boundary.

Under certain specific conditions, stabilized carbanions and heteroatom-based

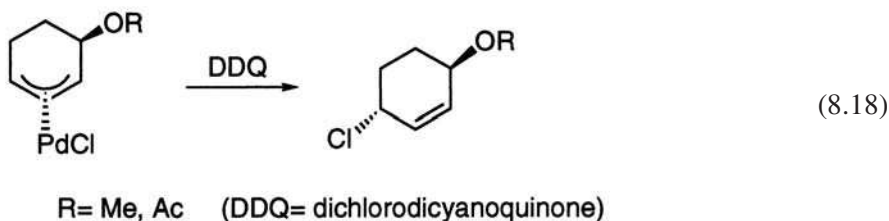


Scheme 8.51.

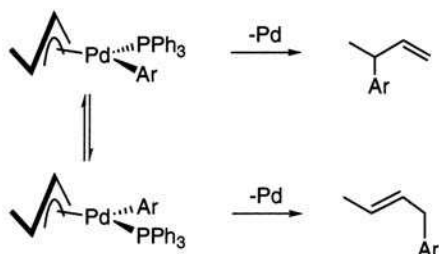


Scheme 8.52.

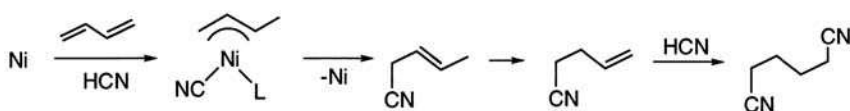
nucleophiles can undergo bond formation with η^3 -allylic group with retention of configuration at the allyl carbon. For example, the occurrence of internal attack of the stabilized carbanion has been postulated to explain the *cis* ring fusion in Pd-catalyzed carboannulation of cyclohexadiene by dimethyl-2-iodophenyl malonate (Scheme 8.52) [87]. Also, as already shown in Scheme 8.50, the OAc ligand was suggested to couple with an allyl ligand bound to Pd in the η^1 -fashion. The chloride anion was also shown to couple with the allyl entity with retention (Eq. 8.18) [88]. In this respect it should be noted that the oxidative addition, the microscopic reverse of the reductive elimination, of allylic halide and carboxylate occurred with unusual retention of stereochemistry under a condition similar to that employed in Eq. 8.18, i.e. in the presence of electron-withdrawing alkene ligands [89,90].



Mechanistic studies on the reductive elimination of square-planar type aryl(η^3 -allyl)palladium complexes demonstrated occurrence of bond formation between the aryl carbon and one of the allyl termini that are located *cis* to each other (Scheme 8.53) [91]. The allyl ligand remained η^3 -coordinated during the coupling. Similar reductive elimination between η^3 -allyl and cyano ligands may be a key step in the industrially important nickel catalyzed hydrocyanation of dienes (Scheme 8.54) [92].



Scheme 8.53.



Scheme 8.54.



Scheme 8.55.

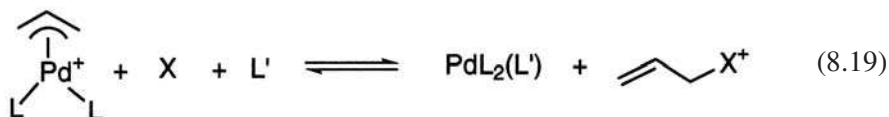
(c) Reversibility of nucleophilic attack

Some theoretical calculations suggested that η^3 -allyl complex was continuously converted to an η^2 -alkene complex as the nucleophile was brought closer to the terminal carbon up to the bonding distance from the backside of the allyl plane (Scheme 8.55) [80a,93]. The profile of the oxidative addition step of allylic electrophile can be traced along the microscopic reverse of the above-mentioned nucleophilic attack. In other words, the initial key step of the oxidative addition may well be assumed to be η^2 -alkene–metal bond formation as in **27** of Scheme 8.55 where Nu may be read as a leaving group such as Cl and OAc. The π -complex formation could then be followed by intramolecular S_N2 path with M–C bond formation and C–X bond rupture with inversion of configuration. Although the importance of such initial η^2 -alkene complex formation in the oxidative addition has been pointed out from the early stage of the development of organometallic chemistry [94], only a limited number of experimental results have been reported which substantiated initial formation of **27**, particularly in reactions of catalytically significant Pd complexes.

Kinetic studies on oxidative allyl transfer from allylammonium ion to Pd implicated transient formation of **27** (Nu = NEt_3^+ with α -diimine ligand) prior

to C–N bond cleavage [95]. Monitoring oxidative addition of allyl acetate with Pd(diphos) species by means of conductivity and UV measurements also provided evidence for transient formation of η^2 -allyl acetate complex of Pd(0) prior to the oxidative addition [96]. Other kinetic evidence has been presented which suggested occurrence of η^2 -alkyne complex formation prior to the oxidative addition of propargyl halides $\text{PhC}\equiv\text{CCH}_2\text{X}$ with $\text{Pt}(\text{PPh}_3)_n$ ($n = 2, 3$) [97]. The most convincing evidence obtained in this study included the overall rate of the oxidative addition with $\text{Pt}(\text{PPh}_3)_2$ being comparable to the rate of η^2 -alkyne complex formation between $\text{Pt}(\text{PPh}_3)_2$ and $\text{PhC}\equiv\text{CMe}$. Moreover, the rate of the overall oxidative addition was insensitive to the nature of the halogen atom of the substrate (Cl, Br), an unusual aspect if the rate-determining step involved the C–halogen bond cleavage.

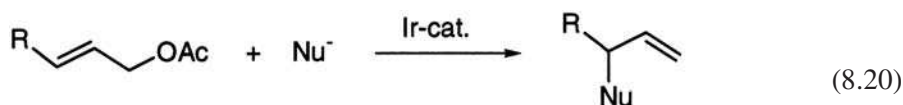
Reversibility of the nucleophilic attack at the η^3 -allylpalladium complexes has been examined in the case where carboxylates and amines were used as nucleophiles. It was shown that η^3 -allylpalladium cation and OAc^- ion are in equilibrium with Pd(0) complex and allyl acetate as shown in Eq. 8.19 ($\text{X} = \text{OAc}^-$), with the equilibrium constant depending on the nature of the auxiliary ligand [96,98,99]. For example, when $\text{L} = \text{L}' = \text{PPh}_3$ the equilibrium lies far to the right, and no apparent reaction occurred between allyl acetate and $\text{Pd}(\text{PPh}_3)_4$ except for deuterium scrambling between $\text{CD}_2=\text{CHCH}_2\text{OAc}$ and $\text{CH}_2=\text{CHCD}_2\text{OAc}$. This suggested only transient formation of an η^3 -allylpalladium species. On the other hand, the analogous reaction using $\text{Pd}(\text{dba})(\text{PPh}_3)_2$ and allyl acetate gave evidence for more abundant existence of the η^3 -allyl cation. The use of chelate diphosphines such as dppf and dppb, instead of PPh_3 , shifted the equilibrium further to the cationic η^3 -allyl side.



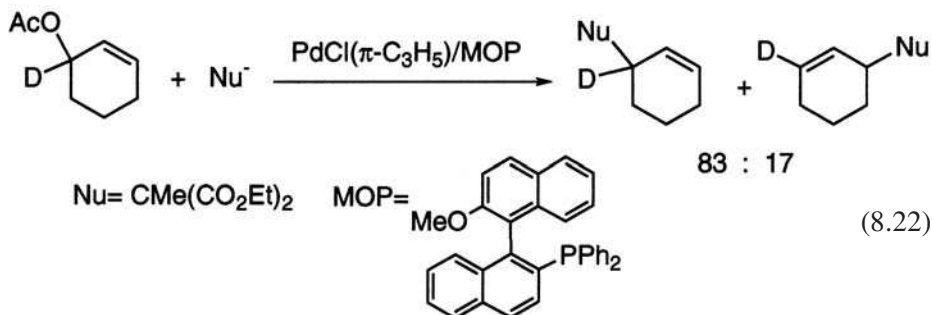
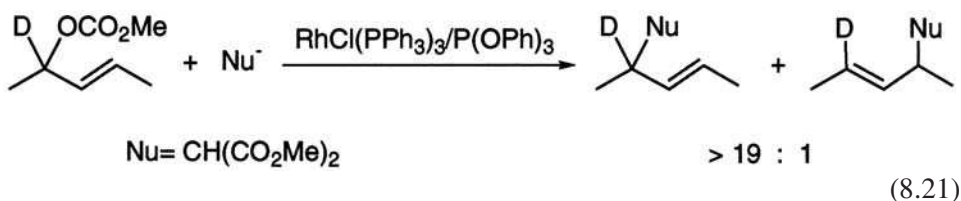
Amination of the allyl ligand in cationic η^3 -allylpalladium complexes was also shown to be a reversible reaction (Eq. 8.19, $\text{X} = \text{NEt}_3$, NHET_2 , py; $\text{L}_2 = \alpha$ -diimine, iminophosphine) [100]. Thus, addition of amine to the η^3 -allyl complex in the presence of excess free alkene, e.g. fumaronitrile and dimethyl fumarate, afforded allylamine or allylammonium cation and Pd(0) complexes of the added activated alkene. The rate of the attack of the amine at the η^3 -allyl ligand increased with increasing basicity of the amine (pyridine < Et_3N ; morpholine < piperidine). The steric effect also played a role in decreasing the rate constant (allyl = CH_2CHCH_2 > $\text{CH}_2\text{CMeCH}_2$; amine = piperidine > Et_2NH). The concentration of the added activated alkene did not affect the rate, suggesting no participation of the alkene in the rate-determining step. Therefore, the primary role of the added alkene may have been to prevent the Pd(0) species from going back to the oxidative addition product.

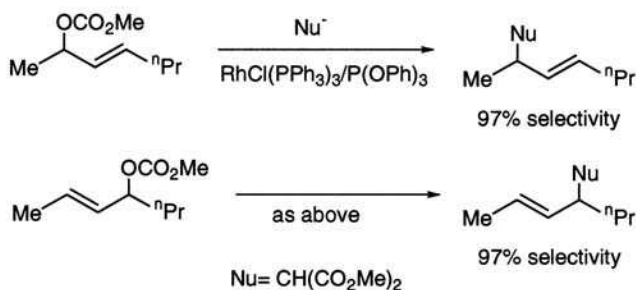
(d) Regioselectivity of terminal attack

Regiochemical control of metal-catalyzed allylic substitution of allylic electrophiles having an unsymmetrical allylic substructure has been a challenging issue for many years. Pd-catalyzed reactions tend to give products of the attack at the less substituted allyl terminus except for a limited number of examples. Recently, a catalyst from precursor $[\text{Ir}(\text{cod})\text{Cl}]_2$ and $\text{P}(\text{OPh})_3$ gave products of alkylation of *E*-2-alkenyl acetates at the more substituted allyl terminus with higher than 90% selectivity (e.g. Eq. 8.20) [101]. Of particular note here is the fact that the alkylation with *Z*-2-alkenyl analogs resulted in the dramatic change of the regioselectivity to a predominant attack at the less substituted terminus. Efficient construction of a quaternary carbon center was also realized using $\text{Me}_2\text{C}=\text{CHCH}_2\text{OAc}$ with the same catalyst system.

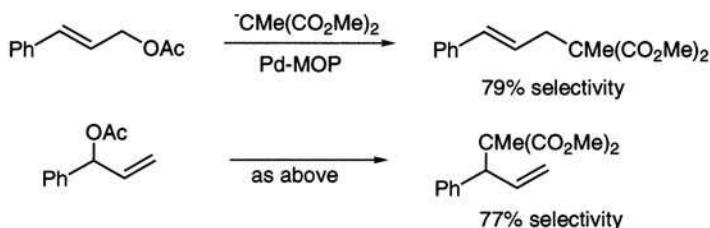


Another intriguing issue in the regiochemistry of allylic substitution is a reaction with a memory effect. This is a reaction in which the nucleophilic attack takes place preferentially at the allyl terminus which originates from the sp^3 carbon, i.e. one bearing the leaving group (a net $\text{S}_{\text{N}}2$ reaction). It is rather astonishing that an $\text{S}_{\text{N}}2'$ reaction is rarely attained even when the substrate is assumed to lead to an intermediate having symmetrically substituted allyl ligand such as 1,3-dimethylallyl and 2-cyclopentenyl. For example, as shown in Eqs. 8.21 and 8.22, reaction of deuterium labeled substrates by the use of Rh or Pd catalyst resulted in high $\text{S}_{\text{N}}2$ selectivity [102,103].





Scheme 8.56.

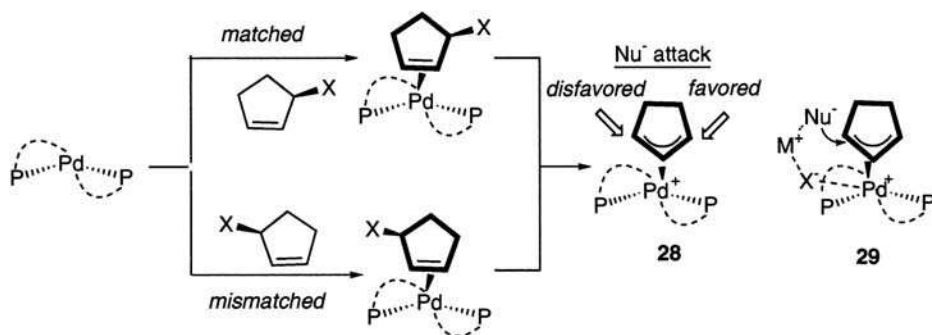


Scheme 8.57.

These catalysts also facilitated remarkable $\text{S}_{\text{N}}2$ reaction of unsymmetrical allylic substrates, as shown in Schemes 8.56 and 8.57 [102,103].

It is not certain whether an intermediate of the reaction exhibiting high memory effect contains an η^3 - or η^1 -allyl ligand. If it were an η^1 -allyl complex, its dynamic 1,3-interconversion, if any, must be slower than the attack of nucleophile specifically at either sp^3 carbon or terminal sp^2 carbon. If it were an η^3 -allyl complex, some unique coordination environment must be at work to provide one allyl terminus originating from the sp^3 carbon with the higher reactivity than the other terminus. In order to explain the MOP-Pd-catalyzed nucleophilic substitution showing the high memory effect shown in Eq. 8.22 and Scheme 8.57, it was postulated that upon η^3 -allyl intermediate formation the original sp^3 carbon becomes the allyl terminus located *trans* to P donor of MOP, while the other terminus is *trans* to Cl. Moreover, the higher *trans* labilizing effect of P was suggested to provide the allyl terminus *trans* to P the greater susceptibility to the nucleophilic attack [103,104].

In the analogous substitution reaction of chiral 2-cyclopentenyl derivatives by the use of Pd-catalyst bearing C_2 -symmetric chelate diphosphine ligand, the degree of the regiochemical memory effect was found to differ according to the absolute configuration of the substrate [105]. As shown in Scheme 8.58, there are configurationally matched and mismatched combinations between C_2 -symmetric Pd(0) moiety and the chiral allyl substrate.



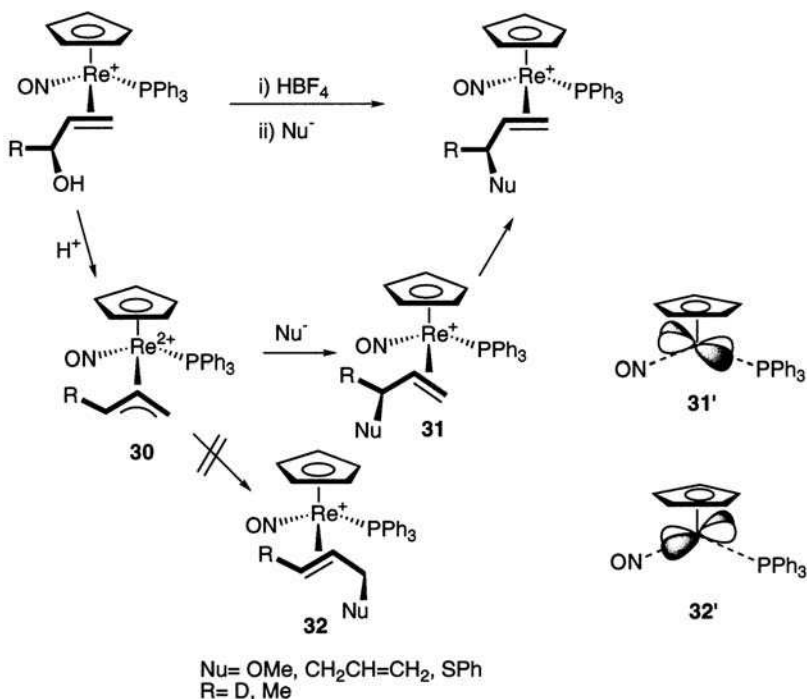
Scheme 8.58.

The stability of η^2 -alkene intermediate in the matched combination would be higher than that in the mismatched one, making the oxidative addition more facile in the former case. The microscopic reversibility principle predicts that among two allyl termini in **28** one originating from the sp^3 carbon in the matched enantiomer of the substrate would be more reactive with nucleophile than the other. So the matched substrate would undergo smoother oxidative addition to afford intermediate **28**, which places the original sp^3 carbon at the more reactive site with respect to the nucleophilic attack, leading to preference of overall S_N2 reaction. In the reaction of the mismatched substrate, the original sp^3 carbon becomes the less reactive allyl terminus of the intermediate **28**, leading to the decrease in the degree of the regiochemical memory effect.

Other explanations for the memory effect have been presented, especially for the reaction of the mismatched combination. One possibility is the occurrence of asymmetrically structured intimate ion pair such as **29** [106]. It was proposed that in this intermediate the leaving group X^- lies at the side proximate to the allyl terminus from which X^- has left. Moreover, electrostatic interactions between X^- , M^+ (counter cation of Nu^-) and Nu^- would direct Nu^- to this particular allylic terminus, as shown in **29**. Yet another explanation was proposed which involved dissociation of one of the two P atoms during the formation of η^3 -allyl intermediate [105].

Though not involved in catalytic systems, a clear case of illustrating the importance of ligand asymmetry in controlling the regioselectivity of the nucleophilic attack appears worth mentioning. Thus, when treated with HBf_4 first and nucleophile second, η^2 -allyl alcohol complex of a half-sandwich Re fragment containing NO and PPh_3 ligands underwent S_N2 reaction with complete retention of configuration (Scheme 8.59) [64]. The first step of the transformation would be protonation of alcoholic OH, followed by oxidation of Re with dehydration to give *exo* η^3 -allyl intermediate **30**.

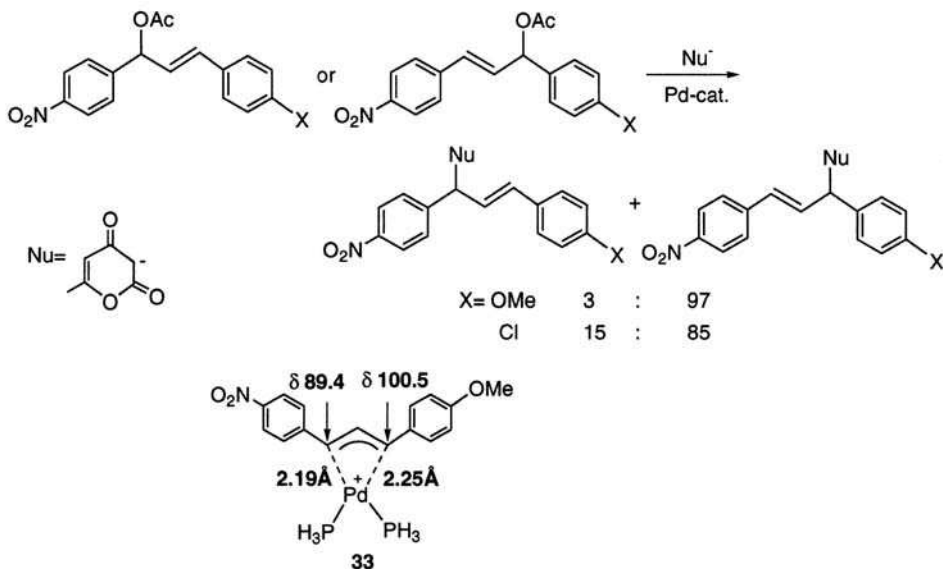
The electronic asymmetry key to the regioselective nucleophilic attack arises from different π -acidity of two ligands, e.g. NO and PPh_3 in **30**, or NO and CO in



Scheme 8.59.

25 of Eq. 8.17 [107]. Upon nucleophilic attack, the η^3 -allyl complex **30** may give two intermediates **31** and **32** depending on the site of the nucleophilic attack. Here **31** is believed to be more stable than **32** for the following reason. In the fragment $\text{M}(\eta^5\text{-C}_5\text{H}_5)(\text{NO})(\text{PPh}_3)$, two $d\pi$ orbitals **31'** and **32'**, orthogonal to each other, are available to have back-donation interaction with π^* of alkene [107a]. Of the two, **32'** capable of overlapping with π^* of the more acidic ligand (NO) is positioned at the lower level than **31'**, destabilizing complex **32** having alkene ligand lying parallel with M–NO. The molecular orbital calculations also suggested that the ligand electronic asymmetry could be transferred to the ground state electronic asymmetry of the η^3 -allyl ligand [107a]. That is, the more reactive allyl terminus (*cis* to NO in **30**) bears the lower electron density and the greater orbital coefficient of LUMO than the other terminus. For the same reason, the allyl terminus *cis* to NO of **25** is more reactive than the other.

Some efforts have been made to understand factors that control the regioselectivity of the Pd-catalyzed allylic substitution, but a delicate superposition of electronic and steric effects of the auxiliary ligand on those of the η^3 -allyl ligand prevents deduction of a general rule for predicting the regioselectivity. On the rough electronic grounds, the attack may be favorable at the terminus bearing substituent(s) (e.g. alkyl, alkoxy) capable of stabilizing the carbonium ion character of this terminus, while the steric hindrance may oppose such an attack.



Scheme 8.60.

An estimation of considerably pure electronic effect of the substituent on the allyl terminus has been made by the Pd-catalyzed alkylation of 1,3-diaryllallyl acetates proceeding through a cationic intermediate $[\text{Pd}\{\eta^3\text{-(4-XC}_6\text{H}_4\text{)CHCHCH(C}_6\text{H}_4\text{NO}_2\text{-4)}\}(\text{PPh}_3)_2]^+$ ($\text{X} = \text{Cl}$ or OMe) [108]. The nucleophilic attack occurred more easily at the carbon bearing the more donating substituent as shown in Scheme 8.60. The more donating substituent was supposed to stabilize more efficiently the carbonium ion character of the terminus to which this substituent is attached. In alternative expression, the terminal carbon with the more withdrawing group would make a stronger bond with Pd. These trends are also reflected in the ^{13}C resonance and Pd–C length. As exemplified in **33** of Scheme 8.60, the terminus bearing the more withdrawing group showed the higher field ^{13}C shift and the shorter Pd–C distance, the latter having been deduced by the DFT calculation [109]. The calculated model reaction between NH_3 and $[\text{Pd}(\eta^3\text{-ArCHCHCHAr}')(\text{PH}_3)_2]^+$ reproduced the preferred attack at the terminus bearing the more donating group. The calculation also suggested that the electronic effect of the substituent appeared at work especially in the transition state, presumably pointing to the involvement of a late transition state of the nucleophilic attack. The issue of an early and a late transition state will be discussed again in the next section.

The correlation between the ^{13}C chemical shift and the preferred site of the nucleophilic attack has also been examined as a function of the nature of auxiliary ligands [110a,b]. Thus, 1,1-dimethylallyl complexes of Pd $[\text{Pd}(\eta^3\text{-Me}_2\text{CCHCH}_2)(\text{L})(\text{L}')]^+$ ligated by more π -acidic phosphines and phosphites

showed the less deshielded ^{13}C shift and the higher reactivity to diethyl methylmalonate anion for the tertiary carbon than the analogous complexes ligated by more donating N-ligands (e.g. TMEDA, pyridine). However, a clearer picture on the analogous correlation for a wider range of ligands and substrates appeared less easy to draw.

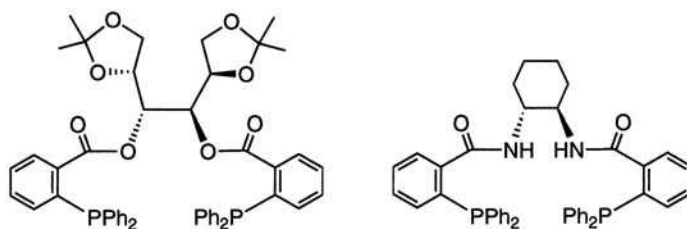
In a series of η^3 -1,1-dimethylallyl complexes of Pd coordinated by diphosphine chelates, attack of malonate anion took place more preferentially at the tertiary carbon as the bite angle of the diphosphine increased; e.g. 8% for dppe and 61% for 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene [110c]. This was attributed to the greater distortion in the coordination mode of the allyl ligand in such a way as to elongate the bond between Pd and the tertiary carbon. Pd-catalyzed reaction of allylic acetates with nucleophiles proceeded through cationic η^3 -allyl intermediates in which one allyl terminus closer to the Si substituent is bound to Pd more weakly than the other terminus, leading to the nucleophilic attack at the former allyl terminus (Eq. 8.23) [110d]. Intramolecular pyridine coordination was shown by an X-ray study to be a cause of such distortion of the allyl coordination.



(e) *Enantioselective allyl coupling*

Unlike some other metal-catalyzed asymmetric transformations such as hydrogenation and oxidation of alkenes, catalytic asymmetric allyl substitution involves the bond-making stage (nucleophilic attack) outside the coordination sphere, distant from the chiral center of auxiliary ligands. In spite of such apparent disadvantageous aspect, progress in Pd-catalyzed enantioselective allyl substitution was very remarkable in recent years, owing to deep understanding of mechanistic features of both catalytic and stoichiometric transformations involving η^3 -allylpalladium complexes. Illustrated below are some unique approaches to the reaction with high enantioselectivity.

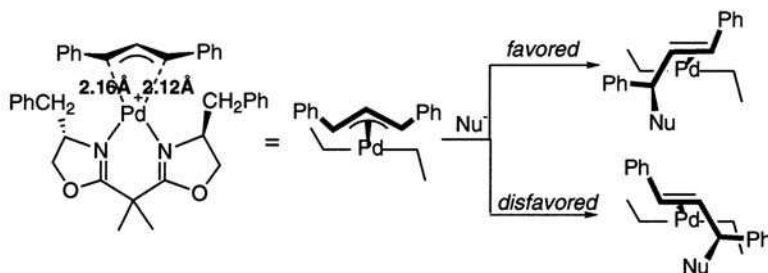
A class of substrates giving an intermediate complex having a symmetrical allyl substructure has been investigated extensively, perhaps owing to conceptual simpleness with regard to the enantio-determining step. The simplest type of intermediate is derived from a reaction of substrates containing the symmetrical allyl substructure using a catalyst having a ligand of C_2 -symmetry. As already shown in **28** of Scheme 8.58, only one isomer is possible for the intermediate except for the intimate ion pair. Provided that both substrate enantiomers lead to **28** efficiently, enantioselectivity of the overall nucleophilic substitution is reduced to the degree of regioselectivity of the nucleophilic attack in **28**. Early stage work along



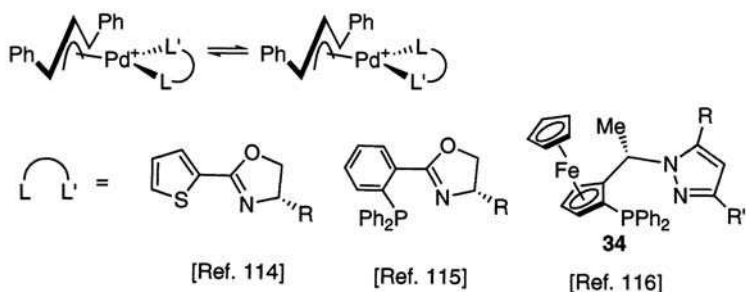
Scheme 8.61.

this strategy employed common C_2 -symmetric diphosphines such as DIOP and BINAP, with modest enantioselectivity having been achieved [111]. More recent efforts employed C_2 -symmetric diphosphines made from a chiral linker containing bifunctional group (e.g. OH, NH_2 , COOH) to which two diphenylphosphino units are bonded (Scheme 8.61), aiming at large ring size chelates (13-membered) with an increased P–Pd–P bite angle [112]. This increase of the bite angle would be expected to create more efficiently working chiral space near the reaction center both at the stage of oxidative addition and nucleophilic attack. By using this strategic tool, highly selective asymmetric substitution of cyclic substrates, e.g. cyclopentenyl analogs, has been achieved. Other than the cyclic substrates giving intermediate with enantiotopic allylic termini, those substrates which bore enantiotopic leaving groups (e.g. meso-2-ene-1,4-diol diester) or those which led to unsymmetrically substituted allyl ligand (e.g. crotyl ester) also underwent highly efficient asymmetric transformations with the new diphosphine auxiliaries.

In addition to the diphosphines, C_2 -symmetric dinitrogen chelates such as bis(oxazoline) also showed remarkable ability to accomplish high enantioselection in allylic substitution [113]. The structural determination of the key intermediate shown in Scheme 8.62 allowed clear explanation of the origin of the high selectivity to be made. Thus, of the two phenyl substituents located syn to the allyl central hydrogen, one at the left side is severely interfered by the benzyl group on the oxazoline ring, making the corresponding Pd–C bond longer than the other



Scheme 8.62.



Scheme 8.63.

Pd–C bond by 0.04 Å. As a result of this lengthening, the left allylic terminus may have become more susceptible to the nucleophilic attack, and this notion was in full agreement with the actual attacking site deduced from the absolute configuration of the product. This kind of ground state activation of one allylic terminus toward nucleophilic attack plays a role in a reaction where the transition state is reached at a relatively early stage of the bond forming profile (early transition state). Alternatively, the difference in the stability of the products of nucleophilic attack, namely η^2 -alkene complexes of Pd(0) shown in Scheme 8.62, may become an important factor in the regioselectivity determination, especially in a reaction proceeding through the late transition state.

Remarkable success has also been seen in the asymmetric allyl coupling involving intermediates with symmetric allyl ligand but with an electronically unsymmetric ligand framework [111]. The two diastereoisomers can be envisaged for intermediates in these reactions as illustrated in Scheme 8.63 [114–116]. Note that even when the attack site is fixed, for example, at a terminus *trans* to the more labilizing ligand, there still remains a case where the different product enantiomer is formed depending on the diastereomeric identity of the intermediate. Therefore, it is essential to rigorously control relative stabilities and/or reactivities of these isomers, in addition to regioselectivity of the nucleophilic attack.

Some efforts have been made to keep stability and/or reactivity of the minor isomer as low as possible by careful design of ligand steric requirement. The important role of the chiral space created by the auxiliary ligand in achieving such thermodynamic and/or kinetic discrimination appears worth noting. Thus, a remarkable structural distortion of one intermediate candidate was elucidated by X-ray structure determination [116]. As shown in Fig. 8.3, the 1,3-diphenylallyl ligand of the major isomer in Scheme 8.63 where L–L' represents **34** (R = Ph, R' = Me) has rotated about the Pd–allyl axis from the ordinary position (the vector connecting two allyl termini being parallel with the coordination plane) to a point where the C–C bond *trans* to N was almost on the coordination plane. The terminus *trans* to P was necessarily out of the plane and located farther from Pd compared to the other terminus *trans* to N by 0.13 Å. The observed orientation of

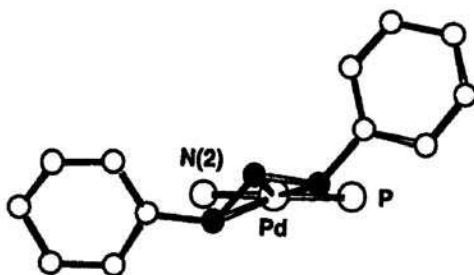
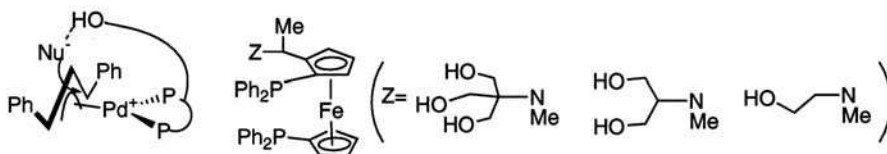


Fig. 8.3. Molecular structure of $[\text{Pd}(\eta^3\text{-PhCHCHCHPh})(\mathbf{34})]^+$ ($\text{R} = \text{Ph}$, $\text{R}' = \text{Me}$). Only donor atoms in the ligand are shown for clarity. Bond lengths ($\text{\AA}$): $\text{Pd-C}(\text{trans-to-N}) = 2.138(16)$; $\text{Pd-C}(\text{center}) = 2.173(16)$; $\text{Pd-C}(\text{trans-to-P}) = 2.268(13)$; $\text{Pd-N} = 2.131(11)$; $\text{Pd-P} = 2.321(4)$; $\text{C}(\text{trans-to-N})\text{-C}(\text{center}) = 1.436(22)$; $\text{C}(\text{trans-to-P})\text{-C}(\text{center}) = 1.380(23)$. Reproduced with permission from American Chemical Society.



Scheme 8.64.

one C–C bond of the η^3 -allyl framework was near to that of the C=C bond of η^2 -alkene complex formed by the nucleophilic attack at the terminus *trans* to P. Other examples of rotationally distorted η^3 -allyl complexes of Pd became available in recent years [117]. Fig. 8.3 corresponds to a kind of ground state deformation in the case of the early transition state reaction. An alternative explanation based on the late transition state condition was given [118]. That is, compared to the sterically matched combination of product alkene and Pd(0)-auxiliary system from the attack at the major isomer, the attack at carbon *trans* to P of the minor isomer would have led to sterically mismatched η^2 -alkene complex.

Another conceptually different approach to discriminating the nucleophilic attack at two allyl terminus of symmetrical η^3 -allyl intermediate was used earlier than those described above [119]. As shown in Scheme 8.64, a functional group capable of interacting with nucleophile was connected by a long tether to the one side of chiral diphosphines in order to bring the nucleophile close to only one allyl terminus. For example, chiral ferrocene diphosphines shown in Scheme 8.64 provided fairly high enantioselectivity in allylic alkylation.

8.2.5 Reaction of unsaturated ligands with carbon number larger than four

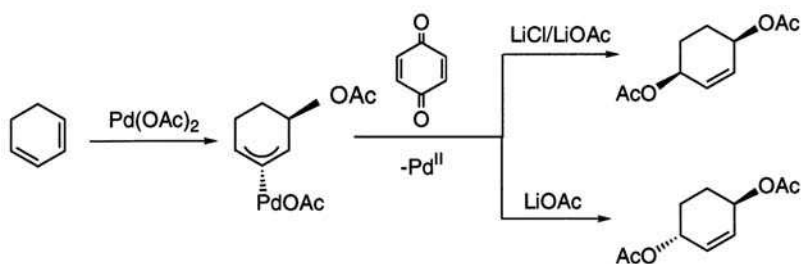
Various nucleophiles such as carbanions, aromatics, amines and phosphines attack metal-bound unsaturated ligands with the carbon number 4, 5 and 6 (cf.

Scheme 8.2) in a manner similar to those described in the reactions of alkene and allyl ligands. However, compared to the latter reactions, the former play a less important role in catalytic synthetic processes, though some stoichiometric reactions indeed represent a useful synthetic tool.

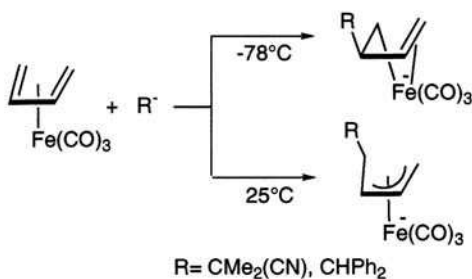
Extensive kinetic studies on reactions of phosphines and amines as nucleophiles with 18-electron complexes involving cyclobutadiene, pentadienyl, hexatriene, benzene and heptatrienyl ligands contributed to deeper understanding of the mechanism of the nucleophilic attack at these unsaturated complexes [120]. In general, the reaction was reversible, and the forward path obeyed simple first-order kinetics with respect to the concentration of each reactant. In the absence of steric effects, reactivity of almost every organometallic electrophile examined showed the common dependency on the nature of nucleophile, where the basicity of the nucleophile governed the reactivity order. Also notable was a conclusion deduced from the kinetic analysis that the transition state of the nucleophilic attack was reached rather early, the C–Nu bond formation being approximately one third complete in the transition state. The following are some synthetically important examples involving reactions at butadiene, pentadienyl and benzene ligands.

Among very rare examples of catalytic transformations involving polyene and polyenyl ligands is Pd-catalyzed oxidation of diene derivatives by the use of acetic acid and quinone with unique stereochemical control being achieved by judicious choice of the reaction condition (Scheme 8.65) [121]. Thus, the oxidation carried out with high Cl^- concentration afforded *cis* diacetate product, while *trans* adduct was obtained in the absence of Cl^- ion. The initial step of the catalytic cycle would be the *exo* attack of OAc^- at the Pd-bound diene, giving rise to η^3 -allyl intermediate with OAc and Pd positioned *trans* to each other. This then underwent either *exo* or *endo* attack of the second OAc^- in the presence or absence of Pd-bound Cl ligand, respectively. The *endo* attack may have proceeded in a manner similar to Scheme 8.50. The final step of the catalysis would be oxidation of $\text{Pd}(0)$, formed by the OAc^- attack at the η^3 -allyl terminus, with benzoquinone as an oxidant.

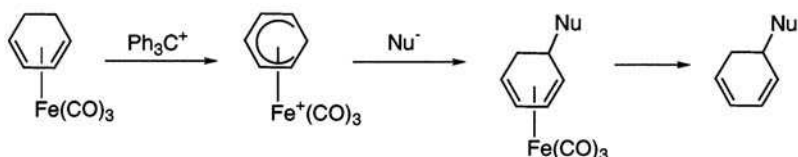
The Davies–Green–Mingos rule predicts that the attack at butadiene ligand should occur at the terminal carbon, as is consistent with the OAc^- attack at the



Scheme 8.65.



Scheme 8.66.

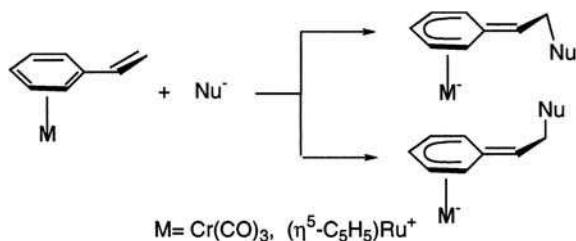


Scheme 8.67.

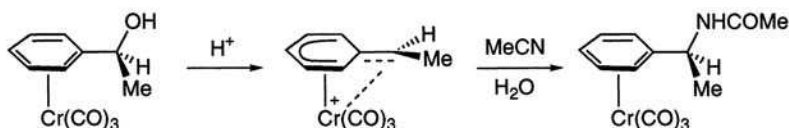
Pd-bound diene shown above. However, the kinetic product in the nucleophilic attack at $(\text{diene})\text{Fe}(\text{CO})_3$ was often due to the attack at internal carbon. Thus, for example, $(\eta^4\text{-CH}_2\text{CHCHCH}_2)\text{Fe}(\text{CO})_3$ reacted with a carbanion at -78°C to give 3-butenyl complex of Fe, which gradually isomerized at the higher temperatures to more stable η^3 -allyliron by terminal attack (Scheme 8.66) [122].

Cyclopentadienyl ligand, a very useful auxiliary in organometallic chemistry, reacts with nucleophiles, but finds a limited synthetic application. Open pentadienyl ligands are more useful for organic synthesis. As typically shown in Scheme 8.67, $\text{Fe}(\text{CO})_3$ -bound diene ligands having hydrogen atom at α -carbon can be converted to open pentadienyl ligands by abstraction of H^- group with Ph_3C^+ . The nucleophilic attack at the terminal carbon of the new ligand is possible since $\text{Fe}(\text{CO})_3^+$ is highly electron-withdrawing, affording substituted hexadiene derivatives [123].

η^6 -Arene ligands coordinated with cationic metal fragment can be attacked by nucleophiles. Even neutral arene complexes of $\text{Cr}(\text{CO})_3$ moiety reacted with anionic nucleophiles to give a transient anionic η^5 -cyclohexadienyl complex in which the negative charge can be delocalized over three CO ligands. The anionic intermediate may then be treated with oxidant such as I_2 to release substituted benzene derivative. The electron-withdrawing ability of $\text{Cr}(\text{CO})_3$ fragment also played a role in stabilizing an anion at aryl carbon generated by metallation. Benzylic anion may also be stabilized by arene-bound metal fragment. As shown in Scheme 8.68, stereochemistry of the nucleophilic attack at styrene derivatives coordinated with $\text{Cr}(\text{CO})_3$ or $\eta^5\text{-C}_5\text{H}_5\text{Ru}^+$ moiety was revealed to be both exo and endo [124].



Scheme 8.68.



Scheme 8.69.

Retention of configuration during nucleophilic substitution of benzylic compound that is η^6 -bound to Cr(CO)_3 , shown in Scheme 8.69, appears to deserve comment [125]. In contrast to stereochemistry of common $\text{S}_{\text{N}}2$ path, the reaction here proceeded with retention presumably because of metal-assisted $\text{S}_{\text{N}}1$ reaction with hindered rotation about the bond between α -carbon and phenyl carbon. The nucleophile (MeCN) then approached the benzylic carbon from the least congested side, which is the same as that on which the leaving group had originally resided. The overall reaction course resembles that encountered in the η^2 -allyl alcohol complex shown in Scheme 8.59. A very similar reaction path involving nucleophilic substitution with retention occurred at the α -carbon of substituted ferrocene derivative [126] as well as that of propargyl-metal complexes [5c,d].

8.3 ELECTROPHILIC ATTACK AT COORDINATED LIGAND

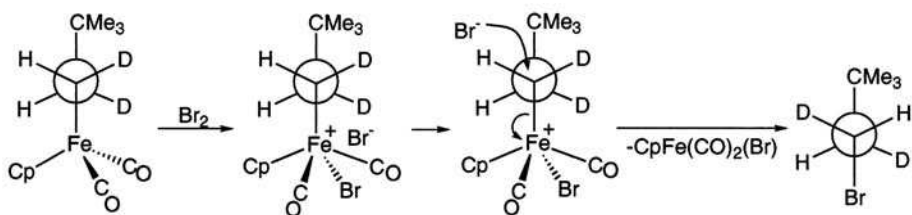
Electrophiles (E) such as H^+ and carbocations can modify organic ligands bound to metal in some ways. The most typical reaction is the cleavage of an M-R σ bond to release an R-E fragment. The electrophile can also add to unsaturated hydrocarbons, e.g. alkenes or alkynes, bound to metal to make new alkyl or alkenyl ligands. In some of these transformations the electrophile may directly approach the electron-rich carbon atom of ligands such as alkyl and alkene. In others, however, availability of relatively high-energy, filled metal d orbital tends to make the metal center a site of the initial electrophilic attack, leading to M-E bond formation (see Scheme 8.1, path B, $\text{S} = \text{E}$). The new ligand group E may

then be brought to reductive elimination with alkyl or alkenyl ligands (R) to form R–E, or migratory insertion with alkene or alkyne ligands to form substituted alkyl or alkenyl ligand. Clear distinction between path A and path B can not always be made without difficulty, as in the case of the nucleophilic attack discussed in 8.2.

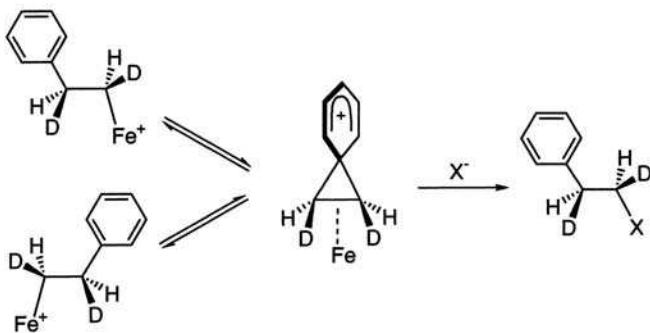
8.3.1 Reaction of alkyl, alkenyl alkynyl and carbene ligands

Stereochemistry of electrophilic substitution of alkylmetal complexes depends on the nature of the electrophile as well as the metal fragment to which the alkyl ligand is attached. Bromodemetalation of alkyliron complex with Br_2 was shown to proceed through inversion of configuration, as shown in Scheme 8.70 [29]. The initial step would be oxidation of Fe with Br^+ , which was followed by $\text{S}_\text{N}2$ cleavage of the Fe–C bond in a manner similar to the reverse of Scheme 8.18. If the phenethyl group, PhCHDCHD or $\text{PhCH}_2^{13}\text{CH}_2$ was used as a stereochemical probe, neighboring group participation by Ph appeared to intervene in the oxidized intermediate to induce both exchange between α - and β -carbons and overall retention of configuration for halogenolysis (Scheme 8.71) [127].

Halogenolysis of alkyl complexes of d^0 or d^{10} metals, e.g. Zr(IV) or Hg(II), did not involve the initial oxidation of the metal atom but proceeded via the direct, front-side attack at the M–C bond ($\text{S}_\text{E}2$) with retention of configuration [128].

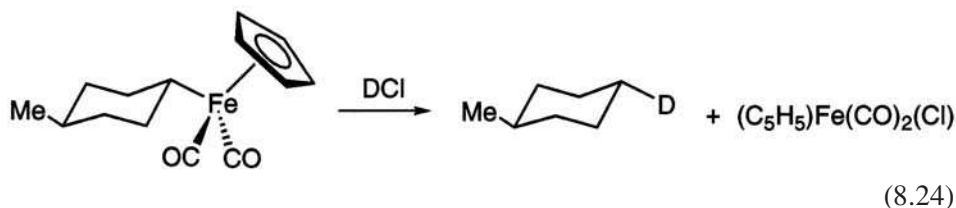


Scheme 8.70.



Scheme 8.71.

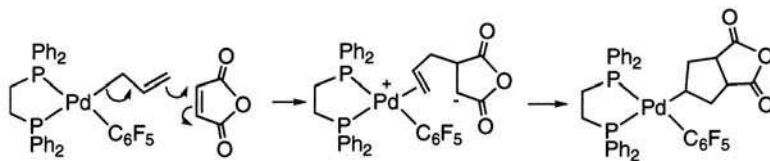
Protonolysis of electron-rich alkylmetals may proceed via initial electrophilic attack at metal, i.e. hydride complex formation. Different from the case of the halogenolysis, the subsequent C–H bond formation occurred via internal reductive elimination with overall retention of configuration (Eq. 8.24) [129].



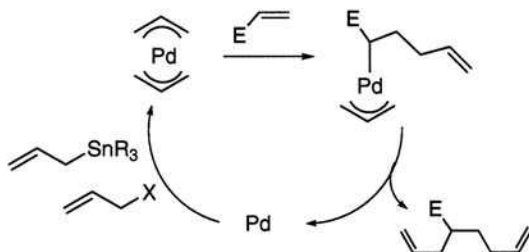
The formation of methane from methyl complexes of Pt(II) and H^+ received considerable attention as the reverse step of methane activation by Pt(II) salts [130]. This protonolysis similarly proceeded via methyl(hydride)platinum(IV) intermediate, the existence of which has actually been confirmed spectrally [131]. Stereochemistry at the α -carbon during SO_2 insertion into alkyl–metal bond is diverse, both retention and inversion of configuration having been observed [29,128,132].

Electrophilic substitution of η^1 -allyl complexes, especially those of Si and Sn, has found extensive synthetic applications, but the overall transformation is stoichiometric with regard to the amount of the metal atom. A catalytically useful reaction of η^1 -allyl intermediate was involved in telomerization of 1,3-dienes in the presence of Pd catalyst shown in Scheme 8.41. η^1 -Allylmetal complexes were reactive with not only H^+ but also electrophilic alkenes (e.g. Scheme 8.72) [62,133]. Recent development in Pd-catalyzed amphiphilic allylation of alkenes and imines (e.g. Scheme 8.73) relied on the high susceptibility of Pd-bound η^1 -allyl ligand to the attack of unsaturated carbon electrophile [134].

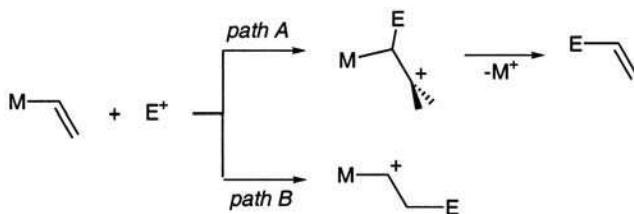
The site of electrophilic attack on alkenyl complexes sometimes differs depending on the electronic requirement of an attaching metal fragment. Alkenyl ligands of some metals tend to undergo the electrophilic attack at the α -carbon, leading to simple electrophilic substitution (Scheme 8.74, path A). It is believed that a positive charge developing on the β -carbon during the α -attack of the electrophile is stabilized, more or less, through σ – π conjugation where σ refers to the M–C σ bond electron pair. On the other hand, the electrophile may attack the β -carbon



Scheme 8.72.



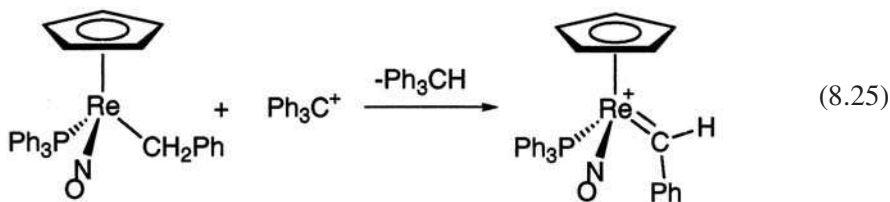
Scheme 8.73.



Scheme 8.74.

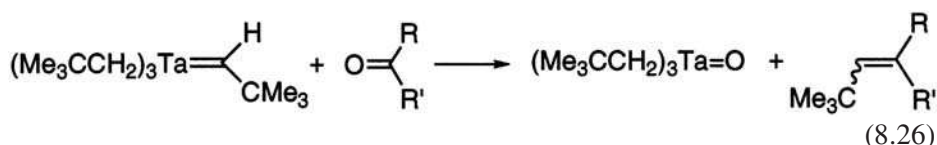
to cause development of a positive charge at the α -carbon if this charge can be stabilized via donation of a metal $d\pi$ orbital (Scheme 8.74, path B). The result is generation of carbene ligand, as exemplified by $M = \text{Fe}(\eta^5\text{-C}_5\text{H}_5)(\text{CO})_2$, $E = \text{H}$ [135].

Scheme 8.74, path B is reminiscent of the electrophilic attack at oxygen of acylmetal complex shown in Eq. 8.5. Another electrophilic route to carbene complex is the reaction of alkylmetals with Ph_3C^+ , as shown in Eq. 8.25 [136]. An electrophilic attack that is similar to Scheme 8.74, path B but appears potentially more significant in catalysis is that of alkynylmetal complex to generate vinylidene ligand. Although Scheme 8.17 described direct formation of the vinylidene complex from M^+ and terminal alkyne, this complex is sometimes derived by treatment of $M\text{-C}\equiv\text{CR}$ with H^+ via β -attack [137].



In contrast to the electrophilic nature of Fischer carbenes described in 8.2.1 (e.g. Scheme 8.16), Schrock carbenes are nucleophilic [138], as typified by

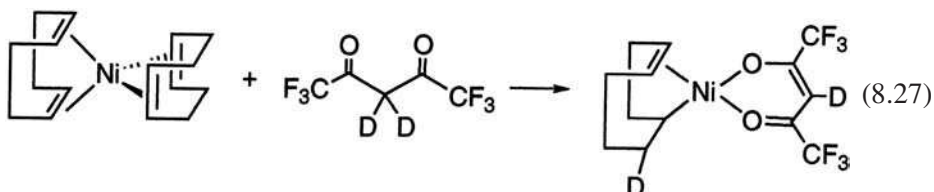
Eq. 8.26. Tebbe's reagent ($\eta^5\text{-C}_5\text{H}_5\text{)}_2\text{Ti}(\mu\text{-CH}_2)(\mu\text{-Cl})\text{AlMe}_2$ similarly reacted with carbonyl compounds.



8.3.2 Reaction of alkene and alkyne ligands

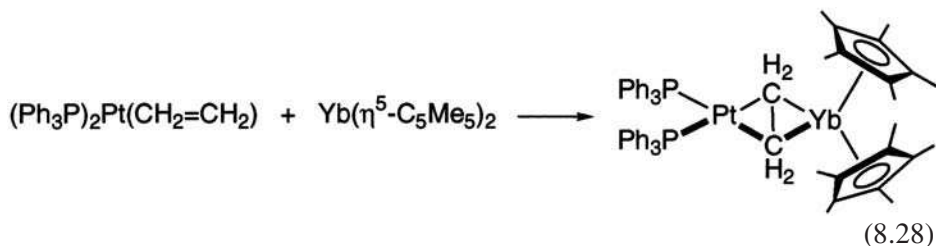
η^2 -Alkene or η^2 -alkyne complexes of transition metals with a low ionization potential could be regarded as metallacyclopropane or metallacyclopropene, and thus it is possible in principle that an electrophile attacks at the 'carbon-metal σ bond' of such metallacycles. Since a high lying MO corresponding to π back-donation from metal to π^* of alkene would extend considerably to a backside region of the carbon with respect to the metal, the electrophile might be capable of approaching the carbon from the backside. Or it may directly attack the metal. The two paths, A and B in Scheme 8.1, for the electrophilic reaction at alkene or alkyne complexes will give products with the same composition but opposite stereochemistry. However, in only very few cases was the occurrence of path A proved.

The first example is the reaction of $\text{Ni}(\text{COD})_2$ with hexafluoroacetylacetone- d_2 shown in Eq. 8.27 [139]. ^1H NMR analysis showed ca. 70% deuterium incorporation at a position anti to Ni, indicating external electrophilic attack of D^+ at the coordinated alkene.



The next example is the reaction of η^2 -propyne complex of Mo, $\text{Mo}(\eta^2\text{-MeC}\equiv\text{CH})(\text{dppe})_2$ with HX to give $\text{MoX}(\text{CH}=\text{CHMe-Z})(\text{dppe})_2$ [140]. No spectral evidence for a hydride complex was obtained. The Z geometry of the propenyl ligand generated was consistent with, though not confirmative of, the external H^+ attack. As a matter of fact, a propylidene ligand has been detected spectroscopically in the course of the reaction presumably via a pathway similar to Scheme 8.74, path B, so that a possibility that the Z-alkenyl structure was of the thermodynamic origin can not be ruled out completely. Finally, ethylene complex $\text{Pt}(\text{CH}_2=\text{CH}_2)(\text{PPh}_3)_2$ was reported to form a novel adduct with an electrophile $\text{Yb}(\text{C}_5\text{Me}_5)_2$ as shown in Eq. 8.28 [141]. Apparently electron deficient Yb atom might have attacked the Pt-bound ethylene carbon with sufficient anionic charge,

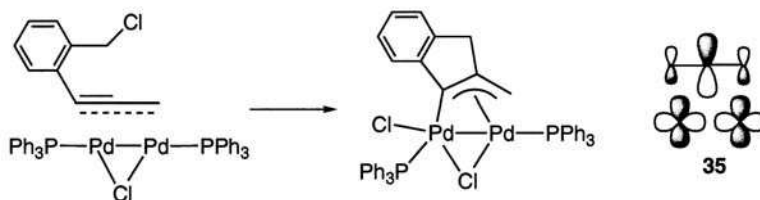
generating a 3-centered-2-electron bridge bond with regard to the Pt-CH₂-Yb skeleton.



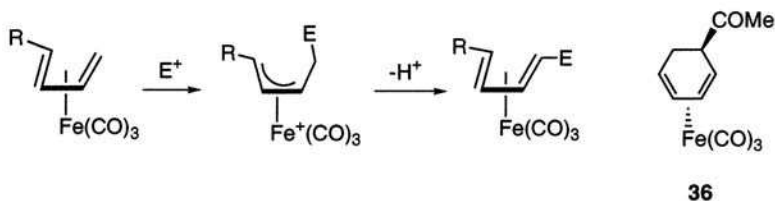
8.3.3 Reaction of unsaturated ligands with carbon number larger than three

Although it may be possible for an electrophile to attack η^3 -allyl ligand, direct proof to substantiate this appears difficult to obtain. An actually active species may be η^1 -allyl form which is in equilibrium with η^3 -allyl form [134]. η^3 -Propargyl or allenyl ligands in mononuclear complexes are susceptible to the nucleophilic attack as already explained in 8.2.4. On the other hand, when bridging over a metal-metal bond, they become susceptible to the attack of electrophiles at the central carbon [142]. As shown in Scheme 8.75, the electrophilic addition occurred at the central carbon to give a μ -vinylcarbene framework. Proton and MeCOCl also underwent intermolecular electrophilic addition. MO calculations suggested that the high susceptibility of the central carbon originated from HOMO (**35** in Scheme 8.75) of the dinuclear complex bearing a big lobe at this carbon. This HOMO was made by mixing of the π^* anti-bonding MO of the ligand into the anti-bonding combination of the Pd-Pd $d\sigma$ - $d\sigma$ orbital and the π bonding MO of propargyl ligand. This mixing takes place in such a way as to weaken the repulsion between the latter two occupied orbitals.

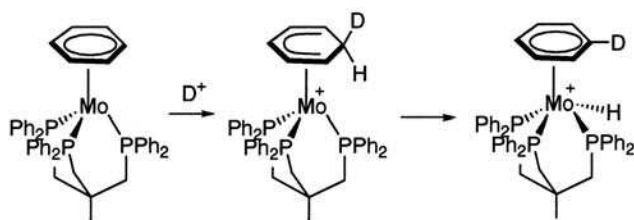
Diene ligands coordinated to $\text{Fe}(\text{CO})_3$ underwent attack of electrophiles such as MeCOCl/ AlCl_3 and $\text{Cl}_2\text{CHOMe}/\text{AlCl}_3$ to afford η^3 -allyl intermediate, followed by proton loss to accomplish electrophilic substitution (Scheme 8.76) [143]. The reaction of cyclohexadiene- $\text{Fe}(\text{CO})_3$ complex with MeCOCl/ AlCl_3 gave 5-acetyl-1,3-cyclohexadiene complex **36** with the exo/endo ratio being 4/1. The electrophilic substitution of $(\eta^5\text{-C}_5\text{H}_5)_2\text{Fe}$ was a marked observation at the



Scheme 8.75.



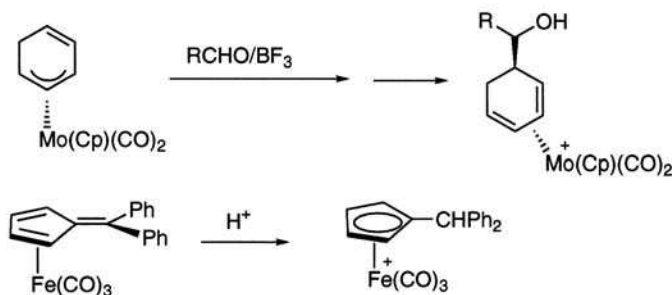
Scheme 8.76.



Scheme 8.77.

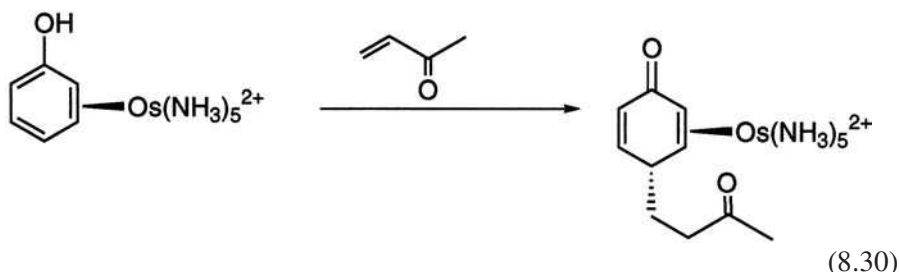
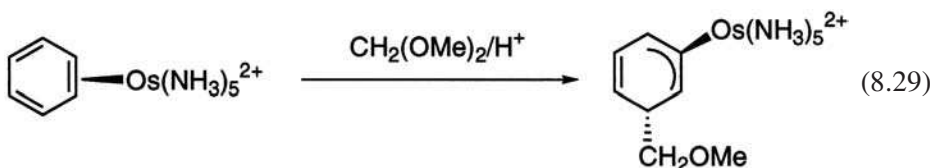
advent of modern organometallic chemistry [144]. A formally 20-electron complex $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Ni}$ reacted with RX to form 18-electron cationic complexes $[(\eta^5\text{-C}_5\text{Me}_5)(\eta^4\text{-C}_5\text{Me}_5\text{R-exo})\text{Ni}]^+\text{X}^-$ ($\text{R} = \text{H}, \text{Me}, \text{PhCH}_2, \text{PhCO}$) [145]. The η^6 -benzene ligand on $\text{Mo}(\text{PR}_3)_3$ was found to undergo protonation to give molybdenum hydride, seemingly via direct attack of H^+ at Mo. However, the use of D^+ demonstrated occurrence of a stepwise protonation–deprotonation sequence shown in Scheme 8.77 [146].

An uncoordinated $\text{C}=\text{C}$ bond of η^3 -hexadienyl [147] and η^4 -fulvene [148] ligands accepted attack of electrophiles to give η^4 -diene and η^5 -cyclopentadienyl ligands, respectively (Scheme 8.78). In all cases the carbon cation generated upon the electrophilic attack would be stabilized by electron donation from the metal center. Especially noteworthy is Eq. 8.29 where the electron-donating character of



Scheme 8.78.

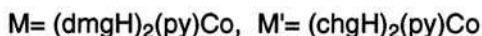
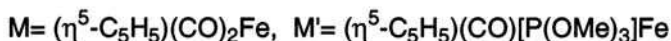
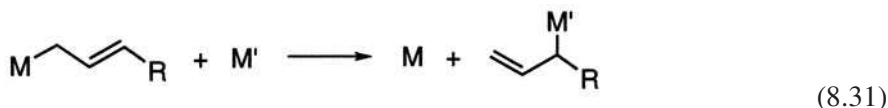
$[\text{Os}(\text{NH}_3)_5]^{2+}$ moiety activated η^2 -bound benzene ligand to the electrophilic attack [149]. α, β -Conjugate enones also reacted with η^2 -phenol ligand on $[\text{Os}(\text{NH}_3)_5]^{2+}$ to give η^2 -dienone complex (Eq. 8.30). These are rare examples of electrophilic reactions involving η^2 -bound benzene ligand.

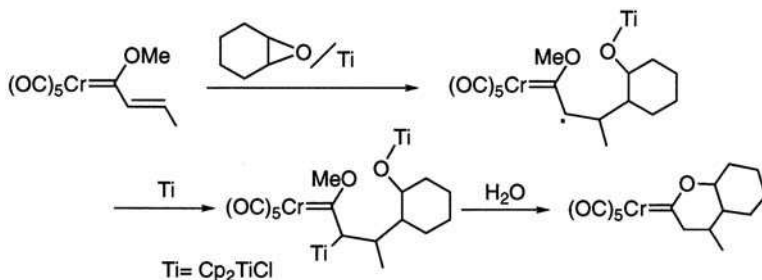


8.4 RADICAL ATTACK AT COORDINATED LIGAND

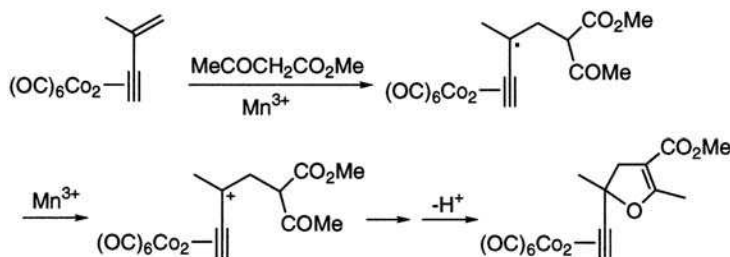
Radical reactions of alkyl and related ligands attached to transition metals have found fewer synthetic applications than those of ligands attached to typical elements such as Sn and Hg. Also, addition of organic free radicals to unsaturated hydrocarbon ligands bound to transition metals remains far less developed than those of nucleophiles and electrophiles. However, future development of organic synthesis may greatly rely on studies of a new methodology to direct the regio- and stereoselectivity of radical reactions by using transition metal fragments as electronic and steric templates.

η^1 -Allyl and η^1 -cyclopentadienyl complexes of Fe and Co have been reported to be susceptible to the attack of metal radical (Eq. 8.31; dmgh = dimethylglyoxamato, chgh = cyclohexanedionedioxamato) [150,151].





Scheme 8.79.



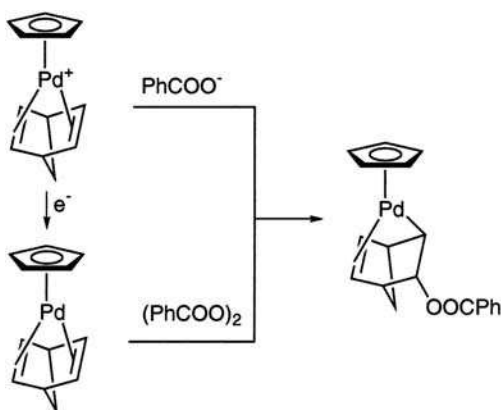
Scheme 8.80.

Both Fe and Co allyls underwent redox transmetallation, which was somewhat similar to Scheme 8.51, but the organic group to be transferred is radical in Eq. 8.31, while it is carbocation in Scheme 8.51. The Co analog also reacted with CCl_3 radical to give $CH_2=CHCH(R)(CCl_3)$ via S_H2' mechanism. η^1 -Allyl complex of Pd also underwent analogous S_H2' reaction with CCl_3 radical [133b].

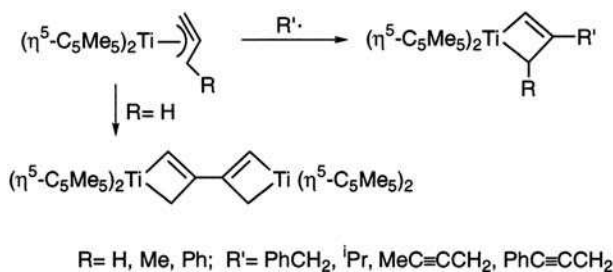
Radical attack at an uncoordinated $C=C$ bond of vinylcarbene or enyne ligands was applied to organic synthesis. Thus, a Ti-induced radical attack at vinylcarbene–Cr complex afforded new carbene–Cr complex (Scheme 8.79) [152], while Mn-induced radical attack at enyne–Co complex led to furan synthesis (Scheme 8.80) [153].

Unsaturated ligands attached to a metal fragment with non-18-electron configuration showed high reactivity to radical attack. Thus, an apparently 19-electron Pd(I) complex $(\eta^5-C_5Ph_5)(diolfin)Pd$ (diolfin = cyclooctadiene, norbornadiene), generated by one electron reduction of the corresponding cation, rapidly reacted with benzoyl peroxide via addition of $PhCOO$ radical to one of the coordinated $C=C$ bonds, giving rise to alkylpalladium(II) complex which was identical with those obtained by attack of $PhCOO^-$ at the alkene of the parent 18-electron cation (Scheme 8.81) [154]. Of further note is that one electron oxidation of the π , σ -Pd(II) product in Scheme 8.81 afforded the parent cation complex presumably via dissociation of the radical species.

17-Electron η^3 -allyl and η^3 -propargyl complexes of Ti(III) accepted attack



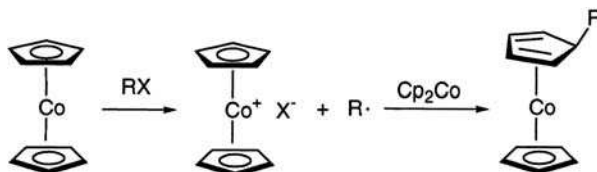
Scheme 8.81.



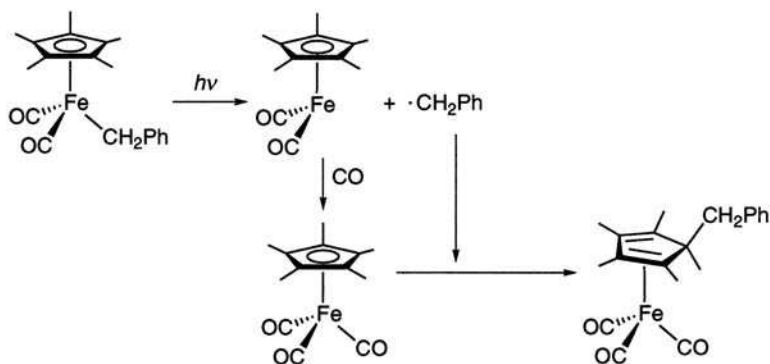
Scheme 8.82.

of organic radicals at the central carbon to give titanacyclobutane and titanacyclobutene complexes, respectively (e.g. Scheme 8.82) [155]. The η^3 -propargyl analogs underwent competitive dimerization.

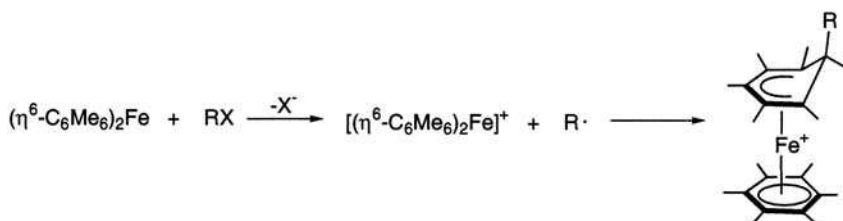
Cobaltocene (formally 19-electron configuration) reacted with RX ($\text{R} = \text{CH}_2\text{Ph}$, $\text{CH}_2\text{CH}=\text{CH}_2$, $\text{CH}_2\text{C}\equiv\text{CH}$) to give Co(I) complex containing η^4 -cyclohexadiene ligand (Scheme 8.83) [156a]. The reaction was proposed to proceed via two steps, the first being electron-transfer from $(\eta^5\text{-C}_5\text{H}_5)_2\text{Co}$ to RX to generate $\text{R}\cdot$ radical, and the second involving attack of the radical at the coordinated $\eta^5\text{-C}_5\text{H}_5$ ligand. A separate experiment confirming the attack of $\text{Me}_2(\text{CN})\text{C}$



Scheme 8.83.



Scheme 8.84.



Scheme 8.85.

radical (from AIBN) at $(\eta^5\text{-C}_5\text{H}_5)_2\text{Co}$ was reported [156b]. Even iodobenzene underwent similar attack of Ph radical if more donating complex $(\eta^5\text{-C}_5\text{Me}_5)_2\text{Co}$ was employed [145]. η^5 -Cyclopentadienyl ligand in transient 19-electron Fe complex accepted attack of radical to give η^4 -cyclopentadiene ligand (Scheme 8.84) [157].

The exo-configuration of the η^4 -diene product was confirmed by X-ray crystallography. Also, 20-electron complex $(\eta^6\text{-C}_6\text{Me}_6)_2\text{Fe}$ reacted with RX ($\text{R} = \text{PhCH}_2$, COPh , CH_2CN , $\text{CH}_2\text{CH}=\text{CH}_2$) via initial electron-transfer to generate R radical and 19-electron intermediate $[(\eta^6\text{-C}_6\text{Me}_6)_2\text{Fe}]^+$ (Scheme 8.85) [158]. Then both radicals underwent mutual coupling to give complexes containing η^5 -cyclohexadienyl ligand. Finally, experiments for testing competition of free benzene and η^6 -benzene of $(\eta^6\text{-C}_6\text{H}_6)\text{Cr}(\text{CO})_3$ in the attack of ketyl radical $(\text{HO})(\text{Me})_2\text{C}$ indicated much greater reactivity (ca. 10^6 times) of the latter ligand than the former [159].

8.5 SUMMARY

A variety of η^1 -bound carbonyl, isocyanide and carbene ligands as well as η^n -bound unsaturated hydrocarbon ligands ($n = 2\text{--}6$) were shown to undergo facile attack of nucleophiles, radicals, or electrophiles to form new ligand frameworks.

The new ligands thus formed can be subjected to ligand substitution to liberate these as the final products of organic synthesis, or to other organometallic reactions including migratory insertion, elimination, and reductive elimination to undergo further transformations on the metal coordination sphere. Both experimental and theoretical insights into the role of the metal atom and its coordination environment in facilitating the addition to the unsaturated ligands have been illustrated. These may contribute to the future design of more sophisticated, more selective organic synthesis using metal complex in both stoichiometric and catalytic amounts.

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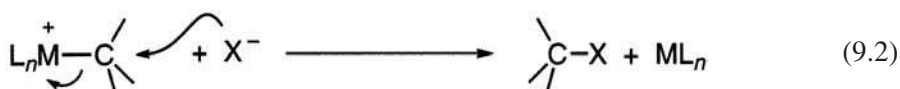
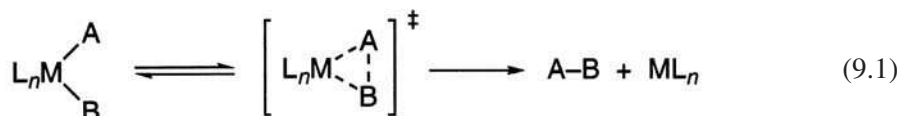
Reductive Elimination

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9.1 INTRODUCTION

Organometallic reactions leading to a new bond formation with reduction in a formal oxidation state of metal center can be classified into two categories from mechanistic viewpoints. One undergoes simultaneous elimination of two anionic ligands (A and B) from an $M(A)(B)L_n$ complex with concomitant formation of an A–B bond via a three-center transition state (Eq. 9.1). The term ‘reductive elimination’ is generally applied to this type. On the other hand, the other involves external attack of a nucleophile on a hydrocarbyl ligand (Eq. 9.2). This reaction resembles the S_N2 process in organic chemistry.

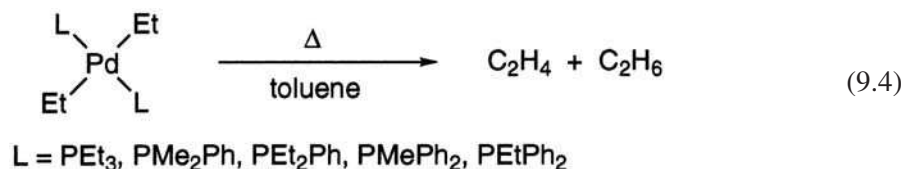
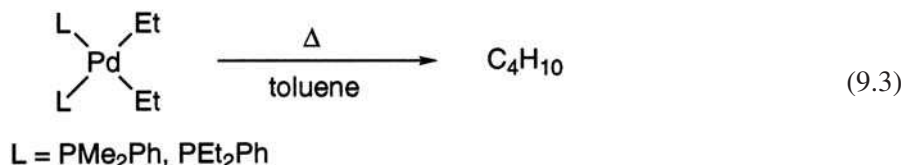


Reductive elimination is a crucial elementary process in organotransition metal chemistry [1]. The reactions causing C–H or C–C bond formation are of particular importance, often constituting a product-forming step in a variety of catalytic transformations. For example, catalytic hydroformylation and hydrogenation of alkenes are accomplished by C–H reductive elimination. Cross-coupling reactions between organic halides and organometallic reagents of main group elements involve C–C reductive elimination at the final stage of catalytic cycle. Reductive elimination giving a C–X bond (X = B, Si, N, O, S, etc.) has also been recognized in many catalytic reactions in recent years. While the importance is obvious, detailed information about reductive elimination is still limited as compared with the other elementary processes. This is mainly because direct observation of this process is often hindered by instability of precursor complexes.

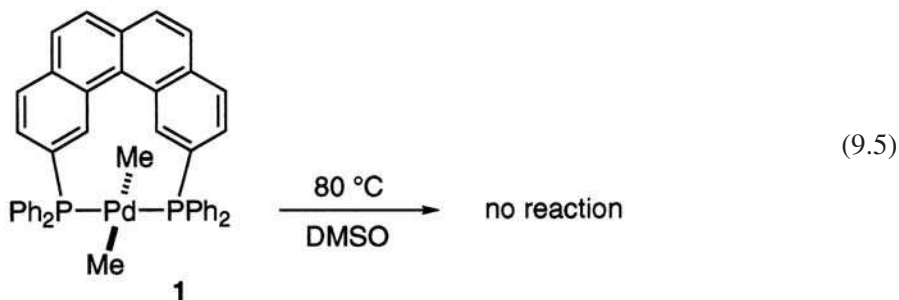
This chapter appraises the current state of mechanistic understanding of reductive elimination. The discussion is subdivided according to the d electron configuration of central metals.

9.2 REDUCTIVE ELIMINATION FROM d^8 *cis*- $MR(R')L_2$ COMPLEXES

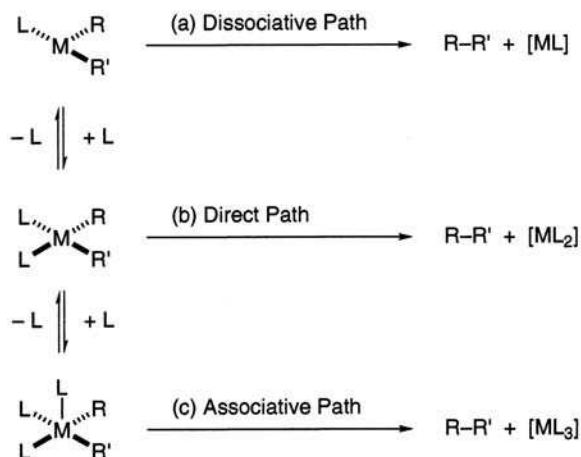
When the reductive elimination proceeds by a concerted mechanism involving a three-center transition state, the two ligands to be eliminated must be situated *cis* to each other. This geometrical requirement has been clearly demonstrated in the thermolysis reactions of *cis*- and *trans*- $PdEt_2L_2$ complexes, which afford entirely different products from one another (Eqs. 9.3 and 9.4) [2]. The *cis* complexes exclusively provide butane as the reductive elimination product, whereas the *trans* isomers selectively afford a 1 : 1 mixture of ethylene and ethane, which are formed by β -hydrogen elimination followed by C–H reductive elimination [3].



The *cis* reductive elimination mechanism was confirmed by another method [4]. Dimethyl complex **1** in Eq. 9.5, whose configuration is fixed to *trans* by the 'TRANSPHOS' ligand, is inactive towards reductive elimination, while *cis*- $PdMe_2L_2$ complexes (L = tertiary phosphine ligands) readily undergo reductive elimination.



Three reaction paths given in Scheme 9.1 have been documented for d^8 *cis*- $MR(R')L_2$ complexes. Path (a) involves preliminary dissociation of one of the



Scheme 9.1.

auxiliary ligands to give a three-coordinate, 14-electron species, which reductively eliminates R–R'.

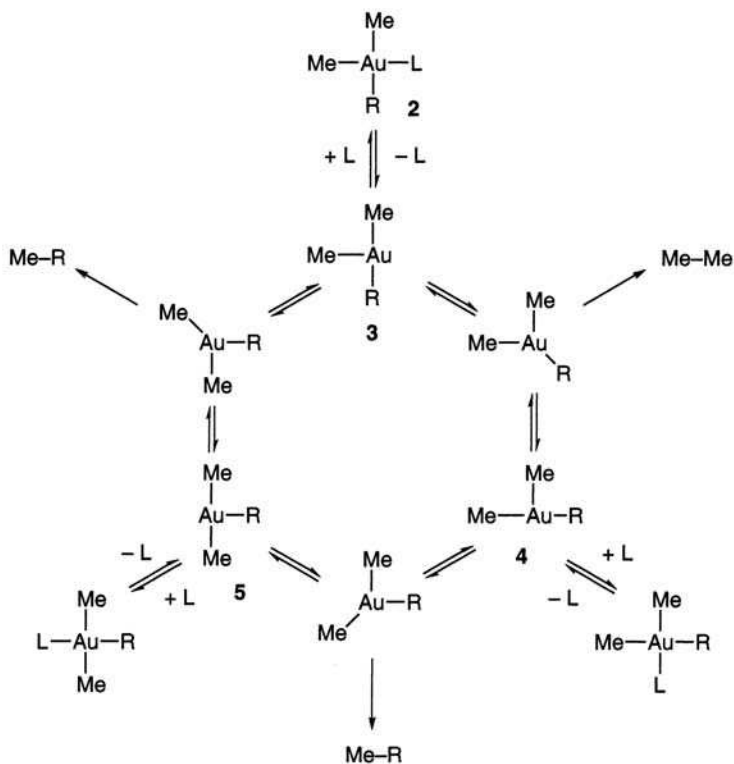
Path (b) is the direct path, simply taking place from a four-coordinate, 16-electron complex. Many intermediates presumed in palladium-catalyzed reactions are considered to follow this path. On the other hand, in path (c), reductive elimination is induced by association with external ligands such as olefins and phosphines. This path has been observed mainly for nickel complexes.

The reason for variation in the reaction path was examined by EHMO calculations [5]. Thus the relative ease of path (a)–(c) was compared starting from *cis*-NiMe₂L_{*n*} (*n* = 1, 2, 3). It was found that path (a) is kinetically favorable, while path (c) is profitable from a thermodynamic point of view. The activation barrier increases in the order [path (a) < path (c) < path (b)], whereas the product stability lowers as [path (c) > path (b) > path (a)]. This study provided a basic framework for considering why the reductive elimination proceeds via different paths dependent on the starting complexes.

9.2.1 Dissociative path (a)

A representative example of path (a) has been reported for AuMe₂R(PPh₃) complexes [6]. A detailed kinetic investigation, together with an MO calculation, indicated the following mechanism involving T- and Y-shaped three-coordinate species (Scheme 9.2) [6a].

Dissociation of PPh₃ (L) from **2** forms a T-shaped intermediate **3**, which undergoes relatively rapid interconversion with other T-shaped intermediates **4** and **5** via transient Y-shaped species. Reductive elimination takes place from any Y-shaped species, giving a kinetic mixture of Me–Me and R–Me. The product distribution varies significantly with R groups, suggesting the following reactivity



Scheme 9.2.

order in reductive elimination [$\text{Me-alkenyl} \geq \text{Me-aryl} > \text{Me-Et} > \text{Me-Me} > \text{Me-CH}_2\text{Ph} > \text{Me-alkynyl}$] [6c].

Path (a) was documented also for *cis*-dialkylpalladium(II) complexes bearing two tertiary phosphine ligands [2,4,7]. Since the three-coordinate, 14-electron intermediate is highly coordinatively unsaturated, its formation should be a very unlikely process in a thermodynamic sense. However, this path becomes feasible owing to the highly reactive nature of the three-coordinate intermediate towards reductive elimination [5,8]. In this situation, phosphine dissociation constitutes the rate-determining step, and generally the complex bearing a diphosphine ligand is poorly reactive [7]. Table 9.1 compares the rates of reductive elimination from *cis*- PdMe_2L_2 having four kinds of phosphine ligands (L). The bulkier ligand, which is more prone to dissociation, tends to give the higher reaction rate [2].

9.2.2 Direct path (b)

Direct path (b) is operative when the reductive elimination is easier than the ligand dissociation. Owing to the simple mechanistic feature, detailed information

TABLE 9.1

Rate of reductive elimination for *cis*-PdMe₂L₂ at 45°C

L	θ (deg) ^a	pK _a ^b	10 ³ k _{obsd} (s ⁻¹)
PEt ₃	132	8.65	0.42
PEt ₂ Ph	136	6.78	0.53
PMePh ₂	136	4.65	1.1
PEtPh ₂	140	4.91	2.0

^a Tolman's cone angle. ^bThe value of conjugate acid.

about the factors controlling reductive elimination has been accumulated for this path. While the nature of metal is among the most important factors, the reactivity is also affected by the sorts of ancillary ligands as well as organic ligands to be eliminated. Each of the factors will be examined in turn below.

(a) Effect of metals

For group 10 metals, the reactivity tends to decrease in the order [Ni > Pd >> Pt]. For example, *cis*-NiMe₂(dppe) decomposes smoothly via path (b) without notable inhibitory effect of free phosphines [9]. In contrast, *cis*-PdMe₂(dppe) does not undergo path (b) but path (a); the reaction is effectively suppressed by added phosphines [2,4]. Platinum(II) dialkyls are inactive towards reductive elimination.

The higher reactivity of nickel complexes than the palladium congeners was examined theoretically. Fig. 9.1 illustrates a schematic diagram for the orbital correlation on the ethane elimination from *cis*-M(CH₃)₂(PH₃)₂ complexes (M = Ni, Pd) [8,10]. This scheme presumes the least motion process that maintains the C_{2v} symmetry of precursor complex throughout the reaction. The C–M–C angle becomes narrow while the P–M–P angle is gradually extended as the reductive elimination proceeds. Finally, ethane is eliminated with formation of a linear M(PH₃)₂ complex.

As seen at the lower left of the figure, the two methyl ligands are linked to the metal by two kinds of bonding orbitals at the 1a₁ and 1b₂ levels, respectively, which are generated by re-combination of two M–CH₃ σ orbitals. The former correlates to the CH₃–CH₃ σ orbital and the latter to the non-bonding metal d orbital of the product M(PH₃)₂ complex. As the reaction proceeds, the 1a₁ level smoothly drops in energy owing to increasing bonding interaction between CH₃ groups. On the other hand, the 1b₂ orbital in the transition state is significantly destabilized by the loss of M–CH₃ bonding as well as the growing anti-bonding interaction between CH₃ groups, while its energy level is thereafter gradually lowered by further structural change of the bent M(PH₃)₂ moiety to the linear final product. Thus, it is found that the activation energy for the reductive elimination is mainly due to the upturn in the 1b₂ level, which is counterbalanced by the stabilization of 1a₁. The activation barrier estimated by EHMO calculations is

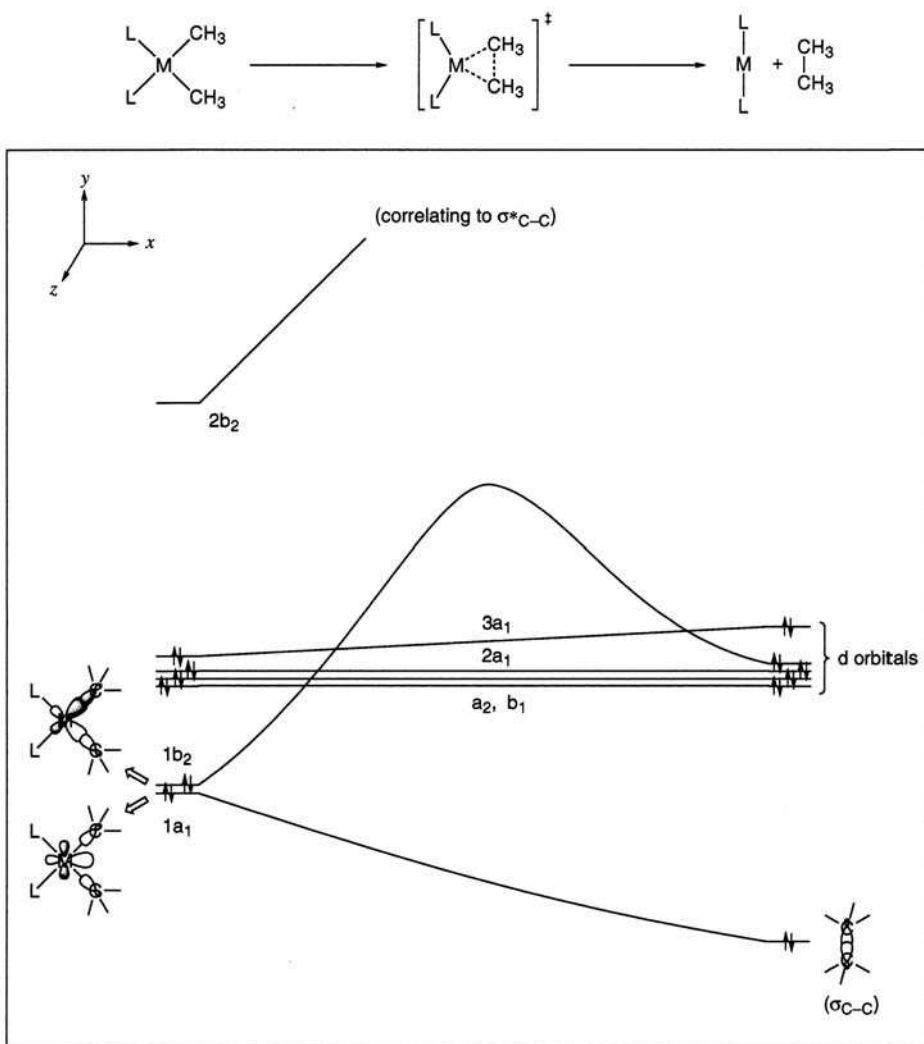


Fig. 9.1. Schematic diagram for the orbital correlation on the ethane elimination from *cis*-M(CH₃)₂(PH₃)₂ complexes (M = Ni, Pd) [8,10].

about 1.1 eV higher for palladium than for nickel. The lower activation energy for nickel is attributed predominantly to the lower d orbital level, which reduces the upturn in the 1b₂ level.

The reason for high stability of platinum complexes towards reductive elimination is more complicated. Thus the difference between d orbital levels of palladium and platinum is not so significant as to rationalize the marked difference in reactivity. Moreover, no notable difference has been observed between the X-ray structures of *cis*-MMe₂(PMePh₂)₂ (M = Pd, Pt) [11]. However, detailed

inspection using *ab initio* MO calculations has provided a convincing argument about this point [12]. Thus the metal in *cis*-MMe₂L₂ type complexes has an s¹d⁹ configuration and forms the M–C covalent bonds through sd hybridization. On the other hand, the product ML₂ species enjoys a d¹⁰ configuration. Therefore, the reductive elimination requires the change in the electron configuration from s¹d⁹ to d¹⁰, and this process is much easier for palladium than for platinum, reflecting the difference in ground state configurations of the two metals [d¹⁰ for Pd, s¹d⁹ for Pt].

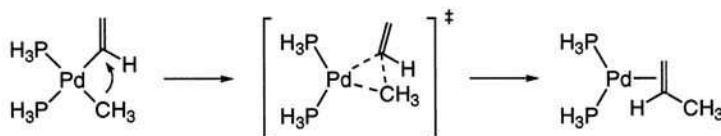
(b) *Effect of leaving groups*

An early theoretical study suggested that better σ donors are eliminated more easily from *cis*-MR(R')L₂ type complexes [8]. However, this prospect is now known to be applicable only to a dialkyl complex series [e.g., Me > Et > Pr > Bu]. Thus the rate of reductive elimination is rather sensitive to the other factors, especially to the orbital hybridization of hydrocarbyl ligands. In general, the reactivity decreases in the order [hydrido (s) ≫ alkenyl (sp²) ≥ aryl (sp²) ≫ alkynyl (sp) ≥ alkyl (sp³)]. While a π-allyl ligand ranks middle, its behavior in reductive elimination will be described separately in Section 9.4.

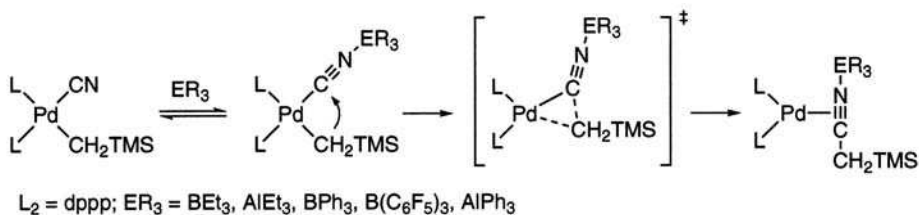
Owing to the extremely high reactivity of hydrido ligand, direct observations of H–H and C–H reductive elimination have been limited to platinum complexes. H–H reductive elimination from *cis*-PtH₂L₂ proceeds without notable activation barrier [13]. C–H reductive elimination is also a facile process; *cis*-PtH(Me)(PPh₃)₂ and *cis*-PtH(CH₂CF₃)(PPh₃)₂ readily decompose at –40°C and room temperature, respectively [14]. These reactions involve a modest kinetic isotope effect ($k_H/k_D = 2.2$ – 3.3) and a small activation entropy (2.0–7.8 eu); the kinetic data are consistent with a concerted mechanism involving a three-center transition state [15].

The highly reactive nature of aryl and alkenyl complexes is significant as compared with dialkyl analogs. For example, *cis*-PdMe(Ph)(PEt₂Ph)₂ smoothly decomposes at room temperature in benzene to give toluene ($k_{\text{obsd}} = 5.0 \times 10^{-4} \text{ s}^{-1}$ at 24°C) [16]. On the other hand, ethane elimination from *cis*-PdMe₂(PEt₂Ph)₂ needs heating ($k_{\text{obsd}} = 5.3 \times 10^{-4} \text{ s}^{-1}$ in Ph₂CH₂ at 45°C) [2]. Note that the former reaction takes place directly from the four-coordinate complex (path (b)), while the latter involves rate-determining dissociation of PEt₂Ph prior to reductive elimination (path (a)). Alkenyl complexes are more reactive; *cis*-PdMe(CH=CHPh)(PMePh₂)₂ and *cis*-Pd(CH₂Ph)(CH=CHAr)(dppf) decompose even at –30°C via path (b) [17,18].

Since sp² carbons generally form a stronger M–C bond than sp³ carbons [19], the highly reactive nature of aryl and alkenyl ligands towards reductive elimination needs a unique rate-acceleration process originated from coordinative unsaturation of sp² carbons. In this regard, Calhorda et al. theoretically proposed a cogent mechanism for the propylene elimination from *cis*-PdMe(CH=CH₂)(PH₃)₂ [20a]. They found that a migration path shown in Scheme 9.3 is energetically advantageous over the simple reductive elimination process with concomitant weakening of both the Pd–Me and Pd–vinyl bonds. A similar mechanism has been proposed



Scheme 9.3.

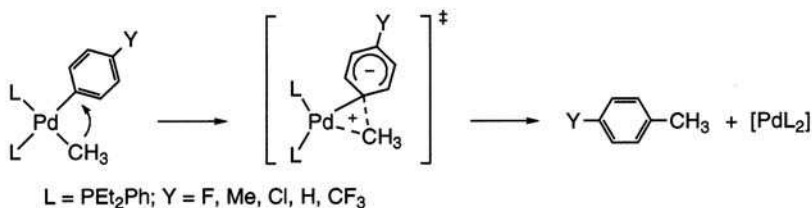


Scheme 9.4.

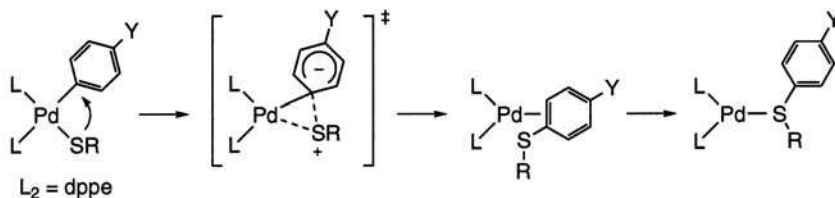
for $\text{cis-}[\text{Pd}(\text{imidazolin-2-ylidene})\text{Me}(\text{PR}_3)_2]^+$ complexes on the basis of kinetic and DFT calculation data [20b].

The initiation step in Scheme 9.3 may be regarded as nucleophilic attack of the methyl ligand on the sp^2 vinylic carbon. This process resembles migratory insertion of CO into an M–C bond. While CO insertion is accelerated by the coordination of CO-oxygen with a Lewis acid which enhances the electrophilicity of carbonyl ligand [21], it has been shown that C–C reductive elimination from $\text{cis-Pd}(\text{CH}_2\text{TMS})(\text{CN})(\text{dppp})$ is similarly accelerated by Lewis acids to a great extent (Scheme 9.4) [22]. The rate constant and Lewis acid strength determined by kinetic and calorimetric analyses are directly correlated with each other.

The ‘migratory reductive elimination process’ is consistent with the kinetic data reported for C–C reductive elimination from $\text{cis-PdMe}(\text{C}_6\text{H}_4\text{-}p\text{-Y})(\text{PEt}_2\text{Ph})_2$ complexes (Scheme 9.5) [16]. The rate constants exhibit a good Hammett correlation with σ_π values of Y, which are synthetic parameters introduced by Yukawa and Tsuno for isolating resonance effects. On the other hand, no correlation was observed with σ_i or σ_p values. Positive sign of the ρ value (+3.2) indicates a major contribution of π -electrophilicity of aryl ligand in the C–C bond formation.



Scheme 9.5.



Scheme 9.6.

The importance of π -electrophilic nature of aryl ligands was noted also in C–N, C–O and C–S reductive elimination from *cis*-Pd(C₆H₄-*p*-Y)(X)(diphosphine) complexes (X = NR₂, OR, SR) [23,24]. A common kinetic feature observed for these systems is the enhancement in the reaction rate by a better π -accepting Y and a better σ -donor ligand X. A kinetic study reported by Hartwig et al. for C–S reductive elimination is particularly detailed, leading to deep insights into the reaction mechanism (Scheme 9.6) [23a].

The rate constants measured with four kinds of *cis*-Pd(C₆H₄-*p*-Bu)(SC₆H₄-*p*-X')(dppe) (X' = Cl, H, Me, OMe) exhibit a linear Hammett correlation with standard σ values of X' in the phenylthiolate ligands ($\rho = -1.5$). On the other hand, the rates of nine *cis*-Pd(C₆H₄-*p*-Y)(S-*t*-Bu)(dppe) complexes are best fit in with the Taft's DSP parameters derived from weighted σ_I and σ_R^- values ($\rho_I = +1.7$, $\rho_R^- = +5.0$). These data are in agreement with the migration mechanism involving a nucleophilic attack of thiolate ligand on phenyl ligand. This mechanism resembles the S_NAr process in organic chemistry. However, since the relative balance of resonance effect is significantly larger than that of the S_NAr, it was considered that π -coordination of the phenyl ring to palladium occurs in conjunction with nucleophilic attack by the thiolate. The overall situation is consistent with Scheme 9.6. Strong retardation effects of sterically demanding aryl ligands also supported the occurrence of π -coordination. The rates of reductive elimination from *cis*-Pd(R)(S-*t*-Bu)(dppe) vary according to the R group [alkenyl > phenyl $\gg$ alkynyl > methyl] (Table 9.2).

TABLE 9.2

Rate of reductive elimination for *cis*-Pd(R)(S-*t*-Bu)(dppe)

R	Reaction temperature (°C)	$t_{1/2}$ (min)
CH=CHMe	50	17
Ph	50	48
C $\equiv$ CPh	95	15
C $\equiv$ CBu	95	87
Me	95	580

Diorganoplatinum(II) complexes are fairly stable towards reductive elimination. On the other hand, *cis*-PtR(SiR'₃)L₂ type complexes have been shown to be reactive towards C–Si reductive elimination [25]. For example, *cis*-Pt(vinyl)(SiPh₃)(PMe₂Ph)₂ undergoes reductive elimination in toluene-*d*₈ at 25°C with the first-order rate constant $1.2 \times 10^{-3} \text{ s}^{-1}$.

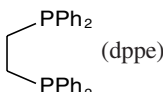
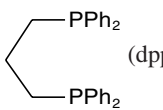
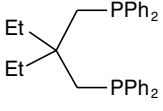
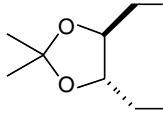
(c) *Effect of supporting ligands*

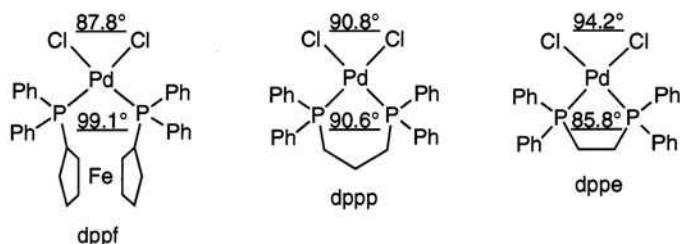
In direct reductive elimination path (b), more electron-donating L tends to reduce the reductive elimination rate and more electron-withdrawing L enhances the reactivity to the contrary. Although no systematic data have been presented, this trend is now widely accepted and supported by theoretical examinations [8].

The other important trend has been observed for diphosphine-coordinated complexes. Thus the rate of path (b) is significantly affected by the chelation size of ligand. For example, the rate of ethane elimination from *cis*-NiMe₂(diphosphine) complexes markedly increases in the order [dppe < dppp < dppb] [9]. Similar trends have been reported for *cis*-PdR(S-*t*-Bu)(diphosphine) complexes [23a] and *cis*-Pd(CH₂TMS)(CN)(diphosphine) [26]. Table 9.3 lists the kinetic data for the latter complexes. The most reactive is the DIOP complex bearing a seven-membered ring, whose rate constant is about 4760 times greater than that of

TABLE 9.3

Rate of reductive elimination for *cis*-Pd(CH₂TMS)(CN)(diphosphine) at 80°C

Diphosphine	$10^5 k_{\text{obsd}} (\text{s}^{-1})$	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (eu)
 (dppe)	0.21	30.8	2.4
 (dppp)	5.0	27.3	–1
 (dppb)	2.1	32.9	13
 (dppf)	7.4	32.5	14
 (DIOP)	1000	28.2	12



Scheme 9.7.

the least reactive dppe complex with a five-membered ring. The six-membered chelate complexes having dppp families exhibit intermediate reactivities, showing relatively small dependence of the rate on substituent of the ligands.

Since the chelate ring size is clearly reflected in the P–Pd–P bite angle [DIOP ($\sim 100^\circ$), dppp ($\sim 90^\circ$), dppe ($\sim 85^\circ$)], it has been considered that the bite angle of diphosphine ligand has a prominent effect on the reductive elimination rate. Thus the wider P–Pd–P angle sterically compresses the C–Pd–C angle to the greater extent, making a carbon–carbon interaction during reductive elimination easier. Such structural variation has been observed for *cis*-PdCl₂(diphosphine) complexes (Scheme 9.7) [27]. Moreover, since the 1b₂ level of transition state in Fig. 9.1 is stabilized by enlargement in the P–Pd–P angle [10], the wider bite angle is profitable for reductive elimination in view of orbital description as well.

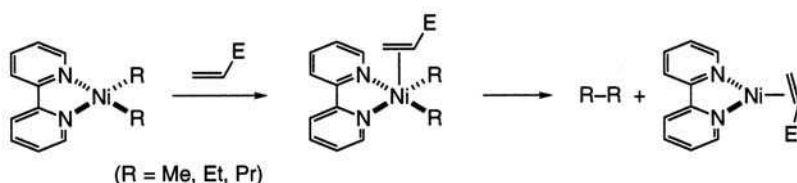
A pronounced acceleration effect of diphosphine ligand with a large bite angle has often been observed in catalytic reactions which involve reductive elimination as the rate-determining step [27–29]. For example, catalytic activity and selectivity of the palladium-catalyzed cross-coupling between PhBr and *sec*-BuMgCl are clearly dependent on the bite angle of diphosphine ligands [27]. As seen from the data given in Table 9.4, the dppf complex having a wide P–Pd–P angle (99.1°) serves as a particularly effective catalyst.

TABLE 9.4

Effect of bite angles of bidentate ligands on palladium-catalyzed cross-coupling reaction between PhBr and *sec*-BuMgCl

Catalyst	Reaction time (h)	Conversion of PhBr (%)	Yield of <i>sec</i> -BuPh (%)
PdCl ₂ (dppf)	1	100	95
PdCl ₂ (dppb)	8	99	51
PdCl ₂ (dppp)	24	77	43
PdCl ₂ (dppe)	48	4	0

At room temperature, in THF. Initial condition: PhBr/*sec*-BuMgCl/catalyst = 1/1.5–3/0.01.



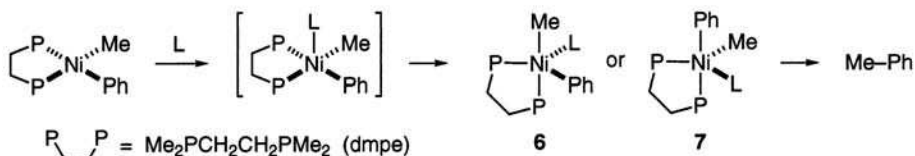
Scheme 9.8.

9.2.3 Associative path (c)

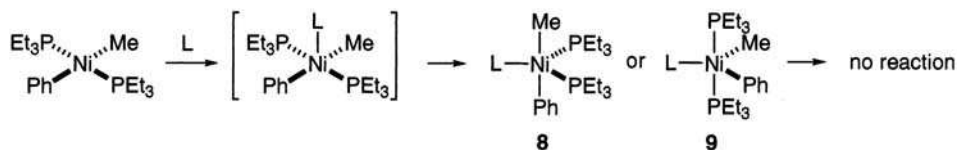
Associative path (c) has been mainly observed for nickel(II) complexes [30–33]. This is because nickel(II) has a higher propensity to make five-coordinate species than palladium(II) and platinum(II). A steric condition is another important factor. Thus the reductive elimination from bipyridine-coordinated dialkyl-nickel complexes is known to be effectively accelerated by addition of π -acceptor olefins such as maleic anhydride and acrylonitrile to the systems (Scheme 9.8) [30]. Owing to the planar coordination structure of bipyridine ligand, the apical site of these complexes is widely open for the coordination of olefins. On the other hand, tertiary phosphine-coordinated analogs are sterically more demanding, and their reductive elimination is much less sensitive towards olefins [9]. Rate-acceleration by π -acceptor olefins was also noted for *cis*-PdR₂(bipy) complexes while the exact mechanistic reason remains unclear [34].

cis-NiMe(Ph)(dmpe) undergoes reductive elimination of toluene in the presence of added phosphines. The more compact phosphine leads to the higher reaction rate [35]. This trend has been rationalized by the mechanism depicted in Scheme 9.9. Coordination of phosphine (L) forms a five-coordinate intermediate **6** or **7**. Reductive elimination from the axial and equatorial sites of five-coordinate structure is allowed by orbital symmetry as confirmed by a theoretical study [5], and indeed proceeds very easily.

In contrast, *trans*-NiMe(Ph)(PEt₃)₂ is fairly stable towards reductive elimination even in the presence of added phosphines. In this case, coordination of phosphine (L) gives two types of five-coordinate species **8** and **9** as shown in Scheme 9.10. Since **8** has the methyl and phenyl groups at mutually trans positions, the reaction is infeasible. On the other hand, **9** has the methyl and



Scheme 9.9.



Scheme 9.10.

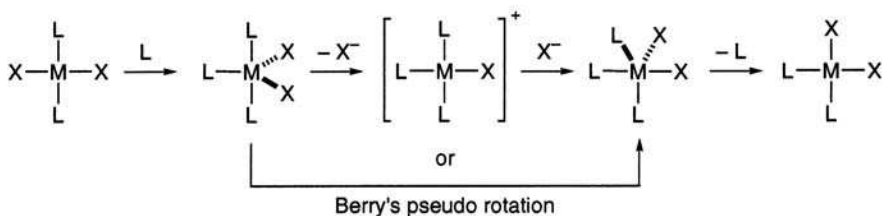
phenyl groups at equatorial positions and seems capable of reductive elimination. However, this reaction is forbidden by orbital symmetry [5].

The reductive elimination process induced by phosphine-coordination has been observed also for *cis*-NiR(CN)L₂ type complexes [36].

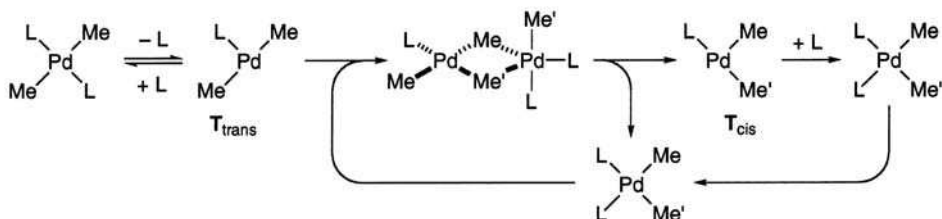
9.3 REDUCTIVE ELIMINATION FROM d⁸ *trans*-MR(R')L₂ COMPLEXES

Owing to the geometrical requirement for reductive elimination, *trans*-MR(R')L₂ complexes must be isomerized to their *cis* isomers prior to reductive elimination. The *trans* to *cis* isomerization of MX₂L₂ type complexes bearing halide ligands (X) is known to proceed by either stepwise ligand displacement or Berry's pseudo rotation of a five-coordinate intermediate (Scheme 9.11) [37]. On the other hand, diorganopalladium complexes have been shown to isomerize via a transmetallation process [38,39].

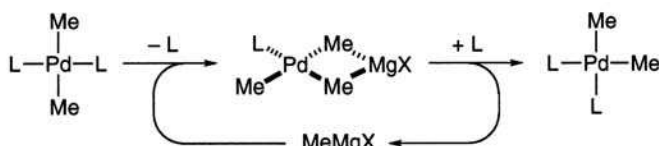
The *trans* to *cis* isomerization of PdMe₂L₂ complex (L = PMePh₂) has been examined by kinetic experiments, showing a unique reaction process promoted by product *cis*-PdMe₂L₂ (Scheme 9.12) [2]. The starting *trans*-PdMe₂L₂ is in a rapid equilibrium with a T-shaped three-coordinate species *trans*-[PdMe₂L] (*T_{trans}*) as supported by NMR observation. Unlike the gold analog [AuMe₂R] in Scheme 9.2, *T_{trans}* in Scheme 9.12 is inert for direct geometrical change to *T_{cis}* via a Y-shaped intermediate, but instead undergoes intermolecular exchange of methyl groups with *cis*-PdMe₂L₂. As seen from the scheme, this transmetallation process results in the conversion of *T_{trans}* to *T_{cis}*. The subsequent coordination of L to *T_{cis}* completes the isomerization. A labeling experiment using CD₃ groups provided an additional support on this mechanism.



Scheme 9.11.

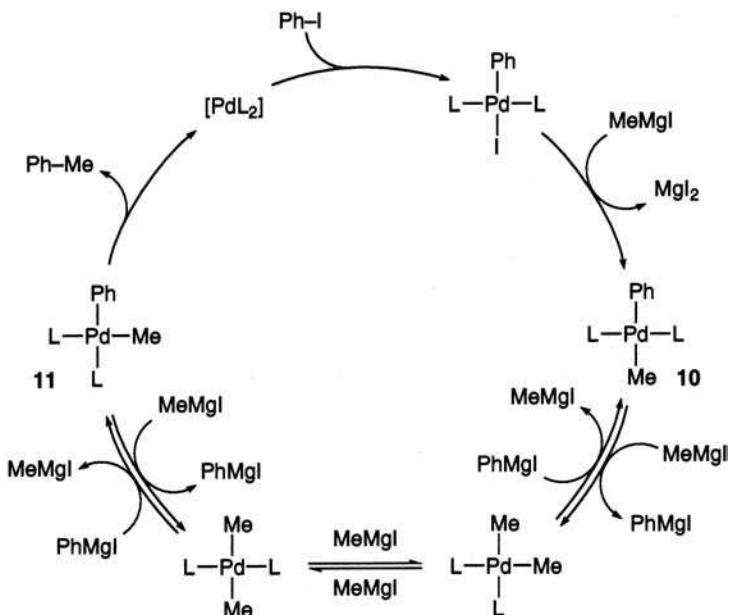


Scheme 9.12.



Scheme 9.13.

Methylmagnesium compounds (MeMgX ; $\text{X} = \text{Me}, \text{I}$) also catalyze the trans-cis isomerization of PdMe_2L_2 (Scheme 9.13) [38]. This reaction was found to serve as a key elementary process in cross-coupling reaction between PhI and MeMgI catalyzed by trans-PdPh(I)L_2 ($\text{L} = \text{PEt}_2\text{Ph}$) (Scheme 9.14) [16]. The trans-PdPh(I)L_2 intermediate, which is formed by oxidative addition of

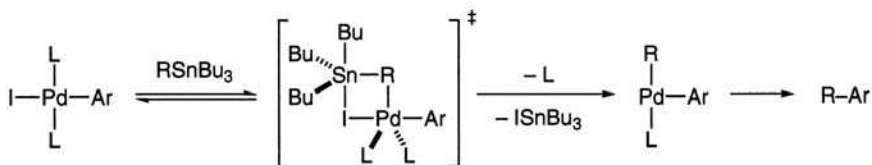
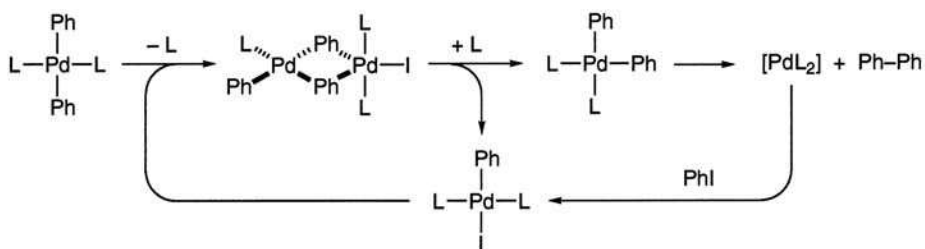


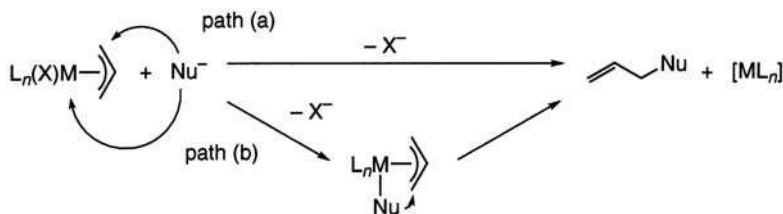
Scheme 9.14.

PhI to a $[\text{Pd}(0)\text{L}_2]$ species, reacts with MeMgI to give *trans*- $\text{PdPh}(\text{Me})\text{L}_2$ (**10**) with retention of the *trans* configuration around palladium. For the reductive elimination of toluene to take place, complex **10** must be converted to its *cis* isomer **11**. This interconversion proceeds by stepwise displacement of the Ph and Me ligands between diorganopalladium complexes and Grignard reagents. Thus the reaction of **10** with MeMgI gives *cis*- PdMe_2L_2 , which is in a rapid equilibrium with *trans*- PdMe_2L_2 . The *trans* dimethyl complex then reacts with PhMgI to give *cis*- $\text{PdPh}(\text{Me})\text{L}_2$ (**11**). Since complex **11** having an sp^2 -hybridized phenyl ligand in a *cis* configuration is much more reactive towards reductive elimination than the other diorganopalladium species, the catalytic reaction exclusively forms toluene.

Trans to *cis* isomerization via a transmetallation process has been observed in several reaction systems giving reductive elimination products [39,40]. For example, *trans*- PdPh_2L_2 ($\text{L} = \text{PEt}_2\text{Ph}$) itself is highly stable towards reductive elimination in a toluene solution, but readily affords biphenyl and *trans*- $\text{PdPh}(\text{I})\text{L}_2$ in the presence of PhI (Scheme 9.15) [39a]. This reaction proceeds by an intermolecular exchange of phenyl groups between *trans*- PdPh_2L_2 and product *trans*- $\text{PdPh}(\text{I})\text{L}_2$. The resulting *cis*- PdPh_2L_2 affords biphenyl. A similar process has been reported for the reaction of *trans*- $\text{PdMe}(\textit{m}\text{-tolyl})\text{L}_2$ with MeI to give *m*-xylene, where *trans*- $\text{PdMe}(\text{I})\text{L}_2$ catalyzes *trans* to *cis* isomerization of $\text{PdMe}(\textit{m}\text{-tolyl})\text{L}_2$ [39b].

It has been shown that direct conversion of *trans*- $\text{PdAr}(\text{I})\text{L}_2$ ($\text{Ar} = \text{C}_6\text{Cl}_2\text{F}_3$, $\text{L} = \text{AsPh}_3$) into *cis*- $\text{PdAr}(\text{R})\text{L}_2$ ($\text{R} = \text{vinyl}$, $\text{C}_6\text{H}_4\text{OMe}$) is accomplished by the reaction with RSnBu_3 in a catalytic cross-coupling system [40a]. Associative displacement of L for R was proposed on the basis of kinetic data (Scheme 9.16).





Scheme 9.17.

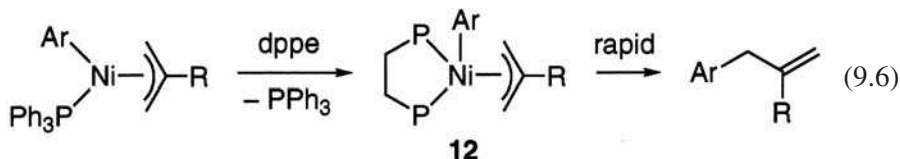
9.4 REDUCTIVE ELIMINATION FROM d^8 π -ALLYL COMPLEXES

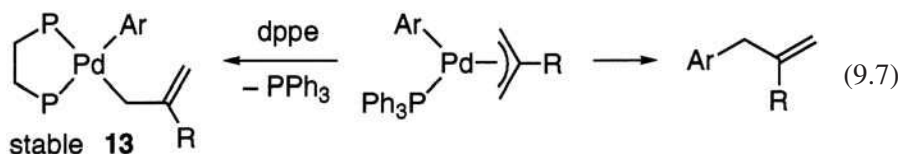
Catalytic organic reactions with a π -allyl intermediate have been explored extensively using Group 10 metals [41]. Two types of reductive elimination processes are known for the catalysis (Scheme 9.17). One is the external attack of a nucleophile on the π -allyl ligand from the opposite side of metal center (path (a)). This type of process is observed with stabilized carbon nucleophiles as well as nitrogen and oxygen nucleophiles, giving rise to the inversion of stereochemistry at the allylic carbon. On the other hand, when non-stabilized carbon nucleophiles (e.g., main group organometallics) and metal hydrides are employed, the π -allyl complex undergoes transmetalation with the nucleophile to form a diorganometal intermediate, which reductively eliminates the allylation product (path (b)). In this process, since the nucleophile is introduced to the π -allyl ligand from the metal center, retention of stereochemistry at the allylic carbon is observed.

Path (a) is discussed in Chapter 8. On the other hand, path (b) was extensively studied by Kurosawa et al. using a series of $M(\pi\text{-allyl})(Ar)L_n$ complexes ($M = Ni, Pd$), and the following mechanistic features emerged [42,43].

(1) π -Allyl complex $M(\pi\text{-allyl})(Ar)L$ is much more reactive than the corresponding σ -allyl complex $M(\sigma\text{-allyl})(Ar)L_2$, showing a direct reductive elimination process with maintenance of the π -allyl structure. This finding has been supported by MO calculations [43c,44].

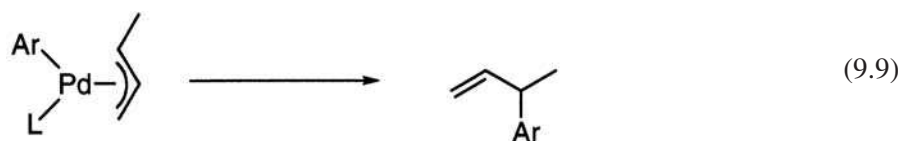
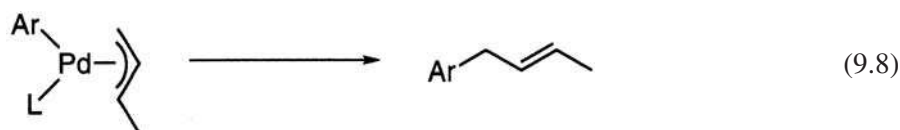
(2) The 18-electron nickel complex $Ni(\pi\text{-CH}_2\text{CRCH}_2)(C_6F_5)(dppe)$ (**12**), which is formed by the ligand displacement of $Ni(\pi\text{-CH}_2\text{CRCH}_2)(C_6F_5)(PPh_3)$ with $dppe$, is about 10^8 times more reactive than the parent PPh_3 complex having a 16-electron configuration (Eq. 9.6). On the other hand, the palladium analog does not adopt an 18-electron π -allyl structure but forms a 16-electron σ -allyl structure $Pd(\sigma\text{-CH}_2\text{CRCH}_2)(C_6H_3Cl_2\text{-2,5})(dppe)$ (**13**), which is much less reactive than the π -allyl complex $Pd(\pi\text{-CH}_2\text{CRCH}_2)(C_6H_3Cl_2\text{-2,5})(PPh_3)$ towards reductive elimination (Eq. 9.7).





(3) The ease of reductive elimination decreases with the sort of metal in the order $[M = \text{Ni} > \text{Pd} \gg \text{Pt}]$. For example, the reaction of $\text{Ni}(\pi\text{-allyl})(\text{C}_6\text{H}_3\text{Cl}_2\text{-2,5})(\text{PPh}_3)$ proceeds 26 times faster than that of $\text{Pd}(\pi\text{-allyl})(\text{C}_6\text{H}_3\text{Cl}_2\text{-2,5})(\text{PPh}_3)$. The platinum analog is totally inactive under the same reaction condition [43b].

(4) The C–C bond formation from π -allyl(aryl)palladium complexes follows the cis elimination process, as confirmed by the following experiments using two geometrical isomers (Eqs. 9.8 and 9.9) [43e].

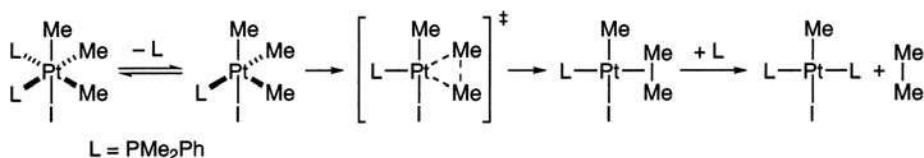


It has been further documented that the rate of reductive elimination from $\text{Pd}(\pi\text{-methallyl})\text{Ar}(\text{olefin})$ complexes increases as the π -acidic nature of the olefin ligand increases (Table 9.5) [43c]. The olefin-coordinated π -allyl complex has been postulated as a key intermediate for rate acceleration by added olefins in the reductive elimination from $\text{Pd}(\pi\text{-allyl})(\text{R})\text{L}$ complexes ($\text{L} = \text{PPh}_3, \text{AsPPh}_3$) [43c,45].

TABLE 9.5

Rate of reductive elimination for $\text{Pd}(\eta^3\text{-methallyl})(\text{C}_6\text{HCl}_4)(\text{olefin})$

Olefin	Reaction temperature (°C)	k_{obsd} (h ⁻¹)
$\text{CH}_2=\text{CH}(\text{C}_6\text{H}_4\text{OMe-4})$	10	0.136
$\text{CH}_2=\text{CH}(\text{C}_6\text{H}_4\text{Me-4})$	10	0.221
$\text{CH}_2=\text{CH}(\text{C}_6\text{H}_5)$	10	0.281
$\text{CH}_2=\text{CH}(\text{C}_6\text{H}_4\text{Cl-4})$	10	1.01
$\text{CH}_2=\text{CH}(\text{C}_6\text{H}_4\text{NO}_2\text{-4})$	10	2.44
	-10	0.175
$\text{CH}_2=\text{CHCO}_2\text{Me}$	-10	1.23
$\text{CH}_2=\text{CHCN}$	-10	2.56
$(Z)\text{-MeO}_2\text{CCH}=\text{CHCO}_2\text{Me}$	-45	2.71



Scheme 9.18.

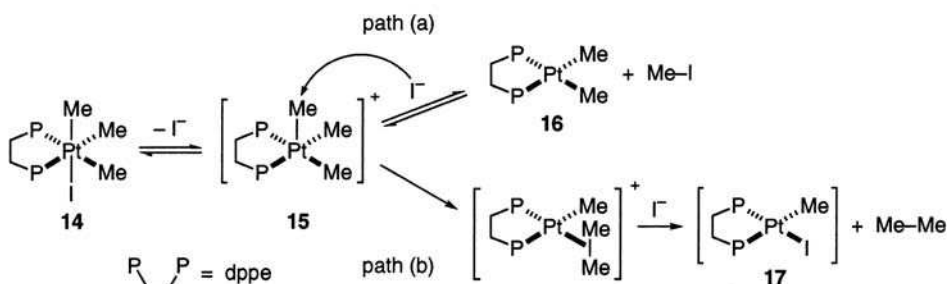
9.5 REDUCTIVE ELIMINATION FROM d^6 METAL COMPLEXES

9.5.1 Group 10 metals

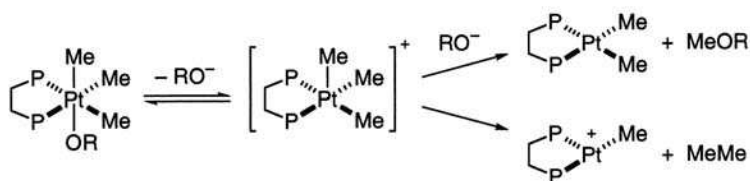
Thermolysis of *fac*- $\text{MR}_3(\text{X})\text{L}_2$ type complexes ($\text{M} = \text{Pt}, \text{Pd}$) bearing a d^6 metal center affords two kinds of reductive elimination products $\text{R}-\text{R}$ and $\text{R}-\text{X}$, along with the formation of $\text{MR}(\text{X})\text{L}_2$ and MR_2L_2 , respectively. A number of kinetic and theoretical examinations suggested a common mechanistic feature involving a five-coordinate intermediate, which is generated by dissociation of either a supporting ligand L or an anionic ligand X [46–53].

When L is a monodentate phosphine, the reaction involves preliminary dissociation of L , as previously documented for *fac*- $\text{PtMe}_3(\text{I})(\text{PMe}_2\text{Ph})_2$ (Scheme 9.18) [47]. Theoretical studies have suggested the formation of a $\text{C}-\text{C}$ σ complex as a transient species, which is subsequently converted into a metastable intermediate with $\text{C}-\text{H}$ bond coordination of ethane [48].

When the dissociation of L is hampered by chelate coordination, anionic dissociation of X takes place. Representative examples have been reported for *fac*- $\text{PdMe}_3(\text{I})(\text{bipy})$ [49b] and *fac*- $\text{PtMe}_3(\text{I})(\text{dppe})$ (**14** in Scheme 9.19) [50]. For the latter complex, a cationic intermediate $[\text{PtMe}_3(\text{dppe})]^+$ (**15**) generated in the system undergoes two competitive reaction paths (a) and (b). Nucleophilic attack of I^- upon the methyl ligand at the apical position leads to the formation of MeI and $\text{PtMe}_2(\text{dppe})$ (**16**) (path (a)), whereas $\text{C}-\text{C}$ reductive elimination from **15** followed by coordination of I^- provides ethane and $\text{PtMe}(\text{I})(\text{dppe})$ (**17**) (path (b)). The former path is the microscopic reverse of oxidative addition of MeI to **16**.



Scheme 9.19.



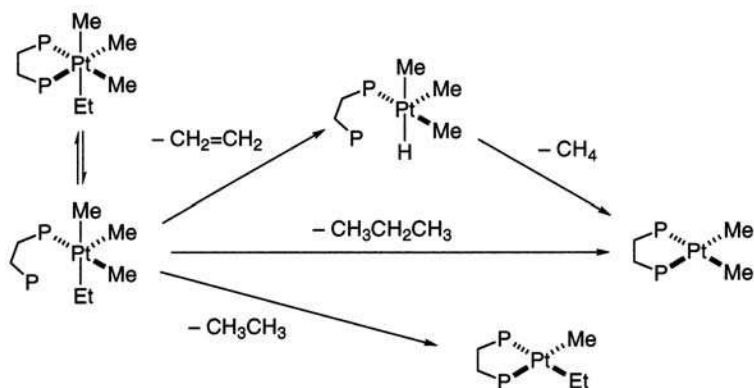
Scheme 9.20.

The interconversion between **14** and **16** can be observed without path (b) in the presence of an excess amount of I⁻ ($\Delta H^0 = 16$ kcal/mol and $\Delta S^0 = 37$ eu). On the other hand, path (b) is exclusively operative when the iodide ion is irreversibly removed from the system as AgI.

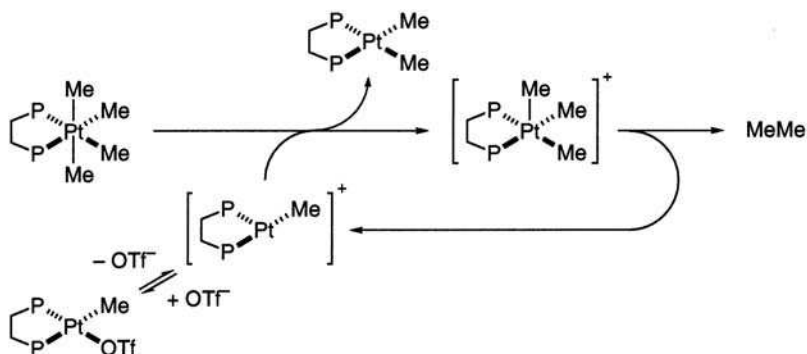
A detailed experimental study has been carried out for competitive formation of C-C and C-O coupling products from *fac*-PtMe₃(OR)L₂ complexes (OR = carboxylato, aryloxo; L₂ = dppe) (Scheme 9.20) [51]. Similarly to the iodo complexes described above, both coupling reactions are initiated by anionic dissociation of the OR ligand to form a five-coordinate intermediate [PtMe₃L₂]⁺. The rate of this preliminary dissociation is significantly enhanced by increasing solvent polarity and by increasing stability of OR⁻ ion. For the complexes having six kinds of *p*-substituted phenoxy ligand (OC₆H₄Y-4), the first-order rate constants exhibit a good Hammett correlation with σ^- values ($\rho = 1.44$). The C-O coupling proceeds by subsequent S_N2 attack of OR⁻ on the methyl ligand, whereas the C-C coupling proceeds by a common reductive elimination process with a three-center transition state. The former reaction is the major path in less polar solvents such as benzene and THF, and facilitated by addition of OR⁻ ion to the system.

Unlike the *fac*-PtR₃(X)L₂, tetraalkyl analogs bearing a bidentate ligand (*i.e.*, *fac*-PtR₄L₂, L₂ = dppe, bipy, etc.), which are unable to undergo anionic dissociation, are fairly stable towards reductive elimination. However, even in such cases, C-C reductive elimination may be operative at high temperature. For example, thermolysis of *fac*-PtMe₃(Et)(dppe) at 165°C affords ethylene, propane, and ethane in a 75:18:7 ratio, whose formation has been rationalized by the following reaction processes involving a partial dissociation of the dppe ligand (Scheme 9.21) [52].

It has been noted that the formation of ethane from PtMe₄(dppe) is markedly accelerated by the aid of a catalytic amount of *cis*-PtMe(OTf)(dppe) [53]. The reaction takes place at room temperature in acetone-d₆, while the parent tetramethyl complex is fairly stable in neat solvent even at 100°C. Based on kinetic and deuterium-labeling experiments an intermolecular process giving a five-coordinate intermediate has been proposed (Scheme 9.22). Thus the transmetalation of a methyl group between PtMe₄(dppe) and three-coordinate [PtMe(dppe)]⁺ affords *cis*-PtMe₂(dppe) and [PtMe₃(dppe)]⁺. Elimination of ethane from the latter complex reproduces [PtMe(dppe)]⁺.



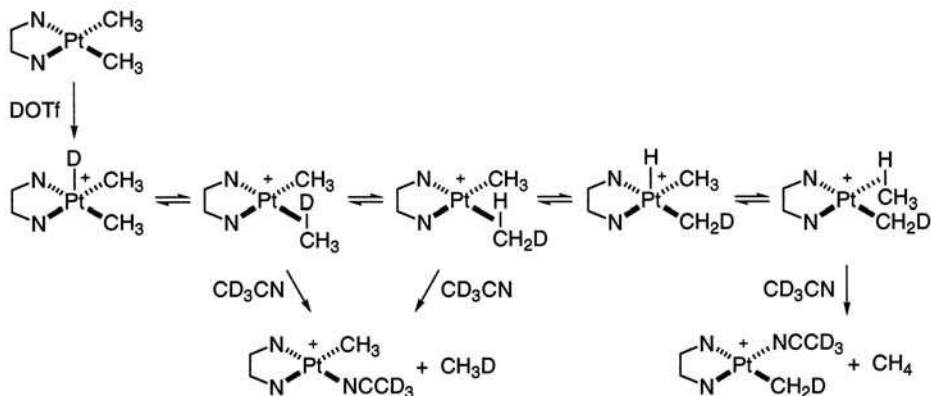
Scheme 9.21.



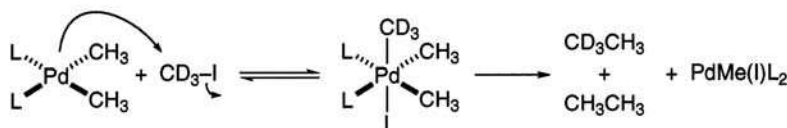
Scheme 9.22.

Reductive elimination of methane from a $[\text{PtMe}_2(\text{H})\text{L}_2]^+$ species has been examined [54] in connection with its microscopic reverse leading to C–H bond activation of methane [55]. Diimine-coordinated complex, which is generated by the treatment of $\text{Pt}(\text{CH}_3)_2\text{L}_2$ ($\text{L}_2 = \text{ArN}=\text{CMe}-\text{CMe}=\text{NAr}$, $\text{Ar} = 3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3$) with DOTf in $\text{CF}_3\text{CH}_2\text{OH}$, affords CH_3D and CH_4 in a 59:41 ratio. Addition of CD_3CN to the system results in higher ratio of CH_3D . These observations have been accounted for by the mechanism depicted in Scheme 9.23. Dimethyl deuterido complex $[\text{Pt}(\text{CH}_3)_2(\text{D})\text{L}_2]^+$ is in a rapid equilibrium with $[\text{Pt}(\text{CH}_3)(\text{CH}_2\text{D})(\text{H})\text{L}_2]^+$ via methane-coordinated platinum(II) intermediates $[\text{Pt}(\text{CH}_3)(\sigma\text{-CH}_3\text{D})\text{L}_2]^+$ and $[\text{Pt}(\text{CH}_2\text{D})(\sigma\text{-CH}_4)\text{L}_2]^+$, which undergo associative displacement of the methane ligand with CD_3CN to give CH_3D and CH_4 , respectively.

Unlike the platinum analogs, direct observation of palladium(IV) alkyls has been limited to those with nitrogen-based ligands such as 2,2'-bipyridine and α -diimines [49]. However, reductive elimination from palladium(IV) complexes has



Scheme 9.23.



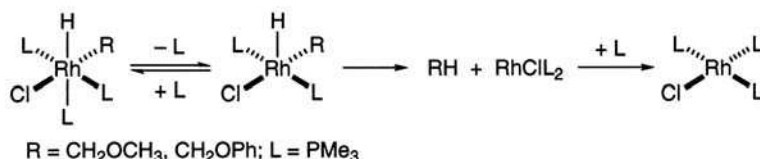
Scheme 9.24.

often been postulated as the product forming step in the reactions of diorganopalladium(II) complexes bearing phosphine ligands (PdR_2L_2) with organic halides ($\text{R}'\text{X}$). The reaction of *cis*- PdMe_2L_2 ($\text{L}_2 = (\text{PMePh}_2)_2$, dppe) with MeI , giving ethane and *trans*- PdMe(I)L_2 , constitutes a representative example [56]. The rate of ethane formation significantly increases with increasing concentration of MeI . A labeling experiment using CD_3I forms a mixture of CD_3CH_3 and CH_3CH_3 . These results are consistent with the mechanism involving a $\text{Pd}(\text{CH}_3)_3(\text{I})\text{L}_2$ intermediate, which is formed by the oxidative addition of MeI to *cis*- PdMe_2L_2 via an $\text{S}_{\text{N}}2$ type process (Scheme 9.24) [49a].

9.5.2 Group 9 and 8 metals

Reductive elimination from octahedral complexes of rhodium(III) and iridium(III) has been examined mainly for C–H bond formation. While some of the complexes undergo a dissociative mechanism similarly to platinum(IV) and palladium(IV) analogs, direct reductive elimination without preliminary ligand loss has also been documented.

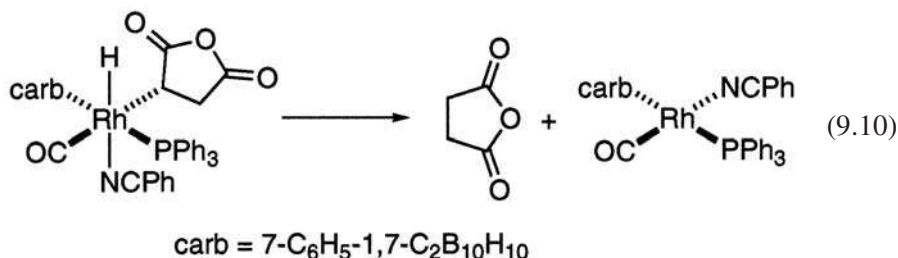
Alkane elimination from *mer*- $\text{RhH(R)Cl(PMe}_3)_3$ involves preliminary dissociation of PMe_3 ligand [57]. Thus $1/k_{\text{obsd}}$ values linearly correlate with the concentration of free PMe_3 added to the system. This observation is consistent with the mechanism involving a five-coordinate intermediate (Scheme 9.25). The reaction



Scheme 9.25.

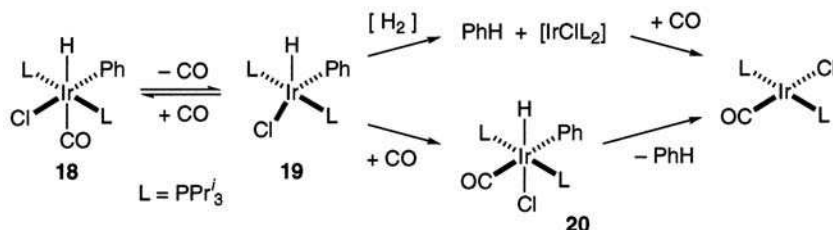
of methoxymethyl complex ($R = \text{CH}_2\text{OCH}_3$) proceeds at 31°C with the following activation parameters [$\Delta H^\ddagger = 25.0$ kcal/mol, $\Delta S^\ddagger = 5.3$ eu, $\Delta G^\ddagger = 23.4$ kcal/mol]. The deuteride complex *mer*-RhD(CD₂OCD₃)Cl(PMe₃)₃ exhibits a small kinetic isotope effect ($k_{\text{H}}/k_{\text{D}} = 1.3$). A similar mechanism has been proposed for the formation of aldehyde from *mer*-RhH(COR')Cl(PMe₃)₃ ($R' = \text{Me}, i\text{-Pr}, \text{Ph}$) [57].

The C–H reductive elimination via ligand dissociation has also been documented for succinic anhydride formation from the iridium(III) complex shown in Eq. 9.10. In this reaction the five-coordinate intermediate is generated by dissociation of the PhCN ligand ($k_{\text{obsd}} = 5.25 \times 10^{-4} \text{ s}^{-1}$ in ClCH₂CH₂Cl at 40°C) [58].

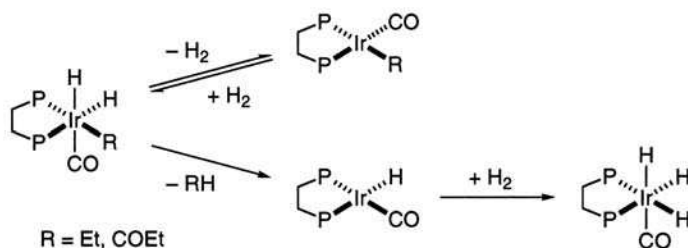


The elimination of H₂ from *cis,cis*-IrH₂Cl(L)(PPh₃)₂ ($L = \text{CO}, \text{PPh}_3$) is induced by flash photolysis [59]. The quantum yield decreases with increase in the concentration of free L, suggesting the mechanism involving a photo-induced dissociation of L, followed by rapid thermal elimination of H₂ from the five-coordinate intermediate IrH₂Cl(PPh₃)₂.

Participation of a five-coordinate intermediate (**19**) has also been suggested by kinetic investigation in the thermolysis of *trans*-IrH(Ph)Cl(CO)(PPr₃^{*i*})₂ (**18**) in toluene (Scheme 9.26) [60]. However, several lines of evidence have indicated that **19** generated by CO dissociation is not the competent intermediate for C–H reductive elimination. Thus the benzene formation proceeds by two other processes. One involves catalytic acceleration by H₂, and the product benzene is eliminated from a six-coordinate species generated by the coordination of H₂ to **19**. On the other hand, the other process involves intermediate **20**, which is a geometrical isomer of **18** and afforded by CO coordination to **19** from the other direction than that for the regeneration of **18**. The reason why **18** is stable while **20** undergoes direct reductive elimination has not been clarified.



Scheme 9.26.



Scheme 9.27.

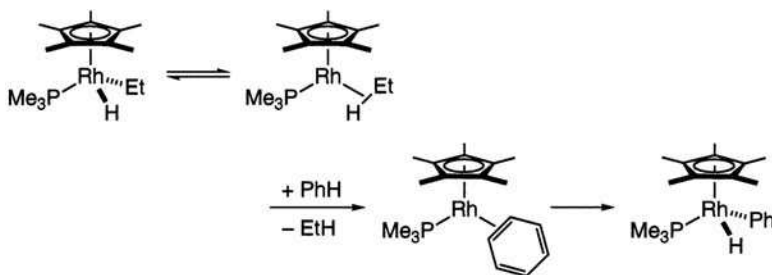
Unlike the above examples, the reductive elimination from *cis,cis*- $IrH_2(R)(CO)(dppe)$ ($R = Et, COEt$) proceeds without ligand loss, as confirmed by kinetic experiments (Scheme 9.27) [61]. The H_2 elimination is a reversible process, whereas the RH elimination proceeds irreversibly. The activation parameters are as follows [EtH elimination: $\Delta H^\ddagger = 20.2$ kcal/mol, $\Delta S^\ddagger = -10.9$ eu, $\Delta G^\ddagger = 23.4$ kcal/mol at $25^\circ C$; EtCHO elimination: $\Delta H^\ddagger = 22.3$ kcal/mol, $\Delta S^\ddagger = -11.0$ eu, $\Delta G^\ddagger = 25.6$ kcal/mol at $25^\circ C$; H_2 elimination: $\Delta H^\ddagger = 15.5$ – 16.5 kcal/mol, $\Delta S^\ddagger = -23.3$ to -23.7 eu, $\Delta G^\ddagger = 22.6$ – 23.4 kcal/mol at $25^\circ C$]. All reactions exhibit a normal primary kinetic isotope effect [$k_H/k_D = 2.4$ (EtH), 1.4 (EtCHO), 1.5–1.6 (H_2)]. The EtH and EtCHO eliminations constitute the product-forming step in hydrogenation and hydroformylation of ethylene catalyzed by $IrH_3(CO)(dppe)$, respectively.

Competitive reductive elimination of C–H and Si–H bonds from $IrH(SiHPh_2)(mesityl)(CO)(dppe)$ has been compared by kinetic experiments [62]. Activation parameters are as follows [C–H bond elimination: $\Delta H^\ddagger = 21.8$ kcal/mol, $\Delta S^\ddagger = -5.0$ eu, $\Delta G^\ddagger = 23.3$ kcal/mol at $25^\circ C$; Si–H bond elimination: $\Delta H^\ddagger = 15.6$ kcal/mol, $\Delta S^\ddagger = -25.2$ eu, $\Delta G^\ddagger = 23.1$ kcal/mol at $25^\circ C$]. The Si–H bond elimination is easier than the C–H bond elimination at lower temperatures, while the former becomes unfavorable at higher temperatures ($>34^\circ C$) owing to the more negative entropy of this path. The hydrido-mesityl-silyl complex does not undergo C–Si reductive elimination to give mesitylsilane. The preferential reductive elimination of C–H and Si–H bond over C–Si bond has been reported also for *mer*- $IrHMe(SiR_3)(PMe_3)_3$ ($SiR_3 = SiPh_3, Si(OEt)_3, SiEt_3$) [63].

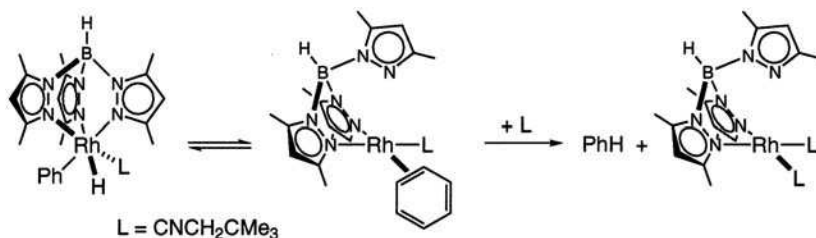
A kinetic study has been carried out for the O–H reductive elimination from *mer*-IrH(OMe)Cl(PR₃)₃ (R = Me, Et) to give methanol [64a]. Unlike the C–H reductive elimination from the alkyl–hydride analogs in Scheme 9.25, the rate of O–H reductive elimination is not influenced by addition of free phosphine, showing the reaction mechanism without preliminary ligand dissociation. Similarly, it has been reported that the thermal elimination of pyrrole from *cis,trans*-IrH₂(*N*-pyrrolyl)(L)(PPh₃)₂ (L = CO, PPh₃) is not affected by added L [64b]. However, in this case, the N–H reductive elimination has been considered to be initiated by irreversible ligand loss to give a five-coordinate intermediate since the reaction is effectively accelerated by photo-induced ligand dissociation [65].

Alkane elimination from Cp^{*}MH(alkyl)L (M = Rh, Ir) and its related complexes bearing Tp^{*} (tris(3,5-dimethylpyrazolyl)borate) or Cn (1,4,7-trimethyl-1,4,7-triazacyclononane) ligand instead of Cp^{*} has been studied in connection with its microscopic reverse process, the oxidative addition of a C–H bond of alkanes [66–68]. A common observation for these systems is the occurrence of intramolecular hydrogen scrambling between the hydrido and alkyl ligands during the reductive elimination. Also observed is an inverse kinetic isotope effect for deuteride complexes: $k_H/k_D = 0.7$ for Cp^{*}IrH(C₆H₁₁)(PMe₃) in C₆D₆ at 130°C [66a], 0.5 for Cp^{*}RhH(C₂H₅)(PMe₃) in toluene-*d*₈ at –30°C [66b], 0.62 for Tp^{*}RhH(CH₃)(CNCH₂CMe₃) in C₆D₆ at 36°C [67], and 0.74 for [CnRhH(CH₃)(PMe₃)] [BAR₄] in C₆D₆ at 75°C [68a]. These observations are consistent with the reductive elimination mechanism involving an alkane-coordinated intermediate, which affords the product alkane via associative displacement of the alkane ligand by an external ligand. Scheme 9.28 shows a typical example, in which solvent benzene serves as the external ligand.

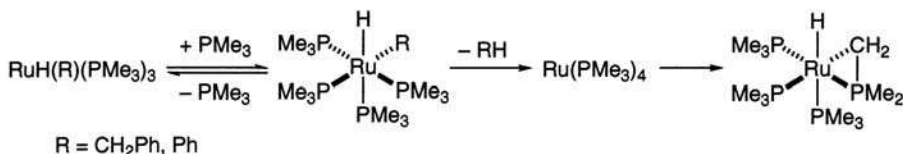
Arene elimination from Cp^{*}- or Tp^{*}-coordinated aryl–hydride complexes follows a similar reaction process, while this reaction involves an η^2 -arene complex as a relatively stable intermediate [69,70]. The mechanism proposed for Tp^{*}RhH(Ph)(CNCH₂CMe₃) is given in Scheme 9.29 [70]. The first step is the formation of a benzene-coordinated intermediate via C–H reductive elimination involving κ^3 – κ^2 rearrangement of the Tp^{*} ligand. The benzene ligand is subsequently displaced by an external L (CNCH₂CMe₃) to afford the final products.



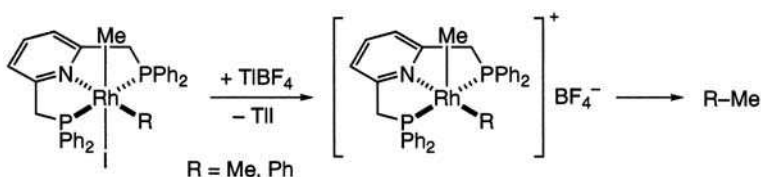
Scheme 9.28.



Scheme 9.29.



Scheme 9.30.

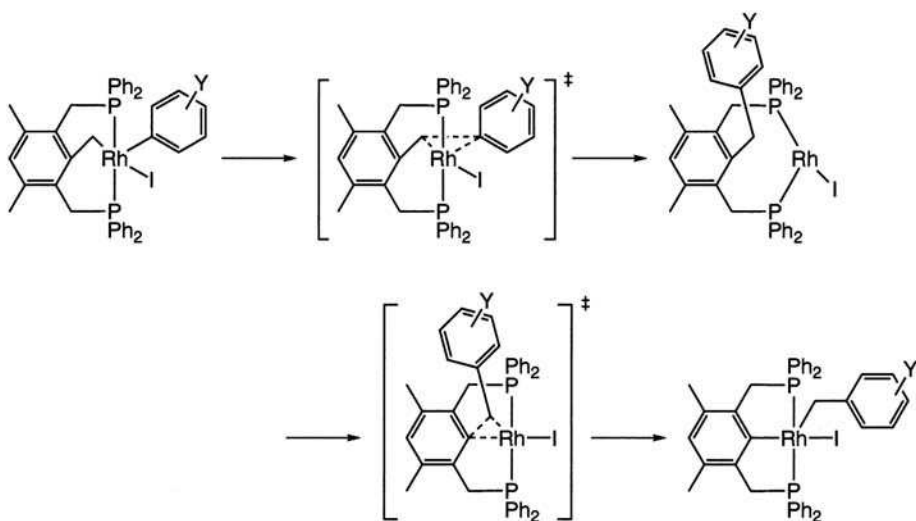


Scheme 9.31.

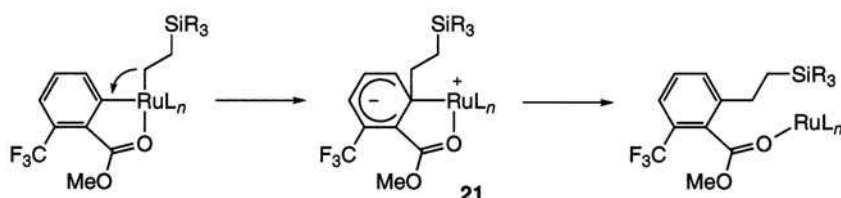
The mechanism of C–H reductive elimination from $\text{RuH(R)(PMe}_3)_4$ ($R = \text{CH}_2\text{Ph}, \text{Ph}$) has been examined in detail [71]. While the ruthenium(II) complexes undergo rapid reversible dissociation of one of the PMe_3 ligands in solution, the reductive elimination has been found to proceed directly from the six-coordinate complexes, not from the five-coordinate species (Scheme 9.30). The resulting $\text{Ru(PMe}_3)_4$ undergoes intramolecular C–H activation to give a ruthenium(II) hydride bearing a metallacyclopropane structure.

Diorganorhodium iodide bearing a PNP ligand (Scheme 9.31) is fairly stable in acetone but undergoes C–C reductive elimination at room temperature by its conversion into a five-coordinate cationic intermediate [72]. It has been pointed out that the reaction is suppressed by the coordination of acetonitrile to the sixth coordination site.

The C–C reductive elimination from a five-coordinate rhodium(III) species has been reported also for the PCP chelate complex given in Scheme 9.32 [73]. While the C–C bond formation is followed by oxidative addition of the resulting benzyl–aryl bond to give a benzylrhodium(III) complex, the reductive elimination constitutes the rate-determining step. The reaction is faster as the aryl ligand is substituted by more electron-donating group(s). This trend is consistent with the observation reported for C–H reductive elimination from $\text{Cp}^*\text{RhH(Ar)(PMe}_3)$ [69c].



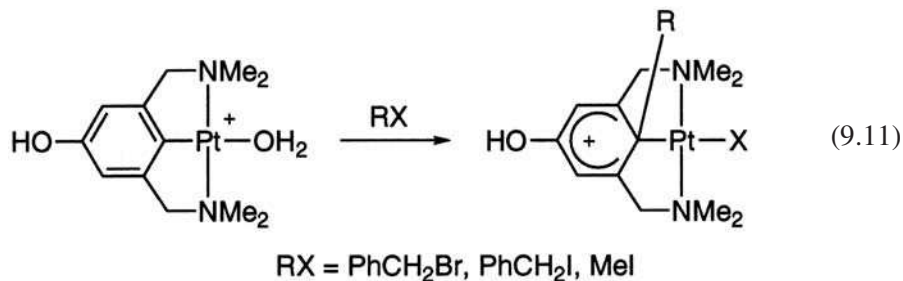
Scheme 9.32.

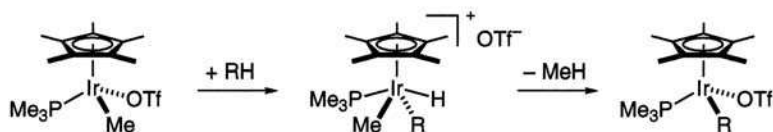


Scheme 9.33.

Ruthenium complex-catalyzed addition of C–H bonds of aromatic esters to olefins involves C–C reductive elimination as the product forming step [74], for which a migratory reductive elimination process involving a zwitter ionic intermediate **21** has been proposed (Scheme 9.33) [75].

Platinum(IV) complexes with a structure analogous to **21** have been isolated (Eq. 9.11) [76].





Scheme 9.34.

9.6 REDUCTIVE ELIMINATION FROM OTHER METAL COMPLEXES

9.6.1 d^4 , d^2 , and d^0 metal complexes

The complexes $\text{Cp}^*\text{IrMe}(\text{OTf})(\text{PMe}_3)$ and $[\text{Cp}^*\text{IrMe}(\text{CH}_2\text{Cl}_2)(\text{PMe}_3)]^+[\text{BAR}_4]^-$ undergo C–H activation of alkanes to give alkyl complexes and methane [77]. Recent theoretical and experimental studies have suggested that this reaction proceeds by a sequence of oxidative addition and reductive elimination processes of C–H bonds involving a d^4 iridium(V) intermediate, rather than a concerted σ -bond metathesis mechanism (Scheme 9.34) [78,79].

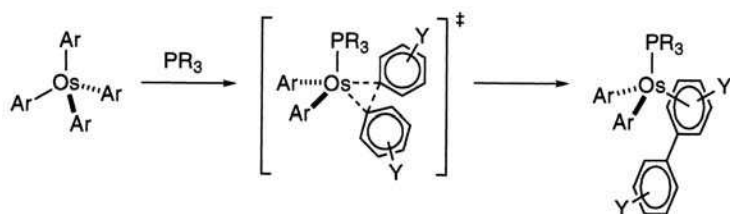
Kinetic studies of C–H reductive elimination from the alkyl–hydrido complexes bearing a d^2 metal center have been reported [80–82]. Similarly to the reactions of d^6 metal complexes, the reductive elimination proceeds via an alkane-coordinate intermediate, as supported by the observation of an inverse kinetic isotope effect. Representative data are as follows: $k_{\text{H}}/k_{\text{D}} = 0.75$ for $\text{Cp}_2\text{W}(\text{H})(\text{Me})$ in CD_3CN at 72.6°C [80], 0.77 for $\text{Cp}^*_2\text{W}(\text{H})(\text{Me})$ in C_6D_6 at 100°C [81], 0.8 for $[\text{Cp}_2\text{Re}(\text{H})(\text{Me})]^+[\text{Cl}]^-$ in CD_2Cl_2 at 9°C [82].

In contrast to the facile C–H reductive elimination from $\text{Cp}^*_2\text{W}(\text{H})(\text{R})$ ($\text{R} = \text{Me}, \text{CH}_2\text{Ph}$), C–C, H–H, and O–H reductive elimination from $\text{Cp}^*_2\text{WMe}_2$, Cp^*_2WH_2 , and $\text{Cp}^*_2\text{W}(\text{H})(\text{OH})$, respectively, have been found to be rather difficult processes [81].

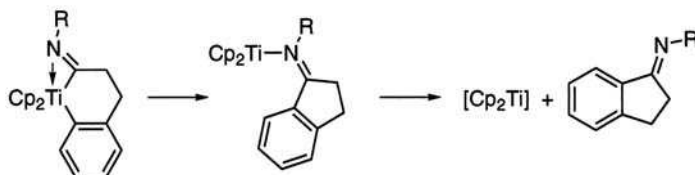
The complex $[\text{Cp}^*\text{Ir}(\text{H})_3(\text{PPh}_3)]^+\text{BF}_4^-$ undergoes solvent-induced elimination of Cp^*H [83]. The reaction readily proceeds in acetonitrile with a good coordination ability [$\Delta H^\ddagger = 16.5$ kcal/mol, $\Delta S^\ddagger = -19.6$ eu, $k_{\text{obsd}} = 1.6 \times 10^{-4} \text{ s}^{-1}$ at 20°C], while no reaction takes place in neat CH_2Cl_2 . A reductive elimination mechanism involving successive η^5 to η^3 to η^1 ring slippage mediated by acetonitrile has been proposed.

On the other hand, biaryl formation from OsAr_4 complexes ($\text{Ar} = \text{MeC}_6\text{H}_4$, $\text{Me}_2\text{C}_6\text{H}_3$, MeFC_6H_3) in toluene- d_8 is induced by the coordination of P-donors such as PMe_3 and $\text{P}(\text{OMe})_3$ [84]. Since the reaction obeys the second-order rate law ($-\text{d}[\text{OsAr}_4]/\text{dt} = k[\text{PR}_3][\text{OsAr}_4]$) and involves an extremely large negative entropy ($\Delta S^\ddagger = -43$ to -53 eu; $\Delta H^\ddagger = 5.0$ – 7.9 kcal/mol at 25°C), it has been considered that the ligand coordination and the C–C bond formation are operative synchronously (Scheme 9.35).

A kinetic examination has been carried out for C–C reductive elimination from the titanocene iminoacyl complexes given in Scheme 9.36 [85]. The reaction



Scheme 9.35.

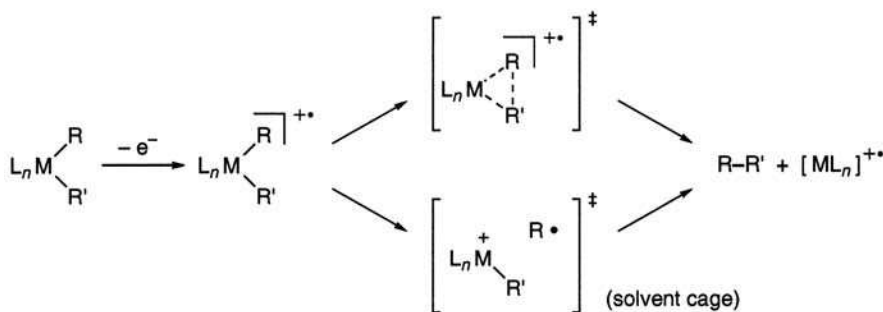


Scheme 9.36.

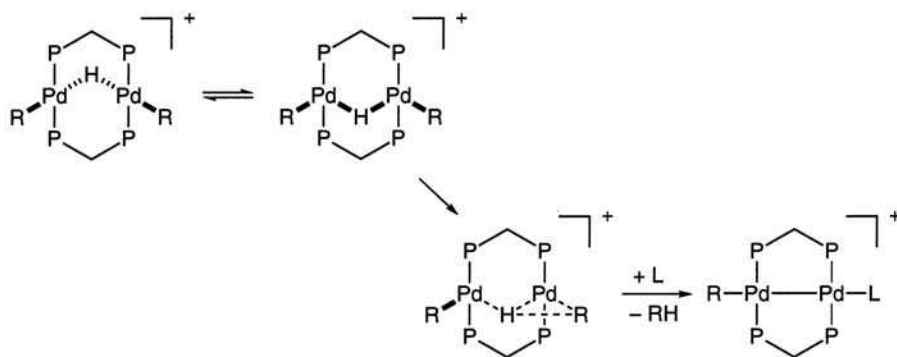
follows first-order kinetics and more readily proceeds as the R substituent on the nitrogen atom is more electron-withdrawing. On the other hand, the reaction rate is little affected by the solvent or by the presence of free PMe_3 . Based on these kinetic observations, a concerted reductive elimination process involving an η^1 -imine intermediate has been proposed.

9.6.2 Oxidatively induced reductive elimination

Since the reductive elimination involves reduction in the formal oxidation state, the reactivity of an organometallic complex may be enhanced by oxidation of the metal center, most typically by two-electron oxidation. For example, dialkylplatinum(II) complexes are fairly stable but after the oxidative addition of alkyl halides the resulting trialkylplatinum(IV) halides readily undergo C–C reductive elimination (see Section 9.5.1). On the other hand, there have been several examples where one-electron oxidation also has a pronounced effect on the rate acceleration of reductive elimination. Early instances have been documented for the complexes bearing the first-row metals (e.g., *trans*- $\text{NiMe}(\text{aryl})(\text{PET}_3)_2$ [86], *cis*- $\text{FeR}_2(\text{bipy})_2$ ($\text{R} = \text{Me}, \text{Et}$) [87], *cis*- $[\text{CoR}_2(\text{bipy})_2]^{2+}$ [88], Cp_2TiR_2 [89]), and more recently for the complexes with the second- and third-row metals (e.g., $\text{Cp}^*\text{RhMe}_2(\text{PPh}_3)$ [90], CnRhMe_3 ($\text{Cn} = 1,4,7\text{-trimethyl-1,4,7-triazacyclononane}$) [91], $\text{Cp}^*\text{Ir}(\text{R})(\text{R}')(\text{PPh}_3)$ ($\text{R}/\text{R}' = \text{H}/\text{H}, \text{H}/\text{Me}, \text{Me}/\text{Me}$) [92], $\text{RuR}_2(\text{CO})(\text{P}(\text{Bu}_2\text{Me})_2)$ [93]). The reductive elimination reaction proceeds by either a concerted mechanism or a stepwise process with homolytic cleavage of one bond followed by radical abstraction within the solvent cage (Scheme 9.37).



Scheme 9.37.



Scheme 9.38.

9.6.3 Reductive elimination from two metals

Reductive coupling of two organic ligands from a pair of metal complexes has already been reviewed [94]. More recently, kinetic studies on reductive elimination from di- and tri-nuclear metal complexes have been reported [95,96]. For C–H reductive elimination reactions from dipalladium complexes with the A-frame structure $[\text{Pd}_2\text{R}_2(\mu\text{-H})(\mu\text{-dppm})_2]^+$, a concerted mechanism involving a W-shaped intermediate has been proposed (Scheme 9.38) [95a].

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