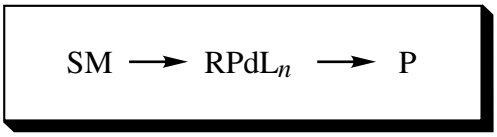

II.3 Organopalladium Compounds Containing Pd(0) and Pd(II)

II.3.1 General Discussion of the Methods of Synthesis and *In Situ* Generation of Organopalladium Compounds

EI-ICHI NEGISHI

A. INTRODUCTION

As indicated in **Table 3** of **Sect. I.2**, there are at least ten general methods for the generation of organopalladium compounds represented by general patterns **1**–**10**. Inasmuch as these processes are generally reversible, their microscopic reversals, that is, general patterns **10**–**19**, provide ten general methods for the decomposition of organopalladium compounds through C—Pd bond cleavage in addition to various types of processes involving nucleophilic and electrophilic attacks on ligands. Although attention will mainly be focused on C—Pd bond formation in this section, it should clearly be noted that the discussions presented for C—Pd bond formation may be adapted to C—Pd bond cleavage with due modifications.

In order to avoid or minimize redundancy, the 19 General Patterns are classified into six categories, as summarized in **Table 1**, and all patterns in each category are discussed as a unit. Many processes of Pd complexes involve a pair of patterns that are microscopic reversals of each other, such as complexation and decomplexation (or dissociation) in ligand substitution. Migration of Pd via a series of hydropalladation–dehydropalladation and reversible carbonylation via migratory insertion–deinsertion are additional representative examples.

B. COMPLEXATION AND DECOMPLEXATION

Most of the stable and isolatable Pd complexes obey the 18- or 16-electron rule.[1] Pd(0) complexes [e.g., $Pd(PPh_3)_4$] tend to exist as coordinatively saturated 18-electron tetrahedral

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TABLE 1. GENERAL PATTERNS OF FORMATION AND CLEAVAGE OF CARBON–PALLADIUM BONDS

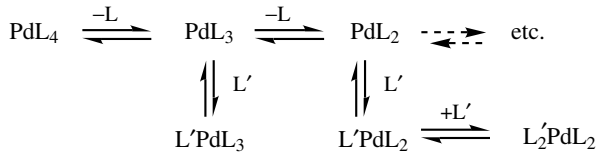
	Category	C—Pd Bond Formation	C—Pd Bond Cleavage
I.	Complexation and decomplexation	*Pattern* **1**: σ-Complesation *Pattern* **2**: π-Complexation *pattern* **3**: Oxidative complexation	*Pattern* **11**: σ-Decomplexation *Pattern* **12**: π-Decomplexation *Pattern* **13**: Reductive decomplexation
II.	Oxidative addition and reductive elimination	*Pattern* **4**: Oxidative addition	*Pattern* **14**: Reductive elimination
III.	Additions and elimination	*Pattern* **5**: Hydropalladation *Pattern* **6**: Metallopalladation *Pattern* **7**: Heteropalladation *Pattern* **9**: Carbopalladation	*Pattern* **15**: Dehydropalladation *Pattern* **16**: Demetallopalladation *Pattern* **17**: Deheteropalladation *Pattern* **19**: Decarbopalladation
IV.	Migatory insertion and migratory deinsertion	*Pattern* **8**: Migratory deinsertion	*Pattern* **18**: Migratory insertion
V.	Transmetallation	*Pattern* **10**: Transmetallation	
VI.	Nucleophilic or electrophilic attack on ligands		*Pattern* **20**

d^{10} complexes, but they can readily dissociate (or decomplex) into coordinatively unsaturated 16- or less-electron d^{10} species (**Scheme 1**). The extent of ligand dissociation with phosphines increases in the order $PMe_3 < PMe_2Ph < PMePh_2 < PEt_3 < PPh_3 < P(Pr\text{-}i)_3 < PCy_3 < PPh(Bu\text{-}t)_2$. On the other hand, Pd(II) complexes [e.g., $Cl_2Pd(PPh_3)_2$] tend to exist as coordinatively unsaturated 16-electron square planar d^8 complexes. Although they are reluctant to form coordinatively saturated 18-electron five-coordinate d^8 complexes, such complexes are kinetically readily accessible, and they can serve as transient intermediates in ligand substitution (**Scheme 1**). Pd(II) d^8 complexes may also undergo substitution by dissociative processes, which must involve 14- or less-electron species as transient intermediate (**Scheme 1**). In all of these three processes, one common crucial requirement is coordinative unsaturation or the presence of one or more valence-shell empty orbitals as Lewis acidic sites.

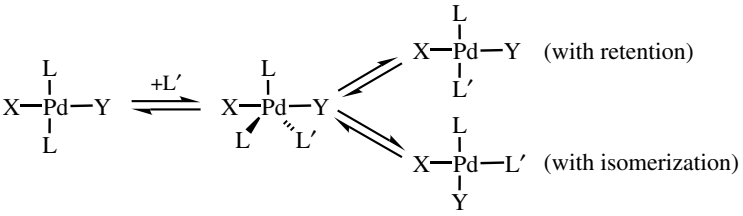
Factors affecting the rate and equilibrium of ligand substitution include (i) the nature of the ligand to be incorporated, especially its nucleophilicity or basicity, (ii) the electrophilicity or acidity of the leaving ligands, and (iii) the nature and stereochemistry of the other ligands. For associative ligand substitution processes of d^8 group 10 metal complexes including Pd(II) complexes, for example, the ligand nucleophilicity order $PR_3 > py > NH_3 > Cl^- > H_2O > OH^-$ and the leaving ability order $NO_3^- > H_2O > Cl^- > Br^- > I^- > N_3^- > SCN^- > NO_2^- > CN^-$ have been reported.[2] The rate of ligand dissociation is also significantly influenced by another ligand *trans* to the one to be dissociated.

This is known as the *trans* effect, which generally decreases in the order $R_3Si^- > H^-$, Me^-, CN^-, olefin, $CO > PR_3$, NO_2, I^-, $SCN^- > Br^- > Cl^- > RNH_2$, $NH_3 > OH^- > NO_3{}^-$, H_2O.[2] It is, however, important to recall that there is no universal acidity or basicity scale and that the orders presented above may be accurate only for those cases that were experimentally examined. So, they should be viewed as vague indications of approximate trends.

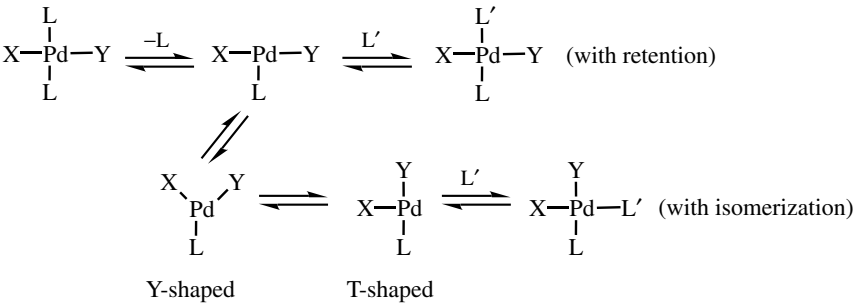
Dissociative ligand substitution reactions of 18-electron d^{10} Pd(0) complexes



Associative ligand substitution reactions of 16-electron d^8 Pd(II) complexes



Dissociative ligand substitution reactions of 16-electron d^8 Pd(II) complexes



Scheme 1

Perhaps more fundamental and important is to recognize the amphiphilic nature of complexation and dissociation, which stems from the fact that the Pd atom in many Pd complexes provides simultaneously one or more empty and filled nonbonding orbitals, as summarized in **Table 2**.

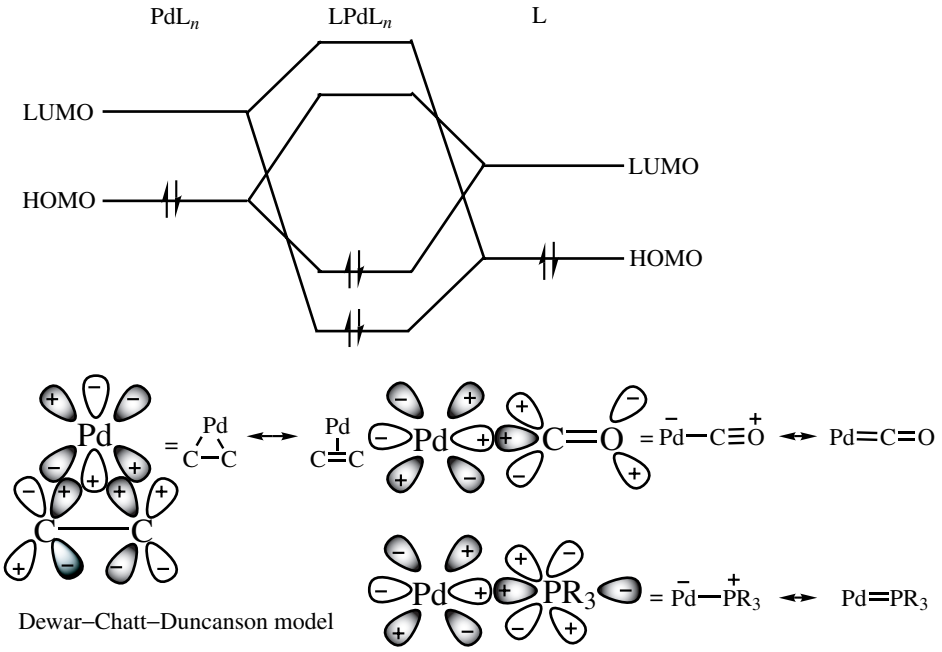
With at least one each of appropriate empty and filled nonbonding orbitals, Pd can be engaged in a synergistic bonding with certain ligands, such as alkenes, CO, and phosphines, leading to strong complexation (**Scheme 2**). The synergistic bonding in alkene–Pd

TABLE 2. NUMBERS OF VALENCE-SHELL EMPTY AND FILLED NONBONDING ORBITALS IN VARIOUS Pd(0) AND Pd(II) COMPLEXES

FOS	d^n	Coordination Number	Electron Count	Number of Empty Orbitals	Number of Filled Nonbonding Orbitals
Pd(O) Complexes					
0	10	4	18	0	5
0	10	3	16	1	5
0	10	2	14	2	5
0	10	1	12	3	5
Pd(II) Complexes					
+2	8	5	18	0	4
+2	8	4	16	1	4
+2	8	3	14	2	4
+2	8	2	12	3	4

complexes is most commonly described in terms of the Dewar–Chatt–Duncanson model[3],[4] (**Scheme 2**), and similar synergistic bonding schemes have been used to explain the bondings in OC—Pd and R_3P—Pd complexes (**Scheme 2**).

One important feature of the synergistic bonding between Pd and ligand is that the directions of electron flow or transfer in donation and backdonation are opposite to each other and that the electronic effects exerted by substitutents in the participating



Scheme 2

ligand and those by other ligands on Pd should therefore be opposite in donation and backdonation. The overall substituent and ligand effects are determined by the relative influences of donation and backdonation, even though donation appears to be always more dominant in the absolute magnitudes of bond energies. As indicated in **Scheme 11** of **Sect. I.2**, Pd(II) complexes tend to act as electrophiles, while Pd(0) complexes are more nucleophilic. Indeed, donation is usually the dominant factor in complexation with Pd(II) complexes, which is promoted by electron-donating substituents of alkenes, while backdonation is generally the more influential of the two with Pd(0) complexes. In such cases, electron-withdrawing substituents promote complexation.

As mentioned earlier, oxidative complexation (pattern **3**) and reductive decomplexation (pattern **13**) are nothing but alternate representations of π-complexation (pattern **2**) and π-decomplexation (pattern **12**), respectively. It might be useful to note that the π-complex formalism and palladacyclopropane formalism correspond to the Walsh model[5] and more commonly used bent σ-bond representation of cyclopropanes, respectively. The palladacyclopropane formalism is useful in discussing the formation of larger palladacycles in terms of carbopalladation of palladacyclopropanes and palladcyclopropenes (**Part IV**).

C. OXIDATIVE ADDITION AND REDUCTIVE ELIMINATION

C.i. Background

Oxidative addition and reductive elimination are two generic chemical terms embracing various types of chemical transformations proceeding by many different mechanisms.[2] In this section, only the mononuclear processes involving a Pd(0) complex and an RX, where R is a C group and X is a halogen or a related leaving group, will be considered mainly from the viewpoint of the formation of organopalladium compounds (**Scheme 3**). On the surface, this process is akin to the formation of the Grignard reagents from RX and Mg, which is indeed an example of oxidative addition. As mentioned earlier, the equation shown in **Scheme 3** merely represents a starting compound–product relationship, and various different reactions represented by **Scheme 3** have indeed been shown to proceed by different mechanisms. The microscopic reversal of the forward process in **Scheme 3** is a reductive elimination reaction, which is not explicitly discussed here. Synthetically more important reductive eliminations are those in which X is a C, H, N, O, or metal group extensively discussed throughout this Handbook, especially in **Parts III** and **VII**, and the mechanistic aspects of carbon–carbon reductive elimination are discussed in detail in **Sect. III.2.19**.

$$Pd(0)L_n + RX \rightleftharpoons RPd(II)L_nX$$

Scheme 3

C.ii. Some Facts

The currently available factual information about **Scheme 3** may be summarized as follows:

1. Organic halides and related electrophiles containing proximal π-electron donors are generally reactive toward Pd(0) complexes. They include the following classes of compounds arranged in decreasing order of reactivity:

Allyl Propargyl	>	Benzyl, Acyl	>	Akenyl Alkynyl	>	Aryl	>>	simple Alkyl

The facts shown above indicate that β,γ-unsaturated halides and other electrophiles are some of the most reactive classes of compounds.[6] Although generally less reactive, α,β-unsaturated derivatives are also generally reactive and practically useful.[7] On the other hand, simple alkyl halides lacking a proximal unsaturation are generally insufficiently reactive. Relatively little is known about the effects of more remote π-bonds and of proximal *n*-electron donors, but the results observed for (*E*)-2-methyl-1,4-diiodo-1-butene shown in **Scheme 2** of **Sect. I.2** clearly indicate that homoallyl halides must be far less reactive than alkenyl halides. These results collectively point to the probable significance of prior π-complexation as a binding process and probable subsequent intramolecular interaction of Pd with C—X bonds.

2. Approximate orders of reactivity of various leaving groups are as follows:

$$I > OTf > Br > Cl >> F$$

$$OZ > NZ_2 > CZ_3, \quad \text{where Z is any atom or group}$$

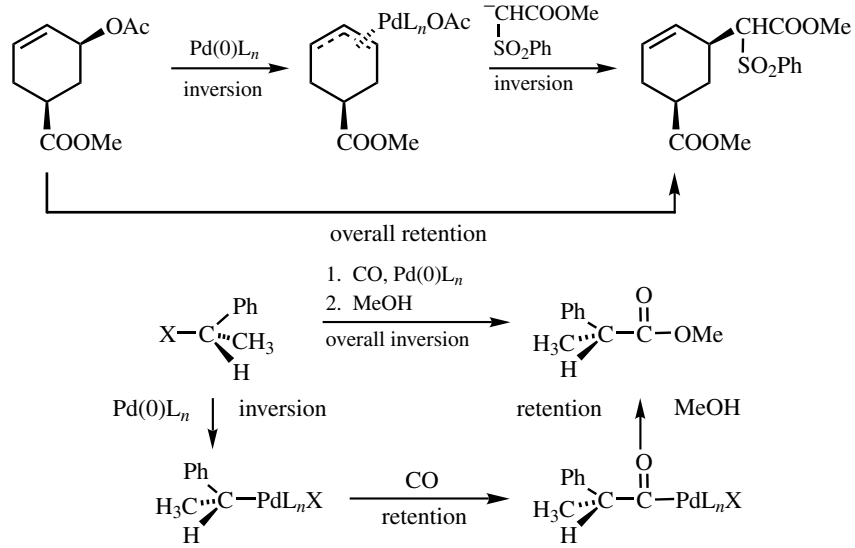
Alkenyl, aryl, and alkynyl derivatives are sufficiently reactive in catalytic processes in cases where X is I, OTf, and Br. Although progress is being made to utilize their chlorides (cf. **Part III**), their synthetic utility is still rather limited. On the other hand, acyl chlorides are very reactive. Likewise, allyl, propargyl, and benzyl chlorides are also very reactive toward Pd(0) complexes. In fact, allyl derivatives are kinetically so reactive that a bewildering array of leaving groups including practically the full range of oxy functionalities, such as various sulfonates, phosphates, carbonates, carboxylates, aryl ethers, and even silyl ethers,[8] can serve as satisfactory leaving groups in a Pd-catalyzed reactions.

3. Oxidative addition of aryl, alkynyl, and acyl derivatives can proceed only with retention of configuration. It is important to note that stereodefined alkenyl derivatives generally undergo oxidative addition with strict retention of configuration, ruling out radical processes for the transformation. On the other hand, allyl, propargyl, and benzyl derivatives generally proceed with strict inversion of configuration, indicating that the mechanism of their oxidative addition is distinct from that observed with alkenyl halide. It is, however, also feasible to observe oxidation or addition of allylic electrophiles proceeding via retention of configuration.

Inversion of configuration observed with allyl[9] and benzyl[10] derivatives has been deduced from the results summarized in **Scheme 4**. In the case of allyl derivatives, a very reasonable and seemingly unmistakable assumption that nucleophilic attack on π-allyl ligands takes place on the side opposite to Pd was made.[9] On the other hand, an equally plausible assumption that migratory CO insertion and methanolysis of acylpalladium derivatives both proceed with retention.[10]

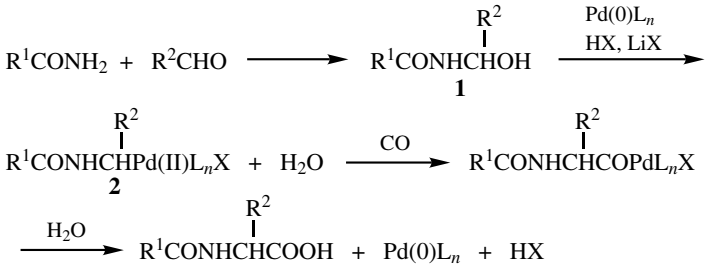
4. In accordance with the general notion that Pd(0) complexes are more nucleophilic than electrophilic, electron-withdrawing substituents in the substrates facilitate oxidative

addition. The observed order of reactivity, such as *p*-NO_2 > *p*-NC > *p*-PhCO > *p*-Cl > H, is roughly proportional with their Hammett σ constants.[11] Also consistent with the notion mentioned above are the effects of ligands on the ease of oxidative addition discussed briefly in **Sect. II.2.3**.



Scheme 4

5. Some appropriately heteroatom-substituted alkyl electrophiles undergo oxidative addition to Pd. For example, the carbonylative synthesis of α-amino acids from aldehydes and carboxamides shown in **Scheme 5**[12] must involve oxidative addition of **1** formed by the reaction of an aldehyde and a carboxamide to Pd to produce an α-amidoalkylpalladium species **2** as intermediate. It is likely that many other proximally heteroatom-substituted alkyl electrophiles will be found to undergo oxidative addition to Pd.



Scheme 5

C.iii. Mechanisms

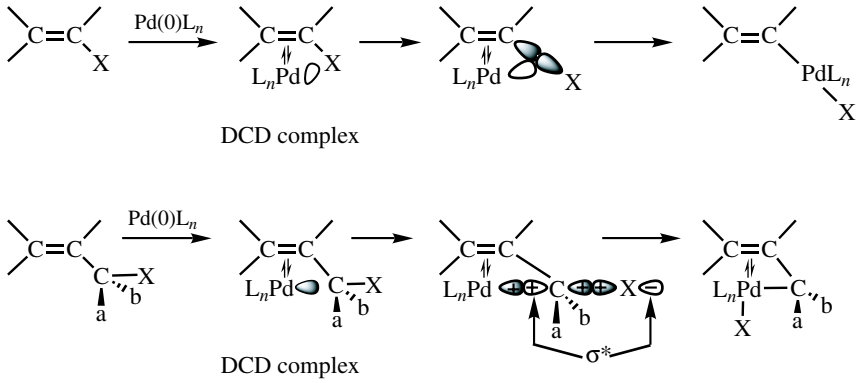
A fair number of investigations have been made on the oxidative addition of Pd(0) complexes with organic halides and related electrophiles, and a reasonable mechanistic

discussion as of the mid-1970s was presented by Stille and Lau.[10] Some notable features with suggested modifications are presented below.

1. The fact that α,β- and β,γ-unsaturated organic derivatives display high reactivity toward Pd(0) complexes indicates that prior or concurrent π-complexation is significant. This in turn indicates that a coordinative unsaturation must be one crucial feature that is either required or highly desirable. In the case of acyl halides C═O π-bonds must be critically involved.

2. Stereospecificity, retention or inversion, tends to rule out radical processes for oxidative addition of proximally unsaturated derivatives and strongly supports concerted processes involving the synergistic interaction represented by the Dewar–Chatt–Duncanson model (**Scheme 2**).

3. Although not yet firmly established, it is likely that a Pd atom bound to a proximal π-bond frontally interacts with its second pair of empty and filled nonbonding orbitals with a C—X bond of alkenyl, alkynyl, and aryl derivatives, as in **Scheme 6**, leading to retention of configuration. In the cases of allyl, propargyl, and benzyl derivatives, a π-bond-captured Pd atom may then undergo an intramolecular "S_N^2-like" substitution leading to Walden inversion (**Scheme 6**). In presenting orbital interaction schemes in **Scheme 6**, only the most crucial features are shown to avoid excessive congestion. For the reaction of benzyl derivatives, frontal attack by Pd at the benzylic carbon center leading to inversion via pseudorotation was suggested,[10] but its plausibility is unclear. It seems certain that Pd(0) complexes must be coordinatively unsaturated for π-complexation. At least in the cases of alkenyl, alkynyl, and aryl derivatives, the ready availability of the second empty orbital appears to be also essential. This does not necessarily require 14-electron Pd complexes, because the overall process can proceed stepwise involving two 16-electron species. In an overall sense, however, Pd(0) complexes that can effectively serve as 14-electron species are required for oxidative addition. In this connection, a recent suggestion based on kinetic studies that oxidative addition of aryl halides with Pd(0) complexes must proceed via monocoordinate 12-electron species[13] is very interesting. The concentration of such species under any conditions must be very low. However, if this suggestion is correct, it would be another eloquent manifestation of the Curtin–Hammett principle.[14]

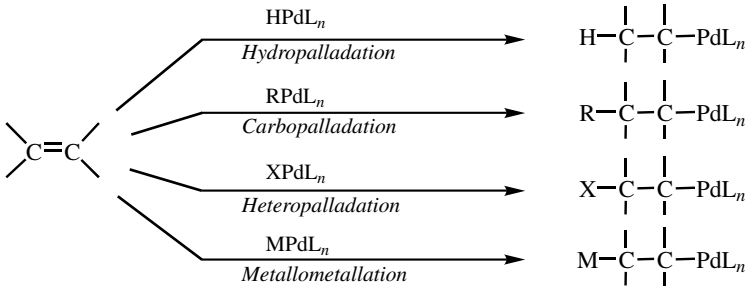


Scheme 6

D. INSERTION OF ALKENES AND ALKYNES VIA ADDITION OF Pd(II) COMPLEXES: HYDROPALLADATION, CARBOPALLADATION, HETEROPALLADATION, AND METALLOPALLADATION

D.i. General Discussion

Various addition reactions of alkenes and alkynes have been termed insertion processes. As the term insertion per se is a nonchemical term, it might be conveniently substituted with hydrometallation (H—M), carbometallation (C—M), heteroatom-metallation or heterometallation (X—M), and metallometallation (M—M), depending on the σ-bond that is added to π compounds. These addition reactions involving Pd are represented by the general equations using alkenes as representative π compounds as shown in **Scheme 7**. The alkenes in **Scheme 7** may be replaced with alkynes and other π compounds.



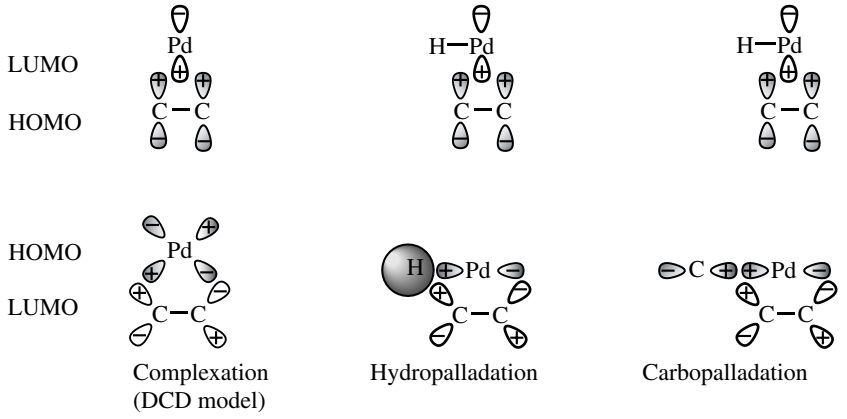
Scheme 7

D.ii. Hydropalladation and Carbopalladation

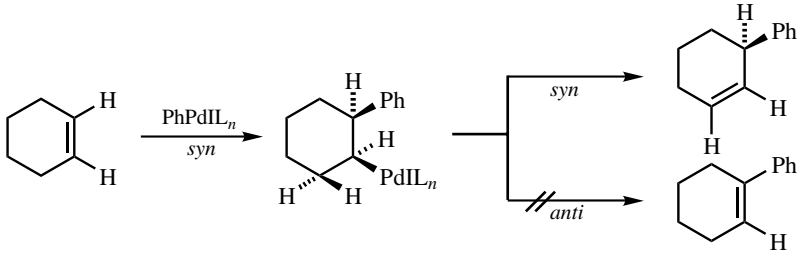
Hydropalladation and carbopalladation can proceed very readily with a variety of alkenes and alkynes, and they share some common critical features. Thus, they generally involve strict *syn* addition of H—Pd and C—Pd bonds, respectively. These features are in agreement with a concerted mechanism involving interaction of an empty orbital of Pd with a π-bond of alkenes or alkynes and that of H—Pd or C—Pd σ-bond with a π^*-orbital, as shown in **Scheme 8**. It should be noted that the overall synergistic bonding scheme for hydropalladation or carbopalladation is very closely related to the Dewar–Chatt–Duncanson (DCD) model[3],[4] for π-complexation. In the schemes for hydropalladation and carbopalladation, the nonbonding Pd d orbital of the DCD model is substituted with a H—Pd and C—Pd σ-orbital, respectively. In all of these concerted processes, the presence or ready availability of a Pd empty orbital is critically important.

Stereochemistry. There are ample experimental indications that both hydropalladation (pattern **5**) and carbopalladation (pattern **8**) as well as their microscopic reversals (patterns **15** and **18**) are, at least in the great majority of cases, strict *syn* addition processes, as predicted by the concerted mechanism shown in **Scheme 8**. In the hydropalladation and carobpalladation reactions of alkynes, the stereochemical course of the reactions is readily seen and unmistakable. However, clear-cut and explicit demonstration of the

stereochemistry of the corresponding reactions of alkenes is rather rare, and their stereochemistry is usually inferred from the overall consequences of some Pd-catalyzed reactions. Thus, for example, the Pd-catalyzed reaction of cyclohexene with PhI gives 3-phenyl-1-cyclohexene rather than the expected and thermodynamically more stable 1-phenyl-1-cyclohexene[15] (**Scheme 9**). The results can readily be accommodated in terms of strict *syn*-carbopalladation and *syn*-dehydropalladation.



Scheme 8

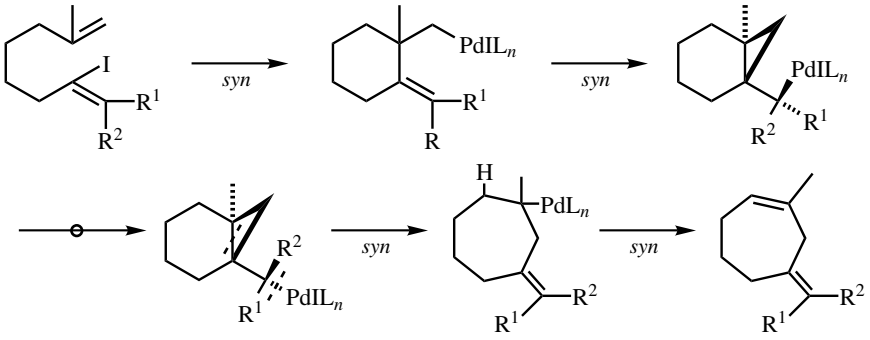


Scheme 9

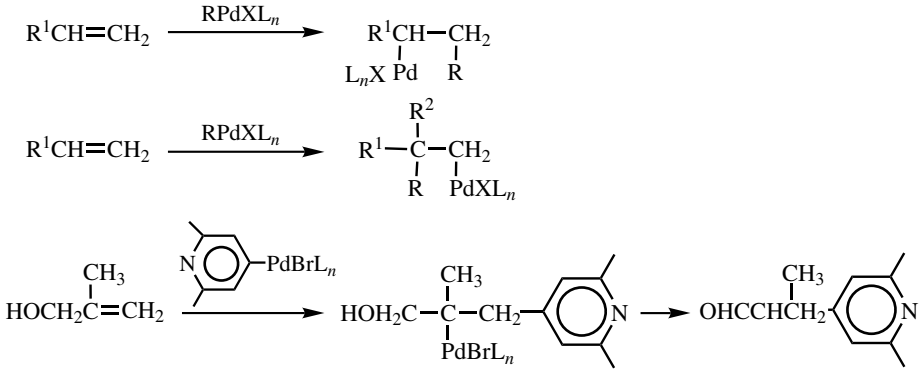
An indication of the strict requirement for *syn*-carbopalladation and *syn*-decarbopalladation can be seen in a complete and initially puzzling stereochemical inversion observed in an apparent endocyclic carbopalladation reaction shown in **Scheme 10**.[16]

Regiochemistry. In contrast with the uniform stereochemistry, the regiochemistry of hydropalladation and carbopalladation depends significantly on various factors, such as substitution pattern and substituents in alkenes and alkynes. In the case of carbopalladation, its cyclic version may display much different regiochemistry than the acyclic version. The capricious nature of the regiochemistry of hydropalladation and carbopalladation is readily seen in the results shown in **Scheme 11**. Thus, the reaction places Pd predominately in the internal position in the cases of monosubstituted alkenes containing simple carbon groups. This is "abnormal" among various hydrometallation reactions, such as hydroboration and hydrozirconation. This regiochemistry can be significantly altered by substitution patterns and substituents. Curiously, 1,1-disubstituted alkenes tend to place Pd in the terminal position, which is opposite to the case of

monosubstituted alkenes. However, there are many exceptions to the above generalization, as exemplified by the reaction of methallyl alcohol shown in **Scheme 11**.



Scheme 10



Scheme 11

Substituent Effects on Hydropalladation and Carbopalladation. As repeatedly mentioned earlier, Pd(II) species are electrophilic. So, hydropalladation and carbopalladation as well as other addition reactions of Pd(II) complexes are accelerated by electron-donating substituents in π-compounds. Any substituents can also exert steric and some other kinds of effects as well. So, the overall substituent effects are the sum of all these factors, of which electronic and steric effects are usually the most dominant ones. The rates of the Heck reaction[17] of various alkenes decrease in the following order: $CH_2{=}CH_2 > CH_2{=}CHOAc > CH_2{=}CHMe > CH_2{=}CHPh > CH_2{=}CMePh$.

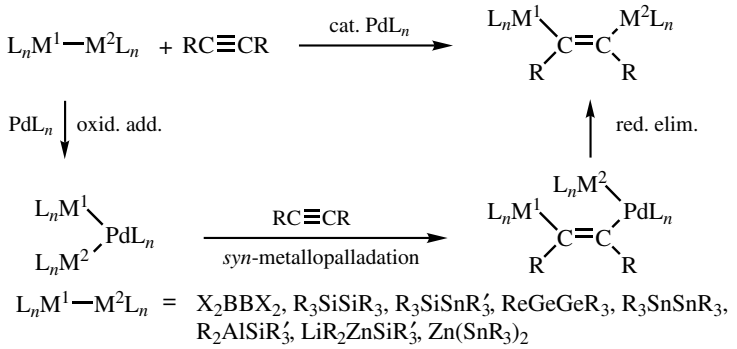
Monosubstituted alkenes with a simple alkyl substituent place about 80% of Pd in the internal position. More electron-withdrawing substituents, such as aryl, carbonyl including ketones and esters, cyano, and nitro groups, place essentially 100% of Pd in the internal position,[17] even though their reactions are relatively slow. Intramolecular cyclic carbopalladation producing three-, five-, and six-membered rings generally favor the "exo" mode of cyclization. On the other hand, the formation of large rings tends to involve the "endo"-mode carbopalladation producing large ring (*E*)-cycloalkenes.[18]

Various aspects of carbopalladation are discussed in detail, mainly in **Part IV**, and those of hydropalladation are discussed mainly in **Part VII**. A large number of Pd-catalyzed reactions involving hydropalladation are also discussed throughout the Handbook.

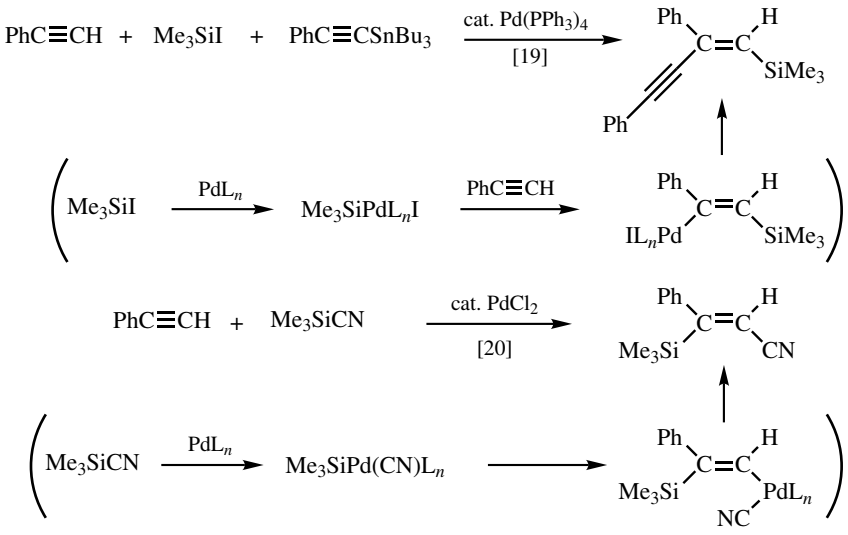
D.iii. Metallopalladation

Various metal–metal bonded compounds containing relatively electronegative metals, such as Si, Ge, Sn, B, Al, and Zn, can undergo Pd-catalyzed metallometallation, which mostly involves *syn*-addition to alkynes. One plausible mechanistic scheme involves (i) oxidative addition of metal–metal bonded compounds to Pd, (ii) metallopalladation (pattern **6**) leading to *syn*-addition of metal–Pd bonds, and (iii) reductive elimination (**Scheme 12**). As such, the overall mechanism resembles that of Pd-catalyzed hydrogenation or hydrosilation, and the critical metallopalladation step must be mechanistically closely related to those of hydropalladation and carbopalladation. These reactions are discussed in detail in **Sect. VII.5**.

Although generation of metal–Pd bonded species for metallopalladation has been achieved mostly via oxidative addition of metal–metal bonded species to Pd, other metal-containing compounds capable of undergoing oxidative addition to Pd may also



Scheme 12

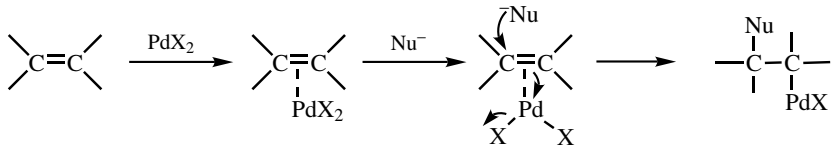


Scheme 13

be used as precursors to metal–Pd bonded species. Some such examples are shown in **Scheme 13**.

D.iv. Halopalladation, Oxypalladation, Aminopalladation, and Other Heteropalladation Reactions

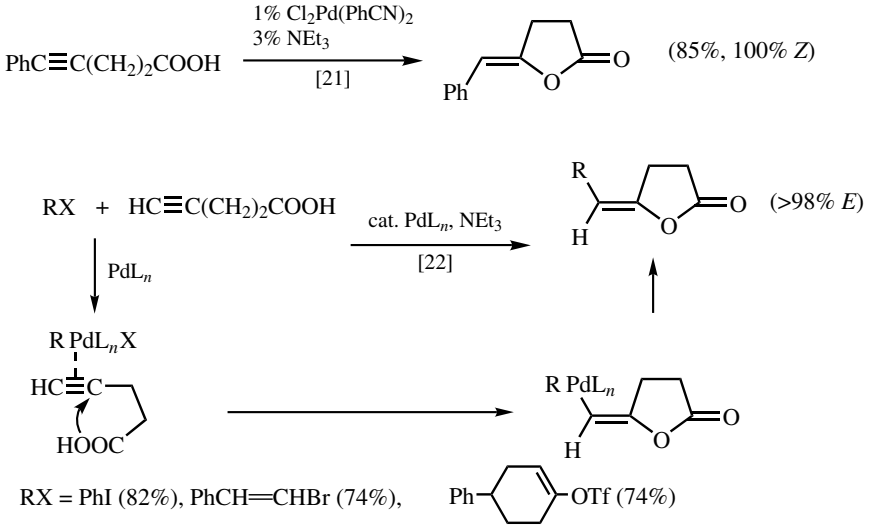
Addition of heteroatom–Pd bonds to alkenes and alkynes may proceed via either *syn*- or *anti*-addition. Although mixtures of stereoisomers may be formed, heteropalladation can be highly stereoselective in many cases. In general, *anti*-addition is more widely observed than *syn*-addition, and this reaction is thought to involve nucleophilic attack on Pd-complexed π-ligands on the side opposite to Pd (**Scheme 14**). A wide variety of nucleophilic heteroatom groups including halides, (i.e., Cl^-, Br^-, and I^-), various oxygen groups, such as H_2O, alcohols, carboxylic acids, and their anions, related S- and Se-containing groups, amines, amides, and their anions participate in this *anti*-addition process, which can also be classified as pattern **20** in **Table 1**.



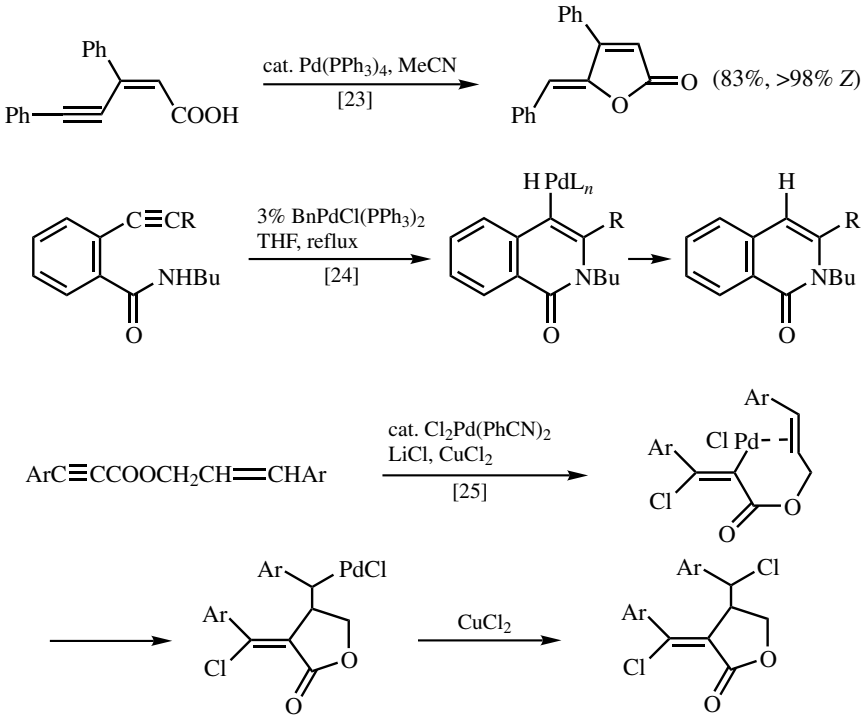
Nu^- = halides (Cl^-, Br^-, and I^-), O, S, Se, N, and other heteroatom nucleophiles

Scheme 14

In cases where alkynes are used as substrates, the overall stereochemical outcome of Pd-catalyzed reactions that are thought to proceed via heteropalladation is unmistakably clear. Some representative examples are shown in **Scheme 15**.



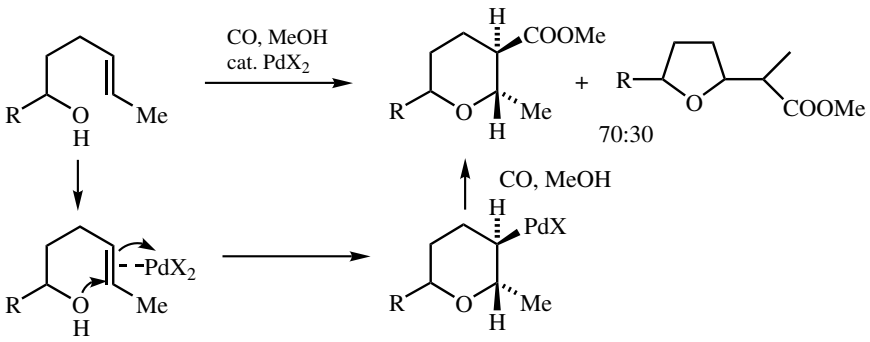
Scheme 15



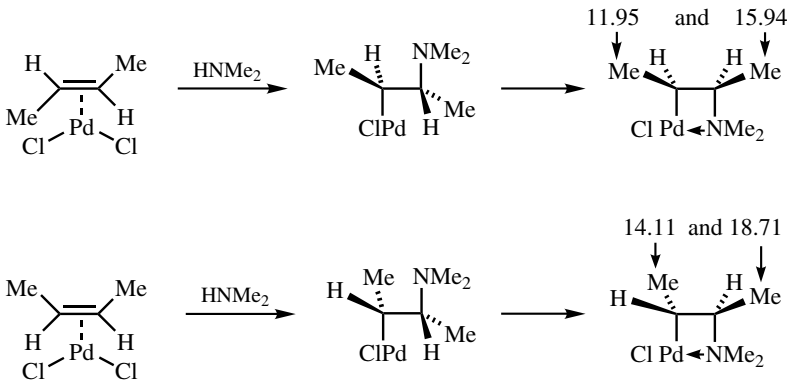
Scheme 15 (*Continued*)

Even in the cases of alkenes, cyclic heteropalladation involving geometrically defined alkenes can provide clear stereochemical information as in **Scheme 16**.[26]

In intermolecular heteropalladation of simple alkenes, clarification of the stereochemistry is somewhat more difficult and involved. Thus, for example, the *anti*-stereochemistry of aminopalladation to alkenes was established by running a pair of reactions using both (*E*)- and (*Z*)-2-butenes and comparing the NMR spectra of the products,[27] as summarized in **Scheme 17**.



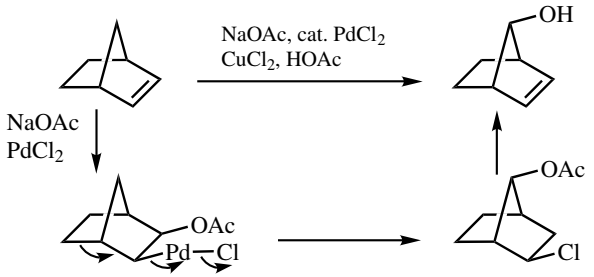
Scheme 16



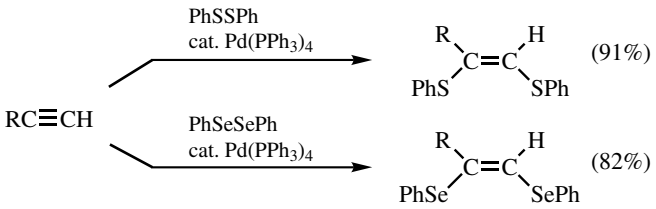
Scheme 17

Although the results shown in **Schemes 15–17** amply demonstrate the predominance of the *anti*-addition in heteropalladation, various factors can readily render the *syn*-heteropalladation reactions more favorable than the corresponding *anti*-addition processes. Such *syn*-addition processes may well be concerted as in the cases of hydropalladation and carbopalladation. As a representative example, norbornene has been converted to *syn*-7-norbornenol,[28] which can readily be explained in terms of *syn*-oxypalladation–rearrangement–elimination, as shown in **Scheme 18**.

Diaryl disulfides and diselenides undergo Pd-catalyzed *syn*-addition of S—S and Se—Se bonds, which may be most readily explained in terms of (i) oxidative addition of S—S and Se—Se bonds, (ii) *syn*-heteropalladation, and (iii) reductive elimination[29] (**Scheme 19**).



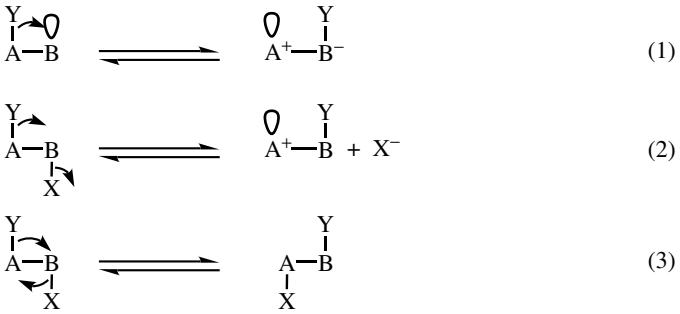
Scheme 18



Scheme 19

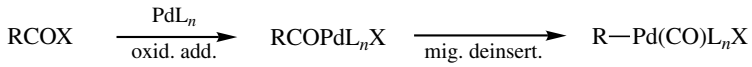
E. MIGRATORY INSERTION AND MIGRATORY DEINSERTION

Migratory insertion (pattern **18**) and migratory deinsertion (pattern **8**) represent some of the most fundamental processes for bond formation and cleavage. These processes are often called 1,2-shifts. Many organic processes, such as Wagner–Meerwein rearrangement, pinocol–pinacolone rearrangement, Beckmann rearrangement, and Bayer–Villiger reaction, are considered to be 1,2-shift processes.[30] The great majority of these reactions appear to contain concerted processes as key elements regardless of whether they are polar or nonpolar, and 1,2-shift processes proceeding by radical mechanisms appear to be very rare. Concerted 1,2-shift processes generally proceed with retention of configuration of the migratory group (Y). They may involve (i) a coordinatively unsaturated migration terminus (i.e., B in Eq. 1), (ii) a coordinatively saturated migration terminus undergoing inversion (i.e., B in Eq. 2), or (iii) double migratory insertion leading to transposition of X and Y as in Eq. 3 (**Scheme 20**).



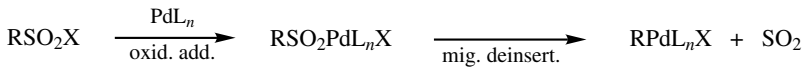
Scheme 20

1,2-Migration of a carbon group from Pd to an adjacent atom (i.e., migratory insertion) (pattern **18**) involves cleavage of a C—Pd bond. On the other hand, its microscopic reversal (i.e., migratory deinsertion) (pattern **8**) generates a C—Pd bond. As is true with many concerted processes, migratory insertion processes are often readily reversible even under mild reaction conditions. Typically, acylpalladium species can readily undergo migratory deinsertion to give decarbonylated organopalladium species (**Scheme 21**), despite the fact that a number of acylpalladium complexes have been isolated and identified (**Sect. II.3.2**). This can be a useful preparative method in cases where RX does not readily undergo oxidative addition, even though the number of examples demonstrating this synthetic option is still very low.[31]



Scheme 21

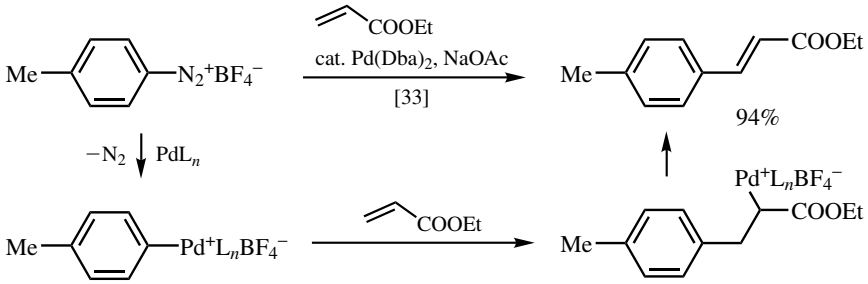
Another potentially useful but not yet widely employed class of electrophiles are sulfonyl chlorides and other halides that can also undergo oxidative addition–migratory deinsertion[32] (**Scheme 22**).



Scheme 22

Despite these interesting and promising possibilities, the current scope of the *in situ* generation of organopalladium derivatives via migratory deinsertion is still rather limited.

Although no 1,2-migratory insertion is involved, aryldiazonium salts have been used to generate organopalladium derivatives via extrusion of a small molecule (i.e., N_2)[33] (**Scheme 23**).

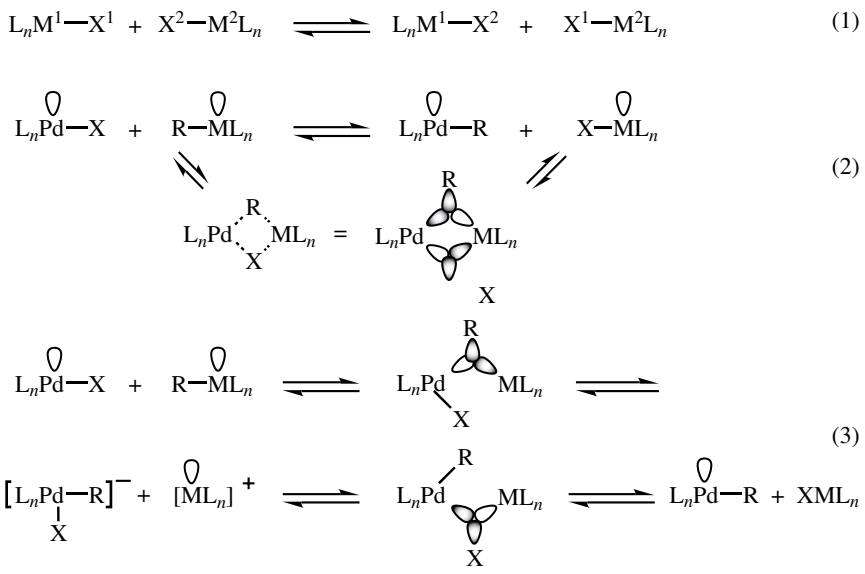


Scheme 23

F. TRANSMETALLATION

Transmetallation represents a class of single bond metathesis reactions in which two organometallic compounds, mostly of two different metals, exchange ligands, as shown in **Scheme 24**.

As indicated in **Scheme 24**, transmetallation is significantly promoted by the presence of a metal empty orbital. In cases where both metals M^1 and M^2 are coordinatively unsaturated, transmetallation is kinetically quite facile, and the eventual equilibrium is thermodynamically dictated. As a rule of thumb, the major driving force is provided by the formation of a bond between the more electropositive metal and the more electronegative ligand. Thus, organometals containing those metals that are more electropositive than Pd including K, Na, Li, Mg, Zn, Al, and Zn undergo facile transmetallation with Pd complexes containing relatively electronegative ligands, as extensively discussed in **Part III**. One must, however, recall the Curtin–Hammett principle[14] discussed in **Sect. I.2**. Thus, thermodynamically unfavorable transmetallation processes may be involved in many Pd-catalyzed reactions provided that the overall process is thermodynamically favorable. Thus, organometals containing relatively electronegative metals, such as organoboranes, organostannanes, and even organosilanes, have participated in Pd-catalyzed reactions (e.g., cross-coupling), which are thought to proceed via transmetallation, as amply discussed in **Part III**. Bases have played important roles in the reactions of organoboranes, suggesting that at least, in some cases, coordinately saturated organoborates might act as reactive species in putative transmetallation processes. In fact, preformed alkynylborates were employed in the initial phase of the Pd-catalyzed cross-coupling of organoboron compounds.[34] In this and many other cases of Pd-catalyzed cross-coupling reactions of



Scheme 24

organoboron, organotin, and organosilicon compounds, nucleophilic organometals may be coordinatively saturated, and their transmetallation processes may not be readily accommodated by the mechanism shown in Eq. 2 of **Scheme 24**. In such cases, a two-stage transmetallation process involving just one empty valence orbital shown in Eq. 3 of **Scheme 24** may be operative. Irrespective of mechanistic details, transmetallation involving Pd complexes has been one of the most general methods for generating σ-bonded organopalladiums along with oxidative addition and several nonredox addition reactions, as discussed throughout this Handbook, especially in **Part III**. As might be expected from the concerted mechanisms shown in **Scheme 24**, transmetallation proceeds with retention of configuration of the R and X groups.

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