

PART I

Introduction and Background

I.1 Historical Background of Organopalladium Chemistry

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This Handbook is all about the use of palladium (Pd) mostly as a component of catalysts for organic synthesis. Today, it is widely recognized that Pd has very significantly changed and improved the art of organic synthesis over the last three decades. It seems reasonable to state that Pd already is one of the most versatile, useful, and hence significant metals in organic synthesis along with Li, Mg, B, Cu and a few others and that its significance is still sharply rising. Over 1000 research publications dealt with the use of Pd mostly in organic synthesis in 1998 alone.

One question this author has frequently encountered is: Why is Pd so versatile and useful? This is indeed a good question, which is not so easy to answer, but some attempts will be made later in **Sect. I.2**. In this section, however, let us look back and try to become acquainted with some of the notable events in the history of organopalladium chemistry with emphasis on the use of Pd in organic synthesis.

In 1912 V. Grignard and P. Sabatier shared, for the first time, a Nobel Prize in chemistry.^[1] It is striking to note that the significance of both Grignard's mostly stoichiometric main group organometallic chemistry and Sabatier's catalytic transition metal chemistry were correctly recognized in a largely prophetic manner by the Royal Swedish Academy of Sciences almost a century ago. It is also striking that the developments of both areas up to that point were rather slow, circuitous, and evolutionary in many ways. The discovery and development of Grignard reagents spanned roughly half a century after Frankland's discovery of Et_2Zn as the first well-recognized main group organometallic compounds in 1849.^[2] It took a few to several decades before organomagnesium chemistry, developed mainly by Barbier,^[3] supplanted that of organozincs. Subsequent studies by Grignard led to the discovery and development of the Grignard reagents.^[4] The significance and synthetic utility of the Grignard reagents have only increased with time. Along with organolithiums developed later,^[5] they continue representing one of the most important classes of organometallic compounds.

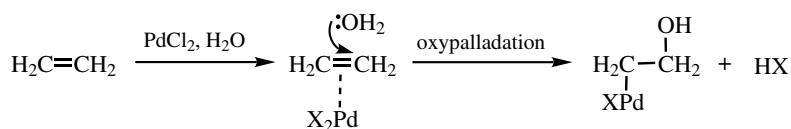
The development of organopalladium chemistry for organic synthesis has been even more sluggish than that of the organometallic chemistry of Mg and Li. It has been reported^[6] that Wollaston in London discovered and isolated Pd in 1803 and named it after the asteroid Pallas, which was discovered a year before. Although an ethylene

complex of Pt, commonly known as Zeise's salt, was reported as early as 1827,^[7] little was known about either organopalladiums or the use of Pd in organic synthesis during the 19th century. Sabatier's systematic investigation of catalytic hydrogenation^{[8],[9]} about a century ago was instrumental in laying the foundation for the widespread use of catalytic hydrogenation in both academia and industry. However, he clearly stated in his Nobel lecture^[9] that catalytic hydrogenation of acetylene with H₂ over Pt black producing ethylene and/or ethane had been reported by von Wilde in 1874.^[10] Moreover, if his Nobel Lecture is an accurate indication, he used mostly Ni along with Pt, Co, Cu, and Ag but perhaps not Pd. As cited by von Wilde, the earliest work on the reduction with H₂ over transition metals appears to be that conceived and suggested by Kolbe^[11] and performed under his guidance and reported by Saytzeff^[12] on the reduction of benzophenone and related carbonyl compounds with H₂ over Pd. By 1912, however, the use of Pd in catalytic reduction including that of alkenes and alkynes had been reported by various chemists including Paal and Amberger^[13] and Wieland,^[14] and the autoclave technology permitting high-pressure catalytic hydrogenation had been introduced by Ipatieff.^[15] As clearly established later, organopalladiums serve as intermediates in these reactions. In this Handbook, catalytic hydrogenation and related addition reactions are discussed mainly in **Part VII**, with other related reactions being discussed in several other sections including **II.2.1**, **II.2.5**, **III.3.1**, and **VI.2.4**. As important as these earlier developments of Pd-catalyzed hydrogenation and related reduction reactions were in the area of organic synthesis, they nevertheless represented an isolated, largely technological, and practical discipline and had remained so until recently.

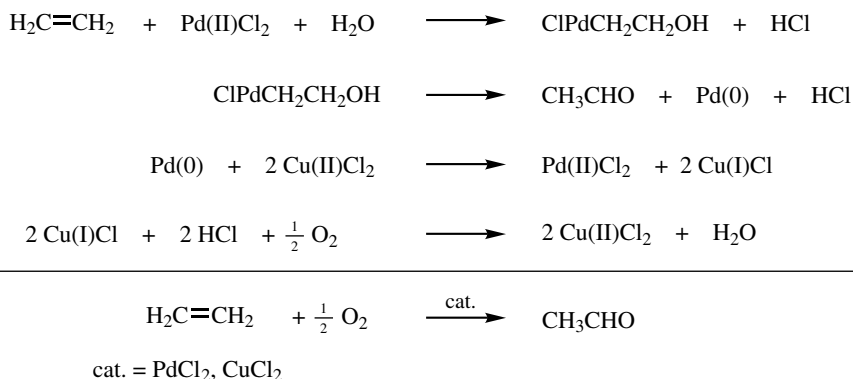
Neither Roelen's development^[16] of the "oxo" process in the 1930s nor the wide-scope investigations of organotransition metal chemistry led by Reppe^[17] during World War II made Pd an important transition metal for organic synthesis, even though Pd may have shown some catalytic activities in these investigations.

Invention of the Wacker process^[18] in 1959 and its subsequent development represent one of the most important milestones in the history of organopalladium chemistry. Although not widely known, the stoichiometric conversion of ethylene to acetaldehyde by the action of PdCl₂ under aqueous conditions, which was accompanied by precipitation of Pd black, was reported as early as 1894.^[19] Aside from the historical intricacy, however, the catalytic hydrogenation and the Wacker oxidation firmly established that Pd and its compounds can serve as catalysts for both reduction and oxidation. At its core, the Wacker process involves a stoichiometric oxypalladation–dehydropalladation tandem (**Scheme 1**), and the development of a catalytic process required an exquisitely engineered two-stage oxidation involving O₂ and CuCl₂.^[18] (**Scheme 2**), as detailed in **Sect. V.3**. More recent results have clearly indicated that the scope of the Wacker oxidation can be and has indeed been expanded far beyond the initial oxidation of ethylene and 1-alkenes to give aldehydes and ketones. Thus, related aminopalladation, halopalladation, and other addition reactions of heteroatom–Pd bonds have been developed. Furthermore, these addition reactions can provide organopalladium intermediates that can be used further for the formation of additional bonds including C—C bonds (**Sect. V.3**).

In the meantime, many other types of oxidation reactions catalyzed by Pd have also been discovered and developed. These other Pd-catalyzed oxidation reactions are discussed in **Part VIII**. For some practical reasons, however, a few additional oxidation reactions involving C—C bond formation are discussed in earlier sections, such as **Sects. III.2.20**, **VI.4.4**, and **VI.7**.



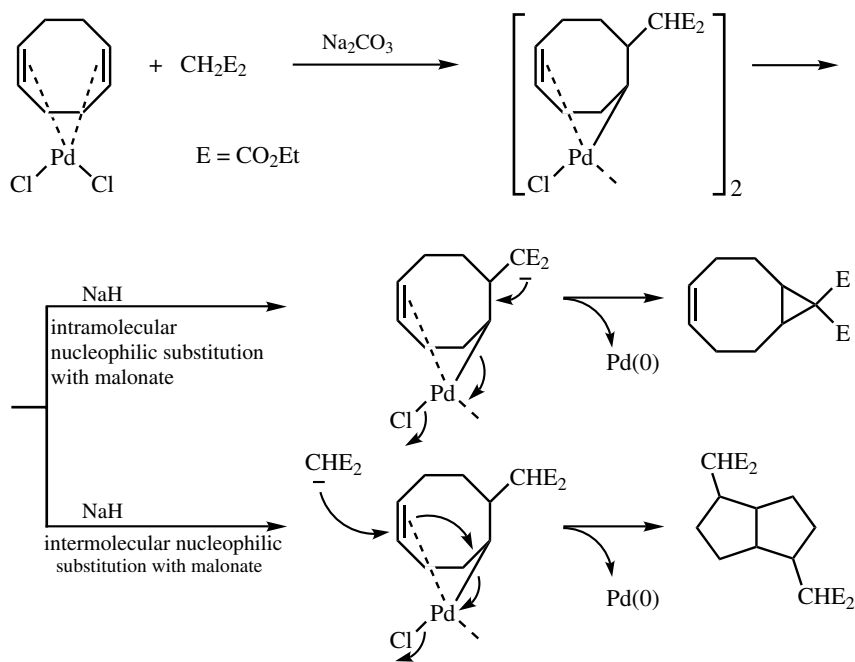
Scheme 1



Scheme 2

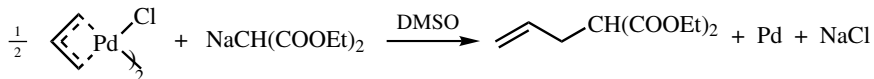
Mechanistic consideration of the Wacker reaction, which is thought to involve nucleophilic attack of ethylene complexed with Pd by H₂O, led to the discovery of a carbon-carbon bond-forming reaction of 1,5-cyclooctadiene-Pd π -complex with ethyl malonate in the presence of Na₂CO₃ by Tsuji et al. in 1965^[20] (**Scheme 3**). Researchers^[21] admit that an analogy between the organopalladium derivatives in **Scheme 3** and π -allylpalladium complexes was drawn and exploited in the discovery of the reaction of π -allylpalladium with malonate also in 1965 (**Scheme 4**). It is noteworthy that this reaction remained only stoichiometric in Pd for several years. Once its catalytic version^{[21],[22]} was developed, however, this reaction has been extensively developed by Tsuji,^[23] Trost,^[24] and many others, as detailed in **Sect. V.2**. Today, it is widely referred to as the Tsuji-Trost reaction, and it represents one of the most widely investigated areas of the organopalladium chemistry (**Scheme 4**).

The birth of the Heck reaction, another important Pd-catalyzed C—C bond-forming reaction, was not straightforward either. In 1968, Heck^[25] reported the reaction of organometals containing Hg, Sn, and Pb with alkenes in the presence of one equivalent of a Pd(II) complex leading to substitution of an alkenyl hydrogen with a carbon group of the organometallic reagent, typically an organomercury (**Scheme 5**). Here again, however, history has been skewed by frequent and unfortunate omission of a closely related stoichiometric reaction by Moritani and Fujiwara^[26] reported in 1967 and shown at the bottom of **Scheme 5**. Unfortunately, both of these stoichiometric reactions were as such not very attractive from the synthetic viewpoint. It was not until three to four years later that Mizoroki et al.^[27] and Heck and Nolley^[27a] reported what is now generally referred to as the Heck reaction, sometimes called the Mizoroki-Heck reaction (**Scheme 5**). As detailed in **Part IV**, this reaction has been shown to proceed via addition of C—Pd bond to alkenes (i.e., carbopalladation), followed by dehydropalladation (**Scheme 6**). The use of the term “Heck reaction” should be limited to those processes that involve this carbopalladation-dehydropalladation sequence, be they stoichiometric or catalytic. It is

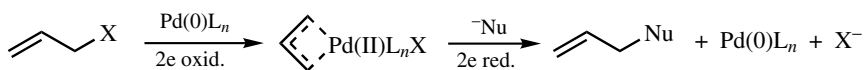


Scheme 3

Original stoichiometric version

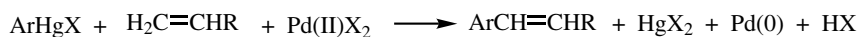


Catalytic version of the Tsuji–Trost reaction

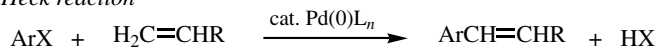


Scheme 4

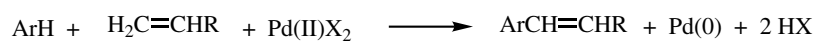
Stoichiometric Heck reaction



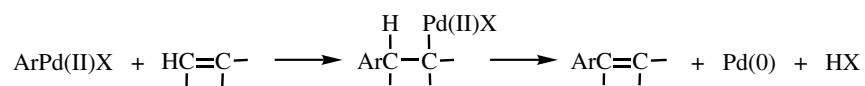
Catalytic Heck reaction



Stoichiometric Moritani–Fujiwara reaction



Scheme 5

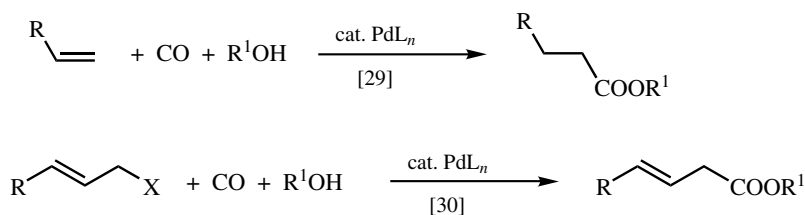


Scheme 6

important to do so because the scope of carbopalladation itself is considerably broader than that of the Heck reaction, as can readily be seen in **Part IV**. For example, Blomquist and Maitlis^[28] earlier investigated Pd-catalyzed cyclic oligomerization reactions of alkynes proceeding via a series of carbopalladation, which do not fall within the definition of the Heck reaction.

The full synthetic scope and utility of those reactions that involve carbopalladation including the Heck reaction became apparent only in the 1980s through extensive investigations by a number of workers, as detailed in **Part IV**. The scope of carbopalladation may conceptually be further expanded so as to include addition reactions of palladium–carbene complexes as well as palladacyclopropanes, palladacycloprenes, and higher palladacycles. These reactions are also discussed in **Part IV** (i.e., **Sects. IV.9** and **IV.10**).

It is generally agreed that Roelen's discovery of the hydroformylation reaction^[16] was the birth of the transition metal-catalyzed carbonylation. Initially, Co catalysts were most extensively used, but the Rh-based processes have since been developed as a superior methods. Although Pd may have been tested along with several other metals, such as Fe, Ru, and Ni, it has never been shown to be very useful in the hydroformylation reaction, sometimes called the "oxo" process. A publication in 1963 by Tsuji et al.^[29] on a related but clearly different reaction of alkenes with CO and alcohols in the presence of a Pd catalyst producing esters was one of the earliest, if not the earliest, reports describing a successful and potentially useful Pd-catalyzed carbonylation reaction. This was soon followed by the discovery of another Pd-catalyzed carbonylation reaction of allylic electrophiles with CO and alcohols^[30] (**Scheme 7**).

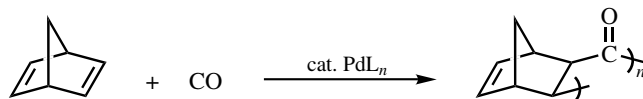


Scheme 7

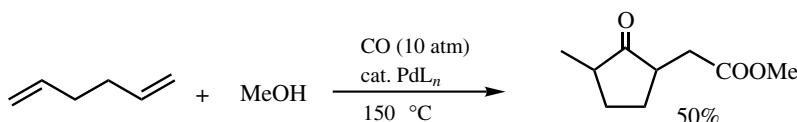
By 1974 the latter reaction had been generalized, and a wide variety of organic halides and other related electrophiles including alkenyl and aryl halides had been used, most notably by Heck and co-workers.^[31] Also developed in his study was a related carbonylation reaction for the synthesis of amides.^[32] Use of organometals and metal hydrides in place of alcohols and amines most notably by Steffy and Stille^[33] further expanded the scope of Pd-catalyzed carbonylation.

Yet another important development in the area of Pd-catalyzed carbonylation is the development of acylpalladation and related carbonyl–Pd bond addition reactions. Acylpalladation may be defined as a process of acyl–Pd bond addition to alkenes and alkynes. Clearly, it is a kind of carbopalladation reaction. For practical reasons, however, it is discussed in **Part VI** together with other carbonylation reactions mentioned above. Tsuji and Hosaka^[34] reported in 1965 what appears to be the first example of the perfectly alternating alkene–CO copolymerization (**Scheme 8**). Independently, Brewis and Hughes^[35] reported also in 1965 a Pd-catalyzed cyclic carbonylation of dienes with CO and methanol (**Scheme 9**). Although the exact mechanism of the initiation is unclear, these reactions

must involve acylpalladation for crucial C—C bond formation. As promising as they were, they remained a couple of isolated studies until about 1980.



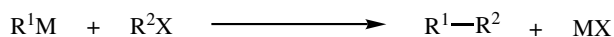
Scheme 8



Scheme 9

The potential for industrial use of the perfectly alternating alkene–CO copolymers recognized primarily by Shell^[36] triggered intensive investigations throughout the world, as detailed in **Sect. VI.4.2**. Independently and concurrently, a systematic investigation of the cyclic acylpalladation was initiated by Negishi and co-workers^{[37]–[40]} using ω -alkene-substituted organic halides. This has led to the discovery and development of several different carbonylation reactions involving CO and π -compounds, as discussed in **Sects. VI.4.1** and **VI.4.3**.

Cross-coupling between organometals and organic electrophiles, such as organic halides, is not only one of the most straightforward methods but also the potentially most general method for the formation of carbon–carbon bonds (**Scheme 10**). Even so, the development of cross-coupling in general and of the Pd-catalyzed version in particular has been surprisingly sluggish. In fact, Pd-catalyzed cross-coupling was one of the last to be developed among the several fundamentally different patterns of C—C bond formation that are widely observable with Pd, as discussed further in **Sect. I.2**.



Scheme 10

Before the 1960s, the scope of cross-coupling as defined above was largely limited to those involving Mg and Li. In general, organometals containing these metals undergo synthetically useful cross-coupling only with certain relatively unhindered alkyl halides, such as those containing methyl, primary alkyl, allyl, and benzyl. Unsaturated organic halides containing C_{sp}²—X and C_{sp}—X bonds do not generally undergo cross-coupling with organolithiums and Grignard reagents. Even their reactions with alkyl halides are subject to various side reactions, such as β and α eliminations, halogen-metal exchange leading to the formation of homocoupled products, and so on, in addition to their competitive reactions with other electrophilic functional groups present in the reactants. Although there were some exceptions, such as alkylation of alkynylmetals containing Li and Mg, direct cross-coupling was, in the main, something to be avoided and substituted with more reliable but more circuitous enolate-based methods. Introduction and development of organocopper-based methods in the 1960s^[41] solved many of the difficulties mentioned above. Nonetheless, a number of other problems remained unsolved.

In 1972, Tamao et al.^[42] as well as Corriu and Masse^[43] reported independently that the reaction of Grignard reagents with alkenyl or aryl halides could be catalyzed by Ni complexes, especially Ni–phosphine complexes. A related study of the stoichiometric carbon–carbon coupling reaction of diorganynickel derivatives by Yamamoto et al.^[44] is also noteworthy. Although many other transition metal-catalyzed reactions of Grignard reagents with organic halides without the use of phosphines were known, these so-called Kharasch-type reactions,^[45] with the exception of the Cu-catalyzed versions,^{[46]–[48]} were not well suited for cross-coupling due to various complications including cross-homo scrambling.

The discovery of Pd-catalyzed cross-coupling was more subtle and evolutionary. Formation of C—C bonds via reductive elimination of diorganypalladium–phosphine complexes was reported in the early 1970s,^[49] but no catalytic procedure was developed. During the 1975–1976 period, several groups of workers including Cassar,^[50] Murahashi et al.^[51] Baba and Negishi,^[52] Fauvarque and Jutand,^[53] and Sekiya and Ishikawa^[54] reported seemingly independently some Pd-catalyzed cross-coupling reactions. The alkyne version of the Heck reaction by Dieck and Heck^[55] and its variant involving the use of Cu(I) salts developed by Sonogashira et al.^[56] were also reported during the same period. In most of these studies, however, one or two papers were published in a rather fragmentary manner, but the systematic studies by Negishi and co-workers^{[52],[57]–[63]} during the 1976–1978 period clearly pointed to the current vision and scope and thus established the foundation for the current broad-spectrum Pd-catalyzed cross-coupling. As detailed in **Sect. III.1**, the studies during this period generated many notable findings, such as (i) generality with respect to the metal counteranions including Zn,^{[57]–[59],[62]} B,^{[62],[63]} Al,^{[52],[61]} Sn,^[62] and Zr,^{[60],[61]} in addition to Mg^[51]; (ii) development of both hydrometallation–cross-coupling^[52] and carbometallation–cross-coupling^[61] tandem procedures with Al and Zr demonstrating some distinct advantages of Pd over Ni; (iii) development of protocols using metals of intermediate electronegativity including Zn, Al, and Zr for superior reactivity and chemoselectivity; and (iv) demonstration of double metal catalysis involving Pd and added metal compounds, especially ZnCl₂ and ZnBr₂.^[61] During this period, related Pd-catalyzed cross-coupling reactions of organotin compounds with aryl^[64] and acyl halides^[65] were reported by Kosugi and co-workers. These first-generation studies were followed by extensive second-generation studies of the Pd-catalyzed cross-coupling involving various metals, most notably Zn,^[66] B,^[67] and Sn^[68] over the past two decades. Today, Pd-catalyzed cross-coupling involving metals of intermediate electronegativity, mostly Zn, Al, and Zr, is often referred to as the Negishi coupling.^[66] No other metals appear to have exhibited a higher reactivity than Zn. However, higher chemoselectivity associated with more electronegative metals, especially B^[67] and Sn,^[68] and their other advantages have been recognized and exploited. Intramolecular cross-coupling of ω -haloorganometals containing B^[69] and Sn^[70] as well as the carbopalladation–cross-coupling tandem and cascade reactions of organotin^[71] are but a few representative examples demonstrating their potential advantages. Coupled with their stability in water, Pd-catalyzed cross-coupling reactions involving B and Sn have become widely used, as discussed in detail in **Part III**. The B protocol is commonly known as the Suzuki reaction, and that involving Sn is often called the Stille reaction. Their first papers on Pd-catalyzed cross-coupling with organoborons and organotin compounds were reported in 1979^[72] and 1978,^[73] respectively. Here again, however, earlier contributions by other workers including the first Pd-catalyzed organoboron cross-coupling reaction by Negishi^{[62],[63]} and seminal contributions with Sn by Kosugi et al.^{[64],[65]} as well as extensive studies with Sn

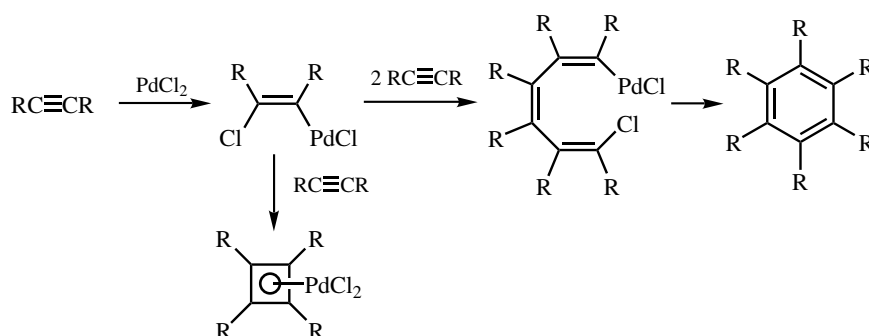
by Beletskaya^[74] should not be overlooked. Extensive developmental studies of the Murahashi Pd-catalyzed cross-coupling with Grignard reagents^{[51],[75]} by several workers including Negishi et al.,^{[57],[76],[76a]} Linstrumelle and co-workers,^{[77]–[79]} and Hayashi et al.^{[80],[81]} initiated in the late 1970s are also noteworthy.

Today, the Negishi, Suzuki, and Stille reactions represent the three most widely used protocols along with the Sonogashira reaction^[82] specializing in the synthesis of alkynes. These reactions are discussed mostly in **Part III** along with the recently developed Si-based cross-coupling (**Sect. III.2.4**) as well as related Pd-catalyzed hydrogenolysis and carbon–heteroatom bond formation reactions (**Sect. III.3**).

Aside from various types of isomerization, rearrangements, and other miscellaneous organopalladium reactions discussed in **Part IX**, most of the fundamental and widely observable patterns of organopalladium reactions had probably been discovered by 1980. However, this was about the time when developments of those reactions discovered earlier as well as their applications, especially in the areas of natural products synthesis and the synthesis of polymers and other compounds of materials chemical interest, began becoming intensive. In recognition of their significance, applications of organopalladium chemistry to the natural products synthesis are highlighted in **Sects. III.2.17.1, III.2.18, IV.8, V.2.6, V.3.6, and VI.6**, while those applications to the synthesis of polymers and other compounds of materials chemical interest are discussed in **Sects. III.2.17.2 and VI.8**.

Development of enantioselective procedures for those reactions discovered earlier also began in the 1980s. Four of the most notable investigations along this line are (i) development of enantioselective cross-coupling by Hayashi et al.^[83] (**Sect. III.2.16**), (ii) development of the enantioselective Heck reaction by Overman^[84] and Shibasaki^[85] (**Sect. IV.2.3**), (iii) development of highly enantioselective procedures for Pd-catalyzed allylation by Trost and Van Vranken^[86] (**Sect. V.2.4**), and (iv) development of enantioselective copolymerization of alkenes and CO by several workers^{[87]–[90]} (**Sect. VI.4.2**).

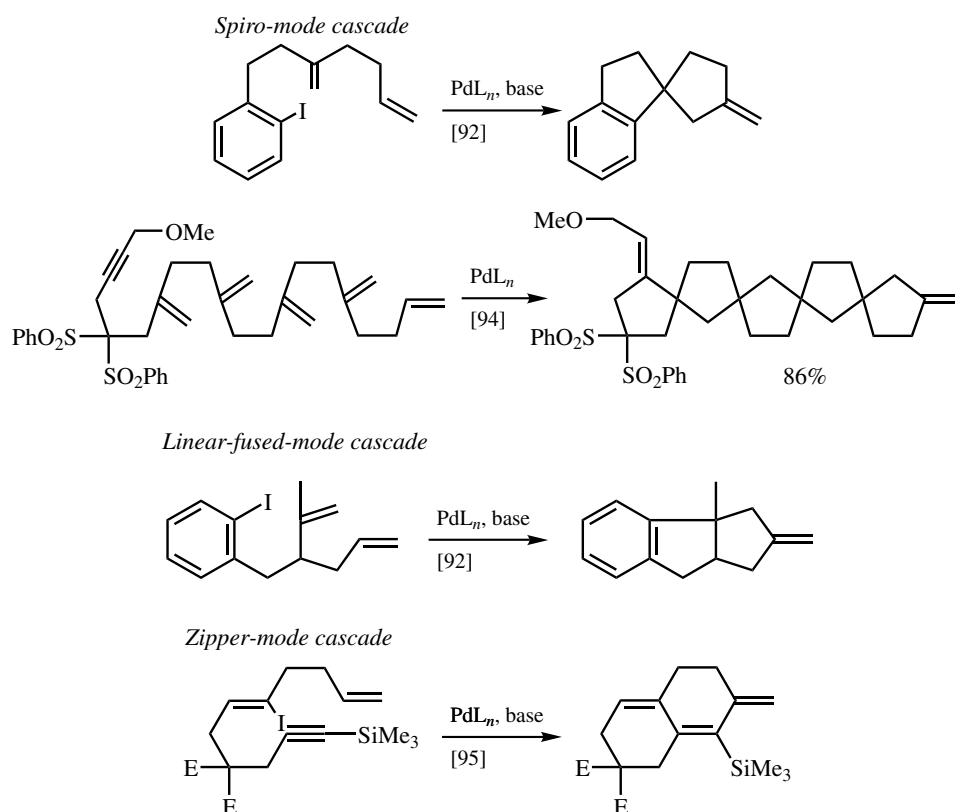
Yet another important aspect of fundamental significance is the “living” and “cascading” nature of some of the organopalladium reactions, especially carbopalladation and migratory insertion. The discovery of “cascading” organopalladium reactions can be traced back to pioneering findings in the 1960s represented by Maitlis’ cyclooligomerization of alkynes^{[28],[91]} that was shown to proceed by a series of carbopalladation (**Scheme 11**) and Tsuji’s alternating copolymerization of norbornadiene and CO^[34] (**Scheme 8**).



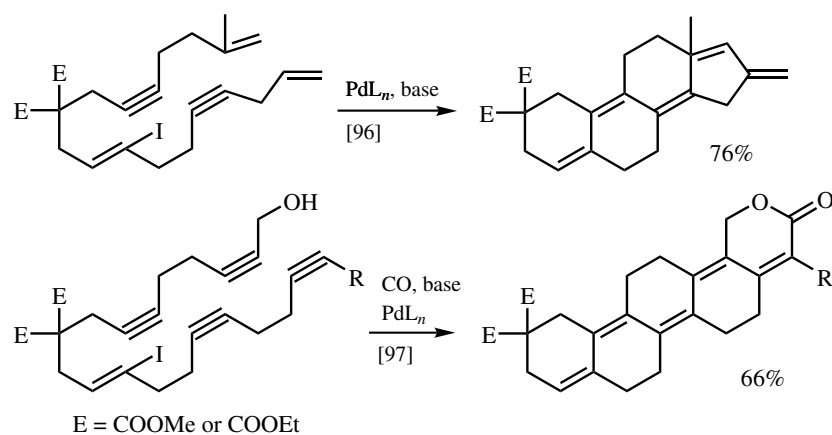
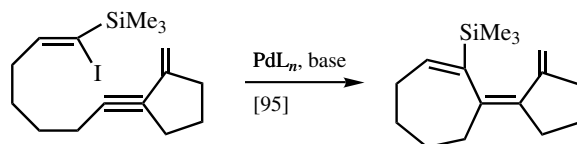
Scheme 11

As such, these reactions may be suited for the synthesis of symmetrically structured oligomers and polymers. In fact, the latter reaction^[36] has been intensively investigated in the 1980s and 1990s primarily for its commercial application (**Sect. VI.4.2**). However, these reactions are not readily adaptable to the selective synthesis of unsymmetrically structured natural products and other molecules of biological and medicinal interest. The feasibility of cascading carbopalladation within the context of the selective synthesis of unsymmetrical molecules was more or less simultaneously demonstrated by Abelman and Overman,^[92] Trost and co-workers,^{[93],[94]} and Negishi and co-workers^{[95]–[97]} only about a decade ago. A related investigation of the cyclic allylpalladation–acylpalladation mainly by Oppolzer^{[98]–[100]} is also noteworthy. Some prototypical and maximally “cascading” examples of cyclic carbopalladation are shown in **Scheme 12**.

These examples have triggered interest in exploiting the “living” and “cascading” possibilities that organopalladium chemistry offers even for the synthesis of unsymmetrical molecules. Some chemists including this author use the term “tandem” process for two-stage cascades, especially in cases where two different kinds of processes are involved, while others have used the term “domino” in place of “cascade.” Usage of these relatively nonscientific but amusing and attractive terms is largely a matter of personal preference, but it is nonetheless important to be familiar with their definitions. In reality, some of the most useful reactions may involve just two- or three-stage “tandem” and “cascade” (or “domino”) processes. Nonetheless, the full and widespread recognition of the “living”



Scheme 12 (Continued)

*Dumbbell-mode cascade*

Scheme 12 (Continued)

characteristics of carbopalladation and migratory insertion has transformed the mostly unidimensional organopalladium chemistry dealing with just one organopalladium reaction at a time into a multidimensional one, thereby significantly expanding its synthetic usefulness. Many “cascading” organopalladium reactions are discussed in **Part IV**, and additional discussions may be found in various sections including **Sects. V.3.2.2, V.3.3.2, V.3.4, V.3.5, VI.2.1.3, VI.4.1, and VI.4.3**.

As further investigations and developments at all fronts of organopalladium chemistry have been continued and intensified, some other largely technological aspects of organopalladium chemistry have also become important. They include such matters as (i) immobilization of Pd catalysts through the use of polymer-bound Pd-complexes and polymer support materials (**Sect. X.2**), (ii) development of aqueous organopalladium chemistry for various purposes (**Sect. X.1**), (iii) applications of organopalladium chemistry within the context of combinatorial chemistry (**Sect. X.3**), and (iv) minimization of unsafe and/or toxic materials such as pyrophoric metals, toxic metals, and toxic ligands, such as As and even P compounds, and (v) use of more economical reagents, for example, organic chlorides in place of iodides and bromides. These dynamic activities incorporate not just fundamental chemical matters but also practical engineering and technological issues that are particularly important in industry. They are clearly adding new dimensions to organopalladium chemistry that cut across the entire field.

REFERENCES

- [1] L. K. James, Ed., *Nobel Laureates in Chemistry, 1901–1992*, American Chemical Society, Washington, DC, **1993**, 798 pp.
- [2] E. Frankland, *Liebigs Ann. Chem.*, **1849**, 71, 171.

- [3] C. Blomberg and F. A. Hartog, *Synthesis*, **1977**, 18, and references therein.
- [4] V. Grignard, *Compt. Rend.*, **1900**, 130, 1322.
- [5] M. Schlosser, in *Organometallics in Synthesis*, M. Schlosser, Ed., Wiley, Chichester **1994**, 1–166. Organoalkali Reagents.
- [6] S. E. Livingstone, *Comp. Inorg. Chem.*, **1973**, 3, 1163–1189, 1274–1329.
- [7] W. C. Zeise, *Pogg. Ann.*, **1831**, 21, 497. (Its original Latin version was published in 1827.)
- [8] P. Sabatier and J. B. Senderens, *Compt. Rend.*, **1897**, 124, 1358.
- [9] P. Sabatier, in *Nobel Lectures: Chemistry, 1901–1921*, Elsevier, Amsterdam, **1966**, 221.
- [10] M. P. von Wilde, *Chem. Ber.*, **1874**, 7, 352.
- [11] H. Kolbe, *J. Prakt. Chem.* [N.F.], **1871**, 4, 418.
- [12] M. Saytzeff, *J. Prakt. Chem.* [N.F.], **1873**, 6, 128.
- [13] C. Paal and C. Amberger, *Chem. Ber.*, **1905**, 38, 1406.
- [14] H. Wieland, *Chem. Ber.*, **1912**, 45, 484.
- [15] W. Ipatieff, *Chem. Ber.*, **1907**, 40, 1270.
- [16] O. Roelen, *German Patent*, **1938**, Nos. 849, 548.
- [17] J. W. Reppe, *Acetylene Chemistry* (P. B. Report–18852-s), C. A. Meyer & Co., New York, **1949**, 209 pp.
- [18] (a) J. Smidt, W. Hafner, R. Jira, J. Sedlmeier, R. Sieber, R. Ruttinger, and H. Kojer, *Angew. Chem.*, **1959**, 71, 176. (b) J. Smidt, W. Hafner, R. Jira, R. Sieber, J. Sedlmeier, and J. Sabel, *Angew. Chem. Int. Ed. Engl.*, **1962**, 1, 80.
- [19] F. C. Phillips, *Am. Chem. J.*, **1894**, 16, 255.
- [20] J. Tsuji, H. Takahashi, and M. Morikawa, *J. Am. Chem. Soc.*, **1965**, 87, 3275.
- [21] J. Tsuji, H. Takahashi, and M. Morikawa, *Tetrahedron Lett.*, **1965**, 4387.
- [22] G. Hata, K. Takahashi, and A. Miyake, *Chem. Commun.*, **1970**, 1392.
- [22a] K. Alkins, W. E. Walker, and R. M. Manyik, *Tetrahedron Lett.*, **1970**, 3821.
- [23] J. Tsuji, *Chem. Met. Carbon Bond*, **1985**, 3, 163–199.
- [24] B. M. Trost, *Acc. Chem. Res.*, **1980**, 13, 385–393.
- [25] R. F. Heck, *J. Am. Chem. Soc.*, **1968**, 90, 5518.
- [26] I. Moritani and Y. Fujiwara, *Tetrahedron Lett.*, **1967**, 1119.
- [27] T. Mizoroki, K. Mori, and A. Ozaki, *Bull. Chem. Soc. Jpn.*, **1971**, 44, 581; **1973**, 46, 1505.
- [27a] R. F. Heck and J. P. Nolley, Jr., *J. Org. Chem.*, **1972**, 37, 2320.
- [28] A. T. Blomquist and P. M. Maitlis, *J. Am. Chem. Soc.*, **1962**, 84, 2329.
- [29] J. Tsuji, M. Morikawa, and J. Kiji, *Tetrahedron Lett.*, **1963**, 1437.
- [30] J. Tsuji, J. Kiji, S. Imamura, and M. Morikawa, *J. Am. Chem. Soc.*, **1964**, 86, 4350.
- [31] A. Schoenberg, J. Bartoletti, and R. F. Heck, *J. Org. Chem.*, **1974**, 39, 3318.
- [32] A. Schoenberg and R. F. Heck, *J. Org. Chem.*, **1974**, 39, 3327.
- [33] F. K. Steffy and J. K. Stille, *J. Am. Chem. Soc.*, **1983**, 105, 7173.
- [34] J. Tsuji and S. Hosaka, *Polym. Lett.*, **1965**, 3, 703.
- [35] S. Brewis and P. R. Hughes, *J. Chem. Soc. Chem. Commun.*, **1965**, 489; **1966**, 6.
- [36] E. Drent and P. H. M. Budzelaar, *Chem. Rev.*, **1996**, 96, 663–681.
- [37] E. Negishi and J. A. Miller, *J. Am. Chem. Soc.*, **1983**, 105, 6761.

- [38] J. M. Tour and E. Negishi, *J. Am. Chem. Soc.*, **1985**, 107, 8289.
- [39] E. Negishi and J. M. Tour, *Tetrahedron Lett.*, **1986**, 27, 4869.
- [40] E. Negishi, G. Wu, and J. M. Tour, *Tetrahedron Lett.*, **1988**, 29, 6745.
- [41] G. H. Posner, *Org. React.*, **1975**, 22, 253.
- [42] K. Tamao, K. Sumitani, and M. Kumada, *J. Am. Chem. Soc.*, **1972**, 94, 4374.
- [43] R. J. P. Corriu and J. P. Masse, *J. Chem. Soc. Chem. Commun.*, **1972**, 144.
- [44] T. Yamamoto, A. Yamamoto, and S. Ikeda, *J. Am. Chem. Soc.*, **1971**, 93, 3350.
- [45] M. S. Kharasch and O. Reinmuth, in *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, New York, **1954**, Chap. 16, 1146–1132.
- [46] M. Tamura and J. Kochi, *Synthesis*, **1971**, 303.
- [47] T. Sato, T. Kawara, M. Kawashima, and T. Fujisawa, *Chem. Lett.*, **1980**, 571.
- [48] B. H. Lipshutz, in *Organometallics in Synthesis*, M. Schlosser, Ed., Wiley, New York, **1994**, 283–382.
- [49] G. W. Parshall, *J. Am. Chem. Soc.*, **1974**, 86, 2360.
- [50] L. Cassar, *J. Organomet. Chem.*, **1975**, 93, 253.
- [51] M. Yamamura, I. Moritani, and S. I. Murahashi, *J. Organomet. Chem.*, **1975**, 91, C39.
- [52] S. Baba and E. Negishi, *J. Am. Chem. Soc.*, **1976**, 98, 6729.
- [53] J. F. Fauvarque and A. Jutand, *Bull. Soc. Chim. Fr.*, **1976**, 765.
- [54] A. Sekiya and N. Ishikawa, *J. Organomet. Chem.*, **1976**, 118, 349.
- [55] H. A. Dieck and R. F. Heck, *J. Organomet. Chem.*, **1975**, 93, 259.
- [56] K. Sonogashira, Y. Tohda, and N. Hagihara, *Tetrahedron Lett.*, **1975**, 4467.
- [57] E. Negishi, A. O. King, and N. Okukado, *J. Org. Chem.*, **1977**, 42, 1821.
- [58] A. O. King, N. Okukado, and E. Negishi, *J. Chem. Soc. Chem. Commun.*, **1977**, 683.
- [59] A. O. King, E. Negishi, F. J. Villani, Jr., and A. Silveira, Jr., *J. Org. Chem.*, **1978**, 43, 358.
- [60] N. Okukado, D. E. Van Horn, W. L. Klima, and E. Negishi, *Tetrahedron Lett.*, **1978**, 1027.
- [61] E. Negishi, N. Okukado, A. O. King, D. E. Van Horn, and B. I. Spiegel, *J. Am. Chem. Soc.*, **1978**, 100, 2254.
- [62] E. Negishi, in *Aspects of Mechanism and Organometallic Chemistry*, J. H. Brewster, Ed., Plenum Press, New York, **1978**, 285–317.
- [63] E. Negishi, *Acc. Chem. Res.*, **1982**, 15, 340–348.
- [64] M. Kosugi, K. Sasazawa, Y. Shimizu, and T. Migita, *Chem. Lett.*, **1977**, 301.
- [65] M. Kosugi, Y. Shimizu, and T. Migita, *Chem. Lett.*, **1977**, 1423.
- [66] E. Negishi and F. Liu, in *Cross-Coupling Reactions*, F. Diederich and P. J. Stang, Eds., VCH, Weinheim, **1998**, 1–47.
- [67] N. Miyaura and A. Suzuki, *Chem. Rev.*, **1995**, 95, 2457–2483.
- [68] V. Farina, V. Krishnamurthy, and W. J. Scott, *Org. React.*, **1997**, 50, 1–652.
- [69] N. Miyaura, H. Suginome, and A. Suzuki, *Tetrahedron Lett.*, **1984**, 25, 761.
- [70] A. Kalivretenos, J. K. Stille, and L. S. Hegedus, *J. Org. Chem.*, **1991**, 56, 2883.
- [71] E. Negishi, Y. Noda, F. Lamaty, and E. J. Vawter, *Tetrahedron Lett.*, **1990**, 31, 4393.
- [72] N. Miyaura, K. Yamada, and A. Suzuki, *Tetrahedron Lett.*, **1979**, 3437.
- [73] D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, **1978**, 100, 3636.
- [74] I. P. Beletskaya, *J. Organomet. Chem.*, **1983**, 250, 551–564.
- [75] S. I. Murahashi, M. Yamamura, K. Yanagisawa, N. Mita, and K. Kondo, *J. Org. Chem.*, **1979**, 44, 2408.

- [76] E. Negishi, L. F. Valente, and M. Kobayashi, *J. Am. Chem. Soc.*, **1980**, *102*, 3298.
- [76a] E. Negishi, F. T. Luo, and C. L. Rand, *Tetrahedron Lett.*, **1982**, *23*, 27.
- [77] H. P. Dang, and G. Linstrumelle, *Tetrahedron Lett.*, **1978**, 191.
- [78] C. Huynh and G. Linstrumelle, *Tetrahedron Lett.*, **1979**, 1073.
- [79] T. Jeffery-Luong and G. Linstrumelle, *Tetrahedron Lett.*, **1980**, *21*, 5019.
- [80] T. Hayashi, M. Konishi, and M. Kumada, *Tetrahedron Lett.*, **1979**, *21*, 1871.
- [81] T. Hayashi, K. Kabeta, I. Hamachi, and M. Kumada, *Tetrahedron Lett.*, **1983**, *24*, 2865.
- [82] K. Sonogashira, in *Metal-Catalyzed Cross-Coupling Reactions*, F. Diederich and P. J. Stang, Eds., Wiley-VCH, Weinheim, **1998**, 203–229.
- [83] T. Hayashi, S. Niizuma, T. Kamikawa, N. Suzuki, and Y. Uozumi, *J. Am. Chem. Soc.*, **1995**, *117*, 9101.
- [84] L. E. Overman, *Pure Appl. Chem.*, **1994**, *66*, 1423–1430.
- [85] M. Shibasaki, *Adv. Metal-Org. Chem.*, **1996**, *5*, 119–151.
- [86] B. M. Trost and D. L. Van Vranken, *Chem. Rev.*, **1996**, *96*, 395–422.
- [87] M. Brookhart, M. Wagner, G. G. A. Balavoine, and H. A. Haddou, *J. Am. Chem. Soc.*, **1994**, *116*, 3641.
- [88] Z. Jiang, S. E. Adams, and A. Sen, *Macromolecules*, **1994**, *27*, 4436.
- [89] S. Bronco, G. Consiglio, R. Hutter, A. Batistini, and U. W. Suter, *Macromolecules*, **1994**, *27*, 4436.
- [90] K. Nozaki, N. Sato, and H. Takaya, *J. Am. Chem. Soc.*, **1995**, *117*, 9911.
- [91] P. M. Maitlis, *Acc. Chem. Res.*, **1976**, *9*, 93–96.
- [92] M. M. Abelman and L. E. Overman, *J. Am. Chem. Soc.*, **1988**, *110*, 2328.
- [93] B. M. Trost and D. C. Lee, *J. Am. Chem. Soc.*, **1988**, *110*, 7255.
- [94] B. M. Trost and Y. Shi, *J. Am. Chem. Soc.*, **1991**, *113*, 701.
- [95] Y. Zhang and E. Negishi, *J. Am. Chem. Soc.*, **1989**, *111*, 3454.
- [96] Y. Zhang, G. Wu, G. Agnel, and E. Negishi, *J. Am. Chem. Soc.*, **1990**, *112*, 8590.
- [97] T. Sugihara, C. Copéret, Z. Owczarczyk, L. S. Harring, and E. Negishi, *J. Am. Chem. Soc.*, **1994**, *116*, 7923.
- [98] W. Oppolzer, T. H. Keller, M. Bedoya-Zurita, and C. Stone, *Tetrahedron Lett.*, **1989**, *30*, 5883.
- [99] K. Yamamoto, M. Terakado, K. Murai, M. Miyazawa, J. Tsuji, K. Takahashi, and K. Mikami, *Chem. Lett.*, **1989**, 955.
- [100] W. Oppolzer, *Pure Appl. Chem.*, **1990**, *62*, 1941.