Chapter 8
Oxidative Carbonylation Reactions

In the last six chapters we discussed the transition metal catalyzed carbonylative activation of organohalogen (C-X, X = I, Br, Cl, OTf, etc.) compounds. They all have one common point in their reaction mechanism; taking a palladium catalyst, for example, the reactions start with Pd(0) and then go to Pd(II) after an oxidative addition. To summarize, the reactions all go through Pd(0) to Pd(II) and a Pd(0) cycle. But for oxidative carbonylation reactions, the reactions go through Pd(II) to Pd(0) and a Pd(II) cycle. Clearly, oxidative carbonylations need additional oxidants to reoxidize the Pd(0) to Pd(II), and various organic nucleophiles were applied as substrates in the presence of CO. One of the most obvious advantages for oxidative carbonylation reactions is the oxidative addition step can be avoid which is more reluctant under CO atmosphere.

The prototype for today's palladium-catalyzed oxidative carbonylations is the well-known "Wacker Process," which was developed already in the late 1950s. Here, ethylene is oxidized to acetaldehyde using a combination of palladium(II) and copper(II) salts. Although no CO was used in this process, all the basic elementary steps for regenerating the catalyst under oxidative conditions are included. Obviously, the mechanism is different from carbonylative coupling reactions, such as reductive carbonylation, alkoxycarbonylation, Suzuki and Sonagashira carbonylations. In the Wacker process, coordination of the olefin onto the electrophilic palladium(II) center allows for a reaction of the double bond with water, alcohols or acetic acid to produce aldehydes, vinylethers or vinylacetates, respectively. Until now, the Wacker process is still the most important route for obtaining acetaldehyde from ethylene. In order to run the reaction catalytic in palladium, the formed Pd(0) species has to be regenerated to Pd(II). This is achieved by adding cupric chloride ($CuCl_2$) to the reaction mixture. Notably, the resulting Cu(I) is regenerated to Cu(II) by molecular oxygen, making the process catalytic in both palladium and copper. This crucial discovery of regenerating the Pd(II) species by $CuCl_2$ was adopted by many palladium-catalyzed oxidative carbonylations of alkenes, which resulted in unsaturated esters or diesters, depending on the catalyst system and the conditions (Scheme 8.1). Nowadays, besides $CuCl_2$, other oxidant reagents, such as direct O_2 or BQ (*p*-benzoquinone), etc., can be used to reoxidize Pd(0) to regenerate the catalytic cycle.

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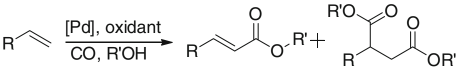

Scheme 8.1 Palladium-catalyzed oxidative carbonylation of olefins

As early as 1963, Tsuji and colleagues described the reaction of olefin-palladium chloride complexes with CO to produce *β*-chloroacyl chlorides [1, 2]. Both internal and terminal aliphatic olefins were transformed into the corresponding chloroesters when the reaction was conducted in alcohols. Later on, in 1969, Yukawa and Tsutsumi reported on the reaction of a styrene-palladium complex with CO in alcohols [3]. Here, various cinnamates and phenylsuccinates were synthesized. Compared with Tsuji's work, they proposed a different reaction mechanism. They assumed that the oxidative addition of the alkyloxycarbonyl groups into styrenes is the key step, but a stoichiometric amount of palladium was still necessary to perform the reaction. Another version of a dialkoxycarbonylation of olefins was reported by Heck [4], using mercuric chloride as additive.

While these initial examples were performed in the presence of stoichiometric amounts of palladium, the first catalytic dialkoxycarbonylation of olefins was independently described by Fenton [5] and Medema [6] in 1969 and 1970. More specifically, a catalytic amount of palladium was used together with an equivalent of $CuCl_2$, and the reactions were run at high pressure of CO and comparatively high reaction temperatures (140–150 °C). Heck demonstrated that $CuCl_2$ is not able to efficiently reoxidize Pd(0) at low temperatures [7–9]. In 1972 Fenton and Steinwand reported on the oxidative carbonylation of olefins to succinates [10]. For the reoxidation of palladium, iron and copper chlorides were used, but oxygen should also have been present—otherwise only low yields of succinates were obtained. A related study of the hydroxycarbonylation of olefins was described by the same group [11]. Nowadays, this type of reaction is efficiently performed in the presence of protic acids.[1]

In order to elucidate the mechanism in more detail, the stereospecific oxidative carbonylation of *cis*- and *trans*-2-butene in methanol was carried out by Stille and colleagues [16]. $PdCl_2$ and $CuCl_2$ were applied as the catalytic system, resulting in a stereospecific *trans*-methoxypalladation. The addition of equimolar amounts of NaOAc changed the course of the reaction completely and led to stereospecific *cis*-carboxymethylpalladation as the exclusive reaction pathway. The authors also investigated the mechanism by means of ^{13}C NMR [17, 18]. Apart from internal and terminal olefins, they extended their methodology to reactions of diolefins [19], vinyl ketones, unsaturated alcohols, and unsaturated esters. All these substrates were dicarboxylated in high yields (Scheme 8.2).

In 1979 Cometti and Chiusoli published their results on the synthesis of methyl cinnamates from styrene [20]. Using a mixture of $PdCl_2$, $CuCl_2$, $MgCl_2$ and

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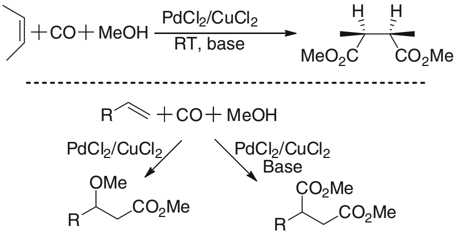
[1] For selected examples, see [12–15].

Scheme 8.2 Palladium-catalyzed oxidative carbonylation of olefins to diesters



NaOAc, the reaction was run in methanol at room temperature under atmospheric pressure of CO to produce methyl cinnamate together with dimethyl phenylsuccinate as the products (Scheme 8.3).

Alper and his group reported on another protocol for the hydroxycarbonylation of alkenes in 1983 [21]. Here, $PdCl_2$ and $CuCl_2$ were applied as the catalytic system. Alkenes were transformed into branched propionic acids in good yields in the presence of water, oxygen, and HCl. Later on, they extended their protocol to monohydroesterification of diols [22–24]. As shown in Scheme 8.4, the reactions could be conducted under mild conditions (room temperature, 1 bar of CO).

Consiglio and colleagues described the enantioselective version of bis-alkoxycarbonylations of alkenes [25–27]. Here, BQ was applied to reoxidize the palladium centre. As chiral ligands, DIOP, BINAP, and some other chiral phosphine ligands were tested. More recently, Chan's group succeeded in using modified dipyridylphosphine cationic Pd(II) complexes to obtain both good *ee* and chemoselectivity.[2]

Instead of using $CuCl_2$ and BQ, butyl nitrite was also applied in the oxidative carbonylation of alkenes by Chauvin and colleagues.[3] When $PdCl_2(PhCN)_2$ and PPh_3 were used as the catalyst system, $PdCl_2(CO_2Bu)NO(PPh_3)$ was isolated and proved to be one of the reaction intermediates. In the gas phase of the reaction, CO_2, N_2O, NO and N_2 were found, but no N_2O.

In 1996 Castanet et al. developed a CO-free procedure for the oxidative carbonylation of alkenes [32]. Instead of a MeOH/CO mixture, methyl formate was used in the presence of a Pd^{II}/Cu system and unsaturated esters were produced in one step. During the reaction, methyl formate acted as the source of both alcohol and CO, but an initial partial pressure of CO was required in order to obtain high yields. Moreover, they demonstrated that by the addition of lithium methoxide, the handling of CO could be avoided.

Inomata and his team described the Pd/C-catalyzed oxidative carbonylation of terminal olefins [33]. The reaction proceeded selectively to mono- or diesters under 1 bar of CO at room temperature in good yields, in the presence of $CuCl_2$ or CuCl as the additive. Interestingly, mainly monoesters were observed when $CuCl_2$

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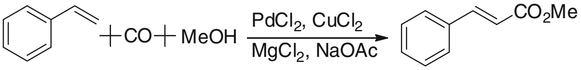
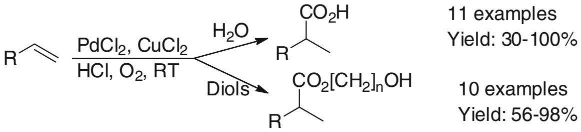
[2] For a summary on the Pd-catalyzed asymmetric alkoxycarbonylation of vinylarenes, see: [28, 29].

[3] For a review on the application of alkyl nitrites as oxidant, see: [30, 31].

Scheme 8.3 Palladium-catalyzed synthesis of methyl cinnamate



Scheme 8.4 Palladium-catalyzed oxidative carbonylation of alkenes to branched products



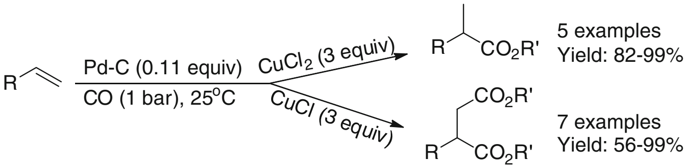
was applied as oxidant, while diesters were formed in good yields by using CuCl as the oxidant reagent (Scheme 8.5). By using $PdCl_2$ (0.1 equiv) instead of Pd/C, in the presence of CuCl (1.5 equiv) and O_2, they were also able to transform 3-buten-1-ols into the corresponding γ-butyrolactones and 2-oxotetrahydrofuran-3-acetic acid esters in high yields [34].

An asymmetric version for the synthesis of diesters was published by the same group in 2001 [35]. By using a chiral bisoxazoline ligand in the presence of copper(I) triflate at 25 °C, terminal olefins were carbonylated to enantiomerically enriched diesters in good yields with up to 66 % *ee* (Scheme 8.6).

Previously, this catalyst system was also used for the oxidative carbonylation of homoallylic alcohols to synthesize lactones with 19–65 % *ee* [36]. In 1998, Saigo and colleagues reported on the use of phosphine sulfides as ligands for the oxidative carbonylation of olefins [37]. Diesters were produced in high yields starting from the corresponding alkenes (Scheme 8.7). Enantioselectivity can be obtained by applying chiral biphosphine sulfides as ligands. Notably, their model system gave 36 and 60 % yield in the absence of ligand and with triphenylphosphine oxide, respectively. However, no reaction took place in the presence of PPh_3.

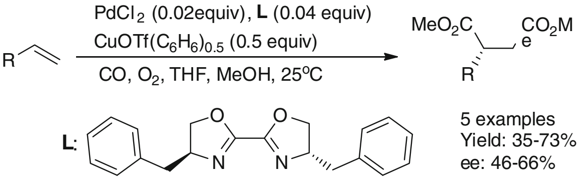
Yang and his team developed a procedure for the oxidative carbonylation of terminal olefins to phenylsuccinate esters by using thioureas as ligands [38]. It was claimed that these ligands can prevent both palladium precipitation and double bond isomerization. Later on, the same authors synthesized a set of thiourea-oxazolines (*S*,*N*-bidentate ligand) which also allowed for enantioselective reactions (Scheme 8.8) [39, 40].

In 2001 Bianchini's group described the oxidative carbonylation of styrene to methyl cinnamate and dimethyl phenylsuccinate. Methyl cinnamate was synthesized starting from styrene with a good yield with excellent selectivity by applying a modified diphosphine as ligand [41], while dimethyl phenylsuccinate was produced by using pyridinimine as the ligand [42]. Jiang and Zhu succeeded in applying the phosphate-based ligand [(*S*)-(+)-BNPPA] in the palladium-catalyzed alkoxycarbonylation of *N*-vinylphalimide [43]. The effects of solvent, temperature, promoters, and other parameters were studied. Good yields and high regioselectivities of either branched or linear products were obtained under optimum conditions.



Scheme 8.5 Pd/C-catalyzed oxidative carbonylation of alkenes

Scheme 8.6 Palladium-catalyzed oxidative carbonylation of olefins



Besides efforts on the development of ligands for oxidative carbonylation of alkenes, Jiang and colleagues performed the oxidative carbonylation of norbornene in supercritical carbon dioxide ($scCO_2$) [44]. Ishii and colleagues were able to develop copper-free reaction conditions by using catalytic amounts of $Pd(OAc)_2$ and molybdovanadophosphate (NPMoV) [45]. With CO and air, cyclopentene was oxidatively carbonylated into dimethyl *cis*-1,2-cyclopentanedicarboxylate and dimethyl *cis*-1,3-cyclopentanedicarboxylate in good yields. The addition of NH_4Cl can improve the yield of this reaction.

The oxidative carbonylation of hydroxy-substituted alkenes can lead to synthetically interesting tetrahydrofurans and pyrans.[4] As early as 1984, Semmelhack and his group developed a methodology for the synthesis of furans and pyrans using a palladium-catalyzed oxidative carbonylation of hydroxyalkenes. In the presence of $CuCl_2$ (3 equiv), $PdCl_2$ (0.1 equiv) and CO (1.1 bar) at 25 °C, the heterocycles were isolated in good yields (Scheme 8.9) [50]. In another study, they performed the carbonylative synthesis of tetrahydrofurans [51, 52], and this procedure was applied to the synthesis of pyran-lactones [53], racemic frenolicin [54], and also plakortones [55–58].

In 1985 Alper and Leonard applied their previously reported reaction conditions [14, 15] in the oxidative carbonylation of alkenones to produce five- and six-membered lactones. The reaction was conducted in THF, in the presence of a $PdCl_2/CuCl_2$ catalyst system yielding lactones in 42–80 % (Scheme 8.10).

That same year, Yoshida and colleagues demonstrated the oxidative carbonylation of 4-penten-1,3-diols. In the presence of $PdCl_2$ (0.1 equiv), $CuCl_2$ (3 equiv), NaOAc (3 equiv) and under CO (1 bar) at room temperature, lactones were achieved stereoselectively [59]. They also succeeded in finding optimal conditions for the oxidative carbonylation of 3-hydroxypent-4-enylamides to produce the

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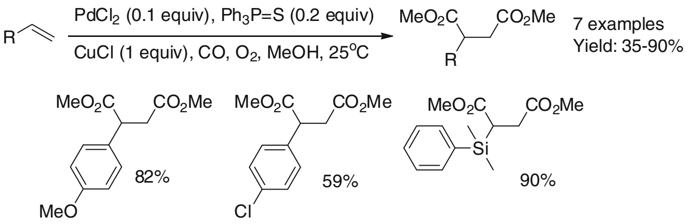
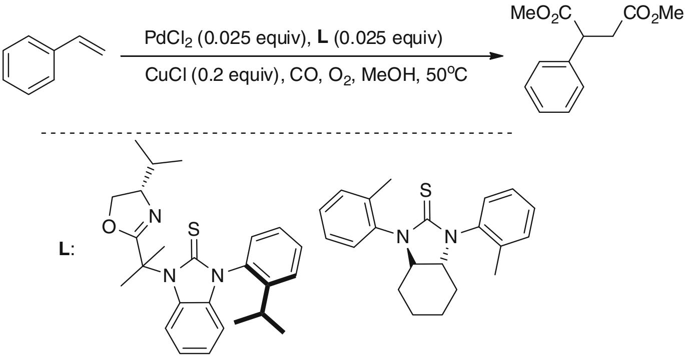
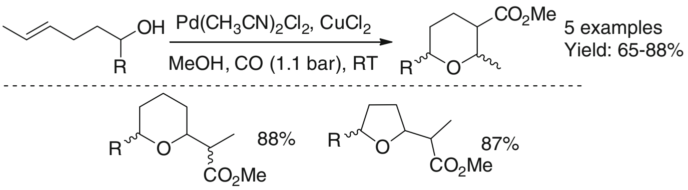
[4] For related reviews on this topic, see: [46–49].



Scheme 8.7 Palladium-catalyzed oxidative carbonylation of olefins using triphenylphosphine sulfide as ligand



Scheme 8.8 Palladium-catalyzed oxidative carbonylation of olefins using thioureas as ligand

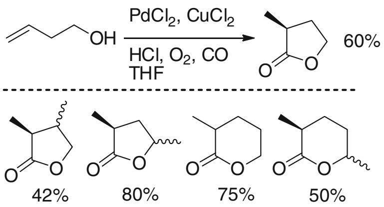


Scheme 8.9 Palladium-catalyzed oxidative carbonylation of hydroxyalkenes

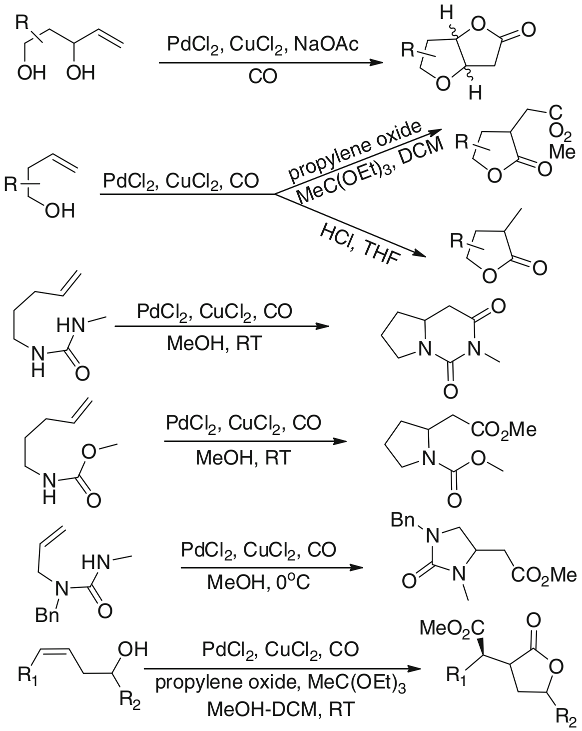
corresponding 3-hydroxy pyrrolidine 2-acetic acid lactones in 66–90 % of yields [60]. The same group also used substituted ureas, 3-hydroxy-4-pentenylamines, 4-hydroxy-5-hexenylamines, 3-buten-1-ols, 3-butyn-1-ols, unsaturated carbamates, unsaturated amides, and even dienyl carbamates as substrates (Scheme 8.11) [61–68]. The related oxidative carbonylation of allenic amides/amines for the synthesis of heterocyclic acrylates was described by Gallagher and colleagues [69].

In 2008 Gracza and Kapitan reported the stereocontrolled oxidative carbonylation of diols [70, 71]. Performing the reaction in AcOH at room temperature,

Scheme 8.10 Palladium-catalyzed oxidative carbonylation of alkenones



Scheme 8.11 Palladium-catalyzed oxidative carbonylation of functionalized alkenes

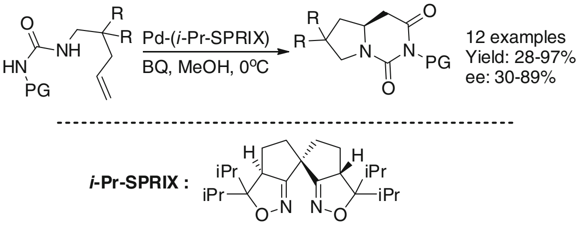


applying Pd(OAc)$_2$, a chiral bis(oxazoline) ligand and BQ as oxidant, the corresponding lactones were produced in good yields.

Recently, Sasai's group published the enantioselective oxidative carbonylation of alkenylureas. By using the palladium-spiro bis(isoxazoline) system, the desired products were produced in good yields and with moderate to good *ee* (Scheme 8.12) [72].

Jiang's group developed a palladium-catalyzed direct oxidative carbonylation of allylic C–H bonds with carbon monoxide [73]. This observation provides a novel route for accessing *β*-enoic acid esters with high regioselectivity (Scheme 8.13). Preliminary results from deuterium-labeling experiments indicated that the allylic C–H activation process is an irreversible rate-determining step.

Scheme 8.12 Palladium-catalyzed oxidative carbonylation of alkenylureas



Although a number of synthetic applications of oxidative carbonylations of alkenes were described in total synthesis, most research efforts focused on finding new ligands and catalyst systems. In general, a large excess of copper salts or other organic oxidants is still needed. Obviously, this creates problems both in the purification of the respective products as well as the environment. Therefore, using air, oxygen, or hydrogen peroxide as more "green oxidants" under mild conditions is an important goal for the future.

In the palladium-catalyzed oxidative carbonylation of alkynes, mixtures of products can often be formed. Nevertheless, these reactions can be valuable and have the potential to be tunable (Scheme 8.14). Costa and Salerno's group has shown that the combination of the palladium catalyst KI and oxidant is a powerful system for the oxidative carbonylation of alkynes.[5]

The examples of oxidative carbonylations of alkynes were reported on in 1964. Here, Tsuji et al. described the palladium-mediated transformation of acetylene into muconyl chloride, fumaryl and maleic acid chloride (Scheme 8.15) [77]. Later on, they used diphenylacetylene as a substrate for the synthesis of lactones in the presence of alcohol and HCl [78, 79].

For ten years, Tsuji and colleagues further developed the palladium-catalyzed oxidative carbonylation of terminal acetylenes. For example, acetylenecarboxylates were produced in high yields at room temperature under atmospheric pressure of CO, but a stoichiometric amount of $CuCl_2$ was needed to reoxidize the Pd(0) (Scheme 8.16) [80]. Temkin and colleagues investigated the mechanism of this reaction [81–84]. They found that σ-alkynylcopper(I) complexes are intermediates in the reaction, and that the addition of CuCl to the initial reaction solution caused a significant decrease in the induction period. A catalytic system consisting of $PdCl_2$, CuCl, LiCl, O_2, and CO was also successfully applied to this reaction. In 1983 Alper's group developed another method using a combination of $PdCl_2$, $CuCl_2$, HCl, and O_2. While *cis*-diesters were synthesized from terminal alkynes, *cis*-monoesters were formed, starting from internal alkynes under atmospheric pressure at room temperature [15].

Ishii and colleagues developed a multicatalytic system for the oxidative carbonylation of terminal alkynes [85]. In the presence of $Pd(OAc)_2$, chlorohydroquinone and NPMoV, under CO and O_2, acetylenecarboxylate or phenylmaleic

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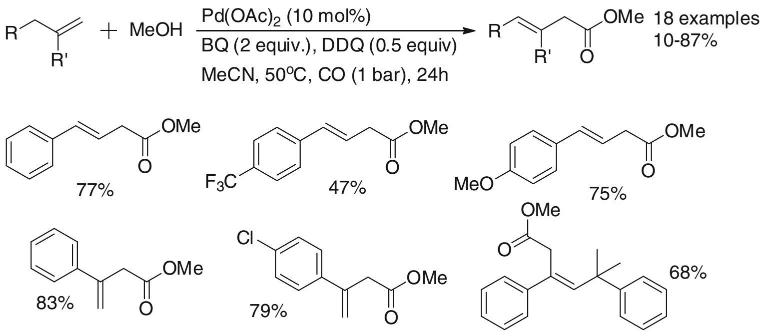
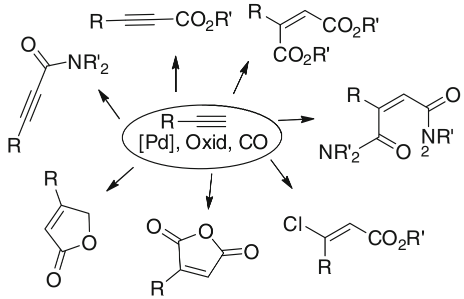
[5] For reviews on PdI_2-catalyzed oxidative carbonylation reactions, see: [74–76].

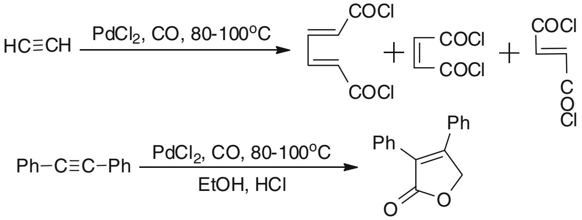


Scheme 8.13 Palladium-catalyzed carbonylation of allylic C–H

Scheme 8.14 Palladium-catalyzed oxidative carbonylations of alkynes

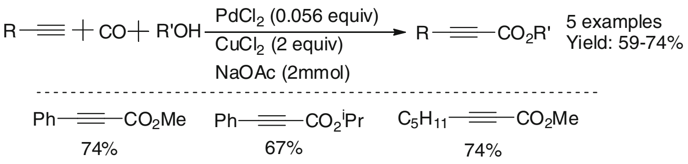


Scheme 8.15 Palladium-mediated oxidative carbonylation of alkynes

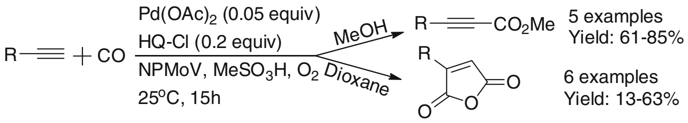


anhydride, were synthesized selectively in various solvents. Interestingly, the presence of O_2 is important; otherwise, no reaction occurred (Scheme 8.17). Notably, Jiang and his research team carried out similar work with the more common $PdCl_2$/$CuCl_2$-catalyst system [86].

Yamamoto and colleagues were able to develop an additive-free palladium catalyst system for the oxidative carbonylation of alkynes [87, 88]. By using their palladium-phosphine catalyst in the presence of molecular oxygen, acetylenecarboxylates were formed under atmospheric pressure of CO at room temperature. A detailed mechanistic study was also carried out proposing a reductive elimination of a palladium species with methoxycarbonyl and alkynyl residues. The oxidation of Pd(0) to Pd(II) species was confirmed to proceed cleanly with



Scheme 8.16 Palladium-catalyzed oxidative carbonylation of acetylenes



Scheme 8.17 Palladium-catalyzed oxidative carbonylation of acetylenes

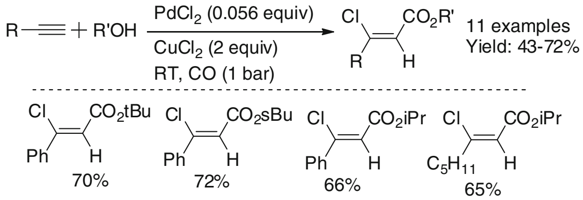
molecular oxygen as the oxidant in the presence of halide ions. On the basis of this work, a heterogeneous variant using Pd/C has also been developed.

Jiang's team described the synthesis of 3-chloroacrylate esters [89]. Their reaction proceeded under 1 bar of CO at room temperature yielding 30–72 % of the desired products in a high regio- and stereoselective manner (Scheme 8.18).

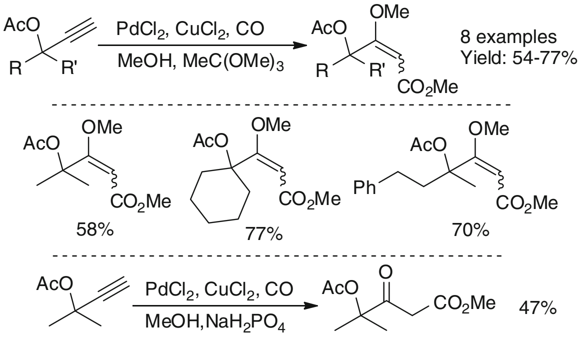
The oxidative carbonylation of 1,1-disubstituted propargyl acetates to unsaturated esters was developed by Okumoto and colleagues in 1999 [90]. A stoichiometric amount of $CuCl_2$ was used as the oxidant and the reaction had to be conducted at 0 °C (Scheme 8.19).

The synthesis of lactones via palladium-catalyzed oxidative carbonylation of hydroxyalkynes was primarily reported by Tamaru and colleagues. Starting from 3-butyn-1-ols, the corresponding lactones were produced at room temperature. An access to ketopyranosides as a subunit of polyketide natural products was reported by Marshall and Yanik [91]. In the presence of 5 mol % $Pd(MeCN)_2Cl_2$ and 1.1–1.5 equivalent of BQ, methyl ketopyranosides were prepared from corresponding hydroxyalkynes with excellent stereoselectivity. A mild and efficient methodology for the palladium-catalyzed carbonylative synthesis of four-membered *β*-lactones has been published by Ma and colleagues [92]. In the presence of $PdCl_2$ and $CuCl_2$, *β*-lactones were produced from 2-alkynols in good yields (Scheme 8.20). Using readily available optically active propargylic alcohols, the corresponding *β*-lactones were generated with high *ee*.

Scheme 8.18 Palladium-catalyzed oxidative carbonylation of acetylenes to chloroacrylates



Scheme 8.19 Palladium-catalyzed oxidative carbonylation of propargylic acetates



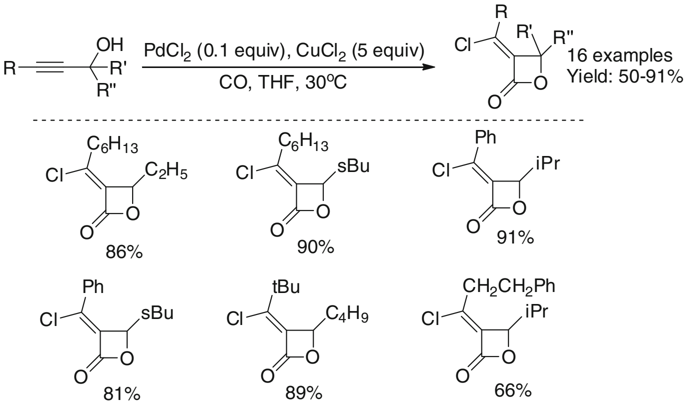
Moreover, an improved method for the oxidative carbonylation of hydroxyalkynes was developed by Kato and colleagues [93]. Applying $Pd(MeCN)_2Cl_2$ (0.05 equiv) and 1.1 equivalent of BQ in methanol at 0 °C under 1 bar of CO, the desired products were obtained from the corresponding cyclic- and acyclic-4-yn-1-ols in good yields (Scheme 8.21). Afterwards, the same group published an asymmetric version of this reaction by applying $Pd(TFA)_2$ with chiral ligands as the catalyst system at lower temperatures (−50 to −30 °C) [94, 95].

Soon afterwards, the same group developed methodologies for the oxidative carbonylation of 4-yn-1-ones and propargylic esters (Scheme 8.22). While 2-cyclopentenone carboxylates were obtained from appropriate carbonyl-substituted alkynes [96], cyclic orthoesters and furanones were successfully synthesized starting from corresponding propargylic compounds [97]. More recently, they also realized the asymmetric version of this reaction [98], which has also been applied in the total synthesis of (−)-AL-2 by Mukai and Miyakoshi [99].

In 2009 Kato and colleagues applied their palladium(II) bis(oxazoline) complexes in the intermolecular methoxycarbonylation of terminal alkynes. Here, terminal alkynes were transformed into *β*-methoxyacrylates in good yields (Scheme 8.23).

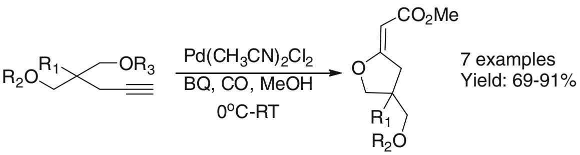
Notably, this methodology tolerates acetyl, ketal, free hydroxy and acid sensitive glycosidic groups. In the case of propargyl alcohol, (±)-dihydrokawain was produced in good yields [100]. In addition, this methodology was applied in the total synthesis of annularin G and annularin H [101].

In 1974, Stille and Wong published the first oxidative carbonylation based on organomercury compounds [102]. Using stoichiometric amount of $PdCl_2$, LiCl, and NaOAc, stereoselective carbonylation took place at room temperature. However, the desired products were obtained only in a low yield. Next, Larock and his team improved the methodology by conducting the reaction at −78 °C [103]. Here, unsaturated carboxylic acids and esters were formed in excellent yields starting from the corresponding vinylmercurials. Although stoichiometric amounts of palladium were still necessary, a catalytic version was realized by the addition of large excess of $CuCl_2$ (Scheme 8.24).



Scheme 8.20 Palladium-catalyzed oxidative carbonylation of alkynes to *β*-lactones

Scheme 8.21 Palladium-catalyzed oxidative carbonylation of alkynes

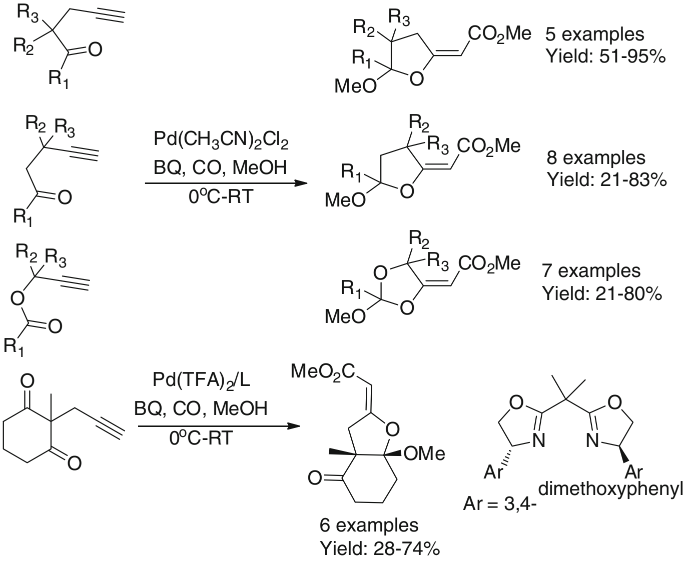


Until now, there has been only one report published concerning the oxidative carbonylation of organosilanes [104]. The reaction was carried out at room temperature and under 1 bar of CO, but a stoichiometric amount of $PdCl_2$ was required to form 61–91 % of the corresponding vinyl esters (Scheme 8.25).

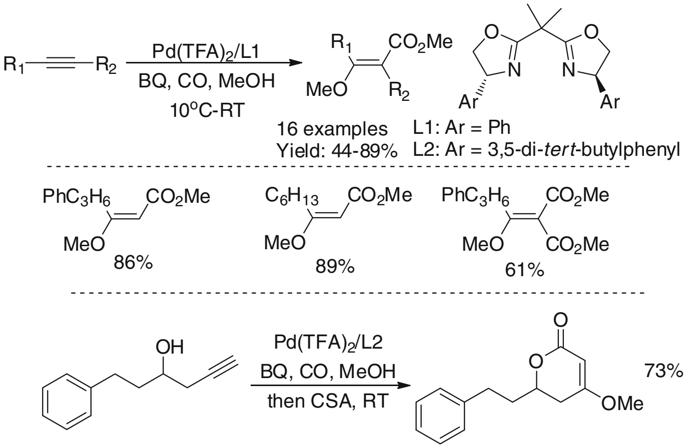
A novel palladium-catalyzed oxidative carbonylation of organoindium compounds with desyl chloride as oxidant was developed by Lei and colleagues in 2008 [105]. Primary and secondary alkyl indium reagents, as well as aryl indium reagents, were carbonylated at 60 °C in the presence of a catalytic amount of palladium catalyst. The corresponding esters were formed in good yields and the methodology showed broad functional group tolerance (Scheme 8.26). The reaction mechanism was discussed in detail.

Suzuki and colleagues described the first palladium-catalyzed oxidative carbonylation of alkenylboranes as early as 1981. They prepared 1-alkenylboranes by hydroboration of alkynes and subsequent oxidative carbonylation mediated by a catalytic amount of $PdCl_2$, in the presence of NaOAc and BQ in methanol, which provided unsaturated esters in good yields (Scheme 8.27a) [106]. Later, a stereoselective synthesis of *β*-mono- and *β*, *β*-disubstituted *α*, *β*-unsaturated esters was established by a stepwise cross-coupling alkylation followed by an oxidative carbonylation of 2-bromo-1-alkenylboranes (Scheme 8.27b) [107]. Good yield and excellent stereoselectivity was achieved.

Interestingly, Uemura and colleagues developed a method for the carbonylation of C–B bonds without any oxidant, using only Pd(0) as the catalyst [108, 109].

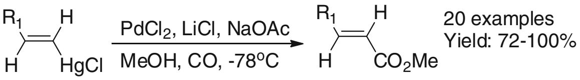


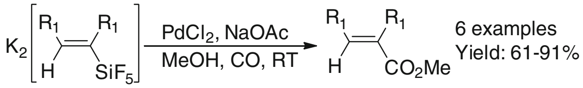
Scheme 8.22 Palladium-catalyzed oxidative carbonylation of carbonyl-substituted alkynes



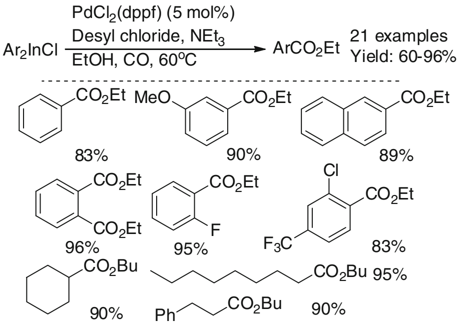
Scheme 8.23 Palladium-catalyzed oxidative carbonylation of alkynes

Scheme 8.24 Palladium-promoted carbonylation of organomercuries

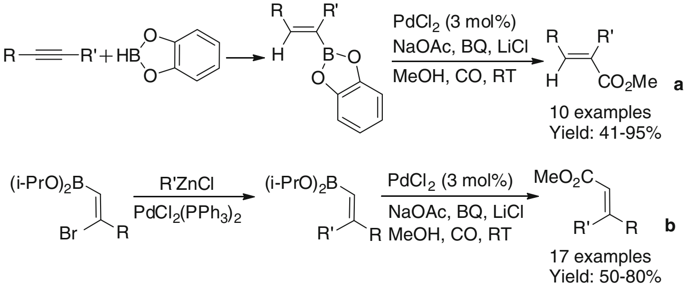




Scheme 8.25 Palladium-promoted carbonylation of organosilanes



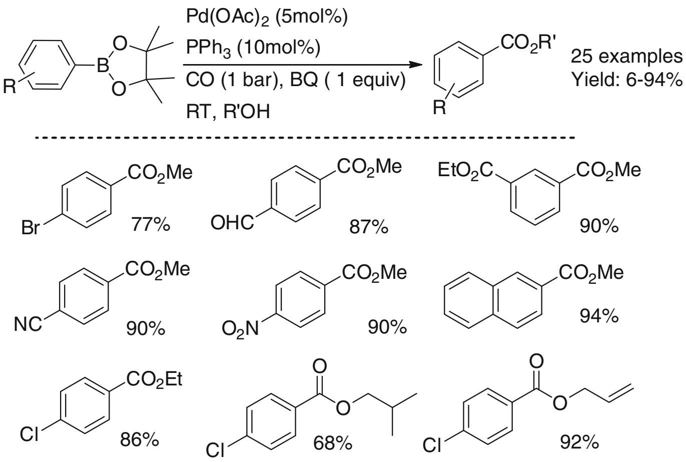
Scheme 8.26 Palladium-catalyzed carbonylation of organoindiums



Scheme 8.27 Palladium-catalyzed oxidative carbonylation of alkenylboranes

Starting from alkenyl- and arylborates and boronic acids, corresponding esters and ketones could be synthesized under the atmospheric pressure of CO in methanol at 25 °C in moderate yields. On the other hand, Yamamoto et al. described a general and selective palladium-catalyzed oxidative carbonylation of arylboronates in alcohols [110]. In the presence of $Pd(OAc)_2/PPh_3$ and BQ, esters were produced from the corresponding arylboronates in good yields at room temperature (Scheme 8.28). A wide range of functional groups, including various carbonyl substituents, nitrile, nitro, sulfone residues, unprotected pyrrole rings and also various alcohols, was tolerated. The reaction was conducted without an acid or base additive and DFT and MP2 calculations were carried out to clarify the reaction mechanism.

Meanwhile, Lei and his colleagues discovered a novel protocol that makes use of air as an oxidant at low temperatures [111]. Using a balloon pressure of CO/air mixture, arylboronates were converted into the corresponding esters in good yields (Scheme 8.29). This was the first example that could apply simply air in the oxidative carbonylation of organoboron compounds with alcohols.



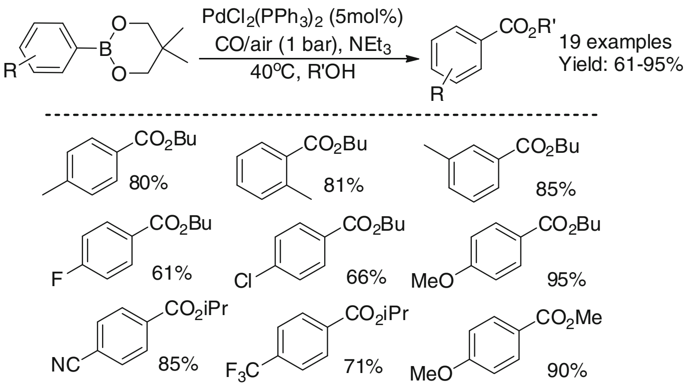
Scheme 8.28 Palladium-catalyzed oxidative carbonylation of arylboronates

The oxidative carbonylation of organoborons has also attracted the interest of Zhou and colleagues, who used 10-hydroxy-9,10-boroxarophenanthrenes in the presence of CO and stoichiometric amounts of $Pd(OAc)_2$ to form tricyclic lactones in high yields (Scheme 8.30) [112].

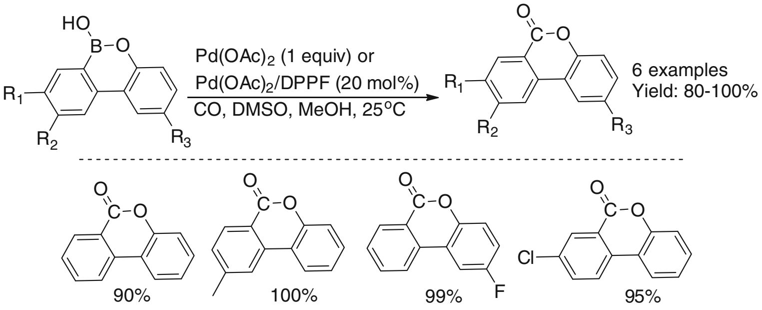
More recently, Beller's group developed a general and efficient protocol for the oxidative carbonylative coupling of arylboronic acids with styrenes [113]. Notably, air was used as a benign terminal oxidant yielding chalcones in moderate to excellent yields (Scheme 8.31). A possible mechanism for the oxidative vinylation of arylboronic acids is proposed in Scheme 8.8. Initially, a transmetalation of the arylboronic acid with the active palladium(II) complex took place. After the coordination and insertion of CO, the corresponding acyl palladium species is formed. Then, the coordination and insertion of styrene to the acyl palladium center should take place. The terminal product was produced after elimination with concomitant generation of a palladium hydride complex. This latter complex was regenerated to the active species in the presence of air, which finished the catalytic cycle.

Kang and colleagues developed a palladium-catalyzed carbonylative coupling of organolead compounds that afforded the symmetrical ketones [114]. In the presence of $Pd_2(dba)_3 \cdot CHCl_3$ (5 mol%) and NaOMe (5 equiv.) in CH_3CN under atmospheric pressure of carbon monoxide at room temperature, symmetrical ketones were produced in good yields (Scheme 8.32).

A palladium-catalyzed oxidative coupling of organozinc reagents were reported by Jackson and colleagues [115]. In the presence of $Pd(PPh_3)_4$ and under CO atmosphere, functionalized zinc reagents were transformed into the desired ketones in good yields. The authors also demonstrated that adventitious molecular oxygen plays a key role in the formation of the symmetrical ketones, and that rigorous exclusion of oxygen can result in substantially higher yields of ketones in the cross-coupling with some aromatic iodides. Cobalt bromide was also applied in



Scheme 8.29 Palladium-catalyzed oxidative carbonylation of arylboronates using air

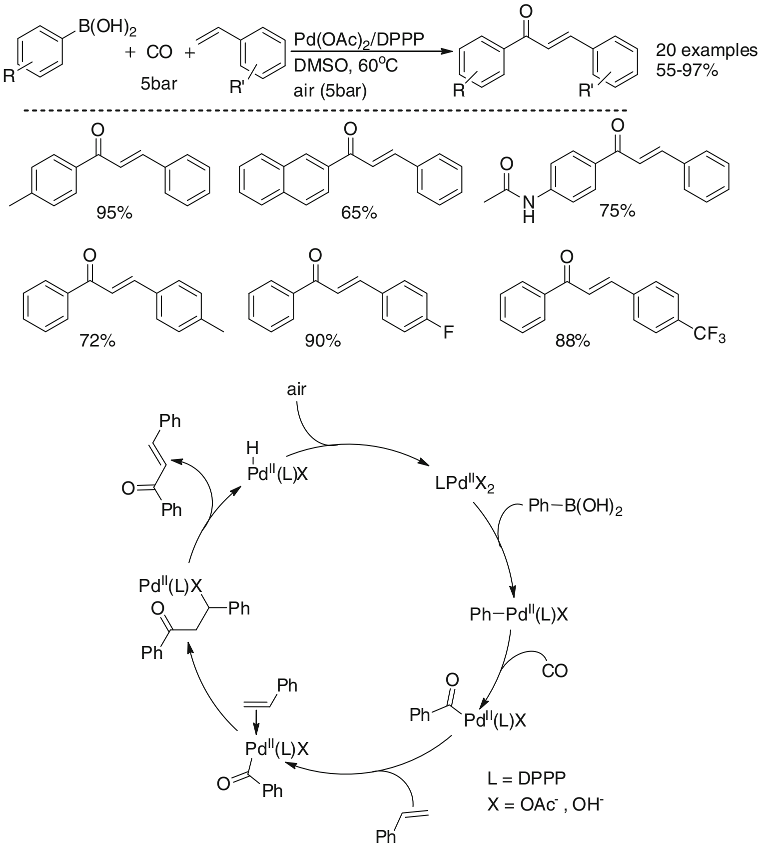


Scheme 8.30 Palladium-mediated oxidative carbonylation towards lactones

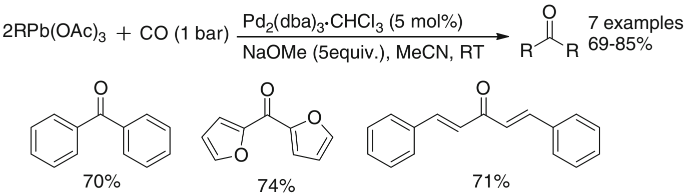
the homo-coupling of organozincs [116]. In the presence of 1.5 equivalents of $CoBr_2$ and bubbling with CO gas, ketones were formed in good yields.

More recently, a rhodium-catalyzed carbonylation of arylzinc compounds was developed by Takagi [117]. In the presence of an Rh-dppf catalyst under 1 bar of CO using 1,2-dibromoethane as the oxidant, carbonylative homo-coupling of arylzinc compounds was achieved, affording symmetrical diaryl ketones in good yields (Scheme 8.33). Under similar conditions, Pd or Ni catalysts induced oxidative homo-coupling of zinc reagents to yield diaryls instead.

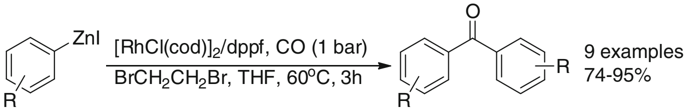
In this chapter we discussed the transition metal catalyzed oxidative carbonylation of alkenes, alkynes and organometallic reagents. In these types of reactions, an additional oxidant is needed to reoxidize the catalyst back to an active state after a reductive elimination step. The oxidants applied are normally $Cu(OAc)_2$ or BQ, air or O_2, as more green oxidants should be investigated and applied in oxidative carbonylation reactions. In contrast, carbonylative reduction reactions using CO as a reductant are also interesting. In the next chapter, the reduction of C-NO_2 with CO will be discussed.



Scheme 8.31 Palladium-catalyzed oxidative carbonylative coupling of arylboronic acids with styrenes and proposed reaction mechanism



Scheme 8.32 Pd-catalyzed carbonylative coupling of organolead compounds



Scheme 8.33 Rh-catalyzed carbonylative synthesis of ketones

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