Chapter 11
A Discussion Between Carbonylation, Noncarbonylation and Decarbonylation

We have discussed various types of carbonylation reactions and their applications in total synthesis in the last ten chapters. In order to evaluate our knowledge of this area, we will discuss the relationship among carbonylation, noncarbonylation and decarbonylation.

Mechanistically, transition metal-catalyzed carbonylation (taking palladium, for example) includes elemental steps such as oxidative addition, coordination and the insertion of carbon monoxide (transmetalation), reductive elimination (Scheme 11.1). In carbonylative coupling reactions, the oxidative additional step needs an electron-rich metal center, but the CO coordination and insertion requires an electron-deficient metal center; the reductive elimination can be promoted by bulky ligands, while the CO coordination and insertion step demand that the ligand not be too bulky. Evaluated temperature can favor an oxidative addition, while it also favors the decarbonylation of an acylpalladium complex (the reverse reaction of CO insertion). The key to developing a successful carbonylative coupling reaction is finding the proper combination of reaction temperature, ligand and the other parameters.

At the stage it is interesting to note the relationship between palladium-catalyzed coupling reactions and their carbonylative coupling reactions. In principle, the reactions work under carbonylative coupling conditions and can also give their noncarbonylation product under CO-free conditions [1, 2]. But it is not restricted that noncarbonylative coupling must be developed before the carbonylative coupling. Such an aminocarbonylation was reported by Heck and colleagues in the 1970s, but the Buchwald-Hartwig amination was established between 1994 and the late 2000s [3–6]. On the other hand, some substrates have been extensively applied in noncarbonylative coupling reactions, but their carbonylative versions are rarely reported, such as aryl chloride, aryl tosylates and aryl mesylates.

Aryl chlorides are important starting materials in palladium-catalyzed coupling reactions [7]. Compared with the corresponding aryl iodides or aryl bromides, the advantages of aryl chlorides are obviously that they are inexpensive, easy to prepare, stable, etc. The same is true if we compare aryl tosylates or aryl mesylates with their aryl triflates analogs. Even though aryl chlorides, aryl mesylates and aryl acetates have been studied and have succeeded in cross-coupling reactions, their

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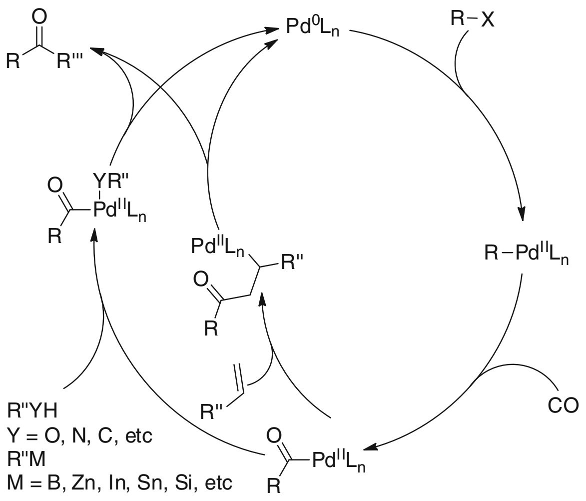
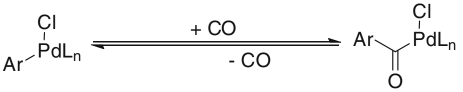
Scheme 11.1 Reaction mechanism for Pd-catalyzed carbonylation reactions



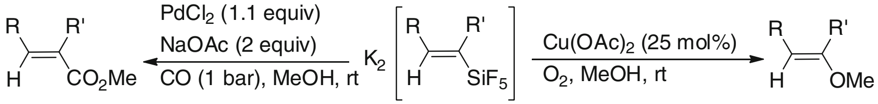
Scheme 11.2 Carbonylation and decarbonylation equilibrium



carbonylative coupling transformations are still rarely reported. Until the present, no general methodology has been developed for the carbonylative coupling of aryl chlorides. All the known procedures need either a high temperature (>140 °C) or a strong base. The possible explanations for this situation are: (1) CO coordinated to metal center decreased the electron density that inhibited the oxidative addition step in some distant; (2) the high temperature required by the oxidative addition or the strong base needed by transmetalation destroyed the formed arylpalladium or acylpalladium species; and (3) in order to avoid the high temperature caused decarbonylation, high pressures of CO are normally applied to drive the reaction, but this may result in the formation of a palladium carbon monoxide complex that is inactive for a cross-coupling reaction (Scheme 11.2).

With this in the background, it will be interesting to discuss the relationship between carbonylation, noncarbonylation and decarbonylation.

Organopentafluorosilicates are recognized as a class of versatile intermediates in various organic syntheses. Kumada and colleagues developed methodologies for the transformation of organopentafluorosilicates into various chemicals [8, 9]. In the case of palladium-mediated carbonylation of silicates, the reaction works at room temperature under atmospheric pressure of carbon monoxide in MeOH. The reaction works with $PdBr_2$ as a promoter as well, but $Pd(OAc)_2$ did not give any carbonylation product. While the direct etherification took place under 25 mol % of $Cu(OAc)_2$ in MeOH at room temperature, the presence of air or O_2 can drive the reaction in a catalytic manner. $CuBr_2$, $CuCl_2$, $Cu(SCN)_2$ only gave the ligand



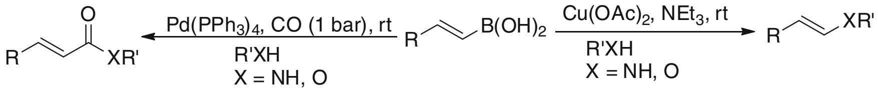
Scheme 11.3 Transformation of alkenylsilicates

transfer products, and no ether was formed. In an inert gas atmosphere, a Cu(I) species was confirmed by titration [10] (Scheme 11.3).

Organoboron reagents are important reagents in organic chemistry that enable many chemical transformations. The reaction of organo boronic acid, vinyl boronate esters and organoborate salts with amines and alcohols give another way for the C–N, C–O bonds to form besides the Buchwald-Hartwig amination. This type of reaction typically uses $Cu(OAc)_2$ as the catalyst, with stoichiometric amounts of $Cu(OAc)_2$ or catalytic amounts of $Cu(OAc)_2$ together with additional oxidants such as air, O_2, TEMPO, in the presence of NEt_3 or pyridine as base; at either room temperature or evaluated temperature, the desired products can be produced in good yields.[1] The carbonylation version of these types of reactions were developed as well [16–20]. In the presence of a palladium catalyst, oxidant and base, esters were produced (Scheme 11.4). Until the present, amines were not used as nucleophiles in the oxidative carbonylation of organoborons; one of the reasons might be the formation of urea.

The oxidative coupling of arylboronic acids with olefins and their carbonylation version are interesting to compare [21–24]. In the report from Wu,[2] they developed the coupling of arylboronic acids with styrenes in the presence of a palladium catalyst in DMF at 50 °C with 1 bar of O_2. In 2012 Beller's team reported on the carbonylation version [24]. In this publication, the use of DMSO as a solvent and DPPP as a ligand are crucial for the success of this transformation (Scheme 11.5).

In 2012 Lei and his colleagues reported the transformation of diaryl ethers to xanthones in the presence of palladium and CO [25]. The noncarbonylation version was reported as well [26, 27]. As shown in Scheme 11.6, the reaction conditions are not very different. All need the presence of TFA to assistant C–H bond activation. One more example is the reaction of aniline with terminal alkynes via an in situ formation of diazonium salts [1, 2]. The carbonylation and



Scheme 11.4 Transformation of organoboron reagents

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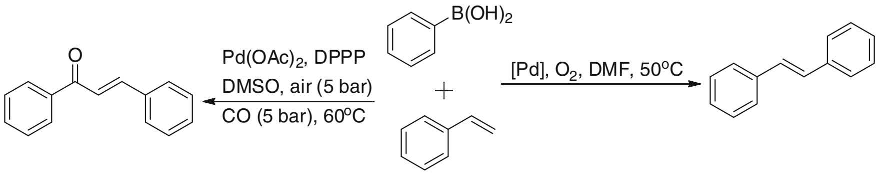
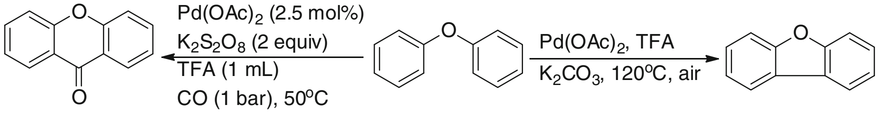
[1] For selected examples, see [11–15].

[2] For selected examples, see [21–23].



Scheme 11.5 Transformation of arylboronic acids



Scheme 11.6 Transformation of diaryl ethers

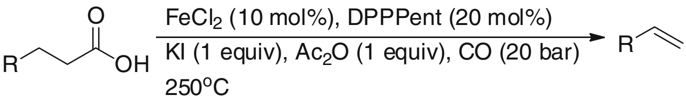
noncarbonylation versions were reported by Beller's group. The difference in the reaction conditions is only at solvent and the presence of CO (10 bar). For the typical cross coupling reactions, the difference between carbonylation and noncarbonylation is even smaller. This is so for Suzuki coupling and carbonylative Suzuki coupling, etc., [28].

Additionally, the carbonylative Heck reaction was developed by Beller's group [29–31]. The reaction condition requires the higher loading of alkenes (6 equiv) and the presence of CO compared with Heck coupling.

The opposite of carbonylation is decarbonylation. In order to understand carbonylation reactions, decarbonylation reactions will be discussed below.

In 2012 Ryu and his colleagues reported the iron-catalyzed decarbonylation of aliphatic carboxylic acids to α-olefins (Scheme 11.7) [32]. In their mechanism study, they found the formation of CO but not CO_2. If the reaction was carried out under low or no pressure (0–5 bar) of carbon monoxide, internal an olefin was observed [33]. In the proposed reaction mechanism, the reaction starts from acid anhydride, which was produced from the reaction of substrate and Ac_2O. Then it reacts with the in situ-formed iron-carbonyl complex, which was generated by $FeCl_2$, phosphine ligand, KI, and CO, and decarbonylation occurred under high temperatures. Notably, $Fe_2(CO)_9$, $Fe_3(CO)_{12}$, $[Fe(CO)_2Cp]_2$ did not give the decarbonylation product.

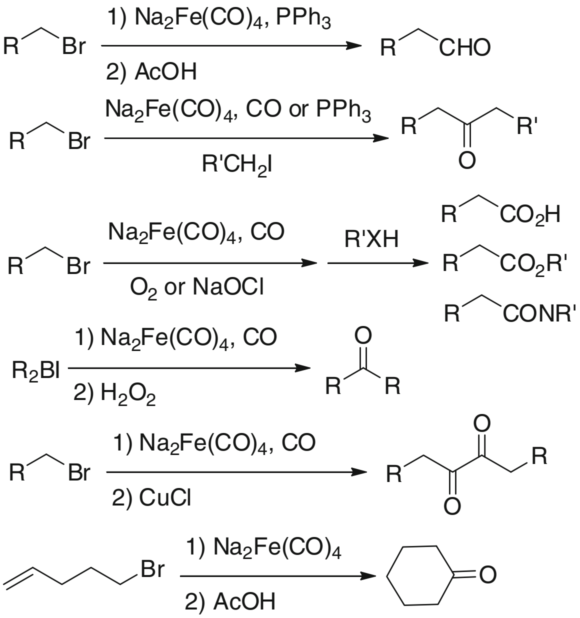
From the other side, the carbonylation of alkyl halides needs stoichiometric amounts of iron salt, such as the Collman reagent $[Na_2Fe(CO)_4]$. The first



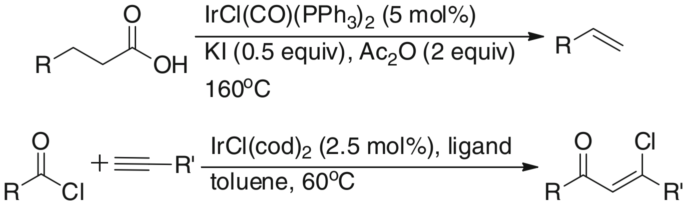
Scheme 11.7 Iron-catalyzed decarbonylation of carboxylic acid

successful application of sodium tetracarbonylferrate (II) in carbonylation was developed by Cooke in 1970 [34]. He synthesized various aldehydes from corresponding alkyl bromides in the presence of a 1.4 equivalent of $Na_2Fe(CO)_4$ and PPh_3. Later on, carboxylic acid derivatives, such as amides, esters and ketones, etc., were prepared by various research groups from corresponding alkyl halides or aryl lithium (Scheme 11.8) [34–44]. The reactions need additional CO or PPh_3 to assist the insertion of CO into the C–Fe bond. The main problem of these methodologies is the necessity for an excess of iron salts, and a catalytic version is still urgently needed.

The above-mentioned decarbonylation of aliphatic acid was also described by the same group, with iridium as the catalyst [45]. Using $IrCl(CO)(PPh_3)_2$ as a catalyst, when combined with KI as an additive, it served as an excellent catalyst for the decarbonylation of long-chain aliphatic carboxylic acids to give internal alkenes with high selectivity. In combination with KI and Ac_2O as additives under controlled temperatures, decarbonylation proceeded to give terminal alkenes with high selectivity. In comparison, Tsuji and colleagues reported an iridium-catalyzed addition of aroyl chlorides and aliphatic acid chlorides to terminal alkynes, and (*Z*)-*β*-chloro-α,*β*-unsaturated ketones were selectively produced (Scheme 11.9) [46]. The additional reactions proceed regio- and stereoselectively with the suppression of decarbonylation and *β*-hydrogen elimination, which might be due to the ligands that were applied. From the point of view of the reaction mechanism, the oxidative addition of aroyl chlorides to [Ir]L (L = IPr) occurs in the presence of alkynes. The insertion of Ir–Cl to alkyne is much faster than decarbonylation.



Scheme 11.8 $Na_2Fe(CO)_4$-mediated carbonylation reactions



Scheme 11.9 Ir-catalyzed reactions of acid and acid chloride

On the other hand, the oxidative addition of aliphatic acid chlorides occurs in the absence of alkyne, but the oxidative addition complex could not be isolated due to fast decarbonylation followed by facile β-hydrogen elimination. The decarbonylation of carboxylic acid was reported with palladium catalysts as well [47–56]. In general, the reactions to acid anhydride as the intermediate need relatively high temperatures.

A brief description of the relationship between carbonylation, noncarbonylation and decarbonylation has been given in this chapter. There are still no general rules for guiding the methodology that is developing on this topic.

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