

Toward development of environmentally benign processes catalyzed by transition-metal complexes*

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Abstract: On the basis of fundamental studies on the carbon–oxygen bond cleavage of various carboxylic acid derivatives, novel, atom-efficient, and environmentally benign catalytic processes to convert them into acids, aldehydes, and ketones have been developed.

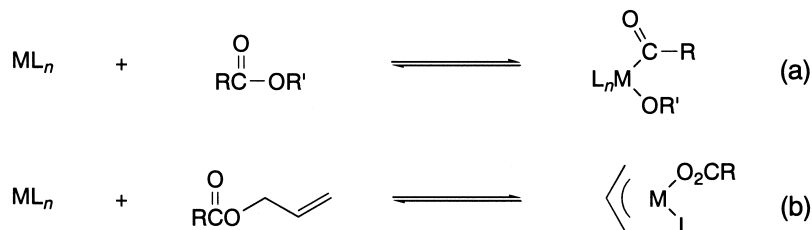
TOWARD DEVELOPMENT OF ENVIRONMENTALLY BENIGN PROCESSES

Increasing attention has been paid to the development of environmentally benign processes in organic synthesis. We need to replace conventional stoichiometric processes by catalytic ones without producing by-products to make the chemical processes more atom-efficient. Recent development of new catalytic processes utilizing transition-metal catalysts has enabled to carry out various synthetic processes under mild conditions with reduction in release of unnecessary by-products. In many of these metal-catalyzed processes, however, processes are often based on the methodology to cause carbon–halogen bond cleavage in organic halides on their reaction with low-valent transition-metal complexes to generate reactive organotransition complexes. The organotransition metal species thus produced undergoes further elementary processes, such as transmetallation and reductive elimination, to generate C–C coupled products (e.g., in Tamao–Kumada–Corriu process) or olefin insertion followed by β -hydrogen elimination to produce arylated olefins (as in Mizoroki–Heck process). Despite the utility of the catalytic processes utilizing the concept of the carbon–halogen bond cleavage, these processes entail an intrinsic problem of starting from organic halides to produce compounds without halogen atoms, and the halogen atom should be eventually discarded as inorganic salts often in combination with a base. In contrast to these processes where the carbon–halogen bond cleavage is utilized, rather limited attention has been paid to application of the concept of carbon–oxygen bond cleavage to organic synthesis, except for the palladium-promoted allyl–oxygen bond cleavage to produce allylation products of nucleophiles (Tsuji–Trost process).

With the intention to develop atom-efficient, environmentally benign synthetic processes, we have been involved in fundamental studies of the C–O bond cleavage in carboxylic esters and anhydrides on interaction with low-valent, transition-metal complexes [1]. Two principal modes of the C–O bond cleavages, i.e., the acyl–O bond cleavage (a), and the allyl–O bond cleavage (b) in carboxylic acid deriv-

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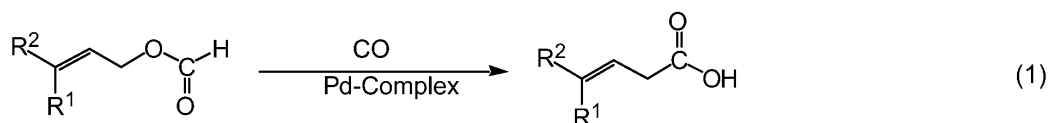
atives, were found to give acyl(aryloxido)metal or acyl(carboxylato)metal complexes in type (a) scission and allyl(carboxylato)metal complexes in the type (b) scission (Scheme 1).



Scheme 1

CATALYTIC PROCESSES BASED ON THE ALLYL–O BOND CLEAVAGE

If one can combine the allyl–O bond cleavage in an allylic carboxylate with CO insertion into the η^3 -allyl–Pd bond to give an acylpalladium complex, a new type of catalytic process can be realized. In fact, by cleaving the C–O bond in allylic formates with a palladium complex under CO pressure, we could develop a new type of catalytic carbonylation process to yield β,γ -unsaturated carboxylic acids from allylic formates under mild conditions (eq. 1) [2]. Since allylic formates can be readily prepared from allylic alcohols and formic acid in the presence of P_2O_5 without using a halogen-containing compound, the carbonylation process provides a new halogen-free route to unsaturated carboxylic acids. The carboxylic acids can be further applied to synthesis of aldehydes and ketones without using halides as described below.



The mechanism of the catalytic carbonylation process can be accounted for by a cycle comprised of elementary processes: (1) oxidative addition of allylic formates to a Pd(0) species to give allyl(formato)palladium(II) species; (2) CO insertion into the allyl–Pd bond to generate acyl(formato)palladium intermediates; (3) reductive elimination of the formato and acyl ligands to produce mixed anhydrides with the formyl entity, which is spontaneously decarbonylated to give the β,γ -unsaturated carboxylic acids; (4) regeneration of the Pd(0) species that further carries the catalytic cycle.

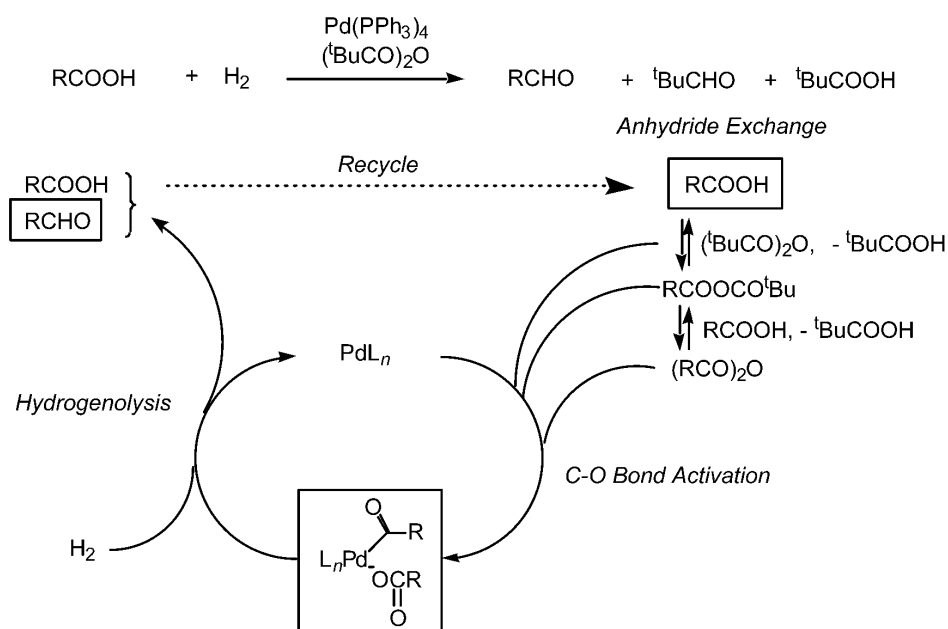
In certain cases, the C–O bond in allylic alcohols can be also cleaved on interaction with a Pd(0) complex to give an η^3 -allylpalladium complex. Nucleophilic attack on the η^3 -allyl ligand yields an allylation product of the nucleophile. An interesting effect of addition of CO_2 gas to the system was observed to promote the allylation process by amine at room temperature and under normal pressure of CO_2 [3].

CATALYTIC PROCESSES BASED ON THE ACYL–O BOND CLEAVAGE

Carboxylic esters and anhydrides undergo oxidative addition on interaction with Pd(0) complexes to give acyl–palladium complexes (Scheme 1, route a). By utilizing the reactivity of the acylpalladium complexes thus generated, we have been able to design a catalytic process to selectively synthesize carboxyl-containing compounds such as aldehydes and ketones under mild conditions [4–7].

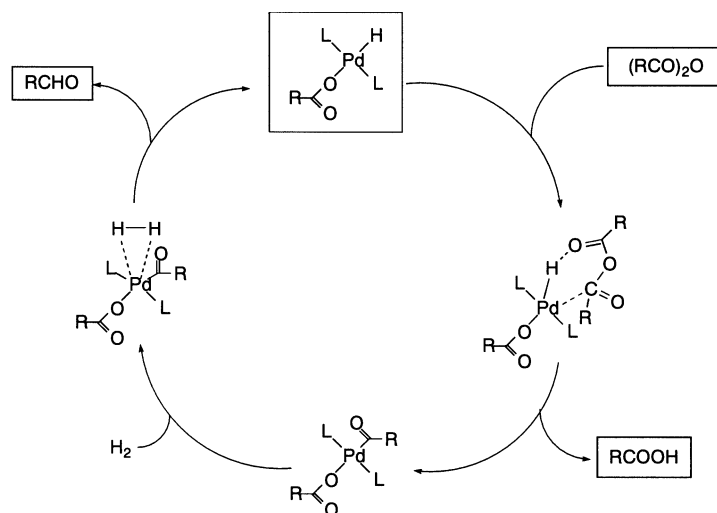
Aldehyde synthesis

Acyl(carboxylato)palladium type complexes formed by oxidative addition of carboxylic anhydrides react with molecular hydrogen to produce 1:1 mixtures of aldehydes and carboxylic acids. By applying the finding as to form a catalytic cycle, catalytic conversion of carboxylic anhydrides into aldehydes and carboxylic acids could be achieved. We could further develop a synthetic method of aldehydes directly from carboxylic acids promoted by a palladium catalyst in the presence of less reactive carboxylic anhydride such as pivalic acid (2,2-dimethylpropionic anhydride). The process is composed of two catalytic cycles as shown in Scheme 2. The main cycle comprises oxidative addition of a carboxylic anhydride to a Pd(0) species to give the acyl(carboxylato)palladium(II) and its reaction with H₂ to liberate aldehyde and the carboxylic acid with regeneration of a Pd(0) species. In the auxiliary cycle, the carboxylic acid produced reacts with a bulky carboxylic anhydride such as pivalic anhydride to form a carboxylic anhydride mixture. The more reactive acyl–O bond in the carboxylic anhydride mixture is cleaved on interaction [4] with a Pd(0) species to convert the carboxylic acid into aldehyde at the cost of pivalic anhydride [4]. Direct hydrogenation of a variety of carboxylic acids, including aliphatic, aromatic, and heterocyclic carboxylic acids as well as di- and tri-basic carboxylic acids, can be effectively performed by the catalytic process.



Scheme 2

Our recent study of the elementary processes of the aldehyde synthesis by computational DFT method revealed the possibility of operation of a mechanism that has not been hitherto proposed. The mechanism shown in Scheme 3 consists of a catalytic cycle involving a palladium hydride species and its interaction with a carboxylic anhydride to cleave the acyl–carboxylate bond in the anhydride.



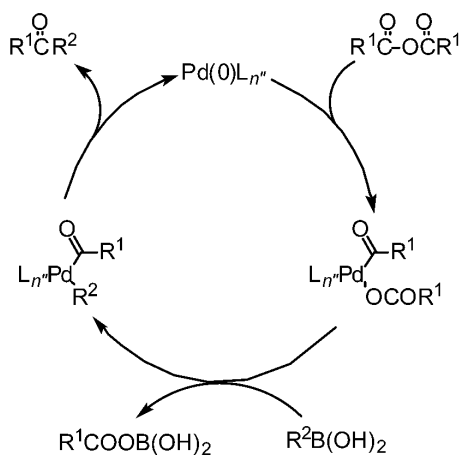
Scheme 3

Ketone synthesis

The concept of palladium-promoted C–O bond cleavage to generate the reactive acylpalladium intermediate led us to further application of the acyl–O bond cleavage to ketone synthesis in combination with the methodology of Suzuki–Miyaura coupling processes utilizing organoboron compounds (eq. 2).

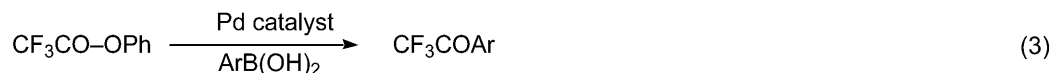


Scheme 4 shows the proposed mechanism for the catalytic conversion of carboxylic anhydrides into ketones catalyzed by palladium catalysts. The catalytic cycle is composed of oxidative addition of the carboxylic anhydride to yield acyl(carboxylato)palladium species, which undergoes the transmetalation with organoboronic acid to give an acyl(alkyl)palladium species that liberates the ketone by reductive elimination.



Scheme 4

In a similar manner, palladium-promoted cleavage of electronegative perfluorocarboxylates can be applied to synthesis of fluorinated ketones in combination with organoboron compounds [6].



These new catalytic processes utilizing the C–O bond cleavage in combination with organoboron compounds provide convenient means to prepare symmetrical and unsymmetrical ketones, some of which are unavailable by other routes, such as conventional Friedel–Crafts acylation. By further combination of the process with an additive that interacts with free carboxylic acids, we could develop a novel method of converting carboxylic acids directly into ketones with organoboronic acids in the presence of a palladium catalyst [7].

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