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Mechanisms of double and single carbonylation reactions catalyzed by palladium complexes

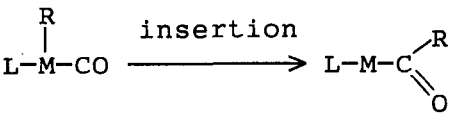
Akio Yamamoto*, Fumiyuki Ozawa, Kohtaro Osakada, Li Huang, Tae–il Son, Nobuo Kawasaski, and Myung–Ki Doh

Research Laboratory of Resources Utilization, Tokyo Institute of Technology, Nagatsuta, Yokohama, 227, Japan

Abstract – Mechanisms of double carbonylation reactions catalyzed by palladium complexs to give α–keto amides and α–keto esters, stoichiometric double carbonylation of allyl carbonates, and cyclization carbonylation of 3–butenoic acid to give cyclic anhydrides are discussed as combination of elementary processes of organometallic reactions.

INTRODUCTION

The carbonylation reaction provides one of the most useful synthetic means in transition metal–catalyzed organic reactions (ref. 1, 2). Clarification of mechanistic details in these carbonylation reactions depends much on understanding of elementary processes of organotransition metal complexes related to the carbonylation reactions, particularly of the behavior of the coordinated CO ligand. Two principal processes are possible for a coordinated CO ligand to be transformed into another type of ligands that can be later released from the transition metal complex as products of the catalytic reaction. One is the CO insertion into a metal–to–carbon bond (eq 1) and the other is attack of an external reagent on the coordinated CO.



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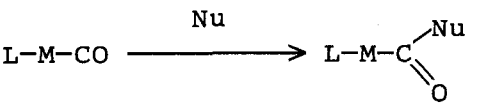

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These elementary processes, when combined with other elementary processes such as oxidative addition and reductive elimination, can be used to construct catalytic cycles for introducing carbon monoxide selectively into organic compounds by means of transition metal complexes.

We wish to present here some of our new findings on elementary processes in recently developed catalytic carbonylation reactions including double carbonylation of organic halides and allylic carbonates to α–keto acid derivatives and cyclic carbonylation of 3–butenoic acid to cyclic acid anhydrides catalyzed by palladium complexes.

*Present address: Department of Applied Chemistry, School of Science and Engineering, Waseda University, 3–4–1 Ookubo, Shinjuku–ku, Tokyo 169.

MECHANISMS OF DOUBLE AND SINGLE CARBONYLATIONS OF ARYL HALIDES CATALYZED BY PALLADIUM COMPLEXES

Catalytic conversion of aryl halides into α–keto acid derivatives has been recently developed by Tanaka's group (ref. 3) as well as our group (ref. 4). α–Keto amides and α–keto esters, respectively, can be produced under relatively mild conditions accompanied by amides and esters as single carbonylation products.

$$ArX + CO + 2HNR_2 \xrightarrow{[Pd]} ArCOCONR_2 + ArCONR_2 \quad (3)$$

X=Halides

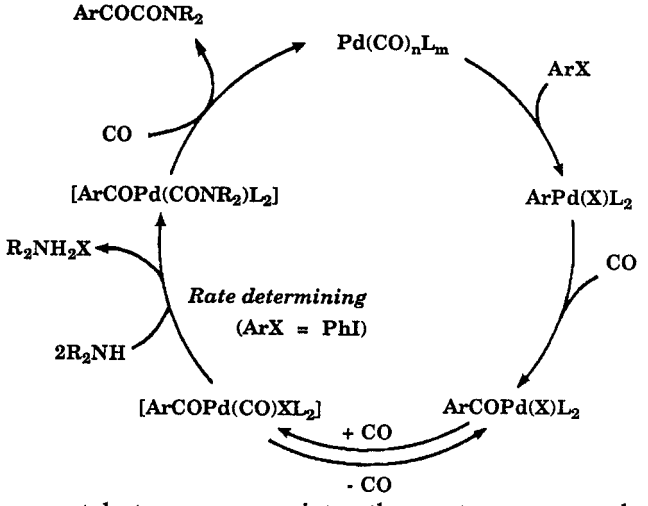
$$ArX + CO + ROH + NEt_3 \xrightarrow{[Pd]} ArCOCOOR + ArCOOR \quad (4)$$

Since these α–keto acid derivatives can be converted into useful biologically active compounds such as α–amino acids and α–hydroxy acids, the newly developed double carbonylation process provides a novel and potentially useful synthetic means for preparing these important compounds.

By detailed mechanistic studies on the double carbonylation reactions we have found that the catalytic process can be reasonably accounted for by the catalytic cycle shown in Scheme 1 (ref. 4–7).

Scheme 1

Proposed mechanism of the palladium–catalyzed double carbonylation of aryl halides to α–keto amides

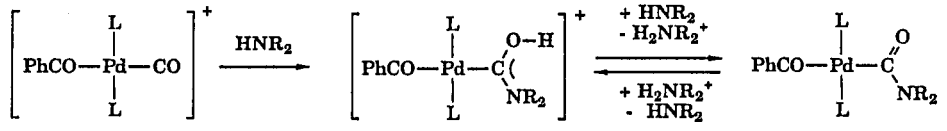


Palladium(II) compounds added as catalyst precursors into the system may be reduced to palladium(0) species on interaction with the secondary amine and carbon monoxide and enter the catalytic cycle. The catalytic cycle is composed of: (1) oxidative addition of aryl halides to the Pd(0) species to give arylpalladium halide complex, (2) CO insertion into the aryl–palladium bond to give an aroylpalladium complex, (3) further CO coordination to the aroylpalladium complex, (4) attack of the secondary amine on the coordinated CO to afford a palladium complex coordinated with the aroyl and carbamoyl ligands, and (5) reductive elimination of the aroyl and carbamoyl ligands to release α–keto amides with regeneration of the Pd(0) species that carries the catalytic cycle.

Of these elementary processes oxidative addition and CO insertion have ample precedents. We have previously obtained evidence for the CO coordination on the acylpalladium complexes by spectroscopic means (ref. 4b). However, the further process involving attack of amine on the coordinated CO ligand and reductive elimination of the acyl and carbamoyl ligands remained to be clarified. A direct approach towards the solution of the problems with the actual catalytic system is not feasible, since the species we wish to characaterize are formed after the rate–determining step of nucleophilic attack of amine on the coordinated CO. We found that by employment of trimethylphosphine, a basic and compact tertiary phosphine, considerable insight into the mechanistic details of the catalytic double and single carbonylation processes could be obtained (ref. 8).

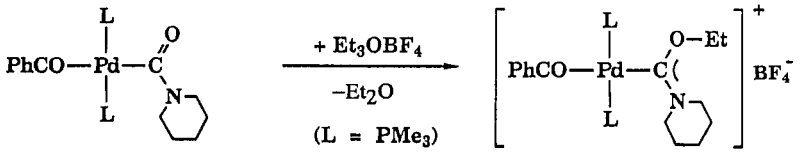
ATTACK OF SECONDARY AMINE ON THE COORDINATED CO

Treatment of a CO–coordinated benzoyl palladium complex having the trimethyl–phosphine ligands (1) with a secondary amine gives an isolable trans–(benzoyl)–(carbamoyl)palladium(II) complex (3) which can be unambiguously characterized by spectroscopy. We have also identified an intermediate species (2) formed by nucleophilic attack of amine on the coordinated CO ligand. Further deprotonation of the intermediate species 2 gives the *trans*-(benzoyl)(carbamoyl)palladium complex 3.



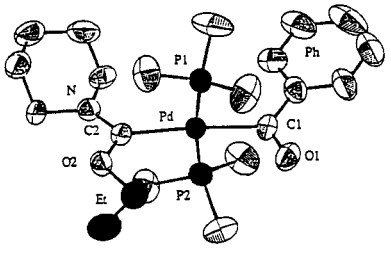
1 (L = PMe_3) 2 3

Isolation of the intermediate species 2 is not feasible, since it is in equilibrium with the deprotonated carbamoyl complex 3. As the model compound of the intermediate protonated species we have isolated its alkylation product 4 by treatment of the carbamoyl complex with an alkylating agent.

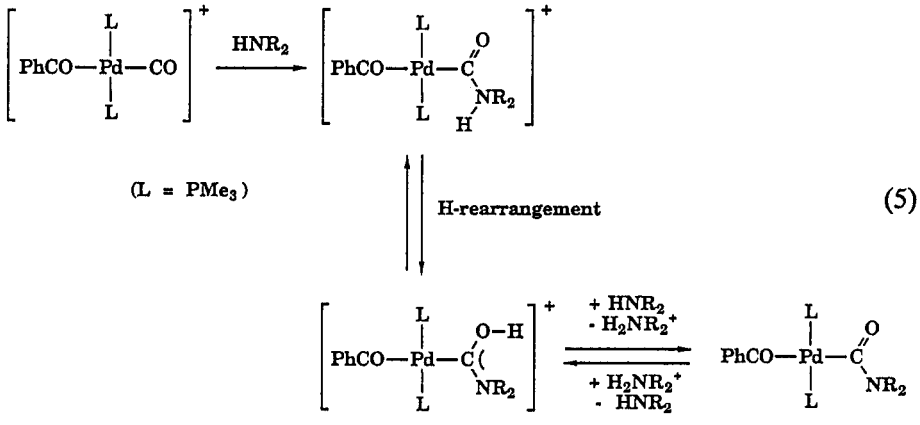


3 4

The molecular structure of the alkylation product 4 was established by X–ray analysis as shown below.

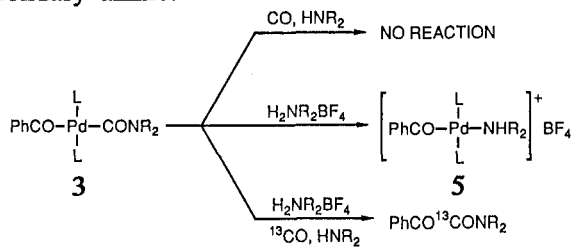


The complex has a square planer geometry with trans configuration where the ethyl group is attached to the oxygen atom of the carbonyl group in the carbamoyl ligand. From these results it is reasonable to assume eq 5 as the process of nucleophilic attack of the coordinated carbonyl ligand by amine to give the carbamoyl complex through intermediate species shown below.



(5)

The isolated *trans*–benzoyl–carbamoyl complex proved to be considerably stable to reductive elimination of the benzoyl and carbamoyl groups to give α–keto amide. The carbamoyl ligand, however, was readily protonated by alkylammonium salt of the amine as weak protic acid to give an amine–coordinated cationic benzoyl complex. Furthermore treatment of the benzoyl–carbamoyl complex with the ammonium salt under carbon monoxide liberated α–keto amide quantitatively. Employment of the ^{13}C–labelled CO in the presence of the secondary amine and its ammonium salt gave the ^{13}C–labelled α–keto amide $PhCO^{13}CONR_2$ indicating that the carbon monoxide was incorporated into the α–keto amide on interaction with the secondary amine.



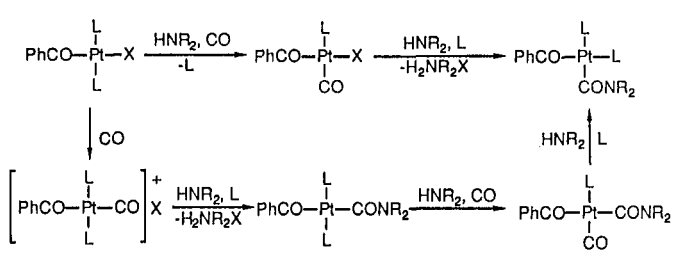
(L = PMe_3; HNR_2 = pyrrolidine)

These results indicate involvement of indirect pathways in liberation of α–keto amide and suggest operation of a new type of trans–cis isomerization.

TRANS–CIS ISOMERIZATION PROCESS

For a trans diorgano isomer to reductively eliminate the coupling product of the organic groups in a concerted manner the ligands to be reductively eliminated are required to be situated in mutually adjacent positions (ref. 3). Therefore, a reaction pathway to cause a trans to cis isomerization should be involved in liberation of the α–keto amide by reductive elimination of the *trans*-(benzoyl)–(carbamoyl)palladium complex. However, study of the isomerization process regarding the palladium complex is hindered because of the lability of the *cis*-(benzoyl)(carbamoyl)palladium complex. Thus we have prepared the corresponding trans and cis isomers of platinum analogs to gain further insight into the mechanism of the trans to cis isomeriztion. Triphenylphosphine–coordinaded benzoylplatinum complexes were found suitable for investigating the mechanism of the trans–cis isomerization. The triphenylphosphine–coordinated *trans*-(benzoyl)–(carbamoyl)platinum complex was readily prepared by treating CO–coordinated benzoylplatinum complex with secondary amine, whereas the *cis*-(benzoyl)–(carbamoyl)platinum complex was obtained by treating the CO–coordinated complex with the amine in the presence of CO. Alternatively, treatment of *trans*-(benzoyl)platinum chloride with the amine and CO afforded the *cis*-(benzoyl)–(carbamoyl) isomer. We have further found that in the reaction of the CO–coordinated trans isomer of cationic benzoylplatinum complex with CO and amine the *trans*-(benzoyl)(carbamoyl)platinum is initially formed and later isomerized to its cis isomer in the presence of amine and CO.

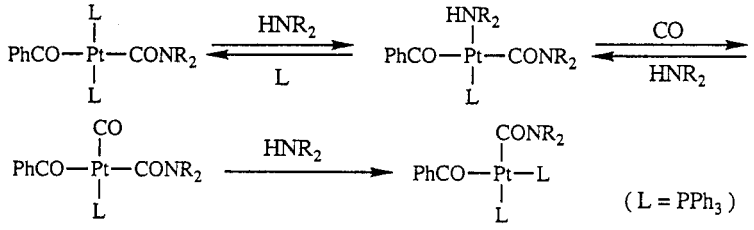
On the other hand, when non–dissociating trimentylphosphine is used as the ligand, no trans–cis isomerization is observed suggesting that dissociation of the tertiary phosphine ligand is essential for bringing about the trans–cis isomerization.



The triphenylphosphine ligand in the *trans*-(benzoyl)bis(triphenylphosphine)–platinum chloride is not readily substituted by CO even under CO pressure, but the triphenylphosphine ligand is replaceable by amine. The amine–coordinated platinum complex once formed is then replaced by carbon monoxide.

The CO ligand thus attached to platinum may be attacked by amine and then deprotonation gives the carbamoyl ligand coordinated to platinum at the positioin cis to the benzoyl ligand. Recoordination of triphenylphosphine to the site trans to the benzoyl ligand forms the *cis*-(benzoyl)(carbamoyl)platinum complex completing the isomerization process. Although the corresponding cis palladium isomer is labile and can not be isolated, the *cis*-(benzoyl)(carbamoyl)platinum analog is quite stable.

These results led us to propose the mechanism of formation of *cis*-(benzoyl)–(carbamoyl)platinum complex from *trans*-(benzoyl)(carbamoyl)platinum as shown below (eq 6).

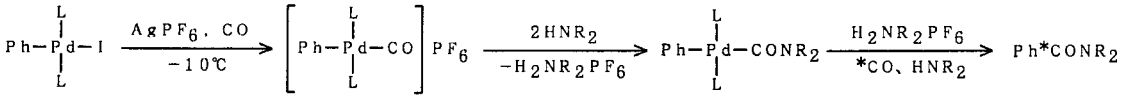


(6)

MECHANISM OF AMIDE FORMATION

The reaction of aryl halide with CO and secondary amine in the presence of the palladium catalyst gives amide as byproduct in addition to α–keto amide. We have previously proposed that formation of the amide can be reasonably explained by assuming nucleophilic attack of amine on CO ligand coordinated to phenylpalldium species (ref. 4b, 5). The reaction was proposed to give a phenyl–carbamoyl palladium complex that reductively eliminates the amide. This proposal was somewhat surprizing, because it is generally believed that the amide is formed by nucleophilic attack of amine on aroylpalladium complex. Employment of the trimethylphosphine ligands allowed us to examine the behavior of the phenyl–palladium complex and provided us conclusive evidence to support operation of reductive elimination of the aryl and carbamoyl ligands to give amide.

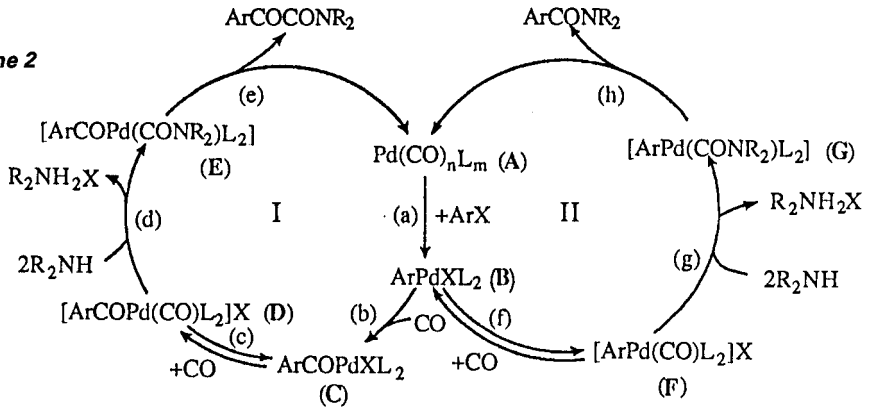
The phenylpalladium complex coordinated with CO and two trimethylphosphine ligands was found to give *trans*-(carbamoyl)(phenyl)bis(trimethylphosphine)palladium on treatment with amine in the presence of CO. The isolated trans isomer having the phenyl and the carbamoyl ligands proved to be stable and did not release amide on treatment with CO and amine. However, analogously to the behavior of the *trans*-benzoyl–carbamoyl–palladium complex the *trans*-phenyl–carbamoyl complex gave amide readily on reaction with alkylammonium salt as weak acid in the presence of amine and CO.



If the reaction of the phenylpalladium complex with CO is carried out at higher temperature, CO insertion into the Ph–Pd bond occurs to give benzoylpalladium complex that undergoes further reaction with CO and amine to give α–keto amide as the double carbonylation product. We have previously observed the employment of less bulky secondary amines in the catalytic process caused decrease in selectivity for the double carbonylation product. The less bulky amines being more reactive toward the coordinated CO ligand are considered to give the aryl–carbamoylpalladium complex without allowing the CO insertion into the aryl–palladium bond to take place, hence leading to formation of the single

carbonylation product. The present study using the trimethylphosphine–coordinated phenylpalladium complex is in accordance with the assumption. The overall mechanisms for the catalytic double and single carbonylations are summarized in Scheme 2.

Scheme 2



Scheme 2 comprises two catalytic cycles I and II with common intermediates A and B. Cycle I gives α–keto amide, the double carbonylation product, whereas cycle II affords amide, the single carbonylation product.

MECHANISMS OF DOUBLE AND SINGLE CARBONYLATION TO GIVE α–KETO ESTER AND ESTER

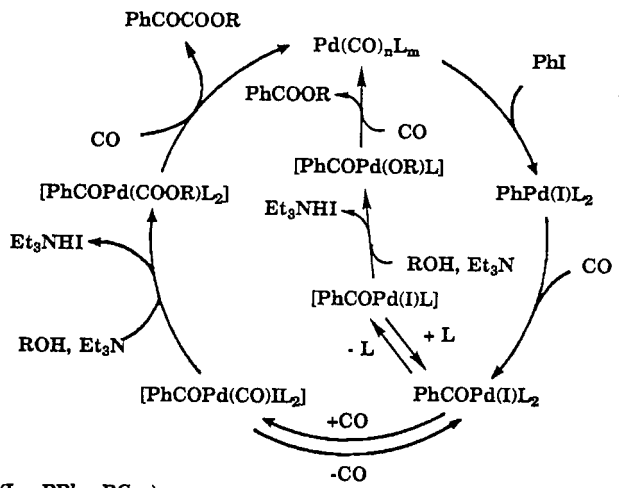
The palladium–catalyzed reaction of aryl iodides with alcohols and tertiary amine in the presence of carbon monoxide yields α–keto esters and esters (ref. 9, 10).

$$PhI + 2CO + ROH + Et_3N \xrightarrow{[Pd]} PhCOCOOR\ (+\ PhCOOR) + Et_3NHI$$

Detailed studies of the double and single carbonylation to give esters revealed operation of the mechanisms as shown in Scheme 3.

Scheme 3

Proposed mechanisms of double and single carbonylation of phenyl iodide with alcohols and triethylamine to give α–keto esters and esters.

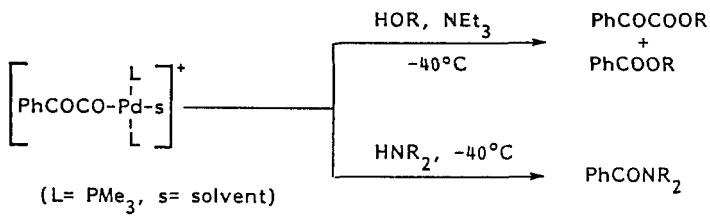


The process is composed of two catalytic cycles. The cycle to give α–keto ester is analogous to the cycle I in Scheme 2 that gives α–keto amide. A zero valent palladium species undergoes oxidative addition of aryl iodide to give arylpalladium iodide which is carbonylated to give aroylpalladium species. Carbon monoxide then coordinates to the aroylpalladium complex and undergoes nucleophilic attack by alcohol and tertiary amine to give aroyl–alkoxycarbonylpalladium that reductively eliminates α–keto ester with regeneration of the Pd(0) species as carrier of the further catalytic cycle.

The mechanism of single carbonylation to give carboxylic ester is somewhat different from the mechanism to give amide. The aroylpalladium spescies serves as the common intermediate to give ester as well as α–keto ester. Preceded by dissociation of the tertiary phosphine ligand an intermediate aroyl–alkoxide complex is formed on reacion with alcohol and amine and reductive elimination of the aroyl and alkoxide ligands affords ester.

ON FEASIBILITY OF DOUBLE CO INSERTION MECHANISM

Although the overall mechanisms of the double carbonylation can be explained in a consistent manner, there still remains the possibility of operation of the CO double insertion mechanism. We have previously prepared diphenylmethylphosphine–coordinated *trans*-α–ketoacylpalladium chloride and found that it was readily decarbonylated to give aroylpalladium complex preceded by phosphine dissociation (ref. 11). The corresponding trimethylphosphine–coordinated complex proved to be more stable to allow study of its reaction with nucleophiles. Cationic phenyl–glyoxylpalladium complex having two trimethylphosphine ligands reacted with alcohols and triethylamine to liberate α–keto ester together with ester, whereas the reaction with amine produced amide.

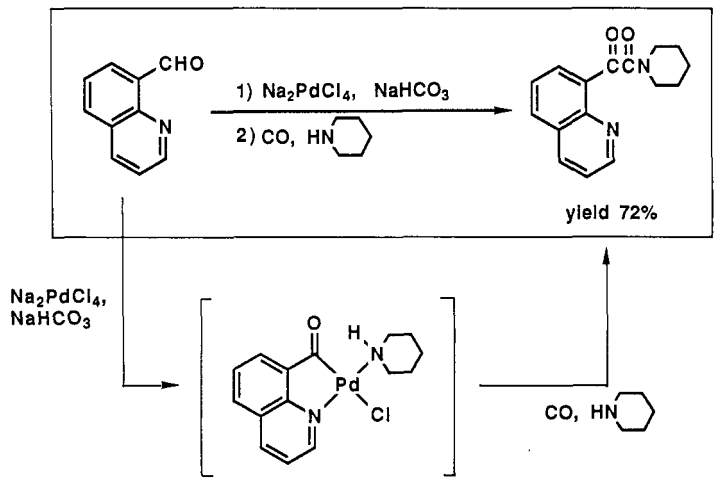


The results indicate the possibility of formation of α–keto ester from a species formed by double CO insertion into the Ph–Pd bond under certain conditions (ref. 12). The formation of amide on treatment of the phenylglyoxylpalladium complex may be accounted for by nucleophilic attack of the amine on the carboxyl group adjacent to the phenyl group in the phenylglyoxyl ligand.

APPLICATION TO OTHER SUBSTRATES

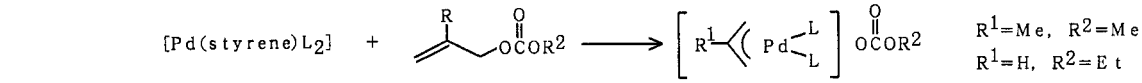
Besides aryl halides other substrates can be led to α–keto acid derivatives by applying the same principle. Alkeny halides having aryl substituent(s) reacted similarly to give α–keto amides (ref. 13) Aromatic aldehydes such as quinoline–8–carbaldehyde and *o*-(*N*,*N*-dimethylamino)benzaldehyde react with tetrachloropalladate through a C–H activation reaction to give the corresponding aroylpalladium complexes that afford α–keto amides in high yields upon carbonylation (ref. 14).

Carbonylation of Aldehyde via C-H Bond Activation

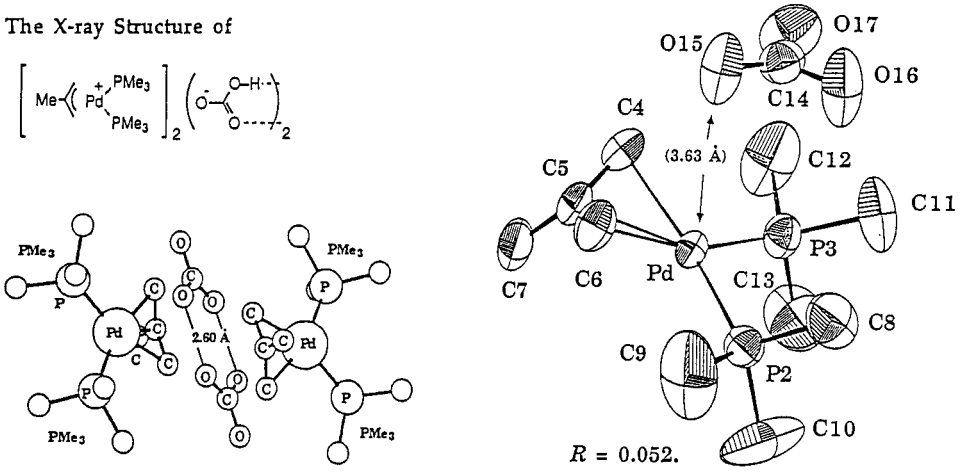


Although the double carbonylation process is suitable to convert aryl halides into α–keto acid derivatives, the method is not applicable to aliphatic halides, since they react with secondary amines to give tertiary amines. Although still stoichioimetric, we have now found a process to double carbonylate allylic carbonates.

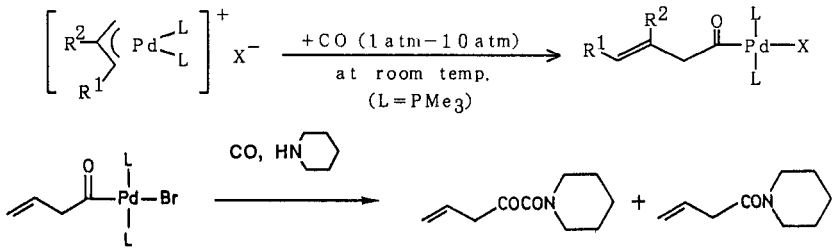
Previously Tsuji found a carbonylation process of converting allyl carbonates to unsaturated carboxylic esters (ref. 15). A π–allylpalladium complex was considered to be a likely intermediate formed by oxidative addition of the allyl carbonates, but no attempt was made to isolate the intermediate and examine its properties. We have isolated the reaction products of alky allyl carbonates with trimethyl–phosphine–coordinated zero–valent palladium complex and characterized them as ionic π–allylpalladium complexes having two trimethylphosphine ligands and an alkyl carbonate anion.



The alkyl carbonate anion was found to be susceptible to hydrolysis and readily converted into hydrogen carbonate anion. The molecular structure of the ionic π–allylpalladium complex having the hydrogen carbonate anions bridging two π–allylpalladium entities has been established as shown below (ref. 16).



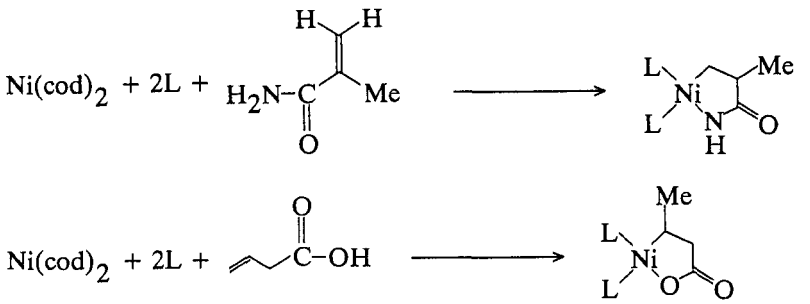
For double carbonylation to proceed from a π–allyl complex it is required that first CO insertion occurs to give acylpalladium complex. The reaction is followed by nucleophilic attack of amine on the coordinated CO to give carbamoyl ligand that subsequently combines with the acyl ligand to release α–keto amide. In fact, occurrence of the CO insertion into the allyl–palladium bond was observed to give acyl type complexes that liberated unsaturated α–keto amide and amide on treatment with amine and CO (ref. 17).



Catalytic double carbonylation of allyl carbamate has been attempted but only stoichiometric amounts of amide and α–keto amide derivatives have been obtained so far.

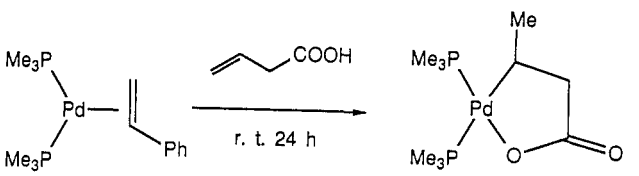
CYCLIZATION CARBONYLATION OF UNSATURATED CARBOSYLIC ACID

We have previously observed that unsaturated acid and amide interact with zero–valent nickel complex to give nickellacyclic ester and amide that can be led to cyclic amide and imide on treatment with carbon monoxide (ref. 18).



Attempts to make the process catalytic has not been successful as far as a nickel complex was used, presumably due to inertness of zero–valent nickel carbonyl complex involved.

We have now prepared the corresponding palladium metallacycloester having two trimethylphosphine ligands by treating zero–valent palladium complex with 3–butenoic acid. The metallacycle was unequivocally characterized by X–ray analysis and spectroscopy. It was futher established that reaction of the metallacycle with CO gave methyl succinic anhydride.



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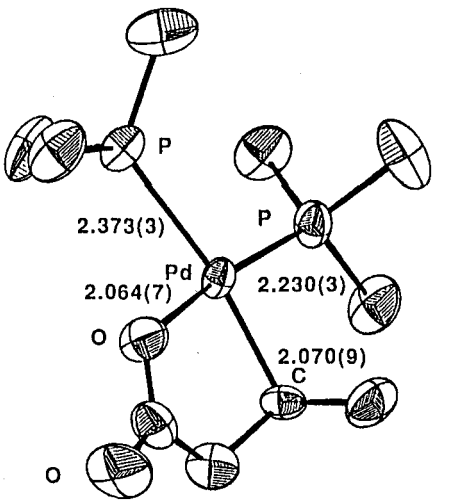
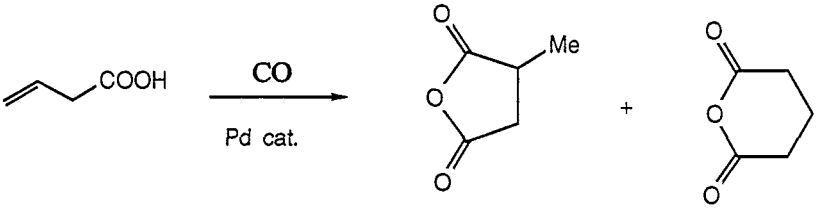


Molecular structure of 6.

Based on the findings catalytic reaction was examined. Indeed, the reaction of 3–butenoic acid with CO in the presence of palladium complex catalytically produced methylsuccinic anhydride and glutaric anhydride (ref. 19).



CONCLUSION

Through studies on elementary processes of organopalladium and –platinum complexes that serve as model compounds in palladium–catalyzed double and single carbonylations important information on the detailed mechanisms of these multistep catalytic reactions has been obtained. Furthermore, some novel catalytic processes have been realized on the basis of the study on the elementary processes regarding carbonylation reactions. The present study proves the utility of this type of approach for understanding the known catalytic processes and for further designing new catalytic processes.

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