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Carbonylation of Metal Carbene with Carbon Monoxide: Generation of Ketene

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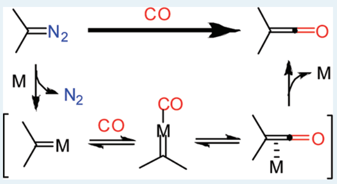
ABSTRACT: Carbonylation of metal carbene complexes, including the carbonylation of Group VI Fischer carbenes, is reviewed in this article. In particular, transition metal-catalyzed carbonylation of metal carbene complexes with carbon monoxide is discussed in detail. This type of carbonylation reactions provides an efficient access to ketene species, which are highly important in organic synthesis.



KEYWORDS: carbonylation, carbon monoxide, metal carbene, ketene, β-lactam synthesis

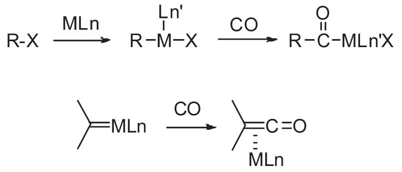
1. INTRODUCTION

Carbonylation of M-C bonds via CO insertion is one of the most important elementary processes in organometallic chemistry. Transition metal-catalyzed carbonylation with CO, in particular Pd-catalyzed carbonylation, has now been well-established as one of the most important ways to synthesize a wide variety of compounds bearing the carbonyl functionality.[1−7] As compared with the CO insertion into M-C bonds, which leads to the formation of acyl-metal species, the carbonylation of metal carbene species would afford metal-complexed ketene intermediates (Scheme 1).

Ketenes are highly useful intermediates in organic synthesis.[8−11] The most common method to access ketenes is from acyl halides through base-promoted dehalogenation. Therefore, carbonylation of metal carbene provides an alternative straightforward approach to the generation of ketene species. However, compared to the carbonylation of M-C bonds, the carbonylation of metal carbene is less developed. Most of the investigations in this area have been focused on stoichiometric transformations, as represented by stoichiometric CO insertion of Fischer carbene complexes under photolytic or thermolytic conditions. The ketenes generated from Fischer carbenes have found important applications in organic synthesis, such as benzannulation (Dötz reaction), and [2 + 2] ketene−imine or ketene-alkene cyclizations.[12−18]

Catalytic carbonylation of metal carbene with CO so far has been only sporadically documented in the literature. Early studies have been focused on the transition metal-catalyzed carbonylation of dihaloalkanes with CO. These reactions are limited by substrate scope and rigorous conditions such as high pressure of CO and high reaction temperature. On the other hand, since diazo compounds are the most common precursor for the generation of metal carbene, it would be natural to conceive the development of transition metal-catalyzed carbonylation with diazo substrates.[19−21] Surprisingly, the investigations along this line have only appeared very recently, mainly by the research groups of Ungváry and Wang.

Scheme 1. Carbonylation of M-C Bond and M═C Bond



This perspective article will focus on the transition metal-catalyzed carbonylation of metal carbene with CO. However since they are closely related, the carbonylation of metal carbene with CO in a stoichiometric process, in particular the carbonylation of Fischer carbene complexes, will be discussed first.

2. CARBONYLATION OF METAL COORDINATED CARBENES WITH CO

2.1. Carbonylation of Stable Mn, Fe, Pt Carbene Complexes. The reactions of stable transition metal carbene complexes with CO have attracted attention over the years, presumably because of their connection with the reaction mechanism of Fischer−Tropsch synthesis.[22] In 1987, Herrmann and Plank reported a carbonylation of diphenylcarbene manganese complexes under high pressure of CO (650 bar initial pressure) (Scheme 2).[23] Diphenylketene complexes **2a** and **2b** were obtained in about 40% yield. The structure of η^2-(C,C)-ketene complex was confirmed by X-ray crystallography. Hydrogenation of the ketene complexes under high pressure led to the formation of a mixture of aldehyde **3** and alcohol **4**.

Following Herrmann's report, several other transition metal carbene carbonylations with CO were documented in the

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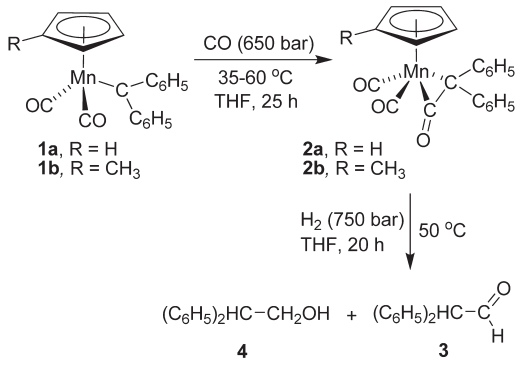
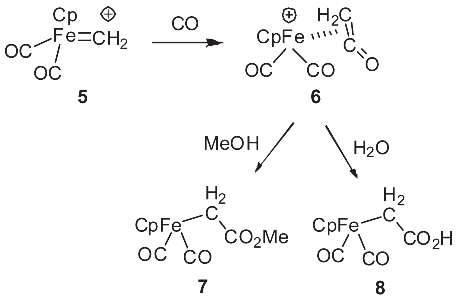
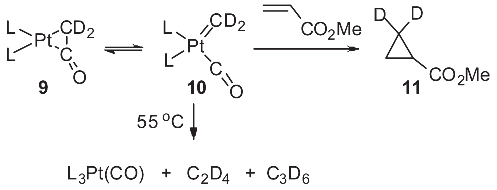
Scheme 2. High Pressure Carbonylation of Mn-Carbene Complexes



Scheme 3. Carbonylation of Iron-Methylidene Complex



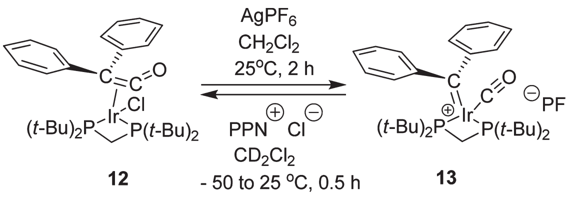
Scheme 4. Reversible Carbonylation Process



literature. Bodnar and Cutler reported formation of a stable η^2-(C,C) ketene compound CpFe $(CO_2)(CH_2{=}C{=}O)^+PF_6^-$ by carbonylation of an iron-methylidene complex.[24] The carbonylation of the iron-methylidene complex **5** occurred under mild conditions, affording iron-ketene complex **6**, which could be isolated as a stable solid at room temperature (Scheme 3). The η^2-(C,C)-ketene complex **6** can be attacked by nucleophiles, such as methanol or H_2O at the ketene carbonyl, to afford iron complexes **7** and **8**. An intriguing question concerning the carbonylation is whether the carbenoid center picks up exogenous CO, or CO comes from a metal center through migratory insertion. ^{13}C Labeling experiment indicates the CO in the iron ketene complex is from exogenous CO. Therefore, in this particular case, the carbonylation resembles the reaction of organic carbenium ion with CO.

Miyashita and co-workers reported the preparation of platinum η^2-(C,C)-ketene complexes $Pt(CH{=}C{=}O)L_2(L{=}PPh_3)$

Scheme 5. Controllable Interconversion between a Ketene Ligand and Carbene and CO Ligands



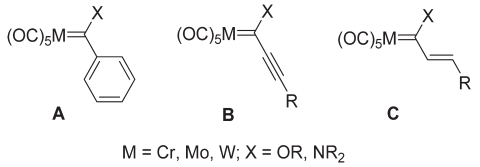


Figure 1. Structure of Group VI Fischer Carbenes.

and $PtCl_2(CH_2{=}C{=}O)$ by the reaction of PtL_4 with CH_2Br_2 and CO in the presence of Zn (eq 1).[25]

$$Pt(PPh_3)_4 + CH_2Br_2 \xrightarrow[\text{Zn, THF}\;\; -30\text{-}20^{\circ}\text{C, 10h}]{\text{CO (3 atm)}} (Ph_3P)_2Pt(H_2C{=}C{=}O) \;\; 23\% \qquad (1)$$

Interestingly, the thermal decomposition at 55 °C of the ketene complexes **9** yielded various hydrocarbons, which indicates the C−C bond cleavage of the ketene ligand to form the metal-carbene−CO intermediate **10** (Scheme 4). The involvement of the intermediate **10** in the rearrangement of **9** is substantiated by the formation of cyclopropanation product **11** in the carbene trapping experiment. These results clearly indicate the reversible nature of the carbonylation process.

The reversible conversion of a ketene ligand to carbene and CO ligands on a single metal center was later further demonstrated by Grotjahn and co-workers in an Ir-ketene complex (Scheme 5).[26] When chloride ligand of the η^2-(C,C) Ir-ketene complex **12** is removed by adding Ag(I) salt, the C=C bond of the ketene ligand is broken to give complex **13**. Interestingly, the ketene complex is reformed upon adding chloride.

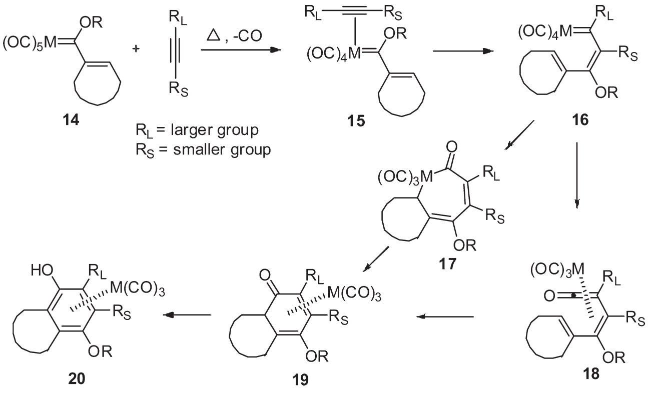
More recently, Goll and Fillion have utilized ketene to generate Pd carbene species, which is subsequently involved in Pd carbene transformations.[27]

2.2. Carbonylation of Group VI Fischer Carbene Complexes.

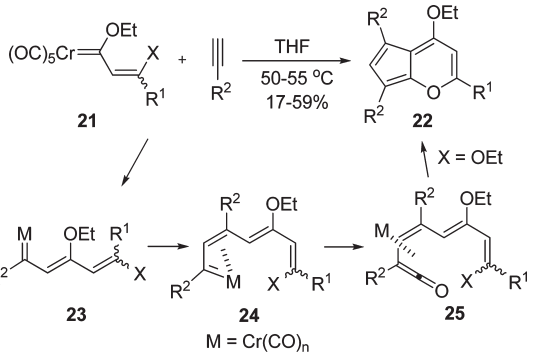
Fischer carbene complexes, which were first reported by Fischer and Maasböl as the pentacarbonyl[methoxybenzylidene] tungsten(0) complex in 1964,[28−32] are heteroatom-stabilized metal carbene complexes (Figure 1). In most cases, they are α, β-unsaturated Group VI metal carbene complexes, which are connected with aryl, alkenyl, or alkyl (X = OR or NR_2, and M = Cr, Mo, or W).

One of the most synthetically useful reactions of Group VI metal carbene complexes is the Dötz benzannulation reaction (eq 2).[33] In the early days since their discovery, Fischer carbene complexes were mainly studied because of mechanistic curiosity, and hardly were considered as potentially useful in preparative organic chemistry. Since the discovery of the Dötz benzannulation reaction in 1975, Group VI metal carbene complexes have gradually attracted attention from synthetic organic chemists. The Dötz benzannulation reaction, which has now been established

Scheme 6. Mechanism of Dötz Benzannulation Reaction



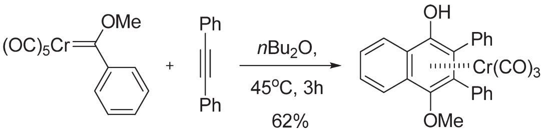
Scheme 7. Carbonylation Subsequent to Two Consecutive Alkyne Insertions



X = OEt, NMe_2

R^1 = *t*-Bu, $C(CH_3)OEt$, C_3H_5OEt; R^2 = *n*-Pr, Ph

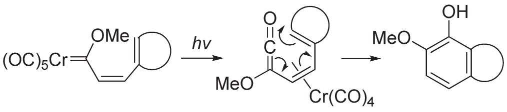
as an important strategy to access fused cyclic or polysubstituted aryl compounds, is particularly useful in the synthesis of naphthoquinone frameworks.[17,29−35]

 (2)

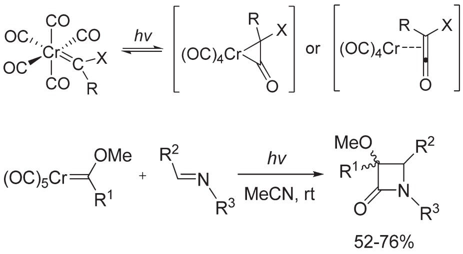
In the mechanism of Dötz benzannulation, the carbonylation of the carbene ligand through migratory insertion of the CO ligand on the metal is suggested as one of the key steps. As shown in Scheme 6, the first step of the Dötz benzannulation reaction is the dissociation of one of the carbonyl ligands located cis to the carbene moiety in Fischer carbene complex **14**, which is suggested to be the rate-determining step.[36−38] Subsequently, the alkyne component coordinates onto the coordinatively unsaturated metal complex, which is followed by the insertion into the metal−carbon bond to form carbene complex **16**. The photochemically induced CO expulsion and the coordination of an alkyne with subsequent phenol formation can be followed directly by online FT-IR spectroscopy.[38]

From the vinylcarbene **16** there are two possible pathways which can lead to **19**. As suggested by Casey, **16** may cyclize to metalacycloheptadienone **17** by CO insertion, which is followed by reductive elimination to afford **19**.[39] Alternatively, the carbonyl ligand may first insert into carbene to form the alkadienylketene complex **18**, and then electrocyclic ring closure occurs to give **19**.[40−42] Finally, **19** tautomerizes to the metal complexed *para*-alkoxyphenol **20**.

Scheme 8. Dötz Benzannulation under Photolytic Conditions



Scheme 9. Photoinduced Carbonylation of Fischer Carbene and *β*-Lactam Synthesis



Carbonyl insertion may occur after two consecutive alkyne insertions. For example, de Meijere and co-workers reported the reaction of ethenylcarbenechromium complexes **21** with terminal alkynes (Scheme 7).[43] The insertion of the first alkyne leads to a 1-chroma-1,3,5-hexatriene **23** with a *Z*-configured double bond at center, which is not capable of 6π-electrocyclization. Consequently, the second alkyne insertion occurs, followed by carbonyl insertion and intramolecular [4 + 2] cycloaddition to afford bicyclic product **22**.

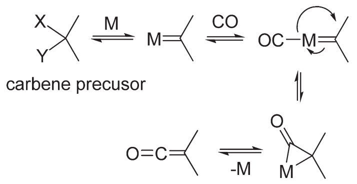
When the photoinduced CO insertion into metal carbene is applied to the diene carbene complex, a metal ketene complex that is analogous to the intermediate **18** in Scheme 5 is generated. This leads to the development of a photochemical variant of the Dötz reaction (Scheme 8).[12,44−46]

Fischer carbene complexes undergo photochemical coupling of a carbonyl ligand to form metal ketene complexes, which react with various nucleophiles. For example, Dorrer and Fischer have shown that the carbonylation reaction of $(CO)_5Cr{=}C(OMe)Ph$ with vinylpyrrolidone under 150 atm of CO leads to the formation of methoxyphenylketene and subsequent [2 + 2] cycloaddition.[47]

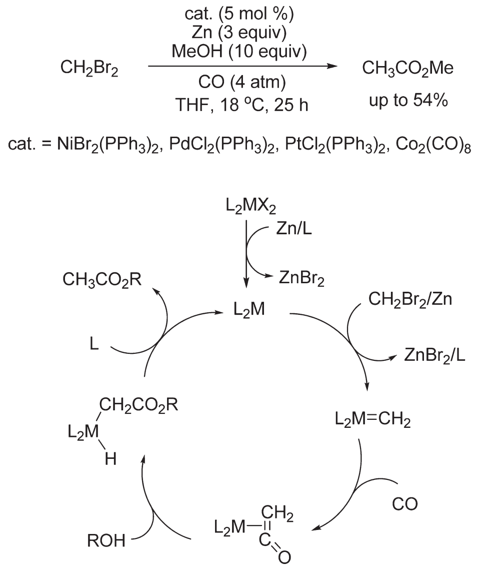
This chemistry has been extensively explored by Hegedus and co-workers. In particular, this photoinduced carbene carbonylation process has been applied in the efficient synthesis of β-lactams (Scheme 9).[12,14,48]

The Staudinger [2 + 2] reaction of ketene and imine to form β-lactam is one of the most important applications of ketene intermediates in organic synthesis. The ketenes are usually generated from acid chlorides with treatment of tertiary amines, or from Wolff rearrangement of α-diazo carbonyl compounds.[8−11] The metal ketene complexes generated from photolysis of Fischer carbene complexes undergo most of the reaction of free ketenes generated by classical means. Moreover, the Fischer carbene approach of ketene in many cases demonstrates greater selectivity and functional group tolerance.

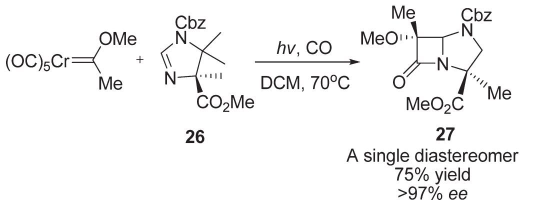
Scheme 10. Transition Metal-Catalyzed Carbonylation of Carbene



Scheme 11. Transition Metal-Catalyzed Carbonylation of *gem*-Dibromide



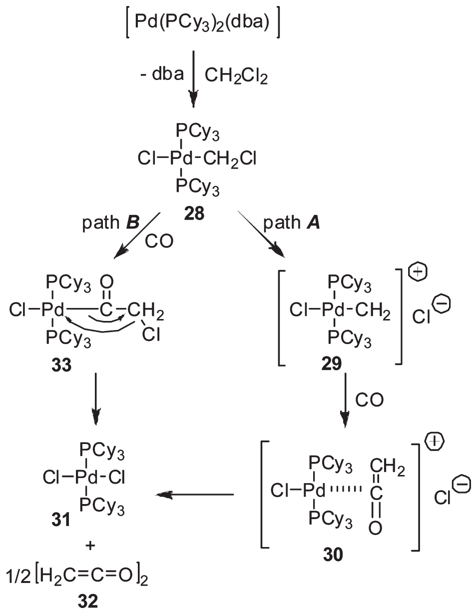
The [2 + 2] reactions of metal ketene complexes and imines are highly diastereoselective in most cases. Cyclic and heterocyclic imines are similarly reactive, producing the *β*-lactam products as single diastereoisomers. For example, when chiral imidazoline **26** was used, very high diastereomeric excess (*de*) (essentially 100%) and enantiomeric excess (*ee*) (>97%) was observed (eq 3).[49]



(3)

Photoinduced insertion of CO into other Group VI metal carbene complexes has also been demonstrated.[8−11,50] Casey and Tuinstra have reported that $(CO)_5WC(C_6H_5)_2$ reacts with CO to afford a diphenylketene intermediate, which leads to the formation of ethyl diphenyacetate in the presence of EtOH.[39] In addition, thermal decomposition of the nonheteroatom-stabilized carbene complexes $(CO)_5M{=}CPh_2$ (M = Cr, W) can produce diphenylketene intermediates.[51]

Scheme 12. Pd-Promoted Carbonylation of CH_2Cl_2 in Stoichiometric Reaction



3. TRANSITION METAL-CATALYZED CARBONYLATION OF CARBENE

Although Fischer carbene carbonylations are highly reliable and versatile, the stoichiometric use of the transition metal limits their wide application in organic synthesis to some extent. Theoretically, catalytic carbene carbonylation with exogenous CO is possible if the steps of metal carbene generation, association of CO to metal, CO migratory insertion to carbene, and dissociation of the ketene from metal (or trapping by nucleophile and then dissociation from metal) are all fast enough and can be matched (Scheme 10).

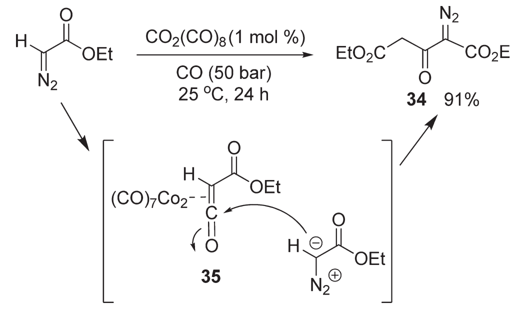
3.1. Transition Metal-Catalyzed Carbonylation of Dihalides.

Although such process seems feasible, catalytic carbonylation reactions of metal carbenes with CO have been much less developed. In the limited reports of early days, dihaloalkanes were used as the source of carbene. Transition metal-catalyzed carbonylation of *gem*-dibromide with CO in the presence of Zn power as a reducing agent was reported by Miyashita and coworkers in 1986 (Scheme 11).[52] Several different kinds of transition metals, such as Ni, Pd, Pt, and Co, have been examined in this transformation. $Co_2(CO)_8$ complex showed the highest efficiency. The ketene intermediate thus generated could be trapped by methanol to give methyl acetate.

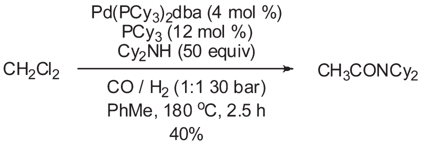
The catalytic carbonylation of less reactive CH_2Cl_2 was studied by Osborn and co-workers. In the beginning, they investigated the activation of CH_2Cl_2 by Pd(0) complex $[Pd(PCy_3)_2(dba)]$ in stoichiometric reaction (Scheme 12).[53] To activate the less reactive C−Cl bond, it has been found that strongly electron donating, but sterically bulky phosphane ligands, such as PCy_3 and P^iPr_3, are required. The Pd(0) complex reacts with CH_2Cl_2 rapidly at 25 °C to afford a colorless chloromethyl complex **28** after recrystallization. When **28** was treated with CO (30 bar) in benzene-d_6 at 25 °C, Pd complex **31** and diketene **32** were formed as characterized by ^1H and ^{31}P NMR. The reaction is suggested to follow the pathway involving Pd carbene **29** formation and subsequent carbonylation of carbene ligand to form **30** (path ***A***). However, an alternative pathway in which CO insertion into Pd−C bond occurs first to form **33** cannot be ruled out (path ***B***).

The carbonylation of CH_2Cl_2 can be carried out under catalytic conditions with Pd(0) complex if the Pd complex **31** can be

Scheme 13. $Co_2(CO)_8$-Catalyzed Carbonylation of Ethyl Diazoacetate



reduced to regenerate the active species $Pd(PCy_3)_2$. This was indeed the case. Thus, under 30 bar of CO and H_2 (1:1) at 180 °C for 2.5 h, dichloromethane could be transferred to a palladium-ketene intermediate, and then was trapped by Cy_2NH with 40% yield (eq 4).

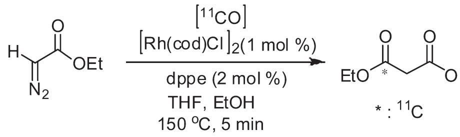


$$CH_2Cl_2 \xrightarrow[\text{CO / } H_2 \text{ (1:1 30 bar)},\ \text{PhMe, 180 °C, 2.5 h},\ 40\%]{Pd(PCy_3)_2dba \text{ (4 mol \%)},\ PCy_3 \text{ (12 mol \%)},\ Cy_2NH \text{ (50 equiv)}} CH_3CONCy_2 \quad (4)$$

The transition metal-catalyzed carbonylation of CH_2Br_2 or CH_2Cl_2 seems appealing in respect of the significance in organic synthesis. However, further studies in this field were rarely reported in the following years. The low efficiency and rigorous conditions of the carbonylation process might be attributed as reasons for the lack of interest.

3.2. Transition Metal Catalyzed Carbonylation of Diazo compounds. Diazo compounds are the most common precursors of metal carbenes.[19−21] They can be decomposed by transition-metal complexes to generate metal carbene intermediates, which can subsequently undergo diverse transformations. These transformations, typically cyclopropanation, C−H bond insertion, and ylide formation, have their various useful applications in organic synthesis. In these catalytic transformations, rhodium and copper are the two most useful metals in terms of efficiency and selectivity, although almost all the transition metals can promote the extrusion of dinitrogen from diazo compounds. Regardless of the extensive studies on transition metal-catalyzed transformations of diazo compounds, transition metal-catalyzed carbonylation of diazo compounds has not been reported until recently.

3.2.1. Rh-Catalyzed Carbonylation of Ethyl Diacetate. In 2006, Långström and co-workers reported a Rh-catalyzed carbonylation of ethyl diazoacetate (EDA) in their synthesis of diethyl [carbonyl-^{11}C] malonate (eq 5).[54]

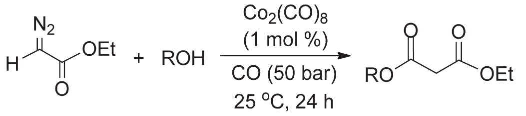


(5)

dppe: 1,2-bis(diphenylphoshino)ethane

3.2.2. $Co_2(CO)_8$-Catalyzed Carbonylation of Ethyl Diazoacetate. Ungváry and co-workers have carried out systematic studies on $CO_2(CO)_8$-catalyzed carbonylation of ethyl diazoacetate since 2003.[55−67] In their initial study, they observed that in the presence of 1 mol % $CO_2(CO)_8$ and under atmospheric pressure of CO at room temperature ethyl diazoacetate (EDA) was slowly converted to a new diazoester **34**. Carrying out the reaction under high pressure of CO (50 bar), the conversion of EDA to **34** could be completed in 24 h (Scheme 13). Ethoxycarbonyl ketene **35**, which is formed through carbonylation of cobalt ethoxycarbonylcarbene complex, is proposed to be the intermediate. This ketene intermediate is attacked by EDA (as nucleophile) to afford **34**.[68]

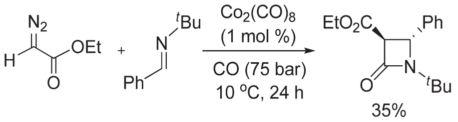
By introduction of a nucleophile, such as alcohol or amine, the ketene intermediate can be trapped by the nucleophile to afford the corresponding malonate derivatives in up to 95% yield (eq 6).



(6)

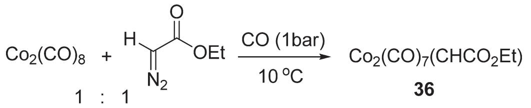
R = Me, Et, ^{t}Bu, Ph

In the presence of *N-tert*-butylbenzaldimine, Staudinger [2 + 2] cycloaddition with the (ethoxycarbonyl)ketene intermediate occurs to afford the corresponding *trans* β-lactam as single isomer.[64,65]



(7)

To gain insight into the reaction mechanism, stoichiometric experiments were carried out.[56] When equimolar amounts of EDA and $CO_2(CO)_8$ were mixed in *n*-octane at room temperature under atmospheric pressure of CO, an orange colored oil of cobalt complex, which was characterized as **36** was isolated in 82% yield by column chromatography at 1 °C under argon (eq 8). Spectroscopic characterization and density functional theory (DFT) calculation suggest ethoxycarbonylcarbene-bridged dicobalt structure for **36**.



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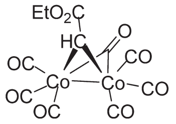

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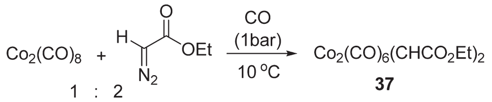
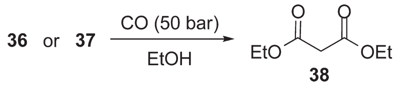
Interestingly, when the reaction was carried out with a 2:1 molar ratio of EDA and $CO_2(CO)_8$, a yellow oil of cobalt complex **37**, in which two of the CO ligands are replaced by ethoxycarbonylcarbene ligands, was isolated (eq 9).



(9)

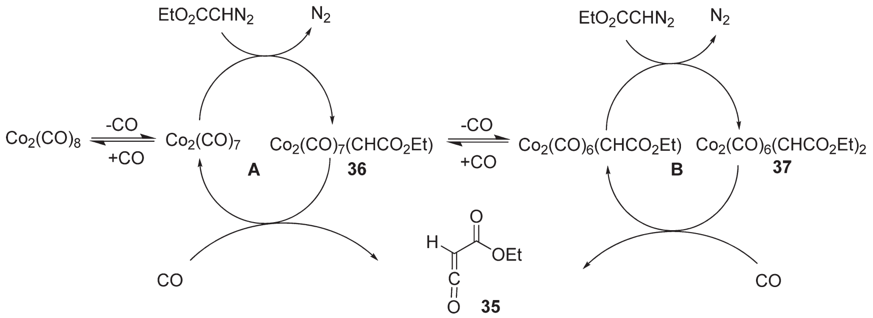
Furthermore, under 50 bar of CO and in the presence of EtOH, both **36** and **37** could be quantitatively converted to diethyl malonate **38** (eq 10).



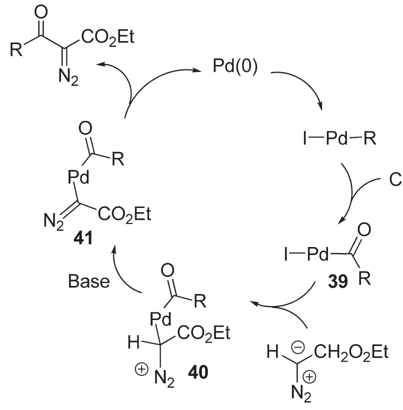
(10)

On the basis of those experimental observations and kinetic studies,[59] the authors have proposed a reaction mechanism for

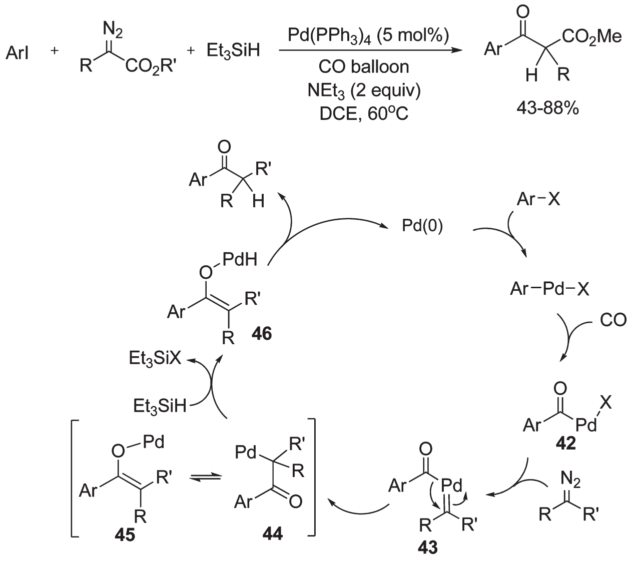
Scheme 14. Mechanism for $Co_2(CO)_8$-Catalyzed Carbonylation of Ethyl Diazoacetate



Scheme 15. Mechanism for Pd-Catalyzed Carbonylation of Diazo Compound

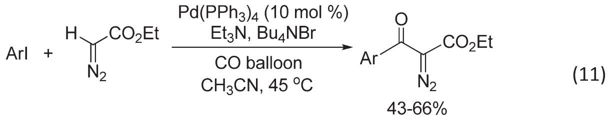


Scheme 16. Pd-Catalyzed Carbonylation/Acyl Migratory Insertion



the $CO_2(CO)_8$-catalyzed carbonylation of EDA (Scheme 14). The mechanism is composed of two catalytic cycles **A** and **B**. In cycle **A**, cobalt complex **36** is the intermediate, while in cycle **B** the active intermediate is cobalt complex **37**. Kinetic data indicate the reaction conditions, in particular the pressure of CO, have significant effect on the reaction pathways.

3.2.3. Pd-Catalyzed Carbonylation of Diazo Compounds. In 2007, Wang and co-workers reported Pd-catalyzed cross-coupling of aryl iodides with EDA.[69] The interesting feature of this coupling reaction is that the diazo functionality can tolerate the Pd-catalyzed reaction conditions. When the coupling reaction was carried out under an atmospheric pressure of CO, the carbonylation occurred to afford β-keto α-diazocarbonyl compounds in moderate yields (eq 11).



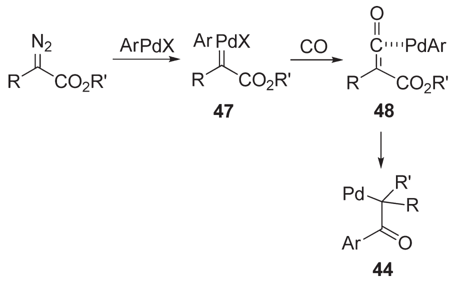
(11)

The reaction mechanism presumably follows the common oxidative addition-CO insertion-diazo complexation-deprotonation-reductive elimination sequence (Scheme 15). The proposed reaction mechanism involves the oxidative addition of Pd(0) to iodide, followed by CO insertion to generate acylpalladium species **39**. Complexation of EDA to **39** gives diazonium complex **40**, which is followed by deprotonation to generate **41**. Finally, reductive elimination from **41** gives the product and completes the cyclic cycle.

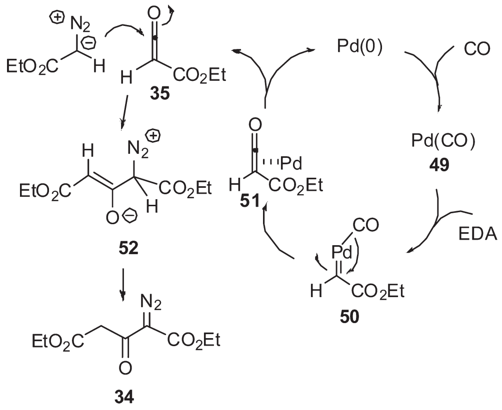
It is noted that in EDA, a relatively acidic proton is present, which makes deprotonation from diazonium complex **40** possible. If such acidic proton is absent, from the analogous diazonium complex, dinitrogen extrusion may occur to generate a Pd carbene species. Recent studies indicate that this is indeed the case. From Pd carbene, migratory insertion occurs and a series of novel coupling reactions have been developed based on this process.[70−72] In the presence of CO, a novel Pd-catalyzed carbonylation reaction was developed by Wang and co-workers, as shown in Scheme 16.[73] In the proposed reaction mechanism, acylpalladium species **42** is first generated through oxidative addition and CO insertion. Subsequently, **42** reacts with diazo substrates to afford Pd carbene intermediate **43**, which is followed by acyl migratory insertion to generate *C*-bound enolate **44**, which is in equilibrium with *O*-bound enolate **45**. Transmetalation with Et_3SiH and subsequent reductive elimination afford the final product.

Although this mechanistic proposal seems reasonable in view of the analogous transformations involving Pd carbene migratory insertion, which have been extensively reported recently,[70−72] an alternative mechanism as shown in Scheme 17 cannot be ruled out. In this reaction mechanism, the Pd-catalyzed carbonylation of diazo compound occurs first to generate a Pd-ketene complex

Scheme 17. Alternative Mechanism for Pd-Catalyzed Carbonylation

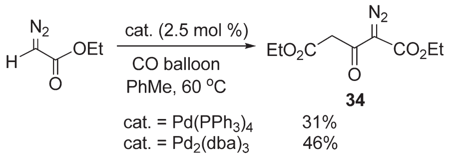


Scheme 18. Proposed Reaction Mechanism for Pd-Catalyzed Carbonylation



48 through Pd carbene **47**, from which migratory insertion occurs to afford *C*-bound palladium enolate **44**.

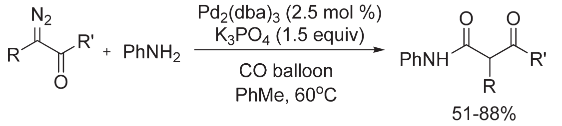
A comprehensive study of Pd-catalyzed carbonylation of diazo compounds was reported by Wang and co-workers in 2011.[74] In the initial study with EDA, similar results as in the $CO_2(CO)_8$-catalyzed system were observed with Pd(0) catalyst under atmospheric CO pressure (eq 12).



(12)

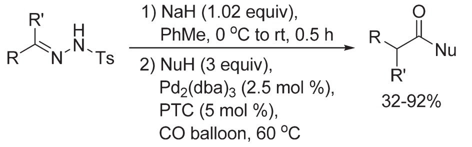
The formation of diazo compound **34** can be rationalized by the mechanism shown in Scheme 18. We assume that CO-complexed Pd species **49** is the active catalyst in the system. Decomposition of the diazo compound induced by the Pd catalyst generates a Pd-carbene **50**, which undergoes carbonylation to give ketene intermediates **51** or **35**. The ketene is then attacked by EDA, which functions as a simple nucleophile in this step, affording intermediate **52**. Intermediate **52** undergoes proton transfer to give the final product **34**.

The ketene intermediate generated by Pd-catalyzed carbonylation of EDA can be trapped by nucleophiles, such as alcohols and amines (eq 13). Compared to the $CO_2(CO)_8$-catalyzed carbonylation of EDA, the Pd-catalyzed carbonylation occurs under low pressure of CO, making it more appealing in organic synthesis. The Pd-catalyzed carbonylation of EDA was further expanded to a series of diazo esters and diazo ketones.



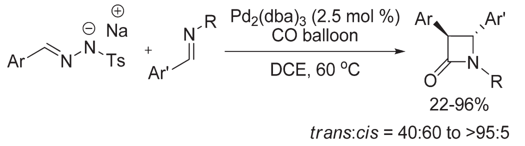
(13)

Since nonstabilized diazo compounds can be generated in situ from *N*-tosylhydrazones, this ketene generation process is further applied to *N*-tosylhydrazones. Under optimized reaction conditions, the Pd-catalyzed carbonylation of *N*-tosylhydrazones occurs smoothly over a wide range of substrates. Because *N*-tosylhydrazones are easily derived from ketones or aldehydes, this reaction is potentially useful in organic synthesis as a general strategy of one-carbon homologation of ketones or aldehydes (eq 14).

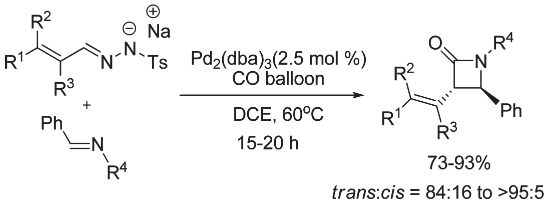


(14)

One of the most important applications of ketenes is the synthesis of *β*-lactams through formal [2 + 2] cycloaddition with imines. Consequently, the *β*-lactam synthesis with the Pd-catalyzed carbonylation of *N*-tosylhydrazones has been explored. Under optimized reaction conditions, the reaction of *N*-tosylhydrazone salt and imines in the presence of $Pd_2(dba)_3$ under CO (1 atm) affords *β*-lactams in good yields with excellent stereoselectivity. Interestingly, in most cases, the *β*-lactam products have trans configuration (eqs 15 and 16).



(15)



(16)

To gain insight into the mechanism of the Pd-carbene formation and the subsequent carbonylation, DFT calculations at the B3LYP/6-31G* level were carried out with phenyldiazomethane as model (Figure 2). The calculation results show that dinitrogen extrusion from the diazo substrate-Pd complex occurs via transition state **TS-AB** over a barrier of 18.5 kcal/mol. In the Pd carbene complex **B**, the distance of C−Pd is 1.970 Å, which is close to the corresponding C−Pd distance observed in the X-ray structure of a reported stable Pd(II)-carbene complex.[75]

The subsequent CO migratory insertion occurs via transition state **TS-BC** over a barrier of 14.5 kcal/mol generating η^2-(C,C) Pd-carbene complex **C-*a***. **C-*a*** is supposed to be in equilibrium

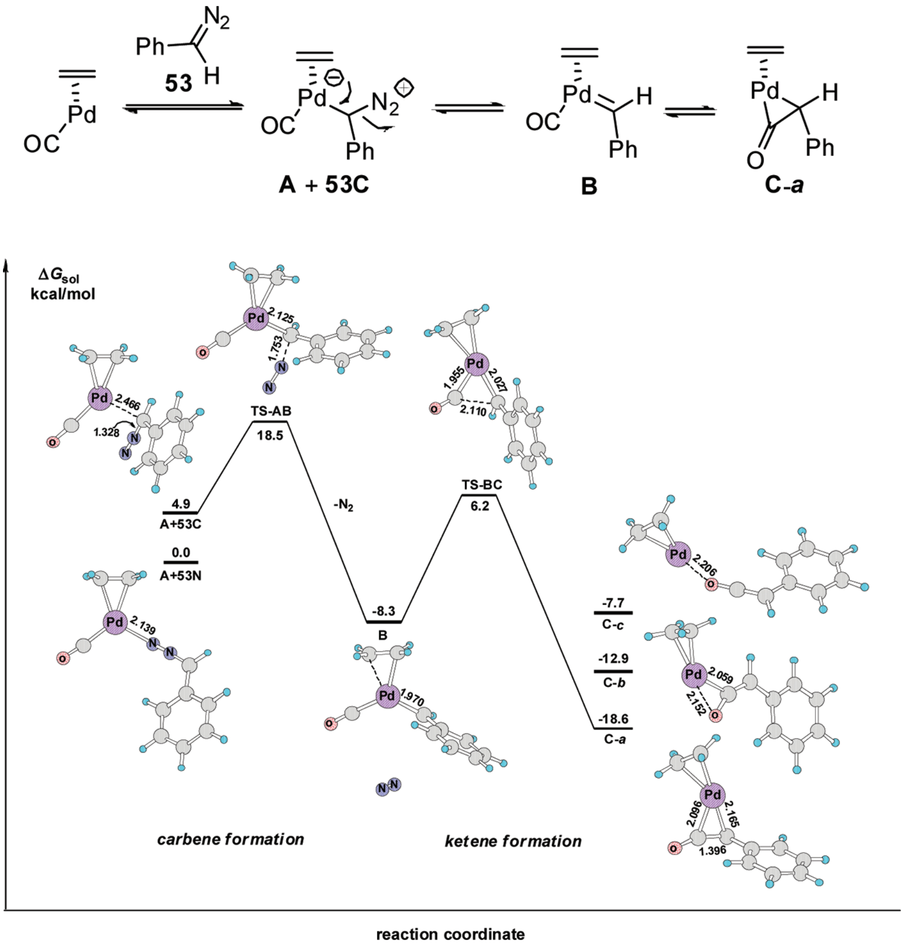


Figure 2. Calculated reaction pathways for the Pd-complexed carbene and ketene formation. The distances are in angstroms. Calculated at B3LYP/6-311+G**//6-31G* level.

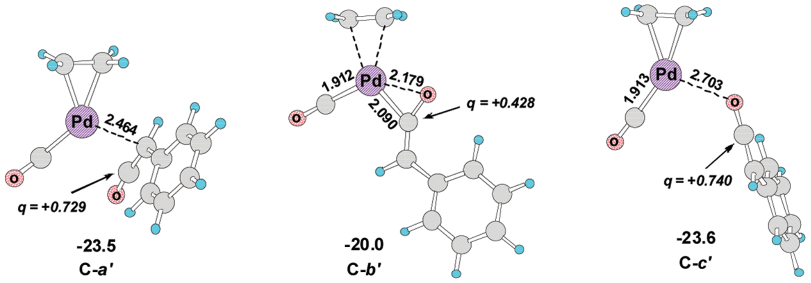


Figure 3. Optimized structures of **C-*a*′**, **C-*b*′**, and **C-*c*′** (at the B3LYP/6-311+G**//6-31G* level). The relative free energies G_{sol} are in kcal/mol, the distances are in angstroms. The NBO charges are given in italic.

with the corresponding η^2-(C,O) Pd-ketene complex **C-*b*** and η^1-(O) Pd-ketene complex **C-*c***. The calculated free energies show that **C-*a*** is 5.7 kcal/mol more stable than **C-*b***, while the **C-*c*** is the least stable complex.

On the Pd center of **C-*a***, **C-*b***, and **C-*c*** there is a vacant orbital, to which another CO may be accommodated as ligand to form complexes **C-*a*′**, **C-*b*′**, and **C-*c*′** (Figure 3). The binding energies of CO to **C-*a***, **C-*b***, and **C-*c*** are 4.9, 7.1, and 15.9 kcal/mol, respectively. As a result, the η^1-(O) Pd-ketene complex **C-*c*′** becomes the most stable one. Moreover, in the oxygen coordinated ketene complex **C-*c*′**, the NBO change (+0.740) on the central carbon atom is the largest one, which indicates that **C-*c*′** is more electrophilic than **C-*a*′** and **C-*b*′**. Therefore we can reasonably suggest the trapping of the ketene complex by nucleophiles (alcohols, amines and imines) occurs preferentially from complex **C-*c*′**.

4. CONCLUDING REMARKS

From the examples presented in this perspective Article, it can be seen that the carbonylation of carbene complexes to generate ketene complexes is a unique process in transition metal chemistry. Carbonylation in stoichiometric reaction, as represented by

Group VI Fischer carbene complexes, have been well explored and have become established as a useful approach for generating ketene complexes. The transition metal-catalyzed carbonylation of metal carbene has been much less developed, but recent developments in this field demonstrate the potential of such reaction as a general methodology for ketene generation under transition metal-catalyzed conditions.

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DEDICATION

This Article is dedicated to Prof. Christian Bruneau on the occasion of his 60th birthday.

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