


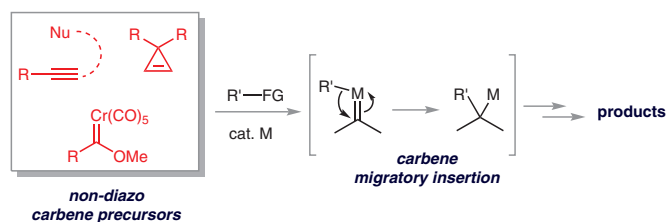
Transition-Metal-Catalyzed Cross-Coupling with Non-Diazo Carbene Precursors

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Abstract Transition-metal-catalyzed cross-coupling reactions through metal carbene migratory insertion have emerged as powerful methodology for carbon–carbon bond constructions. Typically, diazo compounds (or in situ generated diazo compounds from *N*-tosylhydrazones) have been employed as the metal carbene precursors for this type of cross-coupling reactions. Recently, cross-coupling reactions employing non-diazo carbene precursors, such as conjugated ene-yne-ketones, allenyl ketones, alkynes, cyclopropenes, and Cr(0) Fischer carbenes, have been developed. This account will summarize our efforts in the development of transition-metal-catalyzed cross-coupling reactions with these non-diazo carbene precursors.

- 1 Introduction
- 2 Cross-Coupling with Ene-yne-ketones, Allenyl Ketones, and Alkynes
- 3 Cross-Coupling Involving Ring-Opening of Cyclopropenes
- 4 Palladium-Catalyzed Cross-Coupling with Chromium(0) Fischer Carbenes
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Key words cross-coupling, catalysis, carbene migratory insertion, metal carbene, C–C bond formation

1 Introduction

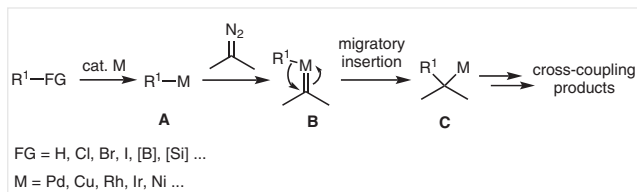
Metal carbene species are versatile intermediates or reagents in organometallics and in organic synthesis.¹ In addition to the traditional metal carbene transformations, the combination of metal carbenes and transition-metal-catalyzed cross-coupling has recently been recognized as powerful methodology for the construction of carbon–carbon and carbon–heteroatom bonds.² In general, the transition-metal-catalyzed cross-coupling reactions involving metal carbenes present two features (Scheme 1): first, metal carbene precursors are employed as the cross-coupling part-

ners; second, in the reaction mechanism a metal carbene migratory insertion process is considered as the key C–C bond-forming process.

The metal carbene species are typically generated from the interaction of metal catalysts and carbene precursors. Diazo compounds or *N*-tosylhydrazones (the precursors for in situ generated diazo compounds) are the most convenient and widely used carbene precursors.^{2,3} Mechanistically, the cross-coupling transformation involving a metal carbene follows the catalytic pathway shown in Scheme 1. The organometallic species **A** is generated from classic cross-coupling steps, such as oxidative addition, transmetalation, and C–H bond activation, which is followed by the reaction with diazo substrate to generate metal carbene intermediate **B**. The intermediate **B** then undergoes migratory insertion of the R group from the metal center to the unsaturated carbon, generating a C–C bond. The migratory insertion thus generates a new organometallic species **C**, which undergoes further transformations to produce the final cross-coupling products.

Although diazo compounds are very useful precursors to generate metal carbene species, they suffer some apparent drawbacks such as instability, explosiveness, and toxicity. Thus, significant efforts have been devoted to investigating alternative carbene precursors, and various carbene precursors have been developed in the past few years.⁴ Some of these alternative carbene precursors have also been explored in carbene-based cross-coupling reactions. It has now been established that a range of non-diazo carbene precursors also generate metal carbene intermediates to participate in the cross-coupling reaction. These reactions do not only provide products with diverse structural features, but also validate the generality of the cross-coupling based on metal carbene migratory insertion. In this account, we will provide the overview of our own efforts in

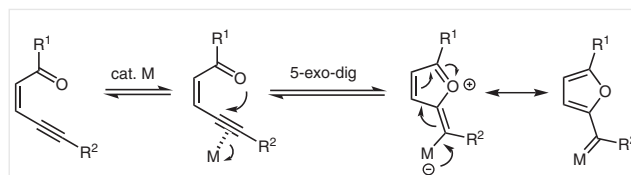
the development of transition-metal-catalyzed cross-coupling reactions of non-diazo carbene precursors.



Scheme 1 Cross-coupling reactions based on metal carbene migratory insertion

2 Cross-Coupling with Ene-yne-ketones, Allenyl Ketones, and Alkynes

Transition-metal catalysts can activate alkynes to trigger an inter- or intramolecular nucleophilic attack to generate metal carbene species.⁵ In particular, conjugated ene-yne-ketones have been reported to produce metal carbene intermediates at the alkyne moiety by transition-metal-catalyzed cycloisomerization. The 5-exo-dig cyclization of conjugated ene-yne-ketone generates metal carbene species, which can undergo various metal carbene transformations (Scheme 2).⁶ We thus conceived that the conjugated ene-yne-ketone could serve as an effective carbene precursor in the cross-coupling reactions based on migratory insertion.

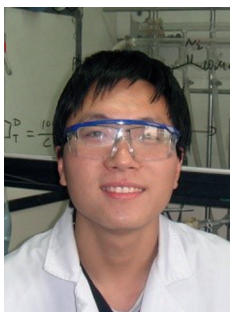


Scheme 2 Generation of a metal carbene from ene-yne-ketone

Along this line, we developed a Pd-catalyzed cross-coupling reaction employing an ene-yne-ketone as the carbene precursor, that afforded 2-vinyl-substituted furan rings in good yields (Scheme 3).⁷ A series of benzyl, allyl, and aryl halides (**2**, **3**, and **7**) were tolerated as the cross-coupling partners. When the alkyne moiety was connected with a bulky group such as a *tert*-butyl or triisopropylsilyl group, the *Z/E* isomer selectivity of product **4** could be improved. The coupling reaction gave furyl-containing 1,3-diene products **5** when allyl bromides were used as the coupling partners.

Regarding the reaction mechanism, it has been proposed that the reaction is initiated by oxidative addition of organic halides to palladium(0) species **9** to form an organopalladium(II) species **10**, which then triggers the 5-exo-dig cyclization by coordinating to the alkyne moiety to generate the furyl palladium(II) carbene intermediate **11**. The migratory insertion process of **11** occurs to give a new organopalladium(II) intermediate **12**, which undergoes β -hydride elimination to afford the alkene product and reproduce the Pd(0) catalytic species (Scheme 4). DFT calculation

Biographical Sketches



Kang Wang was born in Shandong Province. He obtained his B.S. degree in 2013 at the School of Chemistry and Chemical Engineering at Shandong

University. He then became a graduate student in Jianbo Wang's group at Peking University. He obtained his Ph.D. degree in July 2018. The

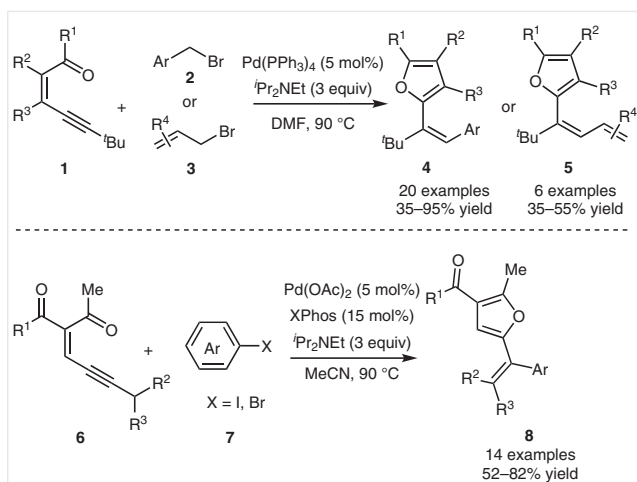
research of his Ph.D. thesis focused on transition-metal-catalyzed cross-coupling with chromium(0) Fischer carbene complexes.



Jianbo Wang received his B.S. degree from Nanjing University of Science and Technology in 1983 and his Ph.D. from Hokkaido University (under the supervision of Prof. H. Suginome)

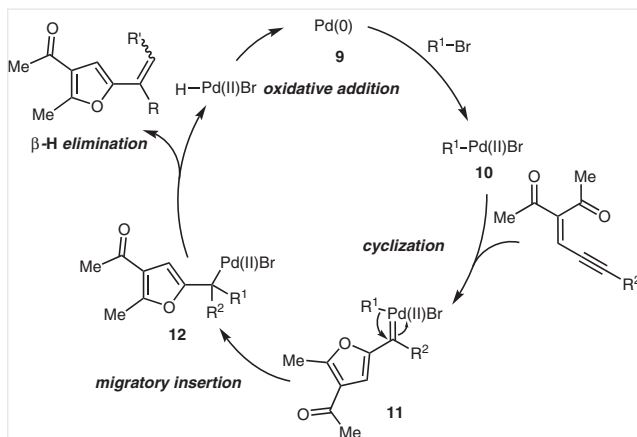
in 1990. He was a postdoctoral associate at the University of Geneva from 1990 to 1993 (with Prof. C. W. Jefford) and University of Wisconsin-Madison from 1993 to 1995 (with

Prof. H. E. Zimmerman and F. A. Fahien). He began his academic career at Peking University in 1995. His research interests have been focused on catalytic metal carbene transformations.



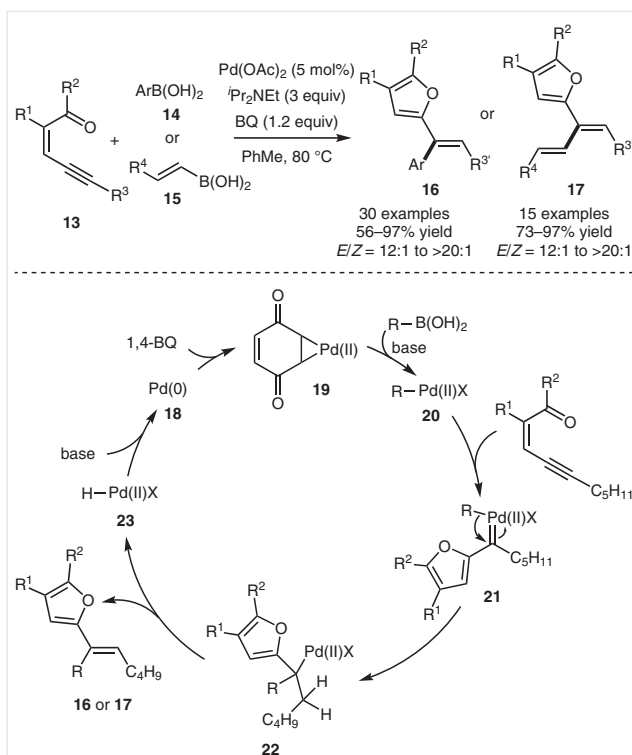
Scheme 3 Palladium-catalyzed cross-coupling of conjugated ene-yne-ketones with benzyl or allyl halides

reveals that the palladium carbene formation is the rate-limiting step and the Pd(II) carbene migratory insertion step occurs readily with a very low energy barrier of less than 5 kcal/mol.



Scheme 4 Proposed mechanism of palladium-catalyzed cross-coupling of conjugated ene-yne-ketones with halides

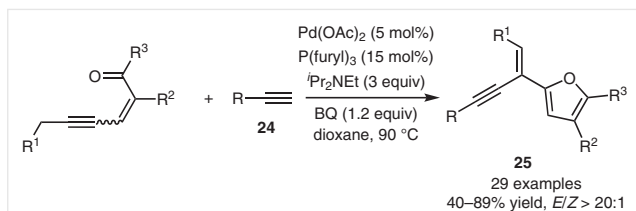
Encouraged by this work, we further explored the palladium-catalyzed oxidative coupling of conjugated ene-yne-ketones **13** with aryl and vinyl boronic acids **14** or **15** (Scheme 5).⁸ This reaction also showed excellent functional group tolerance towards various substituted aryl and alkenyl boronic acids. Conjugated ene-yne-ketones bearing various substituents, such as an ester and a sulfonyl group, were also compatible. Compared with the poor *E/Z* selectivity that was obtained when aryl halides were employed as the coupling partners,⁷ decent *E*-isomer selectivity was observed in this oxidative coupling reaction in almost all the cases.



Scheme 5 Palladium-catalyzed oxidative coupling reaction of conjugated ene-yne-ketones with organoboronic acids

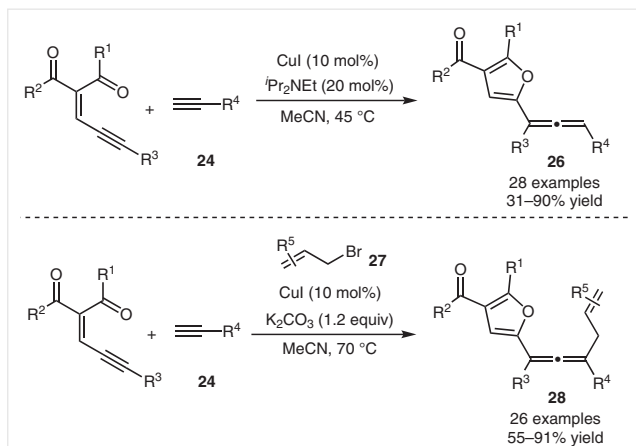
We have proposed a similar reaction mechanism. Thus, the oxidative coupling reaction is initiated by the oxidation of palladium(0) species **18** by 1,4-benzoquinone oxidant. The formed palladium(II) catalytic species **19** undergoes transmetalation with organoboronic acid to produce the organopalladium intermediate **20**, which then activates the ene-yne-ketone substrate to trigger cyclization to produce the furyl palladium carbene intermediate **21**. Migratory insertion of **21** affords intermediate **22**, which further undergoes β -H elimination to give the alkene products. The dissociated Pd(II) species is converted to Pd(0) catalytic species **18** to enter the next catalytic cycle.

Then, we extended this oxidative coupling strategy to a palladium-catalyzed alkyne–alkyne coupling (Scheme 6). We reasoned that the alkyne substrates would form alkynyl palladium species which could activate the ene-yne-ketone to generate the furyl palladium carbene species.⁹ Migratory insertion of the Pd carbene gives the propynyl palladium intermediate, followed by β -hydride elimination to afford furyl-substituted 1,3-enyne product. Indeed, the alkyne–alkyne cross-coupling between various terminal alkyne substrates **24** and differently substituted ene-yne-ketones occurred readily to give the expected 1,3-enyne products **25**. The coupling reaction tolerates a range of aryl-, alkyl-, or silyl-substituted alkyne substrates.



Scheme 6 Palladium-catalyzed oxidative coupling of ene-yne-ketones with terminal alkynes

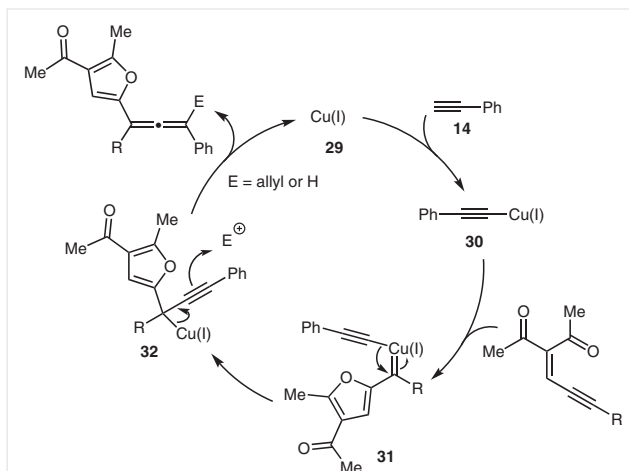
It is worth mentioning that, for the same alkyne substrates and ene-yne-ketone carbene precursors, different transition-metal catalysts may result in different transformations and give different products. Thus, with copper iodide as the catalyst, the cross-coupling between alkynes and ene-yne-ketones gave furfuryl-substituted allene as the products (Scheme 7).¹⁰ This reaction exhibited a good substrate scope; a series of aryl and heteroaryl-substituted terminal alkynes **24** as well as primary, secondary, and tertiary alkyl-substituted terminal alkynes were all tolerated to give various trisubstituted allenes **26**. The reaction also proceeded smoothly in a gram-scale experiment under the standard conditions. We also extended this methodology to the synthesis of tetrasubstituted allenes **28** by introducing allyl bromides as the electrophiles to trap the nucleophilic alkyl copper intermediate.¹¹ The three-component reaction of alkyne, ene-yne-ketone, and allyl bromide **27** proceeded effectively with good functional group compatibility.



Scheme 7 Cu(I)-catalyzed coupling of ene-yne-ketones with terminal alkynes

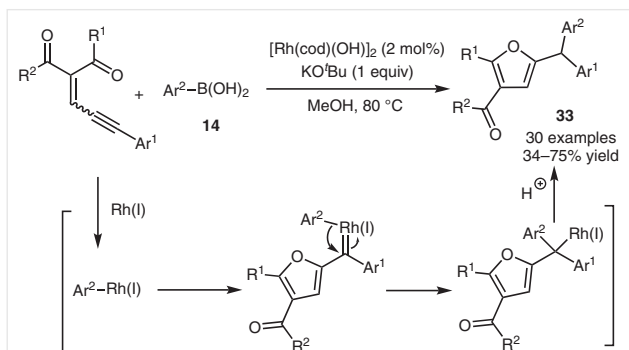
We have proposed the following mechanism as shown in Scheme 8. The copper acetylide **30** is generated from the alkyne substrate and Cu(I) species **29** with the assistance of a base. The ene-yne-ketone then undergoes cyclization to form Cu(I) carbene intermediate **31** by the activation by copper species **30**. After that, copper carbene **31** undergoes migratory insertion to form the propynyl copper interme-

diate **32**. Regioselective protonation occurs at the triple bond carbon atom to give the trisubstituted allene product. When the nucleophilic propynyl copper intermediate **32** is trapped by allyl bromide, the tetrasubstituted allene product is obtained.



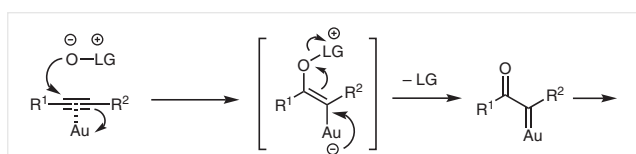
Scheme 8 Proposed reaction mechanism for Cu(I)-catalyzed cross-coupling of an ene-yne-ketone with an alkyne

Because we and other groups have demonstrated that Rh(I) catalysts are also efficient in carbene-involved cross-coupling, we presumed that the conjugated ene-yne-ketones should also undergo a similar cross-coupling reaction under Rh(I) catalysis. Indeed, we further developed the Rh(I)-catalyzed cross-coupling of ene-yne-ketone and organic boronic acid (Scheme 9).¹² Mechanistically, a similar Rh(I) carbene formation and a subsequent metal carbene migratory insertion process are involved in the catalytic cycle. Compared with the Pd(II)-catalyzed coupling of ene-yne-ketone and boronic acid which gives furfuryl-substituted alkene product with β -hydride elimination as the terminating step, the Rh(I)-catalyzed transformation affords furan-containing triarylmethane product **33** with protonation as the terminating step.



Scheme 9 Rh(I)-catalyzed cross-coupling of an ene-yne-ketone with arylboronic acid

In addition to the conjugated ene-yne-ketone, which undergoes intramolecular cyclization to generate the palladium carbene species, an alkyne moiety alone can also be utilized as metal carbene precursor with the assistance of an intermolecular nucleophile (Scheme 10).¹³ Typically, under gold catalysis the alkyne undergoes carbene transformations, such as ylide formation, X–H insertion and cyclopropanation, through the in situ generated α -oxo gold carbenes.¹⁴ The α -oxo carbene is formed through the activation of the triple bond by the gold catalyst, which triggers the nucleophilic attack followed by the oxidation of alkynes by the N–O bond oxidants.

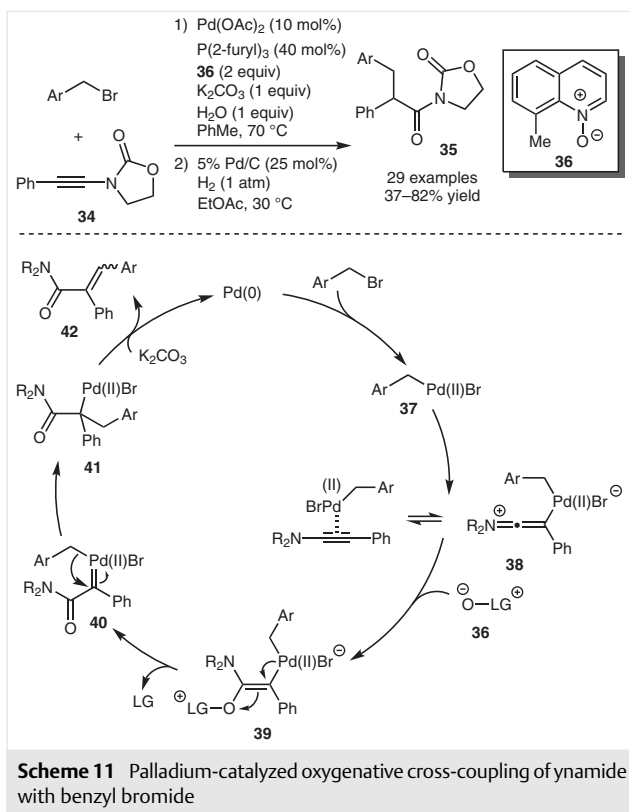


Scheme 10 Generation of α -oxo gold carbene from alkyne

In contrast to the versatile transformations achieved with gold catalysts, the corresponding palladium-catalyzed carbene formations from alkynes are rare, presumably due to the relatively weak π acidity of the Pd(II) complexes as compared with Au(I) complexes. Recently, we developed a Pd(II)-catalyzed oxygenative cross-coupling of alkynes **34** with benzyl bromides, which is proposed to follow the intermolecular oxidation and Pd(II) carbene migratory insertion reaction sequence (Scheme 11).¹⁵

The ynamide substrates **34**, which contain a polarized carbon–carbon triple bond, were utilized as carbene precursors with the assistance of quinoline *N*-oxide **36**. This coupling reaction proceeded smoothly with a range of substituted benzyl bromides and ynamides. A control experiment showed that with α -diazoamide as the carbene precursor similar ynamide products could be obtained, which supports the Pd(II)-carbene migratory insertion mechanism. We have proposed that benzyl palladium species **37**, generated by oxidative addition of benzyl bromide and the Pd(0) catalyst, activates the ynamide triple bond to give keteniminium ion **38**. The following nucleophilic addition by *N*-oxide affords the intermediate **39**, which then generates the α -oxo palladium carbene **40** through γ -elimination by expelling the quinoline part. The Pd(II) carbene **40** then undergoes migratory insertion and subsequent β -hydride elimination to give the coupling product **42**.

Similar to the conjugated ene-yne-ketones, which generate the palladium carbene at the alkyne moiety, allenyl ketones can also generate the palladium carbene species at the allene moiety under palladium catalysis. In this context, we have reported a Pd(II)-catalyzed oxidative cross-coupling of allenyl ketones **43** with organoboronic acids (**14** and **15**), which gives furyl derivatives **44** and **45** (Scheme 12).^{16a} In the reaction mechanism, the aryl palladium(II)



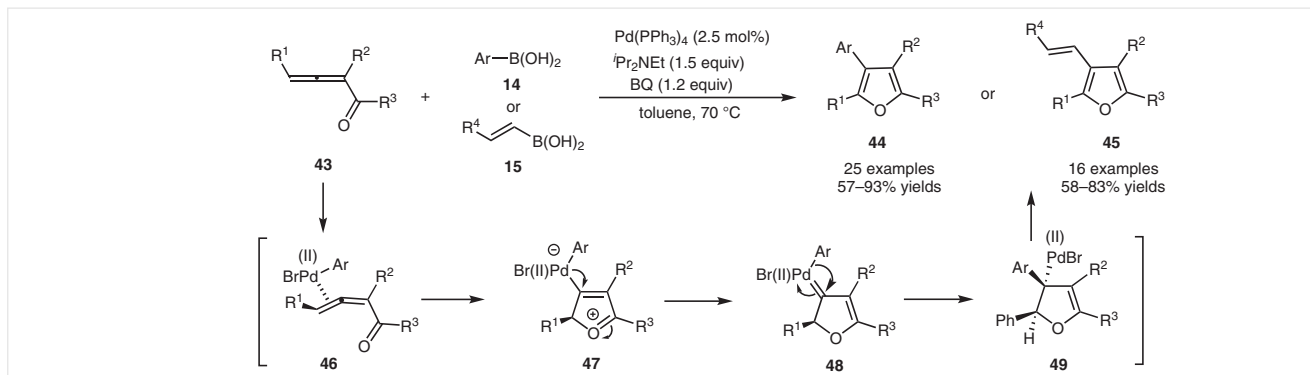
Scheme 11 Palladium-catalyzed oxygenative cross-coupling of ynamide with benzyl bromide

species generated from arylboronic acid coordinates to the allene moiety (**46**) to trigger the cycloisomerization of allenyl ketone, generating palladium carbene intermediate **48**. Subsequently, migratory insertion followed by β -hydride elimination delivers the furan product. The alternative pathways involving the formation of π -allyl palladium species or furyl palladium species could also be possible.^{1b,c}

3 Cross-Coupling Involving Ring-Opening of Cyclopropenes

Cyclopropenes are highly strained unsaturated cyclic compounds and they have emerged as versatile three-carbon units for organic synthesis.¹⁷ Under thermal or transition-metal-catalyzed conditions, cyclopropenes can also act as carbene precursors through ring-opening. The metal carbene species generated through the cyclopropene ring-opening process can participate in typical carbene transformations, which significantly expanded the application of cyclopropenes in organic chemistry.

We have conceived that cyclopropenes may serve as metal carbene precursors in cross-coupling reactions. In this context, we developed an Rh(III)-catalyzed cross-coupling reaction of *N*-phenoxacetamides **50** with cyclopropenes **51**, in which cyclopropenes were utilized as the vinyl carbene precursors in connection with Rh(III)-catalyzed C–H



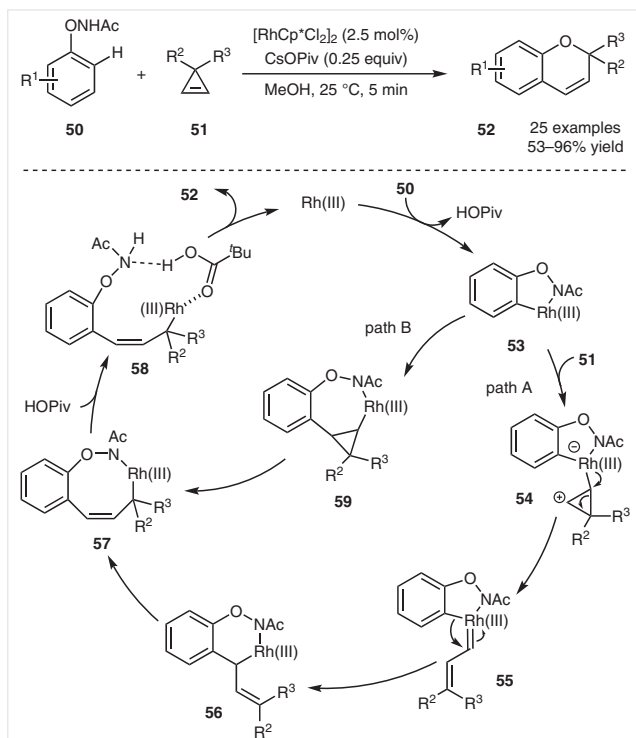
Scheme 12 Palladium-catalyzed oxidative cross-coupling of allenyl ketone with aryl- or vinylboronic acid

activation (Scheme 13).¹⁸ This annulation reaction is highly efficient and can proceed within five minutes at room temperature with a range of different cyclopropenes and *N*-phenoxacetamides, affording the corresponding 2*H*-chromene products **52** in good to excellent yields.

Two probable reaction mechanisms have been proposed to explain this rhodium-catalyzed transannulation reaction (Scheme 13, paths A and B). They share the same C–H activation process which gives the rhodacycle intermediate **53**. In path A, the cyclopropene substrate is coordinated to the rhodium center to generate intermediate **54**, which then undergoes ring-opening to give the vinyl rhodium carbene intermediate **55**. Subsequent migratory insertion and 1,3-

allyl migration reaction give intermediate **57**. Then, the acid-assisted N–O bond cleavage and C–O bond formation sequence (through intermediate **58**) would produce the 2*H*-chromene product. In pathway B, the cyclopropene inserts into the aryl–rhodium bond to form the seven-membered rhodacycle **59**. The subsequent β -carbon elimination process gives the same intermediate **57**. Notably, recent DFT calculation suggests that the aryl–rhodium bond insertion/ β -carbon elimination sequence is more likely to be involved in the reaction mechanism.¹⁹

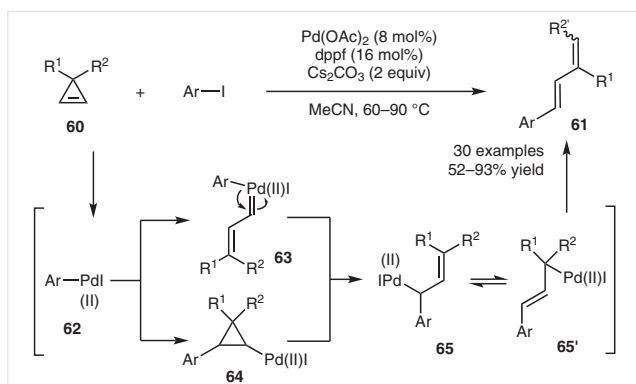
Moreover, we developed the palladium-catalyzed cross-coupling of cyclopropenes **60** with aryl iodides, affording conjugated 1,3-butadiene products **61** (Scheme 14).²⁰ The cyclopropene substrates bearing two identical aliphatic chains produced *E/Z* mixtures of 1,3-dienes with almost 1:1 ratio. Other cyclopropene substrates gave the 1,3-diene products with the *E*-configured isomers as the only or major products. Mechanistically, the aryl palladium species **62** is formed from the oxidative addition step of aryl iodide with the Pd(0) species. Intermediate **62** forms a vinyl palladium carbene intermediate **63** through a ring-opening reaction. The subsequent migratory insertion and β -H elimination then produces the 1,3-diene products. Alternatively, intermediate **62** can insert into the carbon–carbon double bond to form the cyclopropyl palladium intermediate **63** which then undergoes β -carbon elimination to form the same allyl palladium intermediate (**65** or **65'**). The subsequent β -H elimination affords product **61** and releases the palladium catalyst.



Scheme 13 Rh(III)-catalyzed cross-coupling of cyclopropene with *N*-phenoxacetamide

4 Palladium-Catalyzed Cross-Coupling with Chromium(0) Fischer Carbenes

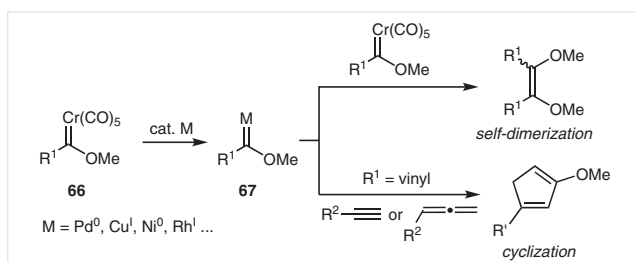
In the past 50 years, Fischer carbene complexes have been extensively explored as valuable reagents in organometallics and in organic synthesis.²¹ Among the various stable metal carbene complexes, chromium(0) Fischer carbene complexes have found wide applications because of their diverse reactivity. A prominent example is the Dötz annula-



Scheme 14 Palladium-catalyzed cross-coupling of cyclopropene with aryl iodide

tion of chromium(0) Fischer carbene complexes with alkynes, which has been extensively applied in the synthesis of densely functionalized arenes.^{21,22}

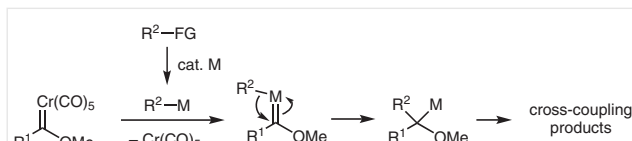
In addition to the traditional reactions, chromium(0) Fischer carbene complexes (**66**) can transfer their carbene ligands to other transition metals to generate new metal carbene intermediates **67**, which undergo further processes to afford various products under catalytic conditions (Scheme 15). The transition metals that have been explored in this type of carbene transfer include palladium, copper, nickel, rhodium, and gold.^{23,24} Transition-metal-catalyzed self-dimerization, cyclopropanation, and cyclization reactions of chromium(0) carbene complexes have been developed on the basis of the carbene transfer process.²³ Although the catalytic carbene transfer process generates reactive metal carbene intermediates, the type and scope of transformations based on such a process are still rather limited. We reasoned that it would be desirable to explore a new type of transformations with chromium(0) Fischer carbene complexes under catalytic conditions.



Scheme 15 Transition-metal-catalyzed carbene transfer reactions of chromium(0) Fischer carbene complexes

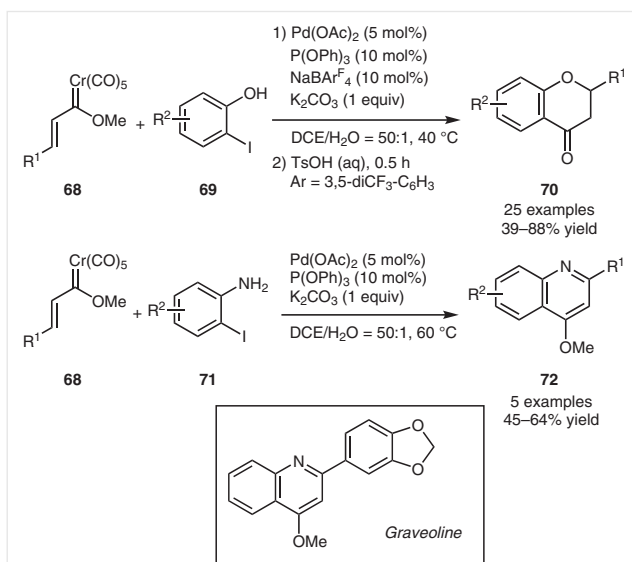
In this context, we have recently initiated a program to study the possibility of employing stable chromium(0) Fischer carbene complexes as the sources of reactive metal carbenes for carbene-based cross-coupling reactions (Scheme 16). The chromium(0) Fischer carbene complex is expected to undergo carbene transfer with organometallic species to generate a new metal carbene intermediate,

which will be followed by migratory insertion. This type of catalytic transformation should open up new opportunities for the application of chromium(0) Fischer carbene complexes in organic synthesis.



Scheme 16 Transition-metal-catalyzed cross-coupling with chromium(0) Fischer carbene

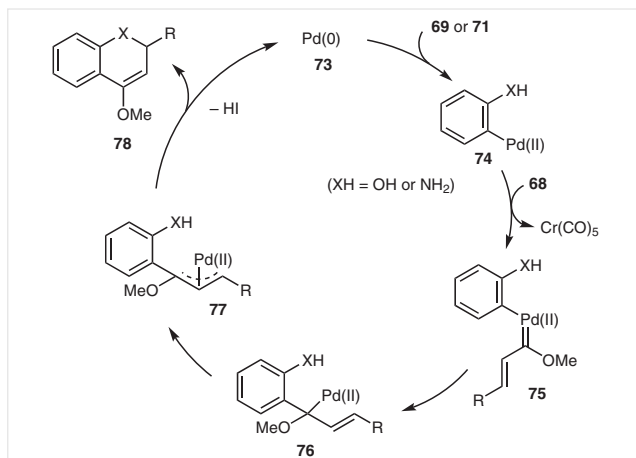
In the beginning, we studied the palladium-catalyzed cross-coupling reaction of vinyl-substituted chromium(0) carbene complexes which were reported to undergo rhodium- or nickel-catalyzed [3+2] cyclization with unsaturated components such as alkynes and allenes.²⁴ In 2017, we reported the palladium-catalyzed [3+3] annulation reaction of vinyl chromium(0) carbenes **68** with 2-iodophenols **69** and 2-iodoanilines **71** (Scheme 17).²⁵ When 2-iodophenols **69** were employed as the coupling partners, this annulation transformation exhibited good functional group compatibility to give a series of substituted flavonones **70**. 2,4-Disubstituted quinoline products **72** were obtained when 2-iodoanilines **71** were utilized as the substrates. To demonstrate the application of this reaction, we could synthesize the natural alkaloid *Graveoline* in good yields.



Scheme 17 Palladium-catalyzed [3+3] annulations of vinyl chromium(0) carbenes with 2-iodophenols and 2-iodoanilines

Mechanistically, 2-iodophenol (or 2-iodoaniline) first undergoes oxidative addition to a Pd(0)-catalytic species to yield aryl palladium(II) intermediate **74** (Scheme 18). Intermediate **74** then undergoes carbene transfer with a vinyl chromium(0) carbene complex to give vinyl Pd(II) carbene

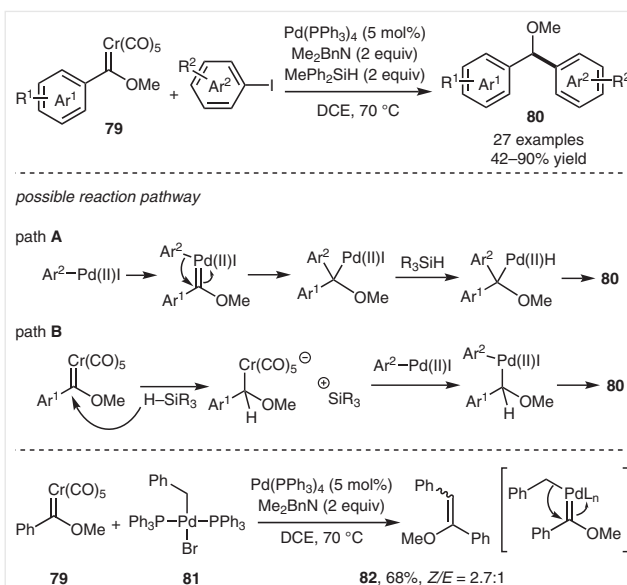
intermediate **75**. The migratory insertion of palladium carbene **75** generates allyl palladium(II) species **77** which is trapped intramolecularly by the nucleophilic hydroxyl group (or amido group) to produce six-membered-ring product **78**.



Scheme 18 Proposed mechanism for palladium-catalyzed [3+3] annulation of vinyl chromium(0) Fischer carbenes

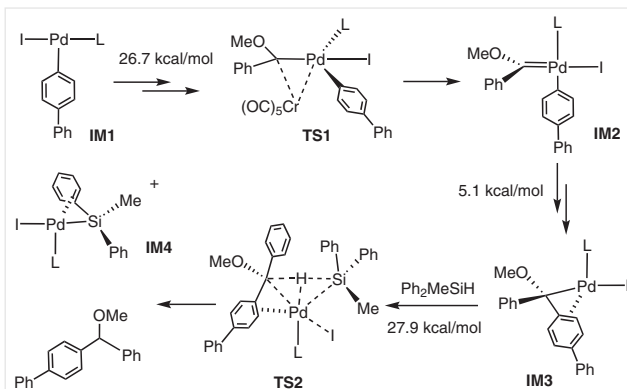
In order to extend this type of transformation with chromium(0) carbenes, we further performed experimental and mechanistic studies on the palladium-catalyzed reductive cross-coupling of aryl halides with aryl chromium(0) carbenes.²⁶ With hydrosilanes as the hydrogen sources and reductants, the coupling products **80** could be obtained through reductive coupling with various substituted aryl chromium(0) carbenes **79** and aryl iodides (Scheme 19). We reasoned that the formation of palladium(II) carbene and its migratory insertion step might be involved in the reaction pathway (path A). However, an alternative mechanism which involves nucleophilic attack of the hydride source to the electrophilic carbenic carbon of chromium(0) carbene followed by transmetalation and reductive elimination cannot be ruled out (path B).

A mechanistic experiment employing stoichiometric benzyl palladium species **81** as the coupling partner supports the palladium carbene pathway, as only a palladium carbene migratory insertion process can lead to the observed vinyl ether products **82** (Scheme 19). Moreover, a Hammett linear free energy correlation study afforded a substantially large negative reaction constant ($\rho = -2.93$), implicating that an electron-donating group on the aryl group of the chromium(0) carbene can promote the coupling reaction. This result also supports the palladium carbene pathway. Since the carbene ligand is transferred from a zero-valued chromium(0) center to a positively charged palladium(II) center in the carbene formation process, the carbenic carbon thus becomes more electron-deficient. Therefore, electron-donating groups promote the carbene transfer process.



Scheme 19 Palladium-catalyzed reductive coupling reactions of aryl chromium(0) Fischer carbenes with aryl iodides

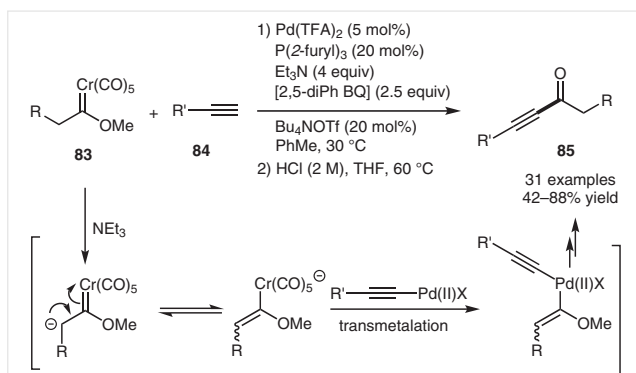
To gain further insights, we also carried out a computational study on the reaction mechanism. The DFT calculation reveals that the palladium carbene intermediate **IM2** is formed through the dimetallacyclopropane transition state **TS1**. The total energy barrier for the palladium(II) carbene formation process is 26.7 kcal/mol (Scheme 20). The subsequent migratory insertion is a facile process with an energy barrier of 5.1 kcal/mol. After that, the concerted hydrogen transfer, depalladation, and Pd–Si bond formation sequence takes place to release the coupling products, crossing over the transition state **TS2** with an energy barrier of 27.9 kcal/mol. The resulting I–Pd–Si species **IM4** undergoes reductive elimination to regenerate the Pd(0) catalytic species. Both carbene transfer and hydrogen transfer processes are the rate-limiting steps in the transformation. Overall, this reductive coupling provides experimental and theoretic



Scheme 20 DFT calculation on the palladium-catalyzed reductive coupling of aryl chromium(0) carbenes with aryl iodides

cal evidence for the palladium-catalyzed cross-coupling of the chromium(0) Fischer carbene complex that involves carbene transfer and migratory insertion.

Furthermore, we explored the oxidative cross-coupling of alkynes with alkyl-substituted chromium(0) Fischer carbene complex (Scheme 21).²⁷ In contrast to the typical benzannulations between alkyne and alkyl chromium(0) carbene complex,²⁸ the presence of a palladium catalyst completely redirected the reaction path toward cross-coupling. A range of substituted terminal alkynes **84** were efficient coupling partners in the palladium-catalyzed cross-coupling reaction with various alkyl chromium(0) carbene complexes **83**. Mechanistic experiments implicate that a pathway involving a sequential deprotonation and transmetalation process is more likely, which is in sharp contrast with the palladium carbene migratory insertion and β -hydride elimination pathway.



Scheme 21 Palladium-catalyzed oxidative coupling reaction of alkyl chromium(0) carbene with terminal alkyne

5 Conclusion

In this account, we have introduced the transformations that employ a range of non-diazo carbene precursors in cross-coupling reactions. The conjugated ene-yne-ketones, allenyl ketones, cyclopropene derivatives along with chromium(0) Fischer carbene complexes have been proved as effective metal carbene precursors to participate in the cross-coupling with migratory insertion as the key step. A range of coupling partners, such as organic halides, boronic acids, terminal alkynes as well as C–H bond activation substrates, were employed in the cross-coupling reactions with the transition-metal catalysis of palladium, rhodium, and copper.

These coupling reactions with non-diazo carbene precursors not only introduce some new synthetic methodologies, but also validate the generality of the metal carbene migratory insertion process. In addition to the cross-coupling transformations described in this account, a series of cross-couplings employing other metal carbene precursors

have also been developed by other groups.^{3a} It can be expected that carbene-based cross-coupling with other non-diazo substrates will continue to emerge in the coming years.

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