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Substrate Activation Strategies in Rhodium(III)-Catalyzed Selective Functionalization of Arenes

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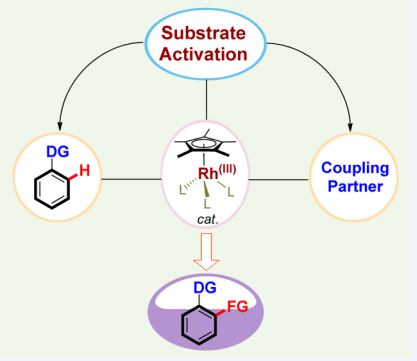
CONSPECTUS: The possibility of developing new methods for the efficient construction of organic molecules via disconnections other than traditional functional group transformations has driven the interest in direct functionalization of C−H bonds. The ubiquity of C−H bonds makes such transformations attractive, but they also pose several challenges. The first is the reactivity and selectivity of C−H bonds. To achieve this, directing groups (DGs) are often installed that can enhance the effective concentration of the catalyst, leading to thermodynamically stable metallacyclic intermediates. However, the presence of a pendant directing group in the product is often undesirable and unnecessary. This may account for the limitation of applications of C−H functionalization reactions in more common and general uses. Thus, the development of removable or functionalizable directing groups is desirable. Another key problem is that the reactivity of the resulting M−C bond can be low, which may limit the scope of the coupling partners and hence limit the reaction patterns of C−H activation reactions.



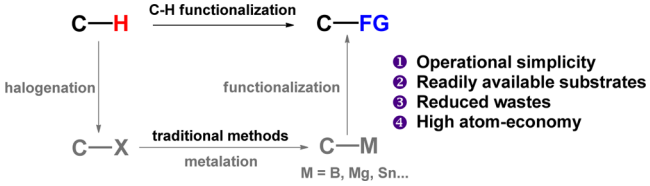
While the first Cp*Rh(III)-catalyzed C−H activation of arenes was reported only 7 years ago, significant progress has been made in this area in the past few years. We began our studies in this area in 2010, and we and others have demonstrated that diversified catalytic functionalization of arenes can be realized using Cp*Rh(III) complexes with high reactivity, stability, and functional group compatibility. This Account describes our efforts to solve some of these challenges using Rh(III) catalysis.

We fulfilled our design and activation of the arene substrates by taking advantage of the nucleophilicity, electrophilicity, oxidizing potential, and properties of a participating ligand of the directing groups when the arenes are coupled with relatively reactive unsaturated partners such as alkenes and alkynes. These in situ funtionalizable roles of the DG allowed extensive chemical manipulation of the initial coupled product, especially in the construction of a diverse array of heterocycles. In the coupling of arenes with polar coupling partners, the polar Rh(III)−C(aryl) bond showed higher reactivity as both an organometallic reagent and a nucleophilic aryl source. The polar coupling partners were accordingly activated by virtue of umpolung, ring strain, and rearomatization. All of these transformations have been made possible by integration of the higher reactivity, stability, and compatibility of Rh(III)−C bonds into catalytic systems. We have demonstrated that to date some of these transformations can be achieved only under rhodium catalysis. In addition, by means of stoichiometric reactions, we have gained mechanistic insights into the interactions between the Rh−C bond and the other coupling partners, which have opened new avenues in future direct C−H functionalization reactions.

1. INTRODUCTION

In the past decades, significant advancements have been made in the area of direct C−H functionalization, and this strategy has delivered various powerful tools that take advantage of the ubiquity of C−H bonds in chemical feedstocks.[1] The direct functionalization of C−H bonds provides a streamlined and step-economical synthesis of desired compounds with no preactivtion of the coupling partner, hence eliminating the generation of a stoichiometric amount of salt waste as in traditional cross-coupling reactions (Scheme 1). Transition metal complexes of palladium, ruthenium, and copper, among others, have been extensively explored and have well served this purpose, and these chemistries have been extensively reviewed. Despite advances in the field, the activation of C−H bonds remains a significant challenge because of their relative inertness and diversification of the arenes and their coupling partners.

Scheme 1. C−H Activation Strategy



The mechanism of the C−H activation reaction can vary with the natures of the arene substrate and the metal. Electron-rich (hetero)arenes may form M−C bonds possibly via an electrophilic C−H activation mechanism. On the other hand, arenes bearing a sufficiently acidic C−H bond are metalated in

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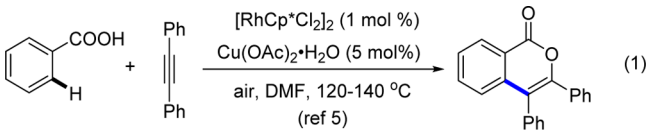
the presence of a base. In both cases, the site reactivity of the C−H activation is dictated by the electronic effect. However, when neither of these features is available, the arene is essentially "unactivated", and it has been widely recognized that the installation of a proximal directing group (DG) can facilitate ortho C−H activation by enhancing the effective concentration of the catalyst, thus giving rise to both higher reactivity and selectivity. Palladium complexes are particularly useful in executing base-assisted cyclometalation.[2] In fact, this strategy has been by extensively applied to a plethora of palladium-catalyzed C−H activation systems, even using various weak directing groups.[3] For this category of substrates, the base-assisted concerted metalation−deprotonation (CMD) mechanism[4] is often followed. This may account for applications of AgOAc and $Cu(OAc)_2$ oxidants in oxidative couplings of arenes, in which the oxidant participates in the reoxidation of the Rh(I) species to the Rh(III) species and also the anion coordinates to the rhodium to effect C−H activation.

In 2007, Miura and Satoh reported the first $[RhCp^*Cl_2]_2$-catalyzed C−H activation of arenes (eq 1).[5] Despite the relatively



(1)

short history, explosive progress has been made in this area, and increasing attention has been devoted to Cp*Rh-catalyzed C−H activation.[6] Cp*Rh(III) catalysts have stood out with high activity, broad substrate scope, mild conditions, and functional group compatibility. This is largely due to the uniqueness of the Cp*Rh(III) complexes, which differ from the well-explored palladium(II) species in the following aspects: (1) The Rh(III)−C(aryl) bond is more polarized and can be more reactive than typical Pd(II)−C and Ru(II)−C bonds. The high valence of the rhodium lowers the tendency for electron back-donation from the metal to the π^* orbital of the arene ring, leading to a more pronounced Rh−C single-bond character. (2) Cp*Rh(III) complexes are octahedral. With the Cp* ligand and the cyclometalated arenes, only one coordination site is left and is reserved for the coupling partner. Therefore, no ligand needs to be added. (3) The proper bulkness of the Cp* ligand offers important assistance. While it might not exert unfavorable steric hindrance during the C−H activation process, the steric hindrance increases to some extent after cyclometalation to offer ground-state destabilization, so that subsequent coordination-number-reducing reactions (reductive elimination or insertion) are favored. (4) Cp*Rh complexes, especially when further stabilized with a cyclometalated group, are thermally stable and less prone to decomposition.

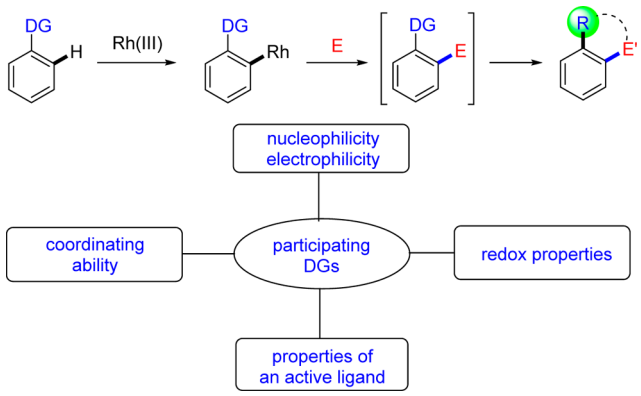
We began our studies of Rh(III)-catalyzed C−H activation in 2010, and we reviewed this exciting chemistry in early 2012,[6b] at which time the majority of the chemistry was limited to couplings using an external oxidant. A large number of exciting C−H activation systems have been developed since then. In this Account, we summarize our strategies for activation of the arene and the coupling partner.

2. ACTIVATION OF ARENE SUBSTRATES

2.1. Criteria for Functionalizable DGs

While DGs are widely employed to enhance both the selectivity and reactivity of C−H activation, the presence of a pendant DG in the product is often undesirable. This limitation might account for the incommensurate applications of C−H activation in total synthesis or synthesis of functional materials given the large volumes of reports on C−H activation systems. To overcome this shortcoming, functionalizable DGs have been introduced.[7] It is preferable that the DG can undergo subsequent in situ transformations leading to useful coupled products (Scheme 2). To achieve this goal, the following criteria of

Scheme 2. Functionalizable DGs in C−H Activation



DGs should be satisfied: (1) they should be sufficiently coordinating to allow for cyclometalation and (2) they should be capable of participating in subsequent transformations as a nucleophile/electrophile, internal oxidant, or active ligand.

2.2. In Situ Generation of DGs

In the olefination of *o*-alkynyl oxime esters (Scheme 3), we initially expected oxime ester-assisted direct olefination.[8] However, under oxidative conditions the Rh(III) catalyst first acts as a Lewis acid catalyst to entail 6-endo-dig cyclization to give an ionic intermediate **Int1** followed by a 3,3-sigmatropic rearrangement to give **Int2**, leading to the formation of isolable isoquinoline intermediate **Int3**. It is the isoquinoline nitrogen that exerts the directing effect for subsequent oxidative olefination. This represents in situ activation of a DG from a readily available functional group. Both mono- and bisolefination products have been observed, and the selectivity can be controlled by adjusting the catalytic conditions.

2.3. DGs as Nucleophiles

In 1998, Miura reported the Pd-catalyzed coupling of arenesulfonamides with acrylates,[9] where the C−H olefination is followed by an intramolecular aza-Michael addition, leading to the construction of six-membered nitrogen heterocycles. Significantly, Yu extended the substrate scope to sp^3 C−H bonds by designing an amide bearing a strongly electron-withdrawing *N*-(p-$C_6F_4CF_3$) group as a nucleophilic DG.[10] Miura and Satoh reported the first rhodium-catalyzed olefination−oxa-Michael cyclization in the coupling of benzoic acids with acrylates.[11] Inspired by these pioneering works, in 2010 we disclosed a rhodium-catalyzed cyclative coupling between secondary carboxamides and activated olefins (Scheme 4).[12] In all cases, C−H activation of the *C*-aryl ring was observed for *N*-aryl benzamides. The reaction may stop at the stage of C−H olefination (**Int4**) when heteroaryl carboxamides are employed. In 2013, Ellman and Lavis applied nitrogen DGs to the nucleophilic cyclative coupling of arenes with benzaldehydes.[13]

To overcome the limitation of DGs in simple nucleophilic cyclization reactions, we designed azomethine imines as arene

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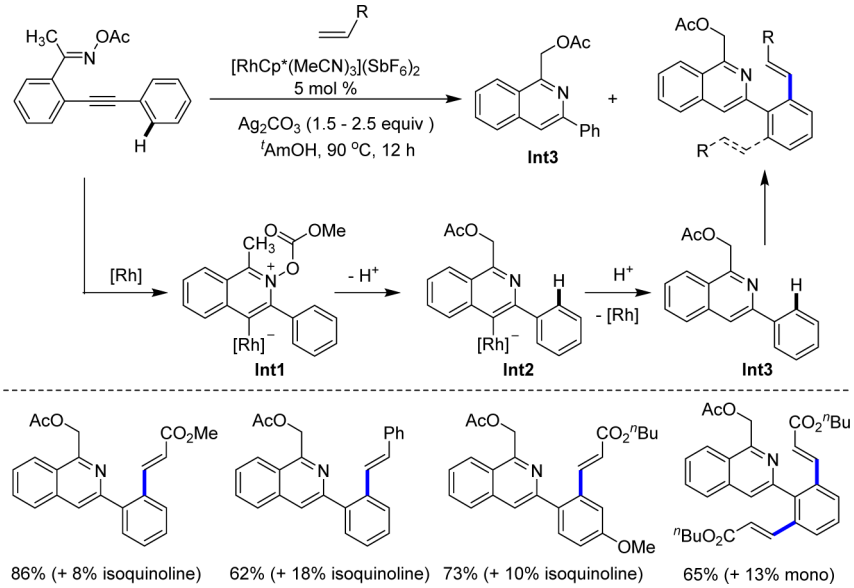
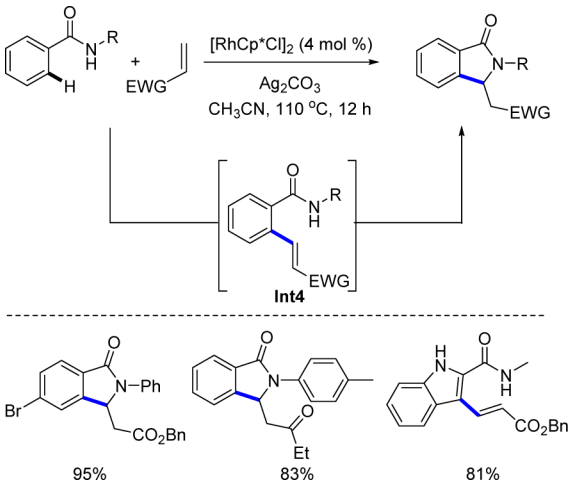
Scheme 3. In Situ Activation/Generation of a DG[8]



Scheme 4. Selected Scope for Oxidative Coupling between Carboxamides and Olefins[12]



substrates that reacted with diverse selectivity (Scheme 5).[14] The oxidative coupling of benzaldehyde-derived azomethine imines with activated olefins occurred via C−H activation and C−N cleavage to give 1,2-dihydrophthalazines (Scheme 5a). Several intermediates were examined, and it was found that the reaction underwent initial oxidative olefination to give intermediate **Int5**, which was followed by rhodium-catalyzed reversible ring scission (retro-Michael addition) to generate protic hydrazone intermediate **Int6**. Subsequent uncatalyzed Michael cyclization afforded the final product.

In contrast, the reaction of heteroaldehyde-derived azomethine imines afforded heteroarene-fused pyridines as a result of C−H activation and N−N cleavage (Scheme 5b). Although the common intermediacy of the hydrazone was followed, it rather underwent six-electron cyclization (**Int7**) followed by elimination of 3-methylbutenamide to furnish the fused pyridine. In these coupling systems, although the azomethine group is sufficiently coordinating to entail C−H activation, the rich postcoupling chemistry stems from in situ functionalizability of a hydrazone intermediate. Moreover, when the oxidant was switched to $Cu(OAc)_2·H_2O$, the reaction of such azomethine imines afforded *o*-olefinated aldehydes (Scheme 5c). The versatility of this reaction system and the diversity of the products resulted from delicate substrate control and condition control.

The role of DGs as nucleophiles is not limited to subsequent addition reactions. By the design of 2-aminopyridyl as a directing group, the coupling of *N*-(2-pyridyl)aniline with benzyl acrylates occurred via initial C−H olefination (**Int8**) followed by intramolecular nucleophilic substitution, leading to the synthesis of quinolones in moderate to high yields (Scheme 6).[15] It is likely that the pyridyl nitrogen binds to the rhodium and facilitates C−H activation and that trans-to-cis isomerization of the olefinated intermediate (**Int8** → **Int9**) is involved.

2.4. DGs as Electrophiles

Amides and imines are bifunctional DGs in that the nitrogen or oxygen donor is attached to an electrophilic C═N or C═O group, and their electrophilicity has been realized in C−H activation.[16] The coupling of benzaldehyde-derived azomethine imines with alkynes follows a sequence of C−H activation, migratory insertion of the Rh−C bond into the alkyne, and nucleophilic attack of the Rh−C(alkenyl) bond into the electrophilic imine group, leading to indenamine products (Scheme 7).[17] This type of reaction was initially reported using Re catalysts.[18] The indenamine product can undergo Cu(II)-catalyzed aerobic oxidation, affording the corresponding indenone in good yield. On the other hand, nitrones are isostructural to azomethine imines. However, their redox-neutral coupling with alkynes directly afforded indenones.[19] In this reaction, a putative *N*-hydroxyindenamine intermediate (**Int10**) was generated; dehydration and subsequent hydrolysis furnished the indenone product.

Tertiary benzamides also function as bifunctional DGs. In the rhodium-catalyzed coupling of benzoyl pyrrolidine with propargyl alcohol, a lactone bearing an exocylic double bond was isolated in high yield (Scheme 8).[20] This reaction proceeded via regioselective hydroaylation of the alkyne (**Int11**) followed by metal-assisted lactonization. Notably, starting from an enantioenriched propargyl alcohol, the enantiopurity of the product was essentially retained. In all such systems of bifunctional DGs, the C−H activation and coupling are promoted by AcOH

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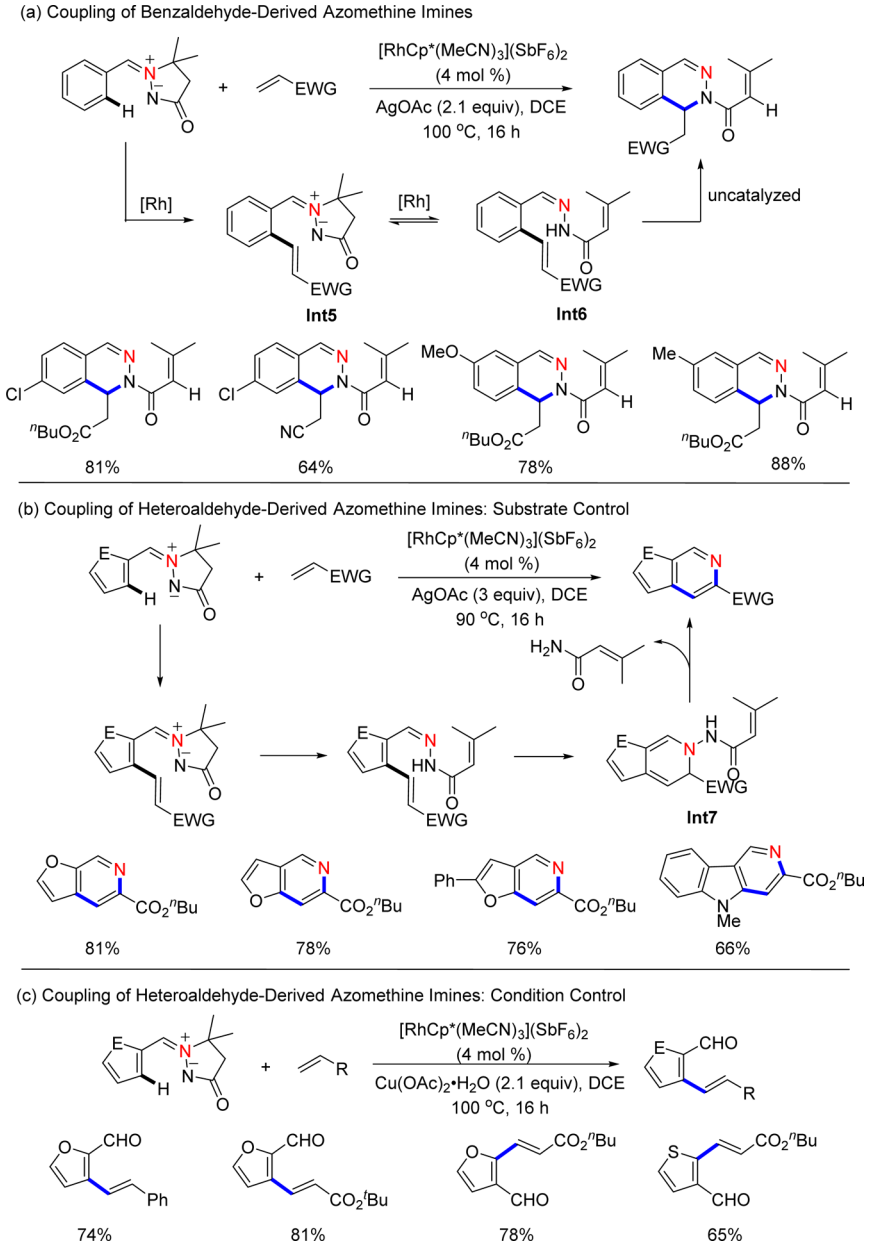
Scheme 5. Selected Scope for Olefination of Azomethine Imines[14]



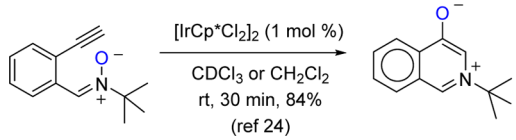
or PivOH, which likely assists C−H activation and subsequently enhances the electrophilicity of the C═N and C═O groups.

2.5. DGs as Internal Oxidants

Inspired by Fagnou and co-workers,[21] we took advantage of the directing effect and oxidizing potential of the N−O bond in oximes. The mild coupling of acetophenone-derived oxime with alkynes afforded isoquinolines (Scheme 9).[22] Although the full mechanistic details remain open to discussion (Rh(III)−Rh(V) and all-Rh(III) mechanisms are possible), the internal oxidizing ability of the N−O bond has been fully recognized, and a number of systems have been developed by taking advantage of the cleavage of N−O and N−N bonds in C−H activation.[23]

Despite the success in the design of C−H activation systems using an internal oxidizing DG, the reactions suffered from limited atom-economy in that a small coproduct was eliminated as a result of N−O or N−N cleavage. In fact, oxygen atom transfer (OAT) with 100% atom economy had not been realized before 2014 in the context of C−H activation, although both C−H activation and OAT represent important areas in catalysis.

Our work in 2011 on the $[IrCp^*Cl_2]_2$-catalyzed intramolecular OAT from nitrone to a proximal terminal alkyne cast new light on this subject (eq 2).[24] This room-temperature reaction



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afforded isolable azomethine ylides with a low catalyst loading. Although the reaction has little to do with C−H activation, $[IrCp^*Cl_2]_2$ and $[RhCp^*Cl_2]_2$ are typical C−H activation catalysts. Therefore, the combination of C−H activation and OAT can be expected. As a proof of concept, we[25a] and Chang[25b] independently realized Rh(III)-catalyzed systems for the

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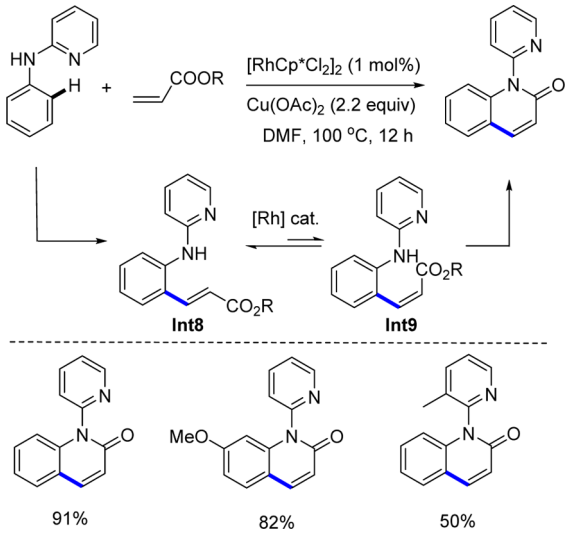
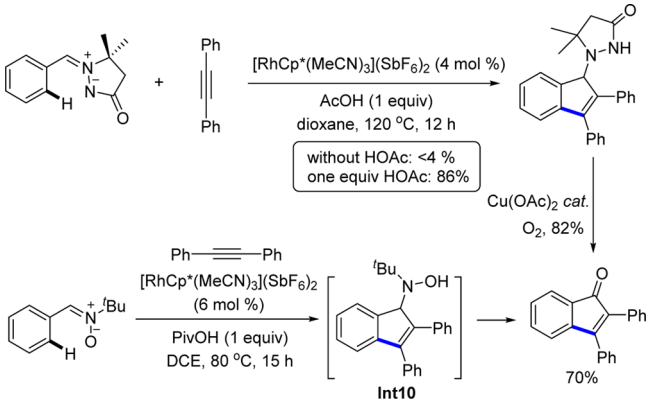
Scheme 6. Tandem Olefination–Nucleophilic Substitution[15]



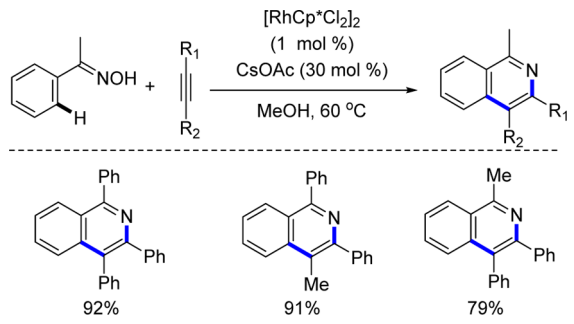
Scheme 7. [3 + 2] Couplings between Alkynes and Azomethine Imines and Nitrones[17]



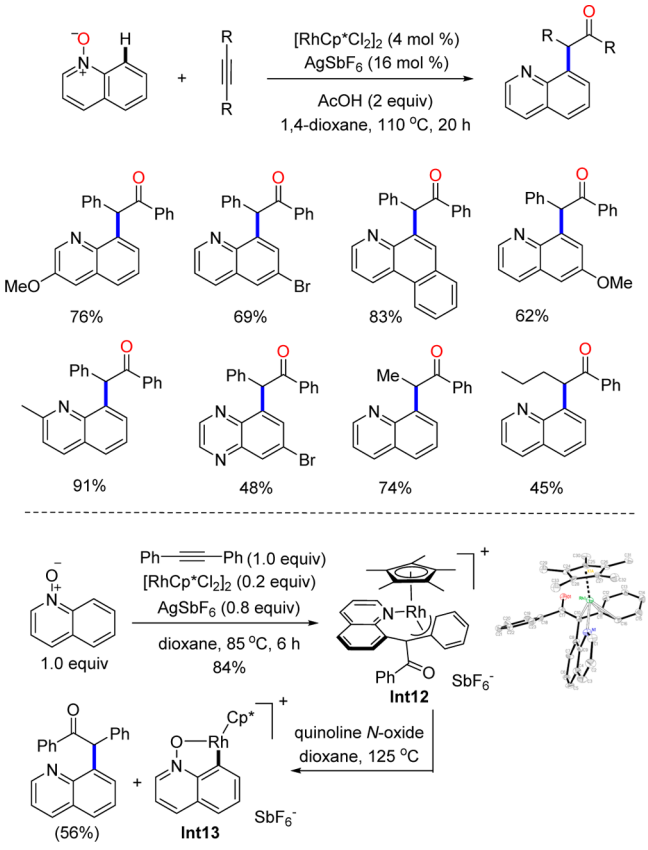
coupling between quinoline *N*-oxides and alkynes that successfully integrated C–H activation with OAT (Scheme 10), leading to the efficient synthesis of α,α-disubstituted acetophenones.

Regarding the mechanism of this system, we successfully isolated a thermodynamically stable η^3-benzyl complex (**Int12**) that was established as the resting state of the catalyst.[25a] Interactions with quinoline *N*-oxide released the coupled product

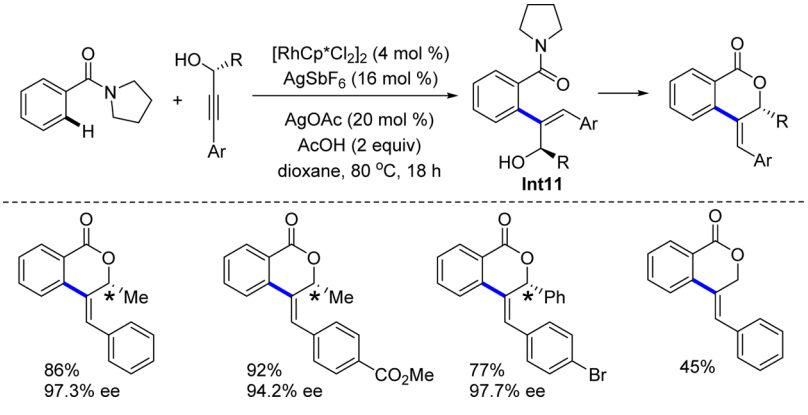
Scheme 9. Selected Scope for Redox-Neutral Synthesis of Isoquinolines[22]



Scheme 10. C–H Activation with Tandem Oxygen Atom Transfer[25a]



Scheme 8. Selected Scope for Hydroarylation–Lactonization[20]



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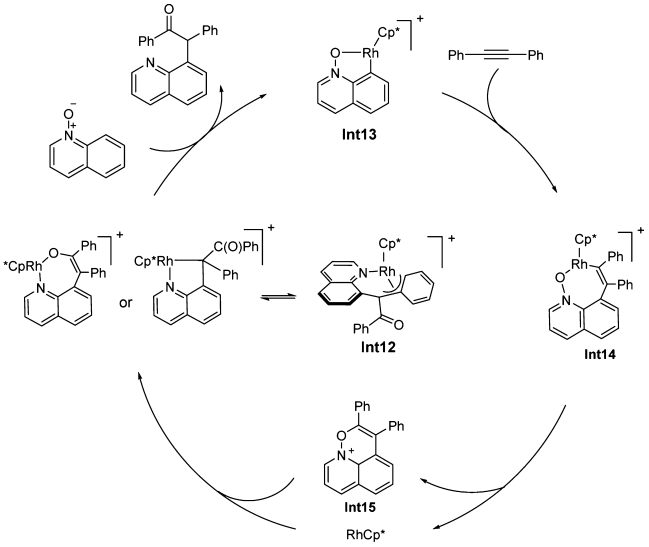
Scheme 11. Proposed Catalytic Cycle for C−H Activation with Subsequent Oxygen Atom Transfer[25a]

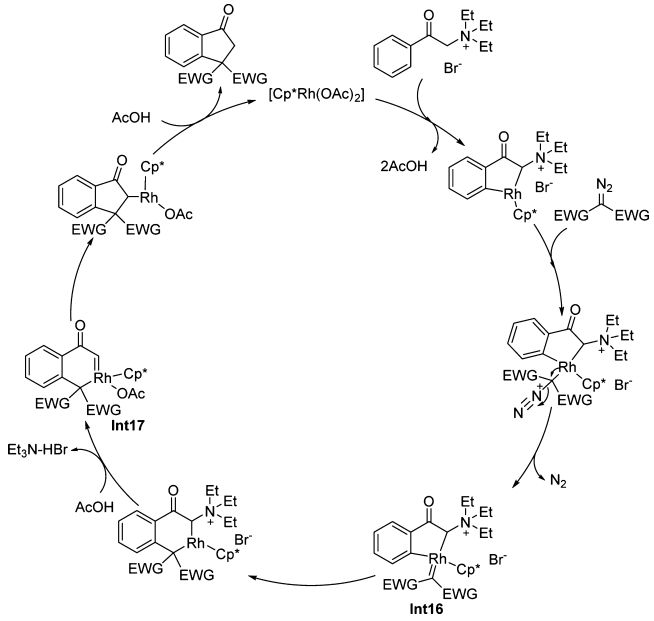


with concomitant cyclometalation of the quinoline *N*-oxide (**Int13**, Scheme 10). Mechanistic studies suggested that a Rh(III)−Rh(I)−Rh(III) pathway is most likely (Scheme 11), in which the seven-membered rhodacyclic intermediate **Int14** undergoes O−C reductive elimination to afford a Rh(I) species and a cationic heterocyclic intermediate (**Int15**). Oxidative addition of **Int15** back to the Rh(I) species leads to the eventual formation of the stable η^3-benzyl intermediate.

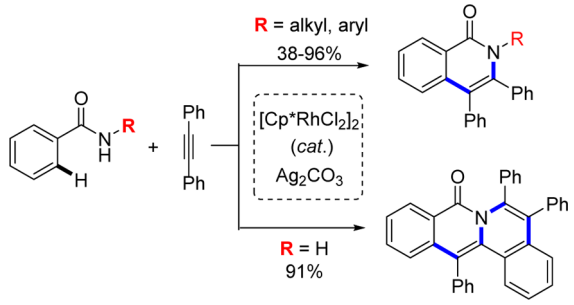
Despite various reports on C−H activation assisted by different oxidizing DGs, redox-neutral coupling delivered by an oxidizing C−N bond had not been reported before 2015. This might be caused by the lower reactivity and larger steric hindrance of C−N bonds. However, this strategy is of great significance because it may allow the efficient construction of complementary carbocycles. We designed phenacyltriethylammonium salts as readily available arene substrates for redox-neutral couplings (Scheme 12).[26] The coupling with α-diazo esters afforded benzocyclopentanones, and this reaction can be performed in one pot starting from α-bromoacetophenones and triethylamine. The coupling with olefins furnished *o*-olefinated acetophenones, and even aliphatic olefins were tolerated. Olefin-dependent selectivity was also observed.

The reaction mechanism for the coupling of phenacyltriethylammonium bromides with diazo esters was explored by a combination of experimental and theoretical methods (Scheme 13).

Scheme 13. Proposed Catalytic Cycle for the Coupling of Phenacyltriethylammonium with a Diazo Substrate[26]

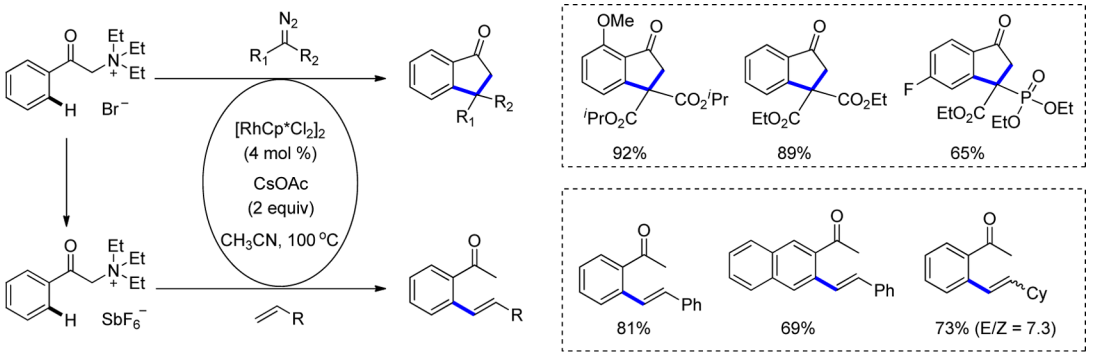


Scheme 14. Oxidative [4 + 2] Coupling between Benzamides and Alkynes[27c]



Density functional theory studies revealed that in the lowest-energy pathway, the turnover-limiting C−H activation process is assisted by C coordination rather than O coordination and occurs via a CMD mechanism. The lowest-energy pathway also involves two Rh(III) carbene species (**Int16** and **Int17**). The first one is generated via coordination and denitrogenation of a diazo ester, and the second α-oxo carbene originates from migratory insertion of the Rh−aryl bond into the first carbene followed by α-elimination of NEt_3.

Scheme 12. Selected Scope for C−H Activation of Phenacyltriethylammonium[26]



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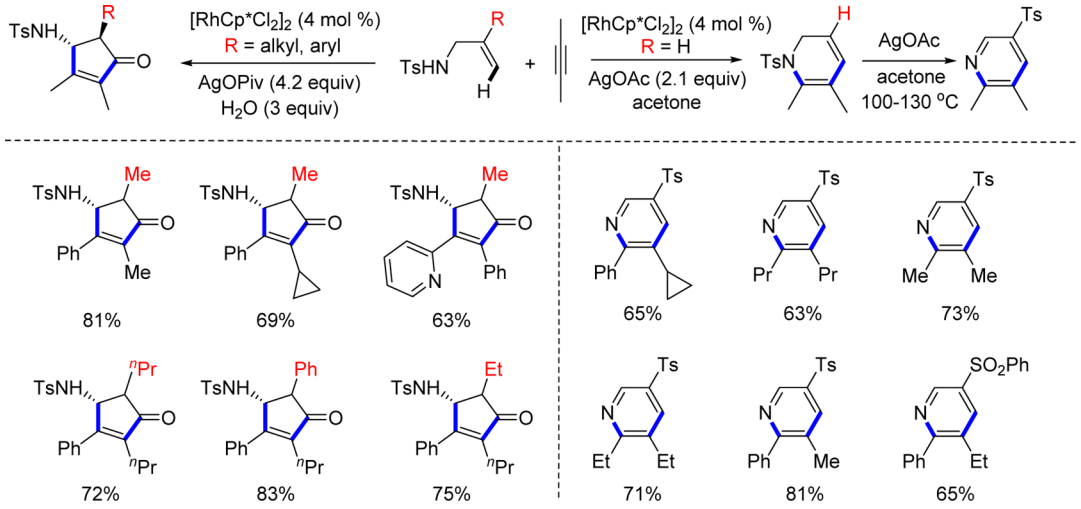
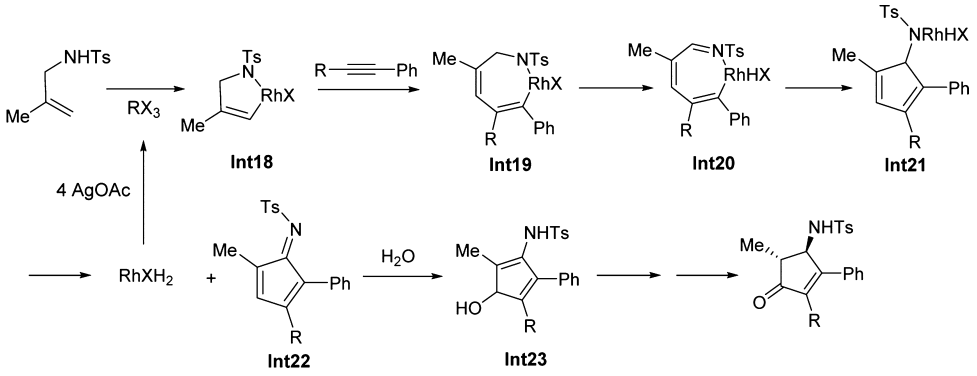
Scheme 15. Selected Scope for the Coupling of *N*-Allyl Sulfonamide with Alkynes[29]



Scheme 16. Proposed Mechanism for the Formation of the *trans*-Cyclopentenone Product[29]



2.6. DGs as Active Ligands

DGs can participate in subsequent electrophilic and redox functionalizations because they are sufficiently reactive or as a result of Rh−DG cooperation. However, when the coupling partners are not sufficiently polarized, the alternative role of the DG can be reflected. In particular, it can act as an active/participating ligand, as in reductive elimination reactions.

In 2010, Miura and Satoh,[27a] Rovis,[27b] and we[27c] independently reported rhodium(III)-catalyzed oxidative C−H/N−H functionalization of benzamides in the coupling with alkynes. The coupling of secondary benzamides afforded isoquinolones as a result of oxidative [4 + 2] reaction coupling. When primary benzamides and aryl-substituted alkynes were coupled, two equivalents of alkyne were incorporated with twofold C−H activation (Scheme 14). In this system, following cyclometalation and migratory insertion into the alkyne, the amide group participates in C−N reductive elimination, exhibiting a typical property of an active ligand. This type of coupling has been further extended to other [4 + 2] and [3 + 2] oxidative couplings.[15,28]

2.7. Participation in Other in Situ Transformations

The role of sulfonamide DGs is mostly limited to subsequent nucleophilic reactions. We extended the role of the NHTs group in *N*-allyl sulfonamides to other interesting substrate-dependent transformations (Scheme 15).[29] The coupling of simple *N*-allyl sulfonamide with diaryl-substituted alkynes afforded 1,2-dihydropyridines via an oxidative [4 + 2] process. In the case of (di)alkyl-substituted alkynes, the isolable 1,2-dihydropyridine intermediate readily underwent further in situ oxidation to give 3-sulfonylpyridine as a result of oxidative intermolecular 1,3-migration of the sulfonyl group. Furthermore, significant substrate- and condition-dependent selectivity was also observed for the olefin moiety of the *N*-allyl sulfonamide substrate. The coupling of 2-substituted *N*-sulfonyl allylamines offered the expected 1,2-dihydropyridine products when a slight excess of the oxidant AgOAc was used. In stark contrast, when water and an excess (4.2 equiv) of AgOAc or AgOPiv were provided, a *trans*-cyclopentenone product was isolated in good yield. Experimental studies confirmed that that these two products were generated from two independent and competing pathways. These results showcased the significance realization of diversified selectivities as a result of substrate control and condition control in rhodium catalysis.

The formation of the *trans*-cyclopentenone product is proposed to occur through common rhodacyclic intermediates **Int18** and **Int19** (Scheme 16). Promoted by an excess of silver oxidant, the amidate moiety undergoes *β*-hydride elimination to afford an *N*-Ts-activated imine (**Int20**). In this process, a nucleophilic amidate ligand is converted to a metal hydride-stabilized electrophilic imine. Subsequent migratory insertion of the Rh−C bond into the imine generates an *N*-cyclopentadienyl amidate intermediate (**Int21**). A second *β*-hydride elimination is proposed to give an activated imine (**Int22**) together with a rhodium dihydride. Subsequent hydration of the imine and tautomerization of **Int23** eventually furnish the final product.

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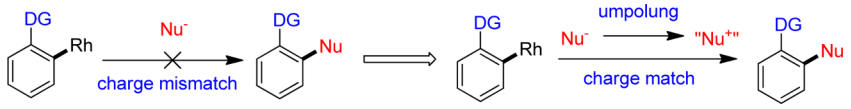
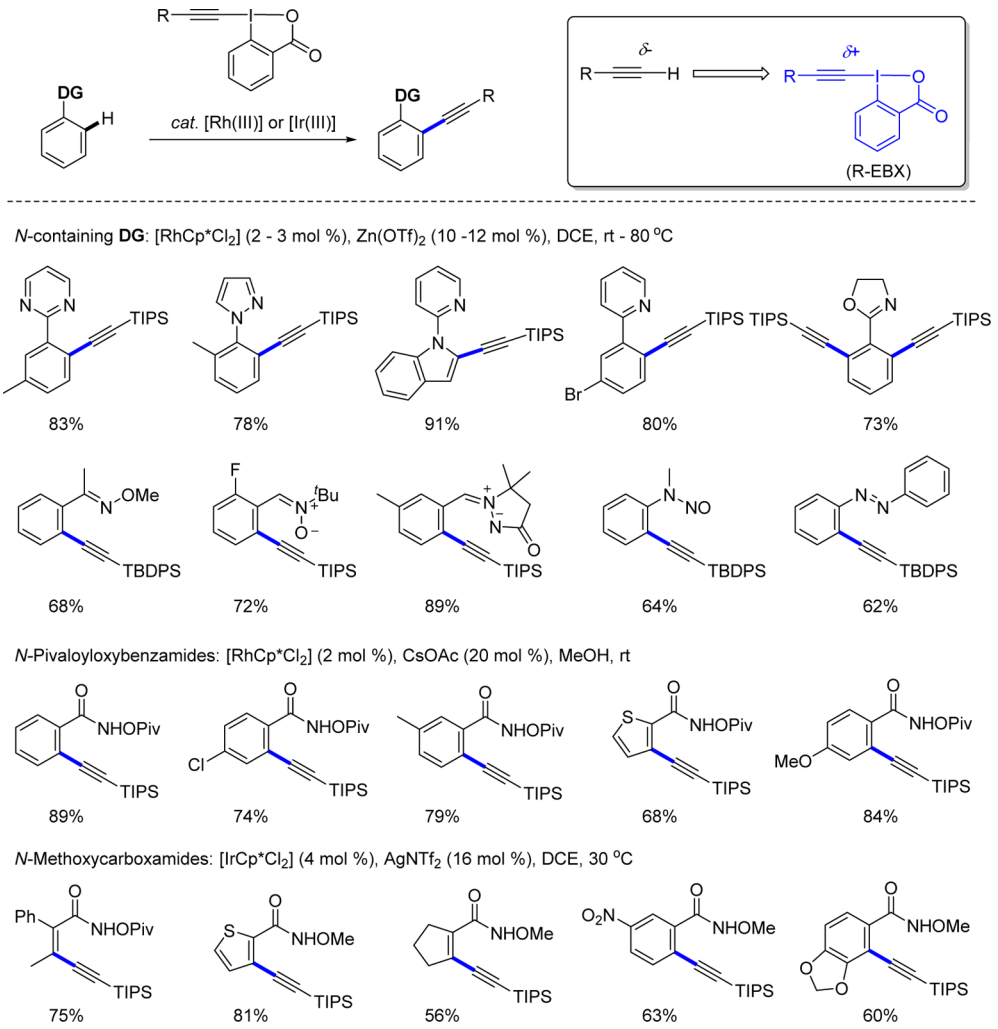
Acc. Chem. Res. 2015, 48, 1007−1020

Scheme 17. Activation of the Coupling Partner via Umpolung



Scheme 18. Selected Scope for Alkynylation of Diverse Arene/Alkene Substrates[30]



3. ACTIVATION OF THE (POLAR) COUPLING PARTNER

In contrast to the higher activity of alkenes and alkynes in coupling reactions, polar coupling partners (aldehydes, imines) often show limited reactivity although they are more reactive toward polar organo−main-group reagents. This is mainly because the M−C bond is often insufficiently polarized. In addition, these polar coupling partners may suffer from limited coordinating ability. A Rh(III)−C bond is typically more polarized and displays not only typical organometallic properties but also mild and controllable nucleophilicity. These properties serve as an advantageous stepping stone into the functionalization of a broad scope of substrates in rhodium-catalyzed coupling reactions because there is no need for a stoichiometric amount of organo−main-group reagent as in traditional functional group transformations. In addition, the mildness of nucleophilic Rh(III)−C bonds contributes to higher substrate compatibility.

3.1. Umpolung

Coupling of Rh−C bonds with nucleophiles is charge-mismatched. To solve this issue, an oxidant is necessary. It should be noted that the role of the oxidant is not simply limited to the reoxidation of a Rh(I) species (typically generated from a product-forming reductive elimination process) to the active Rh(III) species. More specifically, the oxidant may directly interact with the nucleophile, resulting in umploung prior to the coupling (Scheme 17).

3.1.1. Umpolung Using Preformed Reagents. In this context, we applied stable 1-silylethynyl-1,2-benziodoxol-3(1*H*)-ones (silyl-EBXs) as electrophilic alkynylating reagents for the alkynylation of a broad scope of arenes (Scheme 18).[30] These hypervalent iodine reagents circumvented the use of terminal alkynes as alkynylating reagents, which are often troublesome with side reactions. Arenes bearing diversified DGs (pyridine, pyrimidine, pyrazole, oxazoline, oxime, amide, azomethine, nitrone, azo) were smoothly alkynylated, and in many examples the DGs were readily functionalizable.[30a] The C−H bond

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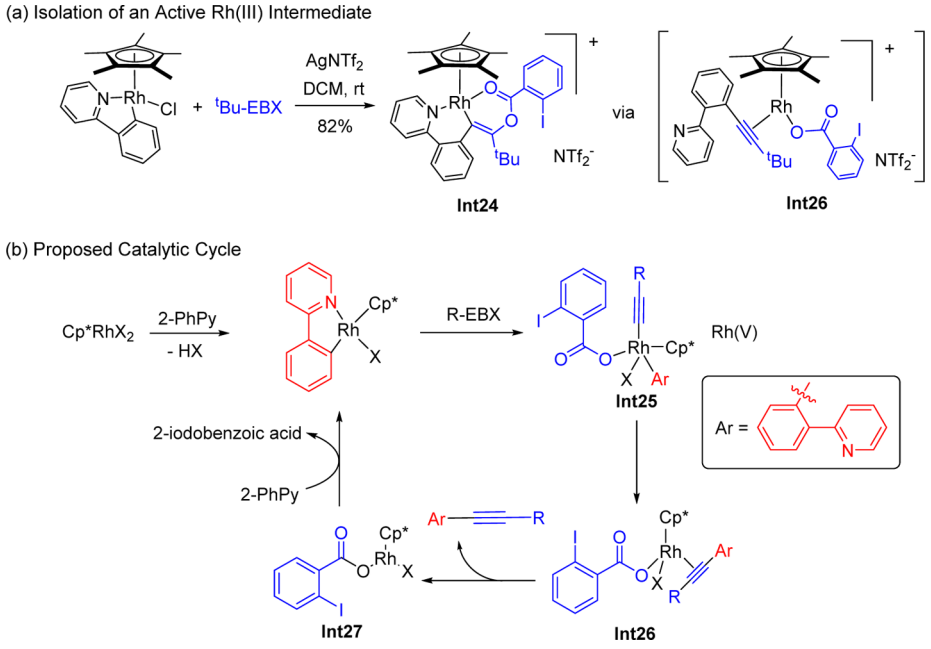
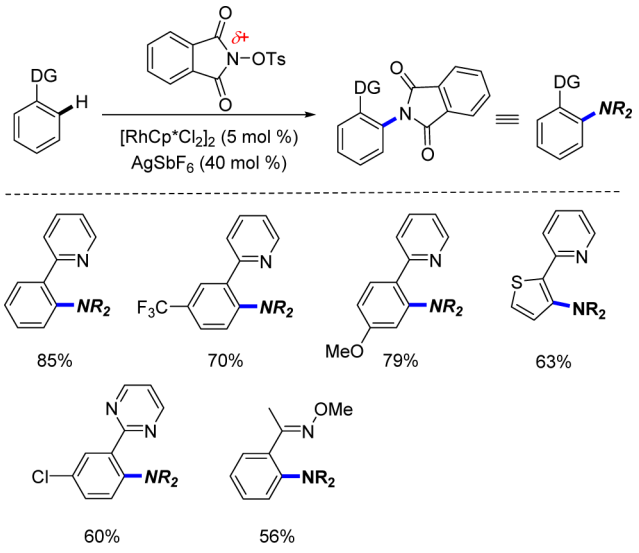
Acc. Chem. Res. 2015, 48, 1007−1020

Scheme 19. Intermediate Studies and Mechanistic Proposal for Rh-Catalyzed Alkynylation[30]



Scheme 20. Selected Scope for Amidation via Umploung[33]



was not limited to an aryl or alkenyl one; formyl C−H as in salicylaldehyde was also applicable.[30b] Rhodium and iridium catalyses exhibited complementary substrate scopes. For example, *o*-alkynylation of *N*-pivaloyloxybenzamides occurred under Rh(III) catalysis, but when the substrate was switched to *N*-methoxybenzamides, Ir(III) catalysis had to be used. It is noteworthy that these systems are complementary to those previously known for the alkynylation of electron-rich (hetero)-arenes under Au(I) and Pd(II) catalysis.[31]

Mechanistic studies were performed for the alkynylation of 2-arylpyridine.[30a] A Cp*Rh(III) tripodal complex was isolated from a stoichiometric reaction with ^{t}Bu-EBX, and it was established as a reactive intermediate (**Int24**, Scheme 19a). The intermediacy of this intermediate in combination with the failure of reductive elimination from the Rh(III) alkynyl complex, [Cp*(N^C)Rh(alkynyl)], led to the proposal of a Rh(III)−Rh(V)−Rh(III) mechanism (Scheme 19b),[30a] where the Rh(V) species (**Int25**) is generated via oxidative addition to the rhodacycle. Reductive elimination affords a Rh(III) alkyne intermediate (**Int26**). In the stoichiometric reaction, migratory insertion of the benzoate ligand afforded the isolate tripodal complex **Int24**. In the catalytic system, dissociation of the alkyne gives rhodium(III) benzoate intermediate **Int27**, which interacts with the arene substrate to initiate the next cycle.

This umpolung strategy has been applied by others to C−H amination/amidation using electrophilic amines/amides.[32] We achieved Rh(III)-catalyzed amidation of 2-arylpyridines and ketoximes using *N*-OTs phthalimide under base-free conditions (Scheme 20).[33] An excess of $AgSbF_6$ additive proved necessary (Ag:Rh = 8:1), which probably activated both the catalyst and the amidating reagent. A possible mechanism includes electrophilic amidation via 1,2-aryl migration with concomitant elimination of OTs^-. However, a Rh(III) to Rh(V) oxidative addition pathway cannot be excluded.

3.1.2. Umpolung under in Situ Conditions. Ideally, umpolung is realized under the catalyzed conditions using a combination of nucleophiles and oxidant, which requires compatibility of the oxidant and the C−H activation. By following an umpolung of azide under rhodium catalysis, we achieved mild azidation of electronically less reactive arenes such as 2-arylpyridines using NaN_3 as an azide source in the presence of $PhI(OAc)_2$/TsOH or a PhI(OH)OTs oxidant (Scheme 21).[34] Arenes bearing a heterocyclic DG such as pyridine, pyrimidine, and pyrazole are viable substrates. Besides azidation, nitration using $NaNO_2$ in the presence of PhI(OH)OTs oxidant occurred with essentially the same substrate scope. It is noteworthy that palladium(II) also catalyzed the oxidative coupling between 2-arylpyridines and NaN_3 under single-electron-oxidation conditions.[35] However, the reaction did not stop at the stage of the azidation; further denitrogenative cylization occurred, and this is likely ascribable to the rather harsh conditions.

Mechanistic studies revealed that C−H activation is involved. However, a cyclometalated Rh(III) azide complex is not an active catalyst. The introduction of TBAC to a coupling catalyzed by the incompetent cyclometalated Rh(III) azide complex

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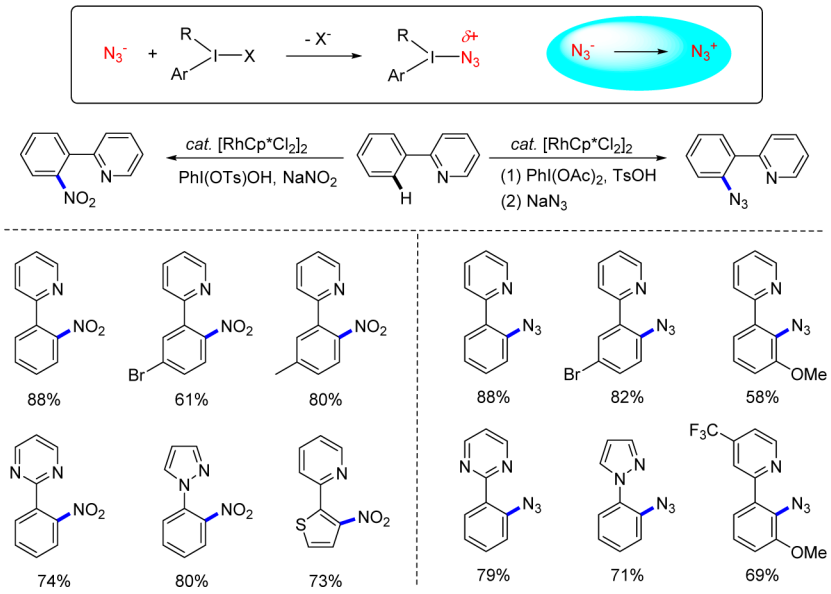
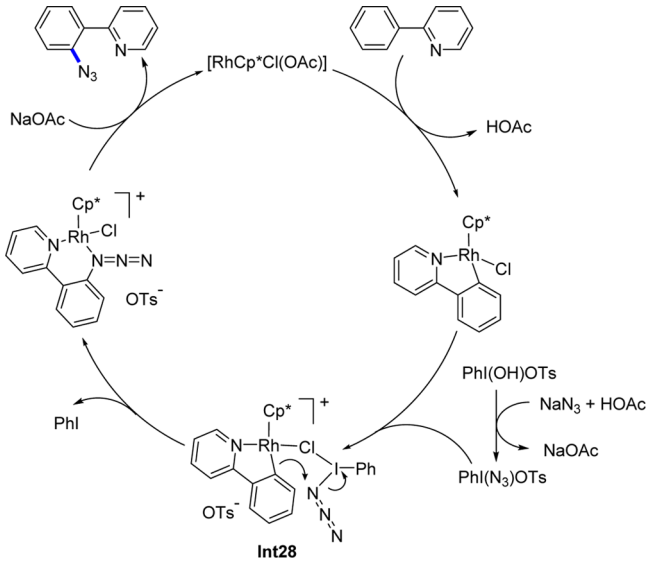
Acc. Chem. Res. 2015, 48, 1007−1020

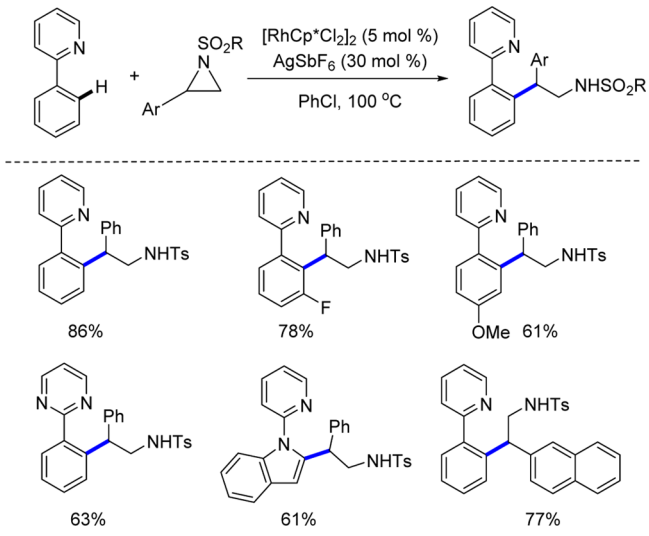
Scheme 21. Selected Scope for C−H Azidation and Nitration of Arenes[34]



Scheme 22. Proposed Catalytic Cycle for the Azidation of 2-Arylpyridines[34]



Scheme 23. Selected Scope for Insertion of Unactivated Arenes into Aziridines[36]

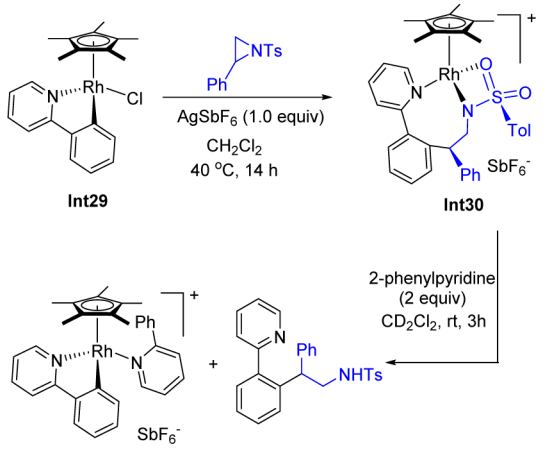


regained the activity, indicating the intermediacy of a rhodium chloride species. A plausible mechanism is given in Scheme 22. It involves the generation of an electrophilic azidating reagent $PhI(N_3)OTs$ via umpolung. The metallacyclic intermediate is bridged to the $PhI(N_3)OTs$ moiety via a chloride ligand (**Int28**), and the C−N bond formation occurs when the Rh(III)−C bond undergoes electrophilic azidation.

3.2. Release of Ring Strain

Strain in three-membered rings can offer substrate activation and streamline further chemical manipulation. Coupling of aziridines with electron-rich arenes under Lewis acid catalysis via the Friedel−Crafts mechanism has been reported. However, until 2013, ring-opening coupling of aziridines with electron-poor arenes via a C−H activation mechanism had not been reported. We achieved the efficient coupling of 2-arylpyridines with *N*-sulfonyl aziridine to give *β*-branched *N*-sulfonyl-ethylamines (Scheme 23).[36] Not only was a combination of

Scheme 24. Stoichiometric Reactions between a Rh−Aryl Bond and an Aziridine[36]



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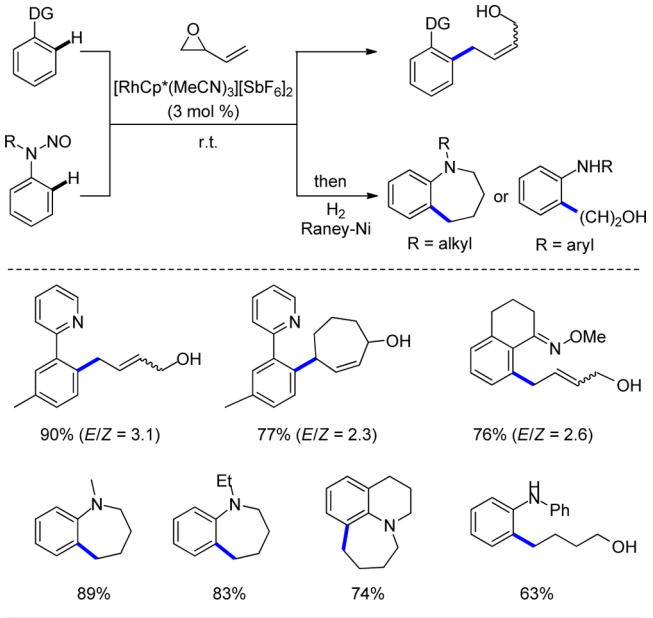
Acc. Chem. Res. 2015, 48, 1007−1020

Scheme 25. Selected Scope for the Coupling of Arenes with Vinyl Oxirane[37]

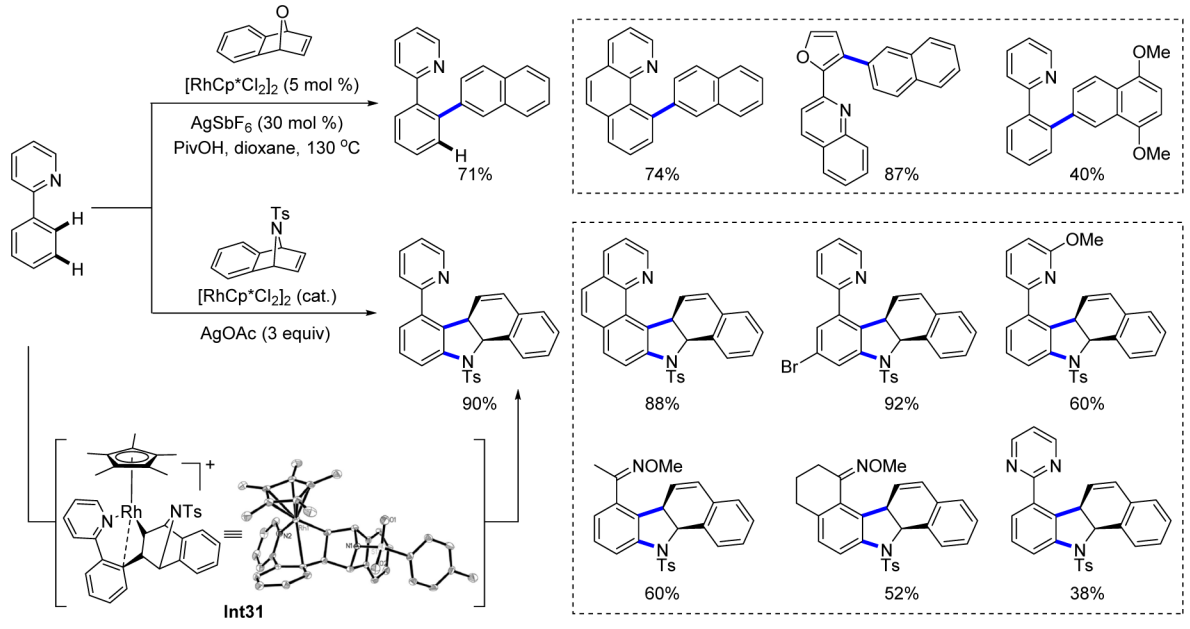


$[RhCp^*Cl_2]_2$ and $AgSbF_6$ necessary, but also the $AgSbF_6$ was used in excess ($AgSbF_6$:$[RhCp^*Cl_2]_2$ = 6:1), allowing it to activate both the aziridine substrate and the catalyst (by chloride abstraction). Mechanistic studies using a stereochemistry probe suggested the intermediacy of a tight ion pair. Significantly, the stoichiometric interactions between rhodacycle **Int29**, an aziridine, and $AgSbF_6$ afforded an eight-membered rhodacycle fused with a four-membed ring (**Int30**, Scheme 24). This complex can readily react with 2-phenylpyridine to release the coupled product and thus has been established as a reactive intermediate. Clearly, the C−C formation originates from the nucleophilic attack of the incipient Rh−C bond at the activated aziridine.

Epoxides are structurally related to aziridines, but styrene oxides failed to couple with arenes under various Rh(III) conditions. The poor reactivity can be ascribed to the low coordinating ability and limited electrophilicity of the epoxide. The introduction of a vinyl group on the epoxide ring provides a handle for functionalization. The room-temperature coupling of arenes with 2-vinyloxiranes afforded allylic alcohols as mixtures of stereoisomers (Scheme 25).[37] The incipient Rh−C bond is proposed to undergo migratory insertion into the olefin, and subsequent β-oxygen elimination and protonolysis yields the product. Although the Rh−C bond does not directly interact with the epoxide ring, it is activated by the strain and by the 2-vinyl group. Significantly, the coupling of *N*-nitrosoanilines with 2-vinyloxirane afforded allylic alcohols bearing a readily functionalizable aminonitroso group; simple hydrogenation catalyzed by Raney Ni then led to the formation of benzoazepanes in high yield.

Olefins as a coupling partner almost inevitably undergo redox-neutral insertion or oxidative olefination in C−H activation chemistry. In the latter reactions, β-hydrogen elimination consists of a key step. However, in the case of activated cyclic olefins such as 7-oxa/azabenzonorbornadienes, β-hydrogen elimination can be suppressed because a syn-coplanar orientation of the Rh−C−C−H moiety cannot be fulfilled, so the alternative β-heteroatom elimination takes place preferentially. Although these bicyclic olefins are known to couple with aryl halides and arylboronic acids, no report on their coupling with arenes had been realized until 2013. Our rhodium-catalyzed oxidative coupling between 2-arylpyridines and 7-azabenzonorbornadienes with AgOAc as an oxidant afforded a *cis*-dihydrocarbazole product (Scheme 26). Importantly, this reaction proceeded with twofold C−H activation in the same arene substrate (ortho then meta C−H activation).[38] Interactions between the incipient Rh(III)−C bond and a 7-azabenzonorbornadiene in a stoichiometric reaction afforded seven-membered rhodacyclic intermediate **Int31**. Further mechanistic studies showed that the first C−H activation is rate-limiting. Mechanistic studies also clarified the sequencing of the second C−H activation (at the meta position, to give **Int32**) versus the β-nitrogen elimination (to give **Int33**), with

Scheme 26. Selected Scope for the Coupling of Arenes with 7-Aza/Oxabenzonorbornadienes[38]



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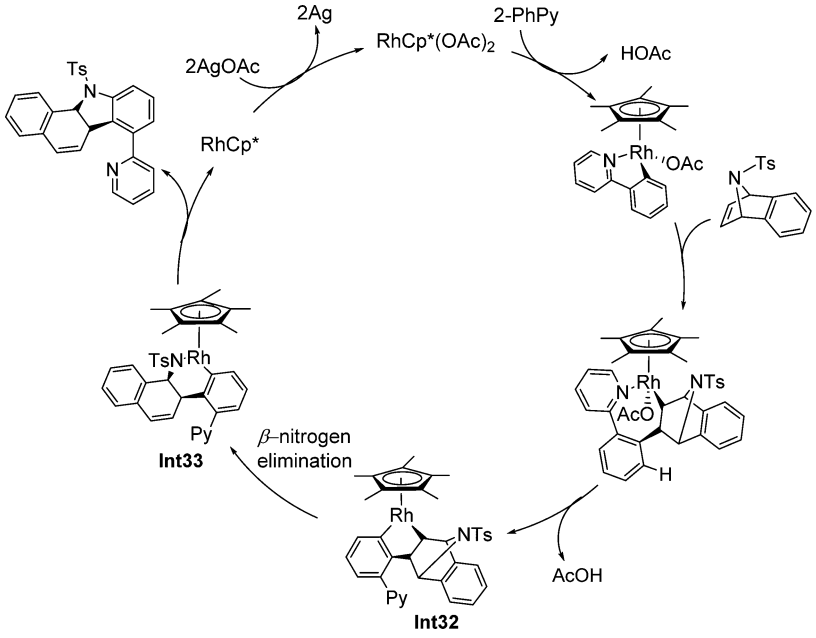
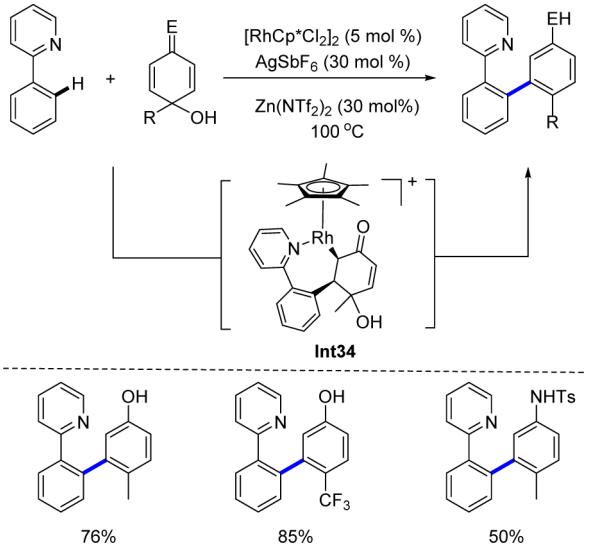
Acc. Chem. Res. 2015, 48, 1007−1020

Scheme 27. Proposed Catalytic Cycle for the Oxidative Coupling of Arenes with 7-Azabenzonorbornadienes[38]



Scheme 28. Coupling of Arenes via Dienones by Rearomatization[39]



the former occurring first (Scheme 27). In contrast to the oxidative coupling of 7-azabenzonorbornadienes, 7-oxabenzonorbornadienes coupled only under redox-neutral conditions in the presence of PivOH to afford the 2-naphthylation product.

3.3. Activation by Rearomatization

By taking advantage of the redox-neutral insertion of arenes into electron-withdrawing group (EWG)-activated olefins, we recently realized the redox-neutral coupling of 2-arylpyridines with 4-hydroxycyclohexa-2,5-dienones, where the rearomatization potential of dienones was utilized as a driving force to accomplish C−C bond formation (Scheme 28).[39] Even though the dienone serves as an activated olefin, zinc triflate is needed as an additive to further enhance the electrophilicity of the carbonyl group. The Rh−C bond is proposed to undergo Zn(II)-assisted 1,4-addition to the enone to give **Int34**. Aromatization to the final product upon release of water presumably occurs after dissociation of an intermediate from the catalyst.

4. SUMMARY AND OUTLOOK

Recent years have witnessed explosive progress in rhodium-catalyzed C−H activation of arenes. This chemistry was initially developed using relatively reactive unsaturated coupling partners such as alkenes and alkynes with catalyzed by Cp*Rh complexes. Mechanistic insights into the Cp*Rh-catalyzed reactions resulted in generally applicable and robust catalysts for diversified C−H bond activations of arenes in couplings with a broader scope of coupling partners, including π bonds, strained rings, and electrophilic reagents. Our contributions to the field started through strategies of substrate activation. In the coupling with π bonds, we focused on the activation of the arene substrates. By the design of directing groups that not only facilitate C−H activation but also participate in the in situ transformations as a nucleophile, electrophile, or internal oxidant, the diverse role of DGs has been fully utilized. In the coupling with polar coupling partners, the Rh(III)−C bond resulting from cyclometalation of the arene is sufficiently polarized and has enhanced reactivity, and consequently, it can act as a valuable surrogate for organo−main-group reagents such as Grignard reagents. By taking advantage of umpolung, ring strain, and rearomatization, we have coupled a range of polar coupling partners with arenes, resulting in C−C, C−O, C−N, and C−Se bond formation. We have demonstrated that to date some of these transformations can be achieved only under rhodium catalysis.

Despite the progress, our strategies are limited to activation of the substrate. Clearly, in order to achieve the activation of challenging sp^3 C−H bonds and asymmetric versions of C−H activation reactions, activation of the catalyst and the design of new (chiral) catalysts need to be actively pursued. We wish to continue our contributions to the field by enabling the functionalization of other classes of C−H bonds and increasing the mechanistic knowledge to further showcase the unique and complementary roles of rhodium catalysis in the construction of complex and useful molecules.

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Xingwei Li was born in Henan, China, in 1971 and obtained his Ph.D. degree in 2005 from Yale University. He then conducted postdoctoral studies at the California Institute of Technology (2005−2006). He started his independent career in 2006 as an Assistant Professor at Nanyang Technological University. He has served as a Professor of Chemistry at Dalian Institute of Chemical Physics, Chinese Academy of Sciences, since 2010. His research interests include organometallic chemistry and the development of new methods in metal-catalyzed organic reactions.

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ABBREVIATIONS

Cp* = pentamethylcyclopentadienyl
DG = directing group
Py = pyridyl
TBAC = tetra-*n*-butylammonium chloride
DCE = 1,2-dichloroethane
Nu = nucleophile
Cy = cyclohexyl
Ts = *p*-toluenesulfonyl
PivOH = pivalic acid
AmOH = amyl alcohol
OAT = oxygen atom transfer
TIPS = triisopropylsilyl
EBX = ethynyl-1,2-benziodoxol-3(1*H*)-one
EWG = electron-withdrawing group
Tol = tolyl
NTf_2 = $N(SO_2CF_3)_2$

REFERENCES

(1) (a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. Rhodium-Catalyzed C−C Bond Formation via Heteroatom-Directed C−H Bond Activation. *Chem. Rev.* **2010**, *110*, 624−655. (b) Ackermann, L.; Vicente, R.; Kapdi, A. R. Transition-Metal-Catalyzed Direct Arylation of (Hetero)Arenes by C−H Bond Cleavage. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792−9826. (c) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. Recent Advances in the Transition Metal-Catalyzed Twofold Oxidative C−H Bond Activation Strategy for C−C and C−N Bond Formation. *Chem. Soc. Rev.* **2011**, *40*, 5068−5083. (d) Yeung, C. S.; Dong, V. M. Catalytic Dehydrogenative Cross-Coupling: Forming Carbon−Carbon Bonds by Oxidizing Two Carbon−Hydrogen Bonds. *Chem. Rev.* **2011**, *111*, 1215−1292. (e) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. Towards Mild Metal-Catalyzed C−H bond Activation. *Chem. Soc. Rev.* **2011**, *40*, 4740−4761. (f) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. Ruthenium(II)-Catalyzed C−H Bond Activation and Functionalization. *Chem. Rev.* **2012**, *112*, 5879−5918. (g) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F.; Beyond Directing Groups. Transition-Metal-Catalyzed C−H Activation of Simple Arenes. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236−10254.

(2) For an early example, see: Gaunt, J. C.; Shaw, B. L. Transition metal−carbon bonds: XL. Palladium(II) complexes of [(dimethylamino)methyl]-ferrocene. *J. Organomet. Chem.* **1975**, *102*, 511−516.

(3) (a) Lyons, T. W.; Sanford, M. S. Palladium-Catalyzed Ligand-Directed C−H Functionalization Reactions. *Chem. Rev.* **2010**, *110*, 1147−1169. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. Weak Coordination as a Powerful Means for Developing Broadly Useful C−H Functionalization Reactions. *Acc. Chem. Res.* **2012**, *45*, 788−802.

(4) (a) Davies, D. L.; Donald, S. M. A.; Al-Duaij, O.; Macgregor, S. A.; Pölleth, M. Electrophilic C−H Activation at {Cp*Ir}: Ancillary-Ligand Control of the Mechanism of C−H Activation. *J. Am. Chem. Soc.* **2006**, *128*, 4210−4211. (b) Ackermann, L. Carboxylate-Assisted Ruthenium-Catalyzed Alkyne Annulations by C−H/Het−H Bond Functionalizations. *Acc. Chem. Res.* **2014**, *47*, 281−295.

(5) Ueura, K.; Satoh, T.; Miura, M. Rhodium- and Iridium-Catalyzed Oxidative Coupling of Benzoic Acids with Alkynes via Regioselective C−H Bond Cleavage. *J. Org. Chem.* **2007**, *72*, 5362−5367.

(6) For selected reviews, see: (a) Kuhl, N.; Schröder, N.; Glorius, F. Formal S_N-Type Reactions in Rhodium(III)-Catalyzed C−H Bond Activation. *Adv. Synth. Catal.* **2014**, *356*, 1443−1460. (b) Song, G.; Wang, F.; Li, X. C−C, C−O and C−N Bond Formation via Rhodium(III)-Catalyzed Oxidative C−H Activation. *Chem. Soc. Rev.* **2012**, *41*, 3651−3678. (c) Satoh, T.; Miura, M. Oxidative Coupling of Aromatic Substrates with Alkynes and Alkenes under Rhodium Catalysis. *Chem.—Eur. J.* **2010**, *16*, 11212−11222.

(7) Zhang, F.; Spring, D. R. Arene C−H Functionalisation Using a Removable/Modifiable or a Traceless Directing Group Strategy. *Chem. Soc. Rev.* **2014**, *43*, 6906−6919.

(8) Zhao, P.; Wang, F.; Han, K.; Li, X. Rhodium(III)-Catalyzed Cyclization−Olefination of *N*-Acetoxyl Ketoimine−Alkynes. *Org. Lett.* **2012**, *14*, 3400−3403.

(9) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. Oxidative Cross-Coupling of *N*-(2′-Phenylphenyl)-benzenesulfonamides or Benzoic and Naphthoic Acids with Alkenes Using a Palladium−Copper Catalyst System under Air. *J. Org. Chem.* **1998**, *63*, 5211−5215.

(10) Wasa, M.; Engle, K. M.; Yu, J.-Q. Pd(II)-Catalyzed Olefination of sp^3 C−H Bonds. *J. Am. Chem. Soc.* **2010**, *132*, 3680−3681.

(11) Satoh, T.; Ueura, K.; Miura, M. Rhodium- and Iridium-Catalyzed Oxidative Coupling of Benzoic Acids with Alkynes and Alkenes. *Pure Appl. Chem.* **2008**, *80*, 1127−1133.

(12) Wang, F.; Song, G.; Li, X. Rh(III)-Catalyzed Tandem Oxidative Olefination−Michael Reactions between Aryl Carboxamides and Alkenes. *Org. Lett.* **2010**, *12*, 5430−5433.

(13) Lian, Y.; Bergman, R. G.; Lavis, L. D.; Ellman, J. A. Rhodium(III)-Catalyzed Indazole Synthesis by C−H Bond Functionalization and Cyclative Capture. *J. Am. Chem. Soc.* **2013**, *135*, 7122−7125.

(14) Zhen, W.; Wang, F.; Zhao, M.; Du, Z.; Li, X. Rhodium(III)-Catalyzed Oxidative C−H Functionalization of Azomethine Ylides. *Angew. Chem., Int. Ed.* **2012**, *51*, 11819−11823.

(15) Chen, J.; Song, G.; Pan, C.-L.; Li, X. Rh(III)-Catalyzed Oxidative Coupling of *N*-Aryl-2-aminopyridine with Alkynes and Alkenes. *Org. Lett.* **2010**, *12*, 5426−5429.

(16) For a review, see: Zhang, X.-S.; Chen, K.; Shi, Z.-J. Transition Metal-Catalyzed Direct Nucleophilic Addition of C−H Bonds to

DOI: 10.1021/acs.accounts.5b00077
Acc. Chem. Res. 2015, 48, 1007−1020

Carbon−Heteroatom Double Bonds. *Chem. Sci.* **2014**, *5*, 2146−2159. For an asymmetric version, see: Wangweerawong, A.; Bergman, R. G.; Ellman, J. A. Asymmetric Synthesis of α-Branched Amines via Rh(III)-Catalyzed C−H Bond Functionalization. *J. Am. Chem. Soc.* **2014**, *136*, 8520.

(17) Chen, Y.; Wang, F.; Zhen, W.; Li, X. Rhodium(III)-Catalyzed Annulation of Azomethine Ylides with Alkynes via C−H Activation. *Adv. Synth. Catal.* **2013**, *355*, 353−359.

(18) Kuninobu, Y.; Kawata, A.; Takai, K. Rhenium-Catalyzed Formation of Indene Frameworks via C−H Bond Activation: [3 + 2] Annulation of Aromatic Aldimines and Acetylenes. *J. Am. Chem. Soc.* **2005**, *127*, 13498−13499.

(19) Qi, Z.; Wang, M.; Li, X. Access to Indenones by Rhodium(III)-Catalyzed C−H Annulation of Arylnitrones with Internal Alkynes. *Org. Lett.* **2013**, *15*, 5440−5443.

(20) Wang, F.; Qi, Z.; Sun, J.; Zhang, X.; Li, X. Rh(III)-Catalyzed Coupling of Benzamides with Propargyl Alcohols via Hydroarylation−Lactonization. *Org. Lett.* **2013**, *15*, 6290−6293.

(21) Guimond, N.; Gouliaras, C.; Fagnou, K. Rhodium(III)-Catalyzed Isoquinolone Synthesis: The N−O Bond as a Handle for C−N Bond Formation and Catalyst Turnover. *J. Am. Chem. Soc.* **2010**, *132*, 6908−6909.

(22) Zhang, X.; Chen, D.; Zhao, M.; Zhao, J.; Jia, A.; Li, X. Synthesis of Isoquinolines via Rhodium(III)-Catalyzed Dehydrative C−C and C−N Coupling between Oximines and Alkynes. *Adv. Synth. Catal.* **2011**, *353*, 719−723.

(23) Huang, H.; Ji, X.; Wu, W.; Jiang, H. Transition Metal-Catalyzed C−H Functionalization of *N*-Oxyenamine Internal Oxidants. *Chem. Soc. Rev.* **2015**, *44*, 1155−1171.

(24) Song, G.; Chen, D.; Su, Y.; Han, K.; Pan, C.-L.; Jia, A.; Li, X. Isolation of Azomethine Ylides and Their Complexes: Iridium(III)-Mediated Cyclization of Nitrone Substrates Containing Alkynes. *Angew. Chem., Int. Ed.* **2011**, *50*, 7791−7796.

(25) (a) Zhang, X.; Qi, Z.; Li, X. Rhodium(III)-Catalyzed C−C and C−O Coupling of Quinoline *N*-Oxides with Alkynes: Combination of C−H Activation with O-Atom Transfer. *Angew. Chem. Int. Ed.* **2014**, *53*, 10794−10798. The group of Chang independently reported the same chemistry. See: (b) Sharma, U.; Park, Y.; Chang, S. Rh(III)-Catalyzed Traceless Coupling of Quinoline *N*-Oxides with Internal Diarylalkynes. *J. Org. Chem.* **2014**, *79*, 9899−9906.

(26) Yu, S.; Liu, S.; Lan, Y.; Wan, B.; Li, X. Rhodium-Catalyzed C−H Activation of Phenacyl Ammonium Salts Assisted by an Oxidizing C−N Bond: A Combination of Experimental and Theoretical Studies. *J. Am. Chem. Soc.* **2015**, *137*, 1623−1631.

(27) (a) Mochida, S.; Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. Rhodium-Catalyzed Oxidative Coupling/Cyclization of Benzamides with Alkynes via C−H Bond Cleavage. *Chem. Lett.* **2010**, *39*, 744−746. (b) Hyster, T. K.; Rovis, T. Rhodium-Catalyzed Oxidative Cycloaddition of Benzamides and Alkynes via C−H/N−H Activation. *J. Am. Chem. Soc.* **2010**, *132*, 10565−10569. (c) Song, G.; Chen, D.; Pan, C.-L.; Crabtree, R.; Li, X. Rh-Catalyzed Oxidative Coupling between Primary and Secondary Benzamides and Alkynes: Synthesis of Polycyclic Amides. *J. Org. Chem.* **2010**, *75*, 7487−7490.

(28) (a) Qi, Z.; Wang, M.; Li, X. Rh(III)-Catalyzed Synthesis of Sultones through C−H Activation Directed by a Sulfonic Acid Group. *Chem. Commun.* **2014**, *50*, 9776−9778. (b) Su, Y.; Zhao, M.; Han, K.; Song, G.; Li, X. Synthesis of 2-Pyridones and Iminoesters via Rh(III)-Catalyzed Oxidative Coupling between Acrylamides and Alkynes. *Org. Lett.* **2010**, *12*, 5462−5465. (c) Wei, X.; Zhao, M.; Du, Z.; Li, X. Synthesis of 1-Aminoisoquinolines via Rh(III)-Catalyzed Oxidative Coupling. *Org. Lett.* **2011**, *13*, 4636−4639.

(29) Wang, D.; Wang, F.; Song, G.; Li, X. Diverse Reactivity in a Rhodium(III)-Catalyzed Oxidative Coupling of *N*-Allyl Arenesulfonamides with Alkynes. *Angew. Chem., Int. Ed.* **2012**, *51*, 12348−12352.

(30) (a) Xie, F.; Qi, Z.; Yu, S.; Li, X. Rh(III)- and Ir(III)-Catalyzed C−H Alkynylation of Arenes under Chelation Assistance. *J. Am. Chem. Soc.* **2014**, *136*, 4780−4787. (b) Wang, H.; Xie, F.; Qi, Z.; Li, X. Iridium and Rhodium-Catalyzed C−H Activation and Formyl Alkynylation of Aldehydes under Chelation Assistance. *Org. Lett.* **2015**, *17*, 920−923. For other related work, see: (c) Feng, C.; Loh, T.-P. Rhodium-Catalyzed C−H Alkynylation of Arenes at Room Temperature. *Angew. Chem., Int. Ed.* **2014**, *53*, 2722−2726. (d) Collins, K. D.; Lied, F.; Glorius, F. Preparation of Conjugated 1,3-Enynes by Rh(III)-Catalysed Alkynylation of Alkenes via C−H Activation. *Chem. Commun.* **2014**, *50*, 4459−4461.

(31) For a review, see: Brand, J. P.; Waser, J. Electrophilic Alkynylation: The Dark Side of Acetylene Chemistry. *Chem. Soc. Rev.* **2012**, *41*, 4165−4179.

(32) (a) Ng, K.-H.; Chan, A. S. C.; Yu, W.-Y. Pd-Catalyzed Intermolecular ortho-C−H Amidation of Anilides by *N*-Nosyloxycarbamate. *J. Am. Chem. Soc.* **2010**, *132*, 12862−12864. (b) Grohmann, C.; Wang, H.; Glorius, F. Rh(III)-Catalyzed Direct C−H Amination Using *N*-Chloroamines at Room Temperature. *Org. Lett.* **2012**, *14*, 656−659.

(33) Yu, S.; Wan, B.; Li, X. Rhodium(III)-Catalyzed C−H Activation and Amidation of Arenes Using *N*-Arenesulfonated Imides as Amidating Reagents. *Org. Lett.* **2013**, *15*, 3706−3709.

(34) Xie, F.; Qi, Z.; Li, X. Rhodium(III)-Catalyzed Azidation and Nitration of Arenes by C−H Activation. *Angew. Chem., Int. Ed.* **2013**, *52*, 11862−11866.

(35) Zheng, Q.-Z.; Feng, P.; Liang, Y.-F.; Jiao, N. Pd-Catalyzed Tandem C−H Azidation and N−N Bond Formation of Arylpyridines: A Direct Approach to Pyrido[1,2-*b*]indazoles. *Org. Lett.* **2013**, *15*, 4262−4265.

(36) Li, X.; Yu, S.; Wang, F.; Wan, B.; Yu, X. Rhodium(III)-Catalyzed C−C Coupling between Arenes and Aziridines by C−H Activation. *Angew. Chem., Int. Ed.* **2013**, *52*, 2577−2580.

(37) Yu, S.; Li, X. Rhodium(III)-Catalyzed C−C Coupling of Arenes with 2-Vinyloxiranes: Synthesis of Allylic Alcohols. *Org. Lett.* **2014**, *16*, 1200−1203.

(38) Qi, Z.; Li, X. Rhodium(III)-Catalyzed Coupling of Arenes with 7-Oxa/Azabenzonorbornadienes by C−H Activation. *Angew. Chem., Int. Ed.* **2013**, *52*, 8995−9000.

(39) Zhang, X.; Wang, F.; Qi, Z.; Yu, S.; Li, X. Rhodium(III)-Catalyzed Redox-Neutral C−H Arylation via Rearomatization. *Org. Lett.* **2014**, *16*, 1586−1589.

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