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Weak-Coordination in C−H Bond Functionalizations Catalyzed by 3d Metals

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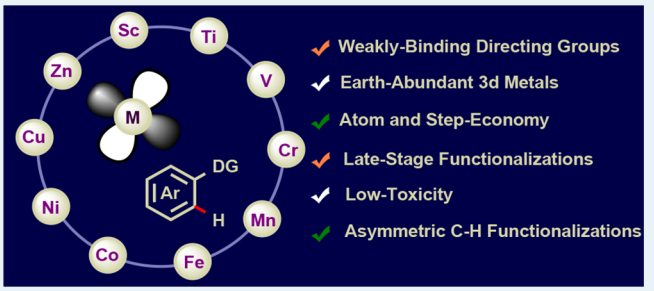
ABSTRACT: Transition-metal-catalyzed C−H bond functionalizations have had an enormous influence on organic synthesis in recent times. However, the use of low-abundance 4d and 5d metals is almost inevitable, and they are in high demand. This will be a cause of concern, and hence, it is important to develop methods based on 3d metals, which are widely present in the Earth's crust. In this regard, the use of 3d metal catalysts or their precursors for catalysis, in general, and C−H bond functionalizations, in particular, has gained significant momentum in the recent times. The major development in catalytic C−H bond functionalizations with 3d metals has been achieved predominantly with strongly coordinating directing groups such as pyridyl, pyrimidinyl, pyrazolyl, and 8-amino-quinolinyl groups. Thus, prefunctionalization of substrates with these directing groups is necessary, which contradicts the step- and atom-economy of C−H bond activation. However, commonly available functional groups such as aldehyde, ketone, carboxylic acid, amide, hydroxy, and *N*-oxides loosely bind to metals through weak-coordination. These weakly coordinating directing groups orient the metal to activate C−H bond regioselectively without the need for preinstalled strongly coordinating directing groups. Although it is challenging, this contemporary topic has been actively pursued by many researchers in recent times. Through this article, we provide a comprehensive overview of 3d metal-catalyzed, weakly coordinating, directing-group-enabled C−H bond functionalizations reported until March 2021.



KEYWORDS: *metal catalysis, C−H bond activation, directing groups, weak-coordination, 3d metals*

1. INTRODUCTION

Transition-metal-catalyzed cross-coupling reactions have revolutionized the area of organic synthesis, and they have been widely applied in the synthesis of natural products, materials, and polyarene synthesis.[1] Despite the significant advances made over the years in transition-metal-catalyzed cross-coupling reactions for the formation of C−C and C−heteroatom bonds, the requirement of prefunctionalized starting material and the ineffectiveness of these methods in minimizing unwanted byproducts are the obstacles of these seminal discoveries.[2−5] In contrast, the direct functionalizations of ubiquitous C−H bonds possess additional advantages in terms of step- and atom-economy.[6−8] However, C−H bonds are inert and ubiquitous which impose significant challenges to the synthetic community to achieve the site-selective functionalizations. In the early days of C−H bond activation, the regioselective C−H bond functionalizations were mainly governed by the steric and electronic parameters associated with the C−H bonds. Generally, the less sterically congested and more acidic C−H bonds are the preferential choice for the transition-metal catalyst over regioselective functionalization of nonbiased C−H bonds.[9,10]

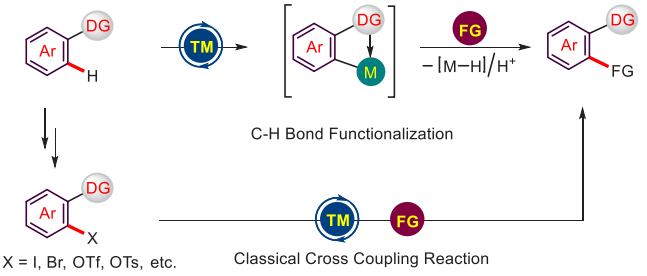


Figure 1. Classical cross-coupling vs directing group-assisted C−H bond functionalization.

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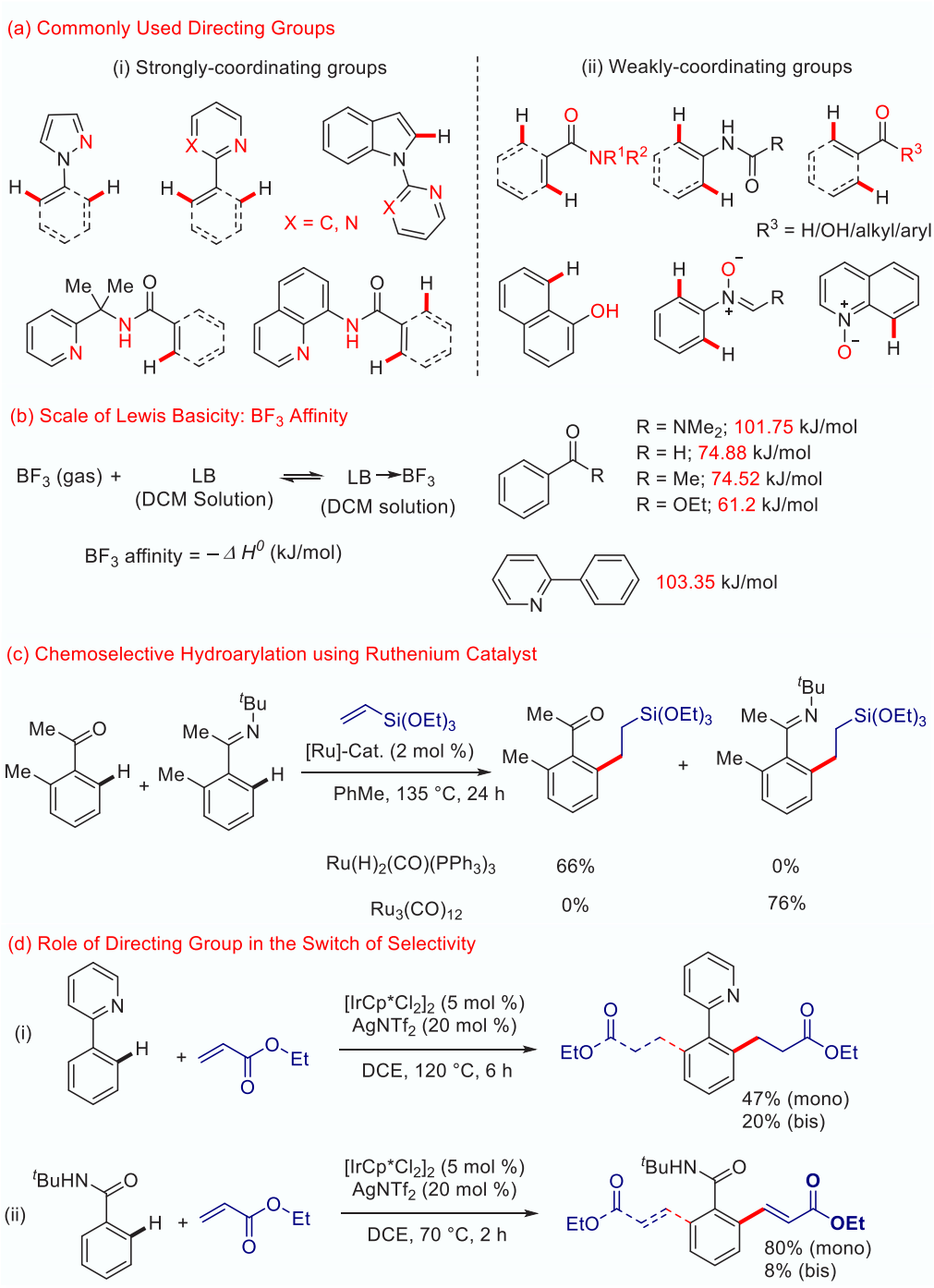
Scheme 1. Classification of Directing Groups and Their Diverse Reactivity



Selective functionalization of a particular C−H bond over the others present in a complex molecule is an extremely difficult task. To accomplish transition-metal-catalyzed regioselective C−H bond activation/functionalizations, Lewis basic functionalities is necessary to be present at the suitable position in the target molecule. The heteroatom present in the functional group or in the heterocycles acts as a directing group, where the Lewis-basic site coordinates to the metal through the dative bond. This brings the metal in close-proximity to a particular C−H bond (can be either *ortho*-, *meta*-, or *para*-) for regioselective C−H activation/functionalizations (Figure 1).

The directing group-assisted catalytic C−H bond functionalizations[11−24] have made a tremendous progress over the last 10 years by virtue of designing new templates, developing active catalysts, creating reactive electrophiles, and so on. Although early stoichiometric C−H bond activation was demonstrated by Bergmann and Jones,[25] it was the seminal work of Murai on catalytic *ortho*-C−H bond functionalization of ketone mediated by low-valent ruthenium that paved the way of C−H activation for further development.[26] Major advancements have been accomplished over the last two decades using platinum group metals such as palladium,[27−30] iridium,[31−33] rhodium,[34] and ruthenium.[35−37] However, their extensive use and low-

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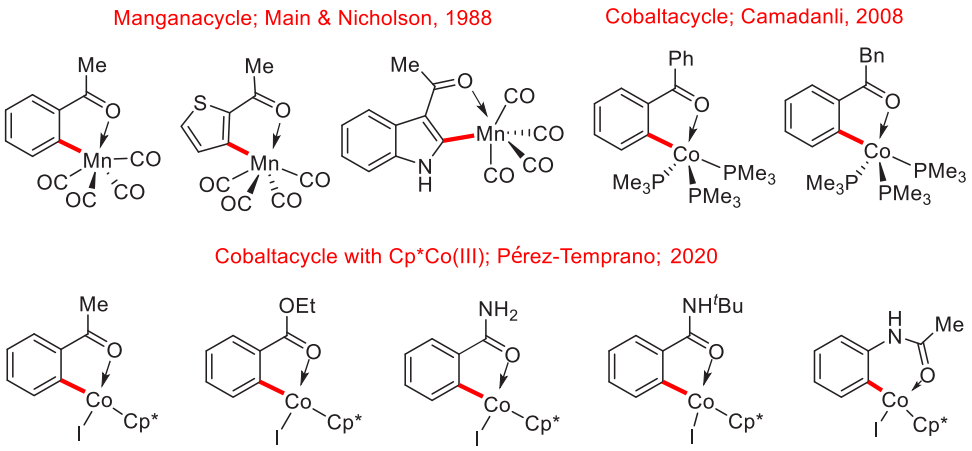

Figure 2. Representative examples of 3d-metalacycle through weak-coordination.

abundance in the Earth's crust put these metals at high-risk for future applications in catalysis.[38,39]

On the contrary, 3d transition metals are widely present in many natural enzymes and are environmental friendly.[40] Moreover, their relative abundance in the Earth's crust is significant, and hence, these earth-abundant metals are an obvious choice for chemists to use in developing C−H bond functionalizations. In addition to the above advantages, the fundamental properties of 3d transition metals should be different from the 4d and 5d metals because of their small size, hard nature at high-valent oxidation state, shorter M−C bond distance, and so on. Further, 3d metals not only proceed through the $2e^-$ pathway but also through the $1e^-$ pathway, and their spin-state should be considered when the reaction pathways are proposed.[41−46]

A nitrogen-containing heterocycle strongly binds with the 3d metals and stabilizes the key cyclometalated intermediate through an inner-sphere mechanism and subsequent coupling of σ-donor/π-donor/π-acceptor partner leading to site-selective functionalization. Over the past few years, strongly coordinating-directing groups such as pyridin-2-yl, 8-amino quinolyl, oxazolin-2-yl, and pyrazol-1-yl have been majorly exploited with the 3d transition metals for direct functionalization of C−H bonds (Scheme 1a(i)).[47−58] However, removal of such directing group is often difficult and requires an additional step(s), which contradicts the atom and step-economy associated with the C−H bond activation process.

However, direct catalytic C−H bond functionalization of molecules using functional groups like carboxylic acid, ester, ketone, hydroxy, amide as directing groups would be ideal (Scheme 1a(ii)). These functional groups not only act as directing groups but also offer a diverse scope for post synthetic modifications. These functional groups bind to metal through weak σ-donation and thereby forms a less thermodynamically stable, more reactive metalacycle for further coupling with the incoming partners.[59,60] Although it has many advantages, the use of abundant 3d transition metals in C−H bond functionalizations directed by weak-coordinating functional groups is challenging and relatively less explored.

The basis of categorization of directing groups into strong- and weak-coordinating sections can arbitrarily defined based on their BF_3 gas affinity with the directing groups (in kJ/mol) (Scheme 1b).[61] The coordinating ability of these directing groups depends on several parameters, such as reaction types, the nature of the metal catalysts, oxidation state, stabilization of metallacycle with the aid of the incoming partner, reaction conditions, and so on. The reactivity of such metalacycle based on their coordination ability provided a switch in selectivity under the same reaction conditions. For example, Murai and co-workers demonstrated the selective C−H alkylation of aryl ketones over imines through intermolecular competitive experiments under the same reaction conditions (Scheme 1c).[62] While $Ru(H)_2(CO)(PPh_3)_3$ selectively provided the *ortho*-alkylation of ketone, the imine was selectively *ortho*-alkylated using $Ru_3(CO)_{12}$ as catalyst. The former favored the reaction through weak-chelation *via* *O*-coordination, and the latter favored the reaction through *N*-coordination from the imine (strong) directing groups. In the same context, Chang reported the switch in selectivity by changing the coordinating ability of the directing group using the $[Cp^*IrCl_2]_2$ catalyst (Scheme 1d).[63] Strongly coordinating pyridine favored the C−H alkylated product, whereas weakly coordinating aryl amide and aryl ketone delivered the C−H alkenylated product exclusively. According to the authors, the rigid iridacycle with phenylpyridine was restricted to attain the *syn*-coplanarity required for the β-hydride elimination to yield the alkenylated product; however, it forced the system for rapid protodemetalation to deliver the hydroarylated product. Conversely, weakly coordinating amide or ketone formed a flexible metallacycle that allowed to attain the *syn*-coplanarity, thereby facilitate the β-hydride elimination over protodemetalation.

Incidentally, weakly bound metalacycle with 3d metals were isolated via C−H bond activation, in particular with manganese and cobalt.[64,65] The representative examples are shown in Figure 2. Very recently, Pérez-Temprano and co-workers isolated various cobaltacycle with various weakly coordinating ligands through the oxidative addition of corresponding *ortho*-iodo derivatives with $Cp^*Co^I(VTMS)_2$ (Figure 2).[66]

Over the past few years, some reviews on 3d metal-catalyzed C−H bond activation reactions were documented. However, to the best of our knowledge, there is no review that explicitly highlights the importance of weakly coordinating directing groups in C−H bond activation with 3d metal catalysts.[67] Considering the growing interest in utilizing functional groups that are present in a molecule as weakly coordinating directing groups for C−H bond functionalizations, we sought to provide a comprehensive overview on the topic covering articles until 2021.

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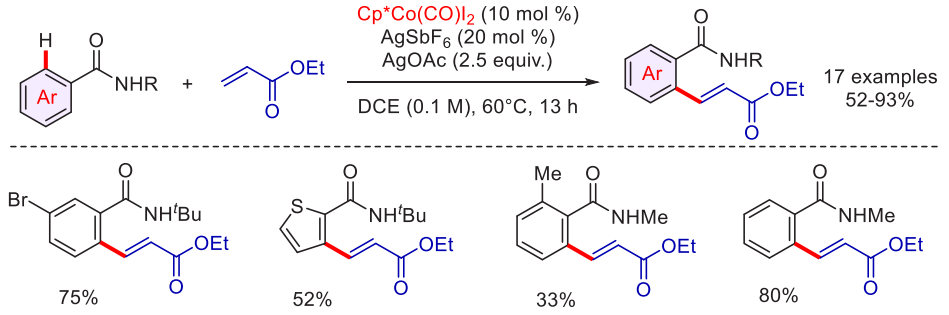
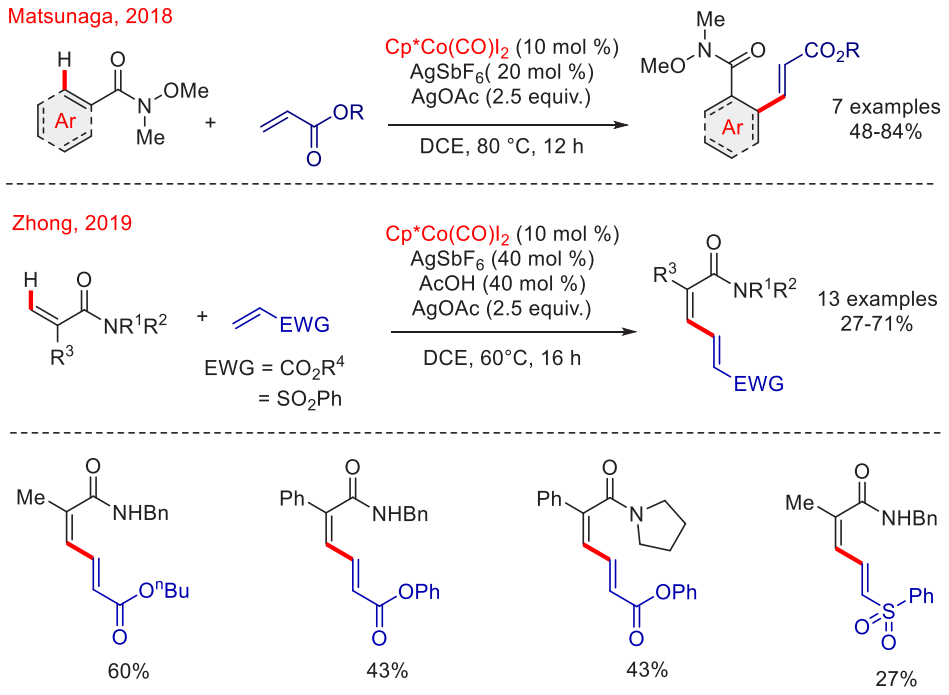
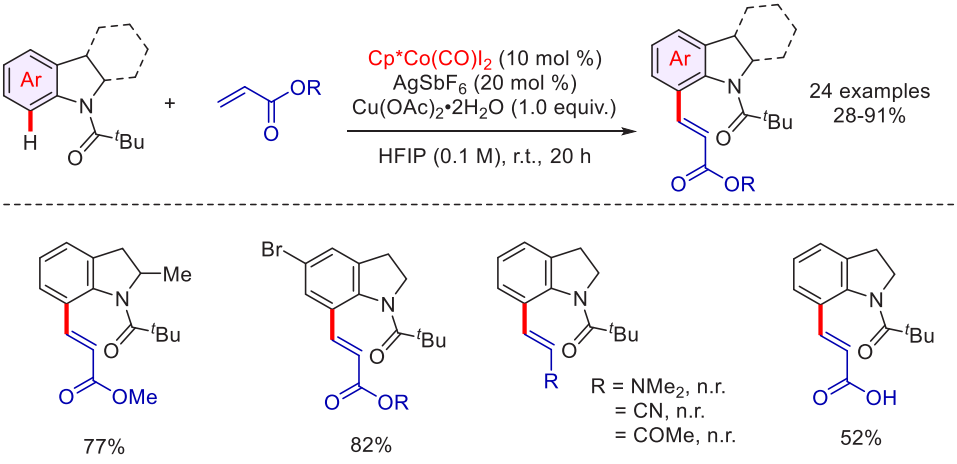
Scheme 2. Cp*Co(III)-Catalyzed Oxidative C−H Olefination using Activated Alkenes



Scheme 3. Amide Directed Oxidative C−H Olefination using Activated Alkenes



Scheme 4. C(7)−H Bond Olefination of Indolines Catalyzed by Cp*Co(III)



2. AMIDE-DIRECTED C−H BOND FUNCTIONALIZATIONS

Among the myriad of directing groups utilized for the site-selective C−H bond functionalizations, the amides are the most powerful directing groups and can be effortlessly installed from carboxylic acids, and their synthetic modification can be accomplished under mild conditions.[68−70] The coordination mode of the amide (O vs N) to the metal depends on the substituent attached on the nitrogen atom and the reaction conditions.

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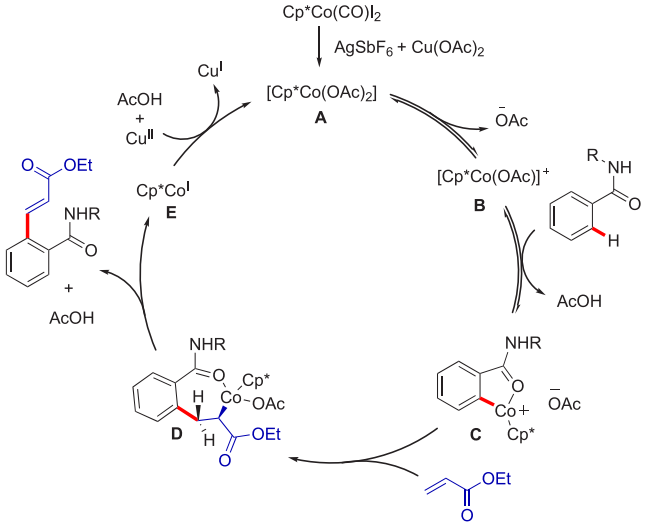
Scheme 5. Plausible Mechanism of the Cp*Co(III)-Catalyzed Oxidative Olefination



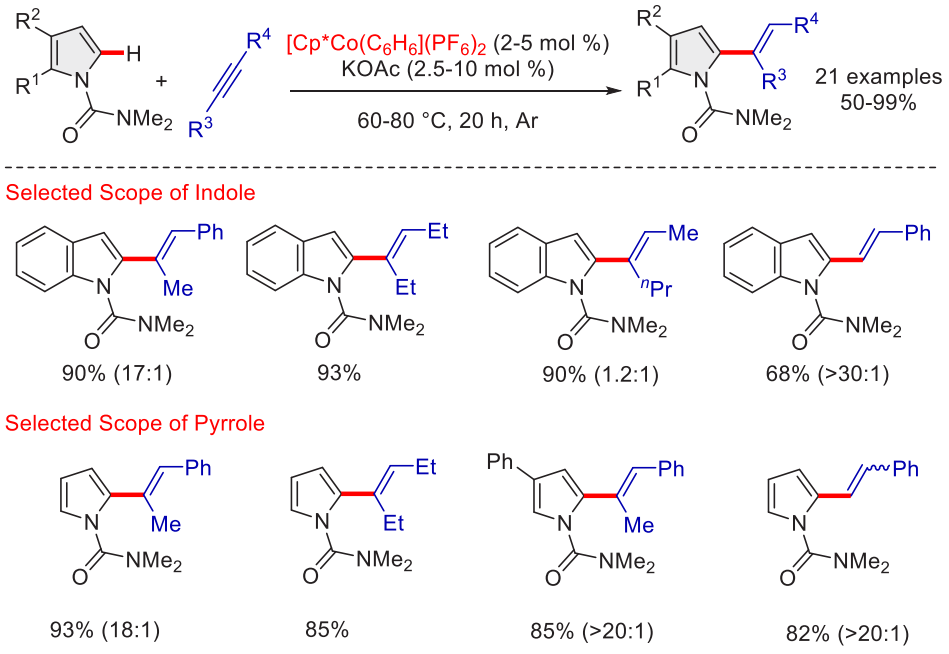
2.1. C−C Bond Formation. *2.1.1. C−H Olefination.* Since the discovery of [Pd]-catalyzed Fujiwara−Moritani reaction, transition-metal-catalyzed C−H olefinations have been witnessing enormous development.[71,72] Evolution of 3d metals in catalytic C−H bond functionalizations provided an additional momentum to this area of reaserch. In 2015, Matsunaga and co-workers utilized an inexpensive, bench-stable Cp*Co(III) catalyst for the oxidative C−H olefination of amides using activated olefins such as ethyl acrylate (Scheme 2).[73] A wide range of aryl amides including heteroaryl amides were successfully olefinated in good yields with good functional group tolerance. However, the presence of *ortho*-substituent in the aromatic amides destabilized the planar metalacyclic intermediate, hence deteriorating the product formation. For *meta*-substituted benzamides, selective functionalization occurred at the less sterically demanding position.

In the subsequent studies, the same group explored the possibility of utilizing Weinreb amide (*N*-methoxy-*N*-methyl amide) as a directing group in high-valent cobalt catalysis.[74] The Weinreb amide possesses high synthetic value and has been widely used in natural product synthesis.[75] Furthermore, their corresponding ketone and aldehyde derivatives could be easily obtained in a single step by employing organo-magnesium/lithium reagents and metal hydrides, that is, lithium aluminum hydride ($LiAlH_4$)/diisobutylaluminum hydride (DIBAL-H). *ortho*-Olefination of Weinreb amides were successfully demonstrated with a wide variety of activated, electron-deficient olefins with good functional group tolerance (Scheme 3). Notably, Weinreb amides derived from acrylic acids were also amenable to the developed methodology to provide synthetically valuable diene with excellent *E*/*Z* selectivity (98:2). However, more challenging unactivated olefins failed to provide the desired product under the established reaction conditions.

Later in 2019, Zhong and co-workers unveiled a Cp*Co(III) catalyzed C−H olefination of acrylamides to access synthetically useful (*Z*,*E*)-1,3-dienamides with high regio- and stereoselectivity (Scheme 3).[76] The reaction tolerates a wide variety of electron-deficient olefins including phenyl vinyl sulfone in moderate-to-good yields. The authors further demonstrated the preference of alkylation over olefination when vinyl ketones were employed as olefins. The dichotomous reactivity of olefins is discussed later in the amide directed C−H alkylation section 2.1.8.

Recently, Ravikumar and co-workers demonstrated the Cp*Co(III)-catalyzed C(7)−H olefination of indoline derivatives at room temperature using activated olefins with the assistance of weakly coordinating pivaloyl group (Scheme 4).[77] The reaction exhibited a broad scope for both indolines and acrylates with good functional group tolerance. Challenging acrylic acid was suitable to provide C-7 olefinated indoline in good yield; however, other electron-deficient olefins such as acrylamide, styrene, acrylonitrile, and methyl vinyl ketone failed to provide the desired olefinated products. It is worth

Scheme 6. Cp*Co(III)-Catalyzed C(2)−H Alkenylation of Indoles and Pyrroles using Alkynes



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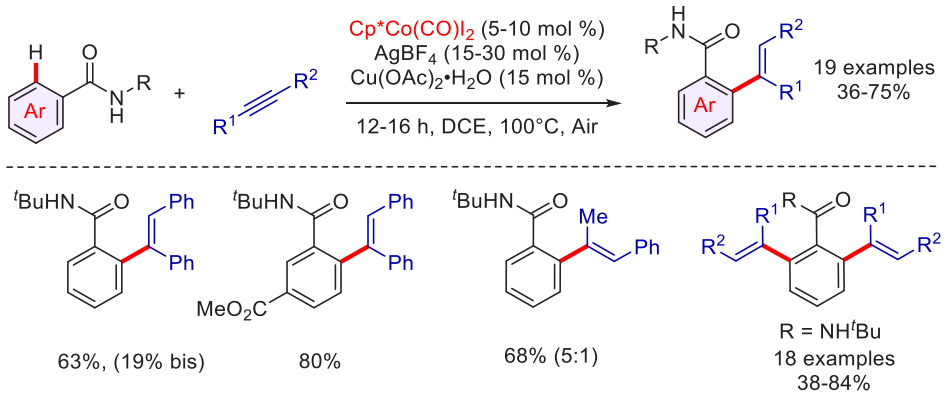
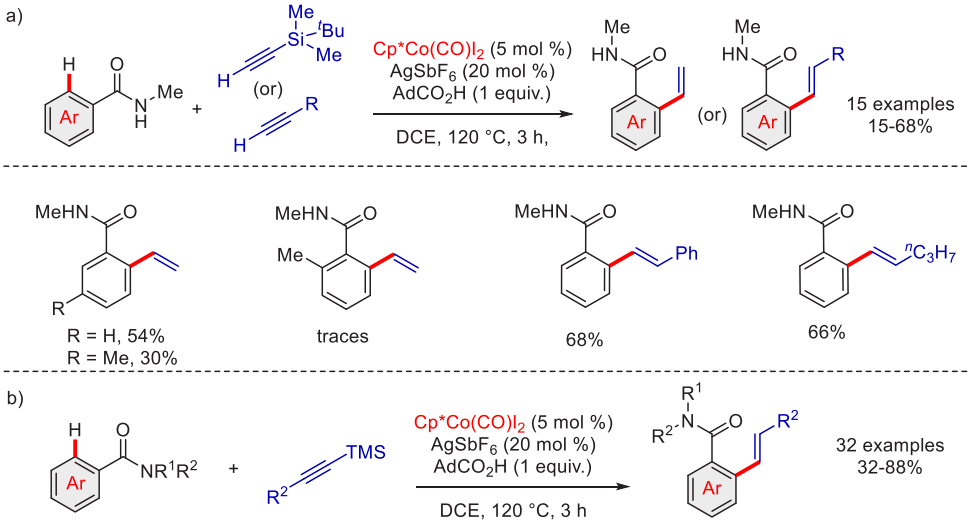
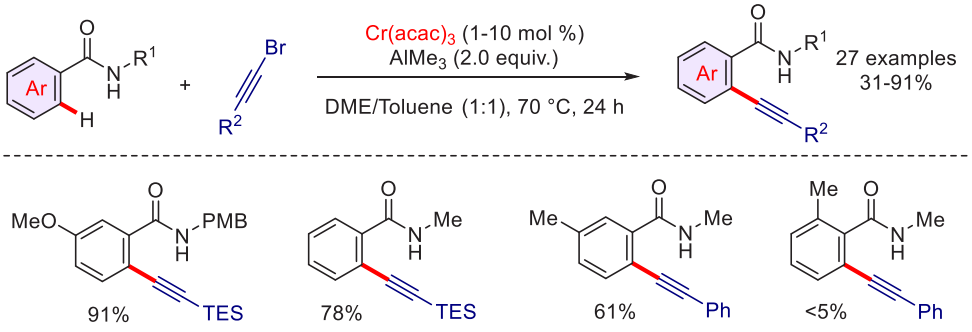
Scheme 7. Cp*Co(III)-Catalyzed *ortho*-C−H Alkenylation of Benzamides using Internal Alkynes



Scheme 8. Cp*Co(III)-Catalyzed *ortho*-C−H Alkenylation of Benzamides using Alkynes



Scheme 9. Chromium-catalyzed C−H Alkynylation of Benzamides using Bromo Alkynes



mentioning that the olefination proceeds via a challenging six-membered metalacycle with cobalt.

The authors proposed a plausible mechanism for C−H olefination as depicted in Scheme 5. The reaction initiates by in situ formation of active cationic cobalt complex [Cp*Co(OAc)]$^{+}$SbF$_6^{-}$ (**B**), which is in equilibrium with kinetically labile neutral cobalt-diacetate complex [Cp*Co(OAc)$_2$] (**A**). The amide coordinates to the electrophilic cobalt through the dative bond followed by acetate-assisted concerted-metalation and deprotonation (CMD) provides intermediate **C**. Subsequent coordination of olefin to the metal in the intermediate **C** and rapid migratory insertion between Co−C leads to intermediate **D**. Finally *β*-hydride elimination furnished the desired product with the release of Cp*Co(I), which was further oxidized by copper(II) acetate to regenerate the active Cp*Co(III) catalyst.

2.1.2. C−H Alkenylation. Transition-metal-catalyzed C−H alkenylation of arenes with alkynes is an elegant and atom-efficient way to construct di- and trisubstituted olefins. Hydroarylation of alkynes possesses an additional advantage over the oxidative olefination using alkenes as the former does not demand an external oxidant to enhance the turnover of the catalyst.[78] In 2016, Matsunaga, Kanai, and co-workers developed a high-valent cobalt-catalyzed hydroarylation of alkynes with indoles assisted by a weakly coordinating carbamoyl directing group (Scheme 6).[79] The cationic

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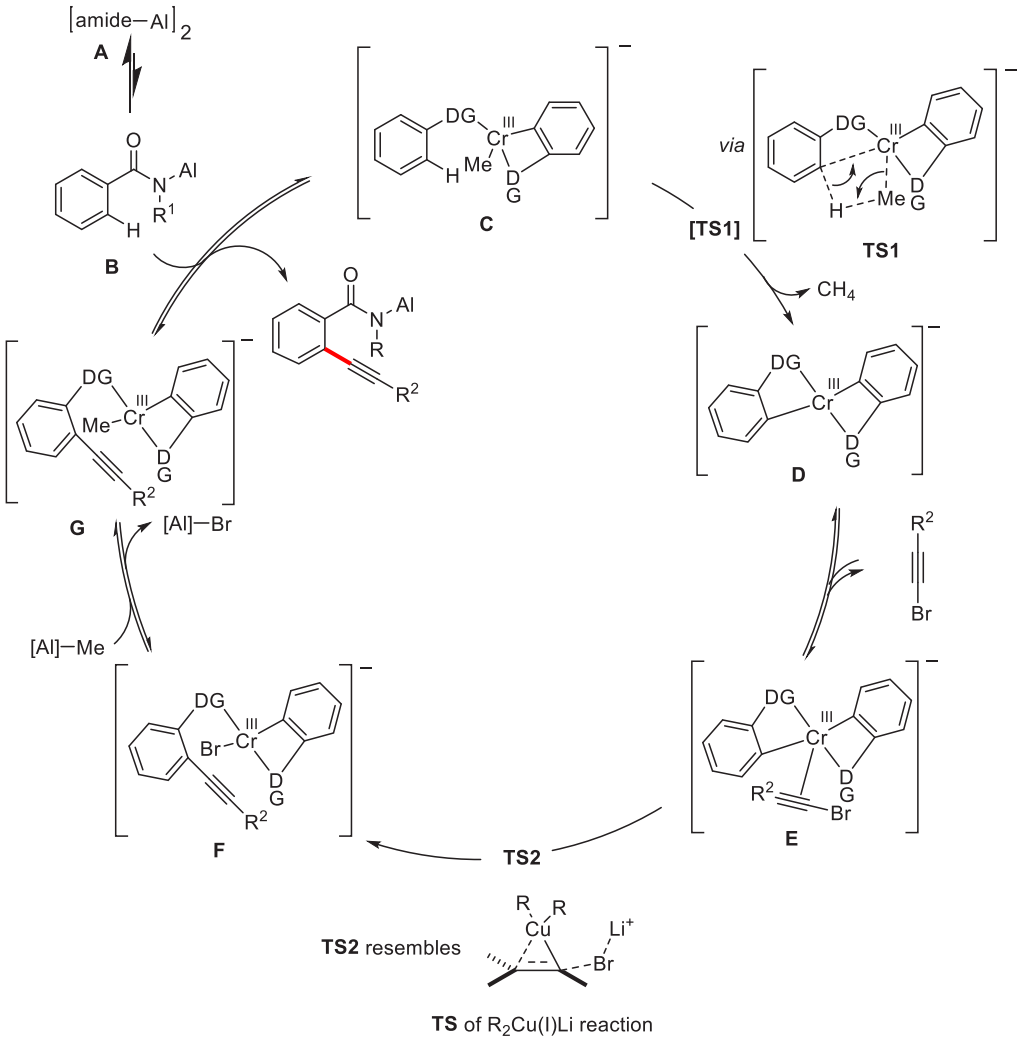
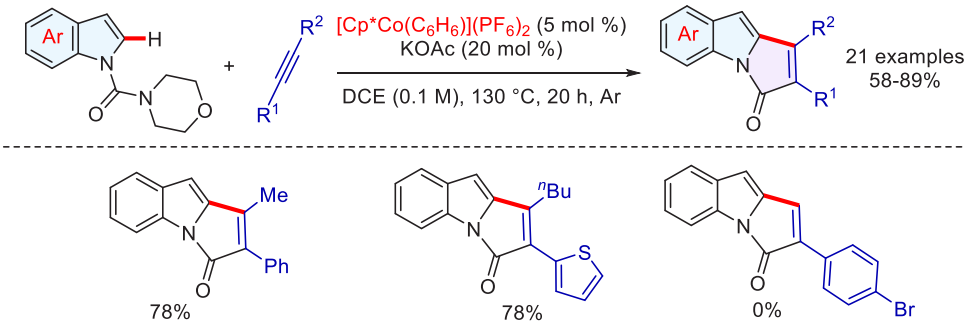
Scheme 10. Plausible Mechanism of the Chromium-Catalyzed C−H Alkynylation



Scheme 11. Cp*Co(III)-Catalyzed Synthesis of Pyrroloindolones



$[Cp^*Co(C_6H_6)]^{2+}$ $(PF_6^-)_2$ was found out to be effective in C-2 selective alkenylation of indoles in good yields. Notably, terminal alkynes which are often considered as difficult substrates in transition-metal-catalyzed hydroarylation, were efficiently hydroarylated with excellent regioselectivity (>30:1). Subsequently, they extended this concept toward C−H hydropyrrolation using alkynes in the presence of a cationic $[Cp^*Co(CH_3CN)_3]^{2+}$ $[2SbF_6^-]$ catalyst.[80]

In 2016, Maji and co-workers disclosed an amide-directed *syn*-selective *mono*- and *bis*-alkenylation using $Cp^*Co(CO)I_2$ catalyst (Scheme 7).[81] The use of silver salt to abstract the iodide ligands from the catalyst was found out to be very crucial in achieving the alkenylation product. Careful tuning of the reaction conditions enabled a selective formation of both *mono*- and *bis*-alkenylated products with excellent isolated mass. However, terminal alkynes were found to be unsuitable under the optimized catalytic conditions. The protocol was further applied for the synthesis of fluorescence active highly π-conjugated framework via 4-fold C−H activation in one step.

Later, Prabhu and co-workers reported a counteranion triggered amide-directed C−H vinylation/olefination of benzamides using terminal alkynes (Scheme 8).[82] Interestingly, a

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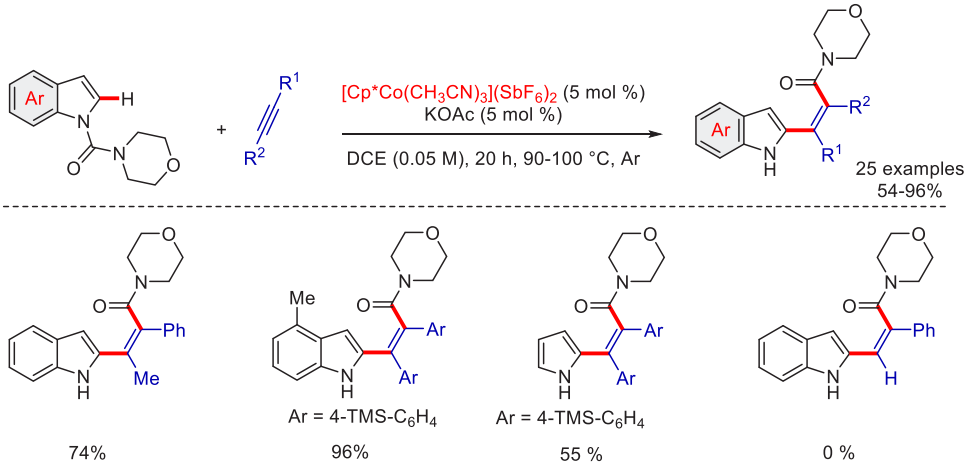
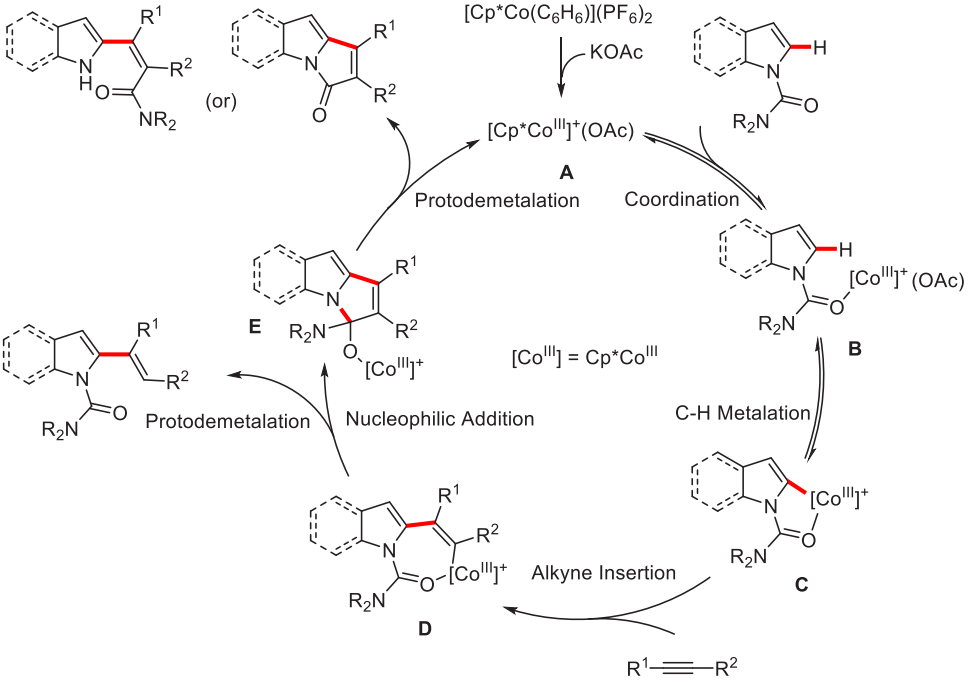
Scheme 12. Cp*Co(III)-Catalyzed C-2 Alkenylation of Indoles using Alkynes



Scheme 13. Plausible Mechanism of the Cp*Co(III)-Catalyzed Coupling of Indoles with Alkynes



variety of alkyl/aryl acetylenes and (aryl-alkynyl)silanes reacted smoothly to deliver the *ortho*-alkenylated products in good yields. The mechanistic studies established the importance of counteranion (e.g., SbF_6^-) in the desilylation process for vinylation reactions. The proposed mechanism for such alkenylation reactions proceeds through 7-membered alkenylated intermediate before it undergoes protodemetalation. The addition of a stoichiometric amount of AdCOOH was crucial in the protodemetalation step. The involvement of key 7-membered cobaltacyclic intermediate was further confirmed by the recent stoichiometric experiments.[83,84]

2.1.3. C−H Alkynylation. Direct incorporation of alkynyl unit into the C−H bond is an interesting and efficient process which enables accessing a wide variety of internal alkynes from terminal alkynes/halo alkynes. In this regard, Nakamura and co-workers developed an efficient chromium-catalyzed amide-directed *ortho*-C−H alkynylation using electrophilic alkynyl bromides (Scheme 9).[85] Various ethynyl bromides having silyl, aryl, heteroaryl, and alkyl substituents were successfully installed at the *ortho*-position of the amides. Along with various aryl amide derivatives, alkene carboxamides were also alkynylated to access enyne derivatives in a single step with good yields. The choice of $AlMe_3$ was found to be crucial in the deprotonation of N−H and C−H bonds as the other organometallic bases like MeMgBr and $ZnMe_2$ failed to carry out the desired C−H alkynylation. The authors further claimed that the two methyl groups of each $AlMe_3$ unit get utilized in the desired transformation. Based on the kinetics and control experiments, the C−H bond activation step was considered as the slowest step in the catalytic cycle.

The C−H activation proceeds via the deprotonation mechanism as shown in **TS1** to obtain second key metalacycle **D** (Scheme 10), which subsequently underwent reversible coordination with an alkyne as evident from the kinetic study. The formation of C−H alkynylated chromate **F** was proposed to proceed through a similar transition state as in the case of the alkenylation of $R_2Cu(I)Li$ that takes place via a cuprio(III)-cyclopropane intermediate as described in **TS2**. Intermediate **F** underwent transmetalation with $AlMe_3$ followed by ligand

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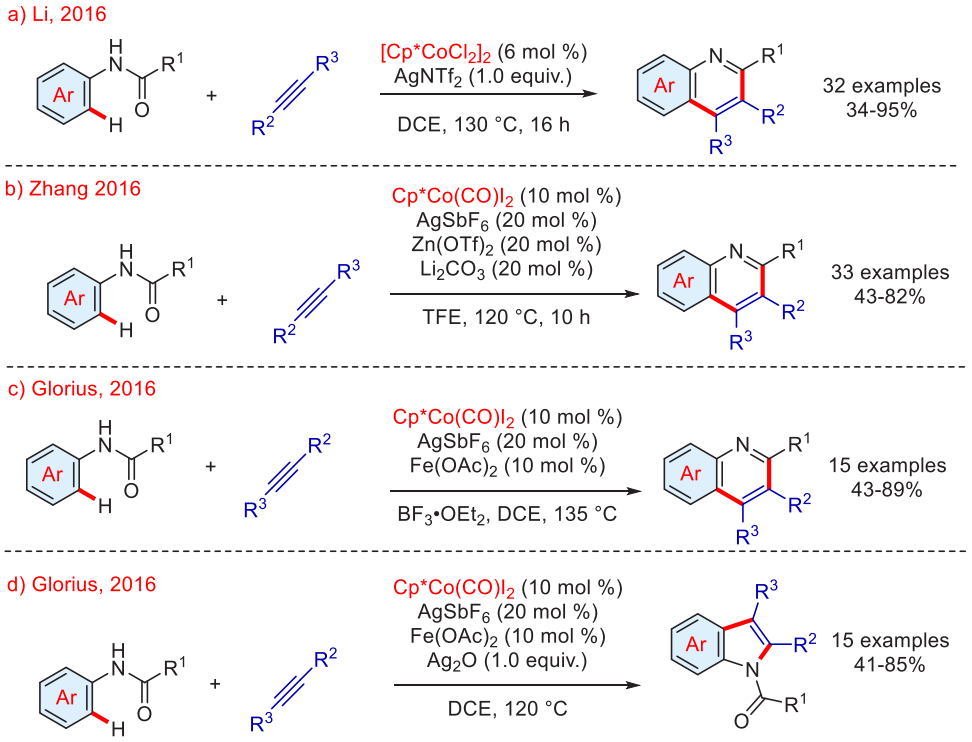
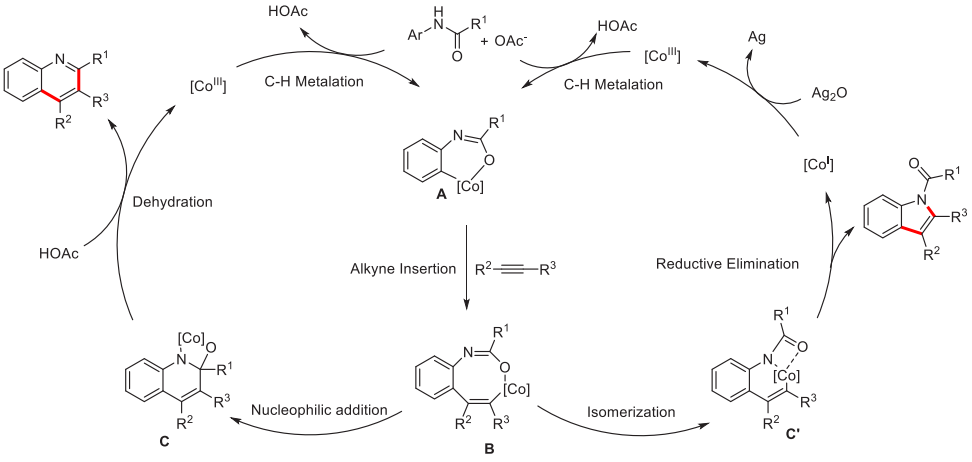
Scheme 14. Cp*Co(III)-Catalyzed Dehydrative Annulation of Anilides with Alkynes



Scheme 15. Plausible Mechanism of the Dehydrative Annulation of Anilides with Alkynes



exchange with amide **B** regenerate the active catalyst along with the alkynylated product.

2.1.4. Annulation Reaction with Alkynes. *N*-Heterocyclic compounds constitute the core structures of many natural products and drugs. Over the years, numerous transition-metal-catalyzed atom- and step-economical protocols have been developed for their synthesis.[86] In 2014, Matsunaga-Kanai reported carbamoyl directed Cp*Co(III)-catalyzed C−H alkenylation followed by annulation of *N*-carbamoyl indoles with alkynes as shown in Scheme 11.[78] In contrast, the congener Cp*Rh(III) provided only a trace amount of the annulated products. This inferior result was attributed to the better nucleophilic reactivity of the carbon connected to Co(III) over Rh(III) species as the Co−C bond is more polarized. The protocol allowed the synthesis of various pyrroloindolones with excellent regioselectivity using symmetrical as well as unsymmetrical internal alkynes. However, the desired annulation did not proceed with terminal and *bis*-aliphatic alkynes.

Thereafter, by careful tuning of reaction parameters, the same group reported the migration of the directing group to give tetrasubstituted alkenes (Scheme 12).[87] The highly substituted alkene products undergo cyclization to yield pyrroloindolones at high temperatures. Various substituted indoles including pyrroles were viable in the established protocol to accomplish highly decorated olefins in moderate to good yields. Furthermore, these tetrasubstituted olefins were utilized to synthesize fluorescent active molecules.

The authors proposed a plausible catalytic cycle as shown in Scheme 13. The reversible cyclometalation followed by alkyne coordination and migratory insertion into Co−C bond generates the key metalacyclic intermediate **D**. Protodemetalation in the intermediate **D** provides the alkenylated product, whereas intramolecular nucleophilic attack of the alkenyl−Co

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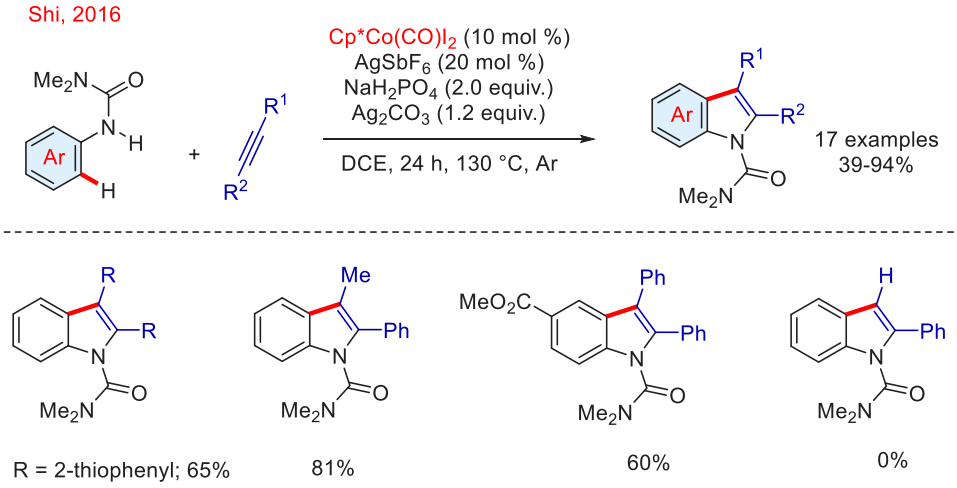
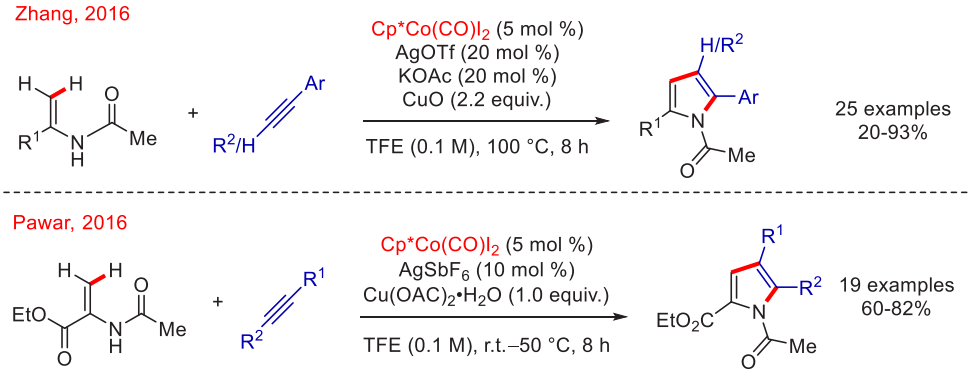
Scheme 16. Cobalt(III)-Catalyzed Oxidative Coupling of *N*-Carbamoyl Anilines with Internal Alkynes



Scheme 17. Cp*Co(III)-Catalyzed Synthesis of Pyrroles



bond to the carbamoyl group followed by the liberation of amine leads to the desired annulation product. Higher nucleophilicity of alkenyl−Co(III) compared with its rhodium analogue drives the nucleophilic attack into the electrophilic carbamoyl group. Migration of the carbamoyl unit proceeds via the cleavage of the C−N bond connected with indole from intermediate **E**. Finally, protodemetalation regenerates the active catalyst **A**.

In 2016, Li,[88] Zhang,[89] and Glorius[90] groups independently developed high-valent cobalt-catalyzed dehydrative annulation of anilides with alkynes to synthesize quinoline derivatives (Scheme 14). The optimized reaction conditions employed for the synthesis of quinolines are slightly different, but in all cases, they used a Lewis acid to enhance the electrophilicity of the carbonyl moiety. Terminal alkynes were not suitable in any of these conditions to achieve the desired products. Additionally, Glorius and co-workers showed that the addition of a stoichiometric amount of an oxidant instead of the Lewis acid resulted in the formation of indole derivatives.

The authors proposed the plausible mechanism as shown in Scheme 15 based on the preliminary experiments. The reaction with silver salt and precatalyst generated more Lewis acidic cationic Cp*Co(III), which coordinates with the substrates. The subsequent C−H metalation led to the metalacycle **A**. The coordination and insertion of an alkyne into **A** delivered an intermediate **B**. Now the nucleophilic addition of alkenyl−Co(III) to the electrophilic carbonyl group followed by dehydration furnished the quinoline product and active Co(III) catalyst. In contrast, the intermediate **B** can undergo isomerization to provide **C′**, which upon reductive elimination provided the final indole product and Cp*Co(I). The regeneration of active Cp*Co(III) species from Cp*Co(I) was achieved by the silver(I) oxide, which serves as an oxidant in the reaction. The use of a Lewis acid in combination with Cp*Co(III) increases the electrophilicity of the carbonyl group and hence triggers the nucleophilic addition of alkenyl−Co(III) to generate the quinoline products.

Subsequently, Shi and co-workers[91] disclosed a similar strategy for the synthesis of indole via oxidative [3 + 2] annulation of anilides with alkynes (Scheme 16). Notably, a less electrophilic directing group prevents the nucleophilic attack of alkenyl−Co(III) and thereby facilitates the reductive elimination to regenerate the active catalyst.

Later, Zhang[92] and Pawar[93] independently reported the synthesis of highly substituted pyrroles using a similar strategy starting from enamides (Scheme 17). The reaction developed by Pawar and co-workers works efficiently at room temperature. In addition to that, *N*−*H* pyrroles can be obtained in a single step by simple tuning of the reaction temperature.

In 2016, Jeganmohan developed an efficient, Cp*Co(III)-catalyzed regioselective protocol for the synthesis of isoquinolone derivatives from readily available *N*-methoxy benzamides and alkynes at 110 °C.[94] It is important to note that the annulation of 3-phenyl prop-2-yn-1-ol provided the annulated product with unprecedented selectivity, with the phenyl group of alkyne resides at the arene side of benzamide. Later, Zhu and co-workers introduced *N*-chloro benzamide as an efficient

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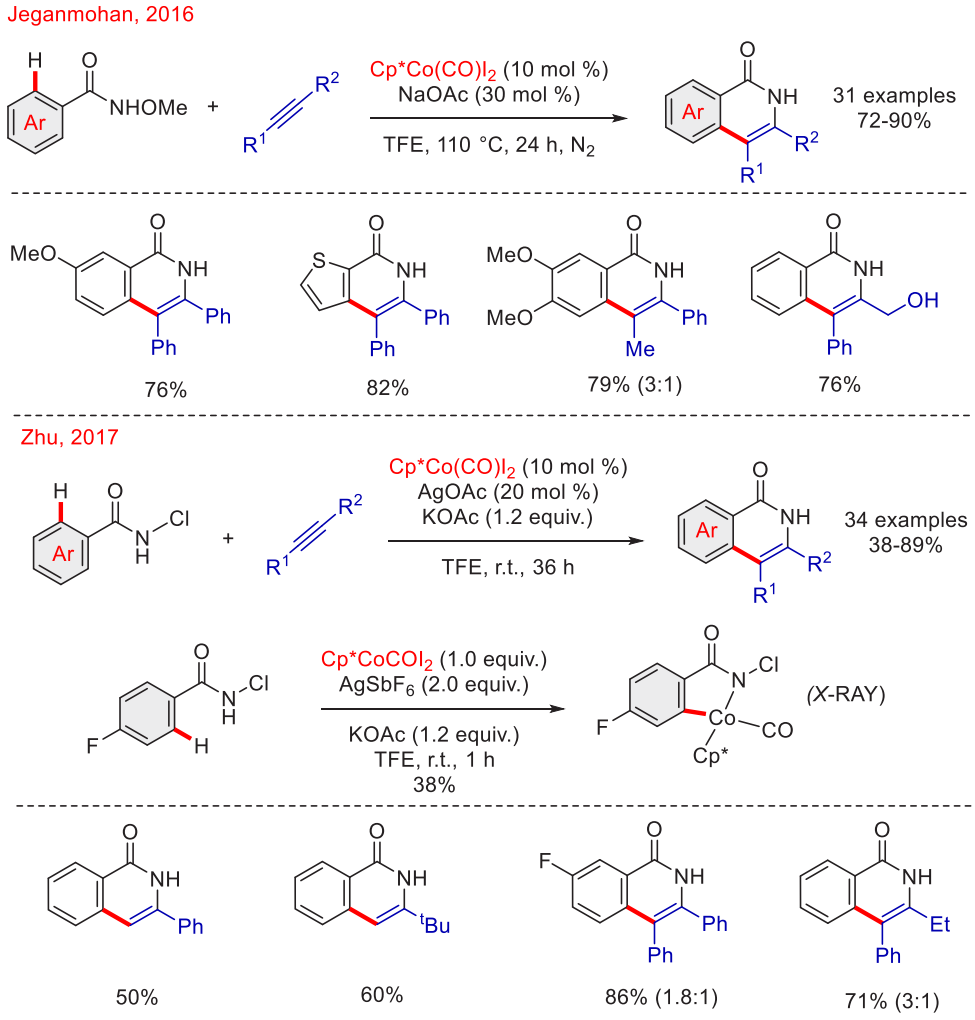
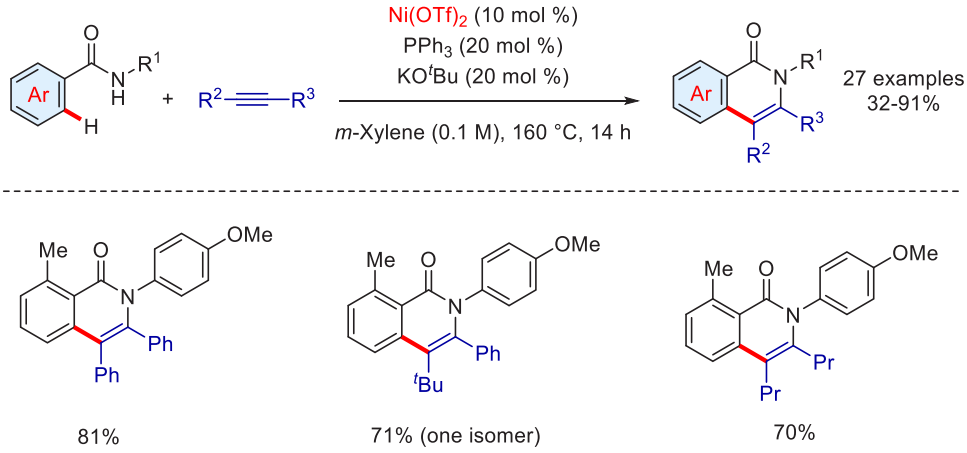
Scheme 18. Cp*Co(III)-Catalyzed Oxidative Annulation of *N*-Methoxy and *N*-Chloro Benzamides with Alkynes



Scheme 19. Nickel-Catalyzed C−H/N−H Annulation of Benzamides with Alkynes



directing group for the oxidative coupling of benzamides with alkynes under Cp*Co(III) catalysis at room temperature.[95] The author isolated the five-membered cobaltacycle with amide at room temperature through a stoichiometric experiment and proposed a Co(III)−Co(V) catalytic cycle considering the high oxidizing property of N−Cl bond (Scheme 18).

In the same line, Chatani and co-workers[96] in 2017 developed an efficient nickel-catalyzed protocol for the *C−H/N−H* annulation of benzamides with alkynes to give 1(2*H*)-isoquinolinones without the need for a specific chelation system (Scheme 19). The use of a strong base like KO^{t}Bu was found to be crucial in the success of the reaction along with the super stoichiometric amount of alkynes (5−10 equiv). An excess quantity of alkyne was necessary to achieve high yields as it not only served as the π-coupling reagent but also played a role as hydrogen acceptor. The protocol displayed a wide scope of

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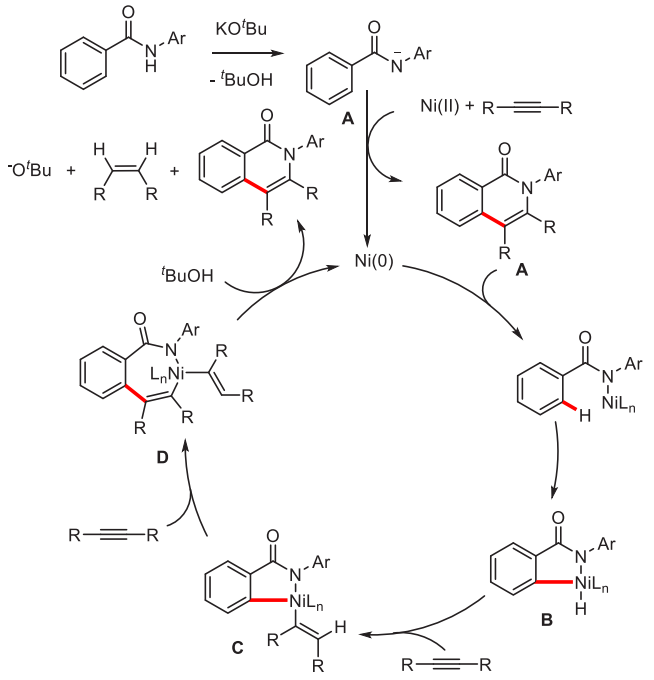
Scheme 20. Plausible Mechanism of Nickel-Catalyzed C−H/N−H Annulation of Benzamides with Alkynes



benzamides and alkynes with good yields and a very high level of regioselectivity in case of unsymmetrical alkynes.

The proposed mechanism began with coordination of Ni(II) to the N atom of amidate anion resulted from the treatment a strong base (Scheme 20). The oxidative addition of low valent Ni(0) resulted from initial electrophilic C−H bond annulation of benzamide with alkyne using Ni(II). Thereafter, low-valent Ni(0) oxidatively added to the proximal *ortho* C−H bond leading to the five-membered metalacycle **B**, which subsequently underwent sequential double insertion with an alkyne to provide intermediate **D**. Finally, reductive elimination provided the isoquinolinones and Ni(0). The authors also proposed the other possible pathway that proceeds via alkyne insertion into the N−Ni bond prior to the C−H activation. The in situ generated alkenyl-Ni species activate the proximal C−H bond and subsequent reductive elimination provided the desired annulated product.

Later, Glorius and co-workers reported an intramolecular oxidative annulation of alkyne tethered benzamides and acrylamides to synthesize various isoquinolone and pyridone derivatives under redox-neutral conditions (Scheme 21).[97] The protocol was applied in the synthesis of two Topo-**I**-Inhibitors and two 8-oxyprotoberberine structural cores toward the synthesis of tetrahydroprotoberberine and the protoberberine alkaloid cores. Practical synthesis of six different tylophora alkaloids was demonstrated in a few steps using intramolecular annulation catalyzed by Co(III).

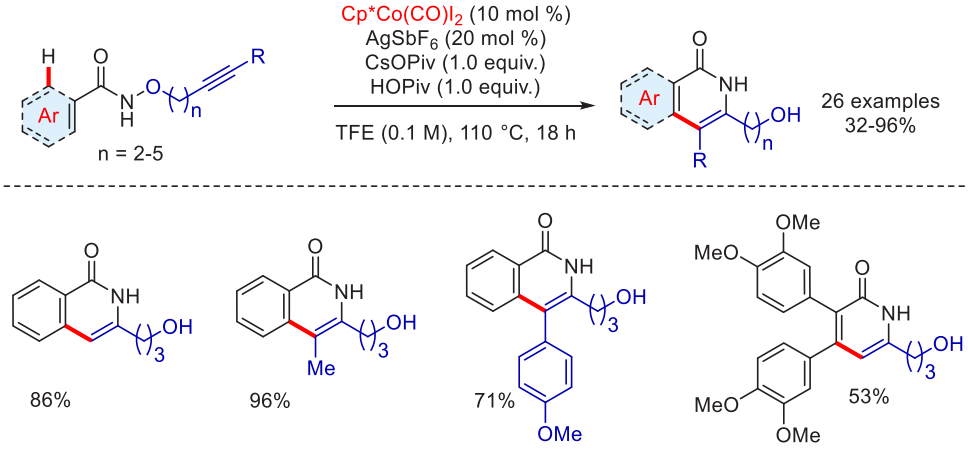
Chegondi and Pawar and their co-workers further exploited an elegant protocol involving a cascade strategy to obtain a tetracyclic indolizidine skeleton (Scheme 22).[98] Notably, reverse regioselectivity was observed in comparison with the earlier reports for annulation using unsymmetrical alkyl/aryl acetylenes. The authors claimed that the opposite regioselectivity in alkyne insertion arises due to weak assistance by the carbonyl oxygen.

In 2017, Sundararaju and co-workers explored the reactivity of diynes toward the oxidative annulation with *N*-methoxy benzamides under Cp*Co(III)-catalysis to access a wide range of isoquinolones with excellent regioselectivity and good functional group tolerance as shown in Scheme 23.[99] The monoannulated products were further diversified by coupling with benzamides under slightly modified conditions and various bis-isoquinolones were obtained with moderate to good yields. Remarkably, high regioselectivity was achieved in both monoannulation and bis-annulation. Based on the experimental results, the authors proposed the preferred order of "R" group at the α-position to the nitrogen of isoquinoline is alkynyl > isoquinolinyl > phenyl > alkyl. The preference could be explained based on the electronic influence of the substituents on either side of the alkyne (R−C$^{\delta+}$≡C$^{\delta-}$−R), thereby prefixing the migratory insertion of alkyne between Co$^{\delta+}$−C$^{\delta-}$ bond.

Subsequently, in 2018 Maji and co-workers developed a strategy for the efficient synthesis of benzofurans and benzofuranones derivatives via an intramolecular hydroarylation of alkyne tethered benzamides using Cp*Co(III) catalyst (Scheme 24).[100] The synthetic utility of the protocol was further expanded via a one-pot sequential 2-fold unsymmetrical C−H bond functionalization under a single directing group operation.

2.1.5. Annulation with Alkenes. Identical to alkynes, alkenes can also be considered as effective π-coupling partners and

Scheme 21. Cp*Co(III)-Catalyzed Intramolecular Oxidative Annulation



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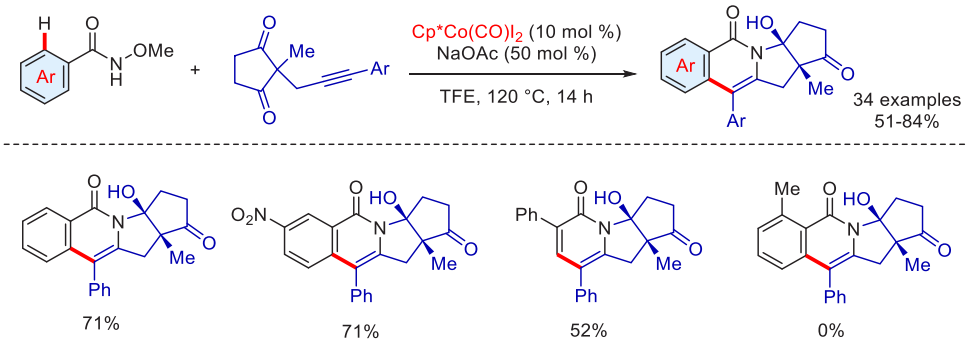
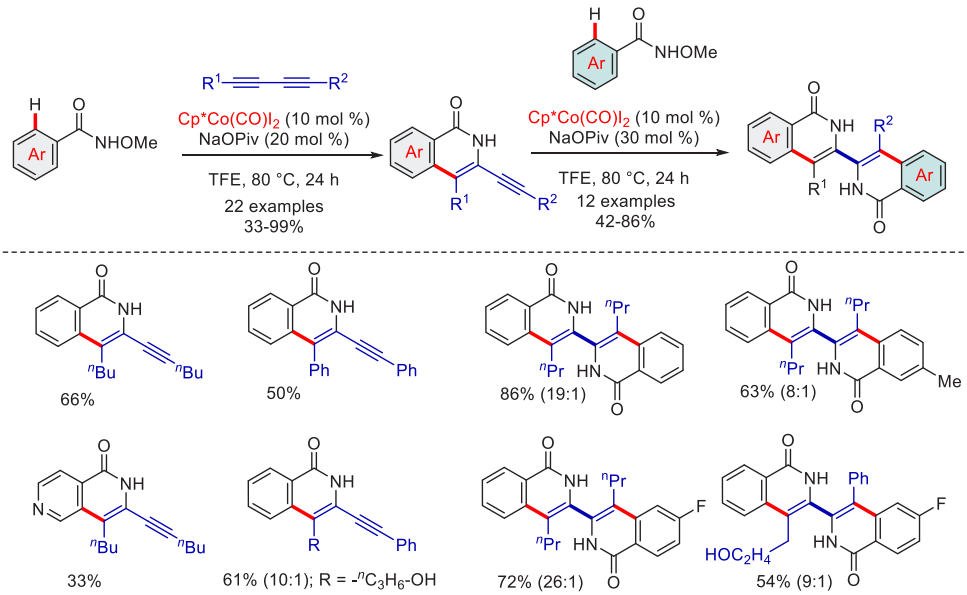
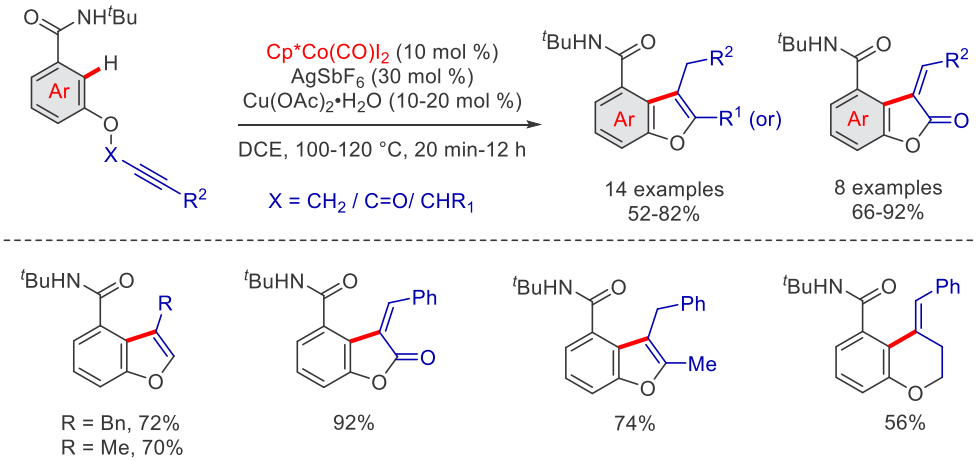
Scheme 22. Cp*Co(III)-Catalyzed Synthesis of Tetracyclic Indolizidines via the Coupling of *N*-Methoxy Benzamides with Alkynes



Scheme 23. Cp*Co(III)-Catalyzed Synthesis of Isoquinolones and *Bis*-Isoquinolones



Scheme 24. Cp*Co(III)-Catalyzed Synthesis of Benzofurans and Benzofuranones



undergo annulation reactions with amides to provide *N*-heterocyclic compounds. Volla and co-workers reported the use of *N*-methoxybenzamide as a weakly coordinating directing group in [4 + 2] annulation of heterobicyclic alkenes, where N−O bond acts as an internal oxidant (Scheme 25a).[101] In addition to various 7-oxabenzonorbornadienes, *N*-protected 7-azabenzonorbornadienes were also amenable for annulation under established reaction conditions. Later, Prabhu and co-workers described Cp*Co(III) catalyzed [4 + 2] annulation of *N*-chlorobenzamides with maleimides (Scheme 25b).[102] Earlier, *N*-hydroxy or *N*-methoxy benzamides were explored for annulation with alkynes; however, in this work, the authors utilized N−Cl bond as an internal oxidant for oxidative annulation.

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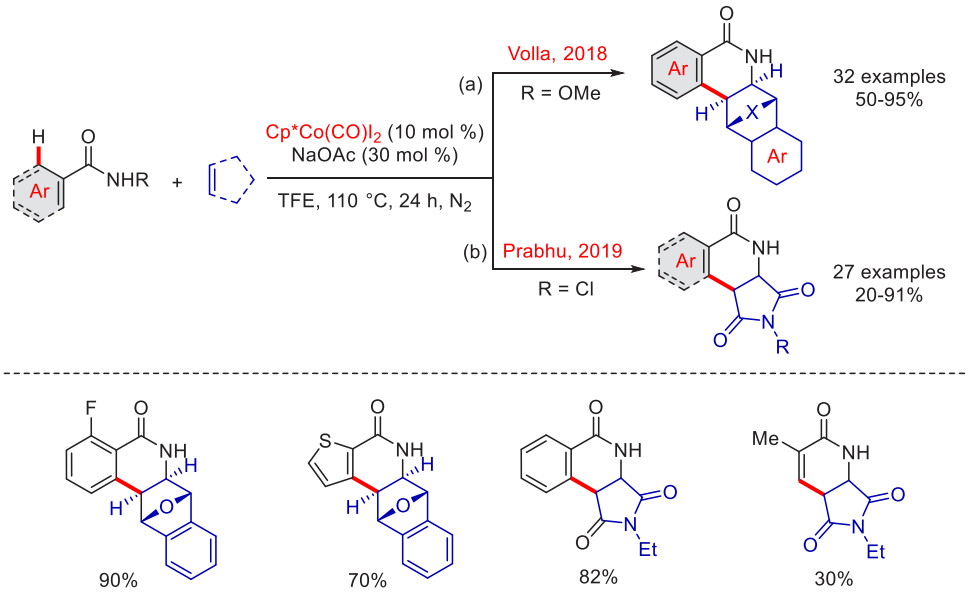
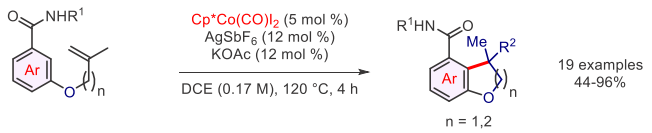
Scheme 25. Cp*Co(III)-Catalyzed Annulation of Benzamides with Alkenes



Scheme 26. Cp*Co(III)-Catalyzed Intramolecular Oxidative Annulation

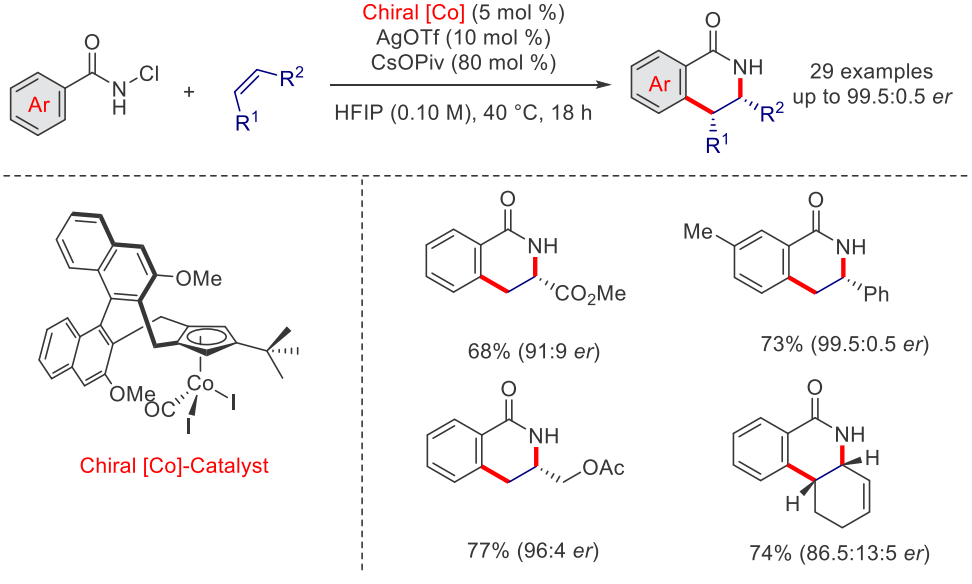


Inspired by these earlier works, Lete and co-workers established an amide-directed Cp*Co(III)-catalyzed intramolecular hydroarylation of unactivated olefins to deliver 3,3-disubstituted dihydrobenzofurans in good yields (Scheme 26).[103] Notably, the tertiary amide (e.g., *N*,*N*-dimethylbenzamide derivative) failed to direct the intramolecular hydroarylation process.

The straightforward synthesis of the enantiopure molecules are in high demand both in industry and academia. The real potential of the 3d metal catalysts in C−H bond activation has been realized recently in the enantioselective C−H bond functionalizations. Very recently, Cramer and co-workers reported the synthesis of chiral C-2 symmetric cyclopentadienyl Co(III) complex and their application in enantioselective [4 + 2] annulation of *N*-chlorobenzamide derivatives with a diverse range of olefins (Scheme 27).[104,105] The annulation provided a series of dihydroisoquinolones in good yields with excellent regio- and enantioselectivity (up to 99.5:0.5). The unique reactivity of the Cp*Co(III)-catalytic system in controlling regio- and enantioselectivity was demonstrated over Cp*Rh(III) with unactivated olefin as coupling partner in C−H and N−H annulation of amides.

2.1.6. Annulation with Allenes. Allenes possess unique reactivity as compared with that of other π-systems due to the presence of two cumulative orthogonal π-bonds.[106] Allenes have been considered as potential π-coupling partners in transition-

Scheme 27. Chiral Cp#Co(III)-Catalyzed Enantioselective [4 + 2] Annulation of *N*-Chloro Benzamides with Alkenes



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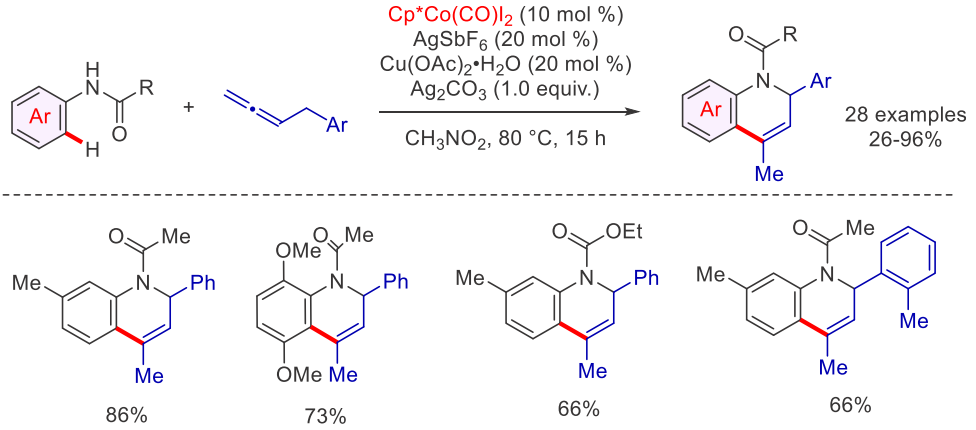
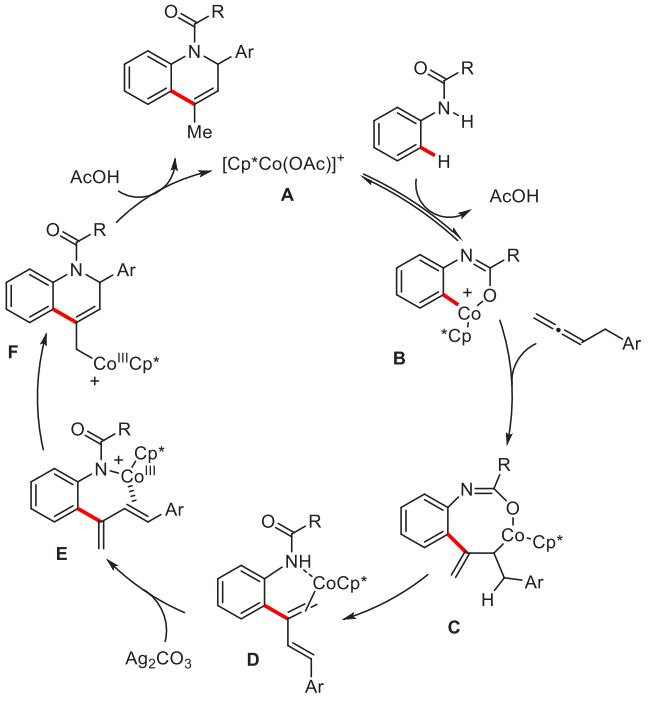
Scheme 28. Cp*Co(III)-Catalyzed [3 + 3] Annulation of Anilides with Allenes



Scheme 29. Plausible Mechanism of the Cp*Co(III)-Catalyzed [3 + 3] Annulation of Anilides with Allenes



metal-catalyzed C−H bond functionalizations. In 2016, Cheng and co-workers utilized benzyl allenes as coupling partners for an anilide-directed [3 + 3] oxidative addition under cobalt(III) catalysis to obtain 1,2-dihydroquinolines(1,2-DHQ) (Scheme 28).[107] The choice of solvent and oxidant was crucial to access products in high yields. The authors demonstrated the excellent scope of benzamide and allene derivatives; however, nonbenzyl aliphatic allene was not amenable under the established conditions.

A plausible mechanism was proposed by the authors as depicted in Scheme 29. The active catalyst [Cp*Co(OAc)]+ (**A**) was generated by in situ ionization followed by metalation and regioselective insertion of allene between Co−C leading to intermediate **C**. The intermediate **C** on subsequent *β*-hydride elimination led to intermediate **D** and Co(I). Oxidative addition, followed by 1,4-cobalt migration, provided the intermediate **F**, which then underwent protodemetalation to furnish the annulated product and regenerate the active catalyst for the next cycle.

The same group further extended their study for [4 + 1] annulation of allenes with benzamides to access isoindolinones and 1,5-dihydro-pyrrol-2-ones as depicted in Scheme 30.[108] A regioisomeric mixture of annulated products were isolated in case of unsymmetrical 1,3-disubstituted allene. In addition, phenyl allene provided [4 + 2] annulated product in 30% yield. The mechanism is quite similar to the one reported above; however, the outcome of the product is largely dependent on the regioselective insertion of allene between the Co−C bond.

2.1.7. C−H Allylation. Allylated arenes and 1,4-dienes are important synthetic building blocks in organic chemistry and are prevalent in many bioactive molecules. Additionally, terminal/internal olefins present in allyl fragments are available for further functional group modifications.[109]

In 2015, Glorius and co-workers reported the first amide-directed C−H allylation of arenes using allyl carbonates as allyl source under mild conditions (Scheme 31a).[110] The scope of various benzamides and heteroatomic amides were explored for allylation under acidic conditions, the role of acid being crucial in obtaining the functionalized products. The KIE values (competitive 6.4 and parallel 2.0) indicated the C−H bond activation step might be the rate-limiting step of the reactions. In 2016, Matsunaga and Kanai demonstrated the direct use of allyl alcohols for the dehydrative allylation of benzamides, secondary amides, and tertiary amides using cobalt(III) catalyst (Scheme 31b).[111] Interestingly, perfluoroalkene also reacted with Weinreb amide possibly via *β*-fluoro elimination, and the desired allylated product was isolated in synthetically viable yield with good *Z*/*E* selectivity (87:13).[74]

According to the authors, the reaction was believed to proceed with the generation of active catalyst **A** which underwent reversible C−H metalation to provide cyclometalated intermediate **B** (Scheme 32). The coordination of allyl substrate to cobalt center followed by insertion into Co−C bond led to seven-membered cobaltacycle **C**. Finally, *β*-oxygen elimination in the intermediate **C** furnished the allylated product, and successive protodemetalation provided the active catalyst back to the cycle.

Very recently, Nakamura and co-workers described an amide directed *ortho*-C(sp^2)−H allylation using allyl bromide under chromium catalysis (Scheme 33).[85] Notably, the protocol was quite selective for *mono*-allylation, and no isomerization of allylated products was observed under the catalytic conditions.

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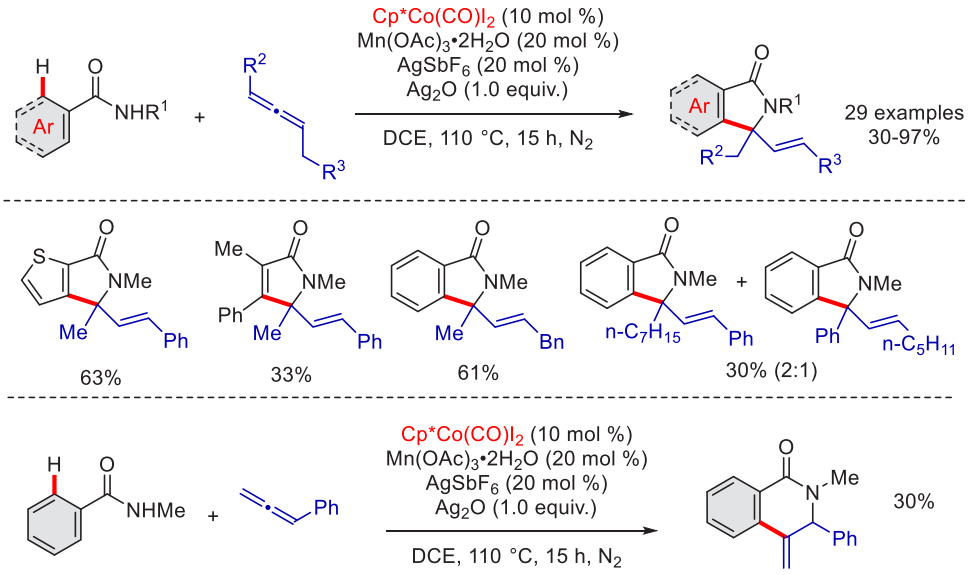
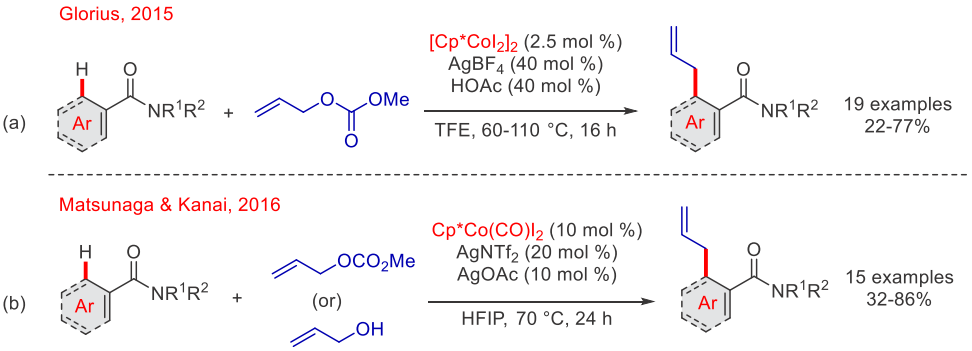
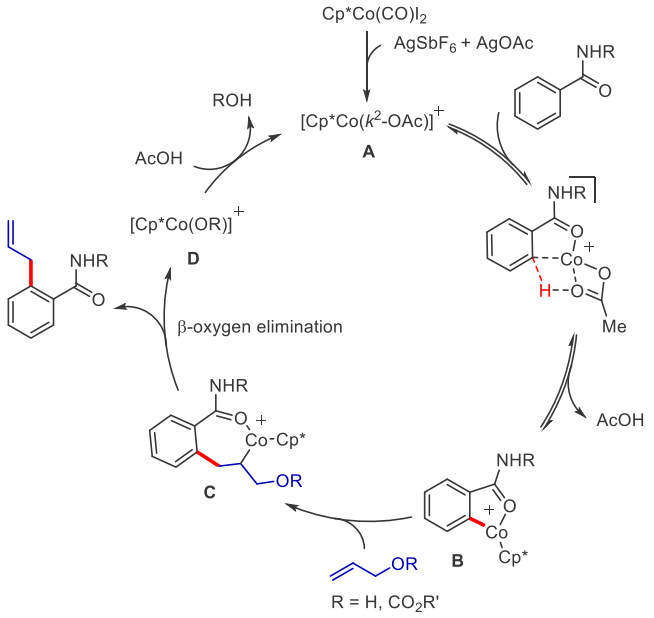
Scheme 30. Cp*Co(III)-Catalyzed Oxidative Annulation with Allenes



Scheme 31. Cp*Co(III)-Catalyzed C−H Bond Allylation with Allyl Carbonates/Alcohols



Scheme 32. Plausible Mechanism of the C−H Allylation with Allyl Carbonates/Alcohols



The crucial role of $AlMe_3$ was discussed for the same catalytic system in section 2.1.3.

2.1.8. C−H Alkylation. Since the pioneering work on the [Ru]-catalyzed hydroarylation of alkenes by Murai,[26] C−H alkylation has been widely explored with noble metals. However, in 2011, Nakamura and co-workers demonstrated the use of earth-abundant 3d metal for the hydroarylation with unactivated alkenes using benzamides as substrate.[112] Though inexpensive cobalt precursor was used as the catalyst, the use of the stoichiometric amount of Grignard reagent is unavoidable. Unactivated terminal and internal alkenes and vinyl silanes were amenable, and in all cases, linear selectivity was achieved (Scheme 34).

Subsequently, the same authors reported [Co]-catalyzed alkylation of benzamides using alkyl chlorides as an alkylating agent (Scheme 35).[113] Several alkyl chlorides containing trimethylsilyl, acetal, pyrrole units underwent alkylation to generate the *ortho*-alkylated benzamides in good to excellent yields. Surprisingly, the authors observed that the less-reactive alkyl chlorides were found to be better suited for the alkylation compared with its bromide partners.

In continuation, the authors further extended their study with manganese for selective *mono*methylation of aryl amides using methyl magnesium bromide (Scheme 36).[114] A wide-range of benzamides, heteroaryl amides, and acrylamides were suitable for *mono* and *bis*-methylation by the control addition of the methylating agent. Based on the preliminary mechanistic investigations, the authors proposed that the active catalyst

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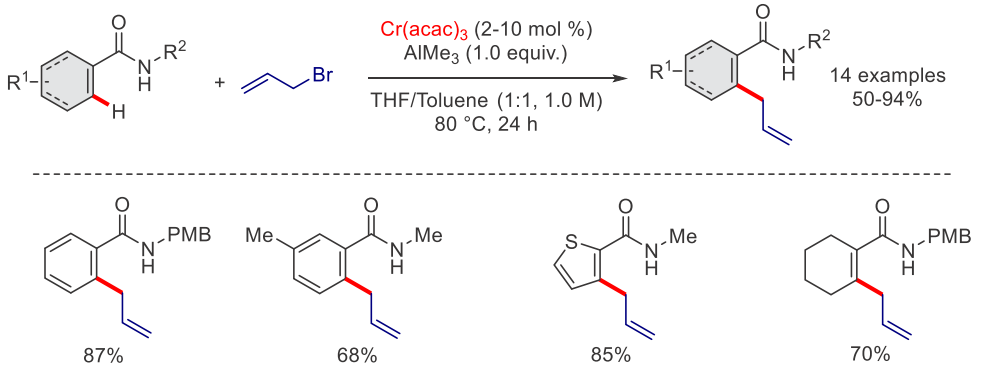
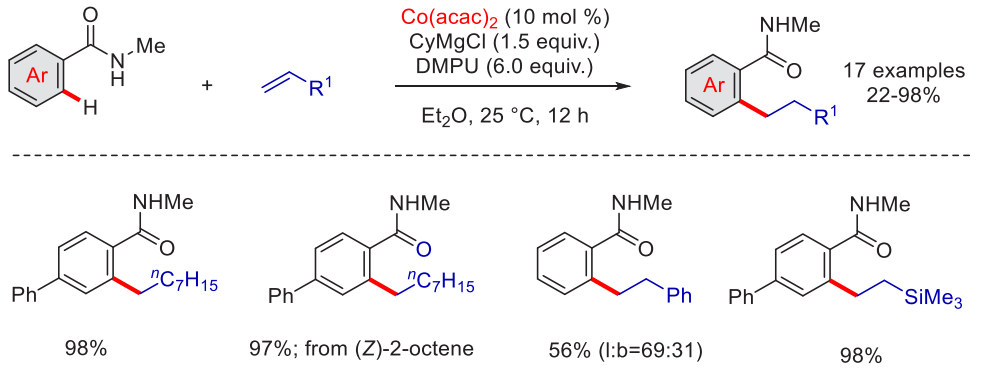
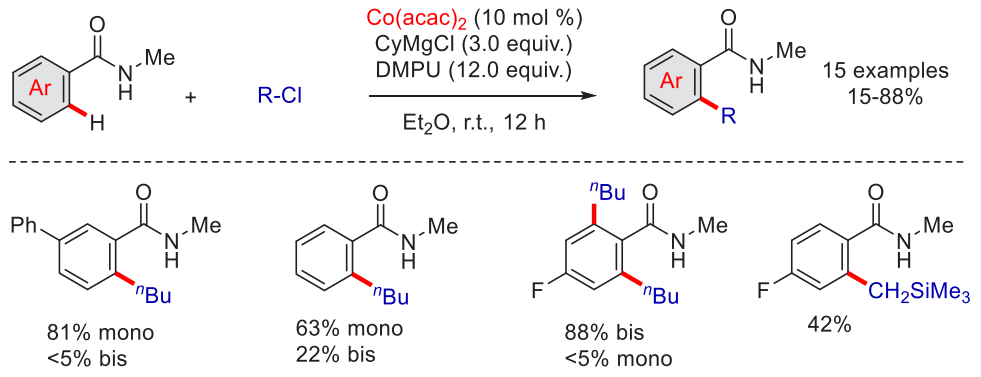
Scheme 33. Chromium-Catalyzed C−H Allylation of Benzamides with Allyl Bromides



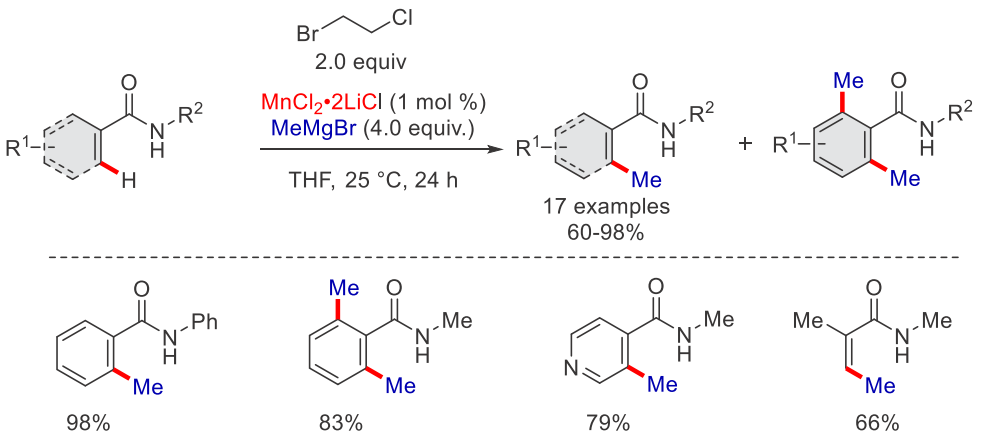
Scheme 34. Cobalt-Catalyzed Amide-Directed C−H Alkylation with Unactivated Olefins



Scheme 35. Cobalt-Catalyzed C−H Alkylation of Benzamides with Alkyl Chlorides



Scheme 36. Manganese-Catalyzed *ortho*-C−H Methylation of Benzamides



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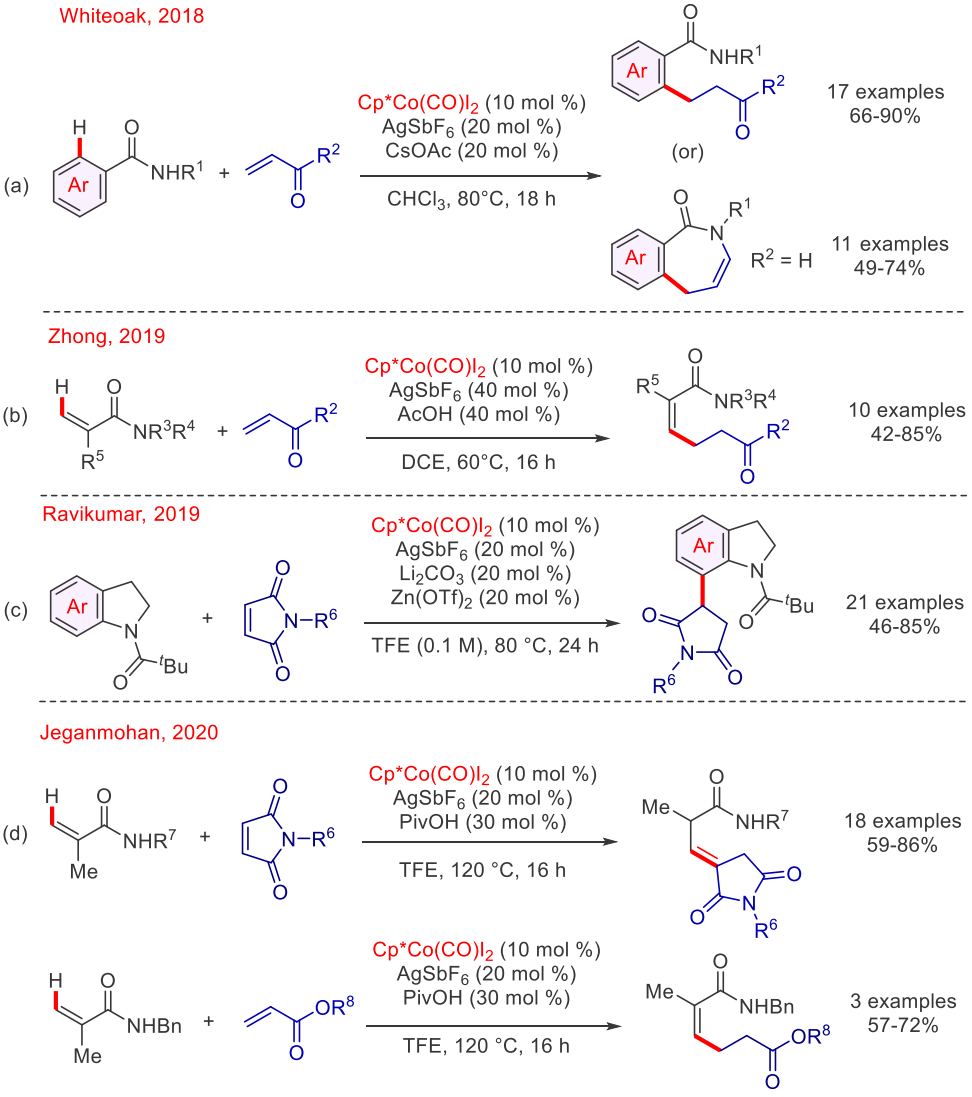
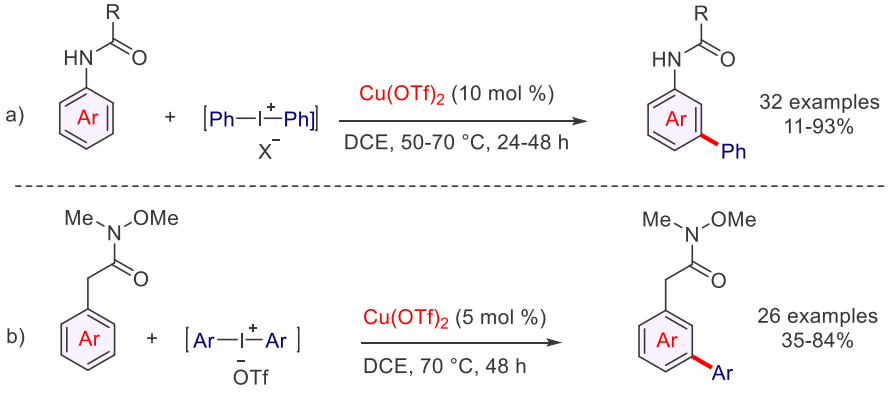
Scheme 37. Cp*Co(III)-Catalyzed C−H Alkylation with Activated Olefins



Scheme 38. Copper-Catalyzed *meta*-Arylation of Aniline and Arylacetamides



Mn(III) is in situ-formed and 1-bromo-2-chloroethane was used as an oxidant in the reaction.

In 2018, Whiteoak[115] and co-workers reported the synthesis of *β*-aryl alkyl ketones through a cobalt-catalyzed *ortho* C−H bond alkylation of benzamides with methyl vinyl ketone. However, when acrolein was used in place of methyl vinyl ketone, azepinones were obtained via cascade C−H alkylation followed by condensation of an aldehyde with nucleophilic amide (Scheme 37a). Inspired by the work of Matsunaga[73] and Whiteoak, Zhong and co-workers reported the vinyl C−H bond alkylation of acrylamides with *α,β*-unsaturated ketones to access *β*-alkylated acrylamides with acceptable yields (Scheme 37b).[76] In 2019, Ravikumar and co-workers disclosed Cp*Co(III)-catalyzed C(7)-selective hydroarylation of indolines using

https://doi.org/10.1021/acscatal.1c05267
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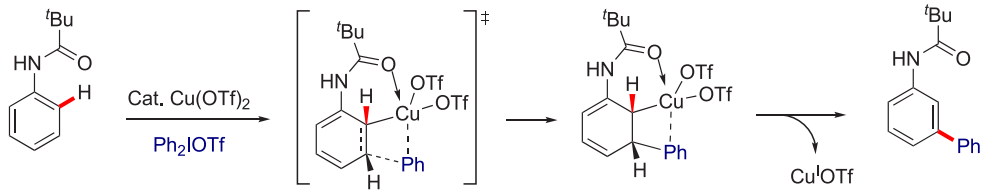
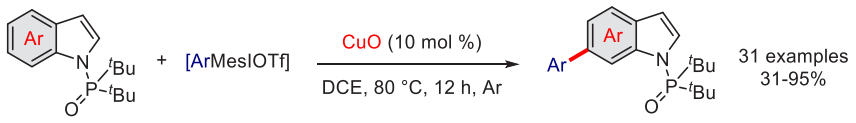
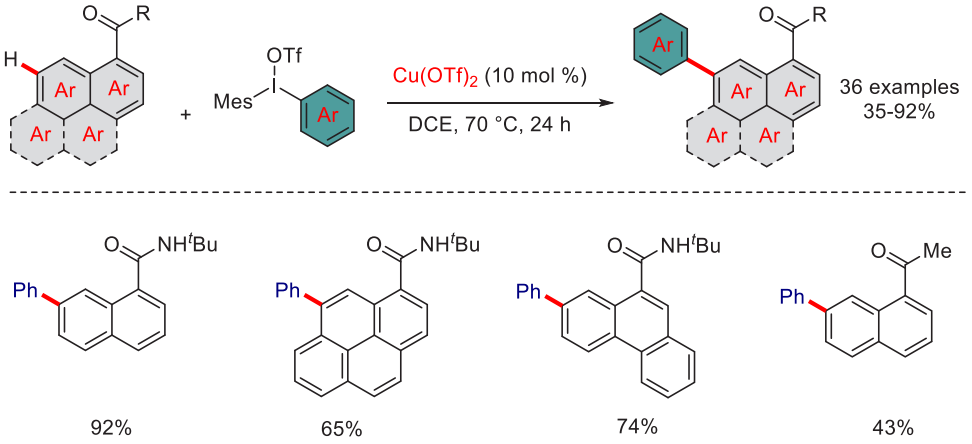
Scheme 39. Plausible Mechanism of the Copper-Catalyzed *meta*-C−H Arylation of Anilides



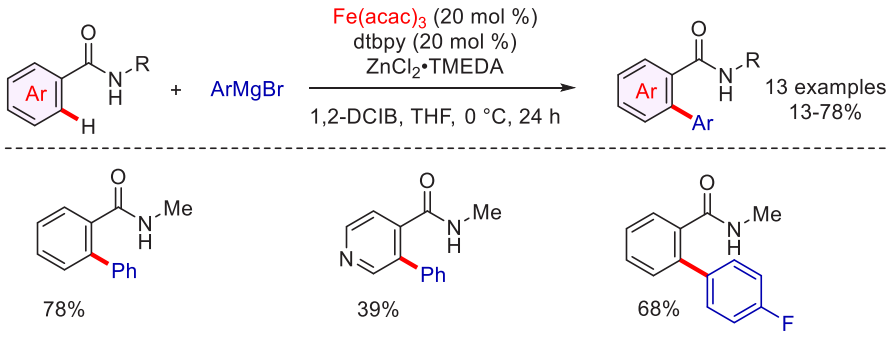
Scheme 40. Copper-Catalyzed C(7)−H Arylation of Indoles



Scheme 41. Copper-Catalyzed Remote C−H Arylation of Polycyclic Aromatic Hydrocarbons



Scheme 42. Iron-Catalyzed *ortho*-C−H Arylation of Benzamides using Aryl Grignard Reagents



maleimides and acrylates (Scheme 37c).[116] The intermolecular competitive experiment revealed better reactivity of acrylate in the alkylation process in comparison with maleimide under the established conditions.

Later, in 2020, Jeganmohan and co-workers described cobalt-catalyzed C−H alkylation of acrylamides with various maleimides to obtain olefins migrated succinimide derivatives in good yields. Migration of double bond is observed only in the case of maleimides, whereas other activated olefins like acrylates provided C−H alkylation products without migration of double bond under the same conditions (Scheme 37d).[117]

2.1.9. C−H Arylation. Biaryl skeletons are widespread in natural products and find important applications in agrochemical and material chemistry. In 2009, Gaunt and co-workers developed an exciting protocol for the *meta*-C−H arylation of anilides using Ph_2IOTf as the arylating agent under copper catalysis (Scheme 38a).[118] A variety of electron-rich arenes were arylated with exquisite *meta* selectivity. Arenes having electron-withdrawing substituents also underwent arylation without compromising the selectivity. In the subsequent years, Gaunt and co-workers further extended the scope of *meta*-C−H arylation to more challenging aryl carboxamides (Scheme 38b).[119] Various alkyl substituted α-aryl ketones were successfully meta arylated with excellent selectivity. The chirality at the α-position of ketone remains unaffected under the optimized conditions. Interestingly, the protocol also works in the absence of copper catalyst at elevated temperatures.

The detailed mechanism of copper-catalyzed *meta*-selective arylation was carried out by Wu and Li groups[120] through experimental and theoretical studies. The authors proposed a four-membered transition state involving Cu(III)−Ph intermediate (Scheme 39). Further, a kinetic study supported the

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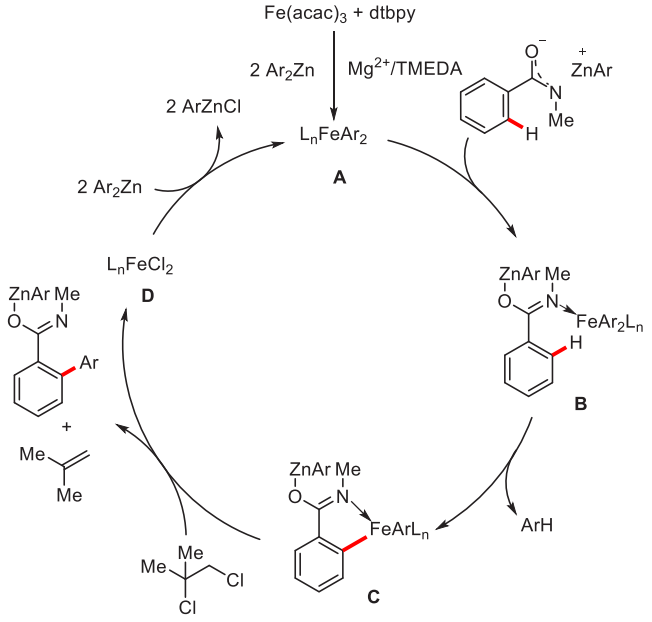
Scheme 43. Plausible Mechanism of the Iron-Catalyzed C−H Arylation



involvement of the Cu(I) catalytic system in the arylation process.

Inspired by these works, Shi, and co-workers demonstrated a directing-group-dependent remote C(6)−H bond arylation of indole using diaryliodonium triflate salts as arylating agents (Scheme 40).[121] The presence of the bulky *tert*-butyl group in the directing group favors the cyclometalation at the C(7) position over the C(2) position. Moreover, the C(6)−H olefination was also achieved using vinyl(aryl)iodonium salt, albeit in low yield.

Very recently, You and co-workers extended the concept of copper-catalyzed meta C−H arylation of amine derivatives and aryl acetic acid derivatives for the remote C−H arylation of substituted polycyclic aromatic hydrocarbons (PAHs) like substituted 1-napthamides phenanthrene-9-carboxamide, pyrene-1-carboxamide, and fluoranthene-3-carboxamide, among others, using aryliodonium salts as the arylating agent (Scheme 41).[122] The protocol was not only limited to the amide directing group; additionally, their ketone derivatives were found to be suitable for the C−H arylation with moderate yields. The reaction proceeded through a similar pathway as proposed by Wu, Li, and their co-workers.

While Gaunt and others showed the utilization of electrophilic arylation using copper, in 2012, Nakamura and co-workers demonstrated iron-catalyzed site-selective *mono*-C−H arylation of benzamide derivatives using aryl magnesium bromide in combination with $ZnCl_2$·TMEDA (Scheme 42) under mild conditions.[123] The presence of the newly installed *ortho*-aryl group restricts the second metalation at another *ortho*-position because of steric congestion, and as a result, only a trace amount of bis-arylated product was observed.

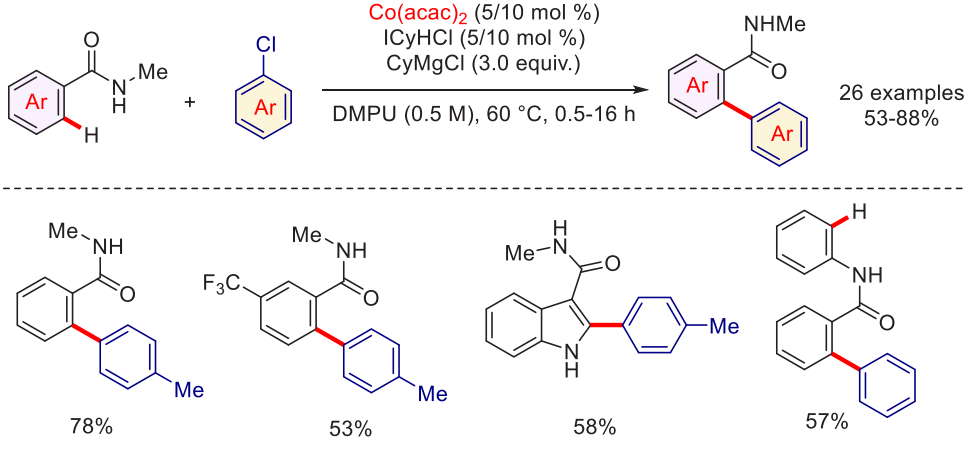
On the basis of previous literature reports, they proposed a plausible mechanism as depicted in Scheme 43. The reaction initiated with the generation of dtbpy stabilized low-valent organoiron species via an *in situ* reduction of Fe(III). The low-valent iron coordinates with deprotonated amide and undergoes *ortho*-metalation to provide the ferracycle intermediate **C**. Finally, oxidation of the ferracycle with 1,2-dichloro-2-methylpropane or 1,2-dichloroisobutane (1,2-DCIB) and subsequent reductive elimination provided the desired arylated product.

Later, Ackerman and co-workers devised an elegant strategy for cobalt-catalyzed synthesis of medicinally important biaryl tetrazole via amide-directed C−H arylation with a strong-σ donating *N*-heterocyclic carbene like 1,3-dicyclohexylimidazolium chloride (ICyHCl) as ligand and chloroarenes as arylating agents (Scheme 44).[124] The reaction works well not only with *N*-methyl aryl amides but also with *N*-aryl benzamides. Interestingly, C−H arylation of *N*-phenyl benzamides occurred selectively at the *ortho*-position of the electron-deficient phenyl group.

Heteroarenes like pyridine are known to coordinate strongly with the metal and thereby poison the catalytic activity. In 2018, Ackermann and co-workers described a scalable site-selective C−H arylation of pyridyl carboxamides in a continuous flow process via amide directed C−H bond activation (Scheme 45).[125] Sustainable and user-friendly $MnCl_2$ was used as catalyst along with neocuproine as ligand and TMEDA as a stabilizer for the Grignard reagent. Detailed computational study and mechanistic investigation suggested a Mn(II)/Mn(III)/Mn(I) catalytic cycle and the C−H activation proceeds likely via ligand-to-ligand−hydrogen transfer (LLHT).

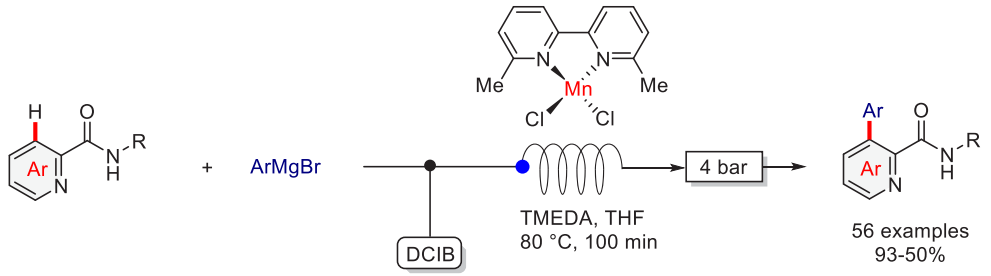
Recently, Duan and co-workers developed an iron-catalyzed phosphine/NHC free, amide-directed C−H arylation of

Scheme 44. Cobalt-Catalyzed *ortho*-C−H Arylation of Benzamides with Aryl Chlorides

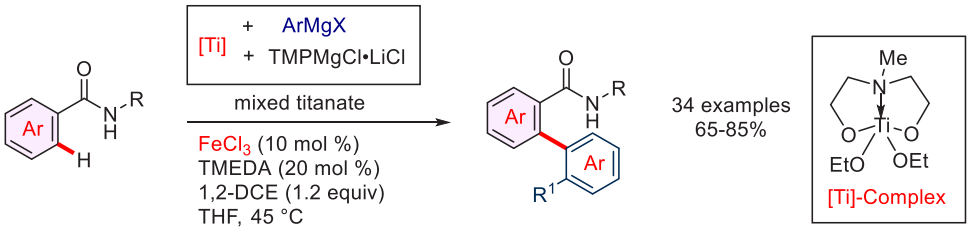


https://doi.org/10.1021/acscatal.1c05267
ACS Catal. 2022, 12, 3452−3506

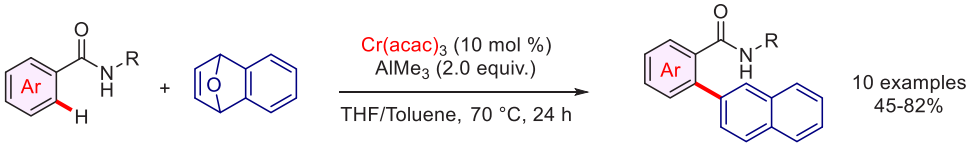
Scheme 45. Manganese-Catalyzed *ortho*-C−H Arylation of Pyridyl Amides in the Flow Process



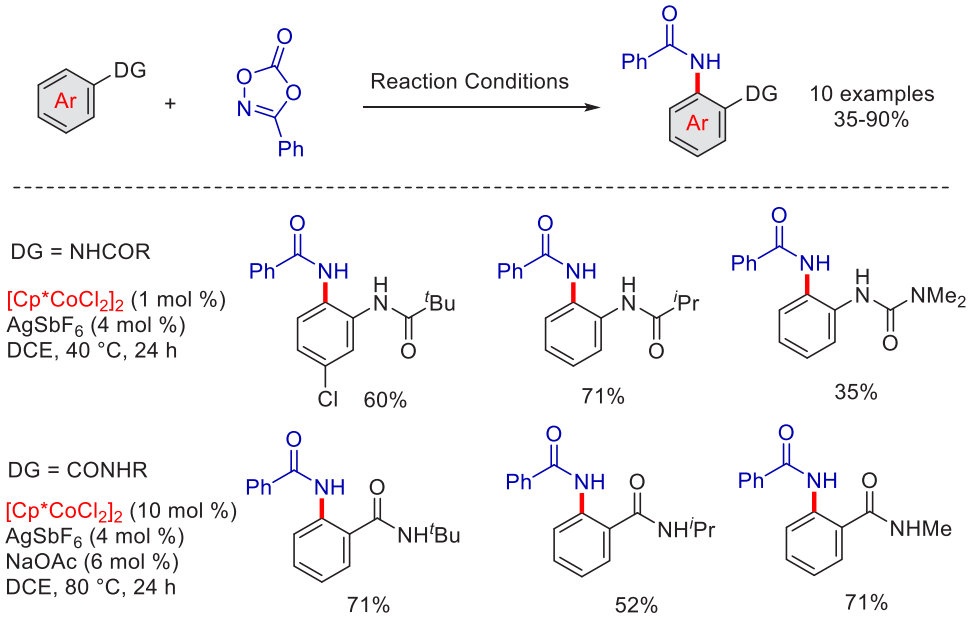
Scheme 46. Iron-Catalyzed *ortho*-C−H Arylation of Benzamides with Grignard Reagents



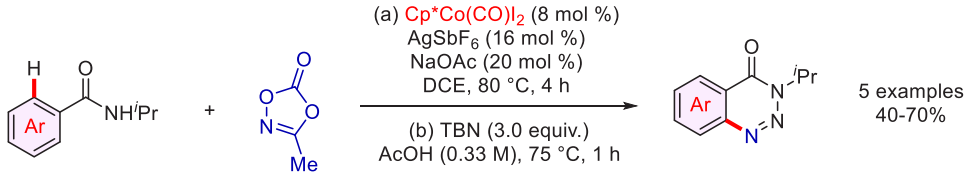
Scheme 47. Chromium(III)-Catalyzed C−H Naphthalenation using 1,4-Dihydro-1,4-epoxynaphthalene



Scheme 48. Cp*Co(III)-Catalyzed *ortho*-C−H Amidation of Anilides and Benzamides using Phenyl Dioxazolones



Scheme 49. Cp*Co(III)-Catalyzed Synthesis of 1,2,3-Benzotriazin-4(3H)-ones



https://doi.org/10.1021/acscatal.1c05267
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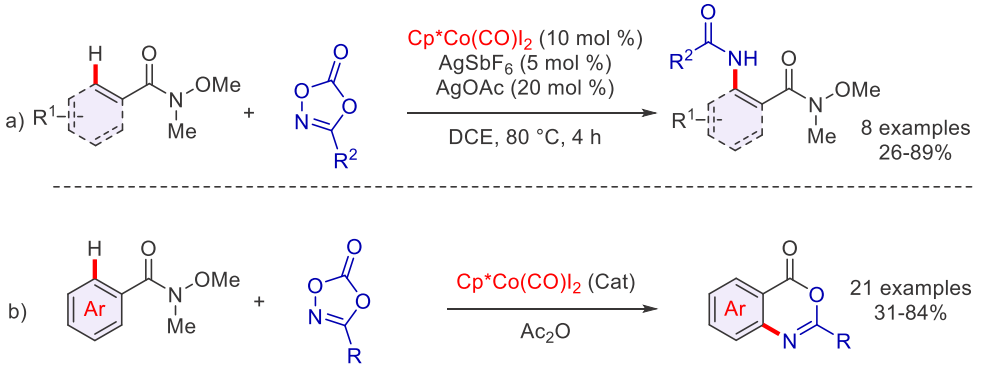
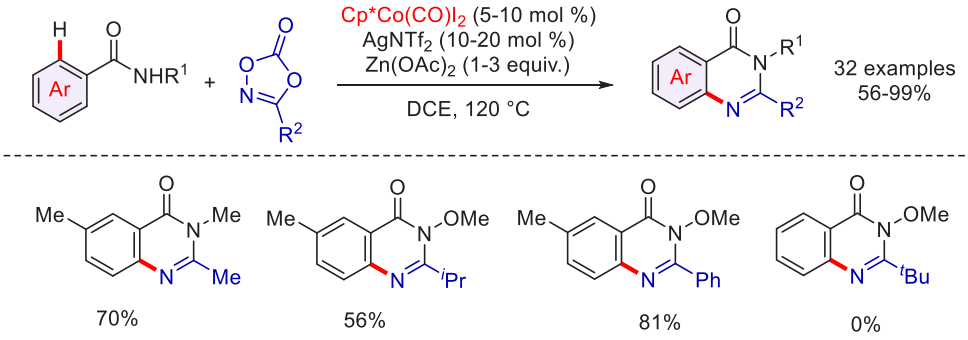
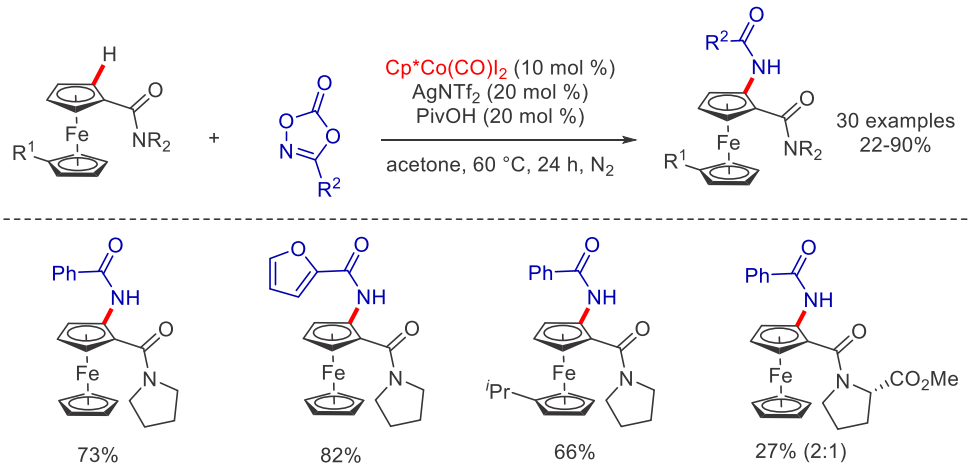
Scheme 50. Cp*Co(III)-Catalyzed *ortho*-C−H Amidation of Benzamides using Dioxazolones



Scheme 51. Cp*Co(III)-Catalyzed Synthesis of Quinazolinone Derivatives via C−H Bond Amidation



Scheme 52. Cp*Co(III)-Catalyzed C−H Amidation of Ferrocene Carboxamides with Dioxazolones



benzamide derivatives using 2-substituted aryl Grignard reagents (Scheme 46).[126] The use of mixed titanate was crucial in the success of the C−H arylation process. Importantly, TMPMgCl·LiCl (2,2,6,6-tetramethylpiperidinylmagnesium chloride) deprotonates the amide acidic hydrogen with concomitant release of TMPH which does not poison the Grignard reagent. Therefore, a small excess of Grignard reagent (1.2 equiv) was sufficient for this arylation. The developed methodology was also extended to the facile syntheses of privileged compounds such as urolithin B and crinasiadine using C−H arylation as the key step.

Very recently, Nakamura and co-workers developed a straightforward protocol for amide directed *ortho*-C−H arylation using 1,4-dihydro-1,4-epoxynaphthalene using abundant, less-toxic chromium catalysis (Scheme 47).[85] Both *N*-methyl benzamide and *N*-PMB-protected benzamide delivered the biaryl products with excellent substrate scope in acceptable yields. The trimethyl aluminum deprotonates the acidic amide N−H as well as the requisite C−H bond during the cyclometalation.

2.2. C−X Bond Formation. C−N Bonds are prevailing in molecules having numerous applications in agrochemicals, materials, and bioactive compounds, and the formation of C−N bond is one of the most important synthetic steps in organic synthesis.[127−131]

2.2.1. C−H Amidation. Among the various C−N bond forming reactions, transition-metal-catalyzed C−H amidation reactions utilizing organic azides and dioxazolones as amidating agents have been widely popular since the pioneering work under Cp*Rh(III) catalysis led by Chang and co-workers.[132]

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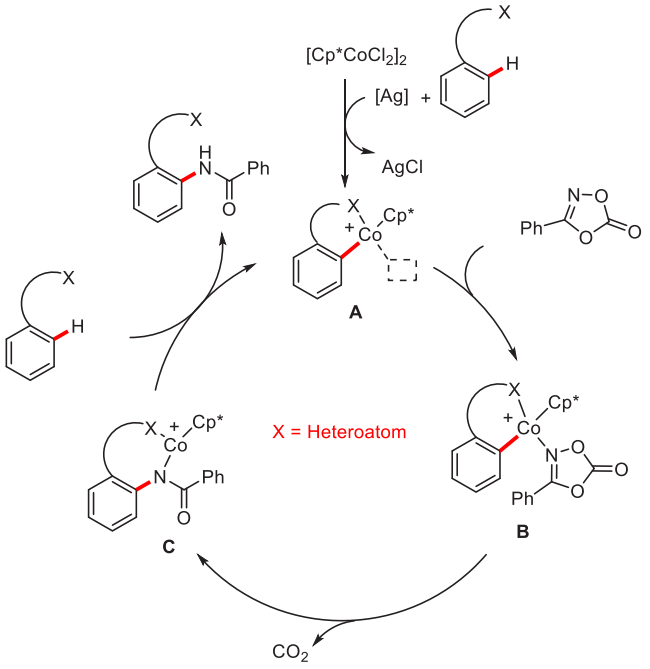
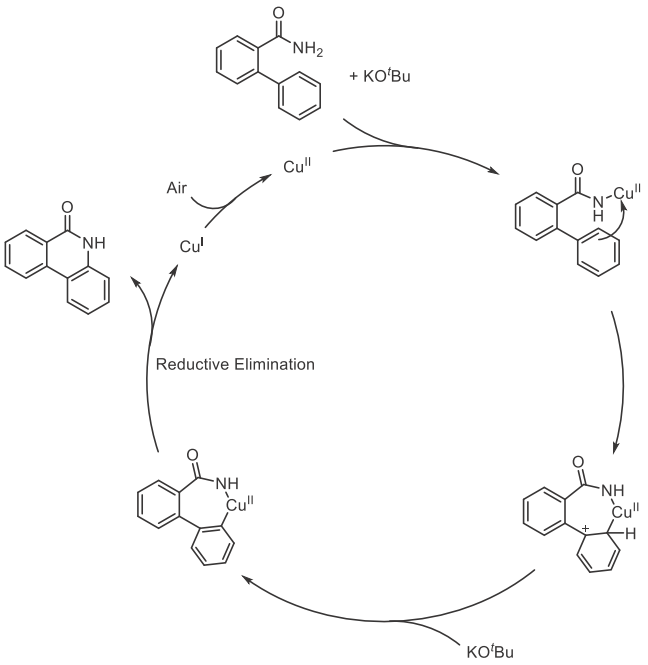
Scheme 53. Plausible General Mechanism for the Arenes C−H Amidation with Dioxazolones



Scheme 55. Plausible Mechanism of the Copper-Catalyzed Intramolecular C−H Bond Functionalization/C−N Bond Formation



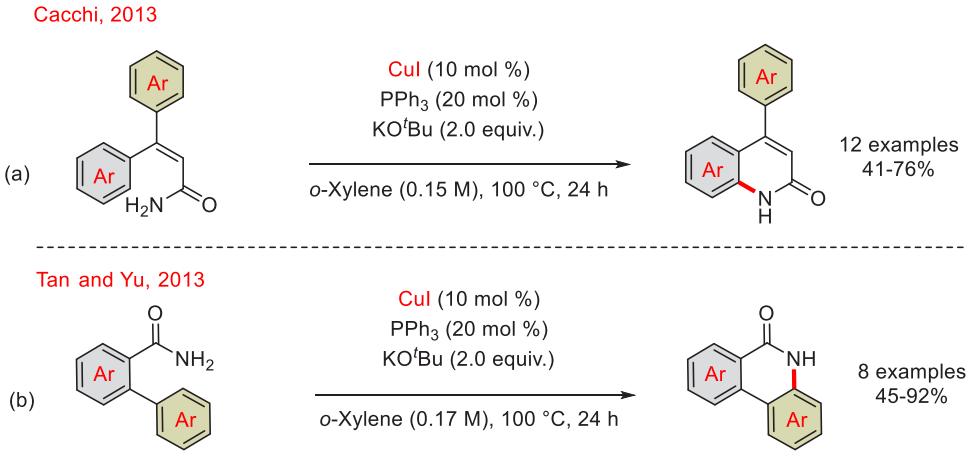
Organic azides or dioxazolones often served as an internal oxidizing agent as well as an amidating agent, which eliminates the necessity of external stoichiometric oxidant for C−H amidation.[133,134] In 2015, *ortho* C−H amidation of arenes under cobalt(III) catalysis was established by the same authors using phenyl dioxazolone as amidating reagent (Scheme 48).[135] Based on a comparative study of reactivity among the group 9 metals, cobalt was found as the most efficient catalyst for *ortho*-amidation of anilides. Both anilide and benzamide derivatives were suitable to deliver the desired amidated products in good yields.

Using this strategy associated with a sequential condensation with *tert*-butyl nitrite (TBN), Whiteoak and co-workers demonstrated the efficient synthesis of 1,2,3-benzotriazin-4(3*H*)-one derivatives which have potential applications as pesticides and in pharmaceuticals (Scheme 49).[136]

Later, Matsunaga and co-workers extended the C−H amidation of benzamides, acrylic amides using *N*-Methyl-*N*-methoxy protected aryl amides in the presence of Cp*Co(III)-catalyst, $AgSbF_6$, and AgOAc (Scheme 50a).[74] Furthermore, to expand the synthetic utility, Weinreb amides were converted to various *ortho*-amidated acetophenones which are otherwise rarely obtained in high yields. The protocol was extended for the synthesis of various 4*H*-3,1-benzoxazin-4-ones in one step (Scheme 50b).[137] The authors claimed that the acetic anhydride traps the liberated amine during the cyclization and therefore facilitates the nucleophilic attack at the Weinreb amide carbonyl.

Subsequently, Dong and Liu reported the facile synthesis of quinazolinone derivatives through cascade C−C and C−N bond formation with benzamides aryl source and dioxazolnes as amidating agent catalyzed by cobalt (Scheme 51).[138] The use of the stoichiometric amount of $Zn(OAc)_2$ was found to be very crucial to get high yields of the desired products. Presumably, Lewis acidic $Zn(OAc)_2$ in combination with Cp*Co(III) enhances the electrophilicity of newly installed amide carbonyl

Scheme 54. Copper-Catalyzed Intramolecular C−H Bond Functionalizations/C−N Bond Formations



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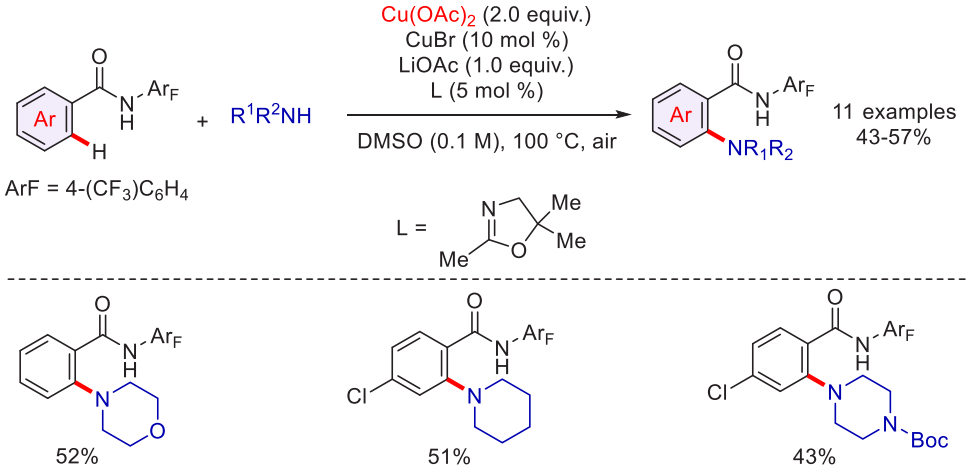
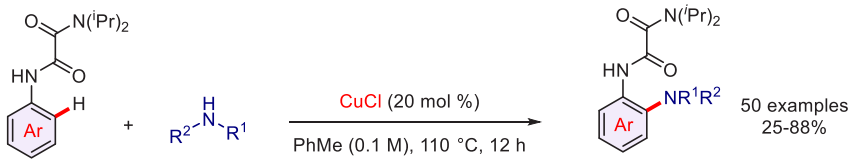
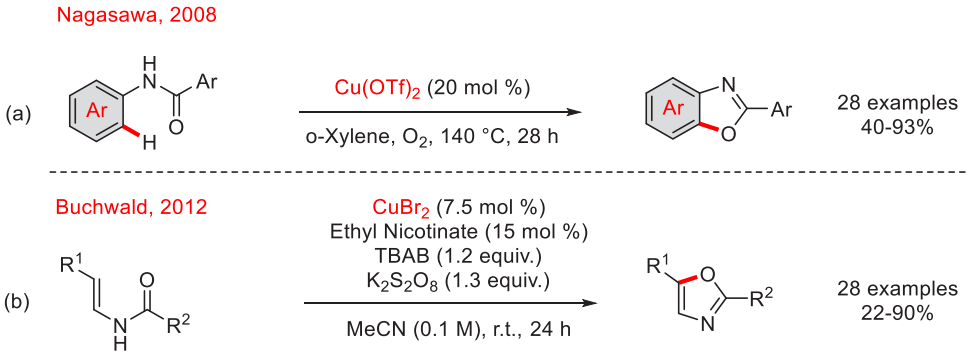
Scheme 56. Copper-Promoted C−H Amination of Benzamides using Secondary Amines



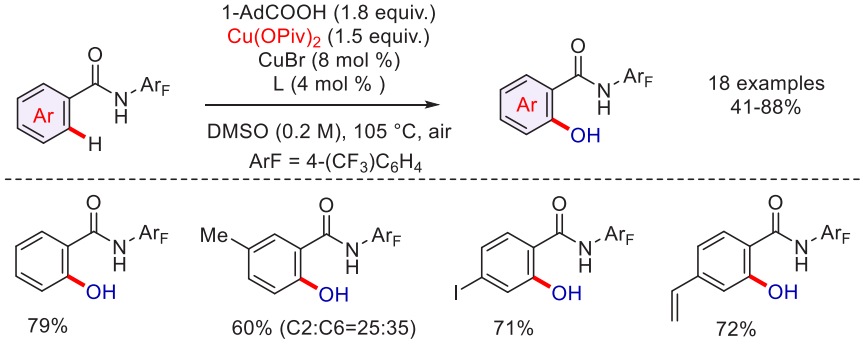
Scheme 57. Copper-Catalyzed C−H Amination of Aniline Derivatives using Secondary Amines



Scheme 58. Copper-Catalyzed Oxidative Cyclization of Anilides and Enamides



Scheme 59. Copper-Promoted C−H Hydroxylation of Benzamides



moiety and therefore facilitated the nucleophilic addition. The protocol has been utilized for the synthesis of the natural product schizocommunin and drug diproqualone. The protocol was further utilized toward the formal synthesis of various bioactive molecules like raltiterxed, (−)-vasicinone, and so on.

Ferrocene and its derivatives have witnessed great applications in asymmetric synthesis, material chemistry, and pharmaceuticals.[139] Shi and co-workers extended the concept of amide-directed site-selective C−H amidation of ferrocene under Cp*Co(III) catalysis, in which it was demonstrated that the electron-deficient dioxazolones were found to be more suitable for the desired amidation under mild conditions (Scheme 52).[140]

https://doi.org/10.1021/acscatal.1c05267
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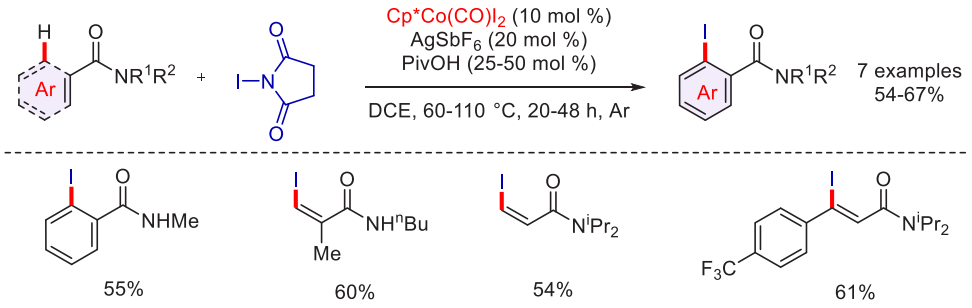
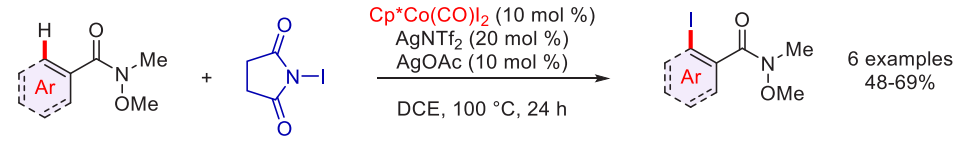
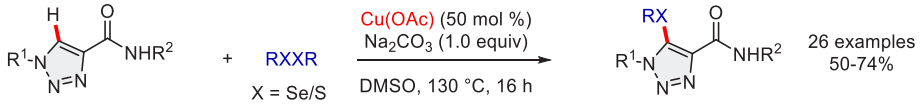
Scheme 60. Cp*Co(III)-Catalyzed C−H Iodination of Aryl/Aliphatic Amides using *N*-Iodo Succinimide



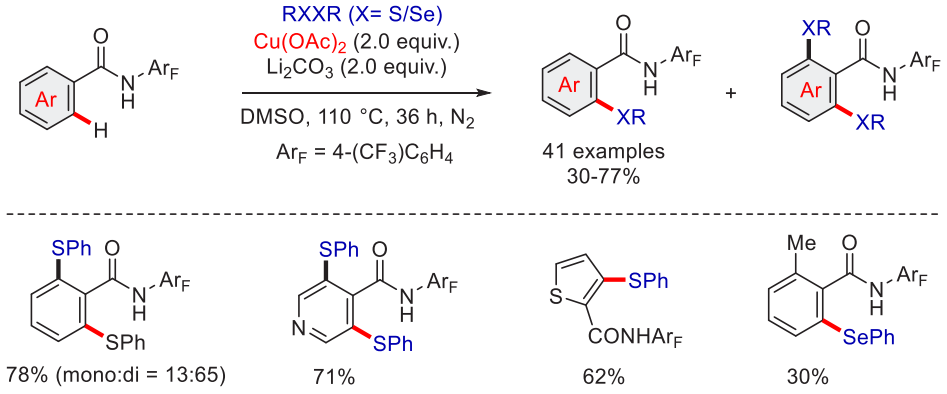
Scheme 61. Cp*Co(III)-Catalyzed C−H Iodination of Weinreb Amides



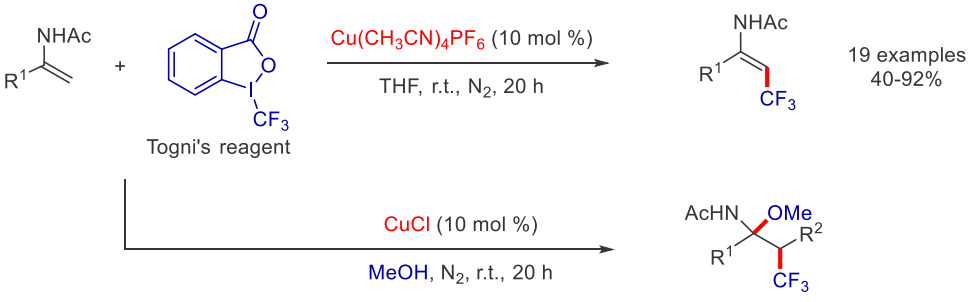
Scheme 62. Copper-Promoted C−H Chalconization of 1,2,3-Triazoles



Scheme 63. Copper-Promoted C−H Chalcogenylation of Benzamides



Scheme 64. Copper-Catalyzed Trifluoromethylation of Enamides



A general plausible mechanism of the C−H amidation process is described in Scheme 53. Coordination of substrate with the catalyst in the presence of silver salt led to catalytically active species **A**. Dioxazolone coordinates with **A** to form **B**, and subsequent amido transfer with the release of CO_2 as the only byproduct generates intermediate **C**. Finally, protodemetalation of **C** delivers the amidated product to regenerate the cationic intermediate **A**.

2.2.2. Intramolecular Amidation Reactions. 2-Quinolone scaffolds are widely found in wide range of bioactive molecules. Considering the importance of 2-quinolone subunits, Cacchi and co-workers developed efficient protocol for the synthesis of 4-aryl-2-quinolones from 3,3-diarylacrylamides via copper-catalyzed intramolecular C−H bond functionalizations and C−N bond formations (Scheme 54a).[141] Importantly, function-alization preferred at the arene, which is present at the same side

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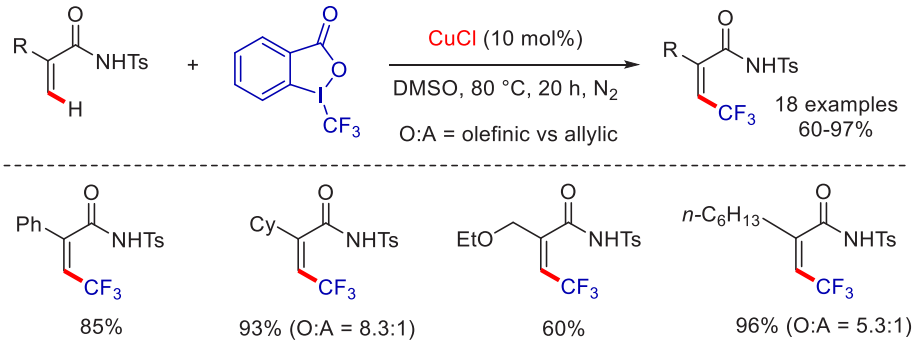
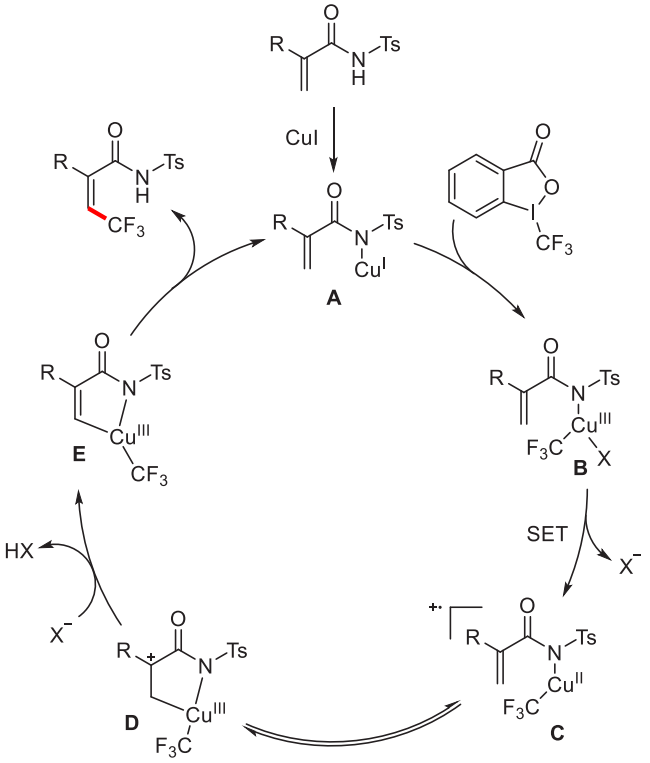
Scheme 65. Copper-Catalyzed Trifluoromethylation of Enamides



Scheme 66. Plausible Mechanism of β-Trifluoromethylation of Acetamides



to the amide irrespective of the substituents present at the arenes. High selectivity was observed to those substrates where the arenes trans to amide contain methyl and chloro and bromo substituents at the ortho position. Inspired from this work, Tan, Yu, and co-workers successfully synthesized various phenanthridin-6(5*H*)-ones from readily available 2-aryl benzamides under similar condition with good yields (Scheme 54b).[142] Notably, the reaction failed to deliver the desired product when *N*-alkyl-2-phenyl benzamide was used as substrate.

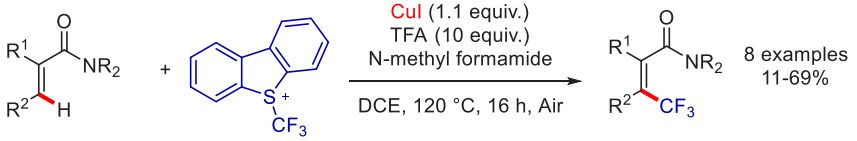
Mechanistically, the reaction began with the oxidation of Cu(I) to Cu(II) in air followed by base-promoted coordination of Cu(II) afforded Cu-amide **A** (Scheme 55). Thereafter, electrophilic attack of the arene ring to the Cu center in the intermediate **A** led to the intermediate **B**. Finally base- mediated elimination of arene rearomatize the arene and successive reductive elimination delivered the desired phenanthridin-6(5*H*)-one.

2.2.3. C−H Amination. Despite major advances in transition-metal-catalyzed C−H amination of arenes, the use of free secondary amine as aminating reagent remains in the early stage.[143] In 2018, Yu and Dai and co-workers successfully described copper-promoted C−H amination of weakly coordinating benzamide using secondary amine (Scheme 56).[144] The use of an external monodentate oxazoline ligand was crucial to obtain the desired product in high yields. The reaction was tolerated with a variety of functional groups present in amide as well as with various aliphatic amides.

The same group recently explored copper-catalyzed oxalamide-directed *ortho*-C−H amination of anilines using O_2 as the sole oxidant (Scheme 57).[145] Pleasingly, besides aniline, the reaction was equally efficient with heteroarenes as observed with benzothiophene, benzothiazole, isoquinoline, and quinoxaline. Various cyclic and acyclic secondary amines were well suited for the transformations. Furthermore, late-stage modification of various drugs like Aminoglutethimide, Mesalazine, Chlorphenesin, Aphotalide, and Anileridine were achieved using this protocol. The authors proposed that the C−H cleavage is not the rate-limiting step of the reaction as evident from KIE experiments.

2.2.4. C−H Oxygenation. The benzoxazole subunits are prevalent in many medicinally important molecules and therefore in 2008, Nagasawa and co-workers developed an protocol for the synthesis of wide variety of 2-arylbenzoxazoles through copper-catalyzed *ortho*-C−H bond functionalizations of easily accessible anilide derivatives at room temperature (Scheme 58a).[146] On a similar note, in 2012, Buchwald and co-workers reported copper-catalyzed oxidative cyclization of enamides to oxazoles via vinylic C−H bond functionalizations (Scheme 58b).[147] A library of 2,5-disubstituted oxazoles bearing aryl, vinyl, alkyl, and heteroaryl substituents with moderate-to-good yields were synthesized using this strategy at very mild

Scheme 67. Copper-Promoted Trifluoromethylation of Acrylamides



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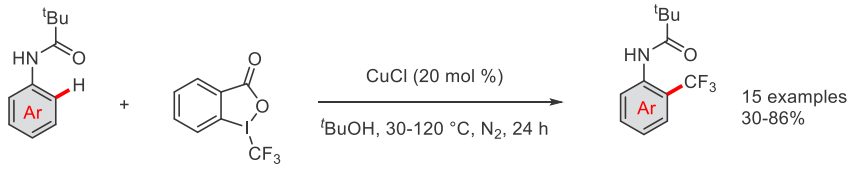
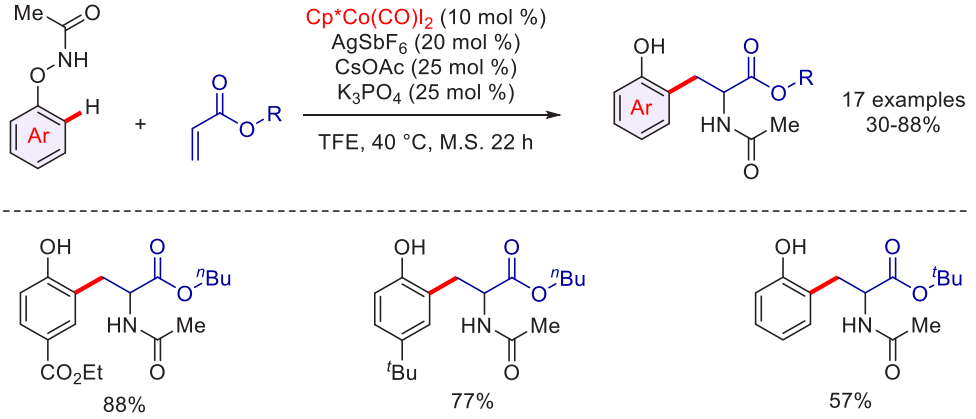
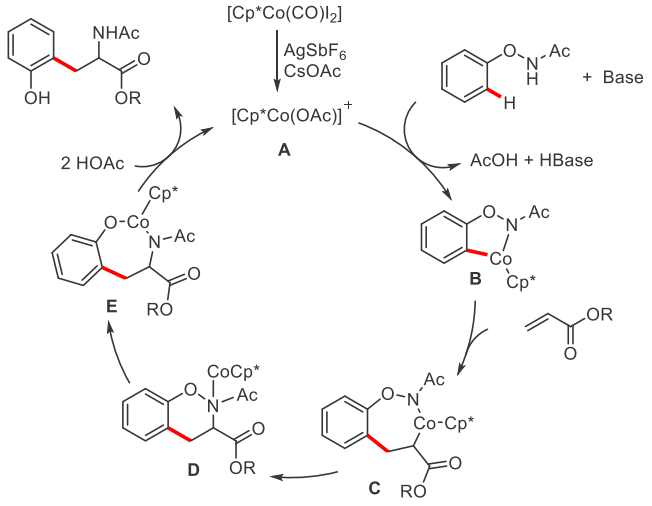
Scheme 68. Copper-Catalyzed *ortho*-Trifluoromethylation of Arenes and Heteroarenes



Scheme 69. Cp*Co(III)-Catalyzed Intermolecular Carboamidation of Alkenes



Scheme 70. Plausible Mechanism of Cp*Co(III)-Catalyzed Carboamidation of Alkenes



conditions. The authors proposed a single-electron pathway for the cyclization, where Cu(II) acts as a single-electron oxidant.

The direct hydroxylation of the arene C−H bond is one of the most efficient ways to produce phenol derivatives which are widely omnipresent in natural products and pharmaceuticals.[148,149] In 2018, Yu and Dai and co-workers reported a copper-promoted *ortho* C−H hydroxylation of benzamide under the assistance of monodentate oxazoline ligand (Scheme 59).[144] The reaction tolerates a wide-range of benzamides under aerobic conditions.

2.2.5. C−H Halogenation. Organohalide compounds are frequently utilized as important building blocks in C−C and C−N bond formations. Among the various methodologies developed for halogenations of organic molecules, transition-metal-catalyzed directed C−H halogenations have been established as one of the most promising tools to synthesize complex molecules and late-stage functionalizations.[150−152] In 2014, Glorius and co-workers demonstrated the synthesis of *ortho*-iodo benzamides using commercially available *N*-iodo succinimide (NIS) via a directed C−H bond activation under cobalt catalysis (Scheme 60).[153] The methodology worked equally well with acrylamide derivatives. According to the authors, pivalic acid might be responsible for the activation of NIS through protonation and in the generation of a highly reactive catalyst for facile coordination of the amide substrates.

In 2018, Matsunaga and co-workers reported the C−H iodination of Weinreb amides under cobalt(III) catalysis (Scheme 61).[64] The commercially available NIS was used as an electrophilic iodinating reagent for the C−H iodination. The reaction scope was very general, and a variety of substituted arenes were amenable for iodination.

2.2.6. C−H Chalcogenylation. Aryl chalconides possess enormous application in material chemistry as well as medicinal chemistry. However, their synthesis under transition-metal catalysis is difficult as the reagents used for chalcogenation often poison the metal catalysts.[154] In 2016, Ackermann and co-workers reported copper-promoted C−H chalcogenation of *N*-(triazolyl)-anilides using dichalconides (PhSSPh/PhSeSePh) with the assistance of weakly coordinating amide (Scheme 62).[155] The protocol was successfully utilized for C−H sulfenylation and selenylation of 1,2,3-triazoles containing secondary amides; however, the tertiary amide containing substrate failed to undergo the desired transformation. The authors also pointed out that the catalytic amount of copper (4 mol %) in combination with $PhI(OAc)_2$ was enough to provide the desired products without compromising the yields.

Recently, Dai and co-workers demonstrated copper-promoted C−H thiolation of hetero(arenes) using weakly coordinating amide as the directing group (Scheme 63).[156] A variety of benzamide derivatives, heteroarenes like indoles, pyrroles, imidazoles, pyridines, and so on, were amenable for functionalization under the optimized protocol. The catalytic system was successfully extended to C−H selenylation with acceptable yields. The kinetic isotope experiments suggested the

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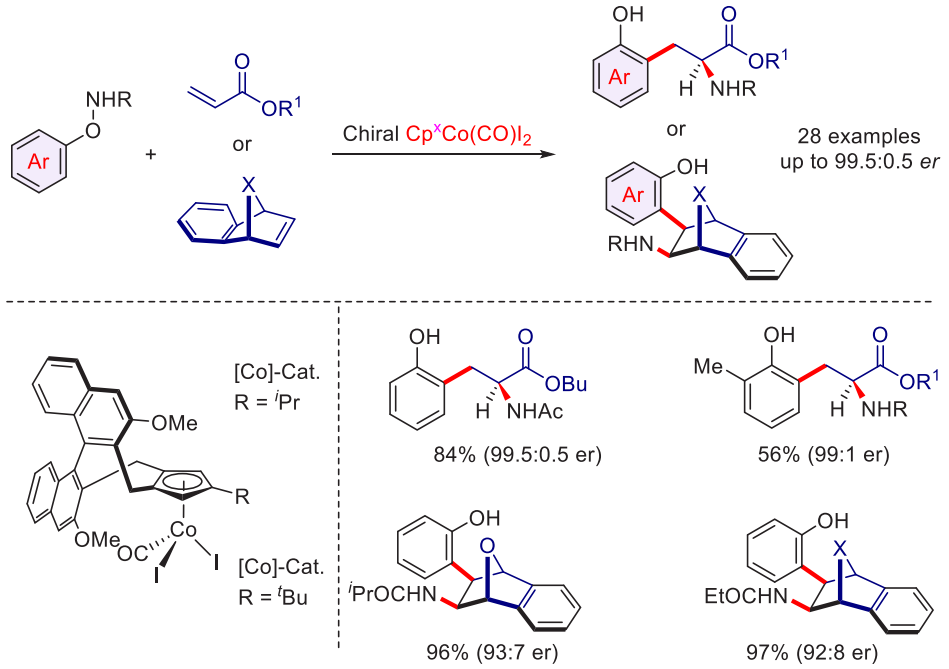
Scheme 71. Chiral Cp^{x}Co(III)-Catalyzed Enantioselective Carboamination of Alkenes



possibility of the involvement of C−H cleavage as the limiting step of the reaction.

2.2.7. C−H Trifluoromethylation. The incorporation of fluorine atom(s), particularly a trifluoromethyl group in an organic molecule, is of great interest as their presence improves the metabolic stability, lipophilicity, and permeability of bioactive molecules.[157−160] In 2012, Loh and co-workers reported a copper-catalyzed trifluoromethylation of enamides using an electrophilic trifluoromethylating Togni's reagent (Scheme 64).[161] The reaction dispensed various trifluoromethylated enamides in good to excellent yields with good functional group tolerance and excellent *E*/*Z* ratio. On the basis of the control experiments, the authors proposed that the reaction proceeded via the formation of an α-trifluoromethyl imine. Thereafter, Lewis acid-induced α-proton elimination transfer furnished the *E*-selective triluoromethylated olefins and regenerate the catalyst. Possibly, the steric interaction between trifluoromethyl group and copper bound imine dictates the stereochemical outcome of the reaction.

In contrast, trifluoromethylation of electron-deficient olefins using Togni's reagent provided the β-trifluoromethylated olefins with excellent (*Z*)-selectivity (Scheme 65).[162] The choice of the directing group turned out to be crucial for the success of the reaction. The reaction was compatible with a broad range of both α-alkyl and α-aryl acrylamide derivatives.

On the basis of the control experiments, the authors proposed a plausible mechanism as shown in Scheme 66. The reaction mechanism proceeds via a ligand exchange between the Cu(I) catalyst and the substrate to generate an intermediate **A**. Oxidative addition of Togni's reagent to **A** provides Cu(III)-CF_3 intermediate **B** which upon intramolecular single-electron transfer (SET) from alkene yields cationic radical intermediate **C**. The in situ-generated metalacycle **D** further underwent α-hydrogen elimination followed by reductive elimination, providing the trifluoromethylated product and regenerating the catalyst for the next cycle.

Later, Besset and co-workers described a copper promoted amide directed trifluoromethylation of acrylamides using electrophilic trifluoromethylating Umemoto's reagent (Scheme 67).[163] The (*Z*)-selective β-trifluoromethylated acrylamide derivatives were obtained in moderate-to-good yields with excellent diastereoselectivity. Notably, the reaction was also viable toward the desired functionalization of the acrylamide containing β-substituent, albeit in low yield.

In the same direction, Xi and co-workers developed a copper-catalyzed C−H trifluoromethylation protocol for the anilides using Togni's reagent (Scheme 68).[164] The *ortho*-trifluoromethylated products were obtained in major amounts along with minor quantities of *meta*- and *para*-isomers. The methodology was equally applicable to the heteroaryl moieties, and the corresponding trifluoromethylated products were isolated in good yields. Furthermore, the mechanistic investigation revealed that the reaction proceeds via a free radical pathway.

2.3. Miscellaneous Reactions. In 2016, Glorius and co-workers devised an elegant protocol for the synthesis of unnatural amino acids via Cp*Co(III)-catalyzed intermolecular carboamination of alkenes (Scheme 69).[165] A wide variety of phenoxyacetamides were readily coupled with different acrylates to obtain various amino acid analogues with good yields at very mild condition. Phenoxyacetamide serves as a directing group as well as an internal oxidant to oxidize the liberated Cp*Co(I) into Cp*Co(III) active species.

On the basis of the control experiments, the authors proposed a plausible mechanism as shown in Scheme 70, which began with the formation of catalytically active Co(III) cationic species **A** with the treatment of $AgSbF_6$, CsOAc, and K_3PO_4 with Cp*Co(CO)I_2 catalyst. The C−H bond activation with the release of AcOH generated the five membered metalacycle **B** which subsequently underwent insertion to olefin leading to intermediate **C**. This intermediate **C** on reductive elimination delivered intermediate **D**. Further, the reduced Co(I) in intermediate **D** oxidatively cleaved the N−O bond to obtain the seven-membered Co(III) intermediate **E**. Finally, the desired amino acid was afforded from the intermediate **E** through protodemetalation.

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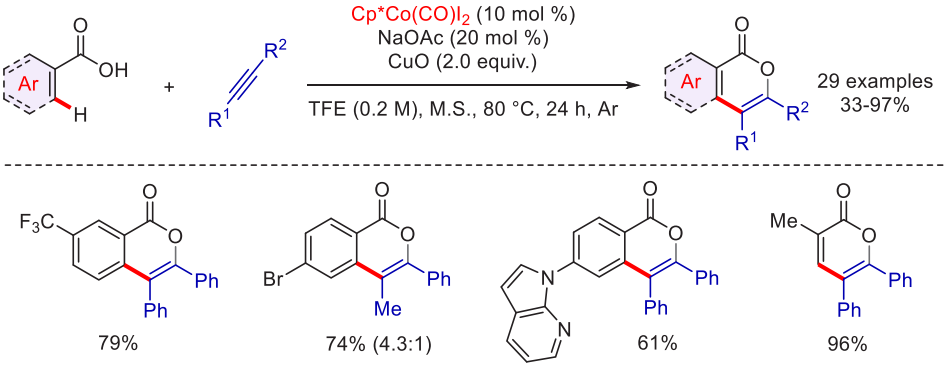
Scheme 72. Cp*Co(III)-Catalyzed Carboxylic Acid-Directed Oxidative Annulation with Alkynes

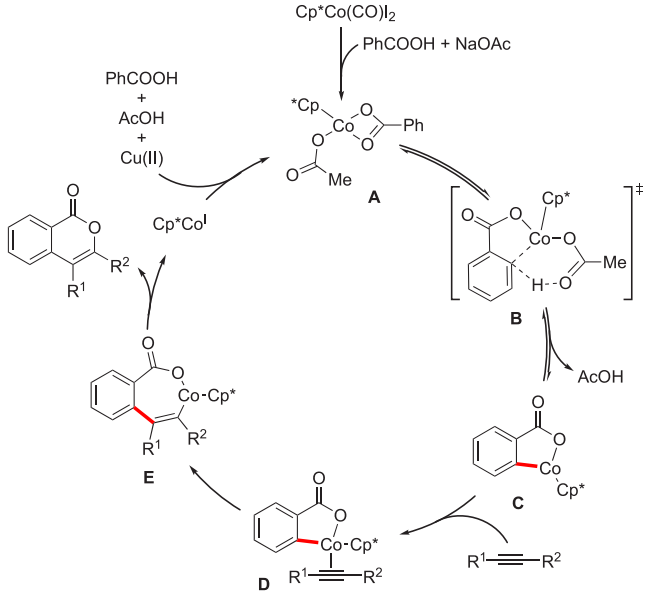


In 2021, Cramer and co-workers unveiled an enantioselective version of the carboamination protocol using chiral cyclopentadienyl cobalt complexes to access various isotyrosine derivatives with excellent enantioselectivity (Scheme 71).[166] The carboamination process was further extended to strained bicyclic alkenes, and the respective amino substituted bicyclic scaffolds were obtained with good-to-excellent enantioselectivity.

3. CARBOXYLIC ACID-DIRECTED C−H BOND FUNCTIONALIZATIONS

Carboxylic acid functionality is abundant in various natural products and biorelevant molecules. Synthetically useful functional groups such as amide, ester, alcohol can be easily obtained from carboxylic acid derivatives. In addition to its known importance in synthesis, it has been established as a potential weakly binding directing group in transition-metal-catalyzed site-selective C−H bond functionalizations.[167,168]

Scheme 73. Plausible Mechanism for the Oxidative Annulation of Benzoic Acid with Alkyne

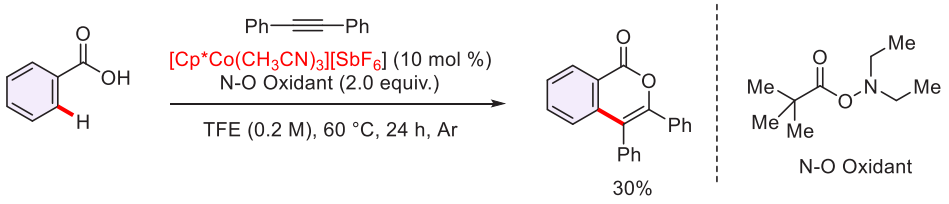


3.1. C−C Bond Formation. *3.1.1. Annulation Reaction.* In the quest to develop Cp*Co(III)-catalyzed C−H activation strategy, in 2017, Sundararaju and co-workers documented oxidative C−H bond annulation with alkynes using carboxylic acid as a directing group (Scheme 72).[169] The optimization study showed that the choice of oxidant was pivotal to carry out this transformation. Biologically important isocoumarin and pyrone derivatives were obtained from various aryl, heteroaryl carboxylic acid, and acrylic acid derivatives bearing electron-donating and electron-withdrawing substituents through C−H bond annulation. Highly regioselective annulation products were obtained when unsymmetrical alkyl/aryl alkynes were used. Further, the authors demonstrated the preferred reactivity of weakly coordinating directing group assisted C−H bond annulation over alkenylation in the presence of a strongly coordinating directing group such as pyridine.

On the basis of the control experiments, a plausible mechanism was proposed as depicted in Scheme 73. Active *bis*-carboxylate Co(III) complex **A** underwent reversible concerted-metalation and deprotonation (CMD) to furnish intermediate **C**. The coordination of alkyne to the cobaltacycle **C** followed by an insertion into the Co−C bond leads to a seven membered alkenyl intermediate **E**. Finally, reductive elimination in the intermediate **E** provides the desired product with the concurrent release of reduced Cp*Co(I) which gets reoxidized to Cp*Co(III) by Cu(II).

Subsequently, in 2017, Wang and co-workers reported that organic molecules bearing N−O bond can be exploited as green oxidants instead of metal oxidants in the oxidative annulation of benzoic acid with diphenylacetylene in the presence of $Cp^*Co(CH_3CN)_3](SbF_6)_2$ catalyst and 2 equiv of N−O oxidant in TFE at 60 °C afforded the isocoumarin derivative in 30% yield (Scheme 74).[170]

Scheme 74. Organic Oxidant Enabled Cp*Co(III)-Catalyzed Synthesis of Isocoumarin



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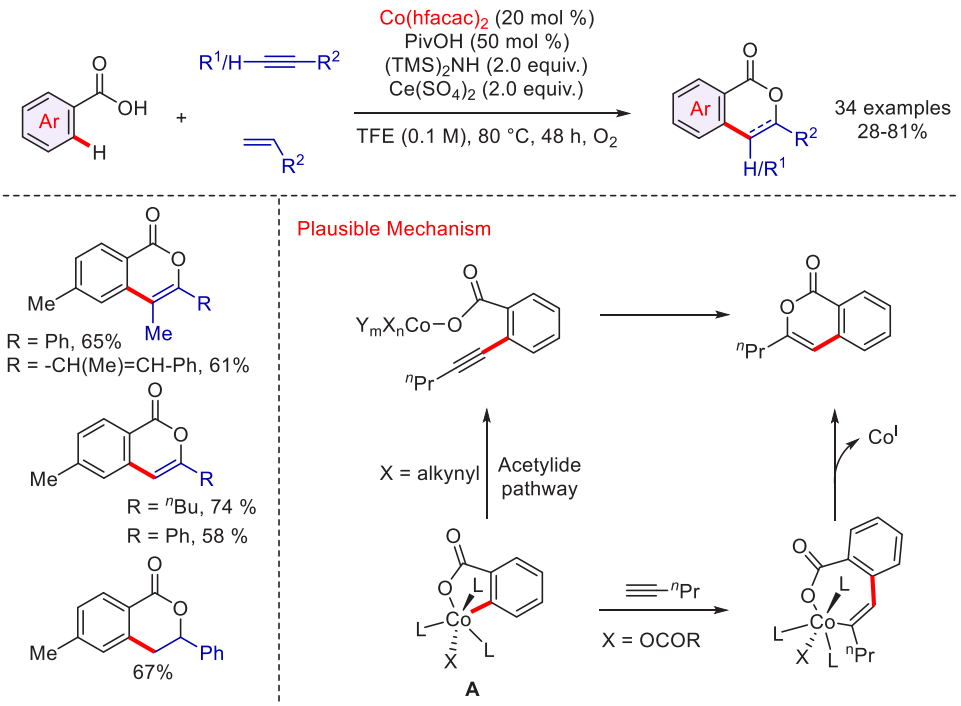
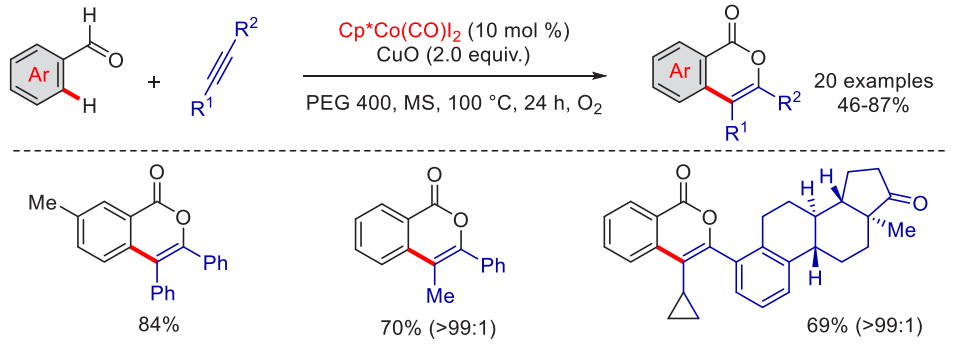
Scheme 75. Cobalt-Catalyzed Annulation of Arene Carboxylic Acids with Alkynes, Alkenes, Dienes



Scheme 76. Cp*Co(III)-Catalyzed Oxidative Annulation of Aryl Aldehydes with Internal Alkynes



Later, Daugulis and co-workers unveiled a novel, regioselective protocol for the oxidative coupling of benzoic acids with π-coupling partners using air-stable cobalt salt (Scheme 75).[171] The oxidative coupling was performed in the presence of 20 mol % $Co(hfacac)_2$, 50 mol % PivOH, 2.0 equiv of $(TMS)_2NH$, and 2.0 equiv of $Ce(SO_4)_2$ in oxygen atmosphere using TFE as solvent at 80 °C. A library of alkynes, alkenes, dienes, and benzoic acid derivatives were engaged in the reaction strategy efficiently and the desired isocoumarin and dihydroisocoumarin scaffolds were isolated in moderate to good yields with excellent regioselectivity. On the basis of the control experiments, a proposed mechanism for oxidative annulation is displayed in Scheme 75, which operated through successive migratory insertion and reductive elimination to provide the desired products. The authors also proposed a different pathway for terminal alkynes via acetylide intermediate formation as extensive deuterium scrambling was noticed in the oxidative coupling of deuterated acetylene.

Subsequently, in 2019, Tao and co-workers demonstrated an efficient, scalable synthesis of isocoumarins directly from aromatic aldehydes and alkynes in the presence of Cp*Co(III) catalyst (Scheme 76).[172] The in situ oxidation of benzaldehyde to benzoic acid followed by carboxylate acid directed C−H bond functionalization delivering isocoumarin scaffold as proposed by the authors. The protocol seems to be very sustainable as it used inexpensive cobalt and the catalytic system is recyclable up to 3 times without compromise in the yield of the isocoumarin derivatives. However, terminal alkynes failed to provide the expected annulation, and only a trace amount of product formation is observed.

3.1.2. C−H Alkylation. In 2016, iron-catalyzed carbonyl directed *ortho*-methylation of arenes was achieved by Nakamura and co-workers as depicted in Scheme 77. This is the first example of carboxylate directed C−H bond functionalizations under iron catalysis.[173] The catalytic system comprises 5 mol % $Fe(acac)_3$, 5 mol % Me_2N-TP as catalyst and ligand in combination with 2 equiv of $AlMe_3$ as methylating reagent, and 2,3-DCB as oxidant furnished the *ortho*-methylated benzoic acid. The optimized conditions tolerates a wide range of functional groups such as fluoro-, bromo-, sulphide and pinacol boronate, among others, present at various positions of the aromatic ring. The use of tridentate phosphine ligand was crucial to carry out the methylation. Importantly, the protocol was successfully extended to the functionalizations of aryl esters and

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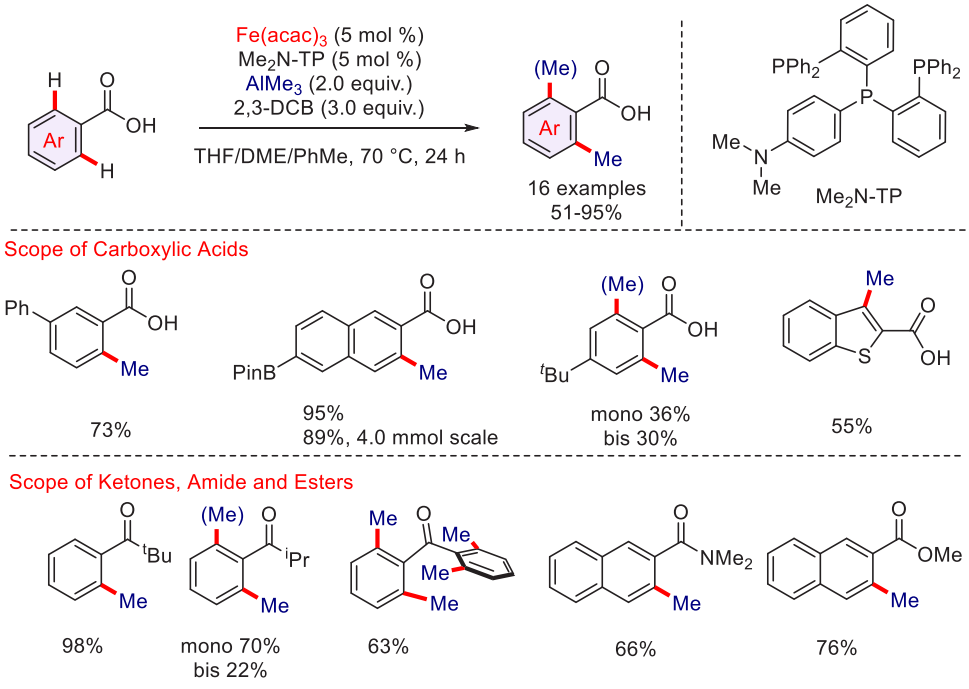
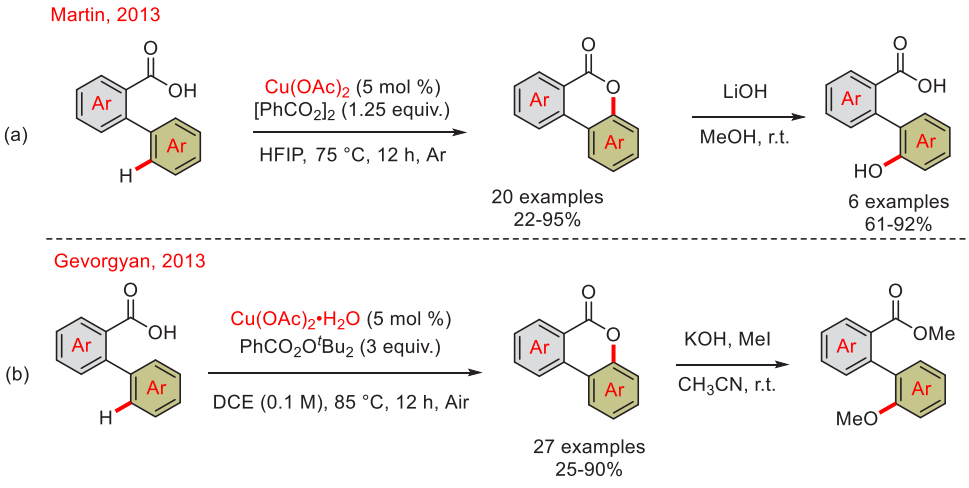
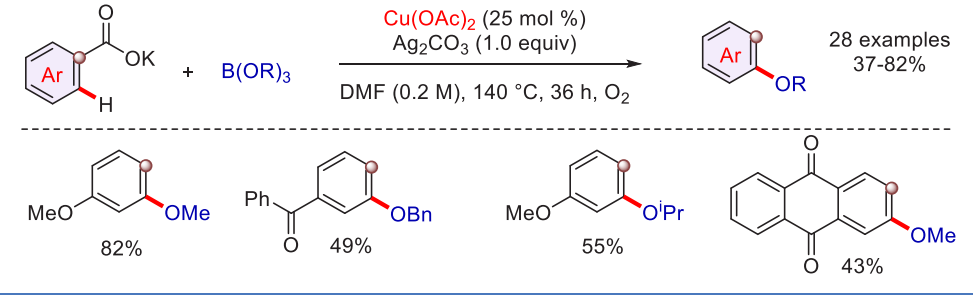
Scheme 77. Iron-Catalyzed Carbonyl-Directed *ortho*-C−H Methylation of Arenes



Scheme 78. Copper-Catalyzed C−H Hydroxylation of 2-Aryl Benzoic Acids



Scheme 79. Copper-Catalyzed Alkoxylation of Benzoic Acid Derivatives



aryl ketones and the corresponding methylated products were obtained in good yields.

3.2. C−X Bond Formation. *3.2.1. C−H Oxygenation.* Martin and co-workers described a copper-catalyzed protocol for the C(sp^2)−H hydroxylation of benzoic acid derivatives using dibenzoyl peroxide as an oxidant. The protocol is involved in two steps through annulation followed by hydrolysis under basic conditions (Scheme 78a).[174] A wide range of substituents were tolerated under the optimized conditions, and both benzolactones and hydroxylated benzoic acid derivatives were isolated in good yields. The intramolecular and intermolecular kinetic isotope experiments revealed that the C−H bond

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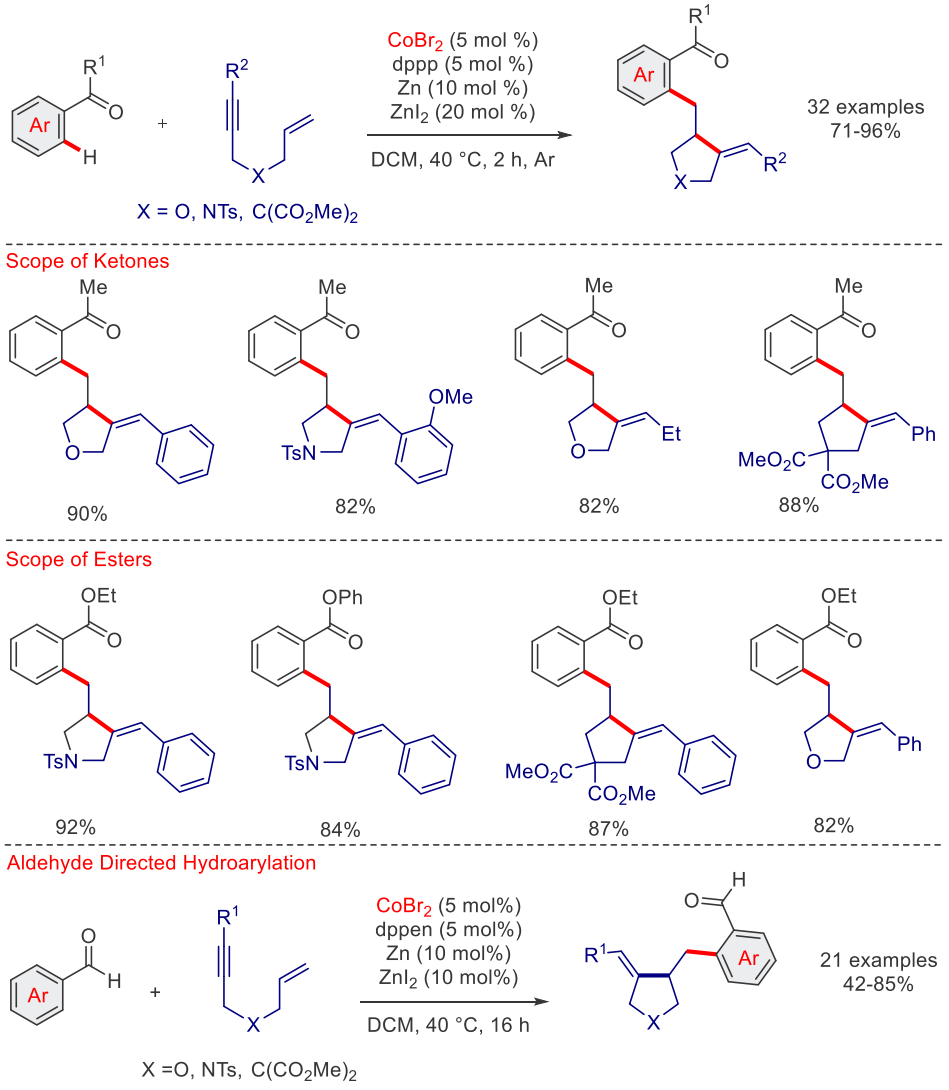
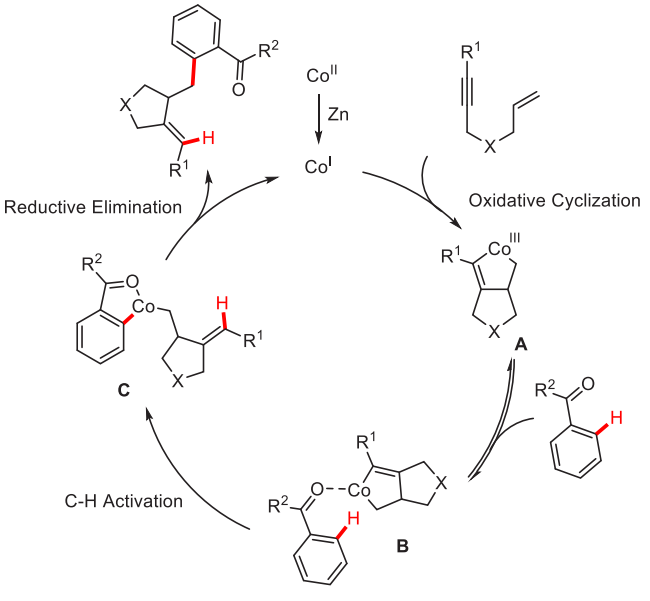
Scheme 80. Cobalt-Catalyzed Carbonyl-Directed Hydroarylation of 1,6-Enynes



cleavage was not involved in the rate-limiting step. In addition to that, the addition of radical scavenger like (2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (TEMPO), butylated hydroxytoluene (BHT) significantly inhibited the formation of benzolactones. At the same time, Gevorgyan and co-workers independently reported a similar transformation using *tert*-butyl peroxybenzoate (TBPB) as an oxidant for the synthesis of various benzolactones/benzocoumarins in good yields (Scheme 78b).[175] Further, the latter group also developed transition-metal-free, $K_2S_2O_8$-mediated transformation of aryl benzoic acids to their respective benzocoumarins in good yields. The authors claimed that the $K_2S_2O_8$-mediated protocol was better in comparison with the metal-catalyzed pathway in terms of selectivity.

In 2013, Gooßen and co-workers devised an *ortho*-selective protocol for C−H alkoxylation of aryl carboxylic acids under copper catalysis with subsequent decarboxylation (Scheme 79).[176,177] Trialkoxy boranes were used as alkoxylating agents, and silver carbonate helped in the decarboxylation as well as in the alkoxylation process. Both primary and secondary alkoxylations were achieved in acceptable yields. Benzoates bearing electron-withdrawing and electron-donating groups readily provided the desired aryl-alkyl ethers with excellent

Scheme 81. Plausible Mechanism of the Ketone-Directed Cobalt-Catalyzed Hydroarylative Cyclizations



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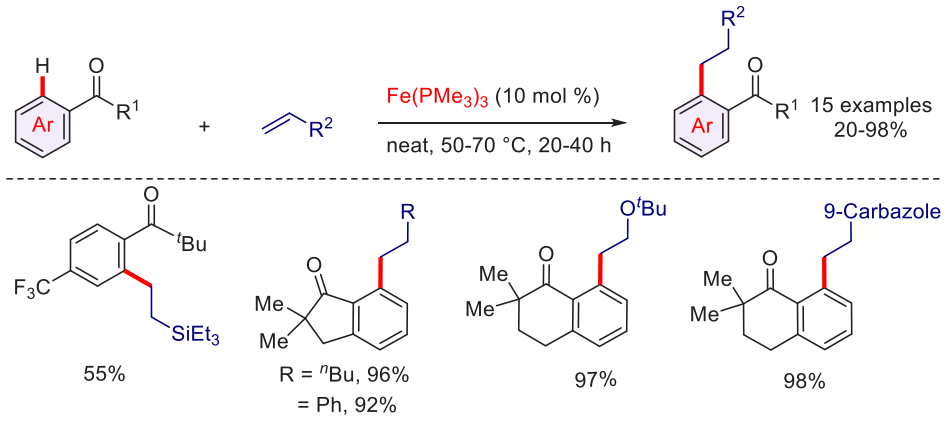
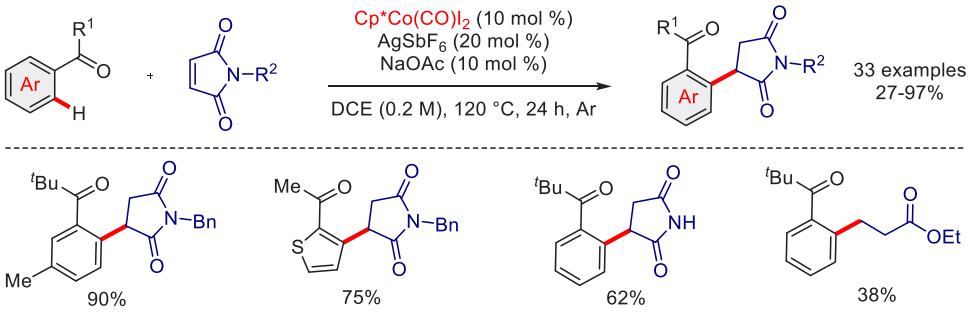
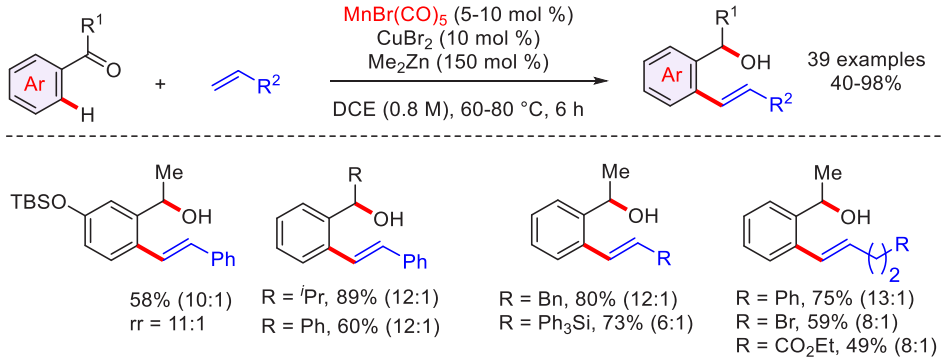
Scheme 82. Iron-Catalyzed Linear C−H Alkylation using Alkenes



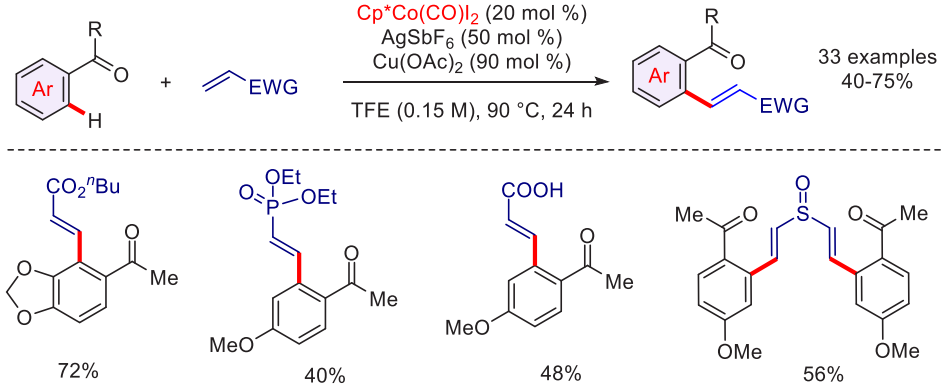
Scheme 83. Cp*Co(III)-Catalyzed C−H Bond Alkylation using Maleimides



Scheme 84. Manganese-Catalyzed C−H Olefination using Unactivated Olefins



Scheme 85. Cp*Co(III)-Catalyzed C−H Bond Olefination using Activated Olefins



functional group tolerance. On the basis of the control experiments, a reaction mechanism was proposed to proceed via the formation of Cu(III)-aryl species. Transfer of alkoxy group to Ar−Cu(III) and successive reductive elimination led to Cu(I)-*ortho*-alkoxy benzoate which upon silver-mediated decarboxylation delivered the desired alkoxy arenes.

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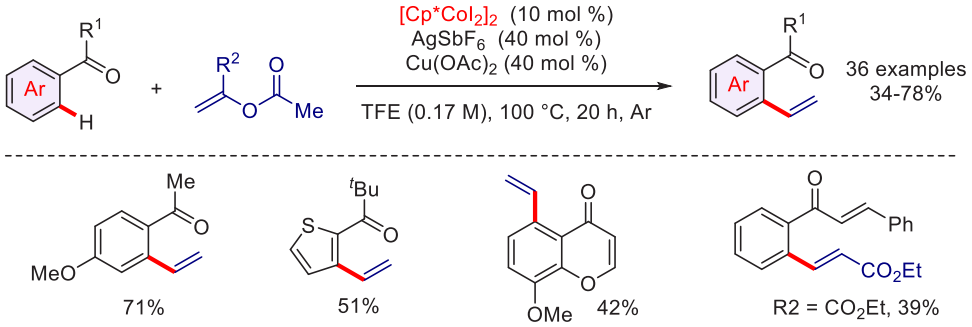
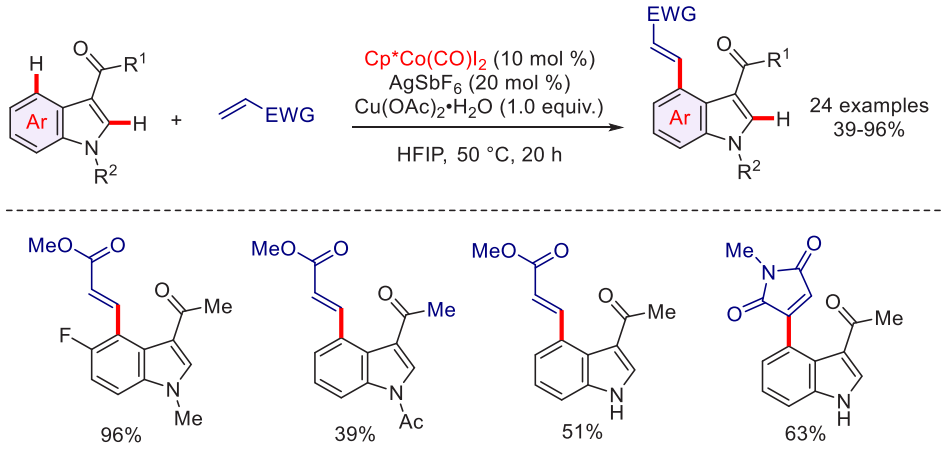
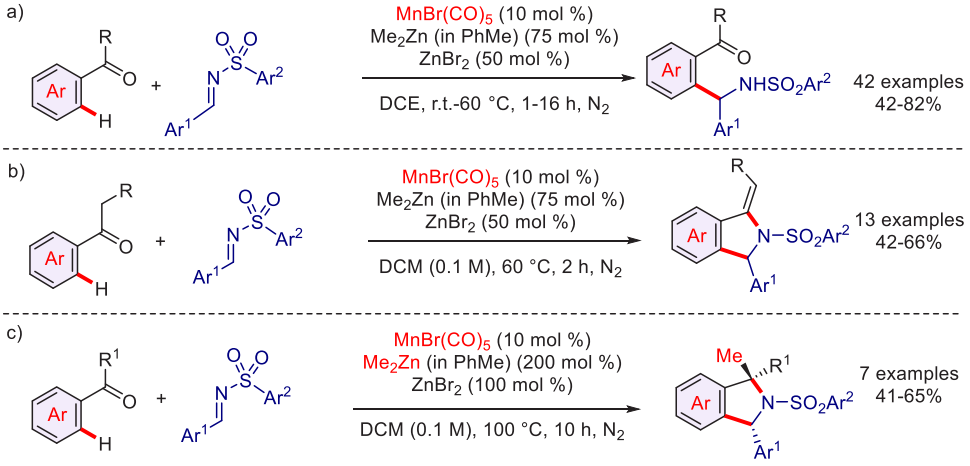
Scheme 86. Cp*Co(III)-Catalyzed *ortho* C−H Vinylation of Aromatic Ketones



Scheme 87. Cp*Co(III)-Catalyzed C-4 Olefination of 3-Acetyl Indoles



Scheme 88. Manganese-Catalyzed Aromatic C−H Addition to Imines



4. KETONE-DIRECTED C−H BOND FUNCTIONALIZATIONS

Ketones are one of the most easily accessible functional groups and provide plenty of opportunities for synthetic transformations. The acidic α-C−H bonds make the ketone a potent nucleophile; however, the electrophilic carbonyl triggers nucleophilic addition.[178]

4.1. C−C Bond Formation. *4.1.1. C−H Alkylation.* A highly chemo- and stereoselective hydroarylative cyclization of 1,6-enynes with aromatic ketones was reported by Cheng and co-workers in 2014 (Scheme 80).[179] The reaction afforded various pyrrolidine and dihydrofuran derivatives in excellent yields in the presence of 5 mol % $CoBr_2$ as catalyst, 5 mol % dppp as ligand, 10 mol % Zn as reductant, and 20 mol % ZnI_2 as additive. Enynes having aryl and aliphatic alkynes were smoothly coupled with aryl ketones to deliver the cyclized products in good yields. Interestingly, terminal alkynes were also found to be suitable for the hydroarylative cyclizations providing a regio-isomeric mixture of the products with moderate selectivity. However, 1,6-enyne bearing internal alkene failed to produce the desired product. The methodology was equally applicable to aryl esters under the same reaction conditions providing the corresponding hydroarylated products in good yields. However, when benzaldehyde was subjected under the standard conditions, hydroacylated product with 1,6 enynes were obtained along with

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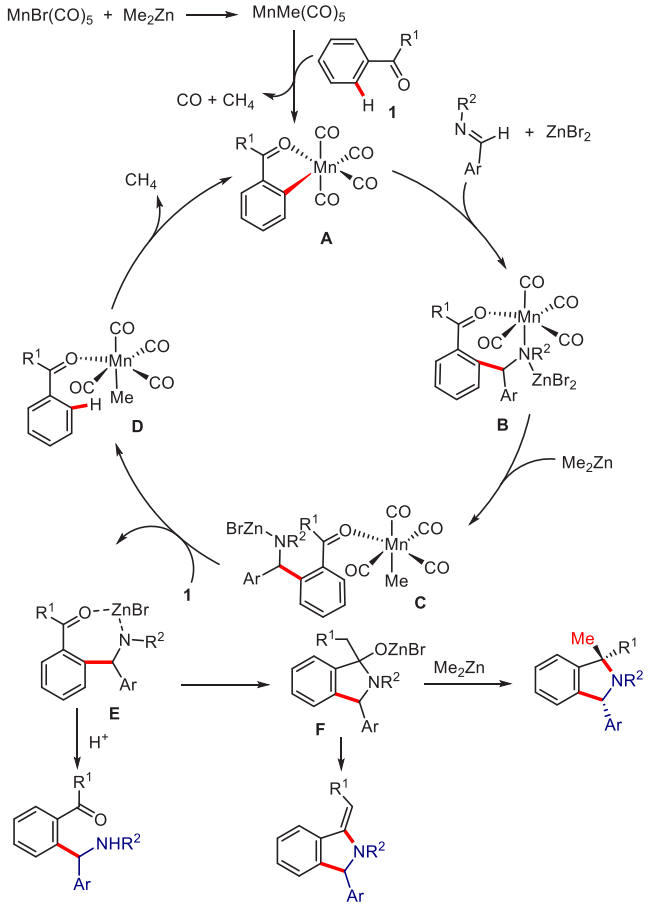
Scheme 89. Plausible Mechanism for Aromatic C−H Addition to Imines



trace amount of desired hydroarylated product. Further screening of the phosphine ligands revealed that the *cis*-1,2-*bis*(diphenylphosphino)ethylene (dppen) proved to be the best ligand and led to the formation of hydroarylated products in good yields with excellent selectivity (99:1) (Scheme 80).[180]

The authors proposed that the in situ-generated low-valent cobalt underwent oxidative cyclization with enyne, leading to Co(III) intermediate **A** (Scheme 81). Further, coordination of ketone followed by successive *ortho* C−H metalation and proton migration leads to intermediate **C** which then undergoes reductive elimination to provide the expected product and regenerates the active Co^{I} for the succeeding cycle.

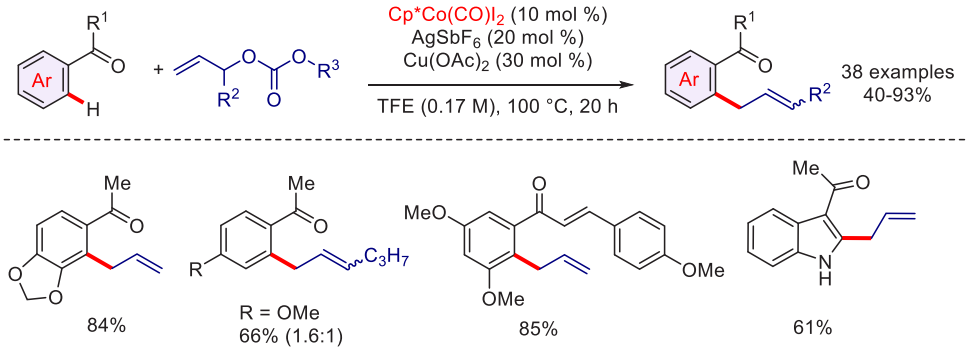
Subsequently, in 2017, Kakiuchi and co-workers reported ketone-directed *ortho* C−H alkylation using simple [Fe-$(PMe_3)_4$] as a catalyst (Scheme 82).[181] The addition of C−H bond to olefins occurs in *anti*-Makovnikov fashion leading to linear products. The reaction scope was quite wide tolerating a variety of functional groups. Notably, enol ethers and styrenes also smoothly underwent the alkylation, affording the linear products selectively in good yields. The kinetic isotope experiments indicate that the C−H activation step is not the rate-determining step. The reaction proceeded through the Fe−H pathway via a formal oxidative addition. The regioselectivity is controlled in the hydrometalation step. Although the actual reason behind the excellent selectivity in the formation of linear products is not clear, the author contemplated that the branched intermediate might be unfavored because of steric congestion around the metal center.

Later, Cp*Co(III) catalyzed *ortho* C−H alkylation of ketones employing bioactive maleimides as alkylating agents was accomplished by Sundararaju and co-workers as shown in Scheme 83.[182] Several aryl alkyl ketones including commercially available acetophenone derivatives smoothly afforded *ortho* alkylated ketones under redox-neutral conditions. The alkylation was not only limited to ketones and maleimides but also extended to other electron-deficient olefins such as acrylates and aryl esters as substrates for C−H bond alkylation. The protocol was also extended to aryl esters derivatives, and the *ortho* corresponding alkylated products were isolated in acceptable yields.

4.1.2. C−H Olefination. Olefination of C−H bonds is one of the facile ways to introduce functional groups into molecules. In this regard, in 2018, Wang and co-workers reported manganese catalyzed redox neutral olefination using unactivated olefins (Scheme 84).[183] The carbonyl moeity has been used as a weakly coordinating directing group as well as hydrogen acceptor. The protocol was well tolerated with diverse functional groups, and several long-chain unactivated aliphatic alkenes, styrenes, and vinyl silanes were amenable with excellent *E*/*Z* selectivity. The authors proposed that the Mn−Zn bimetallic synergistic pathway is key for C−H bond activation which proceeds via unique concerted *bis*-metalation and deprotonation (BCMD) pathway.

Subsequently, oxidative *ortho*-olefination of aryl ketones was achieved by Maji and co-workers using activated olefins that include acrylates, vinyl sulfones, and vinyl sulfonates as shown in Scheme 85.[184] Bioactive molecules such as indanone, a γ-PPAR antagonist, were synthesized using this protocol. The higher reactivity of electron-rich ketones as compared with electron-poor ketones suggested involvement of base-assisted intra-

Scheme 90. Cp*Co(III)-Catalyzed Ketone-Directed C−H Allylation of Arenes



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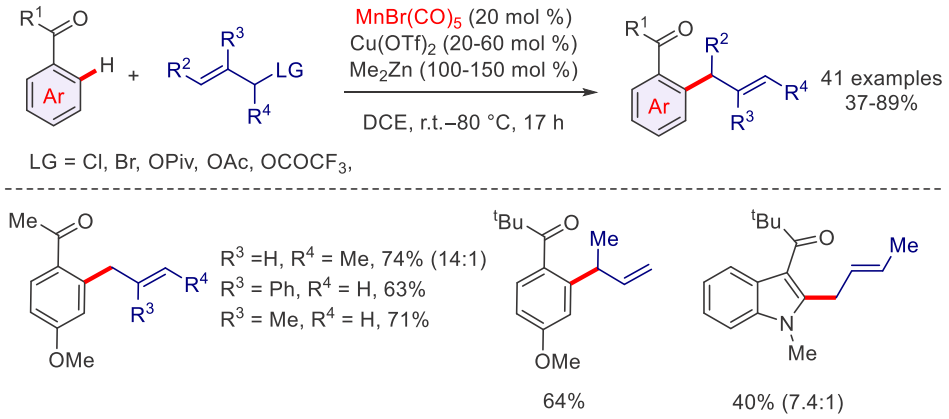
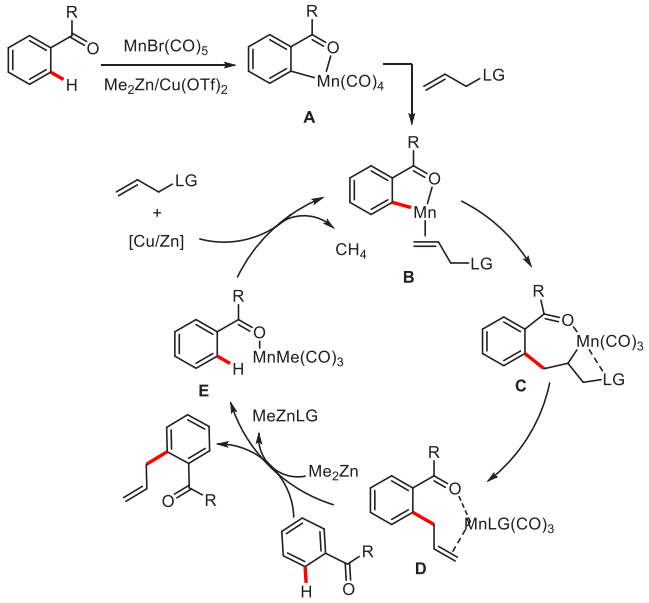
Scheme 91. Manganese-Catalyzed Ketone-Directed C−H Allylation of Arenes



Scheme 92. Plausible Mechanism of the Manganese-Catalyzed C−H Allylation



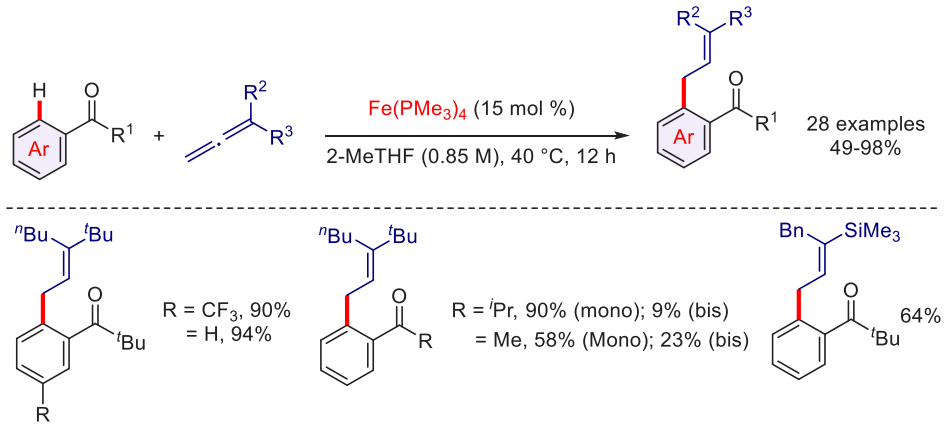
molecular electrophilic type of C−H activation. The C−H bond activation step might not be the rate-limiting step as a small KIE value was obtained in both parallel (k_H/k_D = 1.3) and intermolecular competitive (k_H/k_D = 1.9) kinetic isotope effect experiments.

Subsequently, the same group disclosed a straightforward *ortho*-vinylation of aryl ketones under similar conditions using vinyl acetates under Cp*Co(III)-catalysis (Scheme 86).[185] The vinylated products were utilized in the synthesis of indanone and α-naphthol along with the formal synthesis of natural product bruguierol A. The formation of five-membered cyclometalated intermediate and alkene inserted cyclometalated intermediate were detected by LCMS analysis.

Very recently, Ravikumar and co-workers reported an unusual Cp*Co(III)-catalyzed C-4 olefination of 3-acetyl indoles with activated olefins (Scheme 87).[186] The stoichiometric amount of Cu(II) or Ag(I) is required for the above said oxidative olefination. The preliminary studies suggest that the C−H cleavage step is reversible. The origin of exclusive C-4 selectivity was not well understood, and further studies are required to probe the selectivity.

4.1.3. C−H Addition to Imine. In 2017, Wang and co-workers unveiled the first ketone-directed catalytic C−H bond functionalization using earth-abundant 3d metal. In this report, they described the addition of aromatic C−H bond to imines with the assistance of ketone using manganese catalyst (Scheme 88).[187] Remarkably, the addition of manganese catalyst completely suppressed the competing Mannich reaction. The authors demonstrated three different types of products by altering the reaction conditions that allow them to access *ortho*-C−H aminoalkylated ketones, cyclized exo-olefinic isoindolines,

Scheme 93. Fe-Catalyzed Ketone-Directed Hydroarylation of Allenes



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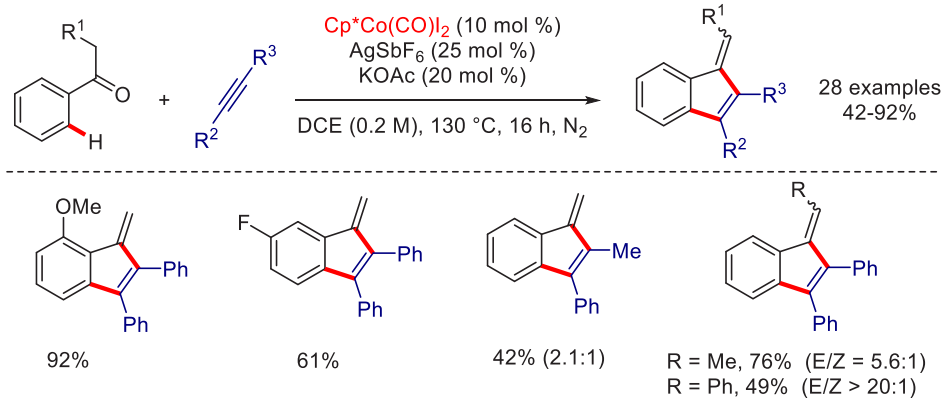
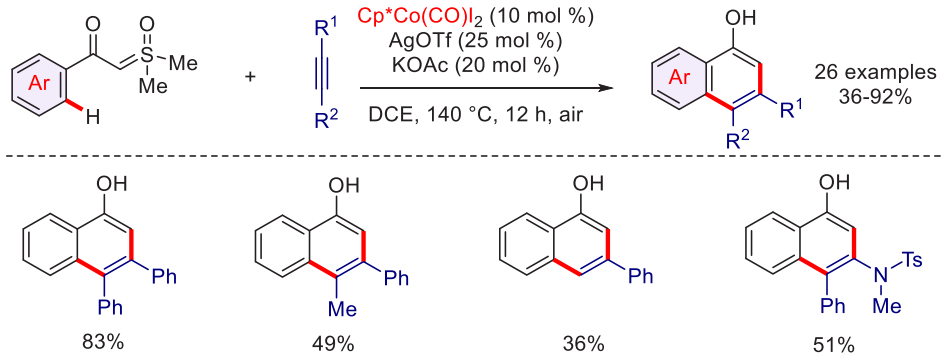
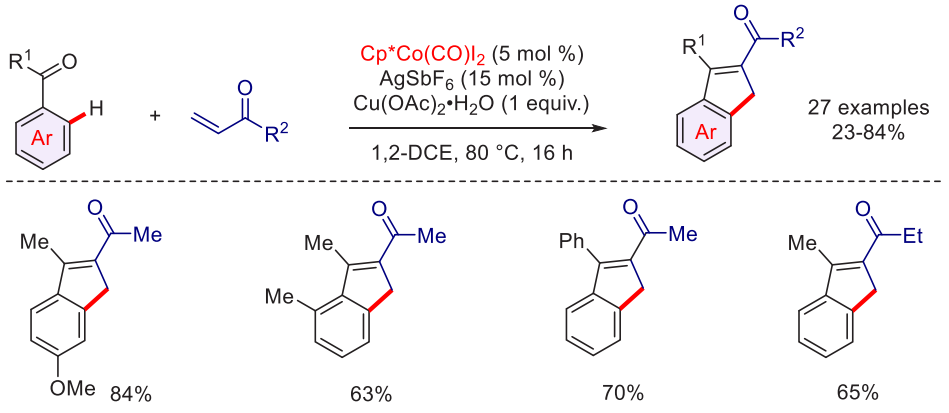
Scheme 94. Cp*Co(III)-Catalyzed Synthesis of Benzofulvenes



Scheme 95. Cp*Co(III)-Catalyzed Synthesis of Substituted Naphthols



Scheme 96. Cp*Co(III)-Catalyzed Synthesis of Indene Derivatives



and three components methylated isoindolines with various aromatic aldimines.

On the basis of the preliminary mechanistic experiments, the authors proposed a plausible pathway as illustrated in Scheme 89. The reaction of Me_2Zn with $MnBr(CO)_5$ produce $MnMe(CO)_5$*in situ*, which further reacts with a ketone to yield manganacycle **A** along with liberation of methane and CO. The addition of imine to **A** led to seven-membered manganacycle **B** which upon transmetalation with Me_2Zn provides an intermediate **C**. This further underwent ligand exchange with the ketone substrate to form an intermediate **D** with subsequent release of Zn coordinated intermediate **E**. Then, intramolecular C−H bond activation in the intermediate **D** regenerates the intermediate **A** by releasing methane. Protonolysis of intermediate **E** deliveres the *ortho*-C−H aminoalkylated ketone. Alternatively, intramolecular cyclization in intermediate **E** leads to **F** which upon release of zinc salt provides exo-olefinic isoindoline. The intermediate **E** can further undergo intermolecular nucleophilic substitution with Me_2Zn to provide methylated isoindoline.

4.1.4. C−H Allylation. Allylated ketones are quite useful substrates in synthetic organic chemistry. Cp*Co(III)-catalyzed *ortho*-selective allylation of aryl ketones using allyl carbonates was accomplished by Maji and co-workers in 2018 (Scheme 90).[188] Various arenes and heteroarenes were successfully functionalized, and the authors proposed that the reaction proceeded via *β*-oxygen elimination as one of the key steps. Some of the allylated products were further diversified to various medicinally important scaffolds.

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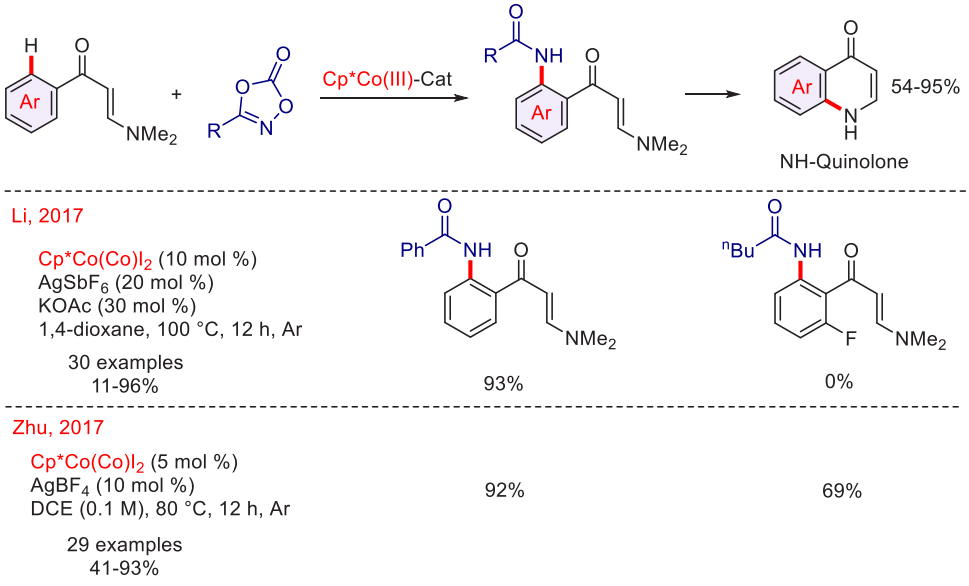
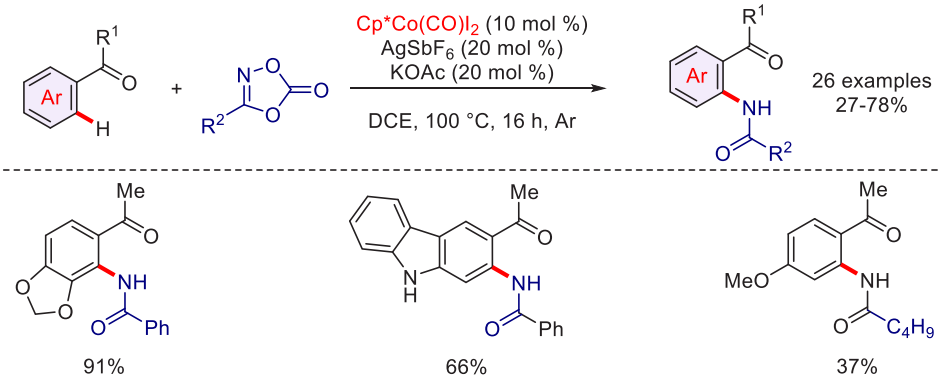
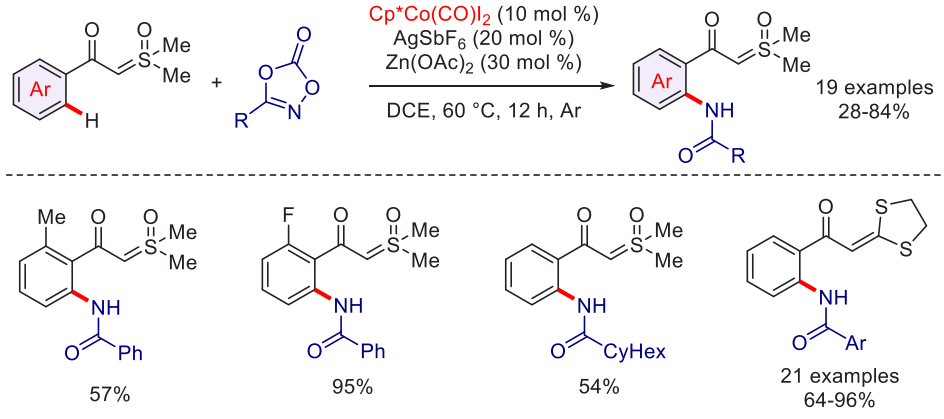
Scheme 97. Cp*Co(III)-Catalyzed Enaminone-Directed C−H Amidation using Dioxazolones



Scheme 98. Ketone-Directed Cp*Co(III)-Catalyzed *ortho*-C−H Bond Amidation using Dioxazolones



Scheme 99. Cp*Co(III)-Catalyzed *ortho*-C−H Amidation of Sulfoxonium Ylides and Ketene Dithioacetals



In 2019, Wang and co-workers demonstrated an elegant strategy to synthesize *ortho*-allylated aryl ketones using environmentally benign manganese catalyst (Scheme 91).[189] The protocol considers allyl chlorides as the most effective allylating agent among others. Using $Cu(OTf)_2$ as an additive, the authors could completely suppress the formation of aldol-type products. The reaction proceeds with complete S_N2' selectivity. Notably, the protocol was compatible with challenging allylic electrophiles and α-, β-, or γ-substituted electrophiles, rendering the allylated products with excellent selectivity. In addition to aryl ketones, the methodology was equally suitable to heteroaryl ketones.

As shown in Scheme 92, the proposed mechanism begins with the formation of five-membered manganacycle **A** through sequential ligand exchange followed by C−H activation. Coordination of the olefin from the allylic substrate through ligand exchange with CO and subsequent insertion generates the seven-membered manganacycle **C**. β-Oxygen elimination in

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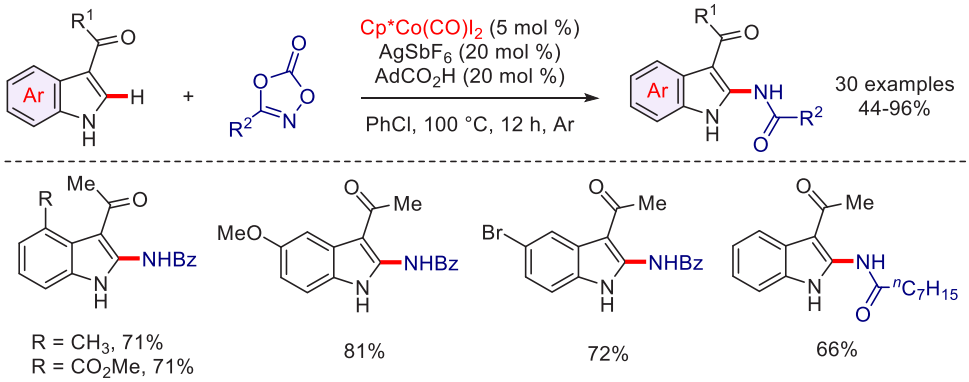
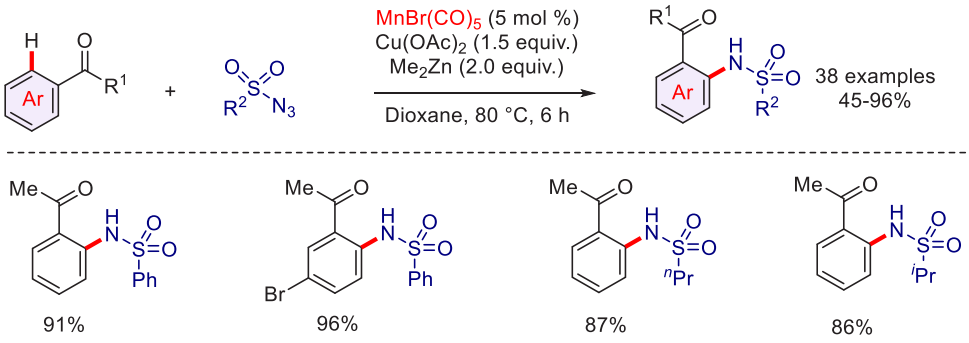
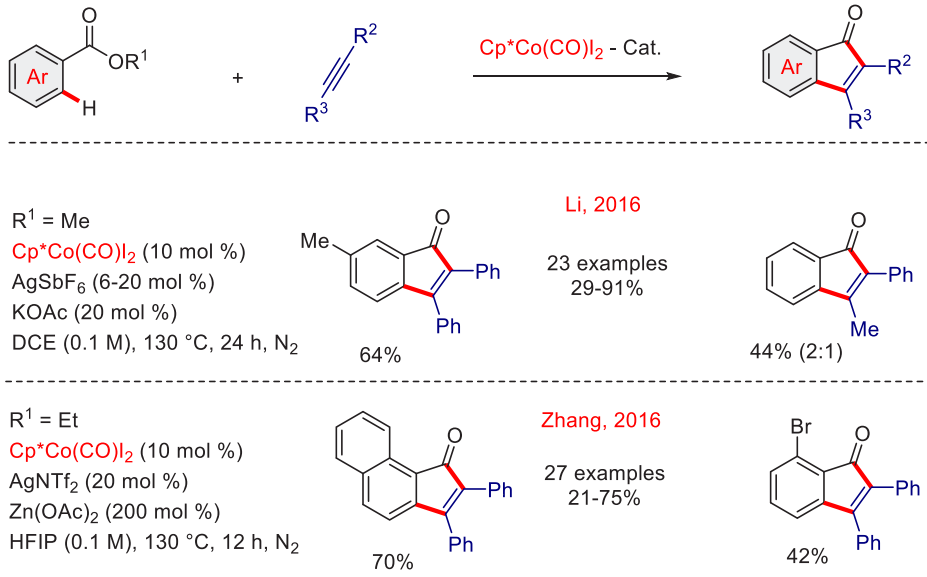
Scheme 100. Ketone-Directed C-2 Amidation of Indole using Dioxazolones



Scheme 101. Manganese-Catalyzed C−H Amidation of Aryl Ketones with Sulfonyl Azides



Scheme 102. Cp*Co(III)-Catalyzed Synthesis of Indenones



the intermediate **C** and ligand exchange with unreacted aryl ketone leads to intermediate **F**. This further generates the manganacycle **B** upon coordination with alkene.

Inspired from the work of Kakiuchi, Ackerman, and co-workers demonstrated the hydroarylation of allenes with aryl ketones under low-valent iron-catalysis (Scheme 93).[190] Remarkably, the hydroarylation proceeds through the selective insertion process, and therefore, complete control in product selectivity was observed. The allylated products were afforded in good yields with excellent functional group tolerance. They further demonstrated that selective *mono*-allylation can be achieved by using the allenes as a limiting reagent. Various terminal allenes having bulky substituents were amenable; however, the scope of mono- and disubstituted allenes was limited.

4.1.5. Annulation Reaction. Recently, with growing interest of ketone as directing group for the site-selective C−H bond functionalizations under high-valent cobalt catalysis, Tan and co-workers disclosed an elegant report on the synthesis of benzofulvenes via ketone-directed C−H bond alkenylation/

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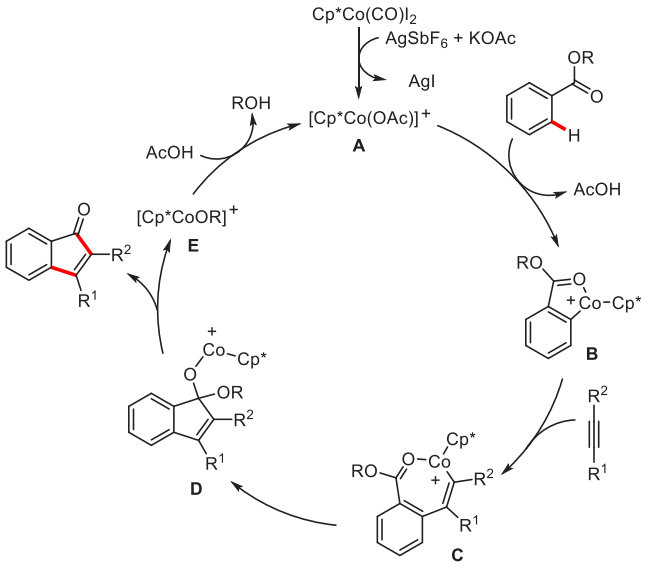
Scheme 103. Proposed Mechanism for the Synthesis of Indanones



nucleophilic-addition/dehydration cascade (Scheme 94).[191] The protocol displayed a wide scope of aryl ketones with good tolerance of functional groups. Unfortunately, terminal alkynes and *bis*-aliphatic internal alkynes did not furnish the desired products. Interestingly, the synthesis of similar benzofulvenes via cyclodimerization of alkynes in slightly different conditions using a cobalt catalyst was also demonstrated. According to the proposed mechanism, ketone directed C−H bond activation, alkyne insertion, and nucleophilic addition of alkenyl−Co(III) into an electrophilic carbonyl, and the subsequent proto-demetalation afforded the desired product after dehydration of tertiary alcohol.

On a similar note, Zhu and co-workers explored the synthesis of 3,4-disubstituted α-naphthol starting from sulfoxonium ylides and internal alkynes using Cp*Co(III)-catalyst (Scheme 95).[192] Notably, the strategy was suitable to terminal alkynes as well as ynamides, albeit in low yields.

Very recently, Dethe and co-workers reported a ketone directed C−H alkylation/aldol condensation cascade sequence for the synthesis of indenes (Scheme 96).[193] Similar to previous work on ketone-directed, Cp*Co(III)-catalyzed C−H bond functionalizations, electron-rich aryl ketones were more reactive than electron-poor ones. The C−H cleavage step was reversible as apparent from the deuterium scrambling study.

4.2. C−X Bond Formation. *4.2.1. C−H Bond Amidation.* In 2017, Li[194] and Zhu[195] and co-workers independently introduced enaminones as potent directing group for the C−H amidation using dioxazolones under Cp*Co(III)-catalysis (Scheme 97). The presence of electron-releasing group in the enaminone makes the carbonyl group more polarized, which favors the coordination of metal to the carbonyl. Wide scope of dioxazolones and enaminones were displayed in both protocols. In addition to the diverse scope of the reactions, the aminated products were utilized in the synthesis of *NH*-isoquinolones which are profound in many drugs like norfloxacin, nedocromil, and so on.

In 2018, Maji and co-workers achieved ketone-directed *ortho*-amidation of arenes under Cp*Co(III)-catalysis using dioxazolones as amidating agent (Scheme 98).[196] It is evident from the substrate scope that the reactivity of electron-rich ketones are much higher compared to electron-deficient ketones in affording the desired amidated products. In addition to its wide scope, the synthesis of acridone alkaloids were also demonstrated using this methodology.

In continuation, Li and co-workers reported cobalt(III)-catalyzed *ortho* C(sp^2)−H amidation of weakly coordinating sulfoxonium ylides and α-benzoylketene dithioacetals using dioxazolone under mild conditions (Scheme 99).[197] The catalytic condition was suitable to a wide variety of substrates and produced corresponding amidated products in acceptable yields.

Later, Wang and co-workers reported a Co(III)-catalyzed C-2 amidation of unprotected indoles using dioxazolones (Scheme 100).[198] The selectivity obtained in this process is in contrast with the previous findings on C−H olefination by Ravikumar and co-workers on C(4)−H bond olefination of indole.

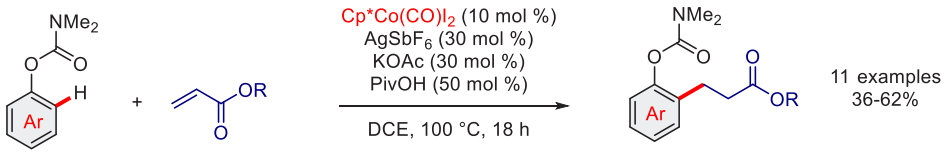
In the meantime, Xu and co-workers delineated a manganese-catalyzed efficient *ortho*-amidation of weakly coordinating aryl ketones using sulfonyl azides as amidating agent (Scheme 101).[199] This is the first example of ketone directed C−H amidation under base-metal catalysis. During the optimization of the reaction, the authors found that the choice of solvent is very important in the success of the reaction. A variety of acetophenones, ketones having long aliphatic chain, cyclic ketones were amidated with good yields. The other weakly coordinating directing groups such as aldehyde, ester, amide were not suitable for this transformation under the optimized conditions. In addition to aromatic sulfonyl azide, aliphatic sulfonyl azide was also tolerable, affording the corresponding amidated products with excellent yields.

5. ESTER-DIRECTED C−H BOND FUNCTIONALIZATIONS

Like other carbonyl functional groups, esters synthetically can also be transferred to various useful functionalities with great ease. Often esters are also serve as useful protecting groups in the synthesis of complex molecules.

5.1. C−C Bond Formation. *5.1.1. Annulation Reactions.* In 2016, Li[200] and Zhang[201] independently developed an efficient strategy toward the synthesis of medicinally important indenones through the annulation of benzoates with internal alkynes (Scheme 102). The stereoelectronic effect of the leaving group has an important role in the success of the reaction. For example, esters bearing electron-withdrawing functional groups were found to be less reactive compared with esters bearing electron-donating groups. Various symmetrical diaryl alkynes

Scheme 104. Cp*Co(III)-Catalyzed Carbamate Directed C−H Alkylation



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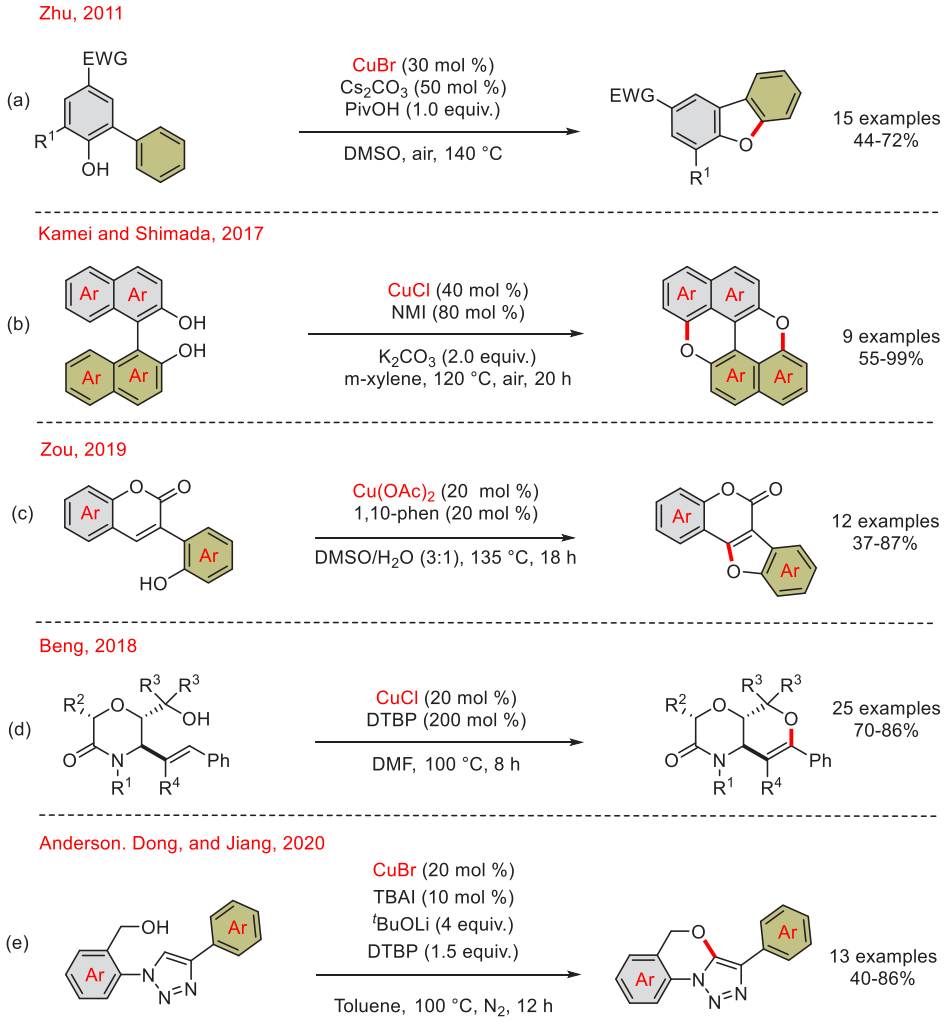
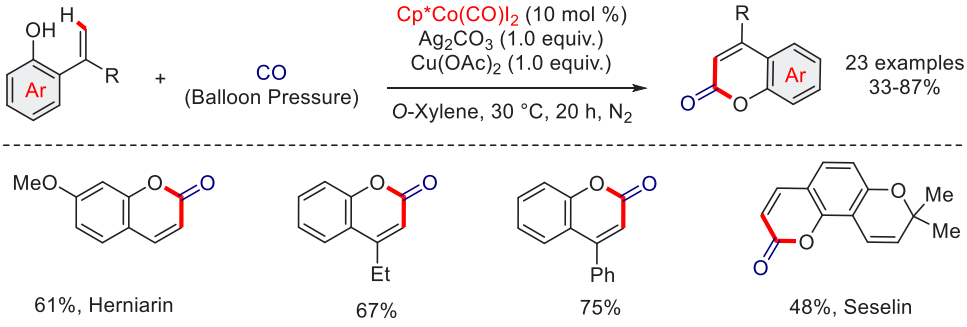
Scheme 105. Copper-Catalyzed Oxidative C−H/C−O Cyclization



Scheme 106. Cp*Co(III)-Catalyzed Annulation of 2-Alkenyl Phenols with CO



were suitable in delivering the product with good yields; however, terminal and internal dialkyl alkynes did not produce satisfactory result under the optimized conditions. Notably, Cp*Rh(III) was not effective in annulation reaction under the optimized conditions. The authors reasoned that the higher nucleophilicity of alkenyl−Co(III) species than that of alkenyl−Rh(III) is attributed to the unique reactivity of Cp*Co(III)-catalyst.

On the basis of the mechanistic studies, a plausible pathway as proposed by the authors is depicted in Scheme 103. First, the precatalyst undergoes ligand substitution with the aid of $Zn(OAc)_2$ and $AgNTf_2$ to provide cationic cobalt species **A**, which further experience ligand exchange and is followed by C−H bond activation leading to five-membered metalacycle **B**. The coordination alkyne to cobalt-center and subsequent insertion and nucleophilic addition of alkenyl−Co(III) species to carbonyl provided the intermediate **D** via intermediate **C**. Finally, alkoxy elimination from complex **D** generates the products and release cobalt alkoxide complex which upon protodemetalation regenerates the active cobalt cationic complex **A**.

5.1.2. C−H Alkylation. Subsequently, Maji and co-workers utilized carbamate as a suitable directing group for *ortho* alkylation of phenols under cobalt catalysis (Scheme 104).[202]

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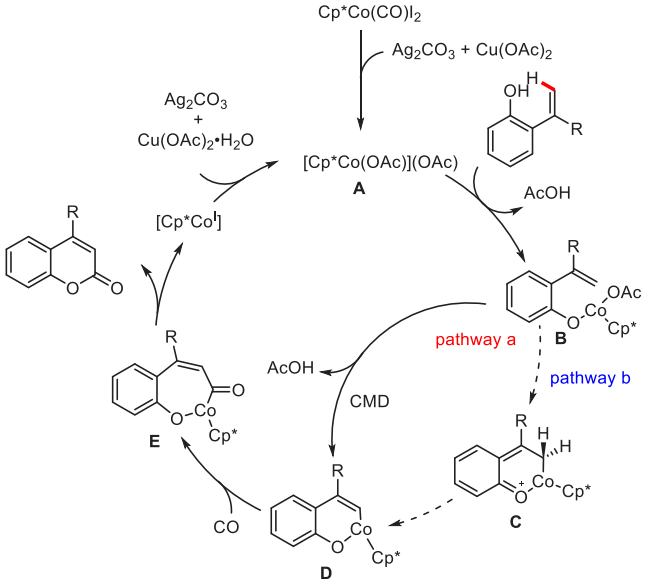
Scheme 107. Plausible Mechanism of Cp*Co(III)-Catalyzed Carbonylation



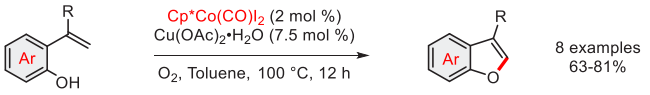
Interestingly, the scope was extended to BINOL and SPINOL carbamate derivatives, delivering the corresponding alkylated products in acceptable yields.

6. HYDROXY-DIRECTED C−H BOND FUNCTIONALIZATIONS

6.1. C−C Bond Formation. *6.1.1. Annulation Reaction.* Phenolic compounds are quite useful building blocks in synthetic organic chemistry. They are often found in medicinally important molecules and natural products. In addition to their wide synthetic importance, they manifest weak coordination to transition metal and are used as directing group to carry out various C−H bond transformations.

In 2011, Zhu group described a copper-catalyzed oxidative C(sp^2)−H cycloetherification of *o*-arylphenols for the preparation of various dibenzofuran derivatives in moderate-to-good yields (Scheme 105a).[203] Author claimed that the presence of electron-withdrawing group like $-NO_2$, −CN, and −CHO at the *para*-position of hydroxy group is important to suppress the oxidation of the substrates. Based on the mechanistic investigations, the authors proposed a irreversible rate-limiting concerted metalation and deprotonation pathway for the C−H bond activation step and subsequent reductive elimination to obtain the dibenzofuran derivatives. Similarly, Kamei and

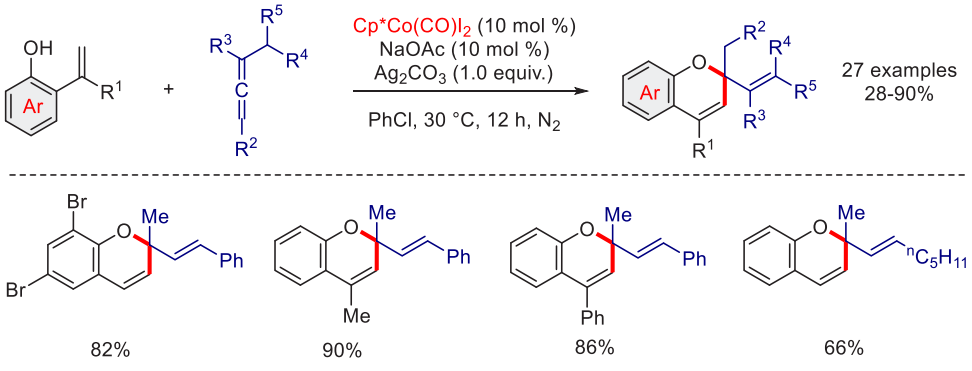
Scheme 109. Oxidative Synthesis of Benzofurans Catalyzed by Cp*Co(III)



Shimada disclosed copper-catalyzed C−H/C−O cyclization of 2,2′ -binapthols using air as an oxidant. The cyclization provided a practical and simple way to access various electronically important *peri*-xanthenoxanthene (PXX) derivatives with good-to-excellent yields (Scheme 105b).[204] The authors also showed that the corresponding PXX molecule could be directly accessed from the 2-napthol at slightly elevated temperature. On the basis of the mechanistic investigations, the authors proposed a radical pathway for this transformation. Later in 2019, Zou and co-workers developed a copper-catalyzed efficient protocol for the synthesis of coumestans from readily available 2-hydroxyl-3-arylcoumarins via cross dehydrogenative C−O coupling reactions (Scheme 105c).[205] The authors successfully implemented this versatile protocol in the synthesis of various natural products such as coumestrol, 9-methoxy-coumestrol, 8,9-dimethoxy-coumestrol, medicagol, and flemichapparin C. In a similar note, copper-catalyzed dehydrogenative C−H alkoxylation of morpholinolyl alkenols were accomplished by Beng and his co-workers using di-*tert*-butyl peroxide (DTBP) as an oxidant (Scheme 105d).[206] The protocol was extended for the synthesis of various spiro-tricyclic dihydropyrans and of *trans*-fused bicyclic morpholines with good yields. Notably, 6-endo cyclization was preferred over the 5-exo cyclization irrespective of the substituents present in the alkenes. Later, Jiang and co-workers reported the synthesis of tricyclic triazole-benzoxazines through copper-catalyzed intramolecular triazole C−H alkoxylation (Scheme 105e).[207] The antifungal properties of the synthesized compounds were tested against *F. oxysporum*, *F. solani*, and *C. destructans* and showed promising levels of inhibition of *F. oxysporum* compared to existing antifungal agents

In 2015, Wang and co-workers reported a straightforward synthesis of coumarin via carbonylation of vinylphenol using carbon monoxide (Scheme 106).[208] They utilized Cp*Co-$(CO)I_2$ as catalyst along with Ag_2CO_3 and $Cu(OAc)_2$ as oxidant as well as carboxylate source. The reaction works under very mild condition with an atmospheric pressure of CO and exhibited wide scope of vinyl as well as 1,1-disubstituted alkenyl phenols with good functional group tolerance. The presence of *ortho*-substituent at the substrate imparts steric crowding during

Scheme 108. Cp*Co(III)-Catalyzed [5 + 1] Annulation of Vinyl Phenols with Allenes



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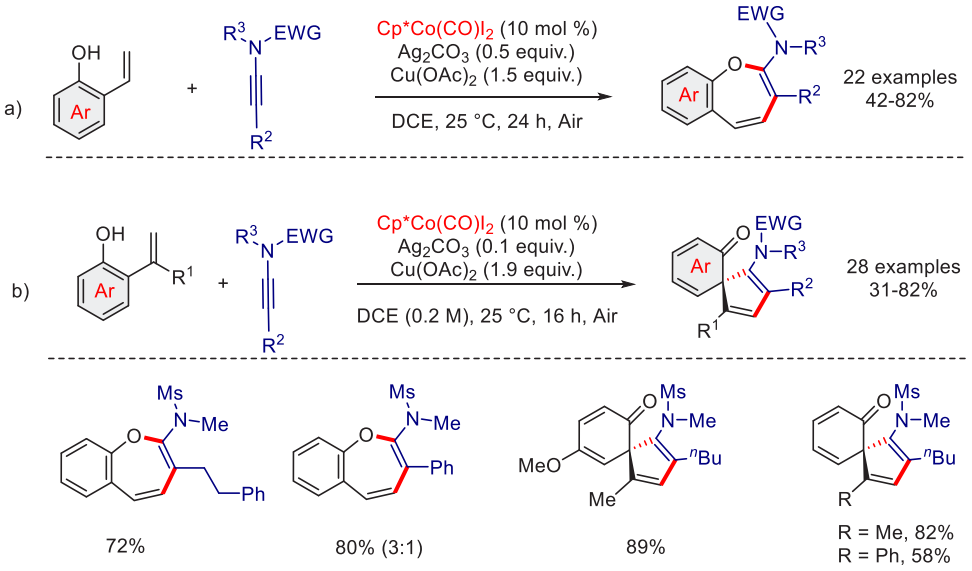
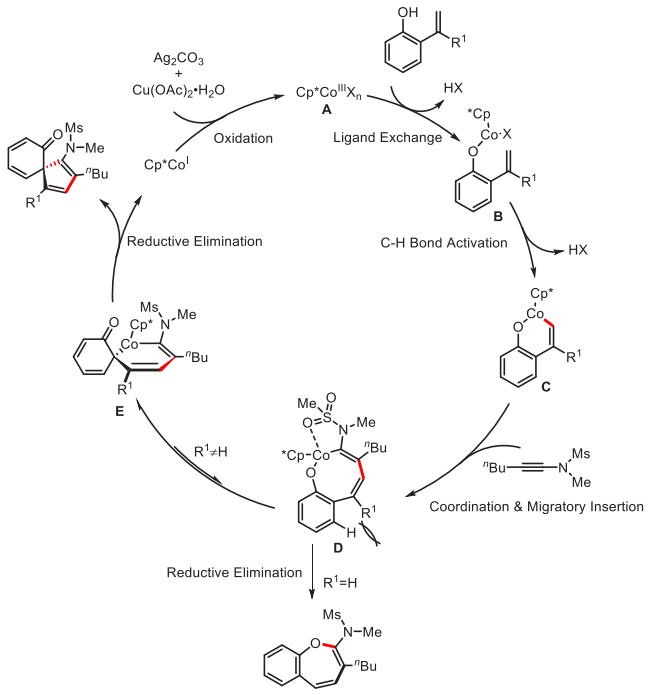
Scheme 110. Cp*Co(III)-Catalyzed Oxidative Annulation of 2-Alkenyl Phenols with Ynamides



Scheme 111. Proposed Mechanism for Oxidative Annulation with Ynamides



cyclometalation and thus lowers the yield of the product. The methodology was further utilized for the total synthesis of natural products like xanthyletin and seselin in moderate yields.

The plausible pathway commences with the formation of active catalyst **A**, which undergoes ligand exchange with the substrate providing intermediate **B** (Scheme 107). Now the concerted-metalation and deprotonation lead to cobaltacycle **D** which also can be formed by intramolecular electrophilic attack of the conjugated alkene to Cp*Co(III) and subsequent deprotonation. The higher value of 3.4 through parallel KIE experiments suggests that the pathway (a) is more probable. Further coordination of CO to cobalt led to intermediate **D** and subsequent insertion and reductive elimination produces the desired carbonylated product and releases Cp*Co(I). Subsequently regeneration of the active catalyst **A** was achieved either by Ag(I) and Cu(II).

In 2016, Cheng and co-workers described an elegant example of hydroxy-directed Cp*Co(III)-catalyzed [5 + 1] annulation of vinyl phenols with allenes (Scheme 108).[209] The choice of acetate and oxidant was vital to access the desired cyclized product in good yield as evident from the reaction optimizations. Various 2H-chromones derivatives were synthesized using this protocol in good-to-excellent yield. Importantly, the strategy was also suitable to 2-alkenyl phenol bearing alkyl/aryl substituents at the α-position and led to the corresponding products in excellent yields. However, 2-alkenyl phenol having substituents at the β-position failed to deliver the desired product. Various *mono*- and *di*-substituted allene were effective under optimal conditions. Unfortunately, allene bearing tertiary carbon at the α-position furnished only a trace amount of desired product. Based on the control experiments, a plausible reaction pathway involves hydroxy directed vinylic C−H bond activation, regioslective insertion of allene, and intramolecular nucleophilic attack by phenoxide to the π-allylic carbon.

In 2016, Anbarasan and co-workers reported the synthesis of benzofuran through Cp*Co(III)-catalyzed cross dehydrogenative C−H/O−H coupling of *ortho* alkenyl phenol (Scheme 109).[210] The protocol efficiently afforded the synthesis of various substituted benzofurans in good yields under oxidative conditions.

Later, Li and co-workers explored the reactivity of the ynamides as coupling reagent in an annulation reaction with 2-alkenyl phenols using $Cp^*Co(CO)I_2$ as a catalyst (Scheme 110). The annulation of vinylphenols with ynamides provided access to a wide variety of benzoxepine derivatives in good yields (Scheme 110a).[211] The aliphatic ynamides were more efficient in delivering the benzoxepines with better yields compared with aromatic ynamides. In contrast, 2-vinylphenol bearing an additional substituent at the internal carbon of alkene did not undergo [5 + 2] annulation with aliphatic yanmides to give benzoxepines, rather it delivered spiro-[4,5]decanes via dearomative oxidative [3 + 2] annulations under almost similar conditions (Scheme 110b).[212] However, the aromatic ynamides were not suitable for the spiroannulation.

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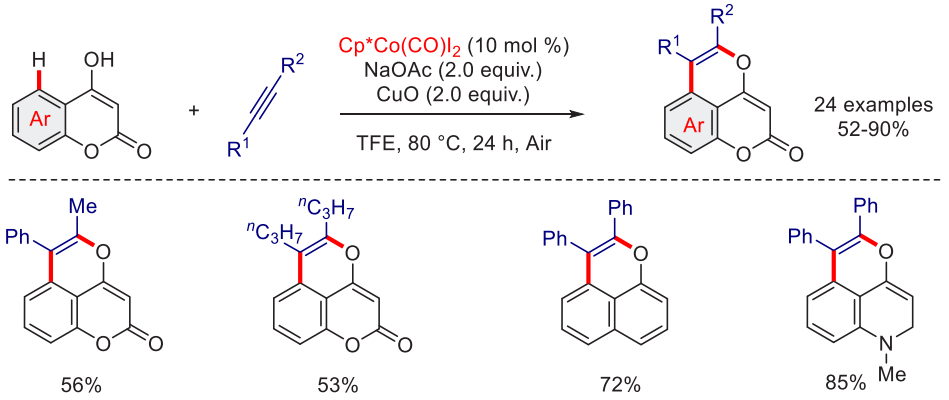
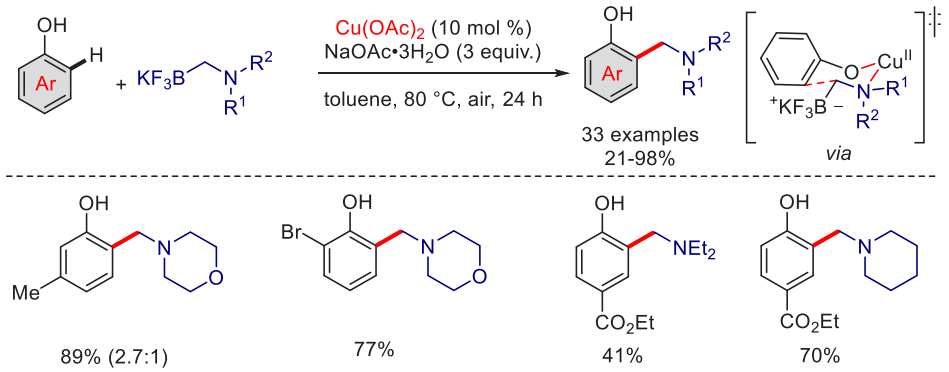
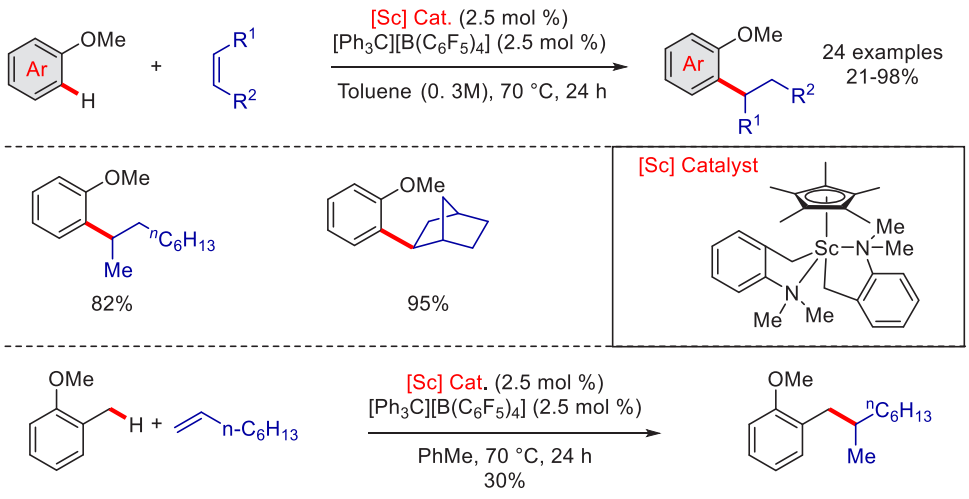
Scheme 112. Cp*Co(III)-Catalyzed Synthesis of Polycyclic Pyrans



Scheme 113. Copper-Catalyzed C−H Aminomethylation of Free Phenols using Trifluoroborate Salts



Scheme 114. Alkoxy-Directed Scandium-Catalyzed C−H Alkylation of Anisoles



According to the authors proposed mechanism as shown Scheme 111, the reaction proceeds through six-membered cyclometalated intermediate **C** via C−H activation. Alkyne coordination followed by migratory insertions leading to intermediate **D**. Now the reaction pathway depends on the substituents present in 2-alkenyl phenol. Presence of substituents at the internal carbon of 2-vinylphenol experiences severe steric repulsion and hence it isomerizes to intermediate **E**, which upon reductive elimination delivers the spiro annulated product. In other words, the intermediate **D** might release the final product benzoxepines upon reductive elimination.

In 2019, Sen and co-workers disclosed Cp*Co(III) catalyzed synthesis of fully decorated pyran[2,3,4-de]chromene-2-one derivatives at relatively mild conditions (Scheme 112).[213] 4-Hydroxycoumarin derivatives smoothly underwent hydroxy directed [4 + 2] annulation with alkynes in the presence of 10 mol % $Cp^*Co(CO)I_2$, 2 equiv of NaOAc, and 2.0 equiv of CuO in TFE, rendering the substituted pyran derivatives in good yields. The protocol works equally well with 1-naphthols to obtain corresponding pyran derivatives.

6.1.2. C−H Aminomethylation. The Wang group developed a copper-catalyzed *ortho*-aminomethylation of free phenols using aminomethyltrifluoroborates (Scheme 113).[214] A variety

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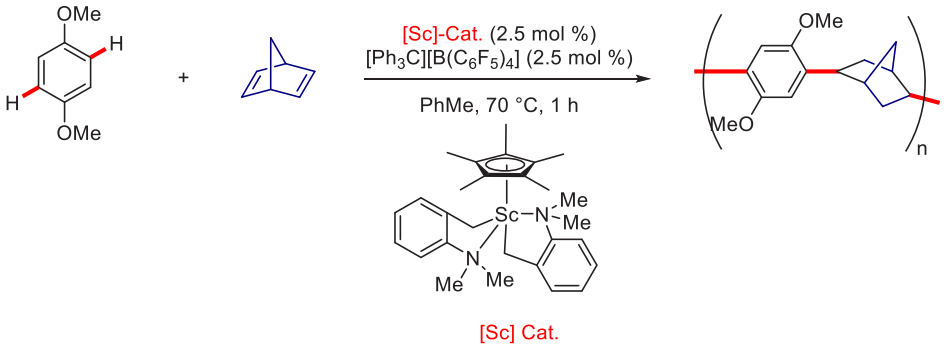
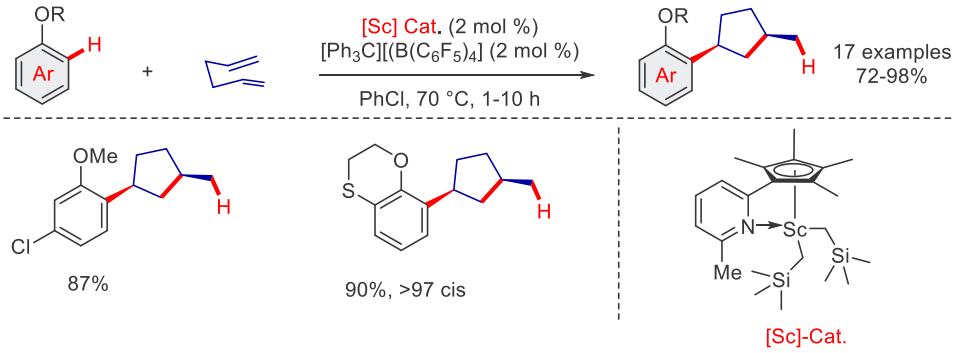
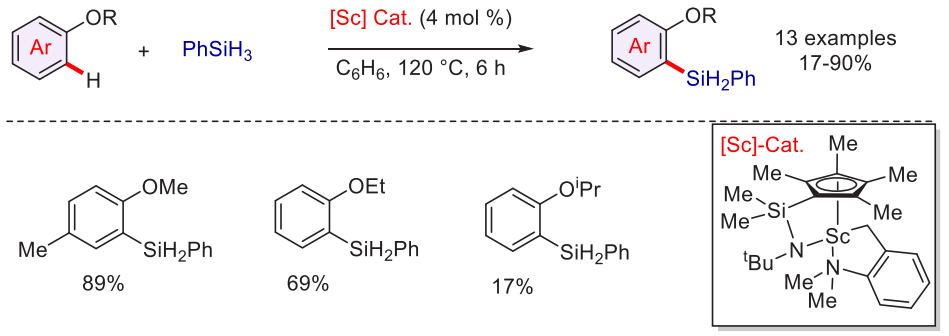
Scheme 115. Alkoxy-Directed Scandium-Catalyzed C−H Polymerization



Scheme 116. Scandium-Catalyzed C−H Hydroarylation of Dienes



Scheme 117. Scandium-Catalyzed Alkoxy Directed C−H Silylation



of phenols and trifluoroboarated were successfully implemented under the optimized conditions, and the corresponding aminomethylated phenol derivatives were isolated with good-to-excellent yields. To explain high level of *ortho*-selectivity author proposed a six membered cyclic transition state through simultaneous coordination of phenol and trifluoroborate to Cu(II) as shown in Scheme 113.

7. ALKOXY-DIRECTED C−H BOND FUNCTIONALIZATION

7.1. C−C Bond Formation. *7.1.1. C−H Bond Alkylation.* In 2012, the Wang group has described half-sandwich scandium dialkyl complex in combination with $[Ph_3C][B(C_6F_5)_4]$-catalyzed alkylation of anisole derivatives (Scheme 114).[215] For *ortho*-unsubstituted anisole derivatives, functionalizations with various alkenes occur at only one *ortho*-position leading to *mono* alkylated products with good yields. However, in the case of *ortho*-methyl anisole, the functionalization happens at the benzylic position.

Later, in 2016, the authors further extended the concept of hydroarylation for the polymer synthesis. The reaction of dimethoxybenzene with unconjugated dienes, such as norbornadiene (NBE) and 1,4-divinylbenzene (DVB) proceeded in step growth fashion in the presence of scandium dialkyl complex (Scheme 115).[216] Later, the polymerization of styrene was also successfully implemented via scandium-catalyzed *ortho* C−H bond activation.[217−219]

Chen and co-workers, in 2019, explored the reactivity of cationic 2-picoline-tethered-half-sandwich scandium alkyl catalyst in combination with $[Ph_3C][B(C_6F_5)_4]$ as catalyst toward the cyclization/hydroarylation reaction of 1,5- and 1,6-dienes with aromatic ethers (Scheme 116).[220] The cyclized products were isolated in good yields with high regio- and diastereoselectivity. Moreover, the utility of the protocol was further explored for the synthesis of spirobicyclization using properly positioned trienes.

7.2. C−X Bond Formation. *7.2.1. C−H Silylation.* Hou and co-workers in 2011, identified scandium alkyl complex as a potent catalyst for the hydrogen-acceptor free silylation of aryl

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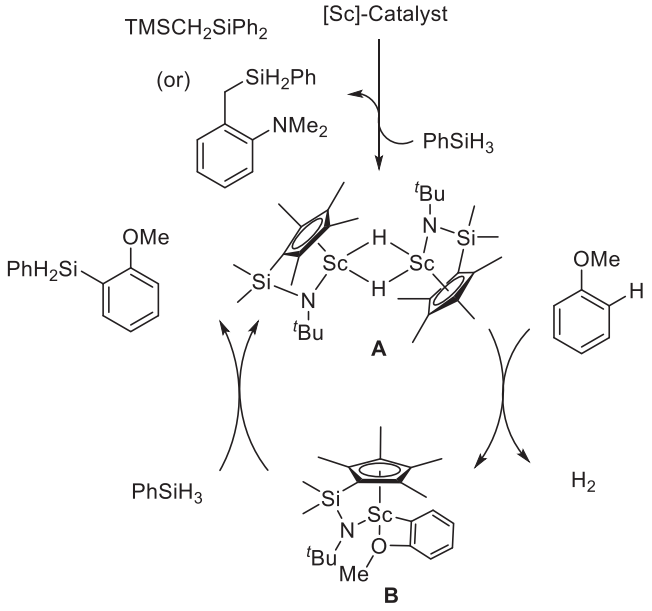
Scheme 118. Proposed Mechanism for *ortho*-Silylation of Arylmethyl Ethers



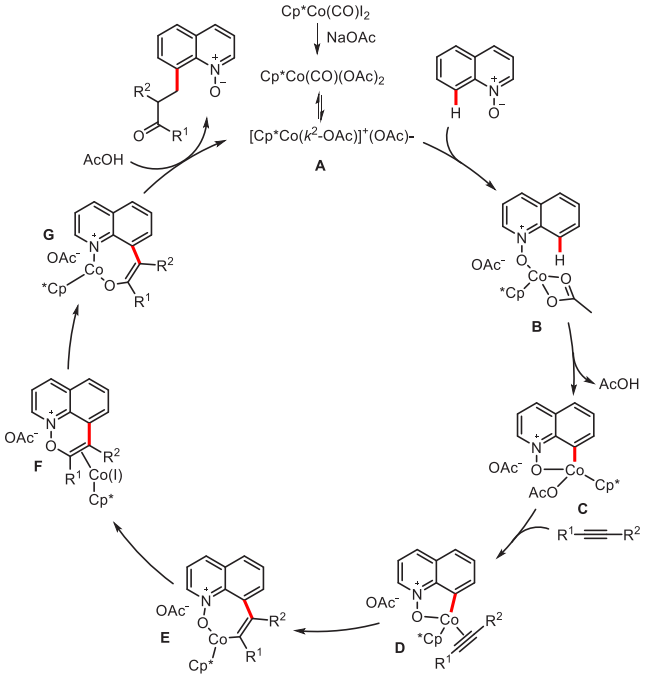
C−H bond (Scheme 117).[221] It is noteworthy to mention that various functional groups like Cl, Br, I, SMe, NMe_2 were suitable to deliver the *ortho*-silylated products in good-to-excellent yields.

On the basis of the control experiments, the authors proposed a plausible mechanism (Scheme 118). The treatment of scandium catalyst with phenyl silane leads to hydride bridge scandanium complex **A** which upon coordination with anisole lead to C−H activated cyclometalated intermediate **B** along with $H_2(g)$. Finally, the sigma-bond metathesis between complex **B** and phenyl silane results the desired *ortho*-silylated product and regenerate the active catalytic species **A**.

8. N-OXIDE-DIRECTED C−H BOND FUNCTIONALIZATION

Quinoline and its derivatives are routinely found in many natural products and biorelevant molecules. The site-selective C(2)−H functionalizations of quinolines is well documented because of the acidic C(2)−H bond;[222] however, very few reports are known in the literature for the challenging C(8)−H functionalizations of quinoline using 3d transition metals. The simple conversion of quinoline to its *N*-oxide bring the metal to be at the proximal position to the C(8)−H bond. This allows the activation of C(8)−H bond of quinoline which are otherwise not easy to functionalize, unlike the C(2)−H bond.

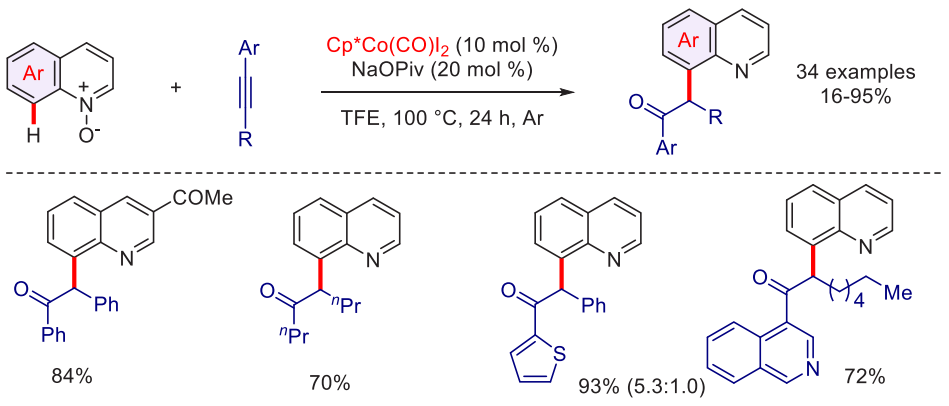
Scheme 120. Proposed Mechanism for the Alkenylation and Oxygen Atom Transfer Protocol



8.1. C−H Alkenylation and Oxygen Atom-Transfer. In 2016, Sundararaju and his co-workers explored an elegant strategy of highly regioselective C−H and C−O coupling of quinoline *N*-oxides with internal alkynes via C−H activation and oxygen atom transfer (OAT) under high-valent cobalt catalysis (Scheme 119).[223] Several symmetrical and unsymmetrical alkynes were smoothly coupled with quinoline *N*-oxides with high regioselectivity to provide *α*-(8-quinolinyl) ketones in good yields. It is noteworthy to mention that the efficiency of the Cp*Co(III) catalytic system is better compared with group 9 congeners Cp*Rh(III) and Cp*Ir(III) catalysts for electron-rich alkynes.

Based on the control experiments, the authors proposed the formation of catalytically active cationic cobalt complex **A** by treatment of NaOAc with the precatalyst (Scheme 120). Complex **A** undergoes an irreversible cyclometalation to provide

Scheme 119. Cp*Co(III)-Catalyzed Coupling of Quinoline *N*-Oxides with Internal Alkynes



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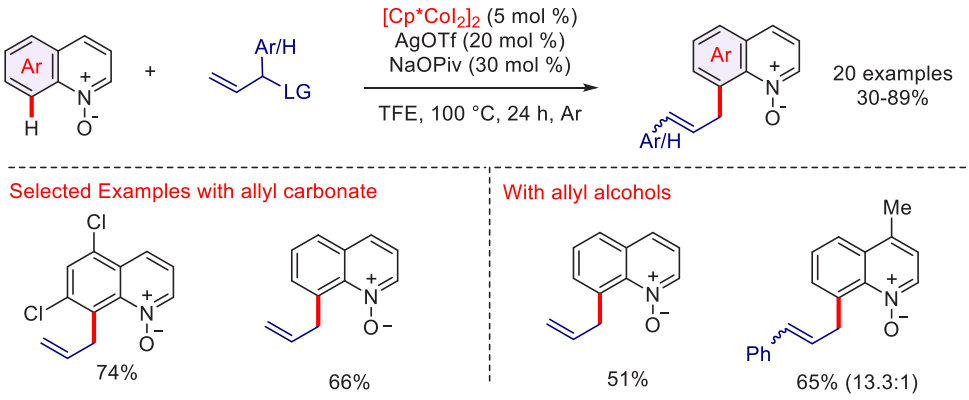
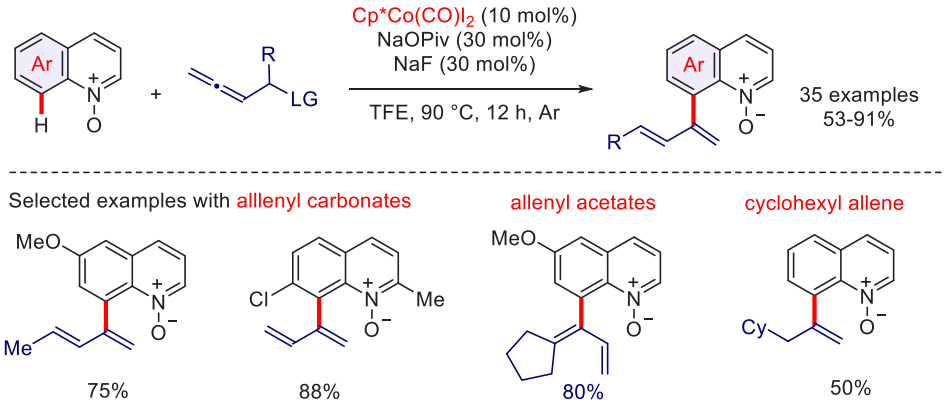
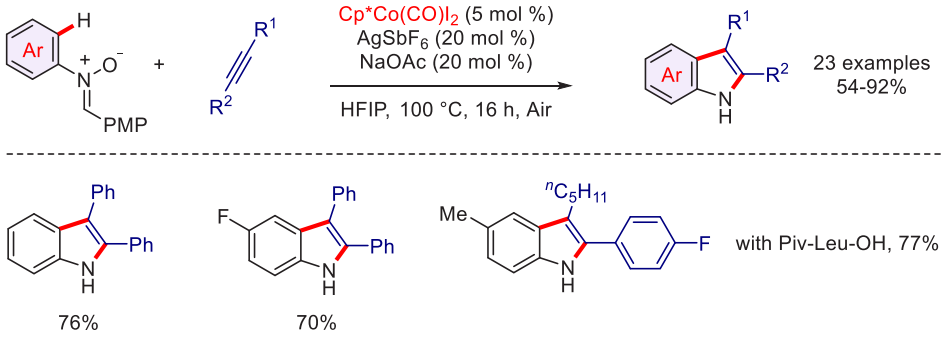
Scheme 121. Cp*Co(III)-Catalyzed C(8)−H Allylation of Quinoline *N*-Oxides with Allyl Alcohols



Scheme 122. Cp*Co(III)-Catalyzed C(8)−H Dienylation of Quinoline *N*-Oxides with Allenylcarbinols/Allenylcarbonates



Scheme 123. Cp*Co(III)-Catalyzed C−H/N−O Functionalizations of Aryl Nitrones with Alkynes



intermediate **C**. Then, coordination followed by insertion of alkyne delivers the intermediate **E**. The reductive elimination in the intermediate **E** provides the Cp*Co(I)-coordinated intermediate **F**. Finally, the oxidative addition of Cp*Co(I) into the N−O bond of the intermediate **F** and successive protodemetalation and keto−enol tautomerization release the final product and regenerate the active catalyst.

8.2. C−H Allylation. Following this study, Sundararaju and co-workers demonstrated C(8)−H selective allylation of quinoline *N*-oxides using both allyl alcohols and allyl carbonate as allylating source (Scheme 121).[224] Quinoline *N*-oxides containing various substituents at a different position were tolerant to the reaction condition and furnished corresponding allylated products in good yields. However, when similar reactions with allyl alcohols were carried out in the presence of Cp*Rh(III), aryl ketones products were obtained exclusively instead of allylated products. The authors explained the dichotomy of the two catalytic systems based on the HSAB principle. As proposed, Rh(III) being a soft metal, prefers to eliminate hydride (soft) rather than hydroxyl (hard) and hence favors the β-hydride elimination affording the ketone product after tautomerism, whereas relatively harder cobalt center choose to proceed via β-hydroxy (hard) elimination, leading to allylated product.

8.3. C−H Dienylation. Recently, Volla and co-workers unfolded Cp*Co(III) catalyzed site-selective C(8)-dienylation of quinoline-*N*-oxides with allenylcarbinol carbonates as dienylating agent (Scheme 122).[225] The reaction displayed good functional group tolerance and a variety of terminalallenyl carbinols carbonate-containing aryl and aliphatic functional groups reacted smoothly to deliver the desired product in good yields. Interestingly, allenylcarbinol carbonates containing biorelevant scaffolds like L-menthol, cholesterol produced the expected products in good yields. Furthermore, the protocol was

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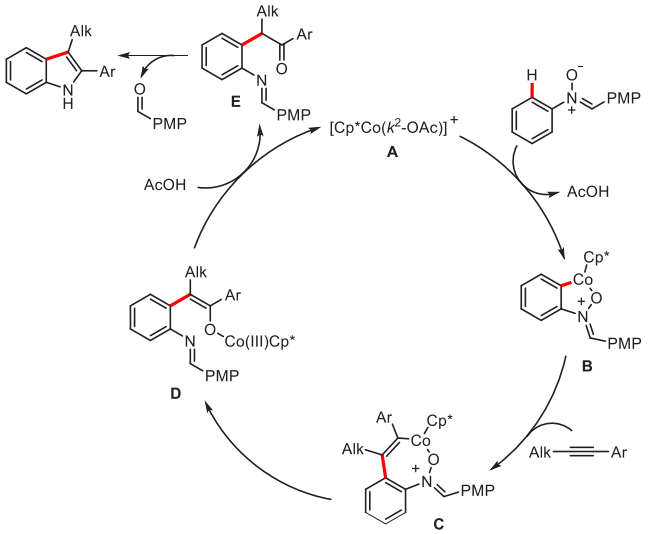
Scheme 124. Plausible Mechanism of Cp*Co(III)-Catalyzed Synthesis of Indoles

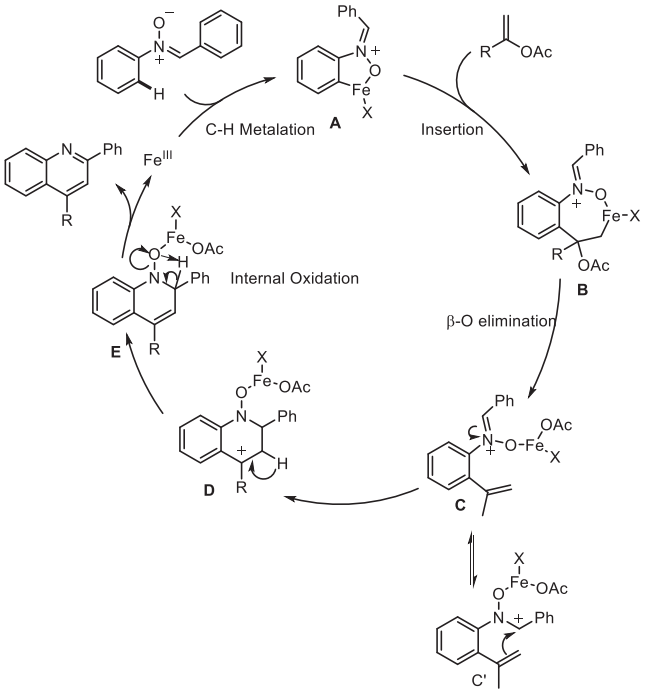


expanded to internal allenylcarbinol carbonates as well. Notably, the C(8)−H alkenylation was observed when cyclohexyl allene was used as a coupling partner, which signifies the importance of leaving group at the β-position to get the dienylation scaffold. Considering the importance of dienes in synthetic organic chemistry, the dienylated products were further diversified to various biorelevant molecules.

8.4. Annulation Reaction. In 2016, Ackermann and co-workers explored the reactivity of aryl nitrones under Cp*Co-(III) catalysis for the first time in the synthesis of indole derivatives under external oxidant-free conditions (Scheme 123).[226] Nitrones efficiently coupled with an internal alkyne in the presence of 5 mol % $Cp^*Co(CO)I_2$, 20 mol % $AgSbF_6$, 20 mol % NaOAC or Piv-Leu-OH in HFIP at 100 °C, rendering indole derivatives in good-to-excellent yields. Notably, the reaction of nitrones with dialkyl-substituted alkynes provided 3,3-disubstituted 3*H*-indole derivatives in moderate yields. Unsymmetrical internal alkynes were also suitable in this transformation and yielded regioselective products with good yields.

The proposed mechanism (Scheme 124) by the authors begins with the formation of cationic complex **A** from precatalyst upon treatment of $AgSbF_6$ and KOAc. Then cationic complex **A** undergoes ligand exchange with the substrate and followed by an acetate-assisted C−H activation to provide a five-membered cobaltacycle **B**. Insertion of alkyne to the cobaltacycle **B** leads to

Scheme 126. Plausible Mechanism of Iron-Catalyzed Annulation of Nitrones with Vinyl Acetates

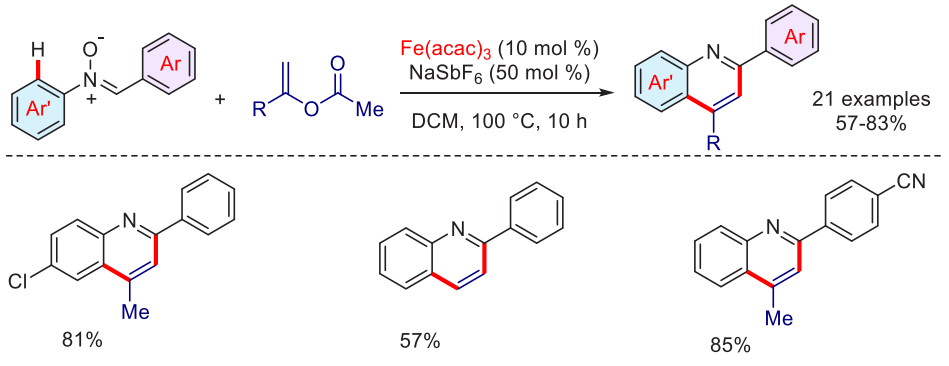


another seven-membered metalacycle **C** which subsequently provides Co(III)-enolate intermediate **D** through successive N−O cleavage and C−O bond formation. Further, proto-demetalation provides protected *ortho* imino ketone **E** which upon hydrolysis followed by intramolecular condensation delivers the desired indole.

Later, Shao and co-workers reported an external oxidant-free, iron-catalyzed annulation of aryl nitrones with geminal substituted vinyl acetates to synthesize 2,4-disubstituted quinolines (Scheme 125).[227] The protocol displayed good functional group tolerance and wide-scope, delivering quinoline derivatives in good yields. Notably, replacing $Fe(acac)_3$ with strong Lewis acids like $Cu(OTf)_2$, $CeCl_3$, $BF_3{\cdot}OEt_2$, or a Brønsted acid like HOTf shut down the reaction. Thus, the authors eliminated the traditional Lewis acid catalyzed pathway for this protocol.

According to the proposed mechanism (Scheme 126), metalacycle **A** is formed from the reaction of $Fe(acac)_3$ and nitrone via N-oxide directed C−H bond activation. Then, insertion of vinyl acetate into **A** leads to intermediate **B** which upon β-oxygen elimination delivers an intermediate **C**. Intra-

Scheme 125. Iron-Catalyzed Annulation of Aryl Nitrones with Vinyl Acetates



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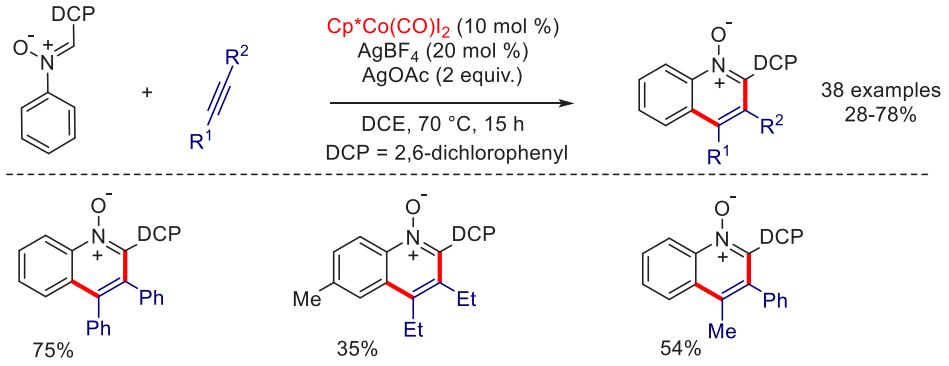
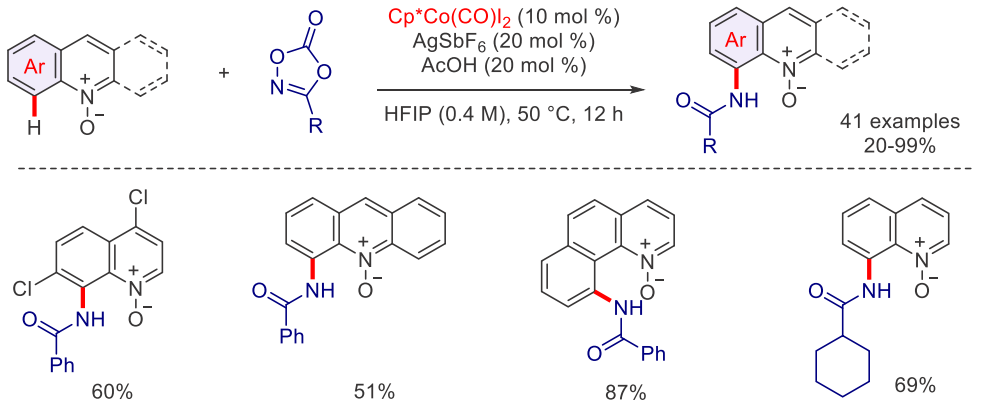
Scheme 127. Cp*Co(III)-Catalyzed Annulation of Aryl Nitrones with Alkynes



Scheme 128. Co(III)-Catalyzed C(8)-Amidation of Quinoline *N*-Oxides



molecular nucleophilic addition of alkene to the carbocation center provides another carbocationic intermediate **D**. Finally, E1 elimination in the intermediate **D** generates the intermediate **E** which upon β-hydride elimination and internal oxidation delivers the desired product.

In the subsequent year, Zhang and co-workers disclosed straightforward synthesis of highly substituted *N*-oxide via aryl nitrone directed annulation with an internal alkyne in the presence of Cp*Co(III) as a catalyst (Scheme 127).[228] Various quinoline *N*-oxide derivatives were synthesized with good functional group tolerance and in good yields. Furthermore, quinoline *N*-oxides have been transferred to various useful products.

8.5. C−H Bond Amidation. Very recently, Sharma and co-workers developed an efficient protocol for the C(8)-amidation of quinoline-*N*-oxides using dioxazolones as amidating agents under very mild conditions (Scheme 128).[229] A wide-variety of dioxzazolones including aromatics, heteroaromatics, aliphatic dioxazolones were found to be suitable under the optimal conditions. In addition to the substituted quinoline-*N*-oxides, phenanthridine-, acridine-, benzo[f]quinoline-, benzo[h]-quinoline-*N*-oxides smoothly underwent amidation at the desired position in good yields.

9. CONCLUSION AND PERSPECTIVES

The directing-group-assisted catalytic C−H bond functionalizations have revolutionized the area of catalysis in organic synthesis. Despite the tremendous success have been made with 4d and 5d transition-metal-based catalysts, only in the recent times, notable progress have been achieved using earth-abundant 3d transition metals for direct C−H bond functionalizations. In this regard, 3d metal catalysts have not only shown similar reactivity with their noble congener metals but also exhibit their unique reactivity in the functionalizations of C−H bonds over the years. The major developments in this area using 3d metals have been noticed using strongly coordinating groups like pyridine, pyrimidine, 8-amino quinolyl, and so on. However, such directing groups often limits their practical applicability as additional steps are necessary for preinstallation and their modification after the functionalizations. Nevertheless, in recent times, a notable emphasis has been put forth on the use of functional groups as directing groups instead of preinstallation of strong coordinating directing groups. In this regard, more practical and useful functional groups such as aldehyde, ketone, carboxylic acid, hydroxy, monodentated amide, and so on, can be considered as weakly coordinating directing groups for site-selective C−H bond functionalizations. These functional groups not only served as weakly coordinating directing groups but also provide sufficient stability to the cyclometalated intermediate for regioselective C−H bond functionalizations. Considering the importance of this emerging topic, herein, we provide a comprehensive overview of C−H bond functionalizations catalyzed by 3d metals through weak chelation. The reported protocols are largely explored using π-bonding coupling partners like alkynes, allenes, alkenes which provide additional stability to the transient cyclometalated intermediate, in addition to highly reactive coupling partners such as dioxazolones, acyl azides. It is very likely that the strategy may be explored to develop various other transformations involving the formation of C−B, C−O, C−P, C−CN, and other bonds . However, the real potential of this powerful strategy is yet to be explored, and it is our anticipation that this field will advance more in the future.

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Further, the more challenging C(sp^3)−H bond functionalizations remained untouched so far through weak-chelation, and hopefully, there will soon be applications in this regard. We hope that the development of enantioselective C−H bond functionalizations with weakly coordinating directing groups will be an exciting area, although the requirement of elevated temperature is a cause of concern. The design of a more efficient catalyst might allow carrying out the C−H bond functionalizations at mild conditions. With the advent of dual catalytic approaches by combining photocatalysts/electricity with 3d metals may indeed favor more advancements on this exciting topic for sustainable applications.

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Notes

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REFERENCES

(1) Biffis, A.; Centomo, P.; Del Zotto, A.; Zecca, M. Pd Metal Catalysts for Cross-Couplings and Related Reactions in the 21st Century: A Critical Review. *Chem. Rev.* **2018**, *118*, 2249−2295.

(2) Jana, R.; Pathak, T. P.; Sigman, M. S. Advances in Transition Metal (Pd, Ni, Fe)-Catalyzed Cross-Coupling Reactions Using Alkylorganometallics as Reaction Partners. *Chem. Rev.* **2011**, *111*, 1417−1492.

(3) Cahiez, G.; Moyeux, A. Cobalt-Catalyzed Cross-Coupling Reactions. *Chem. Rev.* **2010**, *110*, 1435−1462.

(4) Christoffel, F.; Ward, T. R. Palladium-Catalyzed Heck Cross-Coupling Reactions in Water: A Comprehensive Review. *Catal. Lett.* **2018**, *148*, 489−511.

(5) Ruiz-Castillo, P.; Buchwald, S. L. Applications of Palladium-Catalyzed C-N Cross-Coupling Reactions. *Chem. Rev.* **2016**, *116*, 12564−12649.

(6) Dixneuf, P. H.; Doucet, H.*C-H Bond Activation and Catalytic Functionalization I*; Springer, 2016; pp 1−76.

(7) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. Selective Intermolecular Carbon-Hydrogen Bond Activation by Synthetic Metal Complexes in Homogeneous Solution. *Acc. Chem. Res.* **1995**, *28*, 154−162.

(8) Crabtree, R. H. Alkane C-H Activation and Functionalization with Homogeneous Transition Metal Catalysts: A Century of Progress—A New Millennium in Prospect. *J. Chem. Soc., Dalton Trans.* **2001**, *17*, 2437−2450.

(9) Furukawa, T.; Tobisu, M.; Chatani, N. C-H Functionalization at Sterically Congested Positions by the Platinum-Catalyzed Borylation of Arenes. *J. Am. Chem. Soc.* **2015**, *137*, 12211−12214.

(10) Crabtree, R. H.; Lei, A. Introduction: CH Activation. *Chem. Rev.* **2017**, *117*, 8481−8482.

(11) Campeau, L.-C.; Stuart, D. R.; Leclerc, J.-P.; Bertrand-Laperle, M.; Villemure, E.; Sun, H.-Y.; Lasserre, S.; Guimond, N.; Lecavallier, M.; Fagnou, K. Palladium-Catalyzed Direct Arylation of Azine and Azole *N*-Oxides: Reaction Development, Scope and Applications in Synthesis. *J. Am. Chem. Soc.* **2009**, *131*, 3291−3306.

(12) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. Pd(II)-Catalyzed Olefination of Electron-Deficient Arenes Using 2,6-Dialkylpyridine Ligands. *J. Am. Chem. Soc.* **2009**, *131*, 5072−5074.

(13) Murphy, J. M.; Liao, X.; Hartwig, J. F. *Meta* Halogenation of 1,3-Disubstituted Arenes *via* Iridium-Catalyzed Arene Borylation. *J. Am. Chem. Soc.* **2007**, *129*, 15434−15435.

(14) Furukawa, T.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc.* **2015**, *137*, 12211−12214.

(15) Cho, J.-Y.; Tse, M. K.; Holmes, D.; Maleczka, R. E., Jr; Smith, M. R., III Remarkably Selective Iridium Catalysts for the Elaboration of Aromatic C-H Bonds. *Science* **2002**, *295*, 305−308.

(16) Dey, A.; Sinha, S. K.; Achar, T. K.; Maiti, D. Accessing Remote *meta*- and *para*-C(sp^2)-H Bonds with Covalently Attached Directing Groups. *Angew. Chem., Int. Ed.* **2019**, *58*, 10820−10843.

(17) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. Transition Metal-Catalyzed C-H Bond Functionalizations by the Use of Diverse Directing Groups. *Org. Chem. Front.* **2015**, *2*, 1107−1295.

(18) Wencel-Delord, J.; Glorius, F. C-H Bond Activation Enables the Rapid Construction and Late-Stage Diversification of Functional Molecules. *Nat. Chem.* **2013**, *5*, 369−374.

(19) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. Undirected, Homogeneous C-H Bond Functionalization: Challenges and Opportunities. *Chem. Soc. Rev.* **2016**, *45*, 2900−2936.

(20) Hartwig, J. F.; Larsen, M. A. Undirected, Homogeneous C-H Bond Functionalization: Challenges and Opportunities. *ACS Cent. Sci.* **2016**, *2*, 281−292.

(21) Rej, S.; Das, A.; Chatani, N. Strategic Evolution in Transition Metal-Catalyzed Directed C-H Bond Activation and Future Directions. *Coord. Chem. Rev.* **2021**, *431*, 213683.

(22) Sambiagio, C.; Schonbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnurch, M. A Comprehensive Overview of Directing Groups Applied in Metal-Catalysed C-H Functionalisation Chemistry. *Chem. Soc. Rev.* **2018**, *47*, 6603−6743.

(23) Yang, Y.; Lan, J.; You, J. Oxidative C-H/C-H Coupling Reactions between Two (Hetero)arenes. *Chem. Rev.* **2017**, *117*, 8787−8863.

(24) Wang, F.; Yu, S.; Li, X. Transition Metal-Catalysed Couplings Between Arenes and Strained or Reactive Rings: Combination of C-H Activation and Ring Scission. *Chem. Soc. Rev.* **2016**, *45*, 6462−6477.

(25) Jones, W. D.; Feher, F. J. Comparative Reactivities of Hydrocarbon Carbon-Hydrogen Bonds with a Transition-Metal Complex. *Acc. Chem. Res.* **1989**, *22*, 91−100. (b) Crabtree, R. H. The Organometallic Chemistry of Alkanes. *Chem. Rev.* **1985**, *85*, 245−269. (c) Janowicz, A. H.; Bergman, R. G. Carbon-hydrogen activation in completely saturated hydrocarbons: direct observation of M + R-H. fwdarw. M(R)(H). *J. Am. Chem. Soc.* **1982**, *104*, 352−254.

(26) Murai, S.; Kakiuchi, F.; Sekine, S.; Tanaka, Y.; Kamatani, A.; Sonoda, M.; Chatani, N. Efficient Catalytic Addition of Aromatic Carbon-Hydrogen Bonds to Olefins. *Nature* **1993**, *366*, 529−531.

(27) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. Palladium(II)-Catalyzed C-H Activation/C-C Cross-Coupling Reactions: Versatility and Practicality. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094−5115.

(28) Lyons, T. W.; Sanford, M. S. Palladium-Catalyzed Ligand-Directed C-H Functionalization Reactions. *Chem. Rev.* **2010**, *110*, 1147−1169.

(29) Yun, Y.-L.; Yang, J.; Miao, Y.-H.; Sun, J.; Wang, X.-J. Recent Advances in Palladium(II)-Catalyzed Activation of Aromatic Ring C-H Bonds. *J. Saudi. Chem. Soc.* **2020**, *24*, 151−185.

(30) Yang, K.; Song, M.; Liu, H.; Ge, H. Palladium-Catalyzed Direct Asymmetric C-H Bond Functionalization Enabled by the Directing Group Strategy. *Chem. Sci.* **2020**, *11*, 12616−12632.

(31) Wozniak, ř.; Tan, J.-F.; Nguyen, Q.-H.; Madron du Vigné, A.; Smal, V.; Cao, Y.-X.; Cramer, N. Catalytic Enantioselective Functionalizations of C-H Bonds by Chiral Iridium Complexes. *Chem. Rev.* **2020**, *120*, 10516−10543.
(32) Xu, L.; Wang, G.; Zhang, S.; Wang, H.; Wang, L.; Liu, L.; Jiao, J.; Li, P. Recent Advances in Catalytic C-H Borylation Reactions. *Tetrahedron* **2017**, *73*, 7123−7157.
(33) Fernández, D. F.; Mascareñas, J. L.; López, F. Catalytic Addition of C-H Bonds Across C-C Unsaturated Systems Promoted by Iridium(I) and its Group IX Congeners. *Chem. Soc. Rev.* **2020**, *49*, 7378−7405.
(34) (a) Colby, D. A.; Tsai, A. S.; Bergman, R. G.; Ellman, J. A. Rhodium-Catalyzed Chelation-Assisted C-H Bond Functionalization Reactions. *Acc. Chem. Res.* **2012**, *45*, 814−825. (b) Song, G.; Li, X. Substrate Activation Strategies in Rhodium(III)-Catalyzed Selective Functionalization of Arenes. *Acc. Chem. Res.* **2015**, *48*, 1007−1020. (c) 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. (d) 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. (e) Satoh, T.; Miura, M. Oxidative Coupling of Aromatic Substrates with Alkynes and Alkenes under Rhodium Catalysis. *Chem.—Eur. J.* **2010**, *16*, 11212−11222.
(35) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. Ruthenium(II)-Catalyzed C-H Bond Activation and Functionalization. *Chem. Rev.* **2012**, *112*, 5879−5918.
(36) Shan, C.; Zhu, L.; Qu, L.-B.; Bai, R.; Lan, Y. Mechanistic view of Ru-Catalyzed C-H Bond Activation and Functionalization: Computational Advances. *Chem. Soc. Rev.* **2018**, *47*, 7552−7576.
(37) De Sarkar, S.; Liu, W.; Kozhushkov, S. I.; Ackermann, L. Weakly Coordinating Directing Groups for Ruthenium(II)- Catalyzed C-H Activation. *Adv. Synth. Catal.* **2014**, *356*, 1461−1479.
(38) *CRC Handbook of Chemistry and Physics*, 102nd ed.; Rumble, J. R., Ed.; CRC Press/Taylor & Francis: Boca Raton, FL, 2021.
(39) Halka, M.; Nordstrom, B.*Transition Metals; Facts on file*; London, 2011.
(40) Egorova, K. S.; Ananikov, V. P. Which Metals are Green for Catalysis? Comparison of the Toxicities of Ni, Cu, Fe, Pd, Pt, Rh, and Au Salts. *Angew. Chem., Int. Ed.* **2016**, *55*, 12150−12162.
(41) Arevalo, R.; Chirik, P. J. Enabling Two-Electron Pathways with Iron and Cobalt: From Ligand Design to Catalytic Applications. *J. Am. Chem. Soc.* **2019**, *141*, 9106−9123.
(42) Gallego, D.; Baquero, E. A. Recent Advances on Mechanistic Studies on C-H Activation Catalyzed by Base Metals. *Open Chem.* **2018**, *16*, 1001−1058.
(43) Nandy, A.; Chu, D. B. K.; Harper, D. R.; Duan, C.; Arunachalam, N.; Cytter, Y.; Kulik, H. J. Large-Scale Comparison of 3d and 4d Transition Metal Complexes Illuminates the Reduced Effect of Exchange on Second-row Spin-State Energetics. *Phys. Chem. Chem. Phys.* **2020**, *22*, 19326−19341.
(44) Vogiatzis, K. D.; Polynski, M. V.; Kirkland, J. K.; Townsend, J.; Hashemi, A.; Liu, C.; Pidko, E. A. Computational Approach to Molecular Catalysis by 3d Transition Metals: Challenges and Opportunities. *Chem. Rev.* **2019**, *119*, 2453−2523.
(45) Guo, X. K.; Zhang, L. B.; Wei, D.; Niu, J. L. Mechanistic Insights into Cobalt(II/III)-Catalyzed C-H Oxidation: A Combined Theoretical and Experimental Study. *Chem. Sci.* **2015**, *6*, 7059−7071.
(46) Ackermann, L. Carboxylate-Assisted Transition-Metal-Catalyzed C-H Bond Functionalizations: Mechanism and Scope. *Chem. Rev.* **2011**, *111*, 1315−1345.
(47) Shang, R.; Ilies, L.; Nakamura, E. Iron-Catalyzed C-H Bond Activation. *Chem. Rev.* **2017**, *117*, 9086−9139.
(48) Rana, S.; Biswas, J. P.; Paul, S.; Paik, A.; Maiti, D. Organic Synthesis with the Most Abundant Transition Metal-Iron: from Rust to Multitasking Catalysts. *Chem. Soc. Rev.* **2021**, *50*, 243−472.
(49) Rouquet, G.; Chatani, N. Catalytic Functionalization of $C(sp^2)$-H and $C(sp^3)$-H Bonds by Using Bidentate Directing Groups. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726−11743.
(50) Rajesh, N.; Barsu, N.; Sundararaju, B. Recent Advances in $C(sp^3)$-H Bond Carbonylation by First Row Transition Metals. *Tetrahedron Lett.* **2018**, *59*, 862−868.
(51) Liu, W.; Ackermann, L. Manganese-Catalyzed C-H Activation. *ACS Catal.* **2016**, *6*, 3743−3752.
(52) Pototschnig, G.; Maulide, N.; Schnürch, M. Direct Functionalization of C-H Bonds by Iron, Nickel, and Cobalt Catalysis. *Chem.—Eur. J.* **2017**, *23*, 9206−9232.
(53) Gao, K.; Yoshikai, N. Low-Valent Cobalt Catalysis: New Opportunities for C-H Functionalization. *Acc. Chem. Res.* **2014**, *47*, 1208−1219.
(54) Kulkarni, A. A.; Daugulis, O. Direct Conversion of Carbon-hydrogen into Carbon-Carbon Bonds by First-Row Transition-Metal Catalysis. *Synthesis* **2009**, *24*, 4087−4109.
(55) Aneeja, T.; Neetha, M.; Afsina, C. M. A.; Anilkumar, G. Progress and Prospects in Copper-Catalyzed C-H Functionalization. *RSC Adv.* **2020**, *10*, 34429−34458.
(56) Zeng, X. Recent Advances in Chromium-Catalyzed Organic Transformations. *Synlett* **2020**, *31*, 205−210.
(57) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackermann, L. 3d Transition Metals for C-H Activation. *Chem. Rev.* **2019**, *119*, 2192−2452.
(58) Wozniak, L.; Cramer, N. Enantioselective C-H Bond Functionalizations by 3d Transition-Metal Catalysts. *Trends Chem.* **2019**, *1*, 471−484.
(59) 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.
(60) Martinez de Salinas, S.; Sanjosé-Orduna, J.; Odena, C.; Barranco, S.; Benet-Buchholz, J.; Pérez-Temprano, M. H. Weakly-Coordinated Cobaltacycles: Trapping Catalytically Competent Intermediates in Cp^*Co^{III} Catalysis. *Angew. Chem., Int. Ed.* **2020**, *59*, 6239−6243.
(61) Laurence, C.; Gal, J. F.*Lewis Basicity and Affinity Scales: Data and Measurement*; Wiley-Blackwell: 2009.
(62) Kakiuchi, F.; Sato, T.; Tsujimoto, T.; Yamauchi, M.; Chatani, N.; Murai, S. New Protocol for the Siteselective Alkylation and Vinylation of Aromatic Compounds. Catalyst-Specific Reactions. *Chem. Lett.* **1998**, *27*, 1053−1054.
(63) Kim, J.; Park, S.-W.; Baik, M.-H.; Chang, S. Complete Switch of Selectivity in the C-H Alkenylation and Hydroarylation Catalyzed by Iridium: The Role of Directing Groups. *J. Am. Chem. Soc.* **2015**, *137*, 13448−13451.
(64) Gommans, L. H. P.; Main, L.; Nicholson, B. K. Synthesis of *o*-Deuterio- and *o*-Halogeno-acetophenones *via* Oxidation of η^2-(2-acetylphenyl)tetracarbonylmanganese Derivatives and the Determination of a Primary Kinetic Isotope Effect in *ortho*-metalation of Acetophenones. *J. Chem. Soc. Chem. Commun.* **1986**, 12−13.
(65) McKinney, R. J.; Firestein, G.; Kaesz, H. D. Metalation Reaction. VII. Metalation of Aromatic Ketones and Anthraquinone with Methylmanganese and Methylrhenium Carbonyl Complexes. *Inorg. Chem.* **1975**, *14*, 2057−2061.
(66) Martínez de Salinas, S.; Sanjosé-Orduna, J.; Odena, C.; Barranco, S.; Benet-Buchholz, J.; Perez-Temprano, M. H. Weakly Coordinated Cobaltacycles: Trapping Catalytically Competent Intermediates in Cp^*Co^{III} Catalysis. *Angew. Chem., Int. Ed.* **2020**, *59*, 6239−6243.
(67) Banjare, S. K.; Nanda, T.; Pati, B. V.; Biswal, P.; Ravikumar, P. C. *O*-Directed C-H Functionalization *via* Cobaltacycles: A Sustainable Approach for C-C and C-Heteroatom Bond Formations. *Chem. Commun.* **2021**, *57*, 3630−3647.
(68) Zhu, R.-Y.; Farmer, M. E.; Chen, Y.-Q.; Yu, J.-Q. A Simple and Versatile Amide Directing Group for C-H Functionalizations. *Angew. Chem., Int. Ed.* **2016**, *55*, 10578−10599.
(69) Zheng, Q.; Liu, C.-F.; Chen, J.; Rao, G.-W. C-H Functionalization of Aromatic Amides. *Adv. Synth. Catal.* **2020**, *362*, 1406−1446.
(70) Das, R.; Kumar, G. S.; Kapur, M. Amides as Weak Coordinating Groups in Proximal C-H Bond Activation. *Eur. J. Org. Chem.* **2017**, *2017*, 5439−5459.

https://doi.org/10.1021/acscatal.1c05267
ACS Catal. 2022, 12, 3452−3506

(71) Fujiwara, Y.; Moritani, I.; Danno, S.; Asano, R.; Teranishi, S. Aromatic Substitution of Olefins. VI. Arylation of Olefins with Palladium(II) Acetate. *J. Am. Chem. Soc.* **1969**, *91*, 7166−7169.
(72) Moritanl, I.; Fujiwara, Y. Aromatic Substitution of Styrene-Palladium Chloride Complex. *Tetrahedron Lett.* **1967**, *8*, 1119−1122.
(73) Suzuki, Y.; Sun, B.; Yoshino, T.; Kanai, M.; Matsunaga, S. Cp$^{\alpha}$Co(III)-Catalyzed Oxidative C-H Alkenylation of Benzamides with Ethyl Acrylate. *Tetrahedron* **2015**, *71*, 4552−4556.
(74) Kawai, K.; Bunno, Y.; Yoshino, T.; Matsunaga, S. Weinreb Amide Directed Versatile C-H Bond Functionalization under (η5-Pentamethylcyclopentadienyl)cobalt(III) Catalysis. *Chem.—Eur. J.* **2018**, *24*, 10231−10237.
(75) Kalepu, J.; Pilarski, L. T. Weinreb Amides as Directing Groups for Transition Metal-Catalyzed C-H Functionalizations. *Molecules* **2019**, *24*, 830.
(76) Li, T.; Shen, C.; Sun, Y.; Zhang, J.; Xiang, P.; Lu, X.; Zhong, G. Cobalt-Catalyzed Olefinic C-H Alkenylation/Alkylation Switched by Carbonyl Groups. *Org. Lett.* **2019**, *21*, 7772−7777.
(77) Banjare, S. K.; Biswal, P.; Ravikumar, P. C. Cobalt-Catalyzed One-Step Access to Pyroquilon and C-7 Alkenylation of Indoline with Activated Alkenes Using Weakly Coordinating Functional Groups. *J. Org. Chem.* **2020**, *85*, 5330−5341.
(78) Carral-Menoyo, A.; Sotomayor, N.; Lete, E. Cp*Co(III)-Catalyzed C-H Hydroarylation of Alkynes and Alkenes and Beyond: A Versatile Synthetic Tool. *ACS Omega* **2020**, *5*, 24974−24993.
(79) Ikemoto, H.; Yoshino, T.; Sakata, K.; Matsunaga, S.; Kanai, M. Pyrroloindolone Synthesis *via* a Cp*Co^{III}-Catalyzed Redox-Neutral Directed C-H Alkenylation/Annulation Sequence. *J. Am. Chem. Soc.* **2014**, *136*, 5424−5431.
(80) Tanaka, R.; Ikemoto, H.; Kanai, M.; Yoshino, T.; Matsunaga, S. Site- and Regioselective Monoalkenylation of Pyrroles with Alkynes *via* Cp*Co^{III} Catalysis. *Org. Lett.* **2016**, *18*, 5732−5735.
(81) Bera, S. S.; Debbarma, S.; Ghosh, A. K.; Chand, S.; Maji, M. S. Cp*Co^{III}-Catalyzed syn-Selective C-H Hydroarylation of Alkynes Using Benzamides: An Approach Toward Highly Conjugated Organic Frameworks. *J. Org. Chem.* **2017**, *82*, 420−430.
(82) Muniraj, N.; Prabhu, K. R. Cobalt(III)-Catalyzed C-H Activation: Counter Anion Triggered Desilylative Direct *ortho*-Vinylation of Secondary Benzamides. *Adv. Synth. Catal.* **2018**, *360*, 3579−3584.
(83) Sanjose-Orduna, J.; Benet-Buchholz, J.; Perez-Temprano, M. H. Unravelling Molecular Aspects of the Migratory Insertion Step in Cp*Co^{III} Metallacyclic Systems. *Inorg. Chem.* **2019**, *58*, 10569−10577.
(84) Sen, M.; Rajesh, N.; Emayavaramban, B.; Premkumar, J. R.; Sundararaju, B. Isolation of Cp*Co^{III}-Alkenyl Intermediate in Efficient Cobalt-Catalyzed C-H Alkenylation with Alkynes. *Chem.—Eur. J.* **2018**, *24*, 342−346.
(85) Chen, M.; Doba, T.; Sato, T.; Razumkov, H.; Ilies, L.; Shang, R.; Nakamura, E. Chromium(III)-Catalyzed C(sp^2)-H Alkynylation, Allylation, and Naphthalenation of Secondary Amides with Trimethylaluminum as Base. *J. Am. Chem. Soc.* **2020**, *142*, 4883−4891.
(86) Ujwaldev, S. M.; Harry, N. A.; Divakar, M. A.; Anilkumar, G. Cobalt-catalyzed C-H Activation: Recent Progress in Heterocyclic Chemistry. *Catal. Sci. Technol.* **2018**, *8*, 5983−6018.
(87) Ikemoto, H.; Tanaka, R.; Sakata, K.; Kanai, M.; Yoshino, T.; Matsunaga, S. Stereoselective Synthesis of Tetrasubstituted Alkenes *via* a Cp*CoIII-Catalyzed C-H Alkenylation/Directing Group Migration Sequence. *Angew. Chem., Int. Ed.* **2017**, *56*, 7156−7160.
(88) Kong, L.; Yu, S.; Zhou, X.; Li, X. Redox-Neutral Couplings between Amides and Alkynes *via* Cobalt(III)-Catalyzed C-H Activation. *Org. Lett.* **2016**, *18*, 588−591.
(89) Yan, Q.; Chen, Z.; Liu, Z.; Zhang, Y. Cobalt-Catalyzed Synthesis of Quinolines from the Redox-Neutral Annulation of Anilides and Alkynes. *Org. Chem. Front.* **2016**, *3*, 678−682.
(90) Lu, Q.; Vásquez-Cespedes, S.; Gensch, T.; Glorius, F. Control over Organometallic Intermediate Enables Cp*Co(III) Catalyzed Switchable Cyclization to Quinolines and Indoles. *ACS Catal.* **2016**, *6*, 2352−2356.
(91) Zhang, Z.-Z.; Liu, B.; Xu, J.-W.; Yan, S.-Y.; Shi, B.-F. Indole Synthesis *via* Cobalt(III)-Catalyzed Oxidative Coupling of N-Arylureas and Internal Alkynes. *Org. Lett.* **2016**, *18*, 1776−1779.
(92) Yu, W.; Zhang, W.; Liu, Y.; Zhou, Y.; Liu, Z.; Zhang, Y. Cobalt(III)-catalyzed Synthesis of Pyrroles from Enamides and Alkynes. *RSC Adv.* **2016**, *6*, 24768−24772.
(93) Lade, D. M.; Pawar, A. B. Cp*Co(III)-Catalyzed Vinylic C-H Bond Activation Under Mild Conditions: Expedient Pyrrole Synthesis *via* (3 + 2) Annulation of Enamides and Alkynes. *Org. Chem. Front.* **2016**, *3*, 836−840.
(94) Sivakumar, G.; Vijeta, A.; Jeganmohan, M. Cobalt-Catalyzed Cyclization of N-Methoxy Benzamides with Alkynes using an Internal Oxidant through C-H/N-O Bond Activation. *Chem.—Eur. J.* **2016**, *22*, 5899−5903.
(95) Yu, X.; Chen, K.; Guo, S.; Shi, P.; Song, C.; Zhu, J. Direct Access to Cobaltacycles *via* C-H Activation: N-Chloroamide-Enabled Room-Temperature Synthesis of Heterocycles. *Org. Lett.* **2017**, *19*, 5348−5351.
(96) Obata, A.; Ano, Y.; Chatani, N. Nickel-Catalyzed C-H/N-H Annulation of Aromatic Amides with Alkynes in the Absence of a Specific Chelation System. *Chem. Sci.* **2017**, *8*, 6650−6655.
(97) Lerchen, A.; Knecht, T.; Koy, M.; Daniliuc, C. G.; Glorius, F. A General Cp*Co^{III} -Catalyzed Intramolecular C-H Activation Approach for the Efficient Total Syntheses of Aromathecin, Protoberberine, and Tylophora Alkaloids. *Chem.—Eur. J.* **2017**, *23*, 12149−12152.
(98) Chavan, L. N.; Gollapelli, K. K.; Chegondi, R.; Pawar, A. B. Cp*Co(III)-Catalyzed C-H Functionalization Cascade of N-Methoxyamides with Alkynedione for the Synthesis of Indolizidines. *Org. Lett.* **2017**, *19*, 2186−2189.
(99) Sen, M.; Mandal, R.; Das, A.; Kalsi, D.; Sundararaju, B. Cp*Co^{III}-Catalyzed Bis-isoquinolone Synthesis by C-H Annulation of Arylamide with 1,3-Diyne. *Chem.—Eur. J.* **2017**, *23*, 17454−17457.
(100) Bera, S. S.; Debbarma, S.; Jana, S.; Maji, M. S. Cobalt(III)-Catalyzed Construction of Benzofurans, Benzofuranones and One-Pot Orthogonal C-H Functionalizations to Access Polysubstituted Benzofurans. *Adv. Synth. Catal.* **2018**, *360*, 2204−2210.
(101) Dey, A.; Rathi, A.; Volla, C. M. R. Cobalt(III)-Catalyzed [4 + 2] Annulation of Heterobicyclic Alkenes by sp^2 C-H Activation. *Asian J. Org. Chem.* **2018**, *7*, 1362−1367.
(102) Muniraj, N.; Prabhu, K. R. Cobalt(III)-Catalyzed [4 + 2] Annulation of N-Chlorobenzamides with Maleimides. *Org. Lett.* **2019**, *21*, 1068−1072.
(103) Carral-Menoyo, A.; Sotomayor, N.; Lete, E. Amide-Directed Intramolecular Co(III)-Catalyzed C-H Hydroarylation of Alkenes for the Synthesis of Dihydrobenzofurans with a Quaternary Center. *J. Org. Chem.* **2020**, *85*, 10261−10270.
(104) Mas-Roselló, J.; Herraiz, A. G.; Audic, B.; Laverny, A.; Cramer, N. Chiral Cyclopentadienyl Ligands: Design, Syntheses, and Applications in Asymmetric Catalysis. *Angew. Chem., Int. Ed.* **2021**, *60*, 13198−13244.
(105) Ozols, K.; Jang, Y.-S.; Cramer, N. Chiral Cyclopentadienyl Cobalt(III) Complexes Enable Highly Enantioselective 3d-Metal-Catalyzed C-H Functionalizations. *J. Am. Chem. Soc.* **2019**, *141*, 5675−5680.
(106) Ma, S. Transition Metal-Catalyzed/Mediated Reaction of Allenes with a Nucleophilic Functionality Connected to the α-Carbon Atom. *Acc. Chem. Res.* **2003**, *36*, 701−712.
(107) Kuppusamy, R.; Santhoshkumar, R.; Boobalan, R.; Wu, H.-R.; Cheng, C.-H. Synthesis of 1,2-Dihydroquinolines by Co(III)-Catalyzed [3 + 3] Annulation of Anilides with Benzylallenes. *ACS Catal.* **2018**, *8*, 1880−1883.
(108) Boobalan, R.; Santhoshkumar, R.; Cheng, C.-H. Co(III)-Catalyzed [4 + 1] Annulation of Amides with Allenes *via* C-H Activation. *Adv. Synth. Catal.* **2019**, *361*, 1140−1145.
(109) Dutta, S.; Bhattacharya, T.; Werz, B. D.; Maiti, D. Transition-metal-catalyzed C-H allylation reactions. *Chem.* **2021**, *7*, 555−605.
(110) Gensch, T.; Vásquez-Céspedes, S.; Yu, D.-G.; Glorius, F. Cobalt(III)-Catalyzed Directed C-H Allylation. *Org. Lett.* **2015**, *17*, 3714−3717.

https://doi.org/10.1021/acscatal.1c05267
ACS Catal. 2022, 12, 3452−3506

(111) Bunno, Y.; Murakami, N.; Suzuki, Y.; Kanai, M.; Yoshino, T.; Matsunaga, S. Cp*Co^{III}-Catalyzed Dehydrative C-H Allylation of 6-Arylpurines and Aromatic Amides Using Allyl Alcohols in Fluorinated Alcohols. *Org. Lett.* **2016**, *18*, 2216−2219.
(112) Ilies, L.; Chen, Q.; Zeng, X.; Nakamura, E. Cobalt-Catalyzed Chemoselective Insertion of Alkene into the *Ortho* C-H Bond of Benzamide. *J. Am. Chem. Soc.* **2011**, *133*, 5221−5223.
(113) Chen, Q.; Ilies, L.; Nakamura, E. Cobalt-Catalyzed *ortho*-Alkylation of Secondary Benzamide with Alkyl Chloride through Directed C-H Bond Activation. *J. Am. Chem. Soc.* **2011**, *133*, 428−429.
(114) Sato, T.; Yoshida, T.; Al Mamari, H. H.; Ilies, L.; Nakamura, E. Manganese-Catalyzed Directed Methylation of C(sp^2)-H Bonds at 25 °C with High Catalytic Turnover. *Org. Lett.* **2017**, *19*, 5458−5461.
(115) Chirila, P. G.; Adams, J.; Dirjal, A.; Hamilton, A.; Whiteoak, C. J. Cp*Co(III)-Catalyzed Coupling of Benzamides with α,β-Unsaturated Carbonyl Compounds: Preparation of Aliphatic Ketones and Azepinones. *Chem.—Eur. J.* **2018**, *24*, 3584−3589.
(116) Banjare, S. K.; Chebolu, R.; Ravikumar, P. C. Cobalt-Catalyzed Hydroarylation of Michael Acceptors with Indolines Directed by a Weakly Coordinating Functional Group. *Org. Lett.* **2019**, *21*, 4049−4053.
(117) Keerthana, M. S.; Manoharan, R.; Jeganmohan, M. Cobalt(III)-Catalyzed Redox-Neutral Coupling of Acrylamides with Activated Alkenes via C-H Bond Activation. *Synthesis* **2020**, *52*, 1625−1633.
(118) Phipps, R. J.; Gaunt, M. J. A *meta*-selective copper-catalyzed C-H bond arylation. *Science* **2009**, *323*, 1593−1597.
(119) Duong, H. A.; Gilligan, R. E.; Cooke, M.-L.; Phipps, R. J.; Gaunt, M. J. Copper(II)-Catalyzed *meta*-Selective Direct Arylation of α-Aryl Carbonyl Compounds. *Angew. Chem., Int. Ed.* **2011**, *50*, 463−466.
(120) Chen, B.; Hou, X.-L.; Li, Y.-X.; Wu, Y.-D. Mechanistic Understanding of the Unexpected Meta Selectivity in Copper-Catalyzed Anilide C-H Bond Arylation. *J. Am. Chem. Soc.* **2011**, *133*, 7668−7671.
(121) Yang, Y.; Li, R.; Zhao, Y.; Zhao, D.; Shi, Z. Cu-Catalyzed Direct C6-Arylation of Indoles. *J. Am. Chem. Soc.* **2016**, *138*, 8734−8737.
(122) Luo, A.; Zhang, M.; Fu, Z.; Lan, J.; Wu, D.; You, J. Copper-catalyzed remote C-H arylation of polycyclicaromatic hydrocarbons (PAHs). *Beilstein J. Org. Chem.* **2020**, *16*, 530−536.
(123) Ilies, L.; Konno, E.; Chen, Q.; Nakamura, E. Iron-Catalyzed *ortho* Monoarylation of Benzamide Derivatives. *Asian J. Org. Chem.* **2012**, *1*, 142−145.
(124) Li, J.; Ackermann, L. Cobalt-Catalyzed C-H Arylations with Weakly-Coordinating Amides and Tetrazoles: Expedient Route to Angiotensin-II-Receptor Blockers. *Chem.—Eur. J.* **2015**, *21*, 5718−5722.
(125) Zhu, C.; Oliveira, J. C. A.; Shen, Z.; Huang, H.; Ackermann, L. Manganese(II/III/I)-Catalyzed C-H Arylations in Continuous Flow. *ACS Catal.* **2018**, *8*, 4402−4407.
(126) Wei, Y.-M.; Wang, M.-F.; Duan, X. F. Is Fe-catalyzed *ortho* C-H Arylation of Benzamides Sensitive to Steric Hindrance and Directing Group? *Org. Lett.* **2019**, *21*, 6471−6475.
(127) Louillat, M.-L.; Patureau, F. W. Oxidative C-H amination reactions. *Chem. Soc. Rev.* **2014**, *43*, 901−910.
(128) Park, Y.; Kim, Y.; Chang, S. Transition Metal-Catalyzed C-H Amination: Scope, Mechanism, and Applications. *Chem. Rev.* **2017**, *117*, 9247−9301.
(129) Zhao, Y.; Xia, W. Recent advances in radical-based C-N bond formation *via* photo-/electrochemistry. *Chem. Soc. Rev.* **2018**, *47*, 2591−2608.
(130) Rit, R. K.; Shankar, M.; Sahoo, A. K. C-H Imidation: A Distinct Perspective of C-N Bond Formation. *Org. Biomol. Chem.* **2017**, *15*, 1282−1293.
(131) Collet, F.; Lescot, C.; Dauban, P. Catalytic C-H Amination: The Stereoselectivity Issue. *Chem. Soc. Rev.* **2011**, *40*, 1926−1936.
(132) Park, Y.; Park, K. T.; Kim, J. G.; Chang, S. Mechanistic Studies on the Rh(III)-Mediated Amido Transfer Process Leading to Robust C-H Amination with a New Type of Amidating Reagent. *J. Am. Chem. Soc.* **2015**, *137*, 4534−4542.
(133) van Vliet, K. M.; de Bruin, B. Dioxazolones: Stable Substrates for the Catalytic Transfer of Acyl Nitrenes. *ACS Catal.* **2020**, *10*, 4751−4769.
(134) Shin, K.; Kim, H.; Chang, S. Transition-Metal-Catalyzed C-N Bond Forming Reactions Using Organic Azides as the Nitrogen Source: A Journey for the Mild and Versatile C-H Amination. *Acc. Chem. Res.* **2015**, *48*, 1040−1052.
(135) Park, J.; Chang, S. Comparative Catalytic Activity of Group 9 [Cp*M^{III}] Complexes: Cobalt-Catalyzed C-H Amidation of Arenes with Dioxazolones as Amidating Reagents. *Angew. Chem., Int. Ed.* **2015**, *54*, 14103−14107.
(136) Chirila, P. G.; Skibinski, L.; Miller, K.; Hamilton, A.; Whiteoak, C. J. Towards a Sequential One-Pot Preparation of 1,2,3-Benzotriazin-4(3H)-ones Employing a Key Cp*Co(III)-catalyzed C-H Amidation Step. *Adv. Synth. Catal.* **2018**, *360*, 2324−2332.
(137) Tanimoto, I.; Kawai, K.; Sato, A.; Yoshino, T.; Matsunaga, S. One-Step Synthesis of 4H-3,1-Benzoxazin-4-ones from Weinreb Amides and 1,4,2-Dioxazol-5-ones *via* Cobalt-Catalyzed C-H Bond Activation. *HeteroCycles* **2019**, *99*, 118−125.
(138) Yang, J.; Hu, X.; Liu, Z.; Li, X.; Dong, Y.; Liu, G. Cp*Co^{III}-Catalyzed Formal [4 + 2] Cycloaddition of Benzamides to Afford Quinazolinone Derivatives. *Chem. Commun.* **2019**, *55*, 13840−13843.
(139) López, L. A.; López, E. Recent Advances in Transition Metal-Catalyzed C-H Bond Functionalization of Ferrocene Derivatives. *Dalton Trans.* **2015**, *44*, 10128−10135.
(140) Huang, D.-Y.; Yao, Q.-J.; Zhang, S.; Xu, X.-T.; Zhang, K.; Shi, B.-F. Amide-Directed Cobalt(III)-Catalyzed C-H Amidation of Ferrocenes. *Org. Lett.* **2019**, *21*, 951−954.
(141) Berrino, R.; Cacchi, S.; Fabrizi, G.; Goggiamani, A. 4-Aryl-2-quinolones from 3,3-Diarylacrylamides through Intramolecular Copper-Catalyzed C-H Functionalization/C-N Bond Formation. *J. Org. Chem.* **2012**, *77*, 2537−2542.
(142) Gui, Q.; Yang, Z.; Chen, X.; Liu, J.; Tan, Z.; Guo, R.; Yu, W. Synthesis of Phenanthridin-6(5H)-ones via Copper-Catalyzed Cyclization of 2-Phenylbenzamides. *Synlett* **2013**, *24*, 1016−1020.
(143) Yang, Y.; Zhang, D.; Vessally, E. Direct Amination of Aromatic C-H Bonds with Free Amines. *Top. Curr. Chem.* **2020**, *378*, 37.
(144) Shang, M.; Shao, Q.; Sun, S.-Z.; Chen, Y.-Q.; Xu, H.; Dai, H.-X.; Yu, J.-Q. Identification of Monodentate Oxazoline as a Ligand for Copper-Ppromoted *Ortho*-C-H Hydroxylation and Amination. *Chem. Sci.* **2017**, *8*, 1469−1473.
(145) Wu, P.; Huang, W.; Cheng, T.-J.; Lin, H.-X.; Xu, H.; Dai, H.-X. Copper-Catalyzed Oxalamide-Directed *ortho*-C-H Amination of Anilines with Alkylamines. *Org. Lett.* **2020**, *22*, 5051−5056.
(146) Ueda, S.; Nagasawa, H. Synthesis of 2-Arylbenzoxazoles by Copper-Catalyzed Intramolecular Oxidative C-O Coupling of Benzanilides. *Angew. Chem., Int. Ed.* **2008**, *47*, 6411−6413.
(147) Cheung, C. W.; Buchwald, S. L. Room Temperature Copper(II)-Catalyzed Oxidative Cyclization of Enamides to 2,5-Disubstituted Oxazoles via Vinylic C-H Functionalization. *J. Org. Chem.* **2012**, *77*, 7526−7537.
(148) Zheng, Q.; Chen, J.; Rao, G. W. Recent Advances in C-O Bond Construction *via* C-H Activation. *Russ. J. Org. Chem.* **2019**, *55*, 569−586.
(149) Iqbal, Z.; Joshi, A.; Ranjan De, S. Recent Advancements on Transition-Metal-Catalyzed, Chelation-Induced *ortho*-Hydroxylation of Arenes. *Adv. Synth. Catal.* **2020**, *362*, 5301−5351.
(150) Lied, F.; Patra, T.; Glorius, F. Group 9 Transition Metal-Catalyzed C-H Halogenations. *Isr. J. Chem.* **2017**, *57*, 945−952.
(151) Petrone, D. A.; Ye, J.; Lautens, M. Modern Transition-Metal-Catalyzed Carbon-Halogen Bond Formation. *Chem. Rev.* **2016**, *116*, 8003−8104.
(152) Das, R.; Kapur, M. Transition-Metal-Catalyzed Site-Selective C-H Halogenation Reactions. *Asian J. Org. Chem.* **2018**, *7*, 1524−1541.
(153) Yu, D.-G.; Gensch, T.; De Azambuja, F.; Vásquez-Cespedes, S.; Glorius, F. Co(III)-Catalyzed C-H Activation/Formal S_N-Type Reactions: Selective and Efficient Cyanation, Halogenation, and Allylation. *J. Am. Chem. Soc.* **2014**, *136*, 17722−17725.

https://doi.org/10.1021/acscatal.1c05267
ACS Catal. 2022, 12, 3452−3506

(154) Ma, W.; Kaplaneris, N.; Fang, X.; Gu, L.; Mei, R.; Ackermann, L. Chelation-Assisted Transition Metal-Catalysed C-H Chalcogenylations. *Org. Chem. Front.* **2020**, *7*, 1022−1060.
(155) Cera, G.; Ackermann, L. Weak *O*-Assistance Outcompeting Strong *N, N*-Bidentate Directing Groups in Copper-Catalyzed C-H Chalcogenation. *Chem.—Eur. J.* **2016**, *22*, 8475−8478.
(156) Wu, P.; Cheng, T.-J.; Lin, H.-X.; Xu, H.; Dai, H.-X. Copper-Mediated C-H Thiolation of (hetero)arenes Using Weakly Coordinating Directing Group. *Tetrahedron Lett.* **2020**, *61*, 152062.
(157) Bizet, V.; Besset, T.; Ma, J.-A.; Cahard, D. Recent Progress in Asymmetric Fluorination and Trifluoromethylation Reactions. *Curr. Top. Med. Chem.* **2014**, *14*, 901−940.
(158) Liu, H.; Gu, Z.; Jiang, X. Direct Trifluoromethylation of the C-H Bond. *Adv. Synth. Catal.* **2013**, *355*, 617−626.
(159) Ye, Y.; Sanford, M. S. Investigations into Transition-Metal-Catalyzed Arene Trifluoromethylation Reactions. *Synlett* **2012**, *23*, 2005−2013.
(160) Landelle, G.; Panossian, A.; Pazenok, S.; Vors, J.-P.; Leroux, F. R. Recent Advances in Transition Metal-Catalyzed Csp^2-Monofluoro-, Difluoro-, Perfluoromethylation and Trifluoromethylthiolation. *Beilstein J. Org. Chem.* **2013**, *9*, 2476−2536.
(161) Feng, C.; Loh, T.-P. Copper-Catalyzed Olefinic Trifluoromethylation of Enamides at Room Temperature. *Chem. Sci.* **2012**, *3*, 3458−3462.
(162) Feng, C.; Loh, T.-P. Directing-Group-Assisted Copper-Catalyzed Olefinic Trifluoromethylation of Electron-Deficient Alkenes. *Angew. Chem., Int. Ed.* **2013**, *52*, 12414−12417.
(163) Besset, T.; Cahard, D.; Pannecoucke, X. Regio- and Diastereoselective Cu-Mediated Trifluoromethylation of Functionalized Alkenes. *J. Org. Chem.* **2014**, *79*, 413−418.
(164) Cai, S.; Chen, C.; Sun, Z.; Xi, C. CuCl-Catalyzed *Ortho* Trifluoromethylation of Arenes and Heteroarenes with a Pivalamido Directing Group. *Chem. Commun.* **2013**, *49*, 4552−4554.
(165) Lerchen, A.; Knecht, T.; Daniliuc, C. G.; Glorius, F. Unnatural Amino Acid Synthesis Enabled by the Regioselective Cobalt(III)-Catalyzed Intermolecular Carboamination of Alkenes. *Angew. Chem., Int. Ed.* **2016**, *55*, 15166−15170.
(166) Ozols, K.; Onodera, S.; Wozniak, L.; Cramer, N. Cobalt(III)-Catalyzed Enantioselective Intermolecular Carboamination by C-H Functionalization. *Angew. Chem., Int. Ed.* **2021**, *60*, 655−659.
(167) Pichette Drapeau, M.; Gooßen, L. J. Carboxylic Acids as Directing Groups for C-H Bond Functionalization. *Chem.—Eur. J.* **2016**, *22*, 18654−18677.
(168) Shi, G.; Zhang, Y. Carboxylate-Directed C-H Functionalization. *Adv. Synth. Catal.* **2014**, *356*, 1419−1442.
(169) Mandal, R.; Sundararaju, B. Cp*Co(III)-Catalyzed Annulation of Carboxylic Acids with Alkynes. *Org. Lett.* **2017**, *19*, 2544−2547.
(170) Liu, X.-G.; Gao, H.; Zhang, S.-S.; Li, Q.; Wang, H. N-O Bond as External Oxidant in Group 9 Cp*M(III)-Catalyzed Oxidative C-H Coupling Reactions. *ACS Catal.* **2017**, *7*, 5078−5086.
(171) Nguyen, T. T.; Grigorjeva, L.; Daugulis, O. Cobalt-Catalyzed Coupling of Benzoic Acid C-H Bonds with Alkynes, Styrenes, and 1,3-Dienes. *Angew. Chem., Int. Ed.* **2018**, *57*, 1688−1691.
(172) Tao, L.-M.; Li, C.-H.; Chen, J.; Liu, H. Cobalt(III)-Catalyzed Oxidative Annulation of Benzaldehydes with Internal Alkynes *via* C-H Functionalization in Poly(ethylene glycol). *J. Org. Chem.* **2019**, *84*, 6807−6812.
(173) Shang, R.; Ilies, L.; Nakamura, E. Iron-Catalyzed *Ortho* C-H Methylation of Aromatics Bearing a Simple Carbonyl Group with Methylaluminum and Tridentate Phosphine Ligand. *J. Am. Chem. Soc.* **2016**, *138*, 10132−10135.
(174) Gallardo-Donaire, J.; Martin, R. Cu-Catalyzed Mild $C(sp^2)$-H Functionalization Assisted by Carboxylic Acids en Route to Hydroxylated Arenes. *J. Am. Chem. Soc.* **2013**, *135*, 9350−9353.
(175) Wang, Y.; Gulevich, A. V.; Gevorgyan, V. General and Practical Carboxyl-Group-Directed Remote C-H Oxygenation Reactions of Arenes. *Chem.—Eur. J.* **2013**, *19*, 15836−15840.
(176) Bhadra, S.; Dzik, W. I.; Goossen, L. J. Synthesis of Aryl Ethers from Benzoates through Carboxylate-Directed C-H Activating Alkoxylation with Concomitant Protodecarboxylation. *Angew. Chem., Int. Ed.* **2013**, *52*, 2959−2962.
(177) Bhadra, S.; Dzik, W. I.; Goossen, L. J. Decarboxylative Etherification of Aromatic Carboxylic Acids. *SYNTHESIS* **2013**, *45*, 2387−2390.
(178) Huang, Z.; Lim, H. N.; Mo, F.; Young, M. C.; Dong, G. Transition Metal-Catalyzed Ketone-Directed or Mediated C-H Functionalization. *Chem. Soc. Rev.* **2015**, *44*, 7764−7786.
(179) Santhoshkumar, R.; Mannathan, S.; Cheng, C.-H. Cobalt-Catalyzed Hydroarylative Cyclization of 1,6-Enynes with Aromatic Ketones and Esters *via* C-H Activation. *Org. Lett.* **2014**, *16*, 4208−4211.
(180) Santhoshkumar, R.; Mannathan, S.; Cheng, C.-H. Ligand-Controlled Divergent C-H Functionalization of Aldehydes with Enynes by Cobalt Catalysts. *J. Am. Chem. Soc.* **2015**, *137*, 16116−16120.
(181) Kimura, N.; Kochi, T.; Kakiuchi, F. Iron-Catalyzed Regioselective Anti-Markovnikov Addition of C-H Bonds in Aromatic Ketones to Alkenes. *J. Am. Chem. Soc.* **2017**, *139*, 14849−14852.
(182) Mandal, R.; Emayavaramban, B.; Sundararaju, B. Cp*Co(III)-Catalyzed C-H Alkylation with Maleimides Using Weakly Coordinating Carbonyl Directing Groups. *Org. Lett.* **2018**, *20*, 2835−2838.
(183) Hu, Y.; Zhou, B.; Chen, H.; Wang, C. Manganese-Catalyzed Redox-Neutral C-H Olefination of Ketones with Unactivated Alkenes. *Angew. Chem., Int. Ed.* **2018**, *57*, 12071−12075.
(184) Sk, M. R.; Bera, S. S.; Maji, M. S. Cp*Co(III)-Catalyzed C-H Alkenylation of Aromatic Ketones with Alkenes. *Adv. Synth. Catal.* **2019**, *361*, 585−590.
(185) Sk, M. R.; Maji, M. S. Cobalt(III)-Catalyzed Ketone-Directed C-H Vinylation using Vinyl Acetate. *Org. Chem. Front.* **2020**, *7*, 19−24.
(186) Banjare, S. K.; Nanda, T.; Ravikumar, P. C. Cobalt-Catalyzed Regioselective Direct C-4 Alkenylation of 3-Acetylindole with Michael Acceptors Using a Weakly Coordinating Functional Group. *Org. Lett.* **2019**, *21*, 8138−8143.
(187) Zhou, B.; Hu, Y.; Liu, T.; Wang, C. Aromatic C-H addition of Ketones to Imines Enabled by Manganese Catalysis. *Nat. Commun.* **2017**, *8*, 1169.
(188) Sk, M. R.; Bera, S. S.; Maji, M. S. Weakly Coordinating, Ketone-Directed Cp*Co(III)-Catalyzed C-H Allylation on Arenes and Indoles. *Org. Lett.* **2018**, *20*, 134−137.
(189) Ali, S.; Huo, J.; Wang, C. Manganese-Catalyzed Aromatic C-H Allylation of Ketones. *Org. Lett.* **2019**, *21*, 6961−6965.
(190) Messinis, A. M.; Finger, L. H.; Hu, L.; Ackermann, L. Allenes for Versatile Iron-Catalyzed C-H Activation by Weak O-Coordination: Mechanistic Insights by Kinetics, Intermediate Isolation, and Computation. *J. Am. Chem. Soc.* **2020**, *142*, 13102−13111.
(191) Yu, Y.; Wu, Q.; Liu, D.; Hu, L.; Yu, L.; Tan, Z.; Zhu, G. Synthesis of Benzofulvenes *via* Cp*Co(III)-Catalyzed C-H Activation and Carbocyclization of Aromatic Ketones with Internal Alkynes. *J. Org. Chem.* **2019**, *84*, 7449−7458.
(192) Yu, Y.; Wu, Q.; Liu, D.; Yu, L.; Tan, Z.; Zhu, G. Synthesis of 1-naphthols *via* Cp*Co(III)-Catalyzed C-H Activation and Cyclization of Sulfoxonium Ylides with Alkynes. *Org. Chem. Front.* **2019**, *6*, 3868−3873.
(193) Dethe, D. H.; C B, N.; Bhat, A. A. Cp*Co(III)-Catalyzed Ketone-Directed *ortho*-C-H Activation for the Synthesis of Indene Derivatives. *J. Org. Chem.* **2020**, *85*, 7565−7575.
(194) Wang, F.; Jin, L.; Kong, L.; Li, X. Cobalt(III)- and Rhodium(III)-Catalyzed C-H Amidation and Synthesis of 4-Quinolones: C-H Activation Assisted by Weakly Coordinating and Functionalizable Enaminone. *Org. Lett.* **2017**, *19*, 1812−1815.
(195) Shi, P.; Wang, L.; Chen, K.; Wang, J.; Zhu, J. Co(III)-Catalyzed Enaminone-Directed C-H Amidation for Quinolone Synthesis. *Org. Lett.* **2017**, *19*, 2418−2421.
(196) Bera, S. S.; Sk, M. R.; Maji, M. S. Weakly Coordinating, Ketone-Directed (η^5-Pentamethylcyclopentadienyl)cobalt(III)- and (η5-Pentamethylcyclopentadienyl)rhodium (III)-Catalyzed C-H Amidation of Arenes: A Route to Acridone Alkaloids. *Chem.—Eur. J.* **2019**, *25*, 1806−1811.

https://doi.org/10.1021/acscatal.1c05267
ACS Catal. 2022, 12, 3452−3506

(197) Jia, Q.; Kong, L.; Li, X. Cobalt(III)-Catalyzed C-H Amidation of Weakly Coordinating Sulfoxonium Ylides and α-Benzoylketene Dithioacetals. *Org. Chem. Front.* **2019**, *6*, 741−745.
(198) Shi, X.; Xu, W.; Wang, R.; Zeng, X.; Qiu, H.; Wang, M. Ketone-Directed Cobalt(III)-Catalyzed Regioselective C2-Amidation of Indoles. *J. Org. Chem.* **2020**, *85*, 3911−3920.
(199) Kong, X.; Xu, B. Manganese-Catalyzed *ortho*-C-H Amidation of Weakly Coordinating Aromatic Ketones. *Org. Lett.* **2018**, *20*, 4495−4498.
(200) Kong, L.; Yang, X.; Zhou, X.; Yu, S.; Li, X. Cobalt(III)-Catalyzed Efficient Synthesis of Indenones Through Carboannulation of Benzoates and Alkynes. *Org. Chem. Front.* **2016**, *3*, 813−816.
(201) Yu, W.; Zhang, W.; Liu, Z.; Zhang, Y. Cobalt(III)-Catalyzed Annulation of Esters and Alkynes: A Facile Route to Indenones. *Chem. Commun.* **2016**, *52*, 6837−6840.
(202) Bera, S. S.; Maji, M. S. Carbamates: A Directing Group for Selective C-H Amidation and Alkylation under Cp*Co(III) Catalysis. *Org. Lett.* **2020**, *22*, 2615−2620.
(203) Zhao, J.; Wang, Y.; He, Y.; Liu, L.; Zhu, Q. Cu-Catalyzed Oxidative C(sp^2)-H Cycloetherification of *o*-Arylphenols for the Preparation of Dibenzofurans. *Org. Lett.* **2012**, *14*, 1078−1081.
(204) Kamei, T.; Uryu, M.; Shimada, T. Cu-Catalyzed Aerobic Oxidative C-H/C-O Cyclization of 2,2′- Binaphthols: Practical Synthesis of PXX Derivatives. *Org. Lett.* **2017**, *19*, 2714−2717.
(205) Song, X.; Luo, X.; Sheng, J.; Li, J.; Zhu, Z.; Du, Z.; Miao, H.; Yan, M.; Li, M.; Zou, Y. Copper-Catalyzed Intramolecular Cross Dehydrogenative Coupling Approach to Coumestans from 2'-hydroxyl-3-arylcoumarins. *RSC Adv.* **2019**, *9*, 17391−17398.
(206) Beng, T. K.; Bauder, M.; Rodriguez, M. J.; Moreno, A. Copper-Catalyzed Regioselective Dehydrogenative Alkoxylation of Morpholinonyl Alkenols: Application to the Synthesis of Spirotricyclic Dihydropyrans and of Trans-Fused Bicyclic Morpholines. *New J. Chem.* **2018**, *42*, 16451−16455.
(207) Ma, X.; Li, H.; Xin, H.; Du, W.; Anderson, E. A.; Dong, X.; Jiang, Y. Copper-Catalyzed Intramolecular C-H Alkoxylation of Diaryltriazoles: Synthesis of Tricyclic Triazole Benzoxazines. *Org. Lett.* **2020**, *22*, 5320−5325.
(208) Liu, X.-G.; Zhang, S.-S.; Jiang, C.-Y.; Wu, J. Q.; Li, Q.; Wang, H. Cp*Co(III)-Catalyzed Annulations of 2-Alkenylphenols with CO: Mild Access to Coumarin Derivatives. *Org. Lett.* **2015**, *17*, 5404−5407.
(209) Kuppusamy, R.; Muralirajan, K.; Cheng, C.-H. Cobalt(III)-Catalyzed [5 + 1] Annulation for 2H-Chromenes Synthesis *via* Vinylic C-H Activation and Intramolecular Nucleophilic Addition. *ACS Catal.* **2016**, *6*, 3909−3913.
(210) Ghorai, J.; Reddy, A. C. S.; Anbarasan, P. Cobalt(III)-Catalyzed Intramolecular Cross-Dehydrogenative C-H/X-H Coupling: Efficient Synthesis of Indoles and Benzofurans. *Chem.—Eur. J.* **2016**, *22*, 16042−16046.
(211) Han, X.-L.; Liu, X.-G.; Lin, E.; Chen, Y.; Chen, Z.; Wang, H.; Li, Q. Cp*Co(III)-Catalyzed Oxidative [5 + 2] Annulation: Regioselective Synthesis of 2-Aminobenzoxepines *via* C-H/O-H Functionalization of 2-Vinylphenols with Ynamides. *Chem. Commun.* **2018**, *54*, 11562−11565.
(212) Lin, P.-P.; Han, X. L.; Ye, G.-H.; Li, J.-L.; Li, Q.; Wang, H. Cp*Co(III)-Catalyzed Dearomative [3 + 2] Spiroannulation of 2-Alkenylphenols with Ynamides *via* C-H Activation. *J. Org. Chem.* **2019**, *84*, 12966−12974.
(213) Dutta, P. K.; Ravva, M. K.; Sen, S. Cobalt-Catalyzed, Hydroxyl-Assisted C-H Bond Functionalization: Access to Diversely Substituted Polycyclic Pyrans. *J. Org. Chem.* **2019**, *84*, 1176−1184.
(214) Dai, J.-L.; Shao, N.-Q.; Zhang, J.; Jia, R.; Wang, D. H. Cu(II)-Catalyzed *ortho*-Selective Aminomethylation of Phenols. *J. Am. Chem. Soc.* **2017**, *139*, 12390−12393.
(215) Oyamada, J.; Hou, Z. Regioselective C-H Alkylation of Anisoles with Olefins Catalyzed by Cationic Half-Sandwich Rare Earth Alkyl Complexes. *Angew. Chem., Int. Ed.* **2012**, *51*, 12828−12832.
(216) Shi, X.; Nishiura, M.; Hou, Z. C-H Polyaddition of Dimethoxyarenes to Unconjugated Dienes by Rare Earth Catalysts. *J. Am. Chem. Soc.* **2016**, *138*, 6147−6150.
(217) Yamamoto, A.; Nishiura, M.; Oyamada, J.; Koshino, H.; Hou, Z. Cycloterpolymerization of 1,6-Heptadiene with Ethylene and Styrene Catalyzed by a THF-Free Half-Sandwich Scandium Complex. *Macromolecules* **2016**, *49*, 2458−2466.
(218) Zhao, Y.; Luo, G.; Wang, X.; Kang, X.; Cui, D.; Hou, Z.; Luo, Y. DFT Studies on the Polymerization of Functionalized Styrenes Catalyzed by Rare-Earth-Metal Complexes: Factors Affecting C-H Activation Relevant to Step-Growth Polymerization. *Organometallics* **2018**, *37*, 3210−3218.
(219) Yamamoto, A.; Nishiura, M.; Yang, Y.; Hou, Z. Cationic Scandium Anisyl Species in Styrene Polymerization Using Anisole and *N, N*-Dimethyl-*o*-toluidine as Chain-Transfer Agents. *Organometallics* **2017**, *36*, 4635−4642.
(220) Tang, B.; Hu, X.; Liu, C.; Jiang, T.; Alam, F.; Chen, Y. Tandem Cyclization/Hydroarylation of α,ω-Dienes Triggered by Scandium-Catalyzed C-H Activation. *ACS Catal.* **2019**, *9*, 599−604.
(221) Oyamada, J.; Nishiura, M.; Hou, Z. Scandium-Catalyzed Silylation of Aromatic C-H Bonds. *Angew. Chem., Int. Ed.* **2011**, *50*, 10720−10723.
(222) Wang, D.; Désaubry, L.; Li, G.; Huang, M.; Zheng, S. Recent Advances in the Synthesis of C2-Functionalized Pyridines and Quinolines Using *N*-Oxide Chemistry. *Adv. Synth. Catal.* **2021**, *363*, 2−39.
(223) Barsu, N.; Sen, M.; Premkumar, J. R.; Sundararaju, B. Cobalt(III) Catalyzed C-8 selective C-H and C-O Coupling of Quinoline N-Oxide with Internal Alkynes *via* C-H Activation and Oxygen Atom Transfer. *Chem. Commun.* **2016**, *52*, 1338−1341.
(224) Kalsi, D.; Laskar, R. A.; Barsu, N.; Premkumar, J. R.; Sundararaju, B. C-8-Selective Allylation of Quinoline: A Case Study of β-Hydride *vs* β-Hydroxy Elimination. *Org. Lett.* **2016**, *18*, 4198−4201.
(225) Shukla, R. K.; Nair, A. M.; Khan, S.; Volla, C. M. R. Cobalt-Catalyzed C8-Dienylation of Quinoline-N-Oxides. *Angew. Chem., Int. Ed.* **2020**, *59*, 17042−17048.
(226) Wang, H.; Moselage, M.; Gonzalez, M. J.; Ackermann, L. Selective Synthesis of Indoles by Cobalt(III)-Catalyzed C-H/N-O Functionalization with Nitrones. *ACS Catal.* **2016**, *6*, 2705−2709.
(227) Zhong, M.; Sun, S.; Cheng, J.; Shao, Y. Iron-Catalyzed Cyclization of Nitrones with Geminal-Substituted Vinyl Acetates: A Direct [4 + 2] Assembly Strategy Leading to 2,4-Disubstituted Quinolines. *J. Org. Chem.* **2016**, *81*, 10825−10831.
(228) Liu, Y.; Wang, C.; Lv, N.; Liu, Z.; Zhang, Y. Synthesis of Quinoline N-Oxides by Cobalt-Catalyzed Annulation of Arylnitrones and Alkynes. *Adv. Synth. Catal.* **2017**, *359*, 1351−1358.
(229) Dhiman, A. K.; Thakur, A.; Kumar, I.; Kumar, R.; Sharma, U. Co(III)-Catalyzed C-H Amidation of Nitrogen-Containing Heterocycles with Dioxazolones under Mild Conditions. *J. Org. Chem.* **2020**, *85*, 9244−9254.

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