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Transition metal-catalyzed conversion of aldehydes to ketones

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ABSTRACT

Ketones are one of the most important classes of organic compounds, and widely present in various pharmacological compounds, biologically active molecules and functional materials. Over the past few decades, transition metal-catalyzed conversion of aldehydes has been found to be a powerful method. With the continuous development in recent years, it has become an efficient and uncomplicated strategy for constructing ketones. There are four major mechanisms for transition metal-catalyzed ketone synthesis from aldehyde: (1) carbonyl-Heck reaction, that is 1,2-insertion of organometal species to aldehydic C=O double bond, (2) direct insertion of transition metal catalysts to aldehydic C-H bond, (3) aldehyde as acyl radical, (4) aldehyde as carbon radical acceptor. This article summarizes related reports on the transformations of aldehydes to generate corresponding ketones under different reaction conditions.

1. Introduction

Ketones are one of the most important classes of organic compounds, for example, aryl ketones, heteroaryl ketones, and diaryl ketones are common structural motifs in multitudinous natural products [1–9]. A series of derivatives of ketones are versatile building blocks for the synthesis of more complex natural products, biologically active molecules, pharmaceuticals, agricultural chemicals, dyes, and functional materials (Fig. 1) [10–16]. Due to their importance, the development of synthetic methods for the preparation of these scaffolds has received considerable attention.

Traditional methods for the preparation of ketone compounds include Friedel-Crafts reaction of substituted aromatic rings and acylation of organometallic reagents [17–25]. However, the above strategies have some disadvantages to a certain extent. These methods are often painstaking, laborious, and time-consuming multistep processes, making the preparations typically inefficient and uneconomical. For example, when using Friedel-Crafts acylation reaction, an excessive amount of Lewis acid catalyst (such as $AlCl_3$) is usually required, and a large amount of acid gas and sewage are generated during the reaction and post-treatment process, causing environmental pollution [19]. Moreover, the formation of *ortho* and *para* isomers with untunable regioselectivity results in separation problems and makes aryl ketones with *meta* substituents difficult to access. Consequently, there is a great need to develop simple, effective and versatile methods to synthesize these scaffolds.

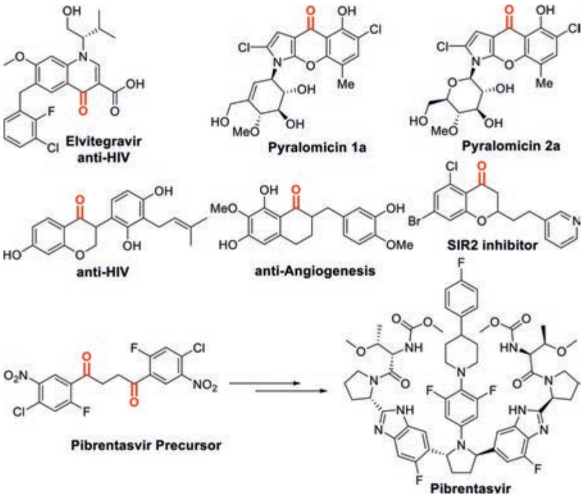

Fig. 1. Selective examples of biologically active ketones.

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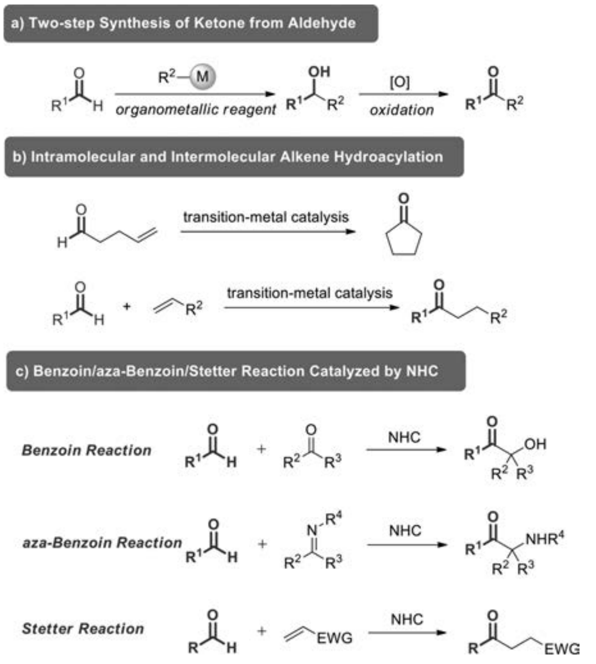


Scheme 1. Selective examples of biologically active ketones and derivatives.

In terms of molecular structure, using aldehyde as starting material to prepare ketone, the conversion would be considered as a much more simple and efficient protocol. And the functionalization of aldehydic C–H bonds has been quite an active research area. However, in the past, the strategy was generally achieved by adding organometallic reagent to aldehyde and then oxidizing the alcohol intermediate (Scheme 1a) [26–30]. The operation procedures of this approach are cumbersome and organometallic reagents are sensitive to air, so further developments are needed to realize the generation of ketones from aldehydes through a one-step process. A large number of studies have shown that the synthesis of ketones through the C–H activation and functionalization of aldehydes under the catalysis of various transition-metals is an effective strategy. The direct hydroacylation of olefins and alkynes is a typical reaction of this conversion, which has been summarized by Willis in 2010 [31]. Hydroacylation generally involves the addition of an acyl unit and a hydrogen atom across a C–C multiple bond, including both intra- and intermolecular type reactions (Scheme 1b) [31–41]. In addition, *N*-heterocyclic carbene (NHC) catalyzed umpolung additions of aldehydes to carbonyl compounds (benzoin reaction) [42–44], imines (aza-benzoin reaction) [45–49], and Michael acceptors (Stetter reaction) [50–58], are also powerful protocols to produce functional ketones by hydroacylation (Scheme 1c) [59–70].

Over the past few decades, transition metal-catalyzed conversions of aldehydes to ketones have been found to be a powerful method. Despite these significant advances, the development of novel strategies to synthesize various ketone derivatives still drawn considerable attention. With the continuous efforts in recent years, transition metal-catalyzed cross-coupling reactions have been the highly versatile methods for the construction of complex molecules from simple building blocks in both research laboratories and industry. Generally, these reactions are tolerant of a variety of functional groups, applicable to a wide range of substrates, and have excellent practical value and broad application prospects [71–76]. In these transformations, the most commonly utilized transition metals may include group VIIB, VII and IB, such as rhodium, ruthenium, palladium, nickel, cobalt, platinum, copper, silver, iron, manganese (Fig. 2). Herein, this article summarizes the related conversions using the different catalytic system with transition metals.

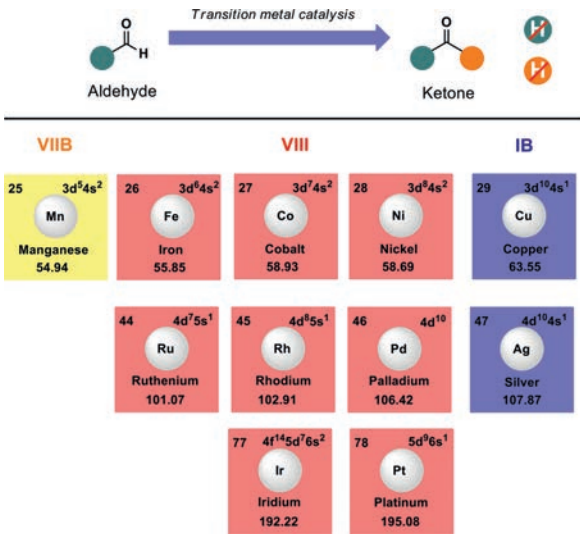
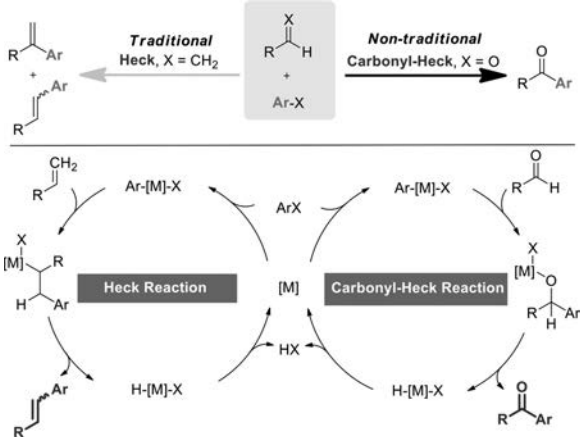


Fig. 2. Transition metals used in the conversions of aldehydes to ketones.



Scheme 2. Heck reaction and carbonyl-Heck reaction.

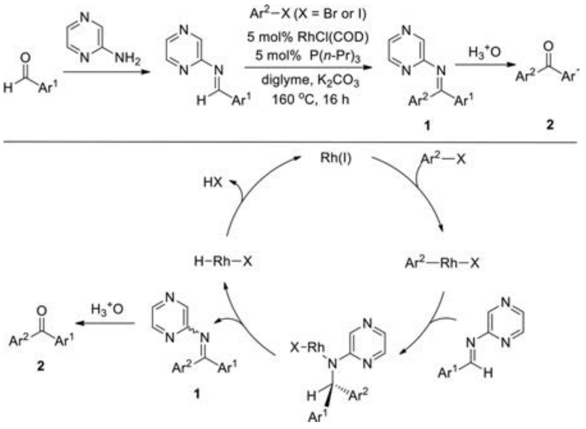
There are four major mechanisms for transition metal-catalyzed ketone synthesis from aldehyde: (1) carbonyl-Heck reaction, that is 1,2-insertion of organometal species to aldehydic C=O double bond, (2) direct insertion of transition metal catalysts to aldehydic C-H bond, (3) aldehyde as acyl radical, (4) aldehyde as carbon radical acceptor.

2. Carbonyl-Heck-type mechanism

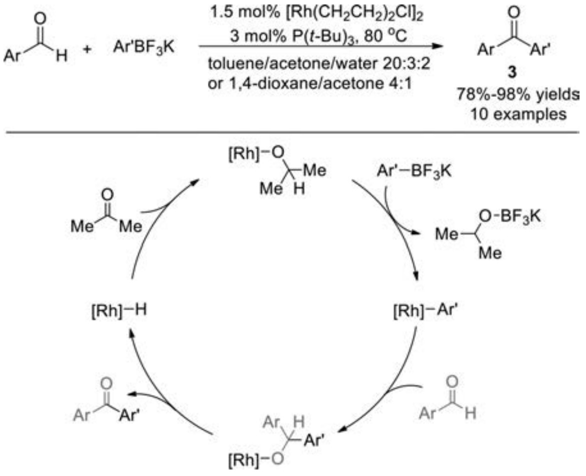
Heck reaction, the coupling of olefins with aryl halides or pseudo-halides, is among the most important transformations in modern synthetic chemistry. In the carbonyl variant of Heck reaction, the C=O bond of aldehyde takes the role of the olefin in the insertion/β-H elimination steps. Conceptually, ketones, instead of substituted olefins, are afforded as the major product of the catalytic cycle (Scheme 2).

2.1. Rh catalysis

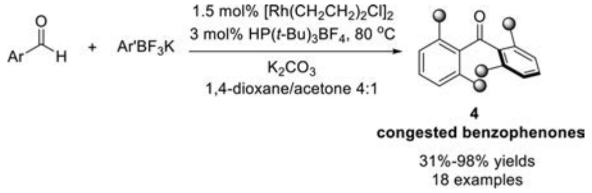
In 2000, Hartwig group reported the rhodium(I)-catalyzed coupling reaction of aryl halides with activated *N*-pyrazyl aldimines through the Heck-type mechanism (Scheme 3) [77]. The *N*-pyrazyl aldimines could be easily prepared by the condensation of aldehydes and 2-aminopyrazine, and the ketones were generated *via*



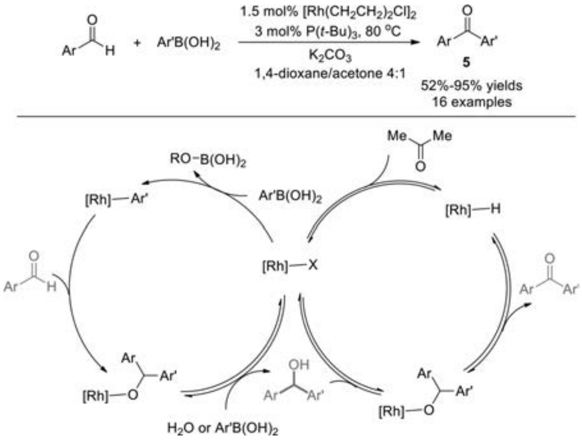
Scheme 3. Synthesis of ketones *via* the coupling of aryl halides with *N*-pyrazyl aldimines.



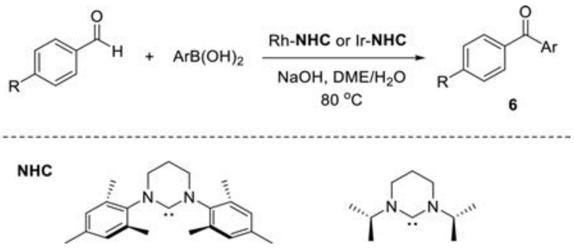
Scheme 4. Rh(I)-catalyzed cross-coupling of arylaldehydes with ArBF$_3$K.



Scheme 5. Sterically hindered benzophenones *via* Rh(I)-catalyzed cross-coupling of arylaldehydes with ArBF$_3$K.



Scheme 6. Rh(I)-catalyzed cross-coupling of arylaldehydes with arylboronic acids.



Scheme 7. Arylation of aryl aldehydes with arylboronic acids.

hydrolysis of the corresponding ketimines. However, the method is not an atom-economic way to access ketones, needing three steps, and the *N*-pyrazyl aldimines should be prepared in advance.

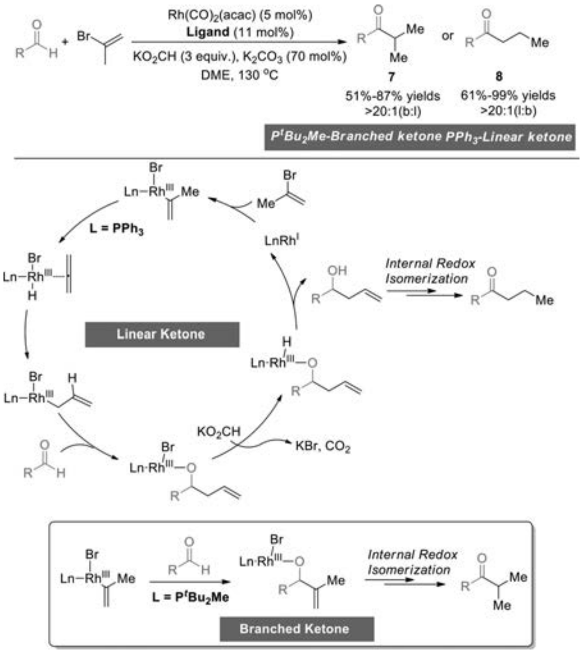
Using P(t-Bu)$_3$ as ligand, in 2004, Darses and Genet *et al*. reported the first rhodium(I)-catalyzed cross-coupling reaction of organoboronic reagents (ArBF$_3$K) with aryl aldehydes to generate diaryl ketones under mild conditions without base (Scheme 4) [78]. Deuterium labeling experiment indicated that this transformation proceeded in a Heck-type mechanism, followed by an unusual hydrogen transfer process, in which acetone worked as a hydride acceptor.

However, the majority of biologically active benzophenones are sterically congested, at least bearing di-*ortho*-substituents, and were mainly obtained *via* the addition of aryllithium or arylmagnesium to aldehydes followed by oxidation. The highly desirable mild transition-metal-catalyzed reactions are limited to reagents that are sterically unencumbered. In 2008, Darses and Genet group employed a rhodium/tri-*tert*-butylphosphane catalyst system with the stable phosphonium salt as the precursor of P(t-Bu)$_3$ instead of highly oxidizable P(t-Bu)$_3$, and for the first time disclosed a straightforward protocol for the synthesis of congested benzophenones from aryl aldehydes and potassium aryltrifluoroborates (Scheme 5) [79]. This reaction was handled in easy-to-operate conditions. A broad substrate scope was tolerated, di-, tri-, and even tetra-*ortho*-substituted benzophenones can be synthesized.

In 2007, Genet *et al*. employed arylboronic acids and developed the rhodium(I)-catalyzed cross-coupling with aryl aldehydes to access directly ketones *via* formal C-H bond activation (Scheme 6) [80]. The reaction pathway was different from their above-mentioned work using ArBF$_3$K which was a tandem catalytic process involving two cycles, an addition cycle and an oxidation cycle combined through β-hydride transfer. In GC/MS monitoring experiment, surprisingly, the aldehyde disappeared very fast to form carbinol *via* the protonation of alkoxo-rhodium intermediate by water formed in the reaction medium (or directly by the boronic acid), giving an active hydroxo-rhodium species. It demonstrated that this reaction may include two consecutive catalytic reactions: rhodium-catalyzed addition of the boronic acid to aldehyde to produce the carbinol; oxidation of the corresponding alcohol to provide the ketone.

In 2004, Buchmeiser and co-workers reported Rh- or Ir-NHC complexes catalyzed arylation of aryl aldehydes with arylboronic acids which described a straightforward access to diaryl ketones with low catalyst loading (0.08-1 mol%) (Scheme 7) [81]. The structure of catalyst strongly affected the activity and selectivity of the reaction, the tetrahydropyrimidin-2-ylidene ligands enhance the efficiency; the propyl groups at both nitrogen atoms of NHC ligands are more effective than other substituents; iridium shows low activity but high selectivity.

In 2019, Krische group developed a regiodivergent rhodium-catalyzed reductive coupling-redox isomerization of aldehydes with vinyl bromide to form branched (P^{t}Bu$_2$Me) or linear (PPh$_3$)



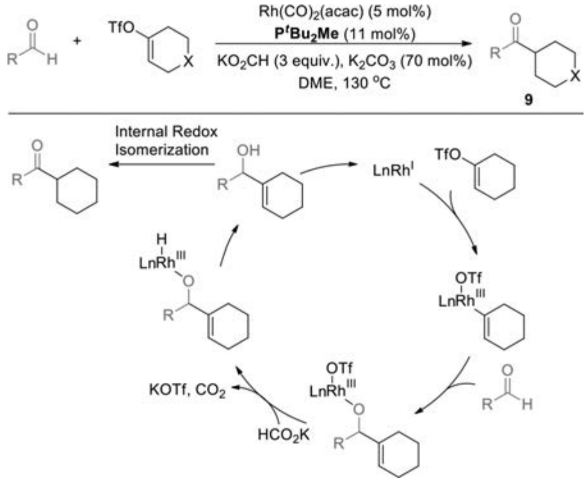
Scheme 8. Regiodivergent Rh-catalyzed vinyl bromide reductive coupling-redox isomerization.

ketones using different ligands (Scheme 8) [82]. A series of deuterium labeling experiments disclosed that a redox isomerization was the critical step. Initially, the oxidative addition of vinyl bromide formed vinyl rhodium(III) species. In the process of the formation of linear ketone, the weak σ-donor ligand PPh_3 dissociated at the vinylrhodium(III) intermediate stage and motivated to form transient allene through β-hydride elimination, and then generated allylrhodium(III) hydride species. Aldehyde insertion provided a homoallylic rhodium alkoxide, and the bromide moiety of the kinetic rhodium alkoxide reacted with HCO_2K to form a hydride. Followed by reductive elimination to afford a homoallylic alcohol which went through isomerization to deliver the linear ketone. For the formation of branched ketone, the strong σ-donor ligand was used. The aldehyde inserted to vinyl rhodium(III) species, converted to the allylic alcohol and, therefrom, the branched ketone in the analogous process.

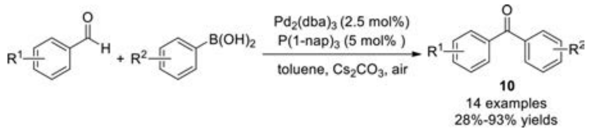
Later, employing the same catalyst system for the branched ketones, and replacing vinyl bromide with vinyl triflate, they developed the vinyl triflate-aldehyde reductive coupling-redox isomerization (Scheme 9) [83]. Many functional aryl or alkyl aldehydes afford the corresponding ketones under the conditions as the previous vinyl bromide adopted.

2.2. Pd catalysis

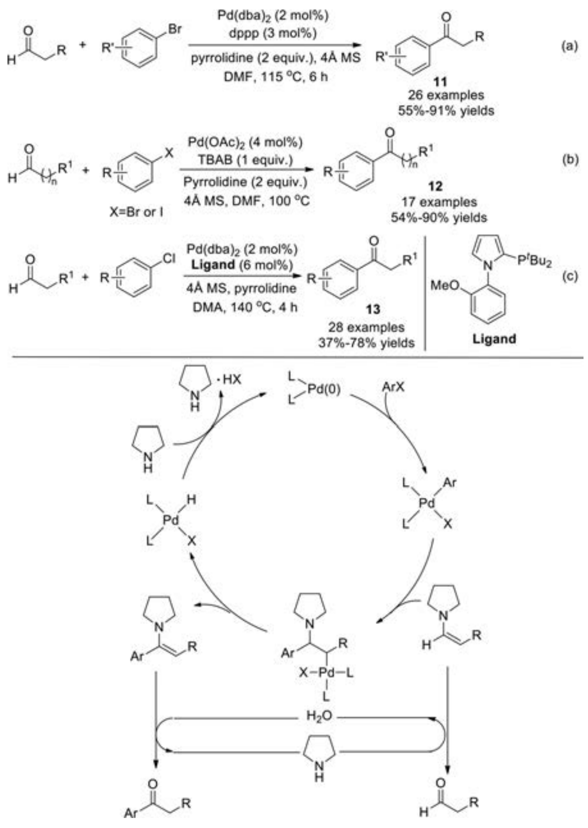
In 2008, Wu and Cheng *et al.* also reported the synthesis of diaryl ketones using a palladium-catalyzed coupling of aromatic aldehydes with aryl boronic acids in moderate to excellent yields (Scheme 10) [84]. The reaction proceeded smoothly in the presence of $Pd_2(dba)_3$ and $P(1\text{-nap})_3$. It is worth noting that Cs_2CO_3 might exhibit a dual ability: (1) Facilitating the addition of organoboronic acids to aldehydes, affording carbinol derivatives; (2) Prompting the aerobic oxidation of the carbinol derivatives *in situ* to aromatic ketones. A variety of functional groups like nitro, cyano, acetoxy, heteroaryl and steric substrates were all well tolerated to access to the desired ketones in good efficiency. All the reactions were carried out under an ambient atmosphere, and rigorous exclusion of air or moisture was not required.



Scheme 9. Rh-catalyzed vinyl triflate-aldehyde reductive coupling–redox isomerization.

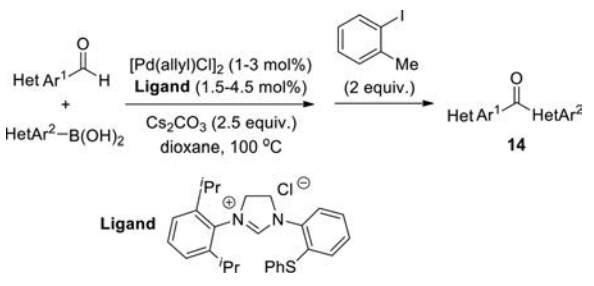


Scheme 10. Pd-catalyzed coupling of aldehydes and organoboronic acid.



Scheme 11. Pd-catalyzed direct acylation of aryl halides.

In 2008, a direct acylation of aryl bromides was developed by Xiao and co-workers, affording alkyl aryl ketones in one step, using palladium and pyrrolidine as the co-catalysts and 4Å MS as additive (Scheme 11a) [85]. In the presence of alkyl aldehydes, the addition of pyrrolidine resulted in the formation of a highly reactive electron-rich enamine, subsequently a Heck-type reaction with pal-



Scheme 12. Heteroaryl and diheteroaryl ketones synthesis *via* Pd-catalyzed 1,2-addition and oxidation.

ladium, followed by hydrolysis to form the corresponding ketones. It is interesting to note that, under similar conditions but without pyrrolidine and 4Å MS, the coupling of aldehydes with aryl bromides led to α-arylated aldehydes instead of ketones.

Furthermore, a palladium(0) nanoparticle-catalyzed direct acylation aryl bromides or iodides was reported by Ranu group in 2010 [86]. Tetrabutylammonium bromide (TBAB) was used as an additive, which stabilized the Pd nanoparticle from gathering. Various aryl iodides and bromides proceeded smoothly with open-chain aldehydes to form the alkyl aryl ketones in good yield (Scheme 11b). A few months later, Xiao group extended the substrate to a wide range of aryl chlorides in high temperature, a bulky electron-rich monophosphine ligand was adopted to enhance the reaction activity, and the reaction was tolerant of functionalities on the aliphatic aldehydes (Scheme 11c) [87].

In 2013, Kuriyama and Onomura *et al.* developed the palladium/imidazolinium carbene-catalyzed 1,2-addition and oxidation to synthesize heteroaryl and diheteroaryl ketones from aldehydes and organoboronic acids (Scheme 12) [88]. The 1,2-addition involves a transmetalation-insertion mechanism, and the oxidation proceeds through oxidative addition, β-hydrogen elimination, and reductive elimination. A high level of catalyst performance was attained in the one-pot process using 1.0-3.0 mol% catalyst loading. Several oxidants were examined, a sterically hindered 2-iodotoluene was the optimal choice, giving the desired ketones in good to excellent yields.

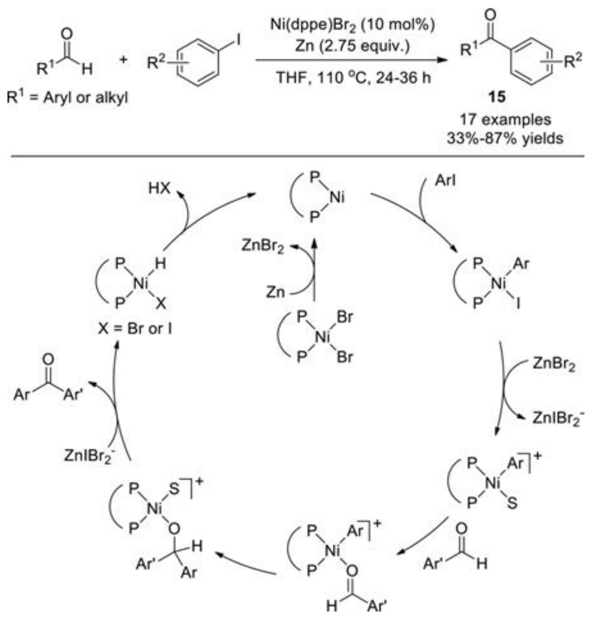
2.3. Ni catalysis

Although Rh-, Ru- and Pd-catalyzed coupling reactions for ketones synthesis from aldehydes were well established, efforts have been made to replace these expensive metals. Owing to its high activity showed in many coupling reactions, nickel is considered as the most promising cheap metal. The first nickel-catalyzed cross-coupling reaction of aldehydes to access ketones was reported by the Cheng group in 2002, providing a new way for chemoselective synthesis of diaryl ketones using aryl aldehydes and aryl iodides in fair to good yields (Scheme 13) [89]. The catalytic reaction proceeds smoothly only with bidentate phosphine nickel complexes as catalysts, such as Ni(dppe)Br$_2$, whereas monodentate phosphine complexes are completely ineffective.

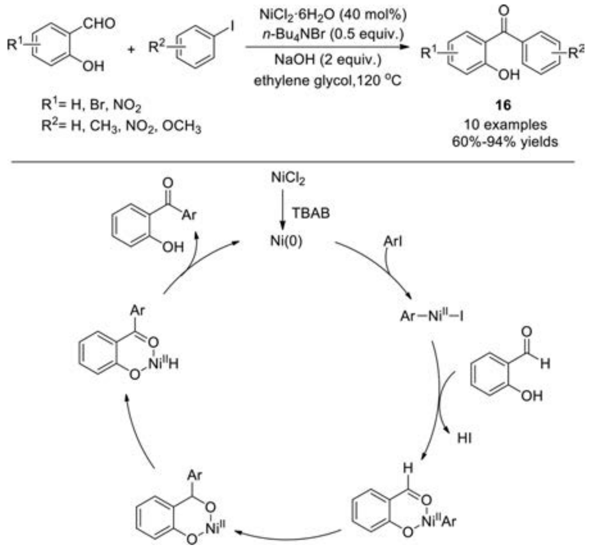
It is worth noting that zinc powder is critical to the coupling. Reduction of Ni(II) to Ni(0) by zinc metal with the formation of zinc halide likely initiates the catalytic reaction. The oxidative addition of aryl iodide, coordination of aldehyde, formation of nickel alkoxide and subsequent β-hydride elimination occurs, and affords the desired ketone.

In 2015, the ligand-free nickel-catalyzed C-H arylation of 2-hydroxybenzaldehydes with aryl iodides to access 2-hydroxybenzophenones was reported by Nowrouzi group, employing the catalyst system of NiCl$_2$·6H$_2$O and n-Bu$_4$NBr (Scheme 14) [90]. Although only 10 examples, this is an efficient, inexpensive, and practicable method for the synthesis of ketones. It is worth noting that the introduction of n-Bu$_4$NBr as an additive not only stabilizes the catalytic system by avoiding undesired agglomeration and deactivation *via* the formation of a monomolecular layer around the metal core, but also plays as a reductant for the generation of Ni(0).

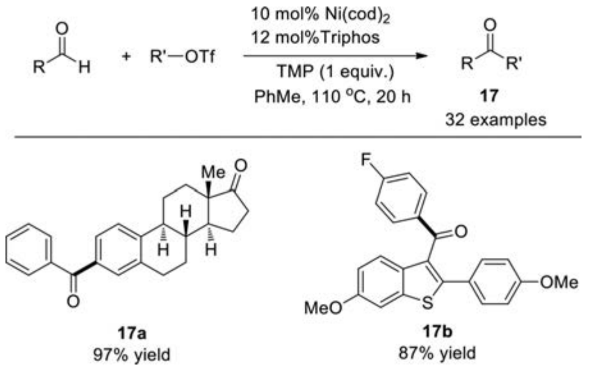
In 2017, Newman and co-workers developed the nickel-catalyzed carbonyl-Heck reaction of aldehydes with organotriflates to make ketones, using Ni(0) precatalyst, tridentate triphos ligand, and bulky amine base (TMP, 2,2,6,6-tetramethylpiperidine) (Scheme 15) [91]. This pathway is supported by the effectiveness of the catalyst in traditional Heck reactions. High-throughput experiment was utilized to uncover the specific combination of halide/pseudohalide, metal, ligand, and base necessary to enable the reaction. The intermolecular coupling demonstrated extensive compatibility, both aryl aldehydes and aryl triflates bearing electron-donating, electron-withdrawing, and sterically hindering



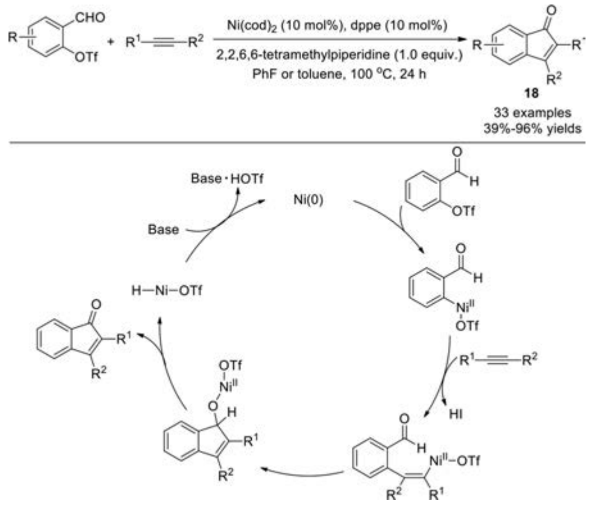
Scheme 13. Ni-catalyzed ketone synthesis *via* coupling of aldehydes and aryl iodides.



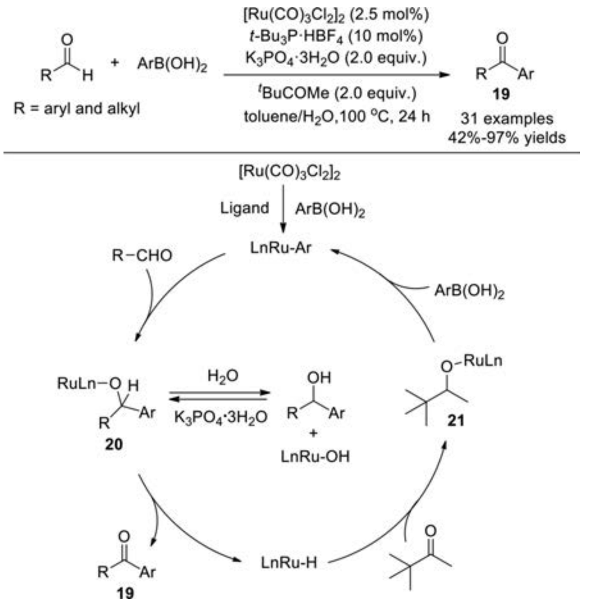
Scheme 14. Ni-catalyzed C-H arylation of 2-hydroxybenzaldehydes with aryl iodides.



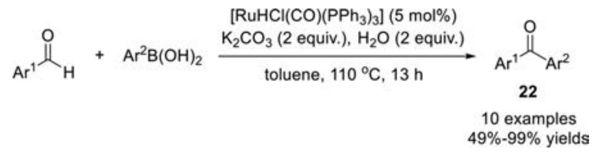
Scheme 15. Ni-catalyzed carbonyl-Heck reaction of aldehydes with organotriflates.



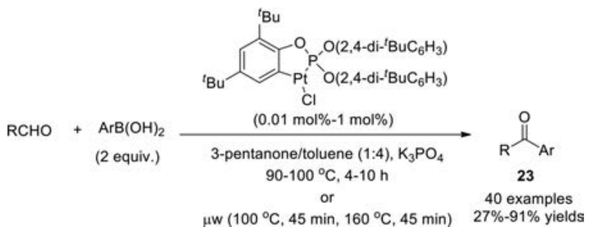
Scheme 16. Ni-catalyzed Larock annulations of substituted 2-formylphenyl trifluoromethanesulfonate with alkynes.



Scheme 17. Ru-catalyzed cross-coupling of aldehydes with arylboronic acids to generate aryl ketones.



Scheme 18. Ru-catalyzed coupling reaction of arylboronic acids with aryl aldehyde.



Scheme 19. Orthoplatinated triarylphosphite-catalyzed ketone synthesis.

functionality were tolerated. Aliphatic aldehydes need quinuclidine as the base to prevent Tishchenko-type side products when using TMP. Some bioactive molecules can be prepared, such as estrone-derived compound **17a** and benzothiophene **17b** (precursor to Raloxifene).

Recently, we present a direct transformation based on nickel-catalyzed Larock annulations of substituted 2-formylphenyl trifluoromethanesulfonate with alkynes to deliver a wide range of indenone analogs that are valuable synthetic intermediates for natural compounds (Scheme 16) [92]. This catalytic system is shown to proceed through a redox neutral arylation in high yields with excellent regioselectivities. Mechanistically, the oxidative addition of a nickel into the weak C–OTf bond, followed by the migratory insertion of the alkyne, and subsequently the intramolecular “carbonyl” variant of the Heck reaction and β-H elimination leads to the formation of the desired indanone.

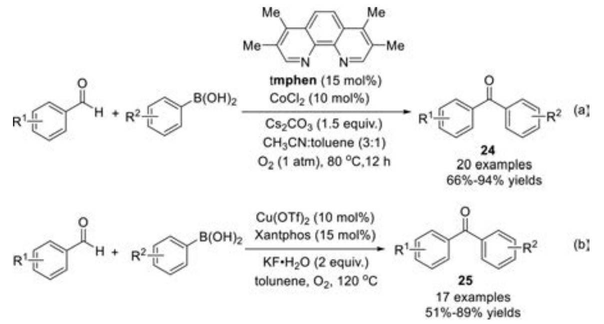
2.4. Ru catalysis

The first Ru-catalyzed cross-coupling reaction of aldehydes with arylboronic acids to generate aryl ketones was described by Wan group in 2011, aliphatic and aromatic aldehydes are effective (Scheme 17) [93]. The kinetic isotope effect experiment demonstrated that C–H activation of aldehyde was not involved in the catalytic cycle, and hydrogen abstraction from alcohol was the probably rate-limiting step. The possible reaction pathway was initiated by transmetalation of boronic acid with $[Ru(CO)_3Cl_2]_2$ to give aryl ruthenium complex, then aldehyde inserted into ruthenium-carbon bond to provide an alkoxo-ruthenium intermediate **20** which underwent β-hydride elimination to afford the final ketone and ruthenium hydride complex. Subsequently, pinacolone inserted into the ruthenium-hydrogen bond to generate alkoxo-ruthenium intermediate **21**, followed by transmetalation wtih boronic acid to regenerate arylruthenium complex.

In the same year, Fukuyama and Ryu *et al.* also reported a ruthenium-catalyzed coupling reaction of aryl aldehydes with arylboronic acids for the synthesis of diaryl ketones using $[RuHCl(CO)(PPh_3)_3]$ as catalyst (Scheme 18) [94]. Various arylboronic acids and aryl aldehydes especially the steric 2-substituted aryl aldehyde work smoothly to give the desired ketones in good yields. This reaction underwent a hydrogen transfer pathway and may contain two consecutive steps: formation of the alcohols and hydrogen transfer to aldehydes to form ketones. Without water, the reaction did not proceed, and no ketone was formed.

2.5. Pt catalysis

In 2010, Hu and co-workers reported an addition reaction followed by an oxidation of aldehydes with arylboronic acids to access aryl ketones (Scheme 19) [95]. The reaction employed ortho-



Scheme 20. Co or Cu-catalyzed arylation of arylboronic acids with aldehydes.

platinated triarylphosphite as catalyst and K_3PO_4 as the best base. The catalyst is an anionic four-electron donor-based metallacycle, which is readily available and air/moisture-stable. 3-Pentanone was identified as a suitable oxidant for the oxidation of alcohol step. Notably, aryl and aliphatic aldehydes can react well with the arylboric acid to obtain the corresponding aryl-aryl and alkyl-aryl ketones in good yield. Besides, a microwave-assisted method was developed with low catalyst loading (0.01 mol%), and the reaction time shortened dramatically. The platinacycle-catalyzed protocols represent the first examples of direct access to aryl alkyl ketones from alkyl aldehydes with arylboronic acids *via* the tandem addition-oxidation reaction.

2.6. Co and Cu catalysis

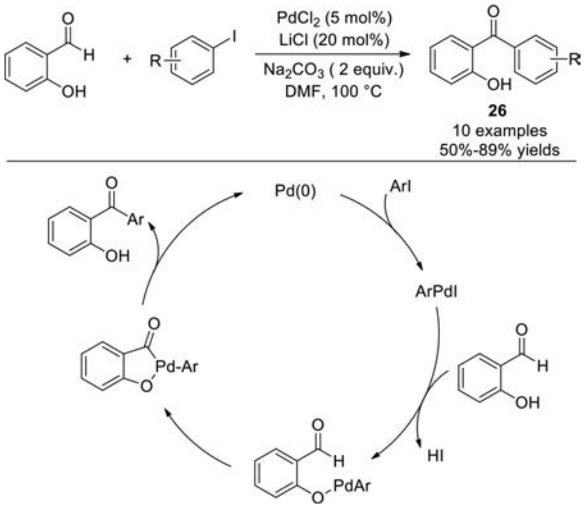
A cobalt-catalyzed arylation of arylboronic acids with aldehydes was developed by the Cheng group in 2011, in the presence of $CoCl_2$ and tmphen under 1 atm of O_2 (Scheme 20a) [96]. Both electron-withdrawing and electron-donating substituted aryl aldehydes and heterocyclic aldehydes reacted smoothly with different substituted boronic acids to afford diaryl ketones in good yields. This cobalt-catalyzed reaction may proceed in a Heck-type mechanism, a cobalt hydride was formed, O_2 as an oxidant to regenerate the active Co(II) species.

Chen and Wu *et al.* achieved this tramsformation using the $Cu(OTf)_2$ and Xantphos catalytic system, aryl ketones were formed in moderate to good yields (Scheme 20b) [97]. As oxidant, oxygen was critical for the reaction. Different aryl aldehydes were well tolerated irrespective of the electronic effect of substituents. However, electron-withdrawing arylboronic acids reacted slowly in lower yields than electron-rich ones owing to the weak transmetalation ability. Although this reaction showed limited examples, the cheap copper was used and a practicable way for the synthesis of ketones was established.

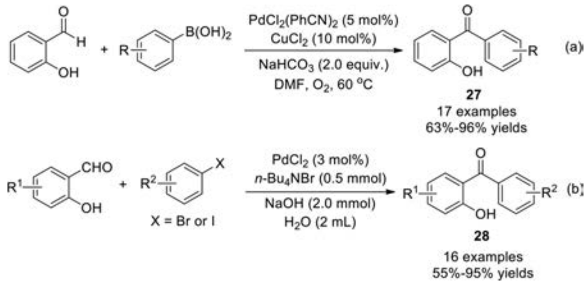
3. Insertion of metal catalysts to aldehydic C-H bonds

In combination with these reports on the transition-metal catalyzed carbonylative Heck reaction of aryl halides, pseudohalides or organometallic reagents, this methodology *via* direct insertion of metal catalysts to aldehydic C—H bond affords another way to complete the Heck reaction on carbonyl groups. Most importantly, it provides efficient synthetic method for preparing the structural motifs of valuable natural products and bioactive molecules such as aurone, flavone, 2′-hydroxychalcone, and flavanone.

3.1. Pd catalysis



Scheme 21. Pd-catalyzed coupling of 2-hydroxybenzaldehyde with aryl iodide.

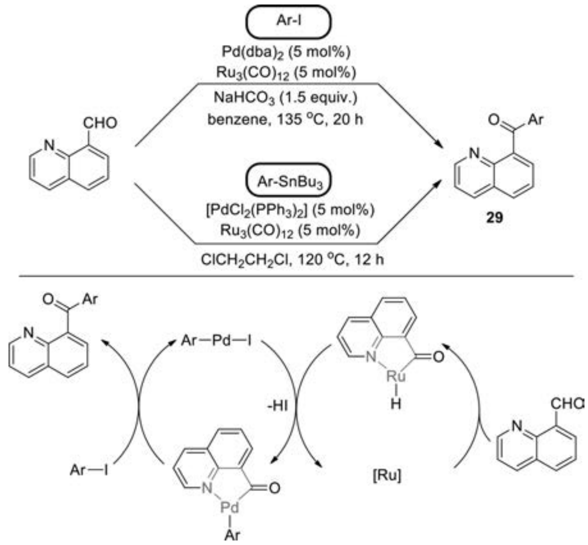


Scheme 22. Pd-catalyzed coupling of 2-hydroxybenzaldehyde with aryl boronic acids or aryl halides.

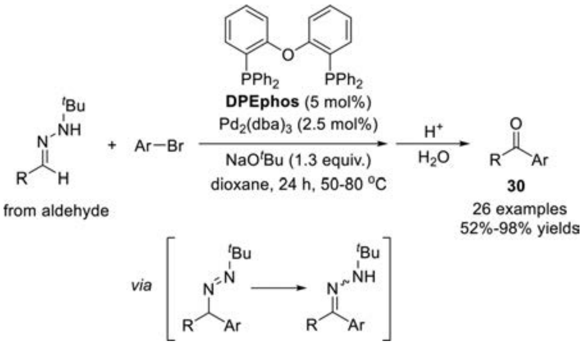
As early as 1996, Miura and co-workers reported the first palladium-catalyzed coupling of 2-hydroxybenzaldehydes with aryl iodides *via* chelation-assisted C—H cleavage of the aldehyde [98]. The direct $PdCl_2$-catalyzed ketone synthesis from aldehyde proceeded smoothly in the presence of Na_2CO_3 (base) and LiCl (additive), although the scope was limited in several examples (Scheme 21). In the plausible catalytic cycle, oxidative addition of aryl iodide to Pd(0) to produce the aryl palladium species which reacted with 2-hydroxybenzaldehyde to generate the aryl(aryloxy)palladium intermediate and released HI. Then, oxidative addition produced the palladium(IV) species, followed by twofold reductive elimination to afford the corresponding ketone.

A similar strategy using arylboronic acid was developed by Xu group in 2010, and various functional 2-hydroxybenzophenones were synthesized under mild conditions in good to excellent yield (Scheme 22a) [99]. This reaction required the use of O_2 as an oxidant to convert the alcohol intermediate into the corresponding ketone. In 2015, aryl iodides, aryl bromides and benzyl bromides were applied in the synthesis of ketones in neat water by Nowrouzi group, no oxidant was needed (Scheme 22b) [100].

In 2005, Chang and co-workers reported the Pd and Ru cooperative catalysis to synthesize ketones *via* the direct coupling of 8-quinolinecarboxaldehyde with iodoarenes or organostannanes [101]. The C-H bond of the aldehyde was activated by ruthenium to generate five-membered cycloacylruthenium hydride intermediate, and then reacted with the aryl palladium species, followed by reductive elimination, the desired ketone was formed finally. The reaction exhibited wide functional group compatibility to aryl iodides and stannanes, ketones were afforded in moderate to good yields (Scheme 23). The transformation demonstrated that the appropriate combination of two compatible metallic catalysts provides a new possibility for the development of novel synthetic methodologies that are difficult to carry out with any single-catalyst systems.



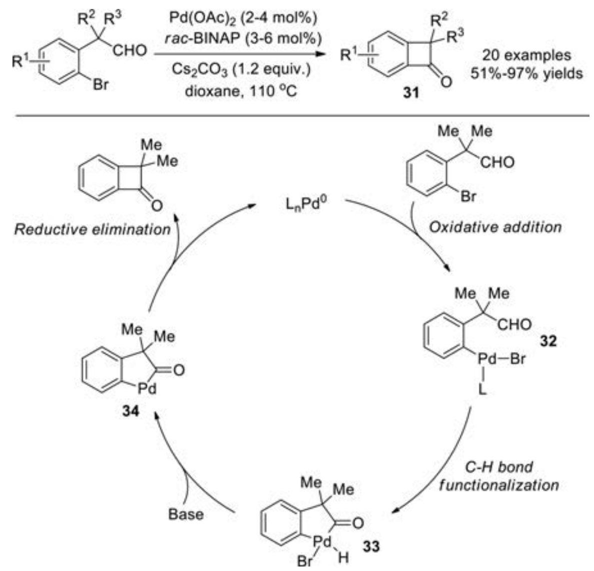
Scheme 23. Pd and Ru co-catalyzed ketone synthesis from aldehyde with iodoarenes or organostannanes.



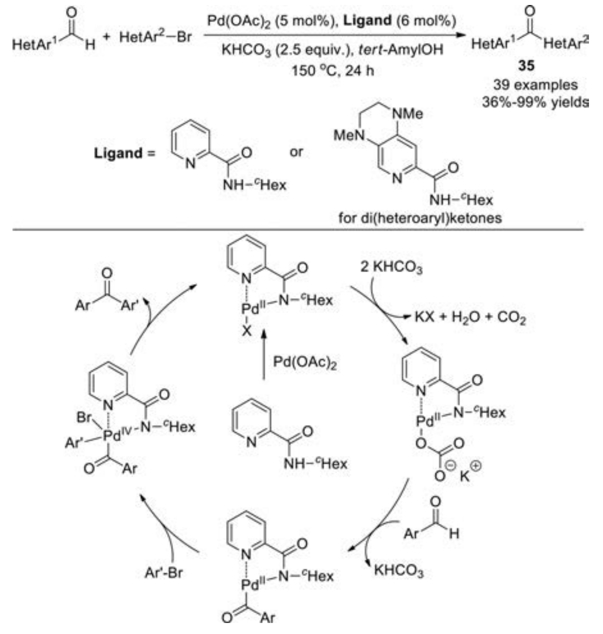
Scheme 24. Pd-catalyzed cross-coupling of *N-tert*-butylhydrazones with aryl bromides.

In 2006, Hartwig group developed palladium-catalyzed arylation of *N-tert*-butylhydrazones with aryl bromides, employing $Pd_2(dba)_3$ and DPEphos as catalyst [102]. These hydrazones, served as acyl anion equivalents, are readily accessible from aldehydes. Under mild conditions, the *N-tert*-butylhydrazones could undergo cross-coupling at the C-position of the diazaallyl unit, isomerization of the initial azo product to the corresponding hydrazones, followed by hydrolysis, would generate the arylketones (Scheme 24).

Owing to the inherent ring stain, active benzocyclobutenone (BCB), a powerful synthetic intermediate, was widely used for many transformations like cycloaddition, C—C bond activation. Previous preparations of this BCB were achieved mainly through [2 + 2] cycloadditions, metal-mediated intramolecular cyclizations, however, functional BCBs cannot easily be obtained from these traditional strategies. In 2010, Martin and co-workers reported a more practicable way for the synthesis of BCBs with intramolecular acylation of aryl bromides *via* C—H functionalization (Scheme 25) [103]. Various substrates with different substituents like alkene, ester, nitrile, aldehyde, ketone, free hydroxy, silyl groups, alkyl halide can be accommodated in this reaction. In the plausible pathway, oxidative addition of Pd(0) to C—Br bond formed intermediate **32**, followed by C—H functionalization to afford intermediate **33** and then released the HBr to generate a five-membered metallacycle **34** under base, finally the reductive elimination gave the corresponding benzocyclobutenone **31**. In addition, the kinetic isotope effect experiment demonstrated that C—H bond cleavage was a rate-limiting step.

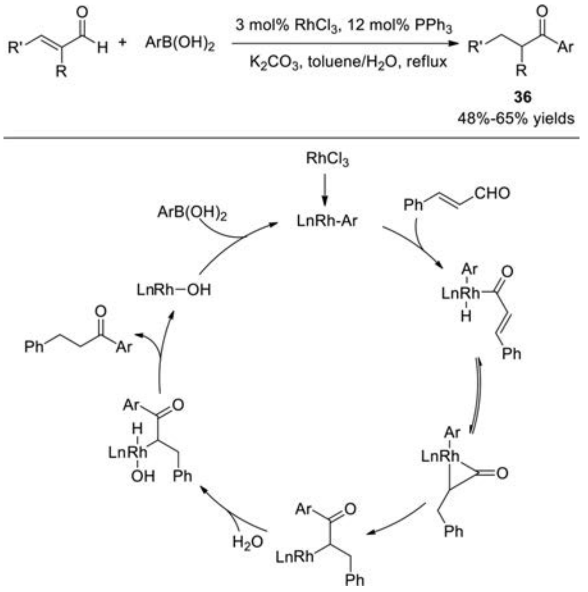


Scheme 25. Pd-catalyzed intramolecular acylation of aryl bromides to synthesize benzocyclobutenones.

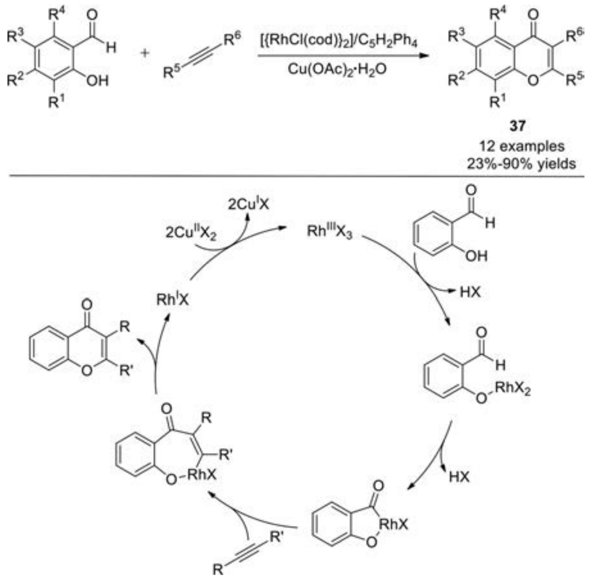


Scheme 26. Pd-catalyzed C—H activation of aldehydes and (hetero)aryl halides to synthesize diaryl ketones.

In 2018, the Kuninobu and Kanai *et al.* developed a practical procedure for the synthesis of diaryl ketones from aldehydes and (hetero)aryl halides *via* palladium-catalyzed C—H activation (Scheme 26) [104]. The picolinamide ligand is the key for this reaction, which activates the C—H bond of aldehyde through a palladium-amide intermediate, then oxidative addition of aryl bromides to this intermediate, eventually a reductive elimination to form the desired ketone. With respect to the substrates, various aryl bromides with aryl or heteroaryl aldehydes were tolerated, and desired diaryl ketones or di(heteroaryl) ketones were formed in good yields, even in gram-scale. The transformation also proceeded using aliphatic aldehydes, whereas the yields of the corresponding ketones were low. Besides, the reaction was applied to the synthesis of Fenofibrate, a commercial drug used to reduce cholesterol levels in patients at risk for cardiovascular disease.



Scheme 27. Arylation of α,β-unsaturated aldehydes with arylboronic acids.



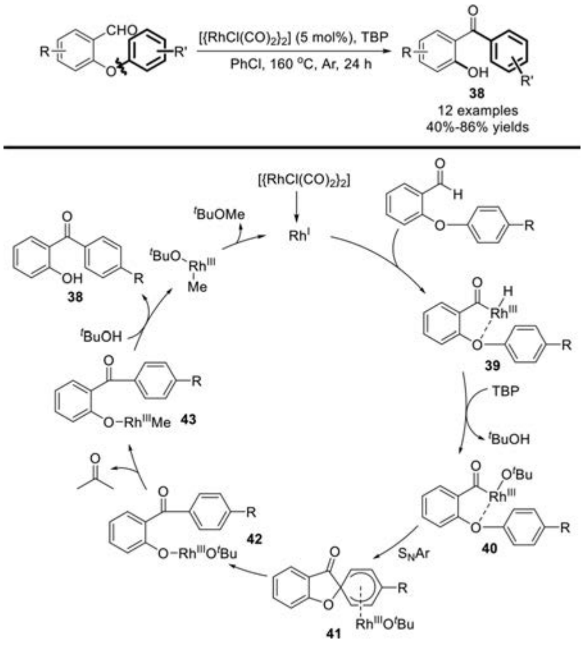
Scheme 28. Rh-catalyzed oxidative coupling of salicylaldehydes with internal alkynes.

3.2. Rh catalysis

Besides the reported palladium catalysts, rhodium is likewise regularly utilized to catalyze the synthesis of ketones from aldehydes, and many research groups have reported on this. In 2004, an unanticipated self-conjugate reduction and cross-coupling tandem reaction of α,β-unsaturated arylaldehydes with arylboronic acids was reported by Zou Group, producing β-phenylpropiophenones as the desired products (Scheme 27) [105]. The pathway catalyzed by the $RhCl_3/PPh_3$ system possibly contains an oxidative addition of the aldehydic C–H bond of α,β- unsaturated aldehyde to the Rh–Ar species that is generated *in situ* by reduction of $RhCl_3$ with arylboronic acids, followed by a three-membered metallocyclopropanone intermediate, subsequently a reductive elimination, oxidative addition of water, and another reductive elimination to afford the desired product.

In 2008, Satoh and Miura *et al.* reported the direct oxidative coupling of salicylaldehydes with internal alkynes to produce 2,3-disubstituted chromone derivatives (Scheme 28) [106]. A rhodium catalyst in combination with a cyclopentadiene ligand and a copper oxidant promote this straightforward annulation. During the reaction process, the coordination of the phenolic oxygen atom to an $Rh^{III}X_3$ species gives a rhodium(III) phenolate. Directed C—H rhodation to form a rhodacycle intermediate is then followed by alkyne insertion and reductive elimination to form the desired chromone. The aldehydic C—H bond-cleavage step may be promoted effectively by the metal-directing hydroxy oxygen atom.

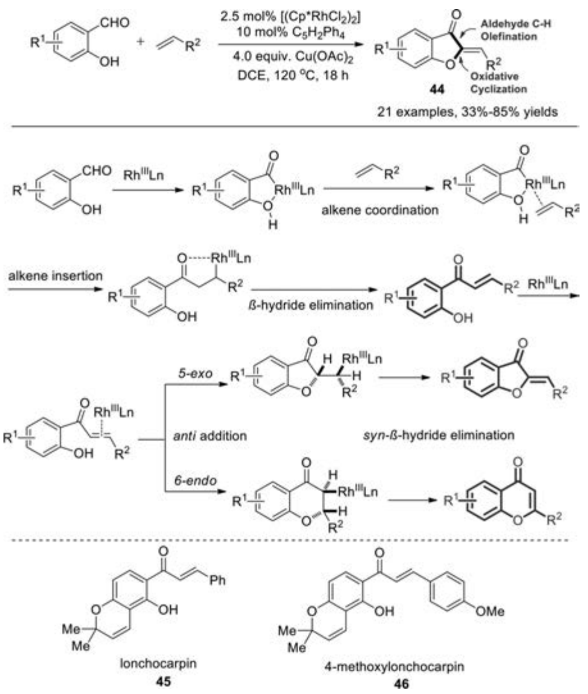
In 2011, Li group disclosed the rearrangement of 2-aryloxybenzaldehydes to 2-hydroxybenzophenones by rhodium-catalyzed cleavage of aryloxy C—O bonds (Scheme 29) [107]. This reaction can tolerate a variety of functional groups, thereby indicating the wide potential of applications. Initially, the aldehydic C—H bond insertion by Rh^I generates the Rh^{III} hydride species **39**. Upon reaction with *tert*-butyl peroxide (TBP), the Rh^{III} complex **40** is formed, thus liberating ^tBuOH. Then complex **40** may undergo an intramolecular S_NAr process to afford the intermediate **41**, thereby generating the Rh^{III} complex **42**, which could release acetone and Rh^{III}/Me complex **43**. Finally, the reaction of the previously liberated ^tBuOH with complex **43** can afford the desired product **38** and form $[Rh^{III}(Me)\text{-}(^tOBu)]$, which could regenerate the Rh^I catalyst *via* a reductive elimination and release ^tBuOMe.



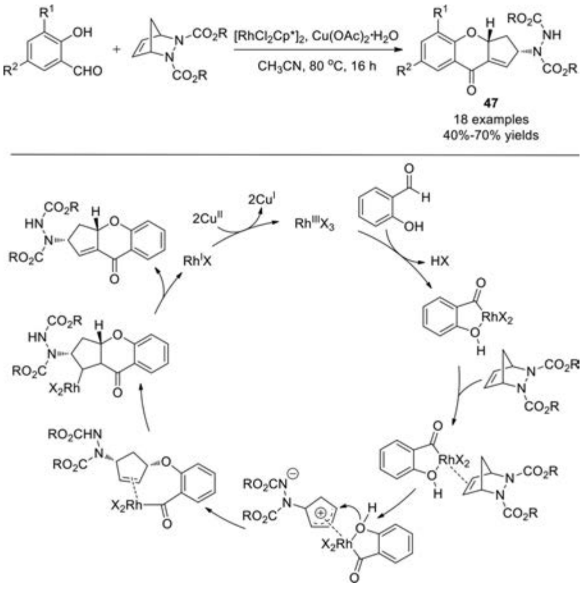
Scheme 29. Rh-catalyzed rearrangement of 2-(aryloxy)-benzaldehydes to 2-hydroxybenzophenones.

In 2012, Glorius and co-workers developed rhodium(III)-catalyzed regioselective dehydrogenative Heck-reaction (DHR) of salicylaldehydes with different classes of olefins (Scheme 30) [108]. A mechanism was proposed in Scheme 31. In the presence of the catalyst $[(Cp^*RhCl_2)_2]$, the products resulted from DHR of aldehydic C—H bonds and subsequent intramolecular oxidative cyclization of C—O bonds. This methodology has been applied to the synthesis of lonchocarpin (**45**) and 4-methoxylonchocarpin (**46**) in just two steps from commercially available reagents. They exhibit a range of biological and pharmacological properties including antimutagenic, antimicrobial, antiulcer, and antitumor activities.

In the presence of an Rh/Cu catalyst system, Pihko and Radhakrishnan *et al.* developed an efficient one pot strategy for the synthesis of cyclopentene fused chromanone derivatives *via* the direct oxidative coupling of salicylaldehydes with azabicyclic olefins in 2013



Scheme 30. Rh(III)-catalyzed cyclization of salicylaldehydes and electron-deficient olefins.

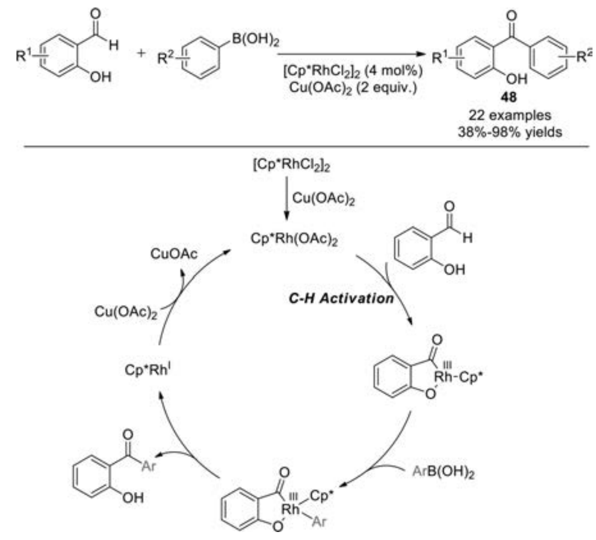


Scheme 31. Oxidative coupling of salicylaldehydes with azabicyclic olefins.

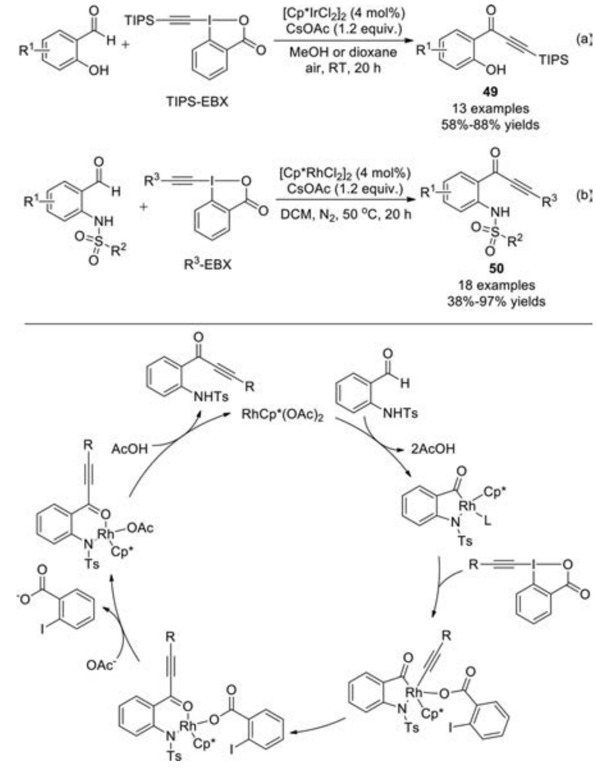
(Scheme 31) [109]. This is the first report on the ring-opening/ring-closing of azabicyclic olefins through a transition-metal catalyzed protocol involving aldehyde C—H cleavage and π-allyl chemistry.

In 2015, Cui group reported Rh(III)-catalyzed salicylaldehydes C—H bond functionalization with arylboronic acids, with features of mild reaction condition and high efficiency (Scheme 32) [110]. Furthermore, the functionalized 2-hydroxybenzophenone could be subject to divergent synthesis of heterocycles.

In 2015, Li group achieved Ir(III) or Rh(III)-catalyzed synthesis of ynones *via* C—H activation of benzaldehydes in the coupling with hypervalent iodine alkynylating reagents (Scheme 33) [111]. Rhodium and iridium catalysis exhibited complementary substrate scope. The iridium(III) catalyst offered high activity for salicylaldehyde substrates, while the rhodium(III) catalyst is necessary when the substrates were *N*-sulfonyl-2-aminobenzaldehydes. In these catalytic systems, the electrophilic aldehyde group is converted to a nucleophilic metal—formyl group, which matches the electrophilic EBX reagents.



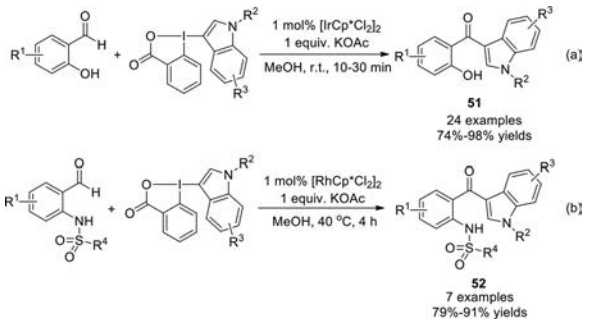
Scheme 32. Rh(III)-catalyzed aldehyde functionalization of salicylaldehydes with arylboronic acids.



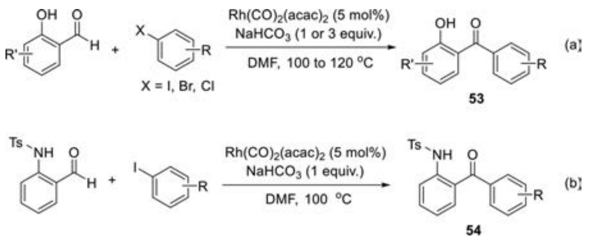
Scheme 33. C—H alkynylation of salicylaldehyde and *N*-sulfonyl-2-aminobenzaldehyde.

Using the similar catalyst systems, Waser group developed the C—H heteroarylation of salicylaldehydes and *N*-sulfonyl-2-aminobenzaldehydes with benziodoxolone hypervalent iodine reagents in 2018 (Scheme 34) [112]. The resulting salicyloyl indoles and (2-sulfonamino)benzoyl indoles were easy to be transformed into other useful building blocks.

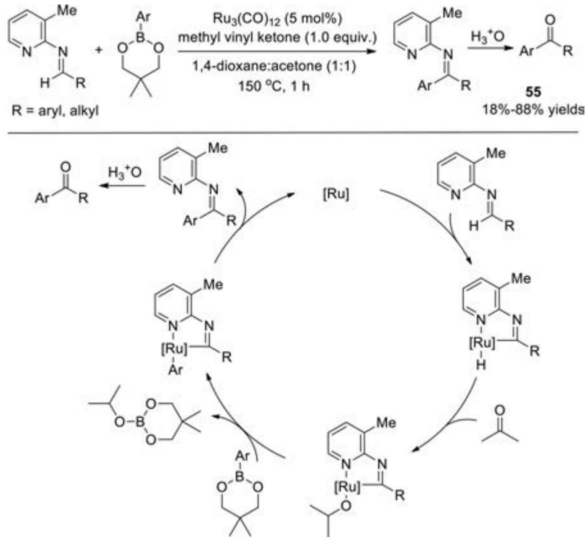
Employing the similar substrates, Rao group reported the directing-group-assisted C—H arylation of aldehydes in 2017, to



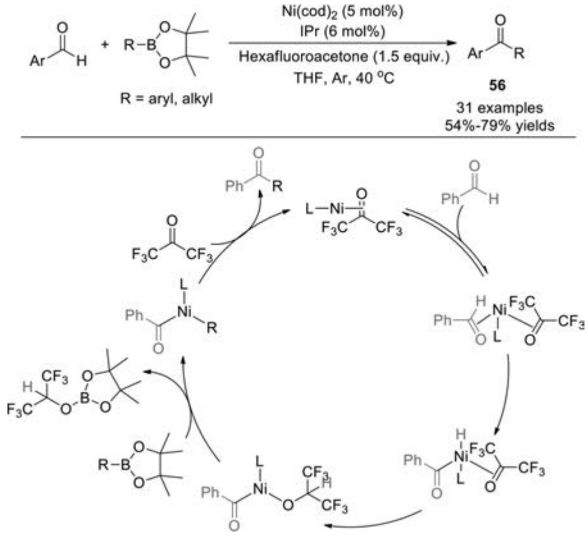
Scheme 34. C−H heteroarylation with benziodoxolone hypervalent iodine reagents.



Scheme 35. Rh-catalyzed directing-group-assisted C–H arylation of aldehydes.



Scheme 36. Ru-catalyzed coupling of aldimines with arylboronates.



Scheme 37. Nickel *N*-heterocyclic carbene catalyzed cross-coupling of aryl aldehydes with boronic esters.

synthesize medicinally valuable 2-hydroxybenzophenones or 2-(*p*-toluenesulfonylamido)benzophenones (Scheme 35) [113]. Multiple functional aldehydes and bulky aryl halides were suitable for the reaction conditions, producing the corresponding ketones in high efficiency. This transformation was initiated by oxidative addition of aryl halides to form arylrhodium species, which sequentially coordinated to the directing atom of aldehydes. Then, C−H activation and reductive elimination occurred, affording benzophenones.

As reviewed above, the most efficient cross-coupling catalysts feature the second- and the third-row transition metals, most notably palladium and rhodium, to achieve high turnover numbers. Despite the wide practicabilities of this methodologies, cross-coupling catalysis continues to attract significant interest, especially with respect to the development of more sustainable catalysts based on abundant first-row transition metals, particularly nickel catalysis.

3.3. Ru catalysis

In 2005, the ruthenium-catalyzed coupling reaction of aldimines bearing the 3-picolin-2-yl group with arylboronates *via* chelation assistance strategy was reported by Jun and coworkers (Scheme 36) [114]. The reaction carried out in a mixture solvent of 1,4-dioxane and acetone, using $Ru_3(CO)_{12}$ as catalyst, methyl vinyl ketone as additive which can suppress the reduction of imines dramatically. Diverse functional arylboronates and aldehydes can be tolerated, furnishing the corresponding ketimines, which were readily converted to ketones by hydrolysis.

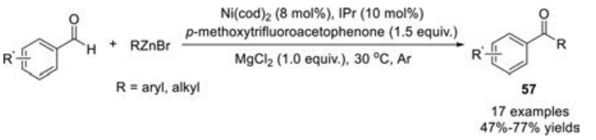
3.4. Ni catalysis

In 2015, Gu group described the nickel *N*-heterocyclic carbene catalyzed cross-coupling reaction of aryl aldehydes with boronic esters. This method provides a practical, neutral, and mild synthetic approach to aryl ketones, employing $Ni(cod)_2$/IPr as the catalyst, hexafluoroacetone as a hydrogen acceptor (Scheme 37) [115]. Different substituted aryl aldehydes and aryl boronic esters were well tolerated in this reaction, irrespective of the position and nature of substituted groups. However, aliphatic aldehydes could not deliver the corresponding ketones under the same reaction conditions. Notably, it was found that the transformations with boronic esters, bearing linear or branched substituents, proceeded smoothly to afford the aryl alkyl ketones in good yields. Moreover, a series of deuterium labeling experiments demonstrated that a nickel hydride species was involved in this reaction, C−H bond activation was the rate-determining step.

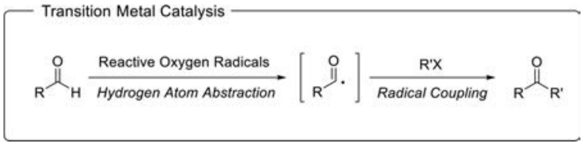
Through the similar reaction mechanism, several months later, Gu, Yuan and co-workers described the nickel *N*-heterocyclic carbene-catalyzed transformation of aromatic aldehydes into aryl ketones utilizing organozinc reagents [116]. $MgCl_2$ was used as an additive, and *p*-methoxytrifluoroacetophenone was used as the hydrogen acceptor. A series of organozinc reagents and aryl aldehydes worked well, the corresponding aryl/aryl or alkyl/aryl ketones were achieved in good yields (Scheme 38).

4. Aldehyde as acyl radical

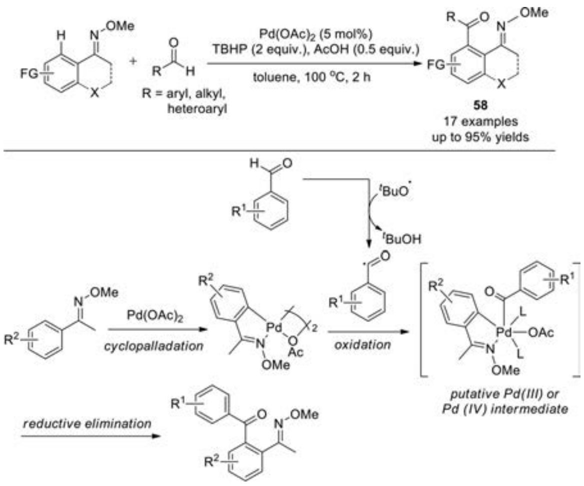
Transition metal-catalyzed C–H activation and radical reactions are two versatile strategies to construct diverse organic skeletons. Aldehydes are known to react with a variety of free radicals to form acyl radicals. And hydrogen atom abstraction from aldehydes



Scheme 38. Nickel *N*-heterocyclic carbene-catalyzed cross-coupling reaction of aryl aldehydes with organozinc reagents.



Scheme 39. Ketone synthesis *via* transition metal-catalyzed C–H activation and radical reactions.



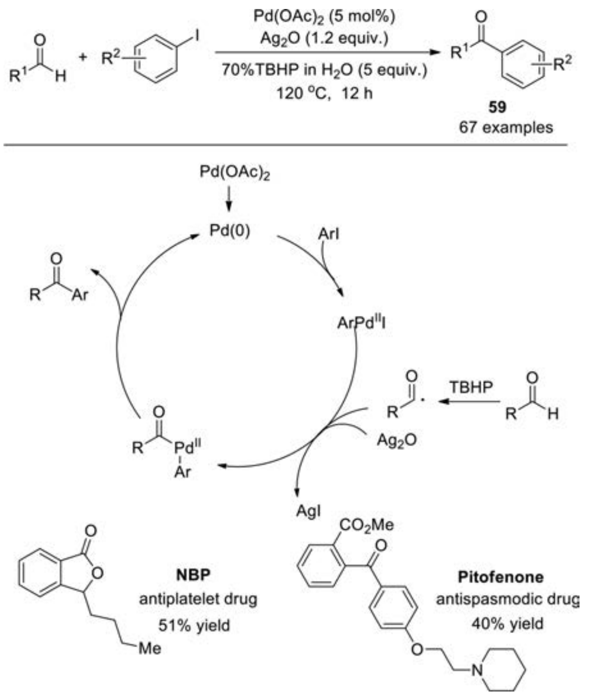
Scheme 40. Pd-catalyzed oxidative C-H bond coupling with aldehydes.

by reactive oxygen radicals (*e.g.,* ^{t}BuO$^·$) is known to be the cleanest way to generate acyl radicals. Due to the widespread applications of acyl radicals, coupled with the great value of ketones in organic synthetic chemistry, there have been a series of systematic studies providing methods for the carbonyl derivatization of aldehydes (Scheme 39).

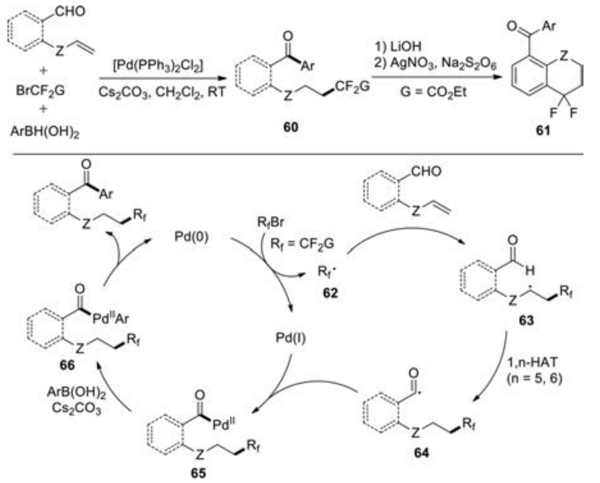
4.1. Pd catalysis

In 2010, Yu group developed the Pd-catalyzed *ortho*-C-H acylation/cross coupling of aryl ketone *O*-methyl oximes with aldehydes using *tert*-butyl hydroperoxide (TBHP) as a source of reactive oxygen radicals (*e.g.,* ^{t}BuO$^·$), which would act upon aldehyde to generate acyl radicals *in situ* (Scheme 40) [117]. With oximes as a directing group, the C–H activation is initiated by *ortho*-selective cyclopalladation on the arene ring. The palladacycle would react with the acyl radicals to afford the product ketones *via* either reactive Pd(IV) or dimeric Pd(III) intermediates. The coupling with aldehydes was achieved with remarkable regioselectivity, and both aliphatic and heteroaromatic aldehydes can be effectively coupled to the oximes. The acylation reactions constitute a versatile route to a diverse library of diaryl ketones, which are difficult to obtain by classical Friedel-Crafts acylation, and exhibit excellent functional group tolerance and regioselectivity.

In 2016, an environmentally benign strategy for the direct acylation of iodo arenes with alkyl/aryl aldehydes was established by Satyanarayana and co-workers, accessing to a wide variety of aryl−aryl and alkyl−aryl ketones in the presence of palladium catalyst (Scheme 41) [118]. TBHP was used as oxidant to generate acyl radical and Ag_2O facilitated the radical generation due to insoluble AgI formed in this biphasic system. This reaction, without activation of the carbonyl group and without directing group assistance, can be applied to the synthesis of antiplatelet drug *n*-butylphthalide (NBP) and the antispasmodic drug Pitofenone.

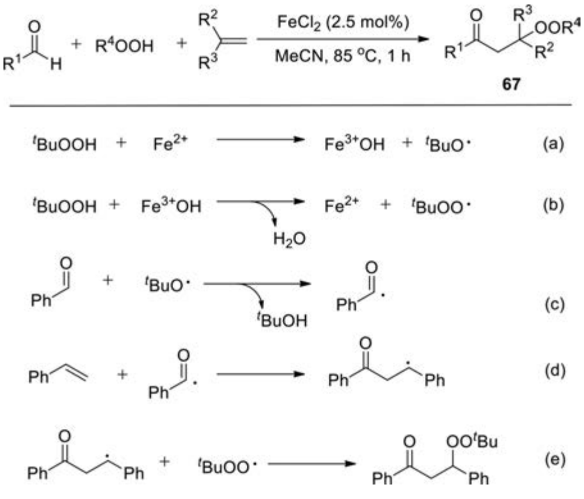


Scheme 41. Pd-catalyzed direct acylation of aryl iodide with alkyl/aryl aldehydes.

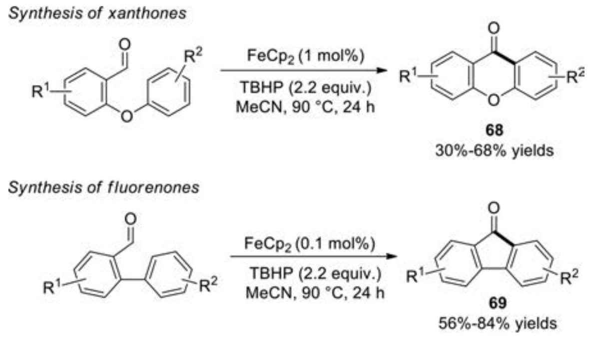


Scheme 42. Pd-catalyzed remote aryldifluoroalkylation of alkenyl aldehydes.

In 2017, Zhu group described the palladium-catalyzed three-component reaction between fluoroalkyl bromides, arylboronic acids, and alkenyl aldehydes, and provides facile access to 5-, 6-, or 7-difluoroalkylated ketones under mild reaction conditions (Scheme 42) [119]. The resultant products can be smoothly converted into CF_2-containing tetrahydronaphthalenes *via* a novel silver-catalyzed intramolecular decarboxylative cyclization of 5-aryl-2,2-difluoropentanoic acids. A radical mechanism is proposed for this palladium-catalyzed remote aryldifluoroalkylation. The reaction is initiated by a single-electron transfer (SET) between Pd(0) and the fluoroalkyl halides, thus producing radical species (**62**) with the concurrent formation of Pd(I). The addition of **62** across the C=C bonds of alkenyl alde-



Scheme 43. Iron-catalyzed carbonylation-peroxidation of alkenes.



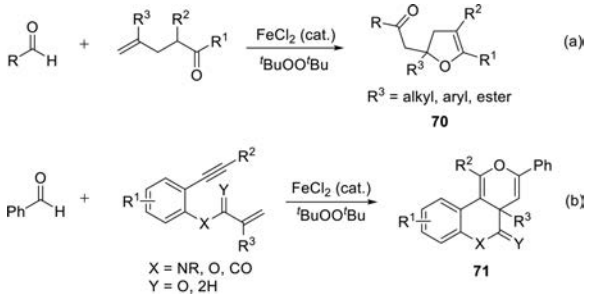
Scheme 44. Synthesis of fluorenones and xanthones *via* cross dehydrogenative coupling.

hyde forms the fluoroalkyl radical **73**, which can be converted into the acyl radical **64** through 1,n-HAT (n = 5 or 6) from intramolecular aldehyde C−H bonds. The coupling of **64** with a Pd(I) species, followed by a transmetalation with $ArB(OH)_2$, produces the intermediate **66**. As a consequence of reductive elimination, the remote aryldifluoroalkylation products are formed, accompanied by the regeneration of Pd(0).

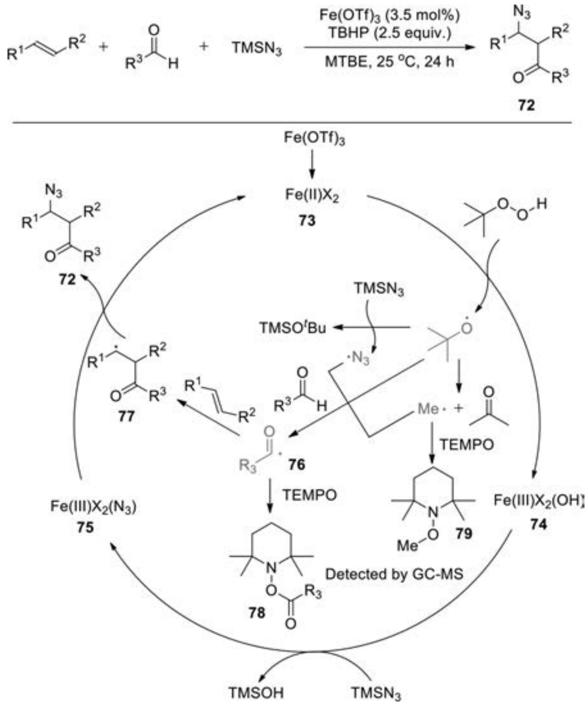
4.2. Fe catalysis

In 2011, Li group achieved the $FeCl_2$-catalyzed three-component reaction of aldehydes, alkenes, and hydroperoxides to synthesize β-peroxy ketones (Scheme 43) [120]. This three- component reaction can be also applied to the synthesis of α-carbonyl epoxides, through either a stepwise base-induced epoxidation of the separated β-peroxy ketones or a one-pot process by simply adding base to the reaction mixture after the completion of the three-component reaction. Mechanistically, alkyloxy and alkylperoxy radicals are generated by iron catalyst. Subsequently, hydrogen atom abstraction by *tert*-butoxyl radical, gives the corresponding acyl radical. The radical addition followed by radical coupling leads to the final product.

In 2013, Studer *et al.* revealed a cross dehydrogenative coupling (CDC) of biphenyl-2-carboxyaldehyde to generate xanthones and fluorenones through base-promoted homolytic aromatic substitutions (BHASs), empolying TBHP as oxidant and $FeCp_2$ (0.1 mol% or 1 mol%) as radical initiator (Scheme 44) [121]. The reaction starting with readily available *ortho*-formyl biphenylethers or biphenyls, was well tolerated to diverse substituents and provided the products in moderate to excellent yields. Mechanistically, the radical process was triggered by the generation of acyl radical from aldehyde in the presence of ^{t}BuOOH and $Fe(II)X_2$. In addition, this work did not require any external strong base.



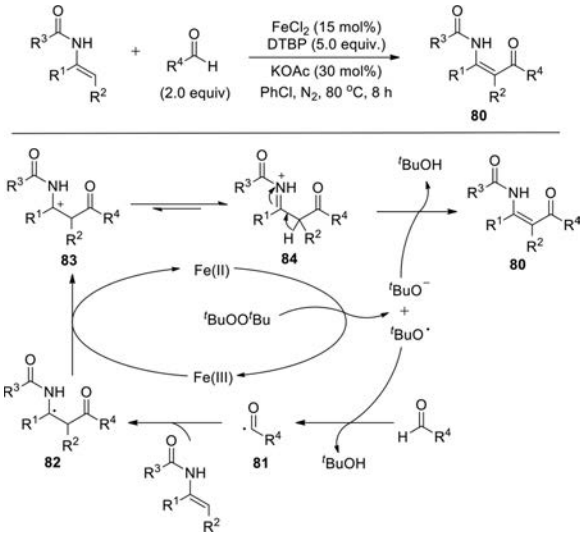
Scheme 45. Iron-catalyzed acylation-oxygenation of terminal alkenes and [2+2+2] annulation of benzene-linked 1,7-enynes with aldehydes.



Scheme 46. Iron-catalyzed radical acyl-azidation of alkenes.

In 2015, Li group reported the iron-catalyzed acylation-oxygenation of terminal alkenes using $FeCl_2$ as catalyst and *di-tert*-butylperoxide as oxidant (Scheme 45a) [122]. Acyl radicals generated by the oxidation of aldehydes add to terminal alkenes and followed by intramolecular oxygenation give functionalized 2,3-dihydrofuran derivatives bearing a quaternary carbon. Using the same reaction conditions, they developed an iron-catalyzed radical [2+2+2] annulation of benzene-linked 1,7-enynes with aldehydes in 2016 (Scheme 45b) [123]. With this method, a variety of fused [6.6.6]pyran molecules are built in an efficient and selective manner. The aldehydic radical-mediated strategy exhibits a particularly attractive dual role, which triggers and terminates the domino cyclization.

In 2019, Bao group developed the iron-catalyzed acyl-azidation of alkenes under mild reaction conditions (Scheme 46) [124]. Aromatic or aliphatic aldehydes can be used as the acyl radical precursors; $TMSN_3$ is employed as the azido source; TBHP is the initiator. The synthesized unsymmetrical β-azido ketones can be easily transformed into valuable functionalized compounds, such as γ-aminol, γ-azido alcohol, β-azido oxime, β-azido ester and tri-



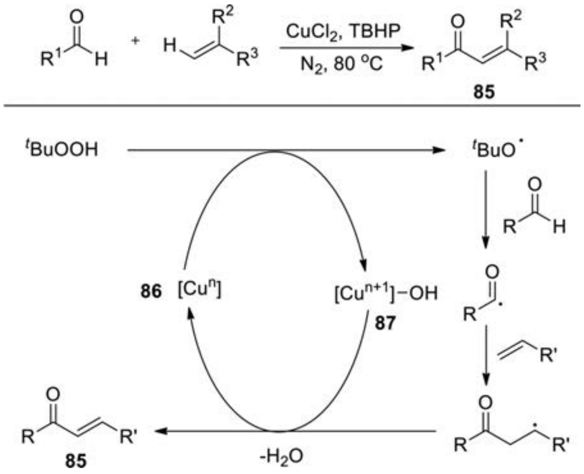
Scheme 47. selective dehydrogenative acylation of enamides with aldehydes leading to β-ketoenamides.

azoles. Initially, an iron(II) species (**73**) undergoes a SET process with TBHP to afford the iron(III) species (**74**) and a *tert*-butyloxyl radical, which can decompose to a methyl radical or release an azido radical from $TMSN_3$. Then, the *tert*-butyloxyl radical (or the methyl radical or the azido radical) abstracts an H-atom from the aldehyde to afford an acyl radical, which is trapped by an alkene to produce a more stable carbon-centered radical **77**. Upon ligand exchange with $TMSN_3$, the iron(III) species (**74**) is converted into an iron(III) species (**75**), which then undergoes azido group transfer with **77** to afford the acyl-azidation product, regenerating the iron catalyst.

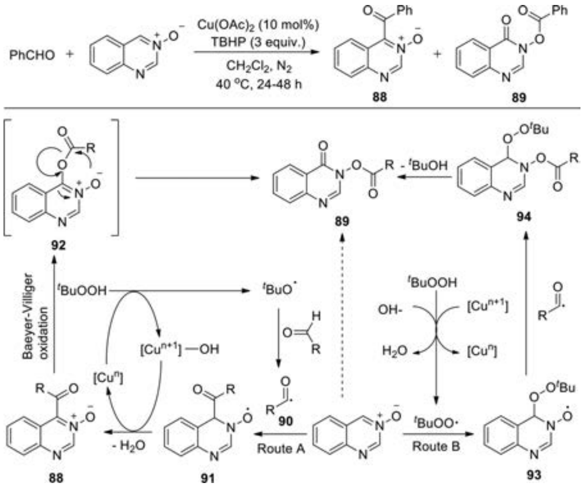
In 2020, Hu group presented the iron-catalyzed dehydrogenative acylation of enamides with aldehydes to afford β-ketoenamides with broad substrate scope, good functional group compatibility, and exquisite stereoselectivity (Scheme 47) [125]. The acyl radical **81** was produced *via* the hydrogen-abstraction from the corresponding aldehyde by the *tert*-butoxyl radical, which was generated *via* the decomposition of DTBP by Fe^{II}. Subsequently, the acyl radical **81** attacked the enamide at the β-position providing the intermediate **82**, which underwent an oxidation by Fe^{III} to afford the tentative cationic species **83. 83** was transformed the iminium intermediate **84**, followed by deprotonation with the aid of the *tert*-butoxide anion to deliver the dehydrogenative acylation product.

4.3. Cu catalysis

In 2013, Lei *et al.* reported the first copper-catalyzed oxidative coupling reaction of aldehydes with alkenes to form α,β-unsaturated ketone compounds using $CuCl_2$ as catalyst (Scheme 48) [126]. Due to the unnecessary pre-functionalization of aldehydes and alkenes, this reaction is a very noticeable and superior protocol to synthesize α,β-unsaturated ketones. The mechanism indicated that alkyloxy radical was formed from TBHP under the action of **86**. Then aldehyde went through a hydrogen atom transfer (HAT) in the presence of the resulting alkyloxy radical to generate an acyl radical. Subsequently, the addition of acyl group to alkene provided benzylic radical, followed by oxidation and deprotonation to obtain the desired product **85** while regenerating **87**.



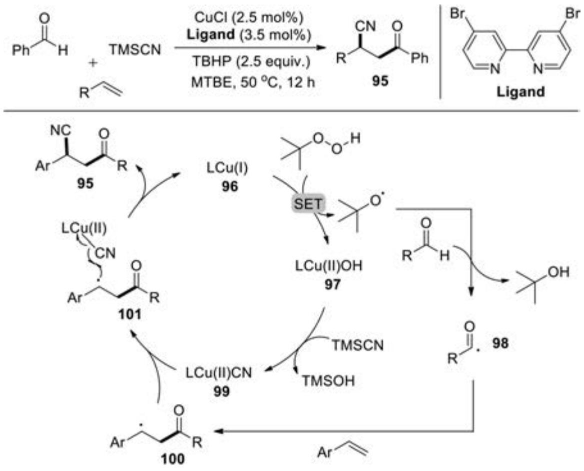
Scheme 48. Copper-catalyzed oxidative coupling of aldehydes with alkenes to synthesize α,β-unsaturated ketones.



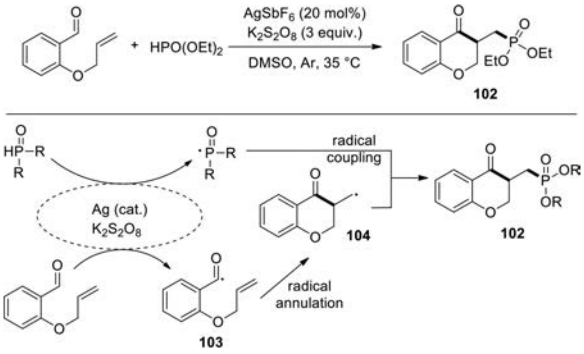
Scheme 49. Copper-catalyzed oxidative coupling of quinazoline 3-oxides with unactivated aldehydes.

Owing to quinazoline derivatives are the core structure of many natural compounds and pharmaceuticals, the effective synthesis of these compounds is of great significance. In 2016, Wang and Zhao *et al.* disclosed a copper-catalyzed oxidative coupling reaction of unactivated aldehydes with quinazoline 3-oxides, providing quinazoline ketones **88** followed by the direct formation of quinazoline esters **89** in one-pot reaction, using $Cu(OAc)_2$ as catalyst and TBHP as oxidant (Scheme 49) [127]. The mechanism illustrated that the final product was formed by two routes: The alkyloxy radical from TBHP abstracted the hydrogen atom from aldehyde to provide the acyl radical **90**, followed by the combination of quinazoline 3-oxide and acyl radical to afford the radical **91**, which was further oxidized to form the ketone. After that, the ketone underwent the Baeyer–Villiger oxidation to deliver an intermediate **92**, and cyclic hydroxamic ester **89** was furnished by the intramolecular acyl transfer (Route A). In another way, TBHP was dehydrogened to obtain a *tert*-butyl peroxy radical, which reacted with quinazoline 3-oxide to give a radical **93**, then **93** combined with the acyl radical to afford ester **94**. At last, ester **94** was transformed into cyclic hydroxamic ester **89** *via* further fragmentation (Route B).

In 2019, Bao group reported the copper-catalyzed radical acylcyanation of alkenes with aldehydes to access various unsymmetrical β-cyano ketones, employing TBHP as initiator (Scheme 50) [128]. The ligated copper(I) catalyst (**96**) and TBHP undergoes a SET process to afford Cu^{II} species (**97**) and O^tBu radical. Then, the O^tBu radical extracts a hydrogen atom from the aldehyde to propagate the acyl radical (**98**) and tert-butanol. Subsequently, the acyl



Scheme 50. Copper-catalyzed radical acyl-cyanation of alkenes.



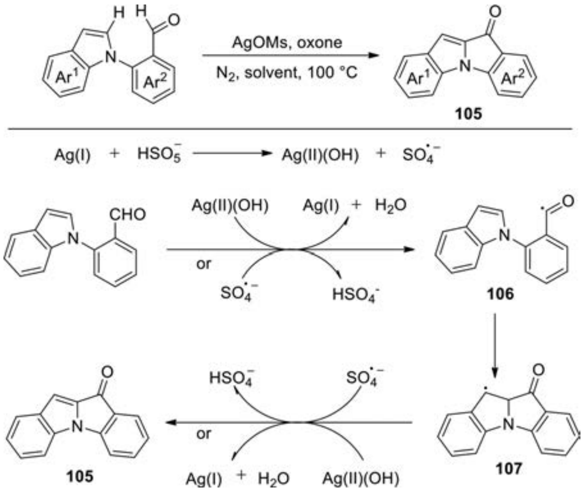
Scheme 51. Synthesis of phosphonate chroman-4-ones through cascade radical cyclization-coupling of 2-(allyloxy)arylaldehydes.

radical captures a vinylarene to form a more stable benzyl radical (**100**). Upon ligand exchange with TMSCN, the Cu^{II} species **97** converts to cyanocopper complex (**99**), which then undergo cyano group transfer with the benzyl radical **100** to access the acyl-cyanation product, meanwhile regenerating the copper(I) catalyst **96**.

4.4. Ag catalysis

The functionalized chroman-4-one skeletons are widely used in biological and pharmaceutical compounds, therefore the development of an effective approach to synthesize such compounds has received much attention. In 2016, Li's group reported a radical cyclization reaction of diethyl phosphite and 2-(allyloxy)-benzaldehyde to form phosphonate chroman-4-one derivatives under mild reaction conditions (Scheme 51) [129]. This reaction proceeded successfully by using AgSbF$_6$ as catalyst and K$_2$S$_2$O$_8$ as oxidant. To explore the process of this reaction, two possible synthetic paths were proposed. Initially, an acyl radical and a phosphonyl radical were generated from aldehyde and diethyl phosphite respectively in the presence of silver catalyst and K$_2$S$_2$O$_8$. The resulting acyl radical **103** underwent intramolecular cyclization to produce an alkyl radical **104**. Subsequently, the coupling between the nucleophilic alkyl radical **104** and the electrophilic phosphonyl radical afforded the desired product **102**. Pleasingly, the protocol also can be used for synthesizing azide and hydroxy functionalized chroman-4-ones.

Indole-indolone compounds always occupy a significant position in the application of various biomedical products and pharmacological compounds. Although great achievements have been made in the development of transition metal-catalyzed direct activation of C—H bonds or the abstraction of hydrogen from the aldehyde, no progress has been made in the catalytic synthesis of indole-indolone. In 2016, Rao's group reported a silver-catalyzed activation of C—H bond of aldehyde for the construction of indole-indolone compounds with good selectivity for the first time (Scheme 52) [130]. The reaction occurred well in the presence of oxone as oxidant and AgOMs as the catalyst, which could obtain the product in good yields. The experiment on the mechanism was conducted. Initially, peroxymonosulfate anion disproportionates into a hydroxide anion and a sulfate radical anion in the presence of [Ag(I)] salt, meanwhile, the [Ag(I)] salt is oxidized to [Ag(II)] species. Then the acyl radical **106** was obtained via the oxidation of C-H bond of aldehyde by [Ag(II)] species or the abstraction of a hydrogen from aldehyde by sulfate radical anion. The acyl radical **106** underwent an intramolecular radical addition to afford the radical **107**, which was subsequently oxidized by sulfate radical anion or [Ag(II)] species, and then underwent the deprotonation to generate the product **105**.



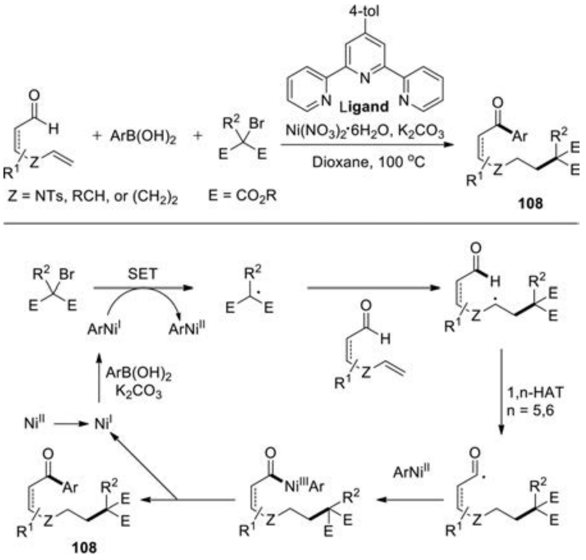
Scheme 52. Silver-catalyzed intramolecular C-2 selective acylation of indoles with aldehydes.

4.5. Ni catalysis

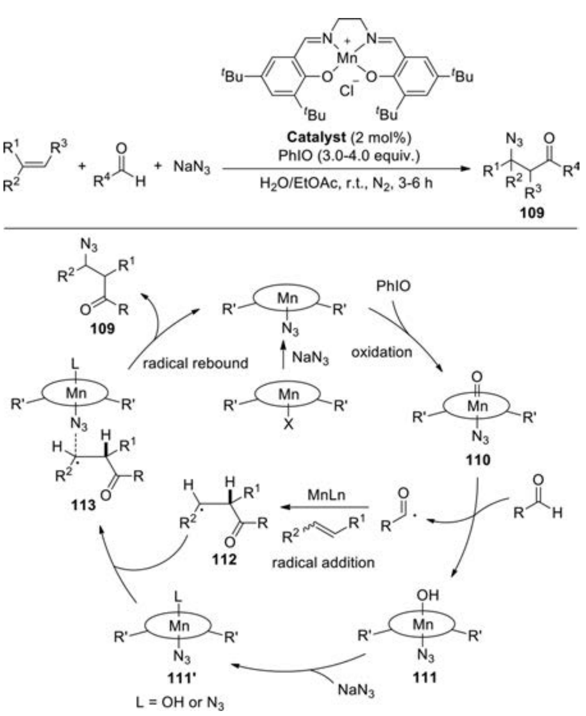
In 2018, Zhu group developed the nickel-catalyzed remote arylation of alkenyl aldehydes triggered by radical alkylation with tertiary α-carbonyl alkyl bromides, thus producing a quaternary carbon center containing ketones in promising yields with broad functional group compatibility (Scheme 53) [131]. Preliminary mechanistic studies suggest that the combination of a 1,n-HAT (n = 5 or 6) from alkyl radicals to aldehyde C—H bonds with nickel catalysis may account for the realization of this reaction.

4.6. Mn catalysis

In 2018, Wang *et al.* describe the three-component reaction of aldehydes, olefins, and sodium azide for the installation of C=O and N$_3$ groups into the double bond based on (salen)Mn(III) catalysis system (Scheme 54) [132]. In the conversion, the manganese-bound azide was oxidized by PhIO, generating the key reactive oxomanganese(V) intermediate **110**, which is capable of abstracting hydrogen from the aldehyde to form intermediate **111** and an acyl radical. The subsequent acyl radical addition of a manganese-activated alkene would generate radical intermediate **112**. Finally, azido-rebound *via* complex **113** released the final product of acylazidation.



Scheme 53. Nickel-catalyzed remote arylation of alkenyl aldehydes.

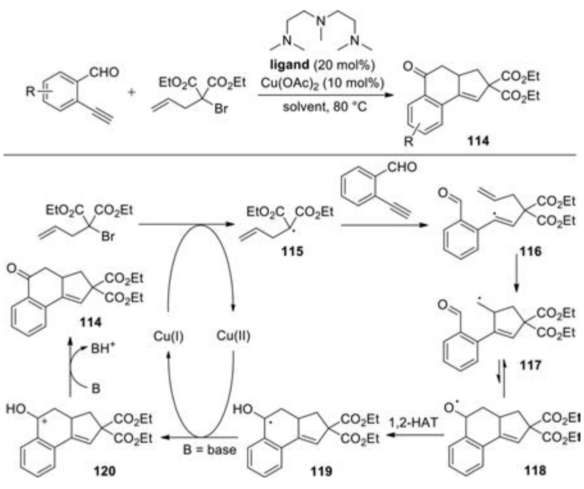


Scheme 54. (Salen)Mn(III)-catalyzed chemoselective acylazidation of olefins.

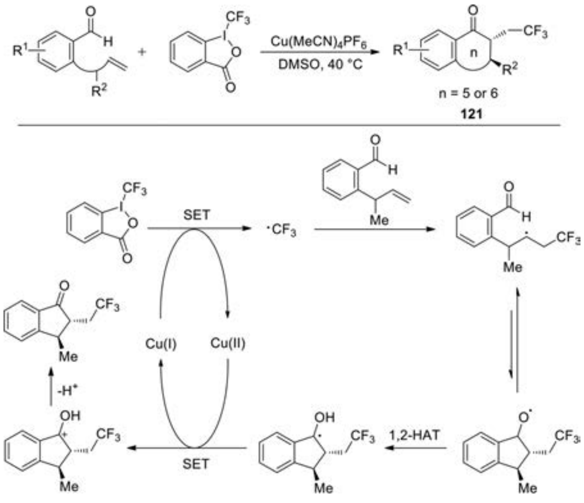
5. Aldehyde as carbon radical acceptor

In the aforementioned work, aldehyde generally was used as a carbon radical donor to initiate ketone synthesis, while employing aldehyde as carbon radical receptor was difficult to achieve. In 2016, Zhu and co-workers developed the copper-catalyzed cascade annulation of enynals with alkenyl or alkynyl α-bromocarbonyls, yielding various cyclohexenone-fused polycyclic compounds, using $Cu(OAc)_2$ as catalyst and pentamethyldiethylenetriamine (PMDETA) as ligand. Diethylazodicarboxylate (DEAD) was used as reductant for *in situ* generation of the Cu^I catalyst (Scheme 55) [133].

The mechanism showed that radical **115** and Cu^{II} were initially obtained by a single electron transfer (SET) between Cu^I and α-bromocarbonyls, then the addition of the resulting radical to C≡C delivered alkenyl radical **116**, which is converted to the alkyl radical species **117** *via* a 5-*exo*-trig cyclization. Then, an intramolecular addition of carbon radical to the aldehyde group led to the generation of alkoxy radical **118**, which underwent 1,2-HAT to provide benzyl radical **119**. Subsequently, the carbon-centered radical **119** was transformed to a cationic intermediate **120** by a second SET process with the aid of Cu^{II}, and Cu^I was simultaneously regenerated. Finally, the intermediate **120** was deprotonated under the action of base to produce target product. Furthermore, the outstanding characteristics of this protocol were excellent step-economics. Up to six new C-C bonds and four new carbocycles can be established in a single reaction.

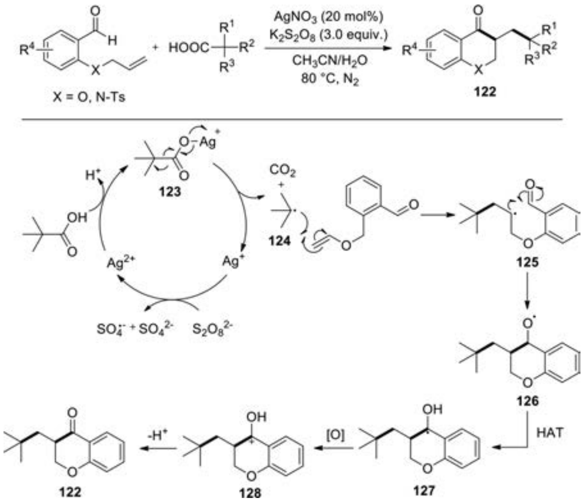


Scheme 55. Copper-catalyzed cascade annulation of enynals with unsaturated α-bromocarbonyls.



Scheme 56. Copper-catalyzed acyltrifluoromethylation of alkenes.

The trifluoromethylation of alkenes, which could straightforwardly construct the C-CF_3 bond, has received extensive attention because of its good step efficiency. In 2017, Zhu *et al.* firstly reported a trifluoromethylation of unactivated alkenes to form trifluoroethyl indanones and related cyclic ketones using $Cu(MeCN)_4PF_6$ as catalyst (Scheme 56) [134]. In this process, the addition of trifluoromethyl radical to alkenes generated the nucleophilic alkyl radical. Subsequently, an alkoxy radical was generated through intramolecular cyclization. And then 1,2-HAT, SET, and deprotonation proceeded successively to provide the final product. This method made a significant contribution to drug application and development through the combination of CF_3 group and an indanone molecule.

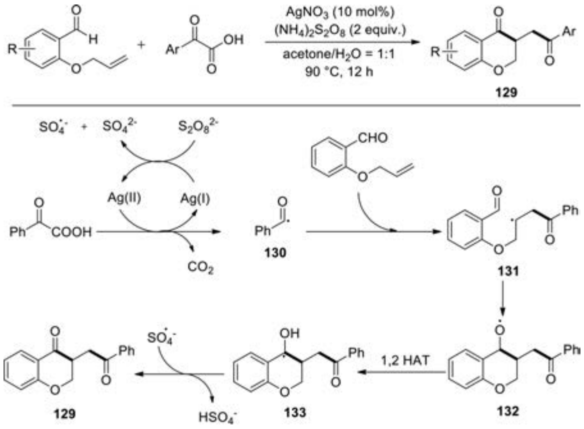


Scheme 57. Silver-catalyzed decarboxylative cascade radical cyclization of *tert*-carboxylic acids and *o*-(allyloxy)arylaldehydes.

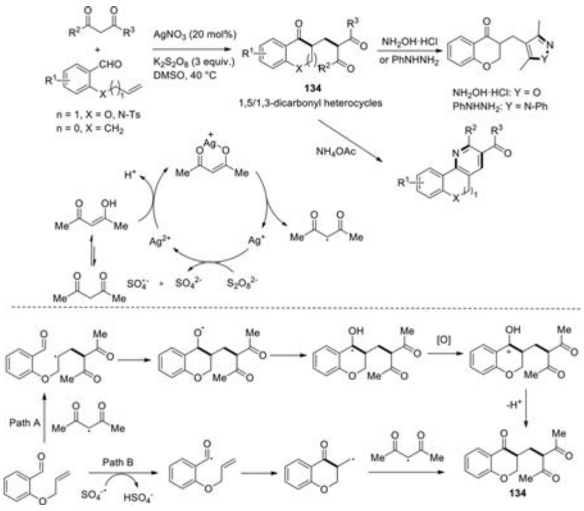
Efficient synthetic protocols of chroman-4-one derivatives have gotten widespread development during the past decades owing to their special physiological and biological properties. The cascade radical cyclization of *o*-(allyloxy)arylaldehydes with different radicals towards the formation of diverse chroman-4-one derivatives has been rapidly developing.

Zhu group disclosed the silver nitrate-catalyzed oxidative radical decarboxylative cyclization reaction of *o*-(allyloxy)arylaldehydes and tertiary carboxylic acids to obtain 3-alkyl-substituted chroman-4-one derivatives under mild conditions (Scheme 57) [135]. The substrate scope of this reaction was inspected, indicating that various *o*-(allyloxy)arylaldehydes and tertiary carboxylic acids with different substituents were well tolerated and generated corresponding products with moderate to good yields. A proposed mechanism illustrated that Ag(I) was firstly transformed into Ag(II) in the presence of persulfate, then Ag(II) combined with tertiary carboxylic acid to produce silver complex **123** which was converted into a radical **124** and regenerated Ag(I) through a single electron transfer, meanwhile CO$_2$ was released. Subsequently, the direct addition of radical **124** to the C=C bond of *o*-(allyloxy)arylaldehyde afforded the radical intermediate **125**, which successively underwent an intramolecular cyclization, a HAT and oxidation to deliver an intermediate **128**. Finally, expected product **122** was obtained by the deprotonation of intermediate **128**.

The utilization of cheap and easily obtainable carboxylic acids as raw materials has great advantages, so that the decarboxylation cross-coupling reaction for the construction of C-C and C-X bonds has received considerable attention in the field of synthesis. Enlightened by previous works, in 2017, Wu *et al.* firstly reported a silver nitrate-catalyzed cascade decarboxylation radical addition/cyclization reaction which performed smoothly between α-oxocarboxylic acids and aromatic aldehydes (Scheme 58) [136]. Eventually, it constructed dihydroflavonoid derivatives with good efficiency and broad substrate scope upon the oxidation of ammonium persulfate. In addition, diverse α-oxocarboxylic acids and 2-(allyloxy)benzaldehyde derivatives bearing different substituents were investigated in this work, and the desirable products exhibited good yields. A feasible mechanism showed that the aldehyde acted as a carbon radical acceptor in this reaction. Initially, the carboxylic acid underwent decarboxylation under the action of silver and persulfate anion to give an acyl radical **130**, then the addition of **130** to the C=C bond of the aldehyde formed radical **131**, which afforded an alkoxyl radical **132** by intramolecular cyclization, followed by 1,2-HAT to produce a benzyl radical **133**. Subsequently, the resulting benzyl radical went through dehydrogenation to generate the final product **129**.



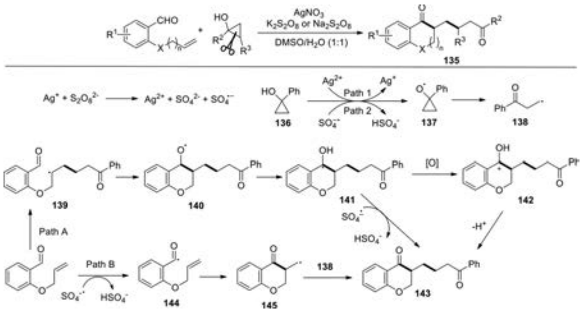
Scheme 58. Silver nitrate-catalyzed cascade decarboxylation and oxidative cyclization.



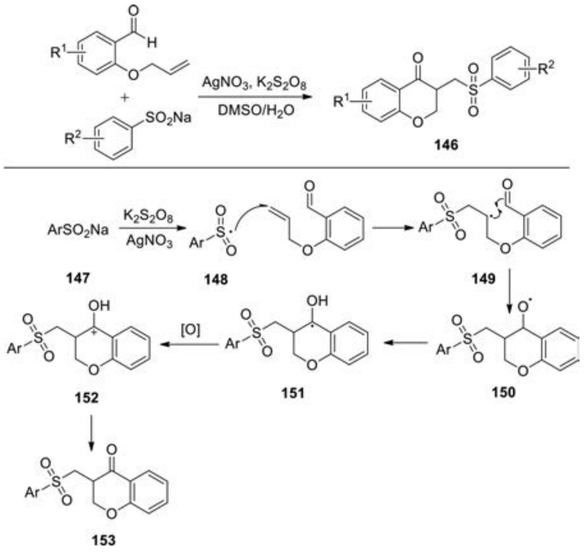
Scheme 59. Silver-catalyzed radical cascade cyclization toward 1,5-/1,3-dicarbonyl heterocycles.

It is well known that dicarbonyl compounds are a sort of important feedstock for the synthesis of various heterocycles. In the past several years, many efforts have been devoted to developing radical cascade reactions to efficiently afford the dicarbonyl heterocycles. A relatively convenient silver-catalyzed radical cascade cyclization was reported by Chen and Yu *et al.* in 2018 (Scheme 59) [137]. In the presence of AgNO$_3$ and K$_2$S$_2$O$_8$, multifarious 2-functionalized benzaldehydes reacted with 1,3-dicarbonyl compounds to form 1,5- or 1,3-dicarbonyl heterocyclic compounds including chroman-4-one, indanone or 2,3-dihydroquinoline-4(1*H*)-one. After that, the generated 1,5-/1,3-dicarbonyl heterocycles could react with NH$_4$OAc, NH$_2$OH·HCl, or PhNHNH$_2$ respectively, and finally produced polycyclic compounds with diverse structures. This is the first example of constructing a large variety of 1,5-/1,3-dicarbonyl heterocycles *via* a silver-catalyzed radical cascade cyclization reaction by directly using 1,3-dicarbonyl compounds as alkyl radical precursors.

Based on the foundation about cascade radical annulation of *o*-(allyloxy)arylaldehydes with different radicals for the preparation of diverse chroman-4-one derivatives, Liu's group reported a novel access to chroman-4-one derivatives by silver-catalyzed cascade radical cyclization of *o*-(allyloxy)arylaldehydes with cyclopropanols



Scheme 60. Silver-catalyzed radical cyclization of 2-(allyloxy)arylaldehydes with cyclopropanols.



Scheme 61. Silver-catalyzed cascade radical cyclization of sodium sulfinates and *o*-(allyloxy)arylaldehydes.

in 2019 (Scheme 60) [138]. Under the mild oxidative conditions, various cyclopropanols and *o*-(allyloxy)arylaldehyde derivatives were explored and rewarded good yields.

Two plausible mechanisms were elucidated by several control experiments. In path A, *o*-(allyloxy)benzaldehyde reacted with β-keto radical **138** which *in situ* generated from the oxidation and rearrangement of cyclopropanol **136** to form the radical intermediate **139**, followed by cyclization to afford an oxygen radical **140**. Then the benzyl radical **141** was formed through a 1,2-HAT process. Finally, the further oxidation and deprotonation yielded the desired product **143**. Alternatively, in path B, sulfate radical anion abstracted the C-H bond of aldehyde, and generated acyl radical **144**. Subsequently the acyl radical **144** underwent 6-*exo*-trig cyclization to provide the radical intermediate **145**, which reacted with radical **138** to generate **143**.

In 2019, Wang and co-workers conducted a similar exploration about the synthesis of chroman-4-one and indanone derivatives through radical cascade ring opening/coupling/cyclization [139]. In addition to the synthesis of chroman-4-one, the indanone derivatives were also successfully prepared in good yields. In terms of the reaction mechanism, different opinions arise from the step that the hydrogen of the benzyl radical **141** was abstracted by the sulfate radical to afford the final products.

In 2020, Wang's group reported silver-catalyzed cascade radical cyclization of *o*-(allyloxy)arylaldehydes with sodium sulfinates to synthesize functionalized chroman-4-ones (Scheme 61) [140]. Under the optimized reaction conditions that using $K_2S_2O_8$ as oxidant and $AgNO_3$ as the catalyst, this reaction displayed a wide substrate scope to yield the desired products in moderate to good yields. In this procedure, *o*-(allyloxy)benzaldehyde reacted with sulfonyl radical **148** which was generated from the sodium benzenesulfinate in the presence of $K_2S_2O_8$ and $AgNO_3$ to produce **149**. Followed by intramolecular cyclization and HAT, it afforded the intermediate **151**. After the oxidation and deprotonation of **151**, the desired product **153** was obtained. This efficient method for the synthesis of functionalized chroman-4-ones derivatives greatly expands the focus on developing economical, practical and environmentally benign protocols for preparation of chroman-4-ones.

6. Conclusions

Ketones have been standing at the center of stage in synthetic organic chemistry, due to their versatile applications in the synthesis of fine chemicals, pharmaceuticals, and agrochemicals, and are already key players in chemical industries and pharmaceutical industries. Over the past few decades, transition metal-catalyzed direct conversions of aldehydes to ketones have drawn great attention. These transformations, in easy and straightforward manners, have excellent practical value, and broad application prospects. Herein, we have provided a comprehensive overview of the historic advancements starting from 2000, and mechanistic details of various aldehydes to generate corresponding ketones under different reaction conditions. We summarize these transformations based on the four major mechanisms: (1) Carbonyl-Heck reaction, that is 1,2-insertion of organometal species to aldehydic C=O double bond, (2) Direct insertion of transition metal catalysts to aldehydic C−H bond, (3) Aldehyde as acyl radical, (4) Aldehyde as carbon radical acceptor. We hope this systematic overview of ketone synthesis employing aldehydes as starting materials will serve as a useful reference for organic chemists and stimulate further innovations in this exciting research field. We are convinced that in the near future the application of these powerful methodologies will accelerate further, not only in academic research but also in industry.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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References

[1] M. Oçafrain, M. Devaud, M. Troupel, J. Périchon, J. Chem. Soc., Chem. Commun. (1995) 2331–2332.
[2] E. Dolhem, M. Oçafrain, J.Y. Nédélec, M. Troupel, Tetrahedron 53 (1997) 17089–17096.
[3] H. Tokuyama, S. Yokoshima, T. Yamashita, T. Fukuyama, Tetrahedron Lett 39 (1998) 3189–3192.
[4] A.C. Wotal, D.J. Weix, Org. Lett. 14 (2012) 1476–1479.
[5] H. Yin, C. Zhao, H. You, K. Lin, H. Gong, Chem. Commun. 48 (2012) 7034–7036.
[6] A.H. Cherney, N.T. Kadunce, S.E. Reisman, J. Am. Chem. Soc. 135 (2013) 7442–7445.
[7] X. Zhang, Z. Wang, X. Fan, J. Wang, J. Org. Chem. 80 (2015) 10660–10667.

[8] C.L. Joe, A.G. Doyle, Angew. Chem. Int. Ed. 55 (2016) 4040–4043.

[9] R. Shi, X. Hu, Angew. Chem. Int. Ed. 58 (2019) 7454–7458.

[10] S. Das, S.K. Parida, T. Mandal, et al., Chem. Asian J. 15 (2020) 568–572.

[11] L. Xiong, H. Hu, C.W. Wei, B. Yu, Eur. J. Org. Chem. 2020 (2020) 1588–1597.

[12] N. Kawamura, H. Nakamura, R. Sawa, et al., J. Antibiot. 50 (1997) 147–149.

[13] P.M. Flatt, X. Wu, S. Perry, T. Mahmud, J. Nat. Prod. 76 (2013) 939–946.

[14] H. Naganawa, H. Hashizume, Y. Kubota, R. Sawa, Y. Takahashi, J. Antibiot. 55 (2002) 578–584.

[15] Z.P. Wang, Y. He, P.L. Shao, Org. Biomol. Chem. 16 (2018) 5422–5426.

[16] R. Wagner, J.T. Randolph, S.V. Patel, et al., J. Med. Chem. 61 (2018) 4052–4066.

[17] S. Nahm, S.M. Weinreb, Tetrahedron Lett 22 (1981) 3815–3818.

[18] T. Hirao, D. Misu, T. Agawa, J. Am. Chem. Soc. 107 (1985) 7179–7181.

[19] , Nucleophilic addition to carboxylic acid derivatives, in: B.T. O'Neill, B.M. Trost, I. Fleming (Eds.), Comprehensive Organic Synthesis, 1, Oxford, Pergamon, 1991, pp. 397–458.

[20] R. Martín, P. Romea, C. Tey, F. Urpí, J. Vilarrasa, Synlett 12 (1997) 1414–1416.

[21] T. Katoh, O. Ohmori, K. Iwasaki, M. Inoue, Tetrahedron 58 (2002) 1289–1299.

[22] Giovanni Sartori, R. Maggi, Chem. Rev. 106 (2006) 1077–1104.

[23] S. Balasubramaniam, I.S. Aidhen, Synthesis 2008 (2008) 3707–3738.

[24] S.G. Davies, A.M. Fletcher, J.E. Thomson, Chem. Commun. 49 (2013) 8586–8598.

[25] M. Nowak, Synlett 26 (2015) 561–562.

[26] Y. Uto, T. Ogata, Y. Kiyotsuka, et al., Biorg. Med. Chem. Lett. 20 (2010) 341–345.

[27] N. Veerasamy, E.C. Carlson, N.D. Collett, M. Saha, R.G. Carter, J. Org. Chem. 78 (2013) 4779–4800.

[28] K. Torikai, R. Koga, X. Liu, et al., Bioorg. Med. Chem. 25 (2017) 5216–5237.

[29] Y.J. Wu, J. Guernon, A. McClure, et al., Bioorg. Med. Chem. 25 (2017) 5490–5505.

[30] H. An, S. Lee, J.M. Lee, et al., J. Med. Chem. 61 (2018) 9266–9286.

[31] M.C. Willis, Chem. Rev. 110 (2010) 725–748.

[32] C.F. Lochow, R.G. Miller, J. Am. Chem. Soc. 98 (1976) 1281–1283.

[33] R.C. Larock, K. Oertle, G.F. Potter, J. Am. Chem. Soc. 102 (1980) 190–197.

[34] D.Y. Lee, C.W. Moon, C.H. Jun, J. Org. Chem. 67 (2002) 3945–3948.

[35] T.A. Betley, J.C. Peters, Angew. Chem. Int. Ed. 42 (2003) 2385–2389.

[36] J.P. Morgan, K. Kundu, M.P. Doyle, Chem. Commun. (2005) 3307–3309.

[37] Y. Oonishi, J. Ogura, Y. Sato, Tetrahedron Lett. 48 (2007) 7505–7507.

[38] E.A. Jo, J.H. Lee, C.H. Jun, Chem. Commun. (2008) 5779–5781.

[39] J.W. Park, J.H. Park, C.H. Jun, J. Org. Chem. 73 (2008) 5598–5601.

[40] E.A. Jo, C.H. Jun, Tetrahedron Lett. 50 (2009) 3338–3340.

[41] J.F. Hooper, S. Seo, F.R. Truscott, J.D. Neuhaus, M.C. Willis, J. Am. Chem. Soc. 138 (2016) 1630–1634.

[42] X. Linghu, J.S. Johnson, Angew. Chem. Int. Ed. 42 (2003) 2534–2536.

[43] H. Takikawa, Y. Hachisu, J.W. Bode, K. Suzuki, Angew. Chem. Int. Ed. 45 (2006) 3492–3494.

[44] K. Thai, S.M. Langdon, F. Bilodeau, M. Gravel, Org. Lett. 15 (2013) 2214–2217.

[45] B.J.E. Reich, A.K. Justice, B.T. Beckstead, J.H. Reibenspies, S.A. Miller, J. Org. Chem. 69 (2004) 1357–1359.

[46] M. He, J.W. Bode, Org. Lett. 7 (2005) 3131–3134.

[47] G.Q. Li, L.X. Dai, S.L. You, Chem. Commun. (2007) 852–854.

[48] D.A. DiRocco, T. Rovis, Angew. Chem. Int. Ed. 51 (2012) 5904–5906.

[49] L.H. Sun, Z.Q. Liang, W.Q. Jia, S. Ye, Angew. Chem. Int. Ed. 52 (2013) 5803–5806.

[50] H. Stetter, Angew. Chem. Int. Ed. 15 (1976) 639–647.

[51] M.S. Kerr, J. Read de Alaniz, T. Rovis, J. Am. Chem. Soc. 124 (2002) 10298–10299.

[52] S.C. Cullen, T. Rovis, Org. Lett. 10 (2008) 3141–3144.

[53] D. Enders, J. Han, A. Henseler, Chem. Commun. (2008) 3989–3991.

[54] J.R. de Alaniz, T. Rovis, Synlett 2009 (2009) 1189–1207.

[55] Q. Liu, T. Rovis, Org. Lett. 11 (2009) 2856–2859.

[56] E. Sánchez-Larios, K. Thai, F. Bilodeau, M. Gravel, Org. Lett. 13 (2011) 4942–4945.

[57] D.A. DiRocco, E.L. Noey, K.N. Houk, T. Rovis, Angew. Chem. Int. Ed. 51 (2012) 2391–2394.

[58] M.M. Heravi, V. Zadsirjan, K. Kafshdarzadeh, Z. Amiri, Asian J. Org. Chem. 9 (2020) 1999–2034.

[59] J.S. Johnson, Angew. Chem. Int. Ed. 43 (2004) 1326–1328.

[60] D. Enders, O. Niemeier, A. Henseler, Chem. Rev. 107 (2007) 5606–5655.

[61] N. Marion, S. Díez-González, S.P. Nolan, Angew. Chem. Int. Ed. 46 (2007) 2988–3000.

[62] Y. Li, Z. Feng, S.L. You, Chem. Commun. (2008) 2263–2265.

[63] D.A. DiRocco, T. Rovis, J. Am. Chem. Soc. 133 (2011) 10402–10405.

[64] T. Jousseaume, N.E. Wurz, F. Glorius, Angew. Chem. Int. Ed. 50 (2011) 1410–1414.

[65] D.M. Flanigan, F. Romanov-Michailidis, N.A. White, T. Rovis, Chem. Rev. 115 (2015) 9307–9387.

[66] E. Ciganek, Synthesis 1995 (1995) 1311–1314.

[67] J. Pesch, K. Harms, T. Bach, Eur. J. Org. Chem. 2004 (2004) 2025–2035.

[68] S. Wei, X.G. Wei, X. Su, J. You, Y. Ren, Chem. Eur. J. 17 (2011) 5965–5971.

[69] M. Gravel, J.M. Holmes, Stetter Reaction, in Comprehensive Organic Synthesis, Second Edition, (Eds.: P. Knochel), Elsevier, Amsterdam, 2014, Vol. 4, pp. 1384-1406.

[70] M.M. Ahire, S.B. Mhaske, ACS Omega 2 (2017) 6598–6604.

[71] B.M. Trost, Science 254 (1991) 1471–1477.

[72] B.M. Trost, Angew. Chem. Int. Ed. 34 (1995) 259–281.

[73] P.A. Wender, V.A. Verma, T.J. Paxton, T.H. Pillow, Acc. Chem. Res. 41 (2008) 40–49.

[74] P.A. Wender, B.L. Miller, Nature 460 (2009) 197–201.

[75] N.Z. Burns, P.S. Baran, R.W. Hoffmann, Angew. Chem. Int. Ed. 48 (2009) 2854–2867.

[76] P. Anastas, N. Eghbali, Chem. Soc. Rev. 39 (2010) 301–312.

[77] T. Ishiyama, J. Hartwig, J. Am. Chem. Soc. 122 (2000) 12043–12044.

[78] M. Pucheault, S. Darses, J.P. Genet, J. Am. Chem. Soc. 126 (2004) 15356–15357.

[79] O. Chuzel, A. Roesch, J.P. Genet, S. Darses, J. Org. Chem. 73 (2008) 7800–7802.

[80] G. Mora, S. Darses, J.P. Genet, Adv. Synth. Catal. 349 (2007) 1180–1184.

[81] C. Qin, J. Chen, H. Wu, et al., Tetrahedron Lett. 49 (2008) 1884–1888.

[82] R.A. Swyka, W.G. Shuler, B.J. Spinello, et al., J. Am. Chem. Soc. 141 (2019) 6864–6868.

[83] W.G. Shuler, R.A. Swyka, T.T. Schempp, B.J. Spinello, M.J. Krische, Chem. Eur. J. 25 (2019) 12517–12520.

[84] N. Imlinger, M. Mayr, D.R. Wang, K. Wurst, M.R. Buchmeiser, Adv. Synth. Catal. 346 (2004) 1836–1843.

[85] J.W. Ruan, O. Saidi, J.A. Iggo, J.L. Xiao, J. Am. Chem. Soc. 130 (2008) 10510–10511.

[86] L. Adak, S. Bhadra, B.C. Ranu, Tetrahedron Lett. 51 (2010) 3811–3814.

[87] P. Colbon, J. Ruan, M. Purdie, J. Xiao, Org. Lett. 12 (2010) 3670–3673.

[88] M. Kuriyama, N. Hamaguchi, K. Sakata, O. Onomura, Eur. J. Org. Chem. 2013 (2013) 3378–3385.

[89] Y.C. Huang, K.K. Majumdar, C.H. Cheng, J. Org. Chem. 67 (2002) 1682–1684.

[90] N. Nowrouzi, M. Zarei, F. Roozbin, RSC Adv. 5 (2015) 102448–102453.

[91] J.K. Vandavasi, X. Hua, H.B. Halima, S.G. Newman, Angew. Chem. Int. Ed. 56 (2017) 15441–15445.

[92] F. Liu, Y. Li, X. Wang, et al., Org. Chem. Front. 8 (2021) 3847–3852.

[93] H. Li, Y. Xu, E. Shi, et al., Chem. Commun. 47 (2011) 7880–7882.

[94] T. Fukuyama, H. Okamoto, I. Ryu, Chem. Lett. 40 (2011) 1453–1455.

[95] Y.X. Liao, Q.S. Hu, J. Org. Chem. 75 (2010) 6986–6989.

[96] J. Karthikeyan, K. Parthasarathy, C.H. Cheng, Chem. Commun. 47 (2011) 10461–10463.

[97] H. Zheng, J. Ding, J. Chen, et al., Synlett 11 (2011) 1626–1630.

[98] T. Satoh, T. Itaya, M. Miura, M. Nomura, Chem. Lett. (1996) 823–824.

[99] F. Weng, C. Wang, B. Xu, Tetrahedron Lett. 51 (2010) 2593–2596.

[100] N. Nowrouzi, S. Motevalli, D. Tarokh, J. Mol. Catal. A: Chem. 396 (2015) 224–230.

[101] S. Ko, B. Kang, S. Chang, Angew. Chem. Int. Ed. 44 (2005) 455–457.

[102] A. Takemiya, J.F. Hartwig, J. Am. Chem. Soc. 128 (2006) 14800–14801.

[103] P. Álvarez-Bercedo, A. Flores-Gaspar, A. Correa, R. Martin, J. Am. Chem. Soc. 132 (2010) 466–467.

[104] T. Wakaki, T. Togo, D. Yoshidome, Y. Kuninobu, M. Kanai, ACS Catal. 8 (2018) 3123–3128.

[105] Z. Wang, G. Zou, J. Tang, Chem. Commun. (2004) 1192–1193.

[106] M. Shimizu, H. Tsurugi, T. Satoh, M. Miura, Chem. Asian J. 3 (2008) 881–886.

[107] H. Rao, C.J. Li, Angew. Chem. Int. Ed. 50 (2011) 8936–8939.

[108] Z. Shi, N. Schröder, F. Glorius, Angew. Chem. Int. Ed. 51 (2012) 8092–8096.

[109] E. Jijy, P. Prakash, M. Shimi, et al., Chem. Commun. 49 (2013) 7349–7351.

[110] D. Wang, S. Cui, Tetrahedron 71 (2015) 8511–8516.

[111] H. Wang, F. Xie, Z. Qi, X. Li, Org. Lett. 17 (2015) 920–923.

[112] E. Grenet, J. Waser, Org. Lett. 20 (2018) 1473–1476.

[113] M.L.N. Rao, B.S. Ramakrishna, Eur. J. Org. Chem. 2017 (2017) 5080–5093.

[114] Y.J. Park, E.A. Jo, C.H. Jun, Chem. Commun. (2005) 1185–1187.

[115] L.J. Gu, C. Jin, H.T. Zhang, Chem. Eur. J. 21 (2015) 8741–8744.

[116] C. Jin, L. Gu, M. Yuan, Catal. Sci. Technol. 5 (2015) 4341–4345.

[117] C.W. Chan, Z. Zhou, A.S.C. Chan, W.Y. Yu, Org. Lett. 12 (2010) 3926–3929.

[118] B. Suchand, G. Satyanarayana, J. Org. Chem. 81 (2016) 6409–6423.

[119] X. Nie, C. Cheng, G. Zhu, Angew. Chem. Int. Ed. 56 (2017) 1898–1902.

[120] W. Liu, Y. Li, K. Liu, Z. Li, J. Am. Chem. Soc. 133 (2011) 10756–10759.

[121] S. Wertz, D. Leifert, A. Studer, Org. Lett. 15 (2013) 928–931.

[122] L. Lv, S. Lu, Q. Guo, B. Shen, Z. Li, J. Org. Chem. 80 (2015) 698–704.

[123] L. Lv, Z. Li, Org. Lett. 18 (2016) 2264–2267.

[124] L. Ge, Y. Li, H. Bao, Org. Lett. 21 (2019) 256–260.

[125] R.H. Liu, Z.Y. Shen, C. Wang, T.P. Loh, X.H. Hu, Org. Lett. 22 (2020) 944–949.

[126] J. Wang, C. Liu, J. Yuan, A. Lei, Angew. Chem. Int. Ed. 52 (2013) 2256–2259.

[127] L. Fan, T. Wang, Y. Tian, et al., Chem. Commun. 52 (2016) 5375–5378.

[128] Y. Jiao, M.-F. Chiou, Y. Li, H. Bao, ACS Catal. 9 (2019) 5191–5197.

[129] J. Zhao, P. Li, X. Li, C. Xia, F. Li, Chem. Commun. 52 (2016) 3661–3664.

[130] X. Wang, Z. Li, S. Cao, H. Rao, Adv. Synth. Catal. 358 (2016) 2059–2065.

[131] W. Jin, Y. Zhou, Y. Zhao, et al., Org. Lett. 20 (2018) 1435–1438.

[132] L. Zhang, S. Liu, Z. Zhao, et al., Chem. Sci. 9 (2018) 6085–6090.

[133] C. Che, Q. Huang, H. Zheng, G. Zhu, Chem. Sci. 7 (2016) 4134–4139.

[134] Z. Liu, Y. Bai, J. Zhang, et al., Chem. Commun. 53 (2017) 6440–6443.

[135] H. Hu, X. Chen, K. Sun, et al., Org. Chem. Front. 5 (2018) 2925–2929.

[136] W.C. Yang, P. Dai, K. Luo, Y.G. Ji, L. Wu, Adv. Synth. Catal. 359 (2017) 2390–2395.

[137] H. Hu, X. Chen, K. Sun, et al., Org. Lett. 20 (2018) 6157–6160.

[138] J. Sheng, J. Liu, L. Chen, et al., Org. Chem. Front. 6 (2019) 1471–1475.

[139] Q. Liu, G. Xie, Q. Wang, et al., Tetrahedron 75 (2019) 130490.

[140] Q.Q. Han, G.H. Li, Y.Y. Sun, et al., Tetrahedron Lett. 61 (2020) 151704.

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