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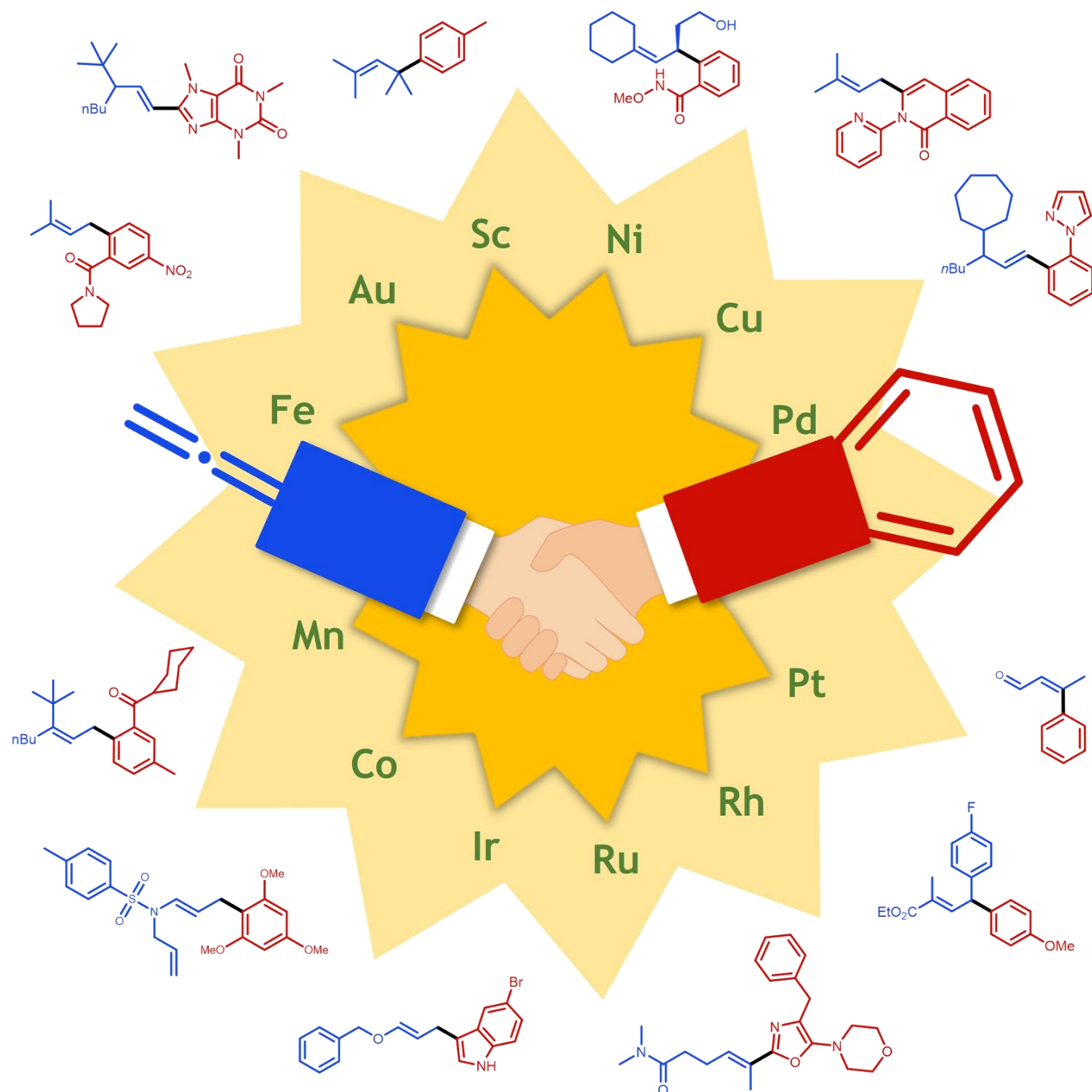
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# Transition Metal-Catalyzed Intermolecular Hydroarylation of Allenes

Lucas Pagès,<sup>[a]</sup> Racha Abed Ali Abdine,<sup>[a]</sup> Florian Monnier <sup>[a], [b],\*</sup> and Marc Taillefer <sup>[a],\*</sup>

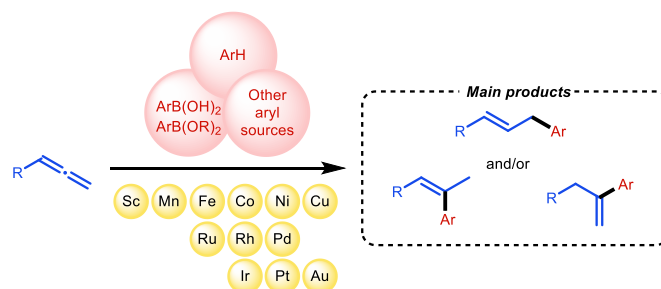


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**Abstract:** The intermolecular transition-metal catalyzed hydroarylation of allenes has been widely explored since the early 1980s. This reaction allows the selective access to high-value allylic or vinylic motifs through the formation of C-C bonds. In this frame, arenes (ArH), which are employed without any pre-functionalisation, represent one of the most used families of aryl sources. Organoboron derivatives (acids  $\text{ArB}(\text{OH})_2$  and esters  $\text{ArB}(\text{OR})_2$ ) constitute alternative, accessible and generally more reactive coupling partners, while aryl halides ( $\text{ArX}$ ) are a third, less used type of aryl source. Whereas gold- and palladium-based catalysts are often used with arenes and aryl boronic derivatives, respectively, as aryl sources, a wide range of other transition metals have also been employed. Experimental and theoretical studies have often been reported, thus affording mechanistic insights and allowing to suggest catalytic cycles.

Although described nearly 135 years ago,<sup>[1]</sup> allenes still remain the least studied all-carbon unsaturated compounds. The first effective synthetic method to obtain this structure was not described until the 1960s, probably because of the unusual linear 3-carbon backbone comprised of two consecutive  $\pi$ -bonds delaying their popularity in organic synthesis. However, since this time, a growing interest in allene chemistry has led to a proliferation of synthetic methods allowing access to a wide variety of these unsaturated molecules,<sup>[2]</sup> particularly in the last 20 years, consequently garnering attention as precursors for organic transformations.<sup>[3]</sup> In this field, hydrofunctionalization mainly for the formation of C-N, C-O and C-C bonds, accomplished mostly with transition metal-based catalysts, has emerged as an atomically efficient tool to exploit the reactivity of allenes while avoiding waste production.<sup>[4]</sup> Thus, these molecules became essential and valuable synthetic building blocks to selectively obtain high value-added allyl or vinyl motifs. The aim of this review is to highlight the importance of hydrofunctionalization of allenes in the frame of C-C bond formation, more particularly focusing the intermolecular hydroarylation of allenes.<sup>[5]</sup> Beginning in the early 80's with a few examples, C-C functionalization has progressively gained interest with the discovery of efficient catalytic systems generally proceeding under mild conditions. The addition of C-pronucleophiles,<sup>[6]</sup> alkynes,<sup>[7]</sup> alkenes,<sup>[8]</sup> cyanide,<sup>[9]</sup> carbon mono-<sup>[10]</sup> and dioxide,<sup>[11]</sup> alcohols<sup>[12]</sup> and aldehydes<sup>[13]</sup> to allenes had thus been described. However, the hydroarylation reaction, which was the first to be performed, has been the most widely studied. In this review, hydroarylation methods are classified into three categories according to the aryl source: (1) aryl nucleophiles, (2) aryl boronic derivatives and (3) miscellaneous (Scheme 1).



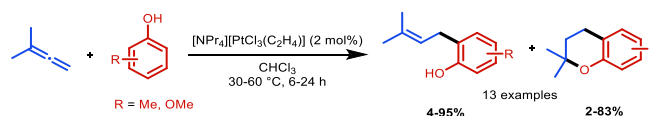
**Scheme 1.** Transition metal-catalyzed intermolecular hydroarylation of allenes.

## 1. Hydroarylation with arenes

The direct addition of an aryl group via a  $\text{C}_{\text{Ar}}\text{-H}$  bond without any pre-functionalisation is a powerful tool in organic synthesis. In this frame, many transition metals have been used over the years to achieve intermolecular hydroarylation of allenes using ArH as the aryl source. The catalytic systems developed, the extent and limitations of methods and the corresponding suggested mechanisms will be described in this part.

### 1.1. Platinum

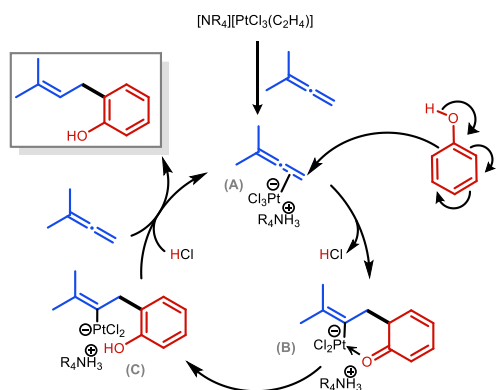
In 1983, Panunzi and coworkers were the first to disclose the hydroarylation of allenes, with the addition of phenols on 1,1-dimethylallene by using a platinum (II) complex as catalyst.<sup>[14]</sup> The allylic product was formed through the regioselective addition of the aryl moiety to the terminal carbon of the allene. The addition occurred in the *ortho* position of the hydroxyl group. The reaction is limited to electron rich phenols and leads, in most cases, to the formation of 2,2-dimethylchromane derivatives, after *in situ* cyclization of the hydroarylation product (Scheme 2).



**Scheme 2.** Platinum-catalyzed hydroarylation of 1,1-dimethylallene with phenols.

The platinum complex would activate the allene through coordination on the less-substituted terminal double bond (Scheme 3), thus favoring a selective *ortho*-addition of a phenolic substrate on the terminal carbon to form the corresponding metallacycle (**B**). The latter undergoes rearomatization to afford the vinyl-Pt intermediate (**C**). Finally, a protodeplatination in the

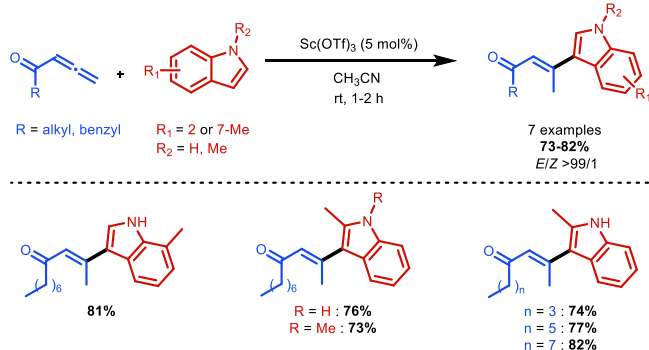
presence of a second molecule of allene allows the formation of the allylic product and the regeneration of the active Pt(II) species.



**Scheme 3.** Proposed mechanism for Pt-catalyzed hydroarylation of 1,1-dimethylallene with phenols.

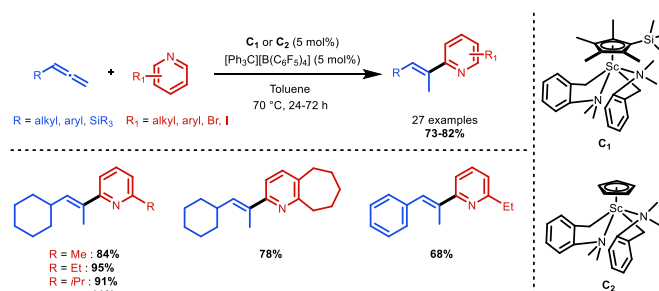
## 1.2. Scandium

S. Ma's group described the hydroarylation of allenic ketones with indole derivatives, by using 5 mol% of scandium triflate ( $\text{Sc}(\text{OTf})_3$ ) at room temperature, to obtain vinyl indole derivatives in good yields with high *E/Z* ratio (Scheme 4).<sup>[15]</sup> The authors mentioned an optimization test with 5 mol% of copper (II) triflate, which afforded the 2,3-addition with the aryl moiety being added on the central carbon of the allene with a good yield (65%) but with a slightly lower *E/Z* ratio (91:9).



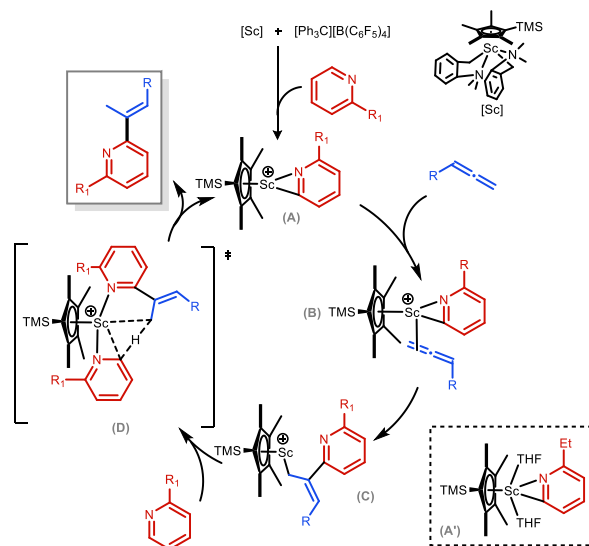
**Scheme 4.** Scandium-catalyzed hydroarylation of allenic ketones with indoles.

Scandium has also been used by Hou and coworkers in 2015 to perform the C-H alkenylation of pyridine derivatives with terminal allenes.<sup>[16]</sup> The addition occurs on the central carbon of the latter in the presence of 5 mol% of scandium half-sandwich **C**<sub>1</sub> and  $[\text{Ph}_3\text{C}][\text{B}(\text{C}_6\text{F}_5)_4]$  as catalyst precursors (Scheme 5).



**Scheme 5.** Scandium-catalyzed hydroarylation of monosubstituted allenes with pyridines.

In the proposed mechanism, the reaction of the scandium precursor with  $[\text{Ph}_3\text{C}][\text{B}(\text{C}_6\text{F}_5)_4]$  and the 2-substituted pyridine produces the cationic scandium-pyridyl complex (**A**) (Scheme 6). Then, after the metal coordinates to the allene through the terminal double bond, the addition of pyridyl moiety on the same insaturation affords the intermediate (**C**). The latter undergoes a protonation reaction with another molecule of pyridine to generate the alkenylated pyridine and regenerate the cationic scandium species. According to deuteration tests and a kinetic isotope effect measurement, the rate-determining step is the C-H activation (from (**A**) to (**B**)). The cationic half-sandwich intermediate (**A'**), similar to species (**A**), with two THF ligands was isolated after recrystallisation in a THF/hexane mixture and can be used as a catalyst to carry out the hydroarylation in deuterated chlorobenzene.

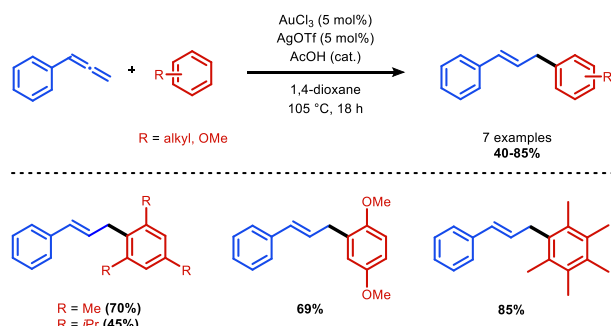


**Scheme 6.** Possible mechanism for Sc-catalyzed hydroarylation of monosubstituted allenes with pyridines.

## 1.3. Gold

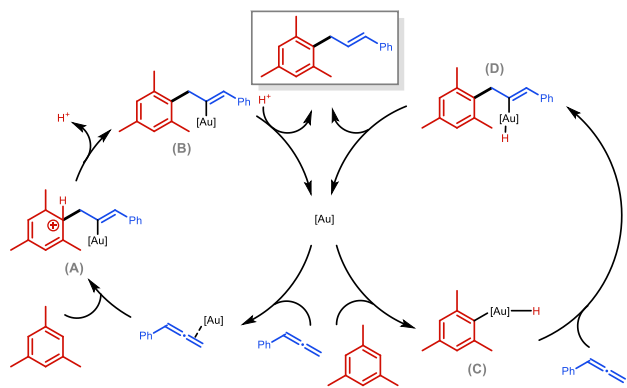
Gold-based catalysts have been the most widely used for the hydroarylation of allenes. Its particularly the case for gold(I) complexes which are known to be excellent  $\pi$ -acidic catalysts that can easily activate unsaturated carbon-carbon bonds.<sup>[17]</sup> In 2008, Li's group reported the regioselective gold-catalyzed addition of

benzene derivatives on the terminal carbon of phenylallene in presence of silver (I) triflate as a co-catalyst (Scheme 7).<sup>[18]</sup>



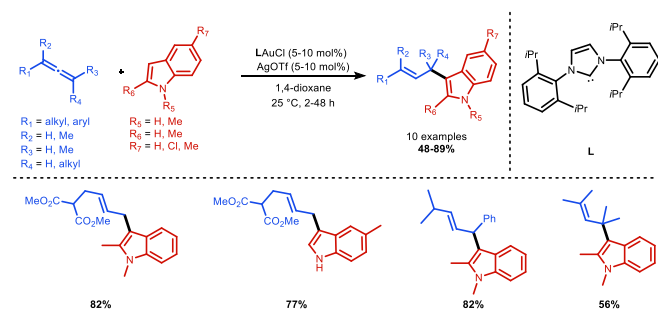
**Scheme 7.** Gold-catalyzed hydroarylation of phenylallene with benzenes.

On the proposed mechanism (Scheme 8, left cycle), gold acts as a Lewis acid and allows the addition of the nucleophilic aryl to the allene by a  $S_EAr$ -type mechanism, leading to the Wheland intermediate **(A)** which undergoes rearomatization to form the vinyl gold species **(B)**. The latter finally affords the hydroarylation compound through reductive elimination. In another hypothesis (Scheme 8, right cycle), the gold firstly inserts into the C-H bond (auration step) to form the aryl gold (III) intermediate **(C)** than can react with the allene to form the vinyl gold (III) intermediate **(D)** which undergoes protodeauration to provide the final product.



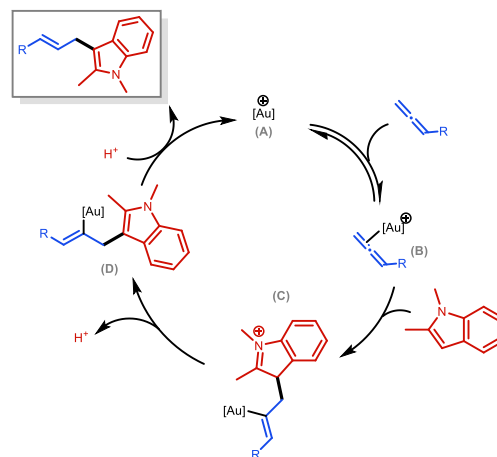
**Scheme 8.** Suggested mechanisms for Au-catalyzed hydroarylation of phenylallene with mesitylene.

One year later, Widenhoefer's group realized an NHC-gold/silver (I) triflate catalyzed hydroarylation of monosubstituted, 1,3-disubstituted and tetrasubstituted allenes with indole derivatives (Scheme 9).<sup>[19]</sup>



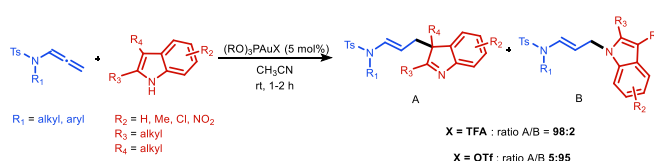
**Scheme 9.** Gold-catalyzed hydroarylation of monosubstituted, 1,3-disubstituted and tetrasubstituted allenes with indoles.

The reaction of LAuCl with AgOTf gives the gold active catalyst LAuOTf through halide displacement. The latter undergoes displacement of the triflate ligand with the allene to afford the gold  $\pi$ -allene complex **(B)** which is in equilibrium with **(A)** (Scheme 10). Then, an outer sphere attack of indole occurs on the gold complex, affording the cationic intermediate **(C)**, the deprotonation of which yields the neutral gold vinyl complex **(D)**, and finally the allylic indole through protonolysis.



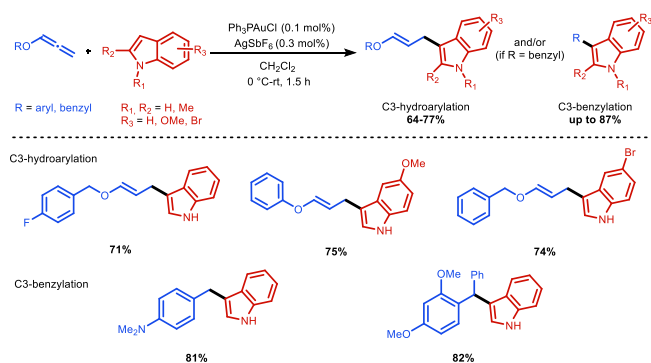
**Scheme 10.** Suggested mechanism for Au-catalyzed hydroarylation of monosubstituted, 1,3-disubstituted and tetrasubstituted allenes with indoles

In the following years, Bandini's group achieved the addition of indoles on the terminal carbon of allenamides with tunable chemoselectivity depending on the counterion of the gold catalyst. In the presence of trifluoroacetate (TFA<sup>-</sup>) anions, the indole acts as a C-nucleophile whereas it acts as an N-nucleophile in presence of triflate (TfO<sup>-</sup>) anions. NMR studies have shown that these two anions do not interact in the same way in terms of coordination capacity and hydrogen bonding, which may explain the difference observed in selectivity.<sup>[20,21]</sup>



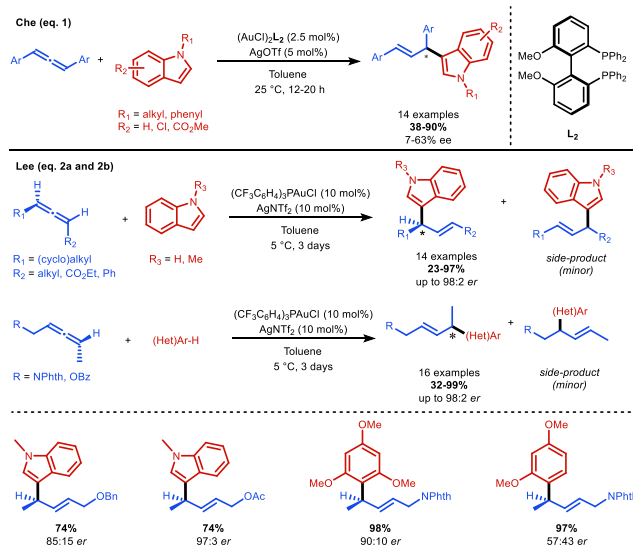
**Scheme 11.** Gold-catalyzed C- or N-hydroindolylolation of monosubstituted allenamides.

Ramana and co-workers developed a gold-catalyzed hydroindolylolation of terminal O-allenyl derivatives thanks to the *in-situ* formed Au(PPh<sub>3</sub>)SbF<sub>6</sub> complex.<sup>[22]</sup> While aryl allenyl ethers afford exclusively the hydroarylation product resulting from the aryl addition on the terminal carbon of the allene, benzyl allenyl ethers suffer from a side-reaction leading to the formation of the benzylation product as secondary or even as the main product (Scheme 12). Control experiments seem to be in favor of an inner sphere mechanism, with an intramolecular transfer of the indole from the gold metal center to the allene.

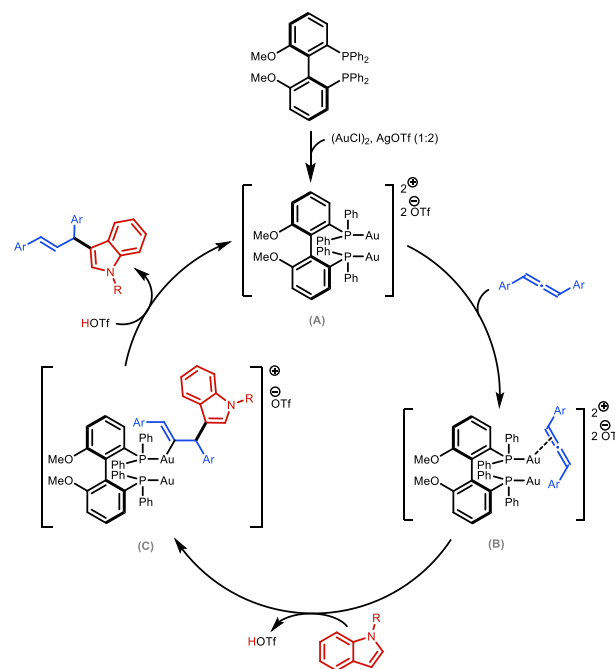


**Scheme 12.** Gold-catalyzed hydroindolylations of monosubstituted allenyl ethers with indoles.

Che and co-workers studied the gold-catalyzed enantioselective addition of indoles to symmetrical 1,3-diaryllallenes in presence of (*S*)-(-)-MeO-biphep **L<sub>2</sub>** (Scheme 13, eq. 1).<sup>[23]</sup> The addition of the aryl moiety occurred on the terminal carbon of the allene and afforded the corresponding products in high yields but with poor to modest enantiomeric excess due to competitive allene racemization. Density function theory (DFT) calculations allow the following mechanism to be proposed (Scheme 14). The cationic complex **(A)** coordinates to the allene to form the intermediate **(B)**. The indole adds to the latter to give the species **(C)** which, by protodeauration in the presence of triflic acid, leads to the hydroarylation product and regenerates the catalytically active species **(A)**. Some years later, Lee's group developed a gold-catalyzed hydroarylation of enantioenriched 1,3-disubstituted allenes with an efficient axial-to-point chirality transfer (Scheme 13, eq. 2a and 2b).<sup>[24]</sup> Pyrrole, indole and polymethoxybenzene derivatives were successfully engaged in this reaction, but systematically led to the formation of a mixture of two regioisomers (at least <20:1).

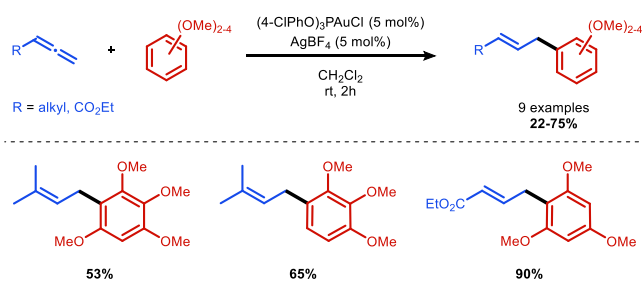


**Scheme 13.** Enantioselective gold-catalyzed hydroarylation of 1,3-disubstituted allenes with indoles.



**Scheme 14.** Proposed mechanism for gold-catalyzed hydroarylation of 1,3-disubstituted allenes with indoles.

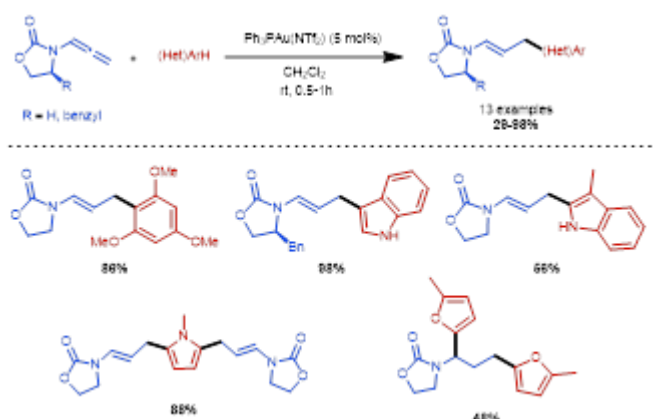
In 2009, Gagné's group reported a (4-ClPhO)<sub>3</sub>PAuCl-catalyzed hydroarylation of terminal allenes with polymethoxybenzene derivatives in presence of AgBF<sub>4</sub> (Scheme 14).<sup>[25]</sup> The reaction is performed under smooth conditions, but the scope was limited to some examples of electron rich arenes containing both *ortho*- and *para*-directing groups. Other electron rich heteroaryl such as indole, benzofuran and pyrrole showed to be unreactive under these conditions.



**Scheme 15.** Gold-catalyzed hydroarylation of monosubstituted allenes with polymethoxybenzenes.

Kimber and coworkers reported a Ph<sub>3</sub>PAu(NTf<sub>2</sub>)<sub>2</sub>-catalyzed stereo- and regioselective addition of electron rich (hetero)aromatics on the terminal carbon of monosubstituted *N*-allenyl oxazolidinone derivatives.<sup>[26]</sup> Under smooth conditions and within short reaction times, various (*E*) enamides were obtained including two original products, one resulting from a double addition of the nucleophile and the other obtained by the addition of the same nucleophile to two allenamide molecules (Scheme 16).

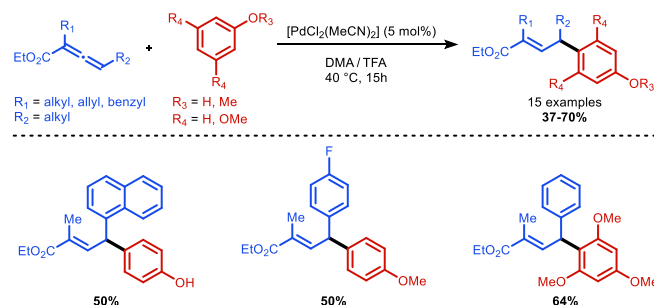




**Scheme 16.** Gold-catalyzed hydroarylation of monosubstituted *N*-allenyl oxazolidinone derivatives with (hetero)aromatics.

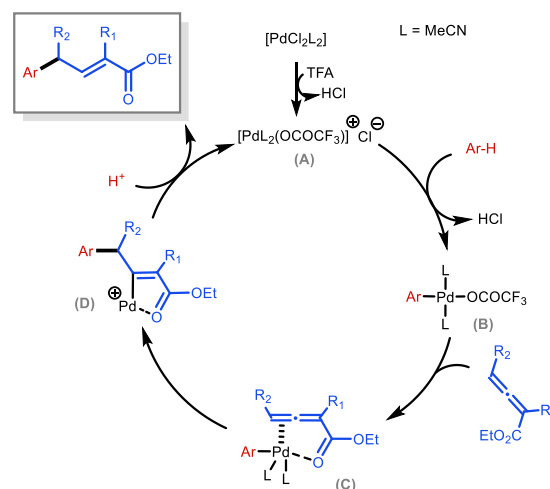
#### 1.4. Palladium

In 2010, S. Ma's group developed a palladium-catalytic system for the hydroarylation of allenates with phenol, anisole and 1,3,5-trimethoxybenzene (Scheme 17).<sup>[27]</sup> The reaction affords selectively the corresponding (*E*)-allylic product through addition on the terminal bond of the allene.



**Scheme 17.** Palladium-catalyzed hydroarylation of 1,1,3-trisubstituted allenates.

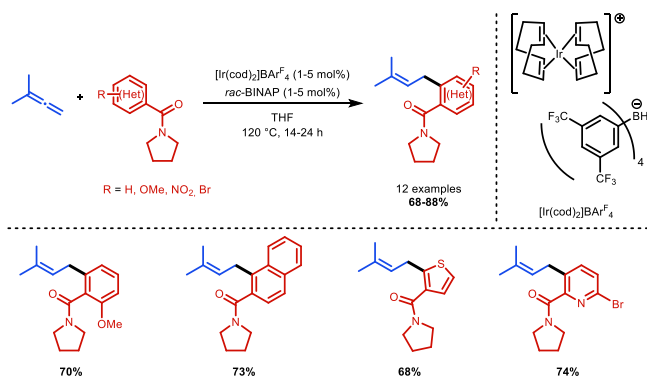
The presence of TFA is crucial to form the active Pd(II) species (**A**) from the starting precatalyst (Scheme 18). The latter then affords the aryl-Pd intermediate (**B**) via electrophilic palladation, which can coordinate to both the allene and carbonyl moieties to form the complex (**C**). Subsequently, a *syn*-insertion of the less hindered, and most electron rich, double bond into the Ar-Pd bond gives the intermediate (**D**) which affords the final stereoselectivity due to the coordination of the metal center to the carbonyl group. Finally, a protodepalladation step gives the linear (*E*)-product and regenerates the active Pd(II) catalyst (**A**).



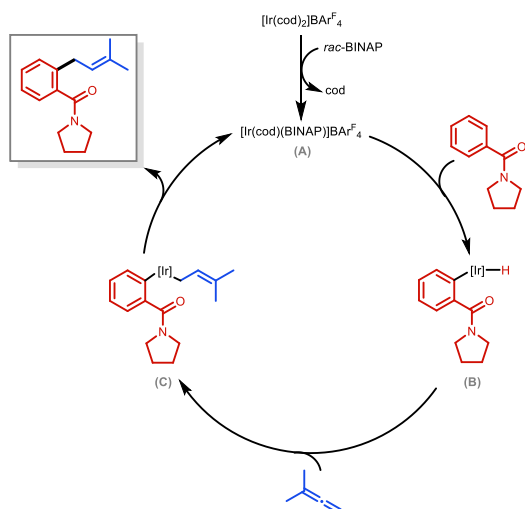
**Scheme 18.** Proposed mechanism for the Pd-catalyzed hydroarylation of 1,1,3-trisubstituted allenates.

#### 1.5. Iridium

Krische and coworkers reported the iridium-catalyzed addition of (hetero)aromatic carboxamides to the terminal carbon of 1,1-dimethylallene.<sup>[28]</sup> This reaction occurs at 120 °C in the presence of 1-5 mol% of cationic iridium catalyst and a racemic diphosphine ligand (Scheme 19). Various substituted benzenes, as well as pyridine, thiophene and indole derivatives, were engaged in this reaction, resulting in the corresponding prenylation products in high yields. The cationic iridium(I) active species (**A**), resulting from the reaction of  $[\text{Ir}(\text{cod})_2]\text{BARF}_4$  with BINAP, undergoes an *ortho* C-H oxidative addition, thus affording the intermediate (**B**) followed by hydrometallation of the allene to form the aryl-allyl iridium complex (**C**) (Scheme 20). The latter finally leads to the prenylation compound through reductive elimination, thereby regenerating the active species (**A**).



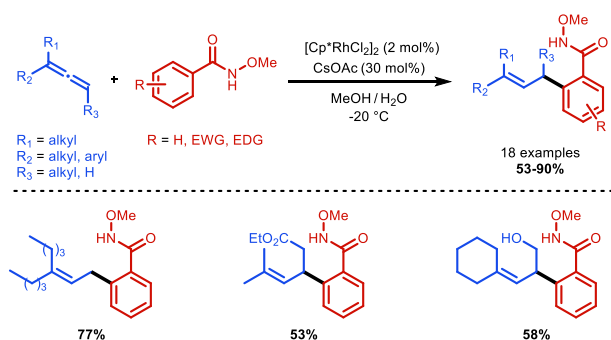
**Scheme 19.** Iridium-catalyzed hydroarylation of 1,1-dimethylallene with (hetero)aromatic carboxamides.



**Scheme 20.** Plausible mechanism for the Ir-catalyzed hydroarylation of 1,1-dimethylallene with (hetero)aromatic carboxamides.

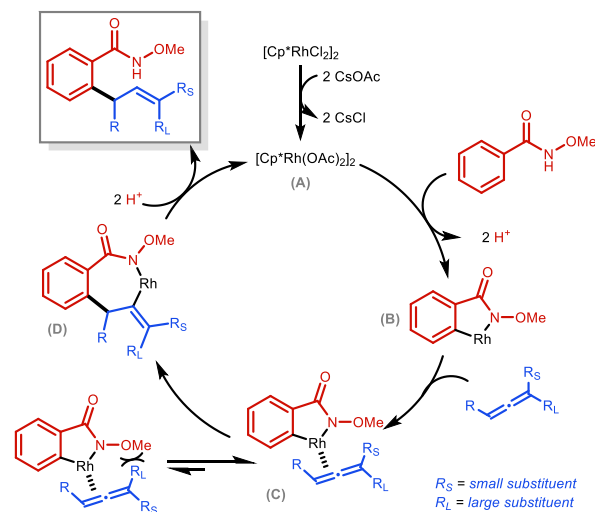
## 1.6. Rhodium

In 2012, Ma's group described the first rhodium-catalyzed hydroarylation of allenes with the addition of *N*-methoxybenzamide derivatives to 1,1-disubstituted and 1,1,3-trisubstituted allenes (Scheme 21).<sup>[29]</sup> The corresponding allylic products resulting from the addition on the terminal position of the allene were obtained with moderate to excellent yields.



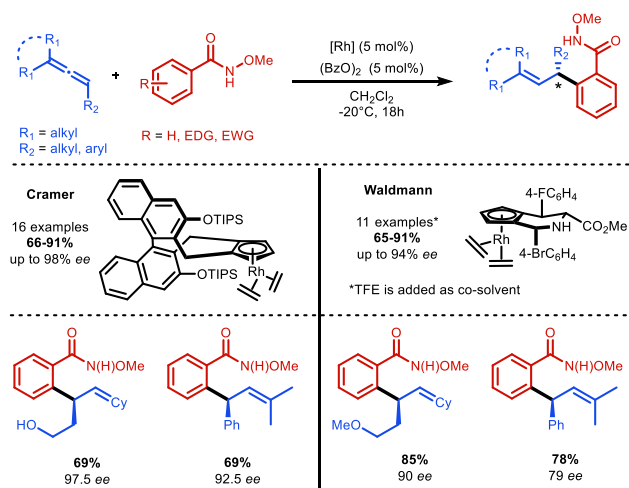
**Scheme 21.** Rhodium-catalyzed hydroarylation of 1,1-disubstituted and 1,1,3-trisubstituted allenes with *N*-methoxybenzamides.

In the proposed mechanism, CsOAc initiates the formation of the catalytic active species (A) from the  $[\text{Cp}^*\text{RhCl}_2]_2$  precatalyst (Scheme 22). The reaction then starts by the arene *ortho*-electrophilic rhodation of the benzamide to form the five membered Rh(III) metallacycle (B). The latter coordinates to the less substituted double bond of the allene, thus favoring its insertion into the Ar-Rh bond to form a  $\text{C}(\text{sp}^2)$ -Rh intermediate (D). A final protonolysis step affords the allylic product and regenerate the active catalyst (A). Kinetic isotope effect (KIE) measurements using deuterated substrates identified the *ortho* C-H bond activation process as the rate-determining step.



**Scheme 22.** Proposed mechanism for Rh-catalyzed hydroarylation of 1,1-disubstituted and 1,1,3-trisubstituted allenes with *N*-methoxybenzamides.

Later, two different chiral, cyclopentadienyl ligands were proposed separately by Cramer<sup>[30]</sup> and Waldmann<sup>[31,32]</sup> to perform the enantioselective rhodium-catalyzed terminal hydroarylation of 1,1,3-trisubstituted allenes with *N*-methoxybenzamide derivatives (Scheme 21). In both cases, a catalytic amount of dibenzoyl peroxide was necessary to oxidize the Rh(I) to Rh(III) which is the active catalytic species promoting the C-H allylation.

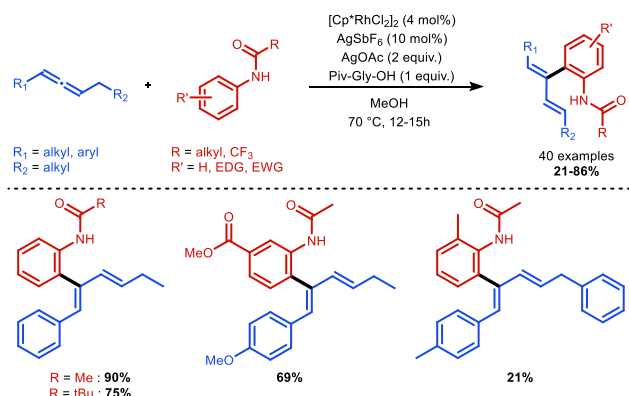


**Scheme 23.** Rhodium-catalyzed enantioselective hydroarylation of 1,1,3-trisubstituted allenes with *N*-methoxybenzamide derivatives.

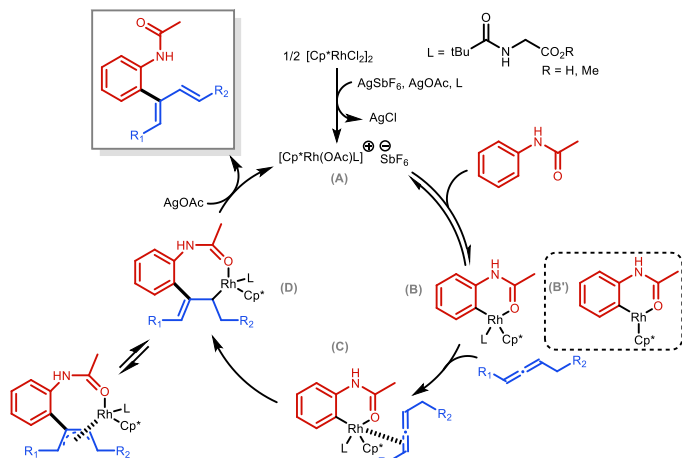
Recently, Kapur and coworkers reported a rhodium-catalyzed hydroarylation of 1,3-substituted allenes with anilide derivatives leading to the formation of 1,3-dienes (Scheme 24).<sup>[33]</sup> In contrary to the regioselectivity generally observed in this type of reaction, unusually the addition of the aryl occurs in the central position of the allene. This reaction was carried out in presence of silver acetate, silver hexafluoroantimonate and an  $\alpha$ -amino acid (both



the acid and the methyl ester forms of *N*-pivaloylglycine) as the ligand. Authors suggest that the active rhodium catalyst (**A**) is able to provide the 6-membered rhodacycle (**B**) through directed C-H activation (Scheme 25). According to KIE measurements and deuteration studies, this step is reversible and not involved in the rate-limiting step. The allene undergoes coordination with intermediate (**B**), thus affording the complex (**C**) which can then lead to the 8-membered rhodacycle (**D**) via carboration. Finally, a  $\beta$ -hydride elimination affords the 1,3-diene and silver(I) can oxidize the rhodium(II) intermediate (**D**), thus regenerating the active rhodium(III) species (**A**). The complex (**B'**), resulting from (**B**) through ligand decooordination, was detected by HRMS.



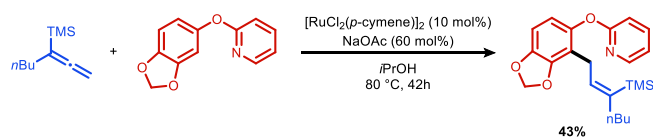
**Scheme 24.** Rhodium-catalyzed hydroarylation of 1,3-disubstituted allenes with anilides.



**Scheme 25.** Suggested mechanism for the Rh-catalyzed hydroarylation of 1,3-disubstituted allenes with anilides.

## 1.7. Ruthenium

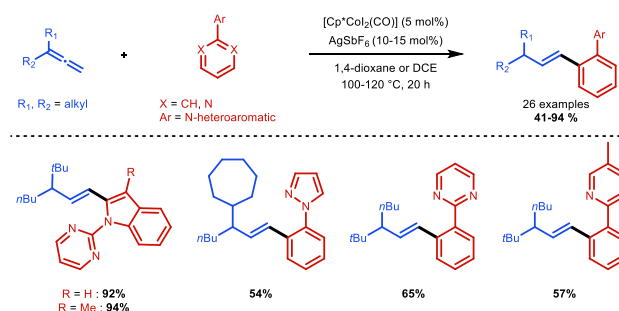
In 2015, Ackermann's group reported a single example of the ruthenium (II)-catalyzed hydroarylation of a 1,1-disubstituted allene with a 2-aryloxypyridine derivative<sup>[34]</sup> (Scheme 26). The addition of the aryl moiety occurred on the terminal carbon of the allene, thus leading to the corresponding allylic compound in moderate yield.



**Scheme 26.** Ruthenium-catalyzed hydroarylation of 1,1-disubstituted allene with a 2-aryloxypyridine derivative.

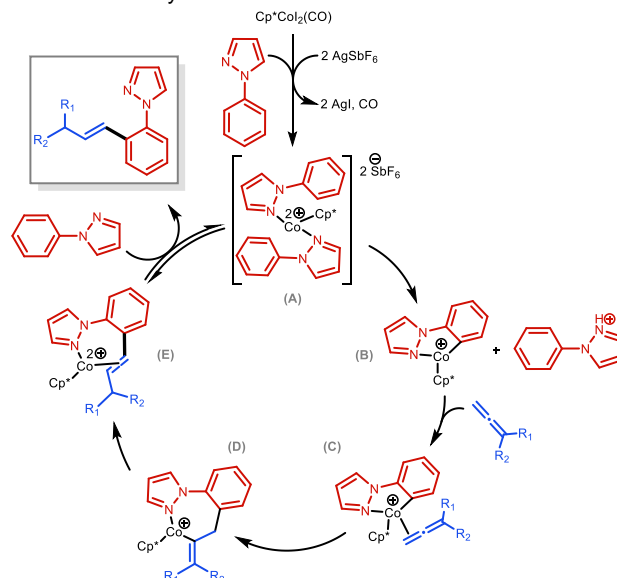
## 1.8. Cobalt

Ackermann's group disclosed in 2017 a general method with a catalytic cobalt (III) system for the addition of (hetero)aromatics to 1,1-disubstituted allenes.<sup>[35]</sup> Various phenyls substituted by a 5 or 6-membered *N*-heteroaromatic cycle as well as indole derivatives were successfully engaged in this reaction, affording the corresponding vinyl aromatic compounds after an isomerization step (Scheme 27).



**Scheme 27.** Cobalt-catalyzed hydroarylation of 1,1-disubstituted allenes with (hetero)aromatics.

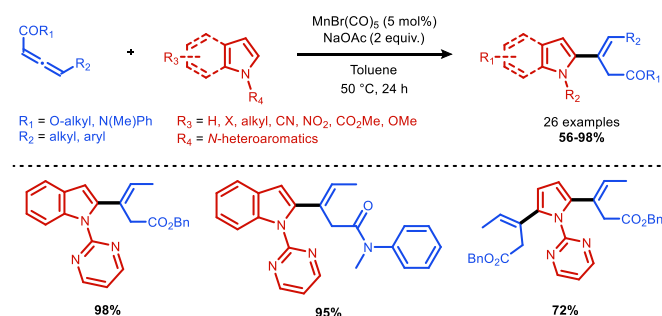
Deuterium labelling, KIE measurements, kinetic studies and DFT calculations allowed the authors to propose a mechanism in which the complex  $\text{Cp}^*\text{Co}_2(\text{CO})$  first leads to an active cationic  $\text{Co}(\text{III})$  species (**A**) in the presence of  $\text{AgSbF}_6$  and two molecules of the heteroaryl (Scheme 28). The latter undergoes a C-H cobaltation by hydrogen transfer to afford the five membered metallacycle (**B**) which can coordinate to the allene through its terminal double bond, leading to the complex (**C**). Then a migratory insertion delivers the seven membered metallacycle intermediate (**D**). Subsequently, a double bond isomerization occurs and is followed by a protonation step in the coordination sphere of the metal catalyst, yielding the intermediate (**E**). A final decobaltation step gives the alkenylated product via a ligand exchange involving a second heteroaryl molecule.



**Scheme 28.** Proposed mechanism for Co-catalyzed hydroarylation of 1,1-disubstituted allenes with (hetero)aromatics.

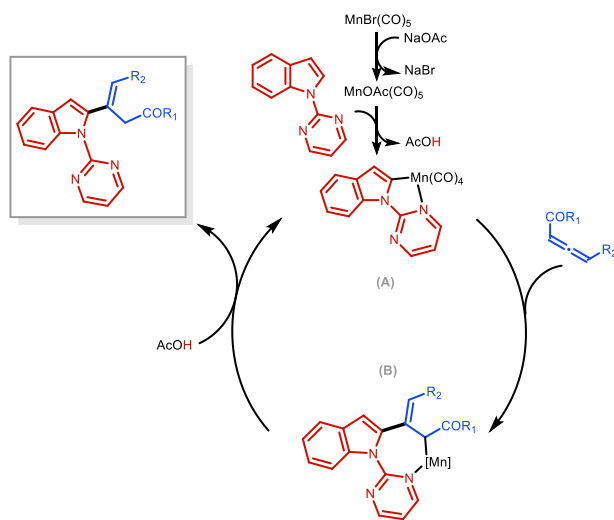
## 1.9. Manganese

Using 5 mol% of  $\text{MnBr}(\text{CO})_5$ , Rueping's group reported the hydroarylation of 1,3-disubstituted allenes with indole and pyrrole derivatives, giving access to alkenyl products through the selective addition to the allene central carbon (Scheme 29) [36].



**Scheme 29.** Manganese-catalyzed hydroarylation of 1,3-disubstituted allenes with indoles and pyrroles.

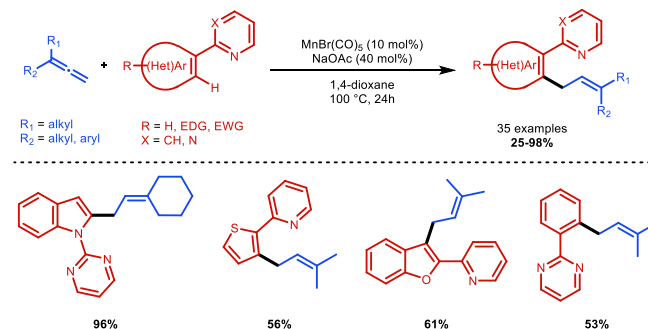
The first step is the formation of  $\text{MnOAc}(\text{CO})_5$  resulting from the reaction of  $\text{MnBr}(\text{CO})_5$  with sodium acetate (Scheme 30). Next, a C-H cleavage on the indole moiety affords the cyclometalated catalytic active species (**A**) that undergoes an allene insertion, allowing the formation of the 7-membered metallacycle intermediate (**B**). Finally, a protonation step involving acetic acid leads to the hydroarylation product, thereby regenerating (**A**). The authors were able to synthesize complex (**A**) and demonstrate its ability to provide the desired hydroarylation product under stoichiometric conditions.



**Scheme 30.** Proposed mechanism for Mn-catalyzed hydroarylation of 1,3-disubstituted allenes with indoles and pyrroles.

Using a similar system, Wang and coworkers reported the hydroarylation of 1,1-disubstituted allenes.[37]. The allylation of a

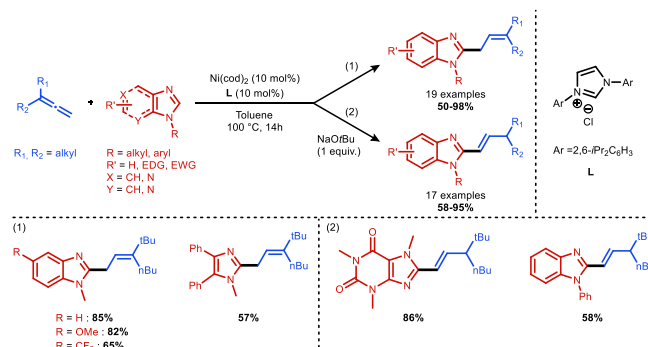
large scope of *N*, *O* and *S*-heteroaromatics as well as benzene derivatives was carried out at the *ortho* position of the directing group (Scheme 31). KIE measurements, H/D scrambling tests and reactions in the presence of a catalytic or stoichiometric amount of a cyclometalated manganese (I) complex intermediate allowed the authors to study the mechanism of the reaction, which is similar to that described the same year by Rueping's team.



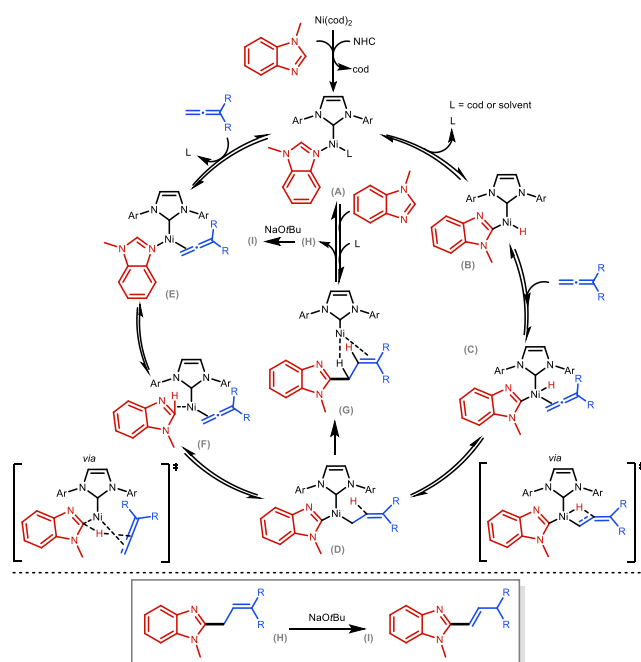
**Scheme 31.** Manganese-catalyzed hydroarylation of 1,1-disubstituted allenes with *N*, *O* and *S*-heteroaromatics.

## 1.10. Nickel

In 2017, Ackermann reported the allylation and the alkenylation of imidazole and purine derivatives by using a  $\text{Ni}(\text{cod})_2/\text{NHC}$  catalytic system.[38] The reaction with 1,1-disubstituted allenes affords selectively the allylic product (Scheme 32, eq. 1), while in the presence of sodium *tert*-butoxide this product undergoes an isomerization to yield only the corresponding vinyl product (Scheme 32, eq. 2). KIE measurements, H/D scrambling tests, NMR studies and DFT calculations allowed the authors to investigate the mechanism of the reaction. The first step is the formation of the active  $\text{Ni}(0)$  species (**A**) through the reaction of  $\text{Ni}(\text{cod})_2$ , NHC and heteroaryl (Scheme 33). The latter can then be involved in two pathways. In one of them (Scheme 33, right cycle), (**A**) firstly undergoes an oxidative addition to afford the  $\text{Ni}(\text{II})$  complex (**B**). This is followed by allene coordination and then a hydronicellation step which successively gives intermediates (**C**), and (**D**), respectively. The formation of the latter can also be explained in another way (Scheme 33, left cycle). The active species (**A**) can give intermediate (**E**) by ligand exchange, which evolves to complex (**F**) by agostic interaction and finally to intermediate (**D**) by C-H activation *via* ligand-to-ligand hydrogen transfer (LLHT). Finally, the  $\text{Ni}(\text{II})$  intermediate (**D**) undergoes reductive elimination to lead to the  $\text{Ni}(0)$  complex (**G**) which provides, *via* ligand exchange, the hydroarylation product (**H**) that isomerizes in the presence of  $\text{NaOtBu}$ , to afford (**I**).



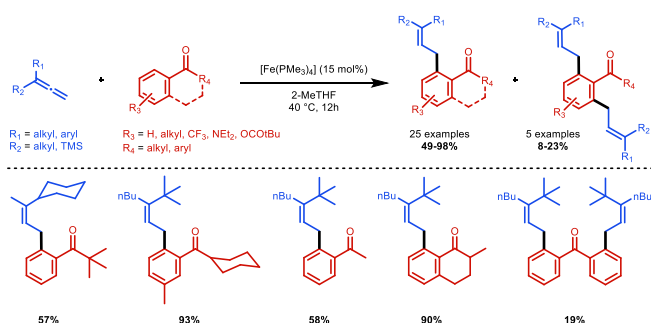
**Scheme 32.** Nickel-catalyzed hydroarylation of 1,1-disubstituted allenes with imidazoles and purines.



**Scheme 33.** Proposed mechanism for the Ni-catalyzed hydroarylation of 1,1-disubstituted allenes with imidazoles and purines.

### 1.11. Iron

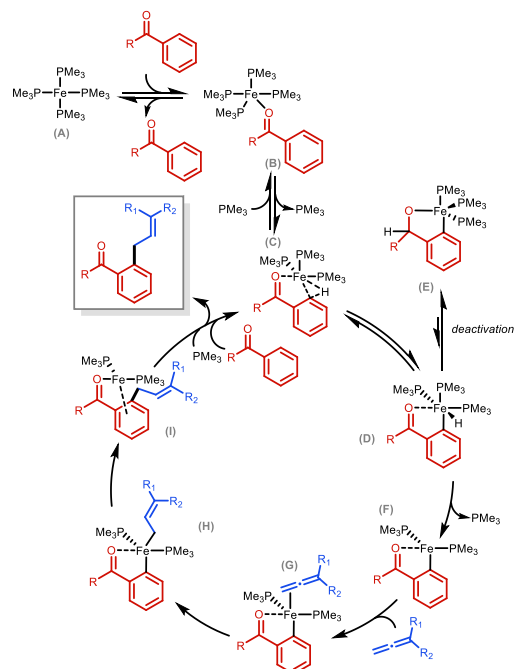
Recently, Ackermann and coworkers reported a  $\text{Fe}(\text{PMe}_3)_4$ -mediated C–H allylation of phenones with 1,1-disubstituted allenes.<sup>[39]</sup> This additive-free catalytic system provided, under mild conditions, good to excellent yields of a broad scope of products resulting from the aryl addition on the terminal carbon of the allene. Some examples of the addition of two allene molecules to the same aryl were also reported in modest yields (Scheme 34).



**Scheme 34.** Iron-catalyzed hydroarylation of 1,1-disubstituted allenes with phenones.

Isolation and structural characterization of iron-metallacycle intermediates, along with detailed mechanistic studies, allowed the authors to suggest the following catalytic cycle (Scheme 35).<sup>[40]</sup> The iron(0) complex (A) firstly undergoes O-coordination with the phenone, thus affording the intermediate (B). Phosphine decooordination then led to the key complex (C) which is then involved in a reversible oxidative addition step to provide the Fe-

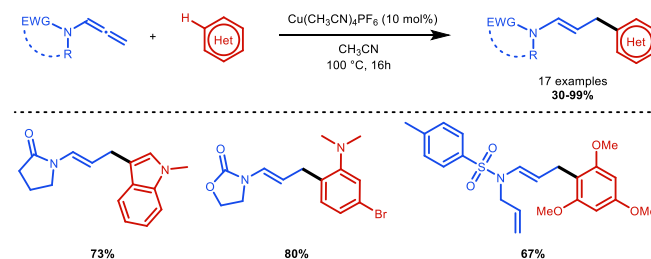
H species (D). This complex can give the catalytically inactive iron (II) alkoxide (E) via a nucleophilic addition of the hydride to the carbonyl (deactivation pathway). A second phosphine decooordination can then occur, leading to the complex (F) which then coordinates to the allene, giving the intermediate (G). Migratory insertion of the allene followed by ligand rearrangement affords (H) and (I) respectively. The latter finally undergoes a rate-determining reductive elimination, thus affording the hydroarylation product and regenerating the intermediate (C).



**Scheme 35.** Proposed mechanism for Fe-catalyzed hydroarylation of 1,1-disubstituted allenes with phenones.

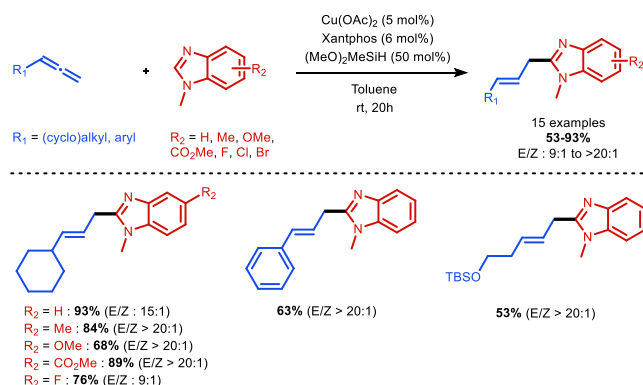
### 1.12. Copper

Recently, our group developed a copper-catalyzed hydroarylation of allenes illustrated by the addition of (hetero)aryl nucleophiles on the terminal carbon of monosubstituted *N*-allenyl derivatives, which afford selectively (*E*)-allylic compounds with medium to excellent yields (Scheme 36).<sup>[41]</sup> Various readily available aromatic compounds were successfully engaged in the reaction with allene substrates, showing the high tolerance of the process. Nevertheless, we noticed that electron-rich substrates are required for the reaction to proceed, which is consistent with the literature and the  $\text{S}_{\text{E}}\text{Ar}$ -type mechanism.



**Scheme 36.** Copper-catalyzed hydroarylation of monosubstituted allenamides with (hetero)aryl nucleophiles.

In 2021, Breit's group reported a copper-catalyzed hydroarylation of monosubstituted allenes using 1-methylbenzimidazole derivatives in the presence of a silane (Scheme 37).<sup>[42]</sup> The addition of heteroaryls occurs selectively on the terminal carbon of the allene, affording the corresponding compounds in moderate to high yields.



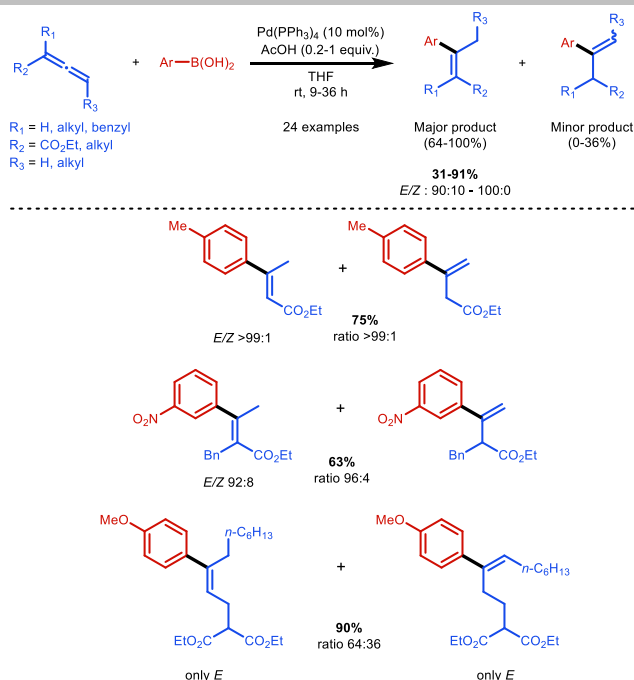
**Scheme 37.** Copper-catalyzed hydroarylation of monosubstituted allenes with 1-methylbenzimidazoles.

## 2. Hydroarylation with aryl boronic derivatives

Organoboronic acids  $\text{Ar-B(OH)}_2$  and esters  $\text{Ar-B(OR)}_2$  are well known aryl sources that can be used as alternative coupling partners for the hydroarylation of allenes. Even if the atom economy is not as good as when the reaction involves arenes nucleophiles, these readily available derivatives are usually more reactive, allowing the extension to less nucleophilic aromatic rings.

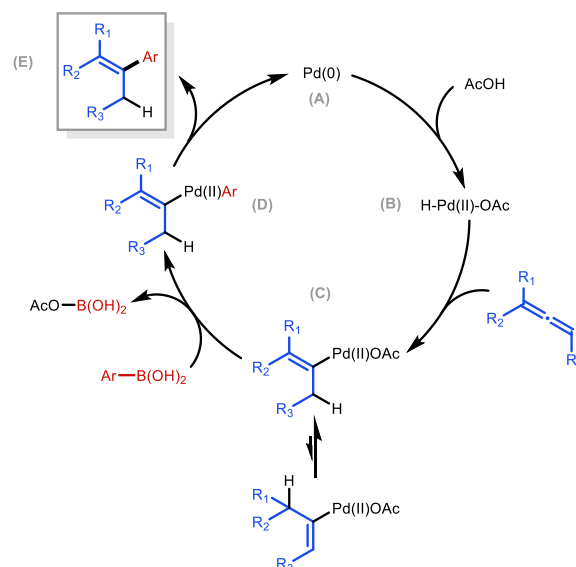
### 2.1. Palladium and platinum

Palladium was the first transition metal involved in allene hydroarylation using aryl boronic derivatives as nucleophiles. By using 10 mol% of tetrakis(triphenylphosphine)palladium(0), in 2003 S. Ma's group reported the addition of aryl organoboronic acids to mono-, 1,1-di, 1,3-di and tri-substituted allenes in the presence of acetic acid (Scheme 38).<sup>[43]</sup> The addition of the aryl moiety occurs on the central carbon of the allene and affords a mixture of two regioisomers in which the major product results from addition to the terminal double bond of the allene. The regioselectivity, *i.e.* the ratio of these two products, is controlled by the steric hindrance of the allene substituents.



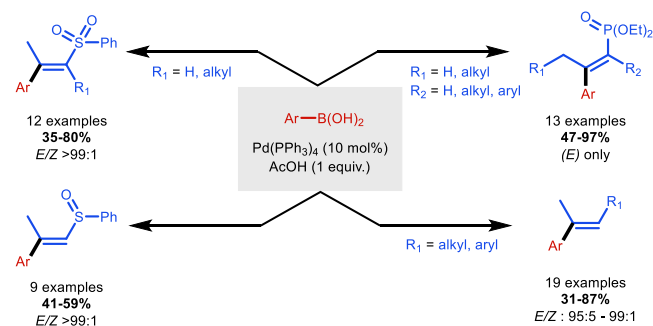
**Scheme 38.** Palladium-catalyzed hydroarylation of mono-, 1,1-di, 1,3-di and tri-substituted allenes with aryl boronic acids.

The authors used control experiments and electrospray ionization Fourier transform mass spectrometry (ESI-FTMS) to investigate the mechanism (Scheme 39).<sup>[44]</sup> The first step of the catalytic cycle is the oxidative addition occurring between the  $\text{Pd(0)}$  (**A**) and acetic acid to give a  $\text{Pd(II)}$  hydride species (**B**). This is followed by the insertion of the allene (hydropalladation step), affording species (**C**). The latter engages in a transmetalation step with the organoboronic acid to give (**D**) which then undergoes reductive elimination to give the desired product (**E**), and regenerates the initial active  $\text{Pd(0)}$  species (**A**).



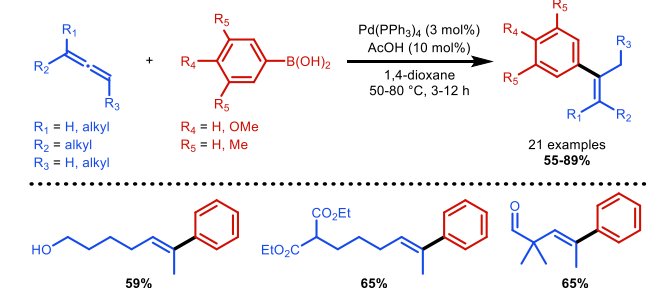
**Scheme 39.** Proposed mechanism for the Pd-catalyzed hydroarylation of mono-, 1,1-di, 1,3-di and tri-substituted allenes with aryl boronic acids.

They later applied this catalytic system to *P*-allenylphosphonates<sup>[45]</sup>, *S*-allenyl-sulfones and -sulfoxides<sup>[46]</sup> to afford (*E*)-vinyl-phosphonates, -sulfones and -sulfoxides respectively. The addition of alkyl- or aryl- substituted allenes with organoboronic acids to afford (*E*)-alkenes was also performed (Scheme 39).

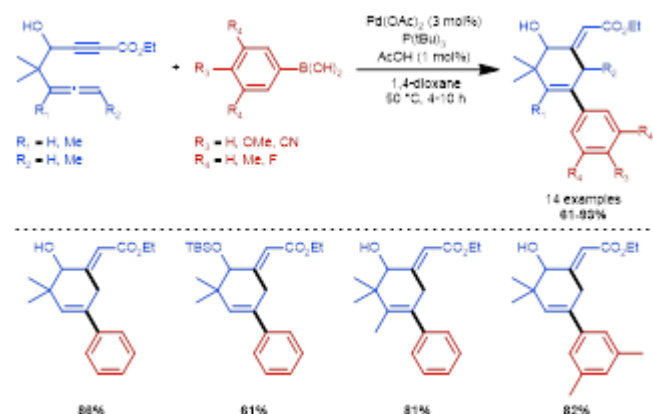


**Scheme 40.** Palladium-catalyzed hydroarylation of *P*-, *S*- and *C*-allenyl derivatives with aryl boronic acids.

At the same time, Oh's group also reported a regio- and stereoselective addition of electron rich aryl organoboronic acids to mono-, 1,1-di and 1,3-disubstituted allenes, in the presence of a catalytic amount of acetic acid (Scheme 40).<sup>[47]</sup> This method is compatible with a range of different functional groups such as alcohols, aldehydes, esters, nitriles and ethers. The addition occurs on the central carbon of the allene, thus affording selectively (*E*)-trisubstituted styrenes, except in the case of 1,3-disubstituted allenes which gives a 50:50 *E/Z* mixture. A few years later, in 2005, the same group reported the palladium-catalyzed hydroarylation of 1,6-allenynes followed by carbocyclization to afford a 6-membered ring (Scheme 42).<sup>[48]</sup>

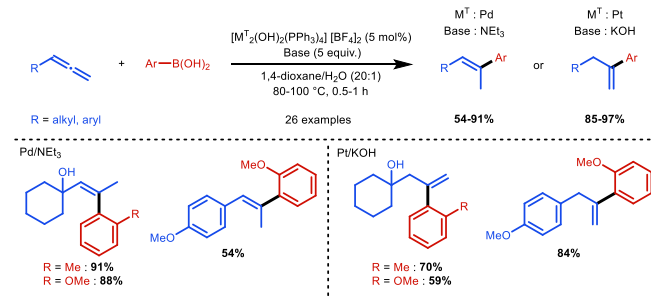


**Scheme 41.** Palladium-catalyzed hydroarylation of mono-, 1,1-di and 1,3-disubstituted allenes with aryl boronic acids.



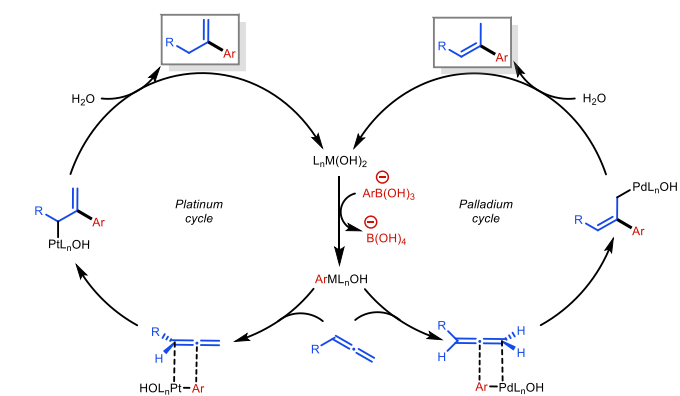
**Scheme 42.** Palladium-catalyzed hydroarylation of 1,6-allenynes with aryl boronic acids.

In 2008, Yoshida and coworkers performed the addition of aryl boronic acids on the central carbon of monosubstituted allenes in the presence of hydroxometal complexes.<sup>[49]</sup> Depending on the metal used, one or the other regioisomer is obtained. Indeed, the use of the hydroxopalladium catalyst in the presence of NEt<sub>3</sub> gave the internal alkene resulting from the addition on the terminal double bond of the allene, whereas the use of hydroxoplatinum catalyst in presence of KOH gave the terminal alkene resulting from the addition on the first double bond of the allene (Scheme 43).



**Scheme 43.** Palladium or platinum-catalyzed hydroarylation of monosubstituted allenes with aryl boronic acids.

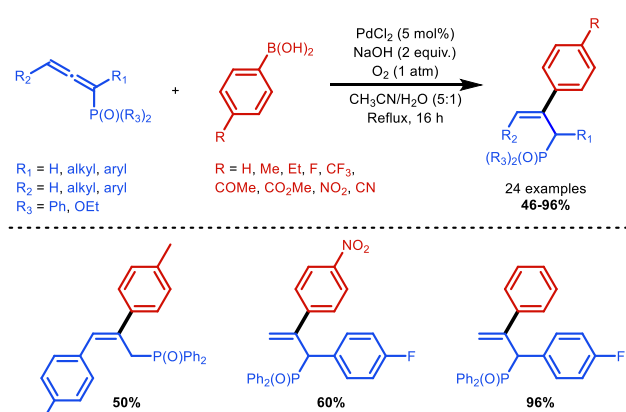
The decisive step to determine the regioselectivity is the coordination of the allene to the [ArML<sub>n</sub>(OH)] species (Scheme 44). If the electron density of the metal complex is low, it will interact with the electron rich double bond *i.e.* the internal one (Scheme 44, right cycle). In the opposite, if the electron density of the metal complex is high, it will interact with the electron poor double bond *i.e.* the terminal one (Scheme 44, left cycle). Then, in both cases, insertion followed by hydrolysis of the corresponding allyl metal intermediate leads to the final compounds.



**Scheme 44.** Proposed mechanism for the Pd- or Pt-catalyzed hydroarylation of monosubstituted allenes with aryl boronic acids.

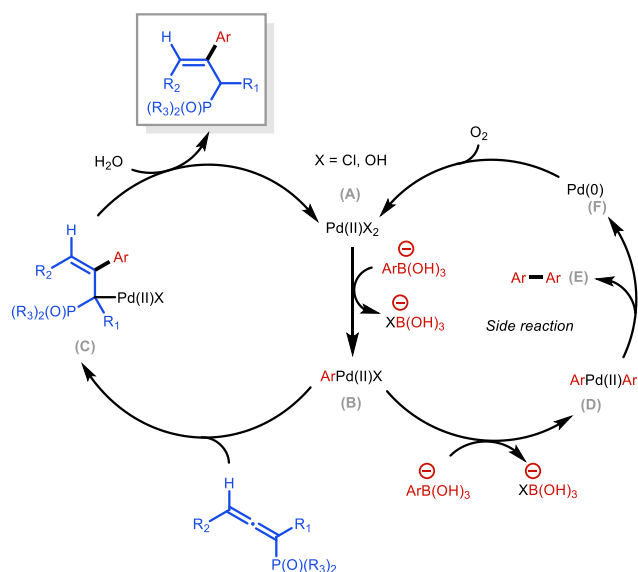
In 2016, Zhou and Zhu reported a ligand-free Pd(II)-catalyzed hydroarylation of mono, 1,1- and 1,3-disubstituted *P*-allenes with aryl boronic acids in the presence of sodium hydroxide as a base and oxygen as an oxidant (Scheme 45).<sup>[50]</sup>





**Scheme 45.** Palladium-catalyzed hydroarylation of monosubstituted, 1,1-disubstituted or 1,1,3-trisubstituted *P*-allenes with aryl boronic acids.

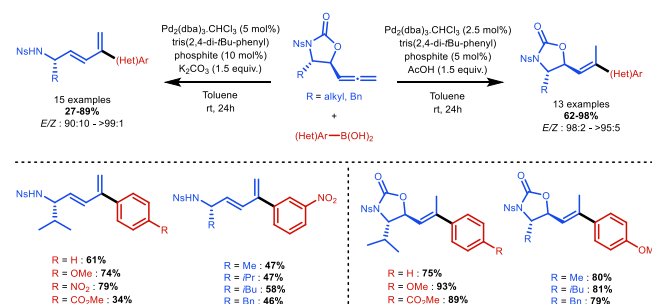
A transmetalation between the active palladium species (**A**) and the aryl boronate firstly affords the  $\text{ArPdX}$  intermediate (**B**) that undergoes allene insertion, thus leading to complex (**C**). Protodepalladation of the latter forms the hydroarylation product and regenerates (**A**). The  $\text{ArPdX}$  species (**B**) can also be involved in an undesired transmetalation step through intermediate (**D**) to give the homocoupling product (**E**) and inactive  $\text{Pd(0)}$  (**F**) that can be oxidized by oxygen in catalytic species  $\text{Pd(II)}$  (**A**) (Scheme 46).



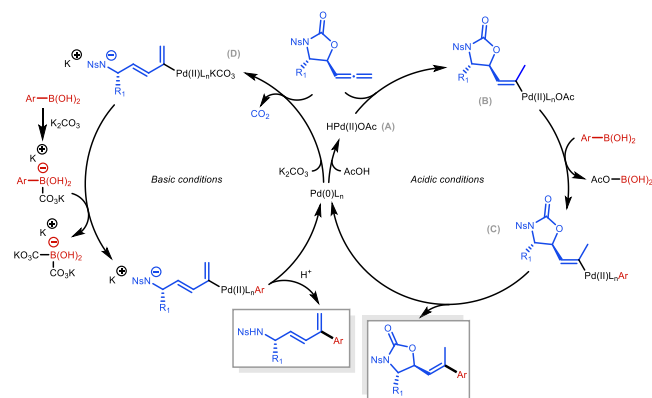
**Scheme 46.** Suggested mechanism for the Pd-catalyzed hydroarylation of monosubstituted, 1,1-disubstituted or 1,1,3-trisubstituted *P*-allenes with aryl boronic acids.

In 2019, Hyland reported a divergent Pd-catalyzed addition of (hetero)aryl boronic acids to the central carbon of enantioenriched 5-allenyloxazolidinones (Scheme 47).<sup>[51]</sup> Based on the palladium/tris(2,4-ditert-butylphenyl) phosphite system, two sets of conditions were established. In the presence of acetic acid vinyloxazolidinones are obtained, whereas in presence of potassium carbonate the reaction is leading to chiral 1,3-dienes through a decarboxylative step. Under acidic conditions, the first step is the formation of the palladium hydride species (**A**) which then affords the vinyl-Pd (**B**) through hydropalladation (Scheme 48, right cycle). Transmetalation between (**B**) and the boronic acid forms the intermediate (**C**), which gives the final product upon reductive elimination. Under basic conditions, the cycle starts with the formation of the 1,3-diene (**D**) through decarboxylative

oxidative addition of  $\text{Pd(0)}$  on the allene (Scheme 48, left cycle). Transmetalation, followed by reductive elimination affords the final compound and regenerates the active palladium catalyst.

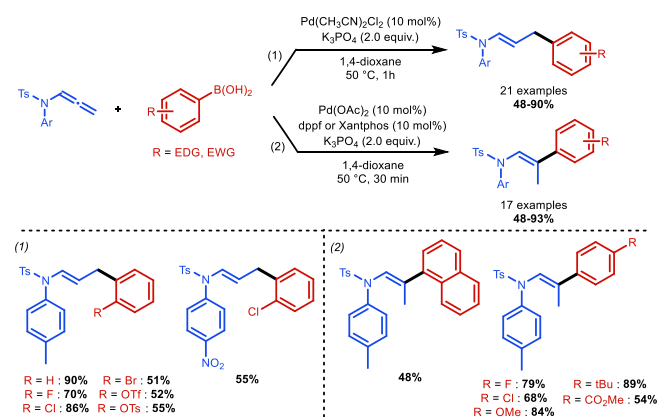


**Scheme 47.** Palladium-catalyzed hydroarylation of enantioenriched 5-allenyloxazolidinones with (hetero)aryl boronic acids.



**Scheme 48.** Plausible mechanism for the Pd-catalyzed hydroarylation of enantioenriched 5-allenyloxazolidinones with (hetero)aryl boronic acids.

In 2021, Liu and coworkers disclosed a palladium-catalyzed hydroarylation of monosubstituted *N*-tosyl allenamides (Scheme 49).<sup>[52]</sup> The use of acetonitrile as a ligand mainly led to the addition of the aryl moiety onto the terminal carbon of the allene (Scheme 49, eq. 1) whereas the use of the bulkier dppf or Xantphos ligand instead afforded the product resulting from the addition on the central carbon of the allene (Scheme 49, eq. 2). Numerous (hetero)aromatic boronic acids were successfully used in this reaction, leading to the corresponding vinylic or allylic hydroarylation products in good yields and relatively short reaction times.

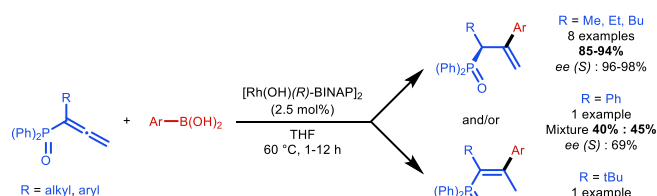


**Scheme 49.** Ligand-controlled palladium-catalyzed hydroarylation of monosubstituted *N*-tosyl allenamides with aryl boronic acid.



## 2.2. Rhodium

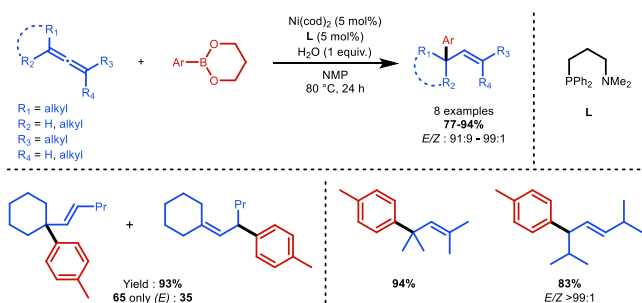
In 2006, the group of Hayashi reported the first catalytic asymmetric hydroarylation of allenes involving aryl boronic acids (Scheme 50).<sup>[53]</sup> Using 2.5 mol% of  $[\text{Rh}(\text{OH})(\text{R})\text{-BINAP}]_2$ , the reaction afforded the chiral allylic phosphine oxides from the corresponding diphenylphosphinyl allenes with high enantioselectivity. However, in the presence of bulky substituents (such as phenyl or *tert*-butyl groups) on the starting allene, the regioselectivity can be reversed to afford the achiral, internal alkene or a mixture of both. This side-product is the same as the one obtained through the palladium(II)-catalyzed hydroarylation of similar allenes reported by Zhou and Zhu in 2016.<sup>[50]</sup>



**Scheme 50.** Rhodium-catalyzed asymmetric hydroarylation of 1,1-disubstituted *P*-allenes with aryl boronic acids.

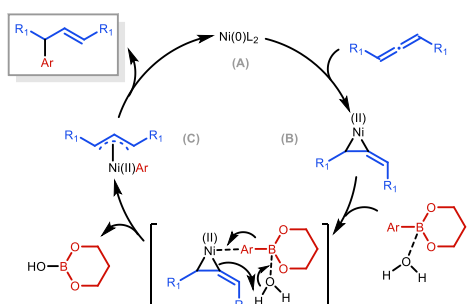
## 2.3. Nickel

In 2006, Shirakawa and coworkers reported a nickel-catalyzed hydroarylation of 1,3-di-, 1,3,3-tri and tetrasubstituted allenes (Scheme 51).<sup>[54]</sup> In contrast to hydroarylations using aryl boronic acids described above, the addition occurs on the terminal carbon of the allene in most cases, except when the terminal substituent is bulky (such as a cyclohexyl group) in which case a mixture of the products resulting from the addition on proximal and terminal carbons is obtained.



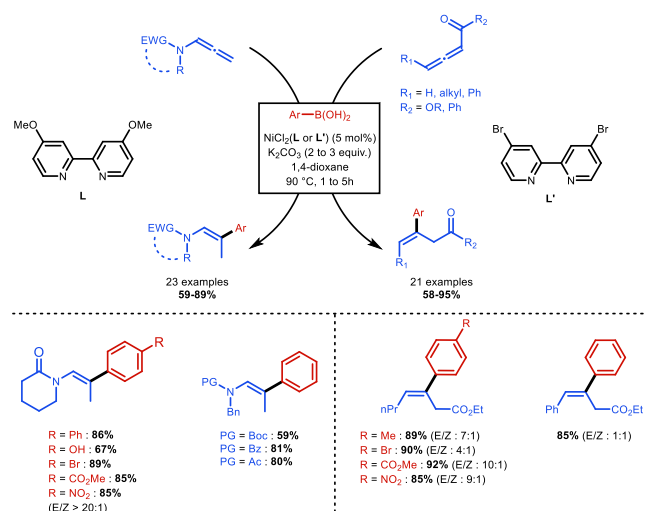
**Scheme 51.** Nickel-catalyzed hydroarylation of 1,3-di-, 1,3,3-tri and tetrasubstituted allenes with aryl boronic acids.

The addition of the Ni(0) species **(A)** on the allene (carbonickelation) firstly gives the Ni(II) nickelacyclopropane intermediate **(B)** (Scheme 52). The latter **(B)** then undergoes a concerted ring opening involving the aryl boronic ester and water, affording a transmetalated  $\pi$ -allylnickel complex **(C)** where the aryl moiety is linked to the metal. Finally, reductive elimination gives the hydroarylation product and regenerates the active species **(A)**.

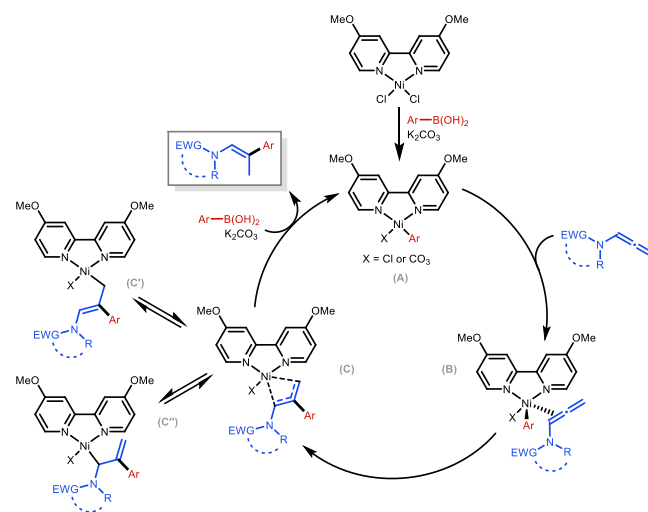


**Scheme 52.** Proposed mechanism for the Ni-catalyzed hydroarylation of 1,3-di-, 1,3,3-tri and tetrasubstituted allenes with aryl boronic acids.

More recently, the group of Bandini reported a nickel-catalyzed hydroarylation of allenamides<sup>[55,56]</sup> and allenates<sup>[57]</sup> performed in the presence of 4,4'-substituted 2,2'-bipyridine ligands (Scheme 53). Both cyclic and acyclic allenamides afforded trisubstituted (*E*)-enamides, resulting from the addition of a wide range of EWG- or EDG-substituted, aryl boronic partners onto the central carbon of the allene. When performed on allenates or allenyl ketones, the reaction afforded (*E*)- $\beta$ -aryl- $\beta,\gamma$ -unsaturated esters and ketones respectively with high regio- and stereoselectivity. The catalytic cycle starts with the formation of the active species **(A)** by transmetalation between the  $\text{NiCl}_2$ -2,2'-bipyridine precursor and the aryl boronic acid in the presence of potassium carbonate. Allene coordination followed by insertion of the Ni-Ar bond into the allene affords **(B)** and  $\pi$ -allylnickel **(C)** respectively. The latter finally undergoes protodemetalation to afford the hydroarylation product and regenerate the active species **(A)**.



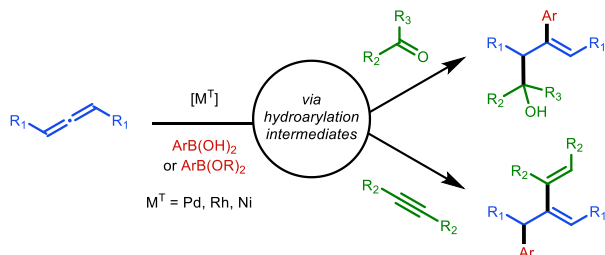
**Scheme 53.** Nickel-catalyzed hydroarylation of allenamides, allenyl ketones and allenates.



**Scheme 54.** Possible mechanism for the Ni-catalyzed hydroarylation of allenamides, allenyl ketones and allenates.

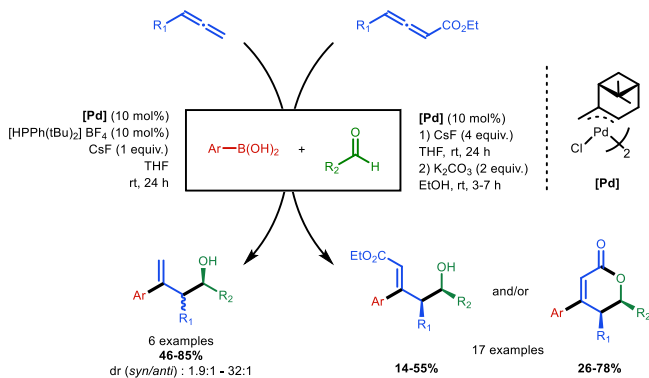
## 2.4. Three-component reactions

Some research teams have taken advantage of the reactivity of the synthetic intermediates formed during the transition metal-catalyzed hydroarylation reactions of allenes to develop three-component reactions (TCR) (Scheme 55).

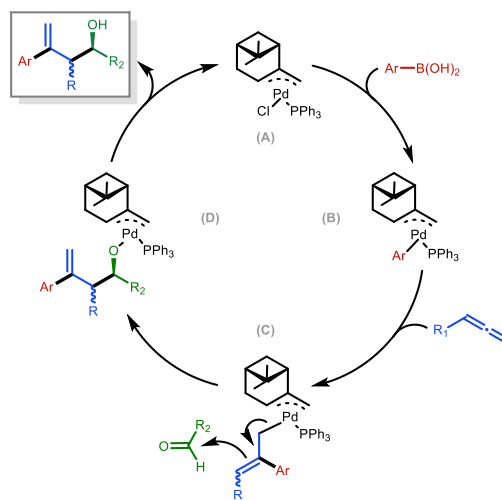


**Scheme 55.** Three-component reactions (TCR) involving hydroarylation intermediates.

Electrophiles as first sight,  $\pi$ -allylmetal intermediates are now well established as ambiphilic reagents. Different methods have been developed since the Tsuji-Trost reaction to take advantage of this dual reactivity<sup>[58]</sup>. Thus, several TCR involving an allene, a boronic acid and a carbonyl derivative were designed in the presence of a transition metal, leading to more substituted and/or complex scaffolds. Thus, Malinakova reported in 2004 the synthesis of homoallylic alcohols through this approach in the presence of a  $\beta$ -pinene bis- $\pi$ -allylpalladium(II) complex and a phosphonium salt (Scheme 54).<sup>[59]</sup> Aliphatic and (hetero)aromatic aldehydes were successfully engaged in this reaction, leading to a mixture of the *syn* (major) and *anti* (minor) diastereoisomers. Based on the same palladium complex, but without the auxiliary ligand, they also developed the first difunctionalization of allenylesters, leading to  $\alpha,\beta$ -unsaturated  $\delta$ -lactones and  $\alpha,\beta$ -unsaturated  $\delta$ -hydroxyesters.<sup>[60]</sup> This regio- and diastereoselective method is tolerant to various substituents, as well as potentially reactive functional groups. The reaction starts with a transmetalation between the active Pd species (A) and the aryl boronic acid which affords the aryl-Pd intermediate (B) (Scheme 57). The latter undergoes migratory insertion with the allene, thus affording (C) which can then react with the aldehyde via nucleophilic addition to give (D). A protodemetalation step finally affords the resulting homoallylic alcohol and regenerates the active catalyst (A).

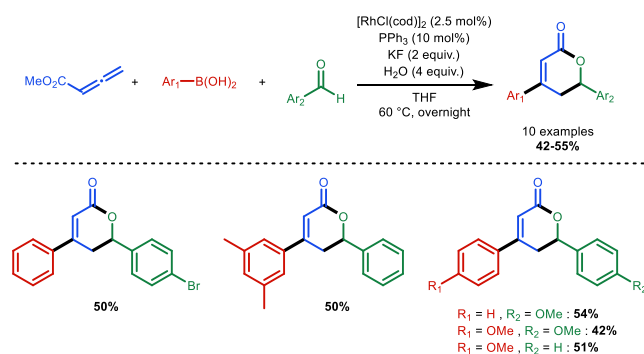


**Scheme 56.** Palladium-catalyzed TCR involving allenes, aryl boronic acids and aldehydes.

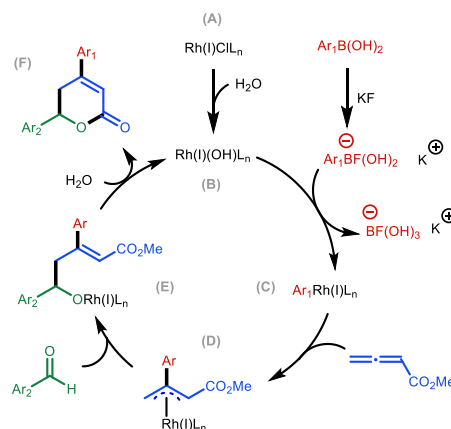


**Scheme 57.** Suggested mechanism for the Pd-catalyzed TCR involving allenes, aryl boronic acids and aldehydes.

A related TCR involving an aryl boronic acid, an allenolate and an aromatic aldehyde, and affording the corresponding  $\alpha,\beta$ -unsaturated  $\delta$ -lactones after cyclization, was reported by Ma and Jia through rhodium catalysis in the presence of triphenylphosphine (Scheme 58).<sup>[61]</sup> The active catalytic species (B), probably formed by the reaction of the rhodium precursor (A) with water, engages in a transmetalation step with the aryl boronate to give the aryl-Rh intermediate (C) (Scheme 56). The latter is then involved in the carboration of the allenolate to afford the  $\pi$ -allylrhodium (D) that can undergo nucleophilic addition to the aldehyde to give (E). Finally, hydrolysis of (E) provides the  $\alpha,\beta$ -unsaturated  $\delta$ -lactone (F) and regenerates the catalytically active species (B).

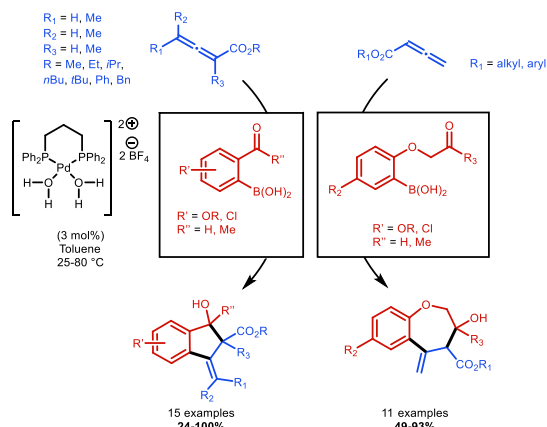


**Scheme 58.** Rhodium-catalyzed TCR involving allenes, aryl boronic acids and aldehydes.

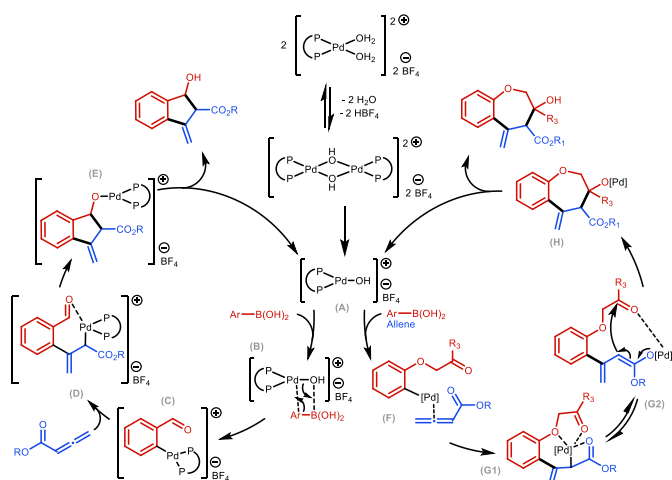


**Scheme 59.** Proposed mechanism for the Ni-catalyzed TCR involving allenenes, aryl boronic acids and aldehydes.

In 2009, Lu performed a [3+2] annulation of 2-formylarylboronic acids with allenates catalyzed by a cationic palladium-complex leading to the formation of racemic indenole derivatives (Scheme 60, left).<sup>[62]</sup> When using a chiral diphosphine ligand, the resulting indenole derivatives were obtained with both good diastereo- and enantioselectivity. The authors also used this catalyst for the [5+2] annulation of 2-acylmethoxyarylboronic acids with allenates to synthesize 1-benzoxepine derivatives (Scheme 60, right).<sup>[63]</sup> These reactions firstly involve the formation of the active palladium hydroxo catalyst (**A**) from its dimeric form (Scheme 61). Then, transmetalation followed by allene coordination affords the allylpalladium species (**D**) and (**G1/G2**) during the formation of indenoles and benzoxepines, respectively. These intermediates can then undergo intramolecular nucleophilic addition on the carbonyl moiety to afford the corresponding 5- or 7-membered cycles (**E**) and (**H**) that can finally deliver the final indenoles and benzoxepines after hydrolysis.



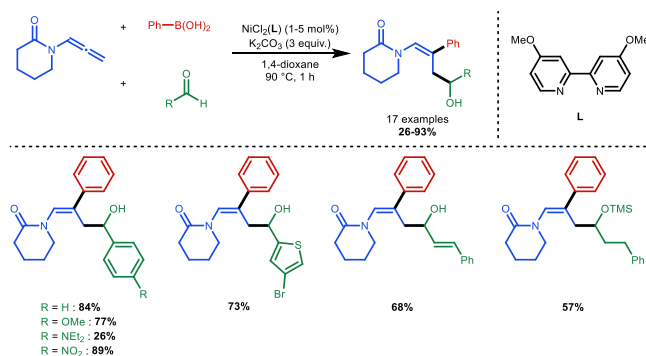
**Scheme 60.** Palladium-catalyzed TCR involving allenenes and 2-formyl or 2-acylmethoxyarylboronic aryl boronic acids.



**Scheme 61.** Suggested mechanism of the Pd-catalyzed TCR involving allenenes and 2-formyl or 2-acylmethoxyarylboronic aryl boronic acids.

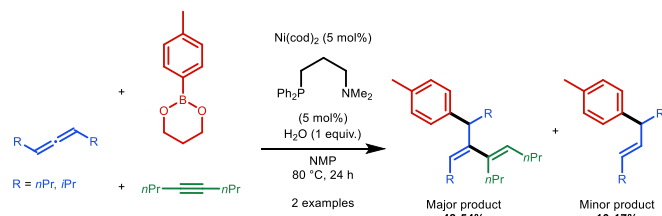
Bandini also took advantage of the nucleophilicity of the transient allylmatal intermediate to design a one-pot nickel-catalyzed reaction of *N*-allenyl-2-piperidinone, phenyl boronic acid, and

aldehydes in the presence of 4,4'-dimethoxy-2,2'-bipyridine, affording homoallylic alcohols in moderate to good yields (Scheme 62).<sup>[55,56]</sup>

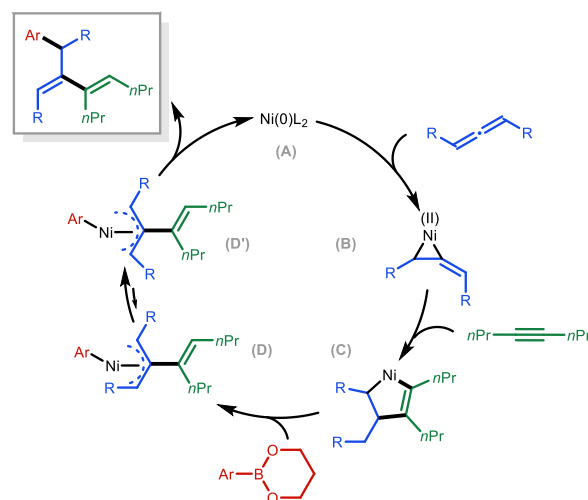


**Scheme 62.** Nickel-catalyzed TCR involving *N*-allenyl-2-piperidinone, phenyl boronic acid and aldehydes.

Shirakawa reported in 2006 the ability of the *in situ* formed nickelacyclopentene to react with an alkyne.<sup>[54]</sup> This nickel-catalyzed one-pot TCR of 1,3-disubstituted allenenes, 2-(*p*-tolyl)-1,3,2-dioxaborinane, and oct-4-yne affords original arylated 1,3-dienes (Scheme 63). The nickelacyclopentene (**B**) resulting from the oxidative cyclization of the allene to nickel (0) species (**A**) can undergo insertion of oct-4-yne to afford the nickelacyclopentene intermediate (**C**) (Scheme 64). The latter then reacts with the aryl-1,3,2-dioxaborinane to afford the *anti*- $\pi$ -allylnickel complex (**D**) which isomerizes to the *syn*- $\pi$ -allylnickel intermediate (**D'**). A reductive elimination finally gives the corresponding 1,3-diene and regenerates the active Ni(0) catalyst.



**Scheme 63.** Nickel-catalyzed TCR involving 1,3-disubstituted allenenes, 2-(*p*-tolyl)-1,3,2-dioxaborinane, and oct-4-yne.



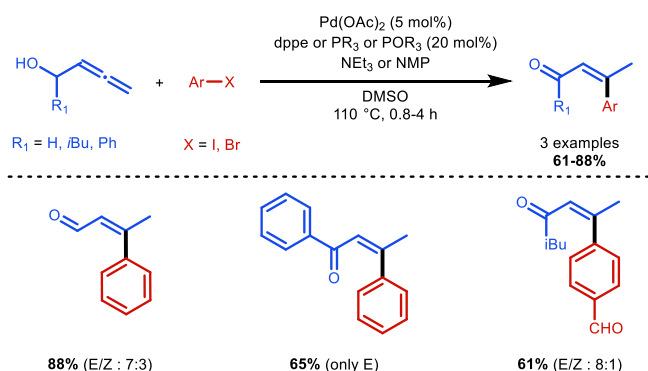
**Scheme 64.** Proposed mechanism for the Ni-catalyzed TCR involving 1,3-disubstituted allenenes, 2-(*p*-tolyl)-1,3,2-dioxaborinane, and oct-4-yne.

### 3. Hydroarylation with other aryl sources

In addition to the arenes and aromatic boronic derivatives, other aryl sources also used in transition metal-catalyzed hydroarylation reactions of allenes will be described in this part: aryl halides,  $\alpha$ -acid isocyanoacetamides and 1,2,3,4-tetrahydronaphthalen-1-ol derivatives.

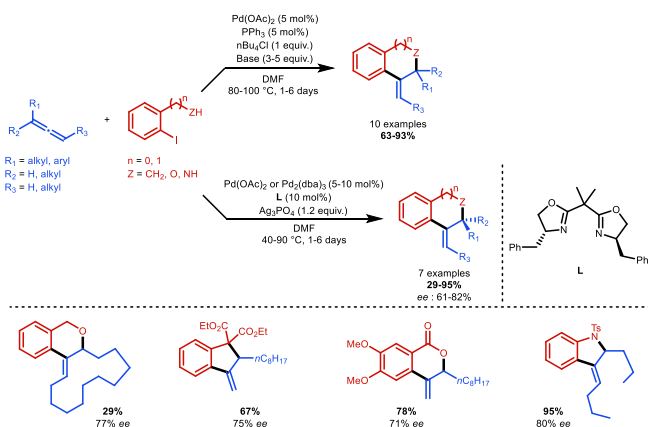
#### 3.1. Palladium

In 1985, Tsuji and coworkers reported a palladium-catalyzed hydroarylation of monosubstituted 1,2-dien-4-ols with aryl iodides or bromides in the presence of a phosphine and a base (Scheme 65).<sup>[64]</sup> This method afforded some  $\beta$ -arylated- $\alpha,\beta$ -unsaturated aldehydes and ketones in good to excellent yields. The lack of stereoselectivity was a major drawback of this method, with a mixture of (*E*) and (*Z*) isomers often being obtained.



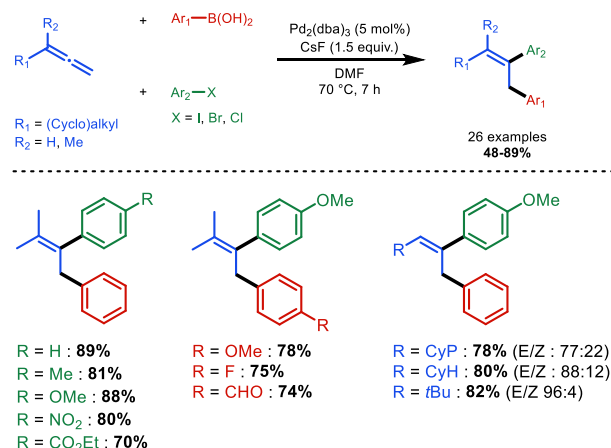
**Scheme 65.** Palladium-catalyzed hydroarylation of monosubstituted 1,2-dien-4-ols with aryl iodides or bromides.

Larock *et al.* described in 1991 a palladium-catalyzed tandem hydroarylation-cyclisation reaction using mono-, 1,3-di and 1,1,3-trisubstituted allenes and aryl iodides.<sup>[65]</sup> Different C-, O- and N-containing 5- or 6-membered ring scaffolds such as 1,2,3,4-tetrahydronaphthalene, indoline or isochromane, were obtained in good to excellent yields (Scheme 66, top). The authors then described new conditions to perform an asymmetric version of this reaction using a bisoxazoline ligand (Scheme 66, bottom).<sup>[66]</sup>

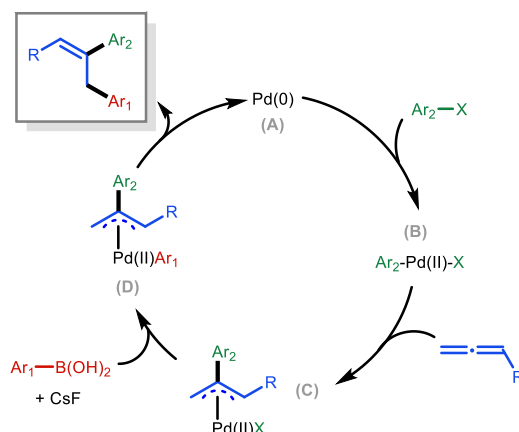


**Scheme 66.** Palladium-catalyzed hydroarylation-cyclisation reactions using mono-, 1,3-di and 1,1,3-trisubstituted allenes and aryl iodides.

In 2002, the team of Cheng reported a palladium-catalyzed three component reaction involving allenes, aryl halides and aryl boronic acids, leading to the addition of two aryl moieties on the mono- or 1,1-disubstituted allene (Scheme 67).<sup>[67]</sup> Oxidative addition of the aryl halide to the palladium (0) species (**A**) firstly affords the palladium (II) species (**B**) which can undergo allene insertion to form the  $\pi$ -allylpalladium intermediate (**C**) (Scheme 68). The latter is then involved in transmetalation with the aryl boronic acid in the presence of  $\text{CsF}$ , thus affording the complex (**D**) from which the final compound is formed, and the active species (**A**) is regenerated upon reductive elimination.



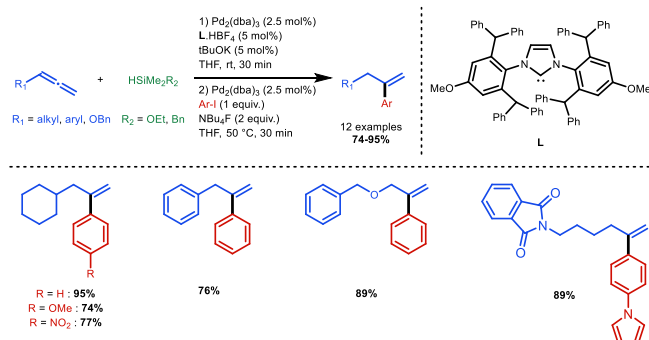
**Scheme 67.** Palladium-catalyzed TCR involving allenes, aryl halides and aryl boronic acids.



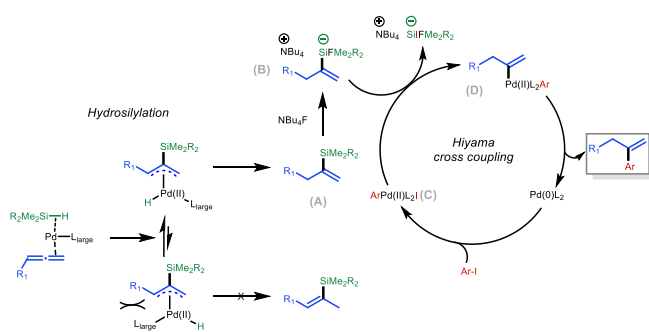
**Scheme 68.** Plausible mechanism for palladium-catalyzed TCR involving allenes, aryl halides and aryl boronic acids.

Montgomery *et al.* recently reported a one-pot monosubstituted allene hydroarylation method based on a palladium-catalyzed hydrosilylation combined with a Hiyama cross-coupling (Scheme 69).<sup>[68]</sup> Regarding the mechanism, the reaction starts with the *N*-heterocycle carbene (NHC) ligand-controlled regioselective palladium-catalyzed hydrosilylation of the allene (Scheme 70). Using bulky ligands such as  $\text{IPr}^{\text{Me}}$  or  $\text{IPr}^{\text{OMe}}$  (**L**) introduces steric repulsion between the organosilane and ligand, thus favoring the formation of the terminal olefinic organosilane intermediate (**A**).

The latter is activated by a fluoride anion *via* TBAF, leading to the anionic compound (**B**). Meanwhile, the aryl iodide undergoes an oxidative addition onto the Pd(0) active species leading to the Pd(II) species (**C**). Then, a transmetalation between (**B**) and (**C**) yields the vinyl palladium complex (**D**). Finally, a reductive elimination affords the hydroarylation product and regenerates the active palladium(0) catalyst.



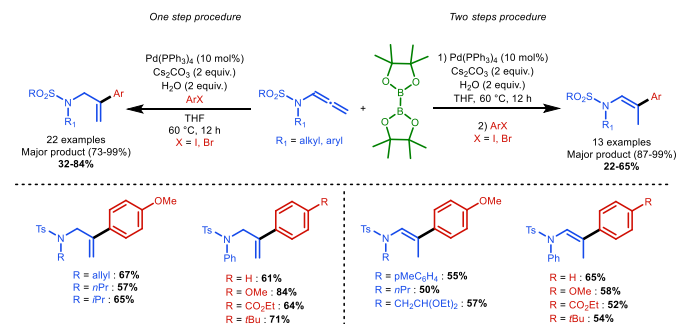
**Scheme 69.** Palladium-catalyzed hydroarylation of monosubstituted allenes through hydrosilylation/Hiyama cross coupling.



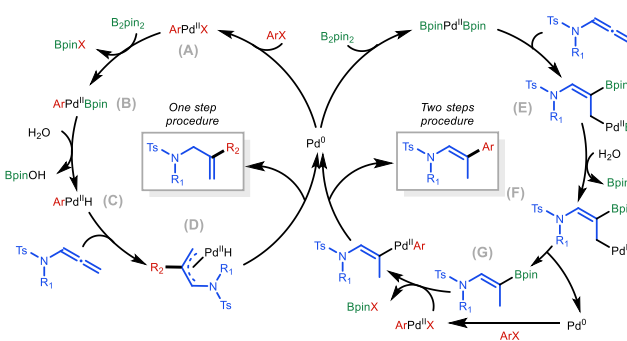
**Scheme 70.** Suggested mechanism for the Pd-catalyzed hydroarylation of monosubstituted allenes through hydrosilylation/Hiyama cross coupling.

Hui Liu reported very recently two complementary hydroarylation methods based on a Pd(0) catalyst and bis(pinacolato)diboron ( $B_2pin_2$ ) (Scheme 71).<sup>[69]</sup> In both systems, the aryl is added to the central carbon of the allene but, depending on the method of addition, two regioisomers can be obtained. When all reagents are added simultaneously, the addition occurs across the internal double bond, thus forming the terminal alkene, whereas when the reagents are added stepwise, this leads to the addition across the terminal double bond, resulting in the internal alkene. The one step procedure (Scheme 72, left cycle) starts with the formation of the intermediate (**A**) resulting from the oxidative addition of the palladium (0) catalyst into the Ar-X bond. Subsequently, transmetalation between this complex and  $B_2pin_2$  yields (**B**) which then reacts with water to form the palladium (II) hydride species (**C**) and thus releases HOBpin. A hydropalladation step then leads to the formation of the  $\pi$ -allylpalladium intermediate (**D**) that gives the final, terminal olefin *via* reductive elimination. The two step procedure (Scheme 72, right cycle) first involves an oxidative addition forming  $Pd(Bpin)_2$ . Borylation-palladation of the starting allenamide then yields the intermediate (**E**) and after reaction with water, the complex (**F**) which undergoes a reductive

elimination releasing the palladium(0) catalyst and yielding the vinyl boronic ester (**G**). The latter is finally involved in a Suzuki-Miyaura coupling, thereby affording the internal alkene.



**Scheme 71.** Palladium-catalyzed one- or two-step hydroarylation of monosubstituted allenamides with aryl iodides or bromides.

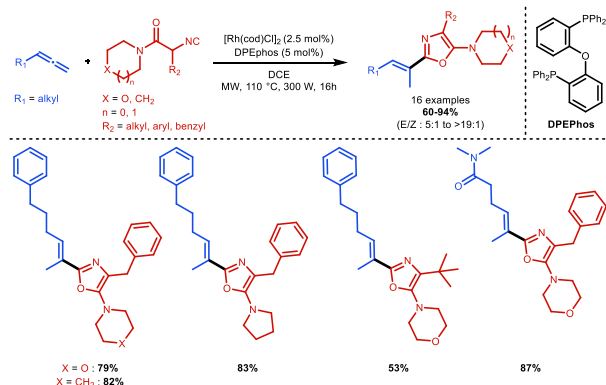


**Scheme 72.** Plausible mechanism for Pd-catalyzed one- or two-steps hydroarylation of monosubstituted allenamides with aryl iodides or bromides.

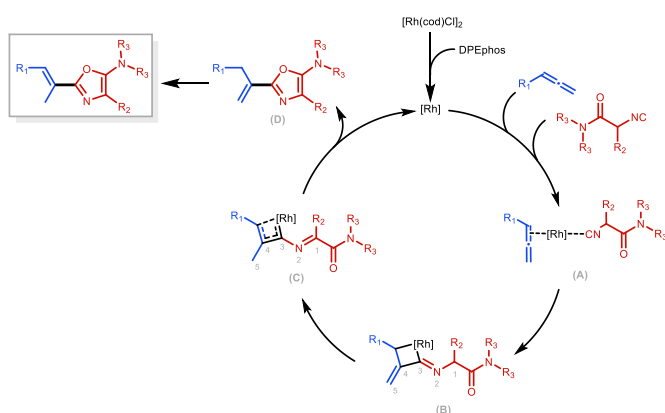
### 3.2. Rhodium

Balalaie and Breit reported an original rhodium-catalyzed hydroarylation of terminal allenes leading to vinyl oxazoles, which are formed *in situ* through an ene reaction starting from enolisable isocyanoacetamides (Scheme 73).<sup>[70]</sup> This reaction is performed under microwave irradiation in the presence of the dimer  $[Rh(cod)Cl]_2$  as the catalyst and DPEphos as the ligand. Sixteen variously 2,4,5-trisubstituted oxazoles were obtained in medium to high yields following these conditions. Based on control experiments and DFT calculations, the authors suggest a 6-step mechanism, the first being the generation of the catalytically active Rh(I) species by ligand exchange from the rhodium precursor  $[Rh(cod)Cl]_2$  (Scheme 74). This species can then coordinate to both the allene and the isocyanoacetamide, leading to the intermediate (**A**) which is subsequently involved in a rhodocyclobutanation followed by a 1,5-hydrogen shift, affording the complexes (**B**) and (**C**), respectively. A reductive elimination, in which the oxazole ring is formed leads to the final compound after isomerization of the double bond of the intermediate (**D**).





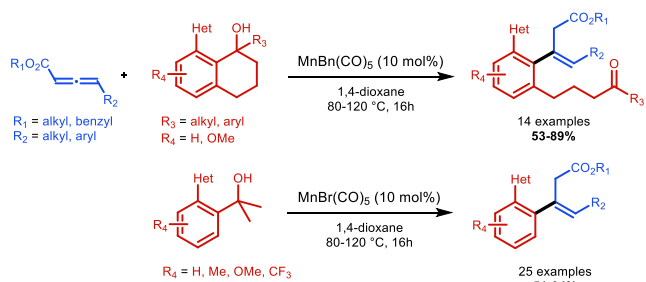
**Scheme 73.** Rhodium-catalyzed hydroarylation of terminal allenes using enolisable isocyanoacetamides.



**Scheme 74.** Plausible mechanism.

### 3.3. Manganese

Ackermann et al. recently disclosed an original hydroarylation of 1,3-disubstituted allenoates through C-C activation based on the use of either pentacarbonylbenzylmanganese  $\text{MnBn}(\text{CO})_5$  or the more common  $\text{MnBr}(\text{CO})_5$  as Mn(I) catalysts (Scheme 75).<sup>[71]</sup> The addition selectively occurs on the central atom of the starting allenoate, leading to the formation of the corresponding vinyl polysubstituted arene in medium to high yields. The mechanism involves breaking of the C-C bond adjacent to the *N*-heterocycle substituent and thus the formation of the corresponding ketone. This ketone is either conserved in the final product, or released as a side-product, depending on the initial aryl source (cyclic or acyclic).



**Scheme 75.** Manganese-catalyzed hydroarylation of 1,3-disubstituted allenoates.

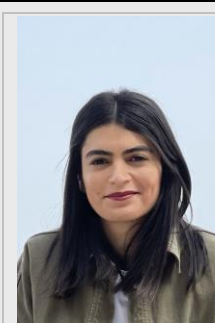
## 4. Conclusion

The hydroarylation of allenes, as well as their hydrofunctionalization, has been the subject of increasing interest in the last decades. First to be performed and broadly studied since, the hydroarylation reaction allowed allenes to be considered as essential and valuable building blocks for the selective synthesis of high-value vinylic or allylic structures via the creation of C-C bonds. In this context, arenes represent the most used type of aryl sources. Proceeding through the direct addition of an aryl group via a  $\text{C}_{\text{Ar}}\text{-H}$  bond functionalization, they are accessible and atom-economic partners. However, they are often limited in terms of reactivity and regioselectivity by their substituents in terms of electron richness and steric hindrance or by the need of a directing group. Organoboron derivatives constitute the other main aryl sources that can be used as alternative coupling partners for the hydroarylation of allenes. These readily available derivatives are usually more reactive, allowing the extension to less nucleophilic aromatic rings, and allow the *ipso* addition without regioselectivity issues. However, this approach requires the incorporation of a boron moiety, and is thus less suitable for late-stage functionalization. In addition other aryl sources, essentially aryl iodides, have been timidly employed in transition metal-catalyzed hydroarylation of allenes and represent a field of investigation that has been less developed until now. Many transition metal-based catalysts have been employed to perform the intermolecular hydroarylation of allenes, mainly gold and palladium using respectively arenes and boronic derivatives as aryl sources. Numerous mechanistic studies, both experimental and theoretical, have been undertaken, very often leading the authors to propose catalytic cycles to describe the hydroarylation of allenes. This rationalization, coupled with the ongoing search for efficient methods using abundant and inexpensive transition metal catalysts, should quickly lead to the consideration of allene hydroarylation as a competitive, sustainable, and central route for obtaining high-value vinyl and allylic fragments.

**Lucas Pagès** completed his M.Sc. in chemistry at the Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM) in 2019 after obtaining a Pharm.D. degree from the Faculty of Pharmacy of the University of Montpellier (2012-2017). He is currently pursuing his Ph.D. at the ICGM with Pr. Florian Monnier and Dr. Marc Taillefer. His research focuses on copper-catalyzed or TFA-mediated hydrofunctionalization of allenes.



**Racha Abed Ali Abdine** obtained a BSc degree in chemistry in 2014 from the Lebanese University in Beirut-Lebanon, then she moved to Paris where she obtained a master degree in molecular chemistry from the Sorbonne University in 2016. She received her PhD from the ENSC-Montpellier in 2019 under the supervision of Prof. Florian Monnier and Dr Marc Taillefer, where her research work focused on the homogeneous



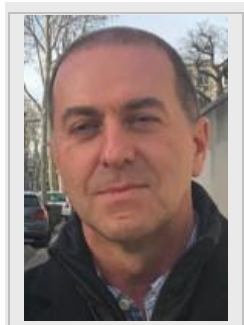


catalysis with transition metals. In 2020, she joined Syncat-H group in Strasbourg as a postdoctoral researcher under the supervision of Dr Joanna Wencel-Delord and Prof. Françoise Colobert. She worked on the design of diphosphine ligands with two atropisomeric axis and their applications in asymmetric catalysis. Currently, she is a temporary research and teaching attaché (ATER) at ECPM in Syncat-H group under the supervision of Dr Sabine Choppin. Her research interests concern the atroposelective C-N coupling.

**Florian Monnier** is a full professor of chemistry at Ecole Nationale Supérieure de Chimie de Montpellier where he has been faculty since 2005 (Assistant Professor in 2005, Associate Professor in 2012, then promoted Full Professor in 2016). He completed his M.Sc. and Ph.D. in Chemistry in 2000 and 2003, respectively, at the University of Rennes under the direction of Professor Pierre H. Dixneuf and Dr. Sylvie Dérien. He studied and developed several original C–C bond formation methodologies involving alkynes under ruthenium catalysis. In 2003 he moved to a postdoctoral position with Pr Professor E. Peter Kündig at University of Geneva, where his studies centered on the development of ruthenium catalysts. In 2004, he arrived in Montpellier for a postdoctoral position with Professor Jean Martinez and Servier Laboratories where he worked on medicinal chemistry. Then he entered the group of Dr. Marc Taillefer in 2005 as an Assistant Professor. His actual research interests cover several areas of catalysis including arylation of nucleophiles, direct amination reactions, and hydrofunctionalization of unsaturated compounds such as alkenes, alkynes, and allenes. In 2013 he was awarded the young research award from the region Languedoc-Roussillon. In 2015 he has been the recipient of Institut Universitaire de France (IUF) award as a junior member.



**Marc Taillefer** studied chemistry and earned his Ph.D. from the University Paul Sabatier, Toulouse, France, under the supervision of Dr Igor Tchatchenko and Dr Jean-Jacques Brunet in 1989. From 1990 to 1994, he was a postdoc at the Technische Universität München, Germany, with Pr Wolfgang A. Herrmann. He became a CNRS researcher at the Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM) in 1992 and CNRS Research Director in 2004. His research focuses on the discovery of breakthrough methodologies in the field of organic synthesis and homogeneous catalysis (C–N, C–O, and C–C bond formation via copper-, iron- and manganese- catalyzed arylation of nucleophiles, transition metal free mediated coupling reaction, and functionalization of unsaturated compounds), as well as phosphorus chemistry (synthesis, reactivity, and applications of phosphonium ylides). Among many other commitments, Marc Taillefer was President of the French Chemical Society's Organic Chemistry Division from 2012 to 2015 and from 2018 to 2021, he was the President of the French Chemical Society (SCF). He was awarded the Grand Prix Emile Jungfleisch de l'Académie des Sciences of the French Academy of Sciences in 2017, and the European Sustainable Chemistry Award of the EuChemS in 2012, among many other honors.



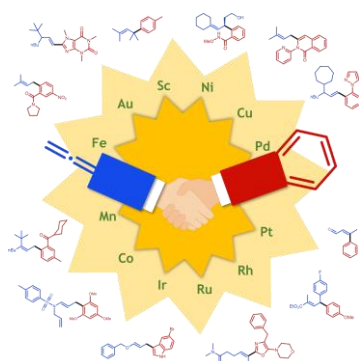
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**Entry for the Table of Contents**

Hydroarylation of allenes leads to the selective formation of highly valuable allylic or vinylic structures through C-C bond formation. In this frame, transition metal-based catalysts have been broadly employed. This review highlights this topic, discussing advantages, limitations and mechanistic aspects of the related methods over the four last decades.