Transition-Metal-Catalyzed Alkenyl sp² C–H Activation: A Short Account

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Abstract
Alkenes are ubiquitous in Nature and their functionalization continues to attract attention from the scientific community. On the other hand, activation of alkenyl sp² C–H bonds is challenging due to their chemical properties. In this short account, we elucidate, discuss and describe the utilization of transition-metal catalysts in alkenylation and provide useful strategies to synthesize organic building blocks in an efficient and sustainable manner.

1 Introduction
Alkenes and their derivatives feature widely in many natural products and advanced materials. Accordingly, significant efforts have been directed towards the development of new synthetic methods to access this class of compounds. Among the many approaches reported, transition-metal-catalyzed cross-coupling reactions are the most commonly employed since they can be carried out on large and industrial scale. However, the need to use prefunctionalyzed environmentally unfriendly organohalides and/or organometallic reagents has encouraged researchers to search for cheaper and greener approaches. We envisaged that a straightforward cross-coupling among cheap alkenes feedstocks would provide one of the most straightforward and practical designs to access this class of important compounds. To be successful, we would need to preferentially C–H functionalize one of the alkenes and effect cross-coupling with the second alkene without them undergoing homo-coupling reactions. We envisaged that by tuning the electronic and steric properties of the olefins, we might be able to preferentially activate one of the two alkenes to effect the desired cross-coupling without the formation of homo-coupling products. If successful, this design might be applicable for the stereoselective synthesis of dienes. Further, an intramolecular version will provide access to cyclic alkenes not available via Diels–Alder or olefin metathesis approaches. However, when we initiated this research program in the early 2000s, very little work had been done in the area of alkenyl sp² C–H bond functionalization. Furthermore, the high activation energy required to activate the alkenyl sp² C–H bond in a highly selective manner poses tremendous challenges for organic chemists. Despite these challenges and considering the many benefits of these methods, we initiated a research program on alkenyl sp² C–H bond functionalization by first investigating the cross-coupling between two distinct olefins.

In early 2001, dimerization of camphene catalyzed by palladium under aerobic oxidative conditions was reported by Gusevskaya et al. in the presence of Pd(OAc)₂/benzoquinone (BQ)/O₂ and Pd(OAc)₂/LiNO₃/O₂ (Scheme 1). They demonstrated that the reaction progressed via formation of a σ-vinyl palladium hydride intermediate.

Scheme 1: Palladium-catalyzed dimerization of camphene
2 Breakthrough

Straightforward cross-coupling reactions using simple alkenes to form dienes had not been explored by virtue of the difficulties in activating the alkenyl C–H bond. The first ever cross-coupling reaction among acrylates and simple olefins by using a catalytic amount of a palladium catalyst was reported by our group (Scheme 3).7

Our initial investigation focused on the coupling of α-alkyl styrenes and acrylates (Heck-type coupling). We envisaged that the α-alkyl substituent on the styrene may preferentially activate the C–H functionalization of the alkene over the acrylate. Furthermore, the steric effect of this alkyl substituent may prevent homo-coupling of the styrene. Additionally, the acrylate may promote cross-coupling. Amidst these simple hypotheses, we carried out the cross-coupling of α-alkyl styrenes with acrylates in the presence of a palladium catalyst. To our delight, the desired cross-coupling products were obtained in moderate yields. Despite this success, this approach had limited scope and applications. (1) A high catalytic loading of the palladium catalyst (20 mol%) was necessary to obtain the products in moderate yields, (2) alkyl-substituted styrenes were necessary as reducing the alkyl substituent resulted in messy reactions, (3) replacing the aryl substituent with an aliphatic substituent resulted in a low yield of the product, and (4) the E/E and E/Z selectivities of the products were low to moderate. In order for this approach to be useful in organic synthesis, we would need to solve some of these problems, if not all.

Later, we modified our previous procedure and developed a coupling reaction among indenes and various electron-deficient alkenes by employing Pd(OAc)$_2$ (10 mol%) as the catalyst and oxygen as the oxidant in AcOH (Scheme 4).8 Various indene derivatives were employed to afford good to moderate yields of the products.
In 2010, an efficient approach to synthesize functionalized 1,3-buta dienes was reported by Yu and co-workers via cross-coupling reactions among terminal alkenes and α-oxoketene dithioacetal s in the presence of Pd(OAc)$_2$ as the catalyst.

In 2012, Liu et al. developed a double C–H bond activation method to access conjugated dienes by straightforward olefination of unactivated alkenes with electron-rich alkenes in the presence of a palladium catalyst (Scheme 5). They even achieved the olefination of styrenes without 2-substituents unlike in the previously reported method. Although they developed an efficient design, it had the disadvantage of overloading of the oxidant (2.5 equiv of AgOAc) in order to achieve the transformation.

Although acrylates are utilized as efficient coupling partners in forming 1,3-diketones, because of the high potential for polymerization, unsaturated ketones such as methyl vinyl ketone are rarely employed in cross-coupling reactions. Later, in 2013, our group developed a general and efficient protocol for the synthesis of conjugated dienyl ketones catalyzed by Pd(OAc)$_2$, involving a coupling reaction among vinyl ketones and simple alkenes (Scheme 6). We showed the importance of this method by synthesizing vitamin A1 and bornelone.

Following this, our group developed ruthenium- and rhodium-catalyzed directing-group-assisted cross-coupling among acrylamides and a broad range of alkenes possessing various functional groups (Scheme 7). In a mixed solvent system of dioxane/water/acetic acid (v/v/v = 8/4/1) in the presence of RuCl$_2$(p-cymene)$_2$ as the catalyst, KPF$_6$ as the additive and Cu(OAc)$_2$·H$_2$O as the oxidant, 1,3-buta diene derivatives were obtained in up to 91% yield and 99/1 (Z/E) selectivity. Similarly, we employed RhCp*Cl$_2$ as the catalyst and Cu(OAc)$_2$ as the oxidant in acetone to prepare substituted dienamides in up to 91% yield and with good to moderate Z/E selectivity. To understand the reaction mechanism, we carried out competition and isotope labelling experiments. Based on the results, we proposed that the reaction is supposedly triggered by cyclometalation of the acrylamide by amide-directed C–H bond activation. Next, the alkene coordinates to the metal center which is followed by the formation of a seven-membered rhodacycle or ruthenacycle species by insertion of the carbon–carbon double bond. Finally, β-elimination results in the formation of the desired dienamide with (Z,E)-configuration. The developed method provides an excellent route to synthesize (Z,E)-dienamides in high yields and with moderate to excellent stereoselectivities.

In organic synthesis functional conjugated muconate subunits are very useful synthons. This class of compounds can be synthesized by a straightforward and atom-economical cross-coupling reaction between two distinct acrylates. The generation of conjugated muconated derivatives with distinctive functional groups from commercially available acrylates through C–H functionalization by straightforward cross-coupling is difficult and challenging. From previous literature, it is evident that the ester group coordinates poorly with the metal center; the most challenging task is to employ the ester as the directing group for the alkenylation of acrylates via chelation assistance. In our previous report, we observed that substitution at the α-position of the alkene is an essential criterium to carry out the alkenyl C(sp$^3$)–H direct functionalization. Later, in 2015, we developed a unique cross-coupling reaction of two distinct acrylates in a highly stereo and chemoselective manner by employing [RuCl$_2$(p-cymene)$_2$] as the catalyst.
Various muconate derivatives with distinct functional groups can be easily synthesized via activation of the vinyl C–H bond. [RuCl₂(μ-p-cymene)]₂ (5 mol%) catalyzed the cross-coupling reaction of n-butyl methacrylate and n-butylnyl acrylate along with AgSbF₆ (20 mol%), and Cu(OAc)₂·H₂O in 1,2-DCE at 135 °C for 24 hours to provide the desired cross-coupled product in 48% isolated yield with a 92/8 Z/E ratio. After further optimization studies, we found that 1,4-dioxane was the most suitable solvent for this transformation, affording the product in 67% yield (Scheme 9). In this report, both aryl- and alkyl-substituted acrylates were utilized to obtain the cross-coupled muconate derivatives in good to excellent yields and with good chemoselectivity and reactivity of the acrylates were influenced by the substituents at the α-position. Through this method multisubstituted (Z,E)-1,3-diene motifs can be synthesized efficiently.

Our continued interest in alkene sp² C–H functionalizations led us to develop a novel and efficient method for the synthesis of 1,4-diene skeletons. In the presence of a transition-metal catalyst the alkene moiety can react with an alkylic source to form allylated alkene products. We chose allyl acetates as the electrophiles for this transformation. In presence of a rhodium catalyst, electron-deficient alkenes undergo olefin allylation with allyl acetates to provide the desired products in good to excellent yields (Scheme 10). A wide variety of acrylamides as well as allyl acetates with distinct functional groups were well tolerated under these catalytic conditions. The alkene substrates were allylated in a simple and straightforward manner, with the aid of directing groups having weak-coordinating assistance, to provide 1,4-diienes that are of high synthetic value.
Alkynes can be transformed into a variety of functional groups and can be merged into the structural backbone of various organic molecules; in synthetic chemistry alkynes are also one of the most versatile functionalities.\textsuperscript{19} The value of alkynes is further highlighted due to their involvement in click chemistry.\textsuperscript{20} In organic synthesis, both non-conjugated and conjugated alkynes are well exploited.\textsuperscript{21} Due to their easy synthetic transformations and useful functionality, 1,3-enynes comprise a class of extensive subunits found widely in pharmaceuticals and natural products of biological interest.\textsuperscript{22}

In 2014, Glorius and co-workers demonstrated pioneering work on the synthesis of enynes via a C–H activation protocol. They reported highly selective alkynylation of benzamides and β-substituted acrylamide derivatives. Reactions of acrylamides with TIPS-EBX (\textsuperscript{1}) in the presence of the cationic rhodium complex \(\text{RhCp}^*(\text{MeCN})_3(\text{SbF}_6)_2\) in dichloromethane at 80 °C afforded alkynylated products in moderate to excellent yields (Scheme 11).\textsuperscript{23}

In the same year, we extended our research of alkylation chemistry and developed a method for olefinic C–H alkylation of electron-deficient alkenes in the presence of a Rh(III) catalyst (Scheme 12).\textsuperscript{24} The tosyl-imide group was selected as a directing group for this transformation. The directing group, with its weak coordinating ability, was responsible for the highly efficient and stereospecific C–H alkylation of alkene C–H bonds. Operational simplicity, gentle reaction conditions and high functional group tolerance were the key advantages of this protocol. Hence this method represents an efficient process for the synthesis of 1,3-enzyme moieties. To show the applicability of the method, the obtained products were further derivatized into a series of pyridinone and triazole moieties of synthetic potential.

Glorius et al., in 2013, reported the straightforward halogenation of readily available acrylamide derivatives in the presence of a Rh(III) catalyst to obtain a variety of substituted Z-haloacrylic acid derivatives.\textsuperscript{25} In the same year, Glorius developed a method to access [3]-dendralenes which involved the coupling reaction of acrylamide derivatives and allenyl carbamino carbamates by allenyl sp\textsuperscript{2} C–H activation using a Rh(III) catalyst (Scheme 13).\textsuperscript{26}

In 2017, we came up with a strategy called ‘substrate control strategy’ with allenyl sp\textsuperscript{2} C–H activation. From our previous report,\textsuperscript{27} we knew that the acylsilane functional group acts as a divergent functionalization tool in synthetic
Transition-metal-catalyzed alkyl C−CF₃ and aryl C−CF₃ bond-forming reactions have been very well developed in recent years. But on the other hand, the trifluoromethyla-
tion of electron-deficient alkenes has not been explored to the same extent. In 2013, we realized that this class of alkenes could be trifluoromethylated by employing suitable directing groups. It was believed that the trifluoromethyla-
tion of electron-deficient alkenes involves hydrogen elimi-
nation and electrophilic addition. However, we postulated two other possibilities in order to understand this transfor-
mation: a radical-addition pathway and another following a se-
quence of directing-group-assisted C−H activation and reductive elimination. We studied the copper-catalyzed tri-
fluoromethylation of N-tosyl acrylamides to obtain trifluo-
romethylated derivatives (Scheme 15), which have enor-
mous potential in materials science, and in agrochemical and pharmaceutical industries etc., owing to the unique ef-
effect of the CF₃ group. The reaction is initiated by ligand exchange between the copper catalyst and acrylamide. Var-
ious functionalized acrylamides have been trifluoromethyl-
ated to afford the corresponding products in excellent yields. Further, we investigated the reaction mechanism through a set of control experiments, which confirmed the involvement of radical species in this catalytic cycle.

3.2 The Chelation versus Non-Chelation Concept

Despite these successes, the reactions of more elaborate aliphatic olefins did not afford the desired products. To overcome this problem, in late 2012, we reported cross-
coupling reactions of acrylates with either TIPS-protected allylic or homoallylic alcohols in the presence of Pd(OAc)₂ as the catalyst. The corresponding dienyl alcohols were ob-
tained with good stereoselectivity and in moderate to high yields. We achieved this transformation employing 10 mol% of Pd(OAc)₂, 2 equivalents of Cu(OAc)₂, 12 mol% of 1,10-
phenanthroline, and 12 mol% of AgSbF₆ with substituted alkenes and acrylates in a solvent mixture of NMP/PivOH (1/1) (Scheme 16). In addition, we demonstrated the ap-
plication of this method by synthesizing the key C13−C21 fragment of palmerolide A.
Over the years, transition-metal-catalyzed arylation of C–H bond functionalization has progressed significantly. On the other hand, stereoselective alkenylation of C–H bond functionalization has not been developed to the same extent. Keeping this in mind, we thought of achieving the C–H bond functionalization of allylic and homoallylic alcohols, which are obtained easily from commercial sources and are much cheaper. We found that we could control the regioselectivity and stereoselectivity in these compounds by choosing appropriate reaction conditions.

In asymmetric synthesis the concept of non-chelation versus chelation has been applied efficiently, but has never been applied for tandem cross-coupling reactions and alkenylation of C–H bond functionalization. We realized and reported the utilization of this strategy for the C–H functionalization of alkenes and alkenyl derivatives (Scheme 17). Highly substituted alkene derivatives are easily obtained through this method in very high stereoselectivities. From the literature, we knew that straightforward C–H bond functionalizations can be easily mediated by the combined catalytic system of an amino acid ligand and a palladium catalyst. In the presence of Ag2CO3 (1.5 equiv) as the oxidant, N-acetyl-l-valine (50 mol%) and Pd(OAc)2 (10 mol%), the desired cross-coupled product was obtained in 59% yield with 84/16 (Z/E) stereoselectivity. Further optimization studies revealed that 1,4-dioxane was the most suitable solvent for this transformation, while N-acetylated-phe-nylalanine was the best ligand (Scheme 18). The alkene starting materials were reacted with distinct acrylates and the products were obtained in good stereoselectivities.

![Scheme 16](image1)

Scheme 16 Palladium-catalyzed cross-coupling reaction of TIPS-protected homoallylic or allylic alcohols with acrylates

![Scheme 17](image2)

Scheme 17 The concept of chelation vs non-chelation

4 Other Alkene Derivatives

By early 2000, many reports had been published on the formation of C–C bonds through aromatic C–H activation catalyzed by transition-metal catalysts. However, alkenylation of C–H activation was in its infancy without many published reports. Our group reported the first palladium-catalyzed ortho-C–H functionalization of cyclic enamides to effect cross-coupling. The enamide, derived from α-tetralone, was coupled with phenylboronic acid in the presence of palladium(II) acetate as the catalyst, an oxidant and a base. After optimization, we found that K2CO3 was a suitable base and that Cu(OTf)2 was a suitable oxidant for this transformation.
This approach was beneficial for the construction of a variety of enamide derivatives with distinct aryl groups at the ortho-\(\text{C}–\text{H}\) position.

As there were only a few reports on the arylation of organic compounds using organosilane compounds\(^{4b,40}\) compared to organoborane reagents, we developed an efficient method for the arylation of alkenyl sp\(^2\) C–H bonds of enamides using a palladium catalyst. In this transformation we employed AgF not only for activating the organosilane compounds, but also as an oxidant to complete the palladium catalytic cycle. We employed 3 equivalents of trialkoxyaryl silanes in the presence of 3 equivalents of AgF and Pd(OAc)\(_2\) (10 mol\%) as the catalyst in dioxane at 80 °C to achieve the arylation of enamides in good to excellent yields (Scheme 20).\(^{41}\)

In late 2011, we reported an elegant catalytic method involving an oxidative cross-coupling reaction of electron-deficient olefins with enamides in the presence of oxygen as the oxidant and palladium(II) acetate as the catalyst (Scheme 21).\(^{42}\) Detailed mechanistic studies have been conducted by synthesizing the six-membered cyclic vinylpalladium complex. This metal complex was explored in detail by X-ray analysis and \(^1\)H NMR spectroscopy. These mechanistic studies provided enough evidence to confirm that the cyclic vinylpalladium complex is the reactive intermediate in the reaction, which leads to olefination of the enamides. The desired products were accessed in moderate to good yields under mild conditions.

Although we reported the arylation of enamides, in our method we employed prefunctionalized coupling partners for this transformation. Hence, we required a method that was able to utilize readily available substances as the coupling partners for the arylation of alkenyl sp\(^2\) C–H bonds. As a result of our investigations, we published the first report employing unactivated arenes as the arylating source in the C–H functionalization of enamides under palladium catalysis. To enhance the chemical stability of the enamides, the enamide nitrogen was doubly protected. This method resulted in the formation of highly substituted enamides in an efficient and cost-effective manner with perfect Z selectivity (Scheme 22).\(^{43}\)

In 2014, Glorius and co-workers demonstrated the first example of the Rh(III)-catalyzed alkenylation of enol-carbamates (Scheme 23).\(^{44}\) This method utilized alkyl, aryl and cyclic enolates to synthesize 1,3-dienes in an efficient manner. The carbamate moiety of the formed products can be easily cleaved, and the products are further transformed into either \((E)\)-3-alkenones or other useful synthetic derivatives.
Following on from the work of Glorius, our lab demonstrated a unique protocol by alkynylating the olefinic C–H bond of enamides in the presence of Rh(III) catalysis for the construction of functionalized 1,3-enyne motifs. The ortho-directing effect of the enamides was explored and utilized for the synthesis of cis-enynamide motifs in a stereospecific manner. In the presence of 2 mol% of Cp*Rh(MeCN)₃(SbF₆)₂, 10 mol% of PivOH and TIPS-EBX, the enamides reacted at room temperature to give alkynylated products in excellent yields (Scheme 24). A wide range of functional groups was tolerated due to the very mild reaction conditions employed. The enynamide products obtained from C–H alkylation were further derivatized into useful organic synths by cycloaddition or Sonogashira coupling reactions.

Until 2012, there were no reports of olefinic C–CF₃ bond formation through the direct replacement of an olefinic C–H moiety. Here in our lab, we developed the first example of enamide C–H trifluoromethylation for the straightforward construction of olefinic C–CF₃ bonds. We employed a novel cationic Cu(I) catalyst to access trifluoromethylated enamides with excellent E selectivity and yields (Scheme 25). We demonstrated the pivotal role of the copper catalyst by...
appropriate mechanistic studies. We also carried out the oxytrifluoromethylation of enamides catalyzed by CuCl.

In continuation of our research on the development of straightforward olefinic C–H functionalizations, we described a palladium-catalyzed cross-coupling reaction of (bromoethynyl)trisopropylsilane and N-vinylacetamides. The combination of solvents DMSO/CH₂Cl₂ (v/v = 3/97) proved to be the best for yielding the desired products (Scheme 26). In this transformation DMSO stabilizes the palladium catalyst by coordinating to the metal center, thus acting as a weak ligand.

Our further studies on the reactivity of enamides with alkynes resulted in our group reporting an efficient method for the formation of substituted pyrrole derivatives in the presence of a palladium catalyst using oxygen as the oxidant (Scheme 27). The method is quite gentle and has broad substrate scope.

In late 2015, the first Rh(III)-catalyzed C–H bond functionalization of enol phosphates with a wide range of activated coupling partners was accomplished by our group. The phosphate group with its strong directing ability facilitates the substrates to participate in synthetically tunable transformations through alkenylation with acrylates and hydroalkenylation with enones (Schemes 28 and 29). The hydroalkenylation process proceeds through C–H activation assisted by chelation, in which the vinylrhodium species undergo conjugate additions to enones. This strategy can further be expanded for the coupling reaction of enol phosphates with other Michael acceptors such as electron-deficient alkynes. Enol phosphates are integral units of many pharmaceuticals and bioactive natural products. In transition-metal-catalyzed cross-coupling reactions, enol phosphates have been utilized as important intermediates. Compared to the triflate and halide partners, enol phosphates are cheap and have higher stability, due to which they are often utilized in these coupling reactions. To show the wide applicability of the method, an array of cross-coupling reactions with other analogues have been performed and highly functionalized conjugated alkenes have been accessed with ease. The outstanding features of this method include the versatile applicability of the coupling products, good functional-group compatibility, and high stereo- and regioselectivity.

Synthetic chemists have been using enamines as synthetic equivalents of metal enolates. Enamines have been demonstrated as useful synthetic intermediates in organic synthesis. Enamines, under very gentle conditions, react with an array of electrophiles. Although enamines are reactive to most electrophiles, they lack reactivity with sterically hindered alkyl halides.

Enamides are often considered as derivatives of enamines. To solve this reactivity problem and in continuation of our studies on the C–H functionalizations of enamides, we were inspired to carry out the transition-metal-catalyzed
cross-coupling of sterically hindered halides with enamides. As expected, this method worked well with a palladium catalyst system, providing access to bulky alkyl-substituted alkenes as versatile precursors of γ-lactams, 1,4-dicarbonyls, δ-amino alcohols and γ-amino acids. Notably, the present reaction conditions not only gave the corresponding products in good yield but also suppressed the side reaction involving β-hydride elimination (Scheme 30).52

Scheme 30 Palladium-catalyzed alkylation reactions of enamides with α-bromo-substituted carbonyl compounds

5 Intramolecular C–H Activation

In early 2017, our group reported an intramolecular C–N bond-forming reaction catalyzed by a palladium catalyst in the presence of chloranil as the additive (Scheme 31).53 This method, involving intramolecular oxidative amination, was widely applicable and various functional groups were well tolerated.

Scheme 31 Palladium-catalyzed formation of multisubstituted dipyrrylroles

Macrocycles are integral units of many pharmaceuticals and bioactive natural products.54 To date, many methods have been reported for the efficient syntheses of macrocycles, e.g., macrolactamizations, macroaldolizations, and macro lactonizations. In the last two decades, ring-closing metathesis (RCM) has been widely applied to construct such macrocycles with double bonds. Though RCM is utilized efficiently to form large rings, the control of E/Z stereo-selectivities in these rings is quite challenging. We have been searching for an efficient method to construct macrocycles with double bonds by applying our well-established method of transition-metal-catalyzed alkenyl sp2 C–H functionalization. With this idea in mind, we envisaged that this class of macrocycles would be easily accessed via an intramolecular cross-coupling among two distinct double bonds. In 2018, we presented the first example of intramolecular oxidative cross-coupling between double bonds catalyzed by a cationic Rh(III) complex (Scheme 32).55 The method is atom economical and the products can be transformed into useful derivatives. Distinctive sized macrocy-

Scheme 32 Intramolecular cross-coupling and derivatization of a cross-coupled product
ciles were obtained with ease in relatively good yields in the presence of $[^\text{RhCp}^\text{*}^\text{C}_{12}]_2$ (5 mol%), NaBARF (40 mol%) and Cu(OAc)$_2$·H$_2$O (2.5 equiv) in acetone at 100 °C. This method features universal utilization of the diene fragment for derivatization, good functional-group compatibility and high stereo- and chemoselectivity.

For the palladium-catalyzed alkenyl sp$^2$ C–H activation we can draw a generalized mechanism as shown in Scheme 33. The palladium catalyst activates the electron-rich alkene by generation of vinyl palladium intermediate A. Next, the incoming electron-deficient alkene coordinates to intermediate A, which is followed by migratory insertion into the palladium–C vinyl bond to form α-Pd intermediate B. Finally, β-H elimination results in formation of the product, while the oxidant employed in the reaction reactivates the catalyst for the next cycle.

![Scheme 33 Generalized mechanism for the palladium-catalyzed alkenyl sp$^2$ C–H activation](image)

6 Conclusion and Future Projects

It is evident from this short account of our group’s research over two decades on alkenyl sp$^2$ C–H activation that these methods have emerged as powerful tools to functionalize and synthesize various alkene derivatives. In particular, transition-metal-catalyzed C–H functionalizations offer more scope and are widely applicable. In continuation of our interest in alkenyl sp$^2$ C–H activation, we are now exploring new arenas for this methodology. After our recent breakthrough macrocyclization report, we are presently looking to expand the application of this method by applying it to distinctive coupling partners in order to obtain more functionalizable products. We are in search of methods that not only activate alkenyl sp$^2$ C–H groups, but that also trigger enantioselective reactions through which we can achieve stereoselective reactions via C–H activation. With our interest in green chemistry and water-promoted reactions, we are also searching for metal-free coupling reactions in water.

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