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Oxazolinyl–Assisted Ru(II)–Catalyzed C-H Allylation with Allyl Alcohols and Synthesis of 4-methyleneisochroman-1-ones.

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Abstract:

We report herein a ruthenium-catalyzed, oxazoline-directed strategy for C–H allylation of aryl oxazolines using allylic alcohols as the coupling partner. The present transformation unravels the unusual reactivity of allylic alcohols in the synthesis of 4-methyleneisochroman-1-ones and C–H allylated products. A complete switch in the product selectivity was observed with substrate control and tuning the reaction conditions. The approach employs allyl alcohols as an efficient alternative to preactivated allylating agents to access diverse products in a highly selective manner.

Introduction:

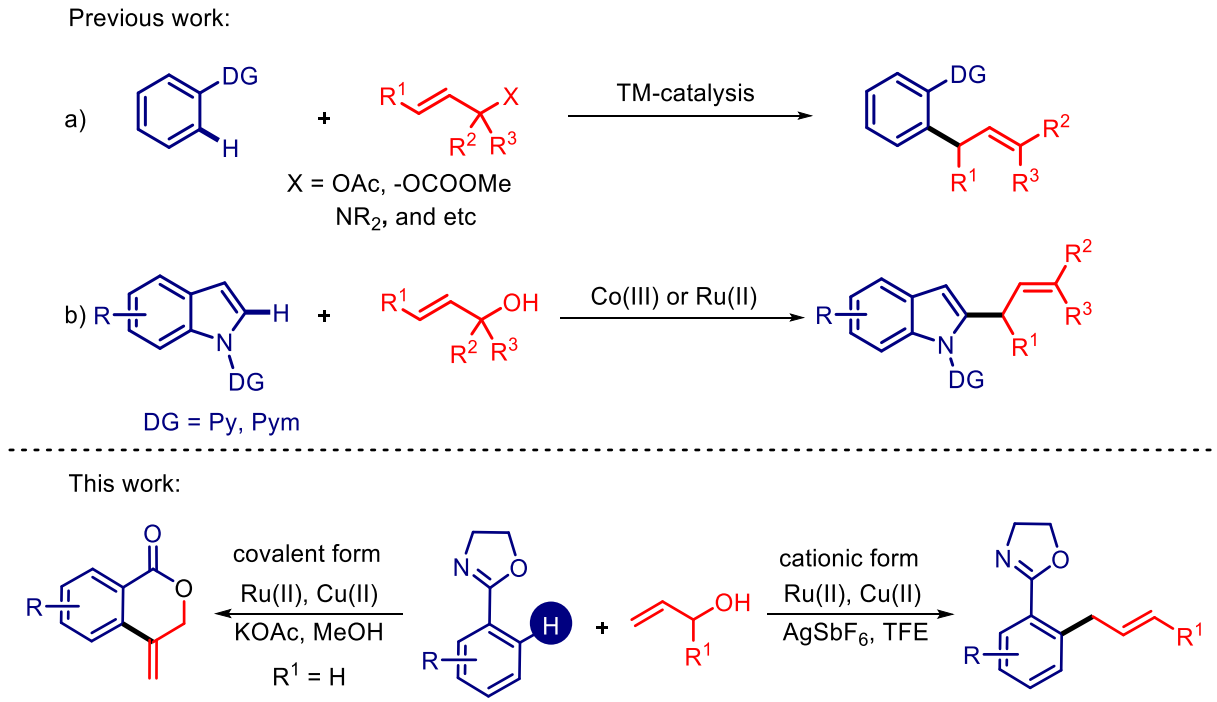
The development of efficient, selective, and sustainable C–H functionalization strategies has gained tremendous importance in the recent years, as they continue to provide solutions to challenging synthetic problems in organic chemistry.[1] In particular, the development of divergent

methods which utilize versatile coupling partners in C–H functionalization and are capable of following two distinct reactive pathways has evolved as a unique approach to access diverse products.[2] In this regard, the use of allyl alcohols as coupling partners in C–H functionalization transformations has emerged as a powerful tool for the construction of C–C bonds due to their unique reactivity, availability and stability.[3] Allyl alcohols have often been employed as alternatives to α,β-unsaturated carbonyl compounds and other pre-activated allylating agents, however, their direct utilization as allylating agents was less explored until recent times. This could be attributed to the reason that allyl alcohols often tend to follow the *β*–hydride elimination pathway preferentially over the *β*–hydroxide elimination pathway. The directed C–H functionalization of arenes with allyl alcohols to obtain C–H alkylated products has received much attention in recent years.[4,5] In this context, tuning the reactivity of the allyl alcohols in transition metal-catalyzed directed C–H functionalizations, to undergo selectively either *β*–hydride elimination or *β*–hydroxide elimination, itself represents a remarkable challenge.

Owing to the importance of the allyl moiety in organic synthesis in the construction of complex molecules, the development of selective C–H functionalization methods for construction of the allylated arenes is of critical importance. In recent years, transition metal-catalyzed C-H allylation of arenes with numerous preactivated allyl surrogates such as allylic acetates, allylic halides, allylic carbonates, allyl phosphates and allyl amines has attracted a lot of interest.[6-10] However, the use of pre-activated allylating agents is in a way not step-economical and at times harsh reaction conditions such as high temperatures, stoichiometric amounts of oxidants need to be employed.[6-8] In this regard, Kanai and co-workers first reported a unique cobalt(III)-catalyzed dehydrative C–H allylation of indoles with allyl alcohols.[11] In 2016, our group demonstrated the use of the allylic alcohols in the ruthenium-catalyzed C–H allylation of indoles.[12] The research groups of Sundararaju, Gooßen and Ji have also reported efficient C–H allylation strategies for the synthesis of allyl arenes with allyl alcohols.[13] Despite these advances, the development of sustainable approaches for C–H allylation of arenes *via* efficient catalytic systems that can enable the *β*–hydroxide elimination still remains a highly desirable target.

The utilization of the oxazolinyl group as a unique directing group in C–H functionalizations has emerged as an important approach because of the prevalence of the oxazoline moiety in natural

products and biologically active compounds.[14] This is due to their ubiquitous availability as well as their unique reactivity of undergoing cascade cyclizations to access nitrogen heterocycles.[15, 16]



Scheme 1: Transition Metal-Catalyzed direct C-H Allylation transformations

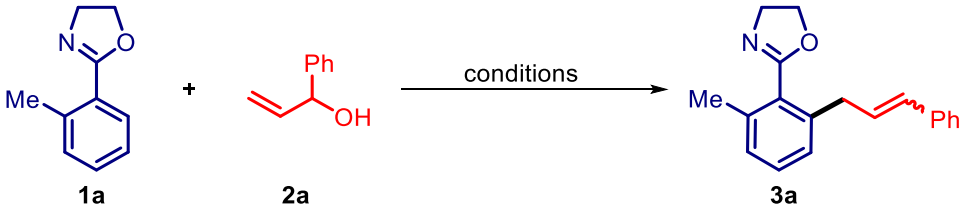
Recently, we have successfully developed a three-component cascade cyclization for the synthesis of isoquinolinones *via* a step-efficient ruthenium-catalyzed, oxazolinlyl-mediated C–H functionalization involving a metal-carbene migratory insertion.[17] To the best of our knowledge, the ruthenium-catalyzed direct C–H allylation of aryl oxazolines with the use of allyl alcohols as allylating agents has never been reported. In continuation to our previous explorations involving the reactivity of allyl alcohols in C–H functionalization of arenes,[18] we have successfully developed a highly selective, ruthenium-catalyzed *ortho*-C–H allylation of aryloxazolines by employing allyl alcohols as coupling partners, under mild reaction conditions (Scheme 1).

Results and Discussion:

We began our optimization studies by probing numerous conditions for the oxazolinyl-assisted Ru(II)-catalyzed C–H allylation by choosing 2-(*o*-tolyl)-4,5-dihydrooxazole (**1a**) and 1-phenylprop-2-en-1-ol (**2a**) as the benchmark substrates for the transformation (Table 1). To our

delight, in preliminary experiments, a very simple catalytic system comprising of $[RuCl_2(p\text{-cym})]_2$, $AgSbF_6$, and $Cu(OAc)_2.H_2O$ delivered the desired C-H allylated product in 15% yield (Table 1, entry 1). The solvent was found to be a critical parameter for the selective formation of C–H allylation product and systematic screening of solvents revealed that TFE was the solvent of choice for the transformation (Table 1, entries 4-9).

Table 1. Optimization studies for C-H allylation:[a]



1a **2a** **3a**

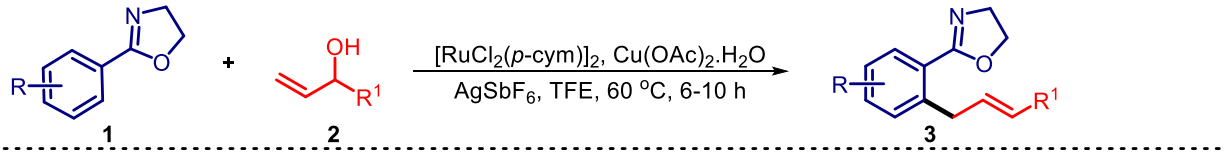
Entry	catalyst/acetate source/additive/solvent/temp/time	Yield 3a (%)
1	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2$ (2 equiv)/$AgSbF_6$/DCE/85 °C/12h	15
2	$[RuCl_2(p\text{-cym})]_2$/$Cu(OTf)_2$(2 equiv)/$AgSbF_6$/DCE/85 °C/12 h	0
3	$[RuCl_2(p\text{-cym})]_2$/$^nBu_4NOAc$ (2 equiv)/$AgSbF_6$/DCE/85 °C/12 h	0
4	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2$ (2 equiv)/$AgSbF_6$/dioxane/85 °C/12 h	10
5	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$/$AgSbF_6$/*t*-BuOH/60 °C/6 h	12
6	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$/$AgSbF_6$/MeOH/60 °C/6 h	15
7	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$/$AgSbF_6$/toluene/85°C/6 h	10
8	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$/$AgSbF_6$/THF/60 °C/6 h	10
9	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$ (2.0 equiv)/$AgSbF_6$/TFE/80 °C/6 h	70
10	$[RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$ (0.25 equiv)/$AgSbF_6$/TFE/60 °C/6 h	81
11	**$RuCl_2(p\text{-cym})]_2$/$Cu(OAc)_2.H_2O$ (0.5 equiv)/$AgSbF_6$/TFE/60 °C/6 h**	**86 (*E*:*Z* = 12:1)**
12	$[RuCl_2(p\text{-cym})]_2$/CsOAc (0.5 equiv)/$AgSbF_6$/TFE/60 °C/6 h	74 (*E*:*Z* = 2.7:1)
13	$[RuCl_2(p\text{-cym})]_2$/AgOAc (1 equiv)/TFE/60 °C/6 h	51 (*E*:*Z* = 2:1)
14	$[RuCl_2(p\text{-cym})]_2$/KOAc (0.5 equiv)/$AgSbF_6$/TFE/60 °C/6 h	63 (*E*:*Z* = 2:1)
15	$[RuCl_2(p\text{-cym})]_2$/NaOAc (0.5 equiv)/$AgSbF_6$/TFE/60 °C/6 h	74 (*E*:*Z* = 8:1)
16	$[RuCl_2(p\text{-cym})]_2$/NaOAc (0.5 equiv)/TFE/60 °C/6 h	81 (*E*:*Z* = 2:1)
17	$[RuCl_2(p\text{-cym})]_2$/$AgSbF_6$/TFE/60 °C/6 h	48
18	$[RuCl_2(p\text{-cym})]_2$/TFE/60 °C/16 h	56
19	$[RuCl_2(p\text{-cym})]_2$/K_3PO_4/TFE/60 °C/16 h	20
20	$Cu(OAc)_2.H_2O$/$AgSbF_6$/TFE/60 °C/6 h	0

[a]Unless otherwise mentioned, all reactions were performed with **1** (0.3 mmol), **2** (0.45 mmol), catalyst (0.015 mmol), $Cu(OAc)_2.H_2O$ (0.15 mmol) and $AgSbF_6$ (0.06 mmol) in 1.5 mL solvent.

Lowering the reaction temperature as well as the loading of $Cu(OAc)_2.H_2O$ resulted in a better yield (Table 1, entries 9–11). Scanning other acetate sources only afforded poor diastereoselectivity (*E*:*Z* ratios), and the best results were obtained with $Cu(OAc)_2.H_2O$ (Table entries 11–16). The presence of the $Cu(OAc)_2.H_2O$ and $AgSbF_6$ plays a crucial role in the *E:Z* selectivity (Table 1 entries 11–16). As expected, control reactions carried out in the absence of the Ru-catalyst did not yield the desired product (Table 1, entry 20).

With the optimized conditions in hand, we sought to explore the versatility of the transformation. The reaction displayed good functional group tolerance and a good substrate scope concerning oxazolines as well as allylic alcohols.

Scheme 2. Substrate scope for C-H allylation:[a]



3a R^1 = Ph, 86% (*E*:*Z* = 12:1) (80%)[b]
3b R^1 = *p*-MeC_6H_4, 65% (*E*:*Z* = 9:1)
3c R^1 = *m*-$MeOC_6H_4$, 70% (*E*:*Z* = 12:1)
3d R^1 = *p*-ClC_6H_4, 74% (*E*:*Z* = 14:1)
3e R^1 = *p*-FC_6H_4, 62% (*E*:*Z* = 10:1)
3f R^1 = H, 61%
3g R^1 = Me, 58% (*E*:*Z* = 1.1:1)
3h R^1 = Et, 55% (*E*:*Z* = 1.2:1)

3i R = Cl, R^1= Ph, 59**%** (*E*:*Z* = 18:1)
3j R = F, R^1= Ph, 55**%** (*E*:*Z* = 13:1)
3k R = Br, R^1= *p*-FC_6H_4, 52% (*E*:*Z* = 14:1)

X-ray structure for **3i**[19a]

3l R^1 = Ph, 73% (*E*:*Z* = 15:1)
3m R^1 = *m*-$MeOC_6H_4$, 65% (*E*:*Z* = 14:1)

3n, 73% (*E*:*Z* = 16:1)

3o, 40%[c] (59%)[e] (*E*:*Z* = 10:1)

3p R = Me, 35%[c, d] (58%)[e] (*E*:*Z* = 12:1)
3q R = OMe, 28%[c,d] (48%)[e] (*E*:*Z* =10:1)

[a]Unless otherwise mentioned all reactions were performed with **1** (0.3 mmol), **2** (0.45 mmol), $[RuCl_2(p\text{-cym})]_2$ (0.015 mmol), $Cu(OAc)_2.H_2O$ (0.15 mmol) and $AgSbF_6$ (0.06 mmol) in 1.5 mL solvent. All yields are isolated yields. *E:Z* ratios were calculated based on integration of isomeric signals in ^1H NMR of the crude reaction mixture. [b]Reaction performed on 1 mmol scale. [c]1.0 equiv of phenylprop-2-en-1-ol was used. [d]diallylated product was also observed along with desired product (See Supporting Information (SI) for details). [e]yield based on recovered starting material.

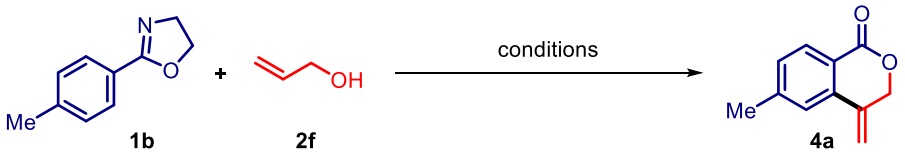
Several allylic alcohols, with varied substitution at the carbinol carbon afforded the allylated products displaying almost exclusive γ-selectivity (**3a**–**3h,** Scheme 2). In most of the cases, the stereochemistry of the resulting olefin was *E*. In the case of but-3-en-2-ol and pent-1-en-3-ol as

coupling partners, poor diastereomeric selectivity was observed (**3g, 3h,** Scheme 2). Steric factors are well tolerated in the transformation and *ortho*–Me, –Cl, –F and –Br substituted aryl oxazolines were found to be suitable substrates for the transformation (**3a-3k**, Scheme 2). The reaction worked with oxazolines containing electron-donating as well as electron-withdrawing substituents (Scheme 2). However, the reaction displayed an electronic bias; oxazolines bearing electron-withdrawing substituents were found to possess relatively decreased reactivity (**3a vs 3i, 3j,** Scheme 2). The reaction of 2-(2-fluorophenyl)-4,5-dihydrooxazole under standard reaction conditions afforded the desired product (**3j**) in 55% yield. Unfortunately for us, the synthesis of methyl 2-(4,5-dihydrooxazol-2-yl)benzoate was unsuccessful in our hands and therefore the substrate scope with an ester substituent could not be tested. Importantly, the desired products were obtained in good yields in the reaction of 2-(naphthalen-1-yl)-4,5-dihydrooxazole (**3k**, **3l**, Scheme 2). The reaction of 5,5-dimethyl-2-(*o*-tolyl)-4,5-dihydrooxazole afforded the desired C–H allylated product in 73% yield (**3m**, Scheme 2). The oxazolines bearing *meta*- and *para*-substituents provided a mixture of di– and monoallylated products under standard reaction conditions (see the Supporting Information (SI) for details).The reduction in the equivalents of the allylic alcohol led to the selective formation of the mono- allylated products (**3o**, **3p**, Scheme 2), however the reaction of the 2-(4-methoxyphenyl)-4,5-dihydrooxazole resulted in the formation of mixture of mono– and di–allylated products (see the Supporting Information (SI) for details). The reaction of 2-(*m*-tolyl)-4,5-dihydrooxazole resulted in the C–H allylation at the sterically less-hindered site to afford the product (**3o**, Scheme 2).

During the optimization studies, we had observed that the reaction of prop-2-en-1-ol with the oxazolines afforded the C–H allylated products along with a trace amount of 4-methyleneisochroman-1-one as the side product. This intriguing nature of annulation to obtain the 4-methyleneisochroman-1-ones, prompted us to probe various conditions for the transformation for the expedient synthesis of 4-methyleneisochroman-1-ones. To the best of our knowledge, the synthesis of the methyleneisochroman-1-one from oxazolines and allylic alcohols has never been reported. We chose 2-(*p*-tolyl)-4,5-dihydrooxazole and prop-2-en-1-ol as standard substrates for the optimization of the annulation of oxazolines with allyl alcohols (Table 2). In an early trial, the catalytic system comprising of $[RuCl_2(p\text{-cym})]_2$, $AgSbF_6$, and $Cu(OAc)_2.H_2O$ yielded the desired product in 23% yield (Table 2, entry 2). The choice of the solvent was again found to be a critical parameter in the transformation. Among the various

solvents screened for the transformation, MeOH was found to be the optimal solvent for the best conversion (Table 2, entries 3–12). Substituting the silver salt with KOAc resulted in a good increment in the yield (Table 2, entry 6).

Table 2. Optimization studies:[a]



Entry	catalyst/acetate source/additive/solvent/temp/time	Yield of 4a (%)
1	$[RuCl_2(p\text{-cym})]_2/K_3PO_4$/DCE/100 °C/12 h	0
2	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O/AgSbF_6$/DCE/100 °C/16 h	23
3	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O/AgSbF_6$/DMF/100 °C/16 h	25
4	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/DCE: H_2O (1:1)/85 °C/16 h	39
5	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/$H_2O$/85 °C/16 h	30
6	**$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/MeOH/85 °C/16 h**	**60**
7	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/*t*-BuOH/85 °C/16 h	5
8	$[RuCl_2(p\text{-cym})]/Cu(OAc)_2.H_2O$/KOAc/toluene/85 °C/16 h	0
9	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/dioxane/85 °C/16 h	5
11	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/THF/85 °C/16 h	0
12	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/KOAc/DMSO/85 °C/16 h	0
13	$[RuCl_2(p\text{-cym})]_2/O_2$balloon/KOAc/MeOH/85 °C/16 h	0
14	$[RuCl_2(p\text{-cym})]_2$/AgOAc/KOAc/MeOH/85 °C/16 h	5
15	$[RuCl_2(p\text{-cym})]_2/Cu(OAc)_2.H_2O$/AcOH/KOAc/MeOH/85 °C/16 h	35
16	$[RuCl_2(p\text{-cym})]/Cu(OAc)_2.H_2O$ (1 equiv)/KOAc/MeOH/85 °C/16 h	30
17	$[RuCl_2(p\text{-cym})]_2$/KOAc/MeOH/85 °C/18 h	5
18	$Cu(OAc)_2.H_2O$/KOAc/MeOH/85 °C/16 h	0

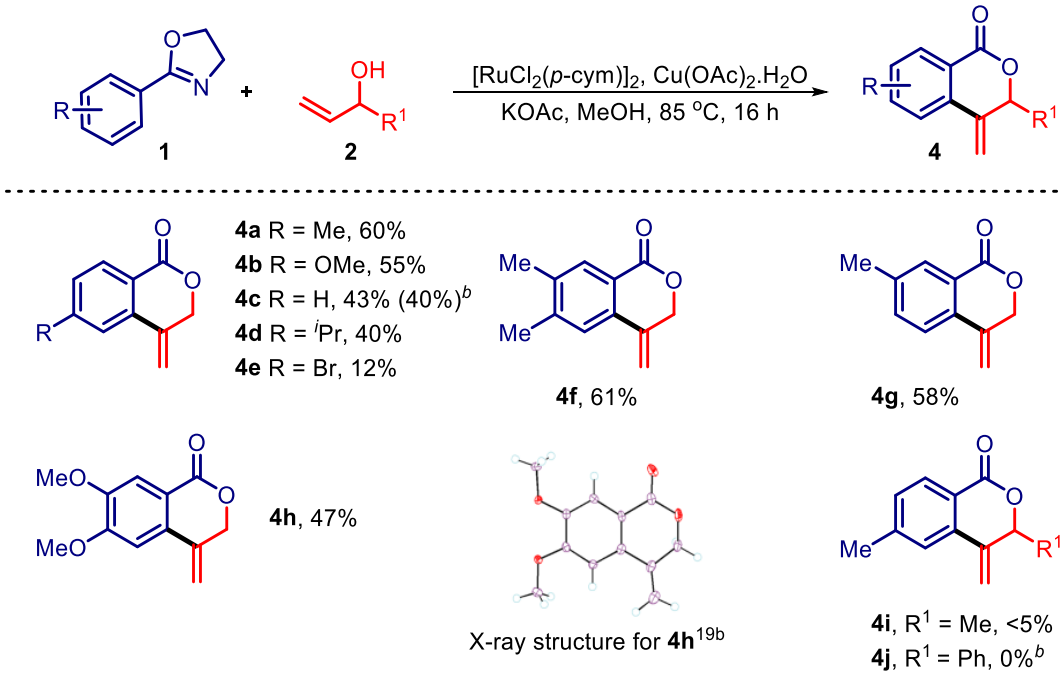
[a]Unless otherwise mentioned, all reactions were performed with **1** (0.3 mmol), **2** (0.45 mmol), catalyst (0.015 mmol), $Cu(OAc)_2.H_2O$ (0.6 mmol) and additive (0.3 mmol) in 2 mL solvent.

Among the various oxidants scanned, the best results were obtained with $Cu(OAc)_2.H_2O$ and poor conversions were observed in the absence of the $Cu(OAc)_2.H_2O$ (Table 2, entries 13–17). A control reaction, carried out without the ruthenium catalyst, did not yield the desired product (Table 2, entry 18). The distinct selectivity in the formation of the C-H allylated products and 4-methyleneisochroman-1-ones was observed with substrate control and tuning the reaction

conditions (Table 1 and Table 2). In C-H allylation reaction, the use of $AgSbF_6$ and $Cu(OAc)_2$ leads to the generation of cationic ruthenium complex [Ru(OH)*p*-cymene][SbF_6] whereas in the synthesis of 4-methyleneisochroman-1-ones the use of KOAc and $Cu(OAc)_2$ generates a covalent system [(*p*-cymene)$Ru(OAc)_2$] as the active catalyst.

With the optimized reaction conditions, we explored the substrate scope for this transformation (Scheme 3).

Scheme 3. Substrate scope:[a]

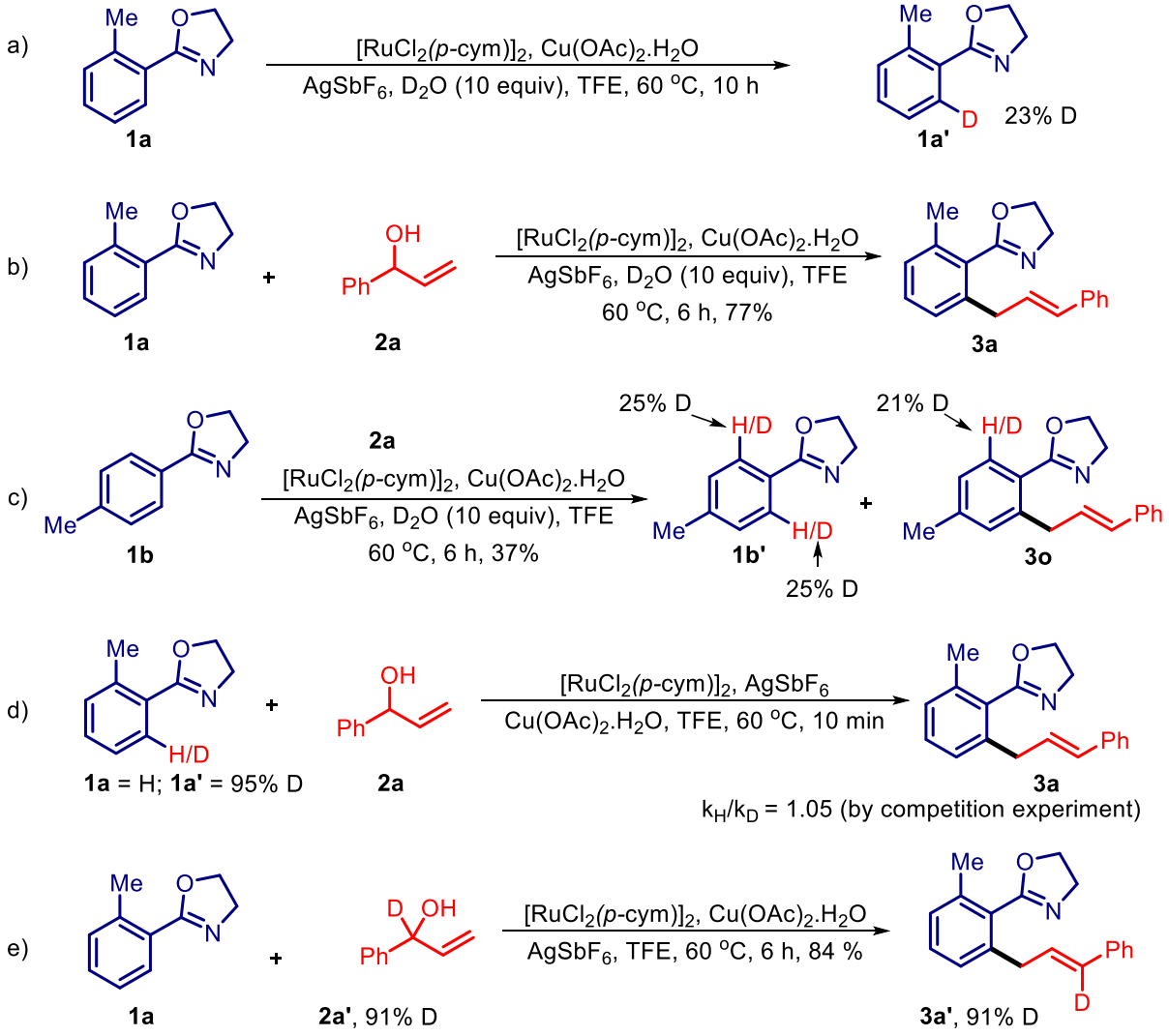


[a]Unless otherwise mentioned, all reactions were performed with **1** (0.3 mmol), **2** (0.45 mmol), catalyst (0.015 mmol), $Cu(OAc)_2.H_2O$ (0.6 mmol) and additive (0.3 mmol) in 2 mL solvent.[b]Reaction performed on 1 mmol scale.

The substrate scope with respect to oxazolines also displayed a distinct electronic-bias and it was observed that the electron-withdrawing substituents greatly hampered the reactivity of the oxazolines (Scheme 3). However, the reaction worked fairly well for most of the electron-rich oxazolines (Scheme 3, **4a–4d, 4f, 4h**). X-ray crystallographic analysis of **4h** unambiguously confirmed the structure of the product (Scheme 3). The reaction of 2-(*m*-tolyl)-4,5-dihydrooxazole resulted in the formation of the desired product (Scheme 3, **4g**) at the less sterically hindered position. The reaction with other allylic alcohols such as 1-phenylprop-2-en-1-ol and crotyl alcohol did not afford the desired product.

To understand the versatile reactivity of Ru(II)-catalyzed C–H allylation in a better manner and to gain more insights into the mechanism of this transformation, a series of studies were conducted (Scheme 4). To check the reversibility of C–H ruthenation step, studies were performed in the presence as well as absence of the allylic alcohol with D_2O under standard conditions.

Scheme 4: **Mechanistic studies:**



In the absence of the coupling partner, the transformation resulted in approximately 23% deuterium incorporation in the starting material at the *ortho*-position (Scheme 4a). In the presence of the coupling partner, desired product formation was observed in 77% yield (Scheme 4b). Similarly, the reaction of 2-(*p*-tolyl)-4,5-dihydrooxazole and **2a** (1 equiv) with D_2O under standard conditions resulted in 21% deuterium incorporation in the product along with the 25 %

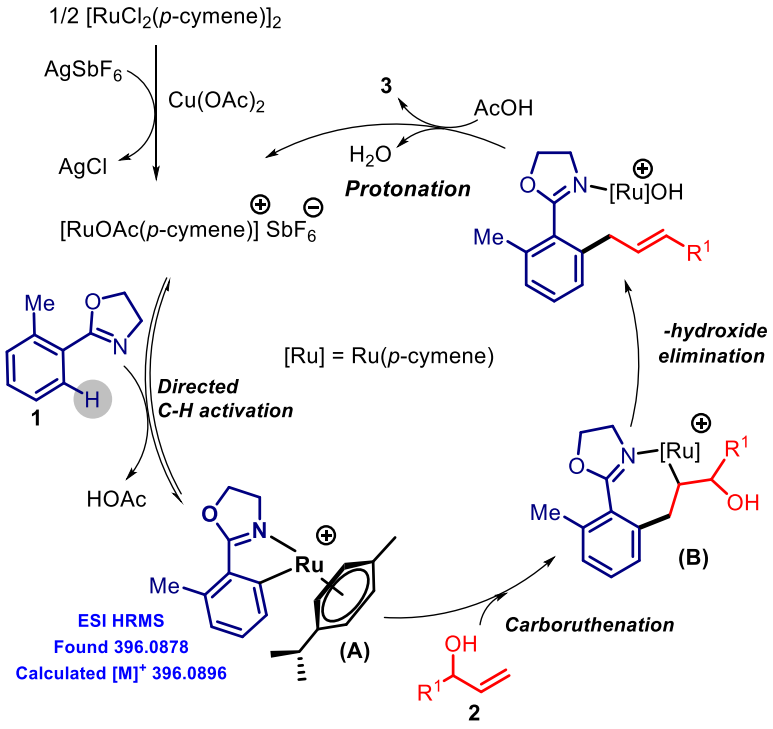
deuterium incorporation in the recovered starting material (Scheme 4c). This significant amount of deuterium incorporation in the recovered starting material indicates that the formation of the ruthenacycle is a reversible transformation (Scheme 4b). To check whether the cleavage of C(sp^2)−H was involved in the rate-determining step, kinetic isotope effect studies were carried out. The value of kinetic isotope effect was found to be approximately 1.0 thereby indicating that the C-H bond cleavage is unlikely to be the rate-limiting step (Scheme 4d). It is possible that either the migratory insertion or the *β*-hydroxide elimination could be the rate-limiting step in the transformation. A control reaction carried out using 1-phenylbut-3-en-2-*d*-2-ol (**2a'**) with **1a** resulted in 91% deuterium incorporation in the resulting product, indicating a high γ-selectivity of the transformation (Scheme 4e).

Based on our previous work and the literature reports,[11-13] a plausible reaction pathway for the C–H allylation is proposed (Scheme 5). The reaction initiates with the generation of the cationic Ru(II) catalyst, followed by the coordination of the metal to the oxazolinyl nitrogen. Subsequent C–H activation at the proximal C-2 position results in the formation of the ruthenacycle **A**. Intermediate **B** results from the insertion of the allyl alcohol *via* carboruthenation. This organometallic intermediate undergoes a selective *β*–hydroxide elimination to afford the desired product. In the C–H allyation transformation, $Cu(OAc)_2$ acts as acetate source in the transformation. Oxidant-free Ru(II)-catalyzed C-H allylation reactions have been reported in the literature in which the regeneration of the catalyst proceeds *via* a protonolysis of the Ru(OH) intermediate (Scheme 5).[13a, 13d-13e] The oxophilicity of the metal and solvent stabilization could be the major factors for the selective *β*–hydroxide elimination. The lack of formation of a π–allyl intermediate is probably the reason for the γ–selectivity observed in the reaction. To obtain additional proofs on the formation of the ruthenacycle, MS studies were performed (Scheme 5) and the ruthenacycle **A** was detected in ESI-HRMS, thereby lending credence to the proposed pathway.

The plausible reaction mechanism for the synthesis of the 4-methyleneisochroman-1-ones is depicted in Scheme 6. The postulated reaction mechanism begins with a nucleophilic attack of the allylic alcohol onto the oxazoline moiety, followed by a subsequent C–H activation to lead to the formation of the intermediate **H** (Scheme 6-I). This intermediate **H** undergoes a migratory insertion with alkene of allylic alcohol to result in intermediate (**I**), which undergoes a *β*-hydride

elimination to deliver the intermediate **E**.This is then followed by a hydrolysis of intermediate **E** to afford 4-methyleneisochroman-1-one as the product (Scheme 6-I).

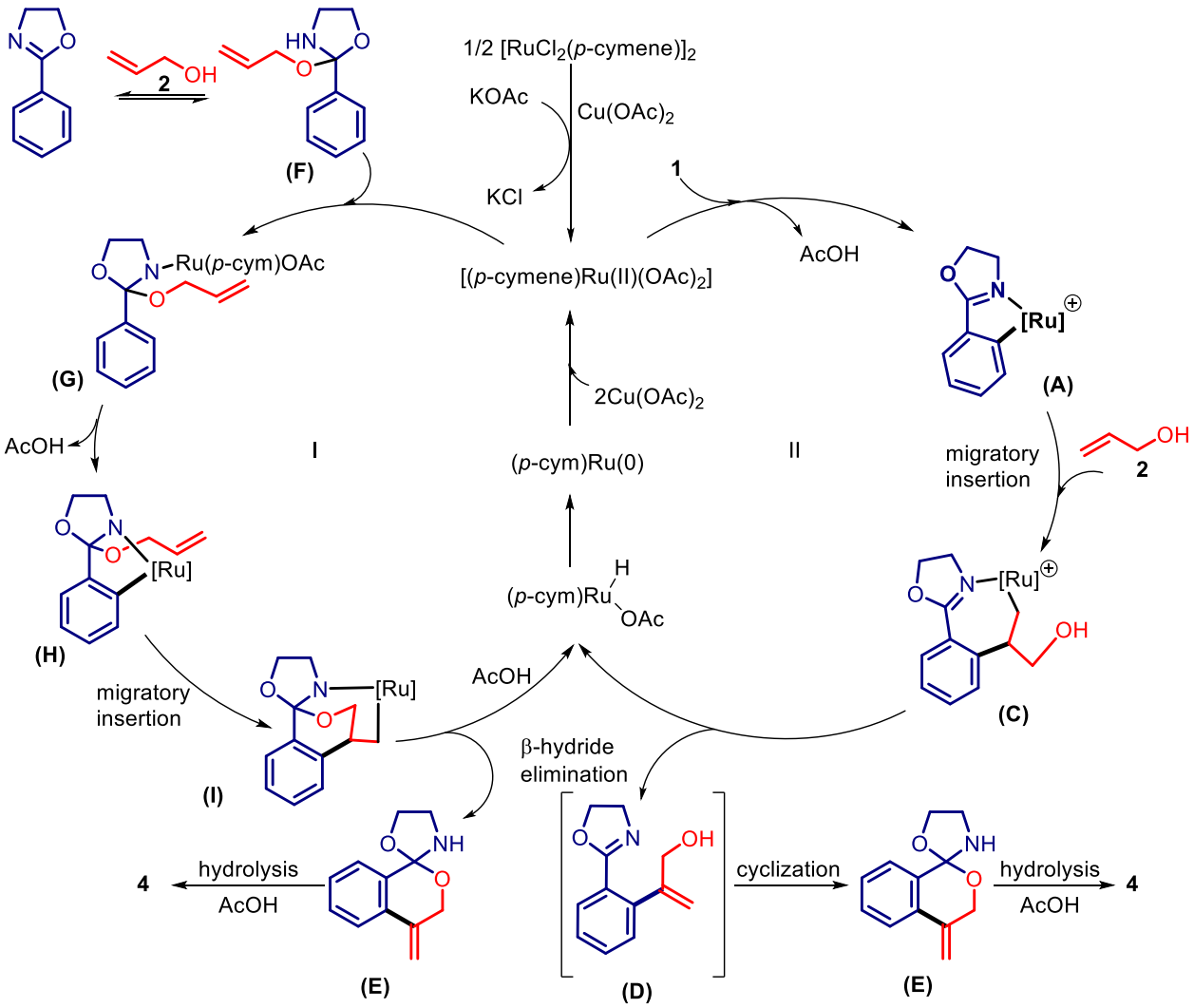
Scheme 5: Plausible reaction mechanism for C-H allylation:



It is also possible that another plausible reaction pathway involving an initial C–H activation and followed by a migratory insertion of the allylic alcohol with the opposite regioselectivity could lead to formation of the desired product (Scheme 6-II). The proposed reaction mechanism begins with an initial C-H activation step followed by the insertion of the allylic alcohol with the opposite regioselectivity to provide intermediate **C**. The subsequent *β*-hydride elimination delivers the intermediate **D**. This is then followed by a cyclization of allylic alcohol onto the oxazolinyl moiety and a hydrolysis to deliver the isochromanone product. The $Cu(OAc)_2.H_2O$ serves as an oxidant in both the reaction plausible mechanisms to complete catalytic cycle by the regeneration of the active catalyst. In C–H allylation transformation, $Cu(OAc)_2.H_2O$ most likely acts as the acetate source in the transformation. This was supported by the observation that the reaction worked with the other acetate sources like NaOAc, CsOAc, *etc*., as well (Table 1, entries 10–16) and the sub-stoichiometric amounts of $Cu(OAc)_2.H_2O$ delivers the final product. The C–H activation step is likely to be a concerted deprotonation/metalation in which –OAc acts

as the base. In the synthesis of the 4-methyleneisochroman-1-ones, $Cu(OAc)_2.H_2O$ acts as oxidant. This is supported by the observation that the absence of the $Cu(OAc)_2.H_2O$ did not lead to the formation of the product (Table 2, entry 10).

Scheme 6. Plausible mechanism for the synthesis of the 4-methyleneisochroman-1-ones:



In summary, we have successfully developed a new ruthenium-catalyzed C–H allylation of aryl oxazolines using allylic alcohols as a coupling partner.The transformation displays a broad substrate scope with excellent γ–selectivity and moderate yields under mild reaction conditions. We have also successfully disclosed the unprecedented reactivity of allylic alcohols in the synthesis of 4-methyleneisochroman-1-one as the products. The current approach represents the

first example of a Ru(II)-catalyzed synthesis of 4-methyleneisochroman-1-one and allylated arenes from oxazolines and allyl alcohols.

Experimental Section:

(1) General Methods:

All commercially available compounds were used as such without any purification. Unless otherwise noted, all reactions were performed in oven-dried glassware. All reactions were run under argon or nitrogen atmosphere. All heating reactions were carried out using an oil bath. All solvents used in the reactions were purified before use. Column chromatography was performed with freshly distilled solvents. Dry tetrahydrofuran and toluene were distilled from sodium and benzophenone, whereas dry dichloromethane, dichloroethane and triethylamine were distilled from CaH_2. Petroleum ether with a boiling range of 40–60 °C was used. Melting points are uncorrected. ^1H, and ^{13}C NMR: Recorded at 295 K in $CDCl_3$; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: $CDCl_3$ (^1H δ 7.24; ^{13}C δ 77.0). LC-HRMS: Analysed using Electron spray ionization (ESI) or Atmospheric pressure chemical ionization (APCI). GC-HRMS: Performed on GC-QToF (with Electron Impact (EI), 70eV). GC-LRMS: Performed on GC-MS (EI, 70 eV) with single quadrupole. FT-IR: Recorded as thin films between KBr plates.

(2) General procedure for the synthesis of oxazolines (1a-1j):[20]

To a solution of corresponding aldehyde (5 mmol) in *tert*-butyl alcohol (25 mL), aminoethanol (5.5 mmol) was added. The reaction mixture was stirred for 30 min at room temperature under argon atmosphere, then K_2CO_3 (15 mmol) and I_2 (10 mmol) were added to the reaction mixture and stirred at 70 °C. After 18 h, the reaction mixture was quenched with saturated $Na_2S_2O_3$ until the iodine-colour almost disappeared and the mixture was then extracted with EtOAc. Upon drying over anhydrous Na_2SO_4, the solvent was removed under reduced pressure and the resulting residue was purified by silica gel flash column chromatography.

2.1. 2-(o-tolyl)-4,5-dihydrooxazole (1a):

Yield: 61% (491 mg); Physical appearance: Yellow oil; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data matched well with those reported in the literature.[16d]

2.2. 2-(*p*-tolyl)-4,5-dihydrooxazole (1b):

Yield: 65% (524 mg); Physical appearance: Off-white solid; TLC R_f 0.4 (3:1, Petroleum ether:EtOAc). Spectral data matched well with those reported in the literature.[20]

2.3. 2-phenyl-4,5-dihydrooxazole (1c):

Yield: 68% (472 mg); Physical appearance: Yellow oil; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[20]

2.4. 2-(4-methoxyphenyl)-4,5-dihydrooxazole (1d):

Yield: 70% (620 mg); Physical appearance: Off-white solid; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[20]

2.5. 2-(4-bromophenyl)-4,5-dihydrooxazole (1e):

Yield: 67% (753 mg); Physical appearance: Off-white solid; TLC R_f 0.4 (3:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[20]

2.6. 2-(naphthalen-1-yl)-4,5-dihydrooxazole (1f):

Yield: 67% (660 mg); Physical appearance: Off-white solid; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[20]

2.7. 2-(3,4-dimethoxyphenyl)-4,5-dihydrooxazole (1g):

Yield: 55% (570 mg); Physical appearance: Off-white solid; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[21]

2.8. 2-(3,4-dimethylphenyl)-4,5-dihydrooxazole (1h):

Yield: 64% (560 mg); Physical appearance: Persian-red solid; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[22]

2.9. 2-(4-isopropylphenyl)-4,5-dihydrooxazole (1i):

Yield: 67% (634 mg); Physical appearance: Off-white gel; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[20]

2.10.5,5-dimethyl-2-(o-tolyl)-4,5-dihydrooxazole (1j):

Yield: 72% (630 mg); Physical appearance: Brown gel; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 7.4 Hz, 1H), 7.23 (t, J = 7.6 Hz, 2H), 3.82 (s, 2H), 2.60 (s, 3H), 1.51 (s, 6H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 163.9, 138.5, 131.1, 130.3, 129.7, 127.9, 125.5, 83.2, 67.3, 27.4, 21.5; **IR** (KBr, cm^{-1}): 2979, 2869, 1643, 1493, 1368, 1050, 963, 780; **ESI-HRMS**: Calculated for $C_{12}H_{15}NO$ $[M+H]^+$ 190.1226, found 190.1216.

(3) General procedure for the synthesis of oxazolines (1k–1n):[21]

Step 1. To a solution of the benzoic acid (1 equiv) in dry DCM (0.3 M) at 0 ºC, oxalyl chloride (3 equiv) and DMF (few drops) were added. The reaction mixture was allowed to warm to room temperature and stirred for 3 hours under an argon atmosphere before removing the solvent under reduced pressure. The crude product was employed immediately in the next step.

Step 2. To the solution of amino ethanol (1 equiv) in methanol (0.25 M), K_2CO_3 (1.1 equiv) was added and the mixture was cooled to 0 ºC. Then, benzoyl chloride (1.1 equiv) was added and the mixture was stirred for 15 hours at room temperature. The solvent was distilled off under reduced pressure and the reaction mixture was diluted with DCM. This was washed with brine and the organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product (*N*-(2-hydroxyethyl)benzamide) was employed in the next step without the further purification.

Step 3. To a solution of DDQ (1.5 equiv) in DCM (0.2 M), PPh_3 (1.5 equiv) was added and the mixture was stirred at room temperature under argon atmosphere for 5 minutes. This was followed by the addition of *N*-(2-hydroxyethyl)benzamide (1 equiv) and the reaction mixture was stirred for 20 minutes. The color of the mixture turned yellow and precipitation occurred. The reaction mixture was washed with NaOH solution (5%) and the separated aqueous layer was extracted with DCM and the organic layer was washed with brine and the organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to afford the desired product.

3.1. 2-(m-tolyl)-4,5-dihydrooxazole (1k):

Yield: 70% (338 mg); Physical appearance: Yellow oil; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[16d]

3.2. 2-(2-chlorophenyl)-4,5-dihydrooxazole (1l):

Yield: 70% (380 mg); Physical appearance: Yellow oil; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[23]

3.3. 2-(2-bromophenyl)-4,5-dihydrooxazole (1m):

Yield: 70% (472 mg); Physical appearance: Pale-yellow clear viscous liquid; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[24a]

3.4. 2-(2-fluorophenyl)-4,5-dihydrooxazole (1n):

Yield: 61% (302 mg); Physical appearance: Pale-yellow clear viscous liquid; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[24b]

(4) Procedure for the synthesis of 2-(2-methylphenyl-6-*d*)-4,5-dihydrooxazole:[18c,25]

Step 1. In a pressure tube equipped with a stir bar, the benzoic acid (100 mg, 0.73 mmol) was dissolved in D_2O (1.5 mL) under N_2 atmosphere. The reaction mixture was degassed for 5-10 min followed by the addition of $[RuCl_2(p\text{-cym})]_2$ (9 mg, 0.015 mmol), and K_2CO_3 (100 mg, 0.73 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 85 °C and allowed to stir for 12 h. Upon cooling to room temperature, the reaction mixture was washed with $NaHCO_3$ and then acidified with 1M HCl, and extracted with DCM, and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure (crude yield, 88%). Further, the product (2-methylbenzoic-6-*d* acid) was employed in the synthesis of 2-(2-methylphenyl-6-*d*)-4,5-dihydrooxazole by using the same procedure as the general procedure **3**.

4.1. 2-(2-methylphenyl-6-*d*)-4,5-dihydrooxazole (1a'):

Yield: 85% (85 mg); Physical appearance: Yellow oil; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.34 (t, J = 7.4 Hz, 1H), 7.24 (t, J = 8.4 Hz, 2H), 4.39 – 4.33 (m, 2H), 4.09 (t, J = 9.4 Hz, 2H), 2.61 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 165.0, 138.7, 131.2, 130.5, 129.5 (t), 127.1, 125.4, 66.8, 55.4, 21.8; **IR** (KBr, cm^{-1}): 2971, 2878, 1643, 1467, 1350, 1046, 946, 773; **ESI-HRMS**: Calculated for $C_{10}H_{11}DNO$ $[M+H]^+$ 163.0976, found 163.0971.

(5) General procedure for the synthesis of the 1-phenyl-prop-2-en-1-ol (2):[26, 27]

To a solution of the aldehyde (5.0 mmol) in dry THF (0.5 M), vinyl magnesium bromide (10.0 mmol, 1.0 M in THF) was added dropwise at 0 °C. After 15 min, the reaction was allowed to warm to r.t. and stirred for additional 3 h. Then the reaction was quenched by adding saturated NH_4Cl aq. and the reaction mixture was extracted with Et_2O. The combined organic extracts were washed with brine, dried over anhydrous $NaSO_4$, filtered, concentrated and purified by silica gel flash chromatography (EtOAc/petroleum ether as eluent) to give the allylic alcohol.

5.1. 1-phenylprop-2-en-1-ol (2a):

Yield: 72% (482 mg); Physical appearance: Pale-yellow clear liquid; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[26]

5.2. 1-(*p*-tolyl)prop-2-en-1-ol (2b):

Yield: 67% (496 mg); Physical appearance: Pale-yellow oil; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[27]

5.3. 1-(4-chlorophenyl)prop-2-en-1-ol (2c):

Yield: 55% (462 mg); Physical appearance: Pale-yellow oil; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data obtained matched well with those reported in the literature.[27]

5.4. 1-(4-fluorophenyl)prop-2-en-1-ol (2d):

Yield: 50% (380 mg); Physical appearance: Pale-yellow oil; TLC R_f 0.4 (9:1, Petroleum ether:EtOAc). Spectral data matched well with those reported in the literature.[26]

5.5. 1-(3-methoxyphenyl)prop-2-en-1-ol (2e):

Yield: 61% (500 mg); Physical appearance: Yellow oil; TLC R_f 0.4 (4:1, Petroleum ether:EtOAc). Spectral data obtained were in good agreement with those reported in the literature.[26]

(6) General procedure for the ruthenium-catalyzed C-H allylation of oxazoline with allyl alcohols:

In a pressure tube equipped with a stir bar, the aryl oxazoline (0.3 mmol) and allylic alcohol (0.45 mmol) were dissolved in TFE (1.5 mL). The reaction mixture was degassed for 5-10 min followed by the addition of $[RuCl_2(p\text{-cym})]_2$ (0.015 mmol), $Cu(OAc)_2.H_2O$ (0.15 mmol), and $AgSbF_6$ (0.06 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 60 °C and allowed to stir for 6–10 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to afford the desired product.

6.1. 2-(2-cinnamyl-6-methylphenyl)-4,5-dihydrooxazole (3a):

Yield: 86% (71 mg) 80% (210 mg, 1 mmol scale); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, DMSO-d_6): δ 7.37 (d, J = 7.4 Hz, 2H), 7.30 (t, J = 7.0 Hz, 3H), 7.24 – 7.12 (m, 3H), 6.45 (d, J = 15.8 Hz, 1H), 6.31 (dt, J = 15.8, 6.8 Hz, 1H), 4.34 (t, J = 9.4 Hz, 2H), 3.99 (t, J = 9.4 Hz, 2H), 3.53 (d, J = 6.8 Hz, 2H), 2.26 (s, 3H);

^{13}C{H} NMR (126 MHz, DMSO-d_6): δ 168.0, 144.1, 142.3, 141.9, 135.8, 134.7, 134.4, 134.1, 133.8, 133.1, 132.4, 132.0, 131.1, 72.1, 60.1, 41.9, 24.5; **IR** (KBr, cm^{-1}): 2928,1660,1449,1352, 1253, 1049, 765; **ESI-HRMS:** Calculated for $C_{19}H_{20}NO$ $[M+H]^+$ 278.1539, found 278.1526.

6.2. (*E*)-2-(2-methyl-6-(3-(*p*-tolyl)allyl)phenyl)-4,5-dihydrooxazole (3b):

Yield: 65% (57 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.29 – 7.23 (m, 4H), 7.12 (t, J = 8.7 Hz, 4H), 6.43 (d, J = 15.8 Hz, 1H), 6.26 (dt, J = 15.7, 6.8 Hz, 1H), 4.37 (t, J = 9.5 Hz, 2H), 4.09 (t, J = 9.6 Hz, 2H), 3.61 (d, J = 6.8 Hz, 2H), 2.37 (s, 3H), 2.34 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.6, 139.4, 137.3, 136.8, 134.8, 130.9, 129.6, 129.2, 128.9, 128.0, 127.9, 126.9, 126.0, 67.2, 55.3, 37.4, 21.2, 19.7; **IR** (KBr, cm^{-1}): 2922,1661, 1348, 1252, 1164, 1045, 764; **ESI-HRMS:** Calculated for $C_{20}H_{22}NO$ $[M+H]^+$ 292.1696, found 292.1683.

6.3. (*E*)-2-(2-(3-(3-methoxyphenyl)allyl)-6-methylphenyl)-4,5-dihydrooxazole (3c):

Yield: 70% (60 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.28 – 7.18 (m, 2H), 7.11 (t, J = 7.2 Hz, 2H), 6.95 (d, J = 7.6 Hz, 1H), 6.89 (s, 1H), 6.78 (dd, J = 8.0, 2.4 Hz, 1H), 6.45 (d, J = 15.6, 1H), 6.37 – 6.25 (m, 1H), 4.37 (t, J = 9.2 Hz, 2H), 4.09 (t, J = 9.2 Hz, 2H), 3.81 (s, 3H), 3.62 (d, J = 6.6 Hz, 2H), 2.35 (s, 3H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 159.8, 139.1, 138.9, 137.4, 130.9, 129.6, 129.5, 129.3, 129.2, 128.8, 128.1, 127.0, 118.8, 112.8, 111.3, 67.3, 55.2, 55.3, 37.3, 19.7; **IR** (KBr, cm^{-1}): 2926,1560,1408,1333, 1258, 1049, 755; **ESI-HRMS**: Calculated for $C_{20}H_{22}NO_2$ $[M+H]^+$ 308.1645, found 308.1627.

6.4. (*E*)-2-(2-(3-(4-chlorophenyl)allyl)-6-methylphenyl)-4,5-dihydrooxazole (3d):

Yield: 74% (72 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.30 – 7.20 (m, 5H), 7.11 (d, J = 7.6 Hz, 2H), 6.38 (d, J = 15.8 Hz, 1H), 6.29 (dd, J = 15.8, 6.4 Hz, 1H), 4.36 (t, J = 9.6 Hz, 2H), 4.08 (t, J = 9.6 Hz, 2H), 3.60 (d, J = 6.4 Hz, 2H), 2.36 (s, 3H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 164.5, 138.9, 137.4, 136.0, 132.6, 129.8, 129.7, 129.6, 128.8, 128.6, 128.2, 127.3, 126.9, 67.2, 55.2, 37.3, 19.7; **IR** (KBr, cm^{-1}): 2924,1651, 1594, 1489, 1260, 1091, 749; **ESI-HRMS**: Calculated for $C_{19}H_{19}ClNO$ $[M+H]^+$ 312.1150, found 312.1145.

6.5. (*E*)-2-(2-(3-(4-fluorophenyl)allyl)-6-methylphenyl)-4,5-dihydrooxazole (3e):

Yield: 62% (55 mg); Physical appearance: brownish-yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 7.35 – 7.24 (m, 3H), 7.16 – 7.10 (m, 2H), 7.03 –

6.96 (m, 2H), 6.41 (d, J = 15.8 Hz, 1H), 6.28 – 6.19 (m, 1H), 4.38 (t, J = 9.4 Hz, 2H), 4.10 (t, J = 9.4 Hz, 2H), 3.60 (d, J = 6.8 Hz, 2H), 2.37 (s, 3H); **^{13}C{H} NMR (**100 MHz, $CDCl_3$): δ 162.0 (J = 246.0 Hz), 138.3 (J = 171.1 Hz), 133.7 (J = 3.3 Hz), 129.8, 129.6, 128.8, 128.8 (J = 2.2 Hz), 128.2, 127.6, 127.5, 126.9, 115.5, 115.2, 67.2, 55.3, 37.3, 19.7; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –115.0; **IR** (KBr, cm^{-1}): 2924, 1659, 1508, 1275, 1157, 937, 750; **ESI-HRMS**: Calculated for $C_{19}H_{19}FNO$ $[M+H]^+$ 296.1445, found 296.1473.

6.6. 2-(2-allyl-6-methylphenyl)-4,5-dihydrooxazole (3f):

Yield: 61% (39 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.34 – 7.18 (m, 1H), 7.08 (d, J = 7.4 Hz, 2H), 6.03 – 5.83 (m, 1H), 5.09 – 5.00 (m, 2H), 4.40 (t, J = 9.4 Hz, 2H), 4.09 (t, J = 9.4 Hz, 2H), 3.44 (d, J = 6.6 Hz, 2H), 2.34 (s, 3H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 164.5, 139.1, 137.3, 137.2, 129.5, 128.7, 127.9, 126.7, 115.7, 67.1, 55.2, 38.1, 19.7; **IR** (KBr, cm^{-1}): 2925, 1662, 1464, 1348, 1251, 1045, 770; **ESI-HRMS**: Calculated for $C_{13}H_{16}NO$ $[M+H]^+$ 202.1226, found 202.1203.

6.7. 2-(2-(but-2-en-1-yl)-6-methylphenyl)-4,5-dihydrooxazole (*E*:*Z*: 1.1:1) (3g):

Yield: 58% (38 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.28 – 7.20 (m, 2H), 7.12 – 7.06 (m, 4H), 5.65 – 5.42 (m, 4H), 4.52 – 4.31 (m, 4H), 4.20 – 4.00 (m, 4H), 3.46 (d, J = 6.4 Hz, 2H), 3.38 (d, J = 6.2 Hz, 2H), 2.35 (s, 6H), 1.75 – 1.63 (m, 6H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.7, 164.6, 140.2, 140.1, 137.2, 137.1, 129.7, 129.5, 129.5, 128.9, 128.7, 128.6, 127.7, 127.7, 126.6, 126.4, 126.3, 124.7, 67.2, 67.1, 55.3, 55.2, 36.9, 31.0, 19.7, 18.0, 12.9; **IR** (KBr, cm^{-1}): 2925, 1662, 1464, 1348, 1251, 1045, 770; **ESI-HRMS**: Calculated for $C_{14}H_{18}NO$ $[M+H]^+$ 216.1383, found 216.1376.

6.8. 2-(2-methyl-6-(pent-2-en-1-yl)phenyl)-4,5-dihydrooxazole (*E*:*Z*: 1.2:1) (3h):

Yield: 55% (42 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.23 (m, 3H), 7.11 – 7.02 (m, 4H), 5.59 – 5.42 (m, 4H), 4.49 – 4.34 (m, 4H), 4.09 (t, J = 9.4 Hz, 4H), 3.52 – 3.31 (m, 4H), 2.33 (s, 6H), 2.22 – 1.97 (m, 4H), 1.08 – 0.92 (m, 6H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.7, 164.6, 140.2, 140.1, 137.2, 137.1, 133.6, 132.5, 129.6, 129.5, 128.7, 128.6, 127.7, 127.6, 127.5, 127.3, 126.6, 126.4, 67.2, 67.1, 55.3, 36.9, 31.2, 25.6, 20.6, 19.7, 14.3, 13.8; **IR** (KBr, cm^{-1}): 2962, 1661, 1463, 1098, 971, 765; **ESI-HRMS**: Calculated for $C_{15}H_{20}NO$ $[M+H]^+$ 230.1539, found 230.1527.

6.9. 2-(2-chloro-6-cinnamylphenyl)-4,5-dihydrooxazole (3i):

Yield: 59% (52 mg); Physical appearance: Yellow solid; M.p. 70 – 76 ºC; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 7.5 Hz, 2H), 7.33 – 7.27 (m, 4H), 7.21 (d, *J* = 6.2 Hz, 2H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.33 – 6.22 (m, 1H), 4.40 (t, *J* = 9.5 Hz, 2H), 4.11 (t, *J* = 9.5 Hz, 2H), 3.62 (d, *J* = 6.6 Hz, 2H);**^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 162.5, 141.6, 137.2, 133.7, 131.7, 130.7, 128.8, 128.5, 127.9, 127.8, 127.5, 127.3, 126.2, 67.7, 55.3, 37.3; **IR** (KBr, cm^{-1}): 2918, 1590, 1437, 1261, 1042, 749; **ESI-HRMS**: Calculated for $C_{18}H_{17}ClNO$ $[M+H]^+$ 298.0993, found 298.0971.

6.102-(2-cinnamyl-6-fluorophenyl)-4,5-dihydrooxazole(3j):

Yield: 55% (44 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether: Acetone); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.40 – 7.27 (m, 6H), 7.27 – 7.20 (m, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.30 (dd, *J* = 15.8, 6.6 Hz, 1H), 4.41 (t, *J* = 9.6 Hz, 2H), 4.11 (t, *J* = 9.6 Hz, 2H), 3.71 (d, *J* = 6.6 Hz, 2H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 161.1 (*J* = 250.6 Hz), 160.6, 142.1, 137.3, 131.62, 131.32 (*J* = 9.0 Hz), 128.5, 128.0, 127.3, 126.1, 125.3 (*J* = 3.2 Hz), 117.3 (*J* = 15.2 Hz), 113.7 (*J* = 21.6 Hz), 67.5, 55.3, 36.9; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –113.2; **IR** (KBr, cm^{-1}): 2905, 1666, 1578, 1463, 1253, 1088, 969, 744; **ESI-HRMS**: Calculated for $C_{18}H_{17}FNO$ $[M+H]^+$ 282.1289 found 282.1310.

6.11. (*E*)-2-(2-bromo-6-(3-(4-fluorophenyl)allyl)phenyl)-4,5-dihydrooxazole (3k):

Yield: 52% (56 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.51 (dd, *J* = 6.6, 2.5 Hz, 1H), 7.35 – 7.28 (m, 3H), 7.25 – 7.20 (m, 1H), 7.03 – 6.96 (m, 2H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.21 (dt, *J* = 15.8, 6.8 Hz, 1H), 4.46 – 4.38 (t, *J* = 9.6 Hz, 2H), 4.12 (t, *J* = 9.6 Hz, 2H), 3.64 – 3.58 (d, *J* = 6.8 Hz, 2H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 162.2 (*J* = 246.4 Hz), 141.6, 133.4 (*J* = 3.4 Hz), 131.0, 130.8, 130.5,128.4, 127.8, 127.7, 127.7, 127.6 (*J* = 8.0 Hz), 122.8, 115.4 (*J* = 21.6 Hz), 67.7, 55.4, 37.4; **^{19}F NMR** (376 MHz, $CDCl_3$): δ –115.0; **IR** (KBr, cm^{-1}): 258, 1651, 1507, 1260, 1227, 1042, 764; **ESI-HRMS**: Calculated for $C_{18}H_{16}BrFNO$ $[M+H]^+$ 360.0394, found 360.0409.

6.12. 2-(2-cinnamylnaphthalen-1-yl)-4,5-dihydrooxazole (3l):

Yield: 73% (68 mg); Physical appearance: Brown gel; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.3 Hz, 1H), 7.86 (dd, *J* = 13.7, 8.2 Hz, 2H), 7.56 – 7.43 (m, 3H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.33 – 7.27 (m, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.40 (dt, *J* = 15.8, 6.6 Hz, 1H), 4.54 (t, *J* = 9.6 Hz, 2H), 4.26 (t, *J*

= 9.6 Hz, 2H), 3.80 (d, *J* = 6.6 Hz, 2H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 164.1, 137.5, 137.4, 132.1, 131.8, 131.3, 130.1, 128.8, 128.5, 128.0, 127.6, 127.2, 126.9, 126.2, 125.7, 125.4, 125.1, 67.4, 55.6, 37.7; **IR** (KBr, cm^{-1}): 2931, 1656, 1531, 1318, 1208, 1010, 756; **ESI-HRMS**: Calculated for $C_{22}H_{20}NO$ $[M+H]^+$ 314.1539, found 314.1537.

6.13. (*E*)-2-(2-(3-(3-methoxyphenyl)allyl)naphthalen-1-yl)-4,5-dihydrooxazole (3m):

Yield: 65% (67 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 7.96 (d, *J* = 8.2 Hz, 1H), 7.86 (dd, *J* = 13.8, 8.2 Hz, 2H), 7.50 (m, 3H), 7.22 (t, *J* = 7.8 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 6.91 (s, 1H), 6.78 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.50 (d, *J* = 15.8 Hz, 1H), 6.39 (dt, *J* = 15.8, 6.6 Hz, 1H), 4.54 (t, *J* = 9.6 Hz, 2H), 4.26 (t, *J* = 9.6 Hz, 2H), 3.81 (s, 3H), 3.79 (s,2H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.0, 159.8, 138.9, 137.5, 132.1, 131.8, 131.2, 130.1, 129.5, 129.1, 128.0, 127.6, 126.9, 125.7, 125.4, 125.1, 118.9, 113.0, 111.3, 67.5, 55.5, 37.7, 29.7; **IR** (KBr, cm^{-1}): 2920, 2850, 2358, 1727, 1614, 1496, 1278, 1031, 790; **ESI-HRMS**: Calculated for $C_{23}H_{22}NO_2$ $[M+H]^+$ 344.1645, found 344.1622.

6.14. 2-(2-cinnamyl-6-methylphenyl)-5,5-dimethyl-4,5-dihydrooxazole (3n):

Yield: 73% (68 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 7.39 – 7.34 (m, 2H), 7.33 – 7.27 (m, 3H), 7.25 – 7.18 (m, 1H), 7.16 – 7.07 (m, 2H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.36 (dt, *J* = 15.8, 6.4 Hz, 1H), 3.85 (s, 2H), 3.64 (d, *J* = 6.4 Hz, 2H), 2.39 (s, 3H), 1.51 (s, 6H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 163.0, 139.1, 137.5, 137.2, 131.1, 129.5, 129.2, 129.8, 128.5, 128.1, 127.0, 126.9, 126.2, 83.7, 67.3, 36.9, 27.6, 19.7; **IR** (KBr, cm^{-1}): 2924, 1708, 1597, 1377, 1275, 1054, 764; **ESI-HRMS**: Calculated for $C_{21}H_{24}NO$ $[M+H]^+$ 306.1852, found 306.1826.

6.15. 2-(2-cinnamyl-5-methylphenyl)-4,5-dihydrooxazole (3o):

Yield: 40% (34 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 7.66 (s, 1H), 7.37 (d, *J* = 7.0 Hz, 2H), 7.30 (t, *J* = 6.9 Hz, 2H), 7.24 – 7.18 (m, 3H), 6.47 – 6.33 (m, 2H), 4.41 (t, *J* = 9.6 Hz, 2H), 4.09 (t, *J* = 9.6 Hz, 2H), 3.92 (d, *J* = 5.8 Hz, 2H), 2.37 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 165.1, 137.8, 137.4, 135.8, 131.6, 130.7, 130.6, 130.5, 129.7, 128.5, 126.9, 126.1, 67.1, 55.3, 37.2, 20.9; **IR** (KBr, cm^{-1}): 2910, 1675, 1551, 1368, 1150, 775; **ESI-HRMS**: Calculated for $C_{19}H_{20}NO$ $[M+H]^+$ 278.1539, found 278.1537.

6.16. 2-(2-cinnamyl-4-methylphenyl)-4,5-dihydrooxazole (3p):

Yield: 35% (30 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, J = 7.8 Hz, 1H), 7.41 – 7.30 (m, 4H), 7.25 – 7.18 (m, 1H), 7.16 – 7.06 (m, 2H), 6.51 – 6.31 (m, 2H), 4.48 – 4.27 (m, 2H), 4.10 (t, J = 9.4 Hz, 2H), 3.94 (d, J = 5.9 Hz, 2H), 2.37 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 166.8, 141.0, 140.4, 133.4, 137.7, 131.2, 130.8, 130.1, 129.6, 128.5, 126.9, 126.3, 126.1, 124.2, 66.9, 55.2, 37.6, 21.4; **IR** (KBr, cm^{-1}): 2917, 1597, 1399, 1274, 1044, 749; **APCI-HRMS**: Calculated for $C_{19}H_{20}NO$ [M+H]+ 278.1539, found 278.1545.

6.18. 2-(2-cinnamyl-4-methoxyphenyl)-4,5-dihydrooxazole (3q):

Yield: 28% (25 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.8 Hz, 1H), 7.38 – 7.30 (m, 4H), 7.25 – 7.18 (m, 1H), 6.86 (d, J = 2.6 Hz, 1H), 6.80 (dd, J = 8.8, 2.6 Hz, 1H), 6.50 – 6.34 (m, 2H), 4.38 (t, J = 9.4 Hz, 2H), 4.08 (d, J = 9.4 Hz, 2H), 4.01 – 3.96 (d, J = 6.2 Hz, 2H), 3.84 (s, 3H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 164.5, 161.3, 142.8, 137.7, 131.9, 131.0, 129.2, 128.4, 126.9, 126.1, 119.5, 116.0, 111.2, 66.7, 55.3, 55.2, 37.8; **IR** (KBr, cm^{-1}): 2929, 1719, 1604, 1496, 1151, 1031, 744; **ESI-HRMS**: Calculated for $C_{19}H_{20}NO_2$ $[M+H]^+$ 294.1489, found 294.1497.

6.9(*E*)-2-(2-methyl-6-(3-phenylallyl-3-*d*)phenyl)-4,5-dihydrooxazole(3a'):

Yield: 85% (69 mg); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44 – 7.19 (m, 6H), 7.13 (t, J = 8.2 Hz, 2H), 6.33 (t, J = 6.4 Hz, 1H), 4.38 (t, J = 9.6 Hz, 2H), 4.10 (t, J = 9.6 Hz, 2H), 3.63 (d, J = 6.4 Hz, 2H), 2.38 (s, 3H); **^{13}C{H} NMR (**126 MHz, $CDCl_3$): δ 139.2, 137.5, 137.4, 129.6, 128.9, 128.9, 128.8, 128.5, 128.3, 128.1, 127.1, 126.9, 126.1, 67.2, 55.3, 37.3, 19.7; **IR** (KBr, cm^{-1}): 2931, 1723, 1643,1316, 1236, 1053, 780; **ESI-HRMS**: Calculated for $C_{19}H_{19}DNO$ $[M+H]^+$ 279.1602, found 279.1595.

(7) General procedure for the ruthenium-catalyzed synthesis of isochromanones:

In a pressure tube equipped with a stir bar, the oxazoline (0.3 mmol) and allylic alcohol (0.45 mmol) were dissolved in 1.5 mL of MeOH. The reaction mixture was degassed for 5-10 min followed by the addition of $[RuCl_2(p\text{-cym})]_2$ (0.015 mmol), $Cu(OAc)_2.H_2O$ (0.45 mmol), and KOAc (0.3 mmol). The tube was fitted with a Teflon screw cap under an argon flow, and the reaction mixture was heated to 85 °C and allowed to stir for 12 – 16 h. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate and washed with brine and the

organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by a silica gel flash column chromatography to yield the desired product.

7.1. 6-methyl-4-methyleneisochroman-1-one (4a):

Yield: 60% (36 mg); Physical appearance: Yellow solid; M.p. 114 – 116 °C; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (500 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.34 – 7.30 (m, 1H), 5.74 (d, J = 1.0 Hz, 1H), 5.41 (t, J = 1.4 Hz, 1H), 5.00 (t, J = 1.2 Hz, 2H), 2.48 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.7, 144.9, 136.8, 135.4, 130.6, 130.4, 123.6, 121.1, 113.3, 71.4, 21.9; **IR** (KBr, cm^{-1}): 2919, 1642, 1271, 1120, 950, 748; **ESI-HRMS:** Calculated for $C_{11}H_{11}O_2$ $[M+H]^+$ 175.0754, found 175.0746.

7.2. 6-methoxy-4-methyleneisochroman-1-one (4b):

Yield: 55% (32 mg); Physical appearance: Off-white solid; M.p. 60 – 62 °C; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (d, J = 8.6 Hz, 1H), 7.01 – 6.92 (m, 2H), 5.67 (s, 1H), 5.36 (s, 1H), 4.93 (s, 2H), 3.87 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.5, 164.0, 138.9, 135.5, 132.9, 116.5, 115.7, 113.7, 107.4, 71.2, 55.7; **IR** (KBr, cm^{-1}): 2918, 1714, 1601, 1316, 1250, 1070, 765; **ESI-HRMS**: Calculated for $C_{11}H_{11}O_3$ $[M+H]^+$ 191.0703, found 191.0684.

7.3.4-methyleneisochroman-1-one (4c):

Yield: 43% (21 mg) 40% (64 mg, 1 mmol scale); Physical appearance: Yellow oil; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR**(400 MHz, $CDCl_3$): δ 8.11 (d, J = 7.8 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.49 – 7.42 (m, 1H), 5.70 (s, 1H), 5.38 (s, 1H), 4.97 (s, 2H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.5, 136.9, 135.2, 133.9, 130.5, 129.4, 123.7, 123.3, 113.7, 71.3; **IR** (KBr, cm^{-1}): 2361, 1719, 1275, 1094, 764; **ESI-HRMS**: Calculated for $C_{10}H_9O_2$ $[M+H]^+$ 161.0597, found 161.0593.

7.4. 6-isopropyl-4-methyleneisochroman-1-one (4d):

Yield: 40% (25 mg); Physical appearance: Pale-yellow gel; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02 (d, J = 8.0 Hz, 1H), 7.40 (s, 1H), 7.35 – 7.28 (m, 1H), 5.70 (s, 1H), 5.36 (s, 1H), 4.95 (s, 2H), 3.04 – 2.89 (m, 1H), 1.26 (d, J = 7.0 Hz, 6H); **^{13}C{H} NMR** (100 MHz, $CDCl_3$): δ 164.6, 155.6, 137.0, 135.6, 130.7, 127.9, 121.5, 121.0, 113.2, 71.4, 34.5, 29.7, 23.6; **IR** (KBr, cm^{-1}): 2918, 1678, 1285, 1122, 955, 745; **ESI-HRMS**: Calculated for $C_{13}H_{15}O_2$ $[M+H]^+$ 203.1067, found 203.1040.

7.5. 6-bromo-4-methyleneisochroman-1-one (4e):

Yield: 12% (10 mg); Physical appearance: White solid; M.p. 102 – 104 °C; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 1.8 Hz, 1H), 7.58 (dd, J = 8.4, 1.8 Hz, 1H), 5.72 (s, 1H), 5.44 (s, 1H), 4.96 (s, 2H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 163.8, 138.4, 134.1, 132.7, 132.2, 129.2, 126.4, 122.5, 115.0, 71.2; **IR** (KBr, cm^{-1}): 2359, 1728, 1589, 1262, 1118, 1085; **ESI-HRMS**: Calculated for $C_{10}H_8BrO_2$ $[M+H]^+$ 240. 9682 and 238.9702, found 240.9663 and 238.9682.

7.6. 6,7-dimethyl-4-methyleneisochroman-1-one (4f):

Yield: 61% (34mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.38 (s, 1H), 5.68 (s, 1H), 5.34 (s, 1H), 4.98 (s, 2H), 2.38 (s, 3H), 2.34 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.9, 143.8, 138.6, 135.3, 134.6, 131.1, 124.2, 121.2, 112.2, 71.5, 20.3, 19.6; **IR** (KBr, cm^{-1}): 2917, 1716, 1613, 1317, 1164, 1046, 751; **ESI-HRMS**: Calculated for $C_{12}H_{13}O_2$ $[M+H]^+$ 189.0910, found 189.0897.

7.7. 7-methyl-4-methyleneisochroman-1-one (4g):

Yield: 58% (46 mg); Physical appearance: Yellow gel; TLC R_f 0.3 (9:1, Petroleum ether:Acetone); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 5.69 (s, 1H), 5.36 (s, 1H), 4.99 (s, 2H), 2.43 (s, 3H); **^{13}C{H} NMR** (126 MHz, $CDCl_3$): δ 164.8, 139.7, 135.1, 134.9, 134.3, 130.6, 123.4, 123.2, 112.6, 71.4, 21.2; **IR** (KBr, cm^{-1}): 2920, 1727, 1614, 1418, 1278, 1031, 790; **ESI-HRMS**: Calculated for $C_{11}H_{10}O_2Na$ $[M+Na]^+$ 197.0573, found 197.0562.

7.8. 6,7-dimethoxy-4-methyleneisochroman-1-one (4h):

Yield: 47% (32 mg); Physical appearance: White solid; M.p. 110 – 116 °C; TLC R_f 0.3 (9:1, Petroleum ether:EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.51 (s, 1H), 6.94 (s, 1H), 5.56 (s, 1H), 5.28 (s, 1H), 4.93 (s, 2H), 3.95 (s, 3H), 3.90 (s, 3H); **^{13}C{H} NMR**(126 MHz, $CDCl_3$): δ 164.6, 154.0, 150.2, 135.2, 131.4, 116.5, 111.7, 111.4, 104.7, 71.5, 56.25, 56.2; **IR** (KBr, cm^{-1}): 2918, 1726, 1615, 1316, 1248, 1092, 760; **ESI-HRMS**: Calculated for $C_{12}H_{13}O_4$ $[M+H]^+$ 221.0808, found 221.0819.

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Notes

The authors declare no competing financial interest.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge via the Internet at **http://pubs.acs.org**.

Copies of ^{1}H and ^{13}C spectra for all new compounds (PDF) and X-ray crystallographic data of **3i** and **4h**.

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References

1. a) McMurray, L.; O'Hara, F.; Gaunt, M. J. Recent Developments in Natural Product Synthesis Using Metal-Catalysed C–H Bond Functionalization. *Chem. Soc. Rev.* **2011**, *40*, 1885 – 1898. b) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. C–H Bond Functionalization: Emerging Synthetic Tools for Natural Products and Pharmaceuticals. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960 – 9009. c) Zhang, M.; Zhang, Y.; Jie, X.; Zhao, H.; Li, G.; Su, W. Recent Advances in Directed C–H Functionalizations Using Monodentate Nitrogen-Based Directing Groups. *Org. Chem. Front.* **2014**, *1*, 843 – 895. d) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. Mild Metal-Catalyzed C–H Activation: Examples and Concepts. *Chem. Soc. Rev.* **2016**, *45*, 2900 – 2936. e) Gandeepan, P.; Müller, T.; Zell, D.; Cera, G.; Warratz, S.; Ackermann, L. 3d Transition Metals for C–H Activation. *Chem. Rev.* **2019**, *119*, 2192 – 2452.

2. a) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. Transition Metal-Catalyzed C–H Bond Functionalizations by the Use of Diverse Directing Groups. *Org. Chem. Front.* **2015**, *2*, 1107 – 1295. b) Sambiagio, C.; Schönbauer, D.; Blieck, R.; Dao-Huy, T.; Pototschnig, G.; Schaaf, P.; Wiesinger, T.; Zia, M. F.; Wencel-Delord, J.; Besset, T.; Maes, B. U. W.; Schnürch, M. A Comprehensive Overview of Directing Groups Applied in Metal-Catalysed C–H Functionalization Chemistry. *Chem. Soc. Rev.* **2018**, *47*, 6603 – 6743. c) Das, R.; Kumar, G. S.; Kapur, M. Amides as Weak Coordinating Groups in Proximal C–H Bond Activation. *Eur. J. Org. Chem*. **2017**, 5439 – 5459.

3. a) Sundararaju, B.; Achard, M.; Bruneau, C. Transition Metal Catalyzed Nucleophilic Allylic Substitution: Activation of Allylic Alcohols via π-Allylic Species. *Chem. Soc. Rev.* **2012**, *41*, 4467 – 4483. b) Lumbroso, A.; Cooke, M. L.; Breit, B. Catalytic Asymmetric Synthesis of Allylic Alcohols and Derivatives and their Applications in Organic Synthesis. *Angew. Chem., Int. Ed.***2013**, *52*, 1890 – 1932. c) Butt, N. A.; Zhang, W. Transition Metal-Catalyzed Allylic Substitution Reactions with Unactivated Allylic Substrates. *Chem. Soc. Rev.* **2015**, *44*, 7929 – 7967.

4. a) Huang, L.; Wang, Q.; Qi, J.; Wu, X.; Huang, K.; Jiang, H. Rh(III)-Catalyzed Ortho-Oxidative Alkylation of Unactivated Arenes with Allylic Alcohols. *Chem. Sci.* **2013**, *4*, 2665 – 2669. b) Shi, Z.; Boultadakis-Arapinis, M.; Glorius, F. Rh(III)-Catalyzed Dehydrogenative Alkylation of (Hetero)arenes with Allylic Alcohols, Allowing Aldol Condensation to Indenes. *Chem. Commun*. **2013**, *49*, 6489 – 6491. c) Manoharan, R.; Jeganmohan, M. Synthesis of Isoindolinones via a Ruthenium-Catalyzed Cyclization of N-Substituted Benzamides with Allylic Alcohols. *Chem. Commun*. **2015**, *51*, 2929 – 2932. d) Han, S. H.; Choi, M.; Jeong, T.; Sharma, S.; Mishra, N. K.; Park, J.; Oh, J. S.; Kim, W. J.; Lee, J. S.; Kim, I. S. Rhodium-Catalyzed C–H Alkylation of Indolines with Allylic Alcohols: Direct Access to β-Aryl Carbonyl Compounds. *J. Org. Chem*. **2015**, *80*, 11092 – 11099.

5. a) Bai, P.; Li, Y.-Q.; Huang, Z.-Z. A Four-Component Cascade C–H Functionalization/Cyclization/Nucleophilic Substitution Reaction To Construct α-Functionalized Tetrahydroquinolines by the Strategy of in situ Directing Group Formation. *Org. Lett.* **2017**, *19*, 1374 – 1377. b) Peneau, A.; Tricart, Q.; Guillou, C.; Chabaud, L. Mild Rhodium(III)-Catalyzed Intramolecular Annulation of Benzamides with Allylic Alcohols to Access Azepinone

Derivatives. *Chem. Commun.* **2018**, *54*, 5891 – 5894. c) Yan, R.; Wang, Z.-X. Rhodium-Catalyzed Alkenyl C−H Activation and Oxidative Coupling with Allylic Alcohols. *Asian J. Org. Chem.* **2018**, *7*, 240 – 247. d) Zhang, J.; Sun, J.-S.; Xia, Y.-Q.; Dong, L. Efficient Synthesis of Functionalized Indene Derivatives via Rh(III)-Catalyzed Cascade Reaction between Oxadiazoles and Allylic Alcohols. *Adv. Synth. Catal.* **2019**, *361*, 2037 – 2041. e) Li, X.; Zhang, F.; Wu, D.; Liu, Y.; Xu, G.; Peng, Y.; Liu, Z.; Huang, Y. Rhodium(III)-catalyzed C–H Alkylation of Heterocycles with Allylic Alcohols in Water: A Reusable Catalytic System for the Synthesis of β-Aryl Ketones. *Tetrahedron* **2018**, *74*, 7364 – 7371.

6. a) Oi, S.; Tanaka, Y.; Inoue, Y. Ortho-Selective Allylation of 2-Pyridylarenes with Allyl Acetates Catalyzed by Ruthenium Complexes. *Organometallics* **2006**, *25*, 4773 – 4778. b) Fan, S.; Chen, F.; Zhang, X. Direct Palladium–Catalyzed Intermolecular Allylation of Highly Electron-Deficient Polyfluoroarenes. *Angew. Chem., Int. Ed.* **2011**, *50*, 5918 – 5923. c) Yao, T.; Hirano, K.; Satoh, T.; Miura, M. Stereospecific Copper-Catalyzed C–H Allylation of Electron–Deficient Arenes with Allyl Phosphates. *Angew. Chem., Int. Ed.* **2011**, *50*, 2990 – 2994. d) Makida, Y.; Ohmiya, H.; Sawamura, M. Regio- and Stereocontrolled Introduction of Secondary Alkyl Groups to Electron-Deficient Arenes Through Copper-Catalyzed Allylic Alkylation. *Angew. Chem., Int. Ed.* **2012**, *51*, 4122 – 4127. e) Yu, Y. B.; Fan, S.; Zhang, X. Copper- and Phosphine-Ligand-Free Palladium-Catalyzed Direct Allylation of Electron-Deficient Polyfluoroarenes with Allylic Chlorides. *Chem. –Eur. J.* **2012**, *18*, 14643 – 14648. f) Wang, H.; Schröder, N.; Glorius, F. Mild Rhodium(III)-Catalyzed Direct C–H Allylation of Arenes with Allyl Carbonates. *Angew. Chem., Int. Ed.* **2013**, *52*, 5386 – 5389. g) Feng, C.; Feng, D.; Loh, T.-P. Oxidant-Free Rh(III)-Catalyzed Direct C–H Olefination of Arenes with Allyl Acetates. *Org. Lett*. **2013**, *15*, 3670 – 3673. h) Yu, S.; Li, X. Rhodium(III)-Catalyzed C–C Coupling of Arenes with 2-Vinyloxiranes: Synthesis of Allylic Alcohols. *Org. Lett*. **2014**, *16*, 1200 – 1203.

7. a) Kuninobu, Y.; Ohta, K.; Takai, K. Rhenium-Catalyzed Allylation of C–H bonds of Benzoic and Acrylic Acids. *Chem. Commun*. **2011**, *47*, 10791 – 10793. b) Zeng, R.; Fu, C.; Ma, S. Highly Selective Mild Stepwise Allylation of N-Methoxybenzamides with Allenes. *J. Am. Chem. Soc*. **2012**, *134*, 9597 – 9600. c) Ye, B.; Cramer, N. A Tunable Class of Chiral Cp Ligands for Enantioselective Rhodium(III)-Catalyzed C–H Allylations of Benzamides. *J. Am. Chem. Soc*.

2013, *135*, 636 – 639. d) Asako, S.; Ilies, L.; Nakamura, E. Iron-Catalyzed Ortho-Allylation of Aromatic Carboxamides with Allyl Ethers. *J. Am. Chem. Soc.* **2013**, *135*, 17755 – 17757. e) Wang, H.; Beiring, B.; Yu, D.-G.; Collins, K.; Glorius, F. [3]Dendralene Synthesis: Rhodium(III)–Catalyzed Alkenyl C–H Activation and Coupling Reaction with Allenyl Carbinol Carbonate. *Angew. Chem., Int. Ed*. **2013**, *52*, 12430 – 12434. f) Asako, S.; Norinder, J.; Ilies, L.; Yoshikai, N.; Nakamura, E. Ortho-Allylation of 1-Arylpyrazoles with Allyl Phenyl Ether via Iron-Catalyzed C–H Bond Activation under Mild Conditions. *Adv. Synth. Catal.* **2014**, *356,* 1481 – 1485.

8. a) Kim, M.; Sharma, S.; Mishra, N. K.; Han, S.; Park, J.; Kim, M.; Shin, Y.; Kwak, J. H.; Han, S. H.; Kim, I. S. Direct Allylation of Aromatic and α, β-Unsaturated Carboxamides under Ruthenium Catalysis. *Chem. Commun*. **2014**, *50*, 11303 – 11306. b) Feng, C.; Feng, D.; Loh, T.-P. Rhodium(III)-catalyzed C–H Allylation of Electron-Deficient Alkenes with Allyl Acetates. *Chem. Commun.* **2015***, 51*, 342 – 345. c) Park, J; Mishra, N. K.; Sharma, S.; Han, S.; Shin, Y.; Jeong, T.; Oh, J. S.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. Mild Rh(III)-Catalyzed C7-Allylation of Indolines with Allylic Carbonates. *J. Org. Chem.* **2015**, *80*, 1818 – 1827. d) Moselage, M.; Sauermann, N.; Koeller, J.; Liu, W.; Gelman, D.; Ackermann, L. Cobalt(III)-Catalyzed Allylation with Allyl Acetates by C–H/C–O Cleavage. *Synlett* **2015**, *26*, 1596 – 1600.

9. a) Cajaraville, A.; López, S.; Varela, J. A.; Saá, C. Rh(III)-Catalyzed Tandem C–H Allylation and Oxidative Cyclization of Anilides: A New Entry to Indoles. *Org. Lett.* **2013**, *15*, 4576 – 4579. b) Kim, M.; Park, J.; Sharma, S.; Han, S.; Han, S. H.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. Synthesis and C2-Functionalization of Indoles with Allylic Acetates under Rhodium Catalysis. *Org. Biomol. Chem*. **2013**, *11*, 7427 – 7434. c) Cong, X.; Zeng, X. Iron-Catalyzed, Chelation-Induced Remote C–H Allylation of Quinolines via 8-Amido Assistance. *Org. Lett.* **2014**, *16*, 3716 – 3719. d) Mei, S.-T.; Wang, N.-J.; Ouyang, Q.; Wei, Y. Rhodium-catalysed Direct C–H Allylation of N-Sulfonyl Ketimines with Allyl Carbonates. *Chem. Commun.* **2015**, *51*, 2980 – 2983. e) Manikandan, R.; Madasamy, P.; Jeganmohan, M. Ruthenium-Catalyzed Oxidant-Free Allylation of Aromatic Ketoximes with Allylic Acetates at Room Temperature. *Chem. –Eur. J.* **2015**, *21*, 13934 – 13938. f) Debbarma, S.; Bera, S. S.; Maji, M. S. Cp*Rh(III)-Catalyzed Low Temperature C–H Allylation of N-Aryl-Trichloro Acetimidamide. *J. Org. Chem.*

2016, *81*, 11716 – 11725. g) Mishra, N. K.; Sharma, S.; Park, J.; Han, S.; Kim, I. S. Recent Advances in Catalytic C(sp^2)–H Allylation Reactions. *ACS Catal.* **2017**, *7*, 2821 – 2847.

10. a) Manikandan, R.; Jeganmohan, M. Temperature-Controlled Redox-Neutral Ruthenium(II)-Catalyzed Regioselective Allylation of Benzamides with Allylic Acetates. *Org. Biomol. Chem.* **2016**, *14*, 7691 – 7701. b) Ramachandran, K.; Anbarasan, P. Cobalt(III)-Catalyzed Allylation of Arene C–H Bonds. *Eur. J. Org. Chem.* **2017**, 3965 – 3968. c) Yan, R.; Wang, Z.-X. Ruthenium-Catalyzed C–H Allylation of Arenes with Allylic Amines. *Org. Biomol. Chem.* **2018**, *16*, 3961 – 3969. d) Trita, A. S.; Biafora, A.; Pichette Drapeau, M.; Weber, P.; Gooßen, L. J. Regiospecific Ortho- C−H Allylation of Benzoic Acids. *Angew. Chem., Int. Ed.* **2018**, *57*, 14580 – 14584. e) Hu, X.-Q.; Hu, Z.; Zhang, G.; Sivendran, N.; Gooßen, L. J. Catalytic C–N and C–H Bond Activation: *Ortho*-Allylation of Benzoic Acids with Allyl Amines. *Org. Lett.* **2018**, *20*, 4337 – 4340. f) Jambu, S.; Tamizmani, M.; Jeganmohan, M. Ruthenium(II)-Catalyzed Cyclization of Aromatic Acids with Allylic Acetates via Redox-Free Two-Fold Aromatic/Allylic C–H Activations: Combined Experimental and DFT Studies. *Org. Lett.* **2018**, *20*, 1982 – 1986. g) Raja Sk, M.; Bera, S. S.; Maji, M. S. Weakly Coordinating, Ketone-Directed Cp*Co(III)-Catalyzed C–H Allylation on Arenes and Indoles. *Org. Lett.* **2018**, *20*, 134 – 137.

11. a) Suzuki, Y.; Sun, B.; Sakata, K.; Yoshino, T.; Matsunaga, S.; Kanai, M. Dehydrative Direct C-H Allylation with Allylic Alcohols under [Cp*Co^{III}] Catalysis. *Angew. Chem., Int. Ed.* **2015**, *54*, 9944 – 9947. b) Bunno, Y.; Murakami, N.; Suzuki, Y.; Kanai, M.; Yoshino, T.; Matsunaga, S. Cp*Co^{III}-Catalyzed Dehydrative C–H Allylation of 6-Arylpurines and Aromatic Amides using Allyl Alcohols in Fluorinated Alcohols. *Org. Lett*. **2016**, *18*, 2216 – 2219.

12. Kumar, G. S.; Kapur, M. Ruthenium-Catalyzed, Site-Selective C–H Allylation of Indoles with Allyl Alcohols as Coupling Partners. *Org. Lett*. **2016**, *18*, 1112 – 1115.

13. a) Kalsi, D.; Laskar, R. A.; Barsu, N.; Premkumar, J. R.; Sundararaju, B. C-8-Selective Allylation of Quinoline: A Case Study of β-Hydride vs β-Hydroxy Elimination. *Org. Lett.* **2016**, *18*, 4198 – 4201. b) Wu, X.; Ji, H. Ruthenium(II)-Catalyzed Regio- and Stereoselective C–H Allylation of Indoles with Allyl Alcohols. *Org. Lett.* **2018**, *20*, 2224 – 2227. c) Wu, X.; Ji, H. Rhodium(III)-Catalyzed C–H Allylation of Indoles with Allyl Alcohols via β-Hydroxide Elimination. *Org. Biomol. Chem.* **2018**, *16*, 5691 – 5698. d) Hu, X.-Q.; Hu, Z.; Trita, A. S.; Zhang, G.; Goossen, L. J. Carboxylate-Directed C–H Allylation with Allyl Alcohols or Ethers.

Chem. Sci. **2018**, *9*, 5289 – 5294. e) Wu, X.; Ji, H. Ruthenium-Catalyzed C–H Allylation of Alkenes with Allyl Alcohols via C–H Bond Activation in Aqueous Solution. *J. Org. Chem.* **2018**, *83*, 12094 – 12102. f) Deng, C.; Hu, P.; Wang, Y.; Wang, S.; Zhang, W.-H. Theoretical Studies on Mechanism of Ru(II)-Catalyzed Regioselective C−H Allylation of Indoles with Allyl Alcohols. *Dalton Trans.* **2019**, *48*, 9181 – 9186.

14. a) Kobayashi, J.; Tsuda, M.; Fuse, H.; Sasaki, T.; Mikami, Y. Halishigamides A−D, New Cytotoxic Oxazole-Containing Metabolites from Okinawan Sponge Halichondria Sp. *J. Nat. Prod.* **1997**, *60*, 150 – 154. b) Giddens, A. C.; Boshoff, H. I. M.; Franzblau, S. G.; Barry, C. E.; Copp, B. R. Antimycobacterial Natural Products: Synthesis and Preliminary Biological Evaluation of the Oxazole-Containing Alkaloid Texaline. *Tetrahedron Letters* **2005**, *46*, 7355 – 7357. c) Mukai, A.; Fukai, T.; Matsumoto, Y.; Ishikawa, J.; Hoshino, Y.; Yazawa, K.; Harada, K.; Mikami, Y. Transvalencin Z, A New Antimicrobial Compound with Salicylic Acid Residue from *Nocardia Transvalensis* IFM 10065. *J. Antibiot.* **2006**, *59*, 366 – 369. d) Sasmal, S.; Sen, I.; Hall, R. G.; Pal, S. A First Synthesis of Bis(benzoxazole) Natural Products: Nataxazole and AJI9561 via Benzoxazole C–H Activation. *Synthesis* **2015**, *47*, 3711 – 3716. e) Robles, A. J.; McCowen, S.; Cai, S.; Glassman, M.; Ruiz, F.; Cichewicz, R. H.; McHardy, S. F.; Mooberry, S. L. Structure–Activity Relationships of New Natural Product-Based Diaryloxazoles with Selective Activity against Androgen Receptor-Positive Breast Cancer Cells. *J. Med. Chem.* **2017**, *60*, 9275 – 9289. f) Ke, S.; Zhang, Z.; Shi, L.; Liu, M.; Fang, W.; Zhang, Y.; Wu, Z.; Wan, Z.; Long, T.; Wang, K. An Efficient Synthesis and Bioactivity Evaluation of Oxazole-Containing Natural Hinduchelins A–D and Their Derivatives. *Org. Biomol. Chem*. **2019**, *17*, 3635 – 3639.

15. a) Chen, X.; Li, J.-J.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. Palladium-Catalyzed Alkylation of Aryl C−H Bonds with sp^3 Organotin Reagents Using Benzoquinone as a Crucial Promoter. *J. Am. Chem. Soc.* **2006**, *128*, 78 – 79. b) Ackermann, L.; Kozhushkov, S. I.; Yufit, D. S. Ruthenium-Catalyzed Hydroarylation of Methylenecyclopropanes through C−H Bond Cleavage: Scope and Mechanism. *Chem. –Eur. J.* **2012**, *18*, 12068 – 12077. c) Ogiwara, Y.; Tamura, M.; Kochi, T.; Matsuura, Y.; Chatani, N.; Kakiuchi, F. Ruthenium-Catalyzed Ortho-Selective C–H Alkenylation of Aromatic Compounds with Alkenyl Esters and Ethers. *Organometallics* **2014**, *33*, 402 – 420. d) Mei, R.; Ackermann, L. Cobalt-Catalyzed C−H Functionalizations by Imidate Assistance with Aryl and Alkyl Chlorides. *Adv. Synth. Catal.* **2016**, *358*, 2443 – 2448. e) Mei,

R.; Loup, J.; Ackermann, L. Oxazolinyl-Assisted C–H Amidation by Cobalt(III) Catalysis. *ACS Catal.* **2016**, *6*, 793 – 797.

16. a) Oi, S.; Aizawa, E.; Ogino, Y.; Inoue, Y. Ortho-Selective Direct Cross-Coupling Reaction of 2-Aryloxazolines and 2-Arylimidazolines with Aryl and Alkenyl Halides Catalyzed by Ruthenium Complexes. *J. Org. Chem.* **2005**, *70*, 3113 – 3119. b) Ackermann, L.; Althammer, A.; Born, R. Catalytic Arylation Reactions by C–H Bond Activation with Aryl Tosylates. *Angew. Chem., Int. Ed.* **2006**, *45*, 2619 – 2622. c) Ouellet, S. G.; Roy, A.; Molinaro, C.; Angelaud, R.; Marcoux, J.-F.; O'Shea, P. D.; Davies, I. W. Preparative Scale Synthesis of the Biaryl Core of Anacetrapib *via* a Ruthenium-Catalyzed Direct Arylation Reaction: Unexpected Effect of Solvent Impurity on the Arylation Reaction. *J. Org. Chem.* **2011**, *76*, 1436 – 1439. d) Maiden, T. M. M.; Swanson, S.; Procopiou, P. A.; Harrity, J. P. A. A Mild and Regioselective Route to Functionalized Quinazolines. *Chem. –Eur. J.* **2015**, *21*, 14342 – 14346. e) Maiden, T. M. M.; Swanson, S.; Procopiou, P. A.; Harrity, J. P. A. Synthesis of Functionalized Pyridines via a Regioselective Oxazoline Promoted C–H Amidation Reaction. *Org. Lett.* **2016**, *18*, 3434 – 3437. f) Liang, S.; Liu, N.-W.; Manolikakes, G. Copper-Mediated Sulfonylation of Aryl C(sp^2)–H Bonds with Sodium and Lithium Sulfinates. *Adv. Synth. Catal.* **2016**, *358*, 159 – 163. g) Wan, L.; Qiao, K.; Yuan, X.; Zheng, M.-W.; Fan, B.-B.; Di, Z. C.; Zhang, D.; Fang, Z.; Guo, K. Nickel-Catalyzed Regioselective C–H Bond Mono- and Bis-Nitration of Aryloxazolines with tert-Butyl Nitrite as Nitro Source. *Adv. Synth. Catal.* **2017**, *359*, 2596 – 2604.

17. Kumar, G. S.; Khot, N. P.; Kapur, M. Oxazolinyl-Assisted Ru(II)-Catalyzed C−H Functionalization Based on Carbene Migratory Insertion: A One-Pot Three-Component Cascade Cyclization. *Adv. Synth. Catal.* **2019**, *361*, 73 – 78.

18. a) Kumar, G. S.; Kumar, P.; Kapur, M. Traceless Directing-Group Strategy in the Ru-Catalyzed, Formal [3 + 3] Annulation of Anilines with Allyl Alcohols: A One-Pot, Domino Approach for the Synthesis of Quinolines. *Org. Lett.* **2017**, *19*, 2494 – 2497. b) Kumar, G. S.; Singh, D.; Kumar, M.; Kapur, M. Palladium-Catalyzed Aerobic Oxidative Coupling of Allylic Alcohols with Anilines in the Synthesis of Nitrogen Heterocycles. *J. Org. Chem.* **2018**, *83*, 3941-3951. c) Kumar, G. S.; Chand, T.; Singh, D.; Kapur, M. Ruthenium-Catalyzed C–H Functionalization of Benzoic Acids with Allyl Alcohols: A Controlled Reactivity Switch between C–H Alkenylation and C–H Alkylation Pathways. *Org. Lett.* **2018**, *20*, 4934 – 4937.

19. a) Crystal Structure submitted to Cambridge Cystallographic Data Centre; CCDC deposition number: CCDC 1915473 (Compound **3i**). b) Crystal Structure submitted to Cambridge Cystallographic Data Centre; CCDC deposition number: CCDC 1907941 (Compound **4h**).

20. Ishihara, M.; Togo, H. Direct Oxidative Conversion of Aldehydes and Alcohols to 2-Imidazolines and 2-Oxazolines Using Molecular Iodine. *Tetrahedron* **2007**, *63*, 1474 – 1480.

21. Wu, X.-F.; Neumann, H.; Neumann, S.; Beller, M. A General and Efficient Palladium-Catalyzed Carbonylative Synthesis of 2-Aryloxazolines and 2-Aryloxazines from Aryl Bromides. *Chem. –Eur. J.* **2012**, *18*, 13619 – 13623.

22. Oi, S.; Sato, H.; Sugawara, S.; Inoue, Y. Nitrogen-Directed Ortho-Selective Homocoupling of Aromatic Compounds Catalyzed by Ruthenium Complexes. *Org. Lett.* **2008**, *10*, 1823 – 1826.

23. Qiao, K.; Yuan, X.; Wan, L.; Zheng, M.-W.; Zhang, D.; Fan, B.-B.; Di, Z.-C.; Fang, Z.; Guo, K. Highly Efficient Synthesis of β-Nitrate Ester Carboxamides through the Ring-Opening of 2-Oxazolines. *Green Chem.* **2017**, *19*, 5789 – 5793.

24. a) Pridgen, L. N. Oxazolines. 3. Regioselective Synthesis of 2-(monosubstituted phenyl) and/or Unsymmetrically 2-(disubstituted phenyl) 2-oxazolines by Cross-Coupling Grignard reagents to (haloaryl)-2-oxazolines. *J. Org. Chem.* **1982**, 47, 4319 – 4323. b) Yu, D.; Shen, Q.; Lu, L. Selective Palladium-Catalyzed C–F Activation/Carbon–Carbon Bond Formation of Polyfluoroaryl Oxazolines. *J. Org. Chem.* **2012**, *77*, 1798 – 1804.

25. a) Winkel, A.; Wilhelm, R. New Chiral Ionic Liquids Based on Imidazolinium Salts. *Tetrahedron: Asymmetry* **2009**, *20*, 2344 – 2350. b) Xu, Q.; Li, Z.; Chen, H.A Convenient Synthesis of 2-Oxazolines and 2-Benoxazoles with PPh_3-DDQ as the Dehydrating Reagent. *Chin. J. Chem.* **2011**, *29,* 925 – 932.

26. Logan, A. W. J.; Parker, J. S.; Hallside, M. S.; Burton, J. W. Manganese(III) Acetate Mediated Oxidative Radical Cyclizations. Toward Vicinal All-Carbon Quaternary Stereocenters. *Org. Lett.* **2012**, *14*, 2940 – 2943.

27. Zheng, H.-X.; Xiao, Z.-F.; Yao, C.-Z.; Li, Q.-Q.; Ning, X.-S.; Kang, Y.-B.; Tang, Y. Transition-Metal-Free Self-Hydrogen-Transferring Allylic Isomerization. *Org. Lett.* **2015**, *17*, 6102 – 6105.