

Ligand-Promoted Rh(I)-Catalyzed C2-Selective C–H Alkenylation and Polyenylation of Imidazoles with Alkenyl Carboxylic Acids

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Abstract: The first Rh(I)-catalyzed directed decarbonylative C2–H alkenylation of imidazoles with readily available alkenyl carboxylic acids is reported. The reaction proceeds in a highly regio- and stereoselective manner, providing efficient access to C2-alkenylated imidazoles that are generally inaccessible by known C–H alkenylation methods. This transformation accommodates a wide range of alkenyl carboxylic acids, including challenging conjugated polyene carboxylic acids, and diversely decorated imidazoles with high functional group compatibility. The presence of a removable pyrimidine directing group, and the use of a bidentate phosphine ligand are pivotal to the success of the catalytic reaction. In addition to imidazoles, this process is also suitable for benzimidazoles. Importantly, the scalability as well as diversification of the products highlight the potential of this protocol in practical applications. Detailed experimental and computational studies provide important insights into the underlying reaction mechanism.

Introduction

C2-substituted imidazoles are the core motifs of diverse bioactive compounds, promising drug candidates and marketed medications. They play an important role in a broad spectrum of biological and pharmacological activities,^[1] such as antihypertension,^[10] antidepression,^[14] inhibition of SAPK2/p38^[14] and inhibition of farnesyltransferase^[11] (Figure 1). Moreover, C2-substituted imidazoles serve as key building blocks for the construction of functional molecules.^[2,3] Thus, it is not surprising that significant efforts have been made to improve access to these *N*-heterocycles over the past several decades.^[4] Nonetheless, the development of more efficient and selective strategies remains a goal within the synthetic community.^[5]

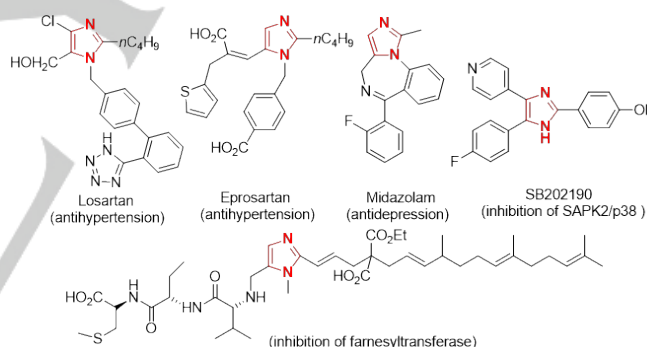
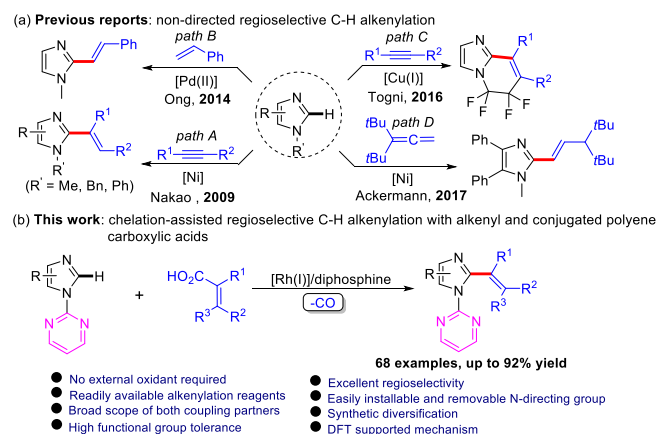


Figure 1. Selected examples of bioactive C2-substituted imidazoles

Transition-metal-catalyzed direct functionalization of unactivated C–H bonds has become a powerful tool for the synthesis and functionalization of various heterocyclic compounds in a selective and atom-economical manner.^[6] In this context, important achievements have been made in directed C–H arylation,^[7] alkylation,^[8] acylation,^[9a–c] alkynylation^[9d–f] and annulation^[10] of imidazoles at the C2 position. However, examples of C2–H olefination of imidazoles are surprisingly rare despite the potential of such products for synthetic diversification.^[11,12] The group of Nakao and Hiyama described the C2-alkenylation of *N*-substituted imidazoles with alkynes using Ni(0)/Lewis acid cooperative catalysis (Scheme 1a, path A).^[12a] The Pd(II)-catalyzed direct C2-alkenylation of *N*-methyl imidazole with styrene was reported by Ong and co-workers (Scheme 1a, path B).^[12b] Togni and co-workers presented the synthesis of fluorinated dihydroimidazopyridines from the tetrafluoroethylimidazole and alkynes under copper(II) catalysis

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(Scheme 1a, path C).^[12c] Very recently, Ackerman and co-workers reported the Ni(0)-catalyzed C2-alkenylation of 1-methyl-4,5-diphenyl-1*H*-imidazole with 1,1-di-*tert*-butylallene (Scheme 1a, path D).^[8h] Despite the encouraging progress, the substrate generality and functional group tolerance in these reactions are limited. Thus, development of a more efficient and general catalytic protocol for direct C2-olefination of imidazoles remains highly desirable.



Scheme 1. Catalytic Direct C2-H Alkenylation of Imidazoles

Intrigued by the recent success in transition-metal-catalyzed C-H alkenylation of heteroarene C-H bonds with the aid of directing groups,^[13] our group recently explored the coupling reaction of *N*-(2-pyrimidyl)imidazoles with alkenes with the idea that the 2-pyrimidyl directing group would coordinate to the metal center and facilitate C-H alkenylation at the C5 position.^[14] However, the C2-H alkenylation failed with a series of Rh(III), Ru(II) or Pd(II) catalysts that were effective in catalyzing alkenylation of various C-H bonds. We found the introduction of a C2-substituent on the imidazole scaffold enables the alkenylation at the C5 position under Rh(III) catalysis.^[14] The failure of C2-H alkenylation of imidazoles under chelation assistance was mainly ascribed to the strong coordination of the imidazole N3 atom with the metal center, which prevents the catalyst from interacting with the imidazole C2-H. In addition, since both C2-H and C5-H can be activated in the presence of *N*-directing groups, the regiocontrol of C-H activation is another concern that must be addressed in our plan for alkenylation.

The recent advances in the application of readily available, stable and structurally diverse alkenyl carboxylic acids as alkene sources for transition-metal catalyzed decarbonylative alkenylation of C-H bonds encouraged us to envision the direct C2-alkenylation of imidazoles with alkenyl carboxylic acids.^[15-17] On the basis of our previous studies on Rh(I)-catalyzed decarbonylative functionalization of (hetero)arene C-H bonds,^[17b,17d-f,h,18] herein we describe the preparation of C2-alkenylated imidazoles through a Rh(I)-catalyzed chelation-assisted decarbonylative alkenylation of *N*-(2-pyrimidyl)imidazoles with alkenyl carboxylic acids (Scheme 1b). The reaction merges C-H bond functionalization and decarbonylation of carboxylic acids while exhibiting broad scope across a wide range of alkenyl and conjugated polyenyl carboxylic acids, imidazoles and benzimidazoles. The reaction allows for the efficient synthesis of various C2-alkenylated imidazole and

benzimidazole products in high yields with excellent regioselectivity and tolerance of a diverse functionality.

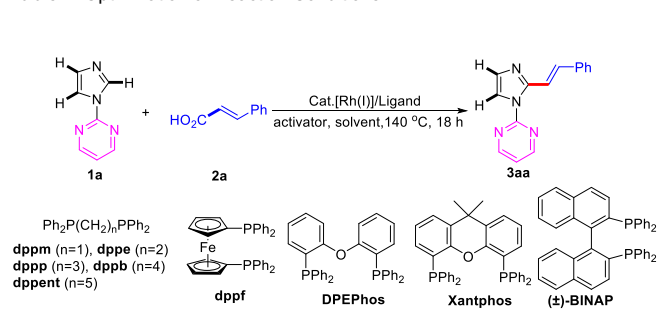
Results and Discussion

To investigate the feasibility of directed C-H alkenylation of imidazoles with alkenyl carboxylic acids we initially chose 2-(1*H*-imidazol-1-yl)pyrimidine (**1a**) and cinnamic acid (**2a**) as the model substrates. To in situ transform acid **2a** into the more reactive anhydrides, Piv₂O or Boc₂O were selected. A variety of Rh(I) complexes, known to be effective for direct C-H alkenylation of (hetero)arenes and cyclic enamines with alkenyl carboxylic acids, failed in the current C-H alkenylation of imidazoles (see the Supporting Information for details). We speculated that the strong coordinating ability of the imidazole N3 with the metal center might be responsible for the lack of reaction. Recent studies have disclosed that the use of a bidentate phosphine ligand facilitates Rh(I)-catalyzed direct C-H bond vinylation and dienylation of arenes with acrylic acid and (*E*)-penta-2,4-dienoic acid^[17i] and Pd(II)-catalyzed arylation and acylation of azole C-H bonds with aryl carboxylic acids.^[7y,19] Based on these works, we speculated that the introduction of a bidentate ligand might enable the desired vinylation reaction. We were pleased to discover that employing 1,3-bis(diphenylphosphino)propane (dppp), [Rh(CO)₂Cl]₂ as the catalyst precursor and Piv₂O as the activator resulted in the exclusive formation of **3aa** in 45% assay yield (Table 1, entry 1). ¹H NMR analysis confirmed that the alkenylation occurred at the C2-position. We next examined the performance of other bidentate phosphine ligands with different bite angles (Table 1, entries 2-9). Of these, DPEphos turned out to be the top choice (Table 1, entry 8). In contrast, catalysts bearing monodentate phosphine and bidentate nitrogen ligands did not promote this transformation (see Supporting Information, Table S4). Solvent effects were next examined (Table 1, entries 10-15). The reaction in 1,4-dioxane resulted in the highest yield and afforded **3aa** in 91% isolated yield (Table 1, entry 11). Inspection of various rhodium precursors revealed that [Rh(CO)₂Cl]₂ was more effective than other commonly employed Rh(I) species, including [Rh(COD)Cl]₂, [Rh(COD)₂]BF₄, [Rh(1,5-HD)Cl]₂ and [Rh(acac)(CO)₂] (see Supporting Information, Table S5).

Reagents to activate the carboxylic acid toward oxidative addition were next examined. Poor outcomes were obtained with other activators, such as Ac₂O, Boc₂O, (CF₃CO)₂O, (MeOCO)₂O or Tf₂O (Table 1, entries 16-20). Notably, no generation of C5-alkenylated product or C2,5-dialkenylated product were detected in the cases above. Notably, only C2-alkenylation was observed upon doubling the amount of **2a** (Table 1, entry 21), indicating the high regioselectivity in this process. Control experiments demonstrated the indispensability of [Rh(CO)₂Cl]₂ and Piv₂O in this transformation (Table 1, entries 22 and 23). Finally, the influence of the *N*-directing group on the alkenylation efficiency was examined (see Supporting Information, Table S6). It was found that the alkenylation reaction was not operative when the 2-pyrimidyl group was replaced with a Me, Ph, benzyl, Ac, Ts, Boc, Piv, Me₂NCO, Me₂NSO₂, 2-pyridyl or *t*Bu₂ groups. The free-NH imidazole also gave no reaction. These results highlight the key role of the 2-pyrimidyl moiety in this C2-H activation of imidazoles.

With the optimized conditions established (Table 1, Entry 11), we investigated the scope of imidazoles by employing cinnamic acid (**2a**) as the coupling partner. As shown in Table 2, a variety

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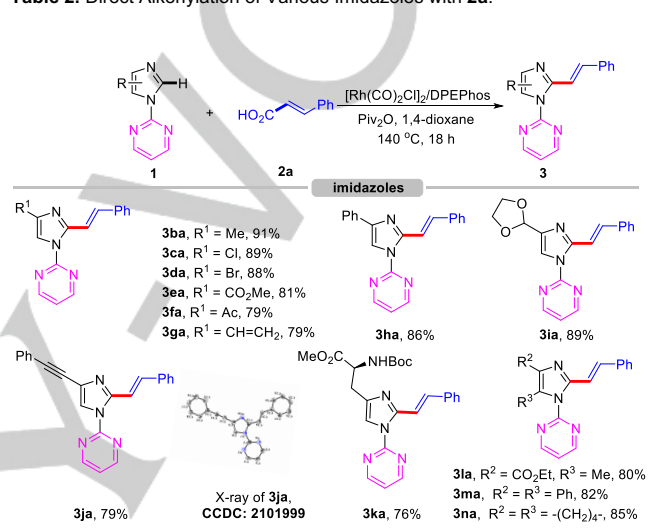
Table 1. Optimization of Reaction Conditions.^[a]

Entry	Ligand	Activator	Solvent	Yield(%) ^[b]
1	dppp	Piv ₂ O	toluene	45
2	dppm	Piv ₂ O	toluene	42
3	dppe	Piv ₂ O	toluene	26
4	dppb	Piv ₂ O	toluene	38
5	dpent	Piv ₂ O	toluene	31
6	dppf	Piv ₂ O	toluene	48
7	DPEPhos	Piv ₂ O	toluene	64
8	Xantphos	Piv ₂ O	toluene	40
9	(±)-BINAP	Piv ₂ O	toluene	25
10	DPEPhos	Piv ₂ O	PhCl	NR
11	DPEPhos	Piv ₂ O	1,4-dioxane	93 (91) ^[c]
12	DPEPhos	Piv ₂ O	THF	82
13	DPEPhos	Piv ₂ O	DMF	48
14	DPEPhos	Piv ₂ O	DMSO	50
15	DPEPhos	Piv ₂ O	MeCN	62
16	DPEPhos	Boc ₂ O	1,4-dioxane	61
17	DPEPhos	Ac ₂ O	1,4-dioxane	22
18	DPEPhos	(CF ₃ CO) ₂ O	1,4-dioxane	NR
19	DPEPhos	(MeOCO) ₂ O	1,4-dioxane	NR
20	DPEPhos	Tf ₂ O	1,4-dioxane	NR
21 ^[d]	DPEPhos	Piv ₂ O	1,4-dioxane	90
22 ^[e]	DPEPhos	Piv ₂ O	1,4-dioxane	NR
23	DPEPhos	none	1,4-dioxane	NR

[a] Reaction Conditions: **1a** (0.1 mmol), **2a** (0.12 mmol), activator (0.15 mmol, 1.5 equiv), [Rh(CO)₂Cl]₂ (2.5 mol %), Ligand (5 mol %), solvent (1.0 mL, 0.1 M), 140 °C, 18 h, N₂. NR: no reaction. [b] Yields were determined by ¹H NMR analysis of unpurified reaction mixtures with internal standard CH₂Br₂. [c] Isolated yield. [d] **2a** (0.24 mmol) was used. [e] In the absence of [Rh(CO)₂Cl]₂.

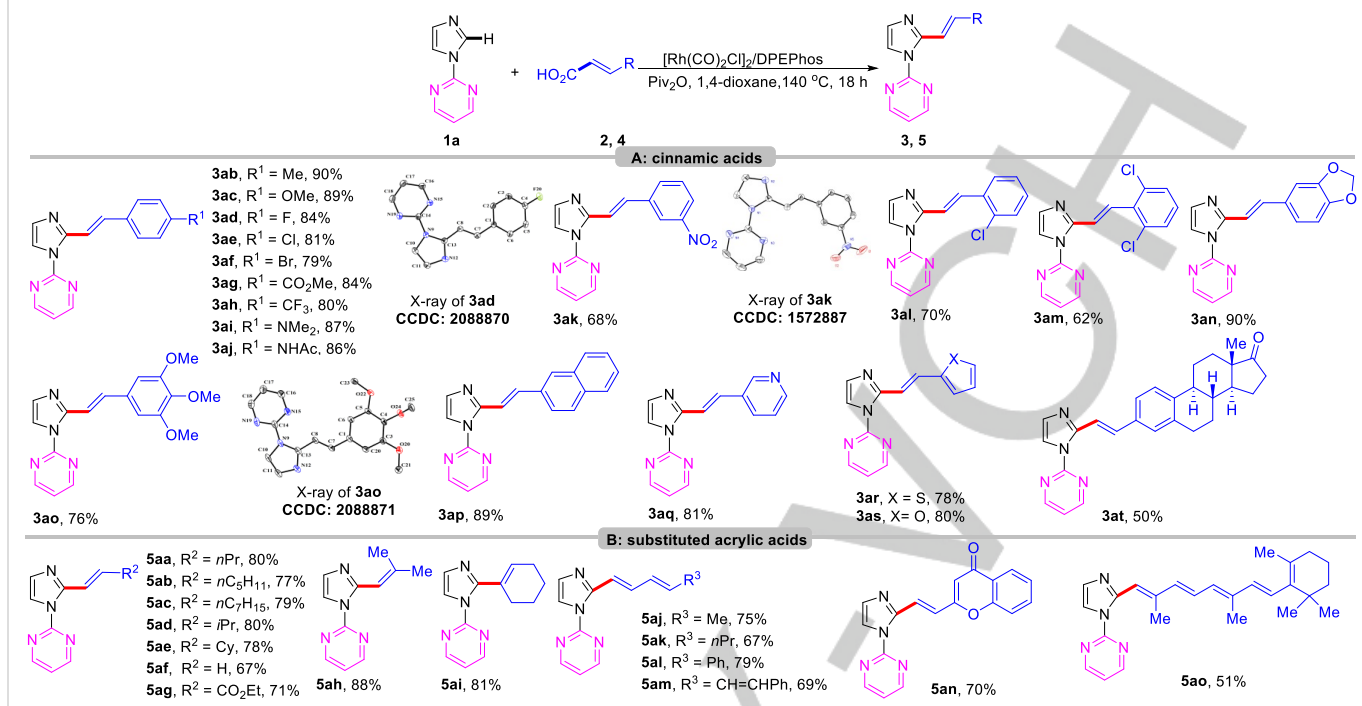
of C4-substituted imidazoles (**1b–1g**) reacted smoothly with **2a** to exclusively provide the C2-alkenylated imidazole products (**3ba–3ga**) in 79–91% yields. The electron density of the imidazole ring only minimally impacted the reaction efficiency, as evidenced by the fact that imidazoles bearing electron-deficient substituents generally gave slightly lower yields (**3ca–3fa** versus **3ba**). Valuable functional groups including, halides (**3ca** and **3da**), ester (**3ea**), ketone (**3fa**), and olefin (**3ga**), were well tolerated, thereby offering ample opportunities for further elaboration. Notably, 2-(4-phenyl-1H-imidazol-1-yl)pyrimidine (**1h**) furnished the target product (**3ha**) in 86% yield. The competing chelation-assisted C–H alkenylation at the phenyl ring was not observed. It is noteworthy that the reaction failed when the electron-deficient 1-(pyrimidin-2-yl)-1H-imidazole-4-carbaldehyde was employed. Conversion of the aldehyde into the corresponding acetal resulted

in a viable substrate that afforded product **3ia** in 89% yield. Interestingly, alkyne containing 2-(4-(phenylethynyl)-1H-imidazol-1-yl)pyrimidine (**1j**) and *L*-histidine (**1k**) were also suitable substrates, generating **3ja** and **3ka** in 79% and 76% yields, respectively. The structure of alkyne **3ja** was confirmed by single-crystal X-ray diffraction (CCDC 2101999). Furthermore, 4,5-disubstituted imidazoles (**1l–1n**) performed well in the alkenylation to generate the target products (**1la–1na**) in 80–85% yields. It should be stressed that this reaction is highly stereoselective, and the alkene products obtained have exclusively the (*E*)-configuration.

Table 2. Direct Alkenylation of Various Imidazoles with **2a**.^[a]

[a] Reaction Conditions: **1** (0.3 mmol), **2a** (0.36 mmol), [Rh(CO)₂Cl]₂ (2.5 mol %), DPEPhos (6.0 mol %), Piv₂O (0.45 mmol, 1.5 equiv), 1,4-dioxane (3.0 mL, 0.1 M), 140 °C, 18 h, N₂. Isolated yield.

The potential of our catalytic system was further examined by the coupling reactions of 2-(1H-imidazol-1-yl)pyrimidine (**1a**) with a series of substituted cinnamic acids (Table 3A). It was found that the regioselective C2-alkenylation of **1a** with cinnamic acids bearing a monosubstituted aryl ring (**2b–2l**) proceeded readily to deliver the desired products (**3ab–3al**) in 68–90% yields. These products bear a range of synthetically valuable functional groups including halides (**3ad–3af**), ester (**3ag**), tertiary amine (**3ai**) and amide (**3aj**). The cinnamic acids (**2m–2p**) bearing multi-substituted aromatic moieties worked well to give the target products (**3am–3ap**) in 62–90% yields with high functional group tolerance. The structures of **3ad**, **3ak** and **3ao** were confirmed by single-crystal X-ray diffraction (CCDC 2088870, 1572887 and 2088871, respectively). Heteroaryl groups are central to the development of biologically active compounds.^[20] We were pleased to find that heteroaryl cinnamic acids (**2q–2s**) could be applied in this reaction without difficulty to deliver products **3aq–3as** in 78–81% yields. Finally, to illustrate the potential of this method for late-stage modification of bioactive molecules, the reaction of **1a** estrone-derived cinnamic acid **2t** was examined. The target product **3at** was obtained in 50% yield.

Table 3. Direct C2-Alkenylation of **1a** with Various Acids.^[a]

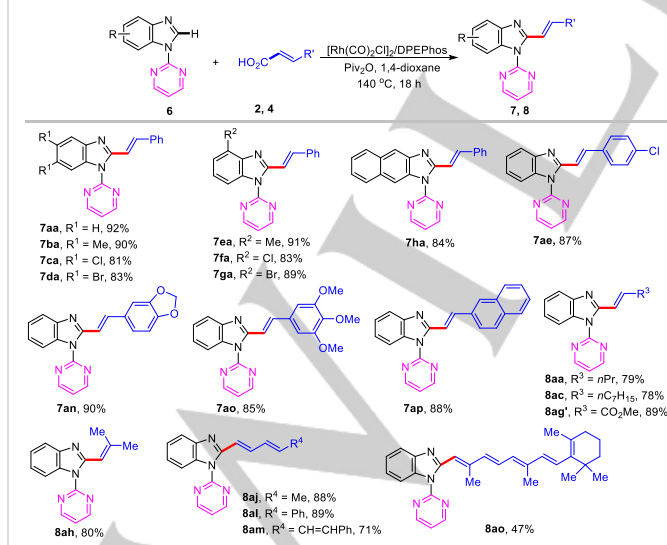
[a] Reaction Conditions: **1** (0.3 mmol), **2a** (0.36 mmol), [Rh(CO)₂Cl]₂ (2.5 mol %), DPEPhos (6.0 mol %), Piv₂O (0.45 mmol, 1.5 equiv), 1,4-dioxane (3.0 mL, 0.1 M), 140 °C, 18 h, N₂. Isolated yield.

Next, we turned our attention to substituted acrylic acids. As can be seen in Table 3B, various β -alkylated acrylic acids (**4a–4e**) reacted efficiently with **1a** to form the alkenylated products (**5aa–5ae**) in 77–80% yields, regardless of the nature of alkyl substituents. Notably, substitution of simple acrylic acid (**4f**), mono-

-ethyl fumarate (**4g**) and the trisubstituted acrylic acids (**4h** and **4i**) to **1a** afforded the corresponding products (**5af–5ai**) in 67–88% yields. However, in the case of trisubstituted alkenyl acid, 2-methyl-3,3-diphenylacrylic acid, the reaction failed (see SI, Table S7). Importantly, the current protocol could be readily extended to conjugated polyenoic acids. The conjugated dienoic and trienoic acids (**4j–4n**) performed well to provide the target products (**5aj–5an**) in 67–79% yields. The present reaction is also applicable to bioactive retinoic acid (**4o**), giving rise to the target product **5ao** in 51% yield. Given the importance of the conjugated polyene motif in organic synthesis and biologically active compounds,^[21] this method fills a gap by enabling straightforward access to imidazole-substituted conjugated polyenes.

Based on the successful vinylation of imidazoles, we wanted to explore the direct C2-alkenylation of 1-(pyrimidin-2-yl)-1H-benzo[d]imidazole derivatives. Under otherwise identical reaction conditions (Table 4), substituted benzimidazoles (**6a–6g**) reacted smoothly with **2a** to furnish the (*E*)-C2-alkenylated benzimidazole products (**7aa–7ga**) in 81–92% yields. Moreover, 1-(pyrimidin-2-yl)-1H-naphtho[2,3-*d*]imidazole (**6h**) was also readily converted to its corresponding C2-alkenylated product (**7ha**) in 84% yield. The substrate scope with regard to the alkenyl carboxylic acid was also surveyed using **6a** as the reaction partner. Gratifyingly, cinnamic acids (**2e**, **2n**, **2o** and **2p**), β -alkylated acrylic acids (**4a**, **4c** and **4h**) and conjugated polyenoic acids (**4j**, **4l**, **4m** and **4o**) all participated, resulting in the target products in 47–90% yields. It is noted that *Z*-configured monomethyl maleate **4g'** only delivered the *E*-configured product **8ag'** in 89% yield.

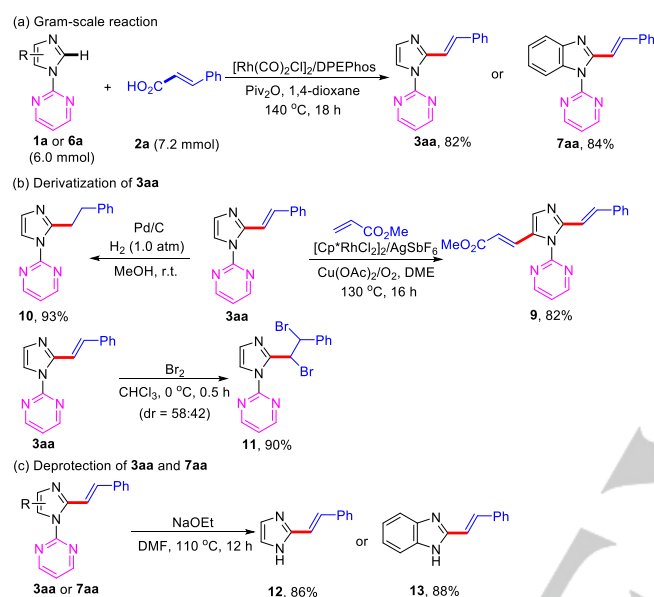
The synthetic utility of this chemistry was next explored. First, the C2-alkenylation of **1a** and **6a** with **2a** on a gram-scale afforded products **3aa** and **7aa** in 82% and 84% yields, respectively (Scheme 2a). Further studies were carried out for the

Table 4. Direct C2-Alkenylation of Benzimidazoles.^[a]

[a] Reaction Conditions: **1** (0.3 mmol), **2a** (0.36 mmol), [Rh(CO)₂Cl]₂ (2.5 mol %), DPEPhos (6.0 mol %), Piv₂O (0.45 mmol, 1.5 equiv), 1,4-dioxane (3.0 mL, 0.1 M), 140 °C, 18 h. Isolated yield.

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derivatization of alkenylation product **3aa** (Scheme 2b). The Cp^{*}Rh(III)-catalyzed direct C5–H alkenylation of **3aa** with methyl acrylate allowed the generation of the desired product **9** in 82% yield by using Cu(OAc)₂ and O₂ as co-oxidant in DME at 130 °C for 16 h.^[14] The C=C moiety of **3aa** was amenable to hydrogenation to give product **10** 93% yield while dibromination provided **11** in 90% yield (as a mixture of diastereomers). Finally, the pyrimidyl directing group in **3aa** and **7aa** could be easily removed by using NaOEt in DMSO at 110 °C to afford the free imidazole **12** and free benzimidazole **13** in 86% and 88% yields, respectively. Of note, the stereochemistry of the alkene moieties was unchanged.

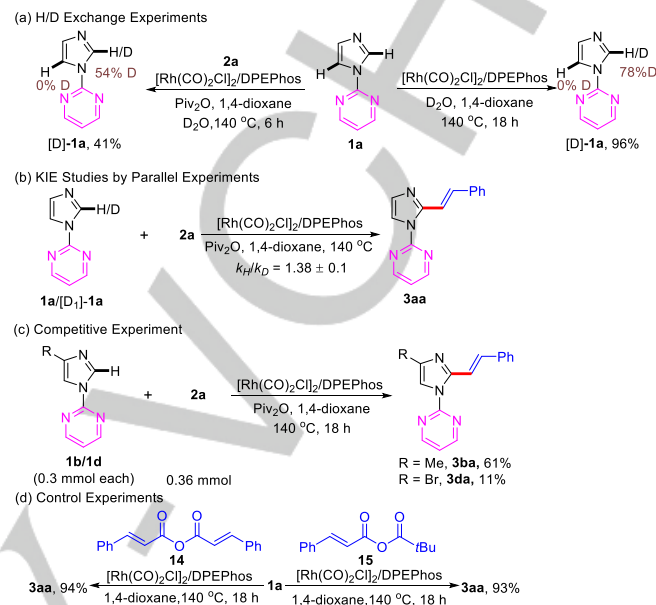


Scheme 2. Synthetic Applications.

To probe the reaction mechanism, a series of experimental investigations were performed (Scheme 3). First, H/D exchange experiments between **1a** and D₂O under the standard conditions in the presence or absence of **2a** and Piv₂O revealed the exclusive deuteration at the C2-position in each case, suggesting the reversibility of the C2–H activation step. These results are also consistent with the observed C2-selectivity in the alkenylation of **1a**. A kinetic isotope effect value of 1.38 ± 0.1 was measured from the two parallel reactions of **1a** and [D]₁-**1a** with **2a**, implying that the cleavage of the C–H bond was not involved in the turnover-limiting step of the catalytic cycle. To probe the impact of electronics of the imidazole on the C–H functionalization, an intermolecular competition experiment was performed. It was determined that the more electron-rich substrate reacted preferentially (Scheme 3c), suggesting the involvement of an electrophilic aromatic substitution type mechanism in the activation of the C–H bond.^[22]

Based on literature precedents on Rh(I)-catalyzed decarbonylative alkenylation of (hetero)arene C–H bonds with alkenyl carboxylic acids,^[17] we speculated that the current alkenylation reaction proceeds via in situ generation of anhydrides from alkenyl carboxylic acids and the Piv₂O activator. This notion was supported by high resolution mass spectrometry of the reaction mixture of **1a** and **2a** after 4 h under the standard conditions, which showed in situ formation of cinnamic anhydride

(**14**) and cinnamic pivalic anhydride (**15**) (see SI). Moreover, the coupling reactions of **1a** with independently prepared **14** or **15** and [Rh(CO)₂Cl]₂/DPEPhos led to product **3aa** in 94% and 93% yields, respectively (see SI). These results confirm that the in situ formed anhydride is indeed involved in the current transformation.



Scheme 3. Mechanistic studies.

To gain additional insight into this Rh(I)-catalyzed C2-alkenylation of imidazoles, density functional theory (DFT) calculations were carried out with **1a** as the substrate and cinnamic anhydride (**14**) as the coupling partner. [Rh(DPEPhos)Cl] (**Int1**) is the starting point of our calculations, since it is viewed as the active catalyst. Figure 2 shows the calculated free energy profile for the reaction. Initially, **1a** can bind to Rh via a pyrimidine N to produce **Int2**. Oxidative addition of the imidazole C2–H bond to Rh(I) has a barrier of 12.1 kcal/mol and generates a hexa-coordinated Rh(III)-hydride complex **Int3**. This oxidative addition process has a relatively low barrier, which can explain the reversibility of the imidazole C2–H bond activation. Furthermore, the C5–H bond activation is calculated to have a higher barrier of 14.4 kcal/mol, consistent with the observed preferential reactivity of C2–H over C5–H. The subsequent reductive elimination of HCl via transition state **TS3-4** affords a 4-coordinate Rh(I) complex **Int4**. This step has an activation free energy of 20.2 kcal/mol and an endothermicity of 13.2 kcal/mol. Next, the oxidative addition of anhydride **14** to tetra-coordinate **Int4** has a free energy barrier of 17.1 kcal/mol, leading to a hexa-coordinated acyl-Rh(III) complex **Int6**, wherein which the cinnamoyl moiety is coordinated to Rh via the carbonyl-carbon. Cinnamic acid (**2a**) can be easily displaced by chloride from HCl in **Int6** to generate a more stable acyl-Rh(III) complex **Int7** ($\Delta G = -11.5$ kcal/mol). Deinsertion of the acyl carbonyl leads to a σ -bound styryl group and the coordinated CO along with dissociation of the P atom *trans* to the cinnamoyl group (**Int8**). This step is found to have a barrier of 25.6 kcal/mol and an endothermicity of 12.3 kcal/mol. After release of CO, the phosphorus center of the DPEPhos ligand re-coordinates to the Rh center, yielding **Int9** ($\Delta G = -6.7$ kcal/mol). This sets the stage

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for C–C reductive elimination to form **Int10**, in which **3aa** is bound to Rh in an $\eta^3(\text{N,C,C})$ mode. The C–C coupling has a free energy barrier of 13.8 kcal/mol and an exothermicity of 9.0 kcal/mol. Finally, the release of **3aa** regenerates the initial catalyst **Int1**. Inspection of Figure 2 reveals that the oxidative addition of **14** (**TS₅₋₆**) is the turnover-limiting transition state (TDTS), according to the energetic span concept.^[23] As such, our computational

results suggest that C–H activation is not the turnover-limiting step, which is consistent with the measured KIE. The calculated high activation barrier (29.0 kcal/mol) matches the prolonged reaction time and high temperature required experimentally. The sequence beginning with oxidative addition of anhydride to **Int1** was also investigated, but the calculations disfavored this possibility (for details, see SI).

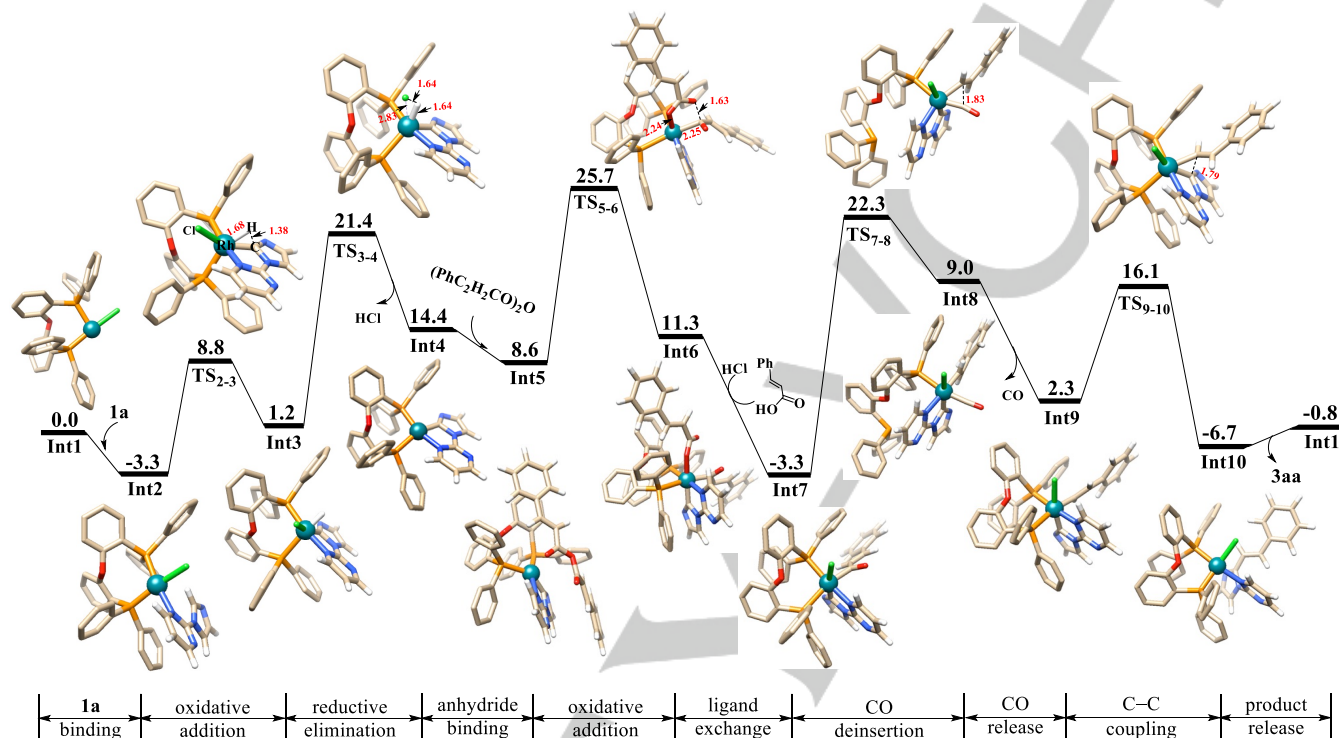
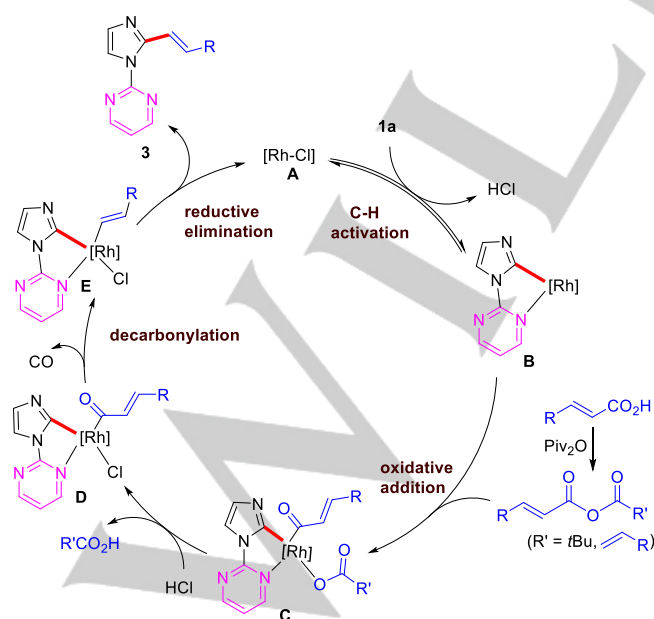


Figure 2. Gibbs free energy profile for the Rh-catalyzed decarbonylative olefination of **1a**. All energies (kcal/mol) are given at the M06-D3/def2-TZVP level in 1,4-dioxane with respect to the energy of [Rh(DPEphos)Cl]. For the sake of simplicity, the H atoms of the DPEphos ligand were omitted.



Scheme 4. Plausible Reaction Mechanism ([Rh] = Rh(DPEPhos)).

On the basis of the above experimental and computational studies, and previous published reports,^[17,18,24] a plausible mechanism is presented in Scheme 4. Initially, coordination of imidazole **1a** to the Rh(I) species **A** followed by pyrimidine-assisted C2–H bond activation affords the 5-membered rhodacycle intermediate **B**. Reaction of **B** with the in situ formed anhydride gives the intermediate **C**, which reacts with HCl to furnish the acid and intermediate **D**. **D** then undergoes decarbonylation to release CO and yield the Rh-alkenyl intermediate **E**. Finally, reductive elimination of **E** affords the product **3** with the concurrent regeneration of the Rh(I) species **A**.

Conclusions

In conclusion, we have developed the first Rh(I)-catalyzed efficient and convenient approach for direct alkenylation of imidazole C2–H bonds with readily available alkenyl carboxylic acids. The judicious choice of the *N*-directing group and bidentate phosphine ligand was crucial to realize this transformation. The reaction is tolerant of a range of substituted imidazoles and benzimidazoles. Notably, a broad scope of acrylic acids and conjugated polyenic acids delivered C2-alkenylated imidazoles and benzimidazoles with high efficiency and trans selectivity.

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Mechanistic studies suggest the reaction involves in situ generation of anhydrides and a reversible, but not turnover-limiting, C–H metalation process. Further studies on C–H functionalization of imidazoles with other carboxylic acids under Rh(I)-catalysis are ongoing in our laboratory.

Experimental Section

Detailed experimental procedures, spectral data for all compounds, copies of ^1H , ^{13}C , and ^{19}F spectra, and X-ray crystallographic analysis for compounds **3ja**, **3ad**, **3ak**, **3ao** are provided in the Supporting Information.

Deposition Numbers 2101999 (for **3ja**), 2088870 (for **3ad**), 1572887 (for **3ak**), 2088871 (for **3ao**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the Cambridge Crystallographic Data Centre <https://www.ccdc.cam.ac.uk/>.

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Conflict of Interest

The authors declare no competing financial interests.

Keywords: imidazole • rhodium • alkenyl carboxylic acid • alkenylation • C–H functionalization

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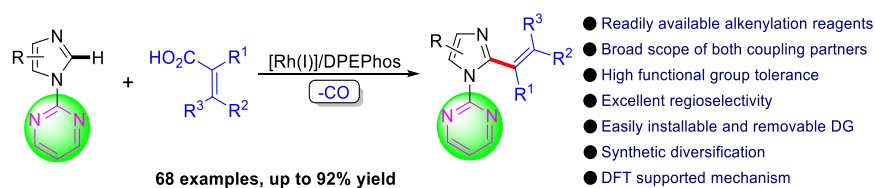
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RESEARCH ARTICLE

Entry for the Table of Contents



A Rh(I)-catalyzed C2-H alkenylation of imidazoles with alkenyl carboxylic acids with highly regio- and stereoselectivity is reported. This protocol merges C-H bond functionalization and decarbonylation of carboxylic acids, accommodates a wide range of substrates with good compatibility of functional groups, and can be easily scaled.