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Olefinic C−H Bond Addition to Aryl Aldehyde and Its *N*-Sulfonylimine *via* Rh Catalysis

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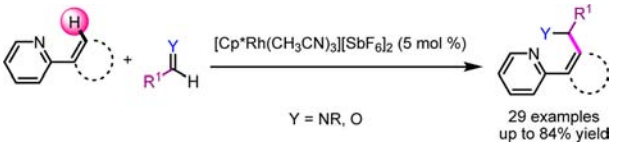
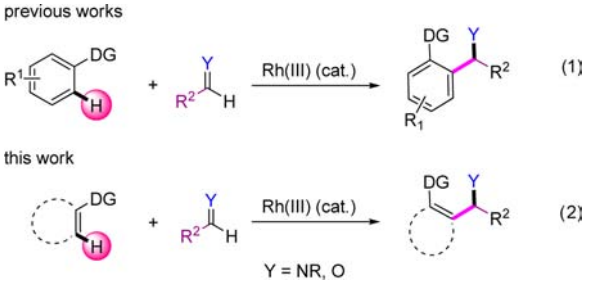
ABSTRACT



The first example of olefinic C−H addition to *N*-sulfonylaldimines and aryl aldehydes is reported. This strategy offered a concise and high atom-economic approach to vinyl amines and vinyl alcohols.

Transition-metal catalyzed C−H functionalization has been demonstrated as one of the most popular methods in



organic synthesis.[1] Although hydroarylation of alkenes and alkynes has been well developed,[2] only a few examples of C−H addition to polar multiple bonds have been reported, the overwhelming majority of which were focused on the aromatic C−H bonds.[3] In recent decades, Rh complexes played active roles in the catalysis of direct C−H transformations.[4] Recently, Ellman and Bergman's group and ours independently reported the rhodium catalyzed aryl C−H addition to imines.[5] Subsequently, Ellman and Bergman's group reported aryl and vinyl C−H addition to *N*-isocyanates.[6] Li's group and ours also extended aryl C−H addition to aryl aldehydes.[7] Inspired by these developments (eq 1), we envisioned that the addition of olefinic C−H bonds to aldimines and aldehyde via Rh catalysis with the assistance of a proper directing group. This strategy offered a concise and high atom-economic approach to allylic amines and alcohols. Containing the double bond,[8] the designed products show potential transformations. Herein, we wish to report our recent research on the first direct alkene C−H bond addition to *N*-sulfonyl aldimines and aryl aldehydes (eq 2).

We first examined the alkenyl C−H addition to imines. The olefin substrate **1a** was synthesized and selected as a model substrate. After the systematic studies we found that

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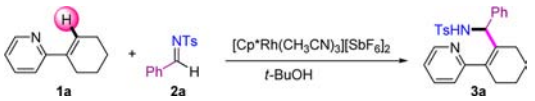
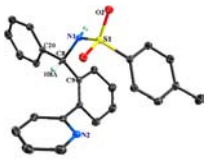
Table 1. Conditions Screening for Alkene C−H Addition to Imine[a]



1a 2a 3a

entry	catalyst (%)	additive	temp (°C)	reaction time (h)	isolated yield (%)
1[b]	10	–	90	72	62
2	5	–	110	48	65
3	5	HOAc (5 mol %)	110	48	63
4	5	HOAc (20 mol %)	110	48	62
5	5	PivOH (5 mol %)	110	48	64
6	5	PivOH (20 mol %)	110	48	69
7	5	PivOH (50 mol %)	110	48	57

[a] **1a** (0.25 mmol), **2a** (0.50 mmol) in *t*-BuOH (0.25 M) under a N_2 atmosphere in a sealed reaction tube. [b] *t*-BuOH (0.50 M). See ORTEP drawing of **3a** below. Thermal ellipsoids are drawn at 30% probability, and H-atoms are omitted for clarity.



3a

the desired addition product **3a** was obtained in 62% isolated yield in the presence of 10 mol % [Cp*Rh-$(CH_3CN)_3$][SbF_6]$_2$ as the catalyst in 72 h (Table 1, entry 1). The structure of the desired compound **3a** was confirmed by the X-ray crystallography of its single crystal. With an increase in temperature to 110 °C, a comparable yield (65%) was obtained with a lower catalyst loading (5.0 mol %) in a much shorter time (48 h) (Table 1, entry 2). Further increasing the temperature to 130 °C induced the partial decomposition of sulfonylaldimine **2a**, which resulted in a difficult separation of the desired product **3a** from the decomposed byproduct. Many other conditions were tested, and we finally found that 20 mol % of PivOH slightly promoted the efficiency (Table 1, entry 6).

With the optimized conditions, the ring size of vinyl substrates was investigated with *N*-tosyl benzaldimine **2a**. To our delight, the five-membered substrate gave an 84% isolated yield (Scheme 1, **3b**). Comparably, the seven-membered substrate gave a much lower efficiency although the catalyst loading was increased to 10 mol % (Scheme 1, **3c**). This result might be attributed to torsional effects. Unfortunately, no desired products were detected when 2-vinylpyridne, 2-(prop-1-en-2-yl)pyridine, and (*E*)-2-(prop-1-enyl)pyridine were submitted. To our delight, heterocyclic substrate **1d** was surveyed and the desired product **3d** was obtained in an acceptable yield. Moreover, various imines were investigated with **1a** as a standard substrate. The following observations were made: (1) An electron-withdrawing substituent on the phenyl group of the imine moiety is beneficial, which arises from enhancement of the electrophilicity of the corresponding *N*-tosylaldimine (**3f**, **3g**). (2) A *meta*-substituted group slightly decreases the efficiency (**3h**). In comparison with the electronic effect, the steric hindrance highly affected this transformation and the *ortho*-methyl substituted *N*-tosylaldimine only exhibited poor efficiency (Scheme 1, **3k**). (3) The heterocyclic *N*-tosylaldimine also showed credible reactivity and the desired product was obtained in an acceptable yield, keeping the heterocyclic ring untouched (Scheme 1, **3l**). (4) With Boc as the protecting group instead of the tosyl group, the desired product was obtained albeit in a much lower yield in the absence of the acid additive by using dichloromethane (DCM) as the solvent, caused by the lower stability of Boc-imine under the optimized conditions (Scheme 1, **3e**).

Next, the alkenyl C−H addition to aldehydes was investigated (Table 2). Due to the high reactivity of alkene **1b** in the above reaction, it was selected as a model substrate to perform the addition with aldehyde **4a**.[7b] Unfortunately, no desired product **5a** was detected when the reported conditions were applied (Table 2, entry 1). To

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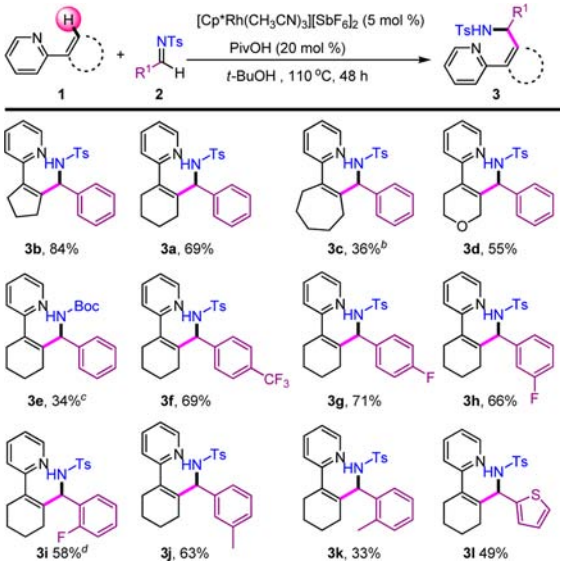
Scheme 1. Substrate Scope of Alkene C−H Addition to Imines[a]

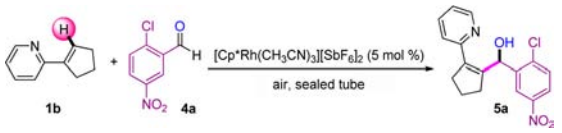


[a] **1a** (0.25 mmol), **2** (0.50 mmol) in *t*-BuOH (0.25 M) under a N_2 atmosphere in a sealed reaction tube at 110 °C for 48 h, and isolated yields were reported. [b] 10 mol % catalyst was used. [c] DCM was used as solvent. [d] ^{1}HNMR yield was reported.

our delight, a 28% ^{1}H NMR yield was observed when the reaction was conducted in DCM (Table 2, entry 2). Compared with catalyst $[Cp^*Rh(CH_3CN)_3][BF_4]_2$, the reaction gave a higher yield with $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ as the catalyst (Table 2, entry 3). When the temperature was increased from 75 to 90 °C, the yield increased correspondingly (Table 2, entry 4). Solvent screening revealed $CHCl_3$, DCE, and *t*-BuOH resulted in similar reaction efficiencies to that using DCM (Table 2, entries 5−7). Although the reaction gave a slightly lower yield using 1,1,1-trichloroethane as solvent, it was selected for the following experiments because the formation of the inseparable byproduct (2-chloro-5-nitrophenyl)methanol was inhibited (Table 2, entry 8). When the reaction temperature was increased to 120 °C, the yield improved slightly (Table 2, entry 9). Higher temperatures did not enhance the yield (Table 2, entry 10). Screening of the amount of PivOH showed that the reaction can reach a better yield (68% isolated yield, Table 2, entry 12) with 10 mol % PivOH. Notably, higher efficiency was obtained when the reaction time was reduced to 4 h (Table 2, entry 15).

Similar to the alkene C−H addition to *N*-Ts imines, the six-membered substrate exhibited a much lower efficiency (Scheme 2, **5b**, 43% yield) compared to the five-membered substrate (Scheme 2, **5a**). However, the desired product was not detected with a seven-membered ring substrate. Different aryl aldehydes were further explored with **1b** as a substrate. First, 4-nitrobenzaldehyde was used and the reaction gave a moderate yield (Scheme 2, **5c**). When a nitro group was introduced at the *m*-position, the reaction exhibited better efficiency (Scheme 2, **5d**). Other different

Table 2. Conditions Screening for Alkene C−H Addition to Aldehydes[a]



entry	solvent	temp (°C)	additive	time (h)	^{1}H NMR yield (%)
1[b]	Et_2O/MeOH (2:1)	90	H_2O (30 equiv)	48	–
2[b]	DCM	75	–	12	28
3	DCM	75	–	12	46
4	DCM	90	–	12	62
5	$CHCl_3$	90	–	12	63
6	DCE	90	–	12	63
7	*t*-BuOH	90	–	12	65
8	CCl_3CH_3	90	–	12	56
9	CCl_3CH_3	120	–	12	57 (60[c])
10	CCl_3CH_3	130	–	12	58[c]
11	CCl_3CH_3	120	PivOH (5%)	12	60
12	CCl_3CH_3	120	PivOH (10%)	12	65 (68[c])
13	CCl_3CH_3	120	PivOH (20%)	12	57
14	CCl_3CH_3	120	PivOH (10%)	8	64
15	CCl_3CH_3	120	PivOH (10%)	4	68 (73[c])
16	CCl_3CH_3	120	PivOH (10%)	2	63
17	CCl_3CH_3	120	PivOH (10%)	1	51

[a] **1b** (0.25 mmol), **4a** (0.75 mmol) in solvent (0.25 M) under an air atmosphere in a sealed reaction tube. [b] $[Cp^*Rh(CH_3CN)_3][BF_4]_2$ was used as the catalyst. [c] Isolated yield.

electron-withdrawing groups on the phenyl part of aldehyde were investigated. The reactions showed moderate efficiency with cyano (Scheme 2, **5e**), trifluoromethyl (Scheme 2, **5f**), and ester (Scheme 2, **5g**) substituents. An acceptable yield was also obtained with dibromo substituted benzaldehyde (Scheme 2, **5h**), which could undergo further transformations to diversify the product.[9] With benzaldehyde as a partner, the reaction gave a low yield (17%), accompanied by a 50% recovery of starting material alkene **1b** (Scheme 2, **5i**). Although the yield of this transformation is relatively lower, this observation is important to show the potential of the vinyl C−H addition to normal aldehyde. Based on the good reactivity of 2-chloro-5-nitrobenzaldehyde and the potential for further transformation of the nitro group, other halides were introduced to nitrobenzaldehyde at different substituted positions. When a nitro group was present on the *meta*- or *para*-position, substrates **5j** to **5p** showed good yields. Notably, in the presence of an

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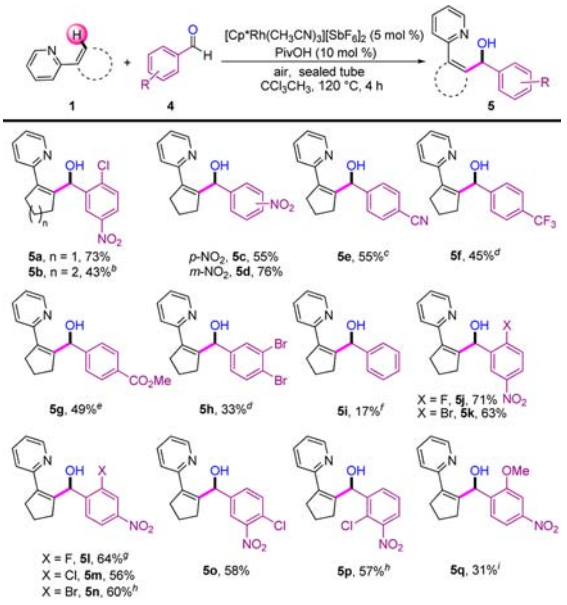
Scheme 2. Substrate Scope of Alkene C−H Addition to Aldehydes[a]

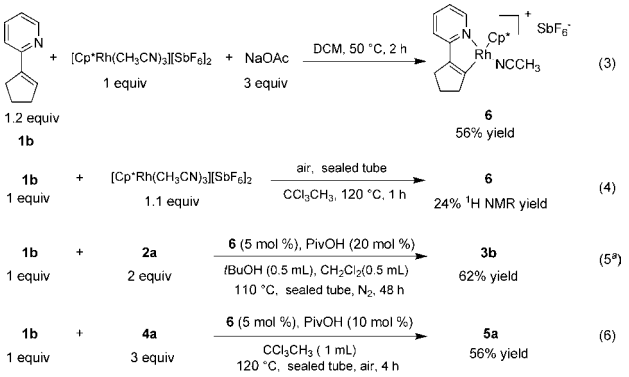


[a] **1** (0.25 mmol), **4** (0.75 mmol) in CCl_3CH_3 (0.25 M) under an air atmosphere in a sealed reaction tube. [b] The reaction was performed in 10 h. [c] The reaction was performed on a 1 mmol scale in 1 mL of solvent. [d] The reaction was performed for 8 h. [e] The reaction was performed on a 1 mmol scale in CH_2Cl_2 for 12 h. [f] This reaction was performed in 1 mL of CH_2Cl_2 on a 1 mmol scale for 14.5 h; 50% of **1b** was recovered. [g] ^{1}HNMR yield. [h] 7% catalyst was used. [i] The reaction was performed with 20 mol % PivOH in 8 h.

electron-donating methoxyl group accompanied by the nitro group, the desired product was isolated in an acceptable yield (Scheme 2, **5q**).

To highlight the synthetic value of this new strategy, we conducted our model reaction (the reaction between **1b** and **4a**) on a 5 mmol scale; the same good yield (73%) as that from the standard conditions was obtained, and up to 1.2 g of product was isolated.

The catalytic pathway was considered as a similar catalytic cycle with aryl C−H addition to imines.[10] To give more evidence, one of the possible key intermediates **6** was synthesized and separated in 56% isolated yield (eq 3).[10,11] It can also be observed under a similar condition with our catalytic system (eq 4). Then the activity of intermediate **6** was invesitgated. Because the lower solubility of intermediate **6** in *t*BuOH, DCM was added when it was used in the catalytic olefinic C−H addition to *N*-sulfonyl aldimines (eq 5). The desired product was obtained with lower efficiency (62% yield) compared with the precatalyst (75% yield). A similar lower efficiency was also observed in the catalytic olefinic C−H addition to aryl aldehydes (eq 6). These lower reactivities might be attributed to the instability of intermediate **6** at high temperature because of the observation of black precipitation under these reaction conditions. Although lower yields occur when using **6** instead of $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$, these results still indicated that **6** is a possible intermediate.



[a] Using $[Cp^*Rh(CH_3CN)_3][SbF_6]_2$ instead of **6** in the same reaction conditions, 75% yield was obtained.

Meanwhile, we also detected the catalytic reactions by ESI-MS. In both the catalytic olefinic C−H addition to *N*-sulfonyl aldimine **2a** and the catalytic olefinic C−H addition to **4a**, the same two peaks were observed. One peak (527.1933) can be assigned to species I (Figure 1). Compared with **6**, the ligand is changed from acetonitrile to **1b** in spieces I. The other peak (382.1043) can be assigned to species II (Figure 1). Compared with **6**, the acetonitrile is dissociated in species II. At the same time, in the catalytic olefinic C−H addition to **4a**, another peak (567.0917) can be assigned to species III and/or IV (Figure 1). Species III is speculated as the coordination of species II with **4a**. Species IV is speculated as the precursor of product **5a** without protonlysis.

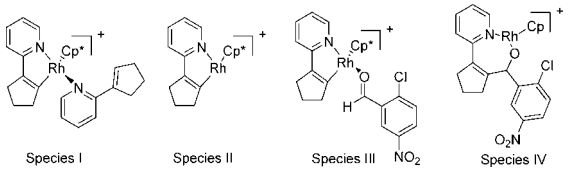


Figure 1. Observed possible intermediates by ESI-MS.

In summary, we developed the first example of direct alkenyl C−H addition to *N*-sulfonyl aldimines and aryl aldehydes. These studies show their significance in enriching the reactivity of broadly existing alkenes. The reactions can occur under mild conditions with high atom-economic efficiency. Further efforts to make this transformation potentially applicable and to find the proper chiral ligand to approach the efficient asymmetric version are underway.

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Supporting Information Available. Brief experimental details and other spectral data for products. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.