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Rh(III)-Catalyzed Oxidative Coupling of Unactivated Alkenes via C−H Activation

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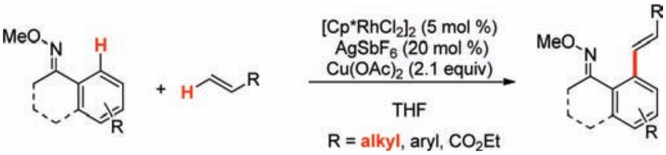
ABSTRACT



Oxime directed aromatic C−H bond activation and oxidative coupling to alkenes is reported using a cationic Rh(III) catalyst. Significantly, the method can be used to oxidatively couple unactivated, aliphatic alkenes.

Directed C−H bond activation and oxidative coupling with alkenes provide an atom economical alternative to traditional transformations such as the Heck reaction. Palladium,[1] ruthenium,[2] and rhodium[3] have been reported to effect the former transformation. However, nearly all oxidative couplings have employed "activated" alkenes such as acrylates and styrenes.[1e,f] Herein, we report a general method for the oxidative coupling of aryl *O*-methyl oximes with unactivated alkenes via C−H bond functionalization using a cationic Rh(III) catalyst.

We began our exploration with attempts to oxidatively couple 1-hexene with imine **1a**. We initially employed conditions reported by Miura for the oxidative coupling of 1-phenylpyrazole with acrylates using $[Cp^*RhCl_2]_2$ as the catalyst in the presence of $Cu(OAc)_2$ as an oxidant and with DMF as the solvent (Table 1, entry 1).[3f] Only trace amounts of the coupled product were observed, and none of the desired product was obtained with other solvents (entries 2 and 3). Prompted by reports that noted a positive effect of

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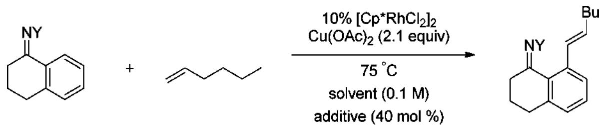
Table 1. Optimization of the Oxidative Coupling Reaction



entry	substrate	additive	solvent	yield[a]
1	Y = Bn (**1a**)	–	DMF	Trace
2	Y = Bn (**1a**)	–	THF	0
3	Y = Bn (**1a**)	–	*t*AmOH	0
4	Y = Bn (**1a**)	$AgSbF_6$	DMF	11%
5	Y = Bn (**1a**)	$AgSbF_6$	*t*AmOH	27%
6	Y = Bn (**1a**)	$AgSbF_6$	EtOH	45%
7	Y = Bn (**1a**)	$AgSbF_6$	THF	10%
8	Y = OMe (**1b**)	$AgSbF_6$	*t*AmOH	60%
9	Y = OMe (**1b**)	$AgSbF_6$	DMF	30%
10	Y = OMe (**1b**)	$AgSbF_6$	THF	85%
11	acetanilide	$AgSbF_6$	THF	0%

[a] NMR yield relative to 2,6-dimethoxytoluene as an internal standard.

halide abstractors for rhodium catalysis, $AgSbF_6$ was added[4] and resulted in improved yields (entries 4–7) with the highest yield being obtained with ethanol as the solvent (entry 6). The combination of rhodium with silver was next tested without copper acetate or using other oxidants (Ag_2CO_3, benzoquinone, $PhI(OAc)_2$), bases (NaOAc, lutidine), or acids (AcOH), but all of these modifications resulted in either a reduced yield or no coupled product (not shown). A survey of other directing groups established that *O*-methyl oxime **1b** (entries 8–10) is superior to the corresponding *N*-benzyl imine **1a**, providing good yields of the trans alkene product in THF (entry 10). Trace amounts of the cis product could also be detected under these conditions (5–10%), and no migration of the double bond was observed. Of note, while the reaction is water sensitive; it is not air sensitive. The reaction mixture could be exposed to the atmosphere with no decrease in yield. No coupled product was observed for acetanilide which has been reported to direct the oxidative coupling of styrenes using the same $[Cp^*RhCl_2]_2/AgSbF_6$ system (entry 11).[3e]

Alkene scope was next explored (Table 2). A *β*-branched alkene provided the coupled product in high yield (entry 2), while an α-branched alkene resulted in a somewhat lower yield (entry 3). The reaction is compatible with chloro and ester functionalities (entries 4 and 5). Notably, diene **2e** preferentially couples at the terminal alkene position in preference to the more electronically activated α,*β*-unsaturated ester (entry 5). Reactions with activated alkenes such as styrene and ethyl acrylate proceed well to give good yields of the alkenylated products (entries 6 and 7). Interestingly, use of allyl acetate as the coupling partner led to formation of the unconjugated terminal alkene **3h** (entry 8). This allylated product presumably forms via a concerted elimination from a rhodium–acetate complex obtained upon insertion of the alkene in the initially generated rhodium-aryl species (eq 1).[5] While this transformation is redox neutral, only trace amounts of product are obtained when $Cu(OAc)_2$ is omitted. However, the reaction can be performed using substoichiometric amounts of $Cu(OAc)_2$ (40 mol %) without a loss in yield.

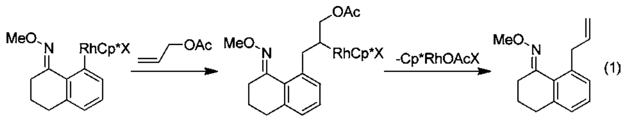
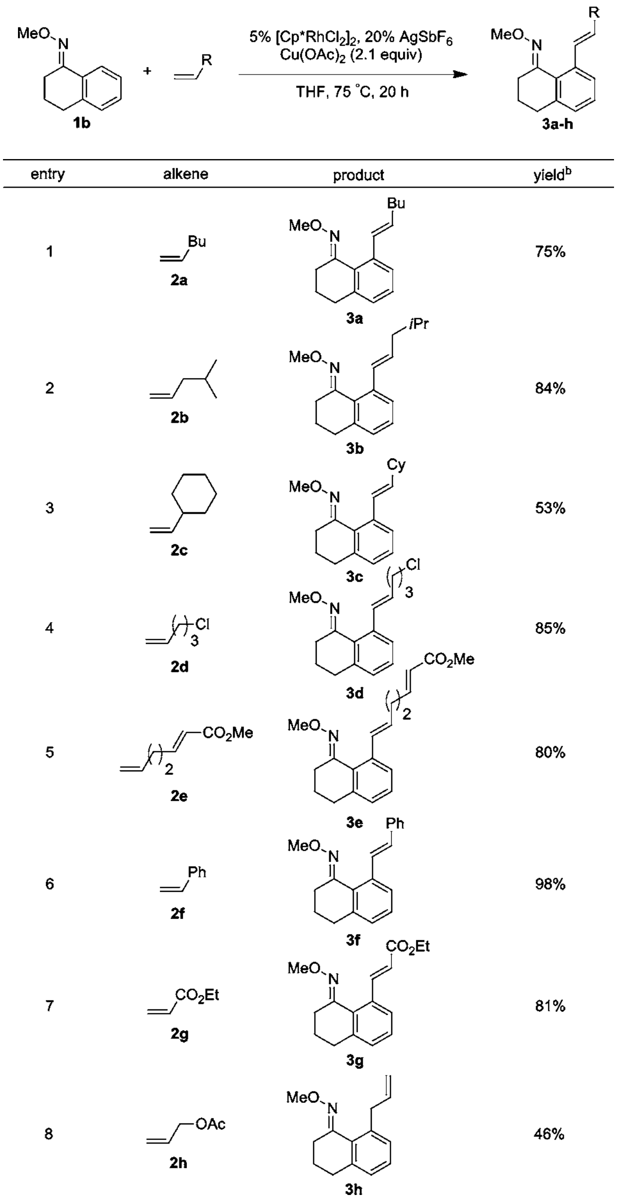


Table 2. Alkene Scope[a]



entry	alkene	product	yield[b]
1	**2a**	**3a**	75%
2	**2b**	**3b**	84%
3	**2c**	**3c**	53%
4	**2d**	**3d**	85%
5	**2e**	**3e**	80%
6	**2f**	**3f**	98%
7	**2g**	**3g**	81%
8	**2h**	**3h**	46%

[a] All reactions were performed by heating the oxime (1 equiv), alkene (3 equiv), $[Cp^*RhCl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2$ (2.1 equiv), and THF (0.1 M) in a sealed vial for 20 h at 75 °C. [b] Isolated yields after purification by chromatography are reported.

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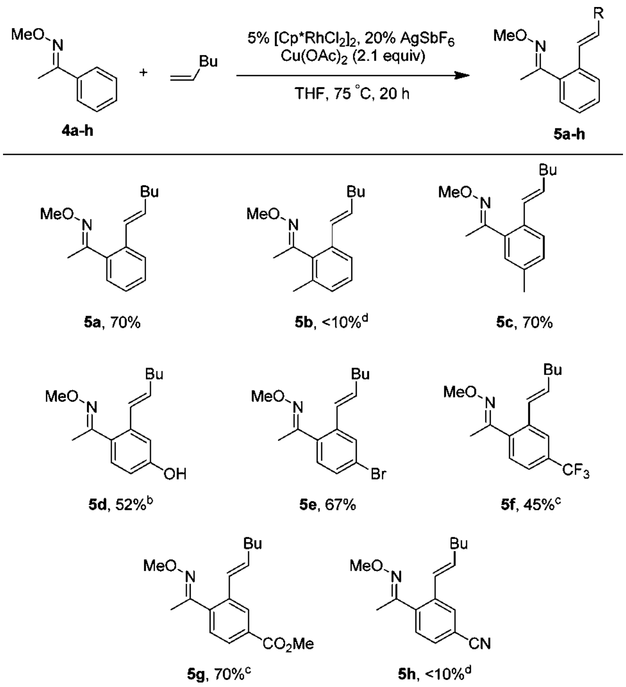
Scheme 1. Aryl *O*-Methyl Oxime Scope[a]



[a] All reactions were performed by heating oxime (1 equiv), 1-hexene (3 equiv), $[Cp^*RhCl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2$ (2.1 equiv), and THF (0.1 M) in a sealed vial for 20 h at 75 °C. Isolated yields after purification by chromatography are reported. [b] 1-Hexene (1.5 equiv). [c] 36 h. [d] NMR yield relative to 2,6-dimethoxytoluene as an internal standard

Under the optimized conditions, a variety of different aryl *O*-methyl oximes could be coupled with alkenes in good yield (Scheme 1). Substrates with *para* (**4d**−**g**) or *meta* (**4c**) substitution patterns and both electron-withdrawing (**4e-g**) and -releasing (**4d**) substituents were effective coupling partners. However, the electron-poor substrates **4f** and **4g** required longer reaction times to achieve full conversion. The brominated analogue **4e** not only underwent coupling efficiently but also did not suffer any Heck coupling or protodebromination. In contrast, the *para*-cyano aryl oxime **4h** gave only a poor yield of coupled product (10% by NMR), probably due to coordination of the nitrile to the catalyst. A small amount of the bis-alkenylated product, less than 10% by NMR, was observed for oximes **4a** and **4e**, and under the standard reaction conditions **4d** resulted in 30% of the bis-alkenylated product. However, this undesired product could be reduced to trace amounts using 1.5 equiv of the alkene. *Ortho*-methyl substituted aryl oxime **4b** resulted in poor conversion, likely due to steric congestion between the directing group and the methyl substituent.[3e]

Recent reports have shown that Rh(III) complexes are efficient catalysts for the oxidative coupling of C−H bonds with acrylates and styrenes. However, the analogous transformation with nonactivated olefins has not previously been demonstrated for Rh catalysts and is generally unknown. We have shown that given an appropriate directing group, the coupling of unactivated as well as functionalized terminal alkenes can be accomplished in moderate to good yields and under conditions that are compatible with commonly encountered functional groups.

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Supporting Information Available: Experimental details, characterization data, and copies of ^{1}H NMR and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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