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Simple Alkenes as Substitutes for Organometallic Reagents: Nickel-Catalyzed, Intermolecular Coupling of Aldehydes, Silyl Triflates, and Alpha Olefins

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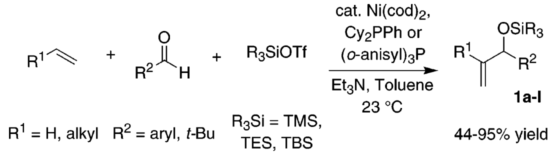
Aliphatic terminal alkenes (alpha olefins) are produced in metric megaton amounts each year, and these chemical feedstocks are starting materials for the preparation of many classes of organic compounds.[1] The value-added component of catalytic intermolecular reactions of these alkenes, such as Ziegler−Natta oligomerization,[2] the Heck reaction,[3] and cross-metathesis,[4] is especially high because they convert an inexpensive raw material into a more highly functionalized compound or polymer with concomitant formation of one or more carbon−carbon bonds. Whereas catalytic carbonyl−ene reactions between alpha olefins and aldehydes provide homoallylic alcohols,[5] there is no method for joining these two building blocks to provide *allylic* alcohols.[6] Herein we report that, in the presence of a nickel catalyst and a silyl triflate, ethylene and alpha olefins can be coupled with aldehydes to form allylic alcohol derivatives (eq 1).



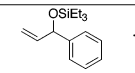
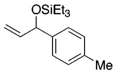
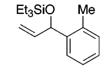
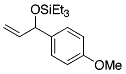
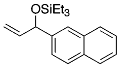
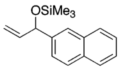
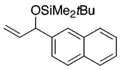
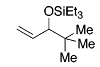
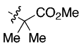
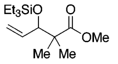
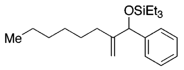
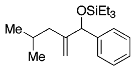
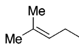
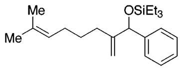
(1)

Several research groups, including our own, have developed metal-catalyzed, intermolecular reductive coupling reactions of aldehydes with alkynes,[7] 1,3-dienes,[8] allenes,[9] enoate esters,[10] enones,[11] and enals.[12] In all of these, an electron-deficient π-bond, in conjunction with a reducing agent, functions as an anion equivalent. On the other hand, catalytic intermolecular coupling (reductive or otherwise) of alpha olefins and aldehydes has not been reported.[13,14] Nickel-promoted, intramolecular alkene−aldehyde reductive coupling was recently described, but this process required a stoichiometric amount of nickel and was not effective in intermolecular cases.[15,16]

We have found that nickel *catalysis* of *intermolecular* alkene−aldehyde coupling is possible when certain phosphine ligands, a silyl triflate, and an amine base are employed. As shown in eq 1 and Table 1, ethylene, aromatic aldehydes, and silyl triflates undergo nickel-catalyzed coupling under very mild conditions (1 atm $H_2C{=}CH_2$, room temperature), yielding a three-component coupling[17] product, a silyl ether of an allylic alcohol (entries 1−7). In some cases, the isolated yield of the product is greater than 90% (entries 3−5), highlighting the efficiency and ease of this method of assembling protected allylic alcohols in a single operation. In general, triethylsilyl triflate is the superior silyl triflate under these conditions, but trimethylsilyl and *tert*-butyldimethylsilyl triflate also provide some flexibility in which protective group appears in the product (entries 6 and 7).

Notably, this transformation is very tolerant of sterically demanding aliphatic aldehydes (entries 8 and 9). Pivaldehyde, ethylene, and Et_3SiOTf undergo smooth coupling to provide the triethylsilyl ether of *tert*-butyl vinyl carbinol in one step and in good yield (entry 8). Entry 9 demonstrates another feature of this reaction, functional group compatibility with esters. A competing (yet unsurprising) side reaction occurs in coupling reactions with aliphatic aldehydes bearing at least one hydrogen adjacent to the carbonyl, enol silane formation.[18]

Table 1. Nickel-Catalyzed, Three-Component Coupling of Alkenes, Aldehydes, and Silyl Triflates [a]

entry	R^1 (alkene)	R^2 (aldehyde)	R_3SiOTf	product	isolated yield (%)
1	H (ethylene, 1 atm)	Ph	Et_3SiOTf	 **1a**	82
2	"	*p*-tolyl	Et_3SiOTf	 **1b**	88
3	"	*o*-tolyl	Et_3SiOTf	 **1c**	93
4	"	*p*-anisyl	Et_3SiOTf	 **1d**	95
5	"	2-naphthyl	Et_3SiOTf	 **1e**	95
6	"	2-naphthyl	Me_3SiOTf	 **1f**	60
7	"	2-naphthyl	*t*$BuMe_2SiOTf$	 **1g**	67
8	"	piv	Et_3SiOTf	 **1h**	70
9	"		Et_3SiOTf	 **1i**	81
10	*n*-hexyl	Ph	Et_3SiOTf	 **1j**	48 [b]
11	isobutyl	Ph	Et_3SiOTf	 **1k**	44 [b]
12		Ph	Et_3SiOTf	 **1l**	50 [b]

[a] See eq 1. Standard conditions (entries 1−9): To a solution of $Ni(cod)_2$ (20 mol %) and tris(*ortho*-methoxyphenyl)phosphine (40 mol %) in toluene at 23 °C under ethylene (balloon, 1 atm) were added triethylamine (600 mol %), the silyl triflate (175 mol %), and the aldehyde (100 mol %). The mixture was stirred 2−8 h at room temperature, and purification by chromatography (SiO_2) afforded products **1a**−**i**. For entries 10−12, dicyclohexylphenylphosphine and the alkene shown were used in place of tris(*ortho*-methoxyphenyl)phosphine and ethylene, respectively (reaction under Ar). See Supporting Information. [b] A silyl ether of a homoallylic alcohol was also isolated in 10−20% yield. See Supporting Information.

Monosubstituted olefins also undergo coupling with aldehydes in the presence of a similar reagent/catalyst combination (entries 10−12). An alpha olefin is thus a functional equivalent of a 2-alkenylmetal reagent, complementary to a 1-alkenylmetal reagent

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in addition reactions to aldehydes. As entry 12 demonstrates, this transformation tolerates more highly substituted alkenes.[19]

The chief byproduct in these reactions is the isomeric *homo*allylic alcohol derivative (**2j** in Figure 1).[20] Remarkably, only one (**1j**) of the three possible allylic alcohol derivatives (**1j**, **3**, and **4**) is formed in greater than 1% yield in all such reactions investigated to date (Figure 1).

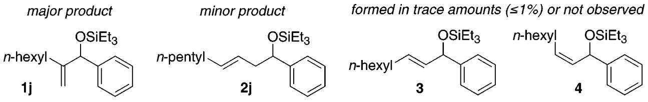
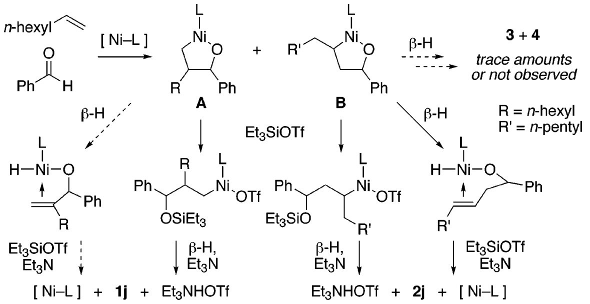


Figure 1. Major and minor products.

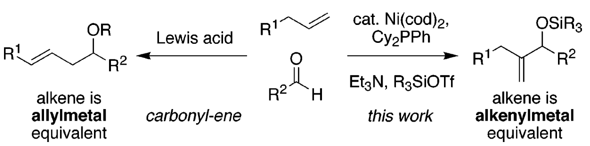
Our explanation for this product distribution and the other observations noted above is summarized in Scheme 1. One of the key intermediates might be oxametallacycle **A**,[15−16] which would lead to the observed allylic product (**1j**) by reaction with the silyl triflate, cleavage of the Ni−O bond, and then β-H elimination. Even though it would represent an alternative means by which **1j** could be formed, β-H elimination directly from **A** is unlikely since the transition state required would be highly strained. This notion is supported by the fact that allylic alcohol products **3** and **4** are generally not formed in the reaction; they would result from the corresponding β-H elimination from regioisomer **B**.

Scheme 1. Mechanistic Hypothesis for Product Distribution



The homoallylic alcohol byproduct is most easily explained by oxametallacycle regioisomer **B**. With the alkyl chain of the olefin adjacent to the Ni center, the transition state for β-H elimination directly from **B** may be less strained than those from **A** and **B** that would lead to allylic alcohol products (see above). Another possibility is that, as in the case of **A**, **B** first reacts with the silyl triflate. Subsequent β-H elimination toward the newly installed carbinol center, which would lead to the generally unobserved allylic alcohol derivatives **3** and **4**, might thus be disfavored for steric and/or electronic reasons.

Scheme 2. Alkenes as Substitutes for Organometallic Reagents



Conceptually, as depicted in Scheme 2, the alkene in a carbonyl−ene reaction serves as a replacement for an allylmetal reagent, and conversely, in the nickel-catalyzed reaction presented here, an alkene functions as an *alkenyl*metal reagent. Compared to the corresponding organometallic reagent, the alkene in this unprecedented bond construction has important advantages, including greater off-the-shelf availability and greater functional group compatibility. The development of an enantioselective version of this process and its use as a fragment coupling reaction in complex molecule synthesis are both underway.

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Supporting Information Available: Experimental procedures and data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) For example, in the case of cyclohexanecarboxaldehyde, the product ratio is about 2:1, favoring the silyl ether.

(19) Di- and tetrasubstituted alkenes also do not react under these conditions.

(20) When tris(*o*-methoxyphenyl)phosphine was employed, the homoallylic product was isolated in greater than 75% yield.

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