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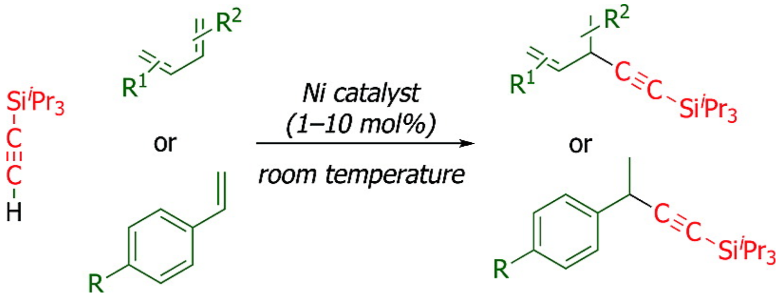

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Nickel-Catalyzed Addition of C−H Bonds of Terminal Alkynes to 1,3-Dienes and Styrenes

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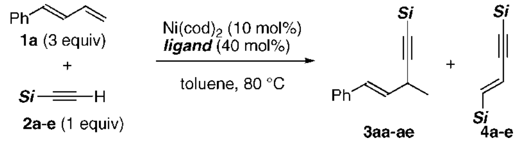
Catalytic reactions involving addition of C−H bonds across carbon−carbon multiple bonds have presented a great challenge in synthetic organic chemistry during the past decade, aiming at exploration of efficient and selective synthetic methods for organic compounds.[1,2] Among the various C−H bonds, sp-C−H bonds have been the primary target for activation by virtue of the relatively high acidity of the hydrogen atoms on the sp-hybridized carbon atom. For instance, addition of hydrogen cyanide to carbon−carbon multiple bonds has been studied extensively, offering convenient methods for the synthesis of nitrile derivatives.[3] Studied even more extensively have been catalytic additions of alkyne C−H bonds. Transition-metal-catalyzed dimerization of alkynes through insertion of the carbon−carbon triple bond into the alkyne C−H bond has been achieved using a variety of transition metal catalysts,[4] leading to success in cross-dimerization systems, in which two different alkynes are selectively coupled.[5] The alkyne dimerization may proceed through oxidative addition of the sp-C−H bond to transition metal catalysts to generate (hydro)(alkynyl)metal intermediates, which undergo further insertion of alkyne. Although it seems easy to extend these reaction intermediates to hydroalkynylation of other unsaturated organic molecules such as alkenes, there have been only a few examples for the hydroalkynylation of unsaturated molecules other than alkynes. Those reported hydroalkynylation reactions require cyclopropenes,[6] allenes,[7] and norbornadiene[8] as the reaction partners, in which the C=C bonds are highly reactive because of the ring strain or the cumulative C=C bonds. Addition to 1,3-dienes has only been partly achieved in the ruthenium-catalyzed codimerization.[9] Expansion of the reaction scope has long been pursued in recognition of the importance of the development of new synthetic routes to alkyne derivatives, but with no particular success. Herein, we describe the nickel-catalyzed addition of the alkyne C−H bond across a carbon−carbon double bond of 1,3-dienes, styrenes, and norbornene.

In the course of our research project aiming at nickel-catalyzed alkynylation of carbon−carbon triple bonds,[10] we carried out reactions of silylacetylenes **2a**−**e** with 1-phenyl-1,3-butadiene **1a** in the presence of nickel catalysts (Table 1). It is interesting to note that reactions of trimethylsilyl- (**2a**), dimethylphenylsilyl- (**2b**), and methyldiphenylsilylacetylene (**2c**) produced the corresponding hydroalkynylation products, albeit in low yields (entries 1–3). The yield was improved by using more bulky silylacetylenes such as *tert*-butyldimethylsilyl- (**2d**) (32%) and triisopropylsilylacetylene (**2e**) (57%) (entries 4 and 5). The effect of the bulky silyl groups can be ascribed to retardation of homodimerization and oligomerization of the alkynes, as pointed out in previous reports on the alkyne cross-dimerization.[5f] The phosphorus ligand was then varied (entries 6–11). A ligand-free catalyst (entry 6), phosphite-based (entry 7), or P^tBu_3-based nickel catalysts (entry 8) resulted in no formation of the hydroalkynylation product. In the ligand-free system, homodimerization of **2e** took place exclusively. A PPh_3−Ni catalyst exhibited catalytic activity comparable to that of the PCy_3−Ni catalyst (entry 9). It was eventually found that sterically less demanding trialkylphosphines such as PMe_3 and PBu_3 invested the catalyst system with remarkable activity toward the hydroalkynylation (entries 10 and 11).

Table 1. Ni-Catalyzed Hydroalkynylation of 1,3-Diene **1a** with **2**[a]



entry	*Si*	ligand	%yield of **3**[b]	%yield of **4**[b]
1	Me_3Si (**2a**)	PCy_3	16	nd
2	$PhMe_2Si$ (**2b**)	PCy_3	15	nd
3	Ph_2MeSi (**2c**)	PCy_3	14	nd
4	*t*-$BuMe_2Si$ (**2d**)	PCy_3	32	nd
5	*i*-Pr_3Si (**2e**)	PCy_3	57	11
6	*i*-Pr_3Si (**2e**)	none	0	83
7	*i*-Pr_3Si (**2e**)	$P(OBu)_3$	0	0
8	*i*-Pr_3Si (**2e**)	P(*t*-Bu)$_3$	0	30
9	*i*-Pr_3Si (**2e**)	PPh_3	65	12
10	*i*-Pr_3Si (**2e**)	PMe_3	95	trace
11	*i*-Pr_3Si (**2e**)	PBu_3	99 (84)	0

[a] All reactions were performed on a 0.1 mmol scale in toluene (0.5 M) for 4 h using 10 mol % of $Ni(cod)_2$ with 40 mol % of phosphine ligands. [b] ^1H NMR yields. Isolated yield is in the parentheses.

In the presence of the $PBu_3/Ni(cod)_2$ catalyst, several 1,3-dienes reacted with **2e** at room temperature (Table 2). In addition to **1a**, 1-aryl-1,3-butadienes bearing electron-donating (**1b**) as well as electron-withdrawing groups (**1c**) on the aromatic ring selectively produced the corresponding 1,4-enynes in high yields (entries 1–3). Note that the reaction proceeded even at room temperature with 1 mol % of catalyst loading. The geometry of the C=C bond of the product was found to be >99% *trans*, in spite of the fact that the starting dienes were used as mixtures of *trans* and *cis* isomers with varied *E*:*Z* ratios. 1,3-Pentadiene (**1d**), an aliphatic terminal conjugated diene, afforded the corresponding 2-alkynylation product **3de** in high yield (entry 4). A conjugated triene **1e** cleanly underwent the addition of **2e**, giving dienyne **3ee** in good yield (entry 5). A conjugated silyl enol ether **1f** also gave the corresponding silyl enol ether **3fe**, in which the siloxy-substituted C=C bond was left untouched (entry 6). In this particular reaction, a decrease in the catalyst loading to 5 mol % in Ni resulted in the reaction remaining incomplete. Reaction of cyclic diene **1g** with **2e** proceeded efficiently at room temperature, giving 3-ethynylcyclohexene derivative **3ge** in high yield (entry 7). Note that isoprene, 2,3-dimethyl-1,3-butadiene, and 1,1-diphenyl-1,3-butadiene were found to be unreactive under the current reaction

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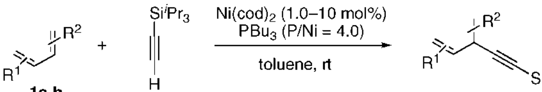
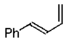
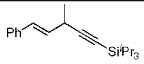
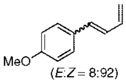
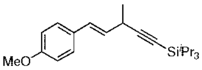
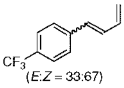
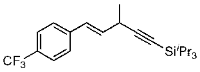
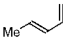
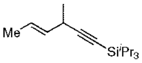
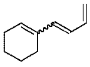
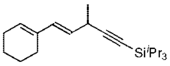
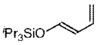
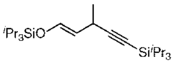
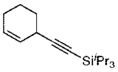
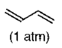
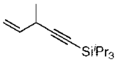
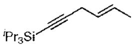
Table 2. Scope of the Nickel-Catalyzed Hydroalkynylation of 1,3-Dienes[a]

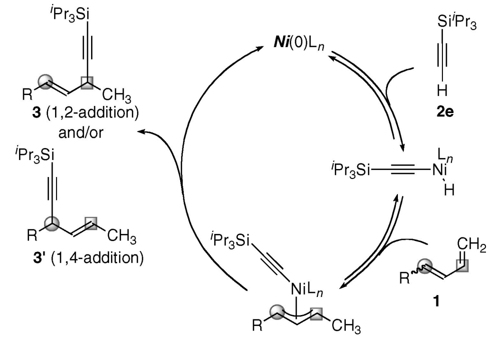


1a-h (3.0 equiv) **2e** **3ae–3he**

entry	1,3-dienes	cat. loading (mol%)	product	%yield[b]
1[c]	 **(1a)**	1	 **(3ae)**	96
2	 (*E*:*Z* = 8:92) **(1b)**	1	 **(3be)**	86
3	 (*E*:*Z* = 33:67) **(1c)**	1	 **(3ce)**	95
4	 **(1d)**	5	 **(3de)**	92
5	 (*E*:*Z* = 59:41) **(1e)**	3	 **(3ee)**	99
6	 **(1f)**	10	 **(3fe)**	73
7	 **(1g)**	5	 **(3ge)**	90
8	 (1 atm) **(1h)**	5	 **(3he)** +  **(3he')**	99 (2:3)

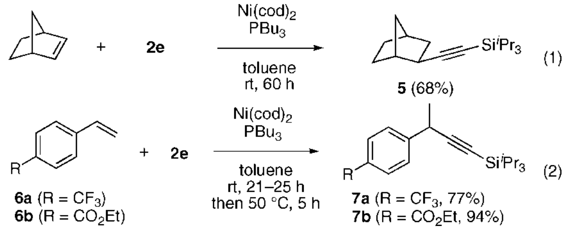
[a] Reactions were performed with 3.0 equiv of dienes on a 0.3 mmol scale in toluene (1.5 M) in the presence of Ni(cod)$_2$ (1.0–10 mol %) with PBu$_3$ (P/Ni ratio = 4/1), unless otherwise noted. [b] Isolated yields. [c] A gram-scale reaction with 1.09 g (6.0 mmol) of **2e** with 1.1 equiv of **1a**.

Scheme 1. Possible Mechanism of the Ni-Catalyzed Hydroalkynylation Reaction



conditions. Gaseous butadiene (**1h**) (1 atm), on the other hand, produced the hydroalkynylation products in good yield (entry 8). In contrast to the hydroalkynylation of other dienes, butadiene produced a 2:3 mixture of two enyne isomers. One isomer (**3he**) formed in a minor quantity has been obtained through the expected 1,2-addition reactions, whereas the major isomer was the 1,4-hydroalkynylation product **3he′**. The formation of the 1,4-addition isomer, as well as the exclusive formation of the *trans*-products from the *E*/*Z* mixtures of the starting 1,3-dienes, indicates that the catalytic hydroalkynylation proceeds through the formation of a π-allylnickel intermediate (Scheme 1). Similar mechanisms involving π-allylnickel species have been proposed in the nickel-catalyzed hydrovinylation[11] and hydrocyanation[12] of 1,3-dienes.

The catalyst system could be applicable to hydroalkynylation of other unsaturated organic compounds. Norbornene underwent 1,2-alkynylation, producing *exo*-addition product **5** stereoselectively (eq 1). The most striking application may be the hydroalkynylation of styrene derivatives **6a** and **6b**, in which the alkynyl groups were introduced to the internal carbon atoms of the C═C bonds to give products **7a** and **7b** (eq 2).



In summary, addition of an alkynyl C−H bond to the C═C bond of 1,3-dienes, styrenes, and norbornene has been developed using nickel catalysts. Use of sterically less demanding trialkylphosphines as a ligand in combination with bulky silylacetylenes such as **2e** as a substrate is crucial to attain a high yield.

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

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