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NICKEL-CATALYZED REGIO- AND STEREO-SELECTIVE SYNTHESIS OF HOMOALLYLIC ALCOHOL DERIVATIVES FROM DIENES AND ALDEHYDES

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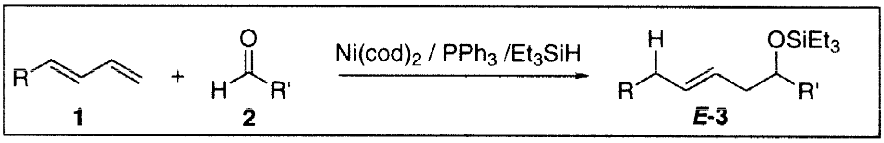
Abstract: The reaction of 1,3-Dienes and aldehydes in the presence of Et_3SiH using a catalytic amount of $Ni(cod)_2$ and PPh_3 gave homoallylic alcohol derivatives in a regio- and stereoselective manner.

Keywords: Aldehydes, Coupling reactions, Dienes, Hydrosilane, Nickel

Many reports concerning nickel-catalyzed reaction of 1,3-dienes and multiple bonds have indicated that these processes are effective for carbon-carbon bond formations[1-4]. However, it is difficult to form a new carbon-carbon bond intermolecularly from two different multiple bonds because of their low selectivities[5,6]. Here, we report a selective intermolecular coupling reaction of 1,3-diene and aldehyde.

In the course of studies on nickel-catalyzed intramolecular diene-aldehyde cyclization, we found that the reaction of 1,3-diene having an aldehyde moiety in a chain in the presence of Et_3SiH proceeded by a catalytic amount of zero-valent nickel complex in a highly regio- and stereoselective manner[7]. Based on these results, it was thought that this intramolecular coupling reaction might be also applicable to highly regio- and stereo-controlled synthesis of homoallylic alcohol derivatives from 1,3-diene and aldehyde (**Scheme 1**).

Scheme 1 Plan for the synthesis of homoallylic alcohol derivatives



Our plan is outlined in **Scheme 2**. In this reaction, nickel hydride complex **4**, generated by the oxidative addition of Et_3SiH to zero-valent nickel complex, is coordinated by diene **1** to give complex **5** (**Scheme 2**). The insertion of the diene moiety of **5** into the nickel-hydride bond produces π-allynickel complexes *anti*-**6** and *anti*-**7**, which would be in a state of

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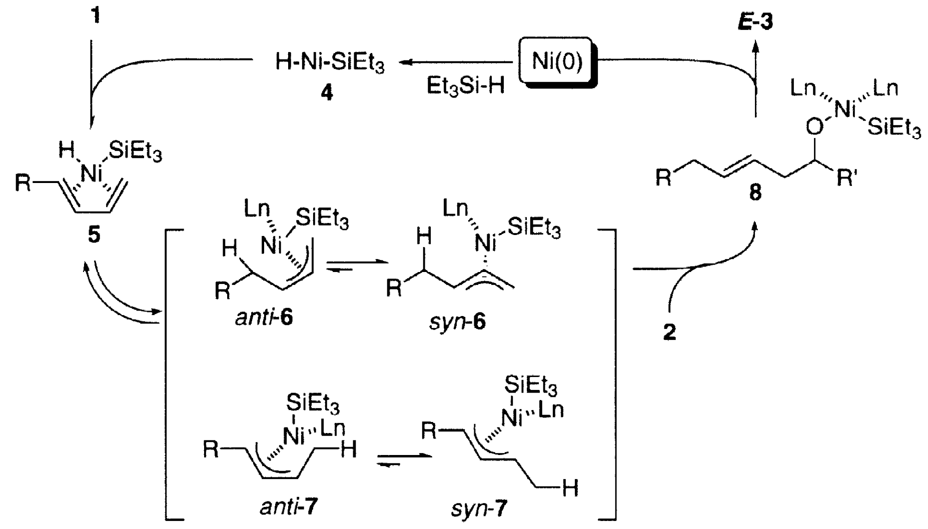
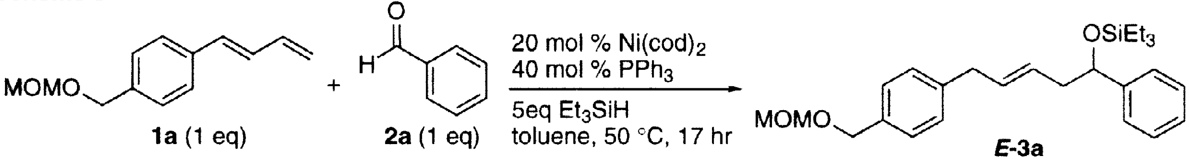
equilibrium with the more stable *syn*-**6** and *syn*-**7**.[8] Then, *syn*-**6** would react with aldehyde **2** at the less substituted terminal carbon of the complex *syn*-**6** to provide complex **8**. Reductive elimination from complex **8** should give silyl-protected homoallyl alcohol derivative ***E*-3**, and zero-valent nickel complex would be regenerated.

Scheme 2



To examine the feasibility of the above plan, the coupling reaction of diene **1a** and benzaldehyde **2a** was carried out (**Scheme 3**). When a toluene solution of diene **1a** (1 eq), aldehyde **2a** (1 eq), and Et_3SiH (5 eq) was stirred in the presence of $Ni(cod)_2$ (20 mol %) and PPh_3 (40 mol %) at 50 °C for 17 hr, triethylsilyl-protected alcohol ***E*-3a** was obtained in 84% yield as a sole product in a regio- and stereoselective manner.

Scheme 3



Encouraged by this result, further investigation of coupling reactions between dienes **1** and various aldehydes **2** were carried out. The results are shown in **Table 1**. The reaction of diene **1a** with aldehyde **2b**, having an electron-donating group at the 4-position on the aromatic ring, gave the desired product in 76% yield (entry 1). In a similar manner, the reaction with **2c**, having an electron-withdrawing group at the same position, also provided a coupling product in moderate yield along with the recovery of diene **1a** in 32% yield (entry 2). In the reactions with aliphatic aldehydes **2d** and **2e**, coupling products were obtained in good yields as a mixture of *E*- and *Z*-isomers. It was interesting that the ratio of *E*- to *Z*-isomers was improved when the initial concentration of the reagents was changed (entries 4 and 5). The reaction of **1b** with various aldehydes (entries 6~9) also afforded coupling products in a regioand stereoselective manner in moderate yields. In these reactions, a fair amount of hydrosilylation product **9** was obtained (entries 6, 7, and 9).

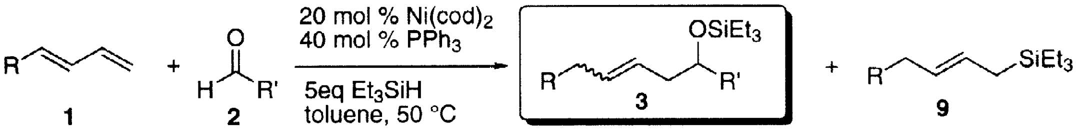
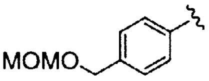
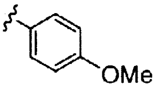
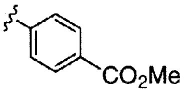
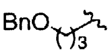
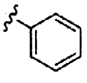
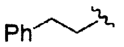


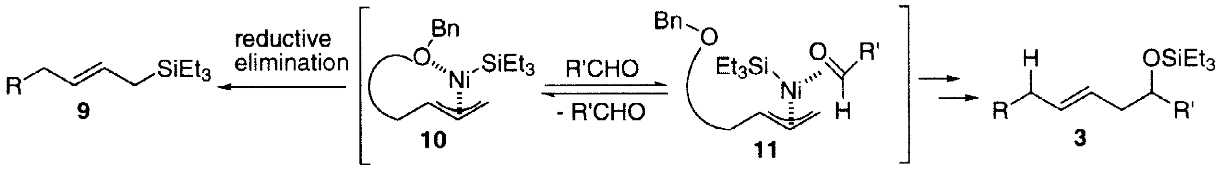
Table 1. Reaction of Various Dienes and Aldehydes in the presence of Et_3SiH and Nickel Catalyst.

entry [a]	diene (R =)	aldehyde (R'=)	time (hr)	yield of **3** (%)	ratio (*E*-**3** / *Z*-**3**)	yield of **9** (%)
1	 **1a**	 **2b**	18	76	100 / 0	0
2	**1a**	 **2c**	44	59 [c]	100 / 0	0
3	**1a**	 **2d**	27	71	3 / 1	0
4	**1a**	 **2e**	23	76	1 / 1	0
5 [b]	**1a**	**2e**	24	81	2 / 1	0
6	 **1b**	 **2a**	18	63	100 / 0	7
7	**1b**	**2b**	19	49	100 / 0	31
8	**1b**	**2c**	44	54 [d]	100 / 0	0
9	**1b**	**2e**	18	63	100 / 0	11
10	 **1c**	**2a**	20	72	100 / 0	0
11	**1c**	**2b**	19	66	100 / 0	0

[a] The initial concentrations of diene and aldehyde were 0.05 M except for entry 5. [b] The initial concentrations of diene and aldehyde were 0.02 M. [c] 32% of **1a** was recovered. [d] 35% of **1b** was recovered.

It seemed likely that the reactivity of π-allylnickel complex generated from diene **1b** was lower than that generated from **1a**. The lower reactivity can be explained by the coordination of oxygen atom of the benzyloxy group onto the nickel center of **10** (**Scheme 4**). Thus, aldehyde could not coordinate to nickel center, and reductive elimination from **10** would occur to give hydrosilylated product **10**.

Scheme 4



To confirm this, coupling reactions of diene **1c** were carried out. In the reaction with aldehyde **2a**, a coupling product was obtained in 72% yield as a sole product (entry 10), and the reaction with aldehyde **2b** also gave only a coupling product in 66% yield (entry 11). These results indicate that the coupling reactions of **1b** were disturbed by coordination of the benzyloxy group onto the nickel center.

In conclusion, we developed a highly regio- and stereoselective synthesis of homoallyl alcohol derivatives by the intermolecular coupling reaction of 1,3-dienes and aldehydes using a catalytic amount of nickel complex in the presence of Et_3SiH. Further studies along this line are in progress.

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References:

[1] For [4 + 4] cycloadditions, see: Wender, P. A.; Tebbe, M. J. *Synthesis* **1991**, 1089 and references cited therein.

[2] For [4 + 2] cycloadditions, see: Wender, P. A.; Smith, T. E. *Tetrahedron* **1998**, *54*, 1255 and references cited therein.

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[8] Hydrosilylation of 1,3-pentadiene using $Ni(acac)_2$-Et_3Al was reported by Lappert. In this case, 1,3-pentadienes gave principally 2-pentenylsilane derivatives. They claimed that secondary alkyl-nickel complex is formed at first and then it rearranged to primary-nickel complex. However, it was considered that these π-allylnickel complexes are in a state of equilibrium and *syn*-**6** should react with aldehyde because *syn*-π-allylnickel complex is more stable than *anti*-complex and the reactivity of *syn*-**6** would be higher than that of *syn*-**7**. See Lappert, M. F.; Nile, T. A.; Takahashi, S. *J. Organomet. Chem.* **1974**, *72*, 425.