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Nickel-Catalyzed Multicomponent Connection of Dimethylzinc, Alkynes, 1,3-Butadiene, Aldehydes, and Amines

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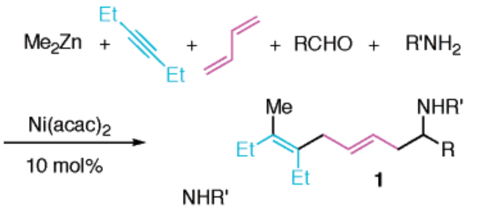
Nickel serves as a versatile catalyst for a variety of oligomerization, co-oligomerization, and polymerization reactions of 1,3-butadiene, which proceed via η^1,η^3-allylalkylnickel(II) **III** as a key intermediate (Scheme 1).[1] Most co-oligomerizations have been limited to the combinations of butadiene and alkenes and/or alkynes. Only a limited number of papers have appeared on the stoichiometric[2,3] and catalytic co-oligomerization[4] of aldehydes and ketones via **III**.

In the past decade, the carbon−carbon bond formation reactions between dienes and aldehydes or ketones in the presence of a nickel catalyst and alkylation or reducing reagents (M−X: e.g., BEt_3,[5] $ZnEt_2$,[6] BMe_3,[7] $ZnMe_2$,[8] Al-*i*-Bu_2(acac),[9] Et_3SiH)[10] have been developed, where both the oxidative cyclization of a diene−nickel(0) complex **I** across a carbonyl compound and transmetalation of X from M to Ni work as key steps to form an oxanickellacycle **IV** as an intermediate.[11,12] In a very rare example, a process involving a bis-diene−nickel(0) complex **II** has been invoked.[8d]

Here we report a useful variation of the pathways, C═N in place of C═O, that might proceed through **I** and **II** as the key intermediates; a nickel(0) catalyst promotes the five-component connection reaction of Me_2Zn, alkynes, 1,3-butadiene, aldehydes, and amines, selectively furnishing dienylamines **1** or trienylamines **2** in good yields (eq 1).[13] Interestingly, the reaction course is strictly affected by the kinds of amines; aromatic amines guide the reaction through **I** and provide **1**, while aliphatic amines provide **2** through **II**, both with high selectivity.



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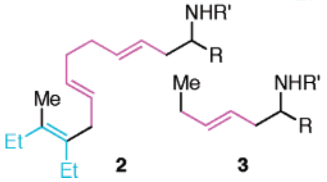
(1)



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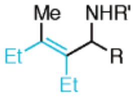

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The reaction shows wide flexibility regarding aldehydes: with *p*-anisidine (AN), aromatic aldehydes bearing either electron-donating or electron-withdrawing groups at either the ortho- or para-position, as well as furyl aldehyde, all worked similarly well and yielded **1** in good to excellent yields (runs 1−7, Table 1). Aliphatic aldehydes also participated nicely in the reaction and furnished **1h** and **1i** in good yields (runs 8 and 9). In sharp contrast to these, when benzylamine (BN) was used in place of AN, no **1** was produced at all; instead, **2**, containing two molecules of 1,3-butadiene, was obtained in an excellent yield (run 10). On the other hand, aliphatic aldehydes−aliphatic amine imines provided intractable mixtures of products (e.g., run 11).

Scheme 1. Reactive Intermediates **I**−**III** for the Nickel-Catalyzed Reactions with 1,3-Butadiene

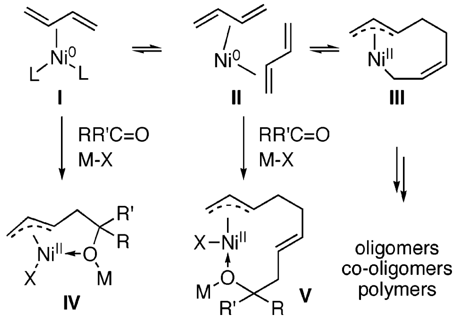

Table 1. Ni-Catalyzed Multicomponent Connection Reaction of Me_2Zn, Alkyne, 1,3-Butadiene, Aldehydes, and Amines[a]

run	aldehyde	amine[b]	time (h)	% yield of **1** or **2**
1	Ph	AN	3	91 (**1a**)
2	*p*-MeC_6H_4	AN	6	96 (**1b**)
3	*o*-$MeOC_6H_4$	AN	2	88 (**1c**)
4	*p*-$MeOC_6H_4$	AN	1	78 (**1d**)
5	*o*-ClC_6H_4	AN	1	91 (**1e**)
6	*p*-ClC_6H_4	AN	2	97 (**1f**)
7	2-furyl	AN	2	98 (**1g**)
8	*n*-pentyl	AN	1	87 (**1h**)
9	*i*-Pr	AN	1	84 (**1i**)
10	Ph	BN	3	94 (**2a**)
11	*n*-pentyl	BN	3	—[c]

[a] Reaction conditions: an aldehyde (1 mmol) and an amine (2 mmol) in THF (2 mL) at 30 °C overnight, and then $Ni(acac)_2$ (0.1 mmol) in THF (3 mL), 3-hexyne (4 mmol), 1,3-butadiene (4 mmol), Me_2Zn (3.6 mmol) at 30 °C for the period of time indicated. [b] AN (PMP-NH_2), *p*-anisidine; BN (Bn-NH_2), benzylamine. [c] Intractable mixture of products.

In view of precedents that, under similar catalytic conditions, dienes react with imines to furnish homoallylamines **3**[13a,b] and also alkynes react with imines to provide allylic amines **4**,[14] both in good yields, the selective formation of either **1** or **2**, without contamination with neither **3** nor **4**, is rather surprising, especially taking into consideration the fact that the formation of **1** and **2** is associated with an unfavorable entropy factor.

The reaction can be undertaken in one flask with great ease (run 1, Table 1): a mixture of benzaldehyde (1 mmol) and *p*-anisidine (2 mmol, AN) in dry THF was stirred at 30 °C overnight under N_2. Into this mixture, without removal of the water produced, were added $Ni(acac)_2$ (0.1 mmol), 1,3-butadiene (4 mmol), 3-hexyne (4 mmol), and Me_2Zn (3.6 mmol, 1M hexane) at 30 °C. The reaction was complete within 3 h and provided **1a** in 91% isolated yield after usual workup and purification by column chromatography over silica gel.

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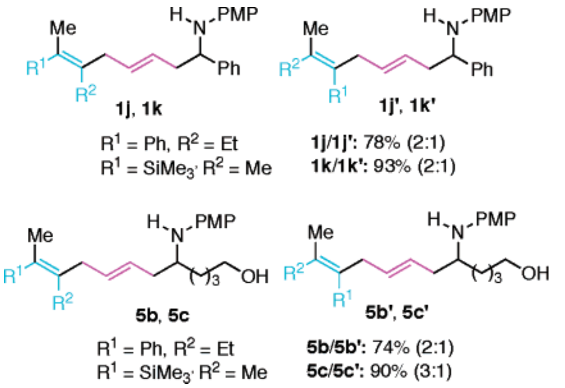
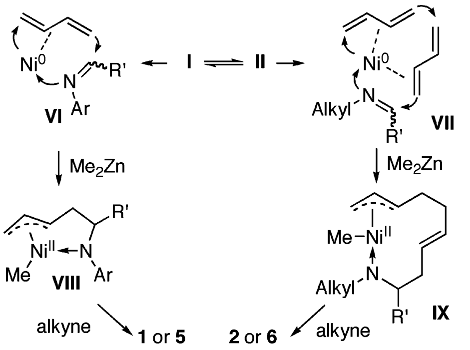
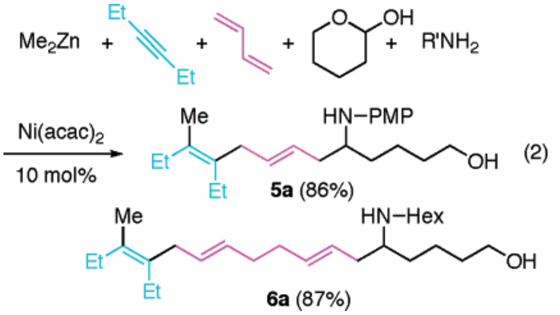


Figure 1. Reaction of AN imines with unsymmetrical alkynes.

Scheme 2. Selective Single (**VI**) or Double Incorporation (**VII**) of 1,3-Butadiene for Aromatic or Aliphatic Amines Imines, Respectively



The compatibility of the present reaction with water, generated during an aldimine formation from an aldehyde and an amine, encouraged us to examine the reaction with lactols (eq 2). 2-Hydroxy-1-oxacyclohexane-AN imine provided **5a** in 86% yield (30 °C, 2 h). To our pleasant surprise, unlike imines formed from aliphatic aldehydes and aliphatic amines (cf., run 11, Table 1), 2-hydroxy-1-oxacyclohexane-*n*-hexylamine imine reacted cleanly and furnished **6a** in 87% isolated yield (30 °C, 3 h).[15]



Unsymmetrical alkynes, despite the large steric or electronic bias of the substituents, did show almost no regioselectivity (Figure 1). The reaction of 1-phenyl-1-butyne and benzaldehyde-AN imine provided a mixture of regioisomers **1j** and **1j′** in a ratio of 2:1. 1-Trimethylsilyl-1-propyne provided a mixture of **1k** and **1k′** in a ratio of 2:1. The poor regioselectivity holds for the reaction with aliphatic aldehydes: **5b**/**5b′** = 2:1 and **5c**/**5c′** = 3:1 for reactions with 2-hydroxy-1-oxacyclohexane-AN imine.

The contrasting reactivity between aromatic amines (giving **1** or **5**) and aliphatic amines (yielding **2** or **6**) might be rationalized invoking **I** and **II**, respectively. Reactive AN imines would react with a diene−nickel(0) complex **I** in the presence of Me_2Zn through a transition state **VI** and form an intermediate **VIII** (Scheme 2). On the other hand, for less reactive aliphatic amine imines, **I** might not be reactive enough; hence, more reactive, less populated bis-butadiene-nickel(0) complex **II** would participate in the reaction through a transition state **VII**.[8d] Cis-insertion of an alkyne to the Ni-allyl bond of **VIII** or **IX** at the distal position, followed by reductive elimination of Ni(0) from a vinyl(methyl)nickel(II) species, thus formed, would lead to **1** or **2**, respectively. The similarity of steric and electronic environments of Ni^{II}-C-allyl and Ni^{II}-Me moieties in **VIII** and **IX** might prevent the regioselective incorporation of unsymmetrical alkynes.[16]

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

References

(1) Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic: New York, 1975; Vol. 2, Chapter 3.
(2) Baker, R.; Crimmin, M. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1264−1267.
(3) Stoichiometric reaction of **I** and two molecules of aldehydes and ketones is reported in reviews without any details: (a) Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 185−206. (b) Baker, R. *Chem. Rev.* **1973**, *73*, 487−530.
(4) Akutagawa, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3646−3648.
(5) (a) Shibata, K.; Kimura, M.; Shimizu, M.; Tamaru, Y. *Org. Lett.* **2001**, *3*, 2181−2183. (b) Kimura, M.; Ezoe, A.; Tanaka, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 3600−3602. (c) Kimura, M.; Ezoe, A.; Shibata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4033−4034.
(6) (a) Loh, T.-P.; Song, H.-Y.; Zhou, Y. *Org. Lett.* **2002**, *4*, 2715−1717. (b) Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, M.; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 397−400.
(7) Kimura, M.; Shibata, K.; Koudahashi, Y.; Tamaru, Y. *Tetrahedron Lett.* **2000**, *41*, 6789−6793.
(8) (a) Kimura, M.; Ezoe, A.; Mori, M.; Tamaru, Y. *J. Am. Chem. Soc.* **2005**, *127*, 201−209. (b) Kimura, M.; Kojima, K.; Inoue, T.; Tamaru, Y. *Synthesis* **2004**, 3089−3091. (c) Ezoe, A.; Kimura, M.; Inoue, T.; Mori, M.; Tamaru, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 2784−2786. (d) Kimura, M.; Matsuo, S.; Shibata, K.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3386−3388.
(9) Sato, Y.; Sawaki, R.; Saito, N.; Mori, M. *J. Org. Chem.* **2002**, *67*, 656−662.
(10) Takimoto, M.; Hiraga, Y.; Sato, Y.; Mori, M. *Tetrahedron Lett.* **1998**, *39*, 4543−4546.
(11) *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, 2005; Chapter 5.
(12) It has been revealed recently that Rh shows a good catalytic performance for the reactions of dienes/alkynes and carbonyls: (a) Kong, J.-R.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 718−719 and references therein. (b) Jang, H.-Y.; Krische, M. J. *Eur. J. Org. Chem.* **2004**, 3953−3958.
(13) Ni-catalyzed C−C bond formation reaction of 1,3-dienes and imines: (a) Kojima, K.; Kimura, M.; Tamaru, Y. *Chem. Commun.* **2005**, 4717−4719. (b) Kimura, M.; Miyachi, A.; Kojima, K.; Tanaka, S.; Tamaru, Y. *J. Am. Chem. Soc.* **2004**, *126*, 14360−14361. (c) Brun, P.; Tenaglia, A. Waegell, *Tetrahedron* **1985**, *41*, 5019−5030.
(14) (a) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1364−1367. For the reactions with aldehydes, see: (b) Oblinger, E.; Montgomery, J. *J. Am. Chem. Soc.* **1997**, *119*, 9065−9066.
(15) Chelation to Zn(II) through its N and O atoms might help the hydroxy imine undergo the reaction as described.
(16) Similar poor regioselectivity has been observed for the related reactions forming the oxygen analogues of **1**.[8a]

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