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Communications

Regio- and Stereoselective Synthesis of 3,6-Dien-1-ynes by Nickel-Catalyzed Coupling Reaction of Allyl Chlorides, 1-Alkynes, and Alkynyltins

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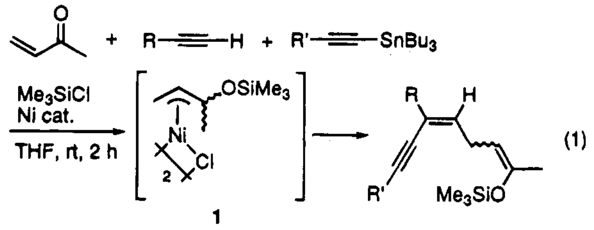
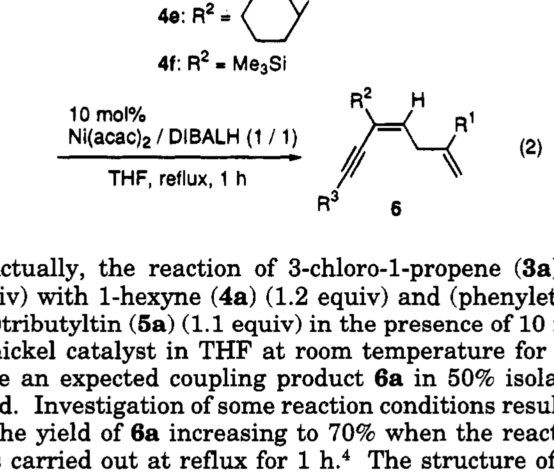
Summary: In the presence of a nickel catalyst prepared from Ni(acac)$_2$ and DIBALH (1/1) *in situ*, three-component coupling reaction of allyl chlorides, 1-alkynes, and alkynyltins yielded regio- and stereoselective 3,6-dien-1-ynes in THF.

We recently reported a new nickel-catalyzed coupling reaction of α,β-conjugated enones with alkynes and alkynyltins to give highly stereodefined enynes (eq 1).[1]



In this reaction, [[(trimethylsilyl)oxy]allyl]nickel complex **1** generated from the reaction of nickel complex with enone and Me$_3$SiCl[2] would be present as a key intermediate. This result suggested that simpler η^3-allylnickel complexes (e.g., **2** in Scheme 1) may also act as catalytic intermediates. It is well known that **2** is easily prepared from allyl halide and nickel(0) complex.[3] Thus, we examined the three-component coupling reaction of allyl chlorides **3** with 1-alkynes **4** and alkynyltins **5** in the presence of nickel catalyst prepared from Ni(acac)$_2$ and DIBALH (1/1) *in situ* (eq 2).



Actually, the reaction of 3-chloro-1-propene (**3a**) (1 equiv) with 1-hexyne (**4a**) (1.2 equiv) and (phenylethynyl)tributyltin (**5a**) (1.1 equiv) in the presence of 10 mol % nickel catalyst in THF at room temperature for 4 h gave an expected coupling product **6a** in 50% isolated yield. Investigation of some reaction conditions resulted in the yield of **6a** increasing to 70% when the reaction was carried out at reflux for 1 h.[4] The structure of **6a**

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[1] Ikeda, S.; Sato, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5975.

[2] Johnson, J. R.; Tully, P. S.; Mackenzie, P. B.; Sabat, M. *J. Am. Chem. Soc.* **1991**, *113*, 6172. Grisso, B. A.; Johnson, J. R.; Mackenzie, P. B. *J. Am. Chem. Soc.* **1992**, *114*, 5160.

[3] Jolly, P. W. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8. Billington, D. C. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, p 423.

[4] The nickel-catalyzed reaction of **3a** (1 equiv) with **5a** (1.1 equiv) in the absence of **4a** at reflux for 4 h gave 1-phenyl-4-penten-1-yne (**7**) in 26% GC yield.

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Table 1. Nickel-Catalyzed Reaction of 3 with 4 and 5[a]

entry	allyl chloride	alkyne	alkynyltin	product	yield[b] %
1	**3a**	**4a**	**5a**	**6a**	70 (>98)
2	**3b**	**4a**	**5a**	**6b**	67 (97)
3	**3a**	**4b**	**5a**	**6c**	80 (>98)
4	**3a**	**4a**	**5b**	**6d**	72 (>98)
5	**3a**	**4c**	**5b**	**6e**	83 (>98)
6	**3a**	**4d**	**5b**	**6f**	76 (98)
7	**3a**	**4e**	**5a**	**6g**	79 (98)
8	**3a**	**4f**	**5a**	**6h**	36[c] (95)

[a] Reaction conditions: allyl chloride (1 mmol), alkyne (1.2 mmol), alkynyltin (1.1 mmol), Ni(acac)$_2$ (0.1 mmol), DIBALH (1 M toluene solution, 0.1 mL), THF (5 mL) at reflux for 1 h under N$_2$. [b] Isolated yield. Isomeric purity is in parentheses. [c] 1-Phenyl-1-penten-1-yne (**7**) was also detected by GC analysis of the reaction mixture (21% yield).

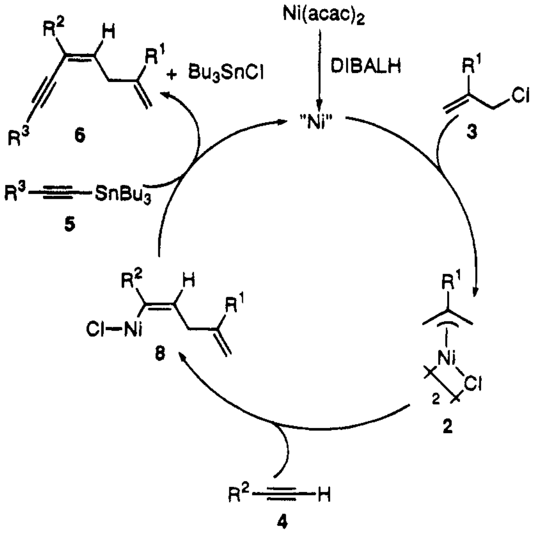
was assigned to (*Z*)-3-butyl-1-phenyl-3,6-heptadien-1-yne by ^{1}H NMR spectra and NOE experiment, and regio- or stereoisomers of **6a** were not detected (isomeric purity of **6a**: >98%).

The three-component coupling of a variety of substrates **3**–**5** proceeds regio- and stereoselectively to yield the corresponding products **6a**–**h**. The product yields and isomeric purities of **6** are summarized in Table 1.[5] A bromine atom in **4c** (entry 5), a (*tert*-butyldimethylsilyl)oxyl group in **4d** (entry 6), and a free hydroxyl group in **4e** (entry 7) remained intact in the reaction. The reaction with **4f** containing a trimethylsilyl group obtained **6h** in only 36% yield along with 1-phenyl-4-penten-1-yne (**7**) (21% GC yield) (entry 8). Interestingly, 3-bromo-1-propene as a substrate under the same reaction conditions gave only 7% of **6a**. The use of allyl- and vinyltins in place of **5** did not react even at prolonged reaction times (20 h).

The proposed reaction mechanism is shown in Scheme 1. The complex **2** was initially generated from the reaction of nickel complex with **3**.[3] Insertion of **4** into **2**, which would be the regio- and stereodetermining step, gives a vinylnickel complex **8**.[6] Transmetallation of **5** with **8** followed by reductive elimination yields the coupling product **6**, regenerating the nickel complex.[7]

In summary, we have described here the three-component coupling of allyl chlorides, 1-alkynes, and alkynyltins in the presence of nickel catalyst.[8,9] The present regio- and stereoselective coupling reaction provides a new synthetic method for the conjugated enynes.[1,10] More detailed studies on the scope of the reaction are in progress.

Scheme 1



Supplementary Material Available: Listing of experimental details and spectral and analytical data for the obtained products (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[5] All new compounds were characterized by NMR, IR, and mass spectral data and by elemental analyses. See supplementary material.

[6] For the insertion of alkynes into η^3-allylnickel intermediates, see: Chiusoli, G. P. *Acc. Chem. Res.* **1973**, *6*, 422. Casser, L.; Chiusoli, G. P.; Guerrieri, F. *Synthesis* **1973**, 509. Llebaria, A.; Moretó, J. M. *J. Organomet. Chem.* **1993**, *451*, 1.

[7] The nickel-catalyzed reaction of alkenyl halides such as β-styryl bromide with **5a** did not afford the corresponding coupling products.

[8] The reaction of organic bromides, norbornenes, alkynes, and alkali carboxylates was investigated in the presence of Ni(cod)$_2$ and P(O^i*Pr*)$_3$ as a catalyst. See: Catallani, M.; Chiusoli, G. P.; Mari, A. *J. Organomet. Chem.* **1984**, *275*, 129.

[9] For recent papers on palladium-catalyzed three-component coupling reactions, see: Torii, S.; Okumoto, H.; Ozaki, H.; Nakayasu, S.; Kotani, T. *Tetrahedron Lett.* **1990**, *31*, 5319. Chatani, N.; Amishiro, N.; Murai, S. *J. Am. Chem. Soc.* **1991**, *113*, 7778. Torii, S.; Okumoto, H.; Ozaki, H.; Nakayasu, S.; Tadokoro, T.; Kotani, T. *Tetrahedron Lett.* **1992**, *33*, 3499. Torii, S.; Okumoto, H.; Kotani, T.; Nakayasu, S.; Ozaki, H. *Tetrahedron Lett.* **1992**, *33*, 3503.

[10] For recent papers on the synthesis of conjugated enynes, see: Okuro, K.; Furuune, M.; Miura, M.; Nomura, M. *Tetrahedron Lett.* **1992**, *33*, 5363. Luo, F.-T.; Fwu, S.-L.; Huang, W.-S. *Tetrahedron Lett.* **1992**, *33*, 6839. Torii, S.; Okumoto, H.; Tadokoro, T.; Nishimura, A.; Rashid, M. A. *Tetrahedron Lett.* **1993**, *34*, 2139. Nuss, J. M.; Rennels, R. A.; Levine, B. H. *J. Am. Chem. Soc.* **1993**, *115*, 6991.