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Nickel-Catalyzed Hydrosilylation/ Cyclization of Difluoro-Substituted 1,6-Enynes

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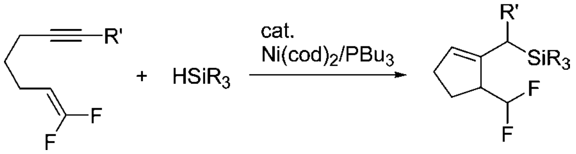
ABSTRACT



Ni-catalyzed hydrosilylative cyclization of difluoro-substituted 1,6-enynes can be carried out. The presence of a geminal-difluoromethylene group at an alkene terminus in enynes is essential for the reaction to proceed.

Catalytic hydrosilylation of unsaturated organic compounds is a process of substantial importance for the synthesis of organosilicon derivatives.[1] Numerous transition metal complexes are known to function as effective catalysts for hydrosilylation. Hydrosilylation of enynes is also an important method for the preparation of cyclic compounds bearing a C−Si bond.[2−4] In most cases, rhodium complexes were used as catalysts for hydrosilylation of enynes reported thus far.[2] Enynes that are applicable to the Rh-catalyzed hydrosilylation are limited to those having no substituents at the alkene moiety except one specific example.[2h] In contrast to the Rh-catalyzed hydrosilylation of enynes, which results in the formation of a C−Si bond at the alkyne carbon, palladium-[3] and yttrium-catalyzed hydrosilylation[4] of enynes yields hydrosilylative cyclization products, in which a C−Si bond forms at the alkene terminus carbon. To the best of our knowledge, there is no example of hydrosilylation of difluoro-substituted enynes, although the expected cyclic products would have both C−Si and C−F bonds that are useful in synthesis—the fluorine atom attached at an alkene is expected to put a unique reactivity to the alkene.[5] We have already reported that the Ni-catalyzed reaction of difluoro-substituted 1,6-enynes with organozinc reagents resulted in alkylative or reductive cyclization in which a trans-C−F bond is selectively substituted during cyclization.[6] We wish to report a new type of Ni-catalyzed hydrosilylative cyclization of difluoro-substituted 1,6-enynes in which the presence of a difluoromethylene group at the alkene carbon is essential for the reaction to proceed.

The reaction of **1** with HSiMe$_2$Ph in the presence of Ni(cod)$_2$/PBu$_3$ as the catalyst in dioxane at 50 °C for 2 h gave **2a** as a single product in 75% isolated yield (Scheme 1). The product obtained was not the expected product, which

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[1] Hiyama, T.; Kusumoto, T. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Elsevier: Oxford, U. K., 1991; Vol. 8, p 763. Ball, Z. In *Comprehensive Organometallic Chemistry III*; Crabtree, R. H., Mingos, M., Eds.; Elsevier: Oxford, U. K., 2007; Vol. 10, p 815. Roy, A. K. *Adv. Organomet. Chem.* **2008**, *44*, 1.

[2] (a) Ojima, I.; Donovan, R. J.; Shay, W. R. *J. Am. Chem. Soc.* **1992**, *114*, 6580. (b) Ojima, I.; Vu, A. T.; Lee, S.-Y.; McCullagh, J. V.; Moralee, A. C.; Fujiwara, M.; Hoang, T. H. *J. Am. Chem. Soc.* **2002**, *124*, 9164. (c) Chakrapani, H.; Liu, C.; Widenhoefer, R. A. *Org. Lett.* **2003**, *5*, 157. (d) Park, K. H.; Kim, S. Y.; Son, S. U.; Chung, Y. K. *Eur. J. Org. Chem.* **2003**, 4341. (e) Park, K. H.; Jung, I. G.; Kim, S. Y.; Chung, Y. K. *Org. Lett.* **2003**, *5*, 4967. (f) Maerten, E.; Delerue, H.; Queste, M.; Nowicki, A.; Suisse, I.; Agbossou-Niedercorn, F. *Tetrahedron: Asymmetry* **2004**, *15*, 3019. (g) Fan, B.-M.; Xie, J.-H.; Li, S.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2007**, *46*, 1275. (h) Denmark, S. E.; Liu, H.-C. J. *J. Am. Chem. Soc.* **2007**, *129*, 3737.

[3] Wakayanagi, S.; Shimamoto, T.; Chimori, M.; Yamamoto, K. *Chem. Lett.* **2005**, *34*, 160.

[4] Molander, G. A.; Retsch, W. H. *J. Am. Chem. Soc.* **1997**, *119*, 8817.

[5] Amii, H.; Uneyama, K. *Chem. Rev.* **2009**, *109*, 2119.

[6] Takachi, M.; Kita, Y.; Tobisu, M.; Fukumoto, Y.; Chatani, N. *Angew. Chem., Int. Ed.*, in press.

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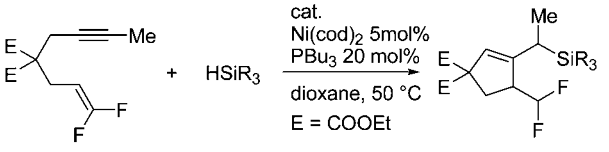
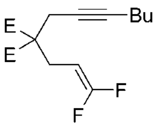
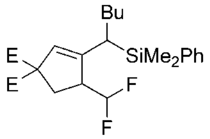
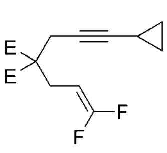
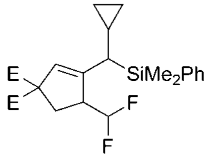
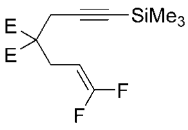
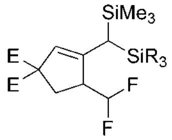
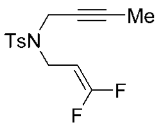
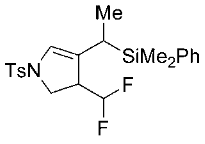
Scheme 1



1	HSiMe$_2$Ph	**2a** 75% (2 h)
	HSiMePh$_2$	**2b** 67% (24 h)
	HSiMe$_2$Et	**2c** 69% (8 h)
	HSiEt$_3$	**2d** 28% (24 h)

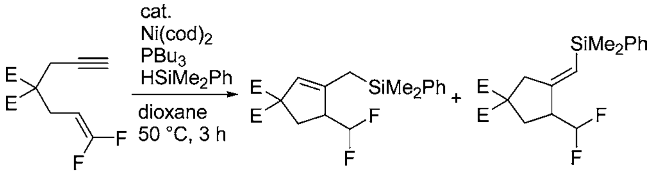
has an exosilylmethylene (vinylsilane) moiety, but instead has an allylsilane moiety[7] unlike reported examples of the Rh-catalyzed hydrosilylation of simple enynes.[2] In addition, the product has a difluoromethyl moiety, which is often used in the medicinal, agricultural, and material sciences.[8] Among the ligands examined, it was found that PBu$_3$ is the ligand of choice: PBu$_3$ (75%, 2 h), PPh$_3$ (56%, 2 h), PCy$_3$ (41%, 24 h), dppe (no reaction, 24 h). While other hydrosilanes also gave the corresponding cyclic allylsilanes, the reaction with HSiMe$_2$Ph gave a better yield in a short reaction time. The reaction was significantly affected by steric factors of hydrosilanes (HSiMe$_2$Ph > HSiMePh$_2$, HSiMe$_2$Et > HSiEt$_3$).

Table 1. Ni-Catalyzed Hydrosilylation of Difluoro-Substituted Enynes[a]

difluoro-enyne	product[b]
 **3**	 **4** 67% (24 h)
 **5**	 **6** 71% (4 h)
 **7**	
HSiMe$_2$Ph	**8a** 95% (6 h)
HSiMePh$_2$	**8b** 94% (6 h)
HSiMe$_2$Et	**8c** 94% (2 h)
HSiEt$_3$	**8d** 90% (6 h)
HSi(OMe)$_3$	**8e** 84% (6 h)
 **9**	 **10** 68% (24 h)

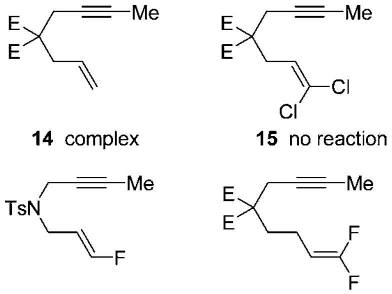
[a] Reaction conditions: enyne (0.3 mmol), HSiR$_3$ (0.60 mmol), Ni(cod)$_2$ (0.015 mmol), PBu$_3$ (0.06 mmol), dioxane (1.5 mL) at 50 °C. [b] Isolated yield.

Scheme 2



11 **12** 18% **13** 11%

Scheme 3. Limitations



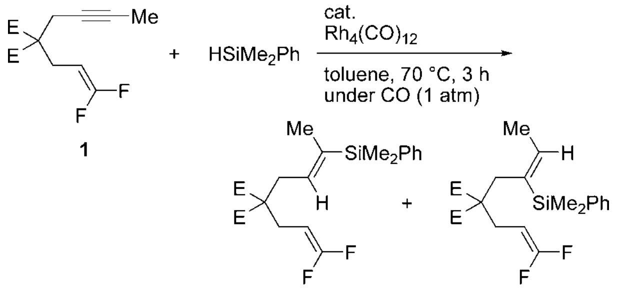
14 complex **15** no reaction

16 complex **17** complex

The results of the Ni-catalyzed hydrosilylation of difluoro-substituted 1,6-enynes are shown in Table 1. Various difluoro-substituted 1,6-enynes having an internal alkyne served as good substrates to give the corresponding cyclic allylsilanes. Curiously, an enyne having a trimethylsilyl group at the alkyne terminus, as in **7**, gave the corresponding products **8** in high yields, irrespective of the structure of the hydrosilanes.[9] An enyne with a nitrogen functional group, as in **9**, also gave the corresponding product **10** in a good yield.

In contrast to enynes having internal alkynes, the reaction of an enyne having a terminal alkyne moiety, as in **11**, gave a mixture of allylsilane **12** and vinylsilane **13** (Scheme 2).

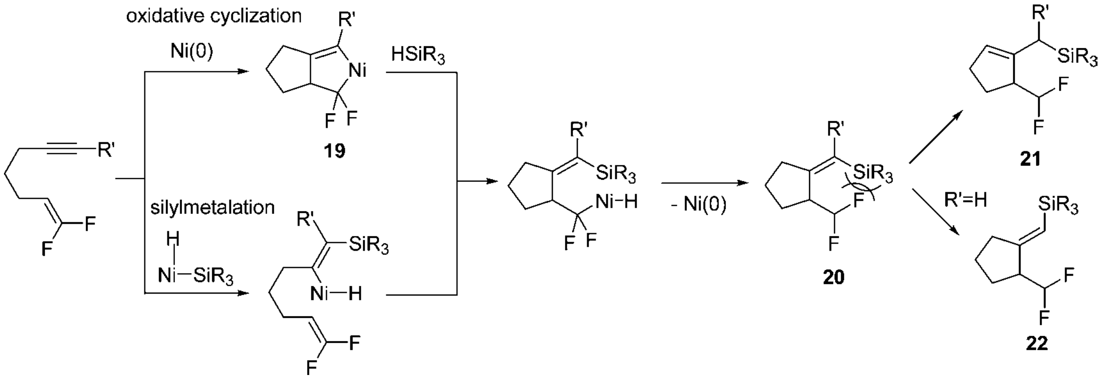
Scheme 4. Rh-Catalyzed Hydrosilylation of **1**



1

18 54% **18'** 15%

Scheme 5. Reaction Mechanism



The presence of a difluoromethylene group at an alkene terminus in enynes was essential for the reaction to proceed (Scheme 3). The reaction of a simple enyne **14**, dichloro-substituted enyne **15**, and monosubstituted enyne **16** gave either complex mixtures or no reaction at all. The length in the tether was also an important factor. Thus, a complex mixture was obtained in the case of 1,7-difluoro-substituted enyne **17**.

Use of $Rh_4(CO)_{12}$ as the catalyst gave a regioisomeric mixture of hydrosilylation products **18**, in which the alkene moiety did not participate (Scheme 4).

The proposed reaction mechanism is shown in Scheme 5. One possibility would have the pathway via a nickelacycle **19** as a key intermediate, which is formed by the oxidative cyclization of an enyne and Ni(0).[10] Another possibility could be the silylmetalation pathway. Tamao and Ito reported the Ni-catalyzed hydrosilylation of diynes in which it was proposed that the reaction is initiated by silylmetalation.[11] Irrespective of the mechanism, an initial product was vinylsilane **20**, which isomerized to thermodynamically stable allylsilane **21** under the reaction conditions. When R′ = H, the isomerization of **20** to **22** also proceeded.

In summary, the first example of hydrosilylation of difluoro-substituted 1,6-enynes is described. A nickel complex showed high catalytic activity.

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

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