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# NICKEL-CATALYZED CARBOMETALLATION OF FUNCTIONALIZED SILYLALKYNES BY GRIGNARD REAGENTS

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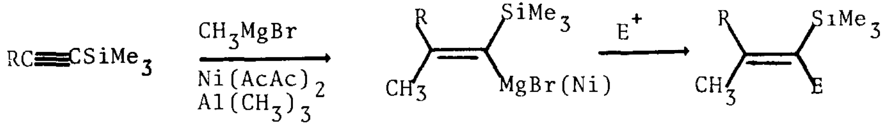
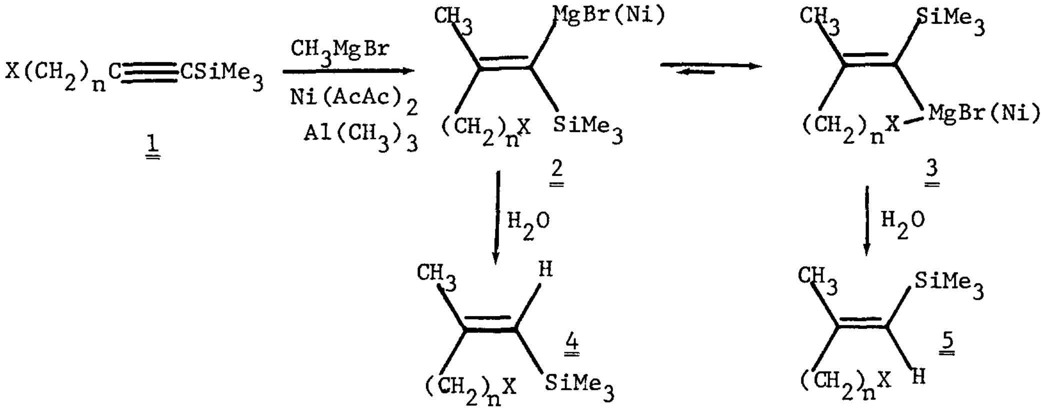
Syntheses of vinylsilanes by the nickel catalyzed addition of methylmagnesium bromide to functionalized silylalkynes are described. Simple syntheses of geraniol and farnesol are reported.

Vinylsilanes have recently been shown to be versatile synthetic intermediates, undergoing electrophilic desilylation with retention of stereochemistry.[1,2] We have reported that the nickel catalyzed addition of methylmagnesium bromide to 1-trimethylsilyl-1-alkynes provides a general route to di- and trisubstituted vinylsilanes (eqn.1).[3] We now wish to report some novel features of the extension of this reaction to functionalized silylalkynes.



eqn. 1

The nickel catalyzed addition of methylmagnesium bromide to 4-trimethylsilyl 3-butyn-1-ol derivatives 1a and 1b gives either the cis or trans adduct selectively depending on the reaction conditions. These additions were carried out as previously described.[3] Trimethylaluminum in hexane (0.1 eq) was added to a solution of nickel acetylacetonate (0.1 eq) in anhydrous tetrahydrofuran giving a homogeneous brown solution. The silylacetylene (1.0 eq) was added immediately, followed rapidly by 4 eq of methylmagnesium bromide in benzene/tetrahydrofuran. The nickel catalyzed addition to the tetrahydropyranyl ether 1a[4] proceeds more rapidly than the analogous reaction with 1-trimethylsilyl-1-octyne. Presumably the electronegative oxygen inductively makes the acetylene electron poor, enhancing complexation to nickel.[5] The silyl ether reacts similarly to 1a and 1b but was not used because of its hydrolytic instability. After 5 hr the reaction with tetrahydropyranyl ether 1a is 80% complete and an 80/20 mixture of 2a and 3a is present. After 11 hr the reaction is complete and a 70/30 mixture of 4a and 5a is isolated in 60% yield.[6,7] The ethoxyethyl ether 1b reacts slightly slower than 1a. After 4 hr the reaction is 60% complete and an 80/20 mixture of 2b and 3b is present. At longer reaction times the reaction goes to completion but isomerization has proceeded further. After 96 hr a 15/85 mixture of 4b and 5b is isolated in 60% yield. We believe that the isomerization is nickel catalyzed[8] and that in the case of 2b/3b the Grignard reagent 3b is more stable as a result of chelation of the magnesium to the oxygen. At short reaction times the initially formed cis addition product 2b is obtained as the major product, while at longer times the thermodynamically more stable chelated isomer 3b predominates.

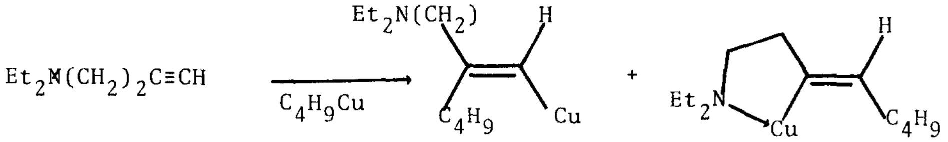


**a**, n = 2, X = OTHP
**b**, n = 2, X = $OCH(CH_3)OC_2H_5$
**c**, n = 2, X = $N(C_2H_5)_2$
**d**, n = 3, X = OTHP
**e**, n = 3, X = $OCH(CH_3)OC_2H_5$
**f**, n = 3, X = $N(C_2H_5)_2$

The diethylamine **1c**[4] reacts more slowly than **1a** or **1b** and isomerizes more rapidly. After 24 hr a 1/9 mixture of **4c** and **5c** is isolated in low yield. After several days exclusively trans adduct **5c** is isolated in 36% yield. The more basic amine not only shifts the equilibrium in favor of **3c** but also accelerates the isomerization. The slower addition may be due to the complexation of the amine with magnesium or nickel.

The trimethylsilylpentynol derivatives **1d**-**1f**[4] behave similarly, although in this case isomerization is slower, since chelation gives a seven rather than a six-membered ring. The tetrahydropyranyl ether **1d** gives a 9/1 mixture of **4d** and **5d** in 52% yield after 16 hr. The ethoxyethyl ether **1e** gives exclusively cis adduct **4e** in 61% yield after 4.5 hr. After 10 days a 1/1 mixture of **2e** and **3e** is present. The diethylamine **1f** gives a 60% yield of an 85/15 mixture of **4f** and **5f** after 5 hr. After 7 days a 35/65 mixture of **2f** and **3f** is present.

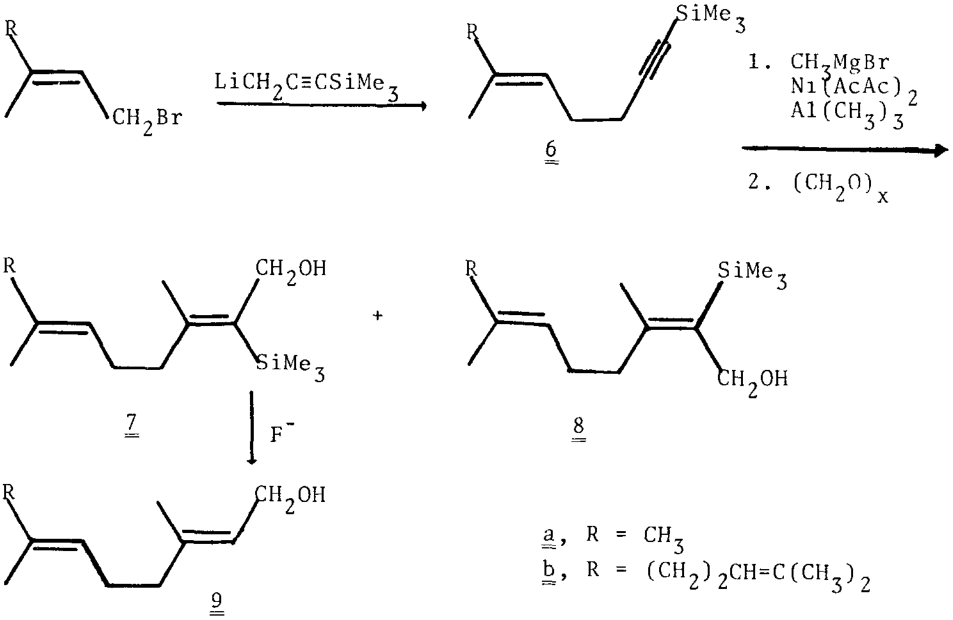
These nickel catalyzed additions to functionalized acetylenes complement the organocopper additions to similar substrates which give mixtures of regioisomers rather than stereoisomers (eqn. 2).[9] We are currently exploring the application of the nickel catalyzed isomerization procedure to the preparation of stable chelated vinylmagnesium reagents starting from readily accessible mixtures of vinyl halides.[10]



eqn. 2

Geraniol and farnesol were synthesized to examine the effect of double bonds on the addition reaction. Nickel catalyzed addition of methylmagnesium bromide to 1-trimethylsilyl-6-methyl-5-hepten-1-yne (6a),[11] prepared from prenyl bromide and lithiotrimethylsilylpropyne in 70% yield, followed by quenching with paraformaldehyde gives 38% of 7a and 5% of 8a.[12] Desilylation of 7a with tetraethylammonium fluoride in DMSO[13] at 60° gives geraniol (9a)[14] in 80% yield. Similarly, 6b[11], prepared from geranyl bromide and lithiotrimethylsilylpropyne in 62% yield, gives 39% of 7b and 5% of 8b. Desilylation[13] of 7b gives trans, trans-farnesol (9b)[14] in 60% yield.

The use of lithiotrimethylsilylpropyne to construct a complex silylacetylene in a single step, followed by nickel catalyzed addition of methylmaganesium bromide and trapping with formaldehyde, thus provides an attractive route for terpene synthesis.



a, R = $CH_3$
b, R = $(CH_2)_2CH{=}C(CH_3)_2$

## References and Notes

1. For reviews see T.H. Chan, *Acc. Chem. Res.*, **10**, 442 (1977); E. Colvin, *Chem. Soc. Rev.*, **7**, 15 (1978).
2. T.H. Chan, P.W.K. Lau and W. Mychajlowskij, *Tetrahedron Lett.*, 3317 (1977) and references cited therein.
3. B.B. Snider, M. Karras and R.S.E. Conn., *J. Am. Chem. Soc.*, **100**, 4624 (1978).
4. Treatment of 3-butynol with 2 eq of butylithium followed by treatment with trimethylsilyl chloride gave trimethylsilylbutynyl trimethylsilyl ether. Hydrolysis gave trimethylsilylbutynol which was converted to **1a** and **1b** by standard methods and to **1c** by tosylation and treatment with diethylamine. **1d-f** were made similarly from 4-pentynol.
5. P.W. Jolly and G. Wilke, "The Organic Chemistry of Nickel", Academic Press, New York, 1974, Vol. 1, pp. 245-252.
6. Yields were not optimized. In most cases the stereoisomers were seperated by column chromatography. The yields given in these cases are the sums of the yields of the isomers.
7. All compounds were characterized by IR, NMR and Mass Spectra and exact masses of chromatographically homogeneous samples. The stereochemistry of the addition products is determined by NMR. The methyl of the cis addition product **4** absorbs as a doublet, J = 1.5Hz. The methyl of the trans addition product **5** absorbs slightly upfield from that of **4** as a doublet, J = 0.8Hz.[3]
8. M. Zembavashi, K. Tamao and M. Kumada, *Tetrahedron Lett.*, 1719 (1975).
9. A. Alexakis, J. Normant and J. Villieras, *J. Organometal. Chem.*, **96**, 471 (1975).
10. J. W. Cornforth, R.H. Cornforth, G. Popják and L. Yengoyan, *J. Biol. Chem.*, **241**, 3970 (1966).
11. E.J. Corey and H. A. Kirst, *Tetrahedron Lett.*, 5041 (1968).
12. The reaction was inhibited by impurities present in the crude **6**. Carefully purified **6** reacted similarly to trimethylsilyloctyne. Complete separation of **7** and **8** was effected by chromatography on silica gel with 8:1 hexane:ethyl acetate.
13. T.H. Chan and W. Mychajlowskij, *Tetrahedron Lett.*, 3479 (1974).
14. Geraniol and farnesol were characterized by GC and NMR; R.B. Bates and D.M. Gale, *J. Am. Chem. Soc.*, **82**, 5749 (1960); R.B. Bates, D.M. Gale and B.J. Gruner, *J. Org. Chem.*, **28**, 1086 (1963).

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