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Facile Synthesis of Both *syn* and *anti* Homoallylic Alcohols from Allyl Chlorides via Organosilicon Intermediates

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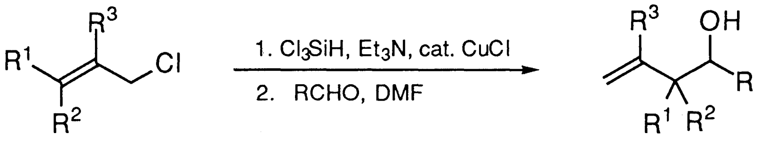
Highly regio- and diastereoselective synthesis of homoallylic alcohols from allyl chlorides via organosilicon intermediates are attained. While *syn* homoallylic alcohols were prepared from (Z)-allyl chlorides, *anti* homoallylic alcohols were obtained from (E)-allyl chlorides. 1-Chloro-2,4-pentadiene reacted at the γ position of the diene system regioselectively.

The stereoselective reactions of allyl organometallics with carbonyl compounds for the synthesis of homoallylic alcohols are one of the most important carbon-carbon bond-forming processes in organic synthesis.1) In order to obtain both *syn* and *anti* homoallylic alcohols in high stereoselectivities, preparation of geometrically pure (E)- and (Z)-allyl organometallics and the reactions via the six membered cyclic transition states are inevitable.1d,e,2) Moreover, it is synthetically desirable to use easily available allyl halides as starting materials. However, although many allyl organometallic reagents have been developed, examples which satisfy the above criteria, direct and highly regio- and stereoselective preparation of homoallylic alcohols from allyl halides, are quite few, and development of new methodologies is strongly desired.

In this paper, we report a solution of this problem; a highly regio- and diastereoselective one-pot synthesis of homoallylic alcohols from allyl chlorides via organosilicon intermediates.

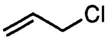
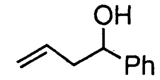
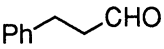
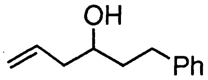
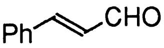
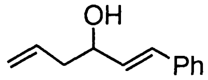
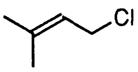
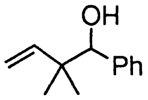
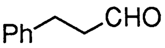
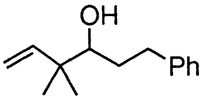
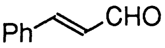
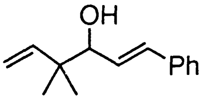
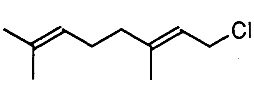
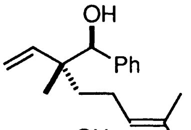
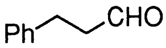
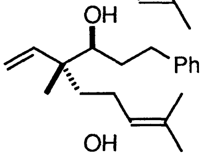
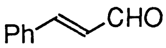
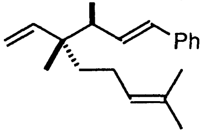
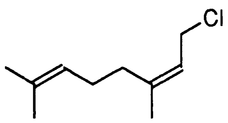
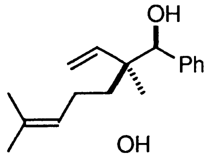
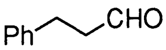
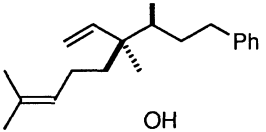
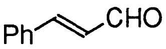
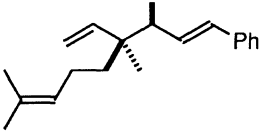
A general scheme for the present one-pot synthesis of homoallylic alcohols from allyl halides is shown below (Scheme 1). An allyl chloride reacts with trichlorosilane (Cl_3SiH) in the presence of triethylamine (1.1 eq.) and cuprous chloride (CuCl, 0.03 eq.) to give an intermediate allyltrichlorosilane.3) To the same pot, an aldehyde in *N,N*-dimethylformamide (DMF) is added.4)



Scheme 1. One-pot Synthesis of Homoallylic Alcohols from Allyl Halides.

Selected examples of the synthesis of homoallylic alcohols from allyl halides are shown in Table 1. In every case, the desired homoallylic alcohols were obtained in high yields. It should be noted that addition of the organosilicon intermediates to the aldehydes proceeded smoothly even in the presence of ether, CuCl, and triethylamine-hydrochloric acid salt ($Et_3N{\bullet}HCl$). The additions occurred exclusively at the γ position of the allyl

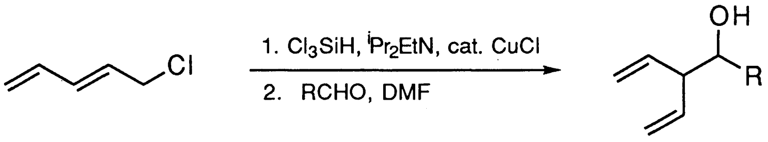
Table 1. One-pot Synthesis of Homoallylic Alcohols from Allyl Chlorides

Entry	Allyl Chloride	Aldehyde	Product	Yield/%a)	*syn*/ *anti*b)
1		PhCHO		89	—
2				89	—
3				88	—
4		PhCHO		82	—
5				83	—
6				88	—
7	 c)	PhCHO		82	<1/>99
8				91	<1/>99
9				97	<1/>99
10	 c)	PhCHO		92	>99/1
11				87	>99/1
12				93	>99/1

a) Isolated yield. b) Determined by ^1H and ^{13}C NMR. c) Diisopropylethylamine was used in stead of triethylamine.

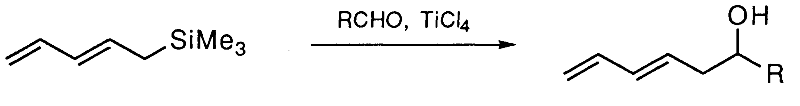
chlorides. Excellent diastereoselectivities were also observed; *syn*-homoallylic alcohols were formed from (Z)-allyl chlorides, whereas *anti*-homoallylic alcohols were produced from (E)-allyl chlorides. These selectivities can be ascribed to the stereospecific formation of (Z)- and (E)-allyltrichlorosilanes from the corresponding allyl chlorides.

1-Chloro-2,4-pentadiene⁵⁾ also worked well under the same reaction conditions, and the reactions occurred at the γ position of the diene system exclusively (Eq. 1). It is noted that the selectivity is quite a contrast to that in the reactions of 2,4-pentadienyltrimethylsilane under the influence of a Lewis acid, which reacted with aldehydes at the terminal position of the diene system (Eq. 2).⁶⁾ This can be rationalized by assuming the six-membered cyclic transition state shown in Scheme 2.

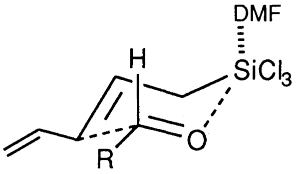


(Eq. 1)

R = Ph	83%
R = $Ph(CH_2)_2$	86%
R = (E)-PhCH=CH	87%



(Eq. 2)



Scheme 2.

A typical experimental procedure is described for the reaction of (E)-1-chloro-3,7-dimethyl-2,6-octadiene (geranyl chloride) with cinnamaldehyde: To a CuCl (0.02 mmol) suspension in Et_2O (0.25 ml) was added diisopropylethylamine (0.66 mmol) in Et_2O (0.5 ml), geranyl chloride (0.6 mmol) in Et_2O (0.5 ml), and trichlorosilane (0.6 mmol) successively at room temperature. The mixture was stirred for 10 h at this temperature and then DMF (2 ml) was added. After cooling to 0 °C, cinnamaldehyde (0.5 mmol) in DMF (1 ml) was added and the mixture was further stirred for 12 h at 0 °C. Cold 1 mol dm^{-3} hydrochloric acid was added to quench the reaction, and the aqueous layer was extracted with Et_2O. After a usual work up, (E)-*anti*-3-hydroxy-4,8-dimethyl-1-phenyl-4-vinyl-1,7-nonadiene⁷,⁸⁾ was obtained in a 97% yield.

Similarly, (E)-*syn*-3-hydroxy-4,8-dimethyl-1-phenyl-4-vinyl-1,7-nonadiene⁷,⁹⁾ was prepared from (Z)-1-chloro-3,7-dimethyl-2,6-octadiene (neryl chloride) and cinnamaldehyde.

In summary, a new and efficient method for the preparation of homoallylic alcohols from allyl chlorides has been developed. Advantages of the present reaction over the conventional methods are: (1) The starting materials, allyl chlorides, are stable and easily available and the procedures are quite simple; (2) Both diastereomer, *syn* and *anti* homoallylic alcohols, can be prepared with high yields and excellent regio- and disatereoselectivities under extremely mild conditions; (3) Unique selectivities were observed in the reactions of 1-chloro-2,4-pentadiene.

High efficiency attained by one-pot process without isolation of hygroscopic allyltrichlorosilanes is noteworthy to refer.

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1) For example, a) A. Yanagisawa, S. Habaue, and H. Yamamoto, *J. Am. Chem. Soc.*, **113**, 8955 (1991); b) C. Jubert, S. Nowotny, D. Kornemann, I. Antes, C. E. Tucker, and P. Knochel, *J. Org. Chem.*, **57**, 6384 (1992); c) P. Wipf and S. Lim, *J. Chem. Soc., Chem. Commun.*, **1993**, 1654, and references cited therein. Review: d) Y. Yamamoto and N. Asao, *Chem. Rev.*, **93**, 2207 (1993); e) W. R. Roush, "Comprehensive Organic Synthesis," Vol. 2, ed by B. M. Trost, Pergamon Press, Oxford (1991), p. 1.

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7) S. Habaue, K. Yasue, A. Yanagisawa, and H. Yamamoto, *Synlett*, **1993**, 788.

8) IR (neat) 3440, 1640, 1450. 970 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.01 (s, 3H), 1.41 (dd, 2H, J = 7.3, 9.9 Hz), 1.57 (s, 3H), 1.66 (s, 3H), 1.89 (m, 2H), 1.97 (br s, 1H), 3.96 (d, 1H, J = 7.4 Hz), 5.09 (d, 1H, J = 17.5 Hz), 5.06-5.17 (m, 1H), 5.24 (d, 1H, J = 10.8 Hz), 5.84 (dd, 1H, J = 10.8, 17.5 Hz), 6.20 (dd, 1H, J = 7.4, 15.9 Hz), 6.56 (dd, 1H, J = 7.4, 15.9 Hz), 7.18-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.8, 17.5, 22.6, 25.6, 37.4, 45.2, 78.5, 115.4, 124.6, 126.4, 127.5, 128.2, 128.4, 132.3, 132.4, 136.7, 143.6. Anal. Found: C, 84.27; H, 9.75%. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69%.

9) IR (neat) 3440, 1640, 1450, 970 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.08 (s, 3H), 1.37-1.51 (m, 2H), 1.57 (s, 3H), 1.66 (s, 3H), 1.87-1.93 (m, 3H), 4.00 (d, 1H, J = 6.3 Hz), 5.03-5.10 (m, 1H), 5.07 (d, 1H, J = 17.4 Hz), 5.20 (d, 1H, J = 10.9 Hz), 5.82 (dd, 1H, J = 10.9, 17.4 Hz), 6.25 (dd, 1H, J = 6.5, 15.8 Hz), 6.39 (d, 1H, J = 15.8 Hz), 7.18-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.5, 18.5, 22.6, 25.6, 36.9, 45.0, 78.7, 115.1, 124.7, 126.4, 127.4, 128.4, 129.0, 131.2, 131.5, 136.8, 142.8. Anal. Found: C, 84.04; H, 9.38%. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69%.

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