SHORT PAPER

J. Chem. Research (S),
2003, 296–298

A stereoselective synthesis of (*E*)-allylic alcohols via the hydromagnesiation of alkynylsilanes†

Mingzhong Cai[a]*, Chunyun Peng[a], Hong Zhao[b] and Wenyan Hao[a]

[a]*Department of Chemistry, Jiangxi Normal University, Nanchang 330027, P.R.China*

[b]*Department of Chemistry, Shangrao Teachers' College, Shangrao 334000, P.R.China*

Hydromagnesiation of alkynylsilanes **1** gives (*Z*)-α-silylvinyl Grignard reagents **2**, which are reacted with aldehydes or ketones to afford (*Z*)-β-silyl allylic alcohols **3** in high yields; intermediates **3** can undergo the desilylation reaction in the presence of anhydrous KF to give (*E*)-allylic alcohols **4** in good yields.

Keywords: hydromagnesiation, alkynylsilane, (*E*)-allylic alcohol, stereoselective synthesis, desilylation reaction

Allylic alcohols are important synthetic intermediates and tertiary allylic alcohols are incorporated in the structure of a variety of natural products and commercially important pharmaceuticals, so the synthesis of allylic alcohols is of considerable interest in organic chemistry.[1] Many methods can be used for the stereoselective synthesis of allylic alcohols,[2] only a few methods, however, are available for preparation of (*E*)-3-monosubstituted allylic alcohols. The reduction of substituted propargyl alcohols with $LiAlH_4$ gave (*E*)-3-monosubstituted allylic alcohols.[3] One-carbon homologation of (*E*)-alkenylboronates using the *in situ* generated chloromethyllithium yielded (*E*)-3-substituted allylboronates, which underwent clean oxidation by alkaline hydrogen peroxide to give the isomerically pure (*E*)-allylic alcohols.[4] The reduction of (*E*)-α,β-unsaturated aldehydes or ketones with sodium monoacetoxyborohydride afforded (*E*)-3-monosubstituted allylic alcohols.[5] These methods so far developed suffer from some disadvantages such as use of two equivalent expensive $LiAlH_4$ as reagent or (*E*)-configuration compounds as starting materials.

Hydromagnesiation has emerged as a unique hydrometallation with some attractive features, such as the high regioselectivity and stereoselectivity observed with alkynylsilanes.[6,7] We now report a facile route for stereoselective synthesis of (*E*)-allylic alcohols via the hydromagnesiation of alkynylsilanes (Scheme 1).

Alkynylsilanes **1** were easily prepared according to the literature procedure.[8] Hydromagnesiation of alkynylsilanes **1** at 25°C in ether for 6h gave (*Z*)-α-silylvinyl Grignard reagents **2**, which reacted with aldehydes or ketones at room temperature for 2h to afford (*Z*)-β-silyl allylic alcohols **3** in high yields. The experimental results are summarised in Table 1.

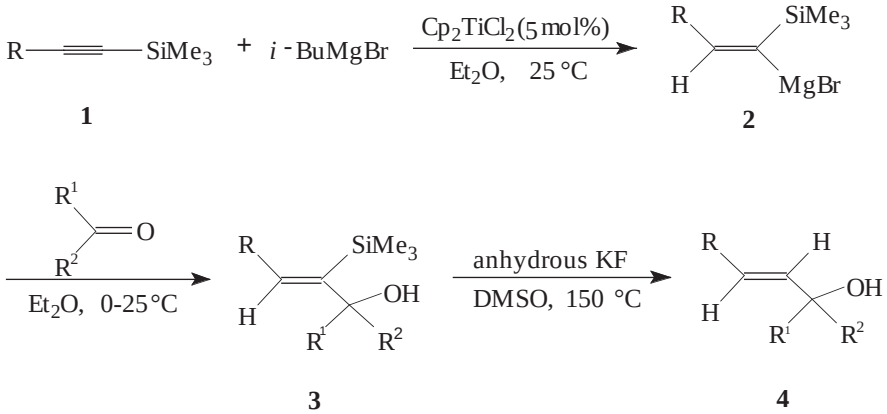
Table 1 Synthesis of (*Z*)-β-silyl allylic alcohols **3**

Entry	R	R^1	R^2	Product[a]	Yield[b](%)
1	*n*-C_4H_9	C_2H_5	H	**3a**	82
2	*n*-C_4H_9	CH_3	CH_3	**3b**	79
3	*n*-C_4H_9	4-ClC_6H_4	H	**3c**	74
4	*i*-C_5H_{11}	C_2H_5	H	**3d**	80
5	*i*-C_5H_{11}	CH_3	CH_3	**3e**	78
6	*i*-C_5H_{11}	Ph	H	**3f**	81
7	*n*-C_6H_{13}	C_2H_5	H	**3g**	83
8	*n*-C_6H_{13}	CH_3	CH_3	**3h**	75
9	*n*-C_6H_{13}	4-ClC_6H_4	H	**3i**	80
10	$PhCH_2$	C_2H_5	H	**3j**	69

[a] All the compounds were characterised using ^{1}H NMR, IR and elemental analyses.
[b] Isolated yield based on the alkynylsilane used.

The isomeric purities of products **3** were determined by ^{1}H NMR spectroscopy (300 MHz) to be more than 96%. One olefinic proton signal of **3** splits characteristically into one triplet with coupling constant J = 7.0 Hz, which indicated that the hydromagnesiation to the alkynylsilanes had taken place with strong preference for the addition of the magnesium atom at the carbon adjacent to the silyl group.

Vinylsilanes are important synthetic intermediates owing to the versatile reactivity of the silyl group and the carbon-carbon double bond.[9] (*Z*)-β-Silyl allylic alcohols **3** are also effective precursors for synthesising (*E*)-allylic alcohols. In the presence of anhydrous KF they can easily undergo the stereospecific



Scheme 1

* To receive any correspondence. E-mail: Caimz618@sina.com
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 2 Synthesis of (*E*)-allylic alcohols **4**

Entry	R	R^1	R^2	Product[a]	Yield[b](%)
1	*n*-C_4H_9	C_2H_5	H	**4a**	73
2	*n*-C_4H_9	CH_3	CH_3	**4b**	70
3	*n*-C_4H_9	4-ClC_6H_4	H	**4c**	76
4	*i*-C_5H_{11}	C_2H_5	H	**4d**	75
5	*i*-C_5H_{11}	CH_3	CH_3	**4e**	71
6	*i*-C_5H_{11}	Ph	H	**4f**	79
7	*n*-C_6H_{13}	C_2H_5	H	**4g**	74
8	*n*-C_6H_{13}	CH_3	CH_3	**4h**	66
9	*n*-C_6H_{13}	4-ClC_6H_4	H	**4i**	78

[a] All the compounds were characterised using ^{1}H NMR, IR and elemental analyses.
[b] Isolated yield based on the (*Z*)-β-silyl allylic alcohol used.

desilylation reaction in DMSO with retention of configuration.[10] Thus, the desilylation reactions of compounds **3** at 150°C in DMSO for 3h in the presence of anhydrous KF afforded (*E*)-allylic alcohols **4** in good yields. The typical results are summarised in Table 2. The stereochemistry of products **4** was easily established, since ^{1}H NMR spectra of **4b**, **4e** and **4h** give rise to a doublet at δ5.4–5.5 with a coupling constant of 16Hz, typical of trans-positioned protons. IR spectra of products **4a–i** show strong IR absorption bands at about 970cm^{-1}, which also indicate the existence of *trans*-positioned protons.[11]

In conclusion, the methodology discussed in this paper provides a convenient and practical route to (*E*)-allylic alcohols, which has advantages of readily available starting materials, straightforward and simple procedures, mild reaction conditions and good yields.

^{1}H NMR spectra were recorded on an AZ-300 MHz spectrometer with TMS as an internal standard. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. Microanalyses were measured using a Yanaco MT-3 CHN microelemental analyser. All solvents were dried, deoxygenated and freshly distilled before use.

(Z)-β-Silyl allylic alcohols 3a-j; general procedure: To a solution of isobutylmagnesium bromide (4.5 mmol) in diethyl ether (7 ml) was added Cp_2TiCl_2 (50 mg, 0.2 mmol) at 0°C under Ar, and the mixture was stirred for 30 min at that temperature. To this solution was added alkynylsilane **1** (4.0 mmol), and the mixture was stirred for 6h at 25°C. After being cooled to 0°C, aldehyde or ketone (4.0 mmol) was added and the mixture was stirred for 2h at 25°C, quenched with sat. aq NH_4Cl (25 ml) and extracted with Et_2O (2 × 30 ml). The organic layer was washed with sat. aq NH_4Cl (20 ml) and water (3 × 30 ml) and dried ($MgSO_4$). Removal of solvent under reduced pressure gave an oil, which was purified by column chromatography on silica gel (eluent: light petroleum – AcOEt, 10:1).

3a: ^{1}H NMR ($CDCl_3$): δ = 6.09 (t, *J* = 7.0 Hz, 1H), 3.95 (t, *J* = 5.7 Hz, 1H), 2.39–1.90 (m, 3H), 1.54–1.14 (m, 6H), 1.12–0.74 (m, 6H), 0.15 (s, 9H). IR (film): ν = 3368, 2958, 2860, 1612, 1458, 1249, 837 cm^{-1}. Anal. calcd for $C_{12}H_{26}OSi$: C, 67.29; H, 12.15. Found: C, 67.04; H, 11.87%.

3b: ^{1}H NMR ($CDCl_3$): δ = 5.96 (t, *J* = 7.0 Hz, 1H), 2.35–1.89 (m, 3H), 1.57–1.14 (m, 10H), 0.92 (t, *J* = 5.4 Hz, 3H), 0.20 (s, 9H). IR (film): ν = 3421, 2959, 2928, 2860, 1603, 1459, 1249, 838 cm^{-1}. Anal. calcd for $C_{12}H_{26}OSi$: C, 67.29; H, 12.15. Found: C, 66.96; H, 11.90%.

3c: ^{1}H NMR ($CDCl_3$): δ = 7.42–7.15 (m, 4H), 6.13 (t, *J* = 7.0 Hz, 1H), 5.12 (s, 1H), 2.45–1.96 (m, 3H), 1.65–1.23 (m, 4H), 0.93 (t, *J* = 5.4 Hz, 3H), 0.03 (s, 9H). IR (film): ν = 3400, 2956, 2858, 1610, 1488, 1249, 840 cm^{-1}. Anal. calcd for $C_{16}H_{25}OClSi$: C, 64.76; H, 8.43. Found: C, 64.45; H, 8.21%.

3d: ^{1}H NMR ($CDCl_3$): δ = 6.06 (t, *J* = 7.0 Hz, 1H), 3.93 (t, *J* = 5.7 Hz, 1H), 2.37–1.90 (m, 3H), 1.57–1.18 (m, 5H), 1.11–0.78 (m, 9H), 0.15 (s, 9H). IR (film): ν = 3399, 2956, 2871, 1603, 1467, 1382, 1365, 1249, 838 cm^{-1}. Anal. calcd for $C_{13}H_{28}OSi$: C, 68.42; H, 12.28. Found: C, 68.59; H, 12.11%.

3e: ^{1}H NMR ($CDCl_3$): δ = 5.96 (t, *J* = 7.0 Hz, 1H), 2.37–1.90 (m, 3H), 1.50–1.23 (m, 9H), 1.11–0.77 (m, 6H), 0.20 (s, 9H). IR (film): ν = 3391, 2955, 2870, 1610, 1467, 1384, 1366, 1248, 839 cm^{-1}. Anal. calcd for $C_{13}H_{28}OSi$: C, 68.42; H, 12.28. Found: C, 68.20; H, 12.04%.

3f: ^{1}H NMR ($CDCl_3$): δ = 7.16 (s, 5H), 6.10 (t, *J* = 7.0 Hz, 1H), 5.12 (s, 1H), 2.48–2.00 (m, 2H), 1.89 (s, 1H), 1.58–1.20 (m, 3H), 1.12–0.85 (m, 6H), 0.05 (s, 9H). IR (film): ν = 3391, 2955, 2870, 1610, 1498, 1467, 1384, 1366, 1248, 839 cm^{-1}. Anal. calcd for $C_{17}H_{28}OSi$: C, 73.91; H, 10.14. Found: C, 73.65; H, 9.89%.

3g: ^{1}H NMR ($CDCl_3$): δ = 6.06 (t, *J* = 7.0 Hz, 1H), 3.93 (t, *J* = 5.7 Hz, 1H), 2.38–1.83 (m, 3H), 1.59–1.09 (m, 10H), 1.05–0.73 (m, 6H), 0.16 (s, 9H). IR (film): ν = 3367, 2961, 2855, 1613, 1462, 1249, 837 cm^{-1}. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.42; H, 12.40. Found: C, 69.65; H, 12.53%.

3h: ^{1}H NMR ($CDCl_3$): δ = 5.96 (t, *J* = 7.0 Hz, 1H), 2.37–1.83 (m, 3H), 1.58–1.10 (m, 14H), 0.89 (t, *J* = 5.4 Hz, 3H), 0.19 (s, 9H). IR (film): ν = 3400, 2958, 2926, 1603, 1460, 1248, 838 cm^{-1}. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.42; H, 12.40. Found: C, 69.21; H, 12.25%.

3I: ^{1}H NMR ($CDCl_3$): δ = 7.41–7.10 (m, 4H), 6.12 (t, *J* = 7.0 Hz, 1H), 5.09 (s, 1H), 2.50–1.98 (m, 3H), 1.67–1.11 (m, 8H), 0.95 (t, *J* = 5.4 Hz, 3H), 0.13 (s, 9H). IR (film): ν = 3418, 2961, 2855, 1609, 1595, 1466, 1248, 840 cm^{-1}. Anal. calcd for $C_{18}H_{29}OClSi$: C, 66.56; H, 8.94. Found: C, 66.23; H, 8.71%.

3j: ^{1}H NMR ($CDCl_3$): δ = 7.40–6.90 (m, 5H), 6.19 (t, *J* = 7.0 Hz, 1H), 3.98 (t, *J* = 5.7 Hz, 1H), 3.45 (d, *J* = 7.4 Hz, 2H), 2.03 (s, 1H), 1.70–1.17 (m, 2H), 0.87 (t, *J* = 5.4 Hz, 3H), 0.13 (s, 9H). IR (film): ν = 3400, 2960, 2876, 1601, 1495, 1249, 838 cm^{-1}. Anal. calcd for $C_{15}H_{24}OSi$: C, 72.58; H, 9.68. Found: C, 72.31; H, 9.46%.

(E)-Allylic alcohols 4a–i; general procedure: To a solution of (*Z*)-β-silyl allylic alcohol **3** (0.5 mmol) in dry dimethyl sulfoxide (2.5 ml) was added anhydrous potassium fluoride (58 mg, 1 mmol). The mixture was heated at 150°C for 3h, quenched with water (10 ml) at 25°C and extracted with Et_2O (3 × 20 ml). The ethereal solution was washed with sat. aq NaCl (3 × 15 ml), dried ($MgSO_4$) and concentrated under reduced pressure. The oily residue was purified by flash column chromatography on silica gel (eluent: light petroleum – AcOEt, 8:1) to give **4a–i** as oils.

4a: ^{1}H NMR ($CDCl_3$): δ = 5.44 (m, 2H), 4.01–3.63 (m, 1H), 2.26–1.76 (m, 3H), 1.64–1.06 (m, 6H), 1.04–0.66 (m, 6H). IR (film): ν = 3355, 2960, 2860, 1670, 1464, 1378, 967 cm^{-1}. Anal. calcd for $C_9H_{18}O$: C, 76.06; H, 12.68. Found: C, 76.25; H, 12.53%.

4b: ^{1}H NMR ($CDCl_3$): δ = 5.50 (d, *J* = 16.0Hz, 1H), 5.39 (m, 1H), 2.25–1.80 (m, 3H), 1.69–1.09 (m, 10H), 0.88 (t, *J* = 5.4Hz, 3H). IR (film): ν = 3360, 2962, 2858, 1669, 1465, 1378, 969 cm^{-1}. Anal. calcd for $C_9H_{18}O$: C, 76.06; H, 12.68. Found: C, 75.83; H, 12.46%.

4c: ^{1}H NMR ($CDCl_3$): δ = 7.34–7.12 (m, 4H), 5.55 (m, 2H), 4.94 (d, *J* = 5.7 Hz, 1H), 2.27–1.78 (m, 3H), 1.58–1.18 (m, 4H), 0.90 (t, *J* = 5.4 Hz, 3H). IR (film): ν = 3343, 2958, 2858, 1667, 1596, 1466, 1378, 969 cm^{-1}. Anal. calcd for $C_{13}H_{17}OCl$: C, 69.49; H, 7.57. Found: C, 69.18; H, 7.40%.

4d: ^{1}H NMR ($CDCl_3$): δ = 5.48 (m, 2H), 4.03–3.66 (m, 1H), 2.25–1.78 (m, 3H), 1.70–1.15 (m, 5H), 1.12–0.71 (m, 9H). IR (film): ν = 3350, 2958, 2850, 1669, 1466, 1384, 969 cm^{-1}. Anal. calcd for $C_{10}H_{20}O$: C, 76.92; H, 12.82. Found: C, 76.68; H, 12.59%.

4e: ^{1}H NMR ($CDCl_3$): δ = 5.49 (d, *J* = 16.0Hz, 1H), 5.37 (m, 1H), 2.11–1.63 (m, 3H), 1.37–1.04 (m, 9H), 1.01–0.62 (m, 6H). IR (film): ν = 3365, 2956, 2870, 1668, 1467, 1384, 1366, 972 cm^{-1}. Anal. calcd for $C_{10}H_{20}O$: C, 76.92; H, 12.82. Found: C, 76.70; H, 12.61%.

4f: ^{1}H NMR ($CDCl_3$): δ = 7.42–7.03 (m, 5H), 5.54 (m, 2H), 4.90 (d, *J* = 5.7 Hz, 1H), 2.58 (s, 1H), 2.25–1.78 (m, 2H), 1.54–1.13 (m, 3H), 1.10–0.73 (m, 6H). IR (film): ν = 3346, 2955, 2869, 1666, 1602, 1492, 1452, 1384, 1366, 971 cm^{-1}. Anal. calcd for $C_{14}H_{20}O$: C, 82.35; H, 9.80. Found: C, 82.04; H, 9.53%.

4g: ^{1}H NMR ($CDCl_3$): δ = 5.50 (m, 2H), 4.05–3.67 (m, 1H), 2.26–1.78 (m, 3H), 1.73–1.10 (m, 10H), 1.09–0.70 (m, 6H). IR (film): ν = 3350, 2959, 2855, 1670, 1459, 1378, 965 cm^{-1}. Anal. calcd for $C_{11}H_{22}O$: C, 77.65; H, 12.94. Found: C, 77.34; H, 12.73%.

4h: ^{1}H NMR ($CDCl_3$): δ = 5.53 (d, *J* = 16.0Hz, 1H), 5.42 (m, 1H), 2.23–1.73 (m, 3H), 1.67–1.07 (m, 14H), 0.87 (t, *J* = 5.4 Hz, 3H). IR (film): ν = 3367, 2961, 2855, 1668, 1464, 1376, 970 cm^{-1}. Anal. calcd for $C_{11}H_{22}O$: C, 77.65; H, 12.94. Found: C, 77.40; H, 12.68%.

4I: ^{1}H NMR ($CDCl_3$): δ = 7.30–7.07 (m, 4H), 5.51 (m, 2H), 4.89 (d, *J* = 5.7 Hz, 1H), 2.66 (s, 1H), 2.22–1.74 (m, 2H), 1.62–1.05 (m, 8H), 0.86 (t, *J* = 5.4 Hz, 3H). IR (film): ν = 3338, 2956, 2855, 1667, 1596, 1490, 1466, 967 cm^{-1}. Anal. calcd for $C_{15}H_{21}OCl$: C, 71.29; H, 8.32. Found: C, 71.38; H, 8.56%.

We thank the National Natural Science Foundation of China (Project: 20062002) and the Natural Science Foundation of Jiangxi Province for financial support.

Received 31 August 2002; accepted 5 December 2002
Paper 02/1536

References

1 T.K.Jones and S.E. Denmark, *Org. Synth.*, 1990, *Coll. Vol.* **7,** 524; D.J. Faulkner, *Synthesis*, 1971, 175; J. Reucroft and P.G. Sammes, *Q. Rev. Chem. Soc.* ,1971, **25**, 135; R.M. Magid, O.S. Fruchey, W.L. Johnson and T.G. Allen, *J. Org. Chem.*, 1979, **44,** 359; E.J. Corey, C.V. Kim and M. Takeda, *Tetrahedron Lett.*, 1972, 4339; S. Okamoto, H. Tsujiyama, T. Yoshino and F. Sato, *Tetrahedron Lett.*, 1991, **32,** 5789.

2 B. Jousseaume and J.G. Duboudin, *J. Organomet. Chem.*, 1975, **91**, C1; M. Zaidlewicz, A. Uzarewicz and R. Sarnowski, *Synthesis*, 1979, 62; A. Ogawa, Y. Tsuboi, R. Obayashi, K. Yokoyama, I. Ryu and N. Sonoda, *J. Org. Chem.*, 1994, **59**, 1600; P.A. Netland, *Org. Prep. Proc. Int.*, 1980, **12**, 216; K. Takai, Y. Kataoka and K. Utimoto, *J. Org. Chem.*, 1990, **55,** 1707; A. Kamimura and N. Ono, *J. Chem. Soc., Chem. Commun.*, 1988, 1278; M. Yukio, S. Kazuhiko and K. Kenji, *Chem. Pharm. Bull.*, 1985, **33,** 2531; M. Julia and J.N. Verpeaux, *Tetrahedron*, 1983, **39,** 3289.

3 M. J. Kang, J. - S. Jang and S. - G. Lee, *Tetrahedron Lett.*, 1995, **36,** 8829.

4 H.C. Brown, A.S. Phadke and N.G. Bhat, *Tetrahedron Lett.*, 1993, **34,** 7845.

5 C.F. Nutaitis and J.E. Bernardo, *J. Org. Chem.*, 1989, **54,** 5629.

6 F. Sato, H. Watanabe, Y. Tanaka, T. Yamaji and M. Sato, *Tetrahedron Lett.*, 1983, **24,** 1041.

7 F. Sato, *J. Organomet. Chem.*, 1985, **285**, 53; F. Sato and H. Urabe, In: *Grignard Reagents – New Developments: Hydromagnesiation of Alkenes and Alkynes*; H. G. Richey, Jr., Ed.; Wiley: Chichester, 2000; p65; Y. Gao and F. Sato, *J. Chem. Soc., Chem. Commun.*, 1995, 659.

8 C. Eaborn and D.R.M. Walton, *J. Organomet. Chem.*, 1964, **2**, 95.

9 T.H. Chan and I. Fleming, *Synthesis*, 1979, 761.

10 T.H. Chan and W. Mychajlowskij, *Tetrahedron Lett.*, 1974, 3479; W.E. Fristad, T.R. Bailey and L.A. Paquette, *J. Org. Chem.*, 1980, **45**, 3028; R.B. Miller and M.I. Al - Hassan, *J. Org. Chem.*, 1983, **48,** 4113.

11 R.S. Rasmussen and R.R. Brattain, *J. Chem. Phys.*, 1947, **15**, 131; O.D. Shreve, M.R. Heether, H.B. Knighf and D. Swern, *Analyt. Chem.*, 1950, **22,** 1261.