One-Pot Synthesis of Homoallylic Alcohols from 1,3-Dienes: Tandem Vicinal Difunctionalization of 1,3-Dienes by Hydride Addition–Aldehyde Coupling Sequence via Organosilicon Intermediates

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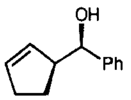
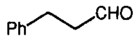
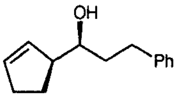
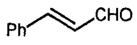
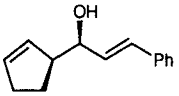
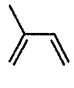
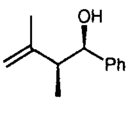
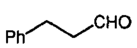
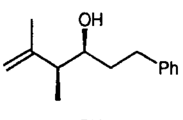
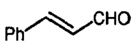
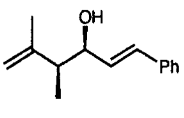
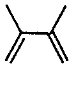
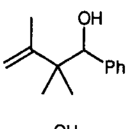
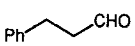
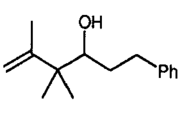
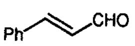
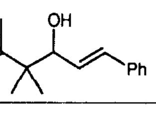
Homoallylic alcohols were directly prepared from 1,3-dienes in high yields with high regio- and stereoselectivity. The process consists of a hydride addition–aldehyde coupling sequence via organosilicon intermediates (an example of tandem vicinal difunctionalization of 1,3-dienes).

Homoallylic alcohols are important intermediates in organic synthesis.[1,2] The reactions of allyl organometallics (usually prepared from allyl halides) with carbonyl compounds are most frequently employed for their preparation.[2] In this paper, we report an alternative one-pot synthesis of homoallylic alcohols from 1,3-dienes.

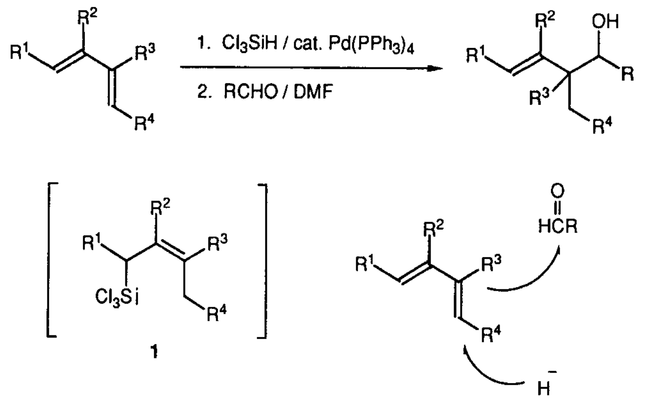
The process is shown in Scheme 1; an initial hydrosilylation of 1,3-diene using a palladium catalyst[3] and successive aldehyde coupling with the intermediate organosilicon compound **1** in dimethylformamide.[4] Consequently, two vicinal σ-bonds are formed in one of the two double bonds of the dienes by hydride addition–aldehyde coupling sequence.

Examples of synthesis of homoallylic alcohols from 1,3-dienes are shown in Table 1. In every case (including both cyclic and acyclic 1,3-dienes), a one-pot reaction of hydride addition–aldehyde coupling sequence proceeded smoothly to afford homoallylic alcohols in high yields. It should be noted that high regio- and diastereoselecti-

Table 1. Synthesis of Homoallylic Alcohols from 1,3-Dienes

Entry	1,3-Diene	Aldehyde	Product		Yield (%)	*syn*/*anti*[a]
1		PhCHO		**2a**	91	>99/1
2				**2b**	87	>99/1
3				**2c**	86	>99/1
4		PhCHO		**2d**	91	94/6
5				**2e**	81	92/8
6				**2f**	92	92/8
7		PhCHO		**2g**	92	–
8				**2h**	83	–
9				**2i**	87	–

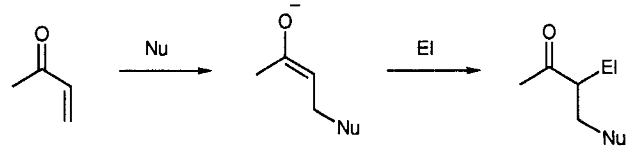
[a] Determined by ^{1}H NMR.



Scheme 1

vity were attained in this process. In the reaction of isoprene, the addition occurred exclusively at the less-substituted olefinic bond. No adduct resulting from addition to the more-substituted olefin part of the isoprene was obtained. Moreover, *syn* homoallylic alcohols were produced in high selectivities, which are ascribed to the geometry of the intermediary organosilicon compounds.[4]

This process is an example of tandem vicinal difunctionalization of 1,3-dienes.[5] Tandem vicinal difunctionalization of α,β-unsaturated carbonyl compounds is well known and provides a convenient method for introducing two functional groups into the olefins (Schemes 2, 3 **A**).[6] One feature of this process is the rapid and convergent access to complex structures in a highly stereocontrolled manner, and considerable utility of this process as a synthetic tool has already been demonstrated in the total synthesis of natural products.[7] However, examples of tandem vicinal difunctionalization of 1,3-dienes (Scheme 3 **B**) are rather limited.[5,8] We believe that the process reported here not only provides a convenient method for the direct preparation of homoallylic alcohols from 1,3-dienes, but also demonstrates the potential utility of this type of tandem vicinal difunctionalization of 1,3-dienes as a versatile synthetic tool.



Scheme 2

Scheme 3

Further studies to apply this methodology to the synthesis of more complicated molecules (including natural products) as well as the development of other examples of tandem vicinal difunctionalization are now in progress.

Melting points are uncorrected. All reagents and solvents were used after purification according to usual methods. ^{1}H and ^{13}C NMR spectra were obtained on a JEOL JNR-EX270L spectrometer and TMS served as internal standard. All reactions were carried out under Ar atmosphere in dried glassware.

Table 2. Physical and Spectroscopic Data of the Homoallylic Alcohols

Product	bp (°C/Torr)[b] or mp (°C)	^{1}H NMR (CDCl$_3$/TMS) δ, J (Hz)	^{13}C NMR (CDCl$_3$/TMS) δ
2a	140/0.4	1.77–1.95 (m, 2H), 2.19 (br s, 1H), 2.26–2.36 (m, 2H), 3.03–3.08 (m, 1H), 4.49 (d, 1H, *J* = 6.6), 5.34–5.38 (m, 1H), 5.80–5.84 (m, 1H), 7.21–7.31 (m, 5H)	25.1, 32.1, 53.8, 76.9, 126.2, 127.2, 128.1, 131.2, 133.4, 143.4
2b	42.5–44.0	1.63 (br s, 1H), 1.69–1.97 (m, 4H), 2.22–2.40 (m, 2H), 2.60–2.71 (m, 1H), 2.76–2.90 (m, 2H), 3.56–3.63 (m, 1H), 5.55–5.60 (m, 1H), 5.84–5.89 (m, 1H), 7.13–7.30 (m, 5H)	23.6, 32.2, 32.3, 36.6, 52.1, 73.0, 125.7, 128.3, 128.4, 131.3, 133.6, 142.2
2c	173/0.05	1.66–2.05 (m, 3H), 2.24–2.42 (m, 2H), 2.92–3.01 (m, 1H), 4.14–4.22 (m, 1H), 5.63–5.67 (m, 1H), 5.87–5.93 (m, 1H), 6.22 (dd, 1H, *J* = 16.2, 6.9), 6.60 (d, 1H, *J* = 16.2), 7.19–7.39 (m, 5H)	24.6, 32.2, 52.2, 75.5, 126.4, 127.5, 128.5, 130.2, 130.7, 130.8, 133.7, 136.8
2d	41.0–42.5	0.99 (d, 3H, *J* = 6.9), 1.73 (s, 3H), 1.98 (br s, 1H), 2.42–2.52 (m, 1H), 4.71 (d, 1H, *J* = 5.3), 4.77 (br s, 1H), 4.84 (d, 1H, *J* = 1.5), 7.21–7.35 (m, 5H)	13.0, 21.8, 47.9, 74.8, 111.9, 126.0, 127.0, 128.0, 143.0, 147.4
2e	145/0.4	1.05 (d, 3H, *J* = 6.9), 1.67 (s, 3H), 1.69–1.81 (m, 3H), 2.14–2.23 (m, 1H), 2.59–2.70 (m, 1H), 2.79–2.90 (m, 1H), 3.53–3.60 (m, 1H), 4.76 (br s, 1H), 4.83 (d, 1H, *J* = 1.6), 7.14–7.30 (m, 5H)	13.5, 21.0, 32.5, 36.5, 46.4, 71.8, 111.5, 125.7, 128.3, 128.4, 142.1, 147.9
2f	149/0.4	1.12 (d, 3H, *J* = 6.9), 1.77 (s, 4H), 2.31–2.42 (m, 1H), 4.29 (t, 1H, *J* = 6.1), 4.83 (d, 1H, *J* = 1.3), 4.89 (t, 1H, *J* = 1.3), 6.23 (dd, 1H, *J* = 16.0, 6.1), 6.61 (d, 1H, *J* = 16.0), 7.20–7.41 (m, 5H)	13.9, 21.3, 47.0, 73.8, 112.1, 126.4, 127.4, 128.5, 130.1, 131.9, 137.9, 147.0
2g	121/0.4	0.93 (s, 3H), 0.98 (s, 3H), 1.85 (s, 3H), 2.13 (br s, 1H), 4.61 (s, 1H), 4.95 (s, 1H), 5.02 (s, 1H), 7.24–7.34 (m, 5H)	19.8, 20.1, 24.2, 44.4, 77.4, 113.1, 127.2, 127.3, 127.9, 140.3, 150.6
2h	157/0.2	0.99 (s, 3H), 1.04 (s, 3H), 1.52–1.82 (m, 3H), 1.68 (s, 3H), 2.56–2.67 (m, 1H), 2.89–3.00 (m, 1H), 3.49 (dd, 1H, *J* = 10.3, 1.1), 4.83 (s, 1H), 4.90 (s, 1H), 7.15–7.31 (m, 5H)	19.6, 21.6, 22.4, 33.0, 33.5, 43.7, 74.8, 112.0, 125.7, 128.3, 128.5, 142.4, 150.8
2i	152/0.04	1.05 (s, 3H), 1.11 (s, 3H), 1.81 (s, 3H), 2.26 (br s, 1H), 4.18 (d, 1H, *J* = 6.6), 4.92 (s, 1H), 4.98 (s, 1H), 6.22 (dd, 1H, *J* = 16.1, 6.6), 6.62 (d, 1H, *J* = 16.1), 7.19–7.40 (m, 5H)	19.8, 21.1, 23.5, 44.2, 76.4, 112.7, 126.4, 127.5, 128.3, 128.5, 131.9, 136.9, 150.3

[a] Satisfactory microanalyses obtained except for **2a** and **2f**: C ±0.18, H ±0.25. **2a**: C −0.62; **2f**: C −0.60.
[b] Bath temperature.

α-(2-Cyclopenten-1-yl)benzyl Alcohol; Typical Procedure:
Trichlorosilane (0.542 g, 4 mmol), cyclopentadiene (264 mg, 4 mmol, freshly distilled before use) and $Pd(PPh_3)_4$ (8 mg) were combined in a sealed glass tube and the mixture was heated at 90 °C for 5 h. The reaction pot was cooled to 0 °C and DMF (5 mL) was added. After stirring for 10 min, benzaldehyde (339 mg, 3.2 mmol) in DMF (5 mL) was added and the mixture was further stirred for 3 h at 0 °C. 1 N HCl was added to quench the reaction, and the product was extracted with Et_2O, after removal of the solvent, the residue was chromatographed on silica gel to give the desired homoallylic alcohol **2a**; yield: 510 mg (91 %) (*syn/anti* = > 99/1) (Table 2).

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