Pergamon

Tetrahedron: *Asymmetry* 10 (1999) 3601–3614

TETRAHEDRON: *ASYMMETRY*

A route to enantiomerically-enriched α-silyl aldehydes from 2,3-epoxy alcohols

Denise C. Chauret, J. Michael Chong * and Qing Ye

Guelph-Waterloo Centre for Graduate Work in Chemistry, Department of Chemistry, University of Waterloo, Waterloo, Ontario, Canada, N2L 3G1

Received 3 August 1999; accepted 23 August 1999

Abstract

Asymmetric epoxidation of (*E*)-3-trialkylsilyl-2-propen-1-ols gives the expected epoxides with high enantioselectivity. Ring opening reactions of these epoxides with organocopper reagents furnishes 1,2-diols which are readily cleaved with $Pb(OAc)_4$ to afford α-silyl aldehydes with no detectable loss of stereochemistry.

1. Introduction

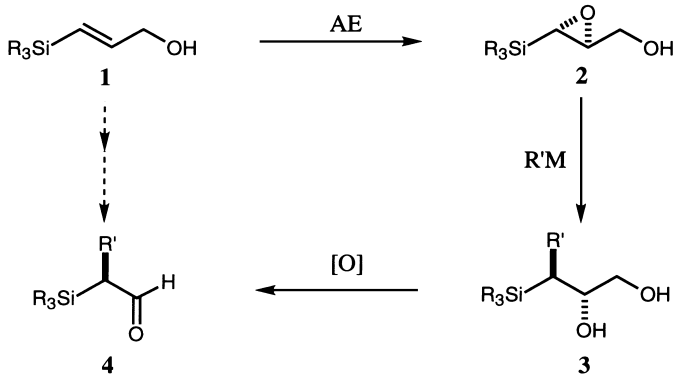
α-Silylcarbonyl compounds have served as important intermediates in organic synthesis.[1] In some applications, such as in the synthesis of stereodefined alkenes, racemic compounds may be employed.[2] However, enantiomerically-enriched compounds are desirable for the synthesis of materials such as enantiomerically-enriched allylsilanes,[3] aldol products[4] and α-hydroxyketones.[5] At present, there are only two enantioselective routes to α-silylcarbonyl compounds: one involves silylation of SAMP/RAMP hydrazones[6] and one involves Pd-catalyzed rearrangement of silyl-substituted vinyloxiranes.[7] The SAMP/RAMP method is very effective for α-silyl ketones but less so for α-silyl aldehydes due to partial *N*-silylation or oxidation of the aldehyde during deprotection of the hydrazone.[6] The vinyloxirane method is limited to β,γ-unsaturated-α-silyl aldehydes containing large (e.g. *i*-Pr_3Si, *t*-BuR_2Si) trialkylsilyl groups.[7] We now report a general efficient route to α-silyl aldehydes which provides these compounds in high enantiomeric purity.

The route that we envisaged is shown in Scheme 1. It is well-established that Sharpless asymmetric epoxidation (AE) of *E*-allylic alcohols proceeds with high enantioselectivity.[8] Use of *E*-3-trialkylsilyl-2-propen-1-ols (**1**) would thus provide epoxides **2** which would be expected to react with organometallic

* Corresponding author. E-mail: jmchong@uwaterloo.ca

0957-4166/99/$ - see front matter
PII: S0957-4166(99)00383-3

reagents to give diols **3**.[2f,9] Oxidative cleavage of diols **3** would then furnish the desired α-silyl aldehydes (**4**).

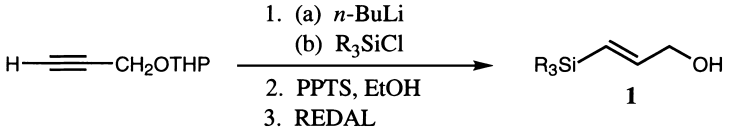


Scheme 1.

2. Results and discussion

2.1. Synthesis of 3-silyl epoxy alcohols

The requisite 3-silylated allylic alcohols were prepared using the sequence shown below. Thus, silylation of the THP ether of propargyl alcohol followed by acid-catalyzed transacetalation gave silylated propargylic alcohols in high yields.[7b] Reduction of these alcohols with REDAL gave exclusively the *E*-allylic alcohols (81–97% yields).[10] This route was superior to the direct silylation of the dianion of propargyl alcohol which usually gave lower yields (50–60%). In general, commercially available trialkylsilyl chlorides were used but in the case of alcohol **1d**, the requisite silyl chloride was prepared in situ from Me_2SiCl_2 and 4-$MeOC_6H_4Li$.[11]



(1)

1a: R_3 = *t*-$BuMe_2$; **1b**: R_3 = $PhMe_2$; **1c**: R_3 = Et_3; **1d**: R_3 = (4-$MeOC_6H_4$)Me_2

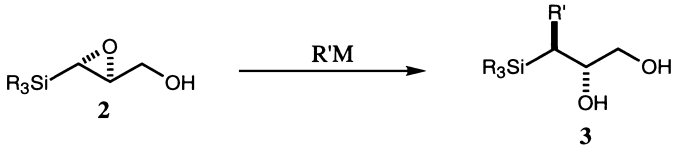
As expected, allylic alcohols **1** underwent Sharpless epoxidation using catalytic amounts of Ti(O-*i*-Pr)$_4$ and tartrate rapidly and highly stereoselectively. In fact, allylic alcohols **1** are almost ideal substrates for AE since the *E* silyl substituent allows for high enantioselectivity and reactivity.[12] Epoxy alcohols **2** are readily isolated in high yields (82–99%) and enantiomeric purities (>95% based on ^{1}H and ^{19}F NMR spectra of MTPA esters).[13–15]

2.2. Ring-opening reactions of 3-silyl epoxy alcohols with organometallic reagents

It has previously been shown that epoxysilanes tend to be opened by nucleophiles at the carbon proximate to the silicon atom.[2f,16] For organocopper reagents, the regioselectivity in the opening of epoxysilanes may be controlled to some extent by varying the nature of the trialkylsilyl group and the organocopper reagent.[2f] For the regiochemistry desired here, 'higher order' cyanocuprates were

preferred.[17] Results are shown in Table 1. In all cases with $Me_2CuCNLi_2$ and $Bu_2CuCNLi_2$, reactions proceeded smoothly with complete regio- and stereoselectivity to give a single diol in high yields.

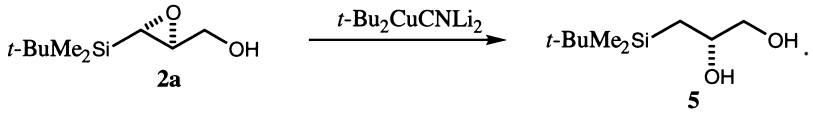
Table 1
Reaction of epoxysilanes **2** with organometallic reagents[a]



Entry	R_3Si	Reagent	Product	Yield (%)[b]
1	*t*-$BuMe_2Si$	$Me_2CuCNLi_2$	**3a**	97
2	*t*-$BuMe_2Si$	$Bu_2CuCNLi_2$	**3b**	85
3	$PhMe_2Si$	$Me_2CuCNLi_2$	**3c**	94
4	$PhMe_2Si$	$Bu_2CuCNLi_2$	**3d**	84
5	Et_3Si	$Me_2CuCNLi_2$	**3e**	93
6	Et_3Si	$Bu_2CuCNLi_2$	**3f**	93
7	(4-$MeOC_6H_4$)Me_2Si	$Me_2CuCNLi_2$	**3g**	95
8	(4-$MeOC_6H_4$)Me_2Si	$Bu_2CuCNLi_2$	**3h**	90
9	*t*-$BuMe_2Si$	BuMgCl/CuI	**3b**	83
10	*t*-$BuMe_2Si$	CH_2=CHMgBr/CuI	**3i**	57
11	*t*-$BuMe_2Si$	CH_2=$CHCH_2$MgCl/CuI	**3j**	33
12	*t*-$BuMe_2Si$	CH_2=$CHCH_2CH_2$MgBr/CuI	**3k**	82
13	*t*-$BuMe_2Si$	EtMgBr/CuI	**3l**	84
14	Et_3Si	BuMgCl/CuI	**3f**	81
15	Et_3Si	CH_2=$CHCH_2$MgCl/CuI	**3m**	57
16	*t*-$BuMe_2Si$	*n*-BuC≡$CAlEt_2$	**3n**	73

a Reactions were carried out using excess (3-5 eq) reagent.
b Isolated yields of chromatographed products.

Unfortunately, the 2° and 3° cuprates *s*-$Bu_2CuCNLi_2$ and *t*-$Bu_2CuCNLi_2$ were either unreactive (at temperatures below −10°C) or gave rise to reduction products (e.g. **5**, equiv. 2) at higher temperatures. The decreased reactivity at lower temperatures may be due to steric factors while the formation of reduction products may be ascribed to thermal decomposition of the cuprates to copper hydrides.[18]



(2)

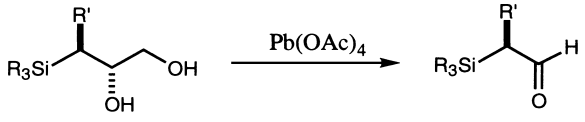
We also examined the opening of epoxysilanes **2** with Grignard reagents in the presence of copper salts (Table 1). In general, reactions with 1° Grignard reagents worked well although yields were slightly lower than with organocuprates and small amounts of by-products were formed. However, it may sometimes be advantageous to use Grignard reagents since they are often more easily prepared than organolithiums (which are used as precursors to the organocuprates.) Also, as with organocuprates, 2° and 3° reagents did not provide the desired products.

To introduce an alkynyl group, organocopper reagents are generally ineffective.[19] Hence, an alkynylaluminum reagent was used.[20] As with the organocopper reagents, only a single regioisomer was observed.

2.3. *Oxidative cleavage of diols **3** to α-silyl aldehydes*

With a series of β,γ-dihydroxysilanes in hand, we turned our attention to the oxidative cleavage of these 1,2-diols to aldehydes. To avoid possible complications under aqueous or acidic conditions, cleavage was carried out using $Pb(OAc)_4$ in dry CH_2Cl_2 containing solid $NaHCO_3$ (Table 2). In each case, the expected α-silyl aldehyde was isolated as the sole product in essentially pure form. They exhibited IR, ^1H and ^{13}C NMR spectral data completely consistent with their assigned structures. However, it was not surprising[6] that they defied purification (silica gel chromatography, distillation) for microanalysis.

Table 2
Preparation of α-silyl aldehydes from diols



3 **4**

Entry	Diol				Aldehyde	
	#	R_3Si	R'	%ee[a]	# (% yield)[b]	%ee[c]
1	**3a**	*t*-BuMe_2Si	Me	97.7	**4a** (96)	>95
2	**3b**	*t*-BuMe_2Si	Bu	97.7	**4b** (97)	97.4
3	**3c**	PhMe_2Si	Me	98.0	**4c** (90)	>95
4	**3d**	PhMe_2Si	Bu	98.0	**4d** (93)	97.8
5	**3e**	Et_3Si	Me	97.3	**4e** (93)	>95
6	**3f**	Et_3Si	Bu	97.3	**4f** (90)	97.5
7	**3g**	(4-MeOC_6H_4)Me_2Si	Me	>95	**4g** (90)	>95
8	**3h**	(4-MeOC_6H_4)Me_2Si	Bu	>95	**4h** (86)	97.3
9	**3i**	*t*-BuMe_2Si	CH_2=CH	97.7	**4i** (85)	86
10	**3j**	*t*-BuMe_2Si	CH_2=$CHCH_2$	97.7	**4j** (93)	>95
11	**3k**	*t*-BuMe_2Si	CH_2=$CHCH_2CH_2$	97.7	**4k** (94)	>95
12	**3l**	*t*-BuMe_2Si	*n*-BuC≡C	97.7	**4l** (89)	97.3

a This is actually the enantiomeric purity (see references 13-15) of epoxy alcohol **2**. Diol **3** is expected to have the same enantiomeric purity based on S_N2 opening of the epoxide.
b Isolated yields of crude aldehydes. Aldehydes were spectroscopically (^1H, ^{13}C NMR) homogeneous and further purification was not attempted.
c Determined by ^1H or ^{19}F NMR analysis of MTPA esters[13-15] after reduction to the 1° alcohols.

The enantiomeric purities of the α-silyl aldehydes were determined by reduction ($LiAlH_4$, Et_2O, 0°C) to the corresponding primary alcohols and preparing the MTPA esters followed by analysis using ^1H and/or ^{19}F NMR spectroscopy. In most cases, the enantiomeric excesses determined were the same as those determined for the corresponding epoxy alcohol precursors. Thus, the epoxide ring opening and the oxidative cleavage reactions must have occurred with little or no loss of stereochemical integrity. Only with aldehyde **4i** (R=CH_2=CH) was racemization observed; it is highly likely that the activating effect of

the vinyl group is responsible for the stereochemical lability of this aldehyde. However, it is interesting to note that an alkynyl group (aldehyde **4l**) does not have this same effect.

We also examined the stereochemical purity of aldehydes after prolonged storage. After one month at 4°C, there was no detectable racemization. However, extensive chemical decomposition occurred after six months at 4°C or after one week at room temperature.

In conclusion, we have developed a general route to enantiomerically-enriched α-silyl aldehydes. Since chirality is introduced using Sharpless asymmetric epoxidation, either enantiomer may be easily accessed (by the appropriate choice of tartrates) with high enantiomeric excess. Many different silyl groups are tolerated; and the α-epoxysilanes may be opened with high regioselectivity and stereoselectivity using organocuprates, Grignard reagents and alkynyl-aluminum reagents.

3. Experimental

3.1. General

All reactions involving air or moisture sensitive reagents were performed under argon using oven-dried glassware. THF and ether were distilled from Na/benzophenone; CH_2Cl_2 and Et_3N were distilled from CaH_2. Anhydrous *t*-butylhydroperoxide in isooctane was prepared and titrated according to the procedure of Sharpless.[8d] Sodium bicarbonate was oven dried prior to use. 4-Bromo-1-butene was passed through a short column of basic aluminum before being used. $CuBr \cdot SMe_2$ was recrystallized from Me_2S/hexane.[21] Allylic alcohols **1a**, **1b** and **1c** were prepared essentially as described by Malacria et al. except that PPTS/EtOH was used instead of *p*-TsOH/MeOH to cleave the THP ether.[7b] Infrared spectra were obtained using a MB-100 FT spectrophotometer as neat liquids (NaCl plates) or as KBr pellets. NMR spectra were recorded using Bruker AM-250 or AC-200 spectrometers as $CDCl_3$ solutions with Me_4Si (^1H δ 0.0) or $CDCl_3$ (^{13}C δ 77.0) as internal standards unless otherwise noted. For ^{19}F NMR spectra, CF_3COOH was used as an external standard (76.53 ppm upfield from $CFCl_3$) and peak positions are reported in ppm upfield from $CFCl_3$. Mass spectra were recorded on a VG Quattro II mass spectrometer (electrospray ionization) or on a Hewlett–Packard 5890 series II/5971A MSD instrument (electron impact ionization). Optical rotations were determined on a Perkin–Elmer 241 digital polarimeter. Elemental analyses were performed by M-H-W Laboratories, Phoenix, Arizona.

All enantiomeric excesses (ee) reported were determined by ^1H NMR or ^{19}F NMR analysis of the derived (+)-MTPA esters obtained by treatment of alcohols with triethylamine, (+)-MTPA-Cl and DMAP in CH_2Cl_2.[22] In each case, an authentic mixture of diastereomers was prepared using (±)-MTPA-Cl[23] as the derivatizing agent.

3.1.1. E-*3-(*p-*Methoxyphenyl)dimethylsilyl-2-propen-1-ol (**1d**)*

p-Bromoanisole (100 mmol) was dissolved in ether (100 mL), then *t*-BuLi (129 mL of a 1.7 M solution in pentane, 220 mmol) was added dropwise into the solution at −78°C. After the reaction mixture was stirred for 15 min at −78°C, it was warmed up to 0°C for 15 min. In order to remove the excess *t*-BuLi, the reaction mixture was stirred for 30 min at rt. Subsequently, dichlorodimethylsilane (13 mL, 100 mmol) was added dropwise to the re-cooled reaction mixture (−78°C). The total reaction mixture was stirred for 2 h at −78°C. The resulting (*p*-methoxyphenyl)dimethylsilyl chloride was used in situ.

To a solution of THP-protected propargyl alcohol in THF (0.5 mL per mmol protected alcohol) at −40°C was added dropwise *n*-BuLi (1.0 equiv., 1.6 M solution in hexane). The reaction mixture was stirred at −40°C for 30 min, then the THF solution of (*p*-methoxyphenyl)dimethylsilyl chloride (1.0

equiv.) was added dropwise. The reaction was warmed to rt and stirred overnight; then the mixture was concentrated to dryness. Ether (50 mL) was added. The organic phase was washed with saturated NH_4Cl solution (50 mL), separated, then dried over $MgSO_4$ and concentrated. Ethanol (1 mL per mmol protected alcohol) and PPTS (0.1 equiv.) were added to the residue, and the resulting mixture was stirred for 7 h at 55°C. At the end of the reaction, solid NaHCO3 was added, ethanol was removed in vacuo and the mixture was diluted with ether (100 mL). The organic phase was washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated. The resulting oil was purified by column chromatography [(20 g silica gel per g residue, hexane:ether (3:1)] to afford the expected 3-trialkylsilylpropargyl alcohol in 64% yield: IR (neat, NaCl) 3358 (br), 3014, 2956, 2837, 1594, 1249, 1182, 779 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.54–7.50 (m, 2H), 6.92–6.89 (m, 2H), 4.28 (s, 2H), 3.80 (s, 3H), 1.56 (br, 1H), 0.38 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 160.7, 135.1, 127.3, 113.7, 105.3, 88.9, 55.0, 51.5, −0.9; MS (EI) *m/z* 220 (M, 37), 205 (100), 167 (17), 145 (40), 121 (25), 75 (25). Anal. calcd for $C_{12}H_{16}O_2Si$: C, 65.41; H, 7.32. Found: C, 65.55; H, 7.26.

A solution of REDAL (2.0 equiv., 75% solution in toluene) was added dropwise into an ether solution of the silylated propargyl alcohol (1 mL per mmol alcohol) at 0°C. At first, the reaction was stirred for 2 h at 0°C, then allowed to warm to rt for 1 h. HCl (1 M) solution was added dropwise to quench the reaction at 0°C until the reaction mixture became clear. The phases were separated and the aqueous phase was extracted with ether (3×30 mL). The total organic layer was washed with water (50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated. The resulting oil (94% yield) was used without further purification. IR (neat, NaCl) 3348 (br), 3040, 1593, 1246, 1182, 818 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H), 6.93–6.87 (m, 2H), 6.23, 6.02 (AB of ABX_2, J_{AB}=18.7 Hz, J_{AX}=4.1 Hz, J_{BX}=1.5 Hz, 1H), 4.20 (dd, J=4.1, 1.5 Hz, 2H), 3.81 (s, 3H), 1.40 (s, 1H), 0.33 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 160.4, 146.4, 135.2, 129.2, 127.6, 113.6, 65.4, 55.0, −2.5; MS (EI) *m/z* 222 (M^+, 4), 207 (15), 189 (83), 165 (39), 151 (37), 135 (28), 115 (16), 99 (41), 75 (100), 59 (20), 45 (16), 43 (16). Anal. calcd for $C_{12}H_{18}O_2Si$: C, 64.82; H, 8.16. Found: C, 64.63; H, 7.91.

*3.2. General procedure A: preparation of (2S,3S)-trialkylsilyl-2,3-epoxy-1-propanols (**2**)*

To a slurry of powdered 3 Å molecular sieves (0.05 g per mmol silylallylic alcohol) in CH_2Cl_2, L-(+)-diethyl tartrate (0.14 equiv.) was added. After cooling to −20°C, titanium tetraisopropoxide (0.12 equiv.) was added dropwise. Pre-dried (4 Å molecular sieves) *t*-butylhydroperoxide (2.0 equiv., 5.1 M solution in isooctane) was subsequently added dropwise. The mixture was stirred at −20°C for 30 min. Then a pre-dried (4 Å molecular sieves) solution of allylic alcohol **1** (X mmol) in CH_2Cl_2 (0.5 mL per mmol silylallylic alcohol) was added dropwise. The reaction was stirred at −20°C for 5 h, whereupon it was added to a 0°C solution of $FeSO_4 \cdot 7H_2O$ (0.33 g per mmol of allylic alcohol) and tartaric acid (0.1 g per mmol of allylic alcohol) in water (1 mL per mmol of allylic alcohol), and stirred for 10 min without a cooling bath. The phases were separated and the aqueous layer was extracted with ether (3×30 mL). The combined organic phase was stirred over 30% NaOH in brine (1 mL per mmol of allylic alcohol) at 0°C for 1 h. After the phases were separated again and the aqueous layer was extracted with ether:hexane 1:1 (3×20 mL), the combined organic phase was dried over $MgSO_4$, concentrated and purified by column chromatography (20 g silica gel per g epoxy alcohol, hexane:ethyl acetate 2:1) to afford (2*S*, 3*S*)-trialkylsilyl-2,3-epoxy-1-propanols (**2**).

*3.2.1. (2S,3S)-t-Butyldimethylsilyl-2,3-epoxy-1-propanol (**2a**)*

Following general procedure A, the title compound was prepared as a colorless oil in 99% yield: $[\alpha]_D^{25}$ −18.5 (c 1.00, MeOH), lit.[7b] $[\alpha]_D^{20}$ −26.9 (c 11.85, $CHCl_3$); IR (neat, NaCl) 3374 (br), 2939, 2884, 2836,

1466, 1442, 1381, 1362, 1252, 1103, 1056, 1007, 837, 901 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.97, 3.57 (AB of ABX, J_{AB}=12.3 Hz, J=4.5, 2.4 Hz, 2H), 2.99 (ddd, X of ABX, J=4.5, 3.7, 2.4 Hz, 1H), 2.31 (d, J=3.7 Hz, 1H), 0.94 (s, 9H), 0.00 (s, 3H), −0.02 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 63.5, 55.7, 46.3, 26.3, 16.4, −8.5, −8.6; MS (EI) *m/z* 171 (M^+−OH, 1), 75 (100), 57 (10). Anal. calcd for $C_9H_{20}O_2Si$: C, 57.39; H, 10.70. Found: C, 57.60; H, 10.55.

*3.2.2. (2S,3S)-Dimethylphenylsilyl-2,3-epoxy-1-propanol (**2b**)*

Following general procedure A, the title compound was prepared as a colorless oil in 82% yield: $[\alpha]_D^{25}$ −11.7 (c 1.00, MeOH), lit.[7b] $[\alpha]_D^{20}$ −11.6 (c 12.85, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.39–7.33 (m, 3H), 3.93, 3.54 (AB of ABX, J_{AB}=12.5 Hz, J=4.7, 2.3 Hz, 2H), 3.00 (ddd, X of ABX, J=4.7, 3.6, 2.3 Hz, 1H), 2.43 (d, J=3.6 Hz, 1H), 0.35 (s, 3H), 0.32 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 135.5, 133.7, 129.4, 127.7, 63.2, 56.3, 47.5, −5.3, −5.5; MS (EI) *m/z* 209 (M+1, 17), 191 (21), 149 (18), 135 (69), 117 (100), 105 (12), 91 (21), 75 (58), 55 (11), 45 (6). Anal. calcd for $C_{11}H_{16}O_2Si$: C, 63.42; H, 7.74. Found: C, 63.43; H, 7.52.

*3.2.3. (2S,3S)-Triethylsilyl-2,3-epoxy-1-propanol (**2c**)*

Following general procedure A, the title compound was prepared as a colorless oil in 97% yield: $[\alpha]_D^{25}$ −8.9 (c 1.00, MeOH); IR (neat, NaCl) 3388 (br), 2954, 1460, 1102, 1055 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.96, 3.53 (AB of ABX, J_{AB}=12.4 Hz, J=4.8, 2.2 Hz, 2H), 3.03 (ddd, X of ABX, J=4.8, 3.7, 2.2 Hz, 1H), 2.28 (d, J=3.7 Hz, 1H), 0.95 (t, J=7.7 Hz, 9H), 0.60 (q, J=7.7 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 63.6, 55.7, 46.6, 7.0, 1.6; MS (EI) *m/z* 207 (M+H+H_2O, 18), 159 (3), 131 (2), 103 (55), 87 (15), 75 (100), 47 (13), 45 (9), 29 (4). Anal. calcd for $C_9H_{20}O_2Si$: C, 57.39; H, 10.70. Found: C, 57.16; H, 10.59.

*3.2.4. (2S,3S)-(p-Methoxyphenyl)dimethylsilyl-2,3-epoxy-1-propanol (**2d**)*

Following general procedure A, the title compound was prepared as a colorless oil in 89% yield: $[\alpha]_D^{25}$ −10.8 (c 1.20, MeOH); IR (neat, NaCl) 3407 (br), 2950, 2837, 1593, 1248, 1183, 1045, 829 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.47–7.42 (m, 2H), 6.93–6.88 (m, 2H), 3.92, 3.56 (AB of ABX, J_{AB}=9.1 Hz, J=4.4, 2.4 Hz, 2H), 3.80 (s, 3H), 2.98 (ddd, X of ABX, J=4.4, 3.7, 2.4 Hz, 1H), 2.40 (d, J=3.7 Hz, 1H), 1.60 (br s, 1H), 0.32 (s, 3H), 0.29 (each s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 160.9, 135.4, 126.3, 113.8, 63.2, 56.0, 55.0, 47.8, −4.9, −5.1; MS (EI) *m/z* 223 (M−Me, 87), 208 (14), 165 (92), 147 (65), 131 (40), 115 (100), 91 (13). Anal. calcd for $C_{12}H_{18}O_3Si$: C, 60.47; H, 7.61. Found: C, 60.38; H, 7.52.

3.3. General procedure B: methyl and butyl cuprate openings of (2S,3S)-trialkylsilyl-2,3-epoxy-1-propanols

To a suspension of CuCN (3.0 equiv., unless otherwise specified) in ether (5 mL per mmol α-epoxysilane) at 0°C or −20 to −40°C was added dropwise MeLi or *n*-BuLi (6.0 equiv., unless otherwise specified). α-Epoxysilane **2** (X mmol) was added dropwise as a solution in ether (1 mL per mmol α-epoxysilane). Then, the reaction was stirred at 0°C or −20 to −40°C for 2 h. Saturated NH_4Cl (pH 8) solution (5 mL per mmol α-epoxysilane) was added dropwise to quench the reaction. The phases were separated and the aqueous layer was extracted with ether (3×3 mL per mmol α-epoxysilane). The combined organic phase was dried over $MgSO_4$, concentrated and purified by column chromatography (20 g silica gel per g residue, CH_2Cl_2:ether 5:1) to afford β,γ-dihydroxysilanes **3**.

*3.3.1. (2S,3S)-3-t-Butyldimethylsilyl-1,2-butanediol (**3a**)*

Following general procedure B, using CuCN (3.0 equiv.) and MeLi (6.0 equiv., 1.4 M solution in ether) at 0°C, the title compound was prepared without purification, as a viscous colorless oil in 97% yield: $[\alpha]_D^{25}$ +9.2 (c 1.00, MeOH); IR (neat, NaCl) 3359 (br), 2954, 1048, 995 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.83 (ddd, X of ABX, J=8.7, 5.5, 2.7 Hz, 1H), 3.63, 3.49 (AB of ABX, J_{AB}=10.9 Hz, J=8.7, 2.7 Hz, 2H), 2.01 (br, 2H), 1.19 (quint, J=7.4 Hz, 1H), 0.94 (d, J=7.4 Hz, 3H), 0.84 (s, 9H), 0.00 (s, 3H), −0.03 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 74.6, 65.1, 27.2, 22.3, 17.3, 10.7, −5.8, −6.2; MS (EI) *m/z* 173 ($M-CH_2OH$, 4), 129 (15), 75 (100), 55 (72). Anal. calcd for $C_{10}H_{24}O_2Si$: C, 58.77; H, 11.84. Found: C, 58.75; H, 11.69.

*3.3.2. (2S,3S)-3-t-Butyldimethylsilyl-1,2-heptanediol (**3b**)*

Following general procedure B, using CuCN (5.0 equiv.) and *n*-BuLi (10.0 equiv., 1.6 M solution in hexane) at −20 to −40°C, the title compound was prepared without purification, as a viscous colorless oil in 85% yield: $[\alpha]_D^{25}$ +10.0 (c 1.00, MeOH); IR (neat, NaCl) 3371 (br), 2942, 1043 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.95 (ddd, X of ABX, J=7.8, 4.1, 3.6 Hz, 1H), 3.65, 3.57 (AB of ABX, J_{AB}=10.8 Hz, J=7.8, 3.6 Hz, 2H), 1.70–1.17 (m, 6H), 1.08–0.75 (m, 13H), 0.10 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 74.6, 66.0, 33.1, 29.6, 28.0, 27.2, 23.0, 18.8, 14.0, −4.5, −6.2; MS (EI) *m/z* 246 (M, 2), 245 (13), 189 (18), 177 (100), 149 (17), 115 (22), 87 (21), 55 (36). Anal. calcd for $C_{13}H_{30}O_2Si$: C, 63.35; H, 12.26. Found: C, 63.18; H, 12.26.

*3.3.3. (2S,3S)-3-Dimethylphenylsilyl-1,2-butanediol (**3c**)*

Following general procedure B, using CuCN (3.0 equiv.) and MeLi (6.0 equiv., 1.4 M solution in ether) at 0°C, the title compound was prepared without purification, as a viscous colorless oil in 94% yield: $[\alpha]_D^{25}$ +4.1 (c 1.00, MeOH); IR (neat, NaCl) 3370 (br), 2954, 1056, 774, 702 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.55–7.51 (m, 2H), 7.38–7.33 (m, 3H), 3.64–3.60 (m, 2H), 3.39 (dd, J=11.4, 8.1 Hz, 1H), 1.22 (quint, J=7.5 Hz, 1H), 0.92 (d, J=7.5 Hz, 3H), 0.35 (s, 3H), 0.34 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 138.6, 133.9, 129.0, 127.8, 75.1, 65.6, 24.4, 11.4, −3.4, −3.5; MS (EI) *m/z* 209 (M−Me, 36), 191 (19), 149 (31), 137 (72), 135 (85), 91 (18), 75 (100), 55 (100), 43 (10). Anal. calcd for $C_{12}H_{20}O_2Si$: C, 64.24; H, 8.98. Found: C, 64.12; H, 9.03.

*3.3.4. (2S,3S)-3-Dimethylphenylsilyl-1,2-heptanediol (**3d**)*

Following general procedure B, using CuCN (5.0 eq) and *n*-BuLi (10.0 equiv., 1.6 M solution in hexane) at −20 to −40°C, the title compound was prepared without purification, as a viscous colorless oil in 84% yield: $[\alpha]_D^{25}$ +22.2 (c 1.00, MeOH); ^1H NMR (250 MHz, $CDCl_3$) δ 7.56–7.51 (m, 2H), 7.38–7.33 (m, 3H), 3.80 (ddd, X of ABX, J=8.7, 5.6, 3.0 Hz, 1H), 3.49, 3.34 (AB of ABX, J_{AB}=10.9 Hz, J_{AX}=8.7, J_{BX}=3.0 Hz, 2H), 1.37–1.13 (m, 6H), 1.02 (q, J=5.6 Hz, 1H), 0.81 (t, J=6.8 Hz, 3H), 0.36 (s, 3H), 0.35 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 139.4, 128.8, 127.7, 74.5, 66.3, 32.1, 30.5, 27.1, 22.8, 13.8, −2.3, −2.6; MS (EI) *m/z* 233 (11), 211 (18), 171 (22), 153 (37), 137 (70), 135 (67), 97 (100), 75 (76), 55 (85). Anal. calcd for $C_{15}H_{26}O_2Si$: C, 67.62; H, 9.83. Found: C, 67.40; H, 9.62.

*3.3.5. (2S,3S)-3-Triethylsilyl-1,2-butanediol (**3e**)*

Following general procedure B, using CuCN (3.0 equiv.) and MeLi (6.0 equiv., 1.4 M solution in ether) at 0°C, the title compound was prepared without purification, as a viscous colorless oil in 93% yield: $[\alpha]_D^{25}$ −1.6 (c 1.00, MeOH); IR (neat, NaCl) 3360 (br), 2952, 1238, 1051, 726 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.74–3.70 (m, 2H), 3.46 (dd, J=11.3, 8.5 Hz, 1H), 2.01–1.90 (m, 2H), 1.09 (quint, J=7.3 Hz, 1H), 0.97–0.91 (m, 12H), 0.58 (q, J=7.7 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 74.9, 65.8,

21.7, 10.9, 7.6, 3.1; MS (EI) *m/z* 204 (M, 1), 151 (17), 133 (30), 115 (49), 103 (100), 87 (53), 75 (99), 55 (99). Anal. calcd for $C_{10}H_{24}O_2Si$: C, 58.77; H, 11.84. Found: C, 58.65; H, 11.90.

*3.3.6. (2S,3S)-3-Triethylsilyl-1,2-heptanediol (**3f**)*

Following general procedure B, using CuCN (5.0 equiv.) and *n*-BuLi (10.0 equiv., 1.6 M solution in hexane) at −20 to −40°C, the title compound was prepared without purification, as a viscous colorless oil in 93% yield: $[\alpha]_D^{25}$ +12.0 (c 1.00, MeOH); IR (neat, NaCl) 3369 (br), 1055, 1011, 723 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.85 (ddd, X of ABX, J=8.7, 5.5, 2.8 Hz, 1H), 3.60, 3.48 (AB of ABX, J_{AB}=10.6 Hz, J_{AX}=8.7, J_{BX}=2.8 Hz, 2H), 1.36–1.15 (m, 7H), 0.94 (t, J=7.7 Hz, 9H), 0.86 (t, J=7.0 Hz, 3H), 0.59 (q, J=7.7 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 74.5, 66.4, 32.7, 27.8, 23.1, 13.9, 7.7, 3.7; MS (EI) *m/z* 246 (M, 2), 189 (18), 177 (100), 167 (7), 149 (17), 115 (22), 87 (21), 55 (36). Anal. calcd for $C_{13}H_{30}O_2Si$: C, 63.35; H, 12.26. Found: C, 63.13; H, 12.32.

*3.3.7. (2S,3S)-3-(p-Methoxyphenyl)dimethylsilyl-1,2-butanediol (**3g**)*

Following general procedure B, using CuCN (3.0 equiv.) and MeLi (6.0 equiv., 1.4 M solution in ether) at 0°C, the title compound was prepared without purification, as a viscous colorless oil in 95% yield: $[\alpha]_D^{25}$ +8.7 (c 1.10, MeOH); IR (neat, NaCl) 3376 (br), 1593, 1247, 1182, 1038, 824, 772 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.47–7.42 (m, 2H), 6.93–6.88 (m, 2H), 3.80 (s, 3H), 3.66–3.62 (m, 2H), 3.52 (dd, J=11.0, 8.2 Hz, 1H), 3.00–2.50 (br, 2H), 1.18 (quint, J=7.5 Hz, 1H), 0.90 (d, J=7.5 Hz, 3H), 0.31 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 160.3, 135.3, 129.2, 113.5, 75.1, 65.5, 54.9, 24.5, 11.2, −3.4; MS (EI) *m/z* 253 (M−1, 1), 223 (2), 207 (40), 165 (100), 133 (35), 105 (6), 91 (8), 75 (7), 55 (24), 45 (3), 43 (5). Anal. calcd for $C_{13}H_{22}O_3Si$: C, 61.38; H, 8.72. Found: C, 61.54; H, 8.57.

*3.3.8. (2S,3S)-3-(p-Methoxyphenyl)dimethylsilyl-1,2-heptanediol (**3h**)*

Following general procedure B, using CuCN (5.0 equiv.) and *n*-BuLi (10.0 equiv., 1.6 M solution in hexane) at −20 to −40°C, the title compound was prepared without purification, as a viscous colorless oil in 90% yield: $[\alpha]_D^{25}$ +20.3 (c 1.00, MeOH); IR (neat, NaCl) 3387 (br), 3045, 1593, 1247, 1182, 1038, 822, 770 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.53–7.49 (m, 2H), 6.96–6.92 (m, 2H), 3.85–3.83 (m, 4H), 3.53, 3.41 (AB of ABX, J_{AB}=13.6 Hz, J_{AX}=8.8, J_{BX}=2.5 Hz, 2H), 2.43 (br, 2H), 1.44–0.84 (m, 10H), 0.38 (s, 3H), 0.37 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 160.2, 135.4, 130.1, 113.5, 74.6, 66.3, 55.0, 32.2, 30.7, 27.2, 22.9, 13.9, −2.2, −2.4; MS (EI) *m/z* 263 ($M-CH_2OH$, 4), 207 (13), 165 (100), 147 (24), 133 (23), 96 (14), 91 (13), 75 (17), 55 (14). Anal. calcd for $C_{16}H_{28}O_3Si$: C, 64.48; H, 9.52. Found: C, 64.83; H, 9.34.

*3.3.9. (2S)-3-t-Butyldimethylsilyl-1,2-propanediol (**5**)*

Following general procedure D, using CuCN (5.0 equiv.) and *t*-BuLi (10.0 equiv., 1.7 M solution in pentane), the title compound was prepared as a white solid by-product from **2a** in 32% yield: mp 63.0–64.0°C; $[\alpha]_D^{25}$ +10.8 (c 0.60, CH_3OH); IR (KBr) 3302 (br), 2950, 2931, 2858, 1469, 1387, 1369, 1253, 1197, 1078, 1054, 1020, 871, 834, 788 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.88–3.78 (m, 1H), 3.61–3.55 (m, 1H), 3.34–3.27 (m, 1H), 2.73 (br, 2H), 0.83 (s, 9H), 0.78–0.62 (m, 2H), 0.00 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 70.435, 69.2, 26.4, 16.4, 17.1, −5.2, −5.7; MS (ES) *m/z* 208 (M+18, 100). Anal. calcd for $C_9H_{22}O_2Si$: C, 56.78; H, 11.65. Found: C, 56.81; H, 11.48.

3.4. General procedure C: epoxysilane ring opening by Grignard reagents

To a slurry of CuI (0.5 equiv.) in ether (5 mL per mmol α-epoxysilane) at −20 to −40°C was added RMgX solution (5.0 equiv.). The mixture was stirred for 5 min at −20 to −40°C, then a solution of α-epoxysilane **2** (X mmol) in ether (1 mL per mmol α-epoxysilane) was added dropwise. The reaction was stirred at −20 to −40°C for 2 h. Then saturated NH_4Cl (pH 8) solution (5 mL per mmol α-epoxysilane) was added to quench the reaction. The phases were separated and the aqueous layer was extracted with ether (3×15 mL). The combined organic phase was dried over $MgSO_4$, concentrated and purified by column chromatography (20 g silica gel per g residue, hexane:ether 3:2), producing the β,γ-dihydroxysilanes **3**.

3.4.1. (2S,3S)-3-t-Butyldimethylsilyl-1,2-heptanediol (3b)

Following general procedure C, using BuMgCl (5.0 equiv., 2.0 M solution in THF), compound **3b** was also prepared in 83% yield. The spectral data observed were identical to those described in Section 3.3.2.

3.4.2. (2S,3S)-3-Triethylsilyl-1,2-heptanediol (3f)

Following general procedure C, using BuMgCl (5.0 equiv., 2.0 M solution in THF), compound **3f** was also prepared in 81% yield. The spectral data observed were identical to those described in Section 3.3.6.

3.4.3. (2S,3S)-3-t-Butyldimethylsilyl-4-pentene-1,2-diol (3i)

Following general procedure C, using CH_2=CHMgBr (5.0 equiv., 1.0 M solution in THF), the title compound was prepared as a white solid in 57% yield: mp 49.5–50.5°C; $[\alpha]_D^{25}$ +9.6 (c 1.00, $CHCl_3$); IR (KBr) 3276 (br), 3070, 2944, 2858, 1627, 1466, 1330, 1254, 1037, 903, 832, 785, 676 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.72–5.52 (m, 1H), 5.05–4.95 (m, 2H), 3.85 (ddd, J=7.9, 4.6, 2.8 Hz, 1H), 3.65–3.57 (m, 2H), 2.04 (m, 1H), 0.90 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 136.1, 116.39, 72.6, 66.1, 38.4, 27.2, 17.7, −5.6, −5.7; MS (ES) *m/z* 234 (M+18, 100). Anal. calcd for $C_{11}H_{24}O_2Si$: C, 61.06; H, 11.18. Found: C, 60.87; H, 10.79.

3.4.4. (2S,3S)-3-t-Butyldimethylsilyl-5-hexene-1,2-diol (3j)

Following general procedure C, CH_2=$CHCH_2MgCl$ was prepared by the reaction of CH_2=$CHCH_2Cl$ (5.0 equiv.) with Mg (5.05 equiv.) in ether at 0°C in the presence of a small amount of iodine, the title compound was prepared as a viscous colorless oil in 33% yield: $[\alpha]_D^{25}$ +8.4 (c 1.10, $CHCl_3$); IR (neat, NaCl) 3372 (br), 3065, 2941, 2858, 1637, 1467, 1412, 1362, 1252, 1045, 910, 825, 767 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.90–5.77 (m, 1H), 5.07–4.96 (m, 2H), 3.87–3.83 (m, 1H), 3.61–3.54 (m, 2H), 2.23–2.09 (m, 4H), 1.24–1.13 (m, 1H), 0.88 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 140.1, 115.4, 74.7, 65.9, 32.3, 27.8, 27.2, 17.4, −4.7, −5.6; MS (ES) *m/z* 246 (M+18, 100). Anal. calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.60; H, 11.57.

3.4.5. (2S,3S)-3-t-Butyldimethylsilyl-6-heptene-1,2-diol (3k)

Following general procedure C, CH_2=$CH(CH_2)_2MgBr$ was prepared by the reaction of CH_2=$CH(CH_2)_2Br$ (5.0 equiv.) with Mg (5.05 equiv.) in ether at rt in the presence of a small amount of iodine, the title compound was prepared as a viscous colorless oil in 82% yield: $[\alpha]_D^{25}$ +8.4 (c 1.00, $CHCl_3$); IR (neat, NaCl) 3376 (br), 3077, 2939, 2857, 1698, 1640, 1466, 1442, 1382, 1251, 1040, 910, 826, 767 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.84–5.68 (m, 1H), 5.03–4.92 (m, 2H), 3.94–3.90 (m, 1H), 3.58–3.53 (m, 2H), 2.23–2.17 (m, 2H), 1.55–1.46 (m, 2H), 1.04–0.97 (m, 1H), 0.88 (s, 9H), −0.01 (s, 3H), −0.02 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 138.7, 114.8, 74.5, 65.9, 34.8, 27.2, 26.5,

26.0, 17.4, −4.5, −5.6; MS (ES) *m/z* 262 (M+18, 100). Anal. calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.55. Found: C, 63.79; H, 11.39.

*3.4.6. (2*S*,3*S*)-3-*t*-Butyldimethylsilyl-1,2-pentanediol (**3l**)*

Following general procedure C, using EtMgBr (5.0 equiv., 2.0 M solution in THF), the title compound was prepared as a viscous colorless oil in 84% yield: $[\alpha]_D^{25}$ +5.9 (c 0.84, $CHCl_3$); IR (neat, NaCl) 3369 (br), 2944, 2858, 1465, 1361, 1251, 1047, 1008, 827, 766 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.95–3.61 (m, 1H), 3.56–3.44 (m, 2H), 1.56–1.42 (m, 2H), 1.21–1.15 (m, 1H), 0.96 (t, J=6.9 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 74.5, 66.01, 30.0, 27.2, 20.7, 17.4, 15.5, −4.4, −5.6; MS (ES) *m/z* 236 (M+18, 100). Anal. calcd for $C_{11}H_{26}O_2Si$: C, 60.49; H, 11.99. Found: C, 60.49; H, 11.81.

*3.4.7. (2*S*,3*S*)-3-Triethylsilyl-5-hexene-1,2-diol (**3m**)*

Following general procedure C, $CH_2{=}CHCH_2MgCl$ was prepared by the reaction of $CH_2{=}CHCH_2Cl$ (5.0 equiv.) with Mg (5.05 equiv.) in ether at 0°C in the presence of a small amount of iodine, the title compound was prepared as a viscous colorless oil in 57% yield: $[\alpha]_D^{25}$ +9.0 (c 1.00 $CHCl_3$); IR (neat, NaCl) 3370 (br), 3076, 2952, 2876, 1637, 1459, 1417, 1320, 1237, 1170, 1037, 909, 851, 725 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.89–5.72 (m, 1H), 5.07–4.96 (m, 2H), 3.86–3.82 (m, 1H), 3.63–3.46 (m, 2H), 2.58 (br, 2H), 2.19 (t, J=6.7 Hz, 2H), 1.23–1.13 (m, 1H), 0.96 (t, J=7.8 Hz, 9H), 0.62 (q, J=7.8 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 139.7, 115.3, 74.3, 66.2, 31.6, 27.8, 7.7. 3.7; MS (ES) *m/z* 246 (M^+18, 100). Anal. calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.39; H, 11.16.

*3.4.8. (2*S*,3*S*)-3-*t*-Butyldimethylsilyl-4-nonyne-1,2-diol (**3n**)*

To a solution of 1-hexyne (0.739 g, 8.7 mmol) in THF (10 mL), *n*-BuLi (5.8 mL, 8.7 mmol, 1.5 M solution in hexane) was added dropwise at −40°C, followed by stirring for 30 min at −40°C. Then, Et_2AlCl (8.7 mL, 8.7 mmol, 1.0 M solution in hexane) was added dropwise. The reaction mixture was stirred at −40°C for 15 min, then permitted to warm to 0°C for 15 min. The mixture was re-cooled to −40°C and a solution of **2a** (0.551 g, 2.9 mmol) in toluene (20 mL) was added dropwise. The final reaction mixture was slowly warmed up to rt and stirred for 5 h at rt. Saturated $NaHCO_3$ solution was added to quench the reaction at 0°C. The phases were separated and the aqueous layer was extracted with ether (3×10 mL). The combined organic phase was dried over $MgSO_4$, concentrated and purified by column chromatography (30 g silica gel, hexane:ether 1:1), affording the title compound (0.572 g) as a viscous colorless oil in 73% yield: $[\alpha]_D^{25}$ −23.4 (c 1.05, $CHCl_3$); IR (neat, NaCl) 3358 (br), 2942, 2858, 1488, 1252, 1059, 1027, 834, 775 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.77–3.55 (m, 3H), 2.42 (br, 2H), 2.21–2.09 (m, 2H), 1.48–1.17 (m, 5H), 0.92 (s, 9H), 0.86 (t, J=6.9 Hz, 3H), 0.13 (s, 3H), 0.09 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 73.3, 71.8, 66.0, 63.7, 31.1, 26.9, 23.0, 22.0, 18.6, 17.4, 13.5, −6.2, −6.4; MS (ES) *m/z* 288 (M+18, 100). Anal. calcd for $C_{15}H_{30}O_2Si$: C, 66.61; H, 11.18. Found: C, 66.30; H, 11.02.

*3.5. General procedure D: preparation of (2*S*)-trialkylsilylaldehydes*

To a solution of lead tetraacetate (1.1 equiv.) in CH_2Cl_2 (5 mL per mmol β,γ-dihydroxysilane) was added $NaHCO_3$ (2.2 equiv.). After the mixture was stirred for 5 min at 0°C, a solution of β,γ-dihydroxysilane **3** (X mmol) in CH_2Cl_2 (2 mL per mmol β,γ-dihydroxysilane) was added dropwise. The reaction was stirred at 0°C for 2 h and quenched by adding saturated $NaHCO_3$ solution (5 mL per mmol β,γ-dihydroxysilane). The phases were separated and the aqueous layer was extracted with

ether (3×5 mL). The combined organic phase was dried ($MgSO_4$) and concentrated to give crude (2*S*)-trialkylsilylaldehydes **4**.

*3.5.1. (S)-2-t-Butyldimethylsilylpropanal (**4a**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 96% yield: $[\alpha]_D^{25}$ −15.9 (c 1.00, MeOH), lit.[6] $[\alpha]_D^{22}$ −114.6 (c 1.27, PhH); IR (neat, NaCl) 2945, 2859, 2800, 2712, 1696, 1467, 1256, 1121, 966, 823, 769 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.74 (d, J=2.1 Hz, 1H), 2.50 (td, J=6.7, 2.1 Hz, 1H), 1.18 (d, J=6.7 Hz, 3H), 0.93 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.5, 41.2, 26.9, 17.7, 9.1, −6.7, −6.8.

*3.5.2. (S)-2-t-Butyldimethylsilylhexanal (**4b**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 97% yield: $[\alpha]_D^{25}$ −6.1 (c 1.00, MeOH); IR (neat, NaCl) 2943, 2858, 2708, 1698, 1466, 1255, 1124, 949, 829, 768 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.65 (d, J=3.6 Hz, 1H), 2.01–1.98 (m, 1H), 1.45–1.09 (m, 6H), 0.90 (s, 9H), 0.87 (t, J=6.8 Hz, 3H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.6, 48.3, 33.3, 26.9, 26.7, 24.8, 22.5, 13.9, −6.4, −6.5.

*3.5.3. (S)-2-Dimethylphenylsilylpropanal (**4c**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 90% yield: $[\alpha]_D^{25}$ −9.6 (c 0.50, MeOH); IR (neat, NaCl) 3070, 2960, 2805, 2704, 1695, 1427, 1254, 1187, 1118, 822, 701 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.62 (d, J=2.2 Hz, 1H), 7.50–7.47 (m, 2H), 7.32–7.28 (m, 3H), 2.60 (td, J=6.7, 2.2 Hz, 1H), 1.13 (d, J=6.7 Hz, 3H), 0.39 (s, 3H), 0.38 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.0, 136.7, 133.7, 129.8, 128.1, 43.0, 8.2, −4.6, −4.7.

*3.5.4. (S)-2-Dimethylphenylsilylhexanal (**4d**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 93% yield: $[\alpha]_D^{25}$ −3.8 (c 1.00, MeOH); IR (neat, NaCl) 3070, 3040, 2957, 2930, 2864, 2715, 1695, 1428, 1254, 1117, 826, 700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.62 (d, J=3.3 Hz, 1H), 7.59–7.33 (m, 5H), 1.94–1.92 (m, 1H), 1.33–1.05 (m, 6H), 0.80 (t, J=6.8 Hz, 3H), 0.37 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.8, 135.6, 133.7, 129.7, 128.0, 50.0, 32.7, 24.0, 22.4, 13.8, −4.1, −4.4.

*3.5.5. (S)-2-Triethylsilylpropanal (**4e**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 93% yield: $[\alpha]_D^{25}$ −12.3 (c 0.50, MeOH); IR (neat, NaCl) 2956, 2878, 2800, 2708, 1694, 1461, 1414, 1229, 1137, 1011, 868, 725 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.70 (d, J=2.2 Hz, 1H), 2.51 (td, J=6.6, 2.2 Hz, 1H), 2.27 (d, J=6.6 Hz, 3H), 0.95 (t, J=7.7 Hz, 9H), 0.64 (q, J=7.7 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.49, 40.81, 8.10, 7.22, 2.55.

*3.5.6. (S)-2-Triethylsilylhexanal (**4f**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 90% yield: $[\alpha]_D^{25}$ −23.6 (c 0.50, MeOH), IR (neat, NaCl) 2949, 2876, 2800, 2705, 1695, 1462, 1415, 1239, 1125, 1010, 725 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.66 (d, J=3.5 Hz, 1H), 2.02–2.01 (m, 1H), 1.38–1.16 (m, 6H), 0.98 (t, J=7.7 Hz, 9H), 0.87 (t, J=6.8 Hz, 3H), 0.64 (q, J=7.7 Hz, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.6, 48.0, 33.3, 24.0, 22.5, 13.8, 7.3, 2.7.

*3.5.7. (S)-2-(p-Methoxyphenyl)dimethylsilylpropanal (**4g**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 90% yield: $[\alpha]_D^{25}$ −2.7 (c 1.00, MeOH); IR (neat, NaCl) 2920, 2850, 2714, 1696, 1594, 1503, 1459, 1278, 1290, 1250, 1113, 822, 774 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.61 (d, J=2.1 Hz, 1H, CH_3CHCHO), 7.49–7.40 (m, 2H, Ar-*H*), 6.93–6.83 (m, 2H, Ar-*H*), 3.80 (s, 3H CH_3O-Ar), 2.55 (td, J=6.5, 2.2 Hz, 1H, CH_3CHCHO), 2.07 (d, J=6.5 Hz, 3H, CH_3CHCHO), 0.35 [s, 6H, $(CH_3)_2Si$]; ^{13}C NMR (63 MHz, $CDCl_3$) δ 203.82, 160.81, 135.37, 127.03, 113.63, 65.81, 31.85, 15.33, −4.38, −4.97.

*3.5.8. (S)-2-(p-Methoxyphenyl)dimethylsilylhexanal (**4h**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 86% yield: $[\alpha]_D^{25}$ −4.0 (c 1.00, MeOH); IR (neat, NaCl) 2956, 3931, 2863, 2713, 1695, 1594, 1503, 1462, 1279, 1250, 1183, 1113, 822, 773 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.56 (d, J=3.4 Hz, 1H), 7.47–7.40 (m, 2H), 6.98–6.91 (m, 2H), 3.81 (s, 3H), 2.08–2.05 (m, 1H), 1.35–1.12 (m, 6H), 0.82 (t, J=6.8 Hz, 3H), 0.37 (s, 3H), 0.36 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 204.0, 160.9, 135.2, 126.3, 113.8, 55.0, 50.3, 32.9, 24.0, 22.4, 13.8, −4.0, −4.2.

*3.5.9. (S)-2-t-Butyldimethylsilyl-3-butenal (**4i**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 85% yield: $[\alpha]_D^{25}$ −8.9 (c 1.10, $CHCl_3$); IR (neat, NaCl) 3057, 2932, 2860, 2810, 2705, 1709, 1466, 1255, 1007, 836, 780 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.66 (d, J=3.3 Hz, 1H), 6.13–6.06 (m, 1H), 5.01–4.85 (m, 2H), 3.31 (dd, J=6.3, 3.3 Hz, 1H), 0.89 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 199.6, 131.2, 114.7, 55.1, 26.8, 18.0, −6.3, −6.8. (Note: the rotation value is not a real result due to the racemization during the reaction.)

*3.5.10. (S)-2-t-Butyldimethylsilyl-4-pentenal (**4j**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 93% yield: $[\alpha]_D^{25}$ −61.5 (c 5.00, $CHCl_3$); IR (neat, NaCl) 3078, 2955, 2951, 2859, 2810, 2715, 1698, 1640, 1468, 1255, 1053, 828, 807 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.59 (d, J=3.1 Hz, 1H), 5.75–5.59 (m, 1H), 5.14–4.80 (m, 2H), 2.72–2.69 (m, 2H), 2.15–2.10 (m, 1H), 0.85 (s, 9H), 0.00 (s, 3H), −0.03 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 202.6, 137.8, 114.9, 47.1, 29.0, 26.8, 17.7, −6.4, −6.6.

*3.5.11. (S)-2-t-Butyldimethylsilyl-5-hexenal (**4k**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 94% yield: $[\alpha]_D^{25}$ −43.2 (c 5.00, $CHCl_3$); IR (neat, NaCl) 3078, 2941, 2859, 2811, 2711, 1697, 1640, 1468, 1255, 1108, 913, 825, 769 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.60 (d, J=3.2 Hz, 1H), 5.75–5.59 (m, 1H) 4.93–4.73 (m, 2H), 2.17–1.77 (m, 4H), 1.46–1.37 (m, 1H), 0.85 (s, 9H), 0.00 (s, 3H), −0.04 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 202.9, 137.6, 115.5, 47.3, 34.5, 26.7, 24.3, 17.7, −6.5, −6.6.

*3.5.12. (S)-2-t-Butyldimethylsilyl-3-octynal (**4l**)*

Following general procedure D, the title compound was prepared without purification, as a colorless oil in 89% yield: $[\alpha]_D^{25}$ −10.6 (c 1.00, $CHCl_3$); IR (neat, NaCl) 2956, 2931, 2859, 2800, 2715, 1702, 1630, 1467, 1365, 1252, 1009, 828, 774 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.47 (d, J=3.8 Hz, 1H), 2.32–2.10 (m, 3H) 1.49–1.25 (m, 4H), 0.90 (s, 9H), 0.86 (t, J=6.9 Hz, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 198.2, 79.2, 72.9, 55.3, 26.3, 23.0, 21.8, 18.6, 17.8, 13.3, −6.7, −7.6.

Acknowledgements

Financial support from the Natural Sciences and Engineering Research Council of Canada in the form of a postgraduate scholarship (to DCC) and a research grant (to JMC) is gratefully acknowledged.

References

1. For reviews, see: (a) Colvin, E. W. *Silicon Reagents in Organic Synthesis*; Academic Press: New York, 1988. (b) Colvin, E. W. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; Vol. 11, pp. 317–354.
2. (a) Hudrlik, P. F.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1981**, *103*, 6251–6253. (b) Hudrlik, P. F.; Hudrlik, A. M.; Misra, R. N.; Peterson, D.; Withers, G. P.; Kulkarni, A. K. *J. Org. Chem.* **1980**, *45*, 4444–4448. (c) Hudrlik, P. F.; Misra, R. N.; Withers, G. P.; Hudrlik, A. M.; Rona, R. J.; Arcoleo, J. P. *Tetrahedron Lett*. **1976**, 1453–1456. (d) Barrett, A. G. M.; Flygare, J. A. *J. Org. Chem*. **1991**, *56*, 638–642. (e) Barrett, A. G. M.; Hill, J. M.; Wallace, E. M. *J. Org. Chem*. **1992**, *57*, 386–389. (f) Chauret, D. C.; Chong, J. M. *Tetrahedron Lett*. **1993**, *34*, 3695–3698.
3. Bhushan, V.; Lohray, B. B.; Enders, D. *Tetrahedron Lett.* **1993**, *34*, 5067–5070.
4. (a) Enders, D.; Lohray, B. B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 581–583. (b) Lohray, B. B.; Zimbiniski, R. *Tetrahedron Lett*. **1990**, *31*, 7273–7276.
5. Enders, D.; Lohray, B. B. *Helv. Chim. Acta* **1989**, *72*, 980–984.
6. (a) Enders, D.; Lohray, B. B. *Angew. Chem., Int. Ed. Engl*. **1987**, *26*, 351–352. (b) Enders, D.; Lohray, B. B.; Burkamp, F.; Bhushan, V.; Hett, R. *Liebigs Ann. Chem.* **1996**, 189–200.
7. (a) Le Bideau, F.; Aubert, C.; Malacria, M. *Tetrahedron: Asymmetry* **1995**, *6*, 697–700. (b) Le Bideau, F.; Gilloir, F.; Nilsson, Y.; Aubert, C.; Malacria, M. *Tetrahedron* **1996**, *52*, 7487–7510. (c) Courillon, C.; Le Fol, R.; Vandendris, E.; Malacria, M. *Tetrahedron Lett*. **1997**, *38*, 5493–5496.
8. (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc*. **1980**, *102*, 5974–5976. (b) Finn, M. G.; Sharpless, K. B. *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Florida, 1985; Vol. 5, pp. 247–308. (c) Sharpless, K. B.; Woodard, S. S.; Finn, M. G. *Pure Appl. Chem*. **1983**, *55*, 1823–1836. (d) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc*. **1987**, *109*, 5765–5780.
9. (a) Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987**, *52*, 4412–4414. (b) Hudrlik, P. F.; Peterson, D.; Rona, R. J. *J. Org. Chem.* **1975**, *40*, 2263–2264.
10. (a) Jones, T. K.; Denmark, S. E. *J. Org. Chem.* **1982**, *47*, 4595–4597. (b) Jones, T. K.; Denmark, S. E. *Org. Synth.* **1986**, *64*, 182–188.
11. The (*p*-methoxyphenyl)dimethylsilyl group were introduced as a possible hydroxyl group equivalent. For a leading reference, see: Fleming, I. *Chemtracts Org. Chem*. **1996**, *9*, 1–64.
12. (a) Kitano, Y.; Matsumoto, T.; Sato, F. *Tetrahedron* **1988**, *44*, 4073–4086. (b) Yoshida, J.; Maekawa, T.; Morita, Y.; Isoe, S. *J. Org. Chem*. **1992**, *57*, 1321–1322.
13. Dale, J. A.; Dull, D. A.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.
14. Hall, W. E.; Seeholzer, K.; Baumeister, M.; Ugi, I. *Tetrahedron* **1986**, *42*, 547–552.
15. Where ^{19}F NMR signals for the two diastereomers were resolved, the signal for the minor isomer could be compared to the ^{13}C satellites (0.55% intensity) of the major signal for a precise assay; with ^{1}H NMR spectra, overlapping ABX patterns were usually observed, and a value of >95% indicates that signals for the minor isomer were not detected.
16. Davis, A. P.; Hughes, G. J.; Lowndes, P. R.; Robbins, C. M.; Thomas, E. J.; Whitman, G. H. *J. Chem. Soc., Perkin. Trans. 1* **1981**, 1934–1941.
17. For recent discussions regarding the nature of 'higher order' cuprates, see: (a) Bertz, S. H.; Nilsson, K.; Davidsson, Ö.; Snyder, J. P. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 314–317. (b) Lipshutz, B. H.; James, B. *J. Org. Chem*. **1994**, *59*, 7585–7587.
18. Whitesides, G. M.; Stedronsky, E. R.; Casey, C. P.; San Fillipo Jr., J. *J. Am. Chem. Soc*. **1970**, *92*, 1426–1427.
19. (a) Corey, E. J.; Beames, D. J. *J. Am. Chem. Soc*. **1972**, *94*, 7210–7211. (b) Mandeville, W. H.; Whitesides, G. M. *J. Org. Chem*. **1974**, *39*, 400–405. (c) Kim, S.; Park, J. H.; Jon, S. Y. *Bull. Korean Chem. Soc*. **1995**, *16*, 783–786.
20. (a) Fried, J.; Lin, C. H.; Sih, J. C.; Dalven, P.; Cooper, G. F. *J. Am. Chem. Soc*. **1972**, *94*, 4342–4343. (b) Suzuki, T.; Saimoto, H.; Tomioka, H.; Oshima, K.; Nozaki, H. *Tetrahedron Lett*. **1982**, *23*, 3597–3600.
21. House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem*. **1975**, *40*, 1460–1469.
22. See footnote 45 in Ref. 8d.
23. Chong, J. M.; Loewith, R. *Synth. Commun*. **1993**, *23*, 2145–2150.