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Stereoselective lithiation of α,β-epoxy-γ,δ-vinylsilanes and transformation into α-silylated ketones

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Abstract—A (*cis*)α,β-epoxy-γ,δ-vinyl-silane undergoes lithiation α to the silicon atom with retention of the configuration of the oxirane. This leads to new silylated vinyloxiranes with a quaternary silylated stereogenic carbon atom. We show here the possible and efficient rearrangement of a methyl substituted adduct into a β,γ-unsaturated-α-silylated ketone.
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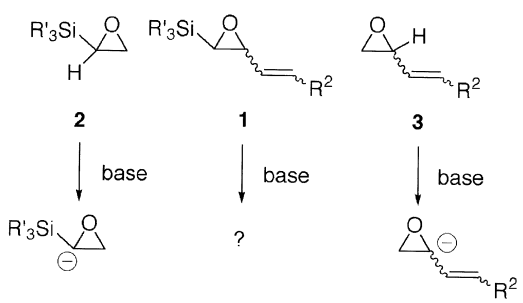
1. Introduction

α,β-Epoxy-γ,δ-vinyl-silanes **1** are highly functionalized substrates of great value in synthetic organic chemistry. Their preparation[1] and reactivity[2] have been rarely described in the literature. One of our projects led us to study the chemical behavior of α,β-epoxy-γ,δ-vinyl-silanes **1** towards nucleophiles and basic reagents and to compare it to the reactivity of α,β-epoxy-silanes **2** or vinyloxiranes **3**. These latter compounds have been thoroughly described in the literature and their reactivity is very well known and widely reported. At the beginning, we could imagine that compounds **1**, which looked like a fused structure made up of compounds **2** and **3**, would display the same reactivity towards deprotonation. Therefore, as depicted in Scheme 1, we could expect the deprotonation α to the silicon atom[3] as in the case of α,β-epoxysilanes **2** and/or the abstraction of the allylic proton[4] as in the case of vinyloxiranes **3**.



Scheme 1.

We recently reported preliminary results in this field showing that *trans* and *cis* α,β-epoxy-γ,δ-vinyl-silanes **1** behaved differently in the presence of lithiated bases.[5] We describe here the preparation of these α-silylated oxiranyl anions and their stereoselective electrophilic trapping. Further synthetic developments of the new thus obtained α-alkylated-α,β-epoxy-γ,δ-vinyl-silanes gave access to α-silylated-β,γ-unsaturated ketones which may be stable entities with no isomerization of the double bond as we report in this paper.

2. Results and discussion

2.1. Reactivity of α,β-epoxy-γ,δ-vinyl-silane 1 on lithiated bases

Our group has already reported the synthesis of enantio-pure *trans* α,β-epoxy-γ,δ-vinyl-silane **1a**[6] through a sequence that presents two stereoselective steps, one of which is the diastereoselective controlled reduction of compound **4** into the silylated (*E*) allylic alcohol **5**, using Red-Al as the reducing agent.[7] The same synthetic pathway has been followed to prepare the *cis* diastereomer **1b** except for the reduction of the triple bond which has been modified by using $LiAlH_4$,[8] crystal clear in dry ether as shown in Scheme 2.[9]

The lithiation reaction has been studied on both compounds *trans*-**1a** and *cis*-**1b**. The *trans* compound **1a** could not be deprotonated neither by *n*-BuLi, *sec*-BuLi nor *tert*-BuLi. It reacted like an electrophilic vinyloxirane[10,11] and underwent a S_N2' reaction instead.[5] The allylic alcohols **9** are thus stereoselectively prepared.(Scheme 3) The study of this

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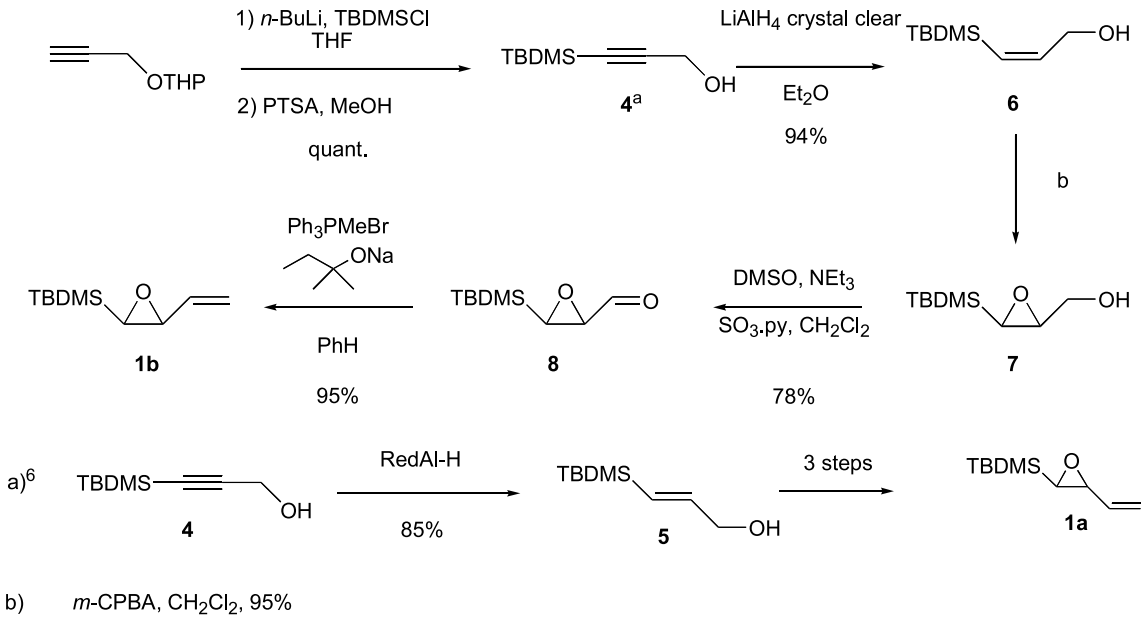
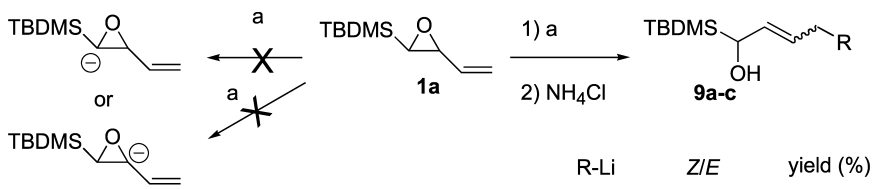


Scheme 2.



	R-Li	*Z*/*E*	yield (%)
9a	*tert*-BuLi	7.4/1	98
9b	*sec*-BuLi	7.8/1	99
9c	*n*-BuLi	7.5/1	69

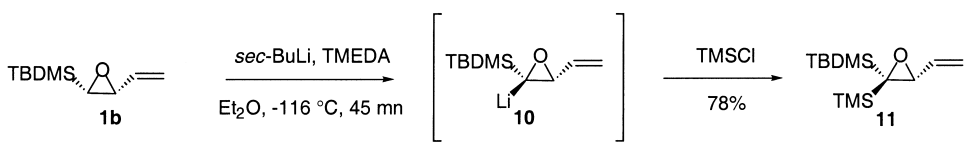
Scheme 3.

S_N2' process is not reported in this paper which is devoted to the oxiranyl anions. However, it is noteworthy to mention that Molander has first reported the importance of the configuration of the starting silylated oxirane on the efficiency of the lithiation reaction.[12] He showed that the *trans* epoxysilanes were uneasily deprotonated after 4 h whereas the *cis* isomers could be lithiated whithin 5 min.

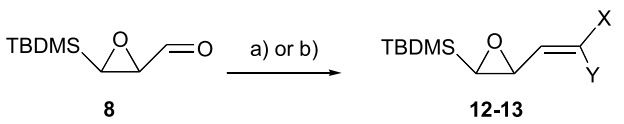
α-Silylated oxiranyl anions have first been obtained by Eisch,[13] they have been reported as configurationally stable species unless a β-substituent induces isomerization of the anion even at low temperature.[14,11] In any case, the yields of the reaction depend very much on the control of the temperature.[15]

The *cis* compound **1b** was therefore successively deprotonated under the classical conditions previously described (*sec*-BuLi, TMEDA, Et_2O, −116°C). Progressive formation of a pale yellow solid as reported[12,13] indicate the likewise formation of the anion **10** stabilized in the α position to the silicon atom.[16] Trapping of this anion with chlorotrimethylsilane led to the α-bis-silylated-α,β-epoxy-γ,δ-vinyl-silane **11** which is partly degraded during the chromatography on silica gel and after this purification the yield falls down to 78%. This is the first example of a new α,β-epoxy-γ,δ-vinyl-silane with a quaternary carbon on the oxirane, β to the C−C double bond (Scheme 4). When the temperature is raised to −30°C, we could neither check the formation of the oxiranyl anion nor the S_N2' process. We registered instead total degradation of compound **1b**. Even with a large excess of the lithiated base, we could not see the formation of any silylated allylic alcohol as expected through an S_N2' reaction.

We wanted to check the influence of a methyl- or a methylester group on the double bond (*Z* or *E* in the case of



Scheme 4.



a) : $(MeO)_2POCH_2COOMe$, DBU, LiCl, **12** X = COOMe, Y = H (67%)

b) : $(CF_3CH_2O)_2POCH_2COOMe$, 18-C-6, KHMDS, **13**: X = H, Y = COOMe (66%)

Scheme 5.

the ester function) of a silylated vinyloxirane towards deprotonation. Therefore we synthesized compounds **12** and **13** starting from epoxyaldehyde **8** respectively through a Wittig Horner Emmons reaction and a Still and Gennari olefination[17] (Scheme 5).

2.2. Electrophilic trapping

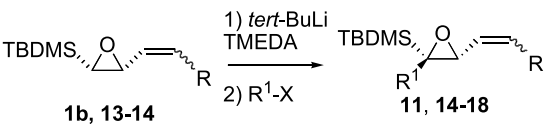
The lithiation reaction was run with *tert*-BuLi and TMEDA in pentane which are efficient experimental conditions that lead to the formation of the anion whithin 30 min, faster than *sec*-BuLi in ether. Addition of an electrophilic agent is then quickly operated and different adducts are stereoselectively synthesized. Obtention of compounds **11**, **14**–**18** (Table 1) indicates two important issues: first the deprotonation occurs chemoselectively at the α-position to the silicon atom and secondly, the vinylic group does not induce the isomerization of the anion with the shift of the negative charge to the β-position as in the case of a phenyl group.[3] In our case the oxiranyl anion could either be stabilized by the silicon atom or by the unsaturation.[4,18] Absence of electrophilic trapping at the allylic position indicates that stabilization of the allylic anion by the unsaturation is not strong enough. Substitution of the double bond with an ester function, probably changes this situation and the consequence is that compounds **12** and **13** could be deprotonated since the caracteristic yellow precipitate of the anion appears clearly at −116°C, but the anion could not be trapped by methyl iodide. Starting material was recovered (40%) and a complex mixture was obtained with evidence of dimerization of the compound.

Trapping of the anion **10** with methyl iodide gave the adduct **14** with 89% yield. On this adduct NMR NOE experiments showed that the silicon atom and the C–C double bond remained *syn* to each other. We can therefore conclude that the deprotonation and the trapping have occured with retention of the configuration of the oxirane. When the electrophile is prochiral like benzaldehyde, the compound **15** is obtained as a 9:1 mixture of two diastereomers **15a** and **15b**. According to Molander,[12] with poorly reactive aldehydes like benzaldehyde the transition state for C–C bond formation is late and therefore the steric effects are more important and induce a greater diastereoselectivity. Especially, in our case we can imagine that the position of the phenyl group should help to avoid it's interaction with the allylic proton. In Scheme 6, we rationalize the major attack of the anion **10** on the *Si* face of the carbonyl which should yield mainly the diastereomer with the new stereogenic carbon having the *R* absolute configuration.

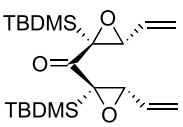
The ester compound **16** was obtained after trapping with methylcyanoformate as well as with methylchloroformate respectively with a yield of 78 and 20%. In the last case a second product **17** was formed by the reaction of the anion **10** on the ester **16** with a yield of 42%. The diene **18** was synthesized by trapping the anion **10** with allyl iodide and the yield after purification is 45%.

These examples demonstrate that *cis* vinylepoxysilane **1b** can be deprotonated by lithiated bases which is not observed in the case of *trans* vinylepoxysilane **1a**. Obviously the relative configuration of the stereogenic carbons of the oxirane is controlling it's reactivity. We can extend the hypothesis proposed by Molander[12] to the case of epoxysilanes and imagine the formation of a complex between the base and the silylated vinyloxirane. Minimizing steric hindrance should imply an *anti* relationship between

Table 1.



Substrate	R^1X	Compound (yield %)
1b: R=H	$(CH_3)_3$ Si–Cl	**11** (78)
1b: R=H	CH_3–I	**14** (89)
1b: R=H	PhCHO	**15** (76)
1b: R=H	$NCCO_2CH_3$	**16** (78)
1b: R=H	$ClCO_2CH_3$	**16** (20)+**17** (42)
1b: R=H		**18** (45)
(*E*)-**12**: R=COOMe	CH_3–I	–
(*Z*)**12**: R=COOMe	CH_3–I	–



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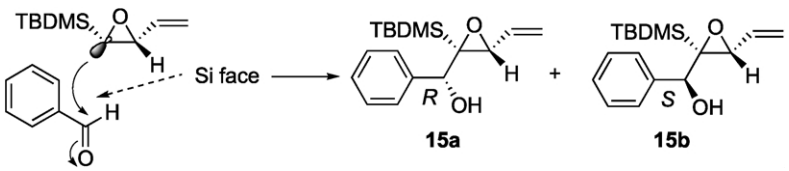
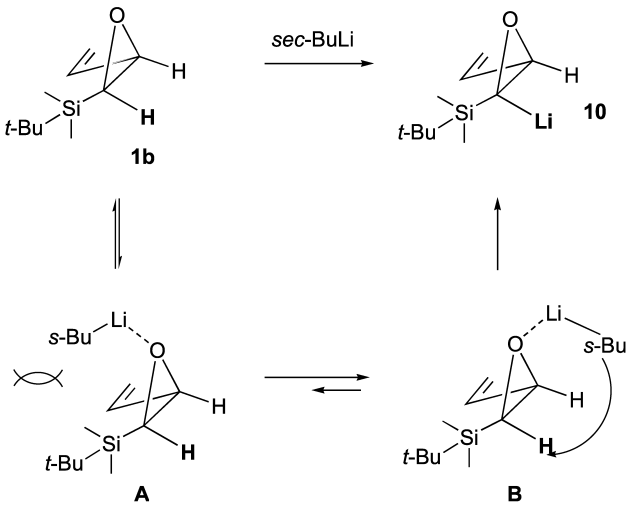


Scheme 6.

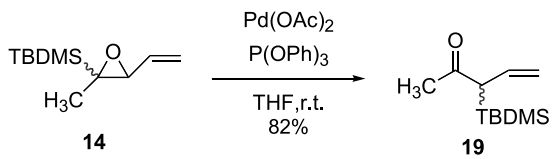


Scheme 7.

the base and the silyl group as in the **B** intermediate of Scheme 7. Since no destabilizing interaction exists in the **B** form, the equilibrium is in favor of **B**, and then the base is well oriented to abstract the proton.

2.3. Stereoselective preparation of a β,γ-unsaturated-α-silylated ketone

The lithiation of silylated vinyloxiranes has given access to new compounds with a quaternary silylated α-carbon. Our group has already studied the palladium catalyzed rearrangement of γ,δ-vinyl-α,β-epoxysilanes and the subsequent formation of β,γ-unsaturated-α-silylated-aldehydes.[19,20] It was interesting to check the transformation of the trisubstituted oxirane **14** with palladium(0) and characterize the newly formed β,γ-unsaturated-α-silylated-ketone **19** which is a highly functionalized compound and therefore a powerful tool for synthetic chemistry. The same rearrangement conducted on the diastereomeric mixture of compound **15** afforded a rapidly degraded compound which could not be fully identified (Scheme 8).



Scheme 8.

3. Conclusion

The lithiation reaction of *cis* silylated vinyloxirane **1b** forms a new type of compounds with a substituent α to the silicon atom and can lead to the formation of highly functionalized ketones. These results show interestingly that the action of a lithiated base on our compounds is totally directed by the relative configuration of the olefin and the silyl group. When they have a *syn* relationship, the base abstracts the proton α to the silicon atom; whereas, when they are *anti* to each other, a S_N2' reaction is observed with addition of the carbanion. In both cases, the diastereoselectivity is high and the chimioselectivity is total. We are currently studying the influence of a substituent on the double bond in the lithiation reaction. This project is investigating the reactivity of α,β-epoxy-γ,δ-vinyl-silanes and therefore their possible applications in synthesis.

4. Experimental

4.1. General

All melting points are uncorrected. THF and Et_2O are distilled from sodium benzophenone ketyl, CH_2Cl_2, pentane and toluene are distilled from CaH_2. Infrared spectra were recorded on a Perkin–Elmer 1420 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on Brucker AC 200 and ARX 400 spectrophotometers. Mass spectra were performed either on Nermag R 30-10 or on MS 700 Jeol apparatus.

4.1.1. (*Z*) 3-*tert*-Butyldimethylsilyl-prop-2-en-1-ol: 6. A solution of 4.6 g of $LiAlH_4$ (powder, 123 mmol, 3.5 equiv.) in 140 mL of anhydrous diethyl ether was stirred overnight at room temperature under argon. The gray $LiAlH_4$ solution was then filtered on celite under inert atmosphere through a Shlenck filtration apparatus into a three-necked round bottom flask equipped with a magnetic stirrer and a condenser. The freshly filtered white solution is heated to reflux. A solution of silylated propargylic alcohol **4** (6.00 g, 35.2 mmol, 1 equiv.) in anhydrous diethyl ether (30 mL) was then transferred via cannula to the reaction mixture and stirred for 1 h. The medium was slowly hydrolyzed with a cold aqueous solution of potassium and sodium tartrate (50 mL) followed by a cold 3.6 M aqueous solution of sulphuric acid (100 mL). The aqueous layer was then extracted with ether and the combined organic phases were neutralized with a saturated $NaHCO_3$ solution. The organic phase was then washed with brine and dried over $MgSO_4$. Purification of the crude product by flash chromatography on silica gel (PE/AcOEt: 90/10) afforded compound **6** as white needles (5.71 g, 33.1 mmol, 94%).

IR (neat) 3300, 2940, 1600, 1250, 820. ^1H NMR (200 MHz, $CDCl_3$) δ 6.50 (dt, 1H, J=14.5, 6.6 Hz), 6.45 (d, 1H, J=14.5 Hz), 4.16 (d, 2H, J=6.6 Hz), 0.87 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 147.5, 129.4, 63.4, 26.3, 16.7, −4.1. HRMS *m/z* calcd for $C_9H_{21}OSi$ (MH^+)

173.1362; found: 173.1353. Anal. calcd for $C_9H_{20}OSi$: C, 62.72; H, 11.70; found: C, 62.57; H, 11.91.

4.1.2. (*cis*) 3-*tert*-Butyldimethylsilyl-2,3-epoxy-propan-1-ol: 7. To a cooled (0°C) solution of allylic alcohol **6** (5.17 g, 30.0 mmol, 1.0 equiv.) in CH_2Cl_2 (60 mL) was slowly added 11.1 g of *m*-CPBA (70% with water and 3-chlorobenzoic acid, 45.0 mmol, 1.5 equiv.). The reaction mixture was allowed to warm up to room temperature and after stirring for 2 h, 20 mL of brine was added to the medium. The organic layer was then dried over $MgSO_4$ and after partial evaporation of the solvent, 10 mL of pentane was added. The precipitate was then filtered off over a short pad of celite. This operation was repeated four times to assure complete removal of the *m*-CPBA and the corresponding acid. The residue was then purified by flash chromatography on silica gel (PE/AcOEt: 80/20) affording epoxyalcohol **7** was obtained quantitatively (5.65 g, 30.0 mmol) as a thick colorless oil.

IR (neat) 3400, 2940, 1250, 850. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (dd, 1H, J=12.2, 3.0 Hz), 3.47 (dd, 1H, J=12.2, 7.8 Hz), 3.35 (ddd, 1H, J=7.8, 5.6, 3.0 Hz), 2.40 (d, 1H, J=5.6 Hz), 0.94 (s, 9H), 0.06 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 63.8, 57.8, 47.9, 26.5, 16.8, −6.0, −6.1. Anal. calcd for $C_9H_{20}O_2Si$: C, 57.39; H, 10.70; found: C, 57.46; H, 10.82.

4.1.3. (*cis*) 3-*tert*-Butyldimethylsilyl-2.3-epoxypropanal: 8. To a cooled (0°C) solution of *cis*-epoxyalcohol **7** (5.00 g, 26.5 mmol, 1.0 equiv.) in CH_2Cl_2 (60 mL) were added successively 43 mL of triethylamine (308 mmol, 10 equiv.) and 48 mL of DMSO (616 mmol, 20 equiv.). After stirring for 5 min at 0°C, 29.4 g of SO_3.pyridine complex (185 mmol, 6 equiv.) was added in small portions. The oxidation occurred at this temperature in 30 min. The reaction mixture was quenched carefully at 0°C by a saturated aqueous NH_4Cl solution (30 mL). The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were washed with brine and dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude product was purified by flash chromatography on silica gel (PE/Et_2O: 90/10) affording the epoxyaldehyde **8** as a colorless oil (3.86 g, 20.7 mmol) with 78% yield.

IR (neat) 2920, 1700, 1230, 820. ^{1}H NMR (200 MHz, C_6D_6) δ 9.07 (d, 1H, J=6.4 Hz), 3.15 (dd, 1H, J=6.4, 5.9 Hz), 2.18 (d, 1H, J=5.9 Hz), 0.78 (s, 9H), −0.10 (s, 3H), −0.25 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 200.0, 59.4, 50.3, 27.2, 17.7, −5.2, −5.3. HRMS *m*/*z* calcd for $C_9H_{19}O_2Si$ (MH^+) 187.1154; found: 187.1156.

4.1.4. (*cis*) 1-*tert*-Butyldimethylsilyl-1.2-epoxybut-3-ene: 1b. To a solution of methyltriphenylphosphonium bromide, Ph_3PCH_3Br, (7.38 g, 20.7 mmol, 1.1 equiv.) in dry toluene (75 mL) was added at room temperature sodium *tert*-pentoxide (2.47 g, 22.5 mmol, 1.2 equiv.) in four times. The medium was warmed up to reflux during 1 h. The mixture was then cooled to room temperature and a solution of the silylated aldehyde **8** (3.5 g, 18.8 mmol, 1 equiv.). In 10 mL of toluene was added dropwise. After 30 min stirring, 30 mL of a saturated aqueous NH_4Cl solution were added. The aqueous layer was extracted with ether and the combined organic phases were washed with brine, dried over Na_2SO_4 and the solvents were removed in vacuo. The crude product was purified by flash chromatography on silica gel (PE/Et_2O: 90/10) to afford the title compound as a colorless oil with 95% yield (3.29 g, 17.8 mmol).

IR (neat) 3060, 2920, 1620, 1240, 830. ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.62 (ddd, 1H, J=17.2, 9.8, 7.4 Hz), 5.45 (dd, 1H, J=17.2, 2.0 Hz), 5.25 (dd, 1H, J=9.8, 2.0 Hz), 3.53 (dd, 1H, J=7.4, 5.4 Hz), 2.46 (d, 1H, J=4.9 Hz), 0.94 (s, 9H), 0.07 (s, 3H), −0.01 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.1, 119.6, 53.4, 50.4, 26.5, 16.8, −6.0, −6.4. HRMS *m*/*z* calcd for $C_{10}H_{21}OSi$ (MH^+) 185.1362; found: 185.1359. Anal. calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.94; found: C, 65.13; H, 10.85.

4.1.5. 1-*tert*-Butyldimethylsilyl-5-methyl-hept-2-en-1-ol: 9a. *General procedure for ring-opening with lithiated carbanions*. The temperature must be rigorously controlled at −116°. To a cooled solution of the *trans* silylated vinyloxirane **1a** (100 mg, 0.54 mmol, 1.0 equiv.) in 5 mL of diethyl ether, was added TMEDA (122 μL, 0.81 mmol, 1.5 equiv.). After 5 min, *s*-BuLi (1.3 M in cyclohexane, 0.63 mL, 0.81 mmol, 1.5 equiv.) was carefully added dropwise. The reaction mixture was stirred for 4 h. The medium was then quenched with a 1/1 solution of propionic acid in diethyl ether. After 15 min, the medium was treated with a saturated aqueous NH_4Cl solution and the organic phase was neutralized with a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted twice with ethyl acetate and the combined organic layers were washed with brine, dried over $MgSO_4$ and the solvents were removed in vacuo. The crude product was purified by flash chromatography on silica gel (PE/CH_2Cl_2: 90/10) and two diastereomers (*Z*)-**9a** (colorless oil) and (*E*)-**9a** (pale yellow oil) were obtained with 88 and 11% yields, each of them being probably a mixture of unseparable diastereomers.

Compound (*Z*)-**9a**. IR (neat) 3450, 3020, 2960, 1650, 1250, 830. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 (t, 1H, J=10.4 Hz), 5.34 (m, 1H), 4.37 (d, 1H, J=10.4 Hz), 1.90 (m, 2H), 1.34 (m, 2H), 1.17 (m, 1H), 0.93 (s, 9H), 0.85 (t, 3H, J=6.6 Hz), 0.84 (d, 3H, J=6.6 Hz), 0.00 (s, 3H), −0.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.2, 128.6, 62.5, 35.4, 34.9, 30.0, 27.4, 19.4, 17.4, 12.0, −7.2, −8.4. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47; found: C, 69.11; H, 12.27.

Compound (*E*)-**9a**. IR (neat) 3460, 3030, 2950, 1670, 1250, 850. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.69 (dd, 1H, J=15.2, 6.6 Hz), 5.52 (dt, 1H, J=15.2, 7.1 Hz), 4.13 (d, 1H, J=6.6 Hz), 2.12 (dt, 1H, J=13.7, 7.1 Hz), 1.94 (dt, 1H, J=13.7, 7.1 Hz), 1.46–1.37 (m, 2H), 1.19 (m, 1H), 1.01 (s, 9H), 0.92 (t, 3H, J=6.6 Hz), 0.91 (d, 3H, J=6.6 Hz), 0.06 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.2, 128.0, 61.8, 34.7 (C_5), 34.2, 29.2, 26.6, 18.8, 16.7, 11.2, −8.0, −9.1. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47; found: C, 69.41; H, 12.55.

4.1.6. 1-*tert*-Butyldimethylsilyl-5,5-dimethyl-hex-2-en-1-ol: 9b. Following the latter procedure, starting from **1a** (100 mg, 0.54 mmol, 1 equiv.) and using *t*-BuLi (1.5 M in pentane, 0.54 mL, 0.81 mmol, 1.5 equiv.), the two separable diastereomers (*E*) (yellow oil) and (*Z*)-**9b** (pale yellow oil)

were obtained as colorless oils respectively with yields of 12 and 86%.

Compound (*E*)-**9b**. IR (neat) 3460, 3020, 2970, 1680, 1270, 850. ^{1}H NMR (400 MHz, C_6D_6) δ 5.59 (dd, 1H, J=15.2, 5.6 Hz), 5.44 (dt, 1H, J=15.2, 6.6 Hz), 3.93 (d, 1H, J=5.6 Hz), 1.90 (d, 2H, J=6.6 Hz), 1.03 (s, 9H), 0.89 (s, 9H), 0.09 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 136.3, 124.8, 67.8, 48.4, 30.6, 28.9, 26.6, 16.5, −6.2, −7.8. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47; found: C, 69.01; H, 12.25.

Compound (*Z*)-**9b**. IR (neat) 3450, 2990, 1650, 1250, 830. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (t, 1H, J=10.7 Hz), 5.43 (dt, 1H, J=10.7, 5.6 Hz), 4.39 (d, 1H, J=10.7 Hz), 2.04 (ddd, 1H, J=14.4, 5.6, 1.0 Hz), 1.78 (ddd, 1H, J=14.4, 5.6, 1.6 Hz), 0.94 (s, 9H), 0.89 (s, 9H), 0.02 (s, 3H), −0.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.4, 126.6, 62.1, 41.5, 30.8, 29.3, 27.1, 17.1, −7.5, −8.6. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47; found: C, 69.04; H, 12.31.

4.1.7. 1-*tert*-Butyldimethylsilyl-oct-2-en-1-ol: 9c. Following the general procedure of ring-opening using 100 mg of **9c** (0.54 mmol, 1.0 equiv.) and *n*-BuLi (2.5 M solution in hexane, 0.32 mL, 0.81 mmol, 1.5 equiv.), the two separable diastereomers (*Z*) (pale yellow oil) and (*E*)-**9c** (colorless oil) were obtained with yields of 61 and 8%.

Compound (*Z*)-**9c**. IR (neat) 3450, 2930, 1660, 1250, 830. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51 (t, 1H, J=10.4 Hz), 5.34 (m, 1H), 4.40 (d, 1H, J=10.4 Hz), 2.06 (m, 1H), 1.92 (m, 1H), 1.36–1.24 (m, 6H), 0.94 (s, 9H), 0.87 (t, 3H, J=7.1 Hz), 0.02 (s, 3H), −0.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.1, 129.6, 62.3, 31.7, 29.5, 27.9, 27.1, 22.6, 17.1, 14.1, −7.6, −8.7. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47; found: C, 69.34; H, 12.51.

Compound (*E*)-**9c**. IR (neat) 3450, 2930, 1680, 1250, 830. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (dd, 1H, J=15.2, 7.1 Hz), 5.46 (dtd, 1H, J=15.2, 7.1, 1.0 Hz), 4.04 (dd, 1H, J=7.1, 1.0 Hz), 2.02 (q, 2H, J=7.1 Hz), 1.37–1.24 (m, 6H), 0.93 (s, 9H), 0.87 (t, 3H, J=7.1 Hz), 0.01 (s, 3H), −0.05 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.2, 127.8, 67.0, 32.5, 31.5, 29.4, 27.1, 22.6, 17.0, 14.1, −7.6, −8.8. Anal. calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47; found: C, 69.20; H, 12.65.

4.1.8. (*cis*) 1-*tert*-Butyldimethylsilyl-1-trimethylsilyl-1,2-epoxybut-3-ene: 11. *General procedure for α-lithiation of (cis) silylated vinyloxirane* **1b**. The temperature was rigorously controlled during the reaction. To a cooled (−116°C) solution of the silylated vinyloxirane **31** (200 mg, 1.08 mmol, 1.0 equiv.) in diethyl ether (10 mL), were added successively TMEDA (0.25 mL, 1.63 mmol, 1.5 equiv.) and *s*-BuLi (1.3 M solution in cyclohexane, 1.67 mL, 2.17 mmol, 1.5 equiv.) or *tert*-BuLi (1.7 M solution in pentane, 1.27 mL, 2.17 mmol, 1.5 equiv.). After 45 min at −116°C, TMSCl (0.28 mL, 2.16 mmol, 2 equiv.) was added rapidly. The medium was maintained at this temperature for 30 min and was warmed up progressively to room temperature. The reaction mixture was then quenched with water (10 mL) and the organic phase was treated with a saturated aqueous NH_4Cl solution, washed with brine and dried over Na_2SO_4. After removal of the solvent, the crude product was purified by flash chromatography on silica gel (PE/CH_2Cl_2: 90/10) affording the substituted silylated vinyloxirane **11** with 78% yield as a pale yellow oil (161 mg, 0.63 mmol). 26% of the starting material was also recovered.

IR (neat) 3050, 2930, 1650, 1250, 830. ^{1}H NMR (200 MHz, C_6D_6) δ 5.92 (ddd, 1H, J=17.2, 10.3, 8.8 Hz), 5.28 (dd, 1H, J=17.2, 1.5 Hz), 5.06 (d, 1H, J=10.3 Hz), 3.45 (d, 1H, J=8.8 Hz), 1.01 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.07 (s, 9H). ^{13}C NMR (100 MHz, C_6D_6) δ 140.0, 120.3, 64.0, 54.7, 29.5, 19.6, 0.0, −0.6, −0.7. HRMS *m/z* calcd for $C_{13}H_{29}OSi_2$ (MH^+) 257.1757; found: 257.1758.

4.1.9. (*E*)(*cis*)5-*tert*-Butyldimethylsilyl-4.5-epoxypent-2-enoic methyl ester: 12. To a suspension of dry LiCl (54.7 mg, 1.29 mmol, 1.2 equiv.) in CH_3CN (6 mL) were successively added, at room temperature, trimethylphosphonoacetate $(MeO)_2POCH_2CO_2Me$ (0.21 mL, 1.29 mmol, 1.2 equiv.), 0.22 mL of diazabicycloundecene DBU (1.07 mmol, 1.0 equiv.) and a solution of the epoxyaldehyde **8** (200 mg, 1.07 mmol, 1.0 equiv.) in CH_3CN (6 mL). The reaction mixture was stirred for 1 h and was diluted with diethyl ether (15 mL) and treated with a saturated aqueous NH_4Cl solution (20 mL). The organic phase was washed with brine and dried over $MgSO_4$. After removal of the solvents in vacuo, the crude product was purified and the two diastereomers (*E*/*Z*=90/10) were separated by flash chromatography on silica gel (PE/Et_2O: 90/10) affording the *trans*-methyl ester **12** with 67% yield (218 mg, 0.90 mmol) as a colorless oil.

IR (neat) 2952, 2927, 2856, 1724, 1655, 1265, 775. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.75 (dd, 1H, J=15.8, 7.9 Hz), 6.21 (d, 1H, J=15.8 Hz), 3.79 (s, 3H), 3.70 (dd, 1H, J=5.7, 7.9 Hz), 2.63 (d, 1H, J=5.7 Hz), 0.99 (s, 9H), 0.14 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.9, 145.9, 123.9, 55.1, 51.7, 51.3, 31.9, 26.5, 16.8, −5.9, −6.2.

4.1.10. (*Z*)(*cis*)5-*tert*-Butyldimethylsilyl-4.5-epoxypent-2-enoic methyl ester: 13. To a cooled (−100°C) solution of crown ether 18-C-6 (1.7 g, 6.46 mmol, 2 equiv.) and phosphonate $(CF_3CH_2O)_2POCH_2CO_2Me$ (0.75 mL, 3.55 mmol, 1.1 equiv.) in THF (70 mL), was slowly added KHMDS (0.5 M in toluene, 6.46 mL, 3.23 mmol, 1.0 equiv.). After 15 min at this temperature, a solution of the aldehyde **8** (600 mg, 3.23 mmol, 1.0 equiv.) in THF (10 mL) was transferred via cannula. After stirring for 40 min at −100°C, the medium was quenched with 15 mL of a saturated aqueous NH_4Cl solution and the temperature was progressively warmed up to 25°C under vigorous stirring. The organic layer was washed with brine and dried over $MgSO_4$. The solvents were removed in vacuo and purification by flash chromatography on silica gel (PE/Et_2O: 90/10) afforded the *Z* epoxyester **14** with 66% yield (516 mg, 2.10 mmol) as a colorless oil.

IR (neat) 2952, 2929, 2857, 1721, 1643, 1439, 1196, 776. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12–5.97 (m, 2H), 4.64 (t, 1H, J=5.9 Hz), 3.79 (s, 3H), 2.72 (d, 1H, J=3.5 Hz), 0.99 (s, 9H), 0.1 (s, 3H), 0.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 148.1, 122.5, 53.4, 51.5, 51.2, 26.7, 26.4, 16.8,

−6.1, −6.6. Anal. calcd for $C_{12}H_{22}O_3Si$: C, 59.46; H, 9.15; found: C, 59.31; H, 9.32.

4.1.11. 2-*tert*-Butyldimethylsilyl-2,3-epoxypent-4-ene: 14. The methylation of the *cis*-silylated vinyloxirane **1b** (100 mg, 0.54 mmol, 1.0 equiv.) was carried out using the same conditions as described for the preparation of **11**, with *t*-BuLi (1.5 M in pentane, 0.54 mL, 0.81 mmol, 1.5 equiv.) in pentane (5 mL). The reaction mixture was quenched with methyl iodide (0.34 mL, 5.42 mmol, 10.0 equiv.). Compound **14** was isolated as a yellow oil with 89% yield (95 mg, 0.48 mmol) after purification of the crude product by flash chromatography on silica gel (PE/CH_2Cl_2: 90/10).

IR (neat) 3040, 2920, 1660, 1230, 820. ^{1}H NMR (200 MHz, C_6D_6) δ 5.74 (ddd, 1H, J=17.4, 10.5, 8.4 Hz), 5.25 (dd, 1H, J=17.4, 1.3 Hz), 5.04 (dd, 1H, J=10.5, 1.3 Hz), 3.01 (d, 1H, J=8.4 Hz), 1.18 (s, 3H), 0.90 (s, 9H), 0.05 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (50 MHz, C_6D_6) δ 138.1, 119.9, 67.0, 56.6, 28.5, 25.9, 18.3, −3.8, −4.2. HRMS *m/z* calcd for $C_{11}H_{23}OSi$ (MH^+) 199.1518; found: 199.1523.

4.1.12. 1-Phenyl-2-*tert*-butyldimethylsilyl-2,3-epoxypent-4-en-1-ol: 15. The procedure was the same as described above for the preparation of **14**, starting from **1b** (100 mg, 0.54 mmol, 1.0 equiv.) and using benzaldehyde (166 μL, 1.63 mmol, 3.0 equiv.) as the electrophile. After usual workup, the crude product was purified and two isomers **15a** and **15b** (9/1) could be separated by flash chromatography on silica gel (PE/CH_2Cl_2: 90/10), affording colorless oils with 76% global yield (119 mg, 0.41 mmol).

Compound **15a**. IR (neat) 3610, 3050, 2950, 1650, 1250, 840. ^{1}H NMR (200 MHz, C_6D_6) δ 7.38–7.08 (m, 5H), 5.86 (ddd, 1H, J=17.5, 10.3, 8.6 Hz), 5.26 (dd, 1H, J=17.5, 1.5 Hz), 5.05 (dd, 1H, J=10.3, 1.5 Hz), 4.84 (s, 1H), 3.82 (d, 1H, J=8.6 Hz), 2.73 (s, 1H), 0.89 (s, 9H), 0.03 (s, 3H), −0.14 (s, 3H). ^{13}C NMR (50 MHz, C_6D_6) δ 141.6, 137.0, 130.0, 129.6, 128.5, 121.1, 75.0, 61.5, 61.2, 28.5, 19.2, −3.0, −3.0. Anal. calcd for $C_{17}H_{26}O_2Si$: C, 70.29; H, 9.02; found: C, 70.31; H, 9.09.

Compound **15b**. IR (neat) 3610, 3040, 2950, 1640, 1250, 830. ^{1}H NMR (400 MHz, C_6D_6) δ 7.47–7.18 (m, 5H), 5.98 (ddd, 1H, J=17.1, 10.2, 8.6 Hz), 5.38 (d, 1H, J=17.1 Hz), 5.16 (d, 1H, J=10.2 Hz), 4.97 (s, 1H), 3.94 (d, 1H, J=8.6 Hz), 1.01 (s, 9H), 0.16 (s, 3H), −0.02 (s, 3H). ^{13}C NMR (100 MHz, C_6D_6) δ 140.5, 135.9, 128.9, 128.5, 128.3, 120.0, 73.9, 60.5, 60.1, 27.4, 18.1, −4.1, −4.1. Anal. calcd for $C_{17}H_{26}O_2Si$: C, 70.29; H, 9.02; found: C, 70.44; H, 9.31

4.1.13. 2-*tert*-Butyldimethylsilyl-2,3-epoxypent-4-enoic methyl ester: 16. Following the procedure for the preparation of **14**, the epoxyester **16** was synthesized starting from **1b** (100 mg, 0.54 mmol, 1.0 equiv.) and using methyl cyanoformate (86 μL, 1.08 mmol, 2.0 equiv.) as the electrophile. After usual workup and flash chromatography on silica gel (PE/CH_2Cl_2: 90/10), the epoxyester **16** was obtained with 78% yield (102 mg, 0.42 mmol) as a colorless oil. Using methyl chloroformate as the electrophile (84 μL, 1.08 mmol, 2.0 equiv.), the compound **16** was obtained as a pale colorless oil with 20% yield (26 mg, 0.11 mmol) in association with dimer **21** (colorless oil) (45 mg, 0.11 mmol, 42% yield) which could be separated by flash chromatography on silica gel (PE/CH_2Cl_2: 90/10).

IR (neat) 3010, 2950, 1730, 1650, 1460, 1240, 850. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.70 (ddd, 1H, J=17.2, 10.2, 8.2 Hz), 5.54 (d, 1H, J=17.2 Hz), 5.38 (d, 1H, J=10.2 Hz), 3.69 (s, 3H), 3.43 (d, 1H, J=8.2 Hz), 0.94 (s, 9H), 0.15 (s, 3H), 0.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 133.6, 122.5, 63.0, 57.2, 52.3, 27.4, 18.1, −4.6, −4.7.

4.1.14. Bis-(2-*tert*-butyldimethylsilyl-2,3-epoxypent-4-en)-ketone: 17. IR (neat) 3060, 2940, 1720, 1660, 1240, 820. ^{1}H NMR (200 MHz, C_6D_6) δ 5.72 (ddd, 2H, J=17.0, 10.2, 8.7 Hz), 5.21 (d, 2H, J=17.0 Hz), 5.04 (d, 2H, J=10.2 Hz), 3.62 (d, 2H, J=8.7 Hz), 1.08 (s, 18H), 0.28 (s, 6H), 0.22 (s, 6H,). ^{13}C NMR (50 MHz, C_6D_6) δ 199.8, 134.8, 121.8, 64.2, 63.8, 28.2, 18.5, −3.5, −3.9. CIMS 395 (MH^+), 379 (82%), 337 (47%), 279 (40%), 205 (30%), 149 (30%).

4.1.15. 4-*tert*-Butyldimethylsilyl-4,5-epoxypent-2,6-diene: 18. The allylation of the *cis*-silylated vinyloxirane **1b** (100 mg, 0.54 mmol, 1.0 equiv.) was carried out using the same conditions as described for the preparation of **11**, with *t*-BuLi (1.5 M in pentane, 0.54 mL, 0.81 mmol, 1.5 equiv.) in pentane (5 mL). The reaction mixture was quenched with allyl iodide (0.25 mL, 2.71 mmol, 5 equiv.). Compound **18** is a colorless oil which was isolated with 45% yield (50 mg, 0.22 mmol) after purification of the crude product by flash chromatography on silica gel (PE/CH_2Cl_2: 90/10).

IR (neat) 3080, 2955, 2927, 2856, 1638, 1464, 1158, 987, 835. ^{1}H NMR (200 MHz, C_6D_6) δ 5.73 (m, 2H), 5.25 (d, 1H, J=17.0 Hz), 4.99 (d, 1H, J=10.2 Hz), 4.95 (d, 1H, J=10.4 Hz), 4.94 (d, 1H, J=17.3 Hz), 3.23 (d, 1H, J=8.9 Hz), 2.41 (dd, 1H, J=15.2, 7.9 Hz), 2.29 (dtd, 1H, J=15.2, 5.7, 1.5 Hz), 0.90 (s, 9H), 0.01 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (50 MHz, C_6D_6) δ 135.4, 132.4, 117.5, 116.1, 61.0, 55.9, 39.6, 26.1, 16.1, −6.0, −6.1. HRMS *m/z* calcd for $C_{11}H_{23}OSi$ (MH^+) 225.1675; found: 225.1676.

4.1.16. 3-*tert*-Butyldimethylsilyl-pent-4-en-2-one: 19. To a solution of $Pd(OAc)_2$ (6 mg, 0.03 mmol, 0.05 equiv.) in THF (1 mL) was added $P(OPh)_3$ (26 μL, 0.10 mmol, 0.2 equiv.). The medium was stirred for 15 min and a solution of methyl substituted silylated vinyloxirane **14** (100 mg, 0.50 mmol, 1 equiv.) in THF (2 mL) was added via cannula. After 2 h, the medium was filtered through a celite pad and the solvent was removed in vacuo. The crude product was then purified by flash chromatography on silica gel (PE/Et_2O: 90/10) affording the α-silylated ketone **19** with 78% yield (77 mg, 0.39 mmol) as a colorless oil.

IR (neat) 2920, 1710, 1650, 1250, 860. ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.06 (dt, 1H, J=17.2, 10.5 Hz), 4.93 (dd, 1H, J=10.5, 1.5 Hz), 4.90 (dd, 1H, J=17.2, 1.5 Hz), 3.41 (d, 1H, J=10.5 Hz), 2.11 (s, 3H), 0.91 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 207.4, 134.4, 114.0, 54.0, 31.3, 26.8, 18.1, −6.1, −6.6. Anal. calcd for $C_{11}H_{22}OSi$: C, 66.60; H, 11.18; found: C, 66.81; H, 11.12.

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