Selective ring opening of silylated vinyloxiranes and reactivity of azido-alcohols

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Dedicated to Professor Lutz F Tietze on the occasion of his 65th birthday

Abstract
The chemoselective ring opening of silylated vinyloxiranes and of silylated epoxy alcohols by sodium azide has been studied. The reactivity of the α-silylated azido-alcohols thus synthesized has been investigated and the formation of highly functionalized products such as acyl azides, azidovinylsilanes, and silylated aldehydes has been rationalized.

Keywords: Azide, chemoselectivity, oxirane, nucleophilic ring opening, rearrangement, silicon

Introduction

The discovery of new functionalized substrates remains an interesting challenge for organic chemists. In this respect, silylated azido-alcohols have a high degree of functionalization, and could be precursors for amino-alcohols which make efficient bidentate ligands for catalytic transformations.[1] Our group has been developing the study of the reactivity of highly functionalized molecules such as silylated vinyloxiranes towards organometallic species,[2] lithiated bases[3] and heterogeneous nucleophiles.[4] These reactions have proved to be extremely stereo- and chemoselective, since the α,β-epoxy-γ,δ-unsaturated silanes **1a–c** have three electrophilic centers and two acidic protons. However, the reactivity of compounds **1a–c** has shown that of the two groups attached to the oxirane, the silyl group has a greater effect than the vinyl moiety. Not only do deprotonations occur preferentially in the position α- to the vinyl functionality, as we previously reported,[3,4] but also nucleophilic openings of the *trans*-oxirane occur preferentially with scission of the C–O bond α– to the silicon atom rather than to the vinyl group.[2,4] We should stress that the ring-opening of both *cis*- and *trans*-α,β-epoxy-γ,δ-unsaturated-silanes **1a–c**, and of the silylated alcohols **2, 3, 4** (epoxy-protected or not) by

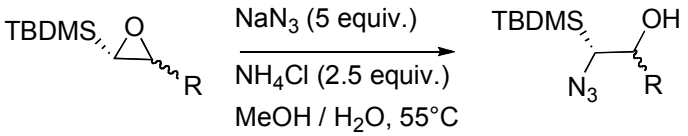
heteroatomic nucleophiles such as azide anion or phenylsulfide lead mainly to substitution in the position α- to the silicon atom. Of particular interest and novelty is the behavior of the consecutively S_N2- formed azido-alcohols towards sulfonyl chlorides.

Results and Discussion

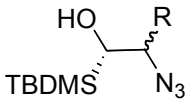
S_N2 ring opening of silylated oxiranes with hetero-nucleophiles

The regio- and stereoselective ring opening[5] of the silylated oxiranes by nitrogen- or sulfur-nucleophiles is an interesting target in the field of organic synthesis. With the purpose of obtaining α-azido-alcohols, we submitted compounds **1a–c**, **2**, **3,** and **4** to sodium azide and ammonium chloride in aqueous methanol.[6]

Table 1. Ring opening of silylated oxiranes with NaN_3



entry	R	substrate	yield(%)	product
1	(*E*)CH=CO_2Me	***trans*-1a-(*E*)**	59	**5**
2	(*Z*)CH=CO_2Me	***trans*-1a-(*Z*)**	0	
3	(*E*)CH=Ph	***trans*-1b-(*E*)**	0[a]	
4	(*Z*)CH=Ph	***trans*-1b-(*Z*)**	13	**6**
5	CH=CH_2	***trans*-1c**	51[b]	**7**
6	CH=CH_2	***cis*-1c**	44[c]	**8**
7	CH_2OH	**2**	87	**9**
8	$CH_2OTBDMS$	**3**	71[d]	**10**
9	CH_2OCH_2Ph	**4**	70	**11**



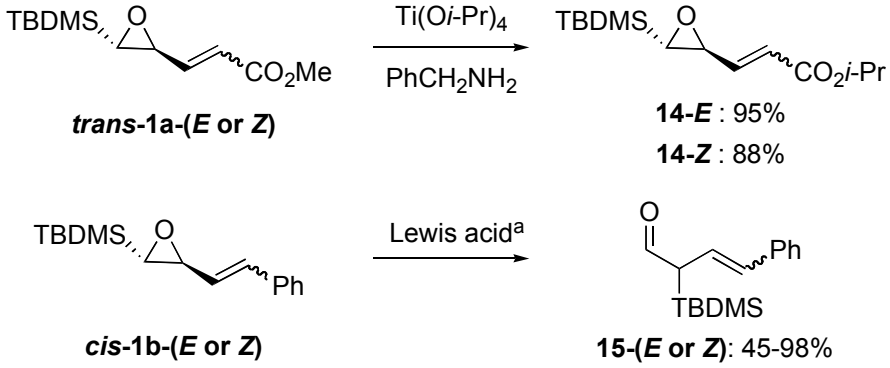
12 : R = CH=CH_2

13: R = $CH_2OTBDMS$

[a] Total degradation of the starting material. [b] Traces of compound **12** arising from the S_N2' reaction of the azide anion on the vinyl-oxirane moiety are obtained in an inseparable mixture with the main product. [c] Secondary product **12** is isolated in 18% yield. [d] Compound **10** is the major regioisomer obtained, with the other S_N2 adduct **13** in a 5.3/1 ratio.

Concerning the ring-opening of the silylated vinyl oxiranes **1a–c**, Table 1 (entries 1–6) shows that only the azido-alcohols issued from the ring opening of the oxirane α– to the silicon atom are obtained in 13 to 59% yield depending on the substituent and the configuration of the alkene

moiety. Compound **(*Z*)- *trans*-1a** was totally recovered under the reaction conditions (entry 2), whereas compound **(*E*)- *trans*-1b** degraded completely (entry 3). The best yield is achieved with the substrate **(*E*)- *trans*-1a** which is substituted by an electron-withdrawing ester group (entry 1). Compound ***cis*-1c** is transformed in an overall yield of 62%, including 44% of the S_N2 azido product and 18% of the diastereoselective S_N2' adduct with the *E*- configuration (entry 6). Degradation (entry 3) and low yield (entry 4) for phenyl derivatives ***trans*-1b** reflect the already reported high sensitivity of these compounds to acidic conditions.[7] Other experimental conditions have been tested on compound **1c** to improve this S_N2 reaction. Different solvents such as DMF, DMSO or CH_3CN gave the azido-alcohol **7** in lower yields than in aqueous methanol. Various nitrogen nucleophiles such as hydrazines (*N*-phenyl-, *N*,*N*-dimethyl-, and unsubstituted hydrazine), trimethylsilyl azide or benzylamine did not transform compound **1c**, which was recovered totally. The addition of Lewis acids was also useless.

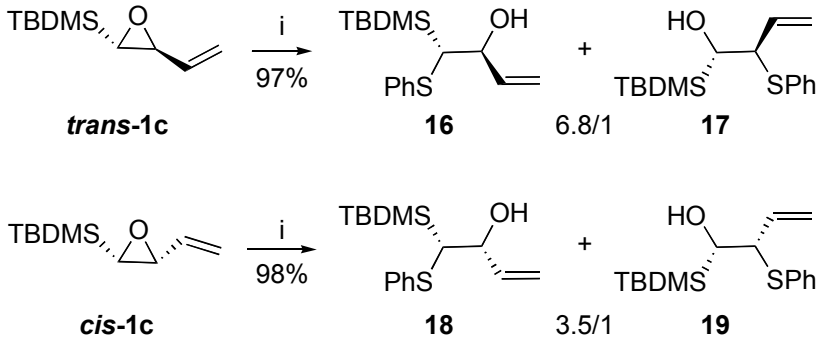


Scheme 1. (a) $BF_3{\cdot}Et_2O$, $ZnCl_2$, $Ti(OPr_i)_4$ or $MgBr_2$.

In the presence of Lewis acids ($BF_3{\cdot}Et_2O$, $ZnCl_2$ or $AlCl_3$) trimethylsilyl azide, potassium phthalimide or benzylamine led only to the degradation of compounds ***trans*-1a- (*E*- or *Z*-)**. When titanium tetra-*iso*-propoxide is used, transesterification products **14- (*E* or *Z*)** were isolated in good yields of 95% (**14-*E***) and 88% (**14-*Z***) (Scheme 1). The phenyl-substituted derivatives ***trans*-1b (*E* or *Z*)** rearranged into α-silylated-β,γ-unsaturated-aldehydes **15- (*E* or *Z*)** in yields depending on the nature of the Lewis acid (Scheme 1).[8]

Concerning the ring-opening of the silylated epoxy alcohol **2** and silylated epoxy ethers **3** and **4**, the azido-alcohols **9**, **10,** and **11** are prepared in better yields (entries 7–9, Table 1) than the vinyl analogs **1a–c**. In the case of the disilylated substrate **3** (entry 8, Table 1), the major azido-alcohol **10** is formed in 60% yield but some ring-opening occurred β- to the silicon atom, yielding also the regioisomer **13** in 11% yield. This latter result indicates that not only is the regioselectivity controlled by the silicon atom linked to the oxirane, but also it is influenced by the hydroxy group, as had been reported previously by Chakraborty.[9,10] However, this lack of regioselectivity could be circumvented, since direct silylation of azido-diol **9** afforded compound **10** in 91% yield.

The ring-opening of the diastereomers ***trans-*** and ***cis*-1c** by thiophenol in the presence of triethylamine in methanol occur efficiently within three hours. The S_N2 reaction is less chemoselective than with sodium azide since the two regioisomeric silylated thio-alcohols are obtained.[4]



(i) PhSH (5 equiv.), NEt_3 (2.5 equiv.), MeOH, 60°C, 3h.

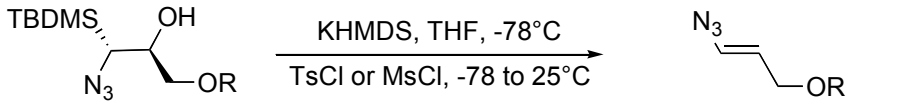
Scheme 2

In the major adduct, the silicon and the sulfur atoms are both linked to the same carbon atom. Compound ***trans*-1c** is transformed into a 6.8/1 ratio of compounds **16** and **17** in a yield of 97% whereas ***cis*-1c** gives a 3.5/1 ratio of compounds **18** and **19** in a yield of 98%. The minor thio-alcohols **17** and **19** could be separated and isolated. The selectivity apparently depends on the relative configuration of the starting oxirane (Scheme 2).

Reaction of silylated oxiranes with nitrogen- and sulfur (in the case of vinyloxiranes)-containing nucleophiles yields substituted alcohols, allylic or not, mainly arising from the opening of the oxirane in the position α- to the silicon atom. The α-azido-alcohols listed in Table 1 were perfect substrates for Staudinger reductive cyclization into aziridines.[11] However, none of these silylated azides could lead to an aziridine, and only degradation was observed. These results prompted us to investigate other aspects of the silylated azido-alcohols' reactivity, among which stands the activation of the hydroxyl group in the β-position to the silicon atom.

Reactivity of silylated α-azido-alcohols

The activation of a secondary hydroxyl group as a sulfonate ester can proceed in a basic medium by reacting the alcohol with sulfonyl chloride derivatives.

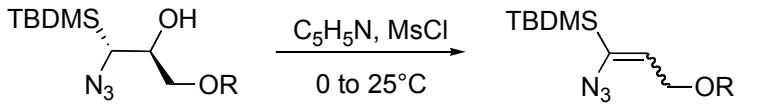


10 : R = OTBDMS
11 : R = OBn

20 (85%) : R = OTBDMS
21 (75%) : R = OBn

Scheme 3

Tosyl- and mesyl- chlorides reacted on compounds **10** and **11** with potassium hexamethylsilylamide to yield respectively the vinyl azides **20** (85%) and **21** (75%) arising from the formal elimination of *t*-butyldimethylsilanol caused by a Peterson elimination reaction (Scheme 3). Although only one diastereomer is obtained, the 13.7 Hz coupling constant of the two vinylic protons in the ^{1}H-NMR could not be attributed unambiguously to one configuration of the carbon–carbon double bond. However, NOE experiments have shown no effect between the vinylic protons and we could propose that the double bond has an *E*- configuration, indicating a *syn*-elimination mechanism which is classically observed for Peterson eliminations run in basic media.



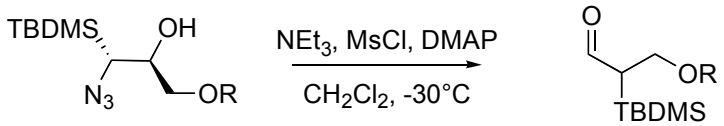
10 : R = OTBDMS
11 : R = OBn

22 (43%) : R = OTBDMS
(*E*)-23 (53%) : R = OBn

Scheme 4

The preparation of the sulfonate esters from azido-alcohols **10** and **11** was tried in pyridine as the solvent. When submitting the silylated azido-alcohols **10** and **11** to mesyl chloride in pyridine we could isolate azido-vinylsilanes **22** and **23** in moderate yields of 43 and 53%, respectively (Scheme 4). In the case of the allylic benzyl ether **23**, NOE irradiation experiments clearly showed a *syn*-relationship between the vinylic proton and the silylated substituent, which indicated that the double bond has the *E*-configuration. At this stage of our study, we could consider different possible dehydration mechanisms without being able to discriminate between E2, E1cb, or E1 pathways. However, we showed that the proton α- to the silicon atom is sufficiently acidic to be abstracted by pyridine.

The great reactivity of the sulfonate ester derivatives of the silylated azido-alcohols has lead us to consider forming them at low temperature and under the reaction conditions usually used for primary alcohols.

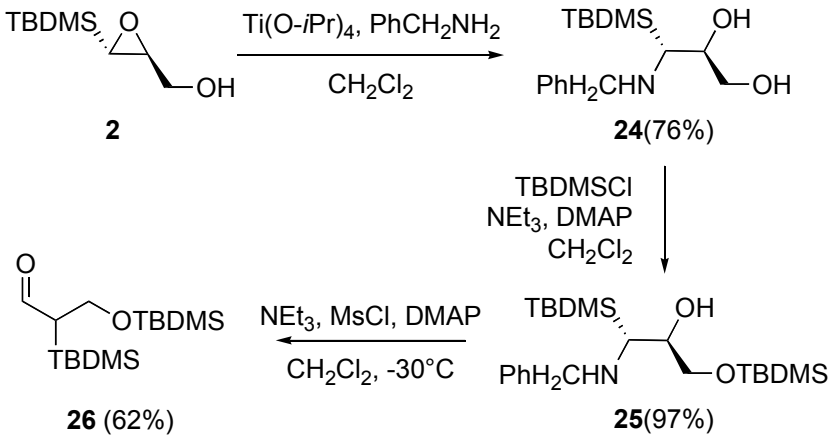


10 : R = OTBDMS
11 : R = OBn

26 (46%) : R = OTBDMS
27 (37%) : R = OBn, **11** (26%)

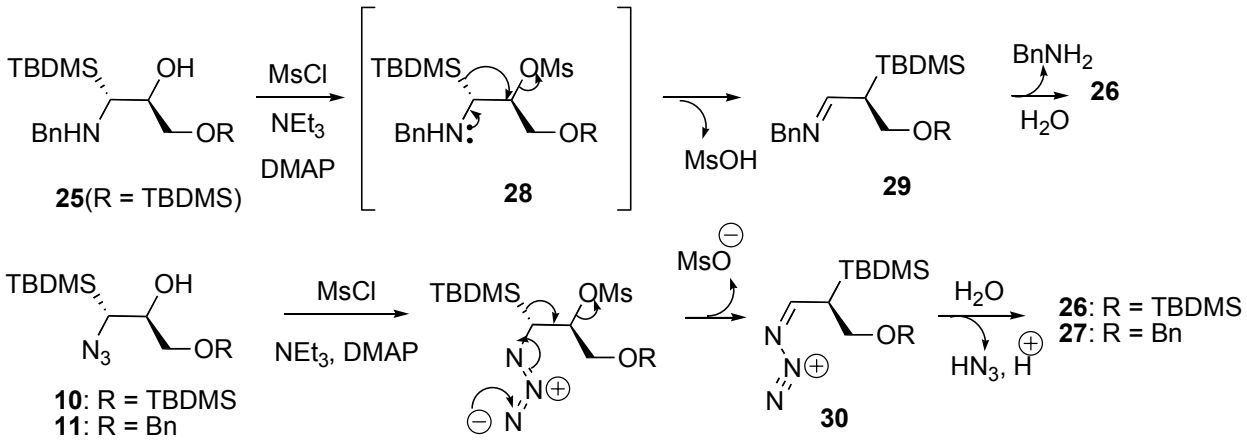
Scheme 5

Unexpectedly, the silylated azido-alcohols **10** and **11** are transformed into the α-silylated aldehydes **26** and **27**, respectively, in 46 and 37% yield (Scheme 5). The formation of the aldehydes **26** and **27** could proceed via the hydrolysis either of the corresponding imines or of the α-silylated-imide anion. The latter anionic intermediates have been reported to be formed by treatment of azido compounds in basic medium. The proton could be abstracted from a carbon atom bearing the azido substituent and an electron-withdrawing group which stabilizes the negative charge. Examples of this electron-deficient substituent being an ester group or a sulfone have been described in the literature.[12–14] In our case, the silylated group could stabilize the negative charge α to the azido function and therefore could favor the formation of the imide anion. To investigate the importance of the azido group in this reaction, we prepared selectively the α-benzylamino- α-silylated alcohols **24** and **25** from the silylated epoxy-alcohol **2**.[15] Compound **25** was submitted to triethylamine, *N*,*N*-dimethylaminopyridine and mesyl chloride (Scheme 6).



Scheme 6

The silicon-rearrangement yields the α-silylated aldehyde **26**, produced similarly from the azido-alcohol **10** (Scheme 5). We can propose a mechanism (Scheme 7) implying the activation of the amino alcohol **25** into the amino-mesylate **28** followed by the spontaneous migration of the silyl group together with elimination of the mesylate anion. The subsequent characterization of benzylamine and aldehyde **26** suggests the possible hydrolysis of the unisolated imine that could be obtained by transformation of intermediate **25**.



Scheme 7

A similar mechanism can be proposed for the azido-alcohols **10** and **11**, in which the transposition/elimination step could yield the diazo-imine intermediate **30** which could react with water and eliminate hydrazoic acid to lead to the α-silylated aldehyde (Scheme 7). To the best of our knowledge, this sila-pinacolic rearrangement of azido-alcohols has not previously been reported in the literature (Scheme 7).

Conclusions

We have investigated the nucleophilic ring-opening of silylated vinyloxiranes and of silylated epoxy alcohols with azide anion and conclude that the reaction is chemoselective and leads to the regioisomer in which the silicon atom and the azido group are α– to each other. The reactivity of the silylated azido-alcohols towards sulfonyl chlorides very much depends on the experimental conditions. We have shown that they can undergo Peterson elimination, dehydration, and silapinacolic rearrangement, leading respectively to acyl azides, azidovinylsilanes, and silylated aldehydes. The latter products are highly functionalized entities and are therefore interesting precursors for organic synthesis.

Acknowledgements

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Experimental Section

General Procedures. RT denotes room temperature; "petroleum" is the fraction having b.p. 40–60ºC.

Methyl 5-azido-5-(*tert*-butyldimethylsilyl)-4-hydroxy-pent-2-enoate (5). General procedure for ring-opening with azide ion. To a solution of the silylated vinyloxirane ***(E)*- 1a** (500 mg, 2.06 mmol, 1.0 equiv.) in MeOH/H_2O (8/1, 5 mL) were successively added, at RT, 671 mg of NaN_3 (10.31 mmol, 5.0 equiv.) and solid NH_4Cl (276 mg, 5.16 mmol, 2.5 equiv.). The mixture was warmed to 55°C and stirred for 12–36 h. It was then quenched with 10 mL of saturated aqueous $NaHCO_3$ solution and the organic phase washed with brine. The combined organic layers were dried over $MgSO_4$ and the solvents removed *in vacuo* after filtration. The crude product was purified by flash chromatography on silica gel (petroleum/Et_2O:80/20) affording the azido-alcohol **5** in 59% yield (347 mg, 1.22 mmol) as a pale yellow oil. IR (neat) (cm^{-1}) 3470, 2950, 2090, 1720, 1640, 1450, 1250, 840. ^{1}H-NMR (400 MHz, $CDCl_3$).δ 6.97 (dd, 1H, J = 15.2, 5.6 Hz, H_3), 6.11 (dd, 1H, J = 15.2, 1.5 Hz, H_2), 4.55 (bt, 1H, J = 4.1 Hz, H_4), 3.73 (s, 3H, H_9), 3.28 (d, 1H, J = 4.1 Hz, H_5), 3.91 (bs, 1H, OH), 0.93 (s, 9H, H_7), 0.07 (s, 3H, H_6), 0.03 (s, 3H, $H_{6'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 147.2, 122.5, 73.5, 57.5, 52.1, 27.0, 17.0, -5.7, -6.6. (Found: C, 50.62; H, 8.41; N, 15.10. $C_{12}H_{23}N_3O_3Si$ requires C, 50.50; H, 8.12; N, 14.72%).

1-Azido-1-(*t*-butyldimethylsilyl)-4-phenyl-but-3-en-2-ol (6). Using the general procedure indicated for the preparation of the azido-ester **5**, the azido-alcohol **6** was synthesized starting from silylated vinyloxirane **1b-*(Z)*** (521 mg, 2.0 mmol, 1 equiv.). After workup, the alcohol **6** was purified by flash chromatography on silica gel (petroleum/Et_2O: 80/20), affording a yellow oil in 13% yield (79 mg, 0.26 mmol). IR (neat) 3380, 2930, 2090, 1630, 1250, 830 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 5H, $H_{6,7,8}$), 6.64 (d, 1H, J = 11.6 Hz, H_4), 5.90 (dd, 1H, J = 11.6, 9.6 Hz, H_3), 4.71 (dd, 1H, J = 9.6, 3.6 Hz, H_2), 3.32 (d, 1H, J = 3.6 Hz, H_1), 2.47 (bs, 1H, OH), 0.84 (s, 9H, H_{10}), 0.03 (s, 3H, H_9), -0.27 (s, 3H, $H_{9'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 134.1, 130.7, 129.5, 129.3, 128.5, 70.6, 59.0, 27.5, 17.4, -6.0, -6.3. Anal. Calcd for $C_{16}H_{25}N_3OSi$: C, 63.32; H, 8.30; N, 13.85. Found: C, 63.63; H, 8.60; N, 13.76.

1-Azido-1-*tert*-butyldimethylsilyl-but-3-en-2-ol (7). Following the general procedure given for the azido-alcohol **5**, the *trans*-silylated vinyloxirane **1c** (200 mg, 1.08 mmol, 1 equiv.) gave **7** in 51% yield as a white solid (125 mg, 0.55 mmol), m.p. 61°C. IR ($CHCl_3$) 3290, 2930, 2100, 1650, 1250, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (ddd, 1H, J = 17.3, 10.2, 7.1 Hz, H_3), 5.32 (dt, 1H, J = 17.3, 1.5 Hz, H_4), 5.23 (dt, 1H, J = 10.2, 1.5 Hz, $H_{4'}$), 4.35 (dd, 1H, J = 7.1, 4.1 Hz, H_2), 3.24 (d, 1H, J = 4.1 Hz, H_1), 2.36 (bs, 1H, OH), 0.92 (s, 9H, H_6), 0.04 (s, 3H, H_5), 0.00 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 118.0, 75.5, 57.6, 27.0, 17.0, -5.9, -6.8 ($C_{5'}$). Anal. Calcd for $C_{10}H_{21}N_3OSi$: C, 52.82; H, 9.31; N, 18.48. Found: C, 52.63; H, 9.15; N, 18.76%. Traces of compound **12** were also detected.

1-Azido-1-*tert*-butyldimethylsilyl-but-3-en-2-ol (8). Following the general procedure given for the azido-alcohol **5**, compound **8** was synthesized starting from the *cis*-silylated vinyloxirane **1c**

(200 mg, 1.08 mmol, 1 equiv.). After the usual workup and flash chromatography on silica gel (petroleum/Et_2O: 80/20), the azido-alcohol **8** was obtained in 44% yield as a colorless oil (109 mg, 0.48 mmol). IR (neat) 3280, 2950, 2100, 1660, 1250, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.03 (ddd, 1H, *J* = 17.3, 10.2, 5.6 Hz, H_3), 5.35 (dt, 1H, *J* = 17.3, 1.0 Hz, H_4), 5.24 (dt, 1H, *J* = 10.2, 1.0 Hz, $H_{4'}$), 4.35 (bs, 1H, H_2), 2.88 (d, 1H, *J* = 3.0 Hz, H_1), 2.12 (bs, 1H, OH), 0.94 (s, 9H, H_6), 0.15 (s, 3H, H_5), 0.10 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 116.3, 74.7, 57.2, 27.0, 17.0, -5.8, -6.2. Anal. Calcd for $C_{10}H_{21}N_3OSi$: C, 52.82; H, 9.31; N, 18.48; Found: C, 52.78; H, 9.42; N, 18.49%. Compound **12** was also isolated in 18% yield (44 mg, 0.19 mmol) as a colorless oil.

***(trans)*-1-*tert*-Butyldimethylsilyl-4-azido-but-2-en-1-ol (12).** IR (neat) 3300, 2940, 2090, 1670, 1240, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.99 (dd, 1H, *J* = 15.3, 5.1 Hz, H_2), 5.61 (dtd, 1H, *J* = 15.2, 5.6, 2.0 Hz, H_3), 4.21 (bd, 1H, *J* = 4.1 Hz, H_1), 3.76 (t, 2H, *J* = 5.6 Hz, H_4), 0.95 (s, 9H, H_6), 0.01 (s, 3H, H_5), -0.03 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 118.6, 66.6, 53.0, 27.2, 17.3, -7.2, -8.9.

(trans)*-Isopropyl 5-*tert*-butyldimethylsilyl-4,5-epoxypent-2-enoate (*(Z)*-14).** To a cooled (0°C) solution of the silylated vinyloxirane ***(Z)*-1a** (363 mg, 1.5 mmol, 1 equiv.) and benzylamine (0.49 mL, 4.5 mmol, 3 equiv.) in CH_2Cl_2 (3 mL) was added titanium tetra-*iso*propoxide (0.90 mL, 3 mmol, 2 equiv.). The reaction mixture was stirred for 1 h at RT then heated at reflux for 12 h. It was then quenched at RT with a satd aq. Na_2SO_4 (10 mL) and filtered through a Celite pad. The mixture was diluted with AcOEt (30 mL), washed with brine, and dried over Na_2SO_4. The solvents were removed *in vacuo* and the crude product purified by flash chromatography (petroleum/Et_2O:90/10), yielding **14-*(Z) as a colorless oil (357 mg, 1.32 mmol, 88%). IR (neat) 2930, 1720, 1650, 1420, 1250, 850cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 (d, 1H, *J* = 11.7 Hz, H_2), 5.68 (dd, 1H, *J* = 11.7, 8.2 Hz, H_3), 5.04 (h, 1H, *J* = 6.6 Hz, H_9), 4.40 (dd, 1H, *J* = 8.1, 3.6 Hz, H_4), 2.20 (d, 1H, *J* = 3.6 Hz, H_5), 1.24 (d, 6H, *J* = 6.6 Hz, H_{10}), 0.93 (s, 9H, H_7), 0.01 (s, 3H, H_6), -0.02 (s, 3H, $H_{6'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 148.8, 123.7, 68.0, 51.3, 50.8, 26.8, 22.2, 17.0, -8.0. Anal. Calcd for $C_{14}H_{26}O_3Si$: C, 62.18; H, 9.69; Found. C, 62.21; H, 9.71%.

(trans)*-Isopropyl 5-*tert*-butyldimethylsilyl-4,5-epoxypent-2-enoate (*(E)*-14).** Following the procedure for the preparation of **14-*(Z), starting from the silylated vinyloxirane **1a-*(E)*** (363 mg, 1.5 mmol, 1 equiv.), the title compound **14-*(E)*** was obtained in 95% yield (385 mg, 1.43 mmol) as a colorless oil. IR (neat) 2960, 1730, 1670, 1430, 1250, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.54 (dd, 1H, *J* = 15.2, 7.6 Hz, H_3), 6.10 (d, 1H, *J* = 15.3 Hz, H_2), 5.02 (h, 1H, *J* = 6.1 Hz, H_9), 3.21 (dd, 1H, *J* = 7.6, 3.1 Hz, H_4), 2.25 (d, 1H, *J* = 3.6 Hz, H_5), 1.22 (d, 6H, *J* = 6.1 Hz, H_{10}), 0.91 (s, 9H, H_7), -0.01 (s, 3H, H_6), -0.08 (s, 3H, $H_{6'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 147.0, 124.1, 68.2, 53.8, 52.5, 26.7, 22.1, 17.0, -7.8, -8.2. Anal. Calcd for $C_{14}H_{26}O_3Si$: C, 62.18; H, 9.69. Found: C, 62.19; H, 9.78.

1-*tert*-Butyldimethylsilyl-1-phenylsulfanyl-but-3-en-2-ol (16). General procedure for ring-opening with thiophenol

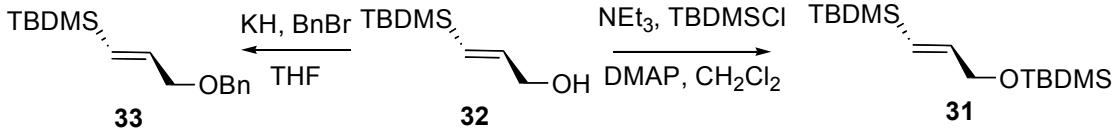
To a solution of the silylated vinyloxirane **1c** (100 mg, 0.54 mmol, 1 equiv.) in MeOH (5 mL) were successively added, at RT, NEt_3 (0.15 mL, 1.08 mmol, 2 equiv.) and PhSH (0.28 mL, 2.71 mmol, 5 equiv.). The reaction mixture was stirred for 1h and then warmed at 60°C for 3 hours. After cooling down to RT, the medium was diluted with 25 mL of CH_2Cl_2, and the organic phase treated with sat. aq. NH_4Cl solution. The aqueous layer was extracted with CH_2Cl_2, washed with brine and dried over Na_2SO_4. After filtration and removal of the solvents *in vacuo*, the residue was purified and the two isomers **16** and **17** could be separated by flash chromatography on silica gel (petroleum/CH_2Cl_2:80/20), affording colorless oils in a total yield of 97% (major, **16**, 135 mg, 0.46 mmol; minor, **17**, 20 mg, 0.07 mmol). IR (neat) 3440, 3040, 2900, 1670, 1240, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.50–7.18 (m, 5H, $H_{9,10,11}$), 6.01 (ddd, 1H, *J* = 17.3, 10.7, 6.1 Hz, H_3), 5.30 (dd, 1H, *J* = 17.3, 1.5 Hz, H_4), 5.22 (dd, 1H, *J* = 10.7, 1.5 Hz, $H_{4'}$), 4.52 (m, 1H, H_2), 3.04 (d, 1H, *J* = 3.0 Hz, H_1), 2.46 (s, 1H, OH), 0.99 (s, 9H, H_6), 0.18 (s, 3H, H_5), 0.18 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 137.9, 129.2, 126.2, 116.3, 74.4, 39.9, 27.4, 17.6, -4.5, -5.6. Exact mass: *m/z* calcd for $C_{16}H_{27}OSSi$ (MH^+) 295.1552, found 295.1548

1-*tert*-Butyldimethylsilyl-2-phenylsulfanyl-but-3-en-1-ol (17). IR (neat) 3450, 3060, 2910, 1660, 1250, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H, $H_{9,10,11}$), 5.98 (dt, 1H, *J* = 17.3, 9.7 Hz, H_3), 5.13 (d, 1H, *J* = 16.2, H_4), 5.13 (d, 1H, *J* = 11.7, $H_{4'}$), 3.97 (dd, 1H, *J* = 9.7, 2.5 Hz, H_2), 3.56 (d, 1H, *J* = 2.5 Hz, H_1), 2.17 (bs, 1H, OH), 0.85 (s, 9H, H_6), 0.06 (s, 3H, H_5), 0.04 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ134.8, 133.9, 133.8, 129.3, 128.1, 118.7, 62.7, 59.4, 27.0, 17.2, -6.7, -7.3.

1-*tert*-Butyldimethylsilyl-1-phenylsulfanyl-but-3-en-2-ol (18). Following the same procedure as for the preparation of **16**, the allylic alcohol **18** was synthesized from the silylated vinyloxirane **1c** (100 mg, 0.54 mmol, 1 equiv.), affording a mixture of two isomers **18** and **19** (ratio 3.5/1, total 98%) which was purified and separated (major **18**, 121 mg, 0.41 mmol; minor, **19**, 35 mg, 0.12 mmol) by flash chromatography on silica gel (petroleum/CH_2Cl_2:80/20). IR (neat) 3420, 3060, 2920, 1650, 1240, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.18 (m, 5H, $H_{9,10,11}$), 5.79 (ddd, 1H, *J* = 17.3, 10.7, 5.6 Hz, H_3), 5.22 (d, 1H, *J* = 17.3 Hz, H_4), 4.94 (d, 1H, *J* = 10.2 Hz, $H_{4'}$), 4.46 (m, 1H, H_2), 2.93 (d, 1H, *J* = 2.6 Hz, H_1), 2.41 (d, 1H, *J* = 8.1 Hz, OH), 1.04 (s, 9H, H_6), 0.22 (s, 3H, H_5), 0.22 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 138.2, 129.3, 128.9, 126.1, 114.8, 73.3, 39.0, 27.5, 17.7, -5.3, -5.7. Exact mass: calcd for $C_{16}H_{27}OSSi$ (MH^+) 295.1552, found 295.1557

1-*tert*-Butyldimethylsilyl-2-phenylsulfanyl-but-3-en-1-ol (19). IR (neat) 3480, 3070, 2960, 1620, 1250, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.26 (m, 5H, $H_{9,10,11}$), 5.68 (dt, 1H, *J* = 17.3, 9.6 Hz, H_3), 5.01 (dd, 1H, *J* = 9.7, 1.5 Hz, H_4), 4.95 (d, 1H, *J* = 16.3, $H_{4'}$), 3.71 (dd, 1H, *J* = 9.6, 9.2 Hz, H_2), 3.37 (dd, 1H, *J* = 9.2, 2.6 Hz, H_1), 2.56 (d, 1H, *J* = 2.5 Hz, OH), 0.96 (s, 9H, H_6), 0.06 (s, 3H, H_5), 0.06 (s, 3H, $H_{5'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.3, 132.9–124.5, 115.3, 63.4, 60.8, 26.0, 16.3, -6.0, -8.9.

***(E)*-3-*tert*-Butyldimethylsilyl-1-*tert*-butyldimethylsilanyloxy-prop-2-ene (31) (Scheme 8)**
To a cooled (0°C) solution of silylated allylic alcohol **32**[16] (1.72 g, 10.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) were successively added NEt_3 (2.78 mL, 20.0 mmol, 2.0 equiv.), DMAP (122 mg, 1.0 mmol, 0.1 equiv.) and, after 5 minutes stirring at 0°C, TBSCl (1.66 g, 11.0 mmol, 1.1 equiv.). The reaction mixture was allowed to warm up to RT and after stirring for 30 minutes was diluted with 40 mL of CH_2Cl_2. The medium was quenched with saturated aq. NH_4Cl solution, washed with brine, and the combined organic layers dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude product was purified by flash chromatography on silica gel (petroleum/Et_2O:95/5) affording the disilylated compound **31** as a white solid, in 93% yield (2.66 g, 9.28 mmol), m.p. = 55°C; IR (CH_2Cl_2) 2950, 1670, 1250, 840 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) δ 6.14 (dt, 1H, J = 18.8, 3.6 Hz, H_2), 5.94 (d, 1H, J = 18.8, H_3), 4.24 (d, 2H, J = 3.6, H_1), 0.95 (s, 9H, H_5), 0.90 (s, 9H, H_8), 0.10 (s, 6H, H_7), 0.05 (s, 6H, H_4). ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.9, 125.6, 66.3, 26.8, 26.3, 18.8, 16.9, -4.8, -5.8. Anal. Calcd for $C_{15}H_{34}OSi_2$: C, 62.86; H, 11.96. Found: C, 62.74; H, 12.08.



Scheme 8

***(trans)*-3-*tert*-Butyldimethylsilyl-2,3-epoxy-1-*tert*-butyldimethylsilanyloxypropane (3)**To a cooled (0°C) solution of the vinylsilane **31** (1.00 g, 3.49 mmol, 1 equiv.) in CH_2Cl_2 (40 mL) was slowly added 7.40 g of *m*-CPBA (70% with water and 3-chlorobenzoic acid, 30.03 mmol, 1.5 equiv.). The reaction mixture was allowed to warm up to RT and after stirring for 2 h, 20 mL of brine was added. 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 using 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 (petroleum/AcOEt:80/20), affording the silylated oxirane **3** as a white solid in 96% yield (1.01 g, 3.35 mmol).

Starting from the silylated epoxy-alcohol **2** (471 mg, 2.5 mmol, 1 equiv.), the silylation of the hydroxyl group was achieved following the procedure described for the preparation of the disilylated compound **31**. Compound **3** was obtained in 91% yield (688 mg, 2.28 mmol). m.p. 95°C; IR (CH_2Cl_2) 2960, 1250, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 3.84 (dd, 1H, J = 11.6, 3.5 Hz, H_1), 3.66 (dd, 1H, J = 11.6, 5.2 Hz, $H_{1'}$), 2.96 (ddd, 1H, J = 5.6, 3.6, 3.5 Hz, H_2), 2.17 (d, 1H, J = 3.6 Hz, H_3), 0.97 (s, 9H, H_5), 0.92 (s, 9H, H_8), 0.10 (s, 3H, H_7), 0.09 (s, 3H, $H_{7'}$), 0.04 (s, 3H, H_4), -0.04 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 65.9, 55.8, 46.7, 26.6, 25.9, 18.4, 16.7, -5.2, -5.3, -8.1, -8.5. Anal. Calcd for $C_{15}H_{34}O_2Si_2$: C, 59.54; H, 11.33. Found: C, 59.34; H, 11.52%.

***(E)*-3-*tert*-Butyldimethylsilyl-1-benzyloxy-prop-2-ene (33) (Scheme 8).** To a cooled (0°C) suspension of KH (30% in mineral oil, 1.60 g, 12.0 mmol, 1.2 equiv.) in dry THF (60 mL), was added dropwise a solution of the allylic alcohol **32** (1.72 g, 10.0 mmol, 1.0 equiv.) in THF (20 mL). After 15 minutes at 0°C, the medium was allowed to warm up to RT for an additional 1 hour, and benzyl bromide (1.67 mL, 14.0 mmol, 1.4 equiv.) was slowly added to the mixture. After stirring for 12 hours, the mixture was quenched with 30 mL of a sat. aq. NH_4Cl solution. The organic phase was washed with brine and the combined organic layers dried over $MgSO_4$. After filtration and evaporation of the solvent, the crude product was purified by flash chromatography on silica gel (petroleum/Et_2O:95/5), affording the benzylic ether **33** as a colorless oil (2.38 g, 9.10 mmol.) in 91% yield. IR (neat) 3050, 2920, 1670, 1240, 820 cm^{-1} ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.32 (m, 5H, H_{Ar}), 6.19 (dt, 1H, J = 18.8, 5.1 Hz, H_2) 5.99 (d, 1H, J = 18.8 Hz, H_3), 4.57 (s, 2H, H_7), 4.12 (d, 2H, J = 5.1 Hz, H_1), 0.93 (s, 9H, H_5), 0.08 (s, 6H, H_4). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 138.6, 129.7, 128.7–128.1, 127.9, 73.5, 72.5, 26.7, 16.8, -5.9. Anal. Calcd for $C_{16}H_{26}OSi$; C, 73.22; H, 9.98. Found: C, 73.06; H, 10.07%.

***trans*-3-*tert*-Butyldimethylsilyl-2,3-epoxy-1-benzyloxypropane (4).** To a cooled (0°C) solution of the silylated allylic benzyl ether **33** (1.31 g, 5.0 mmol, 1 equiv.) in CH_2Cl_2 (40 mL) was slowly added 7.40 g of *m*-CPBA (70% in water; 3-chlorobenzoic acid, 30.03 mmol, 1.5 equiv.). The reaction mixture was allowed to warm up to RT, 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, using 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 (petroleum/AcOEt:80/20), affording compound **4** in 96% yield as a colorless oil (1.34 g, 4.8 mmol). IR (neat) 3010, 2950, 1250, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.32 (m, 5H, H_{Ar}), 4.67 (d, 1H, J = 11.7 Hz, H_7), 4.59 (d, 1H, J = 12.2 Hz, $H_{7'}$), 3.87 (dd, 1H, J = 11.2, 2.6 Hz, H_1), 3.41 (dd, 1H, J = 11.2, 6.1 Hz, $H_{1'}$), 3.09 (ddd, 1H, J = 6.1, 3.1, 2.0 Hz, H_2), 2.18 (d, 1H, J = 2.0 Hz, H_3), 1.00 (s, 9H, H_5), 0.05 (s, 3H, H_4), -0.01 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 128.7–128.0, 128.5, 73.4, 72.8, 54.5, 46.3, 26.8, 16.9, -8.0, -8.2. Anal. Calcd for $C_{16}H_{26}O_2Si$: C, 69.01; H, 9.41.; Found: C, 68.93; H, 9.42%.

3-Azido-3-*tert*-butyldimethylsilyl-propan-1.2-diol (9). Using the general procedure as for the preparation of azidoester **5**, the azido-diol **9** was synthesized starting from the epoxy-alcohol **2** (188 mg, 1.00 mmol, 1 equiv.) in 87% yield as a colorless oil (201 mg, 0.87 mmol). IR (neat) 3380, 2950, 2100, 1250, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 3.92 (m, 1H, H_2), 3.69 (m, 1H, H_1), 3.27 (d, 1H, J = 5.1 Hz, H_3), 0.96 (s, 9H, H_5), 0.10 (s, 3H, H_4), 0.07 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.5, 64.3, 55.5, 26.8, 16.8, -6.2, -6.7.

3-Azido-3-*tert*-butyldimethylsilyl-1-*tert*-butyldimethylsinalyloxy-propan-2-ol (10).
Following the general procedure given for the preparation of the azido-ester **5**, the title compound was synthesized starting from the silylated oxirane **3** (605 mg, 2.00 mmol, 1 equiv.), in 71% global yield (491 mg, 1.42 mmol) as a mixture of two isomers **10** (413 mg, 1.19 mmol) and **13** (78 mg, 0.22 mmol) which could be separated by flash chromatography on silica gel

(petroleum/CH_2Cl_2:80/20). Starting from the azido-diol **9** (347 mg, 1.50 mmol, 1 equiv.), the selective silylation of the primary hydroxyl group was released following the procedure for the preparation of the disilylated compound **31**. The azido-alcohol **10** was obtained in 91% yield as a colorless oil (472 mg, 1.36 mmol). IR (neat) 3350, 2950, 2090, 1230, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 3.85 (m, 1H, H_2), 3.70 (d, 2H, J = 5.4 Hz, H_1), 3.21 (d, 1H, J = 6.2 Hz, H_3), 2.76 (d, 1H, J = 3.6 Hz, OH), 0.97 (s, 9H, H_5), 0.93 (s, 9H, H_8), 0.12 (s, 3H, H_7), 0.11 (s, 3H, $H_{7'}$), 0.10 (s, 3H, H_4), 0.08 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.1, 64.5, 53.8, 26.9, 26.0, 18.4, 17.0, -5.3, -5.9, -6.6. Anal. Calcd for $C_{15}H_{35}N_3O_2Si_2$: C, 52.13; H, 10.21; N, 12.16. Found: C, 51.95; H, 10.25; N, 11.89%.

2-Azido-3-*tert*-butyldimethylsilyl-1-*tert*-butyldimethylsinalyloxy-propan-3-ol (13). IR (neat) 3380, 2940, 2110, 1250, 850 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 4.02 (ddd, 1H, J = 8.0, 3.6, 2.8 Hz, H_2), 3.75 (dd, 1H, J = 11.2, 8.0 Hz, H_1), 3.53 (bd, 1H, J = 10.6 Hz, $H_{1'}$), 3.31 (d, 1H, J = 2.8 Hz, H_3), 1.97 (bs, 1H, OH), 0.96 (s, 18H, $H_{5,8}$), 0.16 (s, 3H, H_7), 0.15 (s, 3H, $H_{7'}$), 0.07 (s, 3H, H_4), 0.04 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.5, 64.1, 57.1, 26.7, 25.9, 18.1, 16.7, -4.1, -4.6, -6.5, -7.1. Anal. Calcd for $C_{15}H_{35}N_3O_2Si_2$: C, 52.13; H, 10.21; N, 12.16. Found: C, 52.29; H, 10.37; N, 11.88%.

3-Azido-3-*tert*-butyldimethylsilyl-1-benzyloxy-propan-2-ol (11). The procedure was exactly the same as described for the synthesis of **5**, starting from the silylated oxirane **4** (278 mg, 1.0 mmol, 1 equiv.). The azido-alcohol **11** was obtained in 70% yield as a colorless oil (225 mg, 0.7 mmol). IR (neat) 3450, 3010, 2930, 2090, 1250, 840 cm^{-1} ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.31 (m, 5H, H_{Ar}), 4.60 (d, 1H, J = 11.7 Hz, H_7), 4.55 (d, 1H, J = 11.7 Hz, $H_{7'}$), 4.01 (ddd, 1H, J = 7.1, 5.6, 3.6 Hz, H_2), 3.60 (dd, 1H, J = 9.6, 7.1 Hz, H_1), 3.56 (dd, 1H, J = 9.6, 3.6 Hz, $H_{1'}$), 3.26 (d, 1H, J = 5.6 Hz, H_3), 0.94 (s, 9H, H_5), 0.05 (s, 3H, H_4), 0.01 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 128.9, 128.3, 128.2, 73.8, 72.4, 72.0, 54.8, 27.1, 17.2, -5.8, -6.5. Anal. Calcd for $C_{16}H_{27}N_3O_2Si$: C, 59.78; H, 8.47; N, 13.07. Found: C, 60.13; H, 8.73; N, 12.95%

***(E)* 1-Azido-3-*tert*-butyldimethylsilanyloxy-prop-1-ene (20)**

To a cooled (–78°C) solution of the azido-alcohol **10** (346 mg, 1.0 mmol, 1.00 equiv.) in THF (10 mL) was slowly added KHMDS (0.5*M* in toluene, 2.1 mL, 1.05 mmol, 1.05 equiv.). The medium was stirred for 10 minutes and mesyl chloride (85 μL, 1.10 mmol, 1.10 equiv.) was added rapidly. The reaction mixture was warmed up to RT and then quenched in water (5 mL). The organic layer was washed with brine and dried over Na_2SO_4. After filtration and removal of the solvents *in vacuo*, a crude product was obtained which was purified by flash chromatography on silica gel (petroleum/Et_2O:98/2), affording the vinyl azide **20** as a pale yellow oil (181 mg, 0.85 mmol) in 85% yield. IR (neat) 2930, 2100, 1660, 1250, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.11 (d, 1H, J = 13.8 Hz, H_1), 5.49 (dt, 1H, J = 13.7, 5.6 Hz, H_2), 4.20 (dd, 2H, J = 5.6, 1.5 Hz, H_3), 0.92 (s, 9H, H_5), 0.09 (s, 6H, H_4). ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.1, 119.3, 61.4, 26.2, 18.7, -5.0

Anal. Calcd for $C_9H_{19}N_3OSi$: C, 50.67; H, 8.98; N, 19.70. Found: C, 50.41; H, 8.76; N, 19.95%.

***(E)* 1-Azido-3-benzyloxy-prop-1-ene (21).** The procedure was as described previously, starting from the azido-alcohol **4** (161 mg, 0.50 mmol, 1 equiv.). The vinyl azide **21** was obtained as a yellow oil in 75% yield (71 mg, 0.37 mmol). IR (neat) 3030, 2850, 2100, 1650 cm^{-1}. ^1H NMR (400 MHz, C_6D_6) δ 7.34 (d, 2H, *J* = 8.3 Hz, H_6), 7.29 (t, 2H, 8.4 Hz, H_7), 7.21 (t, 1H, *J* = 7.8 Hz, H_8), 5.71 (d, 1H, *J* = 13.7 Hz, H_1), 5.37 (dt, 1H, *J* = 13.7, 6.3 Hz, H_2), 4.33 (s, 2H, H_4), 3.71 (d, 2H, *J* = 6.3 Hz, H_3). ^{13}C NMR (100 MHz, C_6D_6) δ 138.6 (C_5), 129.6 (C_1), 128.4 (C_7), 127.6 ($C_{6,8}$), 116.2, 71.8, 67.4.

1-Azido-1-*tert*-butyldimethylsilyl-3-*tert*-butyldimethylsilyloxy-prop-1-ene (22)

To a cooled (0°C) solution of the azido-alcohol **10** (173 mg, 0.50 mmol, 1.00 equiv.) in pyridine (2 mL) was added mesyl chloride (48 μL, 0.63 mmol, 1.25 equiv.). After 1 hour at 0°C, the medium was warmed up to 25°C and stirred overnight. The reaction mixture was then diluted in CH_2Cl_2 (20 mL) and 10 mL of a saturated aqueous NH_4Cl solution was added under vigorous stirring. The organic phase was washed with brine and dried over Na_2SO_4. After filtration and removal of the solvent, the crude product was purified by flash chromatography on silica gel (petroleum/Et_2O:95/5), affording compound **22** as a colorless oil in 43% yield (71 mg, 0.21 mmol). IR (neat) 2980, 2100, 1660, 1250, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.23 (s, 1H, H_2), 4.27 (d, 2H, *J* = 1.0 Hz, H_3), 0.89 (s, 18H, $H_{5,8}$), 0.08 (s, 6H, H_4), 0.05 (s, 6H, H_7). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.1, 128.0, 59.2, 26.0, 25.0, 17.4, 16.2, -6.1, -6.4. Anal. Calcd for $C_{15}H_{33}N_3OSi_2$: C, 54.99; H, 10.15; N, 12.83. Found: C, 55.02; H, 9.92; N, 12.85%.

***(E)* 1-Azido-1-*tert*-butyldimethylsilyl-3-benzyloxy-prop-1-ene (2).** Following the procedure described for the preparation of the compound **22**, the silylated vinyl azide **23** was synthesized as a colorless oil (64 mg, 0.21 mmol; 53% yield), starting from the azido-alcohol **11** (128 mg, 0.40 mmol, 1 equiv.). IR (neat) 3080, 2950, 2100, 1590, 1250, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (m, 5H, $H_{9,10,11}$), 6.29 (s, 1H, H_2), 4.36 (s, 2H, H_7), 4.03 (s, 2H, H_3), 0.80 (s, 9H, H_5), 0.00 (s, 6H, H_4). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 135.9, 128.6, 128.3, 127.9, 126.1, 73.1, 67.2, 27.3, 17.7, -5.1. Anal. Calcd for $C_{16}H_{25}N_3OSi$: C, 63.32; H, 8.30; N, 13.85. Found: C, 63.38; H, 8.08; N, 14.01%.

2-*tert*-Butyldimethylsilyl-3-*tert*-butyldimethylsilanyloxypropanal (26)

To a cooled (-30°C) solution of the azido-alcohol **10** (1.38 g, 4.0 mmol, 1.0 equiv.) in CH_2Cl_2 (16 mL) were successively added NEt_3 (0.67 mL, 4.8 mmol, 1.2 equiv.), DMAP (49 mg, 0.4 mmol, 0.1 equiv.) and, after 10 minutes, MsCl (0.34 mL, 4.4 mmol, 1.1 equiv.). After 1 hour, the reaction mixture was quenched in 10 mL of water and was warmed slowly to RT. The organic phase was 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 (petroleum/Et_2O:90/10), affording the aldehyde **26** as a colorless oil (557 mg, 1.84 mmol, 46% yield). IR (neat) 2940, 1710, 1250, 840 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, 1H, *J* = 4.1 Hz, H_1), 4.21 (t, 1H, *J* = 10.2 Hz, H_3), 3.81 (dd, 1H, *J* = 10.7, 3.6 Hz, $H_{3'}$), 2.67 (dt, 1H, 10.2, 3.6 Hz, H_2), 0.90 (s, 9H, H_5), 0.84 (s, 9H, H_8), 0.05 (s, 3H, H_4), 0.03 (s, 3H, $H_{4'}$), 0.02 (bs, 6H, $H_{7,7'}$). ^{13}C NMR (100 MHz, C_6D_6) δ 200.8, 60.0, 50.9, 26.6, 25.9, 18.3, 17.4, -5.4, -6.3, -6.5. Anal. Calcd for $C_{15}H_{34}O_2Si_2$: C, 59.54; H, 11.33. Found: C, 59.61; H, 11.56%.

2-*tert*-Butyldimethylsilyl-3-benzyloxypropanal (27). Following the same procedure as described for the preparation of the aldehyde **26**, the α-silylated aldehyde **27** was synthesized starting from the azido-alcohol **11** (524 mg, 1.63 mmol, 1 equiv.) in 37% yield (168 mg, 0.6 mmol). Some starting material was recovered (136 mg, 0.42 mmol, 26%). IR (neat) 3010, 2930, 1700, 1250, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 9.75 (d, 1H, J = 3.7 Hz, H_1), 7.37–7.29 (m, 5H, $H_{9,10,11}$), 4.52 (s, 2H, H_7), 4.14 (t, 1H, J = 10.2 Hz, H_3), 3.67 (dd, 1H, J = 9.8, 3.2 Hz, $H_{3'}$), 2.89 (dt, 1H, 10.6, 3.5 Hz, H_2), 0.95 (s, 9H, H_5), 0.09 (s, 3H, H_4), 0.07 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.3 (C_1), 138.2 (C_8), 128.5 (C_{10}), 127.7 ($C_{9,11}$), 73.0 (C_7), 66.6 ($C_{3,3'}$), 48.7 (C_2), 26.8 (C_5), 17.7 (C_6), -6.1 (C_4), -6.2 ($C_{4'}$). Anal. Calcd for $C_{16}H_{26}O_2Si$: C, 69.01; H, 9.41. Found: C, 69.31; H, 9.62%.

3-Benzylamino-3-*tert*-butyldimethylsilyl-propan-1,2-diol (24). To a cooled (0°C) solution of the epoxy alcohol **2** (500 mg, 2.65 mmol, 1.0 equiv.) and benzylamine (0.35 mL, 3.19 mmol, 1.2 equiv.) in CH_2Cl_2 (12 mL), was slowly added titanium tetra-*iso*-propoxide (1.60 mL, 5.31 mmol, 2.0 equiv.). The solution was stirred for 1 hour and was warmed up to 25–30°C. The medium was stirred overnight at this temperature and, after cooling down to 0°C, was carefully quenched with a 10% aqueous NaOH solution (10 mL). After 30 minutes, the mixture was progressively warmed to RT and the titanium salts were filtered off by using a pad of Celite. The salts were washed three times with CH_2Cl_2 and filtered off. The combined organic layers were washed successively with a saturated aq. NH_4Cl solution, then brine, and dried over Na_2SO_4. After removal of the solvents and evaporation *in vacuo*, the crude product was purified by flash chromatography on silica gel (petroleum/AcOEt:80/20), affording the amino-diol **24** as a colorless oil (595 mg, 2.00 mmol, 76% yield). IR (neat) 3460, 3010, 2970, 1240, 850 cm^{-1} ^1H NMR (400 MHz, $CDCl_3$) δ 7.27–7.22 (m, 5H, $H_{9,10,11}$), 4.13 (d, 1H, J = 12.2 Hz, H_7), 3.90 (dd, 1H, J = 11.2, 3.6 Hz, H_1), 3.80 (bq, 1H, J = 3.6 Hz, H_2), 3.79 (dd, 1H, J = 11.2, 3.6 Hz, $H_{1'}$), 3.74 (d, 1H, J = 12.2 Hz, $H_{7'}$), 2.67 (dd, 1H, J = 3.6, 1.6 Hz, H_3), 0.90 (s, 9H, H_5), 0.04 (s, 3H, H_4), 0.01 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 128.8, 128.7, 127.6, 73.0, 66.9, 57.5, 52.3, 27.1, 17.3, -5.9, -7.1.

1-Benzylamino-1-*tert*-butyldimethylsilyl-3-*tert*-butyldimethylsilanyloxy-propan-2-ol (25). The silylation of the primary hydroxyl group of the amino-diol **24** (148 mg, 0.50 mmol, 1 equiv.) was carried out using the procedure described for the preparation of **31**. The amino alcohol **25** was obtained as a colorless oil (198 mg, 0.48 mmol, 97%). IR (neat) 3420, 2900, 1240, 820 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.27 (m, 5H, $H_{12,13,14}$), 4.03 (d, 1H, J = 12.7 Hz, H_{10}), 3.98 (m, 1H, H_2), 3.77 (d, 1H, J = 12.7 Hz, $H_{10'}$), 3.76 (dd, 1H, J = 10.2, 8.1 Hz, H_3), 3.69 (dd, 1H, J = 10.2, 4.0 Hz, $H_{3'}$), 2.49 (d, 1H, J = 4.1 Hz, H_1), 0.96 (s, 9H, H_5), 0.95 (s, 9H, H_8), 0.13 (s, 3H, H_7), 0.13 (s, 3H, H_4), 0.09 (s, 3H, $H_{7'}$), 0.08 (s, 3H, $H_{4'}$). ^{13}C NMR (100 MHz, $CDCl_3$) δ141.0, 128.5, 128.4, 127.0, 74.6, 65.5, 55.7, 49.0, 27.3, 26.0, 18.4, 17.2, -5.1, -5.1, -6.3. Anal. Calcd for $C_{22}H_{43}NO_2Si_2$: C, 64.49; H, 10.58; N, 3.42. Found: C, 64.38; H, 10.77; N, 3.44%.

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