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Regioselective cleavage of 3,4-epoxy alcohols with substituted alkynylaluminum reagents: application to the stereoselective synthesis of polypropionates

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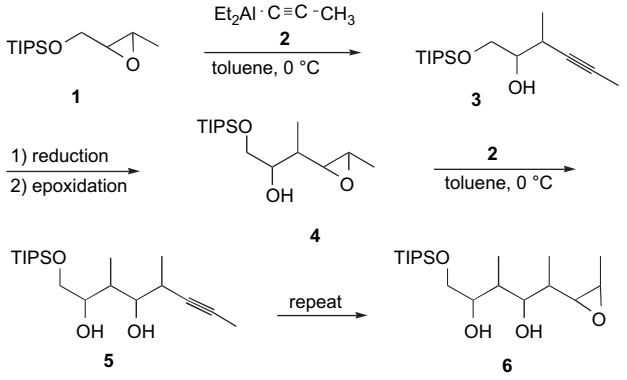
Abstract—The reaction of 3-*O*-substituted propynyl aluminum reagents with a TIPS-protected 2,3-epoxy alcohol and several diastereomeric 2-methyl-3,4-epoxy alcohols offers a convenient synthetic approach for the subsequent preparation and epoxidation of allylic alcohols. The yields are low to moderate and the regioselectivity (internal vs external attack) is similar to that of the standard diethylpropynyl aluminum reagent. The TMS–acetylide alane reagent gives improved yields and good regioselectivity, and is the reagent of choice for the cleavage of the hindered epoxides. This attractive methodology is applied to the elaboration of two advanced polypropionate precursor fragments.

1. Introduction

The regioselective addition of alkynyl nucleophiles to protected and unprotected 2,3-epoxy alcohols using alkynylaluminum reagents is a well-known procedure.[1] Considerably less successful has been the reaction of these reagents with 3,4-epoxy alcohols. Recently, we reported a reiterative epoxide-based approach for the synthesis of polypropionate chains in which the key step is the cleavage of 3,4-epoxy alcohols with an alkynylalane reagent (Scheme 1).[2] In this method, a protected 2,3-epoxy alcohol **1** is submitted to a diethylpropynylalane (**2**)-mediated epoxide cleavage, followed by a cis or trans reduction of the resulting alkyne **3**, and terminated with a stereoselective epoxidation of the alkene product to yield a 2-methyl-3,4-epoxy alcohol **4**. Cleavage of **4** with the same propynyl aluminum reagent produces the stereotetrad **5**. The application of this sequence of steps on the homopropargylic alcohol **5** generates a new 3,4-epoxy alcohol **6**, which allows chain elongation in a reiterative fashion. The configuration of the newly formed hydroxy functionality depends on the epoxide configuration, whereas the *syn*/*anti* relative configuration of the methyl and hydroxy groups is dictated by the cis/trans geometry of the epoxy alcohols; thus, a *cis* epoxide produces an *anti* configuration, while the trans isomer provides the *syn* product.

This process allowed the preparation of a series of diastereomeric stereotetrads (**5**) in good to moderate overall yields. The sequence, although successful for several stereochemical combinations, is not as general as desired, since the regioselectivity of the epoxide cleavage and the stereoselectivity of the epoxidation step may be difficult to control. For example, the *syn*/*trans* homoallylic alcohol **7** gave poor *syn*/*anti* ratios under a variety of epoxidation conditions (Scheme 2).[3] In fact, a lower stereoselectivity for the epoxidation of *trans* homoallylic alcohols has been observed, since various reagents were less selective for the trans than for the cis isomers.[4] In addition, an inherent limitation of hydroxy-directed epoxidations is that they are mostly *syn* selective; hence, the complementary *anti* stereoisomer cannot be obtained as the major isomer because the stereoselectivity of the reaction is substrate controlled.



Scheme 1. Epoxide-based reiterative approach for polypropionate construction.

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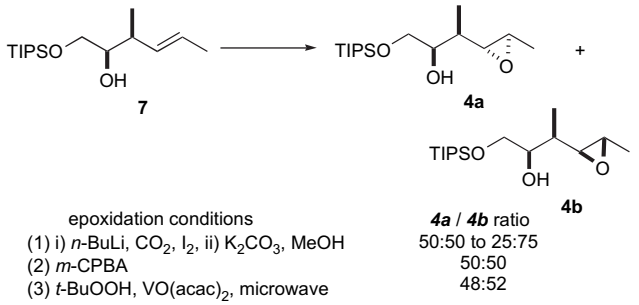
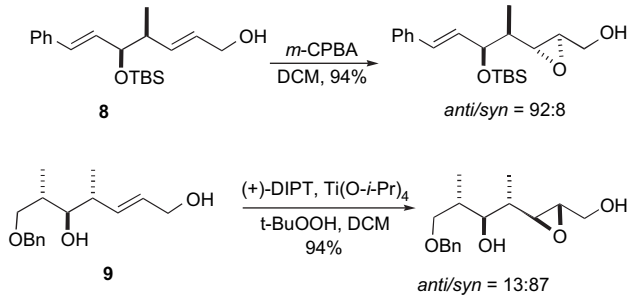


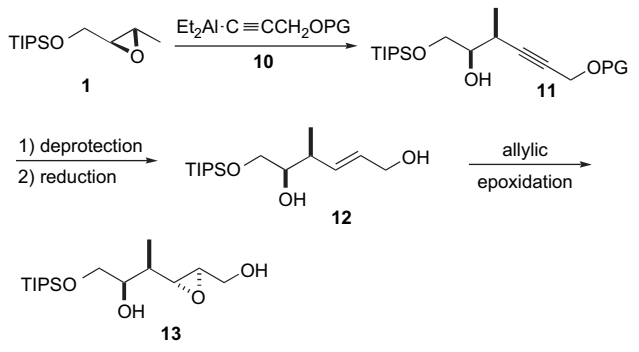
Scheme 2. Stereoselectivity for the epoxidation of *syn*/*trans* homoallylic alcohol **7**.

Unlike the homoallylic alcohols, the epoxidation of acyclic allylic alcohols is well developed and amply understood. Excellent substrate, reagent or catalyst control may be attained, depending on the reagents and conditions, regardless of the alkene geometry. For example, *trans* alkenols such as **8** produce the *anti* epoxide with high stereoselectivity by using *m*-CPBA (Scheme 3).[5] In this epoxidation, the *syn*/*anti* stereoselectivity is controlled by steric hindrance and/or 1,3-allylic strain.[6] On the contrary, the *trans* alkenediol **9** favors the *syn* epoxy alcohol, when subjected to the Sharpless methodology,[7] as a result of the allylic hydroxy-directing effect.[8]



Scheme 3. Stereoselective *anti* and *syn* epoxidation of *trans* allylic alcohols **8** and **9**.

For an efficient stereoselective access to the complementary *anti* 3,4-epoxy alcohol diastereomers in our epoxide-based approach, we decided to use functionalized alkynylaluminum reagents (**10**) for the incorporation of an allylic moiety (**12**) after alkyne reduction (Scheme 4). The plan was to exploit the efficacy and excellent diastereoselectivity obtainable from the epoxidation of allylic alcohols, which would give access to 3,4-epoxy alcohols not readily available by the standard homoallylic alcohol epoxidation methods.



Scheme 4. Second-generation epoxide-based approach for the preparation of polypropionates.

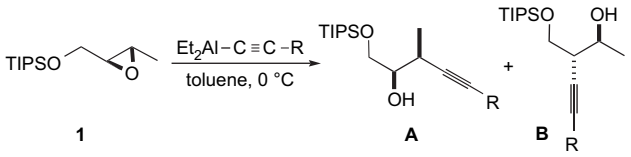
In general, the alkynylaluminum reagents that have been used for the cleavage of epoxides are aliphatic or aromatic.[1,2,9] There are only a few accounts in which a 3-*O*-substituted functionality has been introduced at the propargylic position. In this regard, Fried (in his pioneering studies related to prostaglandin synthesis) employed an alkynylalane reagent derived from (*S*)-3-*tert*-butoxy-1-octyne with a cyclopentane oxide derivative, which afforded the epoxide cleavage product with good regioselectivity.[10a] Prior to this report, other *O*-protected alkynylalane derivatives, e.g., OTMS, gave low yields and poor regioselectivities when subjected to the epoxide cleavage conditions.[10b,c] More recently, Pagenkopf used a 3-OTBS propynyl aluminum reagent in the alkynylation at the more hindered carbon atom of a model trisubstituted 2,3-epoxy alcohol.[1b] The reaction of a series of propynylalane reagents with trisubstituted epoxide was ineffective, however, when the related lithium alanate complex was used in the presence of $BF_3 \cdot OEt_2$, good yields and regioselectivities were obtained.

Herein, we report on the reactivity and regioselectivity of functionalized alkynylalanes for the cleavage of hindered aliphatic epoxy alcohols. The potential use of these reagents in our epoxide-based approach for the synthesis of polypropionate chains was also explored.

2. Results and discussion

Our studies started with the protected *trans*-2,3-epoxy alcohol **1**, which has shown good reactivity and regioselectivity (73% yield; 94:6) when treated with the unsubstituted propynylalane reagent **2** (R=CH_3), to favor external attack.[3] Accordingly, several *O*-protected propargyl alkynylalane reagents (**10a**–**10d**) were explored (Table 1). For the benzyl derivative **10a**, also an excellent regioselectivity was observed, albeit in a disappointingly low 10% yield (entry 2). Several attempts to improve the yield failed; therefore, other propargyl protecting groups were investigated. The 3-OPMB and 3-OTHP propynylalane reagents **10b** and **10c** did not cleave the epoxides (entries 3 and 4), but interestingly, for the 3-OTMS derivative **10d** the yield was improved to 52% although with a lower (67:33) regioisomeric ratio

Table 1. Reaction of epoxide **1** with alkynylalane reagents



Entry	Alane	R	Product	Yield	A/B ratio[a]
1	**2**	CH_3	**3a**	73	94:6
2	**10a**	CH_2OBn	**11a**	10	>95:5[b]
3	**10b**	CH_2OPMB	—	N.R[c]	—
4	**10c**	CH_2OTHP	—	N.R.[d]	—
5	**10d**	CH_2OTMS	**11d**[e]	52	67:33
6	**14**	TMS	**15**	70	>95:5[b]

[a] Determined by NMR spectroscopy.
[b] Only one regioisomer was observed.
[c] Epoxide hydrolysis product (48%) was recovered.
[d] Epoxide hydrolysis product (38%) was recovered.
[e] OTMS hydrolysis product (R=CH_2OH).

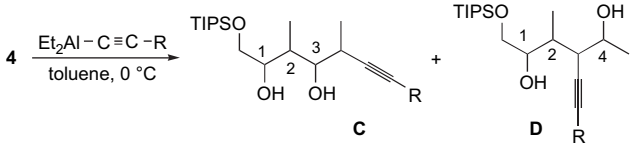
(entry 5). These findings suggest that the poor reactivity observed with the ether-derived alkynylaluminum reagents may arise from deactivation of the alane reagent due to coordination with the propargylic oxygen atom.[11] To ascertain this supposition, the TBDPS protected propargylic alane reagent was tried, but it was unfortunately unreactive. These results imply that steric effects of the protecting group may also play a role in overcoming the reactivity of the alane reagent toward epoxide cleavage.

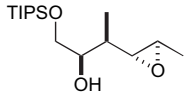
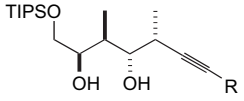
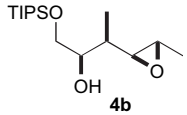
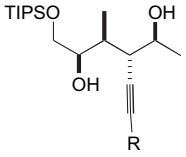
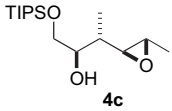
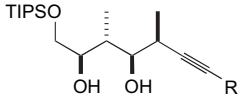
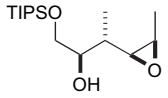
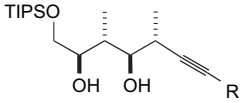
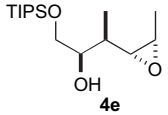
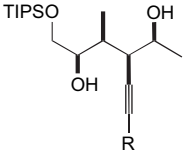
Because of the low yields obtained with the *O*-protected propargylic alanes, we examined the TMS–acetylide derivative **14**. This reagent has been used for the cleavage of 2,3-epoxy alcohol,[1d,1c,12a] vinyl epoxides,[9a] epoxy sulfides,[12b] and epoxy selenides.[12c] When epoxide **1** was treated with **14**, the desired product **15** was obtained in a 70% yield, the highest yield displayed by the functionalized alkynylalane series (entry 6). Also, the regioselectivity was excellent, similar to that of the propynylalane reagent **2**.

The results for the more hindered 2-methyl-3,4-epoxy alcohols **4a**–**4e** are summarized in Table 2. In general, the yields for the cleavage of 3,4-epoxy alcohols **4a**, **4d**, and **4e** with the *O*-protected propargyl alkynylalane reagents were also low (12–55%), but better than that for 2,3-epoxy alcohol **1** (Table 1). The regioselectivity for the epoxide cleavage by the functionalized alkynylalane reagents parallels that of the simple propynylalane reagent **2**. For example, the attack is preferred on the external carbon atom for epoxy alcohols **4a**, **4c**, and **4d**, whereas internal attack is favored for **4b** and **4e**. A reversal of the regioselectivity was obtained when epoxides **4d** and **4e** were treated with the *O*-benzyl alkynylalane **10a** (entry 11) and the 3-methoxyalkynylalane **10e** (entry 16). In contrast to the benzyloxy derivatives, in all cases in which the methoxyalkynylalane **10e** was used, the external attack is favored regardless of the epoxy alcohol, but the yields are lower (entries 4, 13, and 16).

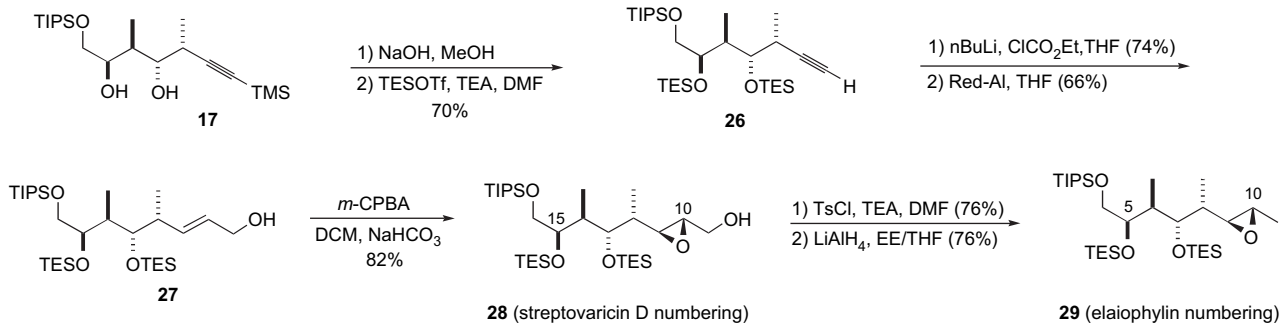
To understand the low reactivity of the propargyl ether derivatives, we carried out the reaction of propynylalane **2** with epoxide **4e** under the standard reaction conditions (toluene, 0 °C), but in the presence of 1 equiv of THF (per alane equiv) to coordinate the THF oxygen atom to the aluminum complex. This modification completely suppressed the formation of the epoxide cleavage product, even on extended warming. Moreover, when the epoxy alcohol **4e**, protected as the

Table 2. Yields and regioselectivities for the reaction of 2-methyl-3,4-epoxy alcohols **4a**–**4d** with alkynylalane reagents



Entry	Epoxide[a]	Alane	R	Major product	Product	Yield %	C/D ratio[b]
1	 **4a**	**2**	CH_3		**5a**	80	89:11
2		**10a**	CH_2OBn		**16a**	55	>95:5[c]
3		**10d**	CH_2OTMS		**16d**[d]	45	90:10
4		**10e**	CH_2OCH_3		**16e**	33[e]	77:23
5		**14**	TMS		**17**	87	85:15
6	 **4b**	**2**[f]	CH_3		**18**	39	15:85
7		**14**	TMS		**19**	45	<5:95[c]
8	 **4c**	**2**[f]	CH_3		**5c**	52	67:33
9		**14**	TMS		**20**	66	77:23
10	 **4d**	**2**[f]	CH_3		**5d**	52	>95:5[c]
11		**10a**	CH_2OBn		**21a**	34	12:88
12		**10d**	CH_2OTMS		**21d**[d]	34	62:38
13		**10e**	CH_2OCH_3		**21e**	29	80:20
14		**14**	TMS		**22**	67	67:33
15	 **4e**	**2**[f]	CH_3		**23**	62	<5:95[c]
16		**10e**	CH_2OCH_3		**24**	12	82:18
17		**14**	TMS		**25**	66	5:95

[a] Prepared by the procedures in Ref. 3.
[b] Determined by NMR spectroscopy.
[c] Only one regioisomer was observed.
[d] OTMS hydrolysis product (R=CH_2OH).
[e] Furan product (15%) was also recovered.
[f] R=CH_3 obtained from Ref. 2.



Scheme 5. Synthesis of the *anti*/*trans* epoxides **25** and **26** by using the allylic epoxidation approach.

benzyl ether, was subjected to the standard epoxide cleavage conditions with the alane **2**, no product was observed. These results are consistent with the deactivation of the alane reagent by coordination with the ether oxygen atom.[11] Although Lewis bases such as phosphines, arsines, stilbanes, and sulfides catalyze the cleavage of simple non-activated epoxides by trialkylaluminum reagents (through the breakage of the alane dimer), ethers and amines do not.[11b] This result contrasts that of benzylated 2,3-epoxy alcohols, where the benzyloxy group does not suppress the reactivity, but through coordination to the alane directs the nucleophilic attack.[9a]

Subsequently, we explored the TMS–acetylide derivative **14** on the hindered diastereomeric 3,4-epoxy alcohols. The literature reports that the use of this reagent deals almost exclusively with vinyl- or hydroxy-substituted epoxides, with no precedent for the more challenging acyclic 3,4-epoxy alcohols.[1,9,12] When epoxides **4a**–**4e** were treated with **14** (entries 5, 7, 9, 14, and 17), the epoxide cleavage products were obtained in better yields (66–87% for epoxides **4a**, **4c**, **4d**, and **4e**), and the regioselectivity was somewhat improved, compared to the standard propynyl aluminum reagent **2**, except in the case of **4d** (entry 14), for which the regioisomeric ratio was 67:33, instead of the ratio >95:5 observed for **2**.

The regioselectivity of the 3,4-epoxy alcohol cleavage reaction was determined by ^{1}H and ^{13}C NMR spectroscopy; the diol products' spectra matched the trends previously established for the diethylpropynylalane cleavage.[2] The TMS alkynyl products revealed the propargyl methine carbon peaks at 43–46 ppm for the internal cleavage products **19** and **25**, while peaks at 31–36 ppm are observed for the desired external cleavage products **17**, **20**, and **22**. In addition, these 1,3-diol products show peaks at 86–87 and 107–109 ppm for the internal and TMS acetylenic carbons atoms, while the 1,4-diol products **19** and **25**, displayed signals at 89–91 and 105–107 ppm for the corresponding carbons atoms. These spectral data provide a reliable tool to assess the regioselectivity of the epoxide cleavage.

Altogether, these results demonstrate that the TMS–acetylene alane reagent **14** is more suitable than the *O*-protected propargyl alane reagents for the aluminum-mediated indirect introduction of a propargylic functionality through epoxide cleavage. Although the conversion of the silylated alkyne products (R=TMS) into an allylic alcohol requires three steps (desilylation, carbomethoxylation, and reduction), it represents only one extra step when compared to the direct introduction of a protected propargyl alcohol derivative (deprotection and reduction). This sequence offers a viable alternative as a propynyl substituted alkynylalane surrogate.

To demonstrate the synthetic usefulness of this functionalized alkynylalane approach for the elaboration of polypropionate-containing natural products, we applied this reaction sequence to the stereoselective construction of the advanced *trans* epoxide **28** (Scheme 5). This compound is a common precursor for our ongoing synthetic efforts toward the polypropionate chains of streptovaricin D and elaiophylin. The challenge here lies in the required *syn*/*anti*/*trans* 2-methyl-3,4-epoxide relative configuration, which cannot be obtained stereoselectively by iodocyclization or transition-metal-catalyzed methods (vide supra). Thus, diol **17** (prepared from epoxide **4a**, Table 1) was efficiently desilylated and protected as the di-TES alkyne **26**. Subsequent *n*-BuLi deprotonation of **26** followed by carbomethoxylation and concomitant reduction of the ester and alkynyl functionalities by Red-Al produced the *trans* allylic alcohol **27**. As required, **27** was stereoselectively epoxidized in 82% yield to the *anti* epoxide **28** with *m*-CPBA. Compound **27** is a masked homoallylic alcohol, which otherwise would have produced a poor *syn*/*anti* mixture of 3,4-epoxy alcohols. The epoxide **28** contains six adjacent stereocenters generated in a highly stereoselective manner, which may serve as a potential precursors to the C(10)–C(15) fragment of streptovaricin D. Most importantly, this epoxide incorporates the demanding and required oxygenated functionality at the C10 position. Similarly, epoxy alcohol **28** is a precursor to the C(5)–C(10) polypropionate chain of elaiophylin. In this case, the directing hydroxy group was removed by tosylation and $LiAlH_4$ reduction to yield the *anti*/*trans* epoxide **29** as a pure diastereomer.

3. Conclusion

We have developed a reaction sequence for the preparation of advanced allylic alcohols for their utilization in complementary stereoselective epoxidation reactions. This approach provides an attractive synthesis of the otherwise challenging 3,4-epoxy alcohol motif with both, an *anti* hydroxy-epoxide relative configuration and a trans geometry. The reiterative epoxide-based sequence offers a general approach for the preparation of polypropionate units. This strategy should be advantageous for the synthesis of the polypropionate units of streptovaricin D and elaiophylin.

4. Experimental

4.1. General comments

All reactions were carried out under nitrogen gas. All solvents were distilled before use, toluene and THF were freshly distilled from sodium/benzophenone. All commercially available compounds were used as received. Epoxides **1** and **4a**–**4e**, and compound **5a** were prepared by published procedures.[3] Unless otherwise noted, all compounds were purified by silica gel column chromatography and fully characterized by 1D and 2D ^{1}H NMR (500 or 300 MHz) and ^{13}C NMR (125 or 75 MHz) as solutions in deuterochloroform. NMR chemical shifts (δ) are given in parts per million relative to TMS, coupling constants (J) in hertz. The elemental analysis was carried out by Atlantic Microlabs, Inc. Norcross, GA.

4.2. General procedure for the alane-mediated epoxide cleavage

The reaction flask was charged with dry toluene (16 mL) and cooled to 0 °C. Then, 1.60 mL (4.10 mmol, 2.6 M) of *n*-BuLi was added, followed by 4.10 mmol of the alkynyl derivative via syringe. After this, 2.30 mL (4.10 mmol) of Et_2AlCl (1.8 M in toluene) was added with a syringe and the solution was stirred at 0 °C for 4 h. The epoxy alcohol (2.05 mmol, 1 equiv) was added to this solution and the reaction was stirred at 0 °C for 18 h. Then, 5% H_2SO_4 was administered dropwise (0 °C) and the phases were separated. After extraction with ethyl acetate, the organic phase was dried ($MgSO_4$) and the crude product purified by flash chromatography to yield the epoxide cleavage products as colorless oil.

4.2.1. (2*R,3*S**)-6-[(Benzyl)oxy]-3-methyl-1-[(triisopropylsilyl)oxy]-6-hexyn-2-ol (11a).** Hexane/ethyl ether 9:1, 10%. ^{1}H NMR ($CDCl_3$) δ: 7.34 (m, 5H), 4.57 (s, 2H), 4.16 (d, J=1.6 Hz, 2H), 3.94 (dd, J=9.7, 3.5 Hz, 1H), 3.79 (dd, J=9.7, 6.3 Hz, 1H), 3.54 (ddd, J=6.3, 4.4, 3.5 Hz, 1H), 2.64 (ddq, J=7.0, 4.4, 1.6 Hz, 1H), 1.61 (s, 1H), 1.30 (d, J=7.0 Hz, 3H), 1.06 (m, 21H). ^{13}C NMR ($CDCl_3$) δ: 137.6, 128.4, 128.0, 127.8, 88.2, 78.0, 74.6, 71.4, 65.3, 57.6, 29.3, 17.9, 17.2, 11.9.

4.2.2. (4*S,5*R**)-4-Methyl-6-[(triisopropylsilyl)oxy]-2-hexyn-1,5-diol (11d).** Hexane/ethyl ether 9:1, 52% (67:33 ratio). ^{1}H NMR ($CDCl_3$) δ: 4.30 (d, J=15.9, 1.9 Hz, 2H), 3.90 (dd, J=9.8, 3.7 Hz, 1H), 3.78 (dd, J=9.8, 6.2 Hz, 1H), 3.53 (m, J=6.2, 5.0, 3.7 Hz, 1H), 2.63 (m, J=7.0, 5.0, 1.9 Hz, 1H), 1.60 (br s, 2H), 1.27 (d, J=7.0 Hz, 3H), 1.08 (s, 18H), 1.07 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 87.4, 80.4, 74.5, 65.1, 51.2, 29.1, 17.9, 16.9, 11.9. Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73. Found: C, 63.65; H, 10.74. Spectral data for the minor isomer (4*R**,5*S**)-4-[(triisopropylsilyloxy)methyl]-2-hexyn-1,5-diol: ^{1}H NMR ($CDCl_3$) δ: 4.19 (d, J=2.0 Hz, 2H), 3.99 (m, J=7.0, 6.3 Hz, 1H), 3.96 (dd, J=10.0, 4.7 Hz, 1H), 3.77 (dd, J=10.0, 9.3 Hz, 1H), 2.68 (m, J=9.6, 7.0, 4.7, 2.0 Hz, 1H), 2.25 (br s, 2H), 1.28 (d, J=6.3 Hz, 3H), 1.04 (s, 18H), 1.02 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 82.6, 82.4, 70.2, 66.1, 50.7, 41.4, 20.5, 17.8, 11.6.

4.2.3. (2*R,3*S**)-3-Methyl-1-[triisopropylsilyl)oxy]-5-trimethylsilyl-4-pentyn-2-ol (15).** Hexane/ethyl ether 4:1, 70%. ^{1}H NMR ($CDCl_3$) δ: 3.95 (dd, J=9.8, 3.6 Hz, 1H), 3.79 (dd, J=9.8, 6.0 Hz, 1H), 3.48 (ddd, J=6.8, 6.0, 3.6 Hz, 1H), 2.60 (s, 1H), 2.56 (dq, J=6.8, 5.4 Hz, 1H), 1.27 (d, J=5.4 Hz, 3H), 1.09 (s, 18H), 1.07 (s, 3H), 0.13 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 108.2, 86.4, 74.8, 65.4, 30.2, 17.9, 17.2, 11.9, 0.0. Anal. Calcd for $C_{18}H_{38}O_2Si_2$: C, 63.09; H, 11.18. Found: C, 63.22; H, 11.25.

4.2.4. (2*R,3*S**,4*S**,5*R**)-8-[(Benzyl)oxy]-3,5-dimethyl-1-(triisopropylsilyl)oxy-6-octyn-2,4-diol (16a).** Hexane/ethyl ether 4:1, 55%. ^{1}H NMR ($CDCl_3$) δ: 7.31 (m, 5H), 4.56 (s, 2H), 4.15 (d, J=2.0 Hz, 2H), 4.17 (m, J=8.5, 4.2, 2.3 Hz, 1H), 3.69 (t, J=9.7, 8.2 Hz, 1H), 3.63 (dd, J=9.7, 4.2 Hz, 1H), 3.49 (dd, J=7.1, 4.7 Hz, 1H), 3.30 (s, 1H), 2.86 (s, 1H), 2.72 (m, J=7.1, 6.8, 2.0 Hz, 1H), 2.11 (m, J=7.2, 4.7, 2.3 Hz, 1H), 1.31 (d, J=6.8 Hz, 3H), 1.03 (d, J=7.2 Hz, 3H), 1.05 (m, 21H). ^{13}C NMR ($CDCl_3$) δ: 137.6, 128.4, 128.0, 127.8, 89.0, 79.2, 78.0, 72.2, 71.4, 65.7, 57.6, 35.7, 31.1, 17.9, 16.9, 11.9. Anal. Calcd for $C_{26}H_{44}O_4Si$: C, 69.60; H, 9.88. Found: C, 69.68; H, 9.80.

4.2.5. (4*R,5*S**,6*S**,7*R**)-4,6-Dimethyl-8-[(triisopropylsilyl)oxy]-2-octyn-1,5,7-triol (16d).** Hexane/ethyl ether 3:2, 45% (90:10 ratio). ^{1}H NMR ($CDCl_3$) δ: 4.22 (s, 2H), 4.14 (m, J=7.5, 5.6, 2.4 Hz, 1H), 3.68 (dd, J=9.8, 5.0 Hz, 1H, TIPSOC*H*$_2$–), 3.66 (dd, J=9.8, 7.1 Hz, 1H), 3.50 (m, J=6.7, 4.4 Hz, 1H), 3.00 (s, 1H), 2.69 (m, J=6.8, 6.7 Hz, 1H), 2.16 (s, 1H), 2.06 (m, J=7.2, 4.4, 2.4 Hz, 1H), 1.86 (s, 1H), 1.26 (d, J=6.8 Hz, 3H), 1.05 (m, 21H), 1.00 (d, J=7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 88.1, 80.3, 78.8, 72.5, 65.5, 51.2, 35.6, 30.8, 17.9, 16.4, 11.9, 11.6. Anal. Calcd for $C_{19}H_{38}O_4Si$: C, 63.64; H, 10.68. Found: C, 63.41; H, 10.86.

4.2.6. (2*R,3*S**,4*S**,5*R**)-3,5-Dimethyl-8-methoxy-1-[(triisopropylsilyl)oxy]-6-octyn-2,4-diol (16e).** Hexane/ethyl acetate 4:1, 33%. ^{1}H NMR ($CDCl_3$) δ: 4.15 (dddd, J=8.4, 4.2, 2.1, 1.5 Hz, 1H), 4.06 (d, J=15.6, 2.0 Hz, 2H), 3.69 (dd, J=9.8, 8.4 Hz, 1H), 3.65 (dd, J=9.8, 4.2 Hz, 1H), 3.45 (ddd, J=7.5, 5.5, 4.6 Hz, 1H), 3.34 (s, 3H), 3.28 (d, J=7.5 Hz, 1H), 2.85 (d, J=1.5 Hz, 1H), 2.70 (dqt, J=6.8, 5.5, 2.0 Hz, 1H), 2.10 (ddq, J=7.0, 4.6, 2.1 Hz, 1H), 1.30 (d, J=6.8 Hz, 3H), 1.06 (m, 21H), 1.02 (d, J=7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 88.8, 79.3, 77.8, 72.3, 65.7, 60.1, 57.4, 35.6, 31.1, 17.9, 16.9, 11.9, 11.6. Anal. Calcd for $C_{20}H_{40}O_4Si$: C, 64.47; H, 10.82. Found: C, 64.46; H, 11.00. Spectral data for the minor isomer (2*R**,3*S**,4*R**)-4-[(1*R**)-1-ethanoyl]-8-methoxy-3-methyl-1-[(triisopropylsilyl)oxy]-5-hexyn-2-ol: ^{1}H NMR ($CDCl_3$) δ: 4.09 (d, J=15.6, 1.9 Hz, 2H), 3.87 (dq, J=9.0, 6.3 Hz, 1H), 3.78 (dd, J=9.3, 3.5 Hz, 1H), 3.73 (ddd, J=7.9, 6.3, 3.5 Hz, 1H), 3.65 (dd, J=9.3, 7.9 Hz, 1H), 3.36 (s, 3H), 2.72 (s, 1H), 2.51 (ddt, J=9.0, 4.4, 1.9 Hz, 1H), 2.05 (ddq, J=7.0, 6.3, 4.4 Hz, 1H), 2.01 (br s, 1H), 1.35 (d, J=6.3 Hz, 3H), 1.10 (d, J=7.0 Hz, 3H), 1.06 (m, 21H). ^{13}C NMR ($CDCl_3$) δ: 85.5, 80.3, 74.0, 68.0, 65.2, 61.5, 57.4, 42.4, 35.3, 22.0, 17.9, 11.9, 11.9.

4.2.7. (2*R,3*S**,4*S**,5*R**)-3,5-Dimethyl-1-[(triisopropylsilyloxy)]-7-(trimethylsilyl)-6-heptyne-2,4-diol (17).** Hexane/ethyl acetate 4:1, 71% (85:15 ratio). ^{1}H NMR

(500 MHz, $CDCl_3$) δ: 4.16 (m, J=8.6, 3.8, 2.2 Hz, 1H), 3.68 (dd, J=9.7, 8.6 Hz, 1H), 3.62 (dd, J=9.7, 3.8 Hz, 1H), 3.40 (m, J=5.6, 4.5 Hz, 1H), 3.25 (s, 1H), 2.83 (s, 1H), 2.65 (m, J=6.8, 5.6 Hz, 1H), 2.07 (m, J=7.0, 4.5, 2.2 Hz, 1H), 1.25 (d, J=6.8 Hz, 3H), 1.05 (m, 21H), 1.00 (d, J=7.0 Hz, 3H), 0.10 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 109.0, 86.3, 79.2, 72.1, 65.8, 38.7, 35.5, 17.6, 16.9, 11.9, 11.5, 0.10. Anal. Calcd for $C_{21}H_{44}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 62.91; H, 11.00. Spectral data for the minor isomer (2*R**,3*S**,4*R**,5*R**)-3-methyl-1-[(triisopropylsilyl)oxy]-4-[(2-trimethylsilyl)ethynyl] hexane-2,5-diol: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.83 (qd, J=8.3, 6.2 Hz, 1H), 3.77 (dd, J=9.3, 3.7 Hz, 1H), 3.71 (m, J=8.0, 5.5, 3.7 Hz, 1H), 3.64 (dd, J=9.3, 8.0 Hz, 1H), 2.48 (dd, J=8.3, 3.9 Hz, 1H), 2.06 (m, J=7.6, 5.5, 3.9 Hz, 1H), 1.33 (d, J=6.2 Hz, 3H), 1.08 (d, J=7.6 Hz, 3H), 1.07 (m, 21H), 0.13 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 105.6, 89.4, 74.3, 68.0, 65.1, 43.1, 35.0, 21.9, 17.9, 11.5, 10.9, 0.0. Anal. Calcd for $C_{21}H_{44}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 63.32; H, 11.23.

4.2.8. (2*R,3*S**,4*S**,5*S**)-3-Methyl-1-[(triisopropylsilyl)-oxy]-4-[(2-trimethylsilyl)ethynyl]hexane-2,5-diol (19).** Hexane/ethyl acetate 4:1, 45%. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.89 (ddd, J=8.0, 5.1, 1.9 Hz, 1H), 3.87 (qd, J=8.3, 6.2 Hz, 1H), 3.73 (dd, J=9.6, 8.0 Hz, 1H), 3.64 (dd, J=9.6, 5.1 Hz, 1H), 2.48 (dd, J=8.3, 5.2 Hz, 1H), 2.07 (ddq, J=7.4, 5.2, 1.9 Hz, 1H), 1.28 (d, J=6.2 Hz, 3H), 1.05 (m, 21H), 0.98 (d, J=7.4 Hz, 3H), 0.10 (s, 9H). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 107.0, 88.7, 74.5, 66.6, 64.9, 46.1, 35.7, 20.9, 17.8, 11.4, 11.3, 0.0. Anal. Calcd for $C_{21}H_{44}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 62.88; H, 11.27.

4.2.9. (2*S,3*S**,4*S**,5*R**)-3,5-Dimethyl-1-[(triisopropylsilyl)oxy]-7-(trimethylsilyl)-6-heptyne-2,4-diol (20).** Hexane/ethyl ether 4:1, 66% (77:23 ratio). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.78 (d, J=2.7 Hz, 1H), 3.78 (m, J=6.7, 2.6, 2.7 Hz, 1H), 3.67 (d, J=2.6 Hz, 1H), 3.53 (t, J=6.2, 6.0 Hz, 1H), 2.72 (m, J=6.9, 6.0 Hz, 1H), 1.97 (m, J=7.0, 6.7, 6.2 Hz, 1H), 1.19 (d, J=6.9 Hz, 3H), 1.05 (m, 21H), 0.93 (d, J=7.0 Hz, 3H), 0.17 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 109.0, 86.3, 79.2, 72.1, 65.8, 38.7, 35.5, 17.6, 16.9, 11.9, 11.5, 0.10. Anal. Calcd for $C_{21}H_{44}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 63.22; H, 11.28. Spectral data for the minor isomer (2*S**,3*S**,4*R**,5*S**)-3-methyl-1-[(triisopropylsilyl)oxy]-4-[(2-trimethylsilyl)ethynyl]hexane-2,5-diol: ^{1}H NMR ($CDCl_3$) δ: 3.88 (d, J=6.2 Hz, 1H), 3.79 (qd, J=8.9, 6.2 Hz, 1H), 3.60 (d, J=9.3, 7.4 Hz, 1H), 3.57 (m, J=9.5, 6.2, 7.4 Hz, 1H), 2.89 (dd, J=8.9, 3.0 Hz, 1H), 2.04 (m, J=9.9, 7.3, 3.0 Hz, 1H), 1.38 (d, J=6.2 Hz, 3H), 1.05 (m, 21H), 0.90 (d, J=7.3 Hz, 3H), 0.13 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 105.3, 89.0, 73.9, 67.8, 65.6, 42.7, 34.7, 22.6, 17.9, 11.9, 10.9, 0.1. Anal. Calcd for $C_{21}H_{44}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 63.05; H, 11.29.

4.2.10. (2*S,3*S**,4*S**,5*S**)-8-Benzyloxy-3,5-dimethyl-1-triisopropylsilyloxy-6-octyne-2,4-diol (21a).** Hexane/ethyl acetate 4:1, 28% (BRSM) of pure internal cleavage product and 0.112 g of a fraction containing the desired external cleavage regioisomer. This fraction was purified again (9:1 hexane/ethyl acetate) to yield 5.5% of the alkynyldiol. ^{1}H NMR ($CDCl_3$) δ: 7.27–7.35 (m, 5H), 4.59 (s, 2H), 4.19 (d, J=1.9 Hz, 2H), 3.84 (dd, J=9.7, 3.5 Hz, 1H), 3.73 (ddd, J=7.8, 7.7, 3.5 Hz, 1H), 3.61 (dd, J=9.7, 7.7 Hz, 1H), 3.45 (dd, J=8.6, 2.9 Hz, 1H), 2.80 (ddq, J=7.0, 2.9, 1.9 Hz, 1H), 1.94 (ddq, J=8.6, 7.8, 6.9 Hz, 1H), 1.31 (d, J=7.0 Hz, 3H), 1.08 (m, 21H), 0.87 (d, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 137.6, 128.4, 128.1, 127.7, 87.5, 78.0, 77.8, 76.1, 71.3, 65.8, 57.7, 39.6, 30.3, 18.4, 17.9, 12.8, 12.0. Spectral data for the minor isomer (2*S**,3*S**,4*R**,5*S**)-(3-Benzyloxy-1-ethynyl)-3-methyl-4-hexane-2,5-diol: ^{1}H NMR ($CDCl_3$) δ: 7.28–7.40 (m, 5H), 4.61 (s, 2H), 4.23 (d, J=1.9 Hz, 2H), 3.86 (dd, J=12.2, 3.1 Hz, 1H), 3.85 (dq, J=6.9, 6.2 Hz, 1H), 3.59 (dd, J=12.2, 7.3 Hz, 1H), 3.57 (ddd, J=8.0, 7.3, 3.1 Hz, 1H), 2.94 (ddd, J=6.9, 4.1, 1.9 Hz, 1H), 1.80 (ddq, J=8.0, 6.9, 4.1 Hz, 1H), 1.26 (d, J=6.2 Hz, 3H), 1.06 (m, 21H), 0.96 (d, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 137.5, 128.4, 128.1, 127.9, 84.9, 81.1, 74.0, 71.4, 68.5, 65.4, 57.6, 42.8, 37.3, 21.1, 17.9, 12.2, 11.9. Anal. Calcd for $C_{26}H_{44}O_4Si$: C, 69.59; H, 9.88. Found: C, 69.54; H, 9.70.

4.2.11. (4*S,5*S**,6*S**,7*S**)-4,5-Dimethyl-8-triisopropylsilyloxy-2-octyne-1,5,7-triol (21d).** Hexane/ethyl acetate 9:1 to 4:1, 21% (BRSM) of pure external cleavage, and 13% (BRSM) of pure internal cleavage product. ^{1}H NMR ($CDCl_3$) δ: 4.22 (d, J=1.9 Hz, 2H), 3.84 (dd, J=9.8, 3.5 Hz, 1H), 3.74 (ddd, J=7.6, 7.5, 3.5 Hz, 1H), 3.62 (dd, J=9.8, 7.5 Hz, 1H), 3.42 (dd, J=8.7, 2.9 Hz, 1H), 2.73 (ddq, J=7.0, 2.9, 1.9 Hz, 1H), 1.95 (ddq, J=8.7, 7.6, 6.9 Hz, 1H), 1.27 (d, J=7.0 Hz, 3H), 1.05 (m, 21H), 0.84 (d, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 86.2, 80.8, 78.0, 75.9, 65.6, 51.0, 39.5, 30.0, 18.0, 17.9, 12.7, 11.8. Anal. Calcd for $C_{19}H_{38}O_4Si$: C, 63.64; H, 10.68. Found: C, 63.82; H, 10.82. Spectral data for the minor isomer (4*R**,5*S**,6*S**)-4-[(1*S**)-(1-hydroxy-ethyl)]-5-methyl-7-triisopropylsilyloxy-hept-2-yne-1,6-diol: ^{1}H NMR ($CDCl_3$) δ: 4.26 (d, J=1.6 Hz, 2H), 3.84 (dd, J=9.4, 2.9 Hz, 1H), 3.86 (dq, J=6.3, 6.2 Hz, 1H), 3.59 (dd, J=9.4, 7.0 Hz, 1H), 3.55 (ddd, J=7.0, 7.0, 2.9 Hz, 1H), 2.84 (ddd, J=6.3, 4.2, 1.6 Hz, 1H), 1.78 (ddq, J=7.0, 6.8, 4.2 Hz, 1H), 1.24 (d, J=6.2 Hz, 3H), 1.05 (m, 21H), 0.92 (d, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 84.0, 83.3, 73.9, 68.4, 65.3, 50.9, 42.7, 37.1, 21.0, 17.9, 11.8, 10.9.

4.2.12. (2*S,3*S**,4*S**,5*S**)-3,5-Dimethyl-8-methoxy-1-triisopropylsilyloxy-6-octyne-2,4-diol (21e).** Hexane/ethyl acetate 4:1, 23% of pure external cleavage product and 6% of pure internal cleavage product. ^{1}H NMR ($CDCl_3$) δ: 4.09 (d, J=1.9 Hz, 2H), 4.04 (s, 1H), 3.83 (dd, J=9.7, 3.1 Hz, 1H), 3.71 (ddd, J=7.6, 7.4, 3.1 Hz, 1H), 3.62 (dd, J=9.7, 7.6 Hz, 1H), 3.43 (dd, J=8.4, 2.0 Hz, 1H), 3.35 (s, 3H), 3.22 (s, 1H), 2.78 (ddq, J=7.0, 2.0, 1.9 Hz, 1H), 1.93 (ddq, J=8.4, 6.9, 7.4 Hz, 1H), 1.28 (d, J=7.0 Hz, 3H), 1.06 (m, 21H), 0.86 (d, J=6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 87.3, 77.9, 77.8, 76.1, 65.7, 60.2, 57.4, 39.6, 30.2, 18.0, 17.9, 12.9, 11.9. Spectral data for the minor isomer (2*S**,3*S**,4*R**,5*S**)-4-(3-methoxy-prop-1-ynyl)-3-methyl-1-triisopropylsilyloxy-hexane-2,5-diol: ^{1}H NMR ($CDCl_3$) δ: 4.15 (d, J=1.2 Hz, 2H), 3.85 (dq, J=6.2, 2.1 Hz, 1H), 3.85 (dd, J=9.4, 2.8 Hz, 1H), 3.58 (dd, J=9.4, 7.3 Hz, 1H), 3.55 (ddd, J=7.3, 7.2, 2.8 Hz, 1H), 3.35 (s, 3H), 2.92 (ddt, J=5.1, 2.1, 1.2 Hz, 1H), 1.79 (ddq, J=7.2, 6.8, 3.7 Hz, 1H), 1.25 (d, J=6.2 Hz, 3H), 1.06 (m, 21H), 0.94 (d, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 84.7, 80.9, 74.0, 68.4, 65.4, 60.1, 57.4, 42.8, 37.3, 21.1, 17.9, 12.1, 11.9.

Anal. Calcd for $C_{20}H_{40}O_4Si$: C, 64.47; H, 10.82. Found: C, 64.41; H, 10.92.

4.2.13. (2*S,3*S**,4*S**,5*S**)-3,5-Dimethyl-1-triisopropylsilyloxy-7-trimethylsilyl-6-heptyn-2,4-diol (22).** Hexane/ethyl acetate 9:1, 67% (2:1 ratio favoring external cleavage). Further purification (12:1 hexane/ethyl acetate) yielded 42% of **22** and 22% of the 1,4-diol product. ^{1}H NMR ($CDCl_3$) δ: 3.83 (dd, J=9.7, 3.3 Hz, 1H), 3.73 (ddd, J=7.6, 7.1, 3.3 Hz, 1H), 3.65 (dd, J=9.7, 7.1 Hz, 1H), 3.40 (dd, J=8.2, 3.5 Hz, 1H), 2.77 (dq, J=7.1, 3.5 Hz, 1H), 1.94 (ddq, J=8.2, 7.6, 7.1 Hz, 1H), 1.26 (d, J=7.1 Hz, 3H), 1.06 (m, 21H), 0.88 (d, J=7.1 Hz, 3H), 0.11 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 107.6, 86.8, 77.6, 75.6, 65.6, 39.5, 31.3, 17.9, 17.8, 13.0, 11.9, 0.18. Anal. Calcd for $C_{21}H_{41}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 63.14; H, 11.36. Spectral data for the minor isomer (2*S**,3*S**,4*R**,5*S**)-3-methyl-1-triisopropylsilyloxy-4-trimethylsilylethynyl-hexane-2,5-diol: ^{1}H NMR ($CDCl_3$) δ: 3.85 (dd, J=9.2, 2.8 Hz, 1H), 3.78 (dd, J=6.2, 3.5 Hz, 1H), 3.59 (dd, J=9.2, 7.2 Hz, 1H), 3.55 (ddd, J=7.2, 4.0, 2.8 Hz, 1H), 2.88 (dd, J=6.6, 3.5 Hz, 1H), 1.75 (ddq, J=6.9, 6.6, 4.0 Hz, 1H), 1.22 (d, J=6.2 Hz, 3H), 1.06 (m, 21H), 0.91 (d, J=6.9 Hz, 3H), 0.16 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 104.6, 90.3, 74.1, 68.3, 65.2, 43.6, 37.0, 21.0, 17.9, 11.9, 11.7, −0.1.

4.2.14. (2*R,3*S**,4*S**,5*S**)-3,5-Dimethyl-8-methoxy-1-triisopropylsilyloxy-6-octyne-2,4-diol (24).** Hexane/ethyl acetate 4:1, 10% of pure external cleavage product and 2.2% of the internal cleavage. ^{1}H NMR ($CDCl_3$) δ: 4.10 (d, J=1.0 Hz, 2H), 4.05 (ddd, J=7.5, 5.3, 1.5 Hz, 1H), 3.73 (dd, J=9.7, 7.5 Hz, 1H), 3.69 (dd, J=9.7, 5.3 Hz, 1H), 3.47 (dd, J=7.0, 4.7 Hz, 1H), 3.36 (s, 3H), 2.77 (ddq, J=7.0, 4.7, 1.0 Hz, 1H), 1.99 (ddq, J=7.0, 7.0, 1.5 Hz, 1H), 1.26 (d, J=7.0 Hz, 3H), 1.06 (m, 21H), 0.94 (d, J=7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 87.2, 78.4, 77.2, 72.6, 64.8, 60.1, 57.4, 37.7, 30.7, 18.0, 17.9, 11.9, 11.4. Spectral data for the minor isomer (2*R**,3*S**,4*R**,5*S**)-4-(3-methoxyprop-1-ynyl)-3-methyl-1-triisopropylsilyloxy-hexane-2,5-diol: ^{1}H NMR ($CDCl_3$) δ: 4.14 (d, J=2.0 Hz, 2H), 3.98 (dq, J=6.2, 4.0 Hz, 1H), 3.96 (ddd, J=7.9, 4.6, 4.0 Hz, 1H), 3.72 (dd, J=9.6, 4.6 Hz, 1H), 3.67 (dd, J=9.6, 7.9 Hz, 1H), 3.36 (s, 3H), 2.53 (ddt, J=5.1, 4.0, 2.0 Hz, 1H), 1.93 (ddq, J=7.1, 5.1, 4.0 Hz, 1H), 1.28 (d, J=6.2 Hz, 3H), 1.05 (m, 21H), 1.05 (d, J=7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ: 85.0, 81.0, 72.2, 65.7, 65.3, 60.1, 57.5, 44.0, 36.5, 21.6, 17.9, 11.9, 11.7.

4.2.15. (2*R,3*S**,4*R**,5*S**)-3-Methyl-4-trimethylsilylethynyl-hexane-2,6-diol (25).** Hexane/ethyl acetate 9:1, 66%. ^{1}H NMR ($CDCl_3$) δ: 3.88 (dq, J=6.1, 4.7 Hz, 1H), 3.88 (ddd, J=7.8, 4.3, 4.2 Hz, 1H), 3.70 (dd, J=9.6, 4.3 Hz, 1H), 3.65 (dd, J=9.6, 7.8 Hz, 1H), 2.49 (dd, J=4.7, 4.7 Hz, 1H), 1.91 (ddq, J=7.2, 4.7, 4.2 Hz, 1H), 1.24 (d, J=6.1 Hz, 3H), 1.05 (m, 21H), 1.02 (d, J=7.2 Hz, 3H), 0.14 (s, 9H). ^{13}C NMR ($CDCl_3$) δ: 104.8, 90.2, 72.6, 66.0, 65.0, 44.5, 36.2, 21.4, 17.9, 11.8, 11.3, 0.1. Anal. Calcd for $C_{21}H_{44}O_3Si_2$: C, 62.94; H, 11.07. Found: C, 63.13; H, 11.18.

4.2.16. (3*R,4*S**,5*S**,6*R**)-3,5-Dimethyl-4,6-bis[(triethylsilyl)oxy]-7-[(triisopropylsilyl)oxy]-hept-1-yne (26).** To the flask containing 2.61 g (6.50 mmol) of diol **17** was added 25 mL of NaOH (0.1 M in MeOH). The solution was stirred overnight. After the disappearance of starting material (TLC), methanol was evaporated under reduced pressure and the resulting slurry was diluted with 30 mL of water. The phases were separated and the aqueous layer was extracted with ether (3×30 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield 2.39 g of the crude TMS–acetylene product that was used for the next step without further purification. To a dried flask was added 24.1 mL of DMF via syringe and cooled to 0 °C. Then, 2.38 g (7.34 mmol) of the alkyne was added followed by the addition of 2.32 mL (16.7 mmol) of TEA. The reaction was stirred for 30 min. After this, 4.10 mL (18.1 mmol) of TESOTf was added via syringe. The reaction was stirred overnight. After the disappearance of starting material (TLC), the reaction was quenched by adding 40 mL of water and extracted with hexane (3×50 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude was purified by flash chromatography (hexane) to yield 2.83 g (70%) of pure product for the two consecutive steps. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.03 (ddd, J=7.5, 5.5, 2.8 Hz, 1H), 3.82 (dd, J=6.6, 3.5 Hz, 1H), 3.66 (dd, J=9.6, 5.5 Hz, 1H), 3.57 (dd, J=9.6, 7.5 Hz, 1H), 2.75 (m, J=7.0, 3.5, 2.5 Hz, 1H), 2.02 (d, J=2.5 Hz, 1H), 1.97 (m, J=7.0, 6.6, 2.8 Hz, 1H), 1.15 (d, J=7.0 Hz, 3H), 1.07 (m, 21H), 0.94 (t, J=8.0 Hz, 18H), 0.83 (d, J=7.0 Hz, 3H), 0.52 (q, J=8.0 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 89.1, 76.6, 73.5, 69.0, 65.8, 40.4, 29.4, 18.0, 15.2, 12.0, 9.6, 7.1, 7.1, 5.7, 5.6. Anal. Calcd for $C_{30}H_{64}O_3Si_3$: C, 64.68; H, 11.58. Found: C, 64.55; H, 11.70.

4.2.17. (2*E*,4*R,5*S**,6*S**,7*R**)-4,6-Dimethyl-5,7-bis[(triethylsilyl)oxy]-8-[(triisopropylsilyl)oxy]-2-octen-1-ol (27).** A dried flask at −78 °C was charged with 5.7 mL of THF. Then, 0.95 g (1.7 mmol) of alkyne **26** was added followed by the addition of 0.94 mL (2.04 mmol) of *n*-BuLi. The reaction was stirred for 30 min, and then 0.25 mL (2.60 mmol) of $ClCO_2Et$ was added via syringe. The reaction was stirred overnight and after the disappearance of starting material (TLC), the reaction was quenched with 20 mL of water. The phases were separated and the aqueous phase was extracted with hexane (3×20 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude was purified by flash chromatography (100:1 hexane/ether) to yield 0.789 g (74%) of pure alkynyl ester product. At this point, a flask at 0 °C was charged with 100 mL of dry THF and 3.19 g (5.07 mmol) of the alkynyl ester followed by the slow addition of 7.24 mL (5 equiv) of Red-Al (3.5 M in toluene). The solution was removed from the ice bath and stirred for several hours until the disappearance of the starting material (TLC). The reaction was cooled to 0 °C and quenched with water, the phases were separated and the aqueous partition was extracted with ether (3×50 mL). The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to yield 2.41 g (81%) of crude material. It was purified by flash chromatography (4:1 hexane/ethyl acetate) to yield 1.96 g (66%) of pure product **27**. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.77 (dd, J=15.5, 7.0 Hz, 1H), 5.61 (dt, J=15.5, 5.9 Hz, 1H), 4.10 (d, J=5.9 Hz, 2H), 3.94 (m, J=8.4, 5.4, 1.7 Hz, 1H), 3.66 (dd, J=7.3, 2.0 Hz, 1H), 3.64 (dd, J=9.7, 5.4 Hz, 1H), 3.55 (t, J=9.7, 8.4 Hz, 1H), 2.42 (m, J=7.0, 7.0, 2.0 Hz,

1H), 1.92 (m, J=7.3, 7.1, 1.7 Hz, 1H), 1.06 (d, J=7.0 Hz, 3H), 1.06 (m, 21H), 0.95 (t, J=8.0 Hz, 18H), 0.82 (d, J=7.1 Hz, 3H), 0.59 (q, J=8.0 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 138.5, 127.6, 77.6, 76.8, 65.7, 64.1, 40.2, 39.3, 17.9, 13.4, 11.9, 9.4, 7.1, 5.8, 5.6. Anal. Calcd for $C_{31}H_{68}O_4Si_3$: C, 63.20; H, 11.63. Found: C, 63.45; H, 11.77.

4.2.18. (2*R,3*S**,4*R**,5*S**,6*S**,7*R**)-2,3-Epoxy-4,6-dimethyl-5,7-bis[(triethylsilyl)oxy]-8-[(triisopropylsilyl)oxy]octan-1-ol (28).** A flask containing 1.0 g of alkenol **27** in 17 mL of CH_2Cl_2 was cooled to 0 °C. Then, 0.59 g (3.4 mmol) of *m*-CPBA was added and stirred until it dissolved followed by the addition of 5.6 mL of a 0.5 M $NaHCO_3$ solution. The reaction was stirred overnight and 25 mL of satd $NaHCO_3$ was added followed by the separation of the layers. The aqueous partition was extracted with ether (20 mL). The combined organic phase was washed with 5% $NaHSO_3$ (2×40 mL), followed by 20 mL of satd $NaHCO_3$ and 20 mL of brine. The solution was dried over $MgSO_4$ and concentrated under reduced pressure. The crude was purified by flash chromatography (4:1 hexane/ether) to yield 0.545 g (53%) of pure epoxide **28**. ^{1}H NMR ($CDCl_3$) δ: 3.93 (dd, J=11.6, 1.9 Hz, 1H), 3.92 (dd, J=6.9, 2.0 Hz, 1H), 3.87 (ddd, J=8.5, 5.2, 1.7 Hz, 1H), 3.65 (dd, J=9.3, 5.2 Hz, 1H), 3.61 (dd, J=11.6, 5.1 Hz, 1H), 3.51 (dd, J=9.3, 8.5 Hz, 1H), 2.93 (m, J=5.1, 2.4, 1.9 Hz, 1H), 2.92 (dd, J=7.4, 2.4 Hz, 1H), 2.03 (m, J=6.9, 7.2, 1.7 Hz, 1H), 1.50 (m, J=7.4, 6.8, 2.0 Hz, 1H), 1.06 (m, 21H), 0.97 (t, J=7.8 Hz, 18H), 0.93 (d, J=6.8 Hz, 3H), 0.81 (d, J=7.2 Hz, 3H), 0.62 (m, J=7.8 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 74.2, 73.3, 65.0, 62.1, 58.9, 58.9, 39.8, 39.0, 17.9, 11.9, 9.9, 8.3, 7.0, 5.7, 5.4. Anal. Calcd for $C_{31}H_{68}O_5Si_3$: C, 61.53; H, 11.33. Found: C, 61.43; H, 11.33.

4.2.19. (2*S,3*S**,4*R**,5*R**,6*S**,7*R**)-2,3-Epoxy-4,6-dimethyl-5,7-bis[(triethylsilyl)oxy]-8-[(triisopropylsilyl)oxy]octane (29).** To a dried flask containing CH_2Cl_2 (2.6 mL) at 0 °C, was added 0.160 g (0.26 mmol) of alcohol **28** followed by the addition of 0.07 mL (0.52 mmol) of TEA. The reaction was stirred (30 min) and 0.10 g (0.52 mmol) of TsCl, dissolved in CH_2Cl_2 (1 mL) was added via syringe. The reaction was stirred overnight and quenched with satd $NaHCO_3$ (15 mL) and water (15 mL). The phases were separated and the aqueous phase was extracted with hexane (3×10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. After column chromatography (4:1 hexane/EtOAc), 76% of the mesylate was obtained. Then, a dry flask at 0 °C was charged with THF (3 mL) and 0.46 mL (0.46 mmol) of $LiAlH_4$. Then, 0.070 g (0.092 mmol) of the tosyl-protected alcohol was added (dissolved in 1 mL of ether). After 1.5 h (TLC), the reaction was quenched with water (10 mL) followed by EtOAc (3.0 mL) and stirred for 15 min. The phases were separated and the aqueous partition was extracted with ether (3×10 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to yield 0.041 g (76%) of product **29**, which was characterized without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.92 (dd, J=6.9, 2.0 Hz, 1H), 3.87 (br t, J=8.8, 5.2, 1.7 Hz, 1H), 3.63 (dd, J=9.5, 5.2 Hz, 1H), 3.51 (br t, J=9.5, 8.8 Hz, 1H), 2.75 (dq, J=5.0, 1.3 Hz, 1H), 2.59 (br d, J=7.4, 1.3 Hz, 1H), 2.00 (m, J=7.1, 6.9, 1.7 Hz, 1H), 1.41 (m, J=7.4, 7.0, 2.0 Hz, 1H), 1.31 (d, J=5.0 Hz, 3H), 1.06 (m, 21H), 0.96 (m, J=8.0 Hz, 18H), 0.91 (d, J=6.8 Hz, 3H), 0.79 (d, J=7.1 Hz, 3H), 0.65–0.58 (q, J=8.0 Hz, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 74.2, 73.3, 65.1, 62.7, 54.9, 39.8, 39.3, 18.1, 17.9, 11.9, 10.0, 8.4, 7.1, 5.8, 5.6.

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Supplementary data

^{1}H and ^{13}C NMR spectral data for all epoxide cleavage products are available in the electronic supplementary information (ESI). Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.05.122.

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