

Stereospecific Formation of Optically Active 5-Alkyl-4-methyl-3-[(trialkylsilyl)oxy]-2-([(trialkylsilyl)oxy]-methyl)tetrahydrofurans via Diastereoselective Epoxidation and Rearrangement of 5-[(Trialkylsilyl)oxy]-2-alken-1-ols¹

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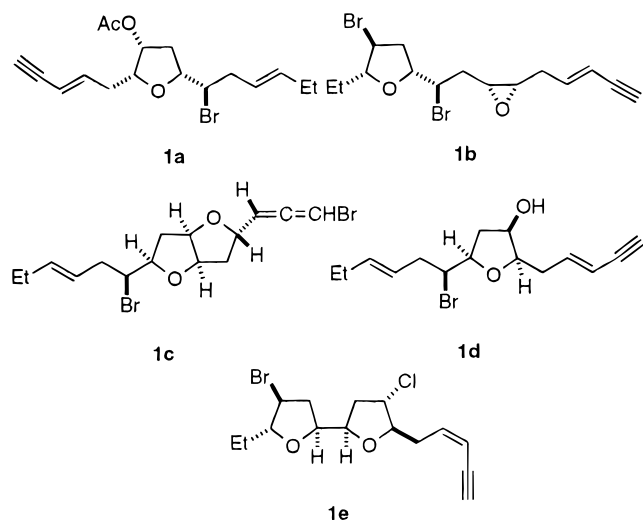
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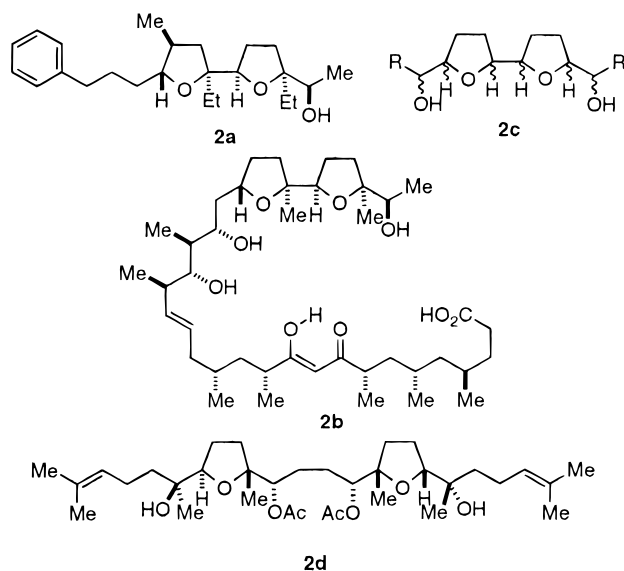
Abstract: A novel method for the synthesis of a series of silyl ethers of 3-(silyloxy)tetrahydrofuran-2-methanols bearing substituents at all four carbon atoms of the ring has been developed. The process involves first non-aldol aldol reaction of the epoxy silyl ether **8** to give the anti aldol product **9**, stereoselective olefination and reduction to the (*E*)- and (*Z*)-allylic alcohols **10** and **11**, diastereoselective epoxidation of these alcohols to give any of the four diastereomeric epoxy alcohols **12–15**, silylation of the alcohols to give the epoxy silyl ethers **27–30**, and final Lewis acid catalyzed rearrangement of the epoxy silyl ethers to give the desired products **31–33** and **36**. In the first three instances, good yields of the desired 3-(silyloxy)-2-((silyloxy)methyl)tetrahydrofurans were obtained. However, rearrangement of the epoxy silyl ether **27** gave a mixture of products, the bis-silyl ether **36** as well as the products of a second non-aldol aldol process. This hydride migration to give the 3,5-bis((trialkylsilyl)oxy)-2,4-dimethylalkanal **35** or its internally protected 1-(silyloxy)pyran **38** can be made to occur in good yield.

Introduction and Background

A large number of biologically active natural products have as an essential part of their structure a tetrahydrofuran unit.⁴ For example, the halogenated sesquiterpenes, kumausyne (**1a**),⁵ laurepoxide (**1b**),⁶ kamausylene (**1c**),⁷ kumasine (**1d**),⁸ and notoryne (**1e**),⁹ all contain one or more tetrahydrofuran units.



2-methanol unit as part of their structure, e.g., the antibiotic isolasolocid A (**2a**),¹⁰ the polyether antibiotic ionophore ionomycin (**2b**),^{4a} and the many bis-tetrahydrofurfuryl alcohol systems, e.g., the annonacins (**2c**)¹¹ and eurylene (**2d**).¹² Finally



A larger group of natural products contain a tetrahydrofuran-

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(2) American Chemical Society Arthur C. Cope Scholar, 1995.

(3) UCLA Department of Chemistry Prize for Excellence in Research 1993–94; UCLA Dissertation Year Fellowship 1994–95. Current address: Zeneca Pharmaceuticals, Wilmington, DE 19850-5437.

(4) (a) *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Westley, J. W., Ed.; Marcel Dekker: New York, 1983; Vols. 1 and 2. (b) Robinson, J. A. *Prog. Chem. Org. Nat. Prod.* **1991**, *58*, 1.

(5) Osumi, K.; Sugimura, H. *Tetrahedron Lett.* **1995**, *36*, 5789.

(6) Fukusawa, A.; Kurosawa, E. *Tetrahedron Lett.* **1980**, *21*, 1471.

there is also an extensive family of naturally occurring compounds that possess 3- or 4-hydroxytetrahydrofuran-2-methanol units, e.g., the α ,5-dialkyl-substituted 4-hydroxytet-

(7) Suzuki, T.; Koizumi, K.; Suzuki, M.; Kurosawa, E. *Chem. Lett.* **1983**, 1639.

(8) Suzuki, T.; Koizumi, K.; Suzuki, M.; Kurosawa, E. *Chem. Lett.* **1983**, 1643.

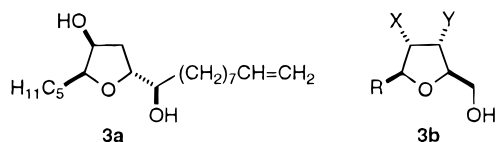
(9) Kikuchi, H.; Suzuki, T.; Kurosawa, E.; Suzuki, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1763.

(10) Horita, K.; Noda, I.; Tanaka, K.; Miura, T.; Oikawa, Y.; Yonemitsu, O. *Tetrahedron* **1993**, *49*, 5979.

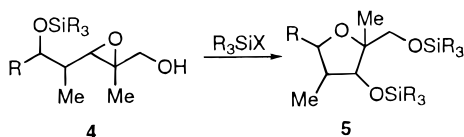
(11) Hoppe, R.; Scharf, H.-D. *Synthesis* **1995**, 1447.

(12) Gurjar, M. K.; Saha, U. K. *Tetrahedron Lett.* **1993**, *34*, 1833.

rahydrofuran-2-methanol norditerpenes (**3a**),¹³ the ribofuranoses, and the nucleic acids and their derivatives (**3b**).¹⁴ Because of

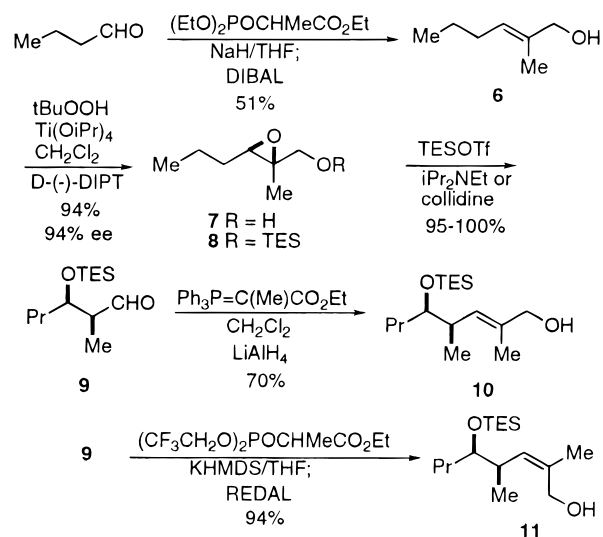


the presence of the tetrahydrofuran structural unit in so many important natural products, many synthetic routes to these compounds have been developed over the last few years.¹⁵ Recently, we have reported the use of Lewis acids for the rearrangement of substituted epoxides, epoxy alcohols, and epoxy silyl ethers to give aldehydes and β -(silyloxy) aldehydes (non-aldol aldol process) in excellent yield and optical purity.¹⁶ We now report herein the use of Lewis acids for the rearrangement of β -(silyloxy)-substituted tertiary epoxy alcohols **4** for the preparation of 2,4-dimethyl-3-(silyloxy)tetrahydrofuran-2-methanols (**5**) with a variety of relative stereochemistries in high yield and optical purity. In this manner, one can prepare in excellent purity and high yield 3-(silyloxy)tetrahydrofuran-2-methanols that bear substituents on every ring carbon.



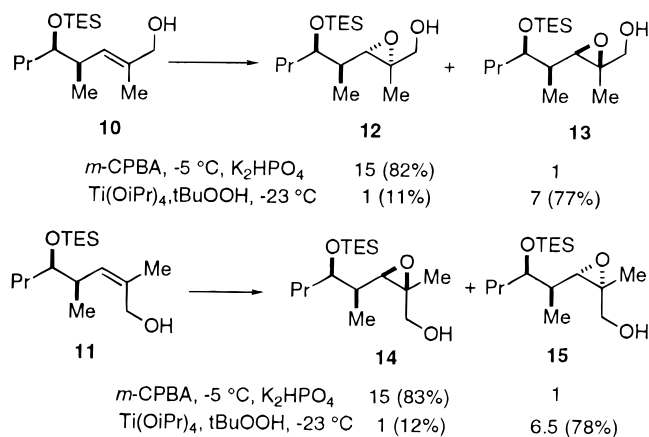
Results and Discussion

Preparation of Substrates. The required substrates for this rearrangement are prepared from simple aldehydes in several high-yielding steps. Thus, butanal was converted via a one-pot Wittig reaction and reduction in 51% yield into (*E*)-2-hexen-1-ol (**6**), which was then epoxidized under Sharpless catalytic conditions using D-(–)-tartrate and *tert*-butyl hydroperoxide to give the epoxy alcohol **7** in 94% yield and 94% enantiomeric excess (ee). The triethylsilyl ether of this epoxy alcohol, compound **8**, was available from **7** in quantitative yield by simple silylation. Rearrangement of either of these two compounds, the simple epoxy alcohol **7** or the silyl epoxide **8**, under any of four different sets of conditions [see the Experimental Section, e.g., those we described earlier,¹⁷ namely triethylsilyl triflate (TESOTf) in the presence of Hünig's base or collidine], afforded the 2-methyl-3-((triethylsilyloxy)hexanal (**9**) in excellent yield (95–100%) and high diastereomeric purity (up to 50:1 at the α -carbon). Normal Wittig reaction on **9** and



in situ reduction with lithium aluminum hydride afforded the (*E*)-allylic alcohol **10** in 70% yield, while the use of the Still modification of the Wittig reaction¹⁷ followed by in situ reduction with Red-Al furnished the (*Z*)-allylic alcohol **11**. Thus, both stereoisomeric allylic alcohols **10** and **11** were available in good yield and high isomeric purity.

Stereoselective epoxidation of both of these allylic alcohols could be carried out using the existing stereocenters to induce the desired sense of facial selectivity. Treatment of the (*E*)-allylic alcohol **10** with *m*-chloroperoxybenzoic acid (mCPBA) afforded a 15:1 mixture of the *anti*- and *syn*-epoxides **12** and **13** from which the *anti*-epoxide **12** could be isolated in 82% yield. On the other hand, epoxidation of **10** using titanium tetrakisopropoxide and *tert*-butyl hydroperoxide afforded a 1:7 ratio of the *anti*- and *syn*-epoxides from which the *syn*-epoxide **13** could be isolated in 77% yield (along with 11% of the *anti*-epoxide). In like fashion, epoxidation of the (*Z*)-allylic alcohol



(13) Warren, R. G.; Wells, R. J.; Blount, J. F. *Aust. J. Chem.* **1980**, *33*, 891.

(14) For an example of unnatural aglycon residues for DNA, see: François, P.; Perilleux, D.; Kempener, Y.; Sonveaux, E. *Tetrahedron Lett.* **1990**, *31*, 6347.

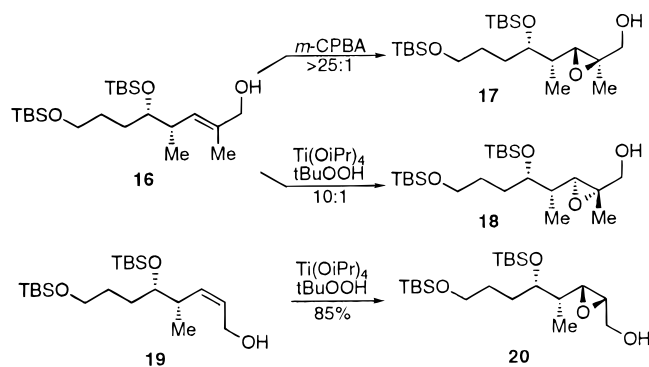
(15) For reviews, see: (a) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. (b) Burns, C. J. *Contemp. Org. Syn.* **1995**, *2.3*, 189–207. For some recent examples, see: (c) Molander, G. A.; Swallow, S. *J. Org. Chem.* **1994**, *59*, 7148. (d) O'Leary, D. J.; Kishi, Y. *J. Org. Chem.* **1994**, *59*, 6629. (e) Zhao, Y.; Beddoes, R. L.; Quayle, P. *Tetrahedron Lett.* **1994**, *35*, 4183. (f) Angle, S. R.; Wei, G. P.; Ko, Y. K.; Kubo, K. *J. Am. Chem. Soc.* **1995**, *117*, 8041. (g) Gurjar, M. K.; Mainkar, P. S. *Heterocycles* **1990**, *31*, 407. (h) Tonn, C. E.; Palazón, J. M.; Ruiz-Pérez, C.; Rodríguez, M. L.; Martín, V. S. *Tetrahedron Lett.* **1988**, *29*, 3149. (i) Bonnaffé, D.; Simon, H. *Tetrahedron* **1992**, *49*, 9695. (j) Andrey, O.; Ducry, L.; Landais, Y.; Planchenault, D.; Weber, V. *Tetrahedron* **1997**, *53*, 4339.

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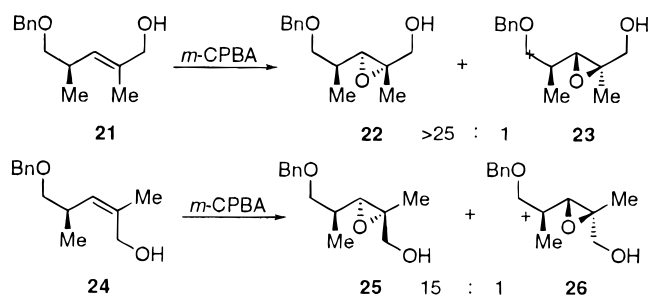
(17) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.

11 with mCPBA gave a 15:1 ratio of epoxides from which the predominating *syn*-diastereomer **14** could be isolated in 83% yield. Treatment of **11** with *tert*-butyl hydroperoxide and titanium tetrakisopropoxide gave a 1:6.5 ratio of the diastereomers from which both could be isolated, the *anti*-isomer **15** in 78% yield and the *syn*-isomer **14** in 12% yield. Thus, both diastereomers of each allylic alcohol **10** and **11**, e.g., **12,13** and **14,15**, respectively, are readily available as the major diastereomer in good isolated yields (77–83%). There is precedence in the literature for this stereochemical outcome in the epoxidation of allylic alcohols containing allylic stereocenters.

Isobe¹⁸ showed that the (*E*)-allylic alcohol **16**, which is extremely similar to **10**, upon treatment with *m*CPBA gave the *anti*-epoxide **17**, in agreement with the stereochemical outcome of the epoxidation of **10** to give **12**. It was also shown that treatment of **16** with *tert*-butyl hydroperoxide and titanium tetraisopropoxide gave a 10:1 mixture of **18** and **17**, which is consistent with the similar epoxidation of **10** to give **13**. Isobe¹⁹ also showed that epoxidation of the *cis*-disubstituted allylic alcohol **19** (similar to **11** but lacking the C₂ methyl) gave an 85% yield of the *anti* epoxide **20**, in accord with the epoxidation of **11** to give mainly **15**. Kishi²⁰ showed that the diastereose-



lectivity of the epoxidation does not depend on the presence of the silyl ether stereocenter. Thus, epoxidation of **21** with *m*CPBA afforded a 25:1 mixture of epoxides **22** and **23**, thereby implying that the methyl stereocenter is the crucial controlling element since alcohol **10**, with the additional silyloxy stereocenter, exhibits the same facial bias for the alkene as does alcohol **22**. However, the diastereoselectivity of epoxidation of the (*Z*)-allylic alcohols is much less clear. For example, Kishi reported that epoxidation of **24** with *m*CPBA gave a 15:1 mixture of **25** and **26**, which is the opposite diastereoselectivity of that seen in the epoxidation of **11**. This suggests that the silyloxy stereocenter reverses the facial preference observed for peracid epoxidations of (*Z*)-allylic alcohols. The diastereomeric relationships for the epoxy alcohols **12**–**15** were proven by NMR spectroscopic techniques on their rearrangement products (see below).



All of the epoxy alcohols were easily transformed into their triethylsilyl (TES) ethers by treatment with triethylsilyl chloride and DIPEA, except for the case of the alcohol **12** where triethylsilyl triflate (TESOTf) was used. Thus, the corresponding bis-triethylsilyl ethers, **27**–**30**, were available in yields of 85–94%.

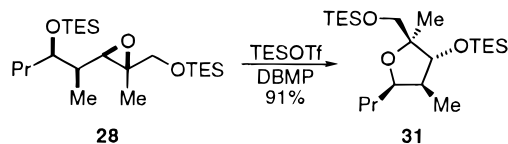
Rearrangements. In our earlier work on the non-aldol aldol process, we showed that treatment of epoxy silyl ethers such

(18) Isobe, M.; Kitamura, M.; Mio, S.; Goto, T. *Tetrahedron Lett.* **1982**, 23, 221.

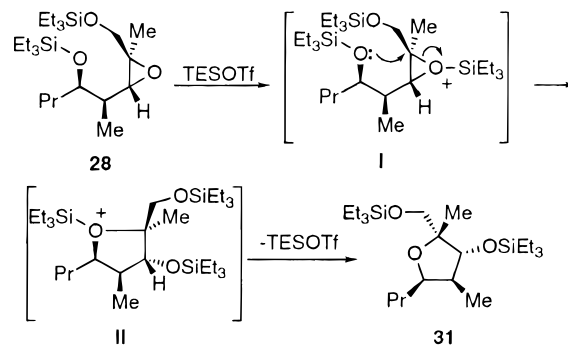
(19) Kitamura, M.; Isobe, M.; Ichikawa, Y.; Goto, T. *J. Org. Chem.* **1984**, 49, 3517.

(20) Johnson, M. R.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4347.

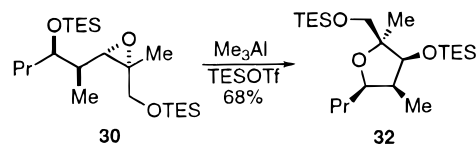
as **8** with a silyl triflate and a hindered base afforded the 2-methyl-3-((triethylsilyl)oxy)alkanal, e.g., **9**, in good yield. With these more substituted substrates, **27**–**30**, the rearrangement was much slower and required longer times and/or higher temperatures to cause loss of starting materials. A wide variety of Lewis acids and bases was used in an attempt to carry out a clean rearrangement of the epoxy alcohols. With only one substrate, the epoxide **27**, were we able to carry out the same type of non-aldol aldol process that we have described for the simple systems, which we will discuss at the end of this section. However, a more general rearrangement occurred readily with all of the other substrates, namely a clean rearrangement to give the tetrahydrofuran-2-methanol silyl ethers. Thus, treatment of the epoxide **28** with TESOTf and 2,6-di-*tert*-butyl-4-methylpyridine (DBMP) afforded the tetrahydrofuran **31** in 91% yield.



The likely mechanism for the synthesis of **31** from **28** is straightforward, namely activation of the epoxide oxygen with TESOTf to give the charged intermediate **I**. The Lewis acid increases the positive character at the tertiary carbon, but before hydride migration can occur, the lone pair of the secondary triethylsilyl ether opens the epoxide to afford the oxonium ion **II**. Finally, loss of TESOTf gives the observed product, namely



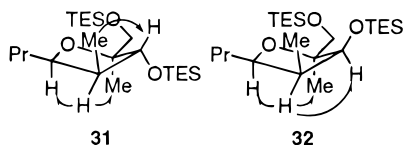
the tetrahydrofuran bis-silyl ether **31**. To ensure that the tetrahydrofuran was formed rather than the oxetane, a proton-coupled (uncoupled) ¹³C NMR was taken which displayed the typical *J*_{C–H} coupling constants consistent with five-membered rings (125 Hz) rather than the larger *J*_{C–H} coupling constants expected for oxetanes.²¹ Treatment of the epoxide **30** with trimethylaluminum and TESOTf afforded the tetrahydrofuran **32** in 68% yield (trimethylaluminum gave a cleaner reaction in this and several other cases than other, nitrogenous bases). The relative stereochemistry of the products were



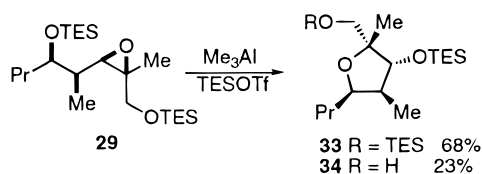
determined by 2D nuclear Overhauser experiments (NOE) which allowed us to relate the known stereocenters (i.e., the propyl group) to the unknown epoxide stereocenters. Specifically, in tetrahydrofuran **31**, the tertiary methyl and the proton α to the (triethylsilyl)oxy group and the quaternary methyl and the proton

(21) (a) Jung, M. E.; Trifunovich, I. D.; Lensen, N. *Tetrahedron Lett.* **1992**, 33, 6719. (b) Foote, C. S. *Tetrahedron Lett.* **1963**, 527.

α to the propyl group and the tertiary methine displayed the mutual correlation shown, thereby allowing one to assign its relative stereochemistry. In tetrahydrofuran **32**, the quaternary methyl, the two protons α to oxygen, and the tertiary methine displayed mutual correlation, thereby verifying the structure of **32**. With the relative stereochemistry of the tetrahydrofurans

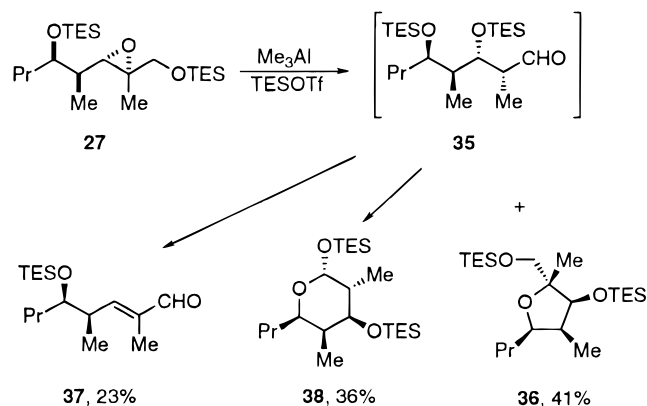


established, the chirality of the starting material can be determined which ultimately proves the diastereoselectivity in the epoxidation step, since the absolute stereochemistry of the propyl group is known because its stereochemistry was set during the first Sharpless–Katsuki epoxidation. This NOE data allows us to assign the absolute stereochemistry of the epoxy alcohols **27–30**. Thus, the stereochemistry of the epoxide ultimately leading to **31** had to be that assigned as **13**, and that leading to **32** had to be that assigned as **15**. Treatment of the epoxide **29** with trimethylaluminum and TESOTf afforded a mixture of the tetrahydrofuran **33** in 68% yield along with the mono-desilylated product **34** (23%). The rearrangement of this



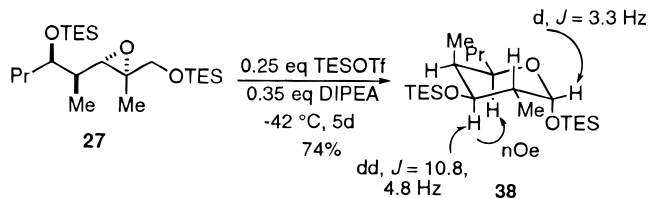
epoxy silyl ether to the tetrahydrofuran occurs in greater than 90% yield. Although NOE studies were not performed on the tetrahydrofuran **33**, the stereochemistry could be inferred because all of the other starting diastereomeric homologated epoxy silyl ethers, namely **27** (see below), **28**, and **30**, gave cyclized products whose stereochemistry was secured by 2D NOESY.

The reaction of the epoxide **27** with trimethylaluminum and TESOTf took a different course, giving a mixture of the tetrahydrofuran **36** and two new products, namely the α,β -unsaturated aldehyde **37** and the tetrahydropyran **38**. The formation of **37** and **38** could only be explained as arising from the common intermediate, the aldol product **35**, where elimination of the β -silyloxy group leads to **37**, while cyclization of the γ -silyloxy oxygen onto a silylated aldehyde intermediate, followed by loss of silicon, gives the tetrahydropyran **38**. Proof



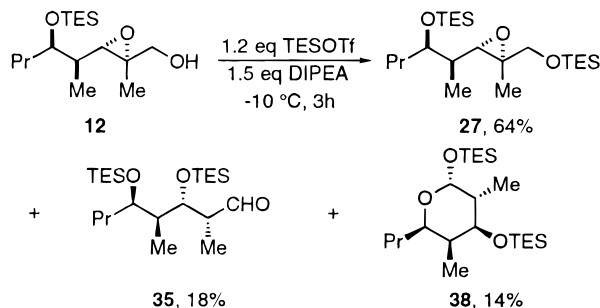
of the intermediacy of the aldol product **35** is based on experiments described below. The production of **38** could be

optimized by prolonged treatment of **27** with catalytic amounts of TESOTf (25 mol % TESOTf and 35 mol % DIPEA) to give the tetrahydropyran **38** in 74% yield, along with 4% of the aldol product **35**. The structure of **38** was assigned based on the coupling constants in its high-field proton NMR spectrum and NOE data, as shown. This represents the first example of



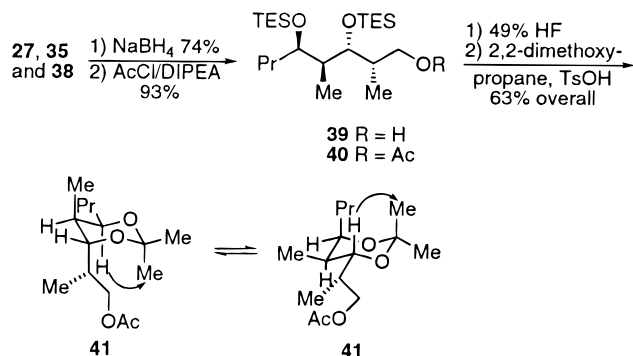
hydride migration to give products formed from this more complex non-aldol aldol process, e.g., those derived from 3,5-bis((trialkylsilyloxy)-2,4-dimethylalkanal, in a preparative sense, while at the same time demonstrating the lability of the triethylsilyl protecting group.

In an attempt to prepare more of the epoxy silyl ether **27** to study this reaction in greater depth, the epoxy alcohol **12** was silylated with TESOTf and DIPEA. When the reaction was carried out at -42 °C for 1 h, as stated previously, compound **27** was isolated in 94% yield. However, when the silylation was conducted at -10 °C for 3 h, the tetrahydropyran **38** was formed in 14% yield along with a 64% yield of **27**. However,



a new product was observed, namely the simple aldol product **35** in 18% isolated yield. This is the first direct observation of an aldol product being formed via hydride migration and silyl transfer on a homologated epoxy silyl ether. Here, the rate of formation for **35** is approximately equal to its rate of cyclization into **38**. One can therefore produce a homologated aldol product in good yield by this non-aldol aldol route.

Since the epoxide **12** was derived from an (*E*)-allylic alcohol, the new aldol compound **35** was assumed to be the *syn*-isomer, by analogy to our earlier work on the rearrangement to give simple aldol products.¹⁷ This was shown to be correct since the absolute and relative configuration was verified in the following ways. Not surprisingly, these compounds (**27**, **35**, and **38**) were unfortunately inseparable by chromatography. Instead, the mixture was reduced with sodium borohydride to give in 74% yield (based on **35**) the primary alcohol **39** which was separable from the recovered starting materials **27** and **38**. The alcohol **39** was then acetylated to give in 93% yield the acetate **40** which was converted in two steps (desilylation with HF followed by acetonide formation) to the cyclic ketal **41**. The key 2D NOESY correlations of **41** show both of the protons α to oxygen are 1,3-diaxial to different acetonide methyl groups (as shown), and therefore the four contiguous stereocenters in **35** are 2,3-*syn*, 3,4-*anti*, and 4,5-*syn*. Thus, the epoxidation that set the stereochemistry at both C₂ and C₃ occurred *anti* to the resident chirality in the reaction of (*E*)-allylic alcohol **10** with mCPBA, thereby securing the structure of epoxide **12**.



Conclusion

We have described a novel preparative route to a series of tetrahydrofuran-2-methanols bearing substituents at all four carbon atoms of the ring. These compounds are prepared by the following: (1) diastereoselective epoxidation of the (*E*)- and (*Z*)-allylic alcohols, **10** and **11**, to give any of the four diastereomeric epoxy alcohols **12–15**; (2) silylation of the alcohol to give the epoxy silyl ethers, **27–30**; (3) Lewis acid catalyzed rearrangement of the epoxy silyl ethers to give the desired products **31–33** and **36**. The use of these compounds in the synthesis of tetrahydrofuran-containing natural products will be reported in due course. Finally, rearrangement of the epoxy silyl ether **27** can be made to occur with hydride migration to give the 3,5-bis((trialkylsilyloxy)-2,4-dimethylalkanal **35** or its internally protected 1-(silyloxy)pyran **38** in good yield by an application of our non-aldol aldol process.

Experimental Section

General. All reactions were carried out under argon with the exclusion of moisture. Solvents were purified as follows: dichloromethane, hexamethylphosphoramide (HMPA), diisopropylethylamine (DIPEA), triethylamine (TEA), and collidine were distilled from calcium hydride and tetrahydrofuran (THF) was from sodium/benzophenone ketyl radical. Titanium tetrakisopropoxide, diisopropyl tartrate (DIPT), triethylsilyl trifluoromethanesulfonate (TESOTf), and *tert*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf), butyraldehyde, and chlorotriethylsilane (TESCl) were distilled before use. Chromatography was conducted on 230–400 mesh silica gel. Bis(2,2,2-trifluoroethyl)-ethyl 2-phosphonopropionate was made by a known procedure¹⁸ and dried by distillation. 18-Crown-6 was recrystallized from acetonitrile.

¹H and ¹³C nuclear magnetic resonance (NMR) were recorded on a Bruker AM360, AM500, ARX400, or ARX500 with tetramethylsilane (TMS) as an external standard. Enantiomeric purities were determined by integration of the diastereomeric ³¹P signals of the compounds prepared by reacting the substrates (ca. 0.05–0.1 mmol) in a sealed NMR tube with 750 μ L of a 10% C₆D₆ in benzene solution (0.22 M) of the chiral phosphonamide²² for 1 day at 25 °C. Other spectroscopic data were obtained as follows: IR spectra on Nicolet 510 FT-IR, Nicolet 205 FT-IR, or Perkin-Elmer series 1600 spectrometers; optical rotations on a Perkin-Elmer 243 Polarimeter; high-resolution mass spectra (MS) on a VG Autospec.

(2R,3R)-2-Methyl-3-propyloxiranemethanol (7). D-(–)-DIPT (311.0 mg, 1.33 mmol, 0.15 equiv) was weighed into a dry, three-neck, 25 mL round bottom flask equipped with 500 mg of powdered 4 Å molecular sieves. The flask was flushed with Ar and fitted with an overhead stirrer, and 10 mL of dichloromethane was added. The solution was cooled to –10 °C and treated successively with titanium tetrakisopropoxide (283 μ L, 0.950 mmol, 0.11 equiv) and 4.25 M *tert*-butyl hydroperoxide (3.1 mL, 13.13 mmol, 1.5 equiv). After 15 min,

the solution was cooled to –32 °C, and the allylic alcohol **6**²³ (999.4 mg, 8.752 mmol) in 2.5 mL of dichloromethane was added via syringe pump over 25 min. At the completion of the reaction (ca. 2 h), the cooling bath was removed, 3 mL of water was added, and the mixture was vigorously stirred until a clear solution resulted (2–6 h). The tartrate was then hydrolyzed by stirring the solution for an additional 3 h with 1 mL of 30% NaOH/saturated NaCl at which time two phases were apparent. The mixture was transferred into 2–15 mL centrifuge tubes and centrifuged, and the dichloromethane layer was drawn out via syringe. The aqueous phase was extracted in a like fashion (4 \times 5 mL each tube), and the combined dichloromethane extracts were stirred over MgSO₄, filtered through a pad of Celite, concentrated, and chromatographed (100 g SiO₂, 80% dichloromethane/20% ethyl acetate, *R_f* = 0.31) to yield 1.0701 g (8.220 mmol, 94%) of the epoxy alcohol **7** as a clear oil: [α] = +26.0 (*c* = 1.05, dichloromethane). ¹H NMR (CDCl₃, 360.130 MHz) δ : 3.66 (1H, dd, *J* = 12.2, 4.68 Hz), 3.54 (1H, dd, *J* = 12.3, 8.3 Hz), 3.02 (1H, t, *J* = 5.4 Hz), 2.06 (1H, dd, *J* = 8.3, 4.8 Hz), 1.6–1.4 (4H, m), 1.26 (3H, s), 0.96 (3H, t, *J* = 7.3 Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ : 65.4, 60.8, 60.0, 30.1, 19.7, 14.2, 13.9. IR (thin film): 3426 cm⁻¹. High-resolution EI MS (*m/z*): 130.0998, calcd for C₇H₁₄O₂ 130.0994. ³¹P NMR (10% C₆D₆ in benzene, 145.786 MHz) δ : 135.2 (3%), 137.2 (97%), 94% ee.

(2R,3R)-2-[[Triethylsilyloxy]methyl]-2-methyl-3-propyloxirane (8). The epoxy alcohol **7** (714.5 mg, 5.488 mmol) was weighed into a dry, 50 mL, one-neck round bottom flask equipped with a magnetic stirbar. The flask was flushed with Ar, treated successively with 30 mL of dichloromethane, DIPEA (1.4 mL, 8.232 mmol, 1.5 equiv), and 4-(dimethylamino)pyridine (DMAP, ca. 50 mg). TESCl (1.2 mL, 7.134 mmol) was added quickly, and a mildly exothermic reaction ensued. After 1 h of stirring, the mixture was poured onto 100 mL of petroleum ether and shaken with 50 mL of 0.2 M pH 7 phosphate buffer. The layers were separated, extracted with petroleum ether (2 \times 50 mL), washed with 0.2 M pH 7 phosphate buffer (1 \times 10 mL), brine (1 \times 10 mL), dried over MgSO₄, concentrated, and distilled via short path (bp = 72–75 °C at 0.09 mm Hg) to give 1.3055 g of the pure silyl epoxide **8** (5.323 mmol, 97%): [α] = +3.7 (*c* = 0.90, dichloromethane). ¹H NMR (CDCl₃, 500.135 MHz) δ : 3.58 (1H, d, *J* = 11.11 Hz), 3.52 (1H, d, *J* = 11.10 Hz), 2.80 (1H, t, *J* = 5.99 Hz), 1.60–1.40 (4 H, m), 1.24 (3H, s), 1.00–0.90 (9H, m), 0.60 (6H, q, *J* = 7.82 Hz). ¹³C NMR (CDCl₃, 90.55 MHz) δ : 67.7, 61.0, 60.8, 30.3, 19.8, 14.2, 13.9, 6.7, 4.3. IR (thin film): 1101 cm⁻¹. High-resolution EI MS (*m/z*): 215.1456, calcd for C₁₁H₂₃O₂Si 215.1467 (M – C₂H₅)⁺.

(2S,3R)-3-[(Triethylsilyloxy)-2-methylhexanal (9). Method i. To the epoxy alcohol **7** (105.0 mg, 0.807 mmol) in 5 mL of dichloromethane was added collidine (160 μ L, 1.210 mmol). The solution was then cooled to –23 °C and reacted with TESOTf (220 μ L, 0.968 mmol) for 45 min at which time the mixture was poured onto 40 mL of ether. The resulting solution was washed with water (2 \times 10 mL), saturated CuSO₄ (2 \times 5 mL), and 5% NaHCO₃ (2 \times 5 mL). Drying over MgSO₄ and removal of solvent yielded 190.8 mg (97%) of the pure aldehyde **9**.

Method ii. The silyl epoxide **7** (97.8 mg, 0.40 mmol) was dissolved in 1.3 mL of dichloromethane and treated successively with 34 mg of powdered 4 Å molecular sieves and DIPEA (21 μ L, 0.12 mmol, 0.30 equiv). The solution was cooled to –42 °C and treated with TESOTf (22 μ L, 0.10 mmol). After 60 min, the solution was poured onto ether (20 mL) and 10 mL of pH 5.5 buffer. The layers were separated, extracted with ether (3 \times 50 mL), washed with water (3 \times 1 mL), 0.2 M pH 7.0 buffer (2 \times 1 mL), and brine (1 \times 5 mL), dried over MgSO₄, and concentrated to yield 98.5 mg (100%) of the pure aldehyde **9**. ¹H NMR shows >50:1 diastereomeric excess (de).

Method iii. The silyl epoxide **8** (143.9 mg, 0.589 mmol) was dissolved in 5 mL of dichloromethane and cooled to –78 °C in an inert atmosphere. BF₃·Et₂O (72 μ L, 0.59 mmol, 1.00 equiv) was added, and the solution was stirred for 1 h. Saturated Na₂CO₃ (2 mL) was then added, and the cooling bath was removed. After the solution reached 25 °C, the layers were separated, and the aqueous layer was extracted with ether (4 \times 1 mL). The combined organic layers were washed with water (3 \times 1 mL), 0.2 M pH 7.0 buffer (2 \times 1 mL), and

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brine (2 × 1 mL), dried over MgSO₄, concentrated, and chromatographed (70 g SiO₂, 95% hexanes/1% TEA/4% ethyl acetate, *R_f* = 0.50) to yield 125.0 mg of the aldehyde **9** (0.506 mmol, 86%, 94:6 de).

Method iv. To a stirring solution of the silyl epoxide **8** (37.0 mg, 0.1514 mmol), 23 mg of molecular sieves, and DIPEA (2.6 μL, 15.1 μmol, 0.10 equiv) in 1.5 mL of dichloromethane at -42 °C was added 0.2 M TESOTf·B(OTf)₃ (37.8 μL, 7.6 μmol, 0.05 equiv), and the solution turned pale yellow. After the reaction was stirred for 10 min, 100 μL of DIPEA was added (color fades) followed by 2.0 mL of 0.2 M pH 7 phosphate buffer. The mixture was poured onto 5 mL of 5% NaHCO₃, the layers were separated, and the aqueous layer was extracted with ether (2 × 5 mL). The combined organic phase was washed with water (3 × 1 mL), 0.2 M pH 7.0 buffer (2 × 1 mL), and brine (1 × 1 mL), dried over MgSO₄, and concentrated to give 36.4 mg of the aldehyde **9** (95%+, >20:1 de): [α]_D = +36.6 (*c* = 1.09, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 9.71 (1H, d, *J* = 1.01 Hz), 4.06 (1H, dt, *J* = 10.98, 3.65 Hz), 2.37 (1H, qdd, *J* = 6.96, 3.65, 1.00 Hz), 1.5–1.15 (4H, m), 0.99 (3H, d, *J* = 6.96 Hz), 0.90–0.80 (9H, m), 0.52 (9H, q, *J* = 7.83 Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ: 205.4, 72.0, 51.4, 36.9, 19.0, 14.1, 7.7, 6.8, 5.1. IR (thin film): 1728 cm⁻¹. High-resolution EI MS (*m/z*): 215.1447, calcd for C₁₁H₂₃O₂Si 215.1467 (M - C₂H₅)⁺.

(4R,5R)-(E)-5-[(Triethylsilyloxy)-2,4-dimethyloct-2-en-1-ol (10). A freshly prepared solution of the aldehyde **9** (168.0 mg, 0.678 mmol) in 5 mL of dichloromethane was refluxed with (1-(ethoxycarbonyl)-ethylidene)triphenylphosphorane (299.0 mg, 0.743 mmol) for 5 d. The solution was then cooled and filtered through a 2 in. plug of SiO₂ (with dichloromethane rinse) yielding 215.0 mg of ethyl (4R,5R)-(E)-5-[(triethylsilyloxy)-2,4-dimethyloct-2-enoate (0.679 mmol, quantitative): [α]_D = +8.25 (*c* = 1.89, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 6.67 (1H, d, *J* = 12.74 Hz), 4.18 (2H, m), 3.58 (1H, m), 2.56 (1H, m), 1.83 (3H, s), 1.39 (2H, m), 1.29 (3H, t, *J* = 8.91 Hz), 1.30–1.20 (2H, m), 0.76 (9H, t, *J* = 7.86 Hz), 0.73 (3H, d, *J* = 7.07 Hz), 0.72 (3H, t, *J* = 7.07 Hz), 0.48 (6H, q, *J* = 7.96 Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 168.2, 145.1, 126.6, 75.2, 60.3, 38.3, 37.5, 18.2, 14.7, 14.12, 14.10, 12.3, 5.1, 6.7. IR (thin film): 1714 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 346.2787, calcd for C₁₈H₄₀NO₃-Si 346.2777 (M + NH₄)⁺; 329.2502, calcd for C₁₈H₃₇O₃Si 329.2512 (M + H)⁺.

This unsaturated ester (230.0 mg, 0.700 mmol) was dissolved in 3.5 mL of ether and cooled to 0 °C. A 1.0 M solution of LiAlH₄ (1.4 mL, 1.400 mmol) was then added, and the temperature of the reaction was allowed to warm to 25 °C over 2 h. Ethyl acetate was added to quench excess reducing agent (2 × 250 μL, cautiously added at first), followed by 3 mL of half-saturated Rochelle's salt. After 3 h of vigorous stirring, the solution was poured onto 5 mL of water and 5 mL of ether. The layers were separated, and the aqueous phase was extracted with ether (3 × 3 mL). The combined organic layers were washed successively with water (2 × 1 mL), 5% NaHCO₃ (1 × 1 mL), and brine (1 × 2 mL). Drying over MgSO₄ and removal of solvent yielded 199.3 mg of material which was chromatographed (30 g SiO₂, 5% ethyl acetate/95% dichloromethane) affording 149.1 mg of the allylic alcohol **10** (0.493 mmol, 70%): [α]_D = +0.65 (*c* = 1.23, dichloromethane). ¹H NMR (CDCl₃, 400.132 MHz) δ: 5.25 (1H, dq, *J* = 9.68, 1.24 Hz), 4.00 (2H, s), 3.50 (1H, m), 2.49 (1H, m), 1.66 (3H, d, *J* = 1.35 Hz), 1.40–1.20 (5H, m), 0.95 (9H, t, *J* = 7.98 Hz), 0.92 (3H, d, *J* = 6.90 Hz), 0.88 (3H, t, *J* = 7.11 Hz), 0.59 (6H, q, *J* = 7.63 Hz). ¹³C NMR (CDCl₃, 100.625 MHz) δ: 133.8, 129.7, 76.2, 69.1, 37.4, 37.2, 18.4, 16.2, 14.4, 13.9, 7.0, 5.2. IR (thin film): 3325.7 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 287.2400, calcd for C₁₆H₃₅O₂Si 287.2406 (M + H)⁺; 304.2662, calcd for C₁₆H₃₈NO₂Si 304.2672 (M + NH₄)⁺.

(4R,5R)-(Z)-5-[(Triethylsilyloxy)-2,4-dimethyloct-2-en-1-ol (11). Ethyl bis(2,2,2-trifluoroethyl)-2-phosphonopropionate (385.4 mg, 1.113 mmol) and 18-crown-6 (1.43 g, 5.410 mmol) in 22 mL of THF was cooled to 0 °C and treated with potassium hexamethyldisilazane (KHMDs) (218.1 mg, 1.100 mmol). After 30 min, the solution was further cooled to -78 °C, when the aldehyde **9** (245.4 mg, 1.004 mmol) in 2.5 mL THF was added dropwise (with 3–0.25 mL rinses). Stirring was continued for 18 h, when the cooling bath was removed and 10 mL of saturated NH₄Cl was added. After reaching 25 °C, the solution was poured onto 25 mL of water and 25 mL of 50/50 pentane/ether.

The layers were separated, and the water layer was extracted with 50/50 pentane/ether (3 × 10 mL). The combined organic extracts were washed with water (3 × 2 mL), 5% NaHCO₃ (1 × 5 mL), and brine (1 × 5 mL), dried over MgSO₄, and freed of solvent to afford 320.0 mg of ethyl (4R,5R)-(Z)-5-[(triethylsilyloxy)-2,4-dimethyloct-2-enoate (0.974 mmol, quantitative): [α]_D = -34.4 (*c* = 1.41, dichloromethane). ¹H NMR (CDCl₃, 360.130 MHz) δ: 5.80 (1H, d, *J* = 10.05 Hz), 4.14 (1H, d, *J* = 7.17 Hz), 4.10 (1H, d, *J* = 7.17 Hz), 3.55 (1H, td, *J* = 6.12, 4.34 Hz), 3.14 (1H, m), 1.83 (3H, s), 1.50–1.30 (4H, m), 1.22 (3H, t, *J* = 7.14 Hz), 0.879 (9H, t, *J* = 7.90 Hz), 0.882 (3H, d, *J* = 6.76 Hz), 0.83 (3H, t, *J* = 7.04 Hz), 0.51 (6H, q, *J* = 7.96 Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ: 168.1, 146.3, 125.9, 75.6, 60.0, 37.8, 37.4, 20.9, 18.6, 14.3, 14.2, 6.9, 5.1. IR (thin film): 1717 cm⁻¹. High-resolution EI MS (*m/z*): 299.2052, calcd for C₁₆H₃₁O₃Si 299.2042 (M - C₂H₅)⁺.

This unsaturated ester (170.0 mg, 0.517 mmol) was dissolved in 3 mL of toluene and cooled to 0 °C. A 3.4 M solution of Red-Al (Aldrich, 230 μL, 0.776 mmol) was added dropwise, and the mixture was reacted at this temperature for 1 h. The cooling bath was removed, and after reaching 25 °C, the reaction was quenched initially with ethyl acetate (250 μL added cautiously) followed by 3 mL of half-saturated Rochelle's salt. After 1 h of stirring, the biphasic mixture was poured onto 5 mL of water and 10 mL of ether. The layers were separated, extracted with ether (3 × 10 mL), and washed with water (2 × 1 mL), 5% NaHCO₃ (1 × 1 mL), and brine (1 × 1 mL). The solution was dried over MgSO₄ and freed of solvent, yielding 156.0 mg of crude material. Chromatography (35 g SiO₂, 3% ethyl acetate/97% dichloromethane) afforded 140 mg of the allylic alcohol **11** (0.489 mmol, 94%): [α]_D = +21.1 (*c* = 2.44, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 5.10 (1H, br d, *J* = 9.86 Hz), 4.13 (1H, d, *J* = 11.78 Hz), 3.89 (1H, d, *J* = 11.53 Hz), 3.48 (1H, m), 2.55 (1H, m), 2.10 (1H, br), 1.81 (3H, d, *J* = 1.41 Hz), 1.40–1.10 (4H, m), 0.95 (9H, t, *J* = 8.07 Hz), 0.93 (3H, d, *J* = 7.42 Hz), 0.87 (3H, t, *J* = 7.02 Hz), 0.62 (6H, m). ¹³C NMR (CDCl₃, 90.560 MHz) δ: 135.1, 131.3, 77.0, 61.6, 38.1, 36.1, 22.1, 19.1, 17.7, 14.4, 6.9, 5.0. IR (thin film): 3339 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 287.2409, calcd for C₁₆H₃₅O₂Si 287.2406 (M + H)⁺.

(2S,3S)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-methyloxiranemethanol (12). The allylic alcohol **10** (207.0 mg, 0.722 mmol) and K₂HPO₄ (500 mg, 2.167 mmol) in 5 mL of dichloromethane at -5 °C was treated with mCPBA (65% purity, 250.0 mg, 0.939 mmol) in 1 mL of dichloromethane. After the reaction was stirred for 1 h, 5% NaHCO₃ was added (2 mL) and the solution was poured onto 10 mL of ether. The layers were separated, and the aqueous phase was extracted with ether (2 × 2 mL). The combined extracts were washed with 5% NaHCO₃ (2 × 1 mL) and brine (1 × 2 mL), dried over MgSO₄, and concentrated to give 200.0 mg of the crude mixture of epoxy alcohols **12** and **13**. ¹H NMR analysis of the crude material indicated ca. 15:1 diastereoselectivity. Chromatography (30 g SiO₂, 5% ethyl acetate/95% dichloromethane) yielded 179.8 mg of the pure epoxy alcohol **12** (0.594 mmol, 82%): [α]_D = -18.8 (*c* = 1.05, dichloromethane). ¹H NMR (CDCl₃, 400.132 MHz) δ: 3.82 (1H, td, *J* = 6.20, 3.78 Hz), 3.67 (1H, dd, *J* = 12.14 Hz), 3.55 (1H, dd, *J* = 12.16 Hz), 2.96 (1H, d, *J* = 9.53 Hz), 1.80 (1H, br), 1.55–1.40 (3H, m), 1.4–1.2 (2H, m), 1.29 (3H, s), 0.96 (9H, t, *J* = 7.94 Hz), 0.903 (3H, t, *J* = 7.33 Hz), 0.884 (3H, d, *J* = 6.93 Hz), 0.61 (6H, q, *J* = 7.73 Hz). ¹³C NMR (CDCl₃, 100.625 MHz) δ: 73.1, 65.6, 62.0, 60.9, 37.6, 36.8, 18.6, 14.4, 14.2, 10.1, 7.0, 5.2. IR (thin film): 3447 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 303.2284, calcd for C₁₆H₃₄O₃Si 303.2273.

(2R,3R)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-methyloxiranemethanol (13). To a solution of the allylic alcohol **10** (119.0 mg, 0.415 mmol) in 3 mL of dichloromethane cooled to -42 °C was added titanium tetrakispropoxide (185 μL, 0.623 mmol). After 15 min, *tert*-butyl hydroperoxide (5.29 M, 94 μL, 0.498 mmol) was added, and the solution was stirred for 9 h at this temperature and then for 12 h at -23 °C. The reaction was stopped with the addition of 2 mL of half-saturated Rochelle's salt with removal of the cooling bath. Stirring was continued at ambient temperature for an additional 2 h, when the solution was poured onto 15 mL of ether. The layers were separated, and the aqueous phase was extracted with ether (3 × 3 mL). The combined ether layers were washed with water (2 × 1 mL) and

brine (1 × 2 mL), dried over MgSO₄, and freed of solvent yielding 125.6 mg of the crude mixture of epoxy alcohols **12** and **13**. ¹H NMR analysis indicated a 1:7 mixture of diastereomers with ca. 7% starting material. Chromatography (30 g SiO₂, 5% ethyl acetate/95% dichloromethane) afforded 90.6 mg of the pure epoxy alcohol **13** (0.299 mmol, 77% based on recovered starting material) ([α] = -0.20 (c = 0.97, dichloromethane)) along with 14.0 mg of **12** (46.2 μmol, 11%) and 7.0 mg of **10**. ¹H NMR (CDCl₃, 500.132 MHz) δ: 3.69 (1H, dd, *J* = 12.38, 4.35 Hz), 3.66 (1H, m), 3.56 (1H, dd, *J* = 12.14, 8.37 Hz), 2.97 (1H, d, *J* = 9.44 Hz), 1.68 (1H, br dd, *J* = 4.58, 8.43 Hz), 1.58–1.45 (2H, m), 1.43–1.35 (1H, m), 1.33–1.20 (2H, m), 1.30 (3H, s), 1.07 (3H, d, *J* = 6.75 Hz), 0.96 (9H, t, *J* = 7.96 Hz), 0.91 (3H, t, *J* = 7.30 Hz), 0.59 (6H, q, *J* = 7.68 Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 73.4, 65.3, 63.5, 61.7, 37.2, 36.9, 18.8, 14.6, 14.1, 11.5, 6.8, 5.1. IR (thin film): 3455 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 303.2360, calcd for C₁₆H₃₅O₃Si 303.2355 (M + H)⁺.

(2S,3R)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-methyloxiranemethanol (14). Allylic alcohol **11** (149.0 mg, 0.520 mmol) was dissolved in 3 mL of dichloromethane, treated with K₂HPO₄ trihydrate (356 mg, 1.560 mmol), and cooled to -5 °C. A solution of mCPBA (65% purity, 0.624 mmol) in 1.5 mL of dichloromethane was added dropwise, and the reaction was stirred for 30 min at which time 1 mL of saturated Na₂S₂O₃ was added and the cooling bath was removed. After 1 h, the mixture was poured onto 25 mL of ether and 8 mL of water. The layers were separated, and the aqueous layer was extracted with ether (3 × 5 mL). The combined extracts were washed with 5% NaHCO₃ (1 × 2 mL) and brine (1 × 3 mL). Further drying over MgSO₄, followed by removal of solvent, gave ca. 150 mg of the crude epoxy alcohols **14** and **15** as a >15:1 mixture of diastereomers (by ¹H NMR). Chromatography (50 g SiO₂, 6% ethyl acetate/94% dichloromethane) afforded 130.3 mg of the pure epoxy alcohol **14** (0.4307 mmol, 83%): [α] = +13.0 (c = 1.35, dichloromethane). ¹H NMR (CDCl₃, 360.130 MHz) δ: 3.80 (1H, td, *J* = 6.32, 3.65 Hz), 3.69 (1H, d, *J* = 11.73 Hz), 3.64 (1H, d, *J* = 11.73 Hz), 2.79 (1H, d, *J* = 9.55 Hz), 1.70 (1H, br), 1.55–1.45 (3H, m), 1.39 (3H, s), 1.35–1.20 (2H, m), 0.96 (9H, t, *J* = 7.96 Hz), 0.900 (3H, d, *J* = 6.90 Hz), 0.896 (3H, t, *J* = 7.33 Hz), 0.62 (6H, q, *J* = 7.77 Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ: 73.0, 67.0, 64.0, 60.9, 37.5, 36.4, 20.5, 18.5, 14.3, 10.3, 6.9, 5.2. IR (thin film): 3449 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 303.2354, calcd for C₁₆H₃₅O₃Si 303.2355 (M + H)⁺.

(2R,3S)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-methyloxiranemethanol (15). To a stirring solution of the allylic alcohol **11** (97.0 mg, 0.3385 mmol) and titanium tetraisopropoxide (151 μL, 0.508 mmol) cooled to -42 °C was added *tert*-butyl hydroperoxide (5.29 M, 96 μL, 0.508 mmol). Stirring was continued at this temperature for 8 h and then for 13 h at -23 °C. The reaction stopped by the addition of 2 mL of half-saturated Rochelle's salt and stirring at 25 °C for 2 h. The resulting mixture was poured onto 10 mL of ether, the layers were separated, and the aqueous layer was extracted with ether (2 × 2 mL). The combined organic extracts were washed with water (3 × 1 mL) and brine (1 × 2 mL), dried over MgSO₄, and freed of solvent yielding 103.2 mg of the crude mixture of epoxy alcohols **14** and **15**. ¹H NMR indicated a 1:6.5 diastereoselectivity. Chromatography (35 g of SiO₂, 5% ethyl acetate/95% dichloromethane) yielded 80.0 mg of the pure epoxy alcohol **15** (0.264 mmol, 78%) and 12.1 mg of the other diastereomer **14** (0.041 mmol, 12%): [α] = +29.1 (c = 2.28, dichloromethane). ¹H NMR (CDCl₃, 360.130 MHz) δ: 3.62 (1H, br), 3.58 (1H, m), 3.46 (1H, d, *J* = 10.18 Hz), 2.57 (1H, d, *J* = 9.51 Hz), 1.62 (1H, m), 1.50–1.30 (3H, m), 1.40 (3H, s), 1.30–1.15 (1H, m), 1.08 (3H, d, *J* = 7.04 Hz), 0.94 (9H, t, *J* = 7.91 Hz), 0.90 (3H, t, *J* = 7.00 Hz), 1.00–0.90 (1H, m), 0.61 (6H, q, *J* = 7.91 Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ: 75.8, 66.6, 64.5, 61.9, 39.8, 35.3, 20.5, 19.7, 15.5, 14.2, 6.8, 6.7. IR (thin film): 3451 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 303.2360, calcd for C₁₆H₃₅O₃Si 303.2355 (M + H)⁺.

(2S,3S)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-[(triethylsilyloxy)methyl]-2-methyloxirane (27). To a solution of the epoxy alcohol **12** (50.0 mg, 0.165 mmol) and DIPEA (43 μL, 0.248 mmol) in 3 mL of dichloromethane cooled to -42 °C was added TESOTf (45 μL, 0.198 mmol). After the reaction was stirred for 1 h, 50 μL of dry MeOH was added and the cooling bath was removed. The mixture was filtered through a plug of SiO₂ (1 g in a pipet) with

a dichloromethane rinse. Removal of solvent yielded 64.8 mg of the pure epoxy silyl ether **27** (0.155 mmol, 94%): [α] = -6.2 (c = 1.01, dichloromethane). ¹H NMR (CDCl₃, 400.132 MHz) δ: 3.83 (1H, td, *J* = 6.29, 3.53 Hz), 3.55 (2H, s), 2.80 (1H, d, *J* = 9.49 Hz), 1.50–1.20 (5H, m), 1.27 (3H, s), 0.96 (9H, t, *J* = 7.73 Hz), 0.95 (9H, t, *J* = 7.75 Hz), 0.90 (3H, t, *J* = 7.38 Hz), 0.88 (3H, d, *J* = 6.92 Hz), 0.62 (6H, q, *J* = 7.75 Hz), 0.60 (6H, q, *J* = 7.94 Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 73.0, 67.8, 63.0, 61.0, 37.8, 36.9, 18.6, 14.4, 14.2, 9.9, 7.0, 6.7, 5.2, 4.4. IR (thin film): 2958 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 417.3179, calcd for C₂₂H₄₉O₃Si₂ 417.3220 (M + H)⁺.

(2S,3R)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-[(triethylsilyloxy)methyl]-2-methyloxirane (28). To a solution of the epoxy alcohol **13** (69.0 mg, 0.228 mmol), DIPEA (60 μL, 0.342 mmol), and ca. 2 mg of DMAP in 1 mL of dichloromethane was added TESCI (46 μL, 0.274 mmol). After 15 min, the solution was diluted to 15 mL with ether and shaken with 1 mL of 0.2 M pH 5.5 phosphate buffer. The layers were separated, and the organic phase was washed with water (2 × 1 mL), 0.2 M pH 7 phosphate buffer (1 × 1 mL), and brine (1 × 2 mL). The extracts were dried over MgSO₄, concentrated, and filtered through a plug of SiO₂ (pipet, dichloromethane rinse). Removal of solvent yielded 85.0 mg of the pure epoxy silyl ether **28** (0.204 mmol, 89%): [α] = -11.6 (c = 2.54, dichloromethane). ¹H NMR (CDCl₃, 360.130 MHz) δ: 3.80 (1H, td, *J* = 6.10, 3.92 Hz), 3.63 (1H, d, *J* = 10.60 Hz), 3.59 (1H, d, *J* = 10.63 Hz), 2.69 (1H, d, *J* = 9.20 Hz), 1.60–1.20 (5H, m), 1.24 (3H, s), 0.904 (9H, t, *J* = 7.19 Hz), 0.896 (9H, t, *J* = 8.03 Hz), 0.86 (3H, d, *J* = 7.07 Hz), 0.84 (3H, t, *J* = 7.33 Hz), 0.56 (6H, q, *J* = 8.06 Hz), 0.55 (6H, q, *J* = 7.20 Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ: 73.2, 66.4, 64.6, 60.8, 37.6, 36.7, 20.5, 18.5, 14.3, 10.4, 7.0, 6.7, 5.2, 4.3. IR (thin film): 2957 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 417.3227, calcd for C₂₂H₄₉O₃Si₂ 417.3220 (M + H)⁺; 387.2445, calcd for C₂₀H₄₃O₃Si₂ 387.2751 (M - C₂H₅)⁺.

(2R,3R)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-[(triethylsilyloxy)methyl]-2-methyloxirane (29). As in the preparation of **28**, the epoxy alcohol **14** (89.0 mg, 0.294 mmol), DIPEA (77 μL, 0.441 mmol), TESCI (60 μL, 0.353 mmol), and ca. 0.5 mg of DMAP yielded 108.5 mg of the pure epoxy silyl ether **29** (0.260 mmol, 89%) after chromatography: [α] = -3.58 (c = 2.12, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 3.65 (1H, td, *J* = 6.29, 3.92 Hz), 3.59 (1H, d, *J* = 11.00 Hz), 3.54 (1H, d, *J* = 11.00 Hz), 2.77 (1H, d, *J* = 9.41 Hz), 1.55–1.45 (2H, m), 1.45–1.35 (1H, m), 1.35–1.20 (2H, m), 1.29 (3H, s), 1.05 (3H, d, *J* = 6.78 Hz), 0.96 (18H, t, *J* = 7.97 Hz), 0.90 (3H, t, *J* = 7.30 Hz), 0.60 (6H, q, *J* = 7.92 Hz), 0.59 (6H, q, *J* = 7.81 Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 73.6, 67.7, 64.4, 61.8, 37.2, 37.0, 18.7, 14.5, 14.1, 11.7, 6.8, 6.6, 5.1, 4.2. IR (thin film): 2960 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 387.2751, calcd for C₂₀H₄₃O₃Si₂ 387.2751 (M - C₂H₅)⁺.

(2R,3S)-3-[(1R,2R)-2-[(Triethylsilyloxy)-1-methylpentyl]-2-[(triethylsilyloxy)methyl]-2-methyloxirane (30). To a solution of the epoxy alcohol **15** (80.0 mg, 0.264 mmol) and DIPEA (69 μL, 0.397 mmol) in 2 mL of dichloromethane was added TESCI (53 μL, 0.317 mmol). After the mixture was stirred for 1 h, it was poured onto 20 mL of ether and shaken with 1 mL of 2.0 M pH 7.0 buffer. The organic layer was further washed with water (2 × 1 mL) and brine (1 × 2 mL), dried over MgSO₄, and concentrated, affording 104.1 mg of crude material. Chromatography (25 g SiO₂, 35% dichloromethane/65% hexanes) yielded 93.5 mg of the pure epoxy silyl ether **30** (0.224 mmol, 85%): [α] = -6.76 (c = 2.13, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 3.78 (1H, ddd, *J* = 7.36, 5.96, 2.86 Hz), 3.65 (1H, d, *J* = 10.70 Hz), 3.61 (1H, d, *J* = 10.71 Hz), 2.75 (1H, d, *J* = 9.46 Hz), 1.50–1.30 (3H, m), 1.30–1.20 (2H, m), 1.36 (3H, s), 1.04 (3H, d, *J* = 6.72 Hz), 0.97 (9H, t, *J* = 7.94 Hz), 0.96 (9H, t, *J* = 7.90 Hz), 0.90 (3H, t, *J* = 7.29 Hz), 0.61 (12H, q, *J* = 7.92 Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 73.2, 68.1, 64.6, 61.6, 37.5, 36.8, 20.2, 18.8, 14.2, 10.8, 6.9, 6.6, 5.1, 4.2. IR (thin film): 2958 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 387.2743, calcd for C₂₀H₄₃O₃Si₂ 387.2751 (M - C₂H₅)⁺.

(2S,3R,4S,5R)-2,4-Dimethyl-5-propyl-3-[(triethylsilyloxy)-2-[(triethylsilyloxy)methyl]tetrahydrofuran (31). To a 5 mL conical vial and spin vane was weighed 2,5-di-*tert*-butyl-4-methylpyridine (25.5 mg, 0.124 mmol) and the bis-silyl ether **16** (23.7 mg, 95.5 μmol). Dichloromethane (1 mL) was added, and the solution cooled to -78

°C; TESOTf (23.7 μ L, 0.105 mmol) was then added. After the reaction was stirred for 3.5 h, 11 μ L of dry 2-propanol was added, and the cooling bath was removed. The mixture was poured onto 20 mL of ether and shaken with 1 mL of 0.2 M pH 5.5 phosphate buffer. The organic layer was further washed with water (2 \times 1 mL), 0.2 M pH 7.0 phosphate buffer (1 \times 2 mL), and brine (1 \times 3 mL). The ether layer was dried over MgSO₄, concentrated, and chromatographed (25 g SiO₂, 25% dichloromethane/75% hexanes) affording 36.2 mg of the pure bis-silyloxy tetrahydrofuran **31** (86.8 μ mol, 91%): $[\alpha]_D^{25} = +13.0$ ($c = 0.74$, dichloromethane). ¹H NMR (CD₂Cl₂, 500.132 MHz) δ : 3.98 (1H, ddd, $J = 8.73, 6.29, 4.90$ Hz), 3.94 (1H, d, $J = 4.49$ Hz), 3.48 (1H, d, $J = 10.15$ Hz), 3.45 (1H, d, $J = 10.14$ Hz), 2.09 (1H, m), 1.50–1.20 (4H, m), 1.09 (3H, s), 1.01 (9H, t, $J = 7.94$ Hz), 1.00 (9H, t, $J = 7.94$ Hz), 0.96 (3H, d, $J = 7.31$ Hz), 0.95 (3H, t, $J = 7.19$ Hz), 0.65 (12H, q, $J = 7.96$ Hz). ¹³C NMR (CD₂Cl₂, 125.767 MHz) δ : 83.9, 79.9, 77.0, 68.0, 44.5, 33.0, 19.6, 18.0, 13.8, 12.1, 6.5, 6.4, 4.7, 4.1. IR (thin film): 2957 cm⁻¹. High-resolution CI (NH₃) MS (m/z): 417.3221, calcd for C₂₂H₄₉O₃Si₂ 417.3220 (M + H)⁺.

(2S,3S,4S,5R)-2,4-Dimethyl-5-propyl-3-[(triethylsilyloxy)-2-[(triethylsilyloxy)methyl]tetrahydrofuran (32). To a solution of the bis-silyl ether **30** (92.0 mg, 0.221 mmol) in 2.2 mL of dichloromethane cooled to -78 °C were added trimethylaluminum (2.0 M in toluene, 27.5 μ L, 55.0 μ mol) and TESOTf (10 μ L, 44.1 μ mol). After the reaction was stirred for 3 h, DIPEA (52 μ L, 0.300 mmol) was added followed by 2-propanol (50 μ L), and the cooling bath was removed. The solution was then poured onto 20 mL of ether and shaken with 1 mL of 0.2 M pH 7.0 buffer. The organic phase was further washed with buffer (2 \times 1 mL) and brine (1 \times 2 mL). Drying over MgSO₄ and removal of solvent yielded 90.1 mg of crude material. Chromatography (25 g SiO₂, 20% dichloromethane/80% hexanes) afforded 62.6 mg of the pure bis-silyloxy tetrahydrofuran **32** (0.151 mmol, 68%): $[\alpha]_D^{25} = +16.4$ ($c = 0.99$, dichloromethane). ¹H NMR (CD₂Cl₂, 500.132 MHz) δ : 3.95 (1H, dt, $J = 7.82, 5.38$ Hz), 3.79 (1H, d, $J = 11.06$ Hz), 3.67 (1H, d, $J = 3.46$ Hz), 3.41 (1H, d, $J = 11.01$ Hz), 1.98 (1H, qdd, $J = 7.33, 5.40, 3.43$ Hz), 1.45–1.20 (4H, m), 0.93 (18H, t, $J = 7.93$ Hz), 0.898 (3H, d, $J = 7.14$ Hz), 0.896 (3H, t, $J = 7.37$ Hz), 0.77 (3H, s), 0.58 (6H, q, $J = 8.17$ Hz), 0.57 (6H, q, $J = 8.02$ Hz). ¹³C NMR (CD₂Cl₂, 125.767 MHz) δ : 85.9, 82.9, 77.1, 64.9, 45.1, 33.2, 23.2, 19.5, 13.9, 12.3, 6.5, 6.4, 4.7, 4.2. IR (thin film): 2958 cm⁻¹. High-resolution CI (NH₃) MS (m/z): 417.3222, calcd for C₂₂H₄₉O₃Si₂ 417.3220 (M + H)⁺.

(2R,3R,4S,5R)-2,4-Dimethyl-5-propyl-3-[(triethylsilyloxy)-2-[(triethylsilyloxy)methyl]tetrahydrofuran (33) and (2R,3R,4S,5R)-2,4-Dimethyl-5-propyl-3-[(triethylsilyloxy)methyl]tetrahydrofuran-2-methanol (34). To a solution of the bis-silyl ether **29** (24.7 mg, 59.2 μ mol) in 300 μ L dichloromethane cooled to -23 °C was added trimethylaluminum (Aldrich, 2.0 M in toluene, 47.4 μ L, 47.4 μ mol) and TESOTf (10 μ L, 44.2 μ mol). After 1 h, 2 mL of half-saturated Rochelle's salt was added and the cooling bath removed. Stirring was continued at 25 °C for an additional 1 h, then the solution was poured onto 2 mL of ether. The layers were separated, and the aqueous layer extracted with ether (3 \times 1 mL). The organic phase was washed with water (3 \times 0.5 mL), brine (1 \times 2 mL), dried over MgSO₄, and freed of solvent to give 25 mg of crude material. Chromatography (5 g of SiO₂, gradient from 5% ethyl acetate/95% dichloromethane to 10% ethyl acetate/90% dichloromethane) afforded 16.8 mg of the pure bis-silyloxy tetrahydrofuran **33** (40.3 μ mol, 68%, $R_f = 0.82$ in 10% ethyl acetate/90% dichloromethane) and 4.1 mg of the pure tetrahydrofuran-2-methanol **34** (13.6 μ mol, 23%, $R_f = 0.20$ in 10% ethyl acetate/90% dichloromethane).

Spectroscopic data for **33**. ¹H NMR (CDCl₃, 500.132 MHz) δ : 4.00 (1H, d, $J = 5.77$ Hz), 3.85 (1H, ddd, $J = 9.09, 5.91, 5.83$ Hz), 3.63 (1H, d, $J = 10.46$ Hz), 3.54 (1H, d, $J = 10.46$ Hz), 2.28 (1H, m), 1.60–1.50 (1H, m), 1.50–1.40 (1H, m), 1.30–1.20 (2H, m), 1.20 (3H, s), 0.964 (9H, t, $J = 8.08$ Hz), 0.960 (9H, t, $J = 7.95$ Hz), 0.90 (3H, t, $J = 7.28$ Hz), 0.89 (3H, d, $J = 7.20$ Hz), 0.617 (6H, q, $J = 7.81$ Hz), 0.608 (6H, q, $J = 7.95$ Hz). ¹³C NMR (coupled, CDCl₃, 125.767 MHz) δ : 83.3 (s), 81.2 (d, $J = 142.1$ Hz), 78.7 (d, $J = 141.2$ Hz), 67.2 (t, $J = 142.0$ Hz), 40.8 (d, $J = 126.8$ Hz), 33.6 (t, $J = 124.4$ Hz), 22.8 (q, $J = 125.6$ Hz), 19.5 (t, $J = 127.2$ Hz), 14.2 (q, $J = 123.0$ Hz), 8.3 (q, $J = 126.4$ Hz), 6.79 (m), 6.72 (m), 4.69 (m), 4.33 (m).

Spectroscopic data for **34**. ¹H NMR (CDCl₃, 500.132 MHz) δ : 4.19

(1H, d, $J = 6.81$), 3.83 (1H, dt, $J = 7.71, 5.20$ Hz), 3.57 (1H, d, $J = 11.69$ Hz), 3.53 (1H, d, $J = 11.67$ Hz), 2.50 (1H, br), 2.19 (1H, m), 1.58 (1H, m), 1.42 (2H, m), 1.30 (1H, m), 1.20 (3H, s), 0.98 (9H, t, $J = 7.98$ Hz), 0.93 (3H, t, $J = 7.22$ Hz), 0.92 (3H, d, $J = 7.28$ Hz), 0.64 (6H, q, $J = 7.99$ Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ : 82.5, 81.7, 77.4, 67.7, 41.4, 32.6, 23.3, 19.4, 14.1, 7.3, 6.6, 4.5.

(2R,3S,4S,5R)-2,4-Dimethyl-5-propyl-3-[(triethylsilyloxy)-2-[(triethylsilyloxy)methyl]tetrahydrofuran (36), (4R,5R)-2,4-Dimethyl-5-[(triethylsilyloxy)-2-octenal (37), and (2R,3R,4S,5S,6R)-(4H)-2,4-Bis[(triethylsilyloxy)-3,5-dimethyl-6-propyltetrahydropyran (38). To a solution of the bis-silyl ether **27** (62.0 mg, 0.149 mmol) in 1.5 mL of dichloromethane cooled to -42 °C were added trimethylaluminum (2.0 M in toluene, 18.6 μ L, 37.2 μ mol) and TESOTf (8.4 μ L, 37.2 μ mol). After the solution was stirred for 2.5 h at this temperature, 100 μ L of DIPEA was added, followed by 1 mL of Rochelle's salt with removal of the cooling bath. The layers were separated, and the aqueous layer was extracted with dichloromethane (4 \times 1 mL). The combined extracts were diluted with 20 mL of ether, washed with water (2 \times 1 mL), 5% NaHCO₃ (1 \times 2 mL), and brine (1 \times 2 mL), dried over MgSO₄, and concentrated affording 48.8 mg (58% molar recovery). ¹H NMR analysis of the crude mixture showed it to contain 41% of the tetrahydrofuran **36**, 23% of the enal **37**, and 36% of the tetrahydropyran **38**, which could not be separated by chromatography. Spectroscopic data for **38** is given later.

Spectroscopic data of **36**. ¹H NMR (CDCl₃, 500.132 MHz) δ : 4.33 (1H, d, $J = 6.20$ Hz), 3.94 (1H, ddd, $J = 7.75, 5.62, 2.13$ Hz), 3.41 (2H, s), 2.20 (1H, m), 1.50–1.20 (4H, m), 1.10 (3H, s), 1.00–0.85 (24H, m), 0.65–0.55 (12H, m).

Spectroscopic data of **37**. ¹H NMR (CDCl₃, 360.130 MHz) δ : 10.10 (1H, s), 6.42 (1H, dd, $J = 10.93, 1.34$ Hz), 3.60 (1H, m), 2.75 (1H, m), 1.78 (3H, d, $J = 1.33$ Hz), 1.60–1.20 (4H, m), 1.06 (3H, d, $J = 6.70$ Hz), 0.95 (9H, t, $J = 7.95$ Hz), 0.89 (3H, t, $J = 7.13$ Hz), 0.59 (6H, q, $J = 7.85$ Hz). ¹³C NMR (CDCl₃, 90.560 MHz) δ : 188.4, 149.8, 132.1, 72.9, 33.9, 33.1, 15.4, 13.6, 13.2, 11.3, 3.9, 2.1. IR (thin film): 1683 cm⁻¹. High-resolution CI (NH₃) MS (m/z): 285.2242, calcd for C₁₆H₃₃O₂Si 285.2250 (M + H)⁺.

(2R,3R,4S,5S,6R)-2,4-Bis[(triethylsilyloxy)-3,5-dimethyl-6-propyltetrahydro-(2H)-pyran (38). The bis-silyl ether **27** (131.0 mg, 0.314 mmol) was dissolved in 600 μ L of dichloromethane, treated with DIPEA (19 μ L, 0.110 mmol), and cooled to -23 °C. TESOTf (18 μ L, 78.6 μ mol) was added, and the reaction flask was placed in a -23 °C refrigerator for 5 d. The reaction was then diluted to 20 mL with ether and shaken with 1 mL of 0.2 M pH 5.5 phosphate buffer. The organic layer was further washed with water (3 \times 1 mL) and brine (1 \times 2 mL), dried over MgSO₄, and concentrated to give 115.0 mg of crude material. ¹H NMR showed an inseparable mixture of the tetrahydropyran **38** (major), along with 3% of the aldehyde **35** and ca. 12–15% of an unassigned compound. This last material and the aldehyde **35** were removed by treatment with 14 mg of sodium borohydride in 3 mL of ether with enough MeOH (0.5 mL) to aid dissolution of the solid. After the mixture was stirred for 1 h, 1 mL of 0.2 M pH 8.0 phosphate buffer was added, and the solution was diluted to 20 mL with ether. After the layers were separated, the organic phase was washed with water (2 \times 1 mL) and brine (1 \times 1 mL). Further drying over MgSO₄, removal of solvent, and chromatography (40 g SiO₂, 2% ethyl acetate/98% hexanes) gave 97.0 mg of the tetrahydropyran **38** (0.233 mmol, 74%). ¹H NMR (CD₂Cl₂, 500.132 MHz) δ : 4.97 (1H, d, $J = 3.26$ Hz), 3.92 (1H, ddd, $J = 7.76, 4.68, 2.16$ Hz), 3.81 (1H, dd, $J = 10.76, 4.82$ Hz), 1.80–1.70 (2H, m), 1.40–1.30 (4H, m), 0.98 (9H, t, $J = 7.94$), 0.97 (9H, t, $J = 7.94$ Hz), 0.92 (3H, t, $J = 7.06$ Hz), 0.87 (3H, d, $J = 6.74$ Hz), 0.85 (3H, d, $J = 6.92$ Hz), 0.63 (6H, q, $J = 7.18$ Hz), 0.61 (6H, q, $J = 7.95$ Hz). ¹³C NMR (CD₂Cl₂, 125.767 MHz) δ : 96.1, 72.2, 70.0, 39.2, 37.5, 34.7, 19.2, 14.3, 13.5, 6.9, 6.7, 5.04, 5.02, 4.7. IR (thin film): 2957 cm⁻¹. High-resolution CI (NH₃) MS (m/z): 417.3206, calcd for C₂₂H₄₉O₃Si₂ 417.3220 (M + H)⁺.

(2S,3R,4S,5R)-3,5-Bis[(triethylsilyloxy)-2,4-dimethyloctan-1-ol (39). A solution of epoxy alcohol **12** (179.0 mg, 0.592 mmol) and DIPEA (154 μ L, 0.888 mmol) in 4 mL of dichloromethane was cooled to -10 °C. TESOTf (160 μ L, 0.710 mmol) was added and stirred for 3 h. After which, the solution was diluted to 10 mL with ether and shaken with 5 mL of 0.2 M pH 5.5 phosphate buffer. The layers were

separated, and the aqueous phase was extracted with ether (3 × 2 mL). The combined organic extracts were washed with water (3 × 1 mL), brine (1 × 2 mL), dried over MgSO₄, and freed of solvent yielding 238.0 mg of an inseparable mixture of the bis-silyl ether **27** (0.382 mmol, 64%), the aldehyde **35** (108.5 μmol, 18%), and the tetrahydropyran **38** (80.5 μmol, 14%) as determined by ¹H NMR integration. The crude was dissolved in 2 mL of 1:1 MeOH:ether and cooled to -5 °C, when sodium borohydride (4.0 mg, 99.0 μmol) was added. After 1 h, the cooling bath was removed and 1 mL of 0.2 M pH 8.0 phosphate buffer was added. The solution was poured onto 20 mL of ether, and the aqueous layer was separated. The organic layer was washed with water (4 × 1 mL), and the combined water layers were extracted with ether. The combined ether layers were finally washed with brine (1 × 2 mL) and dried over MgSO₄, and removal of solvent afforded 206.3 mg of crude material. Chromatography (40 g SiO₂, gradient from 0% ethyl acetate/100% hexanes to 10% ethyl acetate/90% hexanes) afforded 134.8 mg (0.323 mmol, 55% combined recovery) of an inseparable 5:1 mixture of **27** and **38** and 33.6 mg of the alcohol **39** (80.0 μmol, 74% based on **35**): [α] = -1.12 (*c* = 1.52, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 3.86 (1H, dd, *J* = 7.64, 1.06 Hz), 3.80 (1H, m), 3.55 (1H, dd, *J* = 10.29, 7.52 Hz), 3.48 (1H, dd, *J* = 10.29, 6.21 Hz), 1.85 (1H, m), 1.68 (1H, m), 1.60 (1H, br), 1.55–1.45 (2H, m), 1.35–1.20 (2H, m), 0.97 (9H, t, *J* = 7.96 Hz), 0.96 (9H, t, *J* = 7.91 Hz), 0.91 (3H, t, *J* = 6.96 Hz), 0.87 (3H, d, *J* = 6.87 Hz), 0.84 (3H, d, *J* = 6.99 Hz), 0.60 (12H, m). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 73.6, 73.0, 67.0, 42.2, 38.2, 37.6, 18.4, 14.3, 10.7, 9.9, 6.99, 6.94, 5.78, 5.37. IR (thin film): 3353 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 389.2895, calcd for C₂₀H₄₅O₃Si₂ 389.2907 (M - C₂H₅)⁺.

(2S,3R,4S,5R)-1-(Acetyloxy)-3,5-bis[(triethylsilyloxy)-2,4-dimethyloctane (40). To a solution of the alcohol **39** (31.5 mg, 75.2 μmol) and DIPEA (40 μL, 0.226 mmol) was added acetyl chloride (11 μL, 0.150 mmol). After the reaction was stirred for 45 min, 5 drops of dry MeOH was added and the solution was diluted to 2 mL with hexanes. The solution was passed through a plug of SiO₂ (hexanes rinse) yielding, after concentration, 32.2 mg of the acetate **40** (69.8 μmol, 93%): [α] = +2.37 (*c* = 1.52, dichloromethane). ¹H NMR (CDCl₃, 400.132 MHz) δ: 3.95 (1H, dd, *J* = 10.68, 6.12 Hz), 3.80 (3H, m), 2.04 (3H, s), 2.00–1.90 (1H, m), 1.65–1.55 (1H, m), 1.45–1.40 (2H, m), 1.40–1.20 (2H, m), 1.00–0.90 (18H, m), 0.91 (3H, t, *J*

= 6.96 Hz), 0.85 (3H, d, *J* = 6.84 Hz), 0.82 (3H, d, *J* = 6.84 Hz), 0.60 (12H, m). ¹³C NMR (CDCl₃, 100.625 MHz) δ: 171.0, 73.0, 72.2, 67.7, 42.2, 37.8, 34.6, 20.9, 18.5, 14.5, 10.2, 9.9, 7.12, 7.07, 5.95, 5.52. IR (thin film): 1748 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 461.3488, calcd for C₂₄H₅₃O₄Si₂ 461.3482 (M + H)⁺.

(4R,5S,6R)-4-[(S)-(2-(Acetyloxy)-1-methyl)ethyl]-2,2,4-trimethyl-6-propyl-1,3-dioxane (41). The bis-silyl ether acetate **40** (31.0 mg, 67.3 μmol) was dissolved in 2 mL of acetonitrile in a 10 mL Teflon beaker and treated with 49% HF (50 μL). After the reaction was stirred for 1 h, solid NaHCO₃ (100 mg) was added, and the reaction was stirred for another 2 h. The solution was filtered through a plug of SiO₂ (pipet with ether rinse) and concentrated to give 15.5 mg of diol. This was dissolved in 1 mL of 1:1 dichloromethane:2,2-dimethoxypropane (500 μL) and treated with a crystal of TsOH. After the reaction was stirred for 7 h, solid NaHCO₃ (100 mg) was added, the reaction was stirred for another 1 h, and the solution was filtered through a plug of SiO₂ (pipet with ether rinse). Evaporation of solvent and chromatography (5 g SiO₂, dichloromethane, *R_f* = 0.10) afforded 11.6 mg of the acetonide **41** (42.5 μmol, 63% based on **40**): [α] = +9.4 (*c* = 0.55, dichloromethane). ¹H NMR (CDCl₃, 500.132 MHz) δ: 3.97 (1H, dd, *J* = 10.66, 7.62 Hz), 3.90 (1H, dd, *J* = 10.66, 6.74 Hz), 3.71 (1H, m), 3.30 (1H, dd, *J* = 8.19, 2.74 Hz), 2.01 (3H, s), 1.88 (1H, m), 1.78 (1H, m), 1.50–1.30 (2H, m), 1.24 (3H, s), 1.23 (3H, s), 1.30–1.20 (2H, m), 0.90 (6H, m), 0.76 (3H, d, *J* = 6.77 Hz). ¹³C NMR (CDCl₃, 125.767 MHz) δ: 170.6, 100.0, 73.7, 68.9, 66.5, 36.1, 35.1, 32.6, 24.5, 23.1, 20.5, 19.1, 13.7, 11.5, 10.4. IR (thin film): 1745 cm⁻¹. High-resolution CI (NH₃) MS (*m/z*): 271.1917, calcd for C₁₅H₂₇O₄ 271.1909 (M - H)⁺.

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Supporting Information Available: Experimental details (11 pages). See any current masthead page for ordering and Internet access instructions.

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