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Synthesis of chiral alkenyl epoxides: the sex pheromone of the elm spanworm *Ennomus subsignaria* (Hübner) (Lepidoptera: Geometridae)

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ABSTRACT

The identification of the sex pheromone of the elm spanworm *Ennomos subsignaria* (Hübner), as the chiral alkenyl epoxide (6Z)-*cis*-9,10-epoxy-nonadecene has been accomplished. Both enantiomers of (6Z)-*cis*-9,10-epoxy-nonadecene have been synthesized via two routes. The key steps in the first route were to prepare both *threo*-epoxy tosylates and then to perform an alkylative rearrangement of these intermediates to obtain the target molecules. An alternative enantioenriched synthesis that took advantage of the Sharpless dihydroxylation reaction was developed so that a common starting material could be used to access both enantiomers. A field study and GC/EAD testing indicated that *Z*6-*cis*-9*S*,10*R*-epoxy-nonadecene was the sex pheromone of the elm spanworm *E. subsignaria* (Hübner).

1. Introduction

The elm spanworm, *Ennomos subsignaria* (Hübner), occurs across Canada and the eastern United States and, most recently, has appeared at damaging levels in Newfoundland (NL). Its common name is misleading because it is a general feeder on a wide range of deciduous trees, mostly hickory (*Caryra*), ash (*Fraxinus*), oak (*Quercus*), red maple (*Acer rubrum*), elm (*Ulmus*), basswood (*Tilia*), beech (*Fagus*) and horse-chestnut (*Aesculus*) species.[1,2] Larvae pupate on the leaves after about 30 days in netlike cocoons. Snow-white adults emerge from late July to August and lay eggs in clutches that over-winter on the underside of twigs. This insect can be a destructive forest pest particularly in the southern Appalachians where severe outbreaks have occurred.[3,4]

Recently, relationships between egg or larval density and end-of-season defoliation were established,[5] but a means of detecting and predicting outbreaks earlier would be very useful and a trapping system involving the sex pheromone would have improved detection sensitivity and sampling efficiency.

Sex pheromones or attractants have been identified for >120 geometrids but none have been published for the genus *Ennomos*.[7–9] The pheromones usually consist of single or multi-component blends of unsaturated hydrocarbons and/or epoxides with enantiospecificity often found to be critical to bioactivity and for species isolation.[8] Most insect pheromones are volatile and usually obtained in extremely small quantities, ranging from several ng to several μg, thus it is often difficult to unequivocally determine their structure. Our objective was then to identify the sex pheromone of *E. subsignaria* as a tool for further study of its ecology and phenology, and for detection and delimitation surveys. If successful, then it is expected that the sex pheromone may then be useful for controlling future outbreaks using mating disruption or mass trapping techniques.

In 1973, Granett reported that female elm spanworm adults release a male-attracting pheromone,[10] but he did not report the structure of the pheromone. In the Geometridae, it is common for their pheromones to be oxygenated hydrocarbons, usually mono-epoxides, with carbon chain lengths from C-17 to C-21.[7] We have recently reported the identification of the sex pheromone of the elm spanworm[6] using GC/MS (gas chromatography-mass spectrometry), GC/EAD (gas chromatography-electroantennographic detection) and field trapping. Our results indicated that the EAD-active compound was (6*Z*)-*cis*-9,10-epoxy-nonadecene **1**, Fig. 1. The retention time, elution order and the EI-mass spectra of the compounds in the extracts were identical to those produced from authentic racemic synthetic compounds, obtained by nonselective *m*-CPBA oxidation of (6*Z*,9*Z*)-nonadeca-6,9-diene, and confirmed

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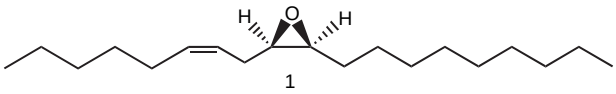


Fig. 1. Structure of the elm spanworm *E. subsignaria* female sex pheromone.

against data previously reported by Millar in 2000.[7] Since it has been shown that insect chemoreception can be highly enantioselective and poor enantiomeric purity can present a problem when studying biological activities, the preparation of chiral epoxides in high enantiomeric purity may be crucial for developing a monitoring tool for this insect. Therefore, the goal became to synthesize both enantiomers of the *cis*-epoxides of (6*Z*)-9,10-epoxy-nonadecene in as highly stereoefficient manner as possible.

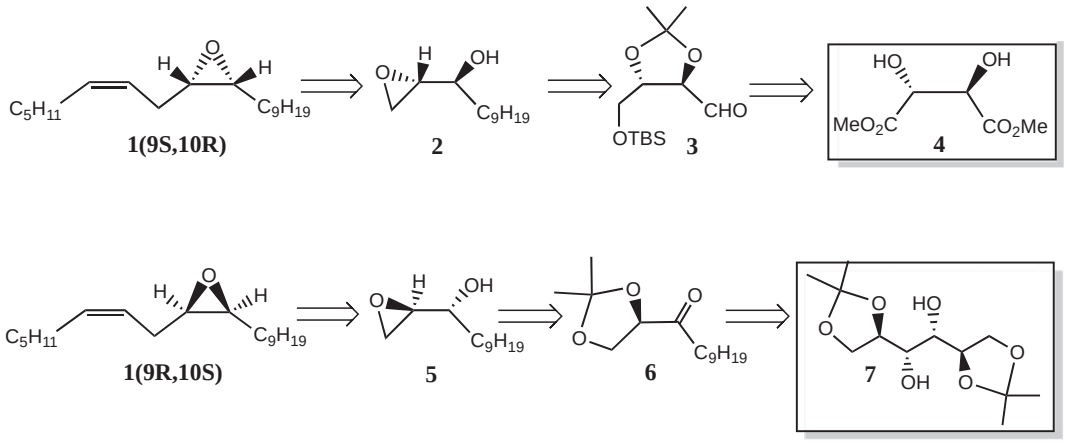
2. Proposed synthetic routes

Examination of the literature revealed several strategies for the synthesis of epoxides in enantiomerically enriched or enantiomerically pure forms.[7,10–16] Given this background it appeared that there were two approaches that would satisfy our requirement for high enantioselectivtiy. Using a 'chiral pool' approach, we could rely on the 'alkylative rearrangement' strategy first outlined by Bell and Ciaccio.[17] In their studies they showed that *threo*- and *erythro*-1,2-epoxy-3-alkanols could efficiently be generated from such readily available natural sources as tartaric acid, sugars, etc. Consequently, a retrosynthetic analysis evolved as shown in Scheme 1. Treating epoxide **2** with 1-heptyne followed by reduction to the *Z*-alkene, enantiomer **1**(9*S*,10*R*) would be generated. Epoxide **2** could be arrived at from aldehyde **3** via a Wittig reaction followed by hydrogenation and functional group manipulation. Aldehyde **3** is easily accessed from L-dimethyl tartrate, **4**. For generation of the enantiomer a similar route could be followed from alcohol **5** to epoxide **1**(9*R*,10*S*). Generation of **5** could be accomplished by stereoselective reduction of ketone **6** followed by epoxide formation. Finally, **6** is easily arrived at from the 1,2: 5,6-diacetonide of D-mannitol, **7**.

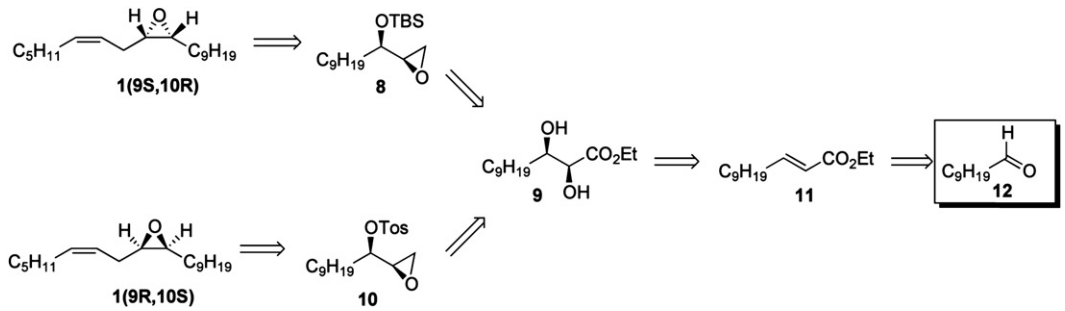
An alternative to this approach uses the Sharpless asymmetric dihydroxylation reaction, Scheme 2.[10,18] Use of the commercially available AD-mix β would generate the *threo*-diol **9**. Conversion of this diol to epoxides **8** and **10** sets the stage for producing the two enantiomers of the alkene/epoxide by taking advantage of chemistry learned from the alkylative rearrangement route. The advantage of this route is clearly the ability of being able to use a common starting material **9**; however, there was a concern as to how enantio-efficient the Sharpless AD would be.

3. Results and discussion

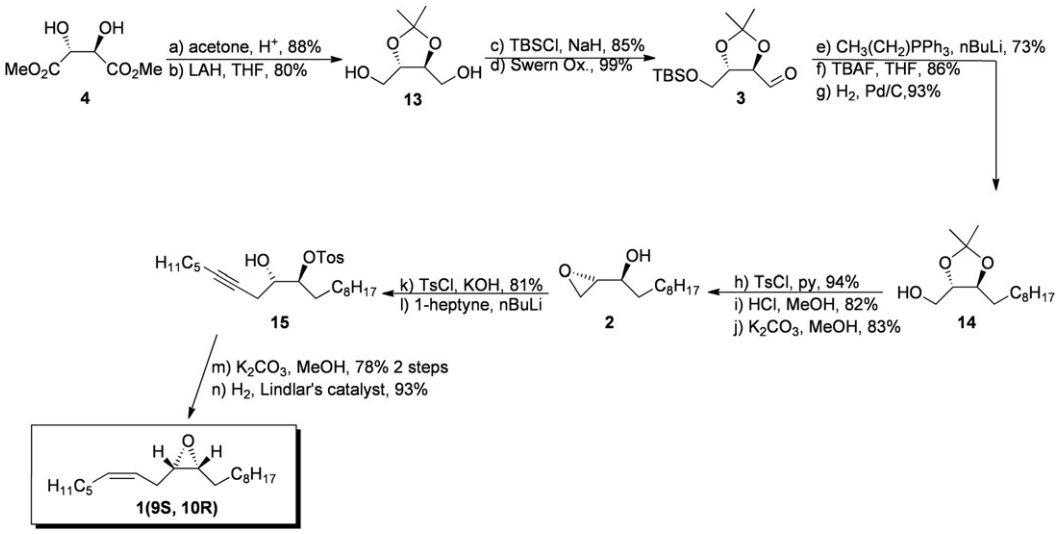
As outlined in Scheme 1, the synthesis of *threo*-(2*S*,3*S*)-epoxy alcohol **2** was initiated by the employment of commercially available L-(+)-dimethyl tartrate as a chiral template. To begin, L-(+)-dimethyl tartrate **4** was treated with acetone, triethylorthoformate and 6 M HCl in DMF at room temperature for 72 h to generate the acetonide, Scheme 3. Conversion of the acetonide to diol **13** proceeded uneventfully by treatment with LAH in THF at 0 °C. While numerous methods have been developed for the selective protection of unsymmetric diols, for example, protection of a primary alcohol in the presence of a secondary alcohol, the selective monoprotection of symmetric diols still presents a problem.[19] Recently, McDougal and co-workers[20] devised a simple method for the selective mono-silylation of symmetrical primary diols. Importantly



Scheme 1. Retrosynthetic analysis for the synthesis of the two enantiomers of (6*Z*)-*cis*-9,10-epoxy-nonadecene using the alkylative rearrangement strategy.



Scheme 2. Retrosynthetic analysis for the synthesis of the two enantiomers of (6*Z*)-*cis*-9,10-epoxy-nonadecene using the Sharpless AD reaction.



Scheme 3. Synthesis of (6Z)-*cis*-9*S*,10*R*-epoxy-nonadecene. Reagents and conditions: (a) CH_3COCH_3, $CH(OC_2H_5)_3$, 6 M HCl in DMF, rt, 72 h, 88%; (b) LAH, THF, 0 °C, 1 h, 80%; (c) TBSCl, NaH, THF, rt, 3 h, 85%; (d) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C, 99%; (e) $CH_3(CH_2)_7PPh_3{}^+Br^-$, *n*-BuLi, THF, −78 °C to rt, 16 h, 73%; (f) TBAF, THF, 1 h, 86%; (g) cat. 30% Pd/C, H_2, MeOH, 93%. (h) TsCl, pyridine, 0 °C–5 °C, 72 h, 94%; (i) 1% methanolic HCl, 5 h, 82%; (j) K_2CO_3, MeOH, 0 °C—rt, 1 h, 83%; (k) TsCl, KOH, Et_2O, 2.5 h, 81%; (l) 1-heptyne, *n*-BuLi, $BF_3{\cdot}Et_2O$, −78 °C, THF; (m) K_2CO_3, MeOH, 0 °C to rt, 1 h, 78% over two steps; (n) cat. 5% Pd/$CaCO_3$ poisoned with lead, C_9H_7N, H_2, 2 h, 93%.

this method makes efficient use of both the diol and protecting reagent.

With this report as a guide, diol **13** was treated with TBSCl in the presence of 1 equiv of NaH to give mono-silyl alcohol in an exceptional 85% yield. It is believed that the success of this reaction lies in the relative insolubility of the mono-sodium salt of **13**, thus effectively removing any excess base. In addition, it is believed that as the reaction proceeds, silylation of the small amount of alkoxide, that is, in solution is faster than proton transfer between the alkoxide and product alcohol.

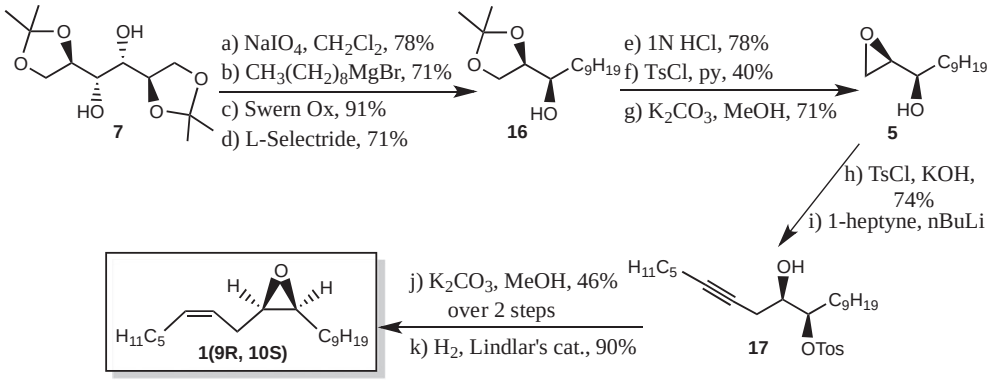
Oxidation of the alcohol to the corresponding aldehyde under Swern conditions[21] generated aldehyde **3** in near quantitative yield. Wittig coupling of **3** with the ylide derived from 1-octyltriphenylphosphonium bromide gave predominantly the *Z*-alkene. The *Z*/*E* ratio was determined by GC to be 30:1, however, this was inconsequential since the olefin was going to be reduced. To fully complete incorporation of one half of the molecule the *E*/*Z* mixture of alkenes was treated with TBAF, to remove the silyl protecting group, followed by catalytic hydrogenation to give alcohol **14**.

With one half of the target pheromone now constructed, the stage was set to incorporate the remaining 7-carbon chain. This began by tosylation of the primary alcohol followed by acid-catalyzed deacetalization to liberate the protected alcohols. Ensuing treatment of the diol with potassium carbonate afforded *threo*-(2*S*,3*S*)-1,2-epoxy-3-dodecanol **2**. At this point the optical purity was assessed to be 93.4% ee as determined by chiral GC after making the derivative of compound **2** using (*S*)-(−)-2-acetoxypropionyl chloride.[22]

To set the final stage for introduction of the 7-carbon chain, the alcohol was converted to its tosylate by treatment with TsCl in the presence of KOH in Et_2O.[23] It should be noted that an acceptable yield of tosylate was only accomplished by using this non-traditional method. When the more standard protocol was used (pyridine, TsCl, CH_2Cl_2, 0 °C—rt, 72 h) only low yields (<20%) and complex reaction mixtures were obtained. The tosylate was treated with 1-lithio-1-heptyne and boron trifluoride etherate,[24] to generate alkynyl alcohol **15**. Although this compound was reasonably stable, no attempts were made to purify it, rather it was directly subjected to epoxide formation by simply treating with potassium carbonate in methanol for a brief period of time. Finally, partial catalytic hydrogenation of the alkyne using Lindlar's catalyst in the presence of a small amount of quinoline produced *cis*-epoxide **1** (9*S*,10*R*). While the sequence was lengthy (14 steps) it did allow for the synthesis of the presumed pheromone with high optical purity (>93.4%) and an overall yield of 13%.

The synthesis of *threo*-(2*R*,3*R*)-epoxy alcohol **5** began with 1,2:5,6-di-*O*-isopropylidene-D-mannitol **7** as the chiral template, Scheme 4. Oxidative cleavage of **7** with sodium metaperiodate[25] afforded the sensitive (*R*)-glyceraldehyde acetonide in 78% yield. Immediate Grignard addition of nonylmagnesium bromide to this aldehyde afforded a mixture of *erythro* and *threo* alcohols, determined to be 6:1 by GC analysis. It should be noted that although the diastereomeric ratio was acceptable it was the undesired stereoisomer that was produced in excess. To reverse this, the mixture of alcohols was oxidized under Swern conditions to smoothly generate ketone **6**. Reduction of the ketone with L-Selectride produced alcohol **16** as a *threo* to *erythro* ratio of 8:1. In this nucleophilic addition reaction, the process does not proceed via a chelate-controlled[26] addition, but rather appears to follow a normal Felkin model.[27] The inhibition of chelate-controlled addition may be a consequence of several factors, including: (a) a significant ring strain which develops in the derived chelate structure, (b) a depressed donor ability of the acetonide oxygen, relative to an ether oxygen, due to an inductive electron withdrawal, and (c) steric inhibition to chelate formation due to non-bonded interactions between the metal ligands and the acetonide methyl group.

With the proper stereochemistry now firmly installed, acid-catalyzed deactalization of **16** gave *threo*-(2*R*,3*R*)-1,2,3-dodecanetriol in 78%. Selective monotosylation of the primary alcohol by reaction with 1 equiv of TsCl in pyridine at 0–5 °C afforded the tosylate in a disappointing 40% yield. Regardless, subsequent treatment of this compound with anhydrous potassium carbonate in anhydrous MeOH yielded *threo*-(2*R*,3*R*)-l,2-epoxy-3-dodecanol **5**. The optical purity of **5** was measured using the same method as described for **2** and was found to have an ee greater than 99%. Completion of the synthesis proceeded as previous described, namely: (1) conversion of **5** to its tosylate, (2) treatment of the tosylate with heptynyl lithium and boron triflouride etherate to give **17**, (3) epoxide formation via K_2CO_3 in methanol, and (4) partial reduction of the alkyne using Lindlar's catalyst. The synthesis of the **1** (9*R*,10*S*) stereoisomer was accomplished in 11 steps with an overall yield of 2.4% and with exceptional stereochemical purity.



Scheme 4. Synthesis of (6Z)-*cis*-9*R*,10*S*-epoxy-nonadecene. Reagents and conditions: (a) $NaIO_4$, $NaHCO_3$, CH_2Cl_2, rt, 2 h, 78%; (b) $CH_3(CH_2)_8Mg^+Br^-$, Et_2O, 0 °C, 3 h, 0–5 °C, overnight, 71%; (c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, −78 °C; 91%; (d) L-Selectride, THF, −78 °C to rt, overnight, 71%; (e) 1 N HCl, THF, 6 h, 78%; (f) TsCl, pyridine, 0 °C–8 °C, 72 h, 40%; (g) K_2CO_3, MeOH, 0 °C to rt, 1 h, 71%; (h) TsCl, KOH, Et_2O, 0 °C, 2.5 h, 74%; (i) 1-heptyne, BuLi, $BF_3{\cdot}Et_2O$, THF, −78 °C; (j) K_2CO_3, MeOH, 0 °C to rt, 1 h, 46% over two steps; (k) cat. 5% Pd/$CaCO_3$ poisoned with lead, C_9H_7N, H_2, 2 h, 90%.

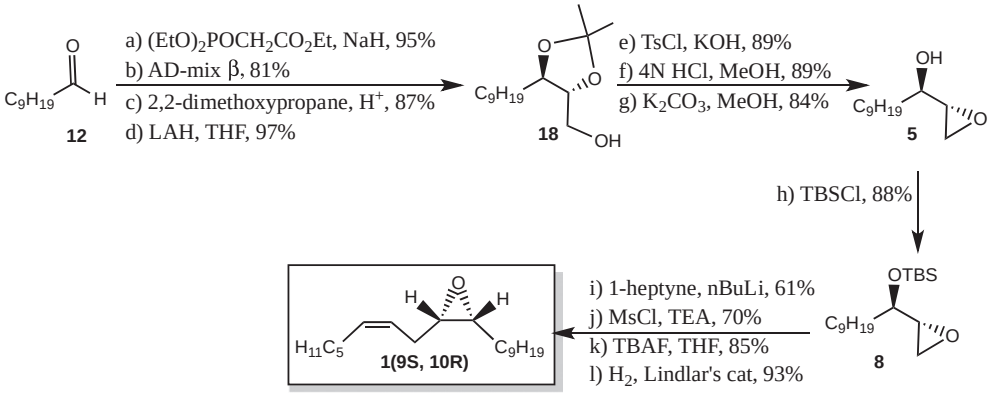
With sufficient material made to allow for field studies, attention was focused on trying to streamline the route. The reasons for this were twofold: firstly, different starting materials were required for the synthesis of the two enantiomers, this was inefficient and unacceptable if the chemistry learned from this project was to be applied to other pheromone syntheses. Secondly, larger quantities of material were going to be required for more extensive field studies, or perhaps for commercial application, therefore efficiencies needed to be found.

With this in mind a second synthetic route involving Sharpless AD[28,29] chemistry was developed. To begin, Scheme 5, decanal **12** was subjected to Horner–Wadsworth–Emmons reaction with triethylphosphonoacetate to furnish the *trans*-olefin **11** exclusively after silica gel chromatography. Olefin **11** was treated with AD-mix-β[30] (Aldrich) to give diol **9** in 81% yield. Attempts were made to reduce **9** with LAH to generate the triol, however, this reaction was somewhat capricious. Therefore conversion of diol **9** to its acetonide followed by reduction with LAH smoothly furnished alcohol **18** in excellent yield. Since **18** was enantiomeric to **14**, optical rotation allowed for an initial assessment of the ee (99%).

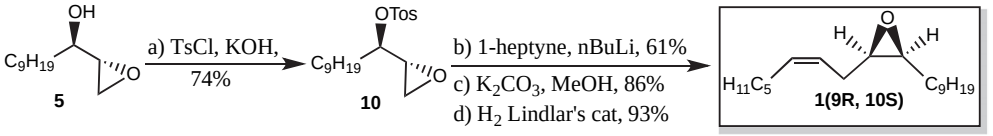
Continuing with the synthesis, alcohol **18** was converted to its tosylate, hydrolyzed to the diol and as expected, when treated with K_2CO_3 in MeOH, epoxy alcohol **5** was efficiently generated. The optical purity was then measured by chiral GC using the same method as for **2** and was determined to be 99%. Alcohol **5** was seen as the lynchpin that would allow for the production of both pheromone enantiomers.

In order to generate **1** (9*S*,10*R*), alcohol **5** was first converted to its TBS-silyl ether via the agency of TBSCl in DMF in the presence of imidazole to give epoxide **8**. Treatment of **8** with 1-lithio-1-heptyne and boron triflouride etherate generated the secondary alcohol in 61% yield. This was then converted to a mesylate, which when subjected to desilylation with TBAF in anhydrous THF followed by partial catalytic hydrogenation to generate the targeted epoxide **1** (9*S*,10*R*). As compared to our previous route, this approach allowed for the synthesis to be accomplished in 2 less steps (12 vs 14), comparable overall yield (12.8% vs 13%) and higher enantiopurity (99% vs 93.4%).

To complete the study, Scheme 6, transformation of alcohol **5** into tosylate **10** proceeded uneventfully. Opening of the epoxide



Scheme 5. Synthesis of 6Z-*cis*-9*S*,10*R*-epoxy-nonadecene. Reagents and conditions: (a) triethyl phosponoacetate, NaH, THF, reflux, 1 h, 95%; (b) AD-mix-β, *t*-BuOH, H_2O, rt, Na_2SO_3, $CH_3SO_2NH_2$, 81%; (c) 2,2-dimethoxypropane, *p*-TSA, CH_2Cl_2, 87%; (d) LAH, THF, 0 °C, 1 h, 97%; (e) TsCl, KOH, Et_2O, 0 °C, 2 h, 89%; (f) 4 N HCl, MeOH, 8 h, 89%; (g) K_2CO_3, MeOH, 0 °C to rt, 1 h, 84%; (h) TBSCl, DMF, imidazole, rt, 16 h, 58%; (i) 1-heptyne, BuLi, $BF_3{\cdot}Et_2O$, THF −78 °C, 61%; (j) MsCl, Et_3N, CH_2Cl_2, 4–8 °C, 72 h, 70%; (k) TBAF, THF, rt, 1 h, 85%; (l) cat. 5% Pd/$CaCO_3$ poisoned with lead, C_9H_7N, H_2, 2 h, 93%.



Scheme 6. Synthesis of 6Z-*cis*-9*R*,10*S*-epoxy-nonadecene. Reagents and conditions: (a) TsCl, KOH, Et_2O, 0 °C, 2.5 h, 74%; (b) 1-heptyne, BuLi, $BF_3{\cdot}Et_2O$, THF −78 °C, 61%; (c) K_2CO_3, MeOH, 0 °C—rt, 1 h, 86%; (d) cat. 5% Pd/$CaCO_3$ poisoned with lead, C_9H_7N, H_2, 2 h, 93%.

with heptynyl lithium as previously, followed by epoxide formation and partial catalytic reduction of the alkyne led to the formation of **1** (9*R*,10*S*). When compared to the route beginning from mannitol, this approach was of equal length (11 steps), much better overall yield (15.6% vs 2.4%) and comparable enantiopurity (99%).

From these studies it is clear that the Sharpless AD route provides an advantage for the synthesis of these types of alkene/epoxides. For one enantiomer the overall yield was improved by 6½ fold, while for the other enantiomer yields were comparable but the overall synthetic sequence was two steps shorter, which in itself is an advantage. Also, the Sharpless AD technology provided superb optical purities for both enantiomers achieving levels that were not obtained using the 'chiral pool' approach. It should be noted that our route used commercially available AD-mix, which is only suitable for small-scale reactions. However, Sharpless[28,29] has provided a 'recipe' that allows for convenient preparation of a large amount of this reagent that has allowed for the facile production of several 10′s–100′s of mmol of these compounds to be efficiently generated.

4. Conclusions

The synthesis of the two enantiomers of the suspected pheromone of the elm spanworm was accomplished. Both enantiomers of (6Z)-*cis*-9,10-epoxy-nonadecene have been synthesized via two routes. The key steps in the first route were to prepare both *threo*-epoxy tosylates and then to perform an alkylative rearrangement of these intermediates to obtain the target molecules. An alternative enantioenriched synthesis that took advantage of the Sharpless dihydroxylation reaction was developed so that a common starting material could be used to access both enantiomers. This has allowed for the facile production of several 10′s–100′s of mmol of these compounds to be efficiently generated, thus making it possible for the possible use of this chiral epoxide as a pest control reagent in pheromone traps or as an early detection monitor for this insect pest. This could lead to an environmental-friendly pest management system for the insect.

5. General experimental procedures

5.1. General

Unless otherwise indicated, all non-aqueous reactions were conducted in oven-dried glassware and under an argon atmosphere. Air-sensitive reagents were transferred via syringe through rubber septa. Reagents were purchased from commercial suppliers and directly used without further purification.

Analytical thin-layer chromatography was performed using SILICYCLE TLC plates, pre-coated with 0.25 mm of UV_{254} Silica Gel. Visualization was done by dipping the TLC plate in potassium permanganate solution or phosphomolybdic acid/ethanol solution followed by baking on a hot plate. Flash column chromatography was performed using a glass column filled with 230–420 mesh silica gel 60 from Fisher. Preparative thin-layer chromatography was carried out on 1 mm SILICYCLE silica gel plates. Reagent grade solvents were used without further purification. All compounds purified by SiO_2 chromatography were greater than 98% purity as determined by GC and/or NMR.

NMR spectra were recorded on a Varian Innova 300 MHz spectrometer. All spectra were recorded in $CDCl_3$ containing TMS as an internal standard or in deuterated DMSO with chemical shifts reported in parts per milloin (δ). GC/MS spectra were measured on an Agilent 6890 N (GC) and 5973 N (MS) model GC/MS or Hewlett–Packard 5890 Series II (GC) and Hewlett–Packard 5971 Series (MS) model GC/MS. High resolution mass spectra were acquired on a Waters Xevo QToF hybrid quadrupole orthogonal time-of-flight mass spectrometer (Xevo QToF). Samples were introduced into the mass spectrometer using a commercially available Atmospheric Solids Analysis Probe (ASAP). Infrared spectra were recorded on a Perkin–Elmer 727B infrared spectrometer using KBr discs. Optical rotations were recorded on a Perkin–Elmer 341 spectrometer using the 589 sodium line. Melting points were measured on a Gallenkamp melting point apparatus and all melting points are uncorrected.

5.1.1. Preparation of (4R,5R)-2,2-dimethyl-1,3-dioxolane-4,5-dimethane. To a round bottom flask were successively introduced (+)-dimethyl L-tartate **4** (25 g, 141 mmol), acetone (38 mL), triethylorthoformate (32 mL) and 6 M HCl solution of dimethylformamide (0.75 mL). The mixture was stirred for 72 h at room temperature and then alkalinized with triethylamine. The mixture was concentrated in vacuo and the residue was diluted with Et_2O (200 mL) and then washed with water (2×30 mL) and dried over $MgSO_4$. The solvent was removed in vacuo to afford 27 g of (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dimethane[31] (88%) as a colourless oil, which was of sufficient purity to be used directly in the next reaction. ^{1}H NMR ($CDCl_3$): δ 4.83 (s, 2H), 3.85 (s, 6H), 1.52 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 170.3, 114.1, 77.2, 53.0, 26.5. IR (KBr) cm^{-1}: 2957 (CH), 1762 (C=O), 1483, 1375. MS m^+/z: 203 (M−15), 175, 159, 141, 133, 117, 101, 85, 73, 59. $[\alpha]_{D^{20}}$ −43.3 (*c* 2.1, CH_2Cl_2).

*5.1.2. Preparation of (4S,5S)-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol (**13**).* To a round bottom flask was put (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dimethane (22.8 g, 0.1 mol) and THF (100 mL). The solution was cooled to 0 °C and LAH (8.0 g, 0.2 mol) was added portion-wise over 15 min. After complete addition the reaction mixture was stirred for 1 h. The reaction was quenched by successive addition of water (8 mL), 15% NaOH (8 mL) and water (24 mL) again. After stirring for 10 min the mixture was filtered through Celite and then dried over $MgSO_4$. The solvent was removed in vacuo to afford 13.5 g (80%) of diol (4*S*,5*S*)-2,2-dimethyl 1,3-dioxolane-4,5-dimethanol[32] **13** as a yellow oil after purification by silica gel chromatography using 1:4 hexanes: ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 3.97 (m, 2H), 3.70–3.76 (m, 4H), 2.96 (br s, 2H), 1.43 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 109.3, 78.3, 62.1, 27.0. IR (KBr) cm^{-1}: 3399 (OH), 2987 (CH), 2936, 1458. MS m^+/z: 147 (M−15), 131, 113, 100, 85, 69, 59, 43. $[\alpha]_{D^{20}}$ −4.7 (*c* 1.5, CH_2Cl_2).

5.1.3. Preparation of (2S,3S)-2,3-O-isopropylidene-1,2,3,4-butanetetrol tert-butyldimethylsilyl ether. To a round bottom flask were added NaH (60% wt dispersion in mineral oil, 3.3 g, 83.6 mmol) and THF (150 mL). Diol **13** (13.5 g, 83.6 mmol) in THF (20 mL) was then added drop-wise over 5 min. After complete addition, the reaction mixture was stirred for 1 h then treated with *tert*-butyldimethylsilyl chloride (12.6 g, 83.6 mmol). After stirring for 3 h the reaction was diluted with water and ether and the layers separated. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed in vacuo to afford 19.7 g (85%) of (2*S*,3*S*)-2,3-*O*-isopropylidene-1,2,3,4-butanetetrol *tert*-butyldimethylsilyl ether[33] as a colourless oil after purification by silica gel chromatography using 2:1 hexane: ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 3.99 (dt, 1H, *J*=7.7, 4.6 Hz), 3.91–3.63 (m, 5H), 2.36 (dd, 1H, *J*=7.5, 4.5 Hz), 1.42 (s, 3H), 1.40 (s, 3H), 0.90 (s, 9H), 0.09 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 109.3, 80.3, 78.3, 63.9, 62.9, 27.2, 27.0, 26.0, 18.5, −5.3 (two signals). IR (KBr) cm^{-1}: 3451 (OH), 2929 (CH), 1468, 1378. MS m^+/z: 261 (M−CH_3), 219, 161, 131, 117, 75, 59, 43. $[\alpha]_{D^{20}}$ +10.9 (*c* 2.1, CH_2Cl_2).

*5.1.4. Preparation of (2S,3S)-2,3-O-isopropylidene-2,3,4-trihydroxybutanal tert-butyldimethylsilyl ether (**3**).* To a round bottom flask were added CH_2Cl_2 (100 mL) and oxalyl chloride (6.3 mL, 72.3 mmol). The solution was cooled to −78 °C and anhydrous DMSO (10.3 mL, 144.6 mmol) was added drop-wise over 5 min.

After stirring at this temperature for 15 min a solution of (2*S*,3*S*)-2,3-*O*-isopropylidene-1,2,3,4-butanetetrol *tert*-butyldimethylsilyl ether (18.1 g, 65.7 mmol) in CH_2Cl_2 (30 mL) was added over 15 min. The resulting mixture was stirred for 1 h at −78 °C and then triethylamine (46 mL, 329 mmol) was added and the cooling bath was removed. After stirring for 5 min the reaction mixture was diluted with H_2O and extracted with ether (3×100 mL). The combined organic phase was washed with water, brine, dried over $MgSO_4$, filtered and the solvent removed in vacuo to afford 18.0 g (99%) of crude (2*S*,3*S*)-2,3-*O*-isopropylidene-2,3,4-trihydroxybutanal *tert*-butyldimethylsilyl ether[33] **3** as a pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 9.78 (dd, 1H, *J*=1.6, 0.8 Hz), 4.33 (dm, 1H, *J*=7.2 Hz), 4.13 (m, 1H), 3.82 (d, 2H, *J*=4.5), 1.49 (s, 3H), 1.42 (s, 3H), 0.91 (s, 9H), 0.093 (s, 3H), 0.091 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 201.8, 111.3, 79.8, 66.2, 26.6, 25.1. IR (KBr) cm^{-1}: 2987 (CH), 1735 (C=O), 1457, 1373. MS m^+/z: 259 (M−CH_3), 245, 217, 199, 187, 171, 159, 145, 129, 117, 101, 85, 75, 59, 43. $[\alpha]_{D^{20}}$ +3.3 (*c* 1.0, CH_2Cl_2).

5.1.5. Preparation of (4E) and (4Z)-(2S,3S)-2,3-O-isopropylidene-4-dodecene-1,2,3-triol tert-butyldimethylsilyl ether. To a round bottom flask were put 1-octyltriphenylphospnonium bromide (13.4 g, 53.0 mmol) and THF (100 mL). The solution was cooled to −78 °C and *n*-BuLi (24 mL, 2.5 M, 59.8 mmol) was added drop-wise over 10 min, after complete addition, stirring was continued at this temperature for 30 min. Then crude aldehyde **3** (12.8 g, 46.9 mmol) was added drop-wise and the reaction mixture was allowed to warm slowly to room temperature and stirred overnight. Anhydrous MeOH (15 mL) was then added to quench the reaction and the resulting mixture was concentrated in vacuo. The residue was purified by silica gel chromatography (10:1 hexane/ethyl acetate, v/v) to afford 12.7 g (73%) of (4*E*) and (4*Z*)-(2*S*,3*S*)-2,3-*O*-isopropylidene-4-dodecene-1,2,3-triol *tert*-butyldimethylsilyl ether as a clear, yellowish oil. ^{1}H NMR ($CDCl_3$): δ 5.66 (m, 1H), 5.39 (m, 1H), 4.78 (m, 1H), 3.79 (m, 1H), 3.69−3.62 (m, 2H), 2.03−2.13 (br m, 2H), 1.44 (s, 3H), 1.43 (s, 3H), 1.24−1.34 (m, 10H), 0.98−0.74 (m, 12H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 136.4, 126.6, 108.9, 82.0, 73.0, 61.7, 32.0, 29.9, 29.4, 28.0, 27.5, 27.2, 26.10 (two signals), 22.9, 18.6, 14.3, −5.9, −5.3. IR (KBr) cm^{-1}: 2928 (CH), 1462, 1379. MS m^+/z: 355 (M−CH_3), 325, 297, 255, 225, 196, 173, 157, 143, 117, 89, 75, 57, 43. HRMS (m^++H) calcd for $C_{21}H_{23}O_3Si$ 371.2982, found 371.2984. $[\alpha]_{D^{20}}$ −6.1 (*c* 1.3, CH_2Cl_2).

5.1.6. Preparation of (4E)- and (4Z)-(2S,3S)-2,3-O-isopropylidene-4-dodecene-1,2,3-triol. Into a round bottom flask were added (4*E*) and (4*Z*)-(2*S*,3*S*)-2,3-*O*-isopropylidene-4-dodecene-1,2,3-triol *tert*-butyldimethylsilyl ether (15.3 g, 41.3 mmol) and THF (100 mL) followed by drop-wise addition of TBAF (123.8 mL, 123.4 mmol). After stirring for 1 h the reaction mixture was diluted with ether and washed with 1 M HCl, water, brine, dried over $MgSO_4$, filtered and the solvent evaporated to yield 9.1 g of (4*E*)- and (4*Z*)-(2*S*,3*S*)-2,3-*O*-isopropylidene-4-dodecene-1,2,3-triol (86%) as a colourless oil after purification by silica gel chromatography with 3:1 hexanes/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 5.73 (m, 1H), 5.40 (m, 1H), 4.74 (t, 1H, *J*=8.6 Hz), 3.86 (m, 1H), 3.76 (m, 1H), 3.58 (m, 1H), 2.22−2.06 (br m, 2H), 1.84 (m, 1H), 1.47 (s, 6H), 1.20 (s, 10H), 0.90 (t, 3H, *J*=6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 137.0, 126.1, 109.3, 81.6, 72.8, 60.9, 32.0, 29.9, 29.4, 29.36, 27.9, 27.5, 27.2, 22.9, 14.3. IR (KBr) cm^{-1}: 3451 (OH), 2927 (CH), 1380. MS m^+/z: 256 (M^+), 241, 196, 181, 167, 155, 137, 121, 107, 97, 83, 67, 59, 43. HRMS (m^++H) calcd for $C_{15}H_{29}O_3$ 257.2117, found 257.2117. $[\alpha]_{D^{20}}$ −7.6 (*c* 2.8, CH_2Cl_2).

*5.1.7. Preparation of (2S,3S)-2,3-O-isopropylidene-l,2,3-dodecantriol (**14**).* (4*E*)- and (4*Z*)-(2*S*,3*S*)-2,3-*O*-Isopropylidene-4-dodecene-1,2,3-triol (1.4 g, 5.4 mmol) was taken up in anhydrous methanol (30 mL) and transferred to a Parr hydrogenation bottle. To this was added a catalytic amount of palladium (30% wt on activated carbon) and the bottle was flushed with hydrogen, and the contents were placed under H_2 pressure (50 psi) and shaken for 16 h. The solution was then filtered through a pad of Celite and rinsed with ether. The solvent was removed in vacuo to yield 1.3 g (93%) of (2*S*,3*S*)-2,3-*O*-isopropylidene-l,2,3-dodecantriol[34] **14** as a colourless oil, which was of sufficient purity for use in the next reaction. ^{1}H NMR ($CDCl_3$): δ 3.94−3.72 (m, 3H), 3.62 (m, 1H), 1.86 (dd, 1H, *J*=7.5, 5.1 Hz), 1.56 (m, 6H), 1.44 (d, 6H, *J*=3.2 Hz), 1.29 (br s, 14H), 0.90 (t, 3H, *J*=6.6 Hz,). ^{13}C NMR ($CDCl_3$): δ 108.6, 81.6, 77.0, 73.9, 72.6, 64.8, 62.2, 33.6, 33.1, 31.9, 29.7, 27.2, 25.8, 22.7, 14.1. IR (KBr) cm^{-1}: 3409 (OH), 2925 (CH), 1643, 1467. MS m^+/z: 243 (M−CH_3), 227, 123, 109, 95, 81, 59. HRMS (m^++H) calcd for $C_{15}H_{31}O_3$ 259.2274, found 259.2273. $[\alpha]_{D^{20}}$ −3.8 (*c* 1.6, CH_2Cl_2).

5.1.8. Preparation of (2S,3S)-2,3-O-isopropylidene-L-(tosyloxy)-2,3-dodecanediol. Into a round bottom flask were put (2*S*,3*S*)-2,3-*O*-isopropylidene-l,2,3-dodecantriol **14** (0.34 g, 5.19 mmol), pyridine (10 mL) and then the solution was cooled to 0 °C. TsCl (0.99 g, 5.19 mmol) was added portion-wise over 15 min. The resulting mixture was stored for 72 h in a fridge (4−8 °C) and then diluted with ice water (10 mL). The solution was extracted with ether (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and the solvent evaporated to yield 2.0 g of (2*S*,3*S*)-2,3-*O*-isopropylidene-L-(tosyloxy)-2,3-dodecanediol (94%) as a pale yellow oil after purification by silica gel chromatography with 5:1 hexanes/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 7.81 (dt, 2H *J*=8.3, 1.7 Hz), 7.39 (dd, 2H, *J*=7.9, 1.0 Hz), 4.11 (m, 2H), 3.80 (m, 3H), 2.48 (s, 3H), 1.38 (s, 3H), 1.32 (s, 3H), 1.29 (br s, 16H), 0.91 (t, 3H, *J*=7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 144.0, 131.8, 128.9 (two signals), 127.1 (two signals), 108.3, 76.1, 75.6, 68.2, 62.8, 32.1, 30.9, 28.5, 28.3, 26.3, 25.7, 24.9, 21.7, 20.7, 16.9, 13.1. IR (KBr) cm^{-1}: 2927 (CH), 2855, 1598 (C=C), 1369, 1190, 1907, 983, 815, 555. HRMS (m^++H) calcd for $C_{22}H_{37}O_5S$ 413.2362, found 413.2365. $[\alpha]_{D^{20}}$ −22.9 (*c* 1.8, CH_2Cl_2).

5.1.9. Preparation of (2S,3S)-1-tosyloxy-2,3-dodecanediol. To a round bottom flask were put (2*S*,3*S*)-2,3-*O*-isopropylidene-L-(tosyloxy)-2,3-dodecanediol (1.0 g, 2.5 mmol) and 1% methanolic HCl (20 mL). The mixture was stirred for 5 h at room temperature, diluted with water (100 mL) and extracted with ether. The combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated, to afford 0.8 g of (2*S*,3*S*)-1-tosyloxy-2,3-dodecanediol (82%) as a white solid after purification by silica gel chromatography with 3:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 7.83 (dt, 2H, *J*=8.3, 1.8 Hz), 7.35 (dd, 2H, *J*=8.6, 0.7 Hz), 4.12 (m, 2H), 3.74 (m, 1H), 3.61 (m, 1H), 2.48 (s, 3H), 1.29 (br s, 18H, 2OH), 0.90 (t, 3H, *J*=6.9 Hz). ^{13}C NMR ($CDCl_3$): δ 145.2, 132.6, 130.0 (two signals), 128.0 (two signals), 77.2, 71.5, 71.4, 70.8, 33.5, 31.9, 30.9, 29.53 (two signals), 29.5, 29.3, 25.5, 22.7, 21.7, 14.1. IR (KBr) cm^{-1}: 3439, 3280 (OH), 2918 (CH), 1599 (C=C), 1353, 962. HRMS (m^++H) calcd for $C_{19}H_{33}O_5S$ 373.2049, found 373.2049. $[\alpha]_{D^{20}}$ −9.9 (*c* 1.1, CH_2Cl_2). Mp: 73.9−75.9 °C.

*5.1.10. Preparation of (2S,3S)-l,2-epoxy-3-dodecanol (**2**).* Into a round bottom flask were placed (2*S*,3*S*)-1-tosyloxy-2,3-dodecanediol (0.75 g, 2.02 mmol) and MeOH (20 mL). This solution was cooled to 0 °C and anhydrous K_2CO_3 (0.55 g, 4.04 mmol) was added and the reaction mixture was allowed to slowly warm to room temperature and stir for 1 h. The mixture was then diluted with an equal volume of water and extracted with ether (3×25 mL). The combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 0.34 g of (2*S*,3*S*)-l,2-epoxy-3-dodecanol[35] **2** (83%) after purification by silica gel chromatography with 3:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 3.46 (br m, 1H), 3.00 (m, 1H), 2.85 (dd, 1H, *J*=5.0, 4.4 Hz), 2.75 (dd, 1H, *J*=4.9, 2.8 Hz), 1.63 (m, 2H), 1.39 (br s, 14H),

0.89 (t, 3H, J=6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 71.7, 55.5, 45.2, 34.4, 31.9, 29.6, 29.5 (two signals), 29.3, 25.3, 22.7, 14.1. IR (KBr) cm^{-1}: 3413 (OH), 2924 (CH). MS m^+/z: 157, 139, 111, 97, 88, 83, 74, 69, 55, 41. $[\alpha]_{D^{20}}$ −4.74 (*c* 1.3, CH_2Cl_2).

5.1.11. Preparation of (2S,3S)-l,2-epoxy-3-(tosyloxy)dodecane. To a round bottom flask were put (2*S*,3*S*)-l,2-epoxy-3-dodecanol **2** (0.34 g, 1.68 mmol), Et_2O (10 mL) and TsCl (0.48 g, 2.52 mmol). The solution was cooled to −5 °C and freshly powdered KOH (1.41 g) was added portion-wise over 15 min. After complete addition, the resulting mixture was stirred for 2.5 h at 0 °C and then ice water (10 mL) was added. The solution was extracted with ether (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to yield 0.48 g of (2*S*,3*S*)-l,2-epoxy-3-(tosyloxy)dodecane[36] (81%) as a tan coloured solid after purification by silica gel chromatography with 3:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 7.82 (d, 2H, J=8.3 Hz), 7.33 (d, 2H, J=8.0 Hz), 4.34 (m, 1H), 3.05 (m, 1H), 2.79 (t, 1H, J=4.2 Hz), 2.63 (dd, 1H, J=4.8, 2.6 Hz), 2.45 (s, 3H), 1.70 (m, 2H), 1.23 (br s, 14H), 0.89 (t, 3H, J=6.6 Hz). ^{13}C NMR ($CDCl_3$): δ 144.6, 134.3, 129.9, 127.9, 83.4, 52.7, 44.8, 31.86, 31.83, 29.4, 19.3, 29.26, 29.2, 24.8, 22.7, 21.7, 14.1. IR (KBr) cm^{-1}: 2924 (CH), 1596 (C═C), 1531 (SO). $[\alpha]_{D^{20}}$ +5.2 (*c* 1.0, CH_2Cl_2). Mp: 60.5–62.1 °C.

5.1.12. Preparation of (9S,10R)-9,10-epoxy-nonadec-6-yne. In a round bottom flask cooled to −78 °C were put 1-heptyne (1.0 g, 3.0 mmol) and THF (20 mL) followed by drop-wise addition of *n*-BuLi (5.6 mL, 1.6 M, 9.0 mmol). The resulting mixture was stirred for 30 min and then $BF_3\cdot Et_2O$ (1.1 mL, 9.0 mmol) was added followed 30 min later by (2*S*,3*S*)-l,2-epoxy-3-(tosyloxy)dodecane (1.1 g, 3.0 mmol) in THF (5 mL). The reaction mixture was stirred for 1 h at −78 °C and was then quenched with saturated aqueous NH_4Cl. The solution was extracted with ether (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 1.5 g of crude **15**. This crude product, **15**, (1.5 g, 3.4 mmol) was dissolved in anhydrous MeOH (15 mL) and cooled to 0 °C at which time anhydrous K_2CO_3 (0.9 g, 6.7 mmol) was added. The reaction mixture was then slowly warmed to room temperature and stirred for 1 h. An equal volume of water was then added and the solution was extracted with ether (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 0.7 g of (9*S*,10*R*)-9,10-epoxy-nonadec-6-yne (78%) as a colourless oil after purification by silica gel chromatography using 8:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 3.14 (m, 1H), 2.97 (ddd, 1H, J=5.7, 5.7, 4.4 Hz), 2.59 (dm, 1H, J=17.0, 2.8 Hz), 2.52–2.13 (m, 3H), 1.57–1.44 (m, 4H), 1.43–1.24 (m, 18H), 0.92 (t, 3H, J=7.0 Hz), 0.91 (t, 1H, J=6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 82.5, 74.8, 57.1, 55.5, 31.9, 31.1, 29.6, 29.5 (two signals), 29.3, 28.6, 27.6, 26.5, 22.7, 22.2, 18.8, 18.7, 14.1, 14.0. IR (NaCl) cm^{-1}: 2926 (CH), 1467. MS m^+/z: 277 (M−1), 263, 249, 235, 221, 207, 193, 179, 165, 151, 137, 123, 109, 95, 81, 67, 55. HRMS (m^++H) calcd for $C_{19}H_{35}O$ 279.2688, found 279.2689. $[\alpha]_{D^{20}}$ +30.3 (*c* 4.5, CH_2Cl_2).

5.1.13. Preparation of (6Z)-cis-9S,10R-epoxy-nonadecene (1(9S,10R)). (9*S*,10*R*)-9,10-Epoxy-nonadec-6-yne (0.78 g, 2.81 mmol) was taken up in anhydrous hexane (20 mL) and transferred to a Parr hydrogenation bottle. Lindlar's catalyst (5% palladium on $CaCO_3$ poisoned with lead, 84 mg) and quinoline (28 mg) were then added and the bottle was flushed with hydrogen and the contents were placed under hydrogen pressure (50 psi) and shaken for 1 h. The solution was then filtered through a pad of Celite and the pad was washed with Et_2O. The solvent was removed in vacuo to yield 0.73 g (93%) of (6Z)-*cis*-9*S*,10*R*-epoxy-nonadecene[37] **1** (9*S*,10*R*) as a colourless oil after purification by silica gel chromatography using 8:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 5.54–5.34 (m, 2H), 2.90–2.87 (m, 2H), 2.32 (m, 1H), 2.18 (m, 1H), 2.06–1.99 (m, 2H), 1.50 (m, 2H), 1.30–1.22 (m, 20H), 0.863 (t, 3H, J=6.6 Hz), 0.86 (t, 3H, J=6.1 Hz). ^{13}C NMR ($CDCl_3$): δ 132.7, 123.8, 57.2, 56.6, 31.9, 31.5, 29.6 (two signals), 29.5, 29.3, 29.3, 27.8, 27.4, 26.6, 26.2, 22.7, 22.6, 14.1, 14.0. IR (NaCl) cm^{-1}: 2925 (CH), 1467. MS m^+/z: 280, 251, 237, 223, 209, 195, 183, 169, 155, 139, 124, 110, 95, 81, 69, 55. HRMS (m^++H) calcd for $C_{19}H_{36}O$ 281.2846, found 281.2846. $[\alpha]_{D^{20}}$ +3.1 (*c* 1.1, CH_2Cl_2).

5.1.14. Preparation of (R)-glyceraldehyde acetonide. To a round bottom flask were placed 1,2:5,6-di-*O*-isopropylidine-D-mannitol **7** (5.0 g, 19.2 mmol), CH_2Cl_2 (20 mL) and saturated aqueous sodium bicarbonate (2 mL). The flask was put in a water bath and then sodium metaperiodate (8.2 g, 38.4 mmol) was added portion-wise over 10 min. The resulting mixture was stirred for 2 h and then $MgSO_4$ (2.5 g) was added. The reaction mixture was stirred for another 20 min and the slurry was vacuum-filtered through a glass frit filter. The filter cake was removed and transferred back into a flask, then CH_2Cl_2 (25 mL) was added, stirred for 10 min and then the slurry was vacuum-filtered again. The filtrates were combined and dried over $MgSO_4$ and then concentrated in vacuo to afford 3.9 g (78%) of crude (*R*)-glyceraldehyde acetonide[25] as a colourless oil. ^{1}H NMR ($CDCl_3$): δ 9.75 (dd, 1H, J=1.9, 0.4 Hz), 4.41 (ddd, 1H, J=7.3, 4.8, 1.9 Hz), 4.23–4.10 (*AB*MX, 2H), 1.51 (m, 3H), 1.44 (t, 3H, J=0.7 Hz). ^{13}C NMR ($CDCl_3$): δ 201.8, 111.3, 79.8, 66.2, 26.6, 25.1. IR (NaCl) cm^{-1}: 2987 (CH), 1735 (C═O), 1457, 1373. MS m^+/z: 31 (M+1), 115, 101, 85, 73, 59, 55. $[\alpha]_{D^{20}}$ +42.2 (*c* 0.55, CH_2Cl_2).

5.1.15. Preparation of (2R,3R)- and (2R,3S)-l,2-O-isopropylidene-1,2,3-dodecanetriol. To a round bottom flask cooled to 0 °C were put (*R*)-glyceraldehyde acetonide (4.0 g, 30.8 mmol) and Et_2O (10 mL). To this was added nonylmagnesium bromide (38.6 mL, 38.6 mmol, 1 M in diethylether) drop-wise over 15 min. After complete addition the reaction mixture was stirred for 3 h at 0 °C and then placed in a refrigerator overnight. Saturated aqueous NH_4Cl was added to destroy excess Grignard reagent and Et_2O (100 mL) was then added. The layers were separated and the organic phase was washed with water, brine, dried over $MgSO_4$, filtered and solvent evaporated to afford 5.7 g of (2*R*,3*R*)- and (2*R*,3*S*)-l,2-*O*-isopropylidene-1,2,3-dodecanetriol[38] (71%) after purification by silica gel chromatography using 3:1 hexane/ethyl acetate (v/v) as eluent. GC analysis indicated a 6:1 mixture of *erythro* to *threo* alcohols. ^{1}H NMR ($CDCl_3$): δ 4.09–3.90 (m, 2H), 3.80 (m, 1H), 3.67 (t, 1H, J=6.6 Hz), 1.96 (s, 1H), 1.46 (m, 3H), 1.39 (m, 3H), 1.60–1.25 (br m, 16H), 0.90 (t, 3H, J=6.6 Hz). ^{13}C NMR ($CDCl_3$): δ 109.3 (108.9), 79.2 (78.7), 72.3 (70.6), 66.1 (64.5), 33.7 (32.6), 31.9, 29.6 (29.6), 29.5 (two signals), (29.5), (29.45), 29.3 (29.3), 26.6 (26.5), (25.8), 25.5, 25.3, 22.6, 14.1. IR (NaCl) cm^{-1}: 3434 (OH), 2925 (CH), 1467, 1370. MS m^+/z: 243 (M−CH_3), 215, 201, 183, 155, 138, 123, 116, 109, 101, 83, 73, 59, 43.

*5.1.16. Preparation of (2R)-l,2-O-isopropylidene-1,2-dihydroxy-3-dodecanone (**6**).* To a round bottom flask cooled to −78 °C were put CH_2Cl_2 (30 mL) and oxalyl chloride (2.7 mL, 21.3 mmol). To this was added anhydrous DMSO (3.3 mL, 42.6 mmol) in CH_2Cl_2 (5 mL) drop-wise over 5 min. After stirring at 78 °C for 15 min, a solution of (2*R*,3*R*)- and (2*R*,3*S*)-l,2-*O*-isopropylidene-1,2,3-dodecanetriol (5.0 g, 19.4 mmol) in CH_2Cl_2 (10 mL) was added drop-wise over 5 min. The solution was stirred at this temperature for 30 min and then triethylamine (13.6 mL, 97.0 mmol) was added, the cold bath was removed and after stirring for 5 min the reaction mixture was diluted with H_2O and extracted with ether (3×100 mL). The combined organic phase was washed with water, brine, dried over $MgSO_4$, filtered and the solvent removed in vacuo to afford to produce 4.5 g (91%) of (2*R*)-l,2-*O*-isopropylidene-1,2-dihydroxy-3-dodecanone[38] **6** as a colourless oil after purification by silica gel chromatography using 3:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 4.39 (m, 1H), 4.29 (m, 2H), 2.58–2.78 (m, 8H), 1.25 (br s, 14H), 0.90 (t, 3H, J=6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 211.0, 110.9,

80.3, 66.5, 38.6, 31.9, 29.5, 29.4, 29.3, 29.2, 26.0, 25.0, 22.9, 22.7, 14.1. IR (NaCl) cm^{-1}: 2929 (CH), 1718 (C=O), 1458, 1373. MS m^+/z: 241 (M−CH_3), 211, 155, 141, 101, 93, 83, 73, 65, 55, 43. $[\alpha]_{D^{20}}$ +22.7 (*c* 1.1, CH_2Cl_2).

*5.1.17. Preparation of (2R,3R)-l,2-O-isopropylidene-1,2,3-dodecanetriol (**16**).* To a round bottom flask were put (2*R*)-l,2-*O*-isopropylidene-1,2-dihydroxy-3-dodecanone **6** (4.8 g, 18.8 mmol) and THF (30 mL). The solution was cooled to −78 °C and L-Selectride (28.0 mL, 28.0 mmol, 1 M in THF) was added drop-wise over 25 min. After complete addition the mixture was slowly warmed to room temperature and stirred overnight. Then 3 M NaOH (29 mL) and 30% H_2O_2 (25 mL) were successively added while maintaining the temperature below 50 °C. The resulting mixture was stirred for 6 h at 35 °C and then Et_2O (100 mL) was added. The layers were separated and the organic phase was washed with water, brine, dried over $MgSO_4$, filtered and solvent evaporated to afford 4.2 g of a mixture of diastereomeric alcohols (the *threo*/*erythro* ratio was estimated as approximately 8:1 by comparison of GC/MS peak areas), which after silica gel chromatography using 5:1 hexane/ethyl acetate (v/v) as eluent gave (2*R*,3*R*)-l,2-*O*-isopropylidene-1,2,3-dodecanetriol[38] **16** as a clear, yellow oil (71%). ^{1}H NMR ($CDCl_3$): δ 4.07−3.97 (m, 2H), 3.75 (m, 1H), 3.50 (m, 1H), 2.15 (d, 1H, *J*=5.2 Hz), 1.46 (s, 3H), 1.39 (s, 3H), 1.62−1.26 (br m, 16H), 0.90 (t, 3H, *J*=7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 109.3, 79.2, 72.3, 66.1, 62.9, 33.7, 31.9, 29.6, 29.5, 29.3, 26.6, 25.5, 25.3, 22.6, 14.1. IR (NaCl) cm^{-1}: 3477 (OH), 2925 (CH), 1467, 1371. MS m^+/z: 243 (M−CH_3), 215, 201, 183, 155, 138, 123, 116, 109, 101, 83, 73, 59, 43. $[\alpha]_{D^{20}}$ +0.9 (*c* 1.1, CH_2Cl_2).

5.1.18. Preparation of (2R,3R)-l,2-3-dodecanetriol. Into a round bottomed flask were put (2*R*,3*R*)-l,2-*O*-isopropylidene-1,2,3-dodecanetriol **16** (3.2 g, 12.4 mmol), THF (60 mL) and 1 N HCl (60 mL). The mixture was stirred for 6 h at room temperature and then neutralized with saturated $NaHCO_3$. Et_2O (100 mL) was added and the layers were separated. The organic phase was washed with water, brine, dried over $MgSO_4$, filtered, and solvent evaporated to afford 2.1 g of (2*R*,3*R*)-l,2,3-dodecanetriol[36] (78%) as an off white solid after purification by silica gel chromatography using 1:2 hexanes/ethyl acetate (v/v) as eluent. ^{1}H NMR (DMSO): δ 4.34 (m, 1H), 4.25 (d, 1H, *J*=5.4 Hz), 4.06 (d, 1H, *J*=6.3 Hz), 3.42−3.24 (m, 4H), 1.42−1.20 (m, 16H), 0.86 (t, 3H, *J*=6.6 Hz). ^{13}C NMR (DMSO): δ 74.5, 70.9, 63.3, 33.2, 31.9, 29.7, 29.6, 29.5, 29.2, 26.1, 22.6, 14.4. IR (NaCl) cm^{-1}: 3286 (OH), 2917 (CH), 1467. $[\alpha]_{D^{20}}$ +10.9 (*c* 1.1, MeOH). Mp: 63.4−64.4 °C.

5.1.19. Preparation of (2R,3R)-L-(tosyloxy)-2,3-dodecanediol. Into a round bottom flask were put (2*R*,3*R*)-l,2,3-dodecanetriol (1.0 g, 4.6 mmol) and pyridine (5 mL). The solution was cooled to 0 °C and TsCl (0.9 g, 4.6 mmol) was added portion-wise over 15 min. After complete addition the resulting mixture was stored for 72 h in a fridge (4−8 °C) and then diluted with ice water (10 mL). The solution was extracted with Et_2O (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and the solvent evaporated to yield 0.7 g of (2*R*,3*R*)-L-(tosyloxy)-2,3-dodecanediol (40%) as a tan coloured solid after purification by silica gel chromatography using 1:1 hexanes/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 7.83 (dt, 2H, *J*=8.3, 1.8 Hz), 7.35 (dd, 2H, *J*=8.6, 0.7 Hz), 4.11 (*AB*X, 2H), 3.72 (m, 1H), 3.60 (m, 1H), 2.47 (s, 3H), 2.38 (b, 1H), 1.92 (b, 1H), 1.56−1.20 (br s, 16H), 0.89 (t, 3H, *J*=6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 145.2, 132.6, 130.0, 128.0, 77.2, 71.5, 71.4, 70.8, 33.5, 31.9, 30.9, 29.53 (two signals), 29.5, 29.3, 25.5, 22.7, 21.7, 14.1. IR (NaCl) cm^{-1}: 3439 (OH), 2918 (CH), 1599 (C=C). HRMS (m^++H) calcd for $C_{19}H_{33}O_5S$ 373.2049, found 373.2049. $[\alpha]_{D^{20}}$ +10.2 (*c* 1.2, CH_2Cl_2). Mp: 75.6−77.0 °C.

*5.1.20. Preparation of (2R,3R)-l,2-epoxy-3-dodecanol (**5**).* To a round bottom flask were placed (2*R*,3*R*)-1-tosyloxy-2,3-dodecanediol (0.7 g, 1.9 mmol) and MeOH (10 mL). This solution was cooled to 0 °C and anhydrous K_2CO_3 (0.5 g, 3.8 mmol) was added and the reaction mixture was allowed to slowly warm to room temperature and stir for 1 h. The mixture was then diluted with an equal volume of water and extracted with Et_2O (3×25 mL). The combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 0.3 g of (2*R*,3*R*)-l,2-epoxy-3-dodecanol **5** (71%) as a colourless oil after purification by silica gel chromatography with 3:1 hexane/ethyl acetate (v/v) as eluent. This material was spectroscopically and chromatographically identical to its enantiomer **237**. HRMS (m^++H) calcd for $C_{12}H_{25}O_2$ 201.1855, found 201.1852. $[\alpha]_{D^{20}}$ +3.8 (*c* 1.3, CH_2Cl_2).

5.1.21. Preparation of (2R,3R)-l,2-epoxy-3-(tosyloxy)dodecane. To a round bottom flask were put (2*R*,3*R*)-l,2-epoxy-3-dodecanol **5** (0.2 g, 1.0 mmol), Et_2O (10 mL) and TsCl (0.3 g, 1.5 mmol). The solution was cooled to −5 °C and freshly powdered KOH (0.8 g) was added portion-wise over 15 min. After complete addition, the resulting mixture was stirred for 2.5 h at 0 °C and then ice water (10 mL) was added. The solution was extracted with Et_2O (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to yield 0.3 g of (2*R*,3*R*)-l,2-epoxy-3-(tosyloxy)dodecane (74%) as a tan coloured solid after purification by silica gel chromatography with 3:1 hexane/ethyl acetate (v/v) as eluent. This material was spectroscopically and chromatographically identical to its enantiomer (2*S*,3*S*)-l,2-epoxy-3-(tosyloxy)dodecane. HRMS (m^++H) calcd for $C_{19}H_{31}O_4S$ 355.1944, found 355.1940. $[\alpha]_{D^{20}}$ −6.0 (*c* 0.72, CH_2Cl_2).

5.1.22. Preparation of (9R,10S)-9,10-epoxy-nonadec-6-yne. In a round bottom flask cooled to −78 °C were put 1-heptyne (0.17 g, 1.78 mmol) and THF (20 mL) followed by drop-wise addition of *n*-BuLi (1.01 mL, 1.6 M, 1.62 mmol). The resulting mixture was stirred for 30 min and then $BF_3\cdot Et_2O$ (0.21 mL, 1.62 mmol) was added followed 30 min later by (2*R*,3*R*)-l,2-epoxy-3-(tosyloxy)dodecane (1.90 g, 0.54 mmol) in THF (5 mL). The reaction mixture was stirred for 1 h at −78 °C and was then quenched with saturated aqueous NH_4Cl. The solution was extracted with Et_2O (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 0.27 g of crude **17** as a brown oil. The crude alcohol **17** (0.27 g, 0.61 mmol), anhydrous MeOH (5 mL) and anhydrous K_2CO_3 (0.17 g, 1.21 mmol) were stirred together for 1 h to afford 0.08 g of epoxide **37** (46%) as a colourless oil after purification by silica gel chromatography using 8:1 hexane/ethyl acetate (v/v) as eluent. This material was spectroscopically and chromatographically identical to its enantiomer (9*S*,10*R*)-9,10-epoxy-nonadec-6-yne. $[\alpha]_{D^{20}}$ −28.8 (*c* 1.0, CH_2Cl_2).

5.1.23. Preparation of (6Z)-cis-9R,10S-epoxy-nonadecene (1(9R,10S)). (9*R*,10*S*)-9,10-Epoxy-nonadec-6-yne (0.1 g, 0.4 mmol) was taken up in hexane (20 mL) and transferred to a Parr hydrogenation bottle. Lindlar's catalyst (5% palladium on $CaCO_3$ poisoned with lead, 12 mg) and quinoline (4 mg) were then added and the bottle was flushed with hydrogen and the contents were placed under hydrogen pressure (50 psi) and shaken for 1 h. The solution was then filtered through a pad of Celite and the pad was washed with Et_2O. The solvent was removed in vacuo to yield 0.09 g (6Z)-*cis*-9*R*,10*S*-epoxy-nonadecene[37] **1**(9*R*,10*S*) (90%) as a colourless oil after purification by silica gel chromatography using 8:1 hexane/ethyl acetate (v/v) as eluent. This material was spectroscopically and chromatographically identical to its enantiomer **1** (9*S*,10*R*). $[\alpha]_{D^{20}}$ −3.5 (*c* 1.0, CH_2Cl_2).

*5.1.24. Preparation of ethyl (E)-dodec-2-enoate (**11**).* To a round bottom flask cooled to 0 °C were put NaH (1.14 g, 28.5 mmol, 60% in

mineral oil) and THF (50 mL) followed by drop-wise addition of triethylphosphonoacetate (5.6 mL, 28.2 mmol). After stirring for 10 min at 0 °C decanal **12** (4.0 g, 25.6 mmol) in THF (10 mL) was added drop-wise. The reaction mixture was allowed to warm to room temperature and then heated at reflux for 1 h. The solution was cooled and diluted with distilled water and ethyl acetate (1:1, 50 mL), the layers were separated and the aqueous layer was extracted with ethyl acetate (2×30 mL). The combined organic layer was washed with 1 M NaOH, H_2O and brine, dried over $MgSO_4$ and the solvent was removed to afford 5.5 g (95%) of ethyl (*E*)-dodec-2-enoate[39] **11** as a colourless oil after purification by silica gel chromatography using 20:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 6.96 (dt, 1H, *J*=15.7, 7.0 Hz), 5.84 (dt, 1H, *J*=15.7, 1.6 Hz), 4.18 (q, 2H, *J*=7.1 Hz), 2.29 (dtd, 2H, *J*=7.0, 7.0, 1.5 Hz), 1.45 (m, 2H), 1.28 (t, 3H, *J*=7.1 Hz), 1.30–1.26 (m, 12H), 0.88 (t, 3H, *J*=6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 166.8, 149.5, 121.2, 60.1, 32.2, 31.8, 29.5, 29.4, 29.3, 29.1, 28.0, 22.7, 14.3, 14.1. IR (NaCl) cm^{-1}: 2927 (CH), 1724 (C=O), 1265, 1181. MS m^+/z: 227 (M+1), 197, 181, 169, 162, 155, 144, 138, 127, 115, 109, 101, 95, 88, 81, 73, 67, 61, 55.

*5.1.25. Preparation of ethyl (2S,3R)-2,3-dihydroxydodecanoate (**9**).* In a round bottom flask were placed *tert*-butyl alcohol (25 mL), H_2O (25 mL) and AD-mix-β (0.7 g). The solution was stirred at room temperature until all the AD-mix-β had dissolved and then methanesulfonamide (0.5 mg, 5.0 mmol) and ethyl (*E*)-dodec-2-enoate **11** (1.1 g, 5.0 mmol) were added. The reaction mixture was stirred at room temperature until TLC showed complete consumption of starting material, Na_2SO_3 (7.5 g) was then added and stirring continued for another 45 min. The reaction mixture was extracted with ethyl acetate (3×50 mL) and the combined organic layer was washed with 2 N KOH, dried over $MgSO_4$, filtered and the solvent was removed to afford 1.1 g (81%) of ethyl (2*S*,3*R*)-2,3-dihydroxydodecanoate[39] **9** as a pale yellow oil after purification by silica gel chromatography using 2:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 4.32 (q, 2H, *J*=7.1 Hz), 4.10 (dd, 1H, *J*=5.2, 2.1 Hz), 3.90 (m, 1H), 3.04 (d, 1H, *J*=5.2 Hz), 1.86 (d, 1H, *J*=9.2 Hz), 1.68–1.57 (m, 2H), 1.38–1.28 (m, 14H), 1.35 (t, 3H, *J*=7.1 Hz), 0.91 (t, 3H, *J*=6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 174.1, 73.0, 72.5, 62.2, 33.9, 31.9, 29.53, 29.5 (two signals), 29.3, 25.7, 22.7, 14.2, 14.1. IR (NaCl) cm^{-1}: 3374 (OH), 2915 (CH), 1713 (C=O), 1292, 1106. $[\alpha]_{D^{20}}$ +9.8 (*c* 1.1, CH_2Cl_2). Mp: 53.4–55.1 °C.

5.1.26. Preparation of ethyl (2S,3R)-2,3-O-isopropylidene-dodecancarboxylate. To a round bottom flask were put ethyl (2*S*,3*R*)-2,3-dihydroxydodecanoate **9** (0.75 g, 2.88 mmol), CH_2Cl_2 (50 mL), *p*-TSA (50 mg) and 2,2-dimethoxypropane (0.45 g, 4.32 mmol). The reaction mixture was stirred overnight at room temperature and then solid $NaHCO_3$ (0.5 g) was added and the reaction mixture was stirred for an additional 30 min. The reaction mixture was filtered through a pad of neutral alumina and the filtrate concentrated to afford 0.75 g of ethyl (2*S*,3*R*)-2,3-*O*-isopropylidene-dodecancarboxylate[40] (87%) as a colourless oil after silica gel chromatography using 10:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 4.24 (qd, 2H, *J*=7.2, 1.2 Hz), 4.13–4.08 (m, 2H), 1.82–1.62 (m, 2H), 1.46 (s, 3H), 1.44 (s, 3H), 1.36–1.24 (m, 14H), 1.29 (t, 3H, *J*=7.1 Hz), 0.88 (t, 3H, *J*=6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 171.0, 110.7, 79.3, 79.2, 61.3, 33.5, 31.9, 29.5 (two signals), 29.47, 29.3, 27.2, 25.7, 25.6, 22.7, 14.2, 14.1. IR (NaCl) cm^{-1}: 2926 (CH), 1761 (C=O), 1213, 1100. $[\alpha]_{D^{20}}$ +14.1 (*c* 1.1, CH_2Cl_2).

*5.1.27. Preparation of (2R,3R)-2,3-O-isopropylidene-1,2,3-dodectriol (**18**).* To a round bottom flask were put (2*S*,3*R*)-2,3-*O*-isopropylidene-dodecancarboxylate (0.20 g, 0.66 mmol) and THF (10 mL). The solution was cooled to 0 °C and LAH (0.03 g, 0.66 mmol) was added. After complete addition the reaction mixture was stirred for 1 h. The reaction was quenched by successive addition of water (0.3 mL), 15% NaOH (0.3 mL) and water (0.9 mL) again. After stirring for 0.5 h the mixture was filtered through Celite and then dried over $MgSO_4$. The solvent was removed in vacuo to yield 0.17 g (97%) of (2*R*,3*R*)-2,3-*O*-isopropylidene-1,2,3-dodecanetriol[40] **18** as a colourless oil, which was of sufficient purity to be used directly for the next reaction. This material was spectroscopically and chromatographically identical to its enantiomer **14**. $[\alpha]_{D^{20}}$ +14.9 (*c* 1.0, CH_2Cl_2).

5.1.28. Preparation of (2R,3R)-2,3-O-isopropylidene-1-(tosyloxy)-2,3-dodecanediol. To a round bottom flask were put (2*R*,3*R*)-2,3-*O*-isopropylidene-1,2,3-dodectriol **18** (0.32 g, 1.16 mmol), Et_2O (10 mL) and TsCl (0.33 g, 1.74 mmol). The solution was cooled to −5 °C and freshly powdered KOH (1.0 g) was added portion-wise over 15 min. After complete addition, the resulting mixture was stirred for 2.5 h at 0 °C and then ice water (10 mL) was added. The solution was extracted with ether (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to give (2*R*,3*R*)-2,3-*O*-isopropylidene-1-(tosyloxy)-2,3-dodecanediol (89%) as a tan coloured oil after silica gel chromatography using 3:1 hexane/ethyl acetate (v/v) as eluent. This material was spectroscopically and chromatographically identical to its enantiomer (2*S*,3*S*)-2,3-*O*-isopropylidene-1-(tosyloxy)-2,3-dodecanediol. $[\alpha]_{D^{20}}$ +9.7 (*c* 1.1, CH_2Cl_2).

*5.1.29. Preparation of (2R,3R)-1,2-epoxy-3-dodecanol tert-butyldimethylsilyl ether (**8**).* In a round bottom flask were placed (2*R*,3*R*)-l,2-epoxy-3-dodecanol **5** (0.2 g, 1.0 mmol), imidazole (0.1 g, 1.5 mmol) and DMF (3 mL). To this solution was then added TBSCl (0.2 g, 1.1 mmol). The reaction mixture was stirred 16 h at room temperature and quenched by addition of H_2O (8 mL). The reaction mixture was extracted with Et_2O (3×10 mL) and the combined extracts were washed with water, brine and dried over $MgSO_4$. The solvent was removed to afford 0.3 g of (2*R*,3*R*)-1,2-epoxy-3-dodecanol *tert*-butyldimethylsilyl ether **8** (88%) as a colourless oil after silica gel chromatography using 5:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 3.27 (m, 1H), 2.93 (m, 1H), 2.79 (m, 1H), 2.56 (m, 1H), 1.58–1.42 (s, 14H), 0.94–0.86 (m, 12H), 0.13 (s, 3H), 0.08 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 74.6, 56.0, 44.9, 34.7, 31.9, 29.6, 29.5, 29.3, 25.9 (two signals), 25.3, 22.7, 18.2, 14.1, −4.4, −5.0. IR (NaCl) cm^{-1}: 2927 (CH), 1102, 837. MS m^+/z: 299, 271, 253, 227, 187, 157, 143, 131, 115, 101, 75, 67, 59. HRMS (m^++H) calcd for $C_{18}H_{39}O_2Si$ 315.2719, found 315.2719. $[\alpha]_{D^{20}}$ −9.5 (*c* 1.0, CH_2Cl_2). $[\alpha]_{D^{20}}$ +6.8 (*c* 1.2, CH_2Cl_2).

5.1.30. Preparation of (9S,10R)-9-hydroxy-10-tert-butyldimethylsilyloxynonadec-6-yne. In a round bottom flask cooled to −78 °C were put 1-heptyne (0.18 g, 1.91 mmol) and THF (20 mL) followed by drop-wise addition of n-BuLi (1.10 mL, 1.6 M, 1.74 mmol). The resulting mixture was stirred for 30 min and then $BF_3\cdot Et_2O$ (0.21 mL, 1.74 mmol) was added followed 30 min later by (2*R*,3*R*)-1,2-epoxy-3-dodecanol *tert*-butyldimethylsilyl ether **8** (0.18 g, 0.58 mmol) in THF (5 mL). The reaction mixture was stirred for 1 h at −78 °C and was then quenched with saturated aqueous NH_4Cl. The solution was extracted with ether (3×25 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 0.14 g (61%) of (9*S*,10*R*)-9-hydroxy-10-*tert*-butyldimethylsilyloxynonadec-6-yne as a yellowish oil after silica gel chromatography using 10:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 3.85 (m, 1H), 3.62 (m, 1H), 2.40–2.29 (m, 3H), 2.20–2.15 (m, 2H), 1.80–1.20 (m, 22H), 0.98–0.88 (m, 15H), 0.13 (s, 3H), 0.12 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 82.4, 76.4, 72.7, 71.3, 33.8, 31.9, 31.1, 29.7, 29.6, 29.5, 29.3, 28.7, 25.9, 25.3, 24.6, 22.7, 22.2, 18.7, 18.1, 14.1, 14.0, −4.2, −4.7. IR (NaCl)

cm^{-1}: 3551 (OH), 2927 (CH). HRMS (m^++H) calcd for $C_{25}H_{50}O_2Si$ 431.3658, found 431.3655. $[\alpha]_{D^{20}}$ −9.5 (*c* 1.0, CH_2Cl_2).

5.1.31. Preparation of (9S,10R)-9-mesyloxy-10-tert-butyldimethylsilyloxynonadec-6-yne. In a round bottom flask cooled to 0 to −10 °C were put (9*S*,10*R*)-9-hydroxy-10-*tert*-butyldimethylsilyloxynonadec-6-yne (0.09 g, 0.23 mmol), dichloromethane (2 mL) and triethylamine (0.05 mL, 0.35 mmol). To this solution was added MsCl (0.02 mL, 0.25 mmol) and the resulting mixture was stored for 72 h in a fridge (4–8 °C). It was then diluted with dichloromethane (5 mL) and was washed with ice water (3 mL), 10% HCl solution, saturated sodium bicarbonate solution and brine. The organic phase was dried over $MgSO_4$, filtered and the solvent evaporated to yield 0.08 g of (9*S*,10*R*)-9-mesyloxy-10-*tert*-butyldimethylsilyloxynonadec-6-yne (70%) as a pale yellow oil after silica gel chromatography using 5:1 hexane/ethyl acetate (v/v) as eluent. ^{1}H NMR ($CDCl_3$): δ 4.57 (m, 1H), 3.96 (m, 1H), 3.14 (s, 3H), 2.74 (dm, 1H, *J*=17.2 Hz), 2.52 (ddd, 1H, *J*=17.0, 8.1, 2.3 Hz), 2.18–2.12 (m, 2H), 1.54–1.26 (m, 22H), 0.92 (m, 15H), 0.14 (s, 3H), 0.10 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 82.9, 82.8, 75.7, 72.0, 38.5, 31.9, 31.4, 31.1, 29.6, 29.5 (two signals), 29.3, 28.5, 25.8 (two signals), 25.4, 22.7, 22.2, 19.9, 18.7, 18.0, 14.1, 14.0, −4.54, −4.59. IR (NaCl) cm^{-1}: 2928 (CH), 1725, 1366, 1178. HRMS (m^++H) calcd for $C_{26}H_{53}O_4SSi$ 489.3434, found 489.3434.

5.1.32. Preparation of (9S,10R)-9,10-epoxy-nonadec-6-yne. In a round bottom flask were put (9*S*,10*R*)-9-mesyloxy-10-*tert*-butyldimethylsilyloxynonadec-6-yne (55 mg, 0.1 mmol) and THF (3 mL) followed by drop-wise addition of TBAF (1 M soln in THF, 0.11 mL, 0.11 mmol). The reaction mixture was stirred for 1 h at room temperature and was then quenched with saturated aqueous NH_4Cl. The solution was extracted with ether (3×5 mL) and the combined organic phase was washed with water, dried over $MgSO_4$, filtered and solvent evaporated to afford 26 mg of (9*S*,10*R*)-9,10-epoxynonadec-6-yne (85%) as a colourless oil after purification by silica gel chromatography using 8:1 hexane/ethyl acetate (v/v) as eluent. This material was identical in all respects to the material synthesized from the previous route. $[\alpha]_{D^{20}}$ +30 (*c* 2.6, CH_2Cl_2).

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.05.015.

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