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Hydrolytic kinetic resolution of terminal mono- and bis-epoxides in the synthesis of insect pheromones: routes to (−)-(*R*)- and (+)-(*S*)-10-methyldodecyl acetate, (−)-(*R*)-10-methyl-2-tridecanone, (−)-(*R*)-(*Z*)-undec-6-en-2-ol (Nostrenol), (−)-(1*R*,7*R*)-1,7-dimethylnonyl propanoate, (−)-(6*R*,12*R*)-6,12-dimethylpentadecan-2-one, (−)-(2*S*,11*S*)-2,11-diacetoxytridecane and (+)-(2*S*,12*S*)-2,12-diacetoxytridecane

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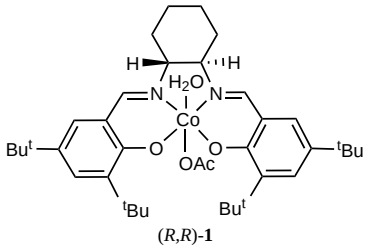
Abstract—Hydrolytic kinetic resolution (HKR) of functionalised epoxides using (salen)Co(OAc) complexes provides enantiomerically enriched epoxides and diols, which have been transformed into important insect sex pheromones. In this general approach, (−)-(*R*)- and (+)-(*S*)-10-methyldodecyl acetates from the smaller tea tortrix moth were obtained, as was (−)-(*R*)-10-methyltridecan-2-one from the southern corn rootworm. The (*S*)-epoxide obtained from undec-1-en-6-yne was transformed to (−)-(*R*)-(*Z*)-undec-6-en-2-ol (Nostrenol) from ant-lions. HKR of appropriate bisepoxides was also investigated, and transformations of the resulting bisepoxides and epoxydiols provided (−)-(1*R*,7*R*)-1,7-dimethylnonylpropanoate from corn rootworms, (−)-(6*R*,12*R*)-6,12-dimethylpentadecan-2-one from the female banded cucumber beetle, and (−)-(2*S*,11*S*)-2,11-diacetoxytridecane and (+)-(2*S*,12*S*)-2,12-diacetoxytridecane from female pea-midges.

1. Introduction

Many chiral insect semiochemicals have been identified in the last 40 years,[1] with the sense of chirality being a crucial determinant of perception and induced behaviour.[2] The determination of the enantiomeric composition by chromatographic methods or biological assays,[3] requires synthetic methods that deliver particular enantiomers of the suspected active component. Quite commonly, insect semiochemicals, including sex pheromones, incorporate a medium to long hydrocarbon chain with some oxygen functionality, often alkyl branching, with a specific or strongly dominating chirality and/or double bond configuration. These structural features, and the regio- and stereo-regularities characterising nucleophilic opening of terminal epoxides, and displacement of sulfonate ester moieties,[4] suggested that a reliable route to epoxides and 1,2-diols of high enantiomeric excesses (e.e.s) would expedite acquisition of such semiochemicals. Jacobsen has introduced procedures for the hydrolytic kinetic resolution (HKR) of terminal epoxides which utilise (salen)Co(OAc) complexes,[5] e.g. **1**.



(*R*,*R*)-**1**

Most reports of successful HKR relate to simple epoxides lacking other functionality. This situation is chang-

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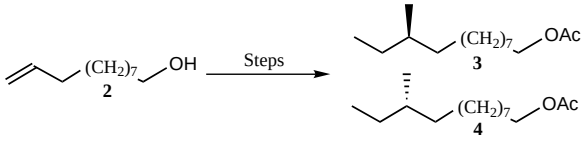
ing, and more varied, but still terminal epoxides may be satisfactorily processed.[6] We now wish to describe the application of the HKR approach to a number of functionalised terminal epoxides, and how the resulting highly enantiomerically enriched epoxides and diols may be transformed to a range of important insect semiochemicals, by routes which are in the main, more direct than those previously described. In situations where acquisition of both enantiomers of an insect component is desirable, the re-constitution of the diol (from the HKR procedure) to the alternate epoxide enantiomer, permits this.

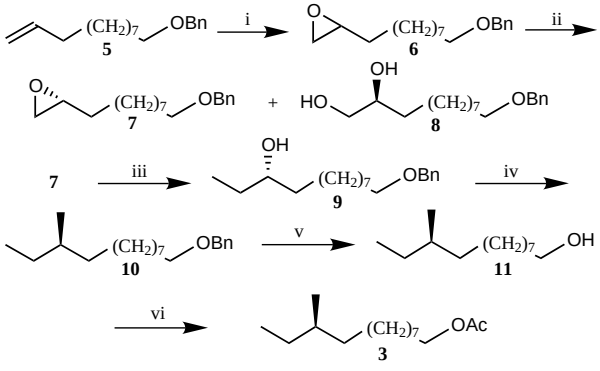
2. Results and discussion

2.1. Hydrolytic kinetic resolution of mono-epoxides

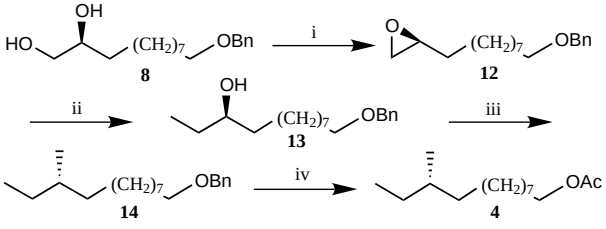
2.1.1. (–)-(*R*)- and (+)-(*S*)-10-Methyldodecyl acetate 3 and 4, respectively. Initially this general approach was directed towards (*R*)-(–)- and (*S*)-(+)-10-methyldodecyl acetate, **3** and **4**, respectively, which are components of the pheromone of the lesser tea tortrix moth, *Adoxophes* spp. (Lepidoptera: Tortricidea).[7]



The (*R*)-isomer **3** was slightly more bioactive than the (*S*), **4**.[8] A number of syntheses of **3** and **4** have been reported and representative approaches utilise chiral auxiliaries, resolution of an intermediate, and organoborane chemistry.[9–11] Our procedure commenced with commercially available 10-undecenol **2**, which as its benzyl ether **5**, was epoxidised with *m*-chloroperbenzoic acid (*m*-CPBA) in dichloromethane (DCM). Epoxide **6**, as the substrate for HKR, was stirred with 0.5 mol% of (*R*,*R*)-**1** and 0.55 mol equiv. of H_2O at room temperature (~22°C) for ca. 24 h. Chromatography on silica easily separated (*R*)-epoxide **7** and (*S*)-diol **8** and with excellent recoveries, 48 and 45%, respectively. Epoxide **7** (>98% e.e. by chiral HPLC) on treatment with Me_2CuLi afforded secondary alcohol **9** in high yield, which was converted to the mesylate in the standard way. Mesylate displacement was effected with an excess of Me_2CuLi in ether, and afforded predominantly benzyl ether **10** of 10-methyldodecanol **11**, of inverted configuration, along with significant elimination products (~30%), which were difficult to suppress. Previous studies have demonstrated that displacement of secondary sulfonate ester groups by simple alkyl cuprates proceeds with inversion of configuration, and is accompanied by varying levels of elimination.[4] An ozonolytic method of debenzylation was adopted, as this would, in addition to transforming the benzyl ether to the benzoate ester, degrade the accompanying alkenes. Thus, treatment of benzyl ether **10** and the accompanying alkenes with ozone–Me_2S, followed by flash chromatography, afforded the benzoate ester, which was hydrolysed with K_2CO_3/MeOH to afford alcohol **11**. Acetylation yielded the target compound (–)-(*R*)-acetate **3**, with $[\alpha]_D^{23}$ –5.4 (*c* 0.97, $CHCl_3$). The (+)-(*S*)-isomer was also acquired. Treatment of (*S*)-diol **8**, from the HKR step, with mesyl chloride (1 equiv.) selectively esterified the primary alcohol, and upon exposure to K_2CO_3/MeOH afforded epoxide **12** which was then processed to benzyl ether **14** as outlined above. (The alternate procedure for converting the diol to the epoxide, through the cyclic sulfate, may have led to a higher yield, on the basis of our experience in closely related systems.) Debenzylation was achieved by hydrogenolysis (H_2, Pd–C, 95%), and then acetylation provided (+)-(*S*)-acetate **4**, with $[\alpha]_D^{23}$ +5.3 (*c* 1.02, $CHCl_3$). These procedures are summarised below in Schemes 1 and 2. Our specific rotation values compare favorably with those reported, which ranged from +4.3 (80% e.e.) to +5.6,[9] +5.9[10] and +4.5[11] (all for $CHCl_3$).



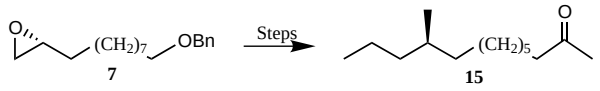
Scheme 1. *Reagents and conditions*: (i) *m*-CPBA, DCM; (ii) 0.5% equiv. (*R*,*R*)-1, 0.55 equiv. H_2O; (iii) Me_2CuLi, Et_2O, 0°C; (iv) 1. MsCl, Et_3N, 2. Me_2CuLi, Et_2O, 0°C; (v) 1. O_3, Me_2S, 2. K_2CO_3, MeOH; (vi) Ac_2O, Py.



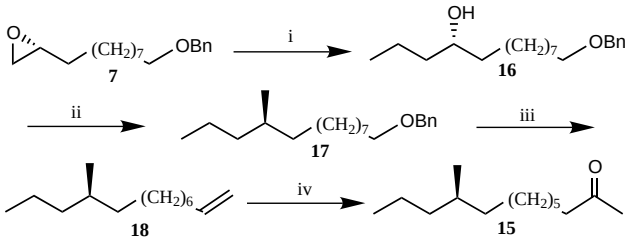
Scheme 2. *Reagents and conditions*: (i) 1. MsCl, Et_3N, 2. K_2CO_3, MeOH; (ii) Me_2CuLi, Et_2O, 0°C, (iii) 1. MsCl, Et_3N, 2. Me_2CuLi, Et_2O, 0°C; (iv) 1. H_2, Pd–C (10%), 2. Ac_2O, Py.

2.1.2. (–)-(*R*)-10-Methyltridecan-2-one 15. Ketone **15** is the sex pheromone of the southern corn rootworm (*Diabrotica undecimpunctata howardi*), and biological evaluation of the enantiomers indicated that the (*R*)-enantiomer was preferred by males.[12] Previous syntheses have relied on resolution,[9] chiral pool starting materials, ((*R*)-citronellyl acetate and (*S*)-3,7-dimethyl-1,6-octadiene),[13] and asymmetric induction in an organocopper addition to the camphorsulfonamide derived crotyl ester.[14] Several of these procedures are

somewhat lengthy, but the reported specific rotations for the (*R*)-enantiomer ($[\alpha]_D$ ($CHCl_3$) of −1.7,[9] −1.4,[13] −1.64,[15] and −1.61[14]) agree well. The lowest value (−1.4) may be associated with some racemisation in a reduction step.[13]

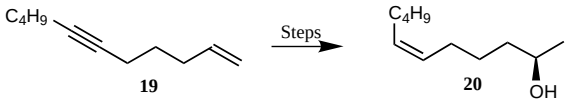


In our approach, (*R*)-epoxide **7** was treated with EtMgBr, in the presence of CuI, to provide the mono-protected (*S*)-diol **16**. The derived secondary mesylate was then treated with an excess of Me_2CuLi in ether to afford the benzyl-protected (*R*)-10-methyltridecanol **17**. Installation of the methyl ketone moiety was achieved by Wacker oxidation of the terminal alkene **18**, in turn generated by [2,3]-Wittig rearrangement of benzyl ether **17**. In this way, (−)-(*R*)-ketone **15**, with $[\alpha]_D^{22}$ −1.6 (*c* 0.7, $CHCl_3$) was obtained in five steps (~10% overall yield) from (*R*)-epoxide **7**. This procedure is shown in Scheme 3.

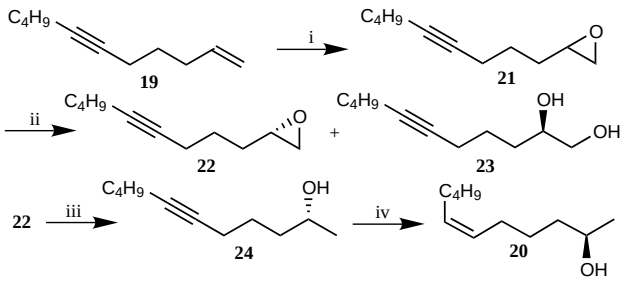


Scheme 3. *Reagents and conditions*: (i) EtMgBr, CuI; (ii) 1. MsCl, Et_3N, 2. Me_2CuLi, Et_2O, 0°C; (iii) ^{n}BuLi, THF, −78°C; (iv) $PdCl_2$, CuCl, DMF–H_2O, O_2.

2.1.3. (−)-(*R*)-(*Z*)-Undec-6-en-2-ol (Nostrenol) 20. Volatile secretions from three sympatric ant-lion species, *Euroleon nostras*, *Grocus bore* and *Myrmeleon formicarius* have been investigated, and (−)-(*R*)-(*Z*)-undec-6-en-2-ol **20** (Nostrenol) of >99.9% e.e. was identified from the former two species.[16] Previous synthesis of the (*S*)-enantiomer (*ent*-**20**) utilised (*S*)-propylene oxide, and a Mitsunobu inversion led to (*R*)-Nostrenol **20**. Our approach sought to utilise HKR, and to demonstrate further the utility of a Ti-based method for stereospecific *Z*-reduction of an isolated yne to the *Z*-ene moiety.



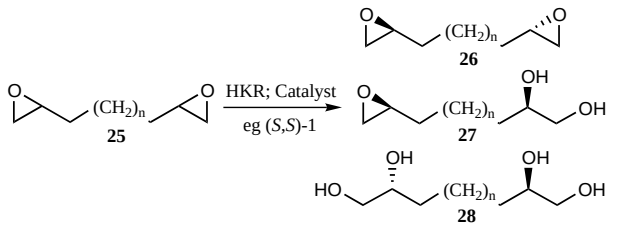
The procedure commenced with 1-hexyne, which on deprotonation and alkenylation with 5-bromo-1-pentene, furnished undec-1-en-6-yne **19** (Scheme 4). Treatment with *m*-CPBA in DCM wrought highly chemoselective alkene epoxidation to provide the volatile epoxy-yne **21**, the required HKR substrate. Use of (*S*,*S*) catalyst and 0.55 equiv. of H_2O in the standard fashion provided (*S*)-epoxide **22** and (*R*)-diol **23**, the latter in 43% yield (maximum of 50%). Regiospecific reductive opening of (*S*)-epoxide **22** with $NaBH_4$/EtOH provided (*R*)-alcohol **24**, which was converted to its Mosher's ester and assayed at >95% e.e. Alcohol **24**, protected as the tetrahydropyran-2′-yl (THP) ether, was now ready for Ti-mediated *Z*-reduction, which was conducted as described in detail elsewhere for analogous systems.[17] Treatment with $Ti(O^iPr)_4$ and ^{i}PrMgBr in ether (−78→−40°C) followed by aqueous quenching provided the *Z*-alkene. Removal of the THP group led to the desired (−)-(*R*)-(*Z*)-enol **20**, with $[\alpha]_D^{23}$ −5.5 (*c* 0.70, $CHCl_3$) which may be compared with the reported value, α_D −6.1 (neat).[16] Our sample of Nostrenol was a single double bond isomer on the basis of the ^{13}C NMR spectrum, and its *Z*-configuration was established by decoupling (of the allylic protons) and measurement of $^3J_{6\text{-}7}$ (10.8 Hz), appropriate for the *Z*-configuration.[18] The Ti-mediated conversion of alkynes to *Z*-alkenes, in all cases we have scrutinised, proceeds in a highly selective *Z*-sense (>99.5%). Although not undertaken, diol **23** from the HKR could have been reconstituted to the (*R*)-epoxide and thence to (+)-(*S*)-(*Z*)-undec-6-en-2-ol.



Scheme 4. *Reagents and conditions*: (i) *m*-CPBA, DCM; (ii) 0.5% equiv. (*S*,*S*)-1, 0.55 equiv. H_2O; (iii) $NaBH_4$, EtOH; (iv) 1. DHP, H^+, 2. $Ti(O^iPr)_4$, ^{i}PrMgBr, Et_2O then H_2O, 3. MeOH, H^+.

2.2. Hydrolytic kinetic resolution of bisepoxides

Terminal bisepoxides (e.g. **25**) should be amenable to the HKR protocol and thereby extend the synthetic utility of this procedure. HKR of bisepoxide **25** should afford unprocessed bisepoxide **26**, epoxydiol **27** and tetrol **28**, all in high e.e. This outcome is shown below, with the theoretical maximal proportions being 25% of (*S*,*S*)-bisepoxide **26**, 50% of (*S*,*R*)-epoxydiol **27**, and 25% of (*R*,*R*)-tetrol **28**.



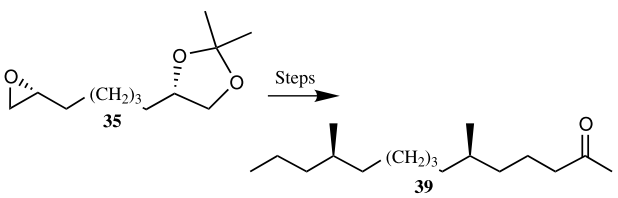
The predominating epoxydiol (e.g. **27**) may provide bi-directional and selective functionalisation, whereas the bisepoxide and tetrol (which may be reconstituted to the enantiomeric bisepoxide) are capable of afford-

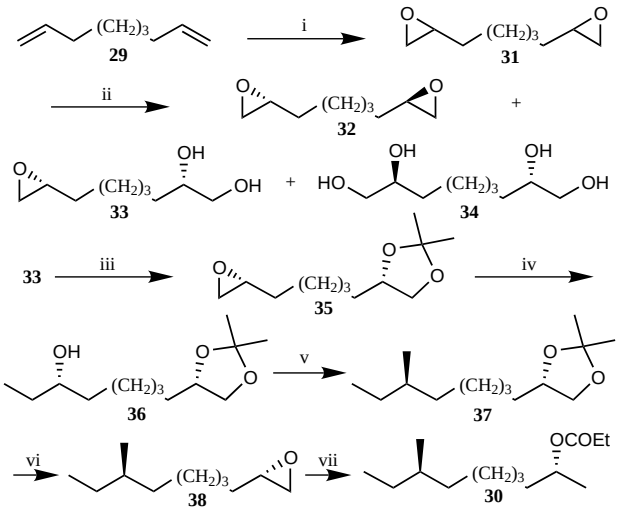
ing C_2-symmetric derivatives. Given the ease of acquiring the starting racemic bisepoxides, examination of their HKR in the context of synthesis of selected insect sex pheromones was undertaken, particularly towards components incorporating two distant stereogenic centres, and possibly additional functionality. At the time this work was commenced, we were unaware of any reports describing HKR of racemic bisepoxides, but Yokota[19] has described the asymmetric cyclisations of a few *meso* bisepoxides, which exhibit quite high e.e.s. It is worthy of emphasis that aliphatic, open-chain systems, with 'non-interacting' remote stereogenic centres, are generally assembled by 'coupling' separately prepared building blocks of appropriate chirality. The HKR of bisepoxides provides an alternative to this approach, and this is now demonstrated with the synthesis of several insect pheromones incorporating two remote stereogenic centres.

2.2.1. (−)-(1*R*,7*R*)-1,7-Dimethylnonyl propanoate 30. Various isomers of 1,7-dimethylnonyl propanoate exhibit attractancy for males of corn rootworms, with western corn rootworm (*Diabrotica virgifera virgifera*) and northern corn rootworm (*D. barberi*) responding strongly to the (1*R*,7*R*)-isomer.[20] Previous syntheses of the four stereoisomers were based on optical resolution of key intermediates[21] or connection of chiral pool-derived units about a one-carbon linker.[22] More recently, Keinan[23] synthesised all four isomers of this propanoate system by exploiting the selectivity of an alcohol dehydrogenase (TBADH) in reduction of nonane-2,8-dione.

In our approach, bisepoxide **31** from 1,8-nonadiene **29** was treated with 1.0% equiv. of (*R*,*R*)-**1** and 0.8 equiv. of H_2O and provided a mixture of bisepoxide **32**, epoxydiol **33** and tetrol **34**. Flash column chromatography permitted easy separation of these components shown below in Scheme 5.

Epoxydiol **33** was converted to acetonide **35**, which was then treated with Me_2CuLi in ether to provide secondary alcohol **36**. Mesylation and further treatment with Me_2CuLi effected methylation with inversion, to furnish acetonide **37**. Deprotection released the diol, which was reconstituted to epoxide **38** by selective mesylation of the primary alcohol and cyclisation with base (K_2CO_3 in MeOH). Reductive opening of epoxide **38** with $NaBH_4$/EtOH, followed by esterification with propanoic anhydride in pyridine, provided the target pheromone, (−)-(1*R*,7*R*)-propanoate **30**, with $[\alpha]_D^{23}$ −7.2 (*c* 0.70, $CHCl_3$). Reported rotations are −8.0[23] and −7.6.[22]

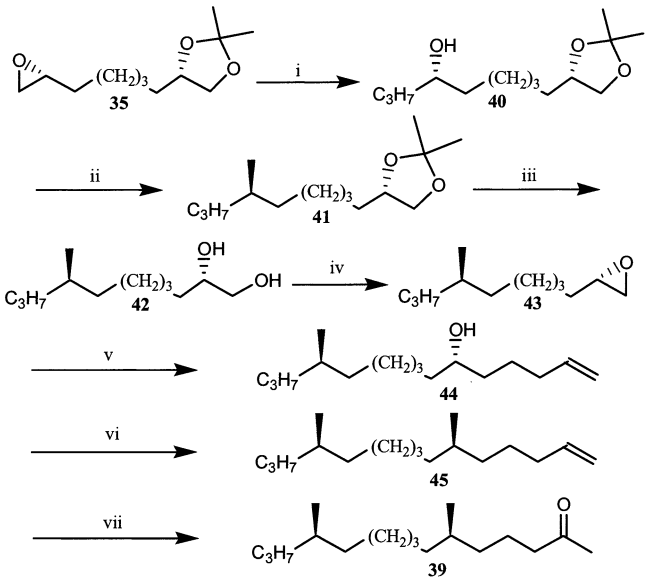




Scheme 5. *Reagents and conditions*: (i) *m*-CPBA, DCM; (ii) 1.0% equiv. (*R*,*R*)-**1**, 0.8 equiv. H_2O; (iii) DMP, H^+; (iv) Me_2CuLi, Et_2O, 0°C; (v) 1. MsCl, Et_3N, 2. Me_2CuLi, Et_2O, 0°C; (vi) 1. MeOH, H^+, 2. MsCl, Et_3N, 3. K_2CO_3, MeOH; (vii) 1. $NaBH_4$, EtOH, 2. $(EtCO)_2O$, Py.

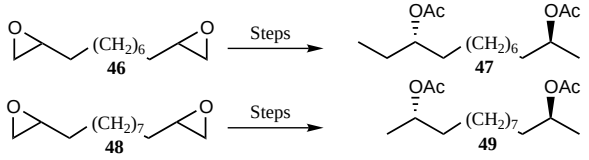
2.2.2. (−)-(6*R*,12*R*)-6,12-Dimethylpentadecan-2-one 36. Ketone **39** is the female produced sex pheromone of the banded cucumber beetle (*Diabrotica balteata*), the larvae of which are serious pests of crops such as cucurbits and sweet potatoes.[24] The route to **39** commenced with epoxy-acetonide **35** is shown in Scheme 6. Treatment of the acetonide with EtMgBr-CuI provided secondary alcohol **40**, which through its mesylate was methylated with Me_2CuLi, to furnish **41**. The released diol **42** was converted to epoxide **43**, treatment of which with but-3-enyl magnesium bromide–CuI yielded hydroxyalkene **44**. Application of the methylation routine (mesylation and treatment with Me_2CuLi) delivered terminal alkene **45**, which under Wacker oxidation conditions was transformed to the target pheromone **39**, with $[\alpha]_D^{23}$ −0.4 (*c* 0.40, $CHCl_3$). In Mori's approach to these stereoisomers, two fragments from citronellol were linked by sulfone mediation, and the resulting (6*R*,12*R*)-isomer exhibited $[\alpha]_D^{22}$ −0.5 ($CHCl_3$).[25] More recently, Enders accessed this isomer by utilizing nucleophilic allylation of an enantiopure π-allyl-tetracarbonyl iron complex, in a longish procedure that ultimately involved linkage of two chiral units by sulfone based coupling. The product had $[\alpha]_D^{20}$ −0.5 (*c* 0.60, $CHCl_3$) and was considered to be >98% e.e.[26]

2.2.3. (−)-(2*S*,11*S*)-2,11-Diacetoxytridecane 47 and (+)-(2*S*,12*S*)-2,12-diacetoxytridecane 49. The diesters **47** and **49** were two of the three active components identified by coupled gas chromatography–electroantennography of extracts from the pheromone glands of female pea midges, *Contarinia pisi*, which are serious pests of commercial peas.[27] As part of that investigation, Hilbur and Francke[27] described the syntheses of these systems in both racemic and enantiomeric forms, and also of the third component, 2-acetoxytridecane. The approach to the optical isomers of these systems was based on alkylation, at both ends of a central carbon chain, with



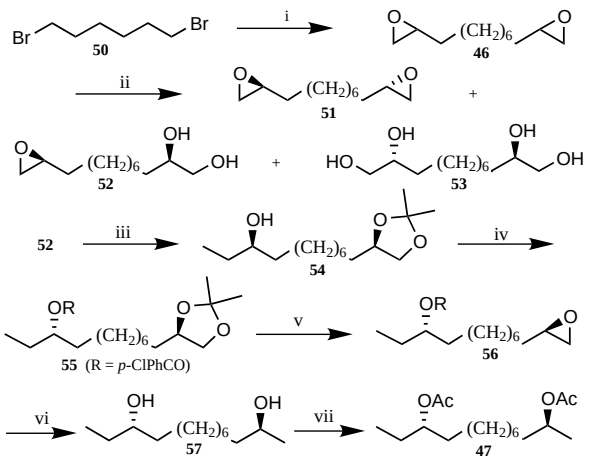
Scheme 6. *Reagents and conditions*: (i) EtMgBr, CuI, Et_2O, 0°C; (ii) 1. MsCl, Et_3N, 2. Me_2CuLi, Et_2O, 0°C; (iii) MeOH, H^+; (iv) 1. MsCl, Et_3N, 2. K_2CO_3, MeOH; (v) $H_2C{=}CH(CH_2)_2MgBr$, CuI, Et_2O, 0°C; (vi) 1. MsCl, Et_3N, 2. Me_2CuLi, Et_2O, 0°C; (vii) $PdCl_2$, CuCl, DMF–H_2O, O_2.

(*S*)- or (*R*)-methyl oxirane, or with epichlorohydrin.[27] It is seen that this procedure represents the general approach to carbon chains carrying remote stereogenic centres.



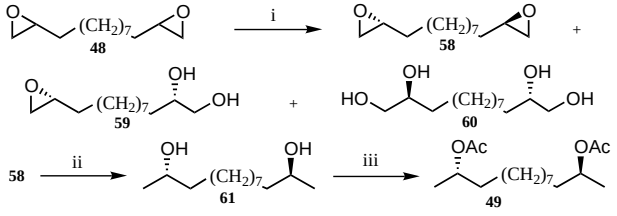
The HKR approach appeared to offer a straightforward alternative for accessing both **47** and **49**. Thus, bisepoxide **46** of dodeca-1,11-diene, acquired by double allylation of 1,6-dibromohexane **50**, was treated with (*S*,*S*) catalyst and H_2O as shown below in Scheme 7. The necessary epoxydiol **52** was acquired in 26% isolated yield. For the target (2*S*,11*S*)-**47**, stereochemical inversion of the secondary alcohol resulting from initial epoxide opening was necessary. Hence, the acetonide from epoxydiol **52** was treated with MeMgBr–CuI to provide **54**, which under Mitsunobu conditions afforded the inverted *p*-chlorobenzoate **55**. Acetonide removal, with Amberlite in MeOH, was followed by re-formation of the epoxide from the 1,2-diol. The now available epoxyester **56**, on reduction with $LiAlH_4$, yielded (2*S*,11*S*)-diol **57** which was converted to the required (–)-(2*S*,11*S*)-diacetate **47**, with $[\alpha]_D^{23}$ –4.0 (*c*, 0.70, $CHCl_3$). This compares favourably with the reported rotation ($[\alpha]_D^{20}$ –4.3 ($CHCl_3$)).[28]

In a similar way, bisepoxide **48** of 1,12-tridecadiene was processed with (*R*,*R*)-**1** to provide the easily separated components **58**, **59** and **60**, as shown below in Scheme 8.



Scheme 7. *Reagents and conditions*: (i) 1. Allyl MgBr, THF, 2. *m*-CPBA, DCM; (ii) 1.0% equiv. (*S*,*S*)-1, 0.6 equiv. H_2O; (iii) 1. DMP, H^+, 2. CH_3MgBr, CuI, Et_2O, 0°C; (iv) Ph_3P, *p*-chlorobenzoic acid, DEAD, THF; (v) 1. MeOH, H^+, 2. MsCl, Et_3N, 3. K_2CO_3, MeOH; (vi) $LiAlH_4$, Et_2O; (vii) Ac_2O, Py.

Bisepoxide **58**, on treatment with $NaBH_4$/EtOH, provided (2*S*,12*S*)-diol **61**, which on acetylation furnished the target (+)-(2*S*,12*S*)-diacetate **49**, with $[\alpha]_D^{23}$ +1.8 (*c* 1.21, $CHCl_3$). The reported value was $[\alpha]_{578}$ +2.0 ($CHCl_3$).[28] In a similar way, epoxydiol **59** and tetrol **60** could be converted to the (2*R*,12*S*)- and (2*R*,12*R*)-stereoisomers, respectively, but this was not undertaken.



Scheme 8. *Reagents and conditions*: (i) 1.0% equiv. (*S*,*S*)-1, 0.6 equiv. H_2O; (ii) $NaBH_4$, EtOH; (iii) Ac_2O, Py.

3. Conclusion

The value of hydrolytic kinetic resolution in providing a range of highly enantiomerically enriched terminal mono- and bisepoxides has been demonstrated by the efficient conversion of such epoxides to a range of important insect sex pheromones.

4. Experimental

4.1. General

NMR spectra were obtained with Bruker EM200, AMX400 and AV400 spectrometers, using $CDCl_3$ or EtOH-d_6 as solvent, and referenced to residual solvents at δ_H 7.24 and δ_C 77.0, and δ_H 5.19 and δ_C 56.8,

respectively. The mass spectra (MS) were recorded on a Hewlett–Packard 5890A GC/Mass Detector at 70 eV. High resolution mass spectrum was performed on a Finnigan MAT 900XL spectrometer. Microanalyses were performed on the Elemental Analyzer Model 1106 from Elemental Microanalysis Limited. Flash chromatography was carried out using Merck silica gel (230–400 mesh). Optical rotations were measured at 589 nm using a 1 dm cell on a Perkin–Elmer 241MC polarimeter.

4.2. (−)-(*R*)- and (+)-(*S*)-10-Methyldodecyl acetate 3 and 4

1-Benzyloxy-undec-10-ene ***5***: Under an inert atmosphere, sodium hydride (60% dispersion in mineral oil, 2.2 g, 55.0 mmol) was washed with hexane, followed by the addition of THF (20 mL) and *t*-butylammonium iodide (0.50 g, 1.4 mmol). After cooling to 0°C, neat 10-undecenol (4.9 g, 29.0 mmol) was added dropwise and the suspension was stirred at room temperature (rt) for 30 min. Benzyl bromide (8.1 g, 47.5 mmol) was slowly added to the above, and the mixture was stirred for 3.5 h. The reaction was quenched by careful addition of H_2O, followed by washing with H_2O. The organic layer was separated, dried over $MgSO_4$, and concentrated. The benzyl ether was distilled at 119–121°C/0.3 mmHg as a slightly yellowish liquid (7.5 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.24 (*m*, 5H), 5.81 (*ddt*, 1H, $J=17.00$, 10.24, 6.72 Hz), 4.98 (*dm*, 1H, $J=17.08$ Hz), 4.92 (*ddt*, 1H, $J=10.20$, 2.32, 1.16 Hz), 4.49 (*s*, 2H), 3.45 (*t*, 2H, $J=6.68$ Hz), 2.03 (*qt*, 2H, $J=6.80$, 1.36 Hz), 1.62–1.27 (*m*, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 138.7, 128.3, 127.6, 127.4, 114.1, 72.8, 70.5, 33.8, 29.8, 29.5, 29.44, 29.41, 29.1, 28.9, 26.2; MS EI *m*/*z* (rel. int.): 260 (M^+, <1), 169 (<1), 151 (1), 109 (6), 107 (15), 91 (100), 69 (10), 55 (29), 41 (38). These data matched those reported.[29]

2-(9-Benzyloxy-nonyl)-oxirane ***6***: A solution of benzyl ether **5** (5.0 g, 19.3 mmol) in DCM (50 mL) was cooled to 0°C. *m*-CPBA was added in small portions, followed by K_2CO_3 (0.67 g, 4.8 mmol). The reaction was stirred at rt for 3 h. The mixture was filtered through a sintered glass funnel, washed repeatedly with saturated $NaHCO_3$, dried ($MgSO_4$) and concentrated. After flash chromatography, the epoxide was obtained as a clear oil (4.1 g, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (*m*, 5H), 4.48 (*s*, 2H), 3.45 (*t*, 2H, $J=6.64$ Hz), 2.88 (*m*, 1H), 2.72 (*dd*, 1H, $J=5.04$, 4.00 Hz), 2.44 (*dd*, 1H, $J=5.04$, 2.72 Hz), 1.63–1.28 (*m*, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 128.3, 127.6, 127.4, 72.8, 70.5, 52.3, 47.0, 32.4, 29.7, 29.43 (2C), 29.39, 29.37, 26.1, 25.9. MS EI *m*/*z* (rel. int.): 276 (M^+, <1), 185 (<1), 149 (1), 121 (1), 107 (39), 91 (100), 71 (10), 55 (20), 43 (11), 41 (30). Anal. calcd for $C_{18}H_{28}O_2$ (%): C, 78.21; H, 10.21. Found: C, 78.41; H, 10.26%.

Hydrolytic kinetic resolution (HKR) of 2-(9-benzyloxy-nonyl)-oxirane ***6***

Preparation of the active catalyst: (*R*,*R*)-*N*,*N*′-Bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexane-diamino cobalt-(II) (0.20 g, 0.3 mmol) and acetic acid (23 μL) were stirred in toluene (1 mL) under air for 1 h. The solvent was removed in vacuo, and the dark brown residue was dried under vacuum, and used directly in the kinetic resolution.[5b]

HKR: Racemic epoxide **6** (3.0 g, 10.8 mmol), H_2O (0.12 mL, 6.7 mmol) and (*R*,*R*)-**1** (17.2 mg, 24.2 μmol) were stirred at rt for 18 h. (*R*)-Epoxide **7** (1.4 g, 46%) and (*S*)-diol **8** (1.4 g, 47%) were separated by flash chromatography. (*R*)-2-(9-Benzyloxy-nonyl)-oxirane **7**: $[\alpha]_D^{23}$ +3.9 (*c* 1.02, $CHCl_3$). Spectral data were identical with those of the racemate **6**. The epoxide was analysed by chiral HPLC using a Chiral OD cel column with a flow rate of 1.0 mL/min and solvent system of 1% isopropanol/hexane. The e.e. was determined to be >98%. (*S*)-11-Benzyloxy-undecane-1,2-diol **8**: $[\alpha]_D^{23}$ +0.7 (*c* 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (*m*, 5H), 4.48 (*s*, 2H), 3.66 (*m*, 2H), 3.44 (*t*, 2H, $J=6.68$ Hz), 3.40 (*dd*, 1H, $J=11.12$, 7.76 Hz), 2.39 (br *s*, 2H), 1.59 (*m*, 2H), 1.40–1.23 (*m*, 14H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.6, 128.3, 127.6, 127.4, 72.8, 72.2, 70.5, 66.7, 33.22, 29.7, 29.6, 29.44, 29.41, 29.39, 26.1, 25.5. These data matched those reported.[29] Anal. calcd for $C_{18}H_{30}O_3$ (%): C, 73.43; H, 10.27. Found: C, 73.26; H, 10.50%.

(S)-12-Benzyloxy-dodecan-3-ol ***9***: Under an inert atmosphere, CuI (0.58 g, 3.0 mmol) in dry ether (30 mL) was cooled to 0°C. MeLi (ca. 0.5 M in ether, 10 mL) was added slowly, and the initiation of cuprate formation was indicated by a bright yellow colour. After the addition, the clear solution was stirred for an extra 10 min. (*R*)-Epoxide **7** (0.31 g, 1.1 mmol) in dry ether (15 mL) was added dropwise at 0°C, and the resulting bright yellow mixture was stirred for 1 h at the same temperature. The reaction was diluted with ether and quenched carefully with saturated NH_4Cl while the ethereal solution was still cold. The aqueous layer was separated and re-extracted with ether. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. The crude product was purified by flash chromatography to provide a clear oil (0.32 g, 100%). $[\alpha]_D^{23}$ +6.0 (*c* 1.18, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32–7.25 (*m*, 5H), 4.48 (*s*, 2H), 3.50 (*m*, 1H), 3.45 (*t*, 2H, $J=6.64$ Hz), 1.61–1.27 (*m*, 19H), 0.92 (*t*, 3H, $J=7.44$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 128.3, 127.6, 127.4, 73.2, 72.8, 70.5, 36.9, 30.1, 29.7, 29.6, 29.51, 29.48, 29.41, 26.1, 25.6, 9.8. Anal. calcd for $C_{19}H_{32}O_2$ (%): C, 78.03; H, 11.03. Found: C, 77.66; H, 11.23%.

(R)-1-Benzyloxy-10-methyldodecane ***10***: Under an inert atmosphere, benzyl ether **9** (0.30 g, 1.0 mmol) was dissolved in DCM (5 mL), and Et_3N (0.40 mL, 2.8 mmol) was added. Mesyl chloride (0.20 mL, 2.4 mmol) was added dropwise to the cool (0°C) solution, and a white precipitate was formed almost immediately. The resulting mixture was stirred at rt for 2 h, and then diluted with ether, and filtered. The filtrate was washed with saturated $NaHCO_3$, dried over $MgSO_4$ and con-

centrated. The crude mesylate was redissolved in anhydrous ether (15 mL). In a separate flask, Me_2CuLi was prepared by slow addition of MeLi (ca. 0.4 M in ether, 10.0 mL, 0.4 mmol) to a suspension of CuI (0.39 g, 2.1 mmol) in ether at 0°C. After the addition, the cuprate was stirred for another 5 min before the crude mesylate was added dropwise. The resulting bright yellow mixture was stirred at 0°C for 2.5 h, followed by dilution with ether and quenched carefully with saturated NH_4Cl. The aqueous layer was separated and re-extracted with ether. The combined organic extract was dried ($MgSO_4$), and concentrated. Flash chromatography afforded a mixture of the unsaturated benzyl ethers and product **10** in a ratio of ca. 2:3. Benzyl ether **10**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.32–7.25 (*m*, 5H), 4.48 (*s*, 2H), 3.45 (*t*, 2H, $J=6.60$ Hz), 1.59–1.06 (*m*, 19H), 0.830 (*t*, 3H, $J=6.84$ Hz), 0.825 (*d*, 3H, $J=6.10$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 138.7, 128.3, 127.6, 127.5, 72.9, 70.5, 36.6, 34.4, 30.0, 29.7, 29.63, 29.59, 29.47, 27.1, 26.2, 19.2, 11.4. MS EI *m*/*z* (rel. int.): 290 (M^+, <1), 199 (3), 108 (11), 92 (67), 91 (100), 69 (16), 57 (18), 55 (13), 41 (20). This ether **10** was then subjected to ozonolysis.

(R)-10-Methyldodecanol ***11***

Ozonolysis: In an attempt to purify benzyl ether **10**, the mixture was subjected to ozonolysis. The benzyl ethers were taken up in DCM, and treated with ozone at −78°C until a pale blue colour persisted. The solution was purged with O_2 until the colour disappeared, and then an excess of Me_2S (0.5 mL) was added. The solution was warmed to rt and stirred for 2 h. The mixture was worked up by washing with H_2O, and the aqueous layer was re-extracted with DCM. The combined organic layers were dried over $MgSO_4$, and concentrated. After column chromatography, the benzoate ester was isolated (0.14 g, 42% over two steps). MS EI *m*/*z* (rel. int.): 304 (M^+, 1), 206 (1), 123 (100), 105 (57), 77 (25), 70 (28), 57 (19), 55 (29), 41 (28). The ester was then hydrolysed immediately.

Saponification: K_2CO_3 (92 mg, 0.67 mmol) was added to a solution of the above benzoate (69 mg, 0.23 mmol) in MeOH (1.5 mL), and the suspension was stirred at rt for 2.5 h. H_2O was then added, followed by extraction with ether. The ethereal solution was washed with H_2O and brine, and dried over $MgSO_4$. After removal of solvent and flash chromatography, alcohol **11** was obtained as a clear oil (30 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 (*t*, 2H, $J=6.64$ Hz), 1.54 (*q*, 2H, $J=6.84$ Hz), 1.35–1.04 (*m*, 18H), 0.83 (*t*, 3H, $J=7.20$ Hz), 0.82 (*d*, 3H, $J=6.36$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 63.1, 36.6, 34.4, 32.8, 30.0, 29.6 (2C), 29.5, 29.4, 27.1, 25.7, 19.2, 11.4. MS EI *m*/*z* (rel. int.): 153 (M^+–C_3H_7, 4), 125 (12), 111 (14), 83 (60), 70 (80), 57 (65), 55 (92), 41 (100). These data matched those reported.[9]

(−)-(R)-10-Methyldodecyl acetate ***3***: An excess of acetic anhydride (0.1 mL) and pyridine (0.1 mL) were added to alcohol **11** (30 mg, 0.15 mmol) in DCM (2 mL). The solution was stirred for 3.5 h, and then washed with aqueous $CuSO_4$. The DCM solution was separated, dried over $MgSO_4$, and then concentrated. After flash chromatography, the acetate was obtained in quantitative yield. $[\alpha]_D^{23}$ −5.4 (*c* 0.97, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.02 (*t*, 2H, $J=6.76$ Hz), 2.01 (*s*, 3H), 1.59 (*q*, 2H, $J=6.91$ Hz), 1.35–1.03 (*m*, 17H), 0.83 (*t*, 3H, $J=7.20$ Hz), 0.81 (*d*, 3H, $J=6.40$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 64.7, 36.6, 30.0, 29.6, 29.50, 29.48, 29.2, 28.6, 27.1, 25.9, 21.0, 19.2, 11.4. MS EI *m*/*z* (rel. int.): 182 (M^+–CH_3CO_2H/C_4H_{12}, <1), 153 (8), 125 7), 111 (10), 97 (35), 83 (34), 70 (47), 55 (47), 43 (10), 41 (48). These data matched those reported.[9–11]

(S)-2-(9-Benzyloxy-nonyl)-oxirane ***12***: (*S*,*S*)-Diol **8** (0.82 g, 2.8 mmol) was dissolved in DCM (8 mL) in an inert atmosphere. Et_3N (0.49 mL, 3.4 mmol) was added and the solution was allowed to stir for 5 min before cooling to 0°C. Mesyl chloride (0.3 mL, 3.3 mmol) was added dropwise, and precipitation was observed almost immediately. The resulting mixture was stirred at rt for 3 h. After diluting with ether, the precipitate was filtered and washed with ether. The combined ethereal solution was washed with saturated $NaHCO_3$, dried ($MgSO_4$) and concentrated. The crude mesylate was redissolved in MeOH (8 mL) and K_2CO_3 (0.8 g, 5.5 mmol) was added. The suspension was stirred at rt for 3 h, and after addition of H_2O, was extracted with DCM. The organic layers were dried over $MgSO_4$, and concentrated. (*S*)-Epoxide **12** was purified by flash chromatography to give a clear oil (0.80 g, 46%). $[\alpha]_D^{23}$ −4.2 (*c* 1.23, $CHCl_3$). The spectral data were identical to those of the racemic epoxy benzyl ether, **6**, described above.

(R)-12-Benzyloxy-dodecan-3-ol ***13***: The procedure followed the protocol described in the formation of (*S*)-hydroxyl benzyl ether **9**. Treatment of epoxide **12** (0.20 g, 0.72 mmol) with Me_2CuLi generated from CuI (0.45 g, 2.4 mmol) and MeLi (ca. 0.4 M in ether, 8.5 mL, 3.4 mmol) yielded the desired alcohol **13** as a clear oil (191 mg, 90%) $[\alpha]_D^{23}$ −5.0 (*c* 1.58, $CHCl_3$). The spectral data matched those for benzyl ether **9** described above.

(S)-1-Benzyloxy-10-methyldodecane ***14***: Following the procedure for the formation of (*R*)-isomer **10**, alcohol **13** (0.15 g, 0.50 mmol) was converted to the corresponding mesylate by treatment with Et_3N (0.30 mL, 2.1 mmol) and mesyl chloride (0.20 mL, 2.5 mmol). The crude mesylate was then reacted with Me_2CuLi, formed from CuI (0.30 g, 1.6 mmol) and MeLi (ca. 0.4 M in ether, 8.0 mL, 3.2 mmol) in anhydrous ether. Benzyl ether **14** was isolated as a colourless oil (50 mg, 34%) after removing the unsaturated component by oxymercuration and careful flash chromatography. The spectral data were identical with those for **10**.

(+)-(S)-10-Methyldodecyl acetate ***4***

Debenzylation: A catalytic amount of Pd–C (10%, 2 mg) was added to benzyl ether **14** (16 mg, 55 μmol) in EtOH (1.5 mL). The suspension was stirred at rt for 7.5 h under a balloon of H_2. The mixture was filtered

through a plug of cotton wool, and the filtrate was dried ($MgSO_4$). Solvent removal yielded (*S*)-10-methyldodecan-1-ol as a clear oil (10 mg, 95%), which was acetylated without further purification. All spectral data matched those for the (*R*)-alcohol **11** above.

Acetylation: (*S*)-Acetate **4** was prepared in the manner described for (*R*)-acetate **3**. The (*S*)-alcohol (9 mg, 45 μmol) was treated with an excess of pyridine and acetic anhydride to yield the required acetate (10 mg, 94%), with spectral data matching those for the (*R*)-acetate described above. The spectral data matched those reported.[9–11] $[\alpha]_D^{23}$ +5.3 (*c* 1.02, $CHCl_3$).

4.3. (−)-(*R*)-10-Methyltridecan-2-one 15

(S)-13-Benzyloxy-tridecan-4-ol ***16***: Under an inert atmosphere, CuI (35 mg, 0.2 mmol) in anhydrous THF (1 mL) was cooled to 0°C and ethyl magnesium bromide, freshly prepared with Mg turnings (49 mg, 2.1 mmol) and ethyl bromide (0.12 mL, 1.5 mmol) in anhydrous ether, was then added. The dark purple mixture was stirred for 10 min, followed by the dropwise addition of (*R*)-epoxide **7** (0.11 g, 0.4 mmol), and stirred at 0°C for 2 h. The reaction was warmed to rt and quenched by slow addition of saturated NH_4Cl, followed by standard workup. Column chromatography yielded mono-protected diol **16** (0.13 g, 75%). $[\alpha]_D^{23}$ +1.0 (*c* 0.97, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.25 (*m*, 5H), 4.48 (*s*, 2H), 3.57 (*m*, 1H), 3.44 (*t*, 2H, $J=6.68$ Hz), 1.63–1.27 (*m*, 21H), 0.91 (*t*, 3H, $J=7.12$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 128.3, 127.6, 127.4, 72.8, 71.7, 70.5, 39.7, 37.5, 29.8, 29.7, 29.54, 29.51, 29.4, 26.2, 25.6, 18.8. MS EI *m*/*z* (rel. int.): 306 (M^+, <1), 288 (7), 197 (2), 155 (1), 123 (3), 107 (24), 91 (100), 83 (6), 69 (6), 55 (22), 41 (12). Anal. calcd for $C_{20}H_{34}O_2$ (%): C, 78.38; H, 11.18. Found: C, 78.52; H, 11.48%.

(R)-1-Benzyloxy-10-methyltridecane ***17***: Reductive methylation of alcohol **16** was performed in the manner described earlier. The alcohol (70 mg, 0.2 mmol) was mesylated with Et_3N (83 μL, 0.6 mmol) and mesyl chloride (56 μL, 0.7 mmol) in DCM. The crude mesylate was then displaced with Me_2CuLi, prepared from MeLi (ca. 0.3 M in ether, 4.0 mL, 1.2 mmol) and CuI (0.10 g, 0.55 mmol) in anhydrous ether, to furnish the alkyl benzyl ether **17** as a colourless oil (28 mg, 40%) after flash chromatography. $[\alpha]_D^{23}$ −2.4 (*c* 0.90, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–7.25 (*m*, 5H), 4.49 (*s*, 2H), 3.44 (*t*, 2H, $J=6.68$ Hz), 1.63–0.80 (*m*, 27H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 128.3, 127.6, 127.4, 72.8, 70.5, 36.6, 34.4, 30.0, 29.7, 29.63, 29.60, 29.5 (2C), 27.1, 26.2, 19.2, 11.4. MS (EI *m*/*z* (rel. int.): 304 (M^+, <1), 213 (3), 151 (1), 125 (4), 108 (11), 91 (100), 83 (14), 69 (15), 55 (15), 41 (28). Anal. calcd for $C_{21}H_{36}O$ (%): C, 82.83; H, 11.92. Found: C, 82.85; H, 12.08%.

(R)-10-Methyltridecene ***18***: A solution of benzyl ether **17** (20 mg, 66 μmol) in dry THF (0.8 mL) was cooled to −78°C under an inert atmosphere. ^{n}BuLi (ca. 1.3 M in hexane, 0.2 mL, 2.5 mmol) was added and the yellow solution was stirred at the same temperature for 30 min. The reaction was warmed to 0°C and quenched with saturated NH_4Cl (1 mL). The mixture was extracted with ether, and the organic extracts were combined, washed with saturated NH_4Cl and brine, separated, dried and concentrated, to afford the alkene. ^1H NMR (200 MHz, $CDCl_3$): δ 5.80 (*m*, 1H), 4.93 (*m*, 2H), 2.02 (*q*, 2H, $J=6.60$ Hz), 1.36–1.02 (*m*, 17H), 0.85 (*t*, 3H, $J=6.85$ Hz), 0.83 (*d*, 3H, $J=6.61$ Hz). MS EI *m*/*z* (rel. int.): 154 ($M^+-C_3H_6$, <1), 153 (3), 111 (10), 97 (29), 84 (35), 83 (26), 69 (42), 55 (72), 43 (100), 41 (90). These data matched those reported.[9,14]

(R)-(−)-10-Methyltridecan-2-one ***15***: Oxygen gas was bubbled through a suspension of $PdCl_2$ (2 mg, 6 μmol) and CuCl (4 mg, 37 μmol) in DMF (0.5 mL) and H_2O (80 μL) for 30 min. Alkene **18** (5 mg, 3 μmol) in DMF (80 μL) was added to the above and O_2 was admitted for a further 4 h, then stirred under a balloon of O_2 overnight. The reaction was quenched by H_2O (15 mL) and extracted with ether. The organic extracts were combined, washed with H_2O, separated and dried ($MgSO_4$). After concentration and chromatography, ketone **15** was furnished as a clear liquid (5 mg, 90%). $[\alpha]_D^{23}$ −1.6 (*c* 0.70, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (*t*, 2H, $J=7.40$ Hz), 2.11 (*s*, 3H), 1.56–1.03 (*m*, 17H), 0.85 (*t*, 3H, $J=6.88$ Hz), 0.81 (*t*, 3H, $J=6.60$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.4, 43.8, 39.9, 37.0, 32.4, 29.83, 29.8, 29.4, 29.1, 27.0, 23.9, 20.1, 19.6, 14.4. MS EI *m*/*z* (rel. int.): 212 (M^+, <1), 194 (1), 151 (1), 123 (2), 110 (4), 95 (4), 85 (7), 71 (22), 58 (58), 43 (100). These data matched those reported.[13–15]

4.4. (−)-(*R*)-(*Z*)-Undec-6-en-2-ol 20

Undec-1-en-6-yne ***19***: MeLi (1.0 M in ether, 20 mL, 20.0 mmol) was added to a solution of hexyne (2.0 mL, 17.4 mmol) in dry THF (20 mL) at −43°C under an inert atmosphere. After stirring for 30 min, freshly distilled HMPA (5 mL) was added, followed by 5-bromo-1-pentene (2.0 mL, 16.9 mmol) in anhydrous THF (2.5 mL). The reaction was allowed to warm slowly to rt, and stirred overnight. The solution was diluted with hexane and washed with H_2O. The aqueous layer was re-extracted with hexane. The combined organic extracts were washed with brine, separated and dried ($MgSO_4$). Removal of the solvent yielded enyne **19** (1.61 g, 63%) as a clear liquid, and used directly in the next reaction. ^1H NMR (400 MHz, $CDCl_3$): δ 5.78 (*ddt*, 1H, $J=17.0$, 10.2, 6.7 Hz), 5.01 (*dq*, 1H, $J=17.2$, 1.72 Hz), 4.95 (*ddt*, 1H, $J=10.2$, 2.2, 1.2 Hz), 2.13 (*m*, 6H), 1.55 (*q*, 2H, $J=6.9$ Hz), 1.42 (*m*, 4H), 0.88 (*t*, 3H, $J=7.1$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.1, 114.9, 80.5, 79.7, 32.8, 31.2, 28.3, 21.9, 18.4, 18.2, 13.6.MS EI *m*/*z* (rel. int.): 135 (M^+-CH_3, 9), 108 (29), 93 (100), 91 (37), 79 (79), 67 (39), 55 (28), 54 (30), 41 (57). These data matched those reported.[30]

2-Non-4-ynyl-oxirane ***21***: *m*-CPBA (7.0 g, 20.3 mmol) was added in small portions to enyne **19** (2.8 g, 18.3 mmol) in DCM (40 mL) at 0°C, followed by K_2CO_3

(ca. 0.3 g). The reaction was stirred at rt for 4 h before being filtered. The filtrate was washed repeatedly with saturated $NaHCO_3$ and brine, separated, dried ($MgSO_4$) and concentrated. Column chromatography afforded epoxide **21** (0.78 g, 29%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.90 (*m*, 1H), 2.73 (*dd*, 1H, $J=5.04$, 4.04 Hz), 2.46 (*dd*, 1H, $J=5.04$, 2.72 Hz), 2.19 (*m*, 2H), 2.11 (*m*, 2H), 1.62 (*m*, 4H), 1.39 (*m*, 4H), 0.88 (*t*, 3H, $J=7.20$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 80.9, 79.3, 51.9, 47.0, 31.5, 31.2, 25.5, 21.9, 18.5, 18.3, 13.6. MS EI *m*/*z* (rel. int.): 151 (M^+-CH_3, 2), 123 (36), 109 (12), 93 (70), 91 (53), 79 (100), 55 (60). This volatile epoxide was immediately subjected to HKR.

HKR: Racemic epoxide **21** (0.55 g, 3.3 mmol), H_2O (47 μL, 2.6 mmol) and (*S*,*S*)-Jacobsen catalyst (16 mg, 22.2 μmol) were stirred at rt for 25 h. The mixture was separated by flash chromatography to give (*S*)-epoxide **22** and (*R*)-diol **23** (0.25 g, 43%), where the epoxide was used immediately. For the ease of characterisation, diol **23** (0.22 g, 1.2 mmol) was converted to the corresponding acetonide in the usual manner. The diol was treated with an excess of dimethoxypropane (DMP) and a catalytic amount of *p*-TsOH in DCM to provide the acetonide as a clear oil (0.25 g, 84%) after column chromatography. (*R*)-2,2-Dimethyl-4-non-4-ynyl-[1,3]dioxolane: $[\alpha]_D^{23}$ −12.7 (*c* 1.42, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.07 (*m*, 1H), 4.02 (*dd*, 1H, $J=7.68$, 5.96 Hz), 3.50 (*t*, 1H, $J=7.32$ Hz), 2.14 (*m*, 6H), 1.50 (*m*, 6H), 1.39 (*s*, 3H), 1.33 (*s*, 3H), 0.88 (*t*, 3H, $J=7.16$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.7, 80.8, 79.4, 75.7, 69.4, 32.7, 31.2, 26.9, 25.7, 25.3, 21.9, 18.7, 18.4, 13.6. MS (EI *m*/*z* (%)): 224 (M^+, <1), 209 (27), 167 (11), 107 (21), 93 (23), 79 (29), 72 (27), 67 (20), 55 (16), 43 (100). Anal. calcd for $C_{14}H_{24}O_2$ (%): C, 74.95; H, 10.78. Found: C, 75.00; H, 11.12%.

(R)-Undec-6-yn-2-ol ***24***: $NaBH_4$ (0.18 g, 4.8 mmol) was added to (*S*)-epoxide **22** in EtOH (5 mL), and the mixture was refluxed for 2 h. After diluting with ether and quenching with saturated NH_4Cl, the mixture was filtered. The precipitate was washed thoroughly with ether. The ether layer was washed with H_2O, and the aqueous layer was re-extracted with DCM. The combined organic phases were dried ($MgSO_4$), concentrated under reduced pressure and purified by flash chromatography to yield alcohol **24** (0.20 g, 73% over two steps). $[\alpha]_D^{23}$ −8.0 (*c* 0.84, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (*s*, 1H, $J=6.16$ Hz), 2.14 (*m*, 4H), 1.38–1.55 (*m*, 10H), 1.18 (*d*, 3H, $J=6.16$ Hz), 0.88 (*t*, 3H, $J=7.16$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 80.7, 79.8, 67.7, 38.4, 31.2, 25.3, 23.5, 21.9, 18.7, 18.4, 13.6. MS EI *m*/*z* (rel. int.): 153 (M^+-CH_3, 11), 111 (51), 97 (16), 93 (89), 79 (100), 67 (63), 54 (36), 45 (66), 41 (56). Anal. calcd for $C_{11}H_{20}O$ (%): C, 78.51; H, 11.98. Found: C, 77.96; H, 12.28%.

Mosher's ester of (R)-undec-6-yn-2-ol ***24***: Under an inert atmosphere, oxalyl chloride (0.57 M in DCM, 0.60 mL, 0.34 mmol) was added to (*S*)-MTPA (88 mg, 0.38 mmol) in dry DCM (0.5 mL). A drop of DMF was added, and after gas evolution ceased, the solution was stirred for a further 35 min. In a separate flask, alcohol **24** (18 mg, 0.11 mmol) and a catalytic amount of DMAP were dissolved in DCM (1 mL), and Et_3N (0.20 mL, 1.4 mmol) was then added. The (*S*)-MTPA solution was syringed into the above and stirred for 1 h. The reaction was diluted with DCM, washed with HCl (1 M) and NaOH (2 M), and the organic phase was dried ($MgSO_4$), concentrated and purified by flash chromatography to afford the Mosher's ester as a viscous oil (30 mg, 73%), and ^{1}H NMR analysis indicated an e.e. of 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (*m*, 2H), 7.38 (*m*, 3H), 5.16 (*s*, 1H, $J=6.46$ Hz), 3.54 (*q*, 3H, $J=1.16$ Hz), 2.09 (*m*, 4H), 1.69 (*m*, 2H), 1.38 (*m*, 6H), 1.33 (*d*, 3H, $J=6.24$ Hz), 0.88 (*t*, 3H, $J=7.16$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 132.5, 129.5, 128.3, 127.2 (*q*, $J=1.3$ Hz), 120.5 (*q*, $J=287.9$ Hz), 84.4 (*q*, $J=27.2$ Hz), 80.8, 79.1, 73.6, 55.4 (*q*, $J=1.3$ Hz), 34.6, 31.2, 24.5, 21.2, 19.8, 18.4, 13.6. MS EI *m*/*z* (rel. int.): 342 ($M^+-C_3H_6$, 2), 189 (100), 119 (11), 109 (29), 95 (88), 81 (37), 67 (36), 55 (31), 41 (20).

(−)-(R)-(Z)-Undec-6-en-2-ol (Nostrenol) ***20***

Protection of secondary alcohol ***24***: Dihydropyran (70 μL, 0.77 mmol) was added dropwise to a solution of alcohol **24** (50 mg, 0.30 mmol) and a catalytic amount of *p*-TsOH in DCM (0.5 mL). The solution was stirred for 2 h. The reaction was diluted with ether and washed with saturated $NaHCO_3$. The aqueous layer was re-extracted with ether and the combined organic extracts were dried ($MgSO_4$) and concentrated. Flash chromatographic purification provided the THP ether as a colourless liquid (two isomers, 63 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.68 (*m*, 1H), 4.62 (*m*, 1H), 3.89 (*m*, 2H), 3.76 (*m*, 2H), 3.47 (*m*, 2H), 2.13 (*m*, 8H), 1.84–1.37 (*m*, 28H), 1.20 (*d*, 3H, $J=6.28$ Hz), 1.10 (*d*, 3H, $J=6.16$ Hz), 0.883 (*t*, 3H, $J=7.20$ Hz), 0.881 (*t*, 3H, $J=7.12$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 98.6, 95.4, 80.4, 80.2, 79.9, 79.7, 73.4, 70.5, 62.7, 62.3, 38.3, 36.5, 35.5, 31.13. 31.12, 31.1 (2C), 25.39, 25.36, 25.0, 21.8 (2C), 21.4, 20.0, 19.6, 19.0, 18.8, 18.7 18.32, 18.30, 13.5 (2C). MS EI *m*/*z* (rel. int.): 252 (M^+, <1), 209 (1), 195 (2), 179 (5), 151 (3), 109 (14), 95 (41), 85 (100), 67 (26), 41 (29); 209 ($M^+-C_4H_9$), 195 (2), 179 (2), 151 (3), 109 (14), 95 (37), 85 (100), 67 (24), 41 (25). This THP ether was then reduced.

Ti^{II}-based reduction of THP ether of alkyne ***24***: Predried Mg turnings (0.76 g, 31.1 mmol) were dry-stirred for 20 min under nitrogen, and anhydrous ether (5 mL) was added. A few drops of neat 2-bromopropane (2.4 mL, 25.4 mmol) were added until the Grignard formation commenced. The remaining bromopropane was diluted with ether (10 mL), while being added to the Mg mixture at such a rate as to maintain gentle refluxing. Occasional cooling in a water-ice bath was necessary. After the addition was completed, the mixture was stirred for 30 min. Anhydrous ether was added to give 20 mL of a ~1.2 M ^{i}PrMgBr solution. To the THP protected alkyne (63 mg, 0.25 mmol) in ether, was added freshly distilled $Ti(O^iPr)_4$ (0.15 mL, 0.51 mmol) in ether (15 mL) under an inert atmosphere. The solution was cooled to −78°C, and ^{i}PrMgBr (ca. 1.2 M in ether, 1.1 mL, 1.3 mmol) was added dropwise to give a

bright yellow solution. The mixture was warmed to –43°C for 2 h, and H_2O (1 mL) was then added to the dark brown reaction mixture, followed by warming to rt overnight. The reaction was quenched with saturated NH_4Cl, and the organic layer was separated, and the aqueous layer was re-extracted with ether. The combined extracts were dried ($MgSO_4$) and concentrated to yield a pale yellow oil (two diastereomers). MS EI *m*/*z* (rel. int.): 254 (M^+, <1), 170 (<1), 152 (1), 110 (8), 97 (11), 85 (100), 67 (15), 55 (25), 41 (22); 170 (<1), 152 (1), 110 (4), 97 (12), 85 (100), 67 (12), 55 (21), 41 (20).

THP deprotection: The above oil was dissolved in MeOH (2 mL) and a catalytic amount of *p*-TsOH was added. The solution was stirred for 1.5 h, and then worked up by addition of aqueous $NaHCO_3$, followed by extraction with DCM. The combined organic layers were dried ($MgSO_4$), concentrated and flash chromatographed to furnish enol **20** in 54% yield over two steps. $[\alpha]_D^{23}$ −5.5 (*c* 0.78, $CHCl_3$). ^1H NMR (400 MHz, CDCl3): δ 5.34 (*m*, 2H), 3.77 (*m*, 1H), 2.03 (*m*, 4H), 1.45–1.29 (*m*, 9H), 1.17 (*d*, 3H, *J*=6.16 Hz), 0.87 (*t*, 3H, *J*=7.08 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 130.3, 129.3, 68.1, 38.9, 31.9, 27.1, 26.9, 25.9, 23.5, 22.3, 14.0. MS EI *m*/*z* (rel. int.): 170 (M^+, 2), 155 (1), 152 (1), 110 (9), 95 (16), 81 (45), 71 (49), 67 (61), 54 (84), 41 (100). These data matched those reported.[16]

4.5. (1*R*,7*R*)-1,7-Dimethylnonyl propanoate 30

1,5-Bisoxiranyl-pentane **31**: At 0°C, *m*-CPBA (70%, 14.8 g, 60.0 mmol) was added in portions to 1,8-nonadiene (3.0 g, 17.8 mmol) in DCM (60 mL). The suspension was stirred at rt overnight. After standard workup and purification, bisepoxide **31** was obtained as a clear oil (1.9 g, 51%). ^1H NMR (400 MHz, $CDCl_3$): δ 2.88 (*m*, 2H), 2.72 (*dd*, 2H, *J*=5.00, 4.00 Hz), 2.44 (*dd*, 2H, *J*=5.04, 2.76 Hz), 1.58–1.40 (*m*, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 47.0, 32.3, 29.2, 25.8. MS EI *m*/*z* (rel. int.): 137 (M^+–H_3O^+, 1), 123 (3), 97 (18), 95 (14), 83 (19), 79 (29), 71 (47), 67 (61), 55 (55), 41 (100). These data matched those reported.[31]

HKR: Bisepoxide **31** (4.0 g, 25.6 mmol), (*R*,*R*)-**1** (0.18 g, 0.3 mmol) and H_2O (0.38 mL, 21.1 mmol) were stirred for 19 h. The products were separated by flash chromatography to afford bisepoxide **32** (1.2 g, 24%), epoxydiol **33** (2.1 g, 46%) and presumably tetrol **34** (0.52 g, 15%). (1*R*,5*R*)-1,5-Bisoxiranyl-pentane **32**: $[\alpha]_D^{23}$ +20.7 (*c* 1.03, $CHCl_3$). The spectral data matched the racemate reported above and those reported.[32] (2*R*,8*S*)-8-Oxiranyl-octane-1,2-diol **33**: ^1H NMR (400 MHz, $CDCl_3$): δ 3.67 (*m*, 1H), 3.61 (*dd*, 1H, *J*=11.04, 3.08 Hz), 3.40 (*dd*, 1H, *J*=11.04, 7.60 Hz), 2.88 (*m*, 1H), 2.72 (*dd*, 1H, *J*=4.96, 4.04 Hz), 2.44 (*dd*, 1H, *J*=4.96, 2.76 Hz), 1.96 (br *s*, 2H), 1.55–1.36 (*m*, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 72.1, 66.8, 52.4, 50.7, 47.1, 32.9, 32.2, 29.2, 25.8, 25.3. This diol was protected as the acetonide, **35**, and fully characterised. For the ease of characterisation, tetrol **34** was directly converted to its bisacetonide by treatment of an excess of 2,2-dimethoxypropane (DMP) (2 mL) in DCM (10 mL) with a catalytic amount of *p*-TsOH. The reaction was stirred overnight, concentrated, and then chromatographed to yield the bisacetonide of **34** as a clear oil (0.61 g, 83%). $[\alpha]_D^{23}$ +25.1 (*c* 1.88, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 4.03 (*m*, 2H), 3.98 (*t*, 2H, *J*=7.40 Hz), 3.45 (*t*, 2H, *J*=7.16 Hz), 1.60–1.24 (*m*, 10H), 1.36 (*d*, 6H, *J*=0.40 Hz), 1.30 (*d*, 6H, *J*=0.48 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6, 76.0, 69.4, 33.5, 29.58, 26.9, 25.7, 25.6. MS EI *m*/*z* (rel. int.): 257 (M^+–CH_3, 74), 199 (2), 139 (6), 121 (14), 101 (13), 81 (19), 72 (39), 59 (18), 43 (100). Anal. calcd for $C_{15}H_{28}O_4$ (%): C, 66.14; H, 10.36. Found: C, 66.02; H, 10.60%.

(4S,5′R′)-2,2-Dimethyl-4-(5-oxiranyl-pentyl)-[1,3]-dioxolane ***35***: Epoxydiol **33** (0.56 g, 3.2 mmol), DMP (1.4 mL) and a few crystals of *p*-TsOH in DCM (5 mL) were stirred overnight. After concentration and column purification, the acetonide was furnished as a clear oil (0.54 g, 78%). $[\alpha]_D^{23}$ +21.9 (*c* 1.15, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 4.03 (*m*, 1H), 3.99 (*t*, 1H, *J*=7.44 Hz), 3.46 (*t*, 1H, *J*=7.16 Hz), 2.86 (*m*, 1H), 2.71 (*dd*, 1H, *J*=5.00, 4.00 Hz), 2.42 (*dd*, 1H, *J*=5.04, 2.27 Hz), 1.61–1.26 (*m*, 10H), 1.37 (*d*, 3H, *J*=0.40 Hz), 1.32 (*d*, 3H, *J*=0.48 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6, 76.0, 69.5, 52.3, 47.0, 33.5, 32.3, 29.4, 26.9, 25.8, 25.70, 25.66. MS EI *m*/*z* (rel. int.): 199 (M^+–CH_3, 43), 121 (2), 101 (8), 93 (17), 81 (11), 79 (18), 72 (31), 57 (10), 43 (100). Anal. calcd for $C_{12}H_{22}O_3$ (%): C, 67.26; H, 10.35. Found: C, 67.47; H, 10.52%.

(3S,8S)-8-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-octan-3-ol ***36***: This epoxide opening by Me_2CuLi was undertaken with the procedure described earlier. Epoxyacetonide **35** (0.45 g, 2.1 mmol) was reacted with Me_2CuLi (from CuI (0.98 g, 5.1 mmol) and MeLi (ca. 0.4 M in ether, 26 mL, 10.4 mmol)) in anhydrous ether at 0°C. The pure hydroxyacetonide was obtained as a clear oil (0.48 g, 98%) after flash chromatography. ^1H NMR (400 MHz, $CDCl_3$): δ 4.04 (*m*, 1H), 4.00 (*m*, 1H), 3.49 (*m*, 1H), 3.47 (*t*, 1H, *J*=7.16 Hz), 1.63–1.27 (*m*, 13H), 1.38 (*s*, 3H), 1.32 (*s*, 3H), 0.91 (*t*, 3H, *J*=7.44 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6, 76.1, 73.2, 60.5, 36.8, 33.5, 30.2, 29.7, 26.9, 25.7, 25.5, 9.8. MS EI *m*/*z* (rel. int.): 215 (M^+–CH_3, 47), 197 (1), 137 (7), 101 (10), 95 (55), 81 (51), 67 (35), 39 (54), 43 (100). Anal. calcd for $C_{13}H_{26}O_3$ (%): C, 67.79; H, 11.38. Found: C, 67.97; H, 11.68%.

(4S,6′R′)-2,2-Dimethyl-4-(6-methyl-octyl)-[1,3]dioxolane ***37***: This reductive methylation was performed in the manner described earlier. Alcohol **36** (0.42 g, 1.7 mmol) was mesylated firstly with Et_3N (0.75 mL, 5.2 mmol) and mesyl chloride (0.34 mL, 4.2 mmol) (3.5 mL) in DCM, followed by treatment with Me_2CuLi in ether, prepared from CuI (0.59 g, 3.1 mmol) and MeLi (ca. 0.3 M in ether, 20 mL, 6.0 mmol) in the standard way. Flash chromatography afforded a clear liquid (0.35 g, 70%), of which contained ca. 15% of the unsaturated acetonide from elimination. ^1H NMR (400 MHz, $CDCl_3$): δ 4.04 (*m*, 1H), 4.00 (*m*, 1H), 3.48 (*t*, 1H, *J*=7.24 Hz), 1.62–1.08 (*m*, 13H), 1.38 (*s*, 3H), 1.33 (*s*, 3H), 0.83 (*t*, 3H, *J*=7.24 Hz), 0.81 (*d*, 3H, *J*=6.40 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6, 76.2, 69.5, 36.5, 34.4, 33.6, 30.0, 29.7, 29.5, 27.0, 25.79, 25.75, 19.2,

11.4. MS EI m/z (rel. int.): 213 (M^+–CH_3, 64), 171 (1), 141 (1), 111 (9), 97 (39), 83 (45), 72 (34), 55 (42), 43 (100). This material was then taken on to epoxide **38**.

(2S,6′R′)-2-(6-Methyl-octyl)-oxirane ***38***

Acetonide deprotection: Amberlite IR120 (ca. 0.2 g) was added to acetonide **37** (0.29 g, 1.3 mmol) in MeOH (2 mL). The mixture was stirred overnight. The beads were filtered off and washed thoroughly with DCM, and the filtrate was dried ($MgSO_4$) and concentrated. After flash chromatography, the diol was obtained as a clear oil (0.18 g, 76%), still containing the 15% unsaturated product from the previous step. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.69 (*m*, 2H), 3.42 (*dd*, 1H, J=10.92 and 7.52), 1.98–1.08 (*m*, 15H), 0.83 (*t*, 3H, J=7.12 Hz), 0.81 (*d*, 3H, J=6.32 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 72.3, 66.7, 36.5, 34.3, 30.0, 29.4 (2C), 27.0, 25.6, 19.2, 11.4. This diol was then processed to epoxide **38**.

Epoxide reconstitution: Under an inert atmosphere, Et_3N (0.19 mL, 1.3 mmol) was added to the diol (0.18 g, 1.0 mmol) in anhydrous DCM (2.5 mL). The solution was cooled to 0°C and mesyl chloride (82 μL, 1.0 mmol) was added, and the mixture was stirred at 0°C for 2 h. The reaction was concentrated, diluted with ether and filtered. The crude mesylate was obtained from the usual workup, and redissolved in MeOH (3 mL). Anhydrous K_2CO_3 (0.41 g, 3.0 mmol) was added to this and the reaction was stirred for 2 h. The solid was filtered off, followed by dilution with H_2O and extraction with DCM. The organic extracts were combined and dried ($MgSO_4$). After concentration and column purification, the volatile epoxide **38** was obtained as a clear oil (43 mg, 27%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.88 (*m*, 1H), 2.73 (*dd*, 1H, J=5.12, 4.20 Hz), 2.45 (*dd*, 1H, J=4.88, 2.68 Hz), 1.52–1.08 (*m*, 13H), 0.83 (*t*, 3H, J=7.12 Hz), 0.81 (*d*, 3H, J=6.40 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 52.4, 47.2, 36.5, 34.3, 32.5, 29.8, 29.5, 27.0, 26.0, 19.2, 11.4. MS EI m/z (rel. int.): 123 (M^+–C_3H_7, 5), 109 (20), 95 (16), 81 (32), 70 (42), 55 (74), 41 (100). These data matched those reported.[32]

(1R,7R)-1,7-Dimethylnonyl propanoate ***30***

Epoxide opening: $NaBH_4$ (20 mg, 0.53 mmol) and epoxide **38** (25 mg, 0.15 mmol) in EtOH (1.5 mL) were refluxed for 1.75 h. The reaction was cooled to rt and quenched with saturated NH_4Cl. The mixture was filtered, and the precipitate was washed with ether. The filtrate was concentrated and extracted with DCM. The organic extracts were combined and dried ($MgSO_4$). The alcohol was isolated as a clear oil (23 mg, 92%) after the removal of solvent and flash chromatography. $[\alpha]_D^{23}$ −13.3 (*c* 1.00, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.76 (*q*, 1H, J=6.10 Hz), 1.42–1.05 (*m*, 14H), 1.16 (*d*, 3H, J=6.10 Hz), 0.83 (*t*, 3H, J=6.82 Hz), 0.80 (*d*, 3H, J=6.40 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 68.2, 39.4, 36.5, 34.4, 30.0, 29.5, 27.0, 25.8, 23.5, 19.2, 11.4. MS EI m/z (rel. int.): 125 (7), 97 (6), 83 (15), 70 (21), 57 (27), 45 (100), 41 (34). These data matched those reported.[21–23]

Esterification: The above alcohol (20 mg, 0.12 mmol), propionic anhydride (0.1 mL), pyridine (0.1 mL) and a catalytic amount of DMAP in DCM (0.3 mL) were stirred for 3.5 h. The reaction was diluted with ether, washed with saturated $CuSO_4$ and dried over $MgSO_4$. Removal of solvent followed by flash chromatography yielded propanoate **30** as a clear oil (21 mg, 79%). $[\alpha]_D^{23}$ −7.2 (*c* 0.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.91 (*tq*, 1H, J=7.00, 6.16 Hz), 2.31 (*q*, 2H, J=7.56 Hz), 1.61–1.08 (*m*, 13H), 1.21 (*d*, 3H, J=6.16 Hz), 1.15 (*t*, 3H, J=7.60 Hz), 0.86 (*t*, 3H, J=7.04 Hz), 0.85 (*d*, 3H, J=6.28 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 70.8, 36.5, 36.0, 34.4, 29.8, 28.0, 27.0, 25.4, 20.0, 19.2, 11.4, 9.2. MS EI m/z (rel. int.): 154 (2), 125 (15), 101 (10), 83 (13), 75 (11), 70 (30), 57 (100), 43 (21), 41 (29). These data matched those reported.[21–23]

4.6. (6*R*,12*R*)-6,12-Dimethylpentadecan-2-one 39

(4S,9S)-9-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-nonan-4-ol ***40***: Under an inert atmosphere, freshly prepared EtMgBr (from Mg turnings (0.66 g, 27.1 mmol) and EtBr (1.8 mL, 23.1 mmol) in anhydrous THF (15 mL)) was added to CuI (0.18 g, 0.9 mmol) in dry THF (10 mL) at 0°C. After stirring for 5 min, epoxy-acetonide **35** (1.5 g, 7.0 mmol) in dry THF (5 mL) was added dropwise to the mixture and stirred at 0°C for 3 h. The reaction was quenched carefully with saturated NH_4Cl, followed by the usual workup and column purification to furnish alcohol **40** as a clear oil (1.6 g, 91%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.01 (*m*, 2H), 3.50 (*m*, 2H), 1.85–1.25 (*m*, 15H), 1.39 (*s*, 3H), 1.34 (*s*, 3H), 0.90 (*t*, 3H, J=6.84 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 108.6, 76.1, 71.5, 69.5, 39.6, 37.3, 33.5, 29.6, 26.9, 25.7 (2C), 25.5, 18.8, 14.1. MS EI m/z (rel. int.): 229 (M^+–CH_3, 19), 211 (1), 169 (1), 125 (4), 109 (17), 95 (35), 72 (28), 55 (45), 43 (100). This was subjected to reductive methylation.

(4S,6′R′)-2,2-Dimethyl-4-(6-methyl-nonyl)-[1,3]dioxolane ***41***: The detailed procedure of this reductive methylation was described earlier. Alcohol **40** (1.1 g, 4.5 mmol) was firstly mesylated by reacting with Et_3N (2.8 mL, 19.0 mmol) and mesyl chloride (0.85 mL, 10.3 mmol), followed by reacting with Me_2CuLi (freshly prepared from CuI (2.2 g, 11.3 mmol) and MeLi (ca.0.4 M in ether, 56 mL, 22.4 mmol)) to afford acetonide **41** as a clear oil (0.35 g, 41%) after flash chromatography. $[\alpha]_D^{23}$ −15.2 (*c* 1.20, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.02 (*m*, 2H), 3.49 (*m*, 1H), 1.57–1.08 (*m*, 15H), 1.39 (*s*, 3H), 1.34 (*s*, 3H), 0.85 (*t*, 3H, J=6.82 Hz), 0.80 (*d*, 3H, J=3.90 Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 108.5, 76.2, 69.5, 39.4, 36.9, 33.6, 32.4, 30.0, 27.0, 26.9, 25.79, 25.77, 20.1, 19.6, 14.4. MS EI m/z (rel. int.): 227 (M^+–CH_3, 21), 141 (1), 123 (1), 97 (21), 83 (22), 72 (23), 55 (20), 43 (100), 41 (30). Anal. calcd for $C_{15}H_{30}O_2$ (%): C, 74.32; H, 12.47. Found: C, 74.56; H, 12.86%.

(2S,8R)-8-Methylundecan-1,2-diol ***42***: Amberlite IR120 (ca. 60 mg) and acetonide **41** (0.30 g, 1.2 mmol) in

MeOH (20 mL) were stirred overnight, followed by filtration and concentration. Flash chromatography afforded diol **42** as a viscous oil (0.25 g, 100%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.62–3.32 (*m*, 3H), 1.35–1.03 (*m*, 17H), 0.84 (*t*, 3H, $J=6.82$ Hz), 0.80 (*d*, 3H, $J=4.14$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 72.4, 66.7, 39.4, 37.0, 33.1, 32.4, 30.0, 27.0, 25.6, 20.1, 19.6, 14.4. This diol was then converted to the epoxide, **43**.

(2S,6′R′)-2-(6-Methyl-nonyl)-oxirane ***43***: The procedure for the epoxide reconstitution was described above in detail. Diol **42** (0.26 g, 1.3 mmol) was mesylated with Et_3N (0.23 mL, 1.6 mmol) and mesyl chloride (0.11 mL, 1.3 mmol), followed by treatment with K_2CO_3 (0.37 g, 2.7 mmol) to furnish epoxide **43** as a clear liquid (0.11 g, 48%) after column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.89 (*m*, 1H), 2.73 (*dd*, 1H, $J=5.00$, 3.96 Hz), 2.45 (*dd*, 1H, $J=5.00$, 2.72 Hz), 1.51–1.18 (*m*, 15H), 0.86 (*t*, 3H, $J=6.96$ Hz), 0.81 (*d*, 3H, $J=6.60$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 47.1, 39.3, 36.8, 32.4, 32.3, 39.7, 26.8, 25.9, 20.0, 19.5, 14.3. MS EI *m*/*z* (rel. int.): 137 ($M^+-C_3H_7$, 1), 123 (7), 109 (16), 95 (20), 81 (36), 69 (38), 55 (76), 43 (98), 41 (100). The volatile epoxide was immediately reacted with the Grignard reagent.

(6S,12R)-12-Methylpentadec-1-en-6-ol ***44***: Under an inert atmosphere, 3-butenyl magnesium bromide was freshly prepared from Mg turnings (67 mg, 2.8 mmol) and 4-bromo-1-butene (0.24 mL, 2.4 mmol) in anhydrous THF (3 mL). The Grignard solution was added to another flask containing CuI (15 mg, 79 μmol) in THF (0.5 mL) at 0°C. Epoxide **43** (0.11 g, 0.60 mmol) in THF (1 mL) was added dropwise to the above, and then stirred for 3 h at this temperature. The reaction was carefully quenched by the addition of saturated NH_4Cl. Standard workup and flash chromatography afforded the corresponding alcohol as a clear oil (48 mg, 34%). $[\alpha]_D^{23}$ −0.1 (*c* 1.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (*ddt*, 1H, $J=17.08$, 10.24, 6.68 Hz), 4.99 (*dq*, 1H, $J=17.12$, 1.88 Hz), 4.92 (*ddt*, 1H, $J=10.2$, 2.04, 1.20 Hz), 3.56 (*m*, 1H), 2.04 (*m*, 2H), 1.51–1.04 (*m*, 20H), 0.84 (*t*, 3H, $J=6.96$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 114.5, 71.8, 39.4, 37.5, 37.0, 36.8, 33.7, 32.4, 30.0, 27.0, 25.7, 24.9, 20.1, 19.6, 14.4. MS EI *m*/*z* (rel. int.): 222 (M^+-H_2O, 1), 194 (1), 151 (3), 123 (4), 97 (30), 81 (100), 69 (37), 57 (46), 43 (94). This alcohol was then converted to alkene **45**.

(6R,12R)-6,12-Dimethylpentadec-1-ene ***45***: By following the standard procedure described previously, alcohol **44** (48 mg, 0.20 mmol) was treated with Et_3N (0.17 mL, 1.2 mmol) and mesyl chloride (50 μL, 0.61 mmol), followed by Me_2CuLi (prepared from CuI (0.10 g, 0.53 mmol) and MeLi (ca. 1.4 M in ether, 0.7 mL, 0.98 mmol)) to give alkene **45** as a clear liquid (25 mg, 53%) after flash chromatography. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.79 (*dt*, 1H, $J=10.28$, 6.68 Hz), 4.98 (*dq*, 1H, $J=17.12$, 1.60 Hz), 4.91 (*dq*, 1H, $J=10.16$, 1.24 Hz), 2.01 (*m*, 2H), 1.41–1.04 (*m*, 20H), 0.86 (*t*, 3H, $J=6.96$ Hz), 0.82 (*d*, 3H, $J=6.60$ Hz), 0.81 (*d*, 3H, $J=6.56$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 114.1, 39.4, 37.1, 37.0, 36.5, 34.1, 32.7, 32.5, 30.4, 27.1, 27.0, 26.4, 20.1, 19.7 (2C), 14.4. MS EI *m*/*z* (rel. int.): 238 (M^+, <1), 210 (<1), 167 (1), 139 (3), 111 (10), 97 (47), 69 (43), 55 (93), 43 (100), 41 (82). These data matched those reported.[26]

(6R,12R)-6,12-Dimethylpentadecan-2-one ***39***: A suspension of $PdCl_2$ (9 mg, 32 μmol) and CuCl (13 mg, 0.13 mmol) in DMF/H_2O (10:1, 0.66 mL) was purged with O_2 for 40 min. Alkene **45** (25 mg, 0.13 mmol) in DMF (0.1 mL) was added and the brownish mixture was bubbled with O_2 for 4 h. The reaction was diluted with H_2O and extracted with DCM. The organic extracts were combined, dried over $MgSO_4$, and concentrated. Column purification furnished **39** as a clear oil (20 mg, 74%). $[\alpha]_D^{23}$ −0.4 (*c* 0.40, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (*t*, 2H, $J=7.44$ Hz), 2.11 (*s*, 3H), 1.55–1.05 (*m*, 20H), 0.86 (*t*, 3H, $J=7.00$ Hz), 0.82 (*d*, 3H, $J=6.60$ Hz), 0.81 (*d*, 3H, $J=6.72$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.4, 44.1, 39.4, 37.1, 36.9, 36.5, 32.6, 32.5, 30.3, 29.8, 27.08, 27.05, 21.4, 20.1, 19.7, 19.5, 14.4. MS EI *m*/*z* (rel. int.): 239 (M^+-CH_3, 2), 236 (7), 211 (3), 165 (1), 152 (2), 123 (4), 110 (10), 85 (15), 71 (24), 58 (57), 43 (100), 41 (27). These data matched those reported.[25,26]

4.7. (2*S*,11*S*)-2,11-Diacetoxytridecane 47

1,8-Bisoxiranyl-octane ***46***. *1,11-Dodecadiene*: Under an inert atmosphere, 1,6-dibromohexane (4.0 g, 16.4 mmol) in anhydrous THF (15 mL) was cooled to 0°C and allyl magnesium bromide (Aldrich, 1.0 M in ether, 93 mL, 93.0 mmol) was added slowly. The mixture was stirred at rt for 2 days. The reaction was re-cooled to 0°C and carefully quenched with MeOH (10 mL). The mixture was filtered, and the filtrate was washed with saturated NH_4Cl, H_2O and brine. The organic solution was dried ($MgSO_4$), and the solvent was distilled off. Flash chromatography afforded 1,11-dodecadiene as a clear liquid (2.0 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (*dt*, 2H, $J=10.20$, 6.72 Hz), 4.98 (*m*, 2H), 4.91 (*m*, 2H), 2.05 (*dq*, 4H, $J=6.80$, 1.36 Hz), 1.42–1.25 (*m*, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.2, 114.1, 33.8, 29.4, 29.1, 28.9. This diene was immediately epoxidised.

Diepoxidation: Based on the procedure for the formation of **31**, 1,11-dodecadiene (2.0 g, 12.0 mmol) was treated with *m*-CPBA (50%, 13.5 g, 39.1 mmol) and K_2CO_3 (1.3 g, 9.4 mmol) to give bisepoxide **46** as a clear oil (1.1 g, 45%) after flash chromatography. ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.87 (*m*, 2H), 2.73 (*dd*, 2H, $J=4.88$, 3.90 Hz), 2.44 (*dd*, 2H, $J=4.88$, 2.68 Hz), 1.49–1.23 (*m*, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.4, 47.1, 32.4, 29.40, 29.36, 25.9. MS EI *m*/*z* (rel. int.): 97 (14), 93 (16), 81 (28), 79 (28), 71 (53), 67 (57), 55 (69), 41 (100).

HKR: Racemic bisepoxide **46** (2.1 g, 10.4 mmol), H_2O (0.15 g, 8.3 mmol) and (*S*,*S*)-Jacobsen catalyst (89 mg, 12.5 μmol) were stirred at rt for 24 h. The (*S*,*S*)-bisepoxide **51** (0.64 g, 23%), (*S*)-epoxy-(*R*)-diol **52** (0.58 g, 26%) and (*R*,*R*)-tetrol **53** (0.27 g, 12%) were separated by flash chromatography. (*S*,*S*)-Bisepoxide **51**: $[\alpha]_D^{23}$

–16.4 (*c* 0.30, $CHCl_3$). The spectral data matched these for the racemic epoxide above. (2*R*,11*S*)-11-Oxiranyl-undecane-1,2-diol **52**: Anal. calcd for $C_{12}H_{24}O_3$ (%): C, 66.63; H, 11.18. Found: C, 66.14; H, 11.47%. (*R*,*R*)-Tetrol **53**: $[\alpha]_D^{23}$ +31.9 (*c* 0.51, MeOH). ^{1}H NMR (400 MHz, EtOH-d_6): δ 5.19 (*s*, 4H), 3.35 (*m*, 6H), 1.42–1.25 (*m*, 16H). ^{13}C NMR (100 MHz, EtOH-d_6): δ 72.7, 67.0, 34.2, 30.6, 30.4, 26.4. Anal. calcd for $C_{12}H_{26}O_4$ (%): C, 61.51; H, 11.18. Found: C, 61.80; H, 11.42%. Epoxydiol **52** was converted to the corresponding acetonide derivative, which was also characterised. (4*R*,8*S*)-2,2-Dimethyl-4-(8-oxiranyl-octyl)-[1,3]dioxolane: ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.01 (*m*, 2H), 3.47 (*t*, 1H, J=7.20 Hz), 2.88 (*m*, 1H), 2.73 (*dd*, 1H, J=5.04, 4.04 Hz), 2.44 (*dd*, 1H, J=5.04, 2.76 Hz), 1.59–1.27 (*m*, 19H), 1.38 (*s*, 3H), 1.33 (*s*, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6, 69.5, 52.4, 47.1, 33.6, 32.5, 29.6, 29.42, 29.38, 26.9, 25.9, 25.7. MS EI *m*/*z* (rel. int.): 241 (M^+–CH_3, 24), 225 (1), 149 (1), 135 (2), 121 (6), 107 (7), 95 (23), 81 (30), 72 (34), 55 (36), 43 (100). This epoxy-acetonide was taken on to organocuprate reaction.

(3R,11R)-11-(2,2-Dimethyl-[1,3]dioxolan-4-yl)-undecan-3-ol ***54***: Under an inert atmosphere, CuI (61 mg, 0.32 mmol) in dry THF (2 mL) was cooled to –40°C. MeMgBr (Aldrich, 3.0 M in ether, 1.0 mL, 3.0 mmol) was added and stirred for 10 min. The above epoxyacetonide (0.37 g, 1.5 mmol) in dry THF (3 mL) was added by syringe to the cuprate, and then stirred for 3.5 h at the same temperature. Saturated NH_4Cl was added carefully to quench the reaction. Standard workup and purification afforded the alcohol as a clear oil (0.36 g, 91%). $[\alpha]_D^{23}$ –17.1 (*c* 1.59, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.01 (*m*, 2H), 3.49 (*m*, 1H), 3.46 (1H, *t*, J=7.24 Hz), 1.59–1.27 (*m*, 19H), 1.38 (*s*, 3H), 1.33 (*s*, 3H), 0.92 (*t*, 3H, J=7.44 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.6, 73.3, 69.5, 36.9, 33.6, 30.1, 29.65, 29.62, 29.5, 29.4, 27.0, 25.7, 25.6, 9.9. MS EI *m*/*z* (rel. int.): 257 (M^+–CH_3, 53), 239 (1), 185 (7), 149 (5), 123 (11), 109 (22), 95 (34), 81 (39), 59 (64), 43 (100). This alcohol was subjected to the Mitsunobu reaction.

(1S,9R)-4-Chloro-benzoic acid 9-(2,2-dimethyl-[1,3]dioxolan-4-yl)-1-ethyl-nonyl ester ***55***: Under an inert atmosphere, alcohol **54** (0.25 g, 0.92 mmol), *p*-chlorobenzoic acid (0.17 g, 1.1 mmol) and triphenylphosphine (0.42 g, 1.6 mmol) in dry THF (10 mL) were cooled to 0°C. DEAD (0.14 mL, 1.1 mmol) in THF (0.5 mL) was added dropwise, and the reaction was stirred for 1 h at the same temperature. After diluting with ether, and washed with H_2O, the aqueous layer was separated and re-extracted with ether. The combined organic extracts were dried ($MgSO_4$), concentrated, and purified by flash chromatography to furnish the benzoate ester as a viscous oil (0.30 g, 80%). $[\alpha]_D^{23}$ +9.2 (*c* 0.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (*m*, 2H), 7.38 (*m*, 2H), 5.03 (*q*, 1H, J=6.36 Hz), 4.02 (*m*, 2H), 3.46 (*t*, 1H, 7.08 Hz), 1.72–1.24 (*m*, 18H), 1.37 (*s*, 3H), 1.33 (*s*, 3H), 0.91 (*t*, 3H, J=7.40 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 139.1, 131.9, 128.6, 128.5, 108.5, 69.5, 33.59, 33.55, 29.6, 29.5, 27.0, 26.9, 25.72, 25.70, 25.3, 9.6. MS EI *m*/*z* (rel. int.): 397 (36), 396 (29), 395 (100), 335 (6), 239 (8), 157 (20), 141 (31), 139 (85), 97 (22), 95 (31), 72 (40), 55 (37), 43 (100). Anal. calcd for $C_{23}H_{35}ClO_4$ (%): C, 67.22; H, 8.58. Found: C, 67.22; H, 8.94%.

(1S,9R)-4-Chloro-benzoic acid 1-ethyl-9-oxiranyl-nonyl ester ***56***. *Acetonide deprotection*: Acetonide **55** (58 mg, 0.14 mmol) and Amberlite IR120 (ca. 20 mg) in MeOH (4 mL) were stirred overnight. After filtration, concentration and column purification, (1*R*,10*R*)-4-chloro-benzoic acid 1-ethyl-10,11-dihydroxy-undecyl ester was obtained as a clear oil (43 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (*m*, 2H), 7.38 (*m*, 2H), 5.03 (*q*, 1H, J=6.64 Hz), 3.65 (2H, *m*), 3.45 (1H, *m*), 1.71–1.24 (*m*, 20H), 0.91 (*t*, 3H, J=7.44 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 139.1, 129.2, 128.6, 72.3, 66.8, 33.6, 33.1, 29.5, 29.4, 29.34, 29.32, 27.0, 25.4, 25.3, 15.2, 9.6. Anal. calcd for $C_{20}H_{31}ClO_4$ (%): C, 64.76; H, 8.42. Found: C, 64.25; H, 8.67%.

Reconstitution to the epoxide: Following the procedure described earlier, the above diol (36 mg, 0.10 mmol) was mesylated with Et_3N (15 μL, 0.10 mmol) and mesyl chloride (8.0 μL, 0.10 mmol) was added, then treated with K_2CO_3 (29 mg, 0.21 mmol) to give epoxy-ester **56** as a clear oil (21 mg, 44%) after flash chromatography. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (*m*, 2H), 7.39 (*m*, 2H), 5.04 (*q*, 1H, J=5.64 Hz), 2.87 (*m*, 1H), 2.71 (*dd*, 1H, J=5.00, 3.96 Hz), 2.43 (*dd*, 1H, J=5.04, 2.72 Hz), 1.68–1.23 (*m*, 18H), 0.91 (*t*, 3H, J=7.44 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 139.1, 130.9, 129.3, 128.6, 52.4, 47.1, 33.6, 32.5, 29.5, 29.41, 29.35, 27.0, 25.9, 25.3, 9.6. HRMS calcd for $C_{20}H_{29}NaClO_3$ 375.1703, found 375.1707 $(M+Na)^+$.

(2S,11S)-Tridecane-2,11-diol ***57***: Under an inert atmosphere, epoxy ester **56** (15 mg, 0.05 mmol) in dry ether (1 mL) was added to $LiAlH_4$ (12 mg, 0.31 mmol) in ether (1.5 mL) at 0°C. The mixture was refluxed for 2 h and stirred overnight at rt. The reaction was diluted with ether, and $Na_2SO_4{\cdot}10H_2O$ (0.12 g) was carefully added and stirred for another 2 h. The mixture was filtered, dried ($MgSO_4$) and concentrated to furnish diol **57** as a clear oil (9 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.77 (*s*, 1H, J=6.00 Hz), 3.50 (*m*, 1H), 1.59–1.27 (*m*, 20H), 1.16 (*d*, 3H, J=6.20 Hz), 0.92 (*t*, 3H, J=7.44 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 73.3, 68.2, 39.3, 36.9, 30.1, 29.7, 29.6, 29.5, 25.7, 25.6, 23.5, 9.9. These data matched those reported.[27]

(2S,11S)-2,11-Diacetoxytridecane ***47***: The above diol (8.0 mg, 0.04 mmol), an excess of pyridine (ca. 0.1 mL) and acetic anhydride (ca. 0.1 mL) and a catalytic amount of DMAP in DCM (1 mL) were stirred for 2 h. The reaction was diluted with ether, washed repetitively with saturated $CuSO_4$, and dried ($MgSO_4$). After concentration and column purification, the title product was yielded as a clear oil (7 mg, 68%). $[\alpha]_D^{23}$ –4.0 (*c* 0.70, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.86 (*tq*, 1H, J=6.24, 6.00 Hz), 4.79 (*tt*, 1H, J=6.72, 5.80 Hz), 2.02

(*s*, 3H), 2.00 (*s*, 3H), 1.57–1.24 (*m*, 18H), 1.18 (*d*, 3H, $J=6.28$ Hz), 0.85 (*t*, 3H, $J=7.40$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.0, 170.8, 75.5, 71.1, 35.9, 33.6, 29.5, 29.42 (2C), 29.40, 26.9, 25.4, 25.3, 21.4, 21.3, 20.0, 9.6. MS EI *m*/*z* (rel. int.): 271 ($M^+-C_2H_5$, <1), 229 (1), 151 (4), 124 (5), 110 (5), 101 (3), 95 (10), 87 (4), 82 (12), 69 (10), 68 (9), 55 (17), 43 (100), 41 (14). These data matched those reported.[27,28]

4.8. (2*S*,12*S*)-2,12-Diacetoxytridecane 49

1,9-Bisoxiranyl-nonane ***48***. *Grignard reaction*: Under an inert atmosphere, allyl magnesium bromide (Aldrich, 1.0 M in ether, 30 mL, 30 mmol) was added to 1,7-dibromoheptane (1.01 g, 3.9 mmol) in dry THF (30 mL) at 0°C. The mixture was stirred at rt for 2 days. After a standard workup and column chromatography, 1,12-tridecadiene was afforded as a clear liquid (0.53 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.80 (*ddt*, 2H, $J=17.08$, 10.26, 6.60 Hz), 5.00 (*m*, 2H), 4.91 (*m*, 2H), 2.02 (*q*, 4H, $J=5.62$ Hz), 1.35 (*m*, 14H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 114.1, 33.8, 29.54, 29.47, 29.1, 28.9. MS EI *m*/*z* (rel. int.): 152 ($M^+-C_2H_4$, <1), 109 (6), 95 (16), 81 (31), 69 (18), 67 (38), 55 (71), 41 (100). This diene was then epoxidised.

Diepoxidation: *m*-CPBA (50%, 3.1 g, 9.0 mmol) was added in portions to 1,12-tridecadiene (0.52 g, 2.9 mmol) in DCM (10 mL) at 0°C, and followed by K_2CO_3 (0.23 g, 1.7 mmol). The resulting suspension was stirred at rt overnight. The solid was filtered and the filtrate was washed thoroughly with saturated $NaHCO_3$, dried ($MgSO_4$) and concentrated. After flash chromatography, bisepoxide **48** was acquired as a clear liquid (0.38 g, 61%). ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.88 (*m*, 2H), 2.72 (*dd*, 2H, $J=5.12$, 4.16 Hz), 2.44 (*dd*, 2H, $J=4.88$, 2.36 Hz), 1.48–1.26 (*m*, 18H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 52.4, 47.1, 32.5, 29.5, 29.4, 25.9. MS EI *m*/*z* (rel. int.): 109 (7), 95 (17), 81 (31), 71 (44), 67 (49), 55 (61), 43 (42), 41 (100). Anal. calcd for $C_{13}H_{24}O_2$ (%): C, 73.54; H, 11.39. Found: C, 73.79; H, 11.69%.

HKR: Racemic bisepoxide **48** (0.36 g, 1.7 mmol), H_2O (25 mg, 1.4 mmol) and (*R*,*R*)-**1** (14 mg, 19.7 μmol) were stirred at rt for 24 h. (*R*,*R*)-Bisepoxide **58** (72 mg, 19%), (*R*)-epoxy-(*S*)-diol **59** (170 mg, 45%) and (*S*,*S*)-tetrol **60** (35 mg, 9%) were separated by flash chromatography. (1*R*,9*R*)-1,9-Bisoxiranyl-nonane **58**: $[\alpha]_D^{23}$ +11.1 (*c* 1.16, $CHCl_3$). The spectral data matched those for the racemic epoxide reported above. (2*S*,12*R*)-12-Oxiranyl-dodecane-1,2-diol **59**: $[\alpha]_D^{23}$ −11.5 (*c* 0.40, MeOH). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.68 (*m*, 2H), 3.39 (*m*, 1H), 2.89 (*m*, 1H), 2.74 (*dd*, 1H, $J=5.12$, 4.20 Hz), 2.44 (*dd*, 1H, $J=4.88$, 2.36 Hz), 1.47–1.26 (*m*, 20H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 71.8, 65.6, 52.4, 47.1, 32.4, 29.6, 29.5, 29.43, 29.38, 29.36, 25.9, 25.0. Anal. calcd for $C_{13}H_{26}O_3$ (%): C, 67.79; H, 11.38. Found: C, 67.56; H, 11.52%. (2*S*,12*S*)-Tridecane-1,2,12,13-tetrol **60**: $[\alpha]_D^{23}$ −26.1 (*c* 0.70, MeOH). ^{1}H NMR (400 MHz, EtOH-d_6): δ 5.19 (*s*, 4H), 3.36 (*m*, 6H), 1.42–1.26 (*m*, 18H). ^{13}C NMR (100 MHz, EtOH-d_6): δ 72.0, 67.0, 34.2, 30.6, 30.42, 30.39, 26.4. Anal. calcd for $C_{13}H_{28}O_4$ (%): C, 62.67; H, 11.36. Found: C, 62.38; H, 11.32%.

(2S,12S)-Tridecane-2,12-diol ***61***: Bisepoxide **58** (65 mg, 0.31 mmol) and $NaBH_4$ (60 mg, 1.6 mmol) in EtOH (3.5 mL) were refluxed for 3 h, followed by quenching with saturated NH_4Cl. The white precipitate was filtered, and the filtrate was concentrated and extracted with DCM. The organic extracts were combined, dried ($MgSO_4$), concentrated and column purified to afford diol **61** (56 mg, 84%). $[\alpha]_D^{23}$ +11.1 (*c* 0.76, MeOH). ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.75 (*m*, 2H), 1.50–1.25 (*m*, 20H), 1.16 (*d*, 6H, $J=6.34$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 68.2, 39.3, 29.59, 29.55, 29.47, 25.7, 23.5. Anal. calcd for $C_{13}H_{28}O_2$ (%): C, 72.17; H, 13.04. Found: C, 72.21; H, 13.52. These data matched those reported.[27]

(2S,12S)-2,12-Diacetoxytridecane ***49***: Diol **61** (44 mg, 0.20 mmol), an excess of pyridine (~0.2 mL) and acetic anhydride (~0.2 mL) and a catalytic amount of DMAP in DCM (2 mL) were stirred for 1.5 h. The reaction was diluted with ether, washed with saturated $CuSO_4$, and dried ($MgSO_4$). After concentration and flash chromatography, the title product was yielded as a clear oil (60 mg, 98%). $[\alpha]_D^{23}$ +1.8 (*c* 1.21, $CHCl_3$). ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.86 (*s*, 2H, $J=6.10$ Hz), 2.00 (*s*, 6H), 1.62–1.23 (*m*, 18H), 1.18 (*d*, 6H, $J=6.10$ Hz). ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.8, 71.0, 35.9, 29.5, 29.4, 25.4, 21.4, 19.9. MS EI *m*/*z* (rel. int.): 257 ($M^+-C_2H_3O^+$, <1), 197 (1), 180 (3), 138 (4), 110 (5), 96 (9), 87 (9), 82 (10), 68 (10), 55 (17), 43 (100), 41 (14). Anal. calcd for $C_{17}H_{32}O_4$ (%): C, 62.67; H, 11.36. Found: C, 62.38; H, 11.32%. These data matched those reported.[27,28]

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