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Synthesis of Sub-units of Marine Polycyclic Ethers by Ring-closing Metathesis and Hydroboration of Enol Ethers

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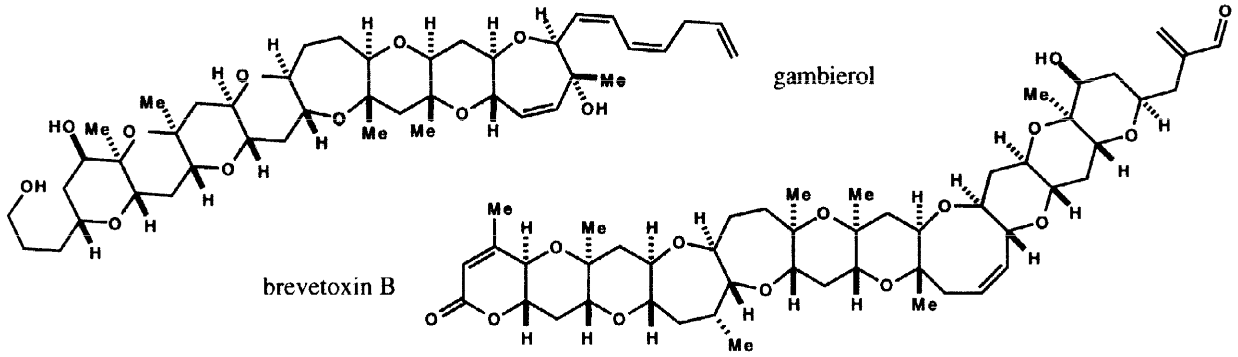
Abstract: The construction of polycyclic ethers by sequential ring-closing metathesis and stereoselective hydroboration of enol ethers has been explored. This reaction sequence has been used to prepare bicyclic ethers corresponding to sub-units found in the brevetoxins and related marine natural products. © 1999 Elsevier Science Ltd. All rights reserved.

The neurotoxin brevetoxin B was isolated from *Gymnodinium breve* Davis, a dinoflagellate organism that often forms large blooms along the coast of Florida, and was characterised by Nakanishi and co-workers in 1981.[1] This compound was just the first of several structurally complex marine polyether natural products to be identified;[2] the family includes brevetoxin A,[3] the ciguatoxins,[4] gambierol,[5] the gambieric acids,[6] yessotoxin,[7] and maitotoxin,[8] the largest non-biopolymeric natural product known.

These polyethers are produced by marine microorganisms and are found in fish that ingest them. They are extremely neurotoxic to vertebrates at low concentrations, and can have a devastating effect of the marine environment and a significant impact on human health. For example, the ciguatoxins, gambierol, maitotoxin and the gambieric acids are produced by the dinoflagellate *Gambierdiscus toxicus* and are transferred to herbivorous fish and then to carnivores that consume them.[2] Ingestion of these agents, through consumption of contaminated fish, leads to ciguatera, a type of food poisoning that is prevalent in tropical and sub-tropical regions.[2]

The neurotoxicity of the brevetoxins and ciguatoxins results from their action at voltage-sensitive sodium channels, and maitotoxin is thought to exert its neurotoxicity by interaction with calcium ion channels.[2,9] Some members of this family of natural products also display potentially beneficial biological activities. For example, the gambieric acids are the most potent anti-fungal agents known, possessing even greater potency than amphotericin.[6]



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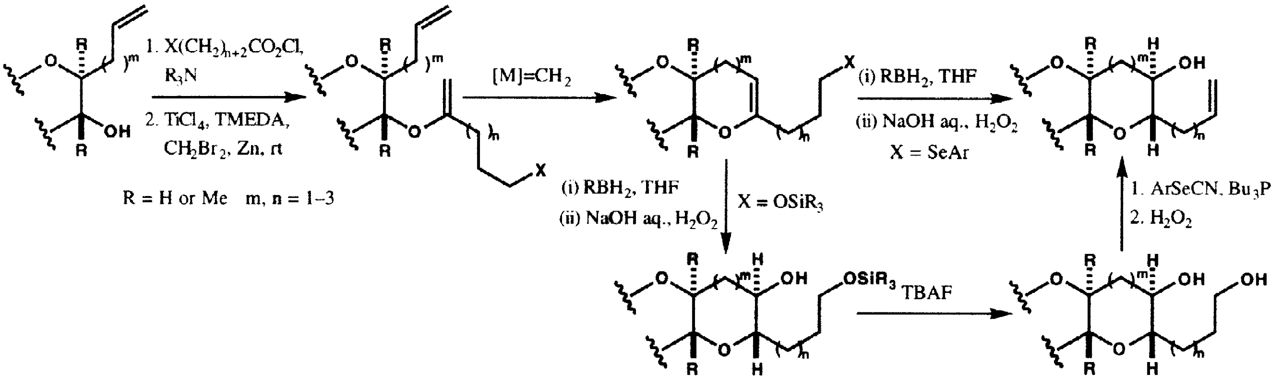
As a consequence of the unique structural features and the synthetic challenges presented by the brevetoxins and related marine toxins, these compounds have attracted considerable attention and have stimulated the development of a host of powerful new synthetic methods for cyclic ether construction.[9] This work has culminated in the recent impressive total syntheses of brevetoxin B and brevetoxin A accomplished by Nicolaou and co-workers,[10,11] and several syntheses of the smaller congener hemibrevetoxin B.[12]

The brevetoxins and ciguatoxins have proved to be extremely challenging synthetic targets, a fact which reflects the limitations of many current methods and strategies. In spite of recent advances, there is a dearth of general and convergent strategies for the rapid assembly of large fused polycyclic ether arrays, and the development of efficient new approaches will be required if other marine polyether toxins are to be realistic targets. In order to address this issue, we sought to develop a novel and efficient general strategy for the construction of *trans*-fused polycyclic ether arrays. We anticipated employing a route involving sequential acylation and methylenation followed by catalytic ring-closing metathesis,[13] promoted by the complexes $2,6\text{-}(i\text{-Pr})_2C_6H_3N{=}Mo[OC(CF_3)_2Me]_2{=}CHCMe_2Ph$ (**1**)[14] or $PhCH{=}Ru(PCy_3)_2Cl_2$ (**2**),[15] and subsequent stereoselective hydroboration (Scheme 1).[16] We were particularly attracted by this approach because it could be used iteratively, permitting sequential ring construction to be performed at the rate of four steps per ring if side-chain functionalisation could be accomplished during the oxidative work-up of the hydroboration reaction (X = SeAr).

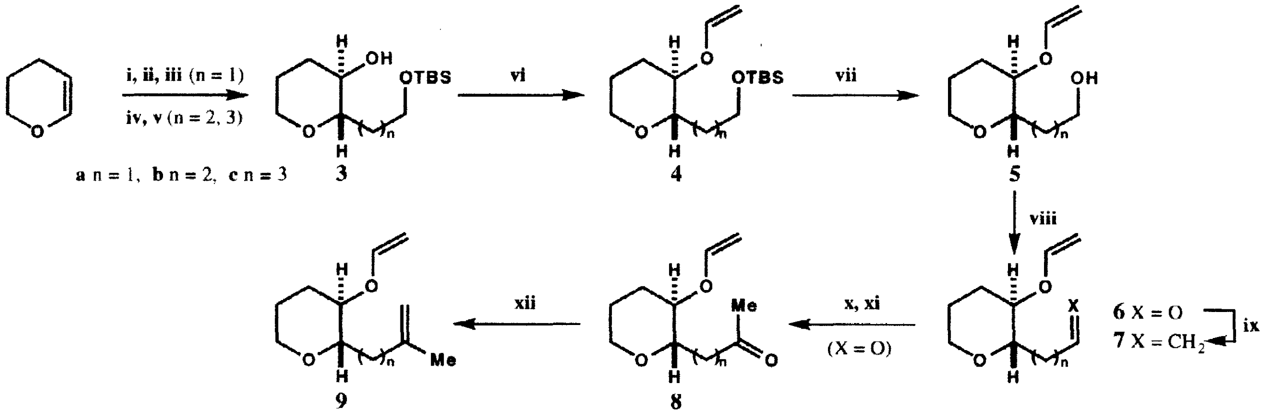


Scheme 1

Prior to our work in this area,[16] Grubbs had shown that it was possible to prepare simple five- and six-membered cyclic ethers by intramolecular metathesis of alkenes with enol ethers using the molybdenum complex **1**,[17] and while our studies were in progress Nicolaou reported that olefinic esters could be converted directly to six- and seven-membered enol ethers in moderate yield by tandem ester methylenation and metathesis using a large excess of Tebbe reagent or dimethyltitanocene.[18]

The aim of the studies described herein, was to demonstrate that ring-closing metathesis could be used to prepare fused bicyclic enol ethers possessing six- or seven-membered rings, and that subsequent stereoselective hydroboration of these compounds would provide *trans*-fused bicyclic ether units of the type found in gambierol, brevetoxin B, and many of the other marine polyether natural products.[16] At the outset, we were confident that hydroboration of the cyclic enol ether ring-closing metathesis products could be accomplished stereoselectively based on literature precedent for the hydroboration of related systems.[19]

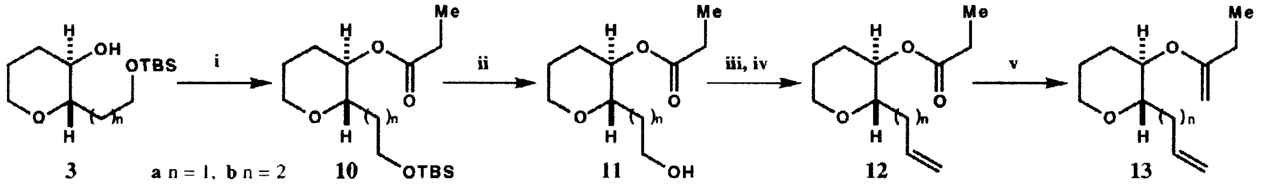
The first objective was the preparation of model systems that could be used to demonstrate the viability of sequential enol ether ring-closing metathesis and hydroboration, as outlined in Scheme 1. The appropriate enol ether cyclisation precursors (**7a–c** and **9a**,**b**) required for our study were prepared as shown in Scheme 2. Deprotonation of 3,4-dihydro-2*H*-pyran with *n*-butyllithium,[20] conversion of the vinyl lithium intermediate into an organocopper reagent by reaction with copper(I) iodide, and subsequent treatment with ethylene oxide afforded 2-(2-hydroxyethyl)-3,4-dihydropyran. This enol ether was then immediately hydroborated with borane-tetrahydrofuran complex to give (2*S**,3*R**)-2-(2-hydroxyethyl)-3-hydroxytetrahydropyran, and the primary hydroxyl group of this diol was then protected as the TBS ether to provide the alcohol **3a**. The homologous alcohols **3b** and **3c** were prepared in good yield by deprotonation of 3,4-dihydro-2*H*-pyran with *n*-butyllithium, alkylation of the vinyl lithium intermediate[20] with either 1-(*t*-butyldimethylsilyloxy)-4-iodobutane[21] or 1-(*t*-butyldimethylsilyloxy)-5-iodopentane[21] and immediate hydroboration of resulting enol ethers. Each of the alcohols **3a–c** was then converted to the corresponding vinyl ether **4a–c** by mercury(II) acetate catalysed reaction with ethyl vinyl ether.[22] Removal of the TBS protecting group afforded the alcohols **5a–c** which were oxidised to give the aldehydes **6a–c**, and Wittig methylenation then completed the synthesis of the cyclisation precursors **7a–c**. The precursors **9a** and **9b** were prepared from the aldehydes **6a** and **6b** by sequential reaction with methylmagnesium bromide, Parikh-Doering oxidation[23] and Wittig methylenation.



Reagents: **i** *n*-BuLi, TMEDA, –78→0 °C, CuI, $(CH_2)_2O$, THF, –78 °C; **ii** BH_3.THF, THF, 0 °C then NaOH aq., 30% H_2O_2 (**a** 51% 2 steps); **iii** *t*-BuMe$_2$SiCl, imidazole, DMF, rt (74%); **iv** *n*-BuLi, rt→50 °C, $I(CH_2)_nCH_2OTBS$, THF; **v** BH_3.THF, THF 0 °C then NaOH aq., 30% H_2O_2 (**b** 98%, **c** 68% 2 steps); **vi** $EtOCHCH_2$, $Hg(OAc)_2$, reflux (**a** 89%, **b** 62%, **c** 83%); **vii** Bu_4NF, THF, rt (**a** 91%, **b** 95%, **c** 94%); **viii** PCC, NaOAc, 4Å sieves, CH_2Cl_2, rt (**a** 62%, **b** 71%); **ix** $Ph_3P^+CH_3Br^-$, *n*-BuLi, THF, rt (**a** 64%, **b** 89%, **c** 59% 2 steps); **x** MeMgBr, THF, 0 °C (**b** 60%); **xi** SO_3.pyr, Et_3N, DMSO, CH_2Cl_2, rt (**a** 67% 2 steps, **b** 64%); **xii** $Ph_3P^+CH_3Br^-$, *n*-BuLi, THF, rt (**a** 67%, **b** 74%).

Scheme 2

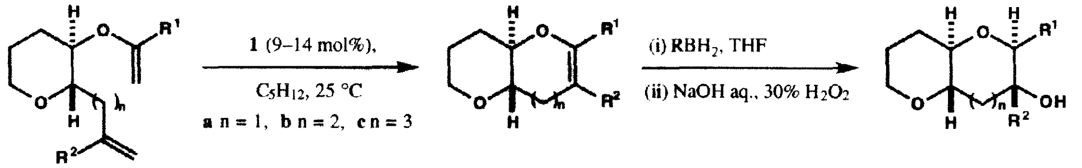
The third set of precursors (**13a** and **13b**) required for our study was prepared as shown in Scheme 3. Acylation of the alcohols **3a** and **3b** with propionic anhydride in the presence of DMAP provided the esters **10a** and **10b** in good yield. Removal of the TBS protecting group afforded the alcohols **11a** and **11b**, which were then converted into the alkenes **12a** and **12b** by sequential oxidation and Wittig reaction. Methylenation of the ester carbonyl group, using Takai's protocol,[24] gave the required cyclisation precursors **13a** and **13b**.



Reagents: **i** $(EtCO)_2O$, DMAP, Et_3N, CH_2Cl_2 (**a** 99%, **b** 73%); **ii** Bu_4NF, THF, rt (**a** 89%, **b** 85%); **iii** SO_3.pyr, Et_3N, DMSO, CH_2Cl_2, rt (**b** 81%); **iv** $Ph_3P^+CH_3Br^-$, *n*-BuLi, THF, rt (**a** 35% 2 steps, **b** 69%); **v** $TiCl_4$, TMEDA, CH_2Br_2, Zn, THF, rt (**a** 70%, **b** 79%).

Scheme 3

Having prepared the required cyclisation precursors, we explored the construction of six- and seven-membered cyclic enol ethers by ring-closing metathesis. Treatment of the enol ethers **7**, **9**, or **13** with a sub-stoichiometric amount (9–14 mol%) of the molybdenum complex **1**,[13,14] afforded the volatile and acid-sensitive cyclic enol ethers **14–16** in good yield (Table). The best results were obtained upon cyclisation of the substrates **9a** and **9b** to give the trisubstituted enol ethers **15a** and **15b** (Table), which suggests that optimum yields are obtained with substrates in which the alkene is hindered with respect to the enol ether group. One possible explanation for this observation is that the metal alkylidene reacts with the substrates **9** at the less hindered enol ether site in the initial intramolecular step of the metathesis sequence, and that ring-closure occurs by rapid reaction of the resulting alkylidene with the electronically more reactive 1,1-disubstituted alkene. In contrast, the substrates **7** and **13** react with the catalyst at the electronically favoured and sterically unencumbered alkene in the initial step, and ring closure proceeds by intramolecular metathesis with the electronically less reactive enol ether. Thus, in the latter case, the lifetime of the intermediate olefin alkylidene is longer and competing non-productive reactions can intervene.



7 $R^1 = H$ $R^2 = H$
9 $R^1 = H$ $R^2 = Me$
13 $R^1 = Et$ $R^2 = H$

14 $R^1 = H$ $R^2 = H$
15 $R^1 = H$ $R^2 = Me$
16 $R^1 = Et$ $R^2 = H$

17 $R^1 = H$ $R^2 = H$
18 $R^1 = H$ $R^2 = Me$
19 $R^1 = Et$ $R^2 = H$

Scheme 4

Substrate	Enol ether	%Yield^{a}	Hydroborating agent	Temp.	Product	%Yield^{b}
7a	**14a**	64	ThxBH$_2$	rt	**17a**	52^{c}
7b	**14b**	65	ThxBH$_2$	-20 °C	**17b**	43^{d}
9a	**15a**	93	BH$_3$.THF	0 °C	**18a**	$72^{c,e}$
9b	**15b**	94	BH$_3$.THF	0 °C	**18b**	0
13a	**16a**	72	ThxBH$_2$	-20 °C	**19a**	61
13b	**16b**	40	ThxBH$_2$	-20 °C	**19b**	41

a Yield of isolated material after purification by chromatography. *b* Total yield of alcohols obtained over two steps without purification of the intermediate enol ether. *c* Yield from the hydroboration reaction only. *d* NMR analysis indicated that a 90:10 mixture of diastereoisomers was obtained with **17b** predominating. *e* NMR analysis indicated that a 68:32 mixture of diastereoisomers with obtained with **18a** predominating.

Table

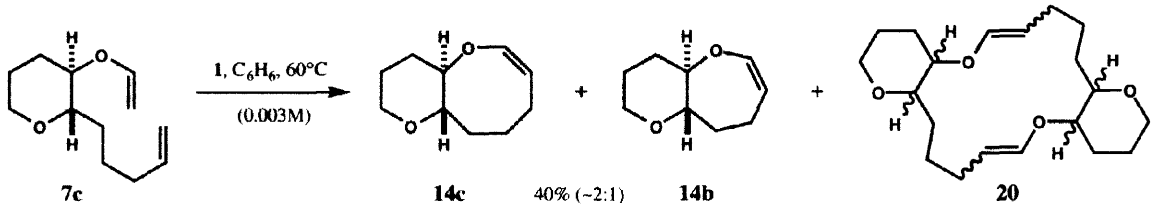
Conversion of the cyclic enol ethers to the required alcohols was accomplished by hydroboration (Table).[19] High levels of diastereocontrol were achieved when this reaction was performed using thexylborane at –20 °C. However, the enol ethers **15a** and **15b** were too hindered to react with thexylborane, and so borane-tetrahydrofuran complex was used instead. This resulted in a poor ratio of diastereoisomers in the case of the enol ether **15a** and decomposition of the intermediate organoborane generated from the enol ether **15b**.[25]

It was possible to hydroborate the acid-sensitive cyclic enol ethers directly without purification after the ring-closing metathesis reaction. The yields of the cyclic ethers (**17–19**) prepared in this way were generally high, and those obtained for the alcohols **19a** and **19b**, whose stereochemistry was rigorously determined by NOE studies, are particularly significant (Table). The yields of the alcohols **17a** and **17b**, produced upon hydroboration of the disubstituted enol ethers **14a** and **14b**, were rather modest and substantial amounts of ring-opened products were obtained from these reactions (Table).[25]

The ruthenium complex **2** was also explored as a catalyst for the ring-closing metathesis reaction of the substrates **7**, **9** and **13**. This catalyst is easier to prepare and handle than the molybdenum complex **1**,[14,15] and the synthetic utility of this and related ruthenium complexes as catalysts for the preparation of heterocycles and carbocycles by ring-closing metathesis had been demonstrated by Grubbs and others.[13] However, the complex **2** proved to be ineffective for the cyclisation of the enol ether substrates used in our study.[26]

The preparation of tetrasubstituted bicyclic enol ethers (R^1 = Et, R^2 = Me, Scheme 4) by ring-closing metathesis was also explored, but this approach was not successful. Although the ring-closing metathesis reaction has been used to prepare tetrasubstituted cycloalkenes from 1,1-disubstituted alkenes,[13,27] the combination of relatively low enol ether reactivity and unfavorable steric interactions seems to preclude the formation of tetrasubstituted enol ethers using this reaction.

It was possible to prepare the bicyclic system **14c** possessing an eight-membered cyclic enol ether by ring-closing metathesis of the substrate **7c** (eq. 1). Treatment of the vinyl ether **7c** with the molybdenum complex **1** (33 mol%) under high dilution conditions afforded an inseparable mixture of the required cyclic ether **14c** and the seven-membered bicyclic enol ether **14b** in a combined yield of 37% (~2:1 ratio). The mass balance was largely accounted for by the formation of substantial amounts of the cyclo-dimer **20**, which was obtained as a complex mixture of stereoisomers and was identified on the basis of NMR and mass spectrometry data.[28,29] Re-submission of the cyclo-dimer **20** to the reaction conditions did not lead to formation of further amounts of the enol ethers **14c** and **14b**.



(1)

The ethyl-substituted cyclisation precursor **13c** (n = 3) was also prepared. However, this compound gave none of the required enol ether **16c** upon treament with the catalyst **1** (Scheme 4). Instead, dimeric products were isolated from this reaction .

The isolation of the cyclic enol ether **14b** from the ring-closing metathesis reaction of the vinyl ether **7c** was unexpected and such a reaction with the catalyst **1** was unprecedented.[16,30] It is likely that this compound was formed by isomerisation of the substrate **7c** prior to metathesis, and that the process was promoted by the molybdenum complex **1** or by trace amounts of an intermediate used to prepare this catalyst. The isomerisation reaction appears to be relatively slow because products arising from analogous isomerisation reactions were not obtained by us from the ring-closing metathesis reactions of other enol ethers or during the preparation of eight- and nine-membered cyclic ethers from the more reactive allylic ether substrates.[31] The putative origin of the smaller ring product is further supported by Overman's recent report of an analogous reaction in which an eight-membered ring was obtained upon attempted formation of a nine-membered ring by ring-closing metathesis using the catalyst **1**.[32]

Our results demonstrate that ring-closing metathesis of enol ethers with alkenes and subsequent stereoselective hydroboration is a viable synthetic sequence for the preparation of six- and seven-membered fused cyclic ethers, but that the reaction is of limited use for the construction of eight-membered cyclic ethers.[30] Application of this sequence to the synthesis of large fragments of the polyether marine toxins is currently under investigation, and the results of these studies will be reported in due course.

Experimental

General

All reactions were performed in oven-dried glassware under an atmosphere of dry nitrogen or argon. Air- and moisture-sensitive liquids and solutions were transferred by syringe or stainless steel cannula. Dry tetrahydrofuran and pentane were distilled from potassium benzophenone ketyl prior to use. Dichloromethane and N,N,N',N'-tetramethylethylenediamine were distilled from calcium hydride under an atmosphere of nitrogen. Other solvents and reagents were used directly as commercially supplied. 2,6-Diisopropylphenylimidoneophylidenemolybdenum (IV) *bis*(hexafluoro-*t*-butoxide) (**1**) was purchased from Strem Chemicals UK.

Flash column chromatography was performed using Fluka silica gel 60 (220–440 mesh ASTM). Thin-layer chromatography was performed using Merck silica gel 60 F_{254} aluminium or glass (250 μm) backed plates, or Polygram sil G/UV_{254} plastic backed plates, Visualisation was accomplished using UV light, or by staining with an ethanolic solution of *p*-anisaldehyde or an aqueous solution of potassium permanganate.

NMR spectra were obtained using Bruker DRX-500, AM-400, WM-250 spectrometers or a Jeol EX-270 spectrometer. The data for ^{1}H spectra are reported as follows: chemical shift (δ), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet,; m, multiplet; br, broad), integration, coupling constant (*J*) in Hz and assignment. IR spectra were recorded on sodium chloride plates using a Perkin Elmer 1600 or 1720-X FTIR instrument; absorption frequencies (ν) are reported in cm^{-1}. High and low resolution mass spectrometry was performed using VG Micromass 70E and AIMS902 instruments; ionisation was accomplished by electron-impact unless otherwise stated. Microanalyses were performed by the microanalysis unit at the Department of Chemistry, University of Nottingham.

(2*S,3*R**)-2-(2-Hydroxyethyl)-3-hydroxytetrahydropyran.** *n*-BuLi (61.1 mL of a 1.38 M solution in hexanes, 84.3 mmol) was added dropwise to a mixture of dihydropyran (11.5 mL, 126 mmol) and TMEDA at 0 °C with stirring. The reaction was allowed to warm to room temperature and a dense white precipitate formed after ca. 2 h. The reaction was stirred overnight and then dry THF (30 mL) was added to dissolve the solid. The mixture was then cooled to –78 °C and then added by cannula to a rapidly stirred suspension of CuI (7.3 g, 38 mmol) in dry THF (50 mL) at –78 °C to give a black suspension. The mixture was stirred for 1 h and then ethylene oxide (7.4 g, 0.16 mol) was added by cannula. The reaction mixture was stirred for a further 1 h at –78 °C and allowed to warm to room temperature slowly. The reaction was stirred for 2 h and then quenched by the addition of a mixture of saturated NH_4Cl and 10% NH_4OH aq. (100 mL). Pet. ether (100 mL) was added to precipitate the solids and the mixture was filtered through basic alumina (Brockman grade III) (Et_2O with 1% Et_3N). Concentration of the filtrate afforded an orange oil (7.17 g) that was used in the subsequent reaction without further purification.

The crude enol ether (7.17 g, 55.9 mmol) was dissolved in dry THF (100 mL) and the solution was cooled to 0 °C. A solution of BH_3.THF complex (112 mL of a ca. 1 M solution in THF, approx. 112 mmol) was added slowly and the reaction stirred at 0 °C for 2 h. The reaction was quenched at 0 °C by the dropwise addition of 3M NaOH aq. (100 mL) followed by 30% H_2O_2 (100 mL). The reaction was stirred at 0 °C for 1 h and then at 25 °C for 2 h. The reaction mixture was filtered and extracted with Et_2O (3 × 100 mL). The product diol was very water soluble, but residual material was recovered by acidification of the aqueous layer and extraction with Et_2O. The crude material was then purified by flash column chromatography on silica gel (Et_2O with 1% MeOH) to give the diol as a colourless oil (4.69 g, 51% for 2 steps) which solidified on standing. IR (thin film) 3324, 2927, 2854, 1094, 1047 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09 (d, *J* = 4.1 Hz, 1H, O*H*), 3.92–3.85 (m, 2H, O*H*, OC*H*), 3.84–3.70 (m, 2H, 2 × OC*H*), 3.38–3.28 (m, 2H, 2 × OC*H*), 3.20–3.13 (m, 1H, OC*H*), 2.14–1.98 (m, 2H, 2 × CH_2), 1.82–1.73 (m, 1H, CH_2), 1.73–1.64 (m, 2H, 2 × CH_2) 1.46–1.35 (m, 1H, CH_2); ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.2, 70.0, 67.6, 60.2, 35.3, 32.4, 25.4; Anal. calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found C, 57.46; H, 9.85.

Alcohol 3a. A solution of *t*-butyldimethylsilyl chloride (4.77 g, 31.6 mmol) in dry DMF (20 mL) was added by cannula to a solution of (2*S**,3*R**)-2-(2-hydroxyethyl)-3-hydroxytetrahydropyran (4.63 g, 31.7 mmol), imidazole (4.31 g, 63.3 mmol) and DMAP (0.1 g) in dry DMF (30 mL) at room temperature. The reaction was stirred for 7 h, after which time tlc indicated complete consumption of starting material. The reaction mixture was poured into water (200 mL) and extracted with ether (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give a colourless oil (6.92 g). The crude product was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 65:35) to give the product as a colourless oil (6.08 g, 74%). IR (thin film) 3422, 2954, 2930, 2856, 1255, 1097 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00–3.97 (m, 1H, O*H*), 3.91–3.82 (m, 2H, 2 × OC*H*), 3.78–3.71 (m, 1H, OC*H*), 3.38–3.28 (m, 2H, 2 × OC*H*), 3.12–3.06 (m, 1H, OC*H*), 2.16–2.09 (m, 1H, CH_2), 1.91–1.87 (m, 2H, 2 × CH_2), 1.72–1.63 (m, 2H, 2 × CH_2) 1.46–1.34 (m, 1H, CH_2), 0.92 (s, 9H, C[CH_3]$_3$), 0.11 (s, 6H, 2 × CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 81.7, 70.4, 67.8, 60.4, 37.5, 32.0, 25.9, 25.7, 18.3, –5.4; HRMS calcd for $C_{19}H_{19}O_3Si$ (M^+–CMe_3): 203.1101, found: 203.1104.

Alcohol 3b. *n*-BuLi (18 mL of a 1.60 M solution in hexanes, 29 mmol) was added dropwise to dihydropyran (4.0 mL, 44 mmol) in THF (50 mL) with stirring at room temperature to give a deep orange solution. The mixture was heated to 50 °C and stirred at this temperature for 2 h. The reaction was cooled to 0 °C and a solution of the 1-(*t*-butyldimethylsilyloxy)-4-iodobutane (4.31 g, 14.4 mmol) in THF (10 mL) was added by cannula. The reaction was heated to 50 °C and stirred at this temperature for 1.5 h. The reaction mixture was cooled, poured into water (200 mL) and then extracted with ether (3 × 100 mL). The combined organic extracts were dried (anh. MgSO$_4$) and the solvent removed *in vacuo* to give the product (4.37 g) as colourless liquid. This crude material was then submitted to hydroboration without further purification.

The enol ether (4.37 g, 17.0 mmol) was dissolved in dry THF (50 mL). A solution of BH$_3$.THF complex (30 mL of a ca. 1 M solution in THF, 30 mmol) was added slowly and the reaction stirred at 0 °C for 2 h. The reaction was quenched at 0 °C by the dropwise addition of water (15 mL) and 2M NaOH aq. (40 mL) followed by 9% H$_2$O$_2$ (50 mL). The reaction mixture was warmed to room temperature and stirred overnight, then filtered and extracted with ether (2 × 100 mL). The combined organic extracts were dried (anh. MgSO$_4$) and the solvent removed *in vacuo* to give a colourless oil (5.00 g). The crude material was purified by flash column chromatography on silica gel (pet. ether-Et$_2$O, 50:50) to afford the product as an oil (3.85 g, 98% for 2 steps). IR (thin film) 3430, 2933, 2858, 2736, 1256, 1097 cm^{-1}; ^{1}H NMR (250 MHz, CDCl$_3$) δ 3.94–3.83 (m, 1H, C*H*$_2$OCH), 3.65 (t, *J* = 7.5 Hz, 2H, C*H*$_2$OTBS), 3.43–3.28 (m, 2H, C*H*$_2$OCH, C*H*OH), 3.02 (ddd, *J* = 9.0, 9.0, 2.6 Hz, 1H, CH$_2$OC*H*), 2.14–1.13 (m, 9H, 8 × C*H*$_2$, O*H*), 0.91 (s, 9H, C[C*H*$_3$]$_3$), 0.07 (s, 6H, 2 × C*H*$_3$); ^{13}C NMR (67.8 MHz, CDCl$_3$) δ 82.6, 70.7, 67.8, 63.7, 33.0, 28.7, 28.3, 26.3, 26.0, 18.7, –5.0; HRMS calcd for C$_{10}$H$_{21}$O$_3$Si (M$^+$–CMe$_3$): 217.1260, found: 217.1257.

Alcohol 3c. *n*-BuLi (18 mL of a 1.6 M solution in hexanes, 29 mmol) was added dropwise to a solution of dihydropyran (4.0 mL, 44 mmol) in THF (60 mL) with stirring at room temperature to give a deep orange solution. The mixture was heated to 50 °C and stirred at this temperature for 2 h. The reaction was cooled to 0 °C and a solution of the 1-(*t*-butyldimethylsilyloxy)-5-iodopentane (4.54 g, 14.4 mmol) in THF (10 mL) was added by cannula. The reaction was heated to 50 °C and stirred at this temperature for 1.5 h. The reaction mixture was cooled, poured into water (200 mL) and then extracted with ether (2 × 100 mL). The combined organic extracts were dried (anh. MgSO$_4$) and the solvent removed *in vacuo* to give the product (4.08 g) as a colourless oil. This crude material was then hydroborated without further purification.

The enol ether (4.08 g, 15.1 mmol) was dissolved in dry THF (50 mL). A solution of BH$_3$.THF complex (30 mL of a ca. 1 M solution in THF, 30 mmol) was added slowly and the reaction stirred at 0 °C for 2 h. The reaction was quenched at 0 °C by the dropwise addition of water (15 mL) and 2M NaOH aq. (40 mL) followed by 9% H$_2$O$_2$ (40 mL). The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was filtered and extracted with ether (2 × 100 mL). The combined organic extracts were dried (anh. MgSO$_4$) and the solvent removed *in vacuo* to give the product as a colourless oil (4.23 g). The crude product was purified by flash column chromatography on silica gel (pet. ether-ether, 50:50) to afford the product as an oil (2.85 g, 68% for 2 steps). IR (thin film) 3439, 2940, 2863, 1356, 1120 cm^{-1}; ^{1}H NMR (250 MHz, CDCl$_3$) δ 3.94–3.83 (m, 1H, C*H*$_2$OCH), 3.62 (t, *J* = 6.4 Hz, 2H, C*H*$_2$OTBS), 3.41–3.23 (m, 2H, C*H*$_2$OCH, C*H*OH), 3.07–2.94 (m, 1H, CH$_2$OC*H*), 2.18–2.03 (m, 1H, C*H*$_2$), 1.95–1.30 (m, 10H, 9 × C*H*$_2$, O*H*), 0.91 (s, 9H, C[C*H*$_3$]$_3$), 0.08 (s, 6H, 2 × C*H*$_3$); ^{13}C NMR (67.8 MHz, CDCl$_3$) δ 82.3, 70.4, 67.5, 63.3, 32.9, 32.9, 31.7, 26.0, 25.6, 21.6, 18.3, –5.3. LRMS *m/z* 231 (10) [M$^+$–CMe$_3$], 57 (19).

Vinyl ether 4a. The alcohol **3a** (1.69 g, 6.49 mmol) and Hg(OAc)$_2$ (0.3 g, 0.9 mmol) were added to ethyl vinyl ether (50 mL) and the mixture was heated at reflux for 6 days. Excess ethyl vinyl ether was then removed *in vacuo* and the residue purified by column chromatography on neutral alumina (pet. ether with 1% Et$_3$N) to give the product (1.65 g, 89%) as an oil. IR (thin film) 2955, 2929, 2856, 1634, 1255, 1182, 1099 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.30 (dd, *J* = 14.1, 6.5 Hz, 1H, OC*H*=CH$_2$), 4.30 (dd, *J* = 14.1, 1.7 Hz, 1H, OCH=C*H*$_2$-*trans*), 4.00 (dd, *J* = 6.5, 1.7 Hz, 1H, OCH=C*H*$_2$-*cis*), 3.90–3.85 (m, 1H, C*H*$_2$OCH), 3.79 (app. dd, *J* = 7.9, 5.3 Hz, 2H, C*H*$_2$OTBS), 3.49–3.42 (m, 1H, C*H*OCH=CH$_2$), 3.35–3.28 (m, 2H, C*H*$_2$OCH, CH$_2$OC*H*), 2.24–2.17 (m, 1H, C*H*$_2$), 2.05 (dddd, *J* = 13.9, 7.9, 7.9, 2.7 Hz, 1H, C*H*$_2$), 1.73–1.60 (m, 2H, 2 × C*H*$_2$), 1.54 (dddd, *J* = 14.1, 9.3, 5.3, 5.3, 1H, C*H*$_2$) 1.50–1.39 (m, 1H, C*H*$_2$), 0.89 (s, 9H, C[C*H*$_3$]$_3$), 0.06 (s, 6H, 2 × C*H*$_3$); ^{13}C NMR (67.8 MHz, CDCl$_3$) δ 150.7, 88.3, 77.9, 76.9, 67.4, 59.3, 35.3, 29.5, 25.9, 25.2, 18.3, –5.4; Anal. calcd for $C_{15}H_{30}O_3Si$: C, 62.89; H, 10.56. Found: C, 63.19; H, 10.98.

Vinyl ether 4b. The alcohol **3b** (1.00 g, 3.64 mmol) and $Hg(OAc)_2$ (0.2 g, 0.6 mmol) were added to ethyl vinyl ether (50 mL) and the mixture was heated at reflux for 6 days. Excess ethyl vinyl ether was then removed *in vacuo* and the residue purified by flash column chromatography on silica gel (pet. ether-Et_2O, 95:5) to give the product (0.68 g, 62 %) as an oil. Further elution (pet. ether-Et_2O, 60:40) provided unreacted starting material (0.22 g, 22%). IR (thin film) 3118, 2930, 2857, 2735, 1634, 1612, 1255, 1183, 1096 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (dd, *J* = 14.0, 6.5 Hz, 1H, OC*H*=CH_2), 4.30 (dd, *J* = 14.0, 1.4 Hz, 1H, OCH=CH_2-*trans*), 3.99 (dd, *J* = 6.5, 1.4 Hz, 1H, OCH=CH_2-*cis*), 3.93–3.86 (m, 1H, CH_2OCH), 3.66–3.54 (m, 2H, CH_2OTBS), 3.47–3.38 (m, 1H, C*H*OCH=CH_2), 3.37–3.28 (m, 1H, CH_2OCH), 3.16 (ddd, *J* = 9.0, 9.0, 2.6 Hz, 1H, CH_2OC*H*), 2.24–2.16 (m, 1H, CH_2), 1.92–1.79 (m, 1H, CH_2), 1.79–1.40 (m, 6H, 6 × CH_2,), 0.86 (s, 9H, C[CH_3]$_3$), 0.03 (s, 6H, 2 × CH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.8, 88.4, 80.3, 77.9, 67.5, 63.2, 29.5, 28.7, 28.4, 26.0, 25.3, 18.3, –5.3; Anal. calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73. Found: C, 64.07; H, 11.20.

Vinyl ether 4c. The alcohol **3b** (0.80 g, 2.7 mmol) and $Hg(OAc)_2$ (0.2 g, 0.6 mmol) were added to ethyl vinyl ether (20 mL) and the mixture was heated at reflux for 8 days. Excess ethyl vinyl ether was then removed *in vacuo* and the residue purified by flash column chromatography on silica gel (pet. ether- Et_2O, 95:5 with 1% Et_3N) to give the product (0.72 g, 83%) as an oil. IR (thin film) 2955, 2929, 2856, 1634, 1255, 1182, 1099 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.30 (dd, *J* = 14.1, 6.5 Hz, 1H, OC*H*=CH_2), 4.30 (dd, *J* = 14.1, 1.7 Hz, 1H, OCH=CH_2-*trans*), 4.02 (dd, *J* = 6.5, 1.7 Hz, 1H, OCH=CH_2-*cis*), 4.00–3.83 (m, 1H, CH_2OCH), 3.62 (t, *J* = 6.4 Hz, 2H, CH_2OTBS), 3.51–3.32 (m, 2H, C*H*OCH=CH_2, CH_2OCH), 3.22–3.13 (m, 1H, CH_2OC*H*), 2.27–2.14 (m, 1H, CH_2), 1.89–1.31 (m, 9H, 9 × CH_2), 0.90 (s, 9H, C[CH_3]$_3$), 0.07 (s, 6H, 2 × CH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.8, 88.4, 80.3, 77.9, 67.5, 63.2, 32.9, 31.8, 29.5, 26.0, 25.3, 18.3, –5.3; Anal. calcd for $C_{17}H_{34}O_3Si$: C, 64.92; H, 10.90. Found: C, 65.09; H, 11.28.

Alcohol 5a. The *t*-butyldimethylsilyl ether **4a** (3.16 g, 11.0 mmol) was dissolved in dry THF (40 mL) and *t*-butylammonium fluoride (30 mL of a 1M solution in THF, 30 mmol) was added. The mixture was stirred at room temperature for 2 h after which time tlc indicated the reaction was complete. The reaction mixture was poured into water (200 mL) and the mixture extracted with ether (3 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed to give an orange oil. The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 50:50 with 1% Et_3N) to afford the product (1.73 g, 91%) as a colourless oil. IR (thin film) 3418, 2943, 2860, 1634, 1178, 1084, 1023 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (dd, *J* = 14.0, 6.5 Hz, 1H, OC*H*=CH_2), 4.31 (dd, *J* = 14.0, 1.7 Hz, 1H, OCH=CH_2-*trans*), 4.03 (dd, *J* = 6.5, 1.7 Hz, 1H, OCH=CH_2-*cis*), 3.95–3.89 (m, 1H, CH_2OCH), 3.79 (app. dd, *J* = 11.3, 5.3 Hz, 2H, CH_2OH), 3.55–3.48 (m, 1H, C*H*OCH=CH_2), 3.44–3.35 (2H, m, CH_2OCH, CH_2OC*H*), 2.61 (t, *J* = 5.6 Hz, 1H, OH), 2.28–2.20 (m, 1H, CH_2), 2.09–2.02 (m, 1H, CH_2), 1.76–1.64 (m, 3H, 3 × CH_2), 1.49–1.40 (m, 1H, CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.5, 88.9, 81.0, 77.4, 67.7, 61.4, 34.1, 29.3, 25.1; HRMS calcd for $C_9H_{14}O_2$ ($M^+–H_2O$): 154.0994, found: 154.0999.

Alcohol 5b. The *t*-butyldimethylsilyl ether **4b** (2.08 g, 6.92 mmol) was dissolved in dry THF (50 mL) and *t*-butylammonium fluoride (20.7 mL of a 1M solution in THF, 20.7 mmol) was added. The mixture was stirred at room temperature for 4 h after which time tlc indicated the reaction was complete. The reaction mixture was poured into water (200 mL) and the mixture extracted with ether (3 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed to give an orange oil. The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 50:50 with 1% Et_3N) to afford the product (1.23 g, 95%) as a colourless oil. IR (thin film) 3401, 2944, 2856, 1635, 1194, 1136, 1083, 1025 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.28 (dd, *J* = 14.0, 6.5 Hz, 1H, OC*H*=CH_2), 4.31 (dd, *J* = 14.0, 1.7 Hz, 1H, OCH=CH_2-*trans*), 4.02 (dd, *J* = 6.5, 1.7 Hz, 1H, OCH=CH_2-*cis*), 3.98–3.87 (m, 1H, CH_2OCH), 3.72–3.55 (m, 2H, CH_2OH), 3.53–3.30 (m, 2H, C*H*OCH=CH_2, CH_2OCH), 3.20 (ddd, *J* = 8.9, 8.9, 2.3 Hz, 1H, CH_2OC*H*), 2.28–2.17

(m, 1H, CH_2), 2.04–1.89 (m, 1H, CH_2), 1.90–1.78 (m, 4H, 4 × CH_2), 1.75–1.40 (m, 2H, 2 × CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.6, 88.7, 80.5, 77.5, 67.7, 62.3, 29.5, 29.0, 28.9, 25.2; Anal. calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74, Found: C, 64.20; H, 10.15.

Alcohol 5c. The *t*-butyldimethylsilyl ether **4c** (0.72 g, 2.3 mmol) was dissolved in dry THF (5 mL) and *t*-butylammonium fluoride (9.2 mL of a 1M solution in THF, 9.2 mmol) was added. The mixture was stirred at room temperature for 3 h after which time tlc indicated the reaction was complete. The reaction mixture was poured into water (50 mL) and the mixture extracted with ether (3 × 50 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed to give an orange oil. The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 40:60) to afford the product (0.43 g, 94%) as a colourless oil. IR (thin film) 3401, 3116, 3022, 2943, 2861, 1635, 1194, 1130, 1083, 1027 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.28 (dd, *J* = 14.0, 6.5 Hz, 1H, $OCH{=}CH_2$), 4.30 (dd, *J* = 14.0, 1.7 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.00 (dd, *J* = 6.5, 1.7 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.96–3.83 (m, 1H, CH_2OCH), 3.62 (t, *J* = 6.4 Hz, 2H, CH_2OH), 3.49–3.37 (m, 2H, $CHOCH{=}CH_2$, CH_2OCH), 3.17 (ddd, *J* = 9.0, 9.0, 2.8 Hz, 1H, CH_2OCH), 2.27–2.13 (m, 1H, CH_2), 1.90–1.27 (m, 10H, 9 × CH_2, *OH*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.9, 88.8, 80.5, 78.0, 77.7, 67.8, 62.8, 32.8, 29.7, 25.5, 21.7; Anal. calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07, Found: C, 65.58; H, 10.53; LRMS *m/z* 200 (2) [M$^+$], 157 (60), 127(2), 71(100).

Aldehyde 6a. The alcohol **5a** (1.70 g, 9.87 mmol) was dissolved in a mixture of dry DMSO (3 mL), dry CH_2Cl_2 (50 mL) and dry Et_3N (13.7 mL, 98.3 mmol). Solid sulfur trioxide-pyridine complex (7.85 g, 49.4 mmol) was added to the solution portionwise and the reaction stirred for 2 h at room temperature. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an orange oil (1.83 g). The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 95:5 with 1% Et_3N) to afford the product (1.04 g, 62%) as a colourless oil. IR (thin film) 3116, 2945, 2855, 2730, 1730, 1633, 1181, 1137, 1099, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.77 (m, 1H, CHO), 6.28 (dd, *J* = 14.0, 6.5 Hz, 1H, $OCH{=}CH_2$), 4.32 (dd, *J* = 14.0, 1.7 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.06 (dd, *J* = 6.5, 1.7 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.94–3.87 (m, 1H, CH_2OCH), 3.76 (ddd, *J* = 9.1, 8.4, 3.7 Hz, 1H, $CHOCH{=}CH_2$), 3.52 (ddd, *J* = 9.9, 9.9, 4.6 Hz, 1H, CH_2OCH), 3.44–3.37 (m, 1H, CH_2OCH), 2.83–2.78 (m, 1H, CH_2CHO), 2.57–2.49 (ddd, *J* = 16.2, 8.4, 1.0 Hz, 1H, CH_2CHO), 2.31–2.24 (m, 1H, CH_2), 1.76–1.64 (m, 2H, 2 × CH_2), 1.53–1.42 (m, 1H, CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 201.2, 150.7, 89.9, 77.6, 76.3, 68.3, 47.1, 29.9, 25.6; HRMS calcd for $C_9H_{14}O_3$: 170.0943, found: 170.0944.

Aldehyde 6b. The alcohol **5b** (0.27 g, 1.4 mmol) was dissolved in a mixture of dry DMSO (2 mL), dry CH_2Cl_2 (10 mL) and dry Et_3N (2.0 mL, 14 mmol). Solid sulfur trioxide-pyridine complex (0.92 g, 5.8 mmol) was added to the solution in a portionwise manner and the reaction stirred for 2 h at room temperature. The reaction mixture was then poured into water (50 mL) and extracted with Et_2O (2 × 50 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an orange oil (0.44 g). The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 80:20 with 1% Et_3N) to afford the product (0.19 g, 71%) as a colourless oil. IR (thin film) 2943, 2854, 2726, 1724, 1636, 1182, 1139, 1100, 1015 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.77 (br s, 1H, CHO), 6.28 (dd, *J* = 14.1, 6.5 Hz, 1H, $OCH{=}CH_2$), 4.31 (dd, *J* = 14.1, 1.7 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.03 (dd, *J* = 6.5, 1.7 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.91–3.84 (m, 1H, CH_2OCH), 3.48–3.41 (m, 1H, $CHOCH{=}CH_2$), 3.36–3.26 (m, 1H, CH_2OCH), 3.17 (ddd, *J* = 9.0, 9.0, 2.8 Hz, 1H, CH_2OCH), 2.63–2.44 (m, 2H, CH_2CHO), 2.27–2.12 (m, 2H, 2 × CH_2), 1.78–1.57 (m, 3H, 3 × CH_2), 1.48–1.35 (m, 1H, CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 202.5, 150.4, 88.8, 79.4, 77.6, 67.6, 40.1, 29.3, 25.2, 24.9; LRMS *m/z* 184 (2) [M$^+$], 141(37), 55 (100), 43 (83); HRMS calcd for $C_8H_{13}O_3$ ($M^+{-}C_2H_3$): 157.0865, found: 157.0865.

Alkene 7a. Methyltriphenylphosphonium bromide (0.79 g, 2.2 mmol) was dissolved in dry THF (45 mL). *n*-BuLi (1.42 mL of a 1.37 M solution in hexanes, 1.95 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 45 min. A solution of the aldehyde (0.30 g, 1.8 mmol) in dry THF (5 mL) was then added and the reaction stirred at room temperature for 1 h. The reaction was quenched by the addition of water (100 mL) and the mixture was extracted with Et_2O (2 × 100 mL). The solvent was removed *in vacuo* to give a colourless semi-solid (0.76 g). Purification by flash column chromatography on silica gel (pet. ether- Et_2O, 95:5 with 1% Et_3N) afforded the product (0.19 g, 64%) as a colourless oil. IR (thin film) 3117, 3076, 2942, 2852, 2727, 1634, 1614, 1183, 1098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.29 (dd, J = 14.1, 6.5 Hz, 1H, $OCH{=}CH_2$), 5.91–5.79 (m, 1H, $CH_2CH{=}CH_2$), 5.12–5.02 (m, 2H, $CH_2CH{=}CH_2$), 4.31 (dd, J = 14.1, 1.7 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.06 (dd, J = 6.5, 1.7 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.95–3.87 (m, 1H, CH_2OCH), 3.53–3.43 (m, 1H, $CHOCH{=}CH_2$), 3.38–3.32 (m, 1H, CH_2OCH), 3.31–3.24 (m, 1H, CH_2OCH), 2.58–2.47 (m, 1H, $CH_2CH{=}CH_2$), 2.26–2.14 (m, 2H, $CH_2CH{=}CH_2$, CH_2), 1.73–1.60 (m, 2H, 2 × CH_2), 1.50–1.34 (m, 1H, CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.9, 135.0, 117.3, 88.9, 80.1, 77.3, 68.0, 36.6, 29.7, 25.5.

Alkene 7b. Methyltriphenylphosphonium bromide (0.48 g, 1.3 mmol) was dissolved in dry THF (50 mL). *n*-BuLi (1.0 mL of a 1.18 M solution in hexanes, 1.2 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 1 h. A solution of the aldehyde (0.19 g, 1.0 mmol) in dry THF (5 mL) was then added and the reaction stirred at room temperature for 1 h. The reaction was quenched by the addition of water (2 mL) and the volatiles removed *in vacuo*. Water (50 mL) was added and the mixture was extracted with Et_2O (2 × 50 mL). The solvent was removed *in vacuo* to give a colourless solid (0.55 g). Purification by flash column chromatography on silica gel (pet. ether-Et_2O, 95:5 with 1% Et_3N) afforded the product (0.17 g, 89%) as a colourless oil. IR (thin film) 3117, 3077, 2944, 2851, 2728, 1636, 1613, 1183, 1100, 1085 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.30 (dd, J = 14.1, 6.5 Hz, 1H, $OCH{=}CH_2$), 5.92–5.73 (m, 1H, $CH_2CH{=}CH_2$), 5.10–4.90 (m, 2H, $CH_2CH{=}CH_2$), 4.30 (dd, J = 14.1, 1.7 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.09 (dd, J = 6.5, 1.7 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.96–3.91 (m, 1H, CH_2OCH), 3.51–3.23 (m, 2H, $CHOCH{=}CH_2$, CH_2OCH), 3.15 (ddd, J = 9.0, 9.0, 2.9 Hz, 1H, CH_2OCH), 2.34–2.01 (m, 3H, $CH_2CH{=}CH_2$, CH_2), 1.97–1.78 (m, 1H, CH_2), 1.77–1.56 (m, 2H, 2 × CH_2), 1.55–1.32 (m, 2H, 2 × CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.7, 138.5, 114.5, 88.5, 79.7, 77.8, 67.5, 31.3, 29.5, 25.3; LRMS *m/z* 183 (100) $[M^++1]$, 85 (15), 55 (24), 43 (27).

Alkene 7c. The alcohol **5c** (0.43 g, 2.15 mmol) was dissolved in a mixture of dry DMSO (2 mL), dry CH_2Cl_2 (20 mL) and dry Et_3N (3.0 mL, 22 mmol). Solid sulfur trioxide-pyridine complex (1.71 g, 10.7 mmol) was added to the solution in a portionwise manner and the reaction stirred for 4 h at room temperature. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an orange oil (0.54 g) which was used for the subsequent Wittig reaction without further purification.

Methyltriphenylphosphonium bromide (1.3 g, 3.6 mmol) was dissolved in dry THF (50 mL). *n*-BuLi (2.33 mL of a 1.38 M solution in hexanes, 3.23 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 1 h. A solution of the crude aldehyde (0.54 g, 2.7 mmol) in dry THF (10 mL) was then added and the reaction stirred at room temperature for 1.5 h. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The solvent was removed *in vacuo* to give a colourless solid (1.05 g). Purification by flash column chromatography on silica gel (pet. ether-Et_2O, 95:5 with 1% Et_3N) afforded the product (0.25 g, 59% for 2 steps) as a colourless oil. IR (thin film) 3117, 3076, 2943, 2851, 2726, 1635, 1613, 1195, 1183, 1100, 1085 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.30 (dd, J = 14.1, 6.5 Hz, 1H, $OCH{=}CH_2$), 5.93–5.72 (m, 1H, $CH_2CH{=}CH_2$), 5.08–4.91 (m, 2H, $CH_2CH{=}CH_2$), 4.31 (dd, J = 14.1, 1.5 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.01 (dd, J = 6.5, 1.5 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.96–3.84 (m, 1H, CH_2OCH), 3.52–3.26 (m, 2H, $CHOCH{=}CH_2$, CH_2OCH), 3.15 (ddd, J = 8.6, 8.6, 2.7 Hz, 1H, CH_2OCH), 2.28–1.97 (m, 3H, $CH_2CH{=}CH_2$, CH_2), 1.87–1.23 (m, 7 × CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.7, 138.8, 114.4, 88.4, 80.2, 77.8, 67.5, 33.7, 31.6, 29.5, 25.3, 24.7; LRMS *m/z* 196 (2) $[M^+]$, 153 (13), 83 (24), 69 (36), 43 (53).

Ketone 8a. The aldehyde **6a** (0.74 g, 4.3 mmol) was dissolved in dry THF (25 mL) and the solution was cooled to 5 °C. A solution of methylmagnesium bromide (1.74 mL of a 3 M solution in THF, 5.22 mmol) was added at this temperature and the reaction allowed to warm to room temperature. After 2 h complete consumption of starting material was indicated by tlc. The reaction was quenched by the addition of water (2 mL) and then poured into water (50 mL) and extracted with ether (2 × 50 mL). The combined organic extracts were then combined and dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an orange oil (0.76 g). This was used for the subsequent oxidation reaction with further purification.

The crude diastereoisomeric mixture of alcohols (0.76 g, 4.1 mmol) was dissolved in a mixture of dry DMSO (2 mL), dry CH_2Cl_2 (25 mL) and dry Et_3N (5.7 mL, 41 mmol). Solid sulfur trioxide-pyridine complex (3.25 g, 20.4 mmol) was added to the solution in a portionwise manner and the reaction stirred for 2 h at room temperature. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an oil. The crude material was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 90:10 with 1% Et_3N) to afford the ketone (0.54 g, 67% for 2 steps) as a colourless oil. IR (thin film) 3116, 2945, 2857, 2727, 1714, 1634, 1359, 1191, 1134, 1097, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.28 (dd, J = 14.0, 6.5 Hz, 1H, $\mathrm{OC}\mathit{H}\mathrm{{=}CH_2}$), 4.31 (dd, J = 14.0, 1.2 Hz, 1H, $\mathrm{OCH{=}C}\mathit{H}_2$-*trans*), 4.04 (dd, J = 6.5, 1.2 Hz, 1H, $\mathrm{OCH{=}C}\mathit{H}_2$-*cis*), 3.89–3.84 (m, 1H, $\mathrm{C}\mathit{H}_2\mathrm{OCH}$), 3.71 (ddd, J = 9.0, 9.0, 3.2 Hz, 1H, $\mathrm{CH_2OC}\mathit{H}$), 3.54–3.46 (m, 1H, $\mathrm{C}\mathit{H}\mathrm{OCH{=}CH_2}$), 3.44–3.35 (m, 1H, $\mathrm{C}\mathit{H}_2\mathrm{OCH}$), 2.81 (dd, J = 15.7, 3.2 Hz, 1H, $\mathrm{C}\mathit{H}_2\mathrm{COCH_3}$), 2.54 (dd, J = 15.7, 8.9 Hz, 1H, $\mathrm{C}\mathit{H}_2\mathrm{COCH_3}$), 2.27–2.20 (m, 1H, $\mathrm{C}\mathit{H}_2$), 2.18 (s, 3H, $\mathrm{C}\mathit{H}_3$), 1.73–1.65 (m, 2H, 2 × $\mathrm{C}\mathit{H}_2$), 1.52–1.41 (m, 1H, $\mathrm{C}\mathit{H}_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 206.7, 150.2, 89.0, 77.0, 76.7, 67.7, 46.4, 30.8, 29.3, 25.1.

Ketone 8b. The aldehyde **6b** (0.66 g, 3.6 mmol) was dissolved in dry THF (5 mL) and the solution was cooled to 0 °C. A solution of methylmagnesium bromide (1.3 mL of a 3 M solution in THF, 3.9 mmol) was added at this temperature and the reaction allowed to warm to room temperature. After 1 h complete consumption of starting material was indicated by tlc. The reaction was quenched by the addition of water (1 mL) and then poured into water (50 mL) and extracted with Et_2O (2 × 50 mL). The combined organic extracts were then combined and dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an orange oil (0.65 g). The residue was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 40:60 with 1% Et_3N) to afford a diastereoisomeric mixture of the product alcohols (0.43 g, 60%) as a colourless oil.

The diastereoisomeric mixture of alcohols (0.41 g, 2.0 mmol) was dissolved in a mixture of dry DMSO (1 mL), dry CH_2Cl_2 (10 mL) and dry Et_3N (2.28 mL, 1.63 mmol). Solid sulfur trioxide-pyridine complex (1.22 g, 7.67 mmol) was added to the solution in a portionwise manner and the reaction stirred for 18 h at room temperature. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an oil (0.34 g). The crude material was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 60:40 with 1% Et_3N) to afford the ketone (0.26 g, 64%) as a colourless oil. IR (thin film) 3115, 2936, 2851, 2726, 1715, 1633, 1359, 1181, 1130, 1098, 1012 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.29 (dd, J = 14.0, 6.5 Hz, 1H, $\mathrm{OC}\mathit{H}\mathrm{{=}CH_2}$), 4.30 (dd, J = 14.0, 1.7 Hz, 1H, $\mathrm{OCH{=}C}\mathit{H}_2$-*trans*), 4.02 (dd, J = 6.5, 1.7 Hz, 1H, $\mathrm{OCH{=}C}\mathit{H}_2$-*cis*), 3.93–3.82 (m, 1H, $\mathrm{C}\mathit{H}_2\mathrm{OCH}$), 3.50–3.38 (m, 1H, $\mathrm{C}\mathit{H}\mathrm{OCH{=}CH_2}$), 3.37–3.24 (m, 1H, $\mathrm{C}\mathit{H}_2\mathrm{OCH}$), 3.14 (ddd, J = 9.0, 9.0, 2.9 Hz, 1H, $\mathrm{CH_2OC}\mathit{H}$), 2.72–2.40 (m, 2H, $\mathrm{C}\mathit{H}_2\mathrm{COCH_3}$), 2.27–2.02 (m, 2H, 2 × $\mathrm{C}\mathit{H}_2$), 2.15 (s, 3H, $\mathrm{CH_2COC}\mathit{H}_3$), 1.75–1.53 (m, 3H, 3 × $\mathrm{C}\mathit{H}_2$), 1.50–1.35 (m, 1H, $\mathrm{C}\mathit{H}_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 208.8, 150.5, 88.7, 79.4, 77.8, 67.5, 39.6, 29.9, 29.4, 26.3, 25.2; HRMS calcd for $C_9H_{15}O_2$ (M^+–OC_2H_3): 155.1072, found: 155.1072.

Alkene 9a. Methyltriphenylphosphonium bromide (1.24 g, 3.47 mmol) was dissolved in dry THF (70 mL). *n*-BuLi (2.22 mL of a 1.37 M solution in hexanes, 3.04 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 45 min. A solution of the ketone **8a** (0.51 g, 2.8 mmol) in dry THF (10 mL) was then added and the reaction stirred at room temperature for 1 h. The reaction was quenched by the addition of water (2 mL) and the volatiles removed *in vacuo*. Water (200 mL) was added and the mixture was extracted with Et_2O (2 × 100 mL). The solvent was removed *in vacuo* to give a colourless solid (1.23 g). Purification of this material by flash column chromatography on silica gel (pet. ether- Et_2O, 95:5 with

1% Et_3N) afforded the product (0.34 g, 67%) as a colourless oil. IR (thin film) 3116, 3075, 2940, 2851, 2726, 1635, 1614, 1194, 1132, 1098, 1083 1053, 1012 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (dd, J = 14.1, 6.5, 1H, $OCH{=}CH_2$), 4.82 (d, J = 0.6 Hz, 1H, $C{=}CH_2$), 4.77 (d, J = 0.6 Hz, 1H, $C{=}CH_2$), 4.30 (dd, J = 14.1, 1.6 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.01 (dd, J = 6.5, 1.6 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.95–3.88 (m, 1H, CH_2OCH), 3.51–3.42 (m, 1H, $CHOCH{=}CH_2$), 3.40–3.28 (m, 2H, CH_2OCH, CH_2OCH), 2.53 (d, J = 14.6 Hz, 1H, $CH_2C{=}CH_2$), 2.27–2.20 (m, 1H, CH_2), 2.12 (dd, J = 14.6, 9.4 Hz, 1H, $CH_2C{=}CH_2$), 1.77 (d, J = 0.5, 3H, CH_3), 1.76–1.64 (m, 2H, 2 × CH_2), 1.51–1.42 (m, 1H, CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.4, 142.5, 112.2, 88.5, 78.6, 77.4, 67.5, 40.2, 29.4, 25.1, 22.5.

Alkene 9b. Methyltriphenylphosphonium bromide (0.54 g, 1.5 mmol) was dissolved in dry THF (50 mL). *n*-BuLi (1.0 mL of a 1.38 M solution in hexanes, 1.4 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 45 min. A solution of the ketone **8b** (0.26 g, 1.3 mmol) in dry THF (2 mL) was then added and the reaction stirred at room temperature for 1 h. The reaction was quenched by the addition of water (1 mL) and the volatiles removed *in vacuo*. Water (100 mL) was added and the mixture was extracted with Et_2O (2 × 100 mL). The solvent was removed *in vacuo* to give a colourless solid (0.63 g). Purification of this material by flash column chromatography on silica gel (pet. ether-Et_2O, 95:5 with 1% Et_3N) afforded the product (0.19 g, 74%) as a colourless oil. IR (thin film) 3116, 3073, 2940, 2851, 2727, 1634, 1613, 1194, 1132, 1099, 1084 1060, 1010 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (dd, J = 14.0, 6.5 Hz, 1H, $OCH{=}CH_2$), 4.70 (br s, 2H, $C{=}CH_2$), 4.31 (dd, J = 14.0, 1.7 Hz, 1H, $OCH{=}CH_2$-*trans*), 4.01 (dd, J = 6.5, 1.7 Hz, 1H, $OCH{=}CH_2$-*cis*), 3.93–3.88 (m, 1H, CH_2OCH), 3.50–3.43 (m, 1H, $CHOCH{=}CH_2$), 3.37–3.29 (m, 1H, CH_2OCH), 3.16 (ddd, J = 9.0, 9.0, 2.5 Hz, 1H, CH_2OCH), 2.26–2.17 (m, 2H, $CH_2C{=}CH_2$), 2.10–2.02 (m, 1H, CH_2), 1.99–1.90 (m, 1H, CH_2), 1.73 (s, 3H, CH_3), 1.73–1.62 (m, 1H, CH_2), 1.53–1.38 (m, 2H, 2 × CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 150.7, 145.7, 109.8, 88.4, 79.9, 77.8, 67.5, 33.3, 30.1, 29.5, 25.3, 22.5.

Ester 10a. The alcohol **3a** (1.0 g, 3.8 mmol), propionic anhydride (0.98 mL, 7.6 mmol), Et_3N (2.14 mL, 15.4 mmol) and DMAP (0.1 g, 0.8 mmol) were dissolved in dry CH_2Cl_2 (25 mL). The reaction mixture was stirred at room temperature for 6 h and then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give a colourless oil (1.33 g). The crude product was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 90:10) to afford the ester (1.20 g, 99%) as a colourless oil. IR (thin film) 2955, 2856, 1742, 1463, 1255, 1183, 1101, 1024 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 (ddd, J = 10.0, 10.0, 4.6 Hz, 1H, $CHOCOEt$), 3.92–3.87 (m, 1H, CH_2OCH), 3.76–3.67 (m, 2H, CH_2OTBS), 3.40–3.29 (m, 2H, CH_2OCH, CH_2OCH), 2.32 (q, J = 7.5 Hz, 2H, CH_2CH_3), 1.88–1.78 (m, 1H, CH_2), 1.77–1.64 (m, 3H, 3 × CH_2), 1.56–1.39 (m, 2H, 2 × CH_2), 1.14 (t, J = 7.5 Hz, 3H, CH_2CH_3), 0.91 (s, 9H, $C[CH_3]_3$), 0.07 (s, 6H, 2 × CH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 173.7, 76.0, 71.9, 67.5, 59.0, 35.2, 29.4, 27.8, 26.0, 25.2, 18.3, 9.1, –5.3; Anal. calcd for $C_{16}H_{32}O_4Si$: C, 60.72; H, 10.19. Found: C, 60.64; H, 10.52.

Ester 10b. The alcohol **3b** (1.0 g, 3.6 mmol) and DMAP (2.24 g, 18.3 mmol) were dissolved in dry CH_2Cl_2 (25 mL). Propionic anhydride (1.41 mL, 11.0 mmol) was added dropwise to the reaction at room temperature and the mixture was stirred at this temperature for 1 h. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give the crude product (1.54 g). This material was then purified by flash column chromatography on silica gel (pet. ether-ether, 90:10) to afford the ester (0.88 g, 73%) as a colourless oil. IR (thin film) 2955, 2857, 1741, 1464, 1386, 1255, 1185, 1096, 1025 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.50 (ddd, J = 10.0, 10.0, 4.6 Hz, 1H, $CHOCOEt$), 3.93–3.84 (m, 1H, CH_2OCH), 3.66–3.50 (m, 2H, CH_2OTBS), 3.38–3.13 (m, 2H, CH_2OCH, CH_2OCH), 2.17 (q, J = 7.5 Hz, 2H, CH_2CH_3), 1.79–1.12 (m, 8H, 8 × CH_2), 1.11 (t, J = 7.5 Hz, 3H, CH_2CH_3), 0.87 (s, 9H, $C[CH_3]_3$), 0.03 (s, 6H, 2 × CH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 173.6, 79.4, 71.9, 67.5, 63.0, 29.4, 28.4, 28.3, 27.7, 26.0, 25.2, 18.3, 9.1, –5.3; Anal. calcd for $C_{17}H_{34}SiO_4$: C, 61.77; H, 10.37. Found: C, 61.59; H, 10.62.

Alcohol 11a. The silyl ether **10a** (1.16 g, 3.67 mmol) was dissolved in dry THF (10 mL) and *t*-butylammonium fluoride (13 mL of a 1M solution in THF, 13 mmol) was added. The mixture was stirred at room temperature for 6 h. The reaction mixture was then poured into water (100 mL) and the mixture extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed to give a red oil (1.12 g). The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 60:40) to afford the product (0.66 g, 89%) as a colourless oil. IR (thin film) 3439, 2941, 2855, 1732, 1463, 1261, 1177, 1098 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.31–4.25 (m, 1H, $CHOCOEt$), 4.21–4.14 (m, 1H, CH_2OH), 3.91–3.84 (m, 1H, CH_2OCH), 3.38–3.27 (m, 2H, CH_2OH, CH_2OCH), 3.10 (ddd, *J* = 8.7, 8.7, 3.0 Hz, 1H, CH_2OCH), 2.33 (q, *J* = 7.6 Hz, 2H, CH_2CH_3), 2.19 (ddddd, *J* = 7.3, 7.3, 7.3, 7.3, 3.0 Hz, 1H, CH_2), 2.14–2.09 (m, 1H, CH_2), 1.79–1.65 (m, 4H, 3 × CH_2, OH) 1.56–1.36 (m, 1H, CH_2), 1.14 (t, *J* = 7.6 Hz, 3H, CH_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.6, 79.5, 70.4, 67.6, 61.3, 33.0. 31.5, 27.7, 25.6, 9.2.

Alcohol 11b. The silyl ether **10a** (1.04 g, 3.15 mmol) was dissolved in dry THF (30 mL) and *t*-butylammonium fluoride (9.1 mL of a 1M solution in THF, 9.1 mmol) was added. The mixture was stirred at room temperature for 3 h. The reaction mixture was then poured into water (100 mL) and the mixture extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed to give an orange oil (1.1 g). The residue was then purified by flash column chromatography on silica gel (pet. ether-Et_2O, 40:60) to afford the product (0.58 g, 85%) as a colourless oil. IR (thin film) 3438, 2945, 2855, 2729, 1737, 1463, 1375, 1350, 1274, 1187, 1139, 1100 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.63–4.50 (m, 1H, $CHOCOEt$), 3.99–3.91 (m, 1H, CH_2OCH), 3.71–3.58 (m, 2H, CH_2OH), 3.45–3.21 (m, 2H, CH_2OCH, CH_2OCH), 2.34 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 2.24–2.11 (m, 1H, CH_2), 1.86–1.62 (m, 5H, 5 × CH_2), 1.54–1.36 (m, 2H, 2 × CH_2), 1.14 (t, *J* = 7.5 Hz, 3H, CH_2CH_3); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 173.6, 77.5, 71.5, 67.5, 62.6, 29.2, 28.6, 28.5, 27.7, 25.0, 9.0.

Alkene 12a. The alcohol **11a** (0.62 g, 3.1 mmol) was dissolved in a mixture of dry DMSO (2 mL), dry CH_2Cl_2 (20 mL) and dry Et_3N (4.64 mL, 33.3 mmol). Solid sulfur trioxide-pyridine complex (2.12 g, 13.3 mmol) was added to the solution in a portionwise manner and the reaction stirred for 6 h at room temperature. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried (anh. $MgSO_4$) and the solvent removed *in vacuo* to give an orange oil (0.46 g) which was used for the subsequent Wittig reaction without further purification.

Methyltriphenylphosphonium bromide (1.16 g, 3.25 mmol) was dissolved in dry THF (45 mL). *n*-BuLi (2.3 mL of a 1.30 M solution in hexanes, 3.0 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 30 min. A solution of the crude aldehyde (0.46 g, 2.3 mmol) in dry THF (5 mL) was then added and the reaction stirred at room temperature for 1 h. The reaction mixture was then poured into water (100 mL) and extracted with Et_2O (2 × 100 mL). The solvent was removed *in vacuo* to give a colourless solid (1.29 g). Purification by flash column chromatography on silica gel (pet. ether-Et_2O, 90:10) afforded the product (0.21 g, 35% for 2 steps) as a colourless oil. IR (thin film) 3077, 2945, 2851, 1740, 1643, 1371, 1349, 1182, 1099, 1068, 1024 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.93–5.80 (m, 1H, $CH{=}CH_2$), 5.10–5.02 (m, 2H, $CH{=}CH_2$), 4.60–4.52 (m, 1H, $CHOCOEt$), 3.98–3.91 (1H, m, CH_2OCH), 3.40–3.29 (m, 2H, CH_2OCH, CH_2OCH), 2.40–2.27 (m, 1H, $CH_2CH{=}CH_2$), 2.31 (q, *J* = 7.6 Hz, 2H, CH_2CH_3), 2.26–2.10 (m, 2H, $CH_2CH{=}CH_2$, CH_2), 1.80–1.62 (m, 2H, 2 × CH_2), 1.51–1.38 (m, 1H, CH_2), 1.15 (t, *J* = 7.6 Hz, 3H, CH_2CH_3); ^{13}C NMR (97.8 MHz, $CDCl_3$) δ 173.4, 134.4, 116.8, 78.9, 71.3, 67.7, 36.5, 29.3, 27.7, 25.1, 9.1.

Alkene 12b. The alcohol **11b** (3.0 g, 14 mmol) was dissolved in a mixture of dry DMSO (5 mL), dry CH_2Cl_2 (50 mL) and dry Et_3N (9.7 mL, 70 mmol). Solid sulfur trioxide-pyridine complex (6.62 g, 41.6 mmol) was added to the solution in a portionwise manner and the reaction stirred for 3 h at room temperature. The reaction mixture was then diluted with ether (200 mL) and washed with water (100 mL), 2M HCl (100 mL) and brine (100 mL). The aqueous layers were then extracted with Et_2O (2 × 100 mL) and the combined organic extracts were dried (anh. $MgSO_4$). The solvent was removed *in vacuo* to give a colourless oil

(2.42 g, 81%) that was judged to be pure enough to be used for the subsequent Wittig reaction without further purification.

Methyltriphenylphosphonium bromide (1.26 g, 3.53 mmol) was suspended in dry THF (90 mL). *n*-BuLi (3.12 mL of a 1.05 M solution in hexanes, 3.28 mmol) was added dropwise to the solution of the salt at room temperature and the mixture was then stirred for 1 h. A solution of the aldehyde (0.54 g, 2.5 mmol) in dry THF (10 mL) was added and the reaction stirred at room temperature for 1 h. The reaction mixture was then poured into water (200 mL) and extracted with Et_2O (2 × 100 mL). The solvent was removed *in vacuo* to give a colourless solid (1.22 g). Purification by flash column chromatography on silica gel (pet. ether-Et_2O, 90:10) afforded the product (0.37 g, 69%) as a colourless oil. IR (thin film) 3077, 2947, 2851, 1741, 1642, 1373, 1351, 1184, 1101, 1024 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.87–5.74 (m, 1H, $C\mathit{H}=CH_2$), 5.06–4.92 (m, 2H, $CH=C\mathit{H}_2$), 4.58–4.50 (m, 1H, $C\mathit{H}OCOEt$), 3.95–3.88 (m, 1H, $C\mathit{H}_2OCH$), 3.40–3.31 (m, 1H, $C\mathit{H}_2OCH$), 3.26–3.19 (m, 1H, $CH_2OC\mathit{H}$), 2.32 (q, J = 7.5 Hz, 2H, $C\mathit{H}_2CH_3$), 2.30–2.02 (m, 3H, $C\mathit{H}_2CH=CH_2$, $C\mathit{H}_2$), 1.80–1.60 (m, 3H, 3 × $C\mathit{H}_2$), 1.53–1.37 (m, 2H, 2 × $C\mathit{H}_2$), 1.16 (t, J = 7.5 Hz, 3H, $CH_2C\mathit{H}_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 173.6, 138.4, 114.6, 78.7, 71.8, 67.5, 31.2, 29.4, 29.3, 27.8, 25.2, 9.1; Anal calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50, Found: C, 67.65; H, 9.98.

Enol ether 13a. $TiCl_4$ (16.7 mL of a 1 M solution in CH_2Cl_2, 16.7 mmol) was added dropwise to dry THF (10 mL) at 0 °C. The solution was warmed to room temperature and TMEDA (5.0 mL, 33 mmol) was added. The mixture was stirred at room temperature for 10 min and zinc powder (2.45 g, 37 mmol) was added. The mixture was stirred for 30 min and then a solution of the ester **12a** (0.38 g, 1.9 mmol) and CH_2Br_2 (0.89 mL, 12.7 mmol) in dry THF (5 mL) was added. The reaction was stirred at room temperature for 3 h, cooled to 0 °C and then quenched by the addition of 2M NaOH aq. (2.5 mL). The reaction was diluted with a mixture of ether and 1% Et_3N(200 mL) then filtered through a short plug of basic alumina (Brockman grade III). The solvent was removed *in vacuo* to give the crude product as an orange oil. Purification of this material on basic alumina (Brockman grade III) (pet. ether with 1% Et_3N) afforded the product as a colourless oil (0.265 g, 70%). IR (thin film) 3076, 2941, 2850, 1653, 1602, 1375, 1330, 1277, 1235, 1099, 1037 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.90–5.80 (m, 1H, $C\mathit{H}=CH_2$), 5.13–5.03 (m, 2H, $CH=C\mathit{H}_2$), 4.00–3.90 (m, 1H, $C\mathit{H}_2OCH$), 3.90 (d, J = 2 Hz, 1H, $OC=C\mathit{H}_2$), 3.85 (d, J = 2 Hz, 1H, $OC=C\mathit{H}_2$), 3.78–3.60 (m, 1H, $C\mathit{H}OC=CH_2$), 3.44–3.23 (m, 2H, $C\mathit{H}_2OCH$, $CH_2OC\mathit{H}$), 2.60–2.40 (m, 1H, $C\mathit{H}_2CH=CH_2$), 2.44–2.10 (m, 2H, $C\mathit{H}_2CH=CH_2$, $C\mathit{H}_2$), 2.06 (q, J = 7.6 Hz, 2H, $C\mathit{H}_2CH_3$), 1.70–1.54 (m, 2H, 2 × $C\mathit{H}_2$), 1.37–1.28 (m, 1H, $C\mathit{H}_2$), 0.99 (t, J = 7.5 Hz, 3H, $CH_2C\mathit{H}_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 162.7, 135.0, 116.7, 80.1, 80.0, 73.3, 67.9, 36.5, 28.3, 28.3, 25.2, 12.0; LRMS 197(3) [M^++1], 196(2), 168(13), 155(3), 141(4), 125(13), 71(100), 55(78), 41(41).

Enol ether 13b. $TiCl_4$ (26.7 mL of a 1 M solution in CH_2Cl_2, 26.7 mmol) was added dropwise to dry THF (50 mL) at 0 °C. The solution was warmed to room temperature and TMEDA (8.0 mL, 114 mmol) was added. The mixture was stirred at room temperature for 10 min and zinc powder (3.95 g, 60.4 mmol) was added. The mixture was stirred for 30 min and then a solution of the ester **12b** (0.70 g, 3.3 mmol) and CH_2Br_2 (1.17 mL, mmol) in dry THF (10 mL) was added. The reaction was stirred at room temperature for 4 h, cooled to 0 °C and then quenched by the addition of 2M NaOH aq. (10 mL) and stirred for 30 min. The reaction was diluted with a mixture of ether and 1% Et_3N (300 mL) then filtered through a short plug of basic alumina (Brockman grade III). The solvent was removed *in vacuo* to give the crude product (1.31 g) as an orange oil. Purification of this material on basic alumina (Brockman grade III) (pet. ether with 1% Et_3N) afforded the product as a colourless oil (0.55 g, 79%). IR (thin film) 3077, 2941, 2850, 1654, 1602, 1375, 1328, 1278, 1236, 1100, 1039 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.85–5.67 (m, 1H), 4.95 (dddd, J = 19.1, 1.8, 1.8, 1.8 Hz, 1H, $CH=C\mathit{H}_2$-*trans*), 4.93–4.84 (m, 1H, $CH=C\mathit{H}_2$-*cis*), 3.88–3.81 (m, 1H, $C\mathit{H}_2OCH$) 3.82 (d, J = 2.0 Hz, 1H, $OC=C\mathit{H}_2$), 3.78 (d, J = 2.0 Hz, 1H, $OC=C\mathit{H}_2$), 3.61 (ddd, J = 10.3, 9.0, 4.3 Hz, 1H, $C\mathit{H}OC=CH_2$), 3.35–3.22 (m, 1H, $C\mathit{H}_2OCH$), 3.16 (ddd, J = 8.9, 8.9, 2.6 Hz, 1H, $CH_2OC\mathit{H}$), 2.32–1.94 (m, 2H, $C\mathit{H}_2CH=CH_2$), 1.99 (q, J = 7.5 Hz, 2H, $C\mathit{H}_2CH_3$), 1.84–1.70 (m, 1H, $C\mathit{H}_2$), 1.67–1.55 (m, 2H, 2 × $C\mathit{H}_2$), 1.47–1.15 (m, 3H, 3 × $C\mathit{H}_2$), 0.97 (t, J = 7.5 Hz, 3H, $CH_2C\mathit{H}_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 162.9, 138.7, 114.4, 80.1, 79.9, 74.0, 67.8, 31.4, 30.2, 29.5, 28.4, 25.3, 12.0; HRMS calcd for $C_{13}H_{22}O_2$: 210.1636, found: 210.1628.

General procedure for the synthesis of cyclic enol ethers by ring-closing metathesis

The substrate (1.0 mmol) was dissolved in dry degassed pentane (1 mL) and the solution added by cannula to a solution of the molybdenum catalyst **1** (13 mol%) in dry degassed pentane (30 mL) at room temperature under argon. The reaction was stirred at room temperature for 4–5 hours and then quenched by exposure to the atmosphere. The solvent was removed *in vacuo* and the resulting material was purified by passage through a short column of basic alumina (Brockman grade III) eluting with a solution of 1% triethylamine in pet. ether. Removal of the solvent afforded the cyclic enol ether as a colourless liquid.

Cyclic enol ether 14a. The enol ether **7a** (160 mg, 0.951 mmol) was reacted with the molybdenum catalyst **1** (100 mg, 0.131 mmol) in pentane (60 mL) according to the general procedure. The product **14a** (85 mg, 64%) was obtained as a colourless oil after purification. IR (thin film) 3064, 2936, 2854, 1647, 1239, 1198, 1180, 1100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33–6.27 (m, 1H, OC*H*=CH), 4.65 (t, *J* = 5.6 Hz, 1H, OCH=C*H*), 3.96–3.90 (m, 1H, C*H*$_2$OCH), 3.49–3.41 (m, 2H, C*H*OCH=CH, C*H*$_2$OCH), 3.36 (ddd, *J* = 9.3, 9.3, 6.2 Hz, 1H, CH$_2$OC*H*), 2.25 (ddd, *J* = 16.3, 5.7, 5.7 Hz, 1H, C*H*$_2$CH=CHO), 2.20–2.11 (m, 1H, C*H*$_2$CH=CHO), 2.08–1.97 (m, 1H, C*H*$_2$), 1.87–1.68 (m, 2H, 2 × C*H*$_2$), 1.59–1.48 (m, 1H, C*H*$_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 143.1, 98.4, 75.0, 74.6, 67.7, 29.0, 27.0, 25.3.

Cyclic enol ether 14b. The enol ether **7b** (50 mg, 0.27 mmol) was reacted with the molybdenum catalyst **1** (30 mg, 0.039 mmol) in pentane (30 mL) according to the general procedure. The product **14a** (27.4 mg, 65%) was obtained as a colourless oil after purification. IR (thin film) 3041, 2920, 2850, 1648, 1268, 1186, 1122, 1086 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.32 (dd, *J* = 6.4, 2.0 Hz, 1H, OC*H*=CH), 4.91 (app. q, *J* = 6.4 Hz, 1H, OCH=C*H*), 3.93–3.87 (m, 1H, C*H*$_2$OCH), 3.45 (ddd, *J* = 11.1, 9.1, 4.6 Hz, 1H, C*H*OCH=CH), 3.37–3.31 (m, 1H, C*H*$_2$OCH), 3.27 (ddd, *J* = 9.1, 7.1, 4.6 Hz, 1H, CH$_2$OC*H*), 2.27–2.19 (m, 1H, C*H*$_2$CH=CHO), 2.14–1.98 (m, 3H, C*H*$_2$CH=CHO, 2 × C*H*$_2$), 1.73–1.67 (m, 2H, 2 × C*H*$_2$), 1.61–1.49 (m, 2H, 2 × C*H*$_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 147.7, 111.5, 82.1, 79.7, 67.5, 33.3, 30.7, 25.7, 20.8; HRMS calcd for $C_9H_{15}O_2$ (M^++H): 155.1072, found: 155.1080.

Cyclic enol ether 14c. The enol ether **7c** (47 mg, 0.24 mmol) was reacted with the molybdenum catalyst **1** (60 mg, 0.078 mmol) in pentane (70 mL) according to the general procedure. A 1:1 mixture of the product **14c** and the cyclic enol ether **14b** (13.3 mg, ~37% based on recovered starting material) was obtained as a colourless oil along with a complex isomeric mixture of the cyclo-dimers **20**[28] and unreacted enol ether **7c** (4 mg) after purification. IR (thin film) 3028, 2938, 2854, 2715, 1647, 1634, 1129, 1095, 1072, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (app. d, *J* = 6.3 Hz, 1H, OC*H*=CH), 4.84 (ddd, *J* = 8.1, 6.4, 6.4 Hz, 1H, OCH=C*H*), 3.90–3.85 (m, 1H, C*H*$_2$OCH), 3.58 (ddd, *J* = 11.1, 9.1, 4.3 Hz, 1H, C*H*OCH=CH), 3.32–3.28 (m, 1H, C*H*$_2$OCH), 3.26 (ddd, *J* = 9.2, 6.7, 2.7 Hz, 1H, CH$_2$OC*H*), 2.32–2.18 (m, 2H, C*H*$_2$CH=CHO), 2.09–2.04 (m, 1H, C*H*$_2$) 1.90–1.73 (m, 2H, 2 × C*H*$_2$), 1.72–1.51 (m, 5H, 5 × C*H*$_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 144.3, 113.5, 82.2, 79.2, 68.0, 32.7, 30.5, 26.1, 23.7, 23.4.

Cyclic enol ether 15a. The enol ether **9a** (255 mg, 1.40 mmol) was reacted with the molybdenum catalyst **1** (100 mg, 0.131 mmol) in pentane (70 mL) according to the general procedure. The product **15a** (200 mg, 93%) was obtained as a colourless oil after purification. IR (thin film) 3062, 2926, 2851, 1671, 1180, 1150, 1089 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (s, 1H, OC*H*=CMe), 3.96–3.90 (m, 1H, C*H*$_2$OCH), 3.43 (ddd, *J* = 11.5, 11.5, 3.1 Hz, 1H, C*H*OCH=CMe), 3.39–3.29 (m, 2H, C*H*$_2$OCH, CH$_2$OC*H*), 2.16–1.98 (m, 3H, C*H*$_2$CMe=CHO, C*H*$_2$), 1.85–1.69 (m, 2H, 2 × C*H*$_2$), 1.57 (s, 3H, C*H*$_3$), 1.59–1.45 (m, 1H, C*H*$_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 137.7, 107.0, 74.9, 73.9, 67.7, 32.6, 30.0, 25.3, 17.8; HRMS calcd for $C_9H_{14}O_2$ (M^++H): 155.0994, found: 155.0980.

Cyclic enol ether 15b. The enol ether **9b** (126 mg, 0.642 mmol) was reacted with the molybdenum catalyst **1** (60 mg, 0.078 mmol) in pentane (30 mL) according to the general procedure. The product **15b** (102 mg, 94%) was obtained as a colourless oil after purification. IR (thin film) 2934, 2848, 2727, 1669, 1196, 1150, 1130, 1098 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.25 (s, 1H, OC*H*=CMe), 3.91–3.82 (m, 1H, C*H*$_2$OCH), 3.58–3.51 (m, 1H, C*H*OCH=CMe), 3.26–3.14 (m, 2H, C*H*$_2$OCH, CH$_2$OC*H*), 2.30–2.16 (m, 1H, C*H*$_2$CMe=CHO), 2.14–2.05 (m, 1H, C*H*$_2$CMe=CHO), 2.03–1.93 (m, 2H, 2 × C*H*$_2$), 1.77–1.62 (m, 2H, 2 × C*H*$_2$), 1.60 (s, 3H, C*H*$_3$), 1.60–1.40 (m, 2H, 2 × C*H*$_2$); ^{13}C NMR (67.8 MHz, CDCl$_3$) δ 142.6, 122.7, 82.9, 80.1, 67.5, 31.8, 30.7, 26.9, 25.8, 19.9.

Cyclic enol ether 16a. The enol ether **13a** (200 mg, 1.02 mmol) was reacted with the molybdenum catalyst **1** (100 mg, 0.131 mmol) in pentane (40 mL) according to the general procedure. The product **16a** (68 mg, 72%) was obtained as a colourless oil after purification. IR (thin film) 3059, 2940, 2852, 2725, 1676, 1653, 1270, 1186, 1164, 1114, 1101 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.42 (d, *J* = 4.6 Hz, 1H, OCEt=C*H*), 3.96–3.88 (m, 1H, C*H*$_2$OCH), 3.49–3.40 (m, 2H, C*H*OCEt=CH, C*H*$_2$OCH), 3.31 (ddd, *J* = 9.3, 6.3, 6.3 Hz, 1H, CH$_2$OC*H*), 2.28–1.95 (m, 4H, C*H*$_2$CH=CEtO, C*H*$_2$CH$_3$), 1.81–1.66 (m, 2H, 2 × C*H*$_2$), 1.62–1.51 (m, 2H, 2 × C*H*$_2$), 1.02 (t, *J* = 7.5 Hz, 3H, C*H*$_3$); ^{13}C NMR (67.8 MHz, CDCl$_3$) δ 155.6, 91.9, 75.2, 74.6, 67.8, 29.3, 27.6, 26.5, 25.4, 11.5.

Cyclic enol ether 16b. The enol ether **13b** (100 mg, 0.48 mmol) was reacted with the molybdenum catalyst **1** (40 mg, 0.052 mmol) in pentane (30 mL) according to the general procedure. The product **16b** (34.8 mg, 40%) was obtained as a colourless oil after purification. IR (thin film) 2937, 2849, 2721, 1677, 1167, 1096 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.87 (dd, *J* = 6.2, 5.4 Hz, 1H, OCEt=C*H*), 3.91–3.84 (m, 1H, C*H*$_2$OCH), 3.38–3.32 (m, 1H, C*H*$_2$OCH), 3.29–3.20 (m, 2H, C*H*OCEt=CH, CH$_2$OC*H*), 2.15–2.00 (m, 4H, C*H*$_2$CH=CEtO, C*H*$_2$CH$_3$), 1.73–1.52 (m, 4H, 4 × C*H*$_2$), 1.45–1.34 (m, 1H, C*H*$_2$), 1.29–1.26 (m, 1H, C*H*$_2$), 1.01 (t, *J* = 7.5 Hz, 3H, C*H*$_3$); ^{13}C NMR (126 MHz, CDCl$_3$) δ 161.4, 106.6, 82.8, 79.7, 67.6, 33.0, 31.0, 28.5, 25.9, 20.9, 11.8. HRMS calcd for $C_{11}H_{18}O_2$: 182.1307, found: 182.1291.

General procedure for the hydroboration of cyclic enol ethers 14, 15 and 16

A solution of thexylborane was prepared by the addition of BH$_3$.THF complex (2.5 mL of 1M solution in THF, 2.5 mmol) to a solution of 2,3-dimethylbut-2-ene (1.25 mL of a 2M solution in THF, 2.5 mmol) in dry THF (2 mL) at 0 °C and the solution stirred for 1 h at this temperature.

The solution of thexylborane was cooled to –20 °C and a solution enol ether **14**, **15** or **16** (0.5 mmol) in dry THF (2 mL) was added dropwise to the solution of the organoborane. The reaction flask was then placed in a freezer at –20 °C for 20 h. The mixture was warmed to 0 °C and oxidation was performed by the slow addition of 3M NaOH aq. (7.5 mL) and the slow addition of 30% H_2O_2 (5 mL). The reaction was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was then extracted with Et$_2$O (3 x 50 mL) and the combined organic extracts were dried (anh. MgSO$_4$). The solvent was removed *in vacuo* and the residue was purified by flash column chromatography on silica gel to afford the alcohol.

Alcohol 17a. The cyclic enol ether **14a** was hydroborated with thexylborane following the general procedure. The cyclic enol ether (24 mg, 0.17 mmol) in dry THF (1.0 mL) was added to a solution of thexylborane (1.0 mmol) at room temperature and the reaction was stirred for 5 h. Oxidation was performed by addition of 3M NaOH aq. (2.0 mL) and 30% H_2O_2 (2.0 mL) at 0 °C. The product was purified by flash column chromatography on silica gel (pet. ether-Et$_2$O, 30:70) to afford the alcohol (14.1 mg, 52%) as a colourless oil. IR (thin film) 3417, 2942, 2854, 1111, 1065, 1021 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.98 (ddd, *J* = 10.6, 5.1, 1.7 Hz, 1H, OC*H*$_2$CHOH), 3.94–3.89 (m, 1H, CH$_2$C*H*$_2$OCH), 3.84 (dddd, *J* = 10.5, 10.5, 5.2, 5.2 Hz, 1H, C*H*OH), 3.41–3.34 (m, 1H, CH$_2$C*H*$_2$OCH), 3.13 (t, *J* = 10.5 Hz, 1H, OC*H*$_2$CHOH), 3.00–2.89 (m, 2H, C*H*OCH$_2$CHOH, C*H*OCH$_2$CH$_2$), 2.41–2.36 (m, 1H, C*H*$_2$), 2.10–2.03 (m, 1H, C*H*$_2$), 1.76–1.66 (m, 3H, 2 × C*H*$_2$, O*H*), 1.46–1.35 (m, 2H, 2 × C*H*$_2$); ^{13}C NMR (67.8 MHz, CDCl$_3$) δ 78.0, 76.8, 72.8, 68.2, 66.1, 39.6, 29.5, 25.7; HRMS calcd for $C_8H_{14}O_3$: 158.0943, found: 158.0948.

Alcohol 17b. The enol ether **7b** (97 mg, 0.532 mmol) was converted to the cyclic enol ether **14b** by ring-closing metathesis following the general procedure. The product was filtered through a short plug of alumina (pet. ether with 1% Et$_3$N) and then immediately hydroborated with thexylborane following the general procedure. The enol ether in dry THF (2.0 mL) was added to a solution of thexylborane (2.3 mmol) at –20 °C.

Reaction at –20 °C for 20 h and then warmed to 0 °C. Oxidation was performed by addition of 3M NaOH aq. (7.5 mL) and 30% H_2O_2 (5 mL) at 0 °C. The product was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 30:70) to afford the alcohol **17b** (35 mg) plus the isomer as colourless oils (combined yield 39 mg, 43% over 2 steps). **IR** (thin film) 3419, 2938, 2864, 1148, 1080 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.13–4.04 (m, 2H, OC*H*$_2$CHOH, C*H*OH), 3.89–3.85 (m, 1H, CH$_2$C*H*$_2$OCH), 3.43 (app. q, *J* = 5.4 Hz, 1H, OC*H*$_2$CHOH), 3.33–3.27 (m, 1H, CH$_2$C*H*$_2$OCH), 3.15 (ddd, *J* = 11.1, 9.1, 4.4 Hz, 1H, C*H*OCH$_2$CHOH), 3.03–2.97 (m, 1H, OC*H*CH$_2$CH$_2$CHOH), 2.09–2.03 (m, 1H, C*H*$_2$), 1.94–1.80 (m, 5H, 4 × C*H*$_2$, O*H*), 1.69–1.63 (m, 2H, 2 × C*H*$_2$), 1.46–1.37 (m, 1H, C*H*$_2$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 82.6, 81.7, 74.8, 69.6, 67.8, 31.3, 30.0, 27.5, 25.8; HRMS calcd for $C_9H_{17}O_3$ (M^++H): 173.1178, found: 173.1172.

Alcohol 18a. The cyclic enol ether **15a** (40.8 mg, 0.265 mmol) was dissolved in dry THF (1.0 mL) and added to a solution of BH_3.THF complex (0.5 mmol) at 0 °C. Reaction performed at 0 °C for 18 h and then oxidation was accomplished by addition of 3M NaOH aq. (2.0 mL) and 30% H_2O_2 (2.0 mL) at 0 °C. The product was purified by flash column chromatography on silica gel (Et_2O) to afford the alcohol **18a** and the diastereoisomer (62:38 ratio of isomers by NMR) as an inseparable mixture (32.9 mg, 72%, 67% over 2 steps). IR (thin film) 3424, 2940, 2852, 1114, 1081 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.94–3.88 (m, 1H, CH$_2$C*H*$_2$OCH), 3.61 (dd, *J* = 11.8, 2.6 Hz, 1H, OC*H*$_2$CMeOH), 3.44–3.35 (m, 1H, CH$_2$C*H*$_2$OCH), 3.36 (d, *J* = 11.8 Hz, OC*H*$_2$CMeOH), 3.30–3.24 (m, 1H, C*H*OCH$_2$CMeOH), 3.03–2.91 (m, 1H, OC*H*CH$_2$CMeOH), 2.13–2.04 (m, 2H, 2 × C*H*$_2$), 1.78–1.69 (m, 2H, 2 × C*H*$_2$), 1.58–1.41 (m, 2H, 2 × C*H*$_2$), 1.37 (br s, 1H, O*H*), 1.18 (s, 3H, C*H*$_3$); HRMS calcd for $C_9H_{16}O_3$: 173.1099, found: 172.1081.

Alcohol 19a. The enol ether **13a** (145 mg, 0.739 mmol) was converted to the cyclic enol ether **16a** by ring-closing metathesis following the general procedure. The product was filtered through a short plug of alumina (pet. ether with 1% Et_3N) and then immediately hydroborated with thexylborane following the general procedure. The enol ether in dry THF (2.5 mL) was added to a solution of thexylborane (4.2 mmol) at –20 °C. Reaction at –20 °C for 20 h and then warmed to 0 °C. Oxidation was performed by addition of 3M NaOH aq. (13 mL) and 30% H_2O_2 (9 mL) at 0 °C. The product was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 30:70) to afford the alcohol (84.4 mg, 61% over 2 steps) as a solid. m.p. 48–49 °C; IR (thin film) 3417, 2940, 2854, 1098, 1059, 1058, 1026 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 3.92 (dd, *J* = 11.3, 4.7 Hz, 1H, C*H*$_2$OCH), 3.40 (dddd, *J* = 9.8, 9.8, 5.0, 5.0 Hz, 1H, C*H*OH), 3.28 (ddd, *J* = 12.1, 11.7, 2.3 Hz, 1H, C*H*$_2$OCH), 3.13 (ddd, *J* = 8.7, 8.7, 2.6 Hz, 1H, OC*H*Et), 3.11–3.02 (m, 2H, C*H*OCHEt, C*H*OCH$_2$CH$_2$), 2.48 (ddd, *J* = 11.4, 4.3, 4.3 Hz, 1H, C*H*$_2$), 2.18–2.09 (m, 2H, C*H*$_2$CH$_3$, C*H*$_2$), 1.76–1.62 (m, 3H, C*H*$_2$CH$_3$, 2 × C*H*$_2$), 1.57–1.48 (m, 1H, C*H*$_2$), 1.45–1.40 (m, 1H, C*H*$_2$), 1.33 (t, *J* = 7.4 Hz, 3H, C*H*$_3$), 1.05 (d, *J* = 5.5 Hz, 1H, O*H*); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 83.4, 77.6, 77.0, 69.5, 67.8, 39.2, 29.2, 25.5, 24.6, 9.9; HRMS calcd for $C_{10}H_{18}O_3$: 186.1256, found: 186.1246.

Alcohol 19b. The enol ether **13b** (100 mg, 0.475 mmol) was converted to the cyclic enol ether **16b** by ring-closing metathesis following the general procedure. The product was filtered through a short plug of alumina (pet. ether with 1% Et_3N) and then immediately hydroborated with thexylborane following the general procedure. The enol ether in dry THF (2.0 mL) was added to a solution of thexylborane (2.5 mmol) at –20 °C. Reaction at –20 °C for 20 h and then warmed to 0 °C. Oxidation was performed by addition of 3M NaOH aq. (7.5 mL) and 30% H_2O_2 (5 mL) at 0 °C. The product was purified by flash column chromatography on silica gel (pet. ether-Et_2O, 30:70) to afford the alcohol (38.6 mg, 41% over 2 steps) as a colourless oil. IR (thin film) 3436, 2937, 2870, 1151, 1091, 1033 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90–3.84 (m, 1H, C*H*$_2$OCH), 3.76–3.70 (m, 1H, C*H*OH), 3.36–3.29 (m, 1H, C*H*$_2$OCH), 3.17 (ddd, *J* = 9.5, 6.6, 3.4 Hz, 1H, OC*H*Et), 3.09 (ddd, *J* = 12.2, 8.0, 4.2, 1H, C*H*OCHEt), 2.98 (ddd, *J* = 8.9, 8.9, 3.7 Hz, 1H, C*H*OCH$_2$), 2.12–2.04 (m, 1H, C*H*$_2$), 1.93–1.80 (m, 3H, 3 × C*H*$_2$), 1.74–1.61 (m, 3H, 3 × C*H*$_2$), 1.51–1.37 (m, 3H, 3 × C*H*$_2$), 0.99 (t, *J* = 7.3 Hz, 3H, C*H*$_3$); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 88.0, 83.3, 83.0, 74.6, 67.8, 31.2, 30.5, 28.0, 27.2, 25.9, 10.7; HRMS calcd for $C_{11}H_{20}O_3$: 200.1412, found: 200.1423.

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