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Anomeric oxygen to carbon rearrangements of alkynyl tributylstannane derivatives of furanyl (γ)- and pyranyl (δ)-lactols

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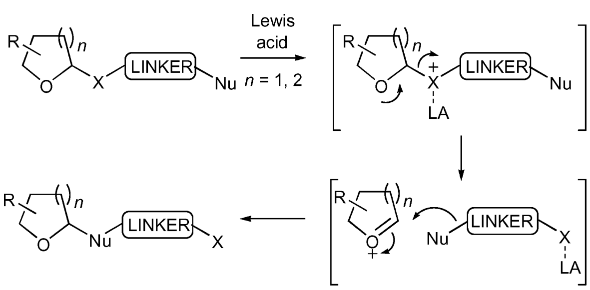
Tetrahydropyran and tetrahydrofuran containing natural products, drugs and agrochemicals often possess carbon–carbon bonds adjacent to the heteroatom. Consequently, new methods for the construction of anomeric carbon–carbon bonds are of considerable importance. We have devised a new strategy to access these systems that requires the treatment of *O*-glycoside alkynyl tributylstannane derivatives of furanyl and pyranyl lactols with Lewis acid to effect oxygen to carbon rearrangements. This leads to the formation of the corresponding carbon linked alkynol products that can be further manipulated to produce key structural motifs and building blocks for the assembly of complex molecules.

Introduction

Tetrahydropyran and tetrahydrofuran ring systems bearing carbon–carbon bonds adjacent to the ring oxygen are commonplace amongst natural products.[1] Such compounds frequently exhibit important biological properties that invariably arise from this particular arrangement of atoms. Accordingly, these structural motifs have been incorporated into synthetic drugs and agrochemicals, many of which exhibit desirable biological activity.[2]

The requirement for new methods of anomeric carbon–carbon bond construction is therefore of considerable importance and consequently a number of solutions have evolved over recent years.[3–5] A popular strategy towards *C*-glycosidation involves the displacement of a group at the 2-position mediated by a Lewis acid. However, the generation of the requisite leaving group followed by displacement often necessitates two separate chemical transformations.[6]

We have recently developed a new synthetic approach towards the formation of carbon–carbon bonds adjacent to the heteroatom in pyran and furan ring systems. This is based on the rearrangement of anomeric oxygen-linked substrates to the corresponding carbon-linked products in a single step, requiring a precursor that contains a carbon centred nucleophile (Nu) covalently linked to the anomeric position through a leaving group (X) (Scheme 1). It has been shown that, upon treatment with Lewis acid, these systems undergo expulsion of the leaving group, to generate a reactive oxonium intermediate that is trapped *in situ* by the nucleophilic component to generate a new carbon–carbon bond.[7] As this generic system encapsulates the three reaction components – substrate, leaving group and nucleophile – it permits one-step *C*-glycosidation.

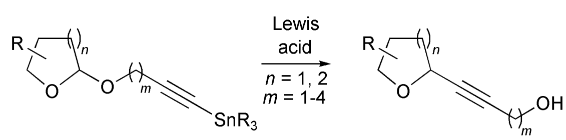


Scheme 1 Anomeric rearrangement. X = leaving group, Nu = nucleophile, LA = Lewis acid.

A few examples of this type of rearrangement had previously been reported for vinylic,[8] phenolic,[9–11] and allylic[12,13] ether systems. However, more general anomeric oxygen to carbon rearrangements using a wider range of more synthetically useful nucleophiles had not been explored in detail.

Our studies have revealed that a range of anomerically linked carbon centred nucleophiles, including electron rich alkenes,[7,14] silyl enol ethers[15] enol ethers[16] and alkynylstannanes[17] undergo rearrangement to afford the corresponding carbon-linked products in good yields. As this method inherently combines anomeric activation with side chain heteroatom protection, it offers good compatibility with target-orientated synthesis.[18–23]

Alkynyl stannanes had previously been used for intermolecular displacement of anomeric halides, but to the best of our knowledge had never been applied to this type of rearrangement.[24] Their ease of preparation and handling, combined with inherent reactivity towards oxonium ion, made alkynyl stannanes ideal for subjection to Lewis acid mediated rearrangement.[17] Herein we discuss the development of this class of the reaction and illustrate its utility by incorporation into the syntheses of a selection of structurally advanced fragments and biologically active natural products (Scheme 2).



Scheme 2 The alkynylstannane rearrangement.

Results and discussion

Rearrangements of mono-substituted pyran derivatives

Initial investigations focused on the rearrangement of tributyl stannane acetylene derivatives of pyran rings. A variety of Lewis acids, concentrations and reaction conditions were tested using the readily obtained tetrahydropyran derivatised propargylic alcohol **1**. Acetylene deprotonation using ^{n}BuLi, followed by addition of tributyltin chloride, gave the desired stannane **2** in high yield. For the rearrangement step, several commonly employed Lewis acids were tested in an effort to synthesise alkynol **3** (Table 1). However, most of these resulted in varying degrees of decomposition, often providing a mix of the identified by-products **1**, **2** and **4**, generated by destannylation of the acetylene or fragmentation of the glycoside linkage (Scheme 3).

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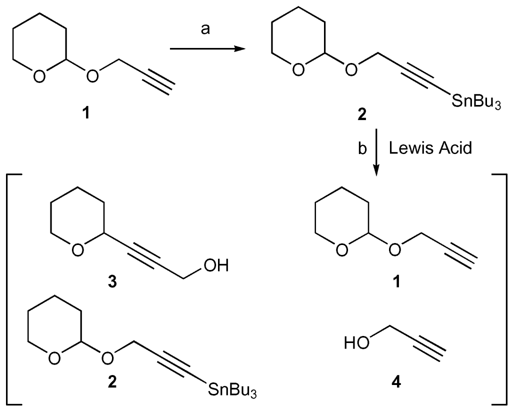
Table 1 Optimization of the rearrangement

Lewis acid	Eq.	Temp./°C	Time/min	Conc./M	Result
$TiCl_4$	3	−78	10	0.46	**1**, **2**, **4**, plus 1 unidentified
$TiCl_4$	4	−78	10	0.19	**1**, **4**, plus 1 unidentified
$SnCl_4$	3	−78⟶−30	30	0.15	**1**, **4**, plus decomposition
$EtAlCl_2$	3	−78⟶25	45	0.15	**1**, **4**, plus 2 unidentified
Me_2AlCl	3	−78⟶25	45	0.15	Complex mixture
BF_3·OEt_2	3	−30	5	0.45	Complex mixture
BF_3·OEt_2	3	−10	5	0.23	Complex mixture
BF_3·OEt_2	3	−10	5	0.45	**3**

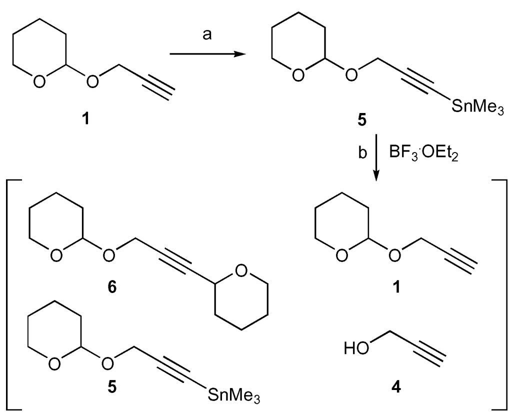


Scheme 3 *Reagents and conditions*: [a]. *n*-BuLi, THF, −78 °C, then Bu_3SnCl, THF; [b] Lewis acid, CH_2Cl_2.

The best results were obtained using boron trifluoride etherate which provided predominantly the desired rearranged material.

Temperature, time and concentration of the reaction were optimized with boron trifluoride etherate as the Lewis Acid. The optimal reaction conditions required a high concentration of substrate (0.45 M) in dichloromethane which was treated with excess boron trifluoride etherate at −10 °C for 5 minutes before quenching with NaOH solution (Table 1).

The analogous trimethylstannane derivative **5** was tested as an alternative under the optimized rearrangement conditions. This proved less stable than the tributyl derivative, decomposing to a mixture of four identified by-products **1**, **4**, **5**, and **6** (Scheme 4). As a result, tributyl stannanes were subsequently adopted for further investigations.

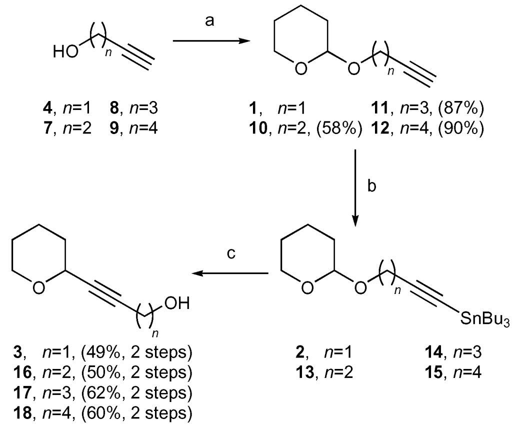


Scheme 4 *Reagents and conditions*: [a]. *n*-BuLi, THF, −78 °C, then Me_3SnCl, THF; [b] BF_3·OEt_2, CH_2Cl_2.

The rearrangement was general for a range of tetrahydropyran "protected" alkynol substrates of differing linker chain lengths (Scheme 5).

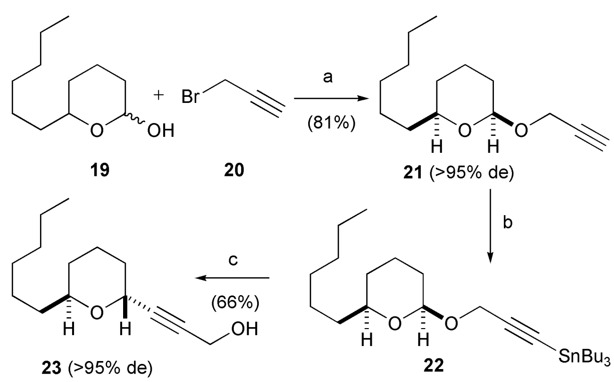
Rearrangements of di-substituted pyran derivatives

With the optimal rearrangement conditions established on simple THP ether derivatives, more complex rearrangement



Scheme 5 *Reagents and conditions*: [a]. DHP, CSA, CH_2Cl_2, 0 °C; [b]. *n*-BuLi, THF, −78 °C, then Bu_3SnCl, THF; [c] BF_3·OEt_2, CH_2Cl_2, −10 °C. DHP = 3,4-dihydropyran, CSA = camphorsulfonic acid.

substrates were considered. On rearrangement, substituted pyranyl ether substrates could lead to the formation of two diastereomeric carbon-linked products. Accordingly, reaction diastereoselectivities and yields were investigated in the rearrangement of 2,6-distubstituted pyran derivatives. Readily available *ⁿ*hexyl-substituted δ-lactol **19**[19] was alkylated by treatment with propargylic bromide **20** and KHMDS to provide terminal acetylene **21** in >95% de, favouring the 2,6-*cis*-products (Scheme 6). Acetylene **21** was stannylated and rearranged to yield the desired alkynol product **23** in 66% yield as a single *trans* diastereoisomer (>95% de). The high level of stereoselectivity in the rearrangement can be readily rationalized by the kinetically favoured axial approach of the nucleophile to the intermediate oxonium ion (Fig. 1).[25]



Scheme 6 *Reagents and conditions*: [a]. KHMDS, THF, −78 °C (81%); [b]. *n*-BuLi, THF, −78 °C, then Bu_3SnCl, THF; [c] BF_3·OEt_2, CH_2Cl_2, −10 °C (66%, 2 steps). KHMDS = potassium hexamethyldisilazide.

Application to the syntheses of spiroketals

The utility of the rearranged tetrahydropyran products was exploited by application to the formation of unsubstituted and substituted 6,6 and 6,5 spiroketals[26] (Scheme 7).

Both propargylic **21** and homo-propargylic **24** ether derivatives of the *ⁿ*hexyl-substituted δ-lactol **19** were synthesized

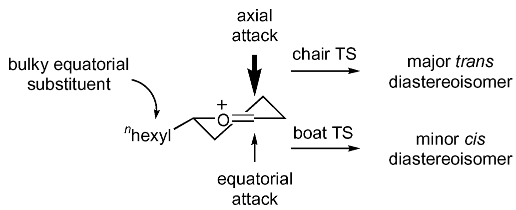
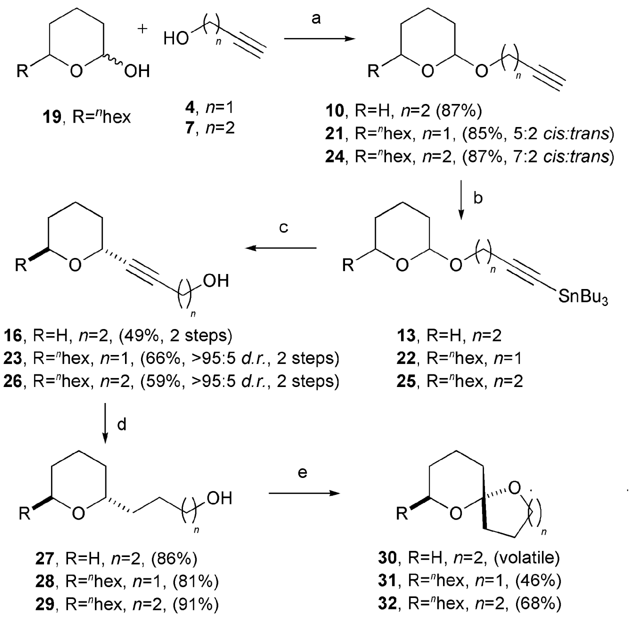


Fig. 1 Diastereoselective rearrangement of disubstituted pyrans.

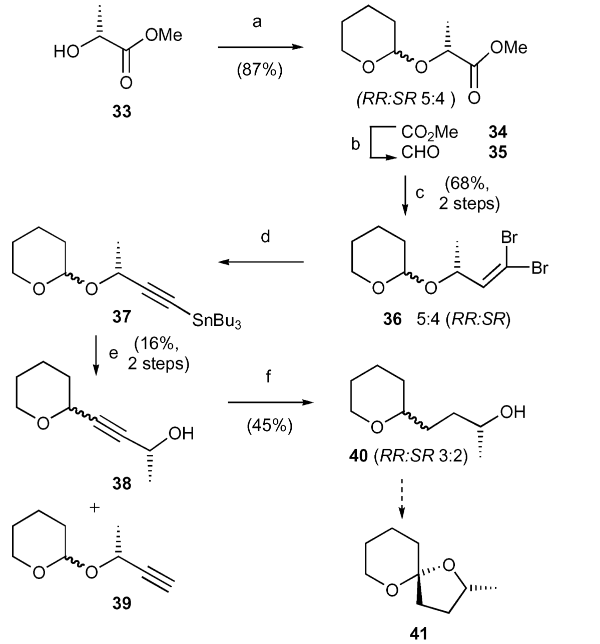


Scheme 7 *Reagents and conditions*: [a]. Amberlyst® A-15, toluene, reflux; [b]. *n*-BuLi, THF, −78 °C, then Bu_3SnCl, THF; [c] $BF_3{\cdot}OEt_2$, CH_2Cl_2, −10 °C; [d]. Raney nickel, H_2, EtOH, rt; [e]. I_2, HgO, cyclohexane, reflux.

by an alternative Fischer glycosidation method employing the corresponding alcohols at reflux in benzene or toluene with catalytic Amberlyst® A-15.[27,28] The resulting alkynes were stannylated and rearranged to provide alkynols **23** and **26** in excellent >95 : 5 d.r. and good yields. Following screening of various hydrogenation catalysts, reduction of alkynes **23** and **26** was facilitated over Raney nickel to provide the corresponding alkanes **28** and **29** in high yield.[29] In accordance with literature procedure,[30,31] the hydroxy alkanes were cyclised by treatment with iodine and mercuric oxide to yield the corresponding 6,5-(**31**) and 6,6-(**32**) spiroketals as single diastereoisomers.[32]

Similarly, rearranged homopropargyl monosubstituted tetrahydropyran **16** was reduced using the Raney nickel hydrogenation to alcohol **27**. Spirocyclisation then accessed the 6,6-spiroketal, olive fly pheromone natural product **30**.

With a versatile method in hand for the rearrangement of unbranched alkyne linkers, rearrangement of an enantiopure branched chain precursor was investigated. Tetrahydropyranyl ether derivative **34** of (*R*)-methyl lactate **33** was synthesised in a 5 : 4 d.r. (Scheme 8). Reduction proceeded smoothly by treatment with DIBAL-H to provide the corresponding aldehyde **35**. This was reacted without further purification under Corey–Fuchs conditions to yield dibromide **36** in 68% yield over the 2 steps, maintaining the 5 : 4 ratio of two diastereoisomers.[33] Dibromide **36** was treated with ^{n}BuLi (2 eq.) to provide the corresponding lithium acetylide that was quenched directly with tributyltin chloride to yield stannane derivative **37**. As before, this was used without further purification in the rearrangement reaction using borontrifluoride etherate. Without further optimisation, the rearrangement provided some alkynol product **38** in 16% yield and 3 : 2 d.r. The corresponding destannylated terminal alkyne **39** was isolated as the main reaction by-product, also in 16% yield. This result highlighted the increased instability of this branched

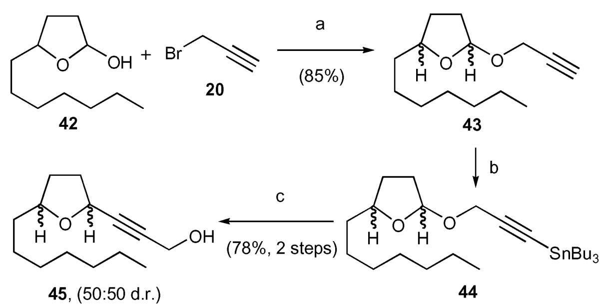


Scheme 8 *Reagents and conditions*: [a]. DHP, CSA, 0 °C, (87%, 5 : 4 d.r.); [b]. DIBAL-H, Et_2O, −78 °C; [c]. PPh_3, CBr_4, CH_2Cl_2, (68%, 2 steps, 5 : 4 d.r.); [d]. *n*-BuLi, THF, −78 °C, then Bu_3SnCl, THF; [e]. $BF_3{\cdot}OEt_2$, CH_2Cl_2, −10 °C, (16%, 3 steps); [f]. Raney nickel, H_2, EtOH, rt, (45%, 3 : 2 d.r.). DHP = 3,4-dihydropyran, DIBAL-H = diisobutylaluminium hydride.

stannane under the reaction conditions, but nonetheless constituted a promising initial attempt for future optimisation. Furthermore, spirocyclisation would complete a short synthesis of wasp pheromone natural product **41**.

Rearrangements of di-substituted furan derivatives

Having investigated the rearrangements and diastereoselectivities across unsubstituted and substituted 6-membered pyran ring systems, the same was attempted for 5-membered furan rings. The known heptane-substituted γ-lactol **42**[19] was alkylated by KHMDS deprotonation and reaction with proparyl bromide to provide terminal alkyne **43** in 85% yield. The identical stannylation-rearrangement conditions as established on the pyranyl ring systems were then applied. This reaction proceeded in a pleasing 78% yield over the two steps to provide the desired rearranged alcohol **45**. As anticipated, the furan displayed diminished diastereoselectivity in the rearrangement compared to the equivalently substituted pyran ring, providing the heptane substituted adduct **45** in an unselective 50 : 50 d.r. (Scheme 9).



Scheme 9 *Reagents and conditions*: [a]. KHMDS, THF, −78 °C (85%); [b]. *n*-BuLi, THF, −78 °C, then Bu_3SnCl, THF; [c] $BF_3{\cdot}OEt_2$, CH_2Cl_2, −10 °C (78%, 2 steps). KHMDS = potassium hexamethyldisilazide.

In order to obtain some stereocontrol in the O to C rearrangements of the furanyl systems, a TBDPS protected hydroxymethyl substituted γ-lactol system was investigated. Lactol **47** was readily prepared from (*R*)-glycidol in three steps as a 3 : 2 mixture of anomers in 70% overall yield (Scheme 10).

Scheme 10 *Reagents and conditions*: [a]. TBDPSCl, NEt_3, DMAP, CH_2Cl_2, rt, 24 h, (85%); [b]. allylMgBr, $CuLi_2Cl_4$, (10 mol%), THF, 15 min, −30 °C, (89%); [c]. O_3, $NaHCO_3$, CH_2Cl_2, 20 min, −78 °C; PPh_3, 14 h, −78 °C ⟶ rt, 14 h, (93%). TBDPS = *tert*-butyldiphenylsilyl.

It was envisaged that the bulky OTBDPS substituent would not only permit a degree of stereocontrol, but the protected oxygen would provide a latent functionality for subsequent development and scaffold elaboration of the rearrangement product (Fig. 2).

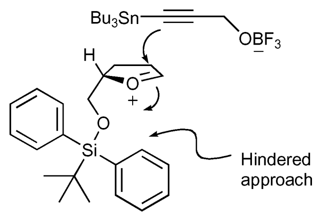
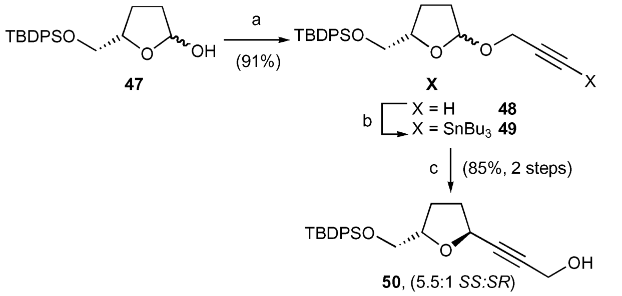


Fig. 2 Steric interactions force a *trans*-delivery of the nucleophile to the THF oxonium intermediate.

Treatment of the lactol **47** with excess propargylic alcohol **4** and catalytic Amberlyst® A-15 provided propargylic ether **48** in high yield, as a 3 : 2 anomeric mixture (Scheme 11). Subjection of this intermediate to the stannylation-rearrangement conditions gave the desired carbon-linked products **50** in a pleasing 5.5 : 1 ratio in favour of the *trans*-adduct in high overall yield. This pleasing result confirmed that the increased bulk offered by the OTBDPS group is able to invoke appreciable levels of diastereoselectivity in the synthesis of versatile alkynol building blocks.



Scheme 11 *Reagents and conditions*: [a]. prop-2-yn-1-ol, Amberlyst A-15®, benzene, 15 min, reflux, (91%); [b]. *n*-BuLi, THF, 30 min, −78 °C; Bu_3SnCl, 30 min, −78 °C ⟶ rt; [c]. $BF_3 \cdot OEt_2$, CH_2Cl_2, 10 min, −10 °C, (85%, 2 steps, 5.5 : 1 *trans* : *cis*).

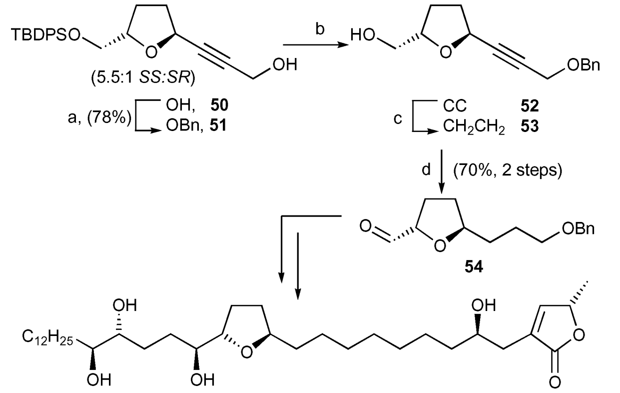
Application to the total synthesis of muricatetrocin C[20,23]

Isolated in limited supply in 1996 by McLaughlin and coworkers, muricatetrocin C had been shown to inhibit the growth of lung and pancreatic carcinomas.[34]

It was envisaged that the versatility of orthogonally functionalized alcohol **50** could be exploited in the total synthesis of this annonaceous acetogenin **55** (Scheme 12).

Inseparable diastereoisomers **50a** and **50b** were benzylated at the primary hydroxyl using KHMDS in the presence of benzyl bromide to provide benzyl ether **51**. At this point the diastereoisomers became separable by chromatography, permitting isolation of isomer **51a** in 78% yield. Analysis by NMR nOe experiments corroborated the predicted *trans*-relationship of the major component **51a** (Fig. 3).

Cleavage of the TBDPS ether **51** to primary alcohol **52** proceeded in an excellent 95% yield under treatment with TBAF. Exhaustive reduction of the alkyne **52** by hydrogenation over Raney nickel, followed by Swern oxidation, permitted



muricatetrocin C, **55**

Scheme 12 *Reagents and conditions*: [a]. KHMDS, THF, 30 min, −78 °C; BnBr, THF, −78°C ⟶ rt, 2 h, (78%); [b]. TBAF, THF, 3 h, rt (95%); [c]. Raney nickel, H_2, EtOH, 30 min, rt, (70%); [d]. DMSO, $(COCl)_2$, CH_2Cl_2, −78 °C, 30 min; NEt_3, −78 °C ⟶ 0 °C, (used crude in coupling). KHMDS = potassium hexamethyldisilazide, Bn-benzyl, TBAF = *tetra*-butylammonium fluoride, DMSO = dimethyl sulfoxide.

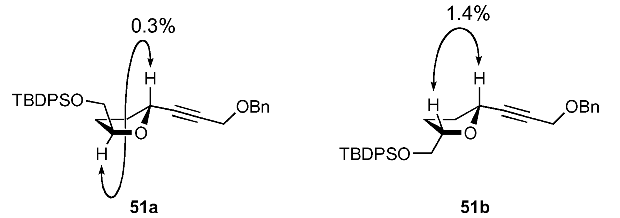


Fig. 3 NOE analysis of rearranged intermediate **51**.

isolation of unstable aldehyde **54** in a 70% yield over the 2 steps. This intermediate was subsequently coupled at each termini to form the central core in the total synthesis of muricatetrocin C.

Application to the total synthesis of CMI-977[21,22]

Drug molecule CMI-977 **56**, a potent 5-lipoxygenase inhibitor that is known to block the generation of leukotriene B_4, was developed for the prophylactic treatment of chronic asthma[35] (Fig. 4).

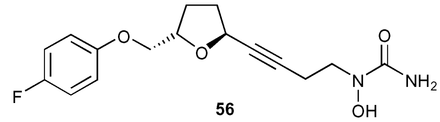
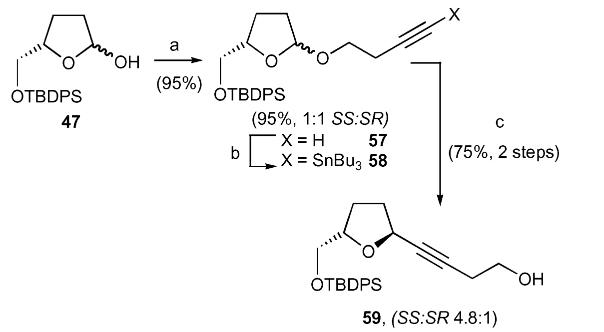


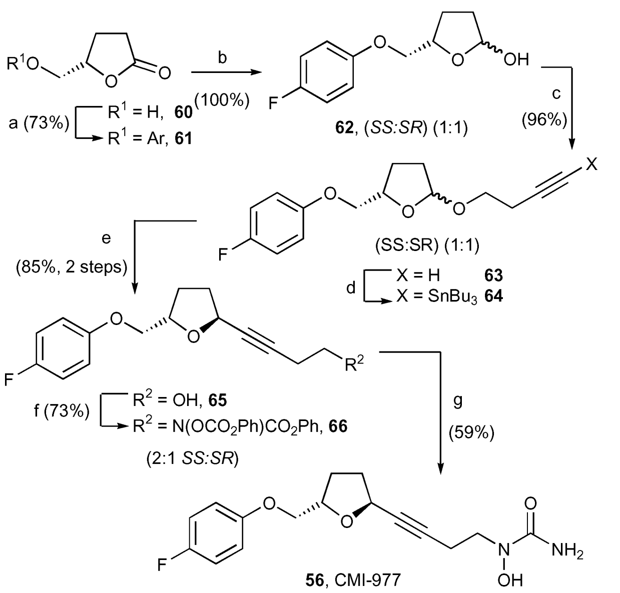
Fig. 4 CMI-977.

It was initially expected that enantiopure lactol **47** could be used in the synthesis of CMI-977, using a homo-proparylic linker. Lactol **47** was heated with homo-propargylic alcohol **7** and catalytic Amberlyst A-15 in benzene to yield tetrahydrofuranyl ether **57** in 95% yield as a 3 : 2 mixture of anomers on multi-gram scale (Scheme 13). The stannylation-rearrangement conditions were successfully applied to provide the carbon linked adducts **59**. Inspection of the crude ^{1}H NMR indicated a 5 : 1 ratio in favour of the desired *trans* product. The rearranged alcohol diastereoisomers proved inseparable by chromatography but the material was carried through the synthesis as a mixture, anticipating the possibility of separation at a later stage. Although the *N*-hydroxy urea portion was installed without difficulty, the subsequent displacement of the hydroxy methyl by *para*-fluoro phenol proved troublesome. After unsuccessfully investigating a range of etherification conditions, this synthetic route was abandoned.[36]

As an alternative to avoid the late stage etherification, the rearrangement was examined for a *p*-fluoro-phenol substituted lactol **62**. This lactol was formed from available (*S*)-γ-hydroxymethyl-γ-butyrolactone **60** (Scheme 14). Conversion to the



Scheme 13 *Reagents and conditions*: [a]. but-3-yn-1-ol, Amberlyst A-15®, benzene, 15 min, reflux, (95%); [b]. *n*-BuLi, THF, 30 min, −78 °C; Bu_3SnCl, 30 min, −78 °C ⟶ rt; [c]. $BF_3{\cdot}OEt_2$, CH_2Cl_2, 5 min, −10 °C, (75%, 2 steps, 4.8 : 1). TBDPS = *tert*-butyldiphenylsilyl.



Scheme 14 *Reagents and conditions*: [a]. *p*-fluorophenol PPh_3, DIAD, THF, 0 °C ⟶ reflux, 3h, (73%); [b]. DIBAL-H, toluene, −78 °C, (100%); [c]. but-3-yn-1-ol, Amberlyst A-15®, benzene, reflux, 15 min, (96%); [d]. *n*-BuLi, Bu_3SnCl, −78 °C ⟶ rt, 30 min; [e]. $BF_3{\cdot}OEt_2$, CH_2Cl_2, −10 °C, 5 min, (2 steps, 85%, 2 : 1); [f]. PPh_3, DIAD, *N,O*-diphenoxycarbonyl hydroxylamine, THF, 0 °C ⟶ rt, (91%); [g]. Ammonia 0.88 sp. gr., rt, 12 h, (59%). DIAD=di-*iso*-propyl azodicarboxylate.

p-fluoro phenyl ether **61** proceeded in 73% yield under modified Mitsunobu conditions, followed by quantitative reduction using DIBAL-H to furnish the desired lactol **62** as a 3 : 2 mixture of anomers.[36] Glycosidation with homo-propargylic alcohol, followed by rearrangement afforded **65** in good yield. Inspection of the crude NMR revealed a 2 : 1 *trans* : *cis* ratio across the ring.

As predicted, the *trans*-selectivity of the reaction was diminished compared to the analogous OTBDPS substituted system **47**, due to the reduced steric bulk of the aryl ether side chain. However, it was pleasing to note the improved selectivity relative to the *n*-alkyl substituted system **43**. Furthermore, the rearrangement diastereoisomers proved readily separable by flash column chromatography, affording diastereomerically pure alkynol **65** in 57% yield. A single crystal X-ray diffraction of **65** was obtained, providing unambiguous proof of the assigned *trans*-stereochemistry (Fig. 5).[37]

Having formed key rearranged intermediate **65**, conversion to CMI-977 **56** was possible following a modification of a 2-step literature procedure (Scheme 14). Mitsunobu reaction with *N,O*-diphenoxycarbonyl hydroxylamine converted the free hydroxyl group of **65** to the protected *N*-hydroxy urea derivative **66**.[36] Direct aminolysis of this material by treatment with concentrated ammonium hydroxide at room temperature

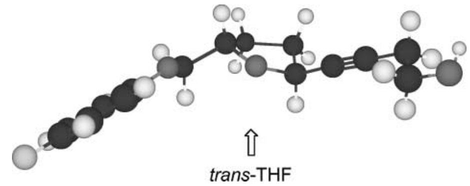


Fig. 5 X-Ray crystal structure of rearranged intermediate **65**.

for 20 hours then gave CMI-977 **56** in 59% yield as a white solid.

Conclusions

In summary, a new anomeric oxygen to carbon rearrangement of alkynyl tributylstananes has been developed. The utility of the procedure has been illustrated by the conversion of rearrangement products into important spiroketal motifs, and by strategic incorporation into the total syntheses of drug molecule CMI-977 and natural product muricatetrocin C. We believe that this method will continue to provide great utility for the synthesis of naturally occurring and biologically important compounds.

Experimental

General

All reactions were carried out under an atmosphere of argon, and those not involving aqueous reagents were carried out in oven-dried (200 °C) glassware, cooled under vacuum. Ether and tetrahydrofuran were distilled from sodium benzophenone ketyl; dichloromethane, benzene and toluene were distilled from calcium hydride; pentane was distilled from sodium; and triethylamine from potassium hydroxide. All other solvents and reagents were used as supplied unless otherwise stated. Ozonolyses were carried out using a Peak Scientific ozone generator. Flash column chromatography was carried out using Merck 60 Kieselgel (230–400 mesh) under pressure unless otherwise stated. Analytical thin layer chromatography (TLC) was performed on glass plates pre-coated with Merck Kieselgel 60 F254, and visualised by ultra-violet irradiation (254 nm), or by staining with aqueous acidic ammonium molybdate, or aqueous acidic potassium permanganate solutions as appropriate. Melting points were measured on a Reichert hot stage apparatus, and are uncorrected. Infra-red spectra were obtained on Perkin Elmer 983G, FTIR 1620, or Spectrum One FT-IR ATR (Attenuated Total Reflectance) spectrometers, from a thin film deposited onto the ATR, a sodium chloride plate, or mixed with potassium bromide as a tablet. Micro-analyses were performed in the microanalytical laboratories at the Department of Chemistry, Lensfield Road, Cambridge using a CE-440 Elemental Analyser. Mass spectra and accurate mass data were obtained on a Micromass Platform LC-MS, Kratos MS890MS, Kratos Concept IH, Micromass Q-TOF, or Bruker BIOAPEX 4.7 T FTICR spectrometer, by electron ionisation, chemical ionisation or fast atom/ion bombardment techniques at the Department of Chemistry, Lensfield Road, Cambridge. ^{1}H NMR spectra were recorded in $CDCl_3$, at ambient temperature on Bruker AM-200, Bruker AM-400, Bruker DPX-400, DRX-400, or Bruker-DRX-600 spectrometers, at 200, 400 or 600 MHz, with residual protic solvent $CHCl_3$ as the internal reference (δ_H = 7.26 ppm); Chemical shifts (δ) are given in parts per million (ppm), and coupling constants (*J*) are given in Hertz (Hz). The proton spectra are reported as follows δ/ppm (number of protons, multiplicity, coupling constant *J*/Hz, assignment). ^{13}C NMR spectra were recorded in $CDCl_3$ at ambient temperature on the same spectrometers at 50, 100 or 150 MHz, with the central peak of $CHCl_3$ as the internal reference (δ_C = 77.0 ppm). DEPT135 and two dimensional (COSY, HMQC, HMBC) NMR spectroscopy were used where appropriate, to aid in the assignment of signals in the ^{1}H and ^{13}C NMR spectra; gradient nOe experiments were also performed in certain cases and their salient results are detailed in the text. Where a compound has been characterised as an inseparable mixture of diastereoisomers, the NMR data for each individual isomer has been reported as far as was discernible from the spectrum of the mixture. Where coincident coupling constants have been observed in the NMR spectrum, the apparent multiplicity of the proton resonance concerned has been reported.

2-(But-1-yne-4-oxy) tetrahydropyran 10[38]. A solution of DHP (5.0 mL, 55.0 mmol) was added dropwise to a solution of 3-butyn-1-ol **7** (3.5 g, 50.0 mmol) and camphorsulfonic acid (0.1 g, 0.50 mmol) in CH_2Cl_2 (25 mL) at 0 °C. The mixture was stirred for 30 min at rt, diluted with CH_2Cl_2 (30 mL) then extracted with a solution of $NaHCO_3$ (25 mL) followed by brine (25 mL). The combined organics were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by flash column chromatography (petroleum ether : ether 15 : 1) yielded alkyne **10** as a colourless oil (4.49 g, 58%); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.49 (1 H, dd, *J* 3.4, 3.1, OC*H*O), 3.76–3.61 (2 H, m, C*H*HO$_{ax}$, OC*H*HCH$_2$CCH), 3.44–3.33 (2 H, m, CH*H*O$_{eq}$, OCH*H*CH$_2$CCH), 2.32–2.30 (2 H, m, C*H*$_2$C≡CH), 1.70–1.39 (6 H, m, 3 × CH$_2$ of THP); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 98.0, 80.8, 68.9, 64.9, 61.3, 30.0, 25.0, 19.4, 18.8.

2-(Pent-1-yne-5-oxy) tetrahydropyran 11[39]. The same procedure was used as for compound **10** to give alkyne **11** as a colourless oil (3.46 g, 87%), obtained after silica gel flash column chromatography (petroleum ether : ether 5 : 1); ν_{max} (film)/cm^{-1} 3298, 2942–2871, 2118, 1034, 1062; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.57 (1 H, t, *J* 3.1, OC*H*O), 3.90–3.75 (2 H, m, C*H*HO$_{ax}$ of THP, OCHOC*H*H), 3.53–3.40 (2 H, m, CH*H*O of THP, OCHOCH*H*), 2.33–2.24 (2 H, m, C*H*$_2$C≡CH), 1.93–1.91 (1H, t, *J* 2.6, C≡C*H*), 1.86–1.72 (4 H, m, C*H*$_2$-CH$_2$C≡CH, 1 × C*H*$_2$ of THP), 1.69–1.49 (4 H, m, 2 × C*H*$_2$ of THP); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 98.7, 83.9, 68.3, 65.7, 62.1, 30.6, 28.6, 25.4, 19.4, 15.2; *m*/*z* (CI) 85 (41%), 102 (100%), 103 (8%), 186 (7%); *m*/*z* (CI) found 169.1228 ([M + H]$^+$ $C_{10}H_{17}O_2$ requires 169.1229).

2-(Hex-1-yne-6-oxy) tetrahydropyran 12[40]. The same procedure was used as for compound **10** to give alkyne **12** as a colourless oil (5.56 g, 90%), obtained after silica gel flash column chromatography (petroleum ether : ether 5 : 1); ν_{max} (film)/cm^{-1} 3298, 2942–2871, 2118, 1034, 1075; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.56 (1 H, t, *J* 2.8, OC*H*O), 3.89–3.69 (2 H, m, C*H*HO$_{ax}$ of THP, OCHOC*H*H), 3.53–3.34 (2 H, m, CH*H*O of THP, OCHOCH*H*), 2.55–2.14 (2 H, m, C*H*$_2$C≡CH), 1.94–1.91 (1 H, t, *J* 1.00, C≡C*H*), 1.89–1.49 (10 H, m, 3 × CH$_2$of THP 2 × C*H*$_2$ of chain); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 98.7, 84.3, 68.2, 66.8, 62.2, 30.6, 28.7, 25.4, 25.3, 19.5, 18.2.

2-(1-Tributylstannyl-3-propynyloxy) tetrahydropyran 2. A solution of butyllithium (11.0 mL, 17.6 mmol, 1.6 M in hexanes) was added dropwise at −78 °C to a solution of alkyne **1** (2.2 mL, 16.0 mmol) in 60 mL of THF. The reaction mixture was stirred for 30 minutes at −78 °C before slow addition of tributyltin chloride. The mixture was stirred for 30 min and allowed to slowly warm from −78 °C to −30 °C. The reaction mixture was extracted using ether (60 mL) and water (60 mL). The aqueous phase was washed using ether (2 × 40 mL) and the combined organic phase dried over $MgSO_4$, filtered and concentrated to yield stannane **2** as a pale yellow oil (6.8 g, 100%). This was used in the subsequent reaction without purification; ν_{max} (film)/cm^{-1} 2954–2860, 2358; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 4.84 (1 H, t, *J* 3.4, OC*H*O), 4.29–4.22 (2 H, m, OC*H*$_2$C≡C), 3.84–3.80 (1 H, m, C*H*HO$_{ax}$), 3.51–3.48 (1 H, m, CH*H*O$_{eq}$ of THP), 1.84–1.69 (2 H, m, C*H*$_2$CHO), 1.62–0.86 (31 H, 2 × C*H*$_2$ of THP, 3 × Bu of SnBu$_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 105.7, 93.3, 89.9, 61.9, 54.9, 30.3, 25.4, 19.1, 28.9, 26.9, 10.9, 13.5; *m*/*z* (EI) 331 (36%), 453 (64%); *m*/*z* (ESI) 453.1792 [M + Na]$^+$; $C_{20}H_{38}O_2SnNa$ requires 453.1791.

2-(1-Tributylstannyl-4-butynyloxy) tetrahydropyran 13. The same procedure was used as for compound **2** to give stannane **13** from alkyne **10** as a pale yellow oil (3.2 g, 100%). This was used in the subsequent reaction without further purification; ν_{max} (film)/cm^{-1} 2920–2870, 2153, 1063, 1122; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.61 (1 H, s, OC*H*O), 3.88–3.70 (2 H, m, C*H*HO, OC*H*H), 3.55–3.43 (2 H, m, CH*H*O, OCH*H*), 2.52–2.45 (2 H, t, *J* 7.3, C*H*$_2$C≡CH), 1.78–0.94 (33 H, m, 3 × C*H*$_2$ of THP and 3 × Bu of SnBu$_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 107.8, 98.4, 82.7, 66.1, 61.8, 30.4, 26.2, 25.4, 19.2, 28.9, 26.8, 10.8, 13.5.

2-(1-Tributylstannyl-5-pentynyloxy) tetrahydropyran 14. The same procedure was used as for compound **2** to give stannane **14** from alkyne **11** as a pale yellow oil (5.4 g, 100%). This was used in the subsequent reaction without further purification; ν_{max} (film)/cm^{-1} 2854–2871, 2149, 1062, 1035; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.60–4.59 (1 H, m, OC*H*O), 3.92–3.80 (2 H, m, C*H*HO, OC*H*H), 3.77–3.43 (2 H, m, CH*H*O, OCH*H*), 2.39–2.29 (2 H, m, C*H*$_2$C≡C), 1.93–1.69 (4 H, m, OCH$_2$C*H*$_2$, C*H*$_2$CHO$_2$ of THP), 1.63–0.87 (31 H, 2 × C*H*$_2$ of THP, 3 × Bu of SnBu$_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 111.3, 98.7, 77.5, 65.9, 62.0, 30.6, 28.8, 25.5, 19.4, 16.9, 29.3, 26.9, 10.9, 13.6.

2-(1-Tributylstannyl-6-hexynyloxy) tetrahydropyran 15. The same procedure was used as for compound **2** to give stannane **15** from alkyne **12** as a pale yellow oil (5.2 g, 100%). This was used in the subsequent reaction without further purification; ν_{max} (film)/cm^{-1} 2939, 2148, 1026, 1056; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.58–4.55 (1 H, m, OC*H*O), 3.90–3.71 (2 H, m, C*H*HO, OC*H*H), 3.53–3.34 (2 H, m, CH*H*O, OCH*H*), 2.30–2.21 (2 H, m, C*H*$_2$C≡C), 1.77–0.81 (39 H, m, 3 × C*H*$_2$ of the chain, 3 × C*H*$_2$ of THP, 3 × Bu of SnBu$_3$); ^{13}C NMR (200 MHz, $CDCl_3$) δ = 111.5, 104.5, 98.7, 66.9, 62.1, 30.7, 28.8, 25.9, 25.4, 19.5, 16.9, 29.0, 26.9, 10.9, 13.6.

2-(Propyn-1-ol) tetrahydropyran 3. A solution of boron trifluoride etherate (0.43 mL, 3.5 mmol) was added dropwise to a solution of stannane **2** (0.5 g, 1.1 mmol) in CH_2Cl_2 (3 mL) at −10 °C. After stirring for 5 min at this temperature the reaction was quenched by the addition of sodium hydroxide solution (2.5 M) and diluted with 4 mL of CH_2Cl_2. The organic phase was washed with water (3 mL) then brine (3 mL), dried over $MgSO_4$, filtered and concentrated. The product was purified by repeated flash column chromatography on silica gel (petroleum ether : Et_2O, 1 : 2 to 1 : 1 to neat Et_2O) to give alkynol **3** as a colourless oil (0.078 g, 49%);ν_{max} (film)/cm^{-1} 3410, 2938–2857, 2190, 1034, 1067; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.65–4.28 (2 H, dd, *J* 5.0, C*H*$_2$OH), 4.02–3.44 (1 H, m, C*H*HO$_{ax}$), 3.52–3.42 (1 H, m, CH*H*O$_{eq}$), 2.22–1.38 (6 H, m, 3 × C*H*$_2$ of THP); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 84.7, 83.4, 66.9, 66.7, 51.0, 31.9, 25.5, 21.7; *m*/*z* (CI) 85 (10%), 158 (100%); *m*/*z* (CI) found 141.0915 ([M + H]$^+$ $C_8H_{13}O_2$ requires 141.0916).

2-(Butyn-1-ol) tetrahydropyran 16. The same procedure was used as for compound **3** to give alkynol **16** from stannane **13** (0.41 M in CH_2Cl_2) as a colourless oil (0.12 g, 50%, 2 steps from alkyne **10**), obtained after repeated flash column chromatography on silica (petroleum ether : Et_2O, 1 : 2 to 1 : 1 to neat Et_2O); ν_{max} (film)/cm^{-1} 3398, 2938–2854, 2141, 1012, 1080, 1035; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.23 (1 H, dd, *J* 8.4, 2.0, OC*H*C≡C), 4.00–3.94 (1 H, m, C*H*HO), 3.72 (2 H, q, *J* 6.2 C*H*$_2$OH), 3.54–3.44 (1 H, m, C*H*HO), 2.50 (2 H, td, *J* 6.2, 1.9, C*H*$_2$CH$_2$OH), 1.97 (1 H, t, *J* 6.0, O*H*), 1.89–1.78 (2 H, m, C*H*$_2$CHO), 1.68–1.50 (4 H, m, 2 × C*H*$_2$); ^{13}C NMR (100 MHz) δ = 82.0, 81.3, 67.3, 66.9, 61.0, 32.4, 25.6, 23.1, 22.0; *m*/*z* (CI)

172 ([M + NH_4]$^+$, 100%); *m*/*z* (EI) found 137.0966 ([M − OH]$^+$ $C_9H_{13}O$ requires 137.0966).

2-(Pentyn-1-ol) tetrahydropyran 17. The same procedure was used as for compound **3** to give alkynol **17** from stannane **14** (0.47 M in CH_2Cl_2) as a colourless oil (0.22 g, 62%, 2 steps from alkyne **11**), obtained after repeated flash column chromatography on silica (petroleum ether : Et_2O, 1 : 2 to 1 : 1 to neat Et_2O); ν_{max} (film)/cm^{-1} 3394, 2998–2857, 2241, 1012, 1079, 1034; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.21–4.17 (1H, m, C*H*O), 3.99–3.90 (1 H, m, C*H*HO), 3.76 (1 H, t, *J* 8.3, O*H*), 3.68–3.31 (1 H, m, CH*H*O), 2.52–2.44 (2 H, dt, C≡CC*H*$_2$), 1.86–1.11 (8 H, m, C*H*$_2$ of the chain, 3 × C*H*$_2$ of THP); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 84,8, 79,1, 67.2, 66.6, 61.5, 32.4, 31.2, 25.5, 21.9, 15.2; *m*/*z* (CI) found 169.1228 ([M + H]$^+$ $C_8H_{13}O_2$ requires 169.1229).

2-(Hexyn-1-ol) tetrahydropyran 18. The same procedure was used as for compound **3** to give alkynol **18** from stannane **15** (0.60 M in CH_2Cl_2) as a colourless oil (0.46 g, 60%, 2 steps from alkyne **12**), obtained after repeated flash column chromatography on silica (petroleum ether : Et_2O, 1 : 2 to 1 : 1 to neat Et_2O); ν_{max} (film)/cm^{-1} 3405, 2937–2859, 2241, 1012, 1081, 1034; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.25–4.19 (1H, m, C*H*O), 4.00–3.90 (1H, m, C*H*HO of THP), 3.64–3.47 (2H, m, CH*H*O of THP, C*H*HOH), 3.45–3.40 (1H, m, CH*H*OH), 2.28–2.21 (2H, m, C*H*$_2$C≡C), 1.81–1.35 (11 H, m, 2 × C*H*$_2$ of chain, 3 × C*H*$_2$ of THP); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 85.2, 79.5, 67.3, 66.6, 62.2, 32.4, 31.7, 25.6, 24.8, 21.9, 18.4; *m*/*z* (EI) found 182.1385 ([M]$^+$ $C_{11}H_{18}O_2$ requires 182.1307).

2-(1-Trimethylstannyl-3-propynyloxy) tetrahydropyran 5. The same procedure was used as for compound **2** to give stannane **5** from alkyne **1** as a pale yellow oil (3.5 g, 100%). This was used in the subsequent reaction without further purification; ν_{max} (film)/cm^{-1} 2954–2860, 2358, 1034, 1120; ^{1}H NMR (200 MHz, $CDCl_3$) δ = 4.82–4.79 (1 H, m, OC*H*O), 4.34–4.12 (2 H, m, OC*H*$_2$C≡C), 3.88–3.68 (1 H, m, C*H*HO$_{ax}$), 3.54–3.40 (1 H, m, CH*H*O$_{eq}$), 1.86–1.48 (6 H, m, 3 × C*H*$_2$ of THP), 0.64–0.11 (9 H, m, 3 × C*H*$_3$ of $SnMe_3$); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 104.5, 73.9, 96.7, 61.9, 54.9, 30.1, 25.2, 18.9, −7.9.

2-(Prop-1-yne-3-oxy)-6-*n*-hexyl tetrahydropyran ether 21. Propargylic alcohol **4** (0.65 mL, 10.6 mmol), was added to a suspension of lactol **19** (1.0 g, 5.3 mmol), Amberlyst® A-15 (150 mg) and toluene (20 mL) and refluxed with stirring for 15 minutes. The reaction mixture was filtered and concentrated *in vacuo* to afford a yellow oil. Purification by silica gel flash column chromatography (petroleum ether : ether 20 : 1, then 10 : 1) afforded ether **21**, as a colourless oil (1.00 g, 85%) and mixture of diastereoisomers (*trans* : *cis* = 5 : 2). Analysis was undertaken on this mixture of isomers; ν_{max}(film)/cm^{-1} 3310, 2931, 2119, 1026, 947; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major *trans*) = 4.99 (1 H, br s, OC*H*O), 4.22 (1 H, dd, *J* 15.6, 2.4, OC*H*HCCH), 4.18 (2 H, dd, *J* 15.6, 2.4, OCH*H*CCH), 3.70–3.60 (1 H, m, $CH_3(CH_2)_5$C*H*O), 2.39 (1 H, t, *J* 2.3, CC*H*), 1.87–1.14 (16 H, m, 8 × C*H*$_2$), 0.88 (3 H, t, *J* 6.68, C*H*$_3$(CH_2)$_5$; δ (minor *cis*) = 4.56 (1 H, dd, *J* 9.4, 2.0, OC*H*O), 4.36 (2 H, d, *J* 2.3, OC*H*$_2$CCH), 3.33–3.38 (1 H, m, $CH_3(CH_2)_5$C*H*O), 2.39 (1 H, t, *J* 2.3, CC*H*), 1.87–1.14 (16H, m, 8 × CH_2), 0.88 (3 H, t, *J* 6.68, C*H*$_3$(CH_2)$_5$); ^{13}C NMR (100MHz) δ (major *trans*) = 96.0, 80.0, 76.3, 69.1, 53.5, 36.2, 31.8, 31.1, 29.4, 25.5, 22.6, 18.0, 14.0; δ (minor *cis*) = 100.0, 80.0, 76.3, 69.1, 54.6, 36.1, 31.8, 31.0, 29.3, 25.5, 22.1, 18.0, 14.0; *m*/*z* (ESI) found 247.1672 ([M + Na]$^+$ $C_{14}H_{24}O_2Na$ requires 247.1674).

2-(3-Hydroxypropyn-1-yl)-6-*n*-hexyl tetrahydropyran ether 23. A 1.6 M solution in hexanes of *n*-butyllithium (2.4 mL, 3.8 mmol) was added dropwise to a −78 °C stirred solution of **21** (0.80 g, 3.6 mmol) in THF (20 mL). The mixture was stirred for 30 minutes at −78 °C before addition of tributyltin chloride (1.29 g, 1.07 mL, 3.9 mmol). After stirring for a further 30 minutes, ether (100 mL) and distilled water (100 mL) were added. The aqueous phase was extracted with ether (50 mL). The combined organic phases were washed with brine (50 mL) and dried over anhydrous $MgSO_4$. The product material was filtered and concentrated *in vacuo* to afford stannane **22**, as a pale yellow crude oil. The stannane **22** was used directly in the next reaction.

Boron trifluoride etherate (1.3 mL, 10.1 mmol) was added dropwise to a stirred solution of stannane **22** in CH_2Cl_2 (1 mL) at −10 °C. After 15 minutes stirring, the reaction was quenched by the addition of a 10 M sodium hydroxide solution (50 mL). Ether was added (50 mL), then distilled water (100 mL). The aqueous layer was extracted with ether (50 mL). The combined organic extracts were washed with brine (50 mL) and dried over anhydrous $MgSO_4$. The material was filtered and then concentrated *in vacuo* to afford a pale yellow oil. Purification by repeated flash chromatography on silica gel (petroleum ether : ether, 50 : 1 then 2 : 1) afforded alkynol **23** (0.496 g, 66%), as a single diastereoisomer and as a colourless oil; ν_{max}(film)/cm^{-1} 3384 2928, 2247, 909, 1029; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.78 (1 H, br s, OC*H*C^{iv}C), 4.34 (2 H, dd, *J* 6.1, 1.7, C*H*$_2$OH), 3.83–3.76 (1 H, m, $CH_3(CH_2)$C*H*O), 1.90–1.12 (16 H, m, 8 × C*H*$_2$), 0.88 (3 H, t, *J* 6.8, C*H*$_3$(CH_2)$_5$); ^{13}C NMR (100 MHz) δ = 84.7, 83.4, 71.8, 65.0, 51.2, 36.1, 31.8, 31.3, 30.5, 29.3, 25.3, 22.6, 19.4, 14.0; *m*/*z* (EI) found 225.1854 ([M + H]$^+$ $C_{14}H_{25}O_2$ requires 225.1855).

2-(3-Hydroxy-*n*-propyl)-6-*n*-hexyl tetrahydropyran ether 28. A 50% Raney nickel slurry in water (1.0 g) was washed with ethanol (3 × 5 mL) and absolute ethanol (3 × 5 mL), before resuspension in absolute ethanol (3 mL). An ethanol solution of alkynol **31** (59 mg, 0.26 mmol) was then added to the nickel suspended in ethanol. The solvent was degassed under vacuum and exposed to an atmosphere of hydrogen. The heterogeneous solution was stirred vigorously for 3 hours at room temperature, then filtered through a plug of silica gel. The silica gel was washed with absolute ethanol and the filtrate concentrated *in vacuo* to yield a colourless oil. Purification by silica gel flash column chromatography (petroleum ether : ether 1 : 1) afforded alcohol **28** (48 mg, 81%) as a colourless oil; ν_{max}(film)/cm^{-1} 3387, 2936; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.75–3.57 (4 H, m, $CH_3(CH_2)_5$C*H*O, OC*H*(CH_2)$_3$OH, C*H*$_2$OH), 2.35 (1 H, s, O*H*), 1.75–1.15 (20 H, m, 10 × C*H*$_2$), 0.88 (3 H, t, *J* 6.3, C*H*$_3$(CH_2)$_5$);^{13}C NMR (100 MHz) δ = 71.5, 70.6, 63.0, 32.8, 31.8, 30.6, 29.5, 29.3, 25.8, 22.6, 21.2, 18.6, 15.2, 14.1; *m*/*z* (EI) found 228.2081 ([M]$^+$ $C_{14}H_{28}O_2$ requires 228.2089).

7-*n*-Hexyl-1,6-dioxaspiro[4,5]decane 31. Iodine (21 mg, 0.080 mmol) and mercuric oxide (20 mg, 0.086 mmol) were added to a solution of **28** (18 mg, 0.078 mmol) in cyclohexane (10 mL) and refluxed for 17 hours. The residual mercury salts were removed by filtration through a plug of silica gel before solvent removal *in vacuo* to yield a deep yellow oil. Purification *via* silica gel chromatography (petroleum ether : ether 2 : 1), then sephadex LH-20 chromatography (CH_2Cl_2 : methanol; 1 : 1) afforded spiroketal **31** (8.2 mg, 46%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 2935; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.92–3.82 (2 H, m, OC*H*$_2$), 3.71–3.66 (1 H, m, $CH_3(CH_2)_5$C*H*O), 2.07–1.99, 1.95–1.72, 1.70–1.55, 1.43–1.11 (20 H, m, 10 × C*H*$_2$), 0.88 (3 H, t, *J* 6.8, C*H*$_3$(CH_2)$_5$); ^{13}C NMR (100 MHz) δ = 105.8, 70.2, 66.6, 37.8, 36.3, 32.9, 31.9, 31.0, 29.3, 25.6, 23.7, 22.6, 20.5, 14.1; *m*/*z* (FAB) found 227.2011 ([M + H]$^+$ $C_{14}H_{27}O_2$ requires 227.2011).

2-(But-1-yne-4-oxy)-6-*n*-hexyl tetrahydropyran ether 24. Amberlyst® A-15 (150 mg) and 3-butyn-1-ol (0.7 mL, 9.26 mmol) were added to a solution of lactol **19** (861 mg, 4.63 mmol) in toluene (20 mL) and refluxed. The toluene–water azeotrope was removed over 15 minutes. The reaction mixture was filtered and concentrated *in vacuo* to afford a pale yellow oil. Purification by silica gel flash column chromatography (petroleum ether : ether 20 : 1, then 10 : 1) afforded alkyne **24** (958 mg, 87%), as a 7 : 2 mixture of diastereoisomers and as a colourless oil. All analysis was undertaken on a mixture of isomers; ν_{max}(film)/cm^{-1} 3313, 3100–2800, 2122, 1090–960; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major *trans* isomer) = 4.85 (1 H, br s, OC*H*O), 3.85–3.70 (1 H, m, OC*H*HCH$_2$C≡CH), 3.70–3.60 (1 H, m, OCH*H*CH$_2$C≡CH), 3.80–3.70 (1 H, m, CH$_3$-(CH$_2$)$_5$*H*CO), 2.54–2.47 (2 H, m, C*H*$_2$C≡CH), 1.97 (1 H, t, *J* 2.6, C≡C*H*), 1.90–1.11 (16H, m, 8 × C*H*$_2$), 0.88 (3 H, t, J 6.4, C*H*$_3$(CH$_2$)$_5$); δ (minor *cis* isomer), 4.41 (1 H, dd, *J* 9.4, 2.0, OC*H*O), 4.0–3.93 (1 H, m, OC*H*HCH$_2$C≡CH), 3.60–3.50 (1 H, m, OCH*H*CH$_2$C≡CH), 3.35–3.32 (1 H, m, CH$_3$(CH$_2$)$_5$*H*CO), 2.54–2.47 (2 H, m, C*H*$_2$C≡CH), 1.97 (1 H, t, *J* 2.6, C≡C*H*), 1.90–1.11 (16H, m, 8 × C*H*$_2$), 0.88 (3 H, t, *J* 6.4, C*H*$_3$(CH$_2$)$_5$; ^{13}C NMR (100 MHz) δ (major *trans* isomer) = 97.2, 80.8, 69.0, 68.8, 64.7, 36.3, 31.8, 31.2, 29.8, 29.4, 25.5, 22.6, 19.9, 18.2, 14.1; δ (minor *cis* isomer) = 97.2, 80.8, 69.0, 68.8, 64.7, 36.3, 31.8, 31.2, 29.8, 29.4, 25.5, 22.6, 19.9, 18.2, 14.1; *m*/*z* (EI) found 239.2006 ([M + H]$^+$ $C_{15}H_{27}O_2$ requires 239.2011).

2-(4-Hydroxy-butyn-1-yl)-6-*n*-hexyl tetrahydropyran ether 26. A solution of ^{n}butyllithium (1.6 M hexanes, 1.5 mL, 2.5 mmol) was added dropwise to a −78 °C stirred solution of **24** (0.56 g, 2.3 mmol) in THF (20 mL). The mixture was stirred for 30 minutes at −78 °C before addition of tributyltin chloride (0.838 g, 0.7 mL, 2.6 mmol). After stirring for a further 30 minutes, ether (100 mL) and distilled water (100 mL) were added. The aqueous phase was extracted with ether (50 mL) and the combined organic phases washed with brine (50 mL) and dried over anhydrous $MgSO_4$. The product material was filtered and concentrated *in vacuo* to afford stannane **25** as a pale yellow crude oil. This oil was used without further purification or characterisation in the next reaction.

Boron trifluoride etherate (1.1 mL, 1.21 g, 8.5 mmol) was added dropwise to a stirred solution of stannane **25** in CH_2Cl_2 (1 mL) at −10 °C. After 15 minutes stirring, the reaction was quenched by the addition of a 10 M sodium hydroxide solution (50 mL). Ether (50 mL) and distilled water (100 mL) were added. The aqueous layer was extracted with ether (50 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered and then concentrated *in vacuo* to afford a pale yellow oil. Purification by repeated flash chromatography on silica gel (petroleum ether : ether, 50 : 1, 2 : 1) afforded alkynol **26** (326 mg, 59%) as a pale yellow oil; ν_{max}(film)/cm^{-1} 3410br, 2932, 2230, 1041; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.72 (1 H, br s, OC*H*C^{IV}C), 3.80–3.78 (1 H, m, CH$_3$(CH$_2$)$_5$C*H*O), 3.72 (2 H, q, *J* 6.2, C*H*$_2$OH), 2.51 (2 H, td, *J* 6.3, 2.0, C^{IV}C^{IV}C*H*$_2$CH$_2$OH), 1.95–1.94, 1.88–1.71, 1.67–1.08, 0.89–0.81 (19 H, m, 8 × C*H*$_2$, 1 × C*H*$_3$);^{13}C NMR (100 MHz) δ = 82.9, 81.0, 71.5, 65.1, 61.2, 36.1, 31.8, 31.4, 30.7, 29.3, 25.3, 23.2, 22.6, 19.4, 14.0; *m*/*z* (FAB) found 239.2004 ([M + H]$^+$ $C_{15}H_{27}0_2$ requires 239.2011).

2-(4-Hydroxy-*n*-butyl)-6-*n*-hexyl tetrahydropyran ether 29. A 50% Raney nickel suspension in water (1.0 g) was washed with ethanol (3 × 5 mL) and absolute ethanol (3 × 5 mL), before resuspension in absolute ethanol (6 mL). A solution of alkynol **26** (106 mg, 0.44 mmol) was added to the suspension of the catalyst. The solvent was degassed under vacuum and the reaction exposed to an atmosphere of hydrogen. The heterogeneous solution was stirred vigorously for 4 hours at room temperature then filtered through a plug of silica gel. The silica gel was washed with absolute ethanol and the filtrate concentrated *in vacuo*. Purification by silica gel flash column chromatography (petroleum ether : ether 1 : 1) afforded alcohol **29** as a colourless oil (98 mg, 91%); ν_{max}(film)/cm^{-1} 3377, 2932, 1041; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.68–3.63 (2 H, m, CH$_3$(CH$_2$)$_5$C*H*O, OC*H*(CH$_2$)$_4$OH), 3.60–3.55 (2 H, m, C*H*$_2$OH), 1.73–1.51, 1.50–1.18, 0.98–0.93, (22 H, m, 11 × C*H*$_2$), 0.88 (3 H, t, *J* 6.7, C*H*$_3$(CH$_2$)$_5$); ^{13}C NMR (100 MHz) δ = 71.0, 70.5, 63.0, 33.2, 32.7, 31.9, 30.3, 30.2, 29.3, 25.8, 22.6, 22.0, 18.7, 15.2, 14.1; *m*/*z* (EI) 242.2 [M]$^+$; *m*/*z* (EI) found 242.2251 ([M]$^+$ $C_{15}H_{30}O_2$ requires 242.2246).

2-*n*-Hexyl-1,7-dioxaspiro[5,5]undecane 32. Iodine (22 mg, 0.085 mmol) and mercuric oxide (20 mg, 0.09 mmol) were added to a solution of alcohol **29** (21 mg, 0.09mmol) in cyclohexane (10 mL). The mixture was refluxed for 17 hours then filtered through a plug of silica gel to remove residual mercury salts. The solvent was removed *in vacuo* to yield a yellow–red oil. Purification *via* silica gel flash column chromatography (petroleum ether : ether, 2 : 1), then sephadex column chromatography (CH_2Cl_2 : methanol, 1 : 1) afforded spiroketal **32** (13.7 mg, 68%), as a pale yellow oil; ν_{max}(film)/cm^{-1} 2941; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.69–3.55 (3 H, m, OC*H*$_2$, CH$_3$(CH$_2$)$_5$C*H*O), 1.91–1.77 and 1.60–1.05 (22 H, m, 11 × C*H*$_2$), 0.89 (3 H, t, *J* 6.7, C*H*$_3$(CH$_2$)$_5$); ^{13}C NMR (100 MHz) δ = 95.4, 69.1, 60.3, 36.5, 36.0, 35.5, 31.9, 31.3, 29.5, 25.8, 25.5, 22.6, 18.9, 18.6, 14.1; *m*/*z* (FAB) 241.8 [M + H]$^+$; *m*/*z* (FAB) found 241.2159 [M + H]$^+$ $C_{15}H_{29}O_2$ requires 241.2168).

2-(4-Hydroxy-*n*-butyl) tetrahydropyran ether 27. A 50% Raney nickel suspension in water (1.8 g) was washed with ethanol (3 × 5 mL) and absolute ethanol (3 × 5 mL), before resuspension in absolute ethanol (6 mL). A solution of alkynol **16** (170 mg, 1.11 mmol) was added to this suspension of catalyst. The solvent was degassed under vacuum then exposed to an atmosphere of hydrogen. The heterogeneous solution was stirred for 4 hours at room temperature then filtered through a plug of silica gel. The silica gel was washed through with absolute ethanol and the filtrate concentrated *in vacuo* to yield a colourless oil. Purification by silica gel chromatography (petroleum ether : ether 1 : 1) afforded alcohol **27** as a colourless oil (148 mg, 86%); ν_{max}(film)/cm^{-1} 3377, 2934, 1091, 1048; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.99–3.94 (1 H, m, C*H*HOCH), 3.65 (2 H, t, *J* 6.4, C*H*$_2$OH), 3.40 (1 H, td, *J* 11.4, 2.6, C*H*HOCH), 3.26–3.21 (1 H, m, CH*H*OCH), 1.82 (1 H, br s, O*H*), 1.60–1.35 and 1.31–1.19 (12 H, m, 6 × C*H*$_2$); ^{13}C NMR (100 MHz) δ = 77.8, 68.5, 62.9, 36.2, 32.7, 32.0, 26.2, 23.6, 21.7; *m*/*z* (EI) 159.20 [M + H]$^+$, 141.14 [M − OH]$^+$; *m*/*z* (EI) found 141.1291 ([M − OH]$^+$ $C_9H_{17}O$ requires 141.1279).

1,7-Dioxaspiro[5,5]undecane (from *Dacus oleae*) 30.[41] Iodine (35 mg, 0.14 mmol) and mercuric oxide (32 mg, 0.15 mmol) were added to a solution of **27** (21 mg, 0.14 mmol) in cyclohexane (5 mL). The mixture was refluxed for 16 hours. The residual mercury salts were removed by filtration through a plug of silica gel and the solvent removed *in vacuo* to yield a yellow–red oil. Purification by silica gel chromatography (petroleum ether : ether 2 : 1), then sephadex LH-20 chromatography afforded spiroketal **30** (<50% – volatile) as a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.70–3.58 (4 H, m, OC*H*$_2$), 1.85–1.74, (4 H, m, C*H*$_2$CO$_2$), 1.61–1.32 (8 H, m, 4 × C*H*$_2$); ^{13}C NMR (100 MHz) δ = 95.0, 60.3, 35.7, 25.3, 18.5; All data identical to that described in the literature.

2-(Ethyl-2-(*R*)-methyl-2-oxy methanoate) tetrahydropyran ether 34. Dihydropyran (4.82 g, 57.2 mmol) and (*R*)-methyl lactate **33** (4.97 g, 47.7 mmol) were dissolved in CH_2Cl_2 (30 mL) at 0 °C. A catalytic amount of camphor sulfonic acid (50 mg) was added to the mixture which was stirred under an atmosphere of argon at 0 °C for 1 h 30 min. A colour change from colourless to deep pink was observed. The reaction was quenched using triethylamine (0.3 mL) which effected a colour change from pink to pale green. The solvent was removed *in vacuo* to yield a yellow oil. Purification by silica gel flash column chromatography afforded tetrahydropyranyl ether **34** (7.79 g, 87%) as a colourless oil and a 5 : 4 mixture of diastereoisomers; ν_{max}(film)/cm^{-1} 3100–2750, 1754, 1036; ^{1}H NMR (400MHz, $CDCl_3$) δ (major) = 4.72–4.67 (1 H, m, OC*H*O), 4.43 (1 H, q, *J* 7.0, OC*H*CO$_2$Me), 3.94–3.81 (1 H, m, C*H*HOCH), 3.73 (3 H, s, OCH_3), 3.53–3.43 (1 H, m, CH*H*OCH), 1.90–1.51 (6H, m, 3 × CH_2 of THP), 1.45 (3 H, d, *J* 7.0, CH_3CH); δ (minor) = 4.72–4.67 (1 H, m, OC*H*O), 4.21 (1 H, q, *J* 7.0, OC*H*CO_2Me), 3.94–3.81 (1 H, m, C*H*HOCH), 3.74 (3 H, s, OCH_3), 3.53–3.43 (1 H, m, CH*H*OCH), 1.90–1.51 (6 H, m, 3 × CH_2 of THP), 1.39 (3 H, d, *J* 7.0, CH_3CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ (major) = 173.9, 97.6, 69.9, 62.5, 51.9, 30.4, 25.3, 19.2, 18.8; δ (minor) = 173.7, 98.3, 72.4, 62.5, 51.9, 30.4, 25.3, 19.2, 18.0; *m*/*z* (CI) 189.31 $[M + H]^+$, 211.16 $[M + Na]^+$; *m*/*z* (EI) found 189.1130 ($[M + H]^+$ $C_9H_{17}O_4$ requires 189.1127).

2-(Prop-1-dibromo-1-ene-3-(*R*)-methyl-3-oxy) tetrahydropyran ether 36. Diisobutylaluminium hydride (19.9 mL, 19.9 mmol) was added dropwise to a stirred solution of ester **34** (3.00 g, 16.0 mmol) in ether (45 mL) at −78 °C under argon. The reaction was stirred for 10 minutes before addition of methanol (0.8 mL) and water (2.0 mL). Rochel salts (150 mL) were added and the mixture was allowed to stir for 1 hour. The aqueous layer was extracted using ether (3 × 50 mL) and the combined organic extract was dried over anhydrous $MgSO_4$ before solvent removal *in vacuo* to yield aldehyde **35**[42] as a colourless oil. This material was used in the next reaction without further analysis or purification.

Triphenylphosphine (16.7 g, 63.8 mmol) was added portionwise over 5 minutes to a stirred solution of carbon tetrabromide (10.6 g, 31.9 mmol) in CH_2Cl_2 (60 mL) at 0°C. After 20 minutes, a solution of crude aldehyde, **35**, in CH_2Cl_2 was added dropwise. The mixture was allowed to stir under argon at 0 °C for a further 30 minutes, before being poured into petroleum ether (1 L). A yellow precipitate formed which was removed *via* filtration through a pad of silica gel. The filtrate was concentrated *in vacuo* to effect the formation of a white precipitate (Ph_3PO) that was removed *via* a second filtration through a pad of silica gel. The solvent was removed *in vacuo* to yield a colourless oil which was purified by silica gel flash column chromatography (petroleum ether : ether 10 : 1 then 5 : 1 then 2 : 1) afforded dibromide **36** (3.39 g, 68 %, 2 steps from ester **34**) as a colourless oil of diastereomeric ratio [5 : 4]; ν_{max}(film)/cm^{-1} 3000–2800, 1617, 1035, 1076; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major) 6.34 (1 H, d, *J* 8.2, C*H*CBr_2), 4.60–4.54 (2 H, m, CH_3C*H*, OC*H*O), 3.91–3.83 (1 H, m, C*H*HO_{ax} of THP), 3.56–3.50 (1 H, m, CH*H*O_{eq} of THP), 1.85–1.78, 1.74–1.68, 1.58–1.50 (6 H, m, 3 × CH_2 of THP), 1.30 (3 H, d, *J* 6.5, CH_3CH); δ (minor) = 6.53 (1 H, d, *J* 8.2, C*H*CBr_2), 4.71–4.69 (1 H, m, OC*H*O), 4.46–4.38 (1 H, m, CH_3C*H*), 3.91–3.83 (1 H, m, CH_2O of THP axial), 3.56–3.50 (1 H, m, CH_2O of THP equatorial), 1.85–1.78, 1.74–1.68, 1.58–1.50 (6 H, m, 3 × CH_2 of THP), 1.25 (3 H, d, *J* 6.5, CH_3CH); ^{13}C NMR (100 MHz) δ (major) = 140.4, 96.5, 90.9, 71.6, 62.9, 30.7, 25.4, 20.1, 19.5; δ (minor) = 141.1, 97.4, 89.2, 73.5, 62.6, 30.7, 25.4, 19.8, 19.1; *m*/*z* (ESI) found 334.9267 ($[M + Na]^+$ $C_9H_{14}O_2Br_2Na$ requires 334.9258).

2-(3-Hydroxy-3-(*R*)-methyl-propyn-1-yl) tetrahydropyran ether 38. A solution of n-butyllithium (1.6 M in hexanes, 10.5 mL, 16.7 mmol) was added dropwise at −78 °C to a stirred solution of dibromide **36** (2.5 g, 7.96 mmol) in THF (60 mL). The mixture was stirred for 30 minutes at −78 °C before addition of tributyltin chloride (2.85 g, 2.4 mL, 8.8 mmol). After stirring for a further 30 minutes, ether (200 mL), then distilled water (200 mL) were added. The aqueous phase was extracted with ether (2 × 100 mL) and brine (100 mL). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford stannane **37** as a pale yellow crude oil. This oil was used without futher purification or characterisation in the next reaction.

A solution of boron trifluoride etherate (3.0 mL, 3.4 g, 23.9 mmol) was added dropwise to a stirred solution of stannane **37** in CH_2Cl_2 (1 mL), at −10 °C. After 15 minutes the reaction was quenched by the addition of a 10 M sodium hydroxide solution (50 mL). Ether (100 mL), then distilled water (100 mL) were added. The aqueous layer was extracted with ether (2 × 100 mL) and the combined organic extracts were washed with brine (100 mL) and dried over anhydrous $MgSO_4$. The product material was filtered before concentration *in vacuo* to afford a pale yellow oil. Purification by repeated flash chromatography on silica gel (petroleum ether : ether, 50 : 1, 10 : 1, 5 : 1, 1 : 1, ether) afforded alkynol **38** (326 mg, 16%) as a pale yellow oil and alkyne byproduct **39** (16%) as a yellow oil; alkynol **38** ν_{max}(film)/cm^{-1} 3398., 3050–2750, 1034, 1082; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major) = 4.63–4.53 (1 H, m, C(Me)*H*OH), 4.29–4.27 (1 H, d, *J* 7.9, C*H*HO_{ax} of THP), 4.00–3.94 (1 H, m, C*H*O), 3.54–3.46 (1 H, m, C*H*HO_{eq} of THP), 1.94 (1 H, dd, *J* 5.0, 2.1, O*H*), 1.84–1.81, 1.71–1.48 (6 H, m, 3 × CH_2 of THP), 1.45 (3 H, d, *J* 6.8, CH_3CH); δ (minor) = 4.63–4.53 (1 H, m, C(Me)*H*OH), 4.29–4.27 (1 H, d, *J* 7.9, C*H*HO_{ax} of THP), 4.00–3.94 (1 H, m, C*H*O), 3.54–3.46 (1 H, m, C*H*HO_{eq} of THP), 1.94 (1 H, dd, *J* 5.0, 2.1, O*H*), 1.84–1.81, 1.71–1.48 (6 H, m, 3 × CH_2 of THP), 1.45 (3 H, d, *J* 6.8, CH_3CH); ^{13}C NMR (100 MHz) δ (major) = 87.1, 83.0, 67.0, 66.7, 58.3, 32.1, 25.6, 21.8, 24.3; δ (minor) = 87.1, 83.0, 67.0, 66.7, 58.3, 32.1, 25.6, 21.8, 24.3; *m*/*z* (EI) found 177.0880 ($[M + Na]^+$ $C_9H_{14}O_2Na$ requires 177.0892); Side product **39** ν_{max}(film)/cm^{-1} 3291, 3000–2800, 1036; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major) = 4.93 (1 H, d, *J* 8.2, OC*H*O), 4.55 (1 H, qd, *J* 6.8, 2.0, CH_3C*H*), 3.85–3.79 (1 H, m, C*H*HO_{ax} of THP), 3.55–3.45 (1 H, m, C*H*HO_{eq} of THP), 2.37 (1 H, d, *J* 2.1, C≡C*H*), 1.87–1.70, 1.65–1.51 (6 H, m, 3 × CH_2 of THP), 1.47 (3 H, d, *J* 6.7, CH_3CH); δ (minor) = 4.77 (1 H, d, *J* 8.2, OC*H*O), 4.46 (1 H, qd, *J* 6.8, 2.0, CH_3C*H*), 4.01–3.96 (1 H, m, C*H*HO_{ax} of THP), 3.55–3.45 (1 H, m, C*H*HO_{eq} of THP), 2.42 (1 H, d, *J* 2.1, C≡C*H*), 1.87–1.70, 1.65–1.51 (6 H, m, 3 × CH_2 of THP), 1.44 (3 H, d, *J* 6.7, CH_3CH); ^{13}C NMR (100 MHz) δ (major) = 95.9, 83.7, 72.4, 62.5, 60.6, 30.5, 25.4, 19.5, 21.8; δ (minor) = 97.1, 84.7, 71.9, 62.2, 60.6, 30.5, 25.4, 19.1, 21.8.

2-(3-Hydroxy-3-(*R*)-methyl-propyl) tetrahydropyran ether 40. A 50% Raney nickel suspension in water (1.8 g) was washed with ethanol (3 × 5 mL) and absolute ethanol (3 × 5 mL), before resuspension in absolute ethanol (6 mL). A solution of alkynol **38** (106 mg, 0.44 mmol) was added to this suspension of catalyst. The solvent was degassed under vacuum then exposed to an atmosphere of hydrogen. The heterogeneous solution was stirred vigorously for 4 hours at room temperature, then the reaction mixture was filtered through a short plug of silica gel. The silica gel was washed with absolute ethanol and the filtrate concentrated *in vacuo* to yield a colourless oil. Purification by silica gel chromatography (petroleum ether : ether 1 : 1) afforded alcohol **40** (21.0 mg, 45%) as a colourless oil; ν_{max}(film)/cm^{-1} 3396, 3050–2750, 1087, 1048; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major) = 4.0–3.96 (1 H, m, OC*H*$(CH_2)_2$CHOH), 3.82–3.75 (1 H, m, C*H*(Me)OH), 3.46–3.38 (1 H, m, C*H*HO_{ax} of THP), 3.28–3.25 (1 H, m, C*H*HO_{eq} of THP), 1.82 (1 H, d, *J* 10.4, O*H*), 1.66–1.20 (10 H, m, 5 × CH_2), 1.17 (3 H, d, *J* 6.2, CH_3); δ (minor) = 4.0–3.96 (1 H, m, OC*H*$(CH_2)_2$CHOH), 3.82–3.75 (1 H, m, C*H*(Me)OH), 3.46–3.38 (1 H, m, C*H*HO_{ax} of THP), 3.28–3.25 (1 H, m, C*H*HO_{eq} of THP), 1.82 (1 H, d, *J* 10.4, O*H*), 1.66–1.20 (10 H, m, 5 × CH_2), 1.17 (3 H, d, *J* 6.2, CH_3); ^{13}C NMR (100 MHz) δ (major) = 79.0, 68.5, 67.6, 35.4, 32.6, 31.8, 26.0, 23.5, 23.5; δ (minor) = 79.0, 68.5, 68.2, 36.3, 32.7, 32.1, 26.0, 23.5, 23.5; *m*/*z* (CI) 159.08 $[M + H]^+$; *m*/*z* (EI) found 181.1200 ($[M + Na]^+$ $C_9H_{18}NaO_2$ requires 181.1204).

2-(Prop-1-yne-3-oxy)-6-*n*-hexyl tetrahydropyran ether 43. KHMDS (0.5 M in toluene, 3.2 mL, 1.6 mmol) was added dropwise to a solution of lactol **42**[19] (0.27 g, 1.45 mmol) in THF (3.2 mL) at −78 °C. The solution was stirred at −78 °C for 30 min, then propargyl bromide (0.52 g, 4.4 mmol) was added dropwise *via* syringe. The reaction was then allowed to warm to rt and stirred for a further 2 h. The reaction mixture was diluted with ether (50 mL), then quenched by the addition of water (5 mL). The organic phase was separated, washed with aqueous hydrochloric acid solution (3 M, 2 × 15 mL) and saturated sodium chloride solution (20 mL), dried ($MgSO_4$) and the volatiles removed *in vacuo* to yield a yellow oil that was purified by silica gel chromatography (petroleum ether : ethyl acetate 50 : 1) to give alkyne **43** (0.28 g, 85%); ν_{max}(film)/cm^{-1} 3312, 2925, 2856, 1460, 1091, 1034, 950; ^{1}H NMR (400 MHz, $CDCl_3$) δ (isomer a) = 5.28 (1 H, d, *J* 8.7, OC*HO*), 4.22 (1 H, d, *J* 2.2, OC*H*HCCH), 4.18 (1 H, d, *J* 2.2, OCH*H*CCH), 4.02 (1 H, m, C_7H_{15}C*H*O), 2.38 (1 H, t, *J* 2.2, CC*H*), 2.12–1.83 (3 H, m, CH_2C(O)O, C_7H_{15}C(O)C*H*H), 1.75–1.52 (1 H, m, C_7H_{15}CH(O)CH*H*), 1.52–1.20 (12 H, m, 5 × CH_2), 0.88 (3 H, t, *J* 6.5, CH_3); δ (isomer b) = 5.21 (1 H, d, *J* 8.9, OC*HO*), 4.22 (1 H, d, *J* 2.2, OC*H*HCCH), 4.18 (1 H, d, *J* 2.2, OCH*H*CCH), 4.02 (1 H, m, C_7H_{15}C*H*O), 2.38 (1 H, t, *J* 2.2, CC*H*), 2.12–1.83 (3 H, m, CH_2C(O)O, C_7H_{15}C(O)C*H*H), 1.75–1.52 (1 H, m, C_7H_{15}CH(O)CH*H*), 1.52–1.20 (12 H, m, 5 × CH_2), 0.88 (3 H, t, *J* 6.5, CH_3); ^{13}C NMR (100 MHz) δ (mix of isomers) = 102.4, 102.0, 81.3, 80.0, 78.4, 73.6, 53.8, 53.4, 37.5, 35.4, 32.1, 31.8, 29.6, 29.2, 29.1, 26.1, 22.63, 22.62, 14.05, 14.04; *m*/*z* (ESI) found 247.1674 ([M + Na]$^+$ $C_{12}H_{24}O_2Na$ requires 247.1674).

2-(3-Hydroxy-propyn-1-yl)-6-*n*-hexyl tetrahydropyran ether 45. The same procedure was used as for compound **2** to give stannane **44** from alkyne **43** as a pale yellow oil. This was used in the subsequent reaction without further purification. The same procedure was used as for compound **3** to give alkynol **45** from stannane **44** as a colourless oil (0.34 g, 78%, 2 steps from alkyne **43**), obtained after repeated flash column chromatography on silica gel (petroleum ether : ether 10 : 1, then 5 : 1, then 2 : 1); ν_{max}(film)/cm^{-1} 3384, 2926, 2857, 2342, 1458, 1331, 1019; ^{1}H NMR (400 MHz, $CDCl_3$) δ (isomer a) = 4.53 (1 H, dd, *J* 7.0 5.9, OC*H*CC), 4.29 (2 H, s, CH_2OH), 3.84–3.80 (1 H, m, C_7H_{15}C*HO*), 2.23–2.08 (1 H, m, C*H*HCHOCC), 2.01–1.94 (2 H, m, C*H*HCHOCC, C_7H_{15}CHOC*H*H), 1.81 (1 H, s, O*H*), 1.70–1.51 (1 H, m, C_7H_{15}CHOCH*H*), 1.50–1.40 (1 H, m, $CH_3(CH_2)_5$C*H*H), 1.38–1.29 (1 H, m, $CH_3(CH_2)_5$CH*H*), 1.28 (10 H, m, 5 × CH_2), 0.87 (3 H, t, *J* 6.5, CH_3); (isomer b) = 4.68 (1 H, dd, *J* 6.8 6.2, OC*H*CC), 4.29 (2 H, s, CH_2OH), 4.07–4.03 (1 H, m, C_7H_{15}C*HO*), 2.23–2.08 (2 H, m, C*H*HCHOCC, C_7H_{15}CHOC*H*H), 2.01–1.94 (1 H, m, C*H*HCHOCC), 1.81 (1 H, s, O*H*), 1.70–1.51 (1 H, m, C_7H_{15}CHOCH*H*), 1.50–1.40 (1 H, m, $CH_3(CH_2)_5$C*H*H), 1.38–1.29 (1 H, m, $CH_3(CH_2)_5$-CH*H*), 1.28 (10 H, m, 5 × CH_2), 0.87 (3 H, t, *J* 6.5, CH_3); ^{13}C NMR (100 MHz) δ (mix of isomers) = 86.1, 86.0, 82.7, 82.6, 80.5, 79.3, 67.8, 67.6, 51.2, 51.1, 35.9, 35.5, 33.4, 33.2, 31.8, 31.7, 31.2, 31.1, 29.6, 29.6, 29.2, 29.2, 26.2, 26.1, 22.6, 14.0; *m*/*z* (ESI) found 247.1666 [M + Na]$^+$ $C_{12}H_{24}O_2Na$ requires 247.1674).

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