Tetrahedron 67 (2011) 5011–5023

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Asymmetric synthesis of the C(6–18) bis(tetrahydropyran)spiroacetal fragment of the lituarines

Jeremy Robertson *, Christopher North, Jessie E.R. Sadig

Department of Chemistry, Chemistry Research Laboratory, University of Oxford, Mansfield Road, Oxford OX1 3TA, UK

ARTICLE INFO

Article history:
Received 1 February 2011
Accepted 29 March 2011
Available online 8 April 2011

Keywords:
Achmatowicz
Asymmetric
Cyanohydrin
Diastereoselective
Oxy-Michael

ABSTRACT

We describe efforts to achieve a multigram synthesis of the tricyclic spiroacetal core of the lituarines based on the addition of acyl anion equivalent to 4-(2-furyl)butan-2-one (**18**). We report the first cases of chemoselective Achmatowicz reaction in the presence of a second furan ring that lacks an α-hydroxyl group. The use of lithiated methoxyallene provides an efficient one-step conversion of ketone **18** into a tricyclic Diels–Alder adduct (**27**). In the final route, asymmetric cyanosilylation of ketone **29** achieved the construction of the stereogenic C(12) 3°-alcohol centre. Subsequent butenylation, diastereoselective reduction of keto-alcohol (+)-**33** and alkene cross metathesis set up an oxy-Michael reaction to close the C(8–12) tetrahydropyran ring. The second ring-closure, which completed the route, was achieved by oxidative spirocyclisation following our earlier work.

1. Introduction

The occurrence in nature of the spiro[furan-2,2′-pyrano[3,2-*b*]pyran] structural motif is limited to marine metabolites of the okadaic acid type[1] and the lituarines[2] (Fig. 1). The latter are a group of three macrolactones isolated from the New Caledonian sea pen *Lituaria australasiae*, with cytotoxicity towards KB cells (IC_{50}=1.0–6.0 ng mL^{-1}) and growth inhibitory effects against the fungi *Fusarium oxysporum*, *Helminthosporium turscicum*, *Penicillium italicum* and *Phytophtora parasitica*. Their structures were proposed on the basis of extensive NMR investigations as samples of the natural products suitable for X-ray crystallographic analysis were not available. However, Smith's group completed total syntheses of the structures proposed for lituarines B and C and found that the spectroscopic data for these compounds did not match those reported.[3] Thus, more recent synthetic efforts have been aimed at securing the correct structures for the lituarines.

In Smith's total synthesis, the C(8–12) tetrahydropyran (**2**, Scheme 1) was formed by acid-mediated O-cyclisation onto allylic epoxide **1** with inversion of stereochemistry at the newly-formed C(12) centre. The second tetrahydropyranyl ring, comprising carbons C(11–15), was then obtained by classical ketodiol spiroacetalisation (**3**→**4**) in a reaction that had to be run at high dilution with a short reaction time in order to minimise epimerisation at the C(15) and C(16) centres.

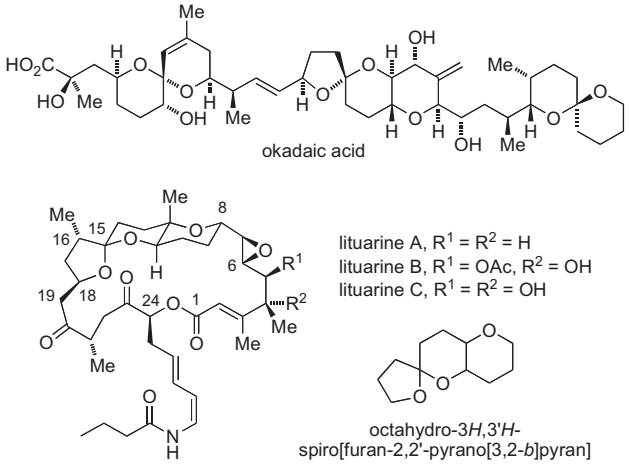
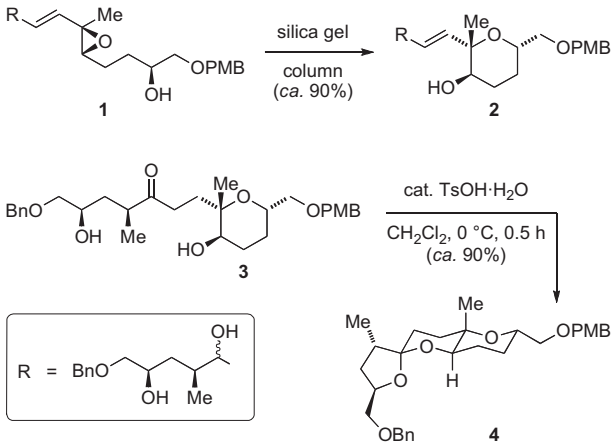


Fig. 1. Natural products containing the spiro[furan-2,2′-pyrano[3,2-*b*]pyran] structural motif.

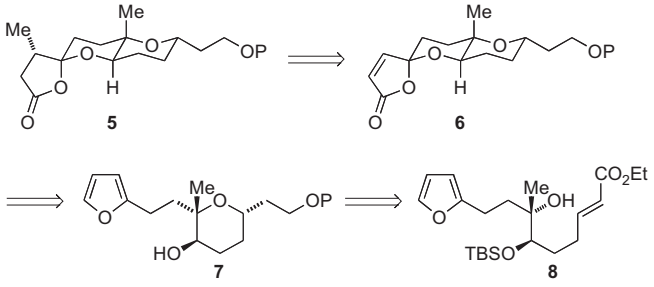
* Corresponding author. E-mail address: jeremy.robertson@chem.ox.ac.uk (J. Robertson).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.03.116



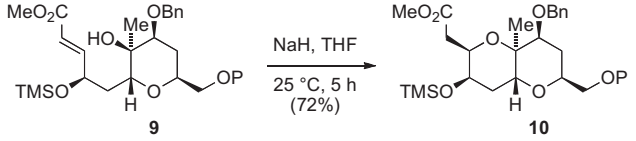
Scheme 1. Key steps in Smith's route to the lituarine tricyclic spiroacetal.

Our own approach to the lituarine tricyclic spiroacetal (**5**, Scheme 2), initiated before Smith's first publications on the subject, was shaped by concerns that we would not be able to achieve spiroacetalisation in a sufficiently stereoselective manner. Thus, we opted to introduce the C(16) methyl substituent by kinetic 1,4-addition to butenolide spiroacetal **6**, which, in turn, was expected to exhibit an essentially complete preference for an axial disposition of the butenolide C–O acyl bond. Shown retrosynthetically, this butenolide would arise by furan oxidative spirocyclisation of tetrahydropyran **7**, a general transformation known since the late 1950s[4] and developed for application in natural product synthesis notably by Bohlmann,[5] Kociensky[6] and more recently by Vassilikogiannakis.[7]



Scheme 2. An approach to the lituarine tricyclic spiroacetal based on oxy-Michael cyclisation and furan oxidative spirocyclisation [P=*t*-BuPh$_2$Si].

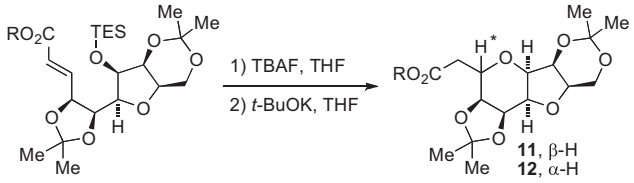
Of the various possibilities for producing the oxidative spirocyclisation substrate (**7**) we selected the oxy-Michael cyclisation of enoate **8**. When we initiated our work the only precedent that we could find for the stereoselective cyclisation of a 3°-alcohol onto an α,β-unsaturated ester was in Nicolaou's assembly of the J-ring of brevetoxin B by base-treatment of alcohol **9** to give bis(tetrahydropyran) **10** (Scheme 3). The stereochemical outcome in this transformation was assumed to be thermodynamically-controlled, leading to an equatorial CH_2CO_2Me substituent.[8]



Scheme 3. Oxy-Michael reaction in Nicolaou's synthesis of brevetoxin B intermediates [P=*t*-BuPh$_2$Si].

Although the oxy-Michael reaction with 3°-alcohols is scarcely precedented, the reaction with 2°-alcohols is a classic strategy for constructing tetrahydropyrans in natural product synthesis. Among over 90 publications referring to the transformation (with enoates), examples include applications to: ambructin,[9] aspergillides A and B,[10] bistramides A and D,[11] brevetoxin B,[12] ciguatoxin fragments,[13] clavosolides A and B,[14] decarestrictine L,[15] gambierol,[16] goniothalesdiol A,[17] halichondrins,[18] herboxidiene,[19] lasonolide A,[20] leucascandrolide A,[21] miyakolide,[22] montanacin,[23] mucocin,[24] neopeltolide,[25] phorboxazoles A and C,[26] polycavernoside A,[27] pyranicin,[28] spirastrellolide A,[29] spongistatin 1,[30] vermiculine[31] and zampanolide.[32]

In general, the geometry of the enoate double bond dictates the stereochemical outcome although the stereoselectivity may vary depending on the reaction conditions. Thus, the most common outcome is for *E*-enoates to cyclise kinetically to give the *trans*-2,6-disubstituted tetrahydropyrans, with the cis-diastereomers predominating under equilibrating conditions. A single example, taken from Yonemistu's PM3 study of the oxy-Michael cyclisation, shows kinetic cyclisation to *trans*-product **11** (Scheme 4), which then converts to the *cis*-product **12** following equilibration with *t*-BuOK.[33] The few reported examples of cyclisations of *Z*-enoates usually afford *cis*-2,6-disubstituted tetrahydropyrans. In both *E*- and *Z*-substrates, substituents in the allylic position can perturb these trends.



Scheme 4. Yonemitsu's results in the context of halichondrin B synthesis.

With this background we were confident that the cyclisation of hydroxy enoate **8** to tetrahydropyran **7** could be achieved and, indeed, this key step, the oxidative spirocyclisation and the stereoselective conjugate addition of methyl, giving tricycle **5**, all proceeded as planned.[34] This intermediate was taken forward to an advanced lituarine B and C precursor (**14**, Fig. 2) in readiness for macrocyclisation and introduction of the C(24) side-chain.[35]

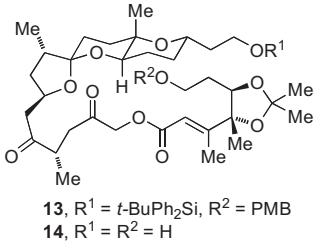
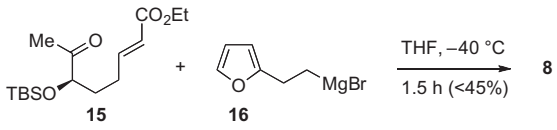


Fig. 2. Advanced intermediates towards lituarines B and C.

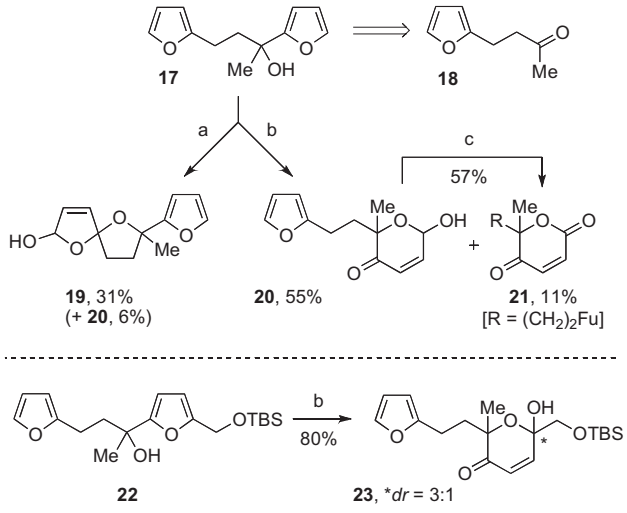
The later stages of our lituarine synthetic route (from **8** all the way through to diol **14**) were reliable but further progress was hampered because of difficulties in scaling up our published route to intermediate **8**. On a multigram scale the addition of organometallics of the form **16** to ketone **15** (Scheme 5) proved to be particularly problematic and the desired product was generated along with the other diastereomer (in variable ratio) and various cyclisation and degradation products, all close-running on TLC. In this paper we describe a more practically reproducible route that allowed us to prepare 1.5 g of tricycle **5** in the first run.[36]



Scheme 5. Low-yielding step in the first route to oxy-Michael precursor **8**.

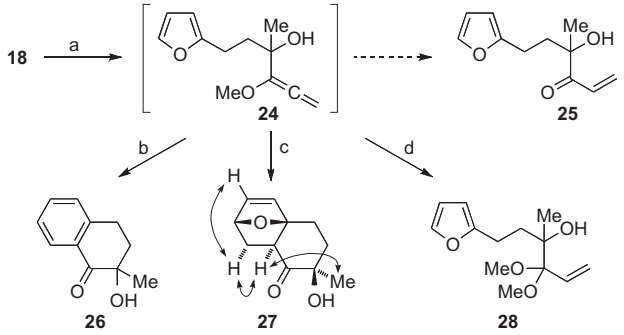
2. Results

The initial challenge was to by-pass the low-yielding bond formation in Scheme 5, corresponding to the C(12–13) bond in the lituarines, and we soon identified furan derivative **18** (Scheme 6) as a starting material, which was readily available[37] on large scale and, which already contained the intact C(12–13) bond. In a preliminary study[38] we envisaged formation of the C(12) 3°-alcohol centre by addition of furyllithium, giving difuran derivative **17** and subsequent Achmatowicz reaction[39] directed by the hydroxyl group.[40] Our preferred peracid conditions for furan oxidation generated spiroacetal **19** by oxidation of the more electron rich furan, distal to the hydroxyl centre, along with a small amount of the desired product (**20**) and recovered starting material. Fortunately, application of Sharpless' conditions for directed epoxidation[41] gave the Achmatowicz product (**20**) and some dione **21**. This idea was applied successfully to substrate **22**, incorporating a C(8) substituent, which was prepared by addition of lithiated 2-[(*tert*-butyldimethylsilyloxy)methyl]furan[42] to ketone **18**. In this case the hydroxypyranone product **23** was formed as a 3:1 mixture of diastereomers but attempts to elaborate this selectively and efficiently to an intermediate similar to **7** failed and work on this route was discontinued.



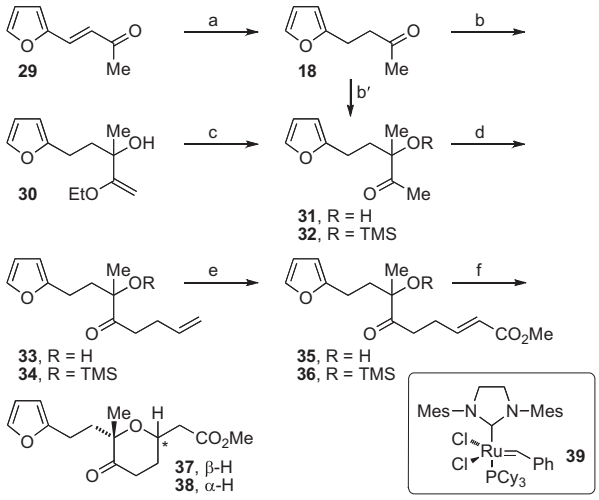
Scheme 6. Reagents: (a) MCPBA, CH_2Cl_2, 0 °C→rt; (b) 0.25 mol % $VO(acac)_2$, *t*-BuOOH, CH_2Cl_2, 20 °C; (c) 10 mol % TPAP, NMO, CH_2Cl_2, 20 °C.

Despite our inability to progress enones **21** or **23** satisfactorily, the use of a lithiated enol ether to construct the 3°-alcohol centre was considered sound and the next development of the proposal evaluated the organolithium reagent derived[43] from methoxyallene. Hydrolysis of the expected adduct **24** (Scheme 7) was expected to lead to enone **25** that we considered could be elaborated to intermediate **8** or its equivalent by conjugate addition to the enone and ketone reduction. Adduct **24** was generated cleanly but could not be isolated as a pure compound owing to its instability on silica or alumina and it was subsequently taken on crude into the hydrolysis conditions. Hydrolysis with dilute hydrochloric acid led to tricycle **27** by intramolecular furan Diels–Alder reaction; the stereochemistry—established by the key NOE correlations shown—corresponds to an *exo*-Diels–Alder transition state. Given the relative ease with which this reaction proceeded we speculate that the enone carbonyl is protonated at the time of cycloaddition. More forcing conditions led to the dehydration product **26**.[44] Milder acid sources led to much the same result under aqueous conditions but the use of camphorsulfonic acid in methanol gave a stable product, acetal **28**.



Scheme 7. Reagents: (a) 1-methoxypropadiene/BuLi, THF, −78 °C; (b) aq HCl (5.0 M), CH_2Cl_2, 0 °C (39%); (c) aq HCl (1.0 M), THF, 0 °C (86%); (d) 1.0 mol % CSA, MeOH, 0→20 °C (58%). [arrows in **27** indicate key NOEs].

Whilst this intermediate (**28**) may ultimately have proven useful, the need to prevent intramolecular Diels–Alder reaction by blocking the carbonyl group created inefficiencies. Use of the simpler organolithium derived[45] from ethyl vinyl ether avoided this problem by omitting the enone C=C, and methyl ketone **31** (Scheme 8) was obtained reliably in good yield after hydrolysis of adduct **30**. This ketone was taken forward by allylation either with the hydroxyl function free or protected as the TMS-ether **32**. Cross metathesis of γ,δ-enones **33** or **34** with methyl acrylate did not proceed at rt with Grubbs II catalyst (**39**) but in dichloromethane at reflux the reaction was essentially complete within 0.5–3 h depending on scale; in both cases, essentially complete *E*-selectivity was observed.

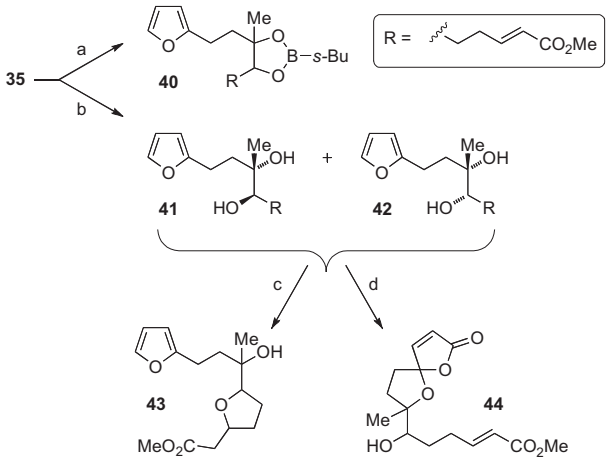


Scheme 8. Reagents: (a) H_2, 0.3 mol % Pd/C (5%), EtOAc, 20 °C (66%); (b) ethyl vinyl ether/*t*-BuLi, THF, −78→20 °C (83%); (b′) (→**32**) ethyl vinyl ether/*t*-BuLi, THF, −78→20 °C then TMSCl, NaI (71%); (c) (→**31**) TsOH, THF, 20 °C (87%); (d) LDA, THF, −78 °C then allyl iodide, −78→20 °C (**33**, 58% from **31**) or LDA, THF, 0 °C then allyl bromide, 0→20 °C (**34**, 75% from **32**); (e) methyl acrylate, 5.0 mol % **39**, CH_2Cl_2, 40 °C (**35**, 87% from **33**; **36**, 57% from **34**); (f) KHMDS, THF, −78→20 °C (69%, **37** and **38**, dr=3:4).

In our earlier work[34] the oxy-Michael reaction (from **8**) was most reliably achieved under equilibrating conditions with LHMDS in THF at −40 °C, generating the tetrahydropyran in 65% yield as a single diastereomer. These and similar conditions led to recovery of

starting material when applied to substrate **35** in which the CH(OTBS) function was replaced by C=O. The best that could be achieved was with a slight excess of KHMDS added at −78 °C and warming to rt; even then, only a moderate yield of a 3:4 diastereomeric mixture of tetrahydropyranones **37** and **38** was obtained.

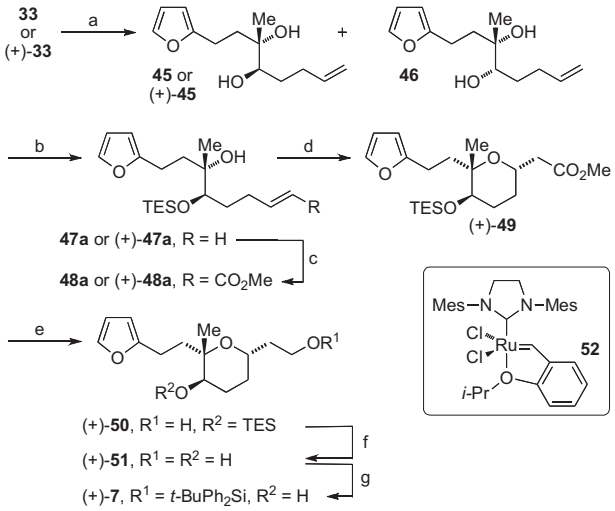
We next attempted to invert the order of steps: ketone reduction then oxy-Michael reaction. Stereoselective reduction of the ketone in substrate **35** turned out to be non-trivial. The simplest reagent, $NaBH_4$, led to non-selective reduction (dr=1.0–1.6:1) and partial oxy-Michael cyclisation of either hydroxyl group. Tetramethylammonium triacetoxyborohydride was an ineffective reducing agent for this hindered ketone, and the combination of L-Selectride and $ZnCl_2$ led to efficient reduction but the initially-formed borate adduct (**40**, Scheme 9) could not be decomposed without disrupting the furan ring. Finally, based on Nakata's precedent,[46] $Zn(BH_4)_2$ was found to give a 4.0–5.0:1 ratio of diastereomers in favour of the desired isomer (**41**) in acceptable yield in trial reactions. Predictably, diol mixture **41** and **42** cyclised to give the tetrahydrofurans **43** and **44** under basic and oxidative conditions, respectively, therefore protection of the 2°-hydroxyl group was indicated (in **41**/**42**). Installation of a *tert*-butyldimethylsilyl group, to give the methyl ester analogue of desired intermediate **8**, was an inefficient process, with yields never surpassing ca. 30%.



Scheme 9. Reagents: (a) $ZnCl_2$, L-Selectride, CH_2Cl_2, −78 °C (65%); (b) $Zn(BH_4)_2$, THF, −20 °C (53%, **41** and **42**, dr=4:1); (c) LHMDS, THF, −40→20 °C (64%); (d) MCPBA, CH_2Cl_2, 0 °C then 1.0 mol % TPAP, NMO, 20 °C (38%).

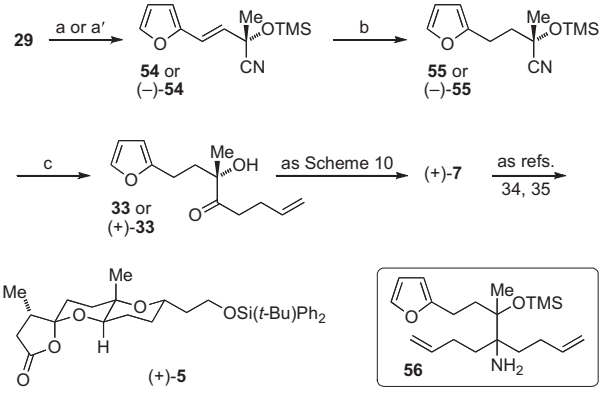
At this point, we decided to defer the cross metathesis step until after the hydroxyketone functionality in **33** had been adjusted to the correct mono-protected diol diastereomer. Rejecting TBS in favour of the less sterically-demanding TES group improved the protection step and intermediate **47** (Scheme 10) was obtained, initially as a 4:1 diastereomeric mixture. Cross metathesis trials with separated diastereomer **47a** showed that switching to the Hoveyda–Grubbs II catalyst **52** allowed the catalyst loading to be reduced to 1% (from 5% with Grubbs II) and slightly increased the yield. The product **48a** was taken through our reported oxy-Michael cyclisation, desilylation and ester reduction steps to provide known intermediate **7** whose spectroscopic data correlated with enantiomerically enriched material,[34] thus confirming the sense of diastereoselective reduction in keto-alcohol **33**.

These studies had mapped out a reproducible route for the production of racemic **7** via **33** but the prospects appeared limited for modifying the organometallic addition step in order to yield enantiomerically enriched keto-alcohol **31**. However, the asymmetric addition of cyanide to methyl ketones is reasonably well-established, particularly for electronically-differentiated



Scheme 10. Reagents: (a) $Zn(BH_4)_2$, THF, 0 °C (dr=4:1); (b) TESCl, imidazole, DMF, 20 °C [(+)-**47a**, 42% from (+)-**33**]; (c) methyl acrylate, 1.0 mol % **52**, CH_2Cl_2, 40 °C [(+)-**48a**, 82%]; (d) LHMDS, THF, −78→−40 °C [76% based on recovered (+)-**48a**]; (e) DIBAL, THF, 0 °C (quant.); (f) TBAF, THF, 20 °C; (g) *t*-$BuPh_2SiCl$, imidazole, DMF, 20 °C [76% from (+)-**50**]. [Yields for the racemic route appear in the Experimental section.].

α,β-unsaturated substrates. After scoping a few of the alternatives, we soon settled on Feng's use of sodium phenylglycinate (**53**) as a Lewis base additive for asymmetric cyanosilylation[47] because of the ready availability of both enantiomers of the catalyst. Application of the reported conditions to ketone **18** with (+)-**53** led, unsurprisingly, to racemic product (**55**, Scheme 11); however, with enone **29**, ees up to 90% could be achieved with high isolated yields. Variability in the ee was attributed to its sensitivity to the levels of water present in the system; nevertheless, in our hands this procedure proved sufficiently reliable that the reaction carried out on a 0.3 mol scale gave the product in 85% ee although the reaction did not run to completion on this scale.



Scheme 11. Reagents: (a) TMSCN, K_2CO_3, DMF, 20 °C (98%); (a′) TMSCN, (−)-**53**, CF_3CH_2OH, THF, −20 °C (43%); (b) H_2, 0.3 mol % Pd/C (5%), EtOAc, 20 °C [**55**, 96%; (−)-**55**, 93%, ee=85%]; (c) 4-butenyllithium, THF, −78→20 °C [**33**, 64%; (+)-**33**, 44%].

Following uneventful hydrogenation [→(−)-**55**] the route connected with the earlier route at ketone **33** by addition of 3-butenyllithium, which was reasonably efficient when only a slight excess (1.3–1.5 equiv) of organolithium was employed. In the racemic series we had noted that addition of a threefold excess, or more, of the organometallic resulted in double addition to produce amine **56**. Completion of the route to intermediate (+)-**7** on large scale was marred only by the oxy-Michael reaction that gave a ca. 50% conversion to the tetrahydropyran, the rest being starting material. Following our previous work, the second tetrahydropyran

ring was formed by oxidative spirocyclisation to give 3.7 g of tricycle (+)-**6**[34] and then 1.5 g of (+)-**5**.[35]

3. Conclusion

Our whole lituarine programme, now running for almost a decade, has been hampered by difficulties in scaling to gram quantities reactions that worked efficiently on multi-milligram scale. The route summarised in Schemes 10 and 11, above, satisfied our immediate needs, with the low-yielding steps [**29**→(−)-**54**, (−)-**55**→(+)-**33** and (+)-**48a**→(+)-**49**] returning mostly unreacted starting materials to account for the mass balance in each case. However, Smith's report, during the course of this work,[3] that the structures of the lituarines are incorrectly assigned, adds to the list of 'molecules that were never there'[48] and a re-evaluation of the original structural data needs to be undertaken before further efforts are expended on this endeavour.

4. Experimental section

4.1. 2,4-Di(furan-2-yl)butan-2-ol (17)

To a stirred solution of furan (0.3 mL, 3.98 mmol) in THF (2.5 mL) at 0 °C was added TMEDA (0.6 mL, 3.98 mmol) followed by butyllithium (2.5 mL, 1.6 M solution in hexanes, 4.0 mmol). After stirring for 0.5 h, ketone **18**[37] (0.50 g, 3.62 mmol) was added and the solution stirred for 2 h. The reaction was quenched with water (50 mL) and the aqueous phase was extracted with ether (2×50 mL). The combined organic phases were washed with satd aq $NaHCO_3$ (2×50 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 5:1) afforded the *title compound* (**17**) as a pale yellow oil (0.57 g, 77%). R_f 0.21 (petrol/ether, 5:1); ν_{max} (thin film)/cm^{-1} 3416br, 2980m, 1597m, 1507m, 1451m, 1372m, 1149m, 1071m, 1010m; δ_H (400 MHz, $CDCl_3$) 1.59 (3H, s, CH_3), 2.04 (1H, s, OH), 2.18–2.23 (2H, m, CH_2C(OH)), 2.61–2.65 (2H, m, FuCH_2), 5.98 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.24 (1H, dd, *J* 3.0, 1.0 Hz, Fu'(H-3)), 6.27 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 6.33 (1H, dd, *J* 3.0, 2.0 Hz, Fu'(H-4)), 7.30 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)), 7.37 (1H, dd, *J* 2.0, 1.0 Hz, Fu'(H-5)); δ_C (100 MHz, $CDCl_3$) 23.0 (CH_2), 26.7 (CH_3), 39.6 (CH_2), 71.3 (C), 104.7 (2× CH), 110.1 (2× CH), 140.9 (CH), 141.7 (CH), 155.6 (C), 159.0 (C); HRMS (ESI^+) found 229.0838, $C_{12}H_{14}NaO_3$ (MNa^+) requires 229.0835.

4.2. 2-[2-(Furan-2-yl)ethyl]-6-hydroxy-2-methyl-2*H*-pyran-3(6*H*)-one (20)

To a stirred solution of difuran **17** (1.0 g, 4.85 mmol) in dichloromethane (20 mL) was added *tert*-butylhydroperoxide (1.0 mL, ca. 5.5 M in decane, ca. 5.50 mmol) and $VO(acac)_2$ (3.0 mg, 11.3 μmol). After 2 h the reaction mixture was poured into water (50 mL) and the aqueous phase extracted with dichloromethane (3×50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 2:1) afforded the *title compound* (**20**) as a pale yellow oil and as a 1:1 mixture of inseparable diastereomers (A and B; 0.59 g, 55%). R_f 0.09 (petrol/ether, 2:1); ν_{max} (thin film)/cm^{-1} 3417br, 2934m, 1687s, 1598m, 1509m, 1448s, 1376m, 1261m, 1148s; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, s, CH_3, A), 1.51 (3H, s, CH_3, B), 1.87–2.03 (2H, m) and 2.19–2.37 (2H, m, CH_2C(CH_3), A and B), 2.58–2.82 (4H, m, FuCH_2, A and B), 3.78 (2H, br s, OH, A and B), 5.71–5.72 (2H, m, C*H*OH, A and B), 5.96 (2H, dd, *J* 3.0, 1.0 Hz, Fu(H-3), A and B), 6.06–6.09 (2H, m, =CHCO, A and B), 6.24–6.26 (2H, m, Fu(H-4), A and B), 6.87 (1H, dd *J* 4.0, 2.5 Hz, C*H*=CHCO, B), 6.89 (1H, dd, *J* 4.0, 2.5 Hz, C*H*=CHCO, A), 7.27–7.28 (2H, m, Fu(H-5), A and B); δ_C (100 MHz, $CDCl_3$) 21.6 (CH_3, A), 22.0 and 22.2 (CH_2, A and B), 25.5 (CH_3, B), 35.8 (CH_2, B), 36.8 (CH_2, A), 81.1 (C, A and B), 87.7 (CH, A and B), 105.0 (CH, A and B), 110.1 (CH, A and B), 126.5 and 126.9 (CH, A and B), 140.9 and 140.1 (CH, A and B), 145.3 and 146.4 (CH, A and B), 155.1 and 155.4 (C, A and B), 198.5 and 198.7 (C, A and B); HRMS (ESI^+) found 245.0787, $C_{12}H_{14}NaO_4$ (MNa^+) requires 245.0784.

4.3. 6-[2-(Furan-2-yl)ethyl]-6-methyl-2*H*-pyran-2,5(6*H*)-dione (21)

To a stirred solution of pyranone **20** (0.58 g, 2.61 mmol) in dichloromethane (20 mL) was added NMO (1.07 g, 9.11 mmol) and, after stirring for 10 min, TPAP (93 mg, 0.26 mmol) was added and the mixture stirred for 3 h. The reaction mixture was passed through a short plug of silica and the filtrate concentrated in vacuo. Flash chromatography (petrol/ether, 1:1) afforded the *title compound* (**21**) as a pale yellow oil (0.33 g, 57%). R_f 0.28 (petrol/ether 1:1); ν_{max} (thin film)/cm^{-1} 3119m, 2981s, 2934s, 1694s, 1622s, 1598s, 1508s, 1450s, 1375s, 1292s, 1011s; δ_H (400 MHz, $CDCl_3$) 1.61 (3H, s, CH_3), 2.13–2.20 (1H, m) and 2.43–2.49 (1H, m, CH_2C(CH_3)), 2.63–2.80 (2H, m, FuCH_2), 5.96 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.24 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 6.65 (1H, d, *J* 10.0 Hz, =CHCO), 6.87 (1H, d, *J* 10.0 Hz, C*H*=CHCO), 7.29 (1H, dd, *J* 2.0. 1.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 22.9 (CH_2), 26.3 (CH_3), 37.9 (CH_2), 89.1 (C), 106.1 (CH), 110.1 (CH), 135.1 (CH), 137.2 (CH), 141.3 (CH), 153.4 (C), 160.4 (C), 195.3 (C); HRMS (CI, NH_3) found 221.0817, $C_{12}H_{13}O_4$ (MH^+) requires 221.0808. Also obtained as a side-product in the preparation of **20**.

4.4. 2-{5-[(*tert*-Butyldimethylsilyloxy)methyl]furan-2-yl}-4-(furan-2-yl)butan-2-ol (22)

To a stirred solution of 2-[(*tert*-butyldimethylsilyloxy)methyl] furan[42] (1.0 g, 4.71 mmol) in THF (10 mL) at −78 °C was added butyllithium (3.2 mL, 1.6 M solution in hexanes, 5.12 mmol) dropwise and the mixture stirred for 1.5 h. The solution was then warmed to 0 °C, stirred for 0.5 h and re-cooled to −78 °C. Ketone **18**[37] (0.59 g, 4.28 mmol) was added dropwise and the mixture stirred for 1.5 h at −78 °C and 0.5 h at rt. Water (30 mL) and ether (20 mL) were added; the aqueous phase was extracted with ether (2×20 mL) and the combined organic portions washed successively with water (2×20 mL) and brine (20 mL). The solution was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 8:1) afforded the *title compound* (**22**) as a pale yellow oil (0.84 g, 56%). R_f 0.18 (petrol/ether, 4:1); ν_{max} (thin film)/cm^{-1} 3423br, 2930m, 2858m, 1256m, 1077m, 1009m; δ_H (400 MHz, $CDCl_3$) 0.09 (6H, s, $Si(CH_3)_2$), 0.91 (9H, s, $C(CH_3)_3$), 1.58 (3H, s, CH_3C(OH)), 2.10 (1H, br s, OH), 2.17–2.22 (2H, m, CH_2C(OH)), 2.62–2.66 (2H, m, FuCH_2), 4.62 (2H, s, FuCH_2OTBS), 5.96–5.97 (1H, m, Fu(H-3)), 6.17 (2H, s, Fu′(H-3) and Fu′(H-4)), 6.27 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.29–7.30 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) −5.2 (2× CH_3), 18.4 (C), 23.0 (CH_2), 25.8 (3× CH_3), 26.7 (CH_3), 39.5 (CH_2), 58.2 (CH_2), 71.3 (C), 104.6 (CH), 105.3 (CH), 107.8 (CH), 110.1 (CH), 140.8 (CH), 153.4 (C), 155.7 (C), 158.6 (C); HRMS (ESI^+) found 373.1806, $C_{19}H_{30}NaO_4Si$ [M (^{28}Si)Na^+] requires 373.1806.

4.5. 6-(*tert*-Butyldimethylsilyloxy)methyl-2-[2-(furan-2-yl) ethyl]-6-hydroxy-2-methyl-2*H*-pyran-3(6*H*)-one (23)

To a stirred solution of difuran **22** (0.84 g, 2.40 mmol) in dichloromethane (10 mL) was added *tert*-butylhydroperoxide (0.50 mL, ca. 5.5 M in decane, ca. 2.75 mmol) and $VO(acac)_2$ (1.5 mg, 5.66 μmol). After 3 h the reaction mixture was poured into water (10 mL), the aqueous phase was extracted with dichloromethane (3×20 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 3:1) afforded the *title compound* (**23**) as a colourless oil and as a 3:1 ratio of diastereomers (0.70 g, 80%). Data for major diastereomer: R_f

0.20 (petrol/ether, 3:1); ν_{max} (thin film)/cm^{-1} 3424br, 2931m, 2858m, 1689m, 1111m, 838m; δ_H (400 MHz, $CDCl_3$) 0.11–0.14 (6H, m, Si(CH_3)$_2$), 0.93 (9H, s, C(CH_3)$_3$), 1.35 (3H, s, CH_3C(OR)), 1.90–2.04 and 2.22–2.30 (2× 1H, 2× m, CH_2C(CH_3)), 2.36–2.55 and 2.66–2.93 (2× 1H, 2× m, FuCH_2), 3.61–3.71 (2H, m, CH_2OSi), 5.94 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.09 (1H, d, *J* 10.0 Hz, =CHCO), 6.24–6.26 (1H, m, Fu(H-4)), 6.80 (1H, d, *J* 10.0 Hz, C*H*=CHCO), 7.27–7.28 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) −5.4 (2× CH_3), 18.3 (C), 22.3 (CH_2), 25.8 (3× CH_3), 27.3 (CH_3), 37.8 (CH_2), 69.2 (CH_2), 80.8 (C), 92.1 (C), 104.7 (CH), 110.1 (CH), 126.6 (CH), 140.8 (CH), 145.1 (CH), 155.6 (C), 199.0 (C); HRMS (ESI$^+$) found 389.1751, $C_{19}H_{30}NaO_5Si$ [M (^{28}Si)Na$^+$] requires 389.1755. Data for minor diastereomer: R_f 0.31 (petrol/ether, 3:1); ν_{max} (thin film)/cm^{-1} 3424br, 2931m, 2858m, 1689m, 1111m, 838m; δ_H (400 MHz, $CDCl_3$) 0.12 and 0.13 (2× 3H, 2× s, Si(CH_3)$_2$), 0.93 (9H, s, C(CH_3)$_3$), 1.36 (3H, s, CH_3C(OR)), 1.96–2.04 and 2.37–2.44 (2× 1H, 2× m, CH_2C(CH_3)), 2.67–2.75 and 2.85–2.93 (2× 1H, 2× m, FuCH_2), 3.62 and 3.68 (2× 1H, 2× d, *J* 10 Hz, CH_2OSi), 3.82 (1H, s, OH), 5.97–5.98 (1H, m, Fu(H-3)), 6.09 (1H, d, *J* 10.0 Hz, =CHCO), 6.26–6.27 (1H, m, Fu(H-4)), 6.78 (1H, d, *J* 10.0 Hz, C*H*=CHCO), 7.28–7.30 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) −5.4 (2× CH_3), 18.3 (C), 21.7 (CH_2), 22.2 (CH_3), 25.8 (3× CH_3), 37.1 (CH_2), 69.4 (CH_2), 80.8 (C), 92.1 (C), 104.7 (CH), 110.1 (CH), 126.0 (CH), 140.8 (CH), 144.9 (CH), 155.6 (C), 199.0 (C); HRMS (ESI$^+$) found 389.1751, $C_{19}H_{30}NaO_5Si$ [M (^{28}Si)Na$^+$] requires 389.1755.

4.6. 2-Hydroxy-2-methyl-3,4-dihydronaphthalen-1(2*H*)-one (26)[44]

To a stirred solution of 1-methoxypropa-1,2-diene[49] (0.15 g, 2.14 mmol) in THF (1.0 mL) at −78 °C was added butyllithium (0.91 mL, 1.6 M solution in hexanes, 1.46 mmol). After 0.5 h the solution was warmed to 0 °C, stirred for 0.5 h and cooled to −78 °C;[†] a solution of ketone **18**[37] (0.10 g, 0.72 mmol) in THF (0.5 mL) was then added. After 3 h the reaction was quenched with satd aq NH_4Cl (1.0 mL) and extracted with dichloromethane (3×5.0 mL). The combined organic extracts were concentrated in vacuo, the residue dissolved in dichloromethane (3.0 mL), cooled to 0 °C and hydrochloric acid (5.0 mL, 5.0 M) was added with stirring. After 15 min solid $NaHCO_3$ was added until gas evolution ceased, the aqueous phase was separated and extracted with ethyl acetate (3×5.0 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 1:1) afforded the title compound (**26**) as a pale yellow oil (49.2 mg, 39%). R_f 0.26 (petrol/ether, 1:1); δ_H (400 MHz, $CDCl_3$) 1.40 (3H, s, CH_3), 2.17–2.30 (2H, m, C(3)H_2), 2.98–3.16 (2H, m, C(4)H_2), 3.85 (1H, br s, OH), 7.26 (1H, d, *J* 8.0 Hz, C(6)H), 7.34 (1H, app. t, *J* 7.5 Hz, C(8)H), 7.52 (1H, app. t, *J* 7.5 Hz, C(7)H), 8.03 (1H, d, *J* 8.0 Hz, C(9)H); δ_C (100 MHz, $CDCl_3$) 23.9 (CH_3), 26.8 (CH_2), 35.9 (CH_2), 73.6 (C), 126.9 (CH), 128.0 (CH), 129.0 (CH), 129.9 (C), 134.1 (CH), 143.4 (C), 201.8 (C).

4.7. (1*R**,4*R**,6*S**,8*R**)-4-Hydroxy-4-methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-one (27)

To a stirred solution of 1-methoxypropa-1,2-diene[49] (0.15 g, 2.14 mmol) in THF (1.5 mL) at −78 °C was added butyllithium (0.91 mL, 1.6 M solution in hexanes, 1.46 mmol). After 0.5 h the solution was warmed to 0 °C, stirred for 0.5 h and cooled to −78 °C; a solution of ketone **18**[37] (0.10 g, 0.72 mmol) in THF (3.0 mL) was then added. After 3 h the reaction was quenched with satd aq NH_4Cl (1.0 mL) and extracted with ethyl acetate (3×5.0 mL). The combined organic extracts were concentrated in vacuo and the residues dissolved in THF (3.0 mL), cooled to 0 °C and hydrochloric acid (0.72 mL, 1.0 M, 0.72 mmol) was added with stirring. After 45 min $NaHCO_3$ (0.06 g, 0.72 mmol) was added and the separated aqueous phase extracted with ethyl acetate (3×5.0 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 2:1) afforded a single diastereomer of the *title compound* (**27**) as a waxy white solid (0.12 g, 86%). R_f 0.11 (petrol/ether, 1:1); mp 74–79 °C; ν_{max} (KBr disc)/cm^{-1} 3450br, 2985m, 2954s, 1710s, 1455m, 1434m, 1367s, 1266s, 1181m, 1170m, 1151s, 1135s, 1087s, 1031s; δ_H (400 MHz, $CDCl_3$) 1.12 (1H, dd, *J* 11.5, 8.0 Hz, C(7)*H*H′), 1.24 (3H, s, CH_3), 1.85–1.95 (2H, m, C(3)*HH*′ and C(2)*H*H′), 2.05 (1H, dd, *J* 8.0, 3.0 Hz, C(6)H), 2.11–2.23 (2H, m, C(3)H*H*′ and C(2)H*H*′), 2.78 (1H, ddd, *J* 11.5, 4.5, 3.0 Hz, C(7)H*H*′), 4.33 (1H, s, OH), 4.58 (1H, d, *J* 4.5 Hz, C(8)H), 5.64 (1H, d, *J* 5.5 Hz, C(10)H), 5.96 (1H, d, *J* 5.5 Hz, C(9)H); δ_C (100 MHz, $CDCl_3$) 24.1 (CH_3), 25.7 (CH_2), 29.4 (CH_2), 36.9 (CH_2), 47.3 (CH), 76.2 (C), 78.0 (CH), 91.1 (C), 136.8 (CH), 138.6 (CH), 211.7 (C); HRMS (ESI$^+$) found 217.0836, $C_{11}H_{14}NaO_3$ (MNa$^+$) requires 217.0835.

4.8. 1-(Furan-2-yl)-4,4-dimethoxy-3-methylhex-5-en-3-ol (28)

To a stirred solution of 1-methoxypropa-1,2-diene[49] (0.15 g, 2.14 mmol) in THF (1.5 mL) at −78 °C was added butyllithium (0.91 mL, 1.6 M solution in hexanes, 1.46 mmol). After 0.5 h the solution was warmed to 0 °C, stirred for 0.5 h and cooled to −78 °C; a solution of ketone **18**[37] (0.10 g, 0.72 mmol) in THF (3 mL) was then added. After 3 h the reaction was quenched with satd aq NH_4Cl (1.0 mL) and extracted with ethyl acetate (3×5 mL). The combined organic extracts were concentrated in vacuo and the residue dissolved in methanol (2.0 mL), cooled to 0 °C and camphorsulfonic acid (1.6 mg, 6.9 μmol) was added to the stirred solution. The mixture was allowed to warm to rt over 5 h and the solvent was removed in vacuo. Flash chromatography on basic alumina (petrol/ether, 5:1) afforded the *title compound* (**28**) as a colourless oil (0.10 g, 58%). R_f 0.50 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3553br, 2945s, 2836m, 1508m, 1453m, 1406m, 1370m, 1180s, 1148s, 1092s, 1064s, 1009s; δ_H (400 MHz, $CDCl_3$) 1.26 (3H, s, C(3)CH_3), 1.90 (1H, ddd, *J* 13.5, 12.5, 5.0 Hz) and 2.23 (1H, app. td, *J* 13.0, 4.5 Hz, C(2)H_2), 2.38 (1H, br s, OH), 2.85 (1H, ddd, *J* 15.5, 12.5, 5.0 Hz) and 3.10–3.19 (1H, m, C(1)H_2), 3.20 and 3.26 (2× 3H, 2× s, 2× OCH_3), 5.23 (1H, dd, *J* 10.5, 2.5 Hz, C(6)*H*H′), 5.57 (1H, dd, *J* 17.0, 10.5 Hz, C(5)H), 5.67 (1H, dd, *J* 17.0, 2.5 Hz, C(6)H*H*′), 6.02 (1H, dd, *J* 3.0, 0.5 Hz, Fu(H-3)), 6.23 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.25 (1H, dd, *J* 2.0, 0.5 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 21.7 (CH_3), 22.5 (CH_2), 36.2 (CH_2), 50.7 and 50.8 (2× CH_3), 77.6 (C), 102.6 (C), 104.9 (CH), 110.4 (CH), 120.1 (CH_2), 136.2 (CH), 141.0 (CH), 157.2 (C); HRMS (ESI$^+$) found 263.1252, $C_{13}H_{20}NaO_4$ (MNa$^+$) requires 263.1254.

4.9. 2-Ethoxy-5-(furan-2-yl)-3-methylpent-1-en-3-ol (30)

To a stirred solution of ethyl vinyl ether (2.08 mL, 21.7 mmol) in THF (6.0 mL) at −78 °C was added *tert*-butyllithium (10.2 mL, 1.7 M solution in pentane, 17.3 mmol). The resulting solution was warmed to 0 °C for 15 min then re-cooled to −78 °C and a solution of ketone **18**[37] (0.60 g, 4.34 mmol) in THF (3.0 mL) added dropwise. After 0.5 h the reaction mixture was allowed to warm to rt over 1 h and quenched with satd aq NH_4Cl (5.0 mL) then extracted with ethyl acetate (3×15 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography on basic alumina (petrol/ether, 2:1) afforded the *title compound* (**30**) as a pale yellow oil (0.76 g, 83%). R_f 0.44 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3476br, 2978s, 2932s, 1710s, 1621m, 1508s, 1448s, 1361s, 1237m, 1148s, 1113s, 1071s, 1009m; δ_H (400 MHz, $CDCl_3$) 1.31 (3H, t, *J* 7.0 Hz, OCH_2CH_3), 1.38 (3H, s, C(3)CH_3), 1.89–2.07 (2H, m, C(4)H_2),

[†] Quenching at this point allows the allene adduct **24** to be observed. NMR data for 1-(*furan-2-yl*)-4-*methoxyhexa*-4,5-*dien*-3-*ol* δ_H (200 MHz, $CDCl_3$) 1.36 (3H, s, C(3)(CH_3)), 1.95–2.05 (2H, m, C(2)H_2), 2.26 (1H, br s, OH), 2.62–2.73 (2H, m, C(1)H_2), 3.45 (3H, s, OCH_3), 5.61 (2H, s, C(6)H_2), 5.98 (1H, dq, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.27 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.30 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)).

2.30 (1H, br s, OH), 2.58–2.72 (2H, m, C(5)H_2), 3.75 (2H, q, *J* 7.0 Hz, OCH_2), 3.99 and 4.24 (2× 1H, 2× d, *J* 2.5 Hz, C(1)H_2), 5.97–5.99 (1H, m, Fu(H-3)), 6.26–6.28 (1H, m, Fu(H-4)), 7.29–7.30 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 14.4 (CH_3), 22.9 (CH_2), 26.6 (CH_3), 38.6 (CH_2), 63.1 (CH_2), 73.6 (C), 79.7 (CH_2), 104.5 (CH), 110.1 (CH), 140.7 (CH), 156.3 (C), 165.7 (C); HRMS (CI, NH_3) found 228.1601, $C_{12}H_{22}NO_3$ (MNH_4^+) requires 228.1594.

4.10. 5-(Furan-2-yl)-3-hydroxy-3-methylpentan-2-one (31)

To a stirred solution of enol ether **30** (68.0 mg, 0.32 mmol) in THF (0.7 mL) at rt was added *p*-toluenesulfonic acid monohydrate (61.6 mg, 0.32 mmol). After 5 min the reaction was partitioned between water (1.0 mL) and ether (1.0 mL); the aqueous phase was extracted with ether (3×1.0 mL) and the combined extracts were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 3:1) afforded the *title compound* (**31**) as a yellow oil (50.7 mg, 87%). R_f 0.24 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3474br, 2976s, 2930s, 1709s, 1598m, 1508s, 1455s, 1359s, 1169s, 1109s, 1072m, 1009s; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, s, C(3)CH_3), 2.01–2.14 (2H, m, C(4)H_2), 2.16 (3H, s, C(1)H_3), 2.42–2.52 (1H, m) and 2.77 (1H, ddd, *J* 15.5, 9.5, 6.0 Hz, C(5)H_2), 3.97 (1H, s, OH), 5.95–5.97 (1H, m, Fu(H-3)), 6.26–6.28 (1H, m, Fu(H-4)), 7.29–7.30 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 22.2 (CH_2), 23.3 (CH_3), 25.6 (CH_3), 37.4 (CH_2), 78.2 (C), 105.6 (CH), 110.3 (CH), 141.0 (CH), 154.8 (C), 211.8 (C); HRMS (CI, NH_3) found 183.1029, $C_{10}H_{15}O_3$ (MH^+) requires 183.1016.

4.11. 5-(Furan-2-yl)-3-methyl-3-(trimethylsilyloxy)pentan-2-one (32)

To a stirred solution of ethyl vinyl ether (0.35 mL, 3.62 mmol) in THF (1.0 mL) at −78 °C was added *tert*-butyllithium (1.71 mL, 1.7 M solution in pentane, 2.91 mmol). The resulting solution was warmed to 0 °C for 15 min then re-cooled to −78 °C and a solution of ketone **18**[37] (0.10 g, 0.72 mmol) in THF (0.5 mL) added dropwise. After 0.5 h at −78 °C the reaction mixture was allowed to warm to rt over 1.5 h and chlorotrimethylsilane (0.37 mL, 2.90 mmol) and NaI (0.43 g, 2.87 mmol) were added causing a white precipitate to form immediately. After stirring for 5 min the reaction mixture was diluted with water (3.0 mL) and extracted with ether (3×5.0 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 20:1) afforded the *title compound* (**32**) as a colourless oil (0.13 g, 71%). R_f 0.54 (petrol/ether, 5:1); ν_{max} (thin film)/cm^{-1} 2958br, 1720s, 1508m, 1453m, 1418m, 1371m, 1353s, 1192s, 1147m, 1120s, 1012s; δ_H (400 MHz, $CDCl_3$) 0.19 (9H, s, $Si(CH_3)_3$), 1.38 (3H, s, C(3)CH_3), 1.84 (1H, ddd, *J* 13.5, 12.0, 4.0 Hz) and 2.14 (1H, ddd, *J* 13.5, 11.5, 5.5 Hz, C(4)H_2), 2.21 (3H, s, C(1)H_3), 2.51 (1H, ddd, *J* 16.0, 12.0, 5.5 Hz) and 2.69 (1H, ddd, *J* 16.0, 11.5, 4.0 Hz, C(5)H_2), 5.96 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.27 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.30 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 2.3 (3× CH_3), 22.6 (CH_2), 25.4 (CH_3), 25.5 (CH_3), 38.7 (CH_2), 82.2 (C), 104.8 (CH), 110.1 (CH), 140.9 (CH), 155.4 (C), 213.7 (C); HRMS (CI, NH_3) found 255.1407, $C_{13}H_{23}O_3Si$ [M (^{28}Si)H^+] requires 255.1411.

4.12. 1-(Furan-2-yl)-3-hydroxy-3-methyloct-7-en-4-one (33)

From **31**: To a stirred solution of diisopropylamine (0.36 mL, 2.60 mmol) in THF (2.0 mL) at −78 °C was added dropwise butyllithium (1.58 mL, 1.6 M solution in hexanes, 2.53 mmol). After stirring for 1 h at −78 °C a solution of ketone **31** (0.12 g, 0.63 mmol) in THF (0.8 mL) was added via cannula and stirring continued for 1 h, whereupon allyl iodide (0.23 mL, 2.53 mmol) was added. The reaction mixture was allowed to warm to rt over 17 h then diluted with ether (5.0 mL) and quenched with satd aq NH_4Cl (8.0 mL). The aqueous phase was separated and washed with ether (3×5.0 mL). The organic extracts were combined, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 5:1) afforded the *title compound* (**33**) as a colourless oil (80.7 mg, 58%) along with a little dialkylated product (11.1 mg, 7%). See below for data.

From **55**: To a stirred solution of 4-iodobut-1-ene (1.00 g, 5.49 mmol) in ether (13 mL) at −78 °C was added *tert*-butyllithium (6.45 mL, 1.7 M solution in pentane, 11.0 mmol) and stirring continued for 1 h at −78 °C and 1 h at rt. The mixture was re-cooled to −78 °C and a solution of nitrile **55** (1.00 g, 4.21 mmol) in ether (10 mL) was added via cannula. The reaction mixture was allowed to warm to rt over 16 h, diluted with ether (10 mL) and quenched by stirring with satd aq NH_4Cl (25 mL) for 0.5 h. The phases were separated, the aqueous phase extracted with ether (3×10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 5:1→1:1) afforded the *title compound* (**33**) as a yellow oil (0.60 g, 64%). R_f 0.47 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3456br, 2958m, 2926m, 1707s, 1642m, 1454m, 1370m, 1250m, 1148m, 1111m, 1069m, 1009s; δ_H (400 MHz, $CDCl_3$) 1.39 (3H, s, C(3)CH_3), 2.00–2.14 (2H, m, C(2)H_2), 2.27–2.40 (2H, m, C(6)H_2), 2.41–2.54 (2H, m, C(1)*H*H′ and C(5)*H*H′), 2.64 (1H, ddd, *J* 17.0, 8.5, 6.5 Hz, C(5)H*H*′), 2.76 (1H, ddd, *J* 15.5, 9.5, 6.0 Hz, C(1)H*H*′), 3.97 (1H, s, OH), 5.01 (1H, ddt, *J* 10.0, 2.0, 1.0 Hz) and 5.06 (1H, app. dq, *J* 17.0, 2.0 Hz, C(8)H_2), 5.79 (1H, ddt, *J* 17.0, 10.0, 6.5 Hz, C(7)H), 5.96 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.27 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.29 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 22.2 (CH_2), 25.7 (CH_3), 27.5 (CH_2), 34.9 (CH_2), 37.6 (CH_2), 78.1 (C), 105.4 (CH), 110.2 (CH), 115.8 (CH_2), 136.7 (CH), 141.0 (CH), 154.8 (C), 213.2 (C); HRMS (ESI^+) found 245.1157, $C_{13}H_{18}NaO_3$ (MNa^+) requires 245.1148.

4.13. (*S*)-1-(Furan-2-yl)-3-hydroxy-3-methyloct-7-en-4-one [(+)-33]

Applying the above procedure from **55** to (−)-**55** (24.4 g, 0.103 mol) afforded the *title compound* (+)-**33** (9.94 g, 44%). Data as above. $[\alpha]_D^{26}$ +18.8 (*c* 1.76, $CHCl_3$).

4.14. 1-(Furan-2-yl)-3-methyl-3-(trimethylsilyloxy)oct-7-en-4-one (34)

To a stirred solution of diisopropylamine (0.03 mL, 0.24 mmol) in THF (0.2 mL) at 0 °C was added dropwise butyllithium (0.14 mL, 1.6 M solution in hexanes, 0.22 mmol). After 0.5 h a solution of ketone **32** (50.0 mg, 0.20 mmol) in THF (0.5 mL) was added dropwise and stirring continued at 0 °C for a further 0.5 h. Allyl bromide (0.02 mL, 0.22 mmol) was added then the reaction mixture was allowed to warm to rt over 16 h and partitioned between ether (2.0 mL) and brine (2.0 mL). The separated organic phase was shaken for 5 min with a buffered acetic acid solution (1.0 mL of a solution made from 15 g anhydrous NaOAc in 50 mL acetic acid and 50 mL water) then washed repeatedly with satd aq $NaHCO_3$ until the washings were basic. The solution was then dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 40:1) afforded the *title compound* (**34**) as a colourless oil (43.9 mg, 75%). R_f 0.63 (petrol/ether, 5:1); ν_{max} (thin film)/cm^{-1} 2958br, 2857m, 1719s, 1642m, 1452m, 1417m, 1372m, 1353m, 1252s, 1191m, 1147m, 1119s, 1077s, 1041m, 1009s; δ_H (400 MHz, $CDCl_3$) 0.20 (9H, s, $Si(CH_3)_3$), 1.37 (3H, s, C(3)CH_3), 1.83 (1H, ddd, *J* 13.5, 12.0, 4.5 Hz) and 2.17 (1H, ddd, *J* 13.5, 12.0, 5.5 Hz, C(2)H_2), 2.25–2.32 (2H, m, C(6)H_2), 2.46 (1H, ddd, *J* 15.5, 12.0, 5.5 Hz, C(1)*H*H′), 2.64–2.74 (3H, m, C(1)H*H*′ and C(5)H_2), 4.98 (1H, app. ddt, *J* 10.0, 2.0, 1.0 Hz) and 5.05 (1H, app. dq, *J* 17.0, 1.5 Hz, C(8)H_2), 5.83 (1H, ddt, *J* 17.0, 10.0, 7.0 Hz, C(7)H), 5.95 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.26 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.29 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 2.3 (3× CH_3), 22.7 (CH_2), 26.0 (CH_3), 27.6 (CH_2), 36.7 (CH_2), 38.9 (CH_2), 82.4 (C), 104.8 (CH), 110.1 (CH), 115.0 (CH_2), 137.6 (CH),

140.9 (CH), 155.4 (C), 214.7 (C); HRMS (CI, NH_3) found 295.1729, $C_{16}H_{27}O_3Si$ [M (^{28}Si)H^+] requires 295.1724.

4.15. (*E*)-Methyl 9-(furan-2-yl)-7-hydroxy-7-methyl-6-oxonon-2-enoate (35)

To a degassed solution of alkene **33** (0.10 g, 0.45 mmol) and methyl acrylate (0.10 mL, 1.40 mmol) in dichloromethane (5.0 mL) was added Grubbs' II catalyst (**39**, 19.0 mg, 22.5 μmol). The reaction mixture was stirred at 40 °C for 0.5 h and then concentrated in vacuo. Flash chromatography (petrol/ether, 3:1→1:1) afforded the *title compound* (**35**) as a pale brown oil (0.11 g, 87%). R_f 0.13 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3482br, 2952s, 2931s, 2854m, 1714s, 1659s, 1508m, 1437s, 1331m, 1278s, 1205s, 1177s, 1149s, 1040s, 1010m; δ_H (400 MHz, $CDCl_3$) 1.38 (3H, s, C(7)CH_3), 2.00–2.15 (2H, m, C(8)H_2), 2.36–2.58 (4H, m, C(9)*H*H′ and C(5)*H*H′ and C(4)H_2), 2.67 (1H, ddd, *J* 11.5, 8.5, 8.0 Hz, C(5)H*H*′), 2.75 (1H, ddd, *J* 15.0, 9.5, 6.0 Hz, C(9)H*H*′), 3.72 (3H, s, OCH_3), 3.85 (1H, s, OH), 5.85 (1H, dt, *J* 15.5, 1.5 Hz, C(2)H), 5.95 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.26 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 6.90 (1H, dt, *J* 15.5, 6.5 Hz, C(3)H), 7.29 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 22.2 (CH_2), 25.8 (CH_2), 25.9 (CH_3), 34.0 (CH_2), 37.6 (CH_2), 51.5 (CH_3), 78.1 (C), 105.7 (CH), 110.3 (CH), 122.0 (CH), 141.1 (CH), 146.9 (CH), 154.6 (C), 166.7 (C), 212.4 (C); HRMS (ESI$^+$) found 303.1205, $C_{15}H_{20}NaO_5$ (MNa^+) requires 303.1203.

4.16. (*E*)-Methyl 9-(furan-2-yl)-7-methyl-6-oxo-7-(trimethylsilyloxy)non-2-enoate (36)

To a degassed solution of alkene **34** (0.10 g, 0.34 mmol) and methyl acrylate (0.09 mL, 1.05 mmol) in dichloromethane (5.0 mL) was added Grubbs' II catalyst (**39**, 14.0 mg, 16.5 μmol). The reaction mixture was stirred at 40 °C for 1 h then concentrated in vacuo. Flash chromatography (petrol/ether, 15:1) afforded the *title compound* (**36**) as a yellow oil (68.6 mg, 57%). R_f 0.06 (petrol/ether, 10:1); ν_{max} (thin film)/cm^{-1} 2954s, 1726s, 1659s, 1508m, 1437s, 1371m, 1253s, 1199s, 1115m, 1077m, 1041s; δ_H (400 MHz, $CDCl_3$) 0.90 (9H, s, Si(CH_3)$_3$), 1.37 (3H, s, C(7)CH_3), 1.83 (1H, ddd, *J* 13.5, 11.5, 4.5 Hz) and 2.19 (1H, ddd, *J* 13.5, 11.5, 5.5 Hz, C(8)H_2), 2.40–2.50 (3H, m, C(4)H_2 and C(9)*H*H′), 2.67 (1H, ddd, *J* 15.5, 11.5, 4.5 Hz, C(9)H*H*′), 2.77 (2H, t, *J* 7.5 Hz, C(5)H_2), 3.73 (3H, s, OCH_3), 5.85 (1H, dt, *J* 15.5, 1.5 Hz, C(2)H), 5.95 (1H, dd, *J* 2.5, 1.0 Hz, Fu(H-3)), 6.25–6.27 (1H, m, Fu(H-4)), 6.96 (1H, dt, *J* 15.5, 7.0 Hz, C(3)H), 7.28–7.29 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 2.3 (3× CH_3), 22.7 (CH_2), 26.0 (CH_2), 26.1 (CH_3), 35.7 (CH_2), 38.9 (CH_2), 51.5 (CH_3), 82.4 (C), 104.9 (CH), 110.1 (CH), 121.5 (CH), 140.9 (CH), 148.1 (CH), 155.2 (C), 167.0 (C), 213.9 (C); HRMS (ESI$^+$) found 375.1598, $C_{18}H_{28}NaO_5Si$ [M (^{28}Si)Na^+] requires 375.1598.

4.17. Methyl 2-{(2*S**,6*S**)-6-[2-(furan-2-yl)ethyl]-6-methyl-5-oxotetrahydro-2*H*-pyran-2-yl}acetate (37) and methyl 2-{(2*S**,6*R**)-6-[2-(furan-2-yl)ethyl]-6-methyl-5-oxotetrahydro-2*H*-pyran-2-yl}acetate (38)

To a stirred solution of alcohol **35** (66.0 mg, 0.23 mmol) in THF (4.0 mL) at −78 °C was added KHMDS (0.70 mL, 0.5 M solution in toluene, 0.35 mmol). The reaction mixture was allowed to warm to rt over 20 h, water (3.0 mL) was added and the separated aqueous phase was extracted with ether (3×5.0 mL). The combined organic portions were washed with brine (3.0 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 5:1) afforded the *title compound* as a colourless oil (45.4 mg, 69%) and as a 3:4 mixture of diastereomers **37** and **38**. Analytical samples were prepared by repeated chromatography. Data for **37**: R_f 0.27 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 2953s, 1738s, 1439s, 1373m, 1344m, 1289s, 1261s, 1207s, 1169s, 1093s, 1011m; δ_H (400 MHz, $CDCl_3$) 1.36 (3H, s, C*H*$_3$C(OR)), 1.86 (1H, ddd, *J* 13.5, 11.5, 5.0 Hz, C*H*H′C(CH_3)), 1.91 (1H, ddd, *J* 13.5, 10.5, 6.5 Hz) and 2.09 (1H, dddd, *J* 13.5, 6.5, 4.0, 3.0 Hz, C*H*$_2$CH$_2$CO), 2.19 (1H, ddd, *J* 13.5, 11.0, 5.5 Hz, CH*H*′C(CH_3)), 2.45–2.66 (5H, m, CH_2CO and CH_2CO_2 and FuC*H*H′), 2.75 (1H, ddd, *J* 15.5, 11.0, 5.0 Hz, FuCH*H*′), 3.73 (3H, s, OCH_3), 4.37 (1H, dddd, *J* 10.5, 8.0, 5.5, 3.0 Hz, C*H*(OR)), 5.97 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.26 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.29 (1H, d, *J* 2.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 21.6 (CH_3), 22.1 (CH_2), 30.3 (CH_2), 35.2 (CH_2), 36.7 (CH_2), 40.6 (CH_2), 51.7 (CH_3), 66.4 (CH), 82.7 (C), 104.7 (CH), 110.0 (CH), 140.7 (CH), 155.7 (C), 171.3 (C), 211.5 (C); HRMS (ESI$^+$) found 303.1201, $C_{15}H_{20}NaO_5$ (MNa^+) requires 303.1203. Data for **38**: R_f 0.32 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 2953m, 1737s, 1508s, 1373m, 1288s, 1260s, 1210s, 1172s, 1089s, 1072s, 1010m; δ_H (400 MHz, $CDCl_3$) 1.29 (3H, s, C*H*$_3$C(OR)), 1.85 (1H, ddd, *J* 14.0, 12.0, 5.5 Hz, C*H*H′C(CH_3)), 1.93 (1H, ddd, *J* 13.5, 11.0, 6.5 Hz) and 2.12 (1H, ddt, *J* 13.5, 6.5, 3.0 Hz, C*H*$_2$CH$_2$CO), 2.24 (1H, ddd, *J* 14.0, 12.0, 4.5 Hz, CH*H*′C(CH_3)), 2.48–2.65 (5H, m, CH_2CO and CH_2CO_2 and FuC*H*H′), 2.76 (1H, ddd, *J* 15.5, 12.0, 4.5 Hz, FuCH*H*′), 3.71 (3H, s, OCH_3), 4.39 (1H, dddd, *J* 11.0, 8.0, 5.0, 3.0 Hz, C*H*(OR)), 6.02–6.04 (1H, m, Fu(H-3)), 6.29 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.31 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 21.0 (CH_2), 22.3 (CH_3), 31.2 (CH_2), 32.0 (CH_2), 36.3 (CH_2), 40.8 (CH_2), 51.7 (CH_3), 66.4 (CH), 82.6 (C), 104.9 (CH), 110.2 (CH), 141.0 (CH), 155.3 (C), 171.2 (C), 211.1 (C); HRMS (ESI$^+$) found 303.1202, $C_{15}H_{20}NaO_5$ (MNa^+) requires 303.1203.

4.18. (*E*)-Methyl 5-{2-*sec*-butyl-5-[2-(furan-2-yl)ethyl]-5-methyl-1,3,2-dioxaborolan-4-yl}pent-2-enoate (40)

To a stirred solution of ketone **35** (0.10 g, 0.36 mmol) in dichloromethane (13.3 mL) at −78 °C was added dropwise $ZnCl_2$ (0.48 mL, 1.0 M solution in ether, 0.48 mmol). After 0.5 h, L-Selectride (1.23 mL, 1.0 M solution in THF, 1.23 mmol) was added dropwise and stirring continued at −78 °C for 1.5 h. The reaction was quenched by the careful addition of methanol (0.31 mL), water (0.16 mL), hydrogen peroxide (0.16 mL, 35% w/w aqueous solution) and aq NaOH (0.16 mL, 6.0 M) and the resulting solution warmed to rt before being diluted with water (5.0 mL) and extracted with dichloromethane (3×15 mL). The combined organic portions were washed with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 1:2→1:5) afforded the *title compound* (**40**), apparently as a single diastereomer, as a colourless oil (81.6 mg, 65%). R_f 0.76 (petrol/ether, 1:2); ν_{max} (thin film)/cm^{-1} 2955s, 2874m, 1726s, 1461m, 1437m, 1384m, 1272m, 1201m, 1147m, 1094m, 1042m, 1010m; δ_H (400 MHz, $CDCl_3$) 0.92 (3H, t, *J* 7.5 Hz, CH_2CH_3), 0.96–1.01 (1H, m) overlapping 0.98 [3H, s (coincident resonances, coupling lost), $CHCH_3$], 1.31–1.34 (1H, m, C*H*H′CH_3) overlapping 1.34 (3H, s, CH_3C(OBO–)), 1.43–1.53 (1H, m, CH*H*′CH_3), 1.56–1.64 (1H, m, C*H*H′CHO), 1.65–1.75 (2H, m, CH*H*′CHO and C*H*H′C(CH_3)), 1.81–1.95 (1H, m, CH*H*′C(CH_3)), 2.26–2.38 (1H, m) and 2.46–2.57 (1H, m, C*H*$_2$CH=), 2.66–2.77 (1H, m) and 2.83 (1H, ddd, *J* 15.5, 11.5, 4.5 Hz, FuC*H*$_2$), 3.74 (3H, s, OCH_3), 3.90–3.95 (1H, m, CHO), 5.88 (1H, d, *J* 16.0 Hz, =CHCO), 5.99 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.29 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 6.96–7.05 (1H, m, C*H*=CHCO), 7.31 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 13.4 (CH_3), 15.1 (CH_3), 18.2–18.7 (CH), 22.5 (CH_2), 25.4 (CH_3), 26.0 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 34.4 (CH_2), 51.4 (CH_3), 82.1 (C), 85.0 (CH), 104.7 (CH), 110.1 (CH), 121.5 (CH), 140.9 (CH), 148.3 (CH), 155.7 (C), 167.0 (C); HRMS (ESI$^+$) found 371.2002, $C_{19}H_{29}BNaO_5$ (MNa^+) requires 371.2000.

4.19. (6*R**,7*S**,*E*)-Methyl 9-(furan-2-yl)-6,7-dihydroxy-7-methylnon-2-enoate (41) and (6*S**,7*S**,*E*)-methyl 9-(furan-2-yl)-6,7-dihydroxy-7-methylnon-2-enoate (42)

To a stirred solution of ketone **35** (50.0 mg, 0.18 mmol) in THF (3.0 mL) at rt was added $Zn(BH_4)_2$ (0.06 mL, 0.35 M solution in THF, 21.0 μmol). After 4.5 h the reaction mixture was diluted with ether

(4.0 mL) and quenched by stirring for 0.5 h with satd aq NaF (3.0 mL). Satd aq NH_4Cl (3.0 mL) was then added, the phases were separated and the organic phase dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (petrol/ether, 1:2) afforded the *title compound* as a colourless oil (26.7 mg, 53%; n.b. hydride in this reaction is limiting in order to minimise conjugate reduction etc.) as a 4:1 mixture of diastereomers **41** and **42**, respectively. R_f 0.10 (petrol/ether, 1:2); ν_{max} (thin film)/cm^{-1} 2956s, 1721s, 1656s, 1508m, 1438s, 1264s, 1207s, 1173s, 1077s, 1041s, 1010s; δ_H (400 MHz, $CDCl_3$) data for **41**: 1.21 (3H, s, C(7)CH_3), 1.50–1.74 (3H, m, C(5)H_2 and C(8)*H*H′), 1.96 (1H, ddd, *J* 14.0, 11.0, 5.5 Hz, C(8)H*H*′), 2.24–2.37 (1H, m) and 2.45–2.55 (1H, m, C(4)H_2), 2.71 (1H, ddd, 15.5, 11.0, 5.5 Hz) and 2.82 (1H, ddd, *J* 15.5, 11.0, 5.5 Hz, C(9)H_2), 3.42 (1H, dd, *J* 10.5, 2.0 Hz, C(6)H), 3.73 (3H, s, OCH_3), 5.87 (1H, dt, *J* 15.5, 1.5 Hz, C(2)H), 6.00 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.28 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.00 (1H, ddd, *J* 15.5, 7.5, 6.5 Hz, C(3)H), 7.30 (1H, dd, 2.0, 1.0 Hz, Fu(H-5)); δ_H (400 MHz, $CDCl_3$) selected data for **42**: 1.16 (3H, s, C(7)CH_3), 1.80–1.88 (2H, m, C(8)H_2), 3.44 (1H, dd, *J* 10.5, 2.5 Hz, C(6)H); δ_C (100 MHz, $CDCl_3$) data for **41**: 22.1 (CH_2), 23.3 (CH_3), 29.3 (CH_2), 29.6 (CH_2), 33.9 (CH_2), 51.5 (CH_3), 74.3 (C), 77.8 (CH), 104.7 (CH), 110.2 (CH), 121.4 (CH), 140.9 (CH), 148.9 (CH), 156.0 (C), 167.1 (C); δ_C (100 MHz, $CDCl_3$) data for **42**: 20.7 (CH_3), 22.1 (CH_2), 29.3 (CH_2), 29.7 (CH_2), 36.9 (CH_2), 51.5 (CH_3), 74.5 (C), 76.2 (CH), 104.9 (CH), 110.2 (CH), 121.4 (CH), 141.0 (CH), 148.9 (CH), 155.9 (C), 166.6 (C); HRMS (ESI^+) found 305.1350, $C_{15}H_{22}NaO_5$ (MNa^+) requires 305.1359.

4.20. Methyl 2-{5-[4-(furan-2-yl)-2-hydroxybutan-2-yl] tetrahydrofuran-2-yl}acetate (43)

To a stirred solution of the diol (29.7 mg, 0.11 mmol, 2:1 mixture of diastereomers **41** and **42**) in THF (2.0 mL) at −40 °C was added LHMDS (0.11 mL, 1.0 M solution in THF, 0.11 mmol). The reaction mixture was then allowed to warm to rt over 18 h then water (2.0 mL) and ether (2.0 mL) were added and the phases separated. The aqueous phase was extracted with ether (3×3.0 mL) and the combined organic phases were washed with brine (2.0 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 1:1) afforded a partially separable mixture of four diastereomers of the *title compound* (**43**) as pale yellow oils (12.0 mg, 40%, 3:1 A and B and 7.1 mg, 24%, 1.35:1 C and D). Data for diastereomers A and B: R_f 0.27 (petrol/ether, 1:2); ν_{max} (thin film)/cm^{-1} 3417br, 2978m, 2953m, 1740s, 1508m, 1438m, 1373m, 1296m, 1278m, 1201s, 1174s, 1147s, 1069s, 1008m; δ_H (400 MHz, $CDCl_3$) 1.10 (3H, s, C*H*$_3$C(OH), B), 1.26 (3H, s, C*H*$_3$C(OH), A), 1.64–1.73 (3H, m, C*H*H′CH(OR)CH_2 in ring, A and B and C*H*H′C(OH), A), 1.77–1.88 (4H, m, C*H*H′CH(OR)C(OH), A and B, C*H*H′C(OH), B and CH*H*′C(OH), A), 1.90–2.00 (3H, m, CH*H*′CH(OR)C(OH), A and B and CH*H*′C(OH), B), 2.05–2.13 (2H, m, CH*H*′CH(OR)CH_2 in ring, A and B), 2.46–2.58 (4H, m, CH_2CO, A and B), 2.62 (2H, br s, OH, A and B), 2.66–2.86 (4H, m, Fu*CH*$_2$, A and B), 3.71 (3H, s, OCH_3, B), 3.71 (3H, s, OCH_3, A), 3.79 (1H, dd, *J* 8.5, 6.5 Hz, C*H*(OR)C(OH), A) overlapping 3.81 (1H, dd, *J* 8.5, 6.5 Hz, C*H*(OR)C(OH), B), 4.37 (2H, app. tt, *J* 7.5, 5.0 Hz, C*H*(OR)CH_2CO, A and B), 5.98–6.01 (2H, m, Fu(H-3), A and B), 6.26–6.29 (2H, m, Fu(H-4), A and B), 7.29 (1H, dd, *J* 1.5, 1.0 Hz, Fu(H-5), B), 7.30 (1H, dd, *J* 1.5, 1.0 Hz, Fu(H-5), A); δ_C (100 MHz, $CDCl_3$) 21.3 (CH_3, B), 22.2 (CH_2, A), 22.6 (CH_2, B), 24.1 (CH_3, A), 24.7 (CH_2, A), 25.0 (CH_2, B), 31.0 (CH_2, B), 31.2 (CH_2, A), 35.5 (CH_2, A), 38.3 (CH_2, B), 40.8 (CH_2, A and B), 51.8 (CH_3, A and B), 72.0 (C, A and B), 75.4 (CH, A), 75.5 (CH, B), 85.4 (CH, B), 86.2 (CH, A), 104.4 (CH, B), 104.5 (CH, A), 110.1 (CH, A and B), 140.7 (CH, B), 140.8 (CH, A), 156.2 (C, A), 156.4 (C, B), 171.8 (C, B), 171.9 (C, A); HRMS (ESI^+) found 305.1357, $C_{15}H_{22}NaO_5$ (MNa^+) requires 305.1359. Data for diastereomers C and D: R_f 0.21 (petrol/ether, 1:2); ν_{max} (thin film)/cm^{-1} 3417br, 2978m, 2953m, 1740s, 1438s, 1373m, 1318m, 1296m, 1259m, 1201s, 1174s, 1147s, 1069s, 1008m; δ_H (500 MHz, $CDCl_3$) 1.11 (3H, s, C*H*$_3$C(OH), D), 1.23 (3H, s, C*H*$_3$C(OH), C), 1.61–1.73 (2H, m, C*H*H′C(OH), C and C*H*H′CH(OR)CH_2 in ring, C), 1.74–1.85 (2H, m, CH*H*′C(OH), C and C*H*H′C(OH), D), 1.86–1.97 (6H, m, C*H*$_2$CH(OR)C(OH), C and D and C*H*H′CH(OR)CH_2 in ring, D and CH*H*′C(OH), D), 2.14–2.21 (2H, m, CH*H*′CH(OR)CH_2 in ring, C and D), 2.45–2.50 (2H, m, C*H*H′CO, C and D), 2.61–2.66 (2H, m, CH*H*′CO, C and D), 2.67–2.85 (4H, m, Fu*CH*$_2$, C and D), 3.69 (3H, s, OCH_3, D), 3.70 (3H, s, OCH_3, C), 3.85 (1H, dd, *J* 6.5, 3.0 Hz, C*H*C(OH), C) overlapping 3.87 (1H, dd, *J* 6.5, 3.5 Hz, C*H*C(OH), D), 4.34–4.42 (2H, m, C*H*(OR)CH_2CO, C and D), 5.98–6.00 (2H, m, Fu(H-3), C and D), 6.27–6.29 (2H, m, Fu(H-4), C and D), 7.29 (1H, dd, *J* 1.5, 1.0 Hz, Fu(H-5), D), 7.30 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5), C); δ_C (125 MHz, $CDCl_3$) data for C: 22.2 (CH_2), 23.6 (CH_3), 26.3 (CH_2), 32.4 (CH_2), 35.0 (CH_2), 40.6 (CH_2), 51.6 (CH_3), 73.0 (C), 76.0 (CH), 85.2 (CH), 104.5 (CH), 110.1 (CH), 140.8 (CH), 156.2 (C), 171.6 (C); data for D: 21.0 (CH_3), 22.3 (CH_2), 26.6 (CH_2), 32.3 (CH_2), 38.1 (CH_2), 40.7 (CH_2), 51.8 (CH_3), 72.8 (C), 76.2 (CH), 84.4 (CH), 104.4 (CH), 110.1 (CH), 140.7 (CH), 156.4 (C), 171.6 (C); HRMS (ESI^+) found 305.1360, $C_{15}H_{22}NaO_5$ (MNa^+) requires 305.1359.

4.21. (3*S**,4*R**)-1-(Furan-2-yl)-3-methyloct-7-ene-3,4-diol (45) and (3*S**,4*S**)-1-(furan-2-yl)-3-methyloct-7-ene-3,4-diol (46)

To a flask containing $NaBH_4$ (41.7 mg, 1.10 mmol) was added $ZnCl_2$ (2.25 mL, 1.0 M solution in ether, 2.25 mmol) and the resulting suspension stirred at 0 °C for 5 min; a solution of ketone **33** (0.50 g, 2.25 mmol) in THF (4.5 mL) was then added via cannula and stirring continued for 2 h at rt. The reaction was quenched by stirring for 0.5 h with satd aq NaF (4.5 mL) and then acidified with hydrochloric acid (1.0 M). The reaction mixture was diluted with dichloromethane (5.0 mL), the phases separated and the aqueous phase extracted with dichloromethane (3×5.0 mL). The organic phases were combined, dried (Na_2SO_4) and concentrated in vacuo. Flash chromatography (petrol/ether, 3:1→1:2) afforded the *title compounds* as a separable mixture of diastereomers [**45** and **46**, dr=4:1, respectively], both viscous yellow oils (0.19 g, 38%, combined). Data for **45**: R_f 0.28 (petrol/ether, 2:1); ν_{max} (thin film)/cm^{-1} 3417br, 2975s, 2948s, 2862m, 1641m, 1597m, 1508m, 1450m, 1415m, 1378m, 1293m, 1147s, 1065s, 1008s; δ_H (400 MHz, $CDCl_3$) 1.21 (3H, s, CH_3), 1.50 (1H, ddd, *J* 10.5, 8.5, 5.5 Hz, C(5)*H*H′), 1.57–1.65 (1H, m, C(5)H*H*′), 1.71 (1H, ddd, *J* 14.0, 11.0, 5.5 Hz, C(2)*H*H′), 1.92–2.21 (4H, m, C(2)H*H*′ and C(6)*H*H′ and 2× OH), 2.29–2.39 (1H, m, C(6)H*H*′), 2.72 (1H, ddd, *J* 15.5, 11.0. 5.5 Hz) and 2.84 (1H, ddd, *J* 15.5, 11.0, 5.0 Hz, C(1)H_2), 3.46 (1H, dd, *J* 10.5, 1.5 Hz, C(4)H), 5.01 (1H, ddd, *J* 10.0, 2.0, 1.0 Hz) and 5.08 (1H, dq, *J* 17.0, 2.0 Hz, C(8)H_2), 5.85 (1H, ddt, *J* 17.0, 10.0, 6.5 Hz, C(7)H), 6.01 (1H, app. dt, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.29 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.31 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 22.2 (CH_2), 23.2 (CH_3), 30.5 (CH_2), 31.0 (CH_2), 33.9 (CH_2), 74.2 (C), 78.2 (CH), 104.6 (CH), 110.2 (CH), 115.2 (CH_2), 138.3 (CH), 140.9 (CH), 156.2 (C); HRMS (ESI^+) found 247.1303, $C_{13}H_{20}NaO_3$ (MNa^+) requires 247.1305. Data for **46**: R_f 0.20 (petrol/ether, 2:1); ν_{max} (thin film)/cm^{-1} 3417br, 2976s, 2947s, 2859m, 1641m, 1508s, 1450s, 1415s, 1381m, 1212m, 1174s, 1147s, 1071s, 1008s; δ_H (400 MHz, $CDCl_3$) 1.17 (3H, s, CH_3), 1.41–1.52 (1H, m, C(5)*H*H′), 1.53–1.65 (3H, m, C(5)H*H*′ and 2× OH), 1.82 (2H, app. q, *J* 8.0 Hz, C(2)H_2), 2.10–2.20 (1H, m) and 2.29–2.39 (1H, m, C(6)H_2), 2.77 (2H, t, *J* 8.0 Hz, C(1)H_2), 3.48 (1H, dd, *J* 10.5, 1.5 Hz, C(4)H), 5.01 (1H, ddt, *J* 10.0, 1.5, 1.0 Hz) and 5.08 (1H, app. dq, *J* 17.0, 1.5 Hz, C(8)H_2), 5.85 (1H, ddt, *J* 17.0, 10.0, 7.0 Hz, C(7)H), 6.00–6.02 (1H, m, Fu(H-3)), 6.28–6.30 (1H, m, Fu(H-4)), 7.30–7.32 (1H, m, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 20.8 (CH_3), 22.1 (CH_2), 30.5 (CH_2), 30.8 (CH_2), 36.9 (CH_2), 74.4 (C), 76.5 (CH), 104.7 (CH), 110.2 (CH), 115.2 (CH_2), 138.3 (CH), 140.9 (CH), 155.9 (C); HRMS (ESI^+) found 247.1303, $C_{13}H_{20}NaO_3$ (MNa^+) requires 247.1305.

4.22. (3*S**,4*R**)-1-(Furan-2-yl)-3-methyl-4-(triethylsilyloxy) oct-7-en-3-ol (47a) and (3*S**,4*S**)-1-(furan-2-yl)-3-methyl-4-(triethylsilyloxy)oct-7-en-3-ol (47b)

To a flask containing $NaBH_4$ (45.5 mg, 1.20 mmol) was added $ZnCl_2$ (2.46 mL, 1.0 M solution in ether, 2.46 mmol) and the resulting suspension stirred at 0 °C until gas evolution ceased; a solution of ketone **33** (0.55 g, 2.47 mmol) in THF (5.0 mL) was then added via cannula and stirring continued for 2 h at rt. The reaction mixture was quenched by stirring for 0.5 h with satd aq NaF (5.0 mL) and then acidified with hydrochloric acid (1.0 M). The reaction mixture was diluted with dichloromethane (5.0 mL), the phases were separated and the aqueous phase was extracted with dichloromethane (3×5.0 mL). The organic phases were combined, dried (Na_2SO_4) and concentrated in vacuo. The residue was dissolved in DMF (8.0 mL) at rt and to this solution were added sequentially imidazole (0.87 g, 12.7 mmol) and chlorotriethylsilane (0.48 mL, 2.85 mol). After 3 h the reaction mixture was partitioned between dichloromethane (10 mL) and satd aq $NaHCO_3$ (5.0 mL). The separated aqueous phase was extracted with dichloromethane (2×5.0 mL); the organic phases were combined, washed with water (2×5.0 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 10:1) afforded separable diastereomers of the *title compound* as pale yellow oils (**47a**, 0.41 g, 49% and **47b**, 0.10 g, 12%). Data for **47a**: R_f 0.61 (petrol/ether, 2:1); ν_{max} (thin film)/cm^{-1} 3474br, 2956s, 2914s, 2878s, 1459m, 1415m, 1295w, 1212m, 1137s, 1106s, 1008s; δ_H (400 MHz, $CDCl_3$) 0.67 (6H, q, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 1.00 (9H, t, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 1.17 (3H, s, C(3)CH_3), 1.47–1.58 (1H, m) and 1.63 (1H, dddd, *J* 14.0, 10.0, 6.0, 3.0 Hz, C(5)H_2), 1.72 (1H, ddd, *J* 13.5, 12.0, 5.5 Hz) and 1.92 (1H, ddd, 13.5, 12.0, 5.0 Hz, C(2)H_2), 2.01–2.19 (2H, m, C(6)*H*H′ and OH), 2.22–2.33 (1H, m, C(6)H*H*′), 2.69 (1H, ddd, *J* 15.5, 12.0, 5.5 Hz) and 2.83 (1H, ddd, *J* 15.5, 12.0, 5.0 Hz, C(1)H_2), 3.54 (1H, dd, *J* 7.5, 3.0 Hz, C(4)H), 4.98 (1H, app. ddt, *J* 10.0, 1.5, 1.0 Hz) and 5.04 (1H, dd, *J* 17.0, 1.5 Hz, C(8)H_2), 5.82 (1H, ddt, *J* 17.0, 10.0, 6.5 Hz, C(7)H), 6.00 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-3)), 6.28–6.30 (1H, m, Fu(H-4)), 7.31 (1H, app. s, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 5.4 (3× CH_2), 7.0 (3× CH_3), 22.2 (CH_2), 23.4 (CH_3), 31.0 (CH_2), 32.2 (CH_2), 34.3 (CH_2), 74.3 (C), 79.7 (CH), 104.4 (CH), 110.1 (CH), 114.7 (CH_2), 138.5 (CH), 140.7 (CH), 156.6 (C); HRMS (ESI^+) found 361.2174, $C_{19}H_{34}NaO_3Si$ [M (^{28}Si)Na^+] requires 361.2169. Data for **47b**: R_f 0.67 (petrol/ether, 2:1); ν_{max} (thin film)/cm^{-1} 3474br, 2956s, 2877s, 1641m, 1597m, 1508m, 1458m, 1416m, 1381m, 1240m, 1147m, 1098s, 1008s; δ_H (400 MHz, $CDCl_3$) 0.67 (6H, q, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 1.00 (9H, t, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 1.14 (3H, s, C(3)CH_3), 1.43–1.66 (2H, m, C(5)H_2), 1.72–1.86 (2H, m, C(2)H_2), 2.00–2.11 (1H, m) and 2.21–2.32 (1H, m, C(6)H_2), 2.72–2.79 (2H, m, C(1)H_2), 3.56 (1H, dd, *J* 7.5, 3.0 Hz, C(4)H), 4.98 (1H, ddt, *J* 10.0, 1.5, 1.0 Hz) and 5.04 (1H, dd, 17.0, 1.5 Hz, C(8)H_2), 5.81 (1H, ddt, *J* 17.0, 10.0, 6.5 Hz, C(7)H), 5.99 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.29 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.30–7.32 (1H, m, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 5.2 (3× CH_2), 6.6 (3× CH_3), 21.1 (CH_3), 22.2 (CH_2), 30.8 (CH_2), 32.3 (CH_2), 37.0 (CH_2), 74.2 (C), 78.2 (CH), 104.5 (CH), 110.1 (CH), 114.8 (CH_2), 138.6 (CH), 140.8 (CH), 156.4 (C); HRMS (ESI^+) found 361.2172, $C_{19}H_{34}NaO_3Si$ [M (^{28}Si)Na^+] requires 361.2169.

4.23. (3*S*,4*R*)-1-(Furan-2-yl)-3-methyl-4-(triethylsilyloxy)oct-7-en-3-ol [(+)-47a]

Applying the above procedure to (+)-**33** (21.4 g, 96.3 mmol) afforded (+)-**47a** (13.6 g, 42%). Data as above. $[\alpha]_D^{25}$ +7.3 (*c* 1.0, $CHCl_3$).

4.24. (6*R**,7*S**,*E*)-Methyl 9-(furan-2-yl)-7-hydroxy-7-methyl-6-(triethylsilyloxy)non-2-enoate (48a) and (6*S**,7*S**,*E*)-methyl 9-(furan-2-yl)-7-hydroxy-7-methyl-6-(triethylsilyloxy)non-2-enoate (48b)

To a degassed solution of the alkene (92.0 mg, 0.27 mmol, 8.6:1 mixture of **47a** and **47b**) and methyl acrylate (0.08 mL, 0.84 mmol) in dichloromethane (3.0 mL) was added Hoveyda–Grubbs II catalyst (**52**, 1.7 mg, 2.7 μmol). The reaction mixture was stirred at 40 °C for 2 h and then cooled and concentrated in vacuo. Flash chromatography (petrol/ether, 25:1→10:1) afforded the *title compound* as a pale yellow oil (96.1 mg, 89%) and as an 8:1 (**48a**:**48b**) ratio of diastereomers. Samples of the separate diastereomers for analysis were obtained by repeat chromatography. Data for **48a**: R_f 0.39 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3507br, 2955s, 2913s, 2877s, 1726s, 1657s, 1457s, 1437s, 1315s, 1277s, 1240s, 1208s, 1173s, 1148s, 1104s, 1046s, 1009s; δ_H (500 MHz, $CDCl_3$) 0.66 (6H, q, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 0.99 (9H, t, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 1.17 (3H, s, C(7)CH_3), 1.62–1.75 (3H, m, C(5)H_2 and C(8)*HH*′), 1.91 (1H, ddd, *J* 13.5, 12.0, 5.0 Hz, C(8)H*H*′), 2.07 (1H, s, br, OH), 2.19–2.28 (1H, m) and 2.38–2.49 (1H, m, C(4)H_2), 2.68 (1H, ddd, *J* 15.5, 12.0, 5.0 Hz) and 2.82 (1H, ddd, *J* 15.5, 11.5, 5.0 Hz, C(9)H_2), 3.55 (1H, dd, *J* 7.5, 3.5 Hz, C(6)H), 3.74 (3H, s, OCH_3), 5.84 (1H, d, *J* 15.5 Hz, C(2)H), 6.00 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.29 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 6.97 (1H, dt, *J* 15.5, 7.0 Hz, C(3)H), 7.30–7.32 (1H, m, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 5.4 (3× CH_2), 7.0 (3× CH_3), 22.2 (CH_2), 23.5 (CH_3), 29.2 (CH_2), 31.2 (CH_2), 34.5 (CH_2), 51.4 (CH_3), 74.3 (C), 79.1 (CH), 104.5 (CH), 110.1 (CH), 121.0 (CH), 140.8 (CH), 149.0 (CH), 156.3 (C), 167.0 (C); HRMS (ESI^+) found 419.2222, $C_{21}H_{36}NaO_5Si$ [M (^{28}Si)Na^+] requires 419.2224. Data for **48b**: R_f 0.48 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3441br, 2955s, 2914m, 2877m, 1726s, 1655s, 1437m, 1277m, 1240m, 1208m, 1172m, 1148m, 1103s, 1044m, 1008s; δ_H (400 MHz, $CDCl_3$) 0.65 (6H, q, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 0.98 (9H, t, *J* 8.0 Hz, Si(CH_2CH_3)$_3$), 1.13 (3H, s, C(7)CH_3), 1.50–1.60 (1H, m) and 1.60–1.70 (1H, m, C(5)H_2), 1.70–1.87 (2H, m, C(8)H_2), 2.11–2.26 (2H, m, C(4)*H*H′ and OH), 2.37–2.48 (1H, m, C(4)H*H*′), 2.71 (1H, ddd, *J* 15.5, 10.5, 6.0 Hz) overlapping 2.77 (1H, ddd, *J* 15.5, 10.5, 6.0 Hz, C(9)H_2), 3.56 (1H, dd, *J* 7.0, 3.5 Hz, C(6)H), 3.72 (3H, s, OCH_3), 5.83 (1H, d, *J* 15.5 Hz, C(2)H), 5.97 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.27 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 6.96 (1H, dt, *J* 15.5, 7.0 Hz, C(3)H), 7.29 (1H, d, *J* 2.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 5.4 (3× CH_2), 7.0 (3× CH_3), 21.2 (CH_3), 22.2 (CH_2), 29.0 (CH_2), 31.3 (CH_2), 37.1 (CH_2), 51.4 (CH_3), 74.2 (C), 77.8 (CH), 104.5 (CH), 110.1 (CH), 121.0 (CH), 140.8 (CH), 149.1 (CH), 156.2 (C), 167.0 (C); HRMS (ESI^+) found 419.2224, $C_{21}H_{36}NaO_5Si$ [M (^{28}Si)Na^+] requires 419.2224.

4.25. (6*R*,7*R*,*E*)-Methyl 9-(furan-2-yl)-7-hydroxy-7-methyl-6-(triethylsilyloxy)non-2-enoate [(+)-48a]

Applying the above procedure to (+)-**47a** (13.6 g, 40.2 mmol) afforded (+)-**48a** as a pale yellow oil (13.0 g, 82%). Data as above. $[\alpha]_D^{18}$ +5.4 (*c* 1.0, $CHCl_3$).

4.26. Methyl 2-{(2*S*,5*R*,6*S*)-6-[2-(furan-2-yl)ethyl]-6-methyl-5-(triethylsilyloxy)tetrahydro-2*H*-pyran-2-yl}acetate [(+)-49]

To a stirred solution of alcohol (+)-**48a** (13.0 g, 32.8 mmol) in THF (380 mL) at −78 °C was added dropwise LHMDS [prepared from hexamethyldisilazane (7.67 mL, 36.1 mmol) and butyllithium (22.6 mL, 1.6 M solution in hexanes, 36.2 mmol) in THF (150 mL)]. The resulting solution was allowed to warm to −40 °C over 3 h then ether (1 L) and satd aq NH_4Cl (100 mL) were added and the phases separated. The aqueous phase was extracted with ether (3×100 mL) and the combined organic portions were washed with brine (200 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, gradient from 20:1→10:1) afforded the *title compound* [(+)-**49**], a colourless oil, as a single diastereomer (6.12 g, 47%) along with recovered starting material [(+)-**48a**,

4.97 g, 38%]. R_f 0.60 (petrol/ether, 1:1); $[\alpha]_D^{25}$ +6.0 (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2954s, 2877s, 1744s, 1508m, 1460s, 1437s, 1377s, 1287s, 1239s, 1197s, 1178s, 1147s, 1100s, 1008s; δ_H (400 MHz, $CDCl_3$) 0.58 (6H, q, *J* 8.0 Hz, $Si(CH_2CH_3)_3$), 0.95 (9H, t, *J* 8.0 Hz, $Si(CH_2CH_3)_3$), 1.17 (3H, s, $CH_3C(OR)$), 1.28–1.37 (1H, m, CHH′$CHCH_2$ in ring), 1.65–1.78 (4H, m, CHH′$C(CH_3)$, $CH_2CH(OTES)$ and CHH′$CHCH_2$ in ring), 1.97 (1H, ddd, *J* 13.5, 12.0, 5.5 Hz, CHH′$C(CH_3)$), 2.35 (1H, dd, *J* 15.0, 5.5 Hz) and 2.45 (1H, dd, *J* 15.0, 7.5 Hz, CH_2CO), 2.62–2.75 (2H, m, FuCH_2), 3.46–3.51 (1H, m, CH(OTES)), 3.69 (3H, s, OCH_3), 3.94 (1H, dddd, *J* 11.5, 7.5, 5.5, 2.0 Hz, CH(OR)CH_2), 5.94 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.26–6.28 (1H, m, Fu(H-4)), 7.29 (1H, d, *J* 1.0 Hz, Fu(H-5)); δ_C (125 MHz, $CDCl_3$) 5.2 (3× CH_2), 6.9 (3× CH_3), 14.8 (CH_3), 21.3 (CH_2), 28.7 (CH_2), 31.0 (CH_2), 38.4 (CH_2), 41.2 (CH_2), 51.5 (CH_3), 66.4 (CH), 73.1 (CH), 76.7 (C), 104.0 (CH), 110.0 (CH), 140.5 (CH), 157.1 (C), 171.9 (C); HRMS (ESI^+) found 419.2227, $C_{21}H_{36}NaO_5Si$ [M (^{28}Si)Na^+] requires 419.2224.

4.27. 2-{(2*S*,5*R*,6*S*)-6-[2-(Furan-2-yl)ethyl]-6-methyl-5-(triethylsilyloxy)tetrahydro-2*H*-pyran-2-yl}ethanol [(+)-50]

To a stirred solution of methyl ester (+)-**49** (6.98 g, 17.6 mmol) in THF (700 mL) at 0 °C was added DIBAL (52.9 mL, 1.0 M solution in cyclohexane, 52.9 mmol) in five portions and the resulting mixture was stirred at rt for 4 h. The reaction was quenched by the addition of potassium sodium tartrate (200 mL, 2.0 M aq) and the phases were separated. The aqueous phase was extracted with ether (2×200 mL), the combined organic phases were washed with brine (200 mL), dried (Na_2SO_4) and concentrated in vacuo to afford the *title compound* [(+)-**50**] as a thick, pale yellow oil, which was used without further purification (6.49 g, quant.). R_f 0.14 (petrol/ether, 1:1); $[\alpha]_D^{25}$ +2.2 (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3385br, 2953s, 2914s, 2877s, 1508s, 1460s, 1415s, 1377s, 1358s, 1239s, 1211s, 1147s, 1100s, 1032s, 1009s; δ_H (400 MHz, $CDCl_3$) 0.59 (6H, q, *J* 8.0 Hz, $Si(CH_2CH_3)_3$), 0.95 (9H, t, *J* 8.0 Hz, $Si(CH_2CH_3)_3$), 1.20 (3H, s, $CH_3C(OR)$), 1.34–1.46 (1H, m, CHH′CH(OTES)), 1.59–1.87 (6H, m, CH_2CH_2OH, $CH_2CHH'CH(OTES)$ and CHH′$C(CH_3)$), 1.99 (1H, ddd, *J* 13.5, 10.5, 6.5 Hz, CHH′$C(CH_3)$), 2.66–2.74 (2H, m, FuCH_2), 2.87 (1H, br s, OH), 3.52 (1H, dd, *J* 11.0, 5.0 Hz, CH(OR)), 3.72–3.81 (3H, m, CH_2OH and CH(OTES)), 5.95 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.27 (1H, dd, *J* 2.5, 2.0 Hz, Fu(H-4)), 7.29 (1H, app. s, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 5.2 (3× CH_2), 6.9 (3× CH_3), 15.3 (CH_3), 21.6 (CH_2), 28.7 (CH_2), 31.4 (CH_2), 37.5 (CH_2), 38.4 (CH_2), 61.7 (CH_2), 70.5 (CH), 72.7 (CH), 77.2 (C), 104.2 (CH), 110.0 (CH), 140.7 (CH), 156.5 (C); HRMS (ESI^+) found 391.2273, $C_{20}H_{36}NaO_4Si$ [M (^{28}Si)Na^+] requires 391.2275.

4.28. (2*S*,3*R*,6*S*)-2-[2-(Furan-2-yl)ethyl]-6-(2-hydroxyethyl)-2-methyltetrahydro-2*H*-pyran-3-ol[34] [(+)-51]

To a stirred solution of silyl ether (+)-**50** (6.23 g, 16.9 mmol) in THF (180 mL) at 0 °C was added dropwise TBAF (44 mL, 1.0 M solution in THF, 44 mmol). The reaction mixture was stirred at 0 °C for 1 h and the reaction was quenched by the addition of water (50 mL); the separated aqueous phase was extracted with ethyl acetate (3×100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to afford the title compound [(+)-**51**] as a pale yellow oil (6.9 g, contains triethylsilyl residues), which was used without further purification. A small amount was purified by chromatography for analysis. R_f 0.09 (petrol/ether, 1:5); $[\alpha]_D^{25}$ +27.9 (*c* 1.0, $CHCl_3$) [lit.[34] $[\alpha]_D^{22}$ +13.0 (*c* 0.50, $CHCl_3$)]; δ_H (400 MHz, $CDCl_3$) 1.22 (3H, s, CH_3), 1.35–1.47 (1H, m, CHH′$CH_2CH(OH)$), 1.60–1.69 (4H, m, CHH′CHH′CH(OH) and CH_2CH_2OH), 1.78–1.92 (2H, m, CHH′$C(CH_3)$ and CHH′CH(OH)), 1.98–2.04 (1H, m, CHH′$C(CH_3)$), 2.15 (1H, br s, OH), 2.73 (2H, app. t, *J* 8.5 Hz, FuCH_2), 2.98 (1H, br s, OH), 3.44–3.52 (1H, m, CH(OH)), 3.73–3.84 (3H, m, CH(OR) and CH_2OH), 5.98 (1H, app. dq, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.26 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.28 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 15.2 (CH_3), 21.5 (CH_2), 28.1 (CH_2), 31.4 (CH_2), 37.5 (CH_2), 38.4 (CH_2), 61.6 (CH_2), 70.5 (CH), 71.7 (CH), 76.7 (C), 104.5 (CH), 110.1 (CH), 140.7 (CH), 156.2 (C).

4.29. (2*S*,3*R*,6*S*)-6-[2-(*tert*-Butyldiphenylsilyloxy)ethyl]-2-[2-(furan-2-yl)ethyl]-2-methyltetrahydro-2*H*-pyran-3-ol[34] [(+)-7]

To a solution of crude diol (+)-**51** (4.29 g, 16.9 mmol) in DMF (100 mL) at rt were added sequentially imidazole (1.38 g, 20.3 mmol) and *tert*-butyldiphenylsilyl chloride (5.28 mL, 20.3 mmol). The reaction mixture was stirred for 16 h and then quenched by the addition of satd aq NH_4Cl (50 mL). The separated aqueous phase was extracted with ether (4×100 mL); the combined organic extracts were washed with brine (50 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 10:1→5:1) afforded the title compound [(+)-**7**] as a viscous, pale yellow oil (6.33 g, 76% from (+)-**50**). R_f 0.36 (petrol/ether, 1:1); $[\alpha]_D^{25}$ +19.3 (*c* 1.0, $CHCl_3$) [lit.[34] $[\alpha]_D^{22}$ +26.3 (*c* 0.88, $CHCl_3$)]; δ_H (400 MHz, $CDCl_3$) 1.09 (9H, s, $C(CH_3)_3$), 1.18 (3H, s, $CH_3C(OR)$), 1.25–1.35 (1H, m, CHH′$CH_2CH(OH)$), 1.57–1.72 (4H, m, CHH′CHH′CH(OH) and CH_2CH_2OSi), 1.77–1.87 (2H, m, CHH′CH(OH) and CHH′$C(CH_3)$), 2.01 (1H, ddd, *J* 13.5, 11.5, 5.5 Hz, CHH′$C(CH_3)$), 2.67 (1H, ddd, *J* 15.5, 11.5, 5.5 Hz) and 2.76 (1H, ddd, *J* 15.5, 11.5, 5.0 Hz, FuCH_2), 3.44–3.52 (1H, m, CH(OH)), 3.66–3.78 (2H, m, CH(OR) and CHH′OSi), 3.82 (1H, ddd, *J* 10.0, 8.5, 5.5 Hz, CHH′OSi), 5.97 (1H, d, *J* 3.0 Hz, Fu(H-3)), 6.27–6.29 (1H, m, Fu(H-4)), 7.30 (1H, d, *J* 1.0 Hz, Fu(H-5)), 7.36–7.45 (6H, m) and 7.66–7.74 (4H, m, 2× Ph); δ_C (100 MHz, $CDCl_3$) 14.8 (3× CH_3), 19.2 (C), 21.4 (CH_2), 26.8 (CH_3), 28.5 (CH_2), 31.7 (CH_2), 38.7 (CH_2), 39.0 (CH_2), 60.3 (CH_2), 65.7 (CH), 73.0 (CH), 75.6 (C), 104.3 (CH), 110.1 (CH), 127.6–135.5 and 140.6 (CH and C), 156.9 (C).[50]

4.30. (*E*)-4-(Furan-2-yl)-2-methyl-2-(trimethylsilyloxy)but-3-enenitrile (54)

To a stirred solution of ketone **29**[37] (2.96 g, 21.4 mmol) and K_2CO_3 (0.15 g, 1.09 mmol) in DMF (10 mL) was added cyanotrimethylsilane (3.77 mL, 28.3 mmol). The resulting mixture was stirred for 1.5 h at rt then diluted with dichloromethane (60 mL), washed with water (3×20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 10:1) afforded the *title compound* (**54**) as a yellow oil (4.94 g, 98%). R_f 0.66 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3419br, 2990m, 2961m, 2342w, 1660m, 1488m, 1448m, 1372m, 1255m, 1214m, 1192m, 1128m, 1107m, 1015m, 1001m; δ_H (400 MHz, $CDCl_3$) 0.25 (9H, s, $Si(CH_3)_3$), 1.74 (3H, s, $C(2)CH_3$), 6.11 (1H, app. dd, *J* 15.5, 0.5 Hz, C(3)H), 6.38 (1H, d, *J* 3.5 Hz, Fu(H-3)), 6.42 (1H, dd, *J* 3.5, 2.0 Hz, Fu(H-4)), 6.69 (1H, d, *J* 15.5 Hz, C(4)H), 7.40–7.41 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 1.4 (3× CH_3), 30.8 (CH_3), 69.7 (C), 110.4 (CH), 111.6 (CH), 119.2 (CH), 120.6 (C), 127.8 (CH), 143.0 (CH), 150.8 (C); HRMS (CI, NH_3) found 209.1013, $C_{11}H_{17}O_2Si$ [M (^{28}Si)–CN]$^+$ requires 209.0992.

4.31. (*S*,*E*)-4-(Furan-2-yl)-2-methyl-2-(trimethylsilyloxy)but-3-enenitrile [(−)-54]

To a stirred solution of sodium (*R*)-phenylglycinate [(−)-**53**, 109 g, 0.63 mol] in THF (300 mL) at −20 °C was added cyanotrimethylsilane (94.0 g, 0.95 mol). The resulting suspension was stirred at rt for 1 h then cooled to −20 °C and a solution of ketone **29**[37] (86.0 g, 0.62 mol) in THF (300 mL) was added via cannula. After 15 min, 2,2,2-trifluoroethanol (23 mL) was added and the reaction mixture stirred for 2 h at −20 °C, then left to stand in the refrigerator (at −20 °C) for 16 h. The reaction mixture was then allowed to warm to rt and concentrated in vacuo. Flash

chromatography (petrol/ether, 25:1) afforded the *title compound* (−)-**54** as a colourless oil (63.3 g, 43%, ee 85% by GC analysis after hydrogenation, see below). Data as above. $[\alpha]_D^{25}$ −58.1 (*c* 1.0, $CHCl_3$).

4.32. 4-(Furan-2-yl)-2-methyl-2-(trimethylsilyloxy) butanenitrile (55)

From **18**: To a stirred solution of ketone **18**[37] (1.50 g, 10.9 mmol) and K_2CO_3 (75.0 mg, 0.54 mmol) in DMF (11 mL) was added cyanotrimethylsilane (1.92 mL, 14.1 mmol). The resulting mixture was stirred for 40 min at rt then diluted with dichloromethane (40 mL) and washed successively with water (3×20 mL) and brine (20 mL). The organic phase was dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 15:1) afforded the *title compound* (**55**) as a yellow oil (2.13 g, 82%). See below for data.

From **54**: A 500 mL two-necked round bottom flask was charged with nitrile **54** (1.00 g, 4.25 mmol), 5% Pd/C (26 mg) and ethyl acetate (35 mL), flush-filled three times with Ar and once with H_2. The reaction mixture was stirred under an atmosphere of H_2 (balloon) and the disappearance of the alkene peaks was monitored by ^{1}H NMR aliquots. On completion (ca. 3–6 h), after flush-filling the flask with Ar, the resulting suspension was filtered through a 1.0 cm plug of Celite®, the plug was eluted with ethyl acetate (100 mL) and the filtrate concentrated in vacuo to afford the *title compound* (**55**) as a pale yellow oil (0.97 g, 96%). R_f 0.68 (petrol/ether, 3:1); ν_{max} (thin film)/cm^{-1} 2963s, 2902m, 2864m, 2232w, 1509s, 1255s, 1215m, 1187s, 1147s, 1118s, 1075s, 1043s, 1012s; δ_H (400 MHz, $CDCl_3$) 0.27 (9H, s, $Si(CH_3)_3$), 1.63 (3H, s, $C(2)CH_3$), 2.06–2.12 (2H, m, $C(3)H_2$), 2.77–2.97 (2H, m, $C(4)H_2$), 6.04 (1H, app. dt, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.29–6.31 (1H, m, Fu(H-4)), 7.32–7.33 (1H, m, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 1.3 (3× CH_3), 23.1 (CH_2), 28.9 (CH_3), 41.5 (CH_2), 69.0 (C), 105.3 (CH), 110.2 (CH), 121.7 (C), 141.1 (CH), 154.2 (C); HRMS (CI, NH_3) found 255.1522, $C_{12}H_{23}N_2O_2Si$ [M (^{28}Si)NH_4^+] requires 255.1523. {Chiral GC trace of **54**: Column: β-cyclodextrin (0.22 mm×30 m), thickness 0.25 μm; carrier gas: He; flow rate: 0.8 mL/min, T injector 220 °C; T detector (FID) 250 °C; T initial 40 °C, 5 min then 20 °C/min to 90 °C, 30 min then 10 °C/min to 95 °C, 20 min then 10 °C/min to 100 °C, 10 min then 20 °C/min to 140 °C t_R=64.98 min [(+)-**54**], 65.83 min [(−)-**54**]}.

4.33. (*S*)-4-(Furan-2-yl)-2-methyl-2-(trimethylsilyloxy) butanenitrile [(−)-55]

Applying the above hydrogenation procedure to two batches of (−)-**54** (total 63.9 g, 0.272 mmol) afforded (−)-**55** as a pale yellow oil (combined 59.9 g, 93%, ee 85% by chiral GC, details above). Data as above. $[\alpha]_D^{17}$ −12.1 (*c* 1.0, $CHCl_3$).

4.34. 5-[4-(Furan-2-yl)-2-(trimethylsilyloxy)butan-2-yl]nona-1,8-dien-5-amine (56)

To a stirred solution of 4-iodobut-1-ene (6.95 g, 38.2 mmol) in ether (90 mL) at −78 °C was added *tert*-butyllithium (44.9 mL, 1.7 M solution in pentane, 76.3 mmol). After 1 h at −78 °C stirring was continued for 1 h at rt then the reaction mixture was cooled to −78 °C and a solution of nitrile **55** (3.02 g, 12.7 mmol) in ether (30 mL) was added via cannula. The reaction mixture was allowed to warm slowly to rt over 16 h then diluted with ether (15 mL) and quenched by stirring for 5 min with satd aq NH_4Cl (20 mL). The separated aqueous phase was extracted with ether (3×15 mL); the organic phases were combined, dried ($MgSO_4$) and concentrated in vacuo. Flash chromatography (petrol/ether, 10:1→3:1) afforded the *title compound* (**56**) as a light brown oil (2.70 g, 61%). R_f 0.05 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 3327br, 2955s, 2862m, 1640m, 1452m, 1251s, 1176m, 1148s, 1111s, 1035s; δ_H (400 MHz, $CDCl_3$) 0.18 (9H, s, $Si(CH_3)_3$), 1.29 (3H, s, CH_3C(OTMS)), 1.43–1.61 (4H, m, 2× $(CH_2)_2C(NH_2)$), 1.81 (1H, ddd, *J* 13.5, 12.0, 5.0 Hz, CHH′C(CH_3)), 1.96–2.24 (5H, m, CHH′C(CH_3), 2× CH_2CH=), 2.65–2.82 (2H, m, FuCH_2), 4.94 (2H, app. dsext, *J* 10.0, 1.0 Hz, 2× =CHH′), 5.03 (2H, ddt, *J* 17.0, 3.5, 1.5 Hz, 2× =CHH′), 5.77–5.88 (2H, m, 2× CH=CH_2), 6.00 (1H, dd, *J* 3.0, 1.0 Hz, Fu(H-3)), 6.29 (1H, dd, *J* 3.0, 2.0 Hz, Fu(H-4)), 7.32 (1H, dd, *J* 2.0, 1.0 Hz, Fu(H-5)); δ_C (100 MHz, $CDCl_3$) 2.9 (3× CH_3), 22.0 (CH_3), 23.7 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 35.0 (CH_2), 35.9 (CH_2), 36.3 (CH_2), 59.6 (C), 82.1 (C), 104.4 (CH), 110.1 (CH), 114.1 (2× CH_2), 139.4 (CH), 139.5 (CH), 140.8 (CH), 156.6 (C); HRMS (ESI$^+$) found 350.2507, $C_{20}H_{36}NO_2Si$ [M (^{28}Si) H^+] requires 350.2510.

Acknowledgements

We thank the University of Oxford and the EPSRC for a studentship (for C.N.), and Drs. Tim Claridge and Barbara Odell, University of Oxford, for supporting NMR studies.

References and notes

1. Tachibana, K.; Scheuer, P. J.; Tsukitani, Y.; Kikuchi, H.; Engen, D. V.; Clardy, J.; Gopichand, Y.; Schmitz, F. J. *J. Am. Chem. Soc.* **1981**, *103*, 2469–2471.
2. Vidal, J.-P.; Escale, R.; Girard, J.-P.; Rossi, J.-C.; Chantraine, J.-M.; Aumelas, A. *J. Org. Chem.* **1992**, *57*, 5857–5860.
3. Smith, A. B., III; Duffey, M. O.; Basu, K.; Walsh, S. P.; Suennemann, H. W.; Frohn, M. *J. Am. Chem. Soc.* **2008**, *130*, 422–423.
4. Ponomarev, A. A.; Markushina, I. A. *Dokl. Akad. Nauk SSSR* **1959**, *126*, 99–102.
5. (a) Bohlmann, F.; Diedrich, B.; Gordon, W.; Fanghänel, L.; Schneider, J. *Tetrahedron Lett.* **1965**, 1385–1388; (b) Bohlmann, F.; Fanghänel, L.; Kleine, K.-M.; Kramer, H.-D.; Mönch, H.; Schuber, J. *Chem. Ber.* **1965**, *98*, 2596–2604; (c) Bohlmann, F.; Kramer, H.-D.; Ertingshausen, G. *Chem. Ber.* **1965**, *98*, 2605–2607.
6. (a) Kocienski, P. J.; Fall, Y.; Whitby, R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 841–844; (b) Brown, R. C. D.; Kocienski, P. J. *Synlett* **1994**, 417–419; (c) Kocienski, P. J.; Brown, R. C. D.; Pommier, A.; Procter, M.; Schmidt, B. *J. Chem. Soc., Perkin Trans. 1* **1998**, 9–39.
7. Montagnon, T.; Tofi, M.; Vassilikogiannakis, G. *Acc. Chem. Res.* **2008**, *41*, 1001–1011.
8. Nicolaou, K. C.; Hwang, C.-K.; Duggan, M. E. *J. Am. Chem. Soc.* **1989**, *111*, 6682–6690.
9. Just, G.; Potvin, P. *Can. J. Chem.* **1980**, *58*, 2173–2177.
10. (a) Fuwa, H.; Yamaguchi, H.; Sasaki, M. *Org. Lett.* **2010**, *12*, 1848–1851; (b) Fuwa, H.; Yamaguchi, H.; Sasaki, M. *Tetrahedron* **2010**, *66*, 7492–7503.
11. (a) Bates, R. W.; Palani, K. *Tetrahedron Lett.* **2008**, *49*, 2832–2834; (b) Hiebel, M.-A.; Pelotier, B.; Lhoste, P.; Piva, O. *Synlett* **2008**, 1202–1204; (c) Hiebel, M.-A.; Pelotier, B.; Piva, O. *Tetrahedron Lett.* **2010**, *51*, 5091–5093.
12. Nicolaou, K. C.; Rutjes, F. P. J. T.; Theodorakis, E. A.; Tiebes, J.; Sato, M.; Untersteller, E. *J. Am. Chem. Soc.* **1995**, *117*, 10252–10263.
13. (a) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron* **1996**, *52*, 12091–12110; (b) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron Lett.* **1997**, *38*, 8053–8056; (c) Oka, T.; Fujiwara, K.; Murai, A. *Tetrahedron* **1998**, *54*, 21–44; (d) Nagumo, Y.; Oguri, H.; Shindo, Y.; Sasaki, S.; Oishi, T.; Hirama, M.; Tomioka, Y.; Mizugaki, M.; Tsumuraya, T. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2037–2040.
14. (a) Son, J. B.; Kim, S. N.; Kim, N. Y.; Lee, D. H. *Org. Lett.* **2006**, *8*, 661–664; (b) Yakambram, P.; Puranik, V. G.; Gurjar, M. K. *Tetrahedron Lett.* **2006**, *47*, 3781–3783; (c) Son, J. B.; Kim, S. N.; Kim, N. Y.; Hwang, M.-H.; Lee, W.; Lee, D. H. *Bull. Korean Chem. Soc.* **2010**, *31*, 653–663; (d) Bates, R. W.; Song, P. *Synthesis* **2010**, 2935–2942.
15. Machinaga, N.; Kibayashi, C. *Tetrahedron Lett.* **1993**, *34*, 5739–5742.
16. (a) Kadota, I.; Park, C.-H.; Ohtaka, M.; Oguro, N.; Yamamoto, Y. *Tetrahedron Lett.* **1998**, *39*, 6365–6368; (b) Kadota, I.; Park, C. H.; Sato, K.; Yamamoto, Y. *Tetrahedron Lett.* **2001**, *42*, 6195–6197; (c) Fuwa, H.; Sasaki, M.; Tachibana, K. *Org. Lett.* **2001**, *3*, 3549–3552; (d) Kadota, I.; Kadowaki, C.; Park, C.-H.; Takamura, H.; Sato, K.; Chan, P. W. H.; Thorand, S.; Yamamoto, Y. *Tetrahedron* **2002**, *58*, 1799–1816; (e) Fuwa, H.; Kainuma, N.; Tachibana, K.; Sasaki, M. *J. Am. Chem. Soc.* **2002**, *124*, 14983–14992.
17. (a) Venkataiah, M.; Somaiah, P.; Reddipalli, G.; Fadnavis, N. W. *Tetrahedron: Asymmetry* **2009**, *20*, 2230–2233; (b) Yadav, J. S.; Rami Reddy, N.; Harikrishna, V.; Subba Reddy, B. V. *Tetrahedron Lett.* **2009**, *50*, 1318–1320.
18. (a) Kim, S.; Salomon, R. G. *Tetrahedron Lett.* **1989**, *30*, 6279–6282; (b) Cooper, A. J.; Salomon, R. G. *Tetrahedron Lett.* **1990**, *31*, 3813–3816; (c) Aicher, T. D.; Buszek, K. R.; Fang, F. G.; Forsyth, C. J.; Jung, S. H.; Kishi, Y.; Scola, P. M. *Tetrahedron Lett.* **1992**, *33*, 1549–1552; (d) Burke, S. D.; Jung, K. W.; Phillips, J. R.; Perri, R. E. *Tetrahedron Lett.* **1994**, *35*, 703–706; (e) Horita, K.; Hachiya, S.-I.; Yamazaki, T.; Naitou, T.; Uenishi, J.-I.; Yonemitsu, O. *Chem. Pharm. Bull.* **1997**, *45*, 1265–1281; (f) Burke, S. D.; Jung, K. W.; Lambert, W. T.; Phillips, J. R.; Klovning, J. J. *J. Org. Chem.* **2000**, *65*, 4070–4087; (g) Jackson, K. L.; Henderson, J. A.; Morris, J. C.; Motoyoshi, H.; Phillips, A. J. *Tetrahedron Lett.* **2008**, *49*, 2939–2941.
19. (a) Banwell, M. G.; Bui, C. T.; Simpson, G. W.; Watson, K. G. *Chem. Commun.* **1996**, 723–724; (b) Banwell, M. G.; Bui, C. T.; Simpson, G. W. *J. Chem. Soc., Perkin Trans. 1* **1998**, 791–800; (c) Edmunds, A. J. F.; Arnold, G.; Hagmann, L.; Schaffner, R.; Furlenmeier, H. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1365–1368.

20. (a) Kang, S. H.; Kang, S. Y.; Kim, C. M.; Choi, H.-W.; Jun, H.-S.; Lee, B. M.; Park, C. M.; Jeong, J. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 4779–4782; (b) Kang, S. H.; Kang, S. Y.; Choi, H.-W.; Kim, C. M.; Jun, H.-S.; Youn, J.-H. *Synthesis* **2004**, 1102–1114.
21. (a) Fettes, A.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4098–4101; (b) Crimmins, M. T.; Siliphaivanh, P. *Org. Lett.* **2003**, *5*, 4641–4644; (c) Fettes, A.; Carreira, E. M. *J. Org. Chem.* **2003**, *68*, 9274–9283; (d) Ferrie, L.; Reymond, S.; Capdevielle, P.; Cossy, J. *Org. Lett.* **2007**, *9*, 2461–2464; (e) Ferrie, L.; Boulard, L.; Pradaux, F.; Bouzbouz, S.; Reymond, S.; Capdevielle, P.; Cossy, J. *J. Org. Chem.* **2008**, *73*, 1864–1880.
22. Evans, D. A.; Ripin, D. H. B.; Halstead, D. P.; Campos, K. R. *J. Am. Chem. Soc.* **1999**, *121*, 6816–6826.
23. Takahashi, S.; Hongo, Y.; Tsukagoshi, Y.; Koshino, H. *Org. Lett.* **2008**, *10*, 4223–4226.
24. Vares, L.; Rein, T. *J. Org. Chem.* **2002**, *67*, 7226–7237.
25. Fuwa, H.; Saito, A.; Sasaki, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 3041–3044.
26. (a) Lee, C. S.; Forsyth, C. J. *Tetrahedron Lett.* **1996**, *37*, 6449–6452; (b) Pattenden, G.; Plowright, A. T. *Tetrahedron Lett.* **2000**, *41*, 983–986; (c) Pattenden, G.; Gonzalez, M. A.; Little, P. B.; Millan, D. S.; Plowright, A. T.; Tornos, J. A.; Ye, T. *Org. Biomol. Chem.* **2003**, *1*, 4173–4208; (d) Yadav, J. S.; Prakash, S. J.; Gangadhar, Y. *Tetrahedron: Asymmetry* **2005**, *16*, 2722–2728.
27. (a) Fujiwara, K.; Amano, S.; Oka, T.; Murai, A. *Chem. Lett.* **1994**, 2147–2150; (b) Blakemore, P. R.; Browder, C. C.; Hong, J.; Lincoln, C. M.; Nagornyy, P. A.; Robarge, L. A.; Wardrop, D. J.; White, J. D. *J. Org. Chem.* **2005**, *70*, 5449–5460.
28. (a) Strand, D.; Rein, T. *Org. Lett.* **2005**, *7*, 199–202; (b) Strand, D.; Norrby, P.-O.; Rein, T. *J. Org. Chem.* **2006**, *71*, 1879–1891.
29. (a) Paterson, I.; Anderson, E. A.; Dalby, S. M.; Loiseleur, O. *Org. Lett.* **2005**, *7*, 4125–4128; (b) Pan, Y.; De Brabander, J. K. *Synlett* **2006**, 853–856; (c) Paterson, I.; Anderson, E. A.; Dalby, S. M.; Genovino, J.; Lim, J. H.; Moessner, C. *Chem. Commun.* **2007**, 1852–1854.
30. (a) Micalizio, G. C.; Roush, W. R. *Tetrahedron Lett.* **1999**, *40*, 3351–3354; (b) Micalizio, G. C.; Pinchuk, A. N.; Roush, W. R. *J. Org. Chem.* **2000**, *65*, 8730–8736.
31. Noda, A.; Aoyagi, S.; Machinaga, N.; Kibayashi, C. *Tetrahedron Lett.* **1994**, *35*, 8237–8240.
32. Uenishi, J.-I.; Iwamoto, T.; Tanaka, J. *Org. Lett.* **2009**, *11*, 3262–3265.
33. Yonemitsu, O.; Yamazaki, T.; Uenishi, J.-I. *Heterocycles* **1998**, *49*, 89–92.
34. Robertson, J.; Meo, P.; Dallimore, J. W. P.; Doyle, B. M.; Hoarau, C. *Org. Lett.* **2004**, *6*, 3861–3863.
35. Robertson, J.; Dallimore, J. W. P. *Org. Lett.* **2005**, *7*, 5007–5010.
36. North, C. D.Phil. Thesis, Oxford, 2010.
37. (a) Leuck, G. J.; Cejka, L. *Org. Synth.*; Wiley, New York, NY, 1941; Collect. Vol. 1; 283–284; (b) Jung, M. E.; Kiankarimi, M. *J. Org. Chem.* **1998**, *63*, 2968–2974.
38. Sadig, J. Chemistry Part II Thesis, Oxford, 2008.
39. Achmatowicz, O., Jr.; Bukowski, P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. *Tetrahedron* **1971**, *27*, 1973–1996.
40. We believe that this is the first reported case of selective oxidation of one of two or more furan rings in which only one bears an α-hydroxyl group. Nelson has reported a variety of mono Achmatowicz oxidations of symmetrical difuryl substrates; see, for example, Hodgson, R.; Majid, T.; Nelson, A. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1631–1643.
41. Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136–6137.
42. Marshall, J. A.; Nelson, D. J. *Tetrahedron Lett.* **1988**, *29*, 741–744.
43. Hoff, S.; Brandsma, L.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 916–924.
44. Yamakawa, K.; Satoh, T.; Ohba, N.; Sakaguchi, R.; Takita, S.; Tamura, N. *Tetrahedron* **1981**, *37*, 473–479.
45. Baldwin, J. E.; Höfle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 7125–7127.
46. (a) Nakata, T.; Tanaka, T.; Oishi, T. *Tetrahedron Lett.* **1983**, *24*, 2653–2656; (b) The reagent was either prepared and used in situ or a THF solution was used, prepared by the procedure reported in: Narasimhan, S.; Madhavan, S.; Prasad, K. G. *J. Org. Chem.* **1995**, *60*, 5314–5315.
47. Liu, X.; Qin, B.; Zhou, X.; He, B.; Feng, X. *J. Am. Chem. Soc.* **2005**, *127*, 12224–12225.
48. Nicolaou, K. C.; Snyder, S. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1012–1044.
49. Pérez, M.; Canoa, P.; Gómez, G.; Teijeira, M.; Fall, Y. *Synthesis* **2005**, 411–414.
50. We note that the ^{13}C NMR listings here are systematically offset relative to those reported in Ref. 34, probably due to a referencing error in the earlier NMR work.