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Conjugate addition of organocopper reagents to γ-alkoxybutenolides and application to the synthesis of non-racemic alkyl cyclopentenones

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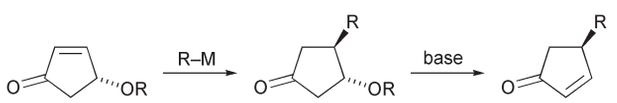
Simple organocopper reagents are shown to undergo *anti*-stereoselective 1,4-addition to menthyloxy-substituted lactone **1** in the presence of $BF_3{\cdot}OEt_2$; the Lewis acid causes partial epimerisation of the acetal centre *after* conjugate addition. Enolate alkylation of the adducts leads to di- and trisubstituted lactones that are converted, in favourable cases, into di- and trisubstituted cyclopentenones.

Introduction

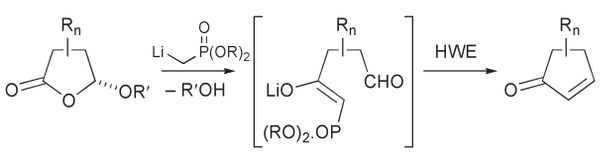
Enantiomerically pure 4-alkylcyclopentenones are of central importance in the construction of a diverse range of natural products and biologically active non-natural analogues, and routes to their synthesis are highly developed, largely driven by prostaglandin research.[1] A classical synthesis of this class of compounds hinges on the *anti*-selective conjugate addition[2] of organometallic reagents, notably dialkyl cuprates, to 4-hydroxycyclopentenone in protected form followed by elimination (Scheme 1). Consequently, the problem is reduced to the need to assemble optically active alkoxy- or silanyloxy-cyclopentenones, for which chemical and chemoenzymatic solutions have been developed and widely adopted.[3]



Scheme 1

We first became interested in this area during the development of our formal synthesis of (±)-roseophilin in which the relative stereochemistry in the natural product derived ultimately from stereoselective 1,4-addition to (±)-4-(6-chlorohexyl)-cyclopentenone.[4] The availability, on a large scale, of both enantiomers of this enone was crucial to our projected synthesis of both enantiomers of roseophilin and hence an assignment of the absolute configuration of the natural product, which was not known at the time. Mindful of the wealth of literature on this general problem,[5] we sought a *practical* alternative solution.

Our approach is based on the known reaction of alkoxybutyrolactones with lithiated phosphonates to yield cyclopentenones directly in a tandem ring-opening/intramolecular Horner–Wadsworth–Emmons olefination (Scheme 2).[6] In the context of the enantioselective synthesis of 4-alkylcyclopentenones, this proposal requires access to 3-alkyl-4-alkoxybutyrolactones in both enantiomeric series, which we envisaged as deriving from (5*R*)-5-(*l*-menthyloxy)-2[5*H*]-furanone **1**[7] or its enantiomer, on the basis of the extensive investigations of Feringa (see below). The realisation of this proposal would constitute an effective four-step asymmetric synthesis of 4-alkylcyclopentenones. However, two factors had to be addressed at the outset: (1) most conjugate additions to lactone **1** involve heteroatoms or heteroatom-stabilised *C*-nucleophiles;[8] we are aware of only a single report[9] describing the direct introduction of a *simple* alkyl group, and problems with this approach have been noted;[10] (2) to the best of our knowledge, the lactone–enone transformation has been reported only for cases where the lactone carbonyl α-position is either fully substituted or forms part of a ring linked to the β-position.[11]



Scheme 2

Results and discussion

Conjugate additions

Attention was first turned to the conjugate addition. Lithium dialkylcuprates were not effective, leading to either incomplete reaction or complex product mixtures within which reduction products were evident (see below), but organocopper reagents could be added reasonably efficiently in the presence of a slight excess of $BF_3{\cdot}OEt_2$.[12] Optimum results were obtained with a three-fold excess of the organocopper/Lewis acid mixture, but use of 1.5 equivalents led to only a slight reduction in yield (Scheme 3, Table 1). The addition of methylcopper proceeded poorly (entry a)—the use of zincate reagents offering only a slight improvement[13]—but organocopper reagents derived from 1°-alkyllithiums added reliably in yields ranging from moderate to excellent (entries b–g); branching at the adding centre was tolerated (entries h and i) albeit with a reduction in yield, and phenylcopper added in poor yield (entry j). Observation of enol ether **5** and butyrolactone **6** implicated reagent-induced reduction as a major contributor to the lowered yields in at least some cases; a plausible mechanism, based on electrocyclic ring-opening of dianion **4** or an equivalent radical anion,[14] is presented in Scheme 4.

In the ^{1}H NMR spectra of adducts **2** and **3**, the acetal proton resonance is a sensitive indicator of the product stereochemistry, and the diastereoselectivity of these reactions was judged by integration of this resonance in the spectra of the crude 1,4-addition products. The data in Table 1 show that for the major isomers (**2**) this resonance shows a very consistent 2.2–2.6 Hz coupling constant;[15] in contrast, this resonance in the minor isomers (**3**) appears as a slightly shifted doublet with a larger coupling constant (4.6–4.8 Hz). On this basis, almost complete stereocontrol was observed in some cases but, in general, the d.r. varied between *ca.* 2–4 : 1; fortunately, the diastereomers could be readily

† Responsible for obtaining the X-ray structure in Fig. 1.

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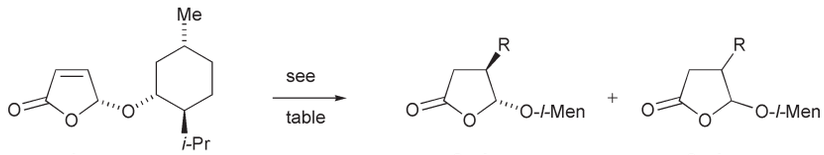
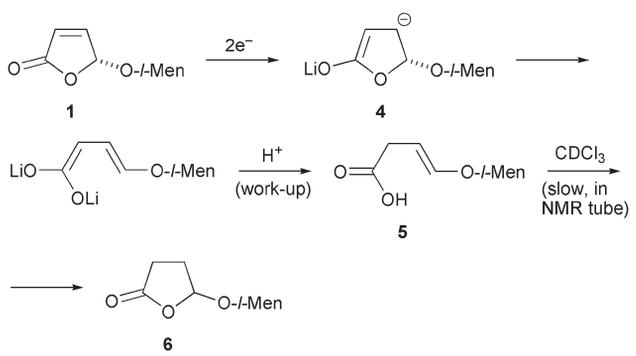


Scheme 3 Reagents: RLi/CuI/$BF_3{\cdot}OEt_2$, THF, −78 °C.

Table 1

Entry	RLi	Yield (%)	d.r. (**2**:**3**)	$[a]_D$[a]	δ_H/ppm (*J*/Hz) for C*H*(OR)$_2$ **2**	**3**
a	MeLi	5	—	—	5.28 (2.2)	—
b	BuLi	76	4.2:1	−145.5	5.34 (2.4)	5.47 (4.8)
c	*i*-BuLi	62	3:1	−107.3	5.33 (2.4)	5.45 (4.8)
d	3-butenyl-Li	63	4:1	−132.9	5.38 (2.4)	5.47 (4.7)
e	6-chlorohexyl-Li	86	3.5:1	−136.3[b]	5.35 (2.4)	5.48 (4.7)
f	7-octenyl-Li	74	2.2:1	−124.6	5.31 (2.3)	5.44 (4.8)
g	8-TBDPSO-octyl-Li	79	2.2:1	−72.2	5.37 (2.3)	5.49 (4.6)
h	*s*-BuLi	41	—[c,d]	—[d]	5.45/5.46 (2.6/2.4)[d]	—
i	*t*-BuLi	44	>95:<5	−157.7	5.52 (2.3)	—
j	PhLi	25	>95:<5	−140.6	5.59 (2.5)	—

[a] Data for **2b**–**g** and **2i**,**j**; *c* 0.15–1.2, $CHCl_3$. [b] Run in ethanol. [c] The ^{1}H NMR spectrum of the crude material was insufficiently clean to allow a ratio to be extracted with confidence. [d] Compound **2h** is a 1:1 mixture of 2′-epimers



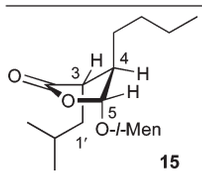
Scheme 4

separated. In addition to this coupling constant information, support for the stereochemical assignment for the major isomers (**2**) was forthcoming from NOE experiments (see, for example, Table 2), from the $[a]_D$ data (the *trans*- diastereomers being characterised by a large negative specific rotation,[16] see Table 1) and, in the case of **2b**, by X-ray crystallography (Fig. 1).[17]

The production of a second diastereomer in these conjugate additions warrants comment. Most nucleophiles add to butenolide **1** with essentially exclusive formation of the *anti*-diastereomer therefore the formation of significant proportions (up to 30%) of what appear to be *cis*-adducts was surprising. However, all published nucleophilic additions to lactone **1** proceed without Lewis acid mediation and it was thought likely that the presence of $BF_3{\cdot}OEt_2$ in the organocopper additions led to this discrepancy. Control experiments were run to establish whether the conjugate addition is inherently poorly diastereoselective, or whether the Lewis acid compromises the stereochemistry of the acetal centre in lactone **1** or adducts **2** (or both). Treatment of a cold (−78 °C) THF solution of lactone **1** with one equivalent of $BF_3{\cdot}OEt_2$ led to rapid epimerisation; on this basis it might be concluded that the diastereomers **2** and **3** result from *anti*-stereoselective conjugate addition to epimeric lactones **1** and **1′**. This possibility was ruled out by performing a conjugate addition on pure lactone **1′**; the major diastereomer **2b′** from this reaction was not the minor isomer (**3b**) obtained from the equivalent reaction with lactone **1**. Secondly, treatment of a cold (−78 °C) THF solution of adduct **2b** with one equivalent of $BF_3{\cdot}OEt_2$ led to the formation of just two major diastereomers, the starting material (**2b**) and the compound obtained as a minor diastereomer from the original conjugate addition experiment. On this basis, the minor diastereomer was assigned as the *cis*-product **3b**, arising from epimerisation at the acetal centre; formation of the alternative *cis*-diastereomer **3b′** was discounted because this would require epimerisation of just the 4-position without concomitant isomerisation of the acetal centre. These experiments are summarised in Scheme 5.

In summary, conjugate addition of alkylcopper reagents, mediated by $BF_3{\cdot}OEt_2$, appears to be highly stereoselective, as expected, but the Lewis acidic environment leads to loss of stereochemical integrity at the acetal centre. Since the stereochemistry at the acetal centre is of no importance to the projected chemistry, this epimerisation is of no consequence.

Table 2

	Irradiate	Enhancement (%) H3	H4	H5	H1′
	H3	—	4.5	1.9	2.0
	H4	4.1	—	4.2	4.1
	H5	1.8	3.8	—	0
	H1′	3.3	6.3	0	—

15

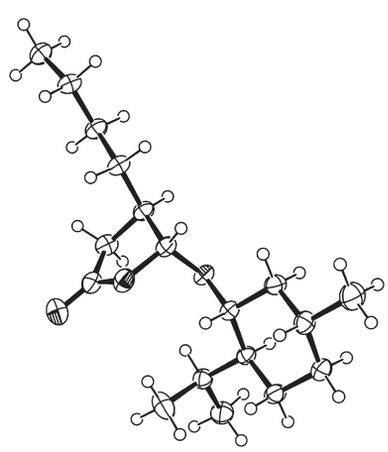
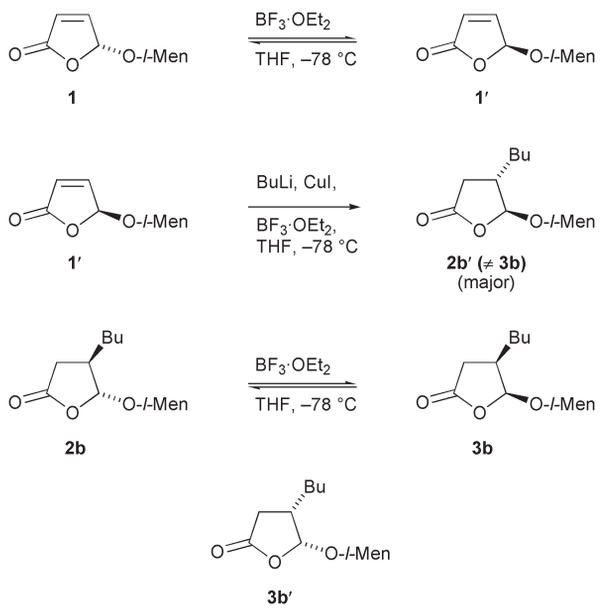


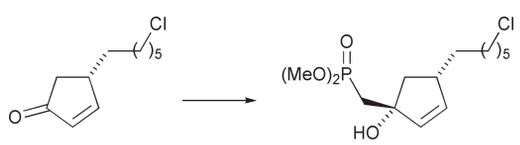
Fig. 1 ORTEP view of lactone **2b** taken from its crystal structure.[17]



Scheme 5

Lactone to enone conversion

Addition of lithiated dimethyl methylphosphonate to a representative lactone (**2e**) under a variety of conditions (T: −78 °C → 20 °C; solvent: Et_2O, THF, or DME; with or without added LiBr[11a]) produced (the enantiomer of) enone **7** in very low yield, the 'best' result being 13% with the majority of the product mixture being intractable polar material. To explore the possibility that product trapping by the lithiated phosphonate could be detrimental to this reaction, enone **7**[18] was treated with the lithiated phosphonate and, indeed, a rapid reaction ensued to generate 3°-alcohol **8** (in 61% yield as a single diastereomer, assigned by NOE experiments; enone **7** was recovered in 20% yield) (Scheme 6). However, inspection of the ^{1}H NMR data obtained on the crude product from the reaction of lactone **2e** showed that none of the alcohol **8** was present, and this was eliminated as a major cause of failure of this reaction.



Scheme 6 Reagents: $MeP(O)(OMe)_2$, BuLi, THF, −78 °C.

Substrate decomposition following enolisation by the lithiated phosphonate was considered as an alternative potential contributor to the failure of this reaction. On the basis of the small $J_{H4,H5}$ value (in lactones **2**) the more populated of the two envelope conformations of the ring is expected[16] to be that in which H3α is pseudoaxial and perfectly aligned for rapid deprotonation (**B**, Figure 2); furthermore, this proton is *anti*- to the C4 alkyl substituent and therefore sterically accessible.

In order to inhibit this mode of decomposition, the 3α position was blocked by enolate alkylation of a representative lactone (**2b**) to generate '3α-blocked' substrate **9** (Scheme 7). It was gratifying to find that this material responded to treatment with the lithiated phosphonate to yield enone **11** in an unoptimised 60% yield (the balance of material being starting

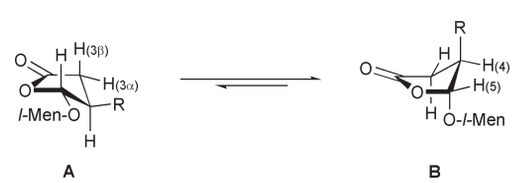
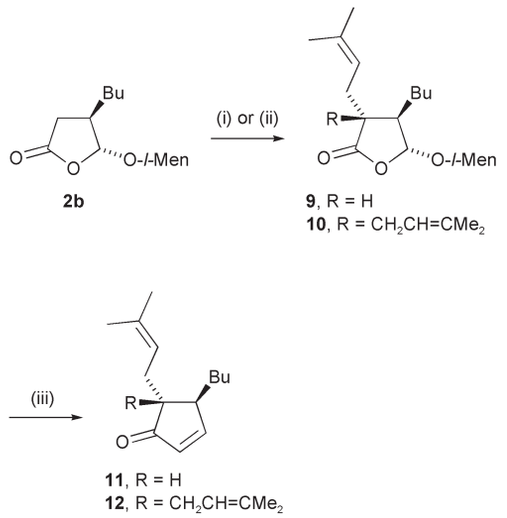
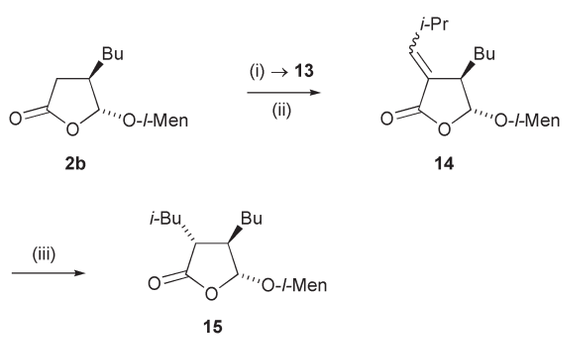


Fig. 2



Scheme 7 Reagents: (i) KHMDS, THF, −78 °C; prenyl bromide (1.0 equiv.); (ii) LiHMDS, THF, −78 °C; prenyl bromide (2.0 equiv.); (iii) $MeP(O)(OMe)_2$, BuLi, LiBr, THF, −78 °C.

lactone). Furthermore, α,α-dialkylated lactone **10** afforded trisubstituted enone **12** in 72% yield. To establish deprotonation of H3α (rather than H3β) as the crucial problem, an attempt was made to produce a 3,4-*cis*-disubstituted lactone by hydrogenation of an alkylidene lactone. Thus, enoate **14** (Scheme 8), produced by condensation of lactone **2b** with isobutyraldehyde, was hydrogenated, but with difficulty and only in the presence of triethylamine.[10b] Under these conditions the 3,4-stereochemistry (in **15**) was shown to be *trans*- by NOE (Table 2), and this aspect of the project was discontinued.



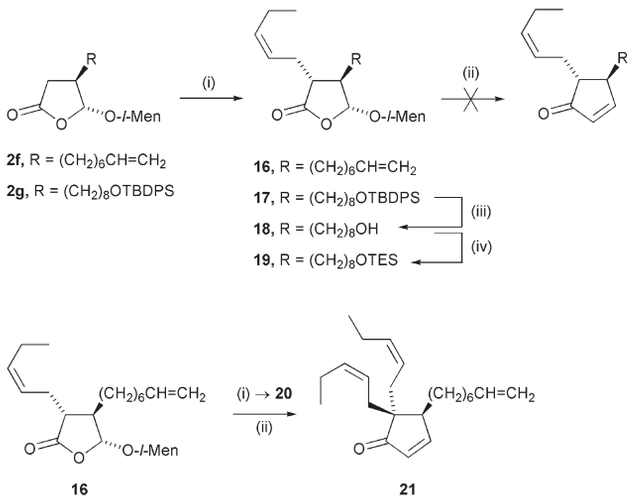
Scheme 8 Reagents: (i) LHMDS, isobutyraldehyde, THF; (ii) MsCl, Et_3N, 1,2-dichloroethane; DBU, CH_2Cl_2; (iii) H_2 (4 bar), Pd/C, Et_3N (0.1 equiv.), EtOH.

Synthetic applications

These studies raised the possibility of producing a variety of biologically significant 3,4-dialkylcyclopentenones; therefore, in anticipation of a synthesis of the methyl ester of chromomoric acid B,[19] lactones **16–19** (Scheme 9) were treated with the lithiated phosphonate. Under the standard conditions, starting lactone was returned in all cases with good mass recovery, just traces of enone being present as inferred from ^{1}H NMR analysis of the crude product. Given the success of the butyl cases, it was concluded that the longer, functionalised side-chains in lactones **16–19**, acted in combination with efficient shielding of the carbonyl α-face by the pentenyl substituent to slow addition to the lactone carbonyl relative to enolisation. In support of this notion, non-enolisable but sterically encumbered substrate **20** was converted into enone **21** in 50% yield (80% based on recovered lactone **20**).

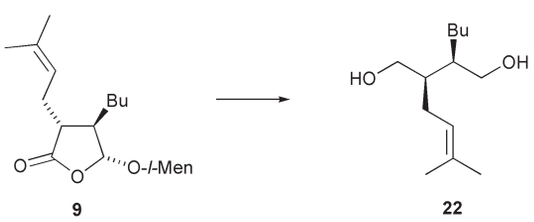
Conclusion

In summary, we have provided a number of *anti*-selective 1,4-additions of simple alkyl copper reagents to γ-alkoxybutenolide **1** in the presence of $BF_3{\cdot}OEt_2$, and shown that the acetal centre



Scheme 9 Reagents: (i) LHMDS, (*Z*)-EtCH=CHCH$_2$Br; (ii) MeP(O)(OMe)$_2$, BuLi, (LiBr), THF, −78 °C → 20 °C; (iii) TBAF; (iv) TESCl, Et$_3$N, DMAP.

is epimerised, under these conditions, subsequent to conjugate addition. We have also shown that tandem lactone cleavage and Horner–Wadsworth–Emmons reaction affords 4-alkylcyclopentenones in a synthetically useful sense to generate di- and tri-substituted cyclopentenones. These latter reactions are sensitive to the steric environment about the lactone carbonyl and large 4-alkyl substituents appear to impede enone formation. During this work we were not able to identify a general practical route to alkylcyclopentenones based on this route, but the availability of simple 3,4-dialkyl derivatives of menthyloxybutyrolactone as single stereoisomers is of considerable synthetic value. For example, as a generic reaction for the construction of 2,3-dialkylbutane-1,4-diols in five steps from furfuraldehyde, lactone **9** was reduced in high yield to give diol **22** (Scheme 10).



Scheme 10 Reagents: LiAlH$_4$, THF, 82%.

Experimental

For general experimental procedures see reference 4b.

Note on numbering: In the menthyloxy dihydrofuranones, C4 side chain protons are indicated with ′; menthyl protons with ″; C3 side chain protons with ‴. In the cyclopentenones, C4 side chain protons are indicated with ′; C5 side chain protons with ″.

General procedure A (for 1,4-addition of organocopper reagents derived from commercial organolithiums)

A solution of organolithium RLi (*x* mmol) was added to a cold (−78 °C) slurry of CuI (*x* mmol, pre-dried by evaporation with toluene) in anhydrous THF (*ca.* 2.5 mL per mmol of RLi). With vigorous stirring, the black reaction mixture was allowed to warm to −25 °C over 20 min, cooled to −78 °C and $BF_3{\cdot}Et_2O$ (*x* mmol) was added followed by a solution of furanone **1** (0.33*x* mmol) in anhydrous THF (*ca.* 3 mL per mmol of furanone **1**). The reaction mixture was stirred at this temperature for 2 h, then quenched with sat. aq. NH_4Cl solution at −78 °C, and allowed to warm to RT; the grey precipitate was filtered off through a plug of Celite® (washing through thoroughly with ether). The filtrate was washed with brine and the organic layer dried ($MgSO_4$), filtered and concentrated *in vacuo* giving, in most cases, a pale yellow solution. Where a mixture of two diastereoisomers was obtained after rough purification by flash column chromatography (95 : 5 petrol : ethyl acetate) the major butyrolactone was isolated by a second, more careful, chromatography step.

General procedure B (for 1,4-addition of organocopper reagents derived from non-commercially available organolithiums)

A solution of the appropriate 1°-iodoalkane (*x* mmol) in anhydrous ether (*ca.* 3.5 mL per mmol of the iodoalkane) was cooled to −78 °C and *tert*-butyllithium (1.7 M solution in pentane, 2*x* mmol) was added. After 20 min, the solution was added by cannula to a cold (−78 °C) slurry of CuI (*x* mmol, predried by evaporation with toluene) in anhydrous THF (30 mL). With vigorous stirring, the black reaction mixture was allowed to warm to −25 °C over 20 min, cooled to −78 °C and $BF_3{\cdot}Et_2O$ (*x* mmol) was added followed by a solution of furanone **1** (0.33*x* mmol) in anhydrous THF (*ca.* 1.5 mL per mmol of furanone **1**). The reaction mixture was stirred at this temperature for 2 h, then quenched with sat. aq. NH_4Cl solution at −78 °C, and allowed to warm to RT; the grey precipitate was filtered off through a plug of Celite® (washing through thoroughly with ether). The filtrate was washed with brine, the combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo* giving, in most cases, a pale yellow solution. A mixture of two diastereoisomers was obtained after rough purification by flash column chromatography (95 : 5 petrol : ethyl acetate), from which the major lactone was then isolated by a second, more careful, chromatography step.

(4*R*,5*R*)-4-Methyl-5-(*l*-menthyloxy)dihydro-2-furanone[8d,g] 2a

General procedure A [furanone **1** (100 mg, 0.42 mmol), R = Me] gave the title compound (**2a**) as a white solid (5 mg, 5%). R_f 0.24 (9 : 1 petrol : ethyl acetate); m.p. 78–80 °C (lit.[8d,g] m.p. 78.2–79.8 °C); ν_{max} (KBr disc)/cm^{-1} 3020s, 2958s, 2927s, 1777s, 1456m, 1215s, 1122m, 931m, 906m, 756s; δ_H (500 MHz, $CDCl_3$) 0.77 (3H, d, *J* 6.9, C(10″)H$_3$), 0.89 (3H, d, *J* 6.6, C(8″)H$_3$), 0.95 (3H, d, *J* 6.6, C(9″)H$_3$), 0.77–0.97 (2H, m, C(4″)H, C(6″)H), 0.95–1.09 (1H, m, C(3″)H), 1.13 (3H, d, *J* 7.2, C(1′)H$_3$), 1.17–1.25 (1H, m, C(2″)H), 1.34–1.43 (1H, m, C(7″)H), 1.59–1.70 (2H, m, C(3″)H, C(4″)H), 2.05–2.10 (2H, m, C(5″)H, C(6″)H), 2.11 (1H, dd, *J* 17.5, 4.0, C(3)H$_A$), 2.38–2.41 (1H, m, C(4)H), 2.84 (1H, dd, *J* 17.5, 8.2, C(3)H$_B$), 3.51 (1H, td, *J* 10.7, 4.2, C(1″)H), 5.28 (1H, d, *J* 2.2, C(5)H); δ_C (125 MHz, $CDCl_3$) 15.6, 17.0, 20.8, 22.1, 22.9, 25.3, 31.5, 34.2, 35.4, 36.2, 39.7, 47.6, 76.6, 106.0, 176.1; *m*/*z* (CI, NH_3) 272 (MNH_4^+, 20%), 255 (MH^+, 60), 134 (100), 99 (60), 81 (60); HRMS (ES) found 272.2227, calculated for $C_{15}H_{30}NO_3$ (MNH_4^+) 272.2226.

(4*R*,5*R*)-4-Butyl-5-(*l*-menthyloxy)dihydro-2-furanone 2b

General procedure A [furanone **1** (100 mg, 0.42 mmol), R = Bu] gave the *title compound* (**2b**) and its C5-epimer (**3b**) in a 4.2 : 1 ratio (95 mg, 76%) from which the major diastereomer (**2b**) was obtained as colourless crystals (76 mg, 61%). R_f 0.34 (95 : 5 petrol : ethyl acetate); m.p. 62–65 °C; $[\alpha]_D^{22} = -145.5$ (*c* 0.4, $CHCl_3$); ν_{max} (KBr disc)/cm^{-1} 2956s, 2927s, 2871s, 1788s, 1457m, 1370s, 1167s, 1129s, 941s; δ_H (400 MHz, $CDCl_3$) 0.77 (3H, d, *J* 6.4, C(10″)H$_3$), 0.90 (3H, d, *J* 6.4, C(8″)H$_3$), 0.90 (3H, t, *J* 8.4, C(4′)H$_3$), 0.93 (3H, d, *J* 6.4, C(9″)H$_3$), 0.77–0.97 (2H, m, C(4″)H, C(6″)H), 0.94–1.05 (1H, m, C(3″)H), 1.17–1.42 (7H, m, C(1′)H, C(2′,3′)$_2$H$_4$, C(2″)H, C(7″)H), 1.50–1.57 (1H, m, C(1′)H), 1.60–1.70 (2H, m, C(3″)H, C(4″)H), 2.02–2.12 (2H, m, C(5″)H, C(6″)H), 2.16 (1H, dd, *J* 17.6, 4.4, C(3)H$_A$), 2.22–2.28 (1H, m, C(4)H), 2.78 (1H, dd, *J* 17.6, 8.4, C(3)H$_B$), 3.49 (1H, td, *J* 10.8, 4.0, C(1″)H), 5.34 (1H, d, *J* 2.4, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 15.6, 20.9, 22.5, 22.6, 23.1, 25.4, 29.1, 31.3, 31.6, 33.9, 34.3, 39.8, 41.6, 47.7, 76.9, 105.0, 176.1; *m*/*z* (CI, NH_3) 297 (MH^+, 15%), 176 (100), 159 (15); HRMS (ES) found 297.2430, calculated for $C_{18}H_{33}O_3$ (MH^+) 297.2430. **(4*R*,5*S*)-4-Butyl-5-**

(*l*-menthyloxy)dihydro-2-furanone (3b) was also obtained, as a colourless oil (18 mg, 15%). R_f 0.33 (95 : 5 petrol : ethyl acetate); δ_H (400 MHz, $CDCl_3$) 0.76 (3H, d, *J* 6.8, C(10″)H_3), 0.89 (3H, d, *J* 6.8, C(8″)H_3), 0.90 (3H, t, *J* 6.4, C(4′)H_3), 0.91 (3H, d, *J* 6.8, C(9″)H_3), 0.76–1.03 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.21–1.65 (10H, m, C(1′–3′)$_3H_6$, C(2″)H, C(3″)H, C(4″)H, C(7″)H), 2.08–2.20 (2H, m, C(5″)H, C(6″)H), 2.29–2.48 (3H, m, C(3)H_2, C(4)H), 3.37 (1H, td, *J* 10.4, 4.4, C(1″)H), 5.47 (1H, d, *J* 4.8, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 15.7, 21.1, 22.1, 22.4, 25.1, 28.0, 29.9, 31.4, 33.1, 34.1, 41.6, 42.7, 48.4, 81.4, 106.0, 176.7 (one resonance not seen); *m*/*z* (CI, NH_3) 314 (MNH_4^+, 20%), 297 (MH^+, 40), 176 (100), 158 (30); HRMS (ES) found 297.2430, calculated for $C_{18}H_{33}O_3$ (MH^+) 297.2430.

(4*S*,5*S*)-4-Butyl-5-(*l*-menthyloxy)dihydro-2-furanone 2b′

General procedure A [furanone **1**′ (100 mg, 0.42 mmol), R = Bu] gave the *title compound* (**2b**′) and its C5-epimer (**3b**′) in a 4.5 : 1 ratio (68 mg, 55%) from which the major diastereomer (**2b**′) was isolated as a colourless oil (56 mg, 45%). R_f 0.70 (7 : 3 petrol : ethyl acetate); $[\alpha]_D^{22}$ = +26.9 (*c* 0.80, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2959s, 2924s, 2872s, 1779s, 1458m, 1422m, 1370s, 1167s, 1129s, 941s; δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 6.9, C(10″)H_3), 0.90 (3H, d, *J* 6.8, C(8″)H_3), 0.91 (3H, t, *J* 6.8, C(4′)H_3), 0.92 (3H, d, *J* 6.8, C(9″)H_3), 0.77–0.97 (2H, m, C(4″)H, C(6″)H), 0.95–1.07 (1H, m, C(3″)H), 1.21–1.39 (7H, m, C(1′)H, C(2′,3′)$_2H_4$, C(2″)H, C(7″)H), 1.51–1.59 (1H, m, C(1′)H), 1.59–1.67 (2H, m, C(3″)H, C(4″)H), 2.03–2.10 (1H, m, C(5″)H), 2.14 (1H, dd, *J* 17.6, 5.2, C(3)H_B), 2.14–2.20 (1H, m, C(6″)H), 2.29–2.35 (1H, m, C(4)H), 2.78 (1H, dd, *J* 17.6, 8.7, C(3)H_A), 3.38 (1H, td, *J* 10.7, 4.4, C(1″)H), 5.23 (1H, d, *J* 3.0, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.8, 16.1, 21.0, 22.1, 22.4, 23.1, 25.6, 29.2, 31.3, 31.6, 34.0, 34.1, 41.9, 42.7, 48.2, 82.2, 110.3, 183.9; *m*/*z* (CI, NH_3) 297 (MH^+, 15%), 176 (100), 159 (15); HRMS (ES) found 297.2430, calculated for $C_{18}H_{33}O_3$ (MH^+) 297.2430.

(4*R*,5*R*)-4-Isobutyl-5-(*l*-menthyloxy)dihydro-2-furanone 2c

General procedure A (furanone **1** (100 mg, 0.42 mmol), R = isobutyl) gave the *title compound* (**2c**) and its C5-epimer (**3c**) in a 3 : 1 ratio (77 mg, 62%) from which the major diastereomer (**2c**) was isolated as a pale yellow oil (57 mg, 46%). R_f 0.61 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22}$ = −107.3 (*c* 0.34, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2960s, 2928s, 2872s, 1777s, 1106m, 930m, 756s, 670s; δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 7.0, C(10″)H_3), 0.89 (3H, d, *J* 6.5, C(8″)H_3), 0.91 (3H, d, *J* 6.5, C(9″)H_3), 0.94 (2 × 3H, 2 × d, *J* 6.5, C(3′)H_3, C(4′)H_3), 0.77–0.97 (2H, m, C(4″)H, C(6″)H), 0.95–1.07 (1H, m, C(3″)H), 1.20–1.34 (2H, m, C(1′)H, C(2″)H), 1.34–1.44 (2H, m, C(1′)H, C(7″)H), 1.59–1.70 (3H, m, C(2′)H, C(3″)H, C(4″)H), 2.05–2.13 (2H, m, C(5″)H, C(6″)H), 2.16 (1H, dd, *J* 17.5, 4.5, C(3)H_A), 2.34–2.40 (1H, m, C(4)H), 2.80 (1H, dd, *J* 17.5, 8.4, C(3)H_B), 3.51 (1H, td, *J* 10.7, 4.2, C(1″)H), 5.33 (1H, d, *J* 2.4, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 15.5, 20.8, 22.1, 22.2, 22.6, 22.9, 25.3, 25.7, 31.2, 34.0, 34.2, 39.5, 39.7, 40.9, 47.6, 76.7, 105.1, 176.1; *m*/*z* (CI, NH_3) 314 (MNH_4^+, 20%), 297 (MH^+, 30), 176 (100), 159 (20); HRMS (ES) found 297.2429, calculated for $C_{18}H_{33}O_3$ (MH^+) 297.2430. The minor diastereomer (**3c**) exhibits a distinctive resonance in the ^1H NMR spectrum at δ 5.45 (1H, d, *J* 4.8).

(4*R*,5*R*)-4-(But-3-enyl)-5-(*l*-menthyloxy)dihydro-2-furanone 2d

General procedure B [furanone **1** (100 mg, 0.42 mmol), R = but-3-enyl] gave the *title compound* (**2d**) and its C5-epimer (**3d**) in a 4 : 1 ratio (78 mg, 63%) from which the major diastereomer (**2d**) was obtained as pale yellow crystals (62 mg, 50%). R_f 0.62 (9 : 1 petrol : ethyl acetate); m.p. 49–53 °C; $[\alpha]_D^{22}$ = −132.9 (*c* 1.0, $CHCl_3$); ν_{max} (KBr disc)/cm^{-1} 2957s, 2928s, 2870s, 1778s, 1456m, 1418m, 1370m, 1170m, 1110m, 937s, 757s; δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 6.8, C(10″)H_3), 0.89 (3H, d, *J* 6.8, C(8″)H_3), 0.95 (3H, d, *J* 6.8, C(9″)H_3), 0.78–0.95 (2H, m, C(4″)H, C(6″)H), 0.95–1.05 (1H, m, C(3″)H), 1.19–1.29 (2H, m, C(2″)H, C(7″)H), 1.33–1.48 (2H, m, C(1′)H_2), 1.60–1.71 (4H, m, C(2′)H_2, C(3″)H, C(4″)H), 2.07–2.19 (2H, m, C(5″)H, C(6″)H), 2.19 (1H, dd, *J* 17.6, 4.6, C(3)H_A), 2.27–2.33 (1H, m, C(4)H), 2.82 (1H, dd, *J* 17.6, 8.4, C(3)H_B), 3.52 (1H, td, *J* 10.8, 4.4, C(1″)H), 4.98–5.07 (2H, m, C(4′)H_2), 5.38 (1H, d, *J* 2.4, C(5)H), 5.78 (1H, app. ddt, app. *J* 17.0, 10.0, 6.4, C(3′)H); δ_C (100.6 MHz, $CDCl_3$) 15.5, 20.9, 22.2, 23.0, 25.4, 31.0, 31.1, 31.3, 33.8, 34.3, 39.8, 41.0, 47.7, 76.7, 104.9, 115.8, 137.0, 175.9; *m*/*z* (CI, NH_3) 312 (MNH_4^+, 5%), 295 (MH^+, 10), 174 (50), 156 (35), 138 (50), 123 (45), 95 (100), 81 (85); HRMS (ES) found 295.2272, calculated for $C_{18}H_{31}O_3$ (MH^+) 295.2273. The minor diastereomer (**3d**) exhibits a distinctive resonance in the ^1H NMR spectrum at δ 5.47 (1H, d, *J* 4.7).

(4*R*,5*R*)-4-(6-Chlorohexyl)-5-(*l*-menthyloxy)dihydro-2-furanone 2e

General procedure B [furanone **1** (700 mg, 2.94 mmol), R = 6-chlorohexyl] gave the *title compound* (**2e**) and its C5-epimer (**3e**) in a 3.5 : 1 ratio (908 mg, 86%) from which a sample of the major diastereomer (**2e**) was isolated, as a colourless oil, for analytical purposes. R_f 0.32 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22}$ = −136.3 (*c* 1.0, EtOH); ν_{max} (thin film)/cm^{-1} 2929s, 2860s, 1787s, 1456s, 1420m, 1370m, 1165s, 1108s, 939s; δ_H (400 MHz, $CDCl_3$) 0.77 (3H, d, *J* 6.5, C(10″)H_3), 0.88 (3H, d, *J* 6.5, C(8″)H_3), 0.94 (3H, d, *J* 6.5, C(9″)H_3), 0.87–0.91 (2H, m, C(4″)H, C(6″)H), 0.98–1.03 (1H, m, C(3″)H), 1.21–1.29 (2H, m, C(2″)H, C(7″)H), 1.32–1.36 (5H, m, C(1′)H, C(2′,3′)$_2H_4$), 1.42–1.46 (2H, m, C(4′)H_2), 1.53–1.57 (1H, m, C(1′)H), 1.62–1.69 (2H, m, C(3″)H, C(4″)H), 1.76 (2H, quin., *J* 6.8, C(5′)H_2), 2.06–2.10 (2H, m, C(5″)H, C(6″)H), 2.17 (1H, dd, *J* 17.5, 4.5, C(3)H_A), 2.23–2.31 (1H, m, C(4)H), 2.80 (1H, dd, *J* 17.5, 8.4, C(3)H_B), 3.50 (1H, td, *J* 10.7, 4.2, C(1″)H), 3.53 (2H, t, *J* 6.8, C(6′)H_2), 5.35 (1H, d, *J* 2.4, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 15.6, 20.9, 22.2, 23.0, 25.4, 26.6, 26.8, 28.6, 31.3, 31.8, 32.4, 33.9, 34.2, 39.8, 41.5, 44.9, 47.7, 76.7, 105.0, 176.1; *m*/*z* (CI, NH_3) 361 ($M^{37}ClH^+$, 3%), 359 ($M^{35}ClH^+$, 10), 238 (95), 202 (100), 185 (30), 167 (30), 38 (65), 95 (40), 81 (45); HRMS (ES) found 359.2353, calculated for $C_{20}H_{36}O_3{}^{35}Cl$ (MH^+) 359.2355. The minor diastereomer (**3e**) exhibits a distinctive resonance in the ^1H NMR spectrum at δ 5.48 (1H, d, *J* 4.7).

(4*R*,5*R*)-5-(*l*-Menthyloxy)-4-(oct-7-enyl)-4-dihydro-2-furanone 2f

General procedure B [furanone **1** (2.5 g, 10.6 mmol), R = oct-7-enyl], gave the *title compound* (**2f**) and its C5-epimer (**3f**) in a 2.2 : 1 ratio (2.74 g, 74%) from which the major diastereomer (**2f**) was isolated as a colourless oil (1.44 g, 39%). R_f 0.48 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22}$ = −124.6 (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2927s, 2856s, 1790s, 1641w, 1456m, 1164m, 1106m, 941m; δ_H (400 MHz, $CDCl_3$) 0.74 (3H, d, *J* 6.8, C(10″)H_3), 0.84 (3H, d, *J* 6.8, C(8″)H_3), 0.90 (3H, d, *J* 6.8, C(9″)H_3), 0.86–0.92 (2H, m, C(4″)H, C(6″)H), 0.91–1.02 (1H, m, C(3″)H), 1.15–1.38 (11H, m, C(1′)H, C(2′–5′)$_3H_8$, C(2″)H, C(7″)H), 1.49–1.53 (1H, m, C(1′)H), 1.57–1.67 (2H, m, C(3″)H, C(4″)H), 1.97–2.07 (4H, m, C(6′)H_2, C(5″)H, C(6″)H), 2.12 (1H, dd, *J* 18.0, 4.4, C(3)H_A), 2.19–2.26 (1H, m, C(4)H), 2.74 (1H, dd, *J* 18.0, 8.4, C(3)H_B), 3.47 (1H, td, *J* 10.4, 4.4, C(1″)H), 4.87–4.97 (2H, m, C(8′)H_2), 5.31 (1H, d, *J* 2.3, C(5)H), 5.76 (1H, app. ddt, app. *J* 17.2, 10.4, 6.8, C(7′)H); δ_C (50.3 MHz, $CDCl_3$) 16.0, 21.3, 22.6, 23.5, 25.8, 27.3, 29.1, 29.2, 29.6, 31.7, 32.3, 34.0, 34.3, 34.7, 40.3, 41.9, 48.1, 77.5, 105.4, 114.7, 139.2, 176.4; *m*/*z* (CI, NH_3) 368 (MNH_4^+, 5%), 351 (MH^+, 15), 230 (100), 214 (20), 212 (15), 156 (10), 138 (20), 95 (20); HRMS (CI) found 368.3177, calculated for $C_{22}H_{42}NO_3$ (MNH_4^+) 368.3165. The minor diastereomer (**3f**) exhibits a distinctive resonance in the ^1H NMR spectrum at δ 5.44 (1H, d, *J* 4.8).

(4*R*,5*R*)-4-[8-(*tert*-Butyldiphenylsilanyloxy)octyl]-5-(*l*-menthyloxy)dihydro-2-furanone 2g

General procedure B [furanone **1** (1.0 g, 4.2 mmol), R = 8-(*tert*-butyldiphenylsilanyloxy)octyl] gave the *title compound* (**2g**) and its C5-epimer (**3g**) in a 2.2 : 1 ratio from which the

major diastereomer (**2g**) was isolated as a colourless oil (1.37 g, 54%). R_f 0.51 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = -72.2$ (*c* 1.2, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3071w, 2929s, 2856s, 1789s, 1462s, 1428s, 1388m, 1361m, 1164s, 1111s, 939s, 823m, 740m, 702s; δ_H (400 MHz, $CDCl_3$) 0.81 (3H, d, *J* 6.8, C(10″)H_3), 0.91 (3H, d, *J* 6.8, C(8″)H_3), 0.96 (3H, d, *J* 6.8, C(9″)H_3), 0.86–1.06 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.08 (9H, s, *t*-Bu), 1.22–1.41 (13H, m, C(1′)H, C(2′–6′)$_5H_{10}$, C(2″)H, C(7″)H), 1.54–1.62 (1H, m, C(1′)H), 1.58 (2H, quin., *J* 6.8, C(7′)H_2), 1.64–1.71 (2H, m, C(3″)H, C(4″)H), 2.09–2.14 (2H, m, C(5″)H, C(6″)H), 2.18 (1H, dd, *J* 17.6, 4.4, C(3)H_A), 2.26–2.30 (1H, m, C(4)H), 2.81 (1H, dd, *J* 17.6, 8.4, C(3)H_B), 3.53 (1H, td, *J* 10.4, 4.4, C(1″)H), 3.68 (2H, t, *J* 6.8, C(8′)H_2), 5.37 (1H, d, *J* 2.3, C(5)H), 7.37–7.46 (6H, m, Ph), 7.69–7.71 (4H, m, Ph); δ_C (100.6 MHz, $CDCl_3$) 15.6, 19.2, 20.9, 22.3, 23.1, 25.4, 25.7, 26.9, 27.0, 29.2, 29.4, 31.4, 31.9, 32.5, 33.9, 34.3, 39.9, 41.6, 47.8, 63.9, 77.0, 105.1, 127.6, 129.5, 134.2, 135.6, 176.1; *m*/*z* (CI, NH_3) 629 (M + Na, 25%), 579 (100), 301 (80), 279 (85%); *m*/*z* (CI, ES) 629 (MNa^+, 25%), 578 (100), 300 (80), 278 (85); HRMS (CI) found 607.4183, calculated for $C_{38}H_{59}O_4Si$ (MH^+) 607.4183. **(4*R*,5*S*)-4-[8-(*tert*-Butyldiphenylsilanyloxy)octyl]-5-(*l*-menthyloxy)dihydrofuran-2-one 3g** was also obtained, as a colourless oil (640 mg, 25%). R_f 0.49 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = -2.5$ (*c* 1.1, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3071w, 3050w, 2929s, 2857s, 1790s, 1464m, 1428m, 1387w, 1361w, 1330w, 1184w, 1112s, 961m, 921m, 823m, 737m, 702m; δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.8, C(10″)H_3), 0.92 (3H, d, *J* 6.8, C(8″)H_3), 0.93 (3H, d, *J* 6.8, C(9″)H_3), 0.86–1.10 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.08 (9H, s, *t*-Bu), 1.25–1.41 (13H, m, C(1′)H, C(2′–6′)$_5H_{10}$, C(2″)H, C(7″)H), 1.50–1.68 (5H, m, C(1′)H, C(7′)H_2, C(3″)H, C(4″)H), 2.13–2.49 (5H, m, C(3)H_2, C(4)H, C(5″)H, C(6″)H), 3.39 (1H, td, *J* 10.8, 4.4, C(1″)H), 3.68 (2H, t, *J* 6.4, C(8′)H_2), 5.49 (1H, d, *J* 4.6, C(5)H), 7.68–7.71 (6H, m, Ph), 7.73–7.76 (4H, m, Ph); δ_C (100.6 MHz, $CDCl_3$) 15.8, 19.2, 21.2, 22.2, 22.7, 25.2, 25.8, 26.6, 26.9, 27.8, 28.3, 29.3, 29.4, 31.6, 32.2, 33.1, 34.2, 41.6, 42.7, 48.4, 63.9, 81.4, 106.0, 127.6, 129.5, 134.1, 134.8, 135.6, 176.7; *m*/*z* (CI, NH_3) 629 (M + Na, 25%), 579 (100), 301 (80), 279 (85%); HRMS (CI) found 607.4177, calculated for $C_{38}H_{59}O_4Si$ (MH^+) 607.4183.

(4*R*,5*R*)-4-(2-Butyl)-5-(*l*-menthyloxy)dihydro-2-furanone 2h

General procedure A [furanone **1** (100 mg, 0.42 mmol), R = *s*-Bu] gave a mixture of two diastereoisomers from which the *major diastereomer* (**2h**) was isolated as a colourless oil (51 mg, 41%) and as a 1 : 1 epimeric mixture at C2′. R_f 0.60 (9 : 1 petrol : ethyl acetate); ν_{max} (thin film)/cm^{-1} 3054s, 2926s, 1778s, 1422s, 1265s, 740s; δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.9, C(10″)H_3), 0.88 (3H, d, *J* 7.0, C(8″)H_3), 0.91 (3H, t, *J* 7.5, C(4′)H_3), 0.93 (3H, d, *J* 6.0, C(2′)H_3), 0.94 (3H, d, *J* 7.0, C(9″)H_3), 0.77–1.05 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.14–1.58 (5H, m, C(2′)H, C(3′)H_2, C(2″)H, C(7″)H), 1.62–1.70 (2H, m, C(3″)H, C(4″)H), 2.06–2.12 (2H, m, C(5″)H, C(6″)H), 2.17–2.41 (2H, m, C(3)H_A, C(4)H), 2.68 (0.5H, dd, *J* 18.5, 10.5) and 2.76 (0.5H, dd, *J* 17.5, 8.5, C(3)H_B), 3.51 (0.5H, td, *J* 10.5, 4.0) and 3.52 (0.5H, td, *J* 10.5, 4.0, C(1″)H), 5.45 (0.5H, d, *J* 2.6) and 5.46 (0.5H, d, *J* 2.4, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 11.6, 11.7, 15.9, 16.1, 16.3, 21.4, 22.7 (C9″), 23.5, 25.8, 27.0, 27.3, 31.0, 31.8, 32.6, 34.7, 36.1, 36.8, 40.3, 46.3, 46.6, 48.2, 77.5, 103.8, 104.4, 176.3; *m*/*z* (CI, NH_3) 314 (MNH_4^+, 10%), 297 (MH^+, 35), 176 (100), 100 (55), 95 (65); HRMS (ES) found 297.2430, calculated for $C_{18}H_{33}O_3$ (MH^+) 297.2430.

(4*R*,5*R*)-4-*tert*-Butyl-5-(*l*-menthyloxy)dihydro-2-furanone 2i

General procedure A [furanone **1** (100 mg, 0.42 mmol), R = *t*-Bu] gave the *title compound* (**2i**) as a colourless oil (55 mg, 44%); no other significant minor diastereomers were visible in the ^{1}H NMR spectrum of the crude material. R_f 0.53 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = -157.7$ (*c* 0.7, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 2954s, 2920s, 2862s, 1774s, 1468m, 1375m, 1179m, 1105m, 905s, 732s; δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.9, C(10″)H_3), 0.89 (3H, d, *J* 6.8, C(8″)H_3), 0.92 (9H, s, *t*-Bu), 0.94 (3H, d, *J* 6.8, C(9″)H_3), 0.77–0.97 (2H, m, C(4″)H, C(6″)H), 0.95–1.07 (1H, m, C(3″)H), 1.17–1.25 (1H, m, C(2″)H), 1.34–1.43 (1H, m, C(7″)H), 1.61–1.68 (2H, m, C(3″)H, C(4″)H), 2.04–2.15 (3H, m, C(4)H, C(5″)H, C(6″)H), 2.35 (1H, dd, *J* 18.4, 4.7, C(3)H_A), 2.69 (1H, dd, *J* 18.4, 9.8, C(3)H_B), 3.52 (1H, td, *J* 10.7, 4.2, C(1″)H), 5.52 (1H, d, *J* 2.3, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 15.6, 20.9, 22.3, 23.0, 25.4, 26.8, 29.9, 31.3, 31.4, 34.3, 39.8, 47.8, 51.4, 76.7, 102.3, 176.6; *m*/*z* (CI, NH_3) 314 (MNH_4^+, 20%), 297 (MH^+, 85), 176 (100), 159 (70), 138 (30); HRMS (ES) found 297.2438, calculated for $C_{18}H_{33}O_3$ (MH^+) 297.2430.

(4*R*,5*R*)-4-Phenyl-5-(*l*-menthyloxy)dihydro-2-furanone 2j

General procedure A [furanone **1** (100 mg, 0.42 mmol), R = Ph] gave the *title compound* (**2j**) as a pale yellow crystalline solid (33 mg, 25%); no other significant minor diastereomers were visible in the ^{1}H NMR spectrum of the crude material. R_f 0.40 (9 : 1 petrol : ethyl acetate); m.p. 79–85 °C; $[\alpha]_D^{22} = -140.6$ (*c* 0.15, $CHCl_3$); ν_{max} (KBr disc)/cm^{-1} 2956s, 2922s, 2855s, 1783s, 1454m, 1100m, 910s, 731s; δ_H (400 MHz, $CDCl_3$) 0.82 (3H, d, *J* 6.9, C(10″)H_3), 0.88 (3H, d, *J* 6.8, C(8″)H_3), 0.90 (3H, d, *J* 6.8, C(9″)H_3), 0.82–0.97 (2H, m, C(4″)H, C(6″)H), 0.95–1.06 (1H, m, C(3″)H), 1.22–1.29 (1H, m, C(2″)H), 1.29–1.39 (1H, m, C(7″)H), 1.63–1.68 (2H, m, C(3″)H, C(4″)H), 1.95–2.00 (1H, m, C(6″)H), 2.04–2.14 (1H, m, C(5″)H), 2.63 (1H, dd, *J* 17.8, 4.6, C(3)H_A), 3.13 (1H, dd, *J* 17.8, 9.1, C(3)H_B), 3.50–3.55 (1H, m, C(4)H), 3.55 (1H, td, *J* 10.8, 4.4, C(1″)H), 5.59 (1H, d, *J* 2.5, C(5)H), 7.15–7.40 (5H, m, Ph); δ_C (100.6 MHz, $CDCl_3$) 15.6, 20.9, 22.2, 23.0, 25.5, 31.3, 34.2, 35.1, 39.7, 47.2, 47.7, 77.3, 105.6, 126.7, 127.7, 129.1, 139.2, 175.8; *m*/*z* (CI, NH_3) 317 (MH^+, 25%), 196 (30), 179 (10), 104 (100); HRMS (ES) found 317.2117, calculated for $C_{20}H_{29}O_3$ (MH^+) 317.2106.

(1*S*,4*S*)-[4-(6-Chlorohexyl)-1-hydroxycyclopent-2-en-1-ylmethyl]phosphoric acid dimethyl ester 8

A solution of dimethyl methylphosphonate (57 μL, 0.53 mmol) in THF (2.0 mL) was treated at −78 °C with *n*-BuLi (328 μL of a 1.6 M solution in hexane, 0.53 mmol). After 30 min, a solution of (*S*)-4-(6-chlorohexyl)cyclopent-2-enone[18] (*ent*-**7**, 100 mg, 0.50 mmol) in THF (0.5 mL) was added to give a yellow solution. After a further 40 min, the reaction was quenched with water (0.5 mL), extracted with ethyl acetate (3 × 5 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The *title compound* (**8**) was obtained as a pale yellow oil (98 mg, 61%; 81% based on recovered *ent*-**7**) after purification by flash column chromatography (99 : 1 dichloromethane : methanol). R_f 0.33 (95 : 5 dichloromethane : methanol); $[\alpha]_D^{22} = -57.8$ (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.25–1.50 (8H, m, C(1′–4′)$_4H_8$), 1.63 (1H, ddd, *J* 13.2, 6.4, 2.4, C(5)H), 1.75 (2H, quin., *J* 6.8, C(5′)H_2), 2.13 (2H, d, *J* 17.2, C(1″)H_2), 2.30 (1H, dd, *J* 13.2, 7.6, C(5)H), 2.57 (1H, app. quin., app. *J* 6.4, C(4)H), 3.51 (2H, t, *J* 6.8, C(6′)H_2), 3.73 (3H, d, *J* 4.4) and 3.76 (3H, d, *J* 4.4, 2 × OCH_3), 3.90 (1H, br.s, –OH), 5.76–5.80 (2H, m, C(2)H, C(3)H); δ_C (100.6 MHz, $CDCl_3$) 26.8, 27.6, 28.9, 32.5, 35.8, 35.9 (d, *J* 133), 44.1, 45.1, 45.9 (d, *J* 10), 52.3 (two peaks, 2 × d, *J* 7), 81.7 (d, *J* 5), 135.5 (d, *J* 10), 137.2; *m*/*z* (ES) 347 ($M^{35}ClNa^+$, 100%), 307 (50); HRMS (ES) found 347.1162, calculated for $C_{14}H_{27}O_4{}^{35}ClPNa$ (MNa^+) 347.1155.

(3*R*,4*R*,5*R*)-4-Butyl-5-(*l*-menthyloxy)-3-(3-methylbut-2-enyl)-dihydro-2-furanone 9

General procedure C (for lactone alkylations)

To a solution of lactone **2b** (380 mg, 1.28 mmol) in THF (6 mL) was added at −78 °C a solution of LiHMDS [prepared from *n*-BuLi (642 μL of a 1.6 M solution in hexanes, 1.03 mmol) and HMDS (214 μL, 1.03 mmol) in THF (4 mL)]. After 30 min, 4-bromo-2-methyl-2-butene (118 μL, 1.03 mmol) was added to the yellow solution and the mixture was stirred at −78 °C for 40 min

then quenched with water (10 mL) before being allowed to warm up to RT. Extraction with ether (3 × 10 mL), drying ($MgSO_4$), solvent evaporation *in vacuo*, and purification by flash column chromatography on silica gel (98 : 2 petrol : ether) afforded the *title compound* (**9**) as a colourless oil (204 mg, 54%; 92% based on recovered **2b**). R_f 0.20 (95 : 5 petrol : ethyl acetate); $[\alpha]_D^{22} = -138.1$ (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2960s, 2921s, 2862s, 1777s, 1679w, 1458s, 1374s, 1320m, 1163m, 1109s, 941s; δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.8, C(10″)H_3), 0.84–0.92 (2H, m, C(4″)H, C(6″)H), 0.89 (3H, d, *J* 6.8, C(8″)H_3), 0.91 (3H, t, *J* 6.8, C(4′)H_3), 0.94 (3H, d, *J* 6.8, C(9″)H_3), 1.00 (1H, qd, *J* 12.8, 3.6, C(3″)H), 1.19–1.50 (8H, m, C(1′–3′)$_3H_6$, C(2″)H, C(7″)H), 1.62–1.70 (2H, m, C(3″)H, C(4″)H), 1.64 (3H, s) and 1.72 (3H, s, $=CMe_2$), 1.98–2.04 (1H, app. dtd, app. *J* 8.4, 6.0, 2.8, C(4)H), 2.07–2.12 (1H, m, C(6″)H), 2.17 (1H, app. quin.d, *J* 7.6, 3.2, C(5″)H), 2.26 (1H, q, *J* 6.0, C(3)H), 2.45 (2H, app. t, *J* 6.0, C(1‴)H_2), 3.52 (1H, td, *J* 10.8, 4.0, C(1‴)H), 5.12 (1H, br t., *J* 6.0, C(2‴)H), 5.30 (1H, d, *J* 2.8, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 15.5, 17.8, 20.9, 22.3, 22.5, 22.9, 25.4, 25.7, 28.8, 29.3, 31.3, 32.0, 34.3, 39.7, 45.5, 46.5, 47.8, 77.2, 104.4, 120.4, 134.6, 178.2; HRMS (CI) found 365.3056, calculated for $C_{23}H_{41}O_3$ (MH^+) 365.3056.

(4*R*,5*R*)-4-Butyl-5-*l*-menthyloxy-3,3-di(3-methylbut-2-enyl)-dihydro-2-furanone 10

General procedure C [using 2.0 equiv. of LiHMDS and 2.0 equiv. of 4-bromo-2-methyl-2-butene relative to lactone **2b** (100 mg, 0.34 mmol)] gave the *title compound* (**10**) as a colourless oil (121 mg, 83%). R_f 0.81 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = -133.2$ (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2953s, 2916s, 2860s, 1770s, 1449s, 1380m, 1152m, 1133m, 1096m, 938m; δ_H (400 MHz, $CDCl_3$) 0.72–0.92 (2H, m, C(4″)H, C(6″)H), 0.81 (3H, d, *J* 6.8, C(10″)H_3), 0.89 (3H, t, *J* 8.0, C(4′)H_3), 0.89 (3H, d, *J* 6.8, C(8″)H_3), 0.93 (3H, d, *J* 6.8, C(9″)H_3), 1.00 (1H, qd, *J* 12.8, 3.6, C(3″)H), 1.16–1.43 (8H, m, C(1′–3′)$_3H_6$, C(2″)H, C(7″)H), 1.60 and 1.61 (2 × 3H, 2 × s) and 1.71 (6H, s, 2 × $=CMe_2$), 1.62–1.71 (2H, m, C(3″)H, C(4″)H), 2.02–2.08 (1H, m, C(6″)H), 2.10–2.16 (3H, m, C(4)H, C(1‴)H, C(5″)H), 2.23 (2H, app. q, app. *J* 6.8, C(1‴)H_2), 2.38 (1H, dd, *J* 14.8, 6.8, C(1‴)H), 3.51 (1H, td, *J* 10.4, 4.0, C(1″)H), 5.04–5.11 (2H, m, 2 × CH=), 5.23 (1H, d, *J* 6.6, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 16.1, 18.0 (two peaks), 20.8, 22.3, 22.8, 23.4, 25.6, 25.9, 26.0, 26.3, 30.1, 31.3, 32.4, 34.3, 34.7, 40.0, 47.1, 47.8, 51.8, 77.9, 104.0, 118.8, 119.2, 134.8, 135.2, 178.9; *m*/*z* (CI, NH_3) 433 (MH^+, 5%), 279 (5), 233 (5), 207 (5), 155 (15), 148 (90), 131 (30), 112 (10), 95 (10), 87 (30), 70 (100); HRMS (CI) found 433.3682, calculated for $C_{28}H_{49}O_3$ (MH^+) 433.3682.

(4*R*,5*R*)-4-Butyl-5,5-di(3-methyl-but-2-enyl)cyclopent-2-en-1-one 11

LiBr (19 mg, 0.22 mmol, dried overnight at 135 °C under high vacuum) was dissolved in anhydrous THF (1.0 mL) and cooled to −78 °C. Dimethyl methylphosphonate (24 μL, 0.22 mmol) and *n*-BuLi (137 μL of a 1.6 M solution in hexanes, 0.22 mmol) were added successively and the mixture was stirred at −78 °C for 30 min. Lactone **9** (80 mg, 0.22 mmol) in THF (0.5 mL) was added, resulting in a yellow solution. The mixture was stirred at −78 °C for 2 h then allowed to reach RT over 3 h. After addition of water (2 mL), the product was extracted with ethyl acetate (3 × 5 mL), dried (Na_2SO_4), filtered, and evaporated *in vacuo*. Purification by flash column chromatography (silica, 95 : 5 petrol : ethyl acetate) gave the *title compound* (**11**) as a colourless oil (27 mg, 60%). R_f 0.45 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = +85.6$ (*c* 0.5, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2960s, 2921s, 2852s, 1705s, 1587m, 1455s, 1376m, 1347m, 1175m; δ_H (400 MHz, $CDCl_3$) 0.92 (3H, t, *J* 6.8, C(4′)H_3), 1.29–1.39 (4H, m, C(2′,3′)$_2H_4$), 1.42–1.53 (2H, m, C(1′)H_2), 1.62 (3H, s) and 1.69 (3H, d, *J* 0.8, $=CMe_2$), 2.00 (1H, ddd, *J* 7.2, 5.6, 2.4, C(5)H), 2.23 (1H, ddd, *J* 14.0, 7.2, 7.2, C(1″)H), 2.42 (1H, ddd, *J* 14.0, 5.6, 5.6, C(1″)H), 2.53–2.60 (1H, m, C(4)H), 5.01–5.08 (1H, m, C(2″)H), 6.12 (1H, dd, *J* 5.6, 2.4, C(2)H), 7.60 (1H, dd, *J* 5.6, 2.4, C(3)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 17.8, 22.7, 25.8, 29.1, 29.7, 34.0, 47.0, 51.7, 120.8, 132.8, 133.7, 167.6, 212.1; *m*/*z* (CI, NH_3) 207 (MH^+, 100%), 191 (10), 148 (10), 138 (15); HRMS (CI) found 207.1749, calculated for $C_{14}H_{23}O$ (MH^+) 207.1749.

(4*S*)-4-Butyl-5,5-bis(3-methyl-but-2-enyl)cyclopent-2-en-1-one 12

LiBr (12 mg, 0.14 mmol, dried overnight at 135 °C under high vacuum) was dissolved in anhydrous THF (0.65 mL) and cooled to −78 °C. Dimethyl methylphosphonate (15 μL, 0.14 mmol) and *n*-BuLi (87 μL of a 1.6 M solution in hexanes, 0.14 mmol) were added successively and the mixture was stirred at −78 °C for 30 min. Lactone **10** (60 mg, 0.14 mmol) in THF (0.3 mL) was added, resulting in a yellow solution. The mixture was stirred at −78 °C for 2 h then allowed to reach RT over 3 h. After addition of water (2 mL), the product was extracted with ethyl acetate (3 × 5 mL), dried (Na_2SO_4), filtered, and evaporated *in vacuo*. Purification by flash column chromatography (silica, 99 : 1 petrol : ether) gave the *title compound* (**12**) as a colourless oil (21 mg, 55%; 72% based on recovered **10**). R_f 0.60 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = +77.7$ (*c* 0.3, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2954s, 2919s, 2850s, 1703s, 1453m, 1379m, 1254w, 1193w, 1103w, 1042w; δ_H (400 MHz, $CDCl_3$) 0.94 (3H, t, *J* 6.8, C(4′)H_3), 1.24–1.43 (6H, m, C(1′–3′)$_3H_6$), 1.57 and 1.59 (2 × 3H, 2 × s) and 1.66 (6H, s, 2 × $=CMe_2$), 2.11–2.22 (4H, m, 2 × C(1″)H_2), 2.61–2.66 (1H, m, C(4)H), 4.94 and 5.05 (2 × 1H, 2 × br t, *J* 7.2, 2 × =CH), 6.12 (1H, dd, *J* 5.6, 2.4, C(2)H), 7.62 (1H, dd, *J* 5.6, 2.4, C(3)H); δ_C (100.6 MHz, $CDCl_3$) 14.0, 17.8, 22.3, 22.6, 25.9, 28.4, 30.6, 32.6, 34.1, 34.5, 49.6, 54.2, 119.7, 120.0, 132.1, 133.0, 134.2, 166.2, 213.9; *m*/*z* (CI, NH_3) 275 (MH^+, 100%), 205 (20), 164 (5), 148 (10); HRMS (CI) found 275.2375, calculated for $C_{19}H_{31}O$ (MH^+) 275.2375.

(3*S*,4*R*,5*R*)-4-Butyl-3-(1-hydroxy-2-methylpropyl)-5-(*l*-menthyloxy)dihydrofuran-2-one 13

General procedure C [using 1.0 equiv. of LiHMDS and 1.0 equiv. of isobutyraldehyde relative to lactone **2b** (195 mg, 0.66 mmol)] gave the *title compound* (**13**) as a colourless oil (200 mg, 83%). R_f 0.34 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = -107.5$ (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3508br, 2957s, 2928s, 2872s, 1760s, 1456s, 1371s, 1242s, 1135s, 1042s, 945s, 733w; δ_H (400 MHz, $CDCl_3$) 0.77 (3H, d, *J* 6.8, C(10″)H_3), 0.88 (3H, d, *J* 6.8, C(8″)H_3), 0.91 (3H, t, *J* 7.6, C(4′)H_3), 0.93 (3H, d, *J* 6.8, C(9″)H_3), 0.94 and 1.01 (2 × 3H, 2 × d, *J* 6.8, –CH(CH_3)$_2$), 0.81–1.05 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.16–1.26 (1H, m, C(2″)H), 1.30–1.42 (5H, m, C(2′,3′)$_2H_4$, C(7″)H), 1.47–1.53 (2H, m, C(1′)H_2), 1.61–1.69 (2H, m, C(3″)H, C(4″)H), 1.93 (1H, oct., *J* 6.8, –CH(CH$_3$)$_2$), 2.06–2.14 (3H, m, C(4)H, C(5″)H, C(6″)H), 2.40 (1H, app. t, app. *J* 6.4, C(3)H), 3.18 (1H, d, *J* 3.2, –OH), 3.49–3.57 (2H, m, C(1‴)H, C(1″)H), 5.34 (1H, d, *J* 3.2, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.8, 15.5, 16.1, 20.0, 20.9, 22.2, 22.5, 22.9, 25.3, 28.8, 30.5, 31.4, 31.9, 34.2, 39.8, 44.5, 47.7, 49.3, 76.2, 77.8, 104.3, 177.7; HRMS (CI) found 369.3005, calculated for $C_{22}H_{41}O_4$ (MH^+) 369.3005.

(4*R*,5*R*)-4-Butyl-3-isobutylidene-5-(*l*-menthyloxy)dihydrofuran-2-one 14

A solution of aldol adduct **13** (100 mg, 0.27 mmol) in 1,2-dichloroethane (1.5 mL) was treated with methanesulfonyl chloride (42 μL, 0.54 mmol) and triethylamine (189 μL, 1.35 mmol) for 30 min at 0 °C, then 4 h at reflux. The cooled reaction was quenched with water (1 mL), extracted with ether (3 × 5 mL), and the extracts were washed with brine (5 mL). The combined organic layers were dried ($MgSO_4$) and evaporated *in vacuo*. Purification by flash column chromatography on silica gel (95 : 5 petrol : ethyl acetate) gave the *mesylate*, which was dissolved in dichloromethane (1 mL) and treated with DBU (57 μL, 0.38 mmol) at RT for 5 h. The solvent was evaporated and the residue purified by flash column chromatography on silica gel

(98 : 2 petrol : ethyl acetate) to give the *title compound* (**14**), an equimolar mixture of the *E* and *Z* stereoisomers, as a colourless oil (80 mg, 84% from **13**). R_f 0.70/0.76 (9 : 1 petrol : ethyl acetate); ν_{max} (thin film)/cm^{-1} 2957s, 2917s, 2870s, 1767s, 1683s, 1456s, 1386w, 1370m, 1344w, 1298w, 1202m, 1107m, 1072w, 944m; δ_H (400 MHz, $CDCl_3$) 0.76–1.08 (21H, m, 6 × CH_3, C(3″)H, C(4″)H, C(6″)H), 1.16–1.56 (8H, m, C(1′–3′)$_3$H$_6$, C(2″)H, C(7″)H), 1.60–1.68 (2H, m, C(3″)H, C(4″)H), 1.94–2.12 (2H, m, C(5″)H, C(6″)H), 2.47–2.57 (0.5H, m, C(2‴)H), 2.60–2.64 (0.5H, m, C(4)H), 2.85 (0.5H, ddd, *J* 7.6, 5.6, 2.0, C(4)H), 3.55 (1H, td, *J* 10.4, 4.0, C(1″)H), 3.69–3.81 (0.5H, m, C(2‴)H), 5.28 (0.5H, d, *J* 2.0) and 5.38 (0.5H, s, C(5)H), 5.92 and 6.56 (2 × 0.5H, 2 × dd, *J* 10.4, 2.0, =CH); δ_C (100.6 MHz, $CDCl_3$) 13.9, 15.8, 20.7, 20.8, 22.0, 22.2, 22.4 (two peaks), 22.5, 23.3, 23.4, 25.5 (two peaks), 26.3, 28.2, 28.5, 29.4, 31.3, 32.2, 32.6, 34.3, 39.8, 44.2, 47.0, 47.7, 47.8, 76.2, 76.3, 101.8, 101.9, 126.2, 127.3, 147.9, 151.4, 168.8, 170.9; *m*/*z* (CI, NH_3) 368 (MNH_4^+, 10%), 351 (MH^+, 60), 230 (50), 214 (70), 197 (100), 195 (50), 166 (20), 148 (100), 138 (15); HRMS (CI) found 351.2891, calculated for $C_{22}H_{39}O_3$ (MH^+) 351.2899.

(3*R*,4*R*,5*R*)-4-Butyl-3-isobutyl-5-(2-*l*-menthyloxy)dihydrofuran-2-one 15

A solution of alkylidene lactone **14** (60 mg, 0.17 mmol), triethylamine (0.02 mmol, 4 μL) and 10% Pd/C (6 mg) in ethanol (1.0 mL) was stirred under a hydrogen atmosphere (4 bar) for 40 h and then filtered through Celite®, washing through with ether (3 × 5 mL). The filtrate was evaporated *in vacuo* and the residue purified by flash column chromatography on silica gel (95 : 5 petrol : ethyl acetate) to give the *title compound* (**15**) as a pale yellow oil (50 mg, 83%). R_f 0.48 (9 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = -98.3$ (*c* 1.7, $CHCl_3$); ν_{max}(thin film)/cm^{-1} 2956s, 2924s, 2863m, 1777s, 1467m, 1367w, 1260m, 1167w, 1104m, 1028w, 942m, 804w; δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.8, C(10″)H$_3$), 0.84–0.92 (2H, m, C(4″)H, C(6″)H), 0.88 (3H, d, *J* 6.8, C(8″)H$_3$), 0.90–0.96 (9H, m, C(4′)H$_3$, –CH(C*H*$_3$)$_2$), 0.95 (3H, d, *J* 6.8, C(9″)H$_3$), 1.00 (1H, qd, *J* 12.8, 3.6, C(3″)H), 1.19–1.56 (9H, m, C(1′–3′)$_3$H$_6$, C(1‴)H, C(2″)H, C(7″)H), 1.61–1.74 (3H, m, C(1‴)H, C(3″)H, C(4″)H), 1.81 (1H, app. sept., app. *J* 6.4, C(2‴)H), 1.96–2.01 (1H, m, C(4)H), 2.08–2.15 (2H, m, C(5″)H, C(6″)H), 2.27 (1H, ddd, *J* 8.4, 6.4, 4.4, C(3)H), 3.51 (1H, td, *J* 10.8, 4.4, C(1″)H), 5.31 (1H, d, *J* 2.4, C(5)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 15.4, 20.9, 22.0, 22.2, 22.5, 22.6, 22.9, 25.4, 25.7, 28.9, 31.3, 32.2, 34.3, 39.5, 40.8, 44.1, 46.9, 47.7, 77.1, 103.9, 179.0; *m*/*z* (CI, NH_3) 370 (MNH_4^+, 15%), 353 (MH^+, 70), 232 (100), 215 (60), 197 (30), 170 (10), 148 (10), 95 (10); HRMS (CI) found 353.3057, calculated for $C_{22}H_{41}O_3$ (MH^+) 353.3056.

(3*R*,4*R*,5*R*)-5-(*l*-Menthyloxy)-4-oct-7-enyl-3-[(2*Z*)-pentenyl]-dihydrofuran-2-one 16

General procedure C [using 1.1 equiv. of LiHMDS and 1.1 equiv. of (*Z*)-1-bromo-2-pentene relative to lactone **2f** (1.44 g, 4.1 mmol)] gave the *title compound* (**16**) as a colourless oil (1.39 g, 81%; NMR spectra indicate slight contamination by the (*E*)-side chain isomer). R_f 0.82 (95 : 5 petrol : ethyl acetate); $[\alpha]_D^{22} = -104.4$ (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2926s, 2856s, 1781s, 1641w, 1457m, 1369m, 1166m, 1108m, 944m; δ_H (400 MHz, $CDCl_3$) 0.79 (3H, d, *J* 6.8, C(10″)H$_3$), 0.89 (3H, d, *J* 6.8, C(8″)H$_3$), 0.94 (3H, d, *J* 6.8, C(9″)H$_3$), 0.84–0.96 (2H, m, C(4″)H, C(6″)H), 0.97 (3H, t, *J* 7.6, C(5‴)H$_3$), 0.96–1.06 (1H, qd, *J* 12.4, 2.8 C(3″)H), 1.19–1.51 (12H, m, C(1′–5′)$_5$H$_{10}$, C(2″)H, C(7″)H), 1.62–1.71 (2H, m, C(3″)H, C(4″)H), 1.99–2.22 (7H, m, C(4)H, C(6′)H$_2$, C(4‴)H$_2$, C(5″)H, C(6″)H), 2.27 (1H, app. q, app. *J* 6.8, C(3)H), 2.50 (2H, app. t, app. *J* 6.8, C(1‴)H$_2$), 3.52 (1H, td, *J* 10.4, 4.4, C(1″)H), 4.90–5.01 (2H, m, C(8′)H$_2$), 5.31 (1H, d, *J* 2.8, C(5)H) overlaying 5.29–5.40 (1H, m) and 5.49–5.61 (1H, m, C*H*=C*H*CH$_3$), 5.81 (1H, app. ddt, app. *J* 17.2, 10.4, 6.8, C(7′)H); δ_C (100.6 MHz, $CDCl_3$) 14.1, 15.5, 20.6, 20.9, 22.3, 22.9, 25.4, 26.6, 28.4, 28.8, 29.2, 31.3, 32.3, 33.7, 34.3, 39.7, 45.2, 45.6, 46.3, 47.8, 77.2, 104.3, 114.3, 124.8, 134.5, 138.9, 177.9; *m*/*z* (CI, NH_3) 419 (MH^+, 25%), 298 (30), 281 (35), 263 (25), 219 (10), 172 (35), 156 (55), 149 (100), 137 (50), 95 (40); HRMS (CI) found 419.3521, calculated for $C_{27}H_{47}O_3$ (MH^+) 419.3525.

(3*R*,4*R*,5*R*)-4-[8-(*tert*-Butyldiphenylsilanyloxy)octyl]-5-(*l*-menthyloxy)-3-[(2*Z*)-pentenyl]dihydrofuran-2-one 17

General procedure C [using 1.0 equiv. of LiHMDS and 1.0 equiv. of (*Z*)-1-bromo-2-pentene relative to lactone **2g** (163 mg, 0.27 mmol)] gave the *title compound* (**17**) as a colourless oil (156 mg,%). R_f 0.24 (95 : 5 petrol : ethyl acetate); $[\alpha]_D^{22} = -67.4$ (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3071w, 3049w, 2929s, 2857s, 1778s, 1742s, 1590w, 1462s, 1428s, 1371m, 1330w, 1240m, 1166s, 1111s, 942s, 823m, 702s, 614m; δ_H (400 MHz, $CDCl_3$) 0.81 (3H, d, *J* 6.8, C(10″)H$_3$), 0.91 (3H, d, *J* 6.8, C(8″)H$_3$), 0.95 (3H, d, *J* 6.8, C(9″)H$_3$), 0.98 (3H, t, *J* 7.6, C(5‴)H$_3$), 1.07 (9H, s, *t*-Bu), 0.86–1.08 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.21–1.50 (14H, m, C(1′–6′)$_6$H$_{12}$, C(2″)H, C(7″)H), 1.58 (2H, quin., *J* 6.8, C(7′)H$_2$), 1.63–1.70 (2H, m, C(3″)H, C(4″)H), 2.01–2.15 (4H, m, C(4)H, C(4‴)H$_2$, C(6″)H), 2.13–2.20 (1H, m, C(5″)H), 2.29 (1H, app. q, app. *J* 6.8, C(3)H), 2.52 (2H, app. t, app. *J* 6.8, C(1‴)H$_2$), 3.53 (1H, td, *J* 10.4, 4.4, C(1″)H), 3.67 (2H, t, *J* 6.8, C(8′)H$_2$), 5.32 (1H, d, *J* 2.8, C(5)H), 5.31–5.37 (1H, m) and 5.51–5.55 (1H, m, C*H*=C*H*CH$_3$), 7.37–7.46 (6H, m) and 7.67–7.70 (4H, m, Ph); δ_C (100.6 MHz, $CDCl_3$) 14.1, 15.5, 19.2, 20.6, 21.0, 22.3, 22.9, 25.4, 25.7, 26.7, 26.9, 28.4, 29.3, 29.4, 31.4, 32.3, 32.6, 34.3, 39.7, 45.7, 46.3, 47.8, 63.9, 77.2, 104.3, 124.7, 127.5, 129.5, 134.1, 134.5, 135.6, 177.9; *m*/*z* (CI, NH_3) 697 (MNa^+, 100%), 692 (40), 575 (10), 459 (10), 381 (10); HRMS (CI) found 675.4803, calculated for $C_{43}H_{67}O_4Si$ (MH^+) 675.4809.

(3*R*,4*R*,5*R*)-4-(8-Hydroxyoctyl)-5-(*l*-menthyloxy)-3-[(2*Z*)-pentenyl]dihydrofuran-2-one 18

A solution of silane **17** (144 mg, 0.21 mmol) in THF (2.0 mL) was treated with TBAF (235 μL of a 1 M solution in THF, 0.24 mmol). After 2.5 h at RT, the reaction mixture was evaporated *in vacuo* and purified by flash column chromatography on silica gel (85 : 15 petrol : ethyl acetate) to give the *title compound* (**18**) as a colourless oil (93 mg, quant.). R_f 0.35 (7 : 3 petrol : ethyl acetate); $[\alpha]_D^{22} = -82.3$ (*c* 1.2, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3440 br s, 2927s, 2855s, 1770s, 1455s, 1370m, 1167m, 1109m, 942m, 755w; δ_H (400 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.8, C(10″)H$_3$), 0.89 (3H, d, *J* 6.8, C(8″)H$_3$), 0.93 (3H, d, *J* 6.8, C(9″)H$_3$), 0.97 (3H, t, *J* 7.6, C(5‴)H$_3$), 0.86–1.07 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.18–1.50 (14H, m, C(1′–6′)$_6$H$_{12}$, C(2″)H, C(7″)H), 1.57 (2H, quin., *J* 6.8, C(7′)H$_2$), 1.60–1.69 (2H, m, C(3″)H, C(4″)H), 1.98–2.10 (4H, m, C(4)H, C(4‴)H$_2$, C(6″)H), 2.09–2.19 (1H, m, C(5″)H), 2.27 (1H, app. q, app. *J* 6.8, C(3)H), 2.49 (2H, app. t, app. *J* 6.8, C(1‴)H$_2$), 3.51 (1H, td, *J* 10.8, 4.4, C(1″)H), 3.64 (2H, t, *J* 6.8, C(8′)H$_2$), 5.30 (1H, d, *J* 2.4, C(5)H), 5.28–5.38 (1H, m) and 5.49–5.55 (1H, m, C*H*=C*H*CH$_3$); δ_C (100.6 MHz, $CDCl_3$) 14.1, 15.4, 20.6, 20.9, 22.3 22.9, 25.4, 25.7, 26.7, 28.4, 29.3, 29.4 (two peaks), 31.3, 32.3, 32.7, 34.3, 39.7, 45.6, 46.3, 47.8, 63.0, 77.2, 104.3, 124.7, 134.6, 180.0; *m*/*z* (CI, NH_3) 454 (MNH_4^+, 65%), 437 (MH^+, 75), 321 (15), 299 (35), 242 (100); HRMS (CI) found 437.3631, calculated for $C_{27}H_{49}O_4$ (MH^+) 437.3631.

(3*R*,4*R*,5*R*)-5-(*l*-Menthyloxy)-3-[(2*Z*)-pentenyl-4-[(8-triethylsilanyloxy)octyl]dihydrofuran-2-one 19

To a solution of chlorotriethylsilane (215 μL, 1.27 mmol), triethylamine (205 μL, 1.47 mmol) and DMAP (8 mg, 0.07 mmol) in dichloromethane (2.0 mL) was added a solution of alcohol **18** (426 mg, 0.98 mmol) in dichloromethane (3.0 mL). The reaction mixture was stirred at RT for 12 h, quenched with sat. aq. NH_4Cl solution (3.0 mL), extracted with dichloromethane (3 × 5 mL) and the extracts dried ($MgSO_4$). Purification by flash column chromatography on silica gel (95 : 5

petrol : ethyl acetate) provided the *title compound* (**19**) (473 mg, 88%) as a colourless oil. R_f 0.43 (95 : 5 petrol : ethyl acetate); $[\alpha]_D^{22} = -82.5$ (*c* 1.0, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 2928s, 2874s, 1779s, 1457s, 1370m, 1240m, 1166s, 1104s, 1016m, 944m, 743m; δ_H (400 MHz, $CDCl_3$) 0.59 (6H, q, *J* 7.6, 3 × $SiCH_2$), 0.78 (3H, d, *J* 6.8, C(10″)H_3), 0.89 (3H, d, *J* 6.8, C(8″)H_3), 0.93 (3H, d, *J* 6.8, C(9″)H_3), 0.96 (9H, t, *J* 8.4, 3 × $SiCH_2CH_3$), 0.97 (3H, t, *J* 7.6, C(5‴)H_3), 0.86–1.05 (3H, m, C(3″)H, C(4″)H, C(6″)H), 1.19–1.48 (14H, m, C(1′–C6′)$_6H_{12}$, C(2″)H, C(7″)H), 1.52 (2H, quin., *J* 6.8, C(7′)H_2), 1.62–1.69 (2H, m, C(3″)H, C(4″)H), 2.00–2.14 (4H, m, C(4)H, C(4‴)H_2, C(6″)H), 2.10–2.18 (1H, m, C(5″)H), 2.26 (1H, app. q, app. *J* 6.8, C(3)H), 2.49 (2H, app. t, app. *J* 6.8, C(1‴)H_2), 3.51 (1H, td, *J* 10.8, 4.4, C(1″)H), 3.59 (2H, t, *J* 6.8, C(8′)H_2), 5.30 (1H, d, *J* 2.8, C(5)H), 5.28–5.35 (1H, m) and 5.49–5.53 (1H, m, C*H*=C*H*CH_3); δ_C (100.6 MHz, $CDCl_3$) 4.4, 6.7, 14.1, 15.5, 20.6, 20.9, 22.2, 22.9, 25.4, 25.8, 26.7, 28.4, 29.3, 29.4, 31.3, 32.3, 32.9, 34.3, 39.7, 45.7, 46.3, 47.8, 62.9, 77.2, 104.3, 124.7, 134.5, 177.9; *m*/*z* (CI, NH_3) 568 (MNH_4^+, 60%), 551 (MH^+, 100), 459 (10), 413 (20), 395 (10), 278 (15); HRMS (CI) found 551.4496, calculated for $C_{33}H_{63}O_4Si$ (MH^+) 551.4496.

(4*R*,5*R*)-5-(*l*-Menthyloxy)-4-oct-7-enyl-3,3-di[(2*Z*)-pentenyl)]-dihydrofuran-2-one 20

General procedure C [using 1.0 equiv. of LiHMDS and 1.0 equiv. of (*Z*)-1-bromo-2-pentene relative to lactone **16** (300 mg, 0.72 mmol)] gave the *title compound* (**20**) as a colourless oil (258 mg, 74%; NMR spectra indicate slight contamination by the (*E*)-side chain isomer). R_f 0.62 (95 : 5 petrol : ether); ν_{max} (thin film)/cm^{-1} 3077w, 3011w, 2962s, 2928s, 2869s, 1774s, 1640w, 1456m, 1370w, 1345w, 1124m, 946m; δ_H (400 MHz, $CDCl_3$) 0.80 (3H, d, *J* 6.8, C(10″)H_3), 0.85–0.89 (14H, m, 2 × C(5″)H_3, C(4″)H, C(6″)H, C(8″)H_3, C(9″)H_3), 0.98–1.06 (1H, qd, *J* 12.4, 2.8 C(3″)H), 1.19–1.47 (12H, m, C(1′–5′)$_5H_{10}$, C(2″)H, C(7″)H), 1.60–1.69 (2H, m, C(3″)H, C(4″)H), 1.96–2.48 (13H, m, C(4)H, C(6′)H_2, 2 × C(1″)H_2, 2 × C(4″)H_2, C(5″)H, C(6″)H), 3.50 (1H, td, *J* 10.8, 4.0, C(1″)H), 4.92–5.02 (2H, m, C(8′)H_2), 5.22–5.59 (4H, m, C(5)H, 2 × C*H*=C*H*CH_3) overlaying 5.29 (1H, d, *J* 6.6, C(5)H), 5.81 (1H, app. ddt, app. *J* 17.2, 10.4, 6.8, C(7′)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 14.1, 15.5, 20.6, 20.8, 20.9, 22.3, 22.9, 25.4, 26.6, 28.4, 28.8, 29.2, 31.3, 32.3, 33.7, 34.3, 39.7, 45.2, 45.6, 46.3, 47.8, 77.2, 104.3, 114.3, 124.8, 134.5, 138.9, 178.4 (some peaks coincident in spectrum); *m*/*z* (CI, NH_3) 487 (MH^+, 100%), 366 (20), 349 (50), 333 (55), 331 (50), 287 (20), 172 (30), 148 (75), 95 (15); HRMS (CI) found 487.4150, calculated for $C_{32}H_{55}O_3$ (MH^+) 487.4151.

(4*S*)-4-Oct-7-enyl-5,5-di[(2*Z*)-pentenyl]cyclopent-2-enone 21

LiBr (15 mg, 0.17 mmol, dried overnight at 135 °C under high vacuum) was dissolved in anhydrous THF (1.0 mL) and cooled to −78 °C. Dimethyl methylphosphonate (18 μL, 0.17 mmol) and *n*-BuLi (103 μL of a 1.6 M solution in hexanes, 0.17 mmol) were added successively and the mixture was stirred at −78 °C for 30 min. Lactone **20** (80 mg, 0.16 mmol) in THF (0.5 mL) was added, resulting in a yellow solution. The mixture was stirred at −78 °C for 2 h then allowed to reach RT over 3 h. After addition of water (2 mL), the product was extracted with ethyl acetate (3 × 5 mL), dried (Na_2SO_4), filtered, and evaporated *in vacuo.* Purification by flash column chromatography (silica, 99 : 1 petrol : ether) gave the *title compound* (**21**) as a colourless oil (27 mg, 50%; 81% based on recovered **21**; NMR spectra indicate slight contamination by the (*E*)-side chain isomer). R_f 0. 30 (95 : 5 petrol : ether); ν_{max} (thin film)/cm^{-1} 3076w, 3010w, 2962s, 2930s, 2856s, 1709s, 1641w, 1590w, 1463m, 1182w, 1069w, 909m, 733m; δ_H (400 MHz, $CDCl_3$) 0.94 and 0.95 (2 × 3H, 2 × t, *J* 7.2, 2 × C(5″)H_3), 1.27–1.69 (10H, m, C(1–5′)$_5H_{10}$), 1.94–2.09 (6H, m, C(6′)H_2, 2 × C(4″)H_2), 2.12–2.32 (4H, m, 2 × C(1″)H_2), 2.62–2.72 (1H, m, C(4)H), 4.93–5.03 (2H, m, C(8′)H_2), 5.12–5.48 (4H, m, 2 × C*H*=C*H*CH_3), 5.82 (1H, app. ddt, app. *J* 16.8.10.4, 6.8, C(7′)H), 6.09–6.25 (1H, m, C(2)H), 7.60–7.65 (1H, m, C(3)H); δ_C (100.6 MHz, $CDCl_3$) 13.9, 14.2, 20.6, 25.6, 28.3, 28.7, 28.8, 28.9, 29.6, 31.5, 33.5, 33.7, 49.7, 53.6, 114.3, 123.8, 124.2, 132.0, 133.5, 134.5, 139.0, 166.1, 213.2; *m*/*z* (CI, NH_3) 346 (MNH_4^+, 10%), 329 (MH^+, 100), 313 (20), 261 (20), 224 (10); HRMS (CI) found 329.2855, calculated for $C_{23}H_{37}O$ (MH^+) 329.2844.

(5*R*,6*R*)-2-Methyl-5,6-di(hydroxymethyl)dec-2-ene 22

A solution of lactone **9** (125 mg, 0.34 mmol) in THF (2.0 mL) was treated with $LiAlH_4$ (26 mg, 0.68 mmol) and the mixture was heated at reflux for 2 h. After cooling to 0 °C, the mixture was quenched with water (1.0 mL) and treated with hydrochloric acid (0.5 mL, 1.0 M). The mixture was extracted with ether (3 × 5 mL) and the organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by flash column chromatography (9 : 1 petrol : ethyl acetate) gave diol **22** as a colourless oil (60 mg, 82%). R_f 0.38 (1 : 1 petrol : ethyl acetate); $[\alpha]_D^{22} = +12.9$ (*c* 0.7, $CHCl_3$); ν_{max} (thin film)/cm^{-1} 3292br s, 2941s, 2927s, 2874s, 2731m, 1456s, 1374s, 1037s, 998s; δ_H (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.2, C(10)H_3), 1.21–1.62 (8H, m, C(5)H, C(6)H, C(7–9)$_3H_6$), 1.64 and 1.71 (2 × 3H, 2 × s, =CMe_2), 2.05 and 2.18 (2 × 1H, 2 × ddd, *J* 13.4, 6.7, 6.7, =CHCH_2), 2.44 (2H, br s, 2 × –OH), 3.56–3.62 (2H, m) and 3.71–3.77 (2H, m, 2 × CH_2OH), 5.13 (1H, br t, *J* 6.7, =CH); δ_C (100.6 MHz, $CDCl_3$) 14.1, 17.8, 22.9, 25.8, 28.3, 29.3, 29.8, 42.3, 43.2, 61.6, 61.7, 123.1, 132.8; *m*/*z* (CI, NH_3) 215 (MH^+, 20%), 197 (100), 179 (25), 123 (15), 109 (20), 95 (25), 82 (15); HRMS (CI) found 215.2017, calculated $C_{13}H_{27}O_2$ (MH^+) 215.2011.

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