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Palladium mediated spiroketal synthesis: application to pheromone synthesis

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Dedicated to Professor S. V. Ley on the occasion of his 60th birthday

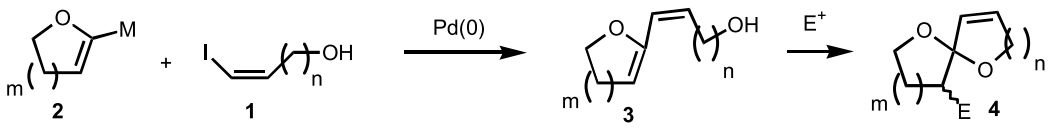
Abstract—Stereospecific Stille coupling reactions of 2-metallo-dihydropyrans with *Z*-vinyl iodo alcohols and subsequent cyclisation provides rapid access to 1,7-dioxaspiro[5.5]undecane family of spiroketals.

1. Introduction

We[1] and others[2] have previously reported on the Stille coupling of tri-butylstannyldihydrofuran and -pyran derivatives. This methodology provides rapid access to a variety of C-glycosides,[2] heterosubstituted dienes[1] and has been employed in the synthesis of benzofused spiroketal-containing systems.[3] Herein we report an extension of this chemistry leading to the rapid synthesis of simple spirocyclic systems which are ubiquitous as pheromones[4a] and is a structural motif present in an ever expanding number of biologically active molecules.[4b] Our basic strategy centred upon the use of Stork's Wittig methodology[5] for the synthesis of *Z*-vinyl iodides **1** followed by a Stille coupling[6] (retention of alkene geometry) with an appropriately metallated enol ether **2** to afford a diene **3** which would undergo cyclisation to afford the desired spiroketal **4**, Scheme 1.

2. Results and discussion

Oxidation of the readily available mono-protected diol **5**[7a] using Swern's procedure afforded the aldehyde **6**[7b] in excellent yield (92%). Olefination[5] ($Ph_3P{=}CHI$, 1.2 equiv; THF; −78 °C) generated **7** which on deprotection (CSA, cat.; MeOH; 25 °C; 78%) led to the isolation of the vinyl iodide $\mathbf{8}_{Z,E}$, as a mixture of geometrical isomers[8] (*Z*:*E*=6.4:1). With the key intermediate $\mathbf{8}_{Z,E}$ in hand, its palladium-mediated coupling with dihydropyran-derived organometallics was next investigated. Reaction of the iodide $\mathbf{8}_{Z,E}$ (1.1 equiv) with the stannane **9** (1 equiv) in the presence of $Pd(OAc)_2$ (5 mol%) and tri-*o*-tolyl phosphine (10 mol%) dissolved in acetonitrile containing triethylamine (Et_3N/CH_3CN; 2.5% v/v) at 80 °C for 1.5 h afforded the labile diene alcohols $\mathbf{10}_{Z,E}$ in moderate yield (33%). As anticipated the coupling reaction proceeds with retention of olefin geometry, generating the dienes $\mathbf{10}_{Z,E}$ as a 6:1 mixture of geometrical isomers.



Scheme 1.

Keywords: Spiroketal; Palladium; Stille; Vinyl iodide; Stork; Selenium.
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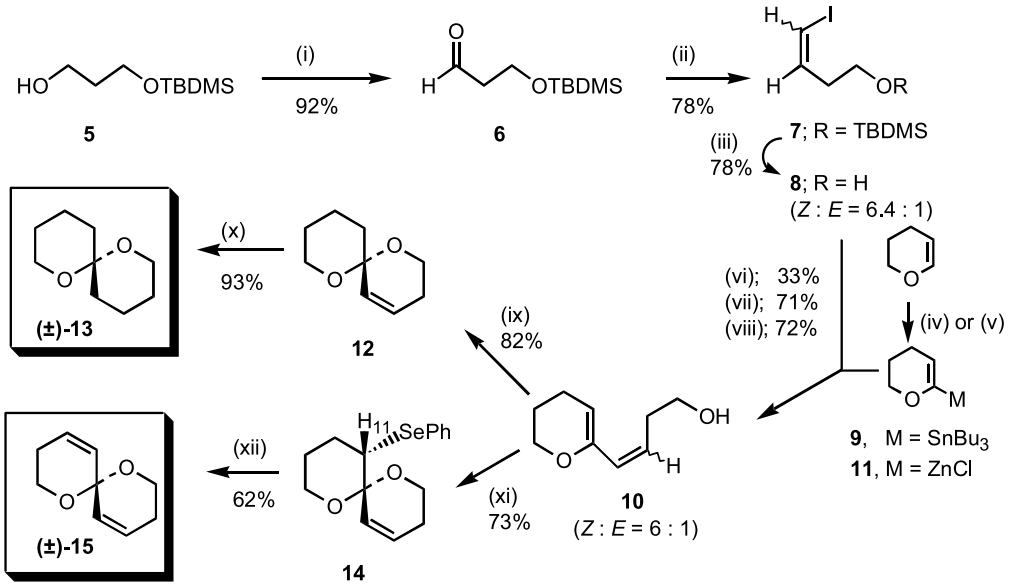
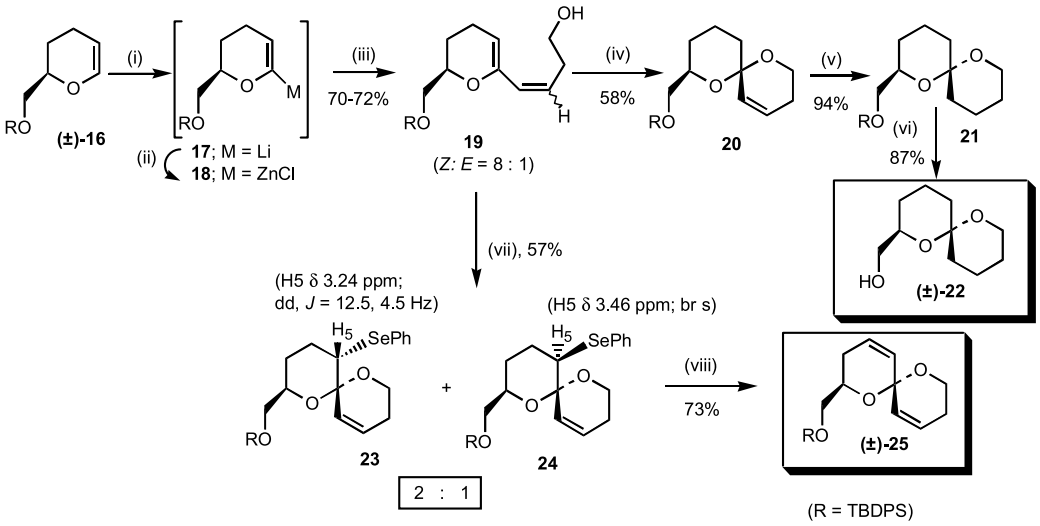
Substantially higher yields (71 and 72%, respectively) of the dienes **10** were obtained under milder reaction conditions (0–10 °C; THF; 1 h) from the coupling reaction of the zinc reagent[9] **11** with the iodide $\mathbf{8}_{Z,E}$ using either 'Pd(PPh$_3$)$_2$'[10] or Pd(PPh$_3$)$_4$ as catalyst. Exposure of the diene-alcohol $\mathbf{10}_{Z,E}$ to a catalytic quantity of CSA in CH_2Cl_2 at ambient temperature resulted in the isolation of the unsaturated spiroketal **12**[11] in 82% yield. A common feature of these spiroketalisation reactions is that, although enriched *Z*/*E*-mixtures of the precursor alcohols were usually employed in the cyclisation reaction, none of the acyclic *E*-double bond isomers could be detected by ^{1}H NMR spectroscopy at the end of reaction.[12] Presumably acid catalysed isomerisation of the unreactive *E*-isomer to the *Z*-isomer and subsequent cyclisation is responsible for this observation. Catalytic hydrogenation (H_2, 1 atm; 5% Pd/C; EtOAc; 25 °C) of **12** afforded the racemic spiroketal **13**, the pheromone[13] of *Dacus oleae*, *D. cacumintus*, in 93% yield. Alternatively, cyclisation[3b,14] of the alcohol $\mathbf{10}_{Z,E}$ with PhSeCl (1.1 equiv; pyridine, 3 equiv; CH_2Cl_2; −78–20 °C) afforded the diastereoisomerically pure selenide **14** (H_{11} δ 3.21 ppm; dd, J=12.5, 4.5 Hz) in good isolated yield (73%). Finally oxidation of **14** followed by in situ thermolysis[3b] (2-benzenesulfonyl-3-phenyloxaziridine, 'Davis oxaziridine',[15] 1.1 equiv; pyridine; $CHCl_3$; 80 °C) afforded the doubly unsaturated spiroketal **15**[16] in 62% yield, Scheme 2.

This basic synthetic strategy was next applied to the protected dihydropyran **16**. Lithiation of **16** using Boeckman's conditions[17] (^{t}BuLi, 2.2 equiv; THF; −78 to 0 °C), transmetallation ($ZnCl_2$, 1.1 equiv; THF; 2 h) to the organozinc **18** and coupling with the vinyl iodides $\mathbf{8}_{Z,E}$ ['Pd(PPh$_3$)$_2$', 5 mol%; THF; 5–20 °C, 1 h] afforded the diene-alcohols $\mathbf{19}_{Z,E}$ in 72% isolated yield. Again, the coupling reaction proceeded with retention of configuration of double bond geometry as $\mathbf{19}_{Z,E}$ was isolated as a 8:1 mixture of diastereoisomers. Exposure of the alcohols $\mathbf{19}_{Z,E}$ to camphorsulfonic acid (0.1 equiv) in CH_2Cl_2 at ambient temperature brought about immediate cyclisation to the spiroketal **20**, which was isolated in 58% yield after chromatography. Catalytic hydrogenation of **20** afforded the spiroketal **21**, which upon fluoride-induced deprotection afforded the functionalised spiroketal **22**[18] in 82% overall yield. Stereochemical assignments in this cyclisation sequence are based on stereoelectronic arguments (vide infra) and are supported by spectroscopic data, most cogently illustrated by the excellent correlation of the ^{13}C NMR of **22** with the published data for this compound.[18b] Alternatively, reaction of the dienes $\mathbf{19}_{Z,E}$ with PhSeCl-pyridine, as above, afforded a diastereoisomeric mixture of the selenides **23** and **24** (57% yield; **23**:**24**=2:1), in which the major diasteroisomer **23** possesses an equatorial phenylseleno-substituent at C_5 (H_5: δ 3.24 ppm; dd, J= 12.5, 4.5 Hz). Removal of the phenylseleno-group was readily accomplished in our standard, two step procedure, affording the unsaturated spiroketal **25**, as a single diastereoisomer, in 73% yield, Scheme 3.

The preparation of branched-chain vinyl iodides and their utilisation in this coupling-cyclisation procedure is also possible, Scheme 4. Reduction of the protected ester **26** to the aldehyde **27**[19] (Dibal-H, 1.6 equiv; toluene; −78 °C; 1 h; 88%) followed by Stork olefination afforded the vinyl iodides[20] $\mathbf{29}_{Z,E}$ in 73% overall yield (*Z*:*E*=8.2:1). In our hands the alternate route to aldehyde **27**, via alcohol **28**, was not as amenable to scale-up when compared to the direct reduction of ester **26**, with the caveat that due care was exercised in quenching the Dibal-H reduction (10% aqueous citric acid). Deprotection of the ethers $\mathbf{29}_{Z,E}$ to the partially separable alcohols[21] $\mathbf{30}_{Z,E}$ proceeded smoothly (CSA, 0.1 equiv; MeOH; 25 °C, 85%), albeit with a slight erosion of stereochemical integrity about the olefinic centre (*Z*:*E*= 6.4:1). Palladium-mediated cross coupling of the

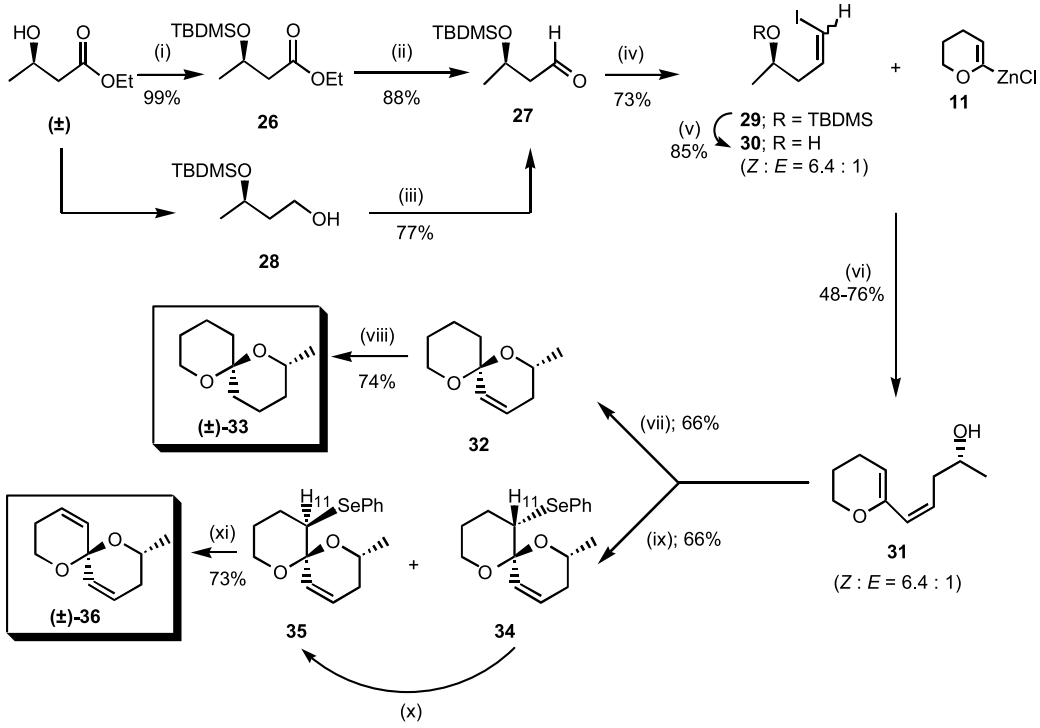


Scheme 2. Reagents and conditions: (i) $(COCl)_2$ (1.1 equiv), DMSO (2.2 equiv), CH_2Cl_2, −78 °C; (ii) Ph_3P=CHI (1.2 equiv), THF, −78 °C; (iii) CSA (0.1 equiv), MeOH, 20 °C, 15 h; (iv) a. ^{t}BuLi (1 equiv), THF, −78 °C to 0 °C, b. Bu_3SnCl (0.75 equiv), −78 °C; (v) a. ^{t}BuLi (1 equiv), THF, −78 to 0 °C, b. $ZnCl_2$ (1.2 equiv), 0–20 °C, 2 h; (vi) **9** (1 equiv), (*o*-Tol)$_3$P (10 mol%), $Pd(OAc)_2$ (5 mol%), Et_3N, CH_3CN, 80 °C, 1.5 h; (vii) **11** (2 equiv), '$(Ph_3P)_2Pd$' (5 mol%), THF, 0 °C, 1 h; (viii) (**11**) (2 equiv), $Pd(Ph_3P)_4$ (5 mol%), THF, 0 °C, 1 h; (ix) CSA (0.1 equiv), CH_2Cl_2, 20 °C; (x) 5% Pd/C, H_2, EtOAc, 1 atm., 6 h; (xi) pyridine (3 equiv), PhSeCl (1.1 equiv), CH_2Cl_2, −78 to 20 °C, 1 h; (xii) Davis oxaziridine (1.1 equiv), pyridine (5 equiv), $CHCl_3$, 80 °C, 15 h.

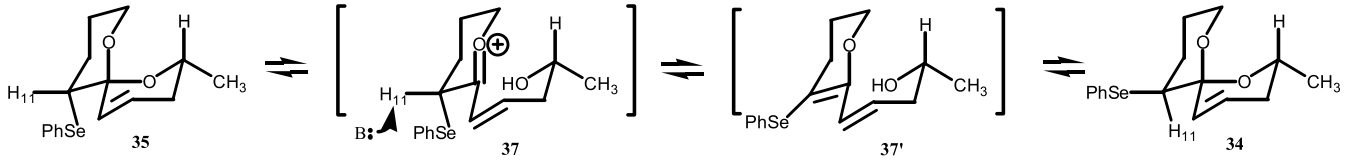


Scheme 3. Reagents and conditions: (i) a. ^{t}BuLi (2.2 equiv), THF, −78–0 °C; b. THF (excess); (ii) $ZnCl_2$ (1.1 equiv); THF, 0 °C, 2 h; (iii) **8**, $Pd(PPh_3)_4$ (5 mol%) or '$Pd(PPh_3)_2$' (5 mol %); see text for conditions; (iv) CSA (0.1 equiv), CH_2Cl_2; (v) 5% Pd/C, H_2, EtOAc, 1 atm.; (vi) TBAF (1 equiv), THF, 20 °C, 12 h; (vii) pyridine (3 equiv), PhSeCl (1.1 equiv), CH_2Cl_2, −78–20 °C, 1 h; (viii) Davis oxaziridine (1.1 equiv), pyridine (5 equiv), $CHCl_3$, 80 °C, 15 h.

geometrically pure *Z*-isomer $\mathbf{30}_Z$ with the zinc reagent **11** proved uneventful, affording the diene-alcohol $\mathbf{31}_Z$ in 76% yield. Acid promoted cyclisation of the alcohol $\mathbf{31}_Z$ generated the spiroketal **32**[22] as a single diastereoisomer (66% yield), which on catalytic hydrogenation afforded the racemic pheromone of *epeolus cruciger* **33**[23] in 74% yield. Cyclisation of the alcohol $\mathbf{31}_Z$ using PhSeCl-pyridine again afforded only two of the possible four diastereoisomeric selenides **34** and **35** (anomeric carbons in ^{13}C NMR {75 MHz $CDCl_3$} at δ 95.02, 95.39 ppm) in a ratio of 7:11. Inspection of the ^{1}H NMR spectra of these compounds indicated that the major product **35** possessed an equatorially disposed selenide group (H_{11}: δ 3.16 ppm, dd, $J=13$, 4.5 Hz) whereas that of **34** was axially disposed (H_{11}: δ 3.40 ppm, tr. $J=4.5$ Hz). Furthermore dissolution of an enriched mixture of **34** and **35** (**34**:**35** = 1:2) in $CDCl_3$ at ambient temperature effected complete isomerisation of this mixture to **35** over a period of 3 days. Notably cyclisation of both **19** (to give **23** and **24**) and **31** (to give **34** and **35**) afforded only two of the possible four diastereoisomeric selenides. Molecular mechanics calculations[24] suggest that in each case the thermodynamically more stable



Scheme 4. Reagents and conditions: (i) TBDMSCl (1.1 equiv), DBU (1 equiv), CH_2Cl_2, 20 °C; (ii) a. Dibal-H (1.6 equiv), toluene, −78 °C, b. citric acid, −78 °C; (iii) a. Dibal-H (3.0 equiv), toluene, −78–20 °C; b. $(COCl)_2$ (1.1 equiv), DMSO (2.2 equiv), −78 °C; (iv) $Ph_3P{=}CHI$ (1.2 equiv); (v) CSA (0.1 equiv), MeOH, 20 °C; (vi) **11**, (2 equiv), $Pd(PPh_3)_4$ (5 mol%), THF, 5 °C, 1 h; (vii) CSA (cat.), CH_2Cl_2, 20 °C; (viii) 5% Pd/C, H_2, EtOAc, 1 atm., 6 h; (ix) pyridine (3 equiv), PhSeCl (1 equiv), CH_2Cl_2, −78–20 °C, 1 h; (x) '$CDCl_3$', 20 °C; (xi) Davis oxaziridine (1.1 equiv), pyridine (5 equiv), $CHCl_3$, 80 °C.



Scheme 5.

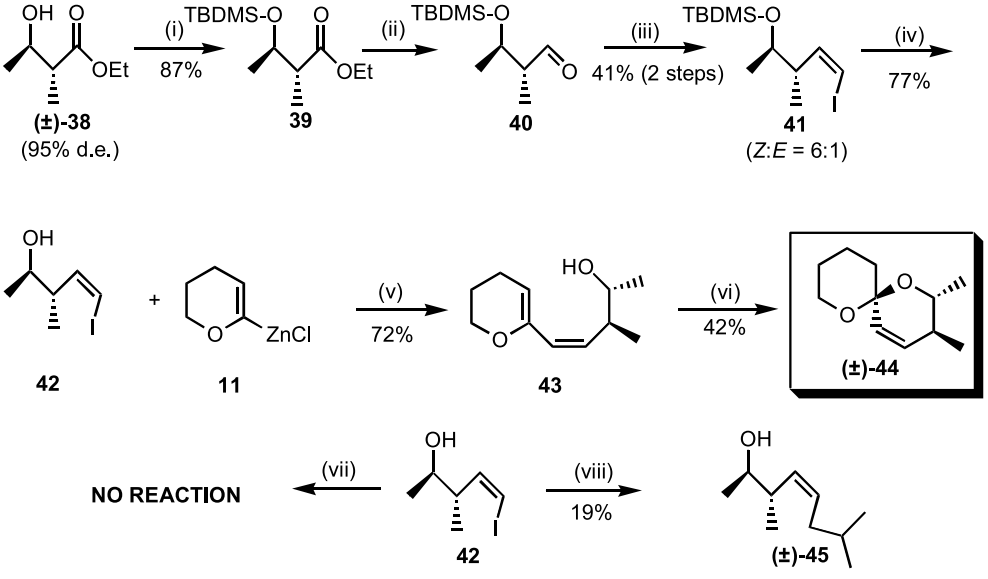
diastereoisomers are isolated: the equatorial selenide **23** being more stable than the axial selenide **24** by ca. 12.5 kJ mol^{-1} whilst **35** is more stable than **34** by ca. 11.2 kJ mol^{-1}.

The equilibration of **34** and **35** can be explained by invoking a reversible[25] ring opening of the selenides **34** and **35** via the oxonium cations **37**. Cation **37** is presumably in equilibrium with the enol ether **37′** thereby providing a pathway for the epimerisation[26] at C_{11}. Ring closure under conditions of thermodynamic control (i.e., maximum anomeric effect in which both exocyclic oxygen substituents are axial with respect to each of the pyranose rings[27]) would account for the interconversion of **34** into the more stable diastereoisomer **35**, Scheme 5. The fact that epimerisation at C_{11} had occurred in this particular reaction is further substantiated by the observation that oxidation of the diastereoisomeric mixture of selenides **34** and **35** (**34**:**35**=7:11) followed by mild thermolysis afforded the doubly-unsaturated sprioketal **36** as a single diastereoisomer in 73% isolated yield.

Finally, the synthesis of spiroketal **44**, which serves as a model for more complex systems present in a number of natural products,[28] has also been achieved using this basic strategy. Protection (DBU, TBDMSCl, dichloromethane; 87% yield) of the hydroxyl group of ethyl (3*R**,2*R**)-3-hydroxy-2-methylbutanoate[29] **38** (95% de) and reduction of the ester group with Dibal-H afforded the known aldehyde **40**.[30] The unstable aldehyde **40** was used immediately in Stork's Wittig olefination sequence affording, without any detectable epimerisation, the light-sensitive vinyl iodide **41** as a mixture of geometric isomers (*Z*:*E*=6:1) in 41% overall yield from the ester **38**.

Deprotection of $\mathbf{41}_{E,Z}$ to $\mathbf{42}_{Z}$ (77% yield) was best accomplished using aqueous hydrogen fluoride in acetonitrile[31] and was then treated with an excess of the organozinc reagent **11** (ca. 4 equiv) in the presence of $Pd(PPh_3)_4$ to afford the diene **43**, as a single geometrical isomer, in 72% yield. The diene **43** was very sensitive to traces of acid and occasionally underwent spirocyclisation in $CDCl_3$ when trying to obtain its ^{1}H NMR spectrum. Cyclisation of **43** on a preparative scale was best accomplished using camphorsulfonic acid as promoter (0.1 equiv) in dichloromethane enabling isolation of the volatile spiroketal **44**[32] in 42% yield.

Presumably cyclisation under these conditions is again subject to thermodynamic control: diastereoisomer **44** benefits from a maximum *exo* anomeric effect (each oxygen is axial to the adjacent pyranose ring) which is augmented by the diequatorial disposition of the methyl groups at C_2 and C_3, Scheme 6. As an excess (ca. 4 equiv) of the organozinc reagent **11** was used in this coupling sequence (1 equiv just serves to deprotonate the free hydroxyl group of **42**), which is obviously wasteful if more elaborate organometallics were to be employed, in situ protection of the hydroxyl group was briefly investigated. Germane to this discussion is Negishi's[33] observation that alkoxyzincs, generated in situ from (*Z*)-iodo-2-buten-1-ol by reaction with EtZnCl, undergo efficient cross-coupling reactions with organometallic reagents, providing a highly



Scheme 6. Reagents and conditions: (i) TBDMSCl (1.1 equiv), DBU (1 equiv), CH_2Cl_2, 0 °C, 3 h; (ii) Dibal-H (1.6 equiv), toluene, −80 °C, 1 h; (iii) Ph_3P=CHI (1.2 equiv); (iv) 60% HF_{aq} in CH_3CN; (v) **11**, (4 equiv), $Pd(PPh_3)_4$ (5 mol%), THF, 5 °C, 1 h; (vi) CSA (0.1 equiv), CH_2Cl_2, 20 °C; (vii) a. EtZnCl (1 equiv), −78–20 °C; b. **11**, $Pd(PPh_3)_4$ (5 mol%), THF, 5 °C, 1 h; (viii) a. Dibal-H (1 equiv), −78–20 °C; b. **11**, $Pd(PPh_3)_4$ (5 mol%), THF, 5 °C, 1 h.

stereoselective procedure for the synthesis of (*Z*)-3-methyl-2-alken-1-ols. Unfortunately, this modification was not successful in our hands. We did observe however that prior treatment of **42** with Dibal-H (1 equiv), followed by reaction with the vinylzinc reagent **11**, as previously described, afforded the coupled product **45** (19% yield) in which transfer of an *iso*-butyl group from aluminium[34] rather than cross coupling with the zinc reagent **11** had taken place, Scheme 6.

3. Conclusion

In conclusion, this study illustrates that the 1,7-dioxa-spiro[5.5]undec-4-ene system is readily accessible using a Wittig–Stille route, and that application of this strategy to the synthesis of more elaborate spiroketals of biological inteserest[28] should be possible. Further studies in this area are in progress the results of which will be reported at a future date.

4. Experimental

4.1. General

All non-aqueous reactions were performed under an atmosphere of dry nitrogen at temperatures which were those of the external bath. Proton and carbon nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded on Bruker AC 300, Varian XL 300, Varian Gemini 200 spectrometers, with residual non-deuterated solvent as internal standard. All chemical shifts are quoted in parts per million downfield from tetramethylsilane. *J* values are given in Hz. Splitting patterns were abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br). Infrared spectra were recorded on a Perkin–Elmer 1710 FT spectrometer as evaporated films unless otherwise stated. Absorption maxima (ν_{max}) were reported in wavenumber (cm^{-1}). Mass spectra were recorded on Kratos MS20 and MS25 spectrometers. The modes of ionisation used were electron impact (EI) and chemical ionisation (CI). Microanalysis was performed at the University of Manchester. Melting points were recorded on a Kofler heated stage microscope, and are uncorrected. Petrol refers to that fraction of light petroleum ether which distils between 40 and 60 °C, and was redistilled prior to use. Tetrahydrofuran (THF) was dried over sodium/benzophenone ketyl and distilled under an atmosphere of dry nitrogen. Dichloromethane was dried over phosphorus pentoxide and distilled. Methanol was dried over magnesium methoxide and distilled. Triethylamine was dried over potassium hydroxide pellets and distilled. Pyridine was dried over potassium hydroxide pellets and redistilled under nitrogen. Dimethyl sulfoxide was dried over calcium hydride and redistilled at atmospheric pressure. Toluene was dried over sodium and redistilled under nitrogen. Where ether is mentioned it refers to diethyl ether. *n*-Butyllithium was supplied as solution in hexanes and *t*-butyllithium as a solution in pentane. Chromatography refers to flash column chromatography and was carried out using Merck silica gel 60H (40–63 μm, 230–400 mesh) as stationary phase. Thin layer chromatography was carried out on plates precoated with Kieselgel 60 F_{254} silica. Visualisation was achieved by ultraviolet absorption or treatment with an ethanolic solution of dodecamolybdophosphoric acid followed by heating.

4.1.1. 3-(*t*-Butyldimethylsilyloxy)propan-1-ol, 5.[7a] Sodium hydride (80% suspension in oil) (1.5 g, 49.8 mmol) was suspended in THF (100 mL) after being washed with hexane. 1,3-Propanediol (3 mL, 3.16 g, 41.5 mmol) was added to the mixture at room temperature and stirred for 45 min, after which time an opaque white precipitate had formed. *t*-Butyldimethylsilyl chloride (6.26 g, 41.5 mmol) was then added, and vigorous stirring was continued for 45 min. The mixture was poured into ether (100 mL), washed with 10% potassium carbonate (30 mL) and brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. The resulting oil was purified by flash column chromatography using ethyl acetate/petrol (1:4) as eluent to afford the title compound **5** (6.3 g, 80%) as a colourless oil; ν_{max} (film) 3353, 2930, 2858, 1472, 1389, 1362, 1256, 1097, 1008, 963, 837, 777, 720 and 663 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.09 (6H, s, MeSi), 0.9 (9H, s, ^{t}BuSi), 1.77 (2H, quintet, $J=5.5$ Hz, 2-H), 2.60 (1H, br s, OH), 3.80 (2H, t, $J=5.5$ Hz, 1-H), 3.82 (2H, t, $J=5.5$ Hz, 3-H); δ_C (75 MHz, $CDCl_3$): −5.50 (MeSi), 18.17 (CMe_3), 25.67 (CMe_3), 34.29 (C-2), 62.27 (C-1), 62.77 (C-3); *m/z* (CI) 191 {$[M+H]^+$, 100%}. Found: *m/z* 191.1465. $C_9H_{23}O_2Si$ {$[M+H]^+$} requires *m/z* 191.1467.

4.1.2. 3-(*t*-Butyldimethylsilyloxy)propanal, 6.[7b] The title compound was prepared from the alcohol **5** (10.43 g, 54.9 mmol) using method A as above. Purification by flash chromatography afforded **6** as a colourless oil (9.46 g, 92%); ν_{max} (film) 2956, 2930, 2858, 1728, 1473, 1390, 1390, 1362, 1257, 1100, 1007, 972, 837 and 778 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 0.09 (6H, s, MeSi), 0.90 (9H, s, ^{t}BuSi), 2.59 (2H, dt, $J=6$, 2 Hz, 2-H), 3.98 (2H, t, $J=6.5$ Hz, 3-H), 9.80 (1H, t, $J=2$ Hz, 1-H); δ_C (75 MHz) −5.46 (MeSi), 18.20 (CMe_3), 25.80 (CMe_3), 46.57 (C-2), 57.41 (C-3), 201.68 (C-1); *m/z* (CI) 189 {$[M+H]^+$, 100%}. Found *m/z* 189.1310. $C_9H_{21}O_2Si$ {$[M+H]^+$} requires *m/z* 189.1311.

4.1.3. Iodomethyltriphenylphosphonium iodide.[36] To a suspension of triphenylphosphine (60 g, 0.23 mol) in toluene (60 mL) was added methylene iodide (24 mL, 0.3 mol). The mixture was kept at 45–50 °C for 15 h after which time the crystals were collected, washed with toluene (3×100 mL), and dried in vacuo (0.1 mmHg) for 4 h affording the title compound (111.2 g, 91.2%) as a white solid, mp 230 °C (dec) [Lit.[35] 228–230 °C (dec)]; ν_{max} (KBr disc) 2919, 2849, 1639, 1618, 1586, 1499, 1482, 1438, 1318, 1111, 1084, 997, 785, 727, 689, 566, 508 and 484 cm^{-1}. δ_H (300 MHz, d_6-DMSO): 5.15 (2H, d, $^2J_{\{P-H\}}=9$ Hz), 7.95 (15H, s, Ar). Found: C, 43.4; H, 3.35; I, 47.4; P, 5.7. $C_{19}H_{17}I_2P$ requires: C, 43.0; H, 3.25; I, 47.9; P, 5.85%.

4.1.4. 2-Tri-*n*-butylstannyl-5,6-dihydro-2*H*-pyran, 9.[35] A solution of *t*-butyl lithium (17.5 mL, 1.7 M solution in pentane) was added dropwise to a stirred solution of 2,3-dihydro-2H-pyran (2.5 g, 2.7 mL, 29.7 mmol) in THF (10 mL) at −78 °C. The mixture was allowed to warm up to 0 °C and was stirred at this temperature for 30 min, then

recooled to −78 °C. Tri-*n*-butyltin chloride (6 mL, 22.3 mmol) was added dropwise and the resulting mixture was allowed to warm up to room temperature and to stir for 2 h. After quenching with aq. ammonium chloride, the product was extracted into ether (3×30 mL), the ethereal extracts dried ($MgSO_4$) and evaporated and the residue purified by column chromatography (triethylamine/petrol 1:19) to afford the title compound **9** (7.23 g, 87%) as a colourless oil; ν_{max} (film) 2955, 2926, 2854, 1606, 1464, 1377, 1221, 1070, 1054, 898, 839, 780 and 666 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.91 (15H, m, $SnCH_2$– and –CH_3), 1.33 (6H, m, –CH_2–, J=7.5 Hz), 1.50 (6H, m, –CH_2–, J=7.5 Hz), 1.85 (2H, m, 4-H, J=5 Hz), 2.01 (2H, m, J=4 Hz, 3-H), 3.90 (2H, t, J=5 Hz, 5-H), 4.72 (1H, t, J=3.5 Hz, 2-H, $^3J_{\{H-Sn\}}$=30 Hz); *m/z* (EI) 317 [[M+ −Bu], ^{120}Sn 100%], 315 {[M+ −Bu], ^{118}Sn 73%}. (CI) 375 {[M+H]$^+$, ^{120}Sn 100%}, 373 {[M+H]$^+$, ^{118}Sn 76%}.

4.1.5. (±)-2-(*t*-Butyldiphenylsilyloxymethyl)-3,4-dihydro-2*H*-pyran, 16. Sodium hydride (80% suspension in mineral oil) (2.12 g, 70.6 mmol) was suspended in THF (100 mL) after being washed with hexane. 2-(Hydroxymethyl)-3,4-dihydro-2*H*-pyran (6.71 g, 58.8 mmol) was added to the mixture at room temperature and left to stir at this temperature for 45 min during which time a light brown precipitate had formed. *t*-Butyldiphenylsilyl chloride (11.76 g, 42.8 mmol) was then added, and vigorous stirring was continued for 40 h. The mixture was poured into ether (100 mL), washed with ammonium chloride, dried ($MgSO_4$) and concentrated in vacuo. The resulting oil was purified by flash column chromatography using ethyl acetate/petrol (1:99) as eluent to afford the title compound **16** (12.53 g, 83%) as a colourless, viscous oil; ν_{max} (film) 3070, 2930, 2857, 1650, 1472, 1428, 1391, 1362, 1242, 1188, 1136, 1112, 1071, 1005, 939, 909, 824, 798, 740 and 702 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.15 (3H, s, ^{t}BuSi), 1.70–1.85 (1H, m, 3-H), 1.95–2.20 (3H, m, 4-H, 3′-H), 3.76 (1H, dd, J=10, 5.5 Hz, CH_2OSi), 3.88 (1H, dd, J=10, 5 Hz, CH_2OSi), 3.90–4.00 (1H, m, 2-H), 4.70 (1H, br s, 5-H), 6.43 (1H, d, J=6.5 Hz, 6-H), 7.40–7.80 (10H, m, Ar); δ_C (75 MHz, $CDCl_3$) 19.27 (C-4), 19.36 (CMe_3), 24.49 (CMe_3), 66.11, 75.38 (C-1), 100.35 (C-5), 127.69, 129.68, 133.69, 135.69 (Ar), 143.64 (C-6); *m/z* (CI) 275 {[M$^+$ −Ph], 100%}; *m/z* (EI) 295 [[M$^+$ −^{t}Bu], 65.1%]. Found: *m/z* (CI); 353.1935 {[M+H]$^+$}. $C_{22}H_{29}O_2^{28}Si$ {[M+H]$^+$} requires *m/z* 353.1937.

4.1.6. Ethyl (±)-3-(*t*-butyldimethylsilyloxy)butanoate, 26.[19] To a solution of racemic ethyl-3-hydroxybutanoate (7.12 g, 53.9 mmol) in dichloromethane (10 mL) was added 1,8-diazobicyclo[5,4,0]undec-7-ene (8.9 mL, 59.25 mmol) at 0 °C followed by a solution of *t*-butyldimethylsilyl chloride (8.53 g, 56.56 mmol) in dichloromethane (10 mL). After 3 h at room temperature, the mixture was poured into water (100 mL) and extracted into ether (100 mL). The organic extracts were washed with water (50 mL), hydrochloric acid (0.1 M, 50 mL), water (50 mL), saturated sodium bicarbonate (50 mL) and water (50 mL). The organic layer was dried ($MgSO_4$), concentrated in vacuo, and the residue chromatographed (1:19 ethyl acetate petrol) to afford the title compound, **26** (13.12 g, 99%) as a colourless oil; ν_{max} (film) 2958, 2931, 2858, 1740, 1474, 1377, 1301, 1256, 1184, 1140, 1084, 1035, 1003, 940, 837, 811 and 777 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.03 (3H, s, MeSi), 0.07 (3H, s, MeSi), 0.85 (9H, s, ^{t}BuSi), 1.19 (3H, d, J=6 Hz, 4-H), 1.25 (3H, t, J=7 Hz, OCH_2CH_3), 2.35 (1H, dd, J=14, 5.5 Hz, 2-H), 2.46 (1H, dd, J=14, 7.5 Hz, 2-H), 4.11 (2H, m, OCH_2), 4.27 (1H, m, 3-H); δ_C (75 MHz, $CDCl_3$) −5.03, −4.51 (Me_2Si), 14.21 (OCH_2CH_3), 17.96 (Me_3C), 23.93 (C-4), 25.73 (Me_3C), 44.96 (C-2), 60.25 (C-3), 65.67 (OCH_2), 171.67 (C-1); *m/z* (EI) 161 [M$^+$ −TBDMS, 100%]. (CI) 45 {[$(CH_3)H_2Si$]$^+$, 82.1%}. Found: *m/z*, 189.0950. $C_8H_{17}SiO_3$ [M$^+$ −^{t}Bu] requires 189.0947. Found: C, 58.7; H, 10.4; Si, 11.7. $C_{12}H_{26}O_3Si$ requires: C, 58.5; H, 10.6; Si, 11.4%.

4.1.7. (±)-3-(*t*-Butyldimethylsilyloxy)butanal, 27.[19] *Method A*. A solution of oxalyl chloride (0.9 mL, 10 mmol) in dichloromethane (100 mL) was cooled to −78 °C to which was added dropwise freshly dried dimethyl sulfoxide (1.5 mL, 20.8 mmol). After 15 min. at −78 °C a solution of (±)-3-(*t*-butyldimethylsilyloxy)butanol **28**[36] (1.75 g, 8.58 mmol) in dichloromethane (20 mL) was added dropwise and the reaction mixture stirred at −78 °C for 25 min. The reaction was quenched by the addition of triethylamine (6 mL) and allowed to warm to room temperature. After 1 h the reaction was poured into saturated aqueous sodium bicarbonate solution (50 mL). The layers were separated and the aqueous layer extracted with dichloromethane. The combined organic layers were washed with brine (50 mL), dried ($MgSO_4$) and concentrated in vacuo. The residue was diluted with hexane (30 mL), washed with water (20 mL), dried ($MgSO_4$) and concentrated in vacuo. Flash column chromatography of the residue using 1:19 ethyl acetate:petrol as eluent, gave the title compound **27** as a colourless oil (1.34 g, 77%).

Method B. Dibal-H in toluene (1 M, 47.3 mL) was added dropwise to a cooled (−80 °C) solution of ethyl (±)-3-(*t*-butyldimethylsilyloxy)butanoate **26** (7.27 g, 29.55 mmol) in anhydrous toluene (210 mL). After 1 h at −78 °C the reaction was quenched by the dropwise addition of methanol (30 mL) whilst keeping the temperature below −78 °C. Citric acid (10% aqueous solution, 300 mL) was then added, the mixture was allowed to warm to room temperature, the organic phase was decanted and the aqueous layer was extracted with dichloromethane (3× 100 mL). The combined organic phases were dried ($MgSO_4$), the solvent was removed under reduced pressure and the residue purified by flash chromatography (ethyl acetate/petrol 1:19) to afford the title compound **27** (5.26 g, 88%); ν_{max} (film) 2957, 2931, 2896, 2858, 2721, 1730, 1473, 1464, 1377,1363, 1257, 1219, 1186, 1138, 1100, 1030, 940, 904, 837, 811 and 777 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.06 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.85 (9H, s, ^{t}BuSi), 1.24 (3H, d, J=6 Hz, 4-H), 2.45 (1H, ddd, J=15, 5, 2 Hz, 2-H), 2.55 (1H, ddd, J=15, 7, 3 Hz, 2-H), 4.35 (1H, sextet, J=5.5 Hz, 2-H), 9.80 (1H, t, J=2.5 Hz, 1-H); δ_C (75 MHz, $CDCl_3$): −4.48, −3.90 (Me_2Si), 18.43 (Me_3C), 24.66 (C-4), 26.2 (Me_3C), 53.45 (C-2), 65.02 (C-3), 202.74 (C-1); *m/z* (EI) 145 [M$^+$ −^{t}Bu, 100%], (CI) 203 {[M+H]$^+$, 100%}. Found: *m/z* (CI) 220.1742. $C_{10}H_{26}NSiO_2$ {[M+NH_4]$^+$} requires *m/z* 220.1733. Found: C, 59.1; H, 11.1. $C_{10}H_{22}O_2Si$ requires: C, 59.4; H, 10.8%.

4.1.8. (±)-3-(*t*-Butyldimethylsilyloxy)butan-1-ol, 28.[37] To a solution of ethyl (±)-3-(*t*-butyldimethylsilyloxy)butanoate

25 (3.02 g, 12.3 mmol) in THF (10 mL) was added Dibal-H (1 M solution in toluene, 27.0 mmol) at −78 °C. The mixture was allowed to warm up to room temperature and stirred for 2–3 h. The reaction was quenched with water (1 mL), poured into diethyl ether (100 mL), sodium hydroxide (3 M, 1 mL) was added and the mixture was stirred until the aluminium salts had precipitated. The supernatant was filtered through celite® and the celite® pad washed with ether (3×30 mL). The combined organic extracts were dried ($MgSO_4$), concentrated and the residue purified by column chromatography (ethyl acetate/petrol 1:4) to afford the title compound (**28**) (1.95 g, 78%) as a colourless oil. ν_{max} (film) 3356, 2957, 2930, 2858, 1473, 1376, 1256, 1141, 1100, 1060, 1030, 943, 904, 837, 776, 718 and 664 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.05 (6H, s, Me_2Si), 0.88 (9H, s, ^tBuSi), 1.22 (3H, d, $J=6$ Hz, 4-H), 1.62 (1H, m, 2-H), 1.75 (1H, m, 2-H), 2.70 (1H, s, OH), 3.70 (1H, m, 1-H), 3.80 (1H, m, 1-H), 4.1 (1H, m, 3-H); δ_C (75 MHz): −4.96, −4.36 (Me_2Si), 17.94 (Me_3C), 23.44 (C-4), 25.80 (Me_3C), 40.57 (C-2), 60.41 (C-1), 68.25 (C-3); *m/z* (EI) 75 [$[(CH_3)_2HSi–O]^+$, 100%], (CI) 205 {$[M+H]^+$,100%} Found: *m/z* (CI) 205.1625. $C_{10}H_{25}O_2Si$ {$[M+H]^+$} requires *m/z* 205.1624. Found: C, 58.7; H, 12.2; Si, 14.2. $C_{10}H_{24}O_2Si$ requires C, 58.8; H, 11.8; Si, 13.7%.

4.1.9. (±)-(*Z*,*E*)-4-(*t*-Butyldimethylsilyloxy)-1-iodopent-1-ene, 29. To a suspension of iodomethyltriphenylphosphonium iodide (16.35 g, 30.85 mmol) in THF (16 mL) at room temperature was slowly added sodium hexamethyldisilazide (1 M solution in THF, 32.4 mL). After stirring for 10 min, the dark red-coloured solution of the yield was cooled to −78 °C and (±)-3-(*t*-butyldimethylsilyloxy)butanal **28** (4.99 g, 24.7 mmol) was added slowly. The mixture was allowed to warm up to room temperature and, after 30 min, the solvent was removed in vacuo. The residue was triturated with petrol (3×50 mL) and the combined extracts filtered through celite® to remove triphenylphosphine oxide. The combined organic extracts were concentrated in vacuo and the residue purified by column chromatography (dichloromethane/hexane 1:19) to afford the title compound **29** (6.7 g, 83%) as a light-sensitive colourless[38] oil, (*Z*:*E*=8.2:1); ν_{max} (film) 2956, 2929, 2894, 2857, 1611, 1472, 1377, 1361, 1308, 1256, 1131, 1089, 1022, 836, 808 and 776 cm^{-1}; δ_H (300 MHz, $CDCl_3$): *Z*-isomer; 0.07 (6H, s, Me_2Si), 0.90 (9H, s, ^tBuSi), 1.19 (1H, d, $J=6$ Hz, 5-H), 2.31 (2H, distorted triplet, 3-H), 3.98 (1H, sextet, $J=6$ Hz, 4-H), 6.28 (2H, m, 2-H). *E*-isomer 0.07 (6H, s, Me_2Si), 0.90 (9H, s, ^tBuSi), 1.15 (1H, d, $J=6$ Hz, 5-H), 2.18 (2H, distorted triplet, 3-H), 3.86 (1H, sextet, $J=6$ Hz, 4-H), 6.03 (1H, d, $J=14.5$ Hz, 1-H), 6.55 (1H, dt, $J=14.5$, 7.5 Hz, 2-H). δ_C (75 MHz, $CDCl_3$): *Z*-isomer −4.69, −4.46 (Me_2Si), 18.11 (Me_3C), 23.59 (C-5), 25.88 (Me_3C), 44.55 (C-3), 67.30 (C-4), 83.69 (C-1), 138.33 (C-2). *m/z* (EI) 269 [M+ $-{}^tBu$, 100%] (CI) *m/e* 327 {$[M+H]^+$, 48%]. Found: *m/z* (CI) 327.0643. $C_{11}H_{24}IOSiO$ requires *m/z* 327.0655.

4.1.10. (*Z*,*E*)-4-(*t*-Butyldimethylsilyloxy)-1-iodobut-1-ene, 7. The title compound was prepared from the aldehyde **6** (5.21 g, 27.7 mmol) using the method described above. Isolated as a light-sensitive, colourless, oil[38] (6.71 g, 78%; *Z*:*E*=7.6:1); ν_{max} (film) 2954, 2929, 2857, 1610, 1472, 1385, 1287, 1257, 1103, 939, 836 and 777 cm^{-1}; δ_H (300 MHz, $CDCl_3$): *Z*-isomer 0.09 (6H, s, MeSi), 0.90 (9H, s, ^tBuSi), 2.36 (2H, m, 4-H), 3.70 (2H, t, $J=6.5$ Hz, 3-H), 6.29 (2H, m, 1-H, 2-H); *E*-isomer 0.08 (6H, s, MeSi), 0.90 (9H, s, ^tBuSi), 2.26 (2H, m, 4-H), 3.65 (2H, t, $J=6.5$ Hz, 3-H), 6.02 (1H, d, $J=14.5$ Hz, 1-H), 6.54 (1H, dt, $J=14.5$, 7.5 Hz, 2-H); δ_C (75 MHz, $CDCl_3$) *Z*-isomer −5.27 (MeSi), 18.33 (CMe_3), 25.93 (CMe_3), 38.37 (C-3), 61.2 (C-4), 83.62 (C-1), 138.31 (C-2); *E*-isomer −5.27, 18.33, 25,93, 39.39, 61.68, 83.63, 143.33; *m/z* (EI) 255 [$M^+ - {}^tBu$, 100%] (CI) 313 {$[[M+H]^+$, 100%}. Found: *m/z* (CI) 313.0485. $C_{10}H_{22}IOSi$ requires *m/z* 313.0486.

4.1.11. (*Z*,*E*)-4-Hydroxy-1-iodobutene, 8. The title compounds were prepared from the vinyl iodide **7** (2.48 g, 7.95 mmol) using the method above. Flash chromatography afforded the iodide as a colourless, light-sensitive oil[38] (1.23 g, 78%), (*Z*:*E*=6.4:1); ν_{max} (film) 3338, 3066, 3948, 2880 1610, 1423, 1336, 1307, 1284, 1254, 1165, 1040, 946, 883, 852 and 691 cm^{-1}; δ_H (300 MHz, $CDCl_3$) *Z*-isomer 1.75 (1H, s, OH), 2.44 (2H, dq, $J=6.5$, 1 Hz, 3-H), 3.75 (2H, t $J=6.5$ Hz, 4-H), 6.28 (1H, q, $J=7$ Hz, 2-H), 6.37 (1H, td, $J=7$, 1 Hz, 1-H); *E*-isomer 1.75 (1H, s, OH), 2.32 (2H, dq, $J=6.5$, 1 Hz, 3-H), 3.68 (2H, t, $J=6.5$ Hz, 1-H), 6.16 (1H, td, $J=14.5$, 1 Hz, 1-H), 6.55 (1H, dt, $J=14.5$, 7 Hz, 2-H); δ_C (75 MHz, $CDCl_3$): *Z*-isomer 38.11 (C-3), 60.96 (C-4), 84.74 (C-1), 137.68 (C-2); *E*-isomer 39.16 (C-3), 61.01 (C-4), 84.74 (C-1), 142.68 (C-2); *m/z* (EI) 198 [M^+, 32.7%]. Found: *m/z* 197.9544. C_4H_7IO [M^+] requires 197.9543.

4.1.12. (±)-(*Z*,*E*)-4-Hydroxy-1-iodopentene, 30. To a solution of (±)-(*Z*,*E*)-4-(*t*-butyldimethylsilyloxy)-1-iodopentene **29** (1.68 g, 5.15 mmol) in methanol (10 mL) was added camphorsulfonic acid (30 mg) and mixture stirred for 15 h at ambient temperature after which time anhydrous potassium carbonate (0.15 g) was added and stirring was continued for 15 min. The mixture was filtered and concentrated in vacuo. The residue was dissolved in dichloromethane (50 mL), washed with saturated aqueous sodium hydrogencarbonate solution, dried ($MgSO_4$), concentrated in vacuo and the residue chromatographed (1:4 ethyl acetate petrol) to afford the title compound **30** (0.93 g, 85%) as a colourless, light-sensitive oil[38] (*Z*:*E*=6.4:1); ν_{max} (film) 3340, 2967, 2925, 1609, 1456, 1376, 1307, 1262, 1121, 1081, 973, 943 and 844 cm^{-1}; δ_H (300 MHz, $CDCl_3$): *Z*-isomer 1.25 (3H, d $J=6.5$ Hz, 5-H), 2.34 (2H, t, $J=6.5$ Hz, 3-H), 3.98 (1H, sextet, $J=6.5$ Hz, 4-H), 6.29 (1H, q, $J=7$ Hz, 2-H), 6.36 (1H, distorted d, $J=8$ Hz, 1-H); *E*-isomer 1.20 (3H, d, $J=6.5$ Hz), 2.10 (2H, t, $J=6.5$ Hz), 3.87 (1H, sextet, $J=6.5$ Hz), 6.13 (1H, d, $J=15$ Hz, 1-H), 6.55 (1H, dt, $J=15$, 7.5 Hz, 2-H); δ_C (75 MHz, $CDCl_3$): *Z*-isomer 23.20 (C-5), 44.10 (C-3), 66.89 (C-4), 84.80 (C-1), 137.56 (C-2); *E*-isomer 22.87, 45.50, 66.58, 84.90, 142.60; *m/z* (EI) 212 [M^+,11.6% (CI) 230 {$[M+NH_4]^+$, 100%}. Found: *m/z* (CI) 211.9704. C_5H_9IO [M^+] requires *m/z* 211.9700.

4.1.13. (±)-(4*Z*,*E*)-5-(3,4-Dihydro-2*H*-6-pyranyl)-4-penten-2-ol, 31. *Method A*. To a stirred mixture of palladium(II) acetate (41 mg, 5 mol%), tri-(*o*-tolyl)phosphine (77 mg, 10 mol%) and triethylamine (0.25 mL) in acetonitrile (10 mL) was added 2-tri-*n*-butylstannyl-5,6-dihydro-2*H*-pyran **9** (1.22 g, 3.22 mmol) followed by (±)-(*Z*,*E*)-4-hydroxy-1-iodopentene **30** (0.73 g, 3.44 mmol). The

reaction mixture was brought to reflux for 1.5 h, cooled to ambient temperature and saturated aqueous potassium fluoride in 10% ammonium hydroxide was added. The resulting mixture was filtered and extracted with ether (3× 30 mL). The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo, and the residue chromatographed (3:1:16 ethyl acetate/triethylamine/petrol) to afford the title compound **31** (261 mg, 48%, colourless oil) as an inseparable mixture of isomers (*Z*:*E*=6:1).

Method B. A solution of *t*-butyl lithium (7.4 mL, 1.7 M solution in pentane) was added dropwise to a stirred solution of 2,3-dihydro-2*H*-pyran (1.15 mL, 12.6 mmol) in THF (8 mL) at −78 °C. The mixture was allowed to warm to 0 °C and was stirred at this temperature for 30 min, then recooled to −78 °C. Zinc chloride (1 M solution in ether, 13.8 mL) was added dropwise and the resulting mixture was allowed to warm up to room temperature and to stir for 2 h. Catalyst generation: in a separate flask, Dibal-H (1 M solution in toluene, 0.33 mL) was added dropwise to $PdCl_2(PPh_3)_2$ (116 mg, 0.16 mmol, 5 mol%) in THF (5 mL) at 0 °C and the resulting mixture was stirred for 30 min. The solution containing the catalyst was then transferred by canula under nitrogen to the solution of the vinyl zinc intermediate **11** at 5–10 °C, followed by a solution of (*Z*,*E*)-4-hydroxy-1-iodopentene **30** (0.72 g, 3.4 mmol) in THF (2 mL) and resulting mixture was stirred for 1 h at ambient temperature. After quenching with sodium hydroxide (10 mL), the product was extracted into ether (3×30 mL), the ethereal extracts dried ($MgSO_4$), concentrated in vacuo, and column chromatography (3:1:16 ethyl acetate/triethylamine/petrol) of the residue afforded the title compound **30** (400 mg, 74%; *Z*:*E*=6:1) as a mobile oil.

Method C. The title compound **31** was prepared in exactly the same way as in method B except that freshly prepared $Pd(PPh_3)_4$ (192 mg, 5 mol%) was used as the catalyst. (±)-(*Z*,*E*)-4-hydroxy-1-iodopentene **30** (0.72 g, 3.4 mmol) afforded **31** (413 mg, 76%; *Z*:*E*=6:1); ν_{max} (film) 3379, 2967, 2929, 1656, 1612, 1414, 1374, 1352, 1310, 1234, 1165, 1122, 1085, 1060, 1002, 922, 886, 846, 814 and 781 cm^{-1}; δ_H (300 MHz, C_6D_6) *Z*-isomer 1.23 (3H, d, *J*= 6 Hz, 1′-H), 1.45 (2H, quintet, *J*=5.5 Hz, 3-H), 1.85 (2H, m, 4-H), 2.05–2.15 (1H, br s, OH), 2.73 (1H, dt, *J*=15, 7 Hz, 3′-H), 2.82 (1H, dt, *J*=15, 7 Hz, 3′-H), 3.76 (1H, t, *J*=6.5 Hz, 2′-H), 3.85 (2H, t, *J*=6.5 Hz, 2-H), 4.72 (1H, t, *J*=4 Hz, 5-H), 5.48 (1H, dt, *J*=12, 6 Hz, 4′-H), 5.82 (1H, d, *J*=12 Hz, 5′-H); *E*-isomer 1.12 (3H, d, *J*=6 Hz, 1′-H), 1.32 (2H, quintet, *J*=5.5 Hz, 3-H), 1.91 (2H, m, 4-H), 2.15–2.30 (3H, m, 3′-H, OH), 3.70 (1H, t, *J*=6.5 Hz, 2′-H), 3.89 (2H, t, *J*=6.5 Hz, 2-H), 4.69 (1H, t, *J*=4 Hz, 5-H), 5.90 (1H, d, *J*=15.5 Hz, 5′-H), 6.27 (1H, dt, *J*=15.5, 7.5 Hz, 4′-H); δ_C (75 MHz, C_6D_6) *Z*-isomer 20.98 (Me), 22.23 (C-4), 23.39 (C-3), 39.01 (C-3′), 65.61 (C-2′), 67.91 (C-2), 103.11 (C-5), 127.02 (C-4′), 127.15 (C-5′), 153.03 (C-6); *E*-isomer 21.03 (Me), 22.23 (C-4), 22.66 (C-3), 42.65 (C-3′), 65.87 (C-2′), 67.35 (C-2), 100.96 (C-5), 125.06 (C-4′), 129.09 (C-5′), 153.03 (C-6); *m*/*z* (EI) 168 [M+, 42.3%] (CI) 169 {[M+H]$^+$, 8.4%}. Found *m*/*z* (CI) 168.1146. $C_{10}H_{16}O_2$ [M^+] requires *m*/*z* 168.1150.

4.1.14. (*Z*,*E*)-4-(3,4-Dihydro-2*H*-6-pyranyl)-3-buten-1-ol, 10. The following coupling procedures were attempted: method A (using 0.5 g, 2.52 mmol vinyl iodide **8**) afforded **10** (127 mg, 33%); method B (using 0.75 g, 3.79 mmol of the iodide **8**) gave **10** (395 mg, 71%) whilst method C (same scale as in method B) afforded the diene **10** in 72% yield (*Z*:*E*=6:1); ν_{max} (film) 3357, 3020, 2930, 2875, 1656, 1612, 1466, 1435, 1414, 1352, 1310, 1234, 1163, 1087, 1060, 966, 934, 890, 865 and 784 cm^{-1}; δ_H (300 MHz, C_6D_6) *Z*-isomer 1.44 (2H, quintet, *J*=5.5 Hz, 3-H), 1.83 (2H, dt, *J*=6, 4 Hz, 4-H), 2.81 (2H, q, *J*=6.5 Hz, 2′-H), 3.6 (2H, t, *J*=6.5 Hz, 1′-H), 3.75 (2H, t, *J*=5 Hz, 2-H), 4.71 (1H, t, *J*=4 Hz, 5-H), 5.40 (1H, dt, *J*=12, 7 Hz, 3′-H), 5.82 (1H, d, *J*= 12 Hz, 4′-H); *E*-isomer 1.52 (2H, quintet, *J*=5.5 Hz, 3-H), 1.90 (2H, dt, *J*=6, 4 Hz, 4-H), 2.21 (2H, q, *J*=6.5 Hz, 2′-H), 3.45 (2H, t, *J*=6.5 Hz, 1′-H), 3.85 (2H, t, *J*=5 Hz, 2-H), 4.68 (1H, t, *J*=4 Hz, 5-H), 5.87 (1H, d, *J*=15.5 Hz, 4′-H), 6.22 (1H, dt, *J*=15.5, 7.5 Hz, 3′-H); δ_C (75 MHz; C_6D_6) *Z*-isomer 20.96 (C-3), 22.22 (C-4), 32.98 (C-2′), 62.58 (C-1′), 65.61 (C-2), 103.08 (C-5), 127.11, 127.19 (C-3′, C-4′), 153.00 (C-6); *E*-isomer 21.01 (C-3), 22.66 (C-4), 36.31 (C-2′), 62.08 (C-1′), 65.86 (C-2), 100.88 (C-5), 124.97 (C-3′), 128. 82 (C-4′), 153.0 (C-6); *m*/*z* (CI) 155 {[M+H]$^+$, 100%}. Found: *m*/*z* (CI) 154.0990. $C_9H_{14}O_2$ [M^+] requires *m*/*z* 154.0994.

4.1.15. (2*R,6*S**)-2-Methyl-1,7-dioxaspiro[5.5]undec-4-ene, 32**[22] To a solution of (*Z*,*E*)-4-(3,4-dihydro-2*H*-6-pyranyl)-3-buten-1-ol, **31** (261 mg, 1.55 mmol) in dichloromethane (5 mL) was added camphorsulfonic acid (30 mg) and the mixture stirred at room temperature for 1 h. After quenching with saturated sodium bicarbonate, the product was extracted into ether (2×20 mL), the ethereal extracts dried ($MgSO_4$), and evaporated and the residue purified by column chromatography (ethyl acetate/petrol 1:19) to afford the title compound **32** (172 mg, 66%) as a colourless oil; ν_{max} (film) 2940, 1658, 1397, 1270, 1201, 1186, 1101, 1072,1046, 1002, 953, 899 and 808 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.27 (3H, d, *J*=6.5 Hz, Me), 1.50–1.65 (5H, m, 9-H, 10-H, 11-H), 1.90–2.00 (3H, m, 3-H, 11′-H), 3.60 (1H, br d, *J*=10 Hz, 8eq-H), 3.85 (1H, dt, *J*=11.5, 2.5 Hz, 8ax-H), 4.01 (1H, ddq, *J*=10, 6, 4.5 Hz, CHMe), 5.61 (1H, ddd, *J*= 10, 2.5, 1 Hz, 5-H), 5.89 (1H, ddd, *J*=10, 5, 2.5 Hz, 4-H); δ_C (50 MHz, $CDCl_3$) 19.01 (C-10), 21.60 (C-Me), 25.59 (C-11), 32.79 (C-9), 35.39 (C-3), 61.18 (C-8), 63.54 (C-2), 94.49 (C-6), 128.31 (C-5), 130.79 (C-4); *m*/*z* (EI) 168 [M+, 79.2%]; (CI) 169 {[M+H]$^+$, 87.9%}. Found: *m*/*z* (CI) 168.1146. $C_{10}H_{16}O_2$ [M^+] requires *m*/*z* 168.1150.

4.1.16. (±)-1,7-Dioxaspiro[5.5]undec-4-ene, 12.[11] The title compound was prepared using the method above from the diene **10** (359 mg, 2.33 mmol) as a colourless oil (293 mg, 82%); ν_{max} (film) 3040, 2940, 2874, 1656, 1428, 1398, 1379, 1353, 1335, 1273, 1201, 1184, 1160, 1138, 1096, 1069, 1053, 1039, 953, 897, 868, 812, 769, 722 and 689 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.4–1.65 (5H, m, 10-H, 11-H, 9ax-H), 1.70–1.90 (2H, m, 9eq-H, 3eq-H), 2.23 (1H, dddt, *J*=18, 10, 5.5, 2.5 Hz, 3ax-H), 3.53–3.60 (1H, m, 8eq-H), 3.70 (1H, dd, *J*=11.5, 6.5 Hz, 2eq-H), 3.80 (1H, dt, *J*= 12, 3 Hz, 8ax-H), 3.87 (1H, dt, *J*=12, 3.5 Hz, 2ax-H), 5.64 (1H, ddd, *J*=10, 3, 1.5 Hz, 5-H), 5.87 (1H, dd, *J*=10, 5 Hz, 4-H); δ_C (75 MHz, $CDCl_3$) 18.53 (C-10), 24.71 (C-3), 24.98 (C-8), 34.79 (C-11), 57. 56 (C-2), 60.78 (C-8), 92.78 (C-6), 127.58 (C-5), 130.66 (C-4); *m*/*z* (CI) 155 {[M+H]$^+$,

100%}; (EI) 154 [M^+, 75.1%]. Found: (CI) *m/z* 154.1001. $C_9H_{14}O_2$ [M^+] requires *m/z* 154.0993.

4.1.17. (2*R,6*S**)-2-Methyl-1,7-dioxaspiro[5.5]undecane, 33.**[23] To a solution of (2*R**,6*S**)-2-methyl-1,7-dioxaspiro[5.5]undec-4-ene, **32** (228 mg, 1.34 mmol) in ethyl acetate (20 mL) was added 5% palladium on carbon (30 mg) and the mixture was hydrogenated at 1 atm for 6 h at room temperature. The catalyst was removed by filtration through celite®, the celite® pad washed with ethyl acetate (25 mL) and the combined organic extracts were concentrated in vacuo. The residue was purified by column chromatography (ethyl acetate/petrol 3:97) to afford the title compound **33** (171 mg, 74%) as a colourless oil; ν_{max} (film) 2939, 2870, 1449, 1384, 1349, 1282, 1257, 1231, 1214, 1182, 1138, 1095, 1065, 1048, 999, 965, 948, 926, 897, 845 and 804 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.15 (3H, d, $J=6$ Hz), 1.20–2.00 (12H, m), 3.50–3.80 (3H, m, 2-H, 8-H); δ_C (75 MHz, $CDCl_3$) 18.57, 18.89 (C-10, C-4), 21.79 (Me), 25.42 (C-9), 32.69 (C-3), 35.08, 35.83 (C-5, C-7), 60.23 (C-8), 65.10 (C-1), 95.54 (C-6); *m/z* (EI) 169 {[M−H]$^+$, 86.2%}. Found: *m/z* (CI) 169.1225. $C_{10}H_{17}O_2$ {[M−H]$^+$} requires *m/z* 169.1228.

4.1.18. (±)-1,7-Dioxaspiro[5.5]undecane, 13[13] The title compound was prepared using the method above from the spiroketal **12** (226 mg, 1.46 mmol) as a colourless oil (213 mg, 93%); ν_{max} (film) 2948, 2870, 1452, 1384, 1280, 1256, 1230, 1208, 1179, 1096, 1068, 991, 935, 913, 876 and 796 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.40–2.00 (12H, m), 3.60–3.80 (4H, m, 2-H, 8-H); δ_C (75 MHz) 18.54 (C-4, C-10), 25.33 (C-5, C-11), 35.76 (C-3, C-9), 60.37 (C-2, C-8), 95.01 (C-6); *m/z* (EI) 155 {[M−H]$^+$, 32.1%}. Found: *m/z* (CI) 155.1068. $C_9H_{15}O_2$ {[M−H]$^+$} requires *m/z* 155.1072.

4.1.19. (2*R,6*R**,11*S**)-2-Methyl-11-phenylselenyl-1,7-dioxaspiro[5.5]undec-4-ene, 34 and (2*R**,6*R**,11*R**)-2-methyl-11-phenylselenyl-1,7-dioxaspiro[5.5]undec-4-ene, 35.** To a solution of (4*Z*,*E*)-5-(3,4-dihydro-2*H*-6-pyranyl)-4-penten-1-ol, **31** (0.36 g, 2.14 mmol) in dichloromethane (5 mL) was added pyridine (0.2 mL, 6.4 mmol). The mixture was cooled to −78 °C, phenylselenyl chloride (0.45 g, 2.35 mmol) was added and the reaction was allowed to warm to room temperature and stir for 1 h. After quenching with ice cold aqueous sodium hydrogencarbonate, the product was extracted into dichloromethane (3× 30 mL), the combined extracts dried ($MgSO_4$), and evaporated and residue purified by column chromatography (ethyl acetate/petrol 3:97) to afford the title compounds **34** and **35** (458 mg, 66%) as an inseparable mixture (**34**:**35**= 7:11). The diastereoisomers equilibrated in $CDCl_3$ after 3 days at 20 °C to **35** as a single diastereoisomer. Mixture: ν_{max} (film) 3053, 2931, 2874, 1658, 1579, 1478, 1437, 1396,1342, 1282, 1231, 1188, 1133, 1101, 1064, 1023, 991, 949, 932, 893, 845, 742 and 709 cm^{-1}; δ_H (300 MHz, $CDCl_3$): Initially 1.30 (33/18H, d, $J=6.5$ Hz, Me), 1.32 (21/18H, d, $J=6.5$ Hz, Me), 1.50–1.80 (3H, m, 9-H, 3ax-H), 1.90–2.10 (2H, m, 10eq-H, 3eq-H), 2.28 (11/18H, qd, $J=$ 13, 4.5 Hz, 10ax-H), 2.50–2.65 (7/18H, m, 10ax-H), 3.16 (11/18H, dd, $J=13$, 4.5 Hz, 11-H), 3.40 (7/18H, t, $J=$ 4.5 Hz, 11-H), 3.62–3.76 (1H, m, 8eq-H), 3.87–4.00 (1H, m, 8ax-H), 4.06 (1H, sextet, $J=6.5$ Hz, 2-H), 5.71 (11/18H, dt, $J=10$, 2 Hz, 5-H), 5.98–6.12 (1H, m, 4-H), 6.36 (7/18H, dt, $J=10$, 2 Hz, 5-H), 7.25–7.62 (5H, m, Ar); Equilibrated (essentially **35**) δ_H 1.30 (3H, d, $J=6.5$ Hz, Me), 1.50–1.80 (3H, m, 9-H, 3ax-H), 1.95–2.10 (2H, 10eq-H, 3eq-H), 2.28 (1H, qd, $J=13$, 4.5 Hz, 10ax-H), 3.16 (1H, dd, $J=13$, 4.5 Hz, 11-H), 3.62–3.76 (1H, m, 8eq-H), 3.87–3.90 (1H, dt, $J=11$, 3 Hz, 8ax-H), 4.04 (1H, sextet, $J=6.5$ Hz, 2-H), 5.71 (1H, dt, $J=10$, 2 Hz, 5-H), 6.05 (1H, dt, $J=9.5$, 4 Hz, 4-H), 7.20–7.65 (5H, m, Ar); δ_C (75 MHz; $CDCl_3$): Initially 21.01, 22.48, 26.63, 27.40, 28.34, 32.09, 31.14, 49.63, 50.21, 60.16, 61.03, 63.84, 64.31, 95.90, 96.09, 126.85, 126.98, 127.17, 128.07, 128.89, 128.96, 129.13, 129.13, 129.32, 130.23, 130.93, 133.38, 134.30; Equilibrated 21.01 (Me), 27.40 (C-9), 28.34 (C-3), 32.09 (C-7), 49.63 (C-11), 60.16 (C-8), 63.84 (C-2), 96.10 (C-6), 127.17, 127.74, 128.88, 129.19 (Ar), 129.13, 129.32 (C-4, C-5), 131.57, 134.30, 134.37 (Ar); *m/z* (EI) 324 [M^+, ^{80}Se 47.5%]; (CI) 325 {[M+H]$^+$, ^{80}Se 38.3%}. Found: *m/z* 324.0616. $C_{16}H_{20}O_2{}^{80}Se$ [M^+] requires *m/z* 324.0628.

4.1.20. (6*S,11*S**)-11-Phenylselenyl-1,7-dioxaspiro[5.5]undec-4-ene, 14.** The title compound was prepared from the diene **10** (382 mg, 2.48 mmol) using the method above and isolated, after flash chromatography, as essentially a single diastereoisomer (559 mg, 73%); ν_{max} (film) 3042, 2935, 2876, 1658, 1599, 1477, 1437, 1395, 1377, 1344, 1316, 1283, 1229, 1209, 1177, 1145, 1070, 1036, 993, 949, 929, 888, 853, 772, 743, 713, 693 and 671 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.55–1.80 (2H, m, 9-H), 1.90–2.10 (2H, m, 3eq-H, 10eq-H), 2.23 (1H, dq, $J=13$, 4.5 Hz, 10ax-H), 2.41 (1H, dddt, $J=18$, 9, 5.5, 2.5 Hz, 3ax-H), 3.21 (1H, dd, $J=12.5$, 4.5 Hz, 11-H), 3.67 (1H, br dd, $J=11$, 5 Hz, 8eq-H), 3.80–4.03 (3H, m, 2-H, 8ax-H), 5.74 (1H, ddd, $J=10$, 3, 1 Hz, 5-H), 6.12 (1H, dd, $J=10$, 5.5 Hz, 4-H), 7.24–7.62 (10H, m, Ar); δ_C (75 MHz, $CDCl_3$) 24.52 (C-3), 27.29 (C-9), 28.83 (C-10), 49.45 (C-11), 58.12 (C-4), 60.32 (C-8), 94.92 (C-6), 127.28, 128.93 (Ar), 129.12 (C-5), 129.60 (C-6), 129.95, 133.45, 134.33, 134.40 (Ar); *m/z* (CI) 311 {[M^+H], 100%]}. Found: *m/z* 310.0473. $C_{15}H_{18}O_2{}^{80}Se$ [M^+] requires *m/z* 310.0472.

4.1.21. (2*R,6*S**)-2-Methyl-1,7-dioxaspiro[5.5]undec-4,10-diene, 36.** The diastereomeric mixture of the selenides **34** and **35** (0.39 g, 1.22 mmol) was dissolved in chloroform (5 mL) to which was added pyridine (0.5 mL, 6.02 mmol) and 2-benzenesulfonyl-3-phenyloxaziridine[15] (413 mg, 1.58 mmol) and the reaction mixture brought to a gentle reflux 15 h. The solvent was removed in vacuo and the residue chromatographed (2:3 dichloromethane/petrol) to afford the title compound **35** (147 mg, 73%) as a yellow oil; ν_{max} (film) 3041, 2974, 2931, 2895, 2828, 1656, 1462, 1446, 1425, 1398, 1386, 1367, 1339, 1270, 1214, 1201, 1183, 1135, 1100, 1076, 1048, 1021, 980, 928, 903, 874, 851, 819, 769, 730 and 701 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.25 (3H, d, $J=6.5$ Hz, Me), 1.80–2.00 (3H, m, 3-H, 9eq-H), 2.29 (1H, dddt, $J=18$, 9, 6, 3 Hz, 9ax-H), 3.76 (1H, dd, $J=12$, 6 Hz, 8eq-H), 4.02 (1H, dt, $J=12$, 3.5 Hz, 8ax-H), 4.00–4.15 (1H, m, 2-H), 5.59 (2H, br d, $J=10$ Hz, 5-H, 11-H), 5.99 (2H, m, 4-H, 10-H); δ_C (75 MHz, $CDCl_3$) 21.29 (Me), 24.53 (C-9), 31.95 (C-3), 58.25 (C-2), 64.01 (C-8), 92.07 (C-6), 128.27, 128.35, 128.54, 129.11 (C-4, C-5, C-10, C-11); *m/z* (CI) 167 {[M+H]$^+$, 72.2%}. Found: *m/z* 166.0993. $C_{10}H_{14}O_2$ [M^+] requires *m/z* 166.0994.

4.1.22. (±)-1,7-Dioxaspiro[5.5]undec-4,10-diene, 15.[16] The title compound was prepared from the selenide **14** (532 mg, 1.71 mmol) using the method described above. Flash chromatography (1:1 dichloromethane/petrol) afforded the title compound as a yellow oil (161 mg, 62%); ν_{max} (film) 3041, 2965, 2933, 2878, 2830, 1654, 1463, 1426, 1395, 1368, 1335, 1271, 1201, 1185, 1157, 1119, 1075, 1023, 901, 862, 778, 735 and 705 cm^{-1}; δ_H (300 MHz, C_6D_6) 1.50 (2H, ddd, J=18, 5, 3 Hz, 9eq-H, 3eq-H), 2.10 (2H, dddt, J=18, 12, 6, 2 Hz, 3ax-H, 9ax-H), 3.67 (2H, dd, J=10, 6 Hz, 2eq-H, 8eq-H), 4.07 (2H, dt, J=11, 3.5 Hz, 2ax-H, 8ax-H), 5.75 (2H, dd, J=10, 3 Hz, 5-H, 11-H), 5.82 (2H, dd, J=10, 5 Hz, 4-H, 10-H); δ_C (75 MHz, C_6D_6) 24.81 (C-3, C-9), 58.33 (C-2, C-8), 91.36 (C-6), 127.82 (C-4, C-10), 130.08 (C-5, C-11); m/z (EI) 152 [M^+, 35.5%]. Found: m/z 152.0834. $C_9H_{12}O_2$ [M^+] requires m/z 152.0837.

4.1.23. (*Z*,*E*)-4-[(2*R)-2-(*t*-Butyldiphenylsilyloxymethyl)-3,4-dihydro-2*H*-6-pyranyl]-3-buten-1-ol, 19.** *Method A*. A solution of *t*-butyllithium (20.6 mL, 1.7 M solution in pentane) was added dropwise to a stirred solution of 2-(*t*-butyldiphenylsilyloxymethyl)-3,4-dihydro-2*H*-pyran **16** (5.61 g, 15.94 mmol) in THF (8 mL) at −78 °C. The mixture was allowed to warm up to 0 °C and was stirred at this temperature for 2 h, then recooled to −78 °C (excess *t*-butyllithium was destroyed by adding more THF [30 mL]). Zinc chloride (1 M solution in ether, 16.9 mL) was added dropwise and the resulting mixture was allowed to warm up to room temperature and to stir for 2 h. In a separate flask, Dibal-H (1 M solution in toluene, 0.4 mL) was added dropwise to $PdCl_2(PPh_3)_2$ (133 mg, 0.19 mmol, 5 mol%) in THF (5 mL) at 0 °C and the resulting mixture was stirred for 30 min. The solution containing the Pd(0) catalyst was then added to the vinyl zinc at 5–10 °C, followed by a solution of (*Z*,*E*)-4-hydroxy-1-iodobut-1-ene **8** (0.69 g, 3.48 mmol) in THF (2 mL) and resulting mixture was stirred for 1 h at 0 °C. After quenching with sodium hydroxide (10 mL), the product was extracted into ether (3×30 mL), the ethereal extracts dried ($MgSO_4$), concentrated in vacuo. The residue was chromatographed (3:1:16 ethyl acetate/triethylamine/petrol) to afford the title compound **19** (1.08 g, 72%; mobile oil) as an inseparable mixture of geometrical isomers (*Z*:*E*=8:1)

Method B. The title compound **19** was prepared from (*Z*,*E*)-4-hydroxy-1-iodobut-1-ene **8** (0.75 g, 3.79 mmol) in exactly the same way as method A except that freshly prepared $Pd(PPh_3)_4$ (213 mg, 5 mol%) was used as the catalyst. Work-up and chromatography (3:1:16 ethyl acetate/triethylamine/petrol) afforded the title compound (1.06 g, 70%, colourless oil), as a mixture of geometrical isomers (*Z*:*E*=8:1); ν_{max} (film) 3385, 2930, 2857, 1655, 1613, 1590, 1472, 1428, 1112, 1068, 1006, 824, 789, 741 and 703 cm^{-1}; δ_H (300 MHz, C_6D_6) *Z*-isomer: 1.25 (9H, s, ^{t}BuSi), 1.49–1.58 (2H, m, 3-H), 1.85–1.95 (2H, m, 4-H), 2.90 (2H, q, J=7 Hz, 3′-H), 3.66 (2H, t, J=6 Hz, 1′-H), 3.77 (1H, dd, J=10, 4.5 Hz, CH_2OSi), 3.80–3.90 (1H, m, CH_2OSi), 3.88–4.00 (1H, m, 2-H), 4.72 (1H, t, J=4 Hz, 5-H), 5.50 (1H, dt, J=12, 8 Hz, 2′-H), 5.85 (1H, d, J=12 Hz, 1′-H), 7.30–8.00 (10H, m, Ar); *E*-isomer: 1.27 (9H, s, ^{t}BuSi), 1.40–1.6 (2H, m, 3-H), 1.61–1.81 (2H, m, 4-H), 2.30 (2H, q, J=7 Hz, 2′-H), 3.50–3.58 (2H, m, 1′-H), 3.77 (1H, dd, J=10, 4.5 Hz, CH_2OSi), 3.80–3.90 (1H, m, CH_2OSi), 3.90–4.00 (1H, m, 2-H), 4.68 (1H, t, J=4 Hz, 5-H), 5.91 (1H, d, J=15.5 Hz, 4′-H), 6.25 (1H, dt, J=15.5, 7.5 Hz, 3′-H), 7.30–8.00 (10H, m, Ar); δ_C (75 MHz, C_6D_6) *Z*-isomer: 19.45 or 19.51 (CMe_3), 20.75 (C-4), 23.84 (C-3), 26.95 or 27.03 (CMe_3), 33.13 (C-2′), 62.54 (C-1′), 66.69 (CH_2OSi), 76.12 (C-2), 102.64 (C-5), 126.76 (C-3′), 127.80 (C-4′), 128.06, 128.09, 130.01, 133.83, 135.97, 136.01 (Ar), 152.63 (C-6); *E*-isomer: 19.45 or 19.51 (CMe_3), 20.75 (C-4), 24.34 (C-3), 26.95 or 27.03 (CMe_3), 36.44 (C-2′), 62.05 (C-1′), 66.69 (CH_2OSi), 75.97, (C-6), 100.97 (C-5), 125.18 (C-3′), 126.76 (C-4′), 128.06, 128.09, 130.01, 133.83, 135.97, 136.01 (Ar), 151.14 (C-6); m/z (CI) 345 {[M^+−Ph], 100%}. Found: m/z (CI) 423.2358. $C_{26}H_{35}O_3^{28}Si$ {[M+H]$^+$} requires m/z 423.2355.

4.1.24. (2*R,6*S**)-2-(*t*-Butyldiphenylsilyloxymethyl)-1,7-dioxa-spiro[5.5]undec-10-ene, 20.** The title compound was prepared from the diene **19** (0.908 g, 2.15 mmol) using the method described above for **32**. Isolated as a colourless, viscous oil after flash chromatography (1:99 ethyl acetate/petrol); yield 0.53 g, (58%); ν_{max} (film) 3071, 3046, 2933, 2858, 1657, 1590, 1473, 1428, 1361, 1273, 1206, 113, 1079, 1029, 998, 958, 919, 904, 889, 862, 824, 805, 739 and 704 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.13 (9H, s, ^{t}BuSi), 1.28 (1H, dq, J=12, 3.5 Hz, 3ax-H), 1.58 (1H, dt, J=13, 5 Hz, 5eq-H), 1.65–2.05 (4H, m, 4-H, 9eq-H, 3eq-H, 5ax-H), 2.35 (1H, dddt, J=18, 9, 5.5, 2.5 Hz, 9ax-H), 3.62 (1H, dd, J=10, 6 Hz, CH_2OSi), 3.70–3.85 (2H, m, CH_2OSi, 8eq-H), 3.90–4.05 (2H, m, 8ax-H, 2ax-H), 5.67 (1H, br d, J=10 Hz, 11-H), 5.99 (1H, br dt, J=10, 5 Hz, 10-H), 7.30–7.80 (10H, m, Ar); δ_C (75 MHz, $CDCl_3$) 18.54 (C-4), 19.33 (CMe_3), 24.80 (C-9), 26.82 (CMe_3), 27.13 (C-3), 34.67 (C-5), 57.58 (C-8), 67.72 (CH_2OSi), 70.57 (C-2), 93.43 (C-6), 127.58 (Ar), 129.54 (C-10), 130.89 (Ar), 133.93 (C-11), 135.67, 135.75 (Ar); m/z (CI) 423 {[M+H]$^+$, 67%} (EI) 365 {[M−^{t}Bu]$^+$, 58.6%}. Found: (CI) m/z 423.2339 {[M+H]$^+$}. $C_{26}H_{35}O_3Si$ requires m/z 423.2355.

4.1.25. (2*R,6*R**)-2-(*t*-Butyldiphenylsilyloxymethyl)-1,7-dioxaspiro[5.5]undecane, 21.** The title compound **21** was prepared from the spiroketal **20** (369 mg, 0.87 mmol) using the method above. Isolated after flash chromatography (1:99 ethyl acetate/petrol) as a colourless, viscous oil (345 mg, 94%); ν_{max} (film) 2937, 2858, 1428, 1386, 1280, 1229, 1211, 1112, 1086, 994, 951, 932, 875, 824, 800, 739 and 702 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.13 (9H, s, ^{t}BuSi), 1.20–1.70 (10H, m, 3-H, 4-H, 5-H, 9-H, 10-H, 11-H), 1.83–2.10 (2H, m, 9-H, 10-H), 3.64 (1H, dd, J=10, 5 Hz, CH_2OSi), 3.58–3.67 (1H, m, 8-H), 3.75 (1H, dd, J=10, 6 Hz, CH_2OSi), 3.80–3.90 (2H, m, 2-H, 8-H) 7.4–7.85 (10H, m, Ar); δ_C (75 MHz, $CDCl_3$) 18.55 (C-4, C-10), 19.27 (CMe_3), 25.39 (C-3), 26.61 (CMe_3), 27.18 (C-9), 35.45, 35.78, (C-5, C-11), 60.25 (CH_2OSi), 67.55 (C-8), 70.15 (C-2), 95.50 (C-6), 127.60, 129.52, 129.55, 133.96, 135.69, 135.73, (Ar); m/z (CI) 442 [[M+NH_4]$^+$,100%]. Found: m/z 425.2516. $C_{26}H_{37}O_3^{28}Si$ {[M+H]$^+$} requires m/z 425.2512.

4.1.26. (2*R,6*R**)-2-(Hydroxymethyl)-1,7-dioxa-spiro[5.5]-undecane, 22.**[18] To a solution of the TBDPS-protected alcohol **21** (275 mg, 0.65 mmol) under nitrogen in THF (10 mL) at ambient temperature was added TBAF (1 M in THF, 1.3 mL) and the resulting pale green solution

was stirred at this temperature for 16 h. Ether (30 mL) was added and the organic solution was washed with saturated aqueous ammonium chloride (2×15 mL) and brine (1× 15 mL), then dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (2:3 ethyl acetate/petrol) of the residue afforded the title compound **22** (105 mg, 87%) as a colourless, viscous oil; ν_{max} (film) 3425, 2941, 2871, 1440, 1384, 1281, 1228, 1210, 1182, 1094, 1077, 1049, 1022, 992, 951, 928, 894, 875 and 808 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.20–1.70 (10H, m, 3-H, 4-H, 5-H, 9-H, 10-H, 11-H), 1.78–2.00 (2H, m, 9-H, 10-H), 2.10 (1H, br s, OH), 3.54 (1H, dd, $J=11$, 7 Hz, CH_2OH), 3.65 (1H, dt, $J=11$, 3 Hz, 8ax-H), 3.60–3.70 (2H, m, CH_2OH and 8eq-H), 3.73–3.83 (1H, m, 2-H); δ_C (75 MHz, $CDCl_3$) 18.18, 18.61 (C-4, C-10), 25.21 (C-3), 26.46 (C-9), 35.42, 35.59 (C-5, C-11), 60.43 (CH_2OH), 66.31 (C-8), 69.67 (C-2), 95.51 (C-6); *m/z* (CI) 187 [$[M+H]^+$, 100%]. Found: *m/z* 186.1252. $C_{10}H_{18}O_3$ [M^+] requires *m/z* 186.1256.

4.1.27. (2*R,5*S**,6*R**)-2-(*t*-Butyldiphenylsilyloxymethyl)-5-phenylselenyl-1,7-dioxaspiro[5.5]-undec-10-ene, 23 and (2*R**,5*R**,6*R**)-2-(*t*-butyldiphenylsilyloxymethyl)-5-phenylselenyl-1,7-dioxaspiro[5.5]undec-10-ene, 24.** The title compounds were prepared from the diene **19** (0.94 g, 2.23 mmol) using the standard cyclisation procedure. Isolated as a 2:1 (**23**:**24**) mixture of diastereoisomers (0.74 g, 57%) after flash chromatography (1:99 ethyl acetate/petrol); ν_{max} (film) 3071, 3049, 2997, 2931, 2857, 1657, 1579, 1475, 1428, 1392, 1361, 1339, 1300, 1271, 1235, 1210, 1189, 1113, 1079, 999, 909, 824, 739 and 705 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.18 (6H, s, ^{t}BuSi, eq. isomer, **23**), 1.21 (3H, s, ^{t}BuSi, ax. isomer, **24**), 1.70–1.80 (2/3H, m), 1.80–2.04 (2H, m), 2.04–2.22 (1H, m), 2.22–2.60 (2H, m), 2.62–2.78 (1/3H, m), 3.24 (2/3H, dd, $J=12.5$, 4.5 Hz, 5-H), 3.46 (1/3H, br s, 5-H), 3.60–4.20 (5H, m, 2-H, 8-H, CH_2OSi), 5.80 (2/3H, d, $J=10$ Hz, 11-H), 6.02–6.10 (1/3H, m, 10-H), 6.12–6.20 (2/3H, m, 10-H), 6.49 (1/3H, d, $J=10$ Hz, 11-H), 7.25–7.85 (15H, m, Ar); δ_C (75 MHz, $CDCl_3$) Equatorial isomer, **23**: 19.37 (CMe_3), 24.62 (C-3), 26.97 (CMe_3), 28.37 (C-9), 29.65 (C-10), 49.37 (C-11), 58.09 (C-2), 67.33 (CH_2OSi), 70.27 (C-8), 95.39 (C-6), 127.80 (Ar), 128.92 (C-4), 129.01, 129.11, 129.66 (Ar), 129.84 (C-6), 133.17, 134.51, 135.81 (Ar); Axial isomer, **24**: 19.41 (CMe_3), 23.73 (C-9), 26.16 (C-9), 26.89 (C-4), 26.97 (CMe_3), 50.16 (C-5), 58.44 (C-8), 67.48 (CH_2OSi), 70.53 (C-2), 95.02 (C-6), 127.80 (Ar), 128.59 (C-10), 129.01, 129.11, 129.66 (Ar), 129.92 (C-11), 133.92, 133.17, 134.51, 135.81 (Ar); *m/z* FAB 579 {$[M+H]^+$, 4.2%}. Found: *m/z* 579.1856. $C_{32}H_{39}O_3^{80}Se^{28}Si$ {$[M+H]^+$} requires 579.1834.

4.1.28. (2*R,6*R**)-2-(*t*-Butyldiphenylsilyloxymethyl)-1,7-dioxaspiro[5.5]undec-4,10-diene, 25.** The title compound was prepared from the diastereomeric mixture of selenides **23** and **24** (503 mg, 0.87 mmol). Isolated as a single isomer, a pale yellow oil, (265 mg, 73%) after flash chromatography (1:99 ethyl acetate/petrol); ν_{max} (film) 3044, 2930, 2857, 1657, 1473, 1428, 1389, 1201, 1113, 1077, 1020, 908, 824, 796, 740 and 702 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.10 (9H, s, ^{t}BuSi), 1.90 (1H, dt, $J=18$, 4.5 Hz, 9eq-H), 2.00–2.10 (2H, m, 3-H), 2.35 (1H, dddt, $J=18$, 9, 5.5, 3 Hz, 9ax-H), 3.70 (1H, dd, $J=10$, 5.5 Hz, CH_2OSi), 3.80 (1H, dd, $J=11$, 6 Hz, 8eq-H), 3.87 (1H, dd, $J=10$, 5 Hz, CH_2OSi), 4.10 (1H, dt, $J=12$, 3.5 Hz, 8ax-H), 4.20 (1H, dq, $J=10$, 5 Hz, 2-H), 5.60–5.70 (2H, m, 5-H, 11-H), 6.12–6.22 (2H, m, 4-H, 10-H), 7.30–7.80 (10H, m, Ar); δ_C (75 MHz, $CDCl_3$) 19.03 (CMe_3), 24.53 (C-9), 26.64 (CMe_3), 27.08 (C-3), 58.32 (C-8), 66.90 (CH_2OSi), 68.66 (C-2), 91.89 (C-6), 127.61, 127.72, 127.80 (Ar), 127.88, 128.15 (C-4, C-10), 128.24, 128.71 (C-5, C-11), 129.57, 129.60, 133.72, 135.50, 135.62, 135.69, 135.76; *m/z* (EI) 362 [$M+-{}^t$Bu, 61%] (CI) 421 [[M+H]+, 100%]. Found: (CI) *m/z* 421.2185. $C_{26}H_{33}O_3^{28}Si$ {$[M+H]^+$} requires *m/z* 421.2200.

4.1.29. Ethyl (2*R,3*R**)-3-(*t*-butyldimethylsilyloxy)-2-methylbutanoate, 39.**[30] To a solution of ethyl (2*R**,3*R**)-3-hydroxy-2-methylbutanoate **38** (9.95 g, 68.1 mmol) in dichloromethane (10 mL) was added 1,8-diazobicyclo-[5,4,0]undec-7-ene (10.2 mL, 65.6 mmol) at 0 °C followed by *t*-butyldimethylsilyl chloride (9.89 g, 65.6 mmol) in dichloromethane (10 mL). After 3 h at room temperature the mixture was poured into water (100 mL), extracted into ether (100 mL) and washed with water (50 mL), hydrochloric acid (0.1 M, 50 mL), water (50 mL), saturated sodium bicarbonate (50 mL) and water (50 mL). The organic layer was dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by flash column chromatography (1:19 ethyl acetate petrol) to afford the title compound **39** (14.02 g, 87%) as a colourless oil; ν_{max} (film) 2958, 2931, 2858, 1737, 1474, 1376, 1320, 1256, 1185, 1113, 1068, 1039, 982, 953, 839, 811 and 776 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.06 (3H, s, CH_3Si), 0.09 (3H, s, CH_3Si), 0.90 (9H, s, CH_3CSi), 1.11 (3H, d, $J=7$ Hz, C2–Me), 1.16 (3H, d, $J=6$ Hz, H-4), 1.25 (3H, t, $J=7$ Hz, OCH_2CH_3), 2.51 (1H, quintet $J=7$ Hz, H-2), 3.95–4.15 (1H, m, H-3), 4.13 (2H, q, $J=7$ Hz, OCH_2); δ_C (75 MHz) −5.12, −4.32, 12.68, 14.19, 17.92, 20.24, 25.72, 48.15, 60.12, 70.15, 175.15; *m/z* (CI) 261 [$M+H]^+$, 100%], 203 [$M^+-{}^t$Bu, 20%]. Found: (CI) *m/z* 261.1884. $C_{13}H_{29}O_3^{28}Si$ {$[M+H]^+$} requires *m/z* 261.1886.

4.1.30. (1*ZE*,3*S,4*R**)-4-(*t*-Butyldimethylsilyloxy)-1-iodo-3-methylpentene, 41.** Dibal-H (1 M in toluene, 15.7 mL, 15.7 mmol) was added dropwise to a cooled (−78 °C) and stirred solution of ethyl (2*R**,3*R**)-3-(*t*-butyldimethylsilyloxy)-2-methylbutanoate **39** (2.42 g, 9.83 mmol) in anhydrous toluene (100 mL). After being stirred at −80 °C for 1 h the reaction was quenched by dropwise addition of methanol (10 mL) keeping the temperature below −78 °C. Citric acid (10% aqueous solution, 80 mL) was then added, the mixture was allowed to warm to room temperature, the organic phase was decanted and the aqueous layer was extracted with dichloromethane (3×100 mL). The combined organic phases were dried ($MgSO_4$), the solvent was removed under vacuum. The crude aldehyde **40**[30] {δ_H (300 MHz, $CDCl_3$): 0.04 (3H, s, CH_3Si), 0.05 (3H, s, CH_3Si), 0.90 (9H, s, CH_3CSi); 1.10 (3H, d, $J=7.5$ Hz, C2–Me), 1.25 (3H, d, $J=6$ Hz, 4-H), 2.30–2.40 (1H, m, H-2); 4.05 (1H, quintet, $J=6$ Hz, H-3), 9.85 (1H, d, $J=2.5$ Hz, H-1)} was used immediately in the next reaction.

To a suspension of iodomethyltriphenylphosphonium iodide (6.51 g, 12.3 mmol) in THF (27 mL) at room temperature was slowly added sodium hexamethyldisilazide (1 M solution in THF, 11.3 mL). After stirring for 10 min, the

dark-coloured solution of the yield was cooled to −78 °C and crude (2*R**,3*R**)-3-(*t*-butyldimethylsilyloxy)-2-methylbutanal **40** in THF (10 mL) was added slowly. The mixture was allowed to warm to room temperature and after 30 min, the solvent was removed in vacuo. The residue was washed with 3×(50 mL 50:1 petrol/diethyl ether) and the supernatant filtered through celite® to remove triphenylphosphine oxide. The combined eluents were concentrated in vacuo and the residue purified by flash column chromatography (dichloromethane /hexane 1:19) to afford the title compound **41** as a light sensitive, colourless, oil[38] (1.38 g, 41% overall yield from **39**; *E*:*Z*=6:1). *Z*-isomer; ν_{max} (film) 2957, 2927, 2885, 2857, 1608, 1472, 1462, 1375, 1259, 1152, 1086, 1064, 1027, 1007, 956, 850, 837, 802, 775, 745, 699 and 665 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.10 (3H, s, CH_3Si), 0.11 (3H, s, CH_3Si), 0.93 (9H, s, CH_3CSi), 1.05 (3H, d, *J*=7 Hz, C3–Me), 1.12 (3H, d, *J*=6.5 Hz, 5-H), 2.50–2.56 (1H, m, 3-H), 3.80–3.88 (1H, m, 4-H), 6.15 (1H, dd, *J*=9, 7.5 Hz, 2-H), 6.25 (1H, d, *J*=7 Hz, 1-H); δ_C (75 MHz; $CDCl_3$): −4.75, −4.23, 15.76, 18.07, 21.45, 25.87, 49.65, 70.87, 81.90, 143.41; *m*/*z* (CI) 341 [[M+H]$^+$,34%]. Found: *m*/*z* (CI) 341.0804. $C_{12}H_{25}IO^{28}Si$ {[M+H]$^+$} requires *m*/*z* 341.0798. *E*-isomer ν_{max} (film) 2957, 2929, 2885, 2857, 1603, 1552, 1472, 1462, 1374, 1361, 1253, 1188, 1157, 1128, 1102, 1064, 1029, 1007, 988, 956, 837, 806, 775 and 663 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.10 (6H, s, CH_3Si), 0.95 (9H, s, CH_3CSi), 1.02 (3H, d, *J*=6.5 Hz, C3–Me), 1.11 (3H, d, *J*=6 Hz, 5-H), 2.15–2.25 (1H, m, 3-H), 3.65–3.72 (1H, m, 4-H), 6.02 (1H, dd, *J*=14.5, 0.5 Hz, H-1), 6.52 (1H, dd, *J*=14.5, 8.5 Hz, H-2); δ_C (75 MHz, $CDCl_3$): −4.78, −4.35, 15.69, 18.07, 21.24, 25.86, 48.37, 71.23, 74.73, 149.04; *m*/*z* (CI) 341 {[M+H]$^+$, 36%}. Found: *m*/*z* (CI) 341.0807. $C_{12}H_{25}IO^{28}Si$ {[M+H]$^+$} requires *m*/*z* 341.0798.

4.1.31. (2*R,3*S**,4*Z*)-5-Iodo-3-methyl-4-penten-2-ol, 42.** To a solution of (1*ZE*,3*S**,4*R**)-4-(*t*-butyldimethyl-silyloxy)-3-methyl-1-iodopentene **41** (1.29 g, 3.79 mmol) in acetonitrile (67 mL) was added 60% aqueous hydrogen fluoride (2.25 mL). The mixture was stirred for 10 min at ambient temperature after which time the reaction mixture was diluted with water (50 mL) and extracted with chloroform (2×50 mL). The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo and the residue purified by flash column chromatography (1:4 ethyl acetate petrol) to afford the title compound **42** (0.66 g, 77%) as a light sensitive, colourless, oil[38]; ν_{max} (film) 3376, 3064, 2969, 2929, 1609, 1452, 1376, 1352, 1262, 1200, 1152, 1112, 1085, 1045, 1015, 995, 929, 886, 797 and 702 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 1.08 (3H, d, *J*=7 Hz, 3′-H), 1.24 (3H, d, *J*=6.5 Hz, 1-H), 2.42–2.56 (1H, m, 3-H), 3.81 (1H, quintet, *J*=6 Hz, 2-H), 6.15 (1H, dd, *J*=9, 7 Hz, 4-H), 6.36 (1H, d, *J*=7.5 Hz, 5-H); δ_C (75 MHz, $CDCl_3$): 15.65, 20.85, 46.70, 70.90, 83.35, 142.86. *m*/*z* (CI) 244 [[M+NH_4]$^+$, 100%]. Found: *m*/*z* (CI) 244.0204. $C_6H_{15}INO$ {[M+NH_4]$^+$} requires *m*/*z* 244.0198.

4.1.32. (2*R,3*S**,4*Z*)-5′-(3′,4′-Dihydro-2*H*-6-pyranyl))-3-methyl-4-penten-2-ol, 43.** A solution of *t*-butyllithium (5.8 mL, 1.7 M solution in pentane) was added dropwise to a stirred solution of 2,3-dihydro-2*H*-pyran (0.8 mL, 9.36 mmol) in THF (5 mL) at −78 °C. The mixture was allowed to warm up to 0 °C and was stirred at this temperature for 30 min, then re-cooled to −78 °C. Zinc chloride (1 M solution in ether, 9.8 mL) was added dropwise and the resulting mixture was allowed to warm up to room temperature and to stir for 2 h, generating a stock solution of the zinc reagent **11**. A solution of (2*R**,3*S**,4*Z*)-5-iodo-3-methyl-4-penten-2-ol **42** (500 mg, 1.17 mmol) and $Pd(PPh_3)_4$ (127 mg, 5 mol%) in THF (5 mL) was added to the vinylzinc **11** at 5–10 °C, and resulting mixture was stirred for 1 h. After quenching with sodium hydroxide (10 mL), the product was extracted with ether (3×30 mL), the ethereal extracts dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by flash column chromatography (3:1:16 ethyl acetate/triethylamine/petrol) to afford the title compound **43** as a colourless oil (290 mg, 72%); ν_{max} (film) 3412, 2969, 2930, 2874, 1723, 1656, 1610, 1450, 1394, 1375, 1353, 1311, 1274, 1234, 1153, 1086, 1060, 999, 972, 936, 893, 862 and 787 cm^{-1}; δ_H (200 MHz, C_6D_6) 1.03 (3H, d, *J*=6 Hz, C-3′Me), 1.18 (3H, d, *J*=6 Hz, H-1′), 1.35 (2H, apparent quintet, *J*=6 Hz, 3-H), 1.76–1.90 (2H, m, 4-H), 3.30–3.50 (1H, m, 3′-H), 3.45–3.55 (1H, m, 2′-H), 3.68 (2H, t, *J*=6 Hz, 2-H), 4.66 (1H, t, *J*=4 Hz, 5-H), 5.15–5.30 (1H, m, 4′-H), 5.75 (1H, d, *J*=12 Hz, 5′-H); *m*/*z* (CI) 183 [[M+H]$^+$, 100%]. Found *m*/*z* (CI) 182.1301. $C_{11}H_{18}O_2$ [M$^+$] requires *m*/*z* 182.1307.

4.1.33. (2*R,3*S**,6*S**)-2,3-Dimethyl-1,7-dioxaspiro[5.5]undec-4-ene, 44.** To a solution of (2*R**,3*S**,4*Z*)-5-(3,4-dihydro-2*H*-6-pyranyl))-3-methyl-4-penten-2-ol **43** (247 mg, 1.35 mmol) in dichloromethane (5 mL) was added camphorsulfonic acid (30 mg) and the mixture stirred at room temperature for 1 h. After quenching with saturated sodium bicarbonate (15 mL), the reaction mixture was extracted with ether (2×20 mL), the ethereal extracts dried ($MgSO_4$), and evaporated and the residue purified by flash column chromatography (ethyl acetate/petrol 1:19) to afford the title compound **44** (105 mg, 42%) as a colourless oil; ν_{max} (film) 3034, 2939, 2872, 1657, 1450, 1398, 1378, 1269, 1225, 1204, 1186, 1169, 1106, 1091, 1074, 1055, 1002, 954, 923, 896, 813 and 723 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.92 (3H, d, *J*=6 Hz, Me) 1.23 (3H, d, *J*=6.5 Hz, Me), 1.45–1.65 (5H, m, 10-H, 11-H, 9ax-H), 1.80–2.00 (2H, m, 3-H, 9eq-H), 3.50–3.61 (2H, m, 8eq-H, 2-H), 3.80 (1H, dt, *J*=11, 3 Hz, 8ax-H), 5.54 (1H, dd, *J*=10, 2 Hz, 5-H) 5.64 (1H, dd, *J*=10, 1.5 Hz, 4-H); δ_C (75 MHz, $CDCl_3$) 16.73, 18.52, 19.14, 25.13, 34.88, 36.22, 60.75, 69.46, 93.59, 129.39, 134.42; *m*/*z* (CI) 182 [M$^+$, 100%]. Found: *m*/*z* (CI) 183.1386. $C_{11}H_{19}O_2$ {[M+H]$^+$} requires *m*/*z* 183.1386.

4.1.34. (2*R,3*S**,4*Z*)-3,7-Dimethyl-4-octen-2-ol, 45.** Dibal-H (2.5 mL of a 1 M solution in toluene) was added to the vinyl iodide **42** (570 mg, 2.5 mmol) at −78 °C and then allowed to warm up to room temperature. This solution was then added, via cannula, to a mixture of the zinc reagent **11** (2.5 mmol) and $Pd(PPh_3)_4$ (5 mol%) in THF. After 1 h at 5 °C work-up and chromatography as above afforded the title compound **45** as a colourless oil (75 mg, 19%); ν_{max} (film) 3363, 2958, 2871, 1465, 1368, 1164, 1091, 1044, 1014, 924, 877, 831 and 792 cm^{-1}; δ_H (300 MHz, $CDCl_3$): 0.95–1.10 (9H, m, 3×Me), 1.22 (3H, d, *J*=7 Hz, Me), 1.65 (1H, apparent septet, *J*=6.5 Hz, 7-H), 1.82 (1H, br d s, OH), 2.00–2.20 (2H, m, 6-H), 2.45–2.60 (1H, m, 3-H), 3.52 (1H, quintet, *J*=6.5 Hz, 2-H), 5.28–5.40 (1H, m, 4-H), 5.59 (1H, dt, *J*=11, 7 Hz, 5-H); δ_C (50 MHz, $CDCl_3$) 16.9, 20.0, 22.1,

22.5, 28.6, 36.8, 39.9, 71.6, 131.3, 132.4; *m/z* (CI) 156 [M^+, 38%], 174 [[$M+NH_4$]$^+$, 100%]. Found: *m/z* (CI) 174.1855. $C_{10}H_{24}NO$ {[$M+NH_4$]$^+$} requires *m/z* 174.1858.

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