Synthesis of Cyclic Alkenyl Dimethylsiloxanes from Alkynyl Benzyldimethylsilanes, and Application in Polyene Synthesis

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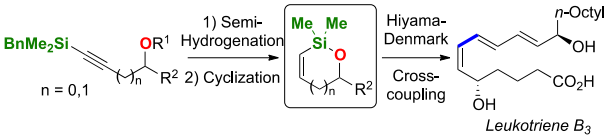
Supporting Information Placeholder

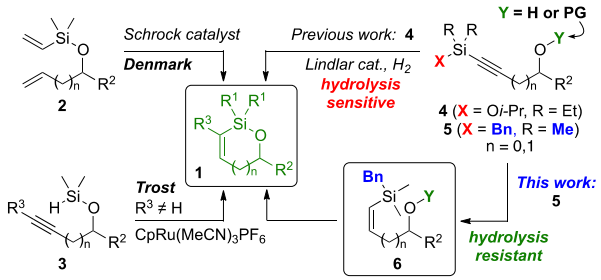


ABSTRACT: Cyclic dimethylalkenylsiloxanes, useful motifs for (*Z*)-selective Hiyama cross-coupling, are accessed from alkynyl benzyldimethylsilanes featuring adjacent allylic or homoallylic oxygen substituents by semi-hydrogenation / debenzylation / cyclization. While formation of 5- and 6-membered rings can be achieved from the free alcohols using fluoride or silanolate, allylic acetate precursors to 5-membered rings display distinct modes of activation. The utility of these compounds is demonstrated through the preparation of a variety of (*Z*)-alkene-containing polyenes, and application to a concise total synthesis of leukotriene B_3.

Cyclic alkenylsiloxanes (**1**, Scheme 1) are versatile synthetic intermediates. On activation by silaphilic nucleophiles, they enable the synthesis of (*Z*)-allylic or homoallylic alcohols *via* palladium-catalyzed Hiyama-Denmark cross-coupling,[1] and serve as precursors to β- or γ-hydroxycarbonyls through Tamao oxidation.[2] In the cross-coupling setting, cyclic alkenylsiloxanes offer benefits over other organometallic reagents:[3] they are non-toxic (compared to organotin compounds), inexpensive, and ensure the (*Z*)-stereochemistry of the coupled alkene product due to the constrained (cyclic) nature of the alkenylsiloxane. They also offer transient protection for the proximal allylic or homoallylic alcohol, thereby avoiding unnecessary protecting group manipulations of the latter.

These motifs have typically been accessed by ring-closing metathesis (RCM, **2**→**1**),[4] or intramolecular alkyne hydrosilylation (**3**→**1**).[2a, 2b, 5] While such methods have been applied in a number of settings,[1c, 2a, 6] the RCM approach requires the air-sensitive Schrock catalyst to overcome the steric hindrance imparted by the silicon substituents, while hydrosilylation is limited to internal alkynes and necessarily forms a trisubstituted alkenylsilane product.[7] We previously reported an alternative strategy based on the semi-hydrogenation of diethylisoproxyalkynylsilanes **4** to acyclic (*Z*)-alkenylsiloxanes, which afford cyclic diethyl alkenylsiloxanes on reaction with a proximal alcohol.[8] The use of a diethylsilane was required due to the hydrolytic sensitivity of equivalent dimethylalkoxyalkynylsilanes; however, the stability conferred by the ethyl substituents also reduced reactivity towards cross-coupling.[9]

Scheme 1. Approaches to cyclic alkenylsiloxanes

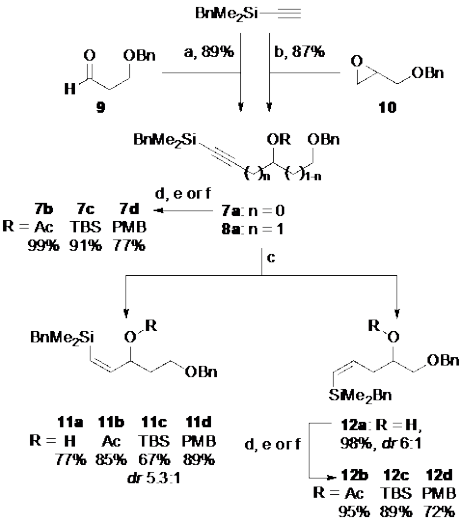


To overcome this limitation, we targeted a hydrolytically- resistant silane, where the silanol (and cyclic siloxane) would be unmasked only after alkyne semi-hydrogenation. The benzyldimethylsilyl (BDMS) group was an attractive candidate (**5**), as it is well-established to act as a surrogate for a dimethylsilanol, but is stable to a wide variety of conditions in its latent form. In seminal work, Eaborn demonstrated its lability towards aqueous

base (under warming),[10] while later studies revealed a more 'orthogonal' cleavage by the action of hydrated fluoride (e.g. TBAF).[11]

(*Z*)-Alkenylbenzylsilanes (**6**) have previously been generated via hydrozirconation or diimide reduction of BDMS-alkynylsilanes.[11a, 12] Here we describe development of the semihydrogenation approach to these motifs, and the implementation of various methods for benzyl cleavage / cyclization to the cyclic siloxane. We also compare the coupling efficiency of 5- and 6-membered cyclic dimethylsilanes to give (*Z*)-alkene containing polyenes, where the 5-membered dimethylsiloxanes were found to exhibit significantly enhanced coupling efficiency and reactivity compared to their acyclic counterparts. We further apply the chemistry to a concise seven-step synthesis (linear sequence) of the anti-inflammatory natural product leukotriene B_3.

Scheme 2. Synthesis of cyclic siloxane precursors



Reagents and conditions: a) *n*-BuLi, THF, -78 °C; **9**; 89% (**7a**); b) *n*-BuLi, THF, -78 °C; BF_3•Et_2O, **10**, 87% (**8a**); c) H_2, $Pd/CaCO_3$, quinoline, toluene; **11a**: 77%, *dr* 20:1; **11b**: 85%, *dr* 20:1; **11c**: 67%, *dr* 5.3:1; **11d**: 89%, *dr* 20:1; **12a**: cyclohexene included as co-solvent, 98%, *dr* 6:1; d) Ac_2O, DMAP, Et_3N, CH_2Cl_2; **7b**: 99%; **12b**: 95%; e) TBSCl, imid., CH_2Cl_2; **7c**: 91%; **12c**: 89%; f) PMBTCA, $Sc(OTf)_3$, CH_2Cl_2; **7d**: 77%; **12d**: 72%.

BDMS-substituted propargylic and homopropargylic alcohols **7a** and **8a** (Scheme 2) were prepared by addition of lithium benzyldimethylsilylacetylide to aldehyde **9** and epoxide **10** respectively. Semi-hydrogenation of **7a** afforded the (*Z*)-BDMS alkene **11a** as a single diastereomer, which was somewhat unexpected in light of our previous work in which acetate protection was required for high selectivity in the reduction.[8a, 13] Hydrogenation of **8a** also proceeded in excellent yield, albeit a small amount of the (*E*)-alkene was observed (**12a**, *Z*:*E* = 6:1); this observation is in keeping with other Lindlar reductions of alkynylsilanes.[8b, 14] While these alcohols are direct precursors to cyclic siloxanes, we also wished to compare the efficiency of debenzylation / cyclization of protected alcohol derivatives, as might be found in synthetic contexts. Acetate-, TBS- and PMB-protected alcohols were thus prepared, with these groups introduced either before (n=0) or after (n=1) semi-hydrogenation (**7**/**12b–d** respectively). The reductions to produce **7b–d** proceeded in high yield and with good selectivity, with the exception of silyl ether **11c** (*Z*:*E* = 5.3:1). This latter result likely relates to the increased steric crowding in this substrate, although the mechanistic basis of the isomerization is not clear.

With various potential precursors to 5- and 6-membered cyclic dimethylsiloxanes in hand, debenzylation / cyclization conditions were examined (Table 1). Treatment of alcohol **11a** with TBAF effected rapid debenzylation and complete conversion to the cyclic siloxane **13**, while the homoallylic alcohol **12a** gave a mixture of cyclic siloxane **14** and acyclic silanol, which cyclized to **14** on workup (74%). Interestingly, complete debenzylation could be achieved with just 0.25 equivalents of TBAF, with products **13** and **14** isolated after either acidic or basic workup, on multi-gram scale. **11a** and **12a** were also converted to their cyclic siloxanes on treatment with KOTMS, which could permit fluoride-free activation / *in situ* cross-coupling of the masked silanol.[15] This represents the first use of KOTMS to unmask a BDMS group.

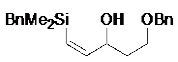
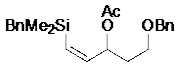
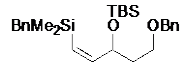
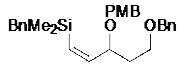
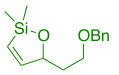
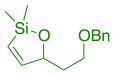
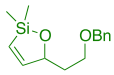
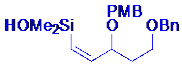
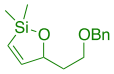
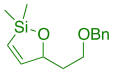
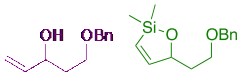
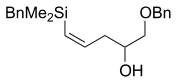
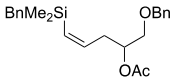
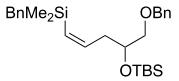
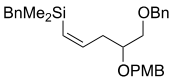
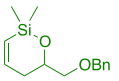
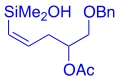
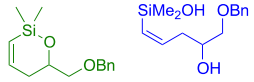
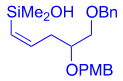
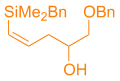
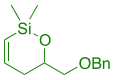
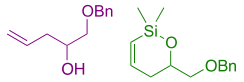
For the protected alcohol derivatives, we expected that a two step process would be required to reveal the cyclic siloxanes; however, **13** was unexpectedly generated on treatment of allylic acetate **11b** with TBAF•$3H_2O$, albeit this reaction now required a full equivalent of fluoride. Equally surprisingly, solvolysis of **11b** (K_2CO_3 / MeOH) also led to exclusive formation of **13**. In contrast, reaction of homoallylic acetate **12b** with TBAF gave the acyclic silanol **16b** with the acetate intact, while methanolysis afforded the expected acyclic alcohol **18** with the BDMS group remaining untouched. Sluggish reactions were observed for both acetates **11b** and **12b** on treatment with KOTMS, resulting in a 1:2 mixture of the cyclic siloxanes and desilylated products **19** and **20**.

Reaction of silyl ether **11c** with TBAF also gave the cyclic siloxane **13**, while for **12c** a 4.5:1 mixture of cyclic siloxane **14** and silanol **16a** was produced. In contrast to the alcohol and acetate substrates, KOTMS or K_2CO_3/MeOH could not achieve cleavage of the benzylsilane or TBS ethers. Similarly, PMB ethers **11d** and **12d** remained intact on treatment with any of the 'activators', with debenzylation to **15** / **16d** only possible under TBAF activation.

These observations suggest that neighbouring group participation is crucial in the unexpected debenzylation / cyclizations of allylic acetate **11b** (Scheme 3). Under methanolysis conditions (Scheme 3a), attack of methoxide on the acetate leads to a tetrahedral intermediate **21**, the alkoxide derived from which may be ideally placed to engage with the adjacent silicon atom, promoting benzyl cleavage (**22**); indeed, the enhanced rate of cleavage of trialkylbenzylsilanes by proximal alcohols had been noted by Eaborn, but is rarely exploited.[16] As no debenzylation /cyclization is observed for alcohol **11a** under the same conditions, the proximity of the alkoxide (released on ester hydrolysis) to the silicon atom appears to be important.[16-17] On treatment of **11b** with TBAF (Scheme 3b), the silanol generated by benzyl cleavage (**23**) could un-

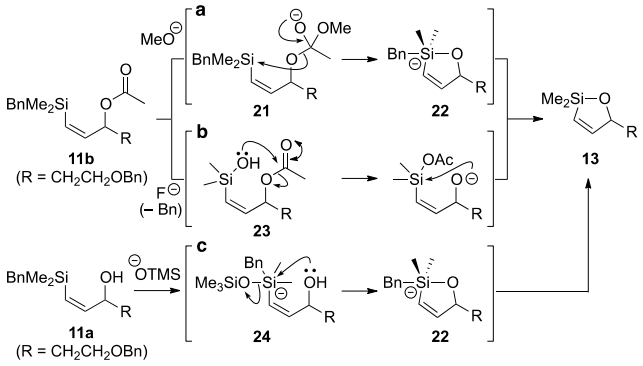
dergo transesterification with the adjacent acetate, the liberated alkoxide (or alcohol) then cyclizing onto the acetoxysilane. The efficient and rapid cyclization of alcohols **11a**/**12a** on treatment with KOTMS (Scheme 3c), but not of silyl ethers **11c**/**12c**, implies that a proximal alcohol is beneficial for this unusual debenzylation. We suggest that reversible addition of

Table 1. Debenzylation and cyclization studies.

Conditions[a]	 **11a**	 **11b**	 **11c**	 **11d**
TBAF[c]	 **13** (99)	 **13** (99)	 **13** (99)[f]	 **15** (n.d.)[f]
K_2CO_3/MeOH[d]	no reaction	 **13** (99)	no reaction	no reaction
KOTMS[e]	 **13** (99)	 **19**, **13** (2:1)[g]	no reaction	no reaction
Conditions[b]	**12a** 	**12b** 	**12c** 	**12d** 
TBAF[c]	 **14** (74)	 **16b** (n.d.)	 **14**, **16a** (4.5:1)[f,g]	 **16d** (n.d.)[f]
K_2CO_3/MeOH[d]	no reaction	 **18** (93)	no reaction	no reaction
KOTMS[e]	 **14** (71)	 **20**, **14** (2:1)[h]	no reaction	no reaction

[a] Values in parentheses represent conversions for 5-membered ring products (as judged by ^{1}H NMR spectroscopic analysis of the crude reaction mixture). [b] Yields in parentheses represent isolated yields for 6-membered ring products. [c] TBAF•3H$_2$O (0.25 equiv.), THF, rt. [d] K_2CO_3 (1.5 equiv.), MeOH, rt. [e] KOTMS (1.5 equiv.), THF, rt. [f] 1 equiv. TBAF. [g] Product ratio; yield not determined. [h] **14** was isolated in 34% yield. For other entries, n.d. = not determined.

the silanolate ion to the benzylsilane could lead to an electrophilic ate complex **24**, which promotes attack by the neighboring alcohol. An alternative role of silanolate as general base cannot be ruled out, but would seem inconsistent with the lack of debenzylation observed with K_2CO_3 / MeOH. Given that 5-membered cyclic dimethylalkenylsiloxanes are sensitive towards silica gel column chromatography, these various modes of activation – which require no purification other than an aqueous work up – could improve access to the cyclic species from stable precursors.



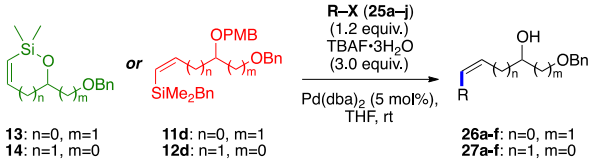
Scheme 3. Possible mechanisms for debenzylation of **11a** / **11b**.

Hiyama-Denmark couplings of these 5- and 6-membered cyclic siloxanes were next studied, with a focus on polyene synthesis, which has been less extensively explored than equivalent arene couplings. We aimed to compare the efficiency of reaction of the two ring sizes with that of the previously studied cyclic diethylsilanes,[8] and acyclic (*Z*)-benzyldimethylsilanes **11d** and **12d**, as well as to evaluate the influence of the substitution pattern and halide of the alkene coupling partner. As described by Denmark *et al.*, either Pd(dba)$_2$ (5 mol%) or [Pd(allyl)Cl]$_2$

(2.5 mol%) were used as pre-catalysts, with 2–3 equiv. of TBAF as activator, in THF at room temperature.[4d]

An initial study of reactions with iodobenzene using $Pd(dba)_2$ and 2.0 equiv. of TBAF revealed very rapid cross-coupling of both the 5-membered cyclic siloxane **13** (98%, 5 min) and the 6-membered counterpart **14** (99%, 15 min) (Table 2, Entry 1). These reactions were markedly more rapid than the equivalent cyclic diethylsilanes (which required 24 h to achieve similar yields),[8] underlining the critical importance of the size of the silane substituents. Compared to **13**, the acyclic benzyldimethylsilane **11d** (Entry 2) required extended reaction times, and gave a mixture of stereoisomers (*Z*:*E* = 3:1) as well as significant desilylation of the starting material, which clearly illustrates the advantage of the cyclic silane in this coupling. Interestingly, the acyclic homoallylic PMB ether **12d** coupled with equal efficiency to cyclic siloxane **14**, which

Table 2. Substrate scope in Hiyama-Denmark coupling



Entry	Substrate	Product from **13** Time, Yield (%)[a]	Product from **14** Time, Yield (%)[a]
1	Ph—I **25a**	**26a** 5 min,[b] 98%	**27a** 15 min,[b] 99%
2	Ph—I **25a**	**26b** 30 min,[b,c] 38% + 48% desilylation	**27b** 30 min,[b,d] 94%
3	**25b** (X=I) **25c** (X=Br)	**26c** (X=I) 45 min, 78% (X=Br) 15 min, 78%	**27c** (X=I) 16 h, 75% (X=Br) 5 h,[e] 68%
4	**25d** (X=I) **25e** (X=Br)	**26d** (X=I) 15 min,[f] 73% (X=Br) 3 h,[e] 57%	**27d** (X=I) 16 h, 65% (X=Br) 16 h, 60%
5	**25f**	**26e** 1 h, 84%	**27e** 16 h, 73%
6	**25g** (X=I)	**26f**	
	25h (X=Br)	(X=I) 30 min, 81% (X=Br) 2 h,[g] 56%	**27f** (X=I) 30 min, 64% (X=Br) 16 h, 53%
7	**25i**	**26g** 4 h, 52% Fostriecin fragment	
8	**25j**	**26h** 2 h, 66% Phoslactomycin B fragment	

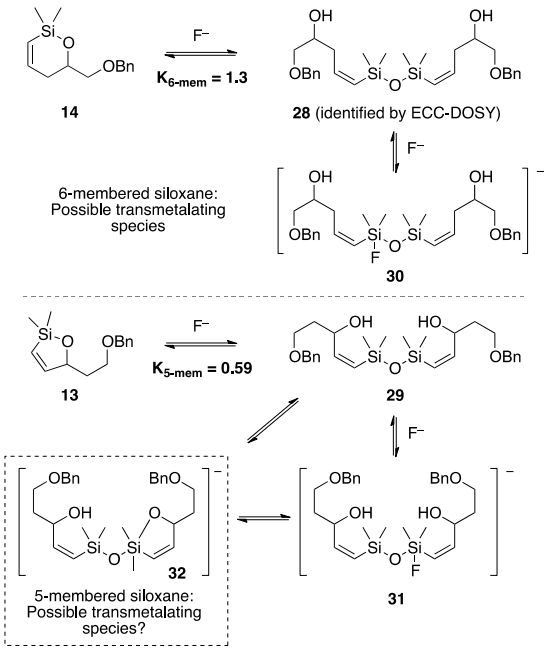
[a]Isolated yields. Couplings in Entry 2 used **11d** and **12d** as substrates. [b]2 equiv. TBAF•$3H_2O$. [c] Coupling of **11d**. Product isolated in a 3:1 *Z*:*E* ratio. [d] Coupling of **12d**. [e][allylPdCl]$_2$ (2.5 mol%), 1.2 equiv. siloxane. [f]1.2 equiv. siloxane. [g][allylPdCl]$_2$ (2.5 mol%).

may imply that these two reactions proceed through a similar acyclic silane species.[18]

Application of these conditions to iodostyrene **25b** (Entry 3), resulted in sluggish coupling of 5-membered siloxane **13**, with incomplete reaction after 1.5 h. However, use of an additional equivalent of fluoride enabled complete conversion in 45 min (**26c**, 78%). When bromostyrene **25c** was employed, **26c** was obtained in equivalent yield but, surprisingly, in a shorter reaction time (15 min). The 6-membered siloxane **14** displayed a similar trend, albeit both couplings required longer reaction times (iodostyrene: **27c**, 75%, 16 h; bromostyrene: **27c**, 68%, 5 h). These modified conditions were applied to a range of mono- and dienyl halides **25f–j**, giving products **26d–h** / **27d–f** in moderate to excellent yields (52–90%, Entries 4-6). In all cases, shorter reaction times were observed for **13** (15 min–3 h) compared to **14** (typically 16 h), and aside from the halostyrenes, vinyl iodides showed superior reactivity compared to vinyl bromides. Most notable were the comparatively rapid[8] syntheses of the triene / diene portions of fostriecin and phoslactomycin B (**26g** and **26h** respectively, entries 7, 8), which involve coupling of hindered (*Z*)-alkenyl iodides.

The different reactivity of the five- and six-membered ring siloxanes is worthy of discussion. Under conditions equivalent to those employed in the present work, Denmark proposed that the transmetalation step for fluoride-promoted cross-coupling of acyclic alkenylsilanols involves a key fluoride ate-complex of an alkenyl disiloxane.[19] We explored the behaviour of the 5- and 6-membered siloxanes **13** and **14** on treatment with TBAF by NMR spectroscopy (in d_8-THF), and observed for both the immediate establishment of an equilibrium with what we propose to be acyclicdisiloxanes **28** and **29** (Scheme 4).[20] While the 5-membered siloxane undergoes gradual desilylation under these conditions, we

Scheme 4. Possible mechanisms for transmetallation of cyclic siloxane-derived intermediates

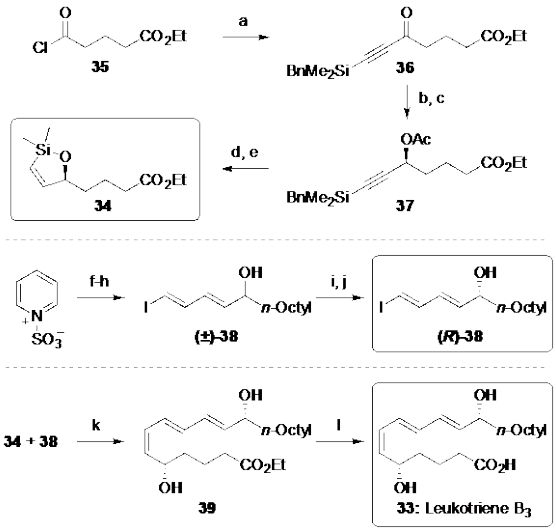


were able to use ECC-DOSY NMR spectroscopy[21] to support the assignment of disiloxane **28**, with an estimated molecular weight of ~600 (actual M_W of silanol monomer: 248; M_W of disiloxane **28**: 515).[20]

We therefore propose that the action of fluoride on **14** establishes a rapid equilibrium of **14** with disiloxane **28**, and that this speciesundergoes transmetalation via a Denmark ate complex **30**. The question therefore remains as to the nature of the transmetalating species derived from the 5-membered siloxane **13** (or, its acyclic disiloxane **29**), where experimental observations show enhanced and distinct reactivity compared to acyclic alkenylsilanes (see above). We suggest that while the reactions of **13** could certainly proceed via an equivalent fluoride ate complex **31**, there is potential for intramolecular engagement by the proximal alcohol to form complex **32**. Whether this complex exists in higher concentration, or is more reactive than its fluoride counterpart remains unclear, but given the precedent for the enhanced reactivity of other γ-hydroxysilanes in alkoxide-promoted cross-coupling,[22] this seems a reasonable mechanistic proposal.

Finally, the utility of this methodology was demonstrated through a concise total synthesis of leukotriene B_3 (**33**, Scheme 5), an important agent in the inflammatory response process.[23,24] The synthesis of cyclic siloxane **34**, containing the C6–C7 (*Z*)-alkene of the natural product, commenced with addition of the zinc acetylide of BDMS acetylene to commercially available acid chloride **35**. Noyori asymmetric transfer hydrogenation[25] (99% *ee*) followed by acetate protection afforded alkyne **37**, which gave the 5-membered cyclic siloxane **34** after treatment with fluoride. Its coupling partner, dienyl iodide (*R*)-**38**, was prepared from SO_3•pyridine via hydrolysis / iodination to an intermediate semi-hydrogenation of iododienal,[26] addition of *n*-octylmagnesium bromide to which gave dienyl iodide (±)-**38** as a mixture of stereoisomers (1.2:1, *E,E*:*E,Z*) which could be enriched in the desired isomer *via* recrystallization (10:1, *E,E*:*E,Z*). Swern oxidation, followed by CBS reduction[27] of the resulting enone, gave dienyl iodide (*R*)-**38** (90% *ee*, after recrystallization). Fluoride-promoted cross-coupling of **34** and (*R*)-

Scheme 5. Synthesis of leukotriene B_3



Reagents and conditions: a) *n*-BuLi, $BnMe_2SiCCH$, $ZnCl_2$, THF, 0 °C, 52%; b) RuCl(*S,S*)TsDPEN (2 mol%), *i*-PrOH, CH_2Cl_2; c) Ac_2O, DMAP, Et_3N, CH_2Cl_2, 90% over two steps, 99% *ee*; d) H_2, $Pd/CaCO_3$ (5 mol%), quinoline, cyclohexene, toluene, 82%, *dr* >20:1; e) TBAF•$3H_2O$ (1.05 equiv), THF, 87%; f) KOH, H_2O; g) PPh_3, I_2, CH_2Cl_2; h) 1-bromooctane, Mg, THF, 8% over three steps (10:1 *E,E*:*E,Z* after recrystalization); i) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2; j) (*S*)-(−)-2-methyl-CBS-oxazaborolidine, BH_3.THF, THF, 33% over two steps (90% *ee*, 12% yield after recrystalization); k) $Pd(dba)_2$ (5 mol%), TBAF•$3H_2O$ (3 equiv), THF, 73%; l) LiOH, H_2O, *i*-PrOH, 99%.

38 gave triene **39** in 73% yield. Finally, ester hydrolysis afforded leukotriene B_3 (**33**, 99%) in a total of seven steps in the longest linear sequence from commercially available starting materials, which corresponds to the shortest synthesis of this natural product to date.

In conclusion, 5- and 6-membered cyclic dimethyl alkenylsiloxanes can be prepared by the semi-hydrogenation of benzyldimethyl alkynylsilanes, with the resultant (*Z*)-benzyldimethyl alkenylsilanes serving as masked cyclic siloxane precursors. Cyclization of both allylic and homoallylic alcohols adjacent to BDMS (*Z*)-alkenes can be effected through both fluoride- and silanolate-promoted benzyl cleavage, and allylic acetate 5-membered ring siloxane precursors display unique modes of activation under mild conditions. Cross-coupling was used to access a range of (*Z*)-alkene containing polyenes, including fragments of the natural products fostriecin and phoslactomycin B. Finally, this chemistry was applied to a concise total synthesis of leukotriene B_3.

EXPERIMENTAL SECTION

General considerations. Commercial reagents were used directly as supplied. Solvents were dried using an alumina column solvent drying system. Unless otherwise

stated, all non-aqueous reactions were performed in oven-dried apparatus under a nitrogen atmosphere at room temperature. Tetrabutylammonium fluoride (TBAF•$3H_2O$) solution was prepared by dissolving solid tertabutylammonium fluoride trihydrate in anhydrous THF. Column chromatography was performed using Macherey-Nagel Kieselgel 60M (230-400 mesh) silica gel as the stationary phase. Specific rotations were recorded on a Perkin-Elmer 341 polarimeter with a 1 dm path length cell (sodium D line, 589 nm); specific rotations [α] are given in deg dm^2g^{-1}, concentration (*c*) is reported in g 100 mL^{-1}. Enantiomeric excesses (*ee*) were determined by HPLC using a DAICEL CHIRALPAK IB or IC column (250 mm × 4.6 mm ID). Infrared spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer equipped with a diamond ATR module. ^1H and ^{13}C NMR spectra were recorded on Bruker DPX200, AVIII400 or AVIII500 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm), referenced to the solvent residual ($CDCl_3$ δ_H/δ_C = 7.26/77.2; C_6D_6 δ = 7.16/128.1; CD_3OD δ = 3.31/49.0). Signals are recorded as singlet (s), broad singlet (br s), doublet (d), triplet (t), quartet (q), quintet (quin), and multiplet (m). Coupling constants (*J*) are reported to the nearest 0.5 Hz. High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics microTOF spectrometer (resolution = 5000 FWHM).

Benzyl(ethynyl)dimethylsilane was prepared by variation of a literature procedure.[12a] To a suspension of Mg turnings (4.74 g, 195 mmol, 1.4 equiv.) in Et_2O (20 mL, sufficient to cover the turnings) was added a solution of benzyl chloride (16.0 mL, 139 mmol, 1.0 equiv.) in Et_2O (120 mL) at a rate sufficient to maintain controlled reflux. After addition, the mixture was heated at reflux for 2 h, then cooled to room temperature. The resulting solution of benzylmagnesium chloride (140 mL, ca. 1.0 M in Et_2O, 1.0 equiv.) was added to dichlorodimethylsilane (24.0 ml, 199 mmol, 1.4 equiv.) *via* cannula. The mixture was heated at reflux for 1 h, then cooled to room temperature. The suspension was filtered under nitrogen *via* cannula, and concentrated *in vacuo* to give crude benzyldimethylchlorosilane as a pale yellow oil. The silane was redissolved in THF (240 mL) and cooled to 0 °C. To this stirred solution was added dropwise a solution of ethynylmagnesium bromide (304 mL, 0.5 M in THF, 152 mmol, 1.3 equiv.). The resulting mixture allowed to warm to room temperature, and was stirred for a further 3 h. The reaction was quenched by addition of NH_4Cl (240 mL, sat., aq.). The organic phase was separated, and the aqueous phase was further extracted with Et_2O (2 × 200 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (5% EtOAc / petroleum ether) gave benzyl(ethynyl)dimethylsilane (19.7 g, 113 mmol, 81%) as a pale yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.27-7.21 (2H, m), 7.14-7.0 (3H, m), 2.42 (1H, s, CC*H*), 2.23 (2H, s), 0.16 (6H, s, $Si(CH_3)_2$); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.9, 130.7, 130.6, 126.8, 96.7, 90.9, 28.2, 0.0. Spectroscopic data in agreement with the literature.[12a]

*1-(Benzyldimethylsilyl)-5-(benzyloxy)pent-1-yn-3-ol (**7a**).* To a solution of benzyldimethylsilylacetylene (4.37 g, 25.1 mmol, 1.1 equiv.) in THF (76 mL) at –78 °C was added a solution of *n*-BuLi (9.6 mL, 2.5 M in hexanes, 23.9 mmol, 1.05 equiv.) dropwise *via* syringe. The resulting mixture was stirred for 1 h, after which 3-(benzyloxy)propanal (**9**) (3.74 g, 22.8 mmol, 1.0 equiv.) was added. After stirring at –78 °C for 30 min, the cooling bath was removed and the reaction allowed to reach room temperature and stirred for a further 30 min. The reaction was quenched by addition of NH_4Cl (80 mL, sat., aq.), the organic phase was separated and the aqueous phase further extracted with Et_2O (3 × 80 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (10% EtOAc / petroleum ether) gave **7a** (6.88 g, 2.32 mmol, 89%) as a clear oil. R_f 0.17 (10% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3410, 2958, 2100, 832, 697; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-6.95 (10H, m), 4.56-4.48 (1H, m), 4.48-4.38 (2H, m), 3.79-3.69 (1H, m), 3.63-3.52 (1H, m), 2.99-2.92 (1H, m), 2.12 (2H, s), 2.06-1.93 (1H, m), 1.93-1.80 (1H, m), 0.06 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.0, 139.9, 130.6, 130.5, 130.3, 129.9, 129.8, 126.5, 109.6, 90.0, 75.5, 69.8, 64.0, 38.7, 28.3, 0.0; HRMS (ESI+) calc. for $C_{21}H_{26}O_2NaSi$ $[M+Na]^+$ 361.1594, found 361.1595.

*1-(Benzyldimethylsilyl)-5-(benzyloxy)pent-1-yn-3-yl acetate (**7b**).* To a solution of **7a** (950 mg, 2.81 mmol, 1.0 equiv.), acetic anhydride (0.53 mL, 5.6 mmol, 2.0 equiv.) and Et_3N (1.2 mL, 8.6 mmol, 3.0 equiv.) in CH_2Cl_2 (19 mL) was added a crystal of 4-dimethylaminopyridine. The mixture was stirred for 2 h, then water (15 mL) was added. The organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (5%→10% Et_2O / petroleum ether) gave **7b** (1.07 g, 2.80 mmol, 99%) as a clear oil. R_f 0.37 (10% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2961, 2180, 1745, 1229, 837; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.02 (10H, m), 5.56 (1H, t, J = 7.0 Hz), 4.53-4.45 (2H, m), 3.62-3.50 (2H, m), 2.18 (2H, s), 2.15-1.97 (2H, m), 2.06 (3H, s), 0.12 (3H, s), 0.11 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.8,138.9, 138.3, 128.6, 128.5, 128.3, 127.8, 127.7 124.5, 103.8, 89.1, 73.2, 65.9, 61.9, 35.1, 26.1, 21.1 ,–2.1, –2.2; HRMS (ESI+) calc. for $C_{23}H_{28}O_3NaSi$ $[M+Na]^+$ 403.1700, found 403.1692.

*Benzyl(5-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy) pent-1-yn-1-yl)dimethylsilane (**7c**).* To a solution of *tert*-butyldimethylsilyl chloride (468 mg, 3.11 mmol, 2.1 equiv.) in CH_2Cl_2 (3.0 mL) was added imidazole (221 mg, 3.25 mmol, 2.2 equiv.). After stirring for 10 min, **7a** (500 mg, 1.48 mmol, 1.0 equiv.) was added and the mixture was stirred overnight. The mixture was diluted with CH_2Cl_2 (15 mL), then NH_4Cl (15 mL, sat., aq.) was added. The organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 15 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (2% Et_2O / petroleum ether) gave **7c** (610 mg, 1.35 mmol, 91%) as a colourless oil. R_f 0.79 (25% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2956, 2173, 1250, 1020, 697; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.09 (6H, m), 7.07-6.96 (4H, m), 4.50 (1H, t,

J = 6.5 Hz), 4.46-4.35 (2H, m), 3.52 (2H, qt, *J* = 9.5 and 6.0 Hz), 2.10 (2H, s), 1.90 (2H, q, *J* = 6.0 Hz), 0.83 (9H, s), 0.05 (3H, s), 0.04-0.01 (9H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ* 139.1, 138.6, 128.5, 128.3, 127.8, 127.7, 124.5, 108.9, 87.3, 73.2, 66.5, 60.5, 38.8, 26.3, 26.0, 18.4, −2.0, −2.1, −4.4, −4.9; HRMS (ESI+) calc. for $C_{27}H_{40}O_2Si_2Na$ $[M+Na]^+$ 475.2459, found 475.2453.

General Procedure A: PMB protection. To a solution of the alcohol (1.0 equiv.) and scandium(III) triflate (0.15 equiv.) in toluene (0.16 M, 6.4 mL / mmol substrate) was added 4-methoxybenzyl 2,2,2-trichloroacetimidate (1.5 equiv.). The mixture was stirred for 2 h, then $NaHCO_3$ (15 mL $mmol^{-1}$ substrate) and Et_2O (15 mL $mmol^{-1}$) were added. The organic phase was separated, and the aqueous phase extracted with Et_2O (x 2, 15 mL $mmol^{-1}$). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated.

*Benzyl(5-(benzyloxy)-3-((4-methoxybenzyl)oxy)pent-1-yn-1-yl)dimethylsilane (**7d**).* Prepared following general procedure A with **7a** (500 mg, 1.48 mmol), toluene (9.5 mL), *4-methoxybenzyl 2,2,2-trichloroacetimidate* (616 mg, 2.22 mmol) and scandium(III) triflate (109 mg, 0.221 mmol). Purification *via* column chromatography (10% Et_2O / petroleum ether) gave **7d** (521 mg, 1.14 mmol, 77%) as a colourless oil. R_f 0.45 (25% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3027, 2169, 1248, 1095, 698; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.36-6.80 (14H, m), 4.68 (1H, d, *J* = 11.5 Hz), 4.49-4.42 (2H, m), 4.39 (1H, d, *J* = 11.5 Hz), 4.27 (1H, dd, *J* = 7.0 and 6.5 Hz), 3.79 (3H, s), 3.64-3.55 (2H, m), 2.21 (2H, s), 2.11-1.93 (2H, m), 0.15 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ* 159.4, 139.1, 138.6, 130.1, 129.9, 128.5, 128.5, 128.3, 127.8, 127.7, 124.5, 113.9, 106.1, 89.2, 73.1, 70.5, 66.5, 66.0, 55.4, 36.1, 26.3, −1.9; HRMS (ESI+) calc. for $C_{29}H_{34}O_3SiNa$ $[M+Na]^+$ 481.2169, found 481.2167.

*5-(Benzyldimethylsilyl)-1-(benzyloxy)pent-4-yn-2-ol (**8a**).* To a solution of glycidol (3.0 mL, 45 mmol, 1.0 equiv.) and benzyl bromide (7.0 mL, 59 mmol, 1.3 equiv.) in DMF (113 mL) at 0 °C was added NaH (1.81 g, 60 wt% dispersion in mineral oil, 45.3 mmol, 1.0 equiv.). The cooling bath was removed and the reaction mixture was stirred vigorously at room temperature overnight. The mixture was then diluted with CH_2Cl_2 (60 mL) and quenched by addition of water (300 mL). The organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (5 × 60 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. Purification via column chromatography (20% Et_2O / petroleum ether) gave 2-((benzyloxy)methyl)oxirane (**10**) (7.23 g, 44.0 mmol, 98%) as a colourless oil. Data identical to literature values.[28] To a solution of benzyldimethylsilylacetylene (4.83 g, 27.7 mmol, 1.3 equiv.) in THF (100 mL) at −78 °C was added a solution of *n*-BuLi (15.3 mL, 1.6 M in hexanes, 24.5 mmol, 1.15 equiv.) dropwise *via* syringe. After stirring for 30 min at −78 °C, $BF_3{\cdot}Et_2O$ (3.40 mL, 27.7 mmol, 1.3 equiv.) was added over 5 min, followed by epoxide **10** (3.50 g, 21.3 mmol, 1.0 equiv.). After stirring for 1 h, the resulting mixture was quenched by addition of HCl (30 mL, 1 M, aq.). The cooling bath was removed and the mixture was allowed to warm to room temperature. The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 × 30 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), filtered, and concentrated. Purification *via* column chromatography (30% Et_2O / petroleum ether) gave **8a** (6.21 g, 18.4 mmol, 87%) as a colourless oil. R_f 0.19 (30% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3410, 2981, 1383, 1152, 954; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.02 (10H, m), 4.57 (2H, s), 3.98-3.3.89 (1H, m), 3.57 (1H, dd, *J* = 9.5 and 4.0 Hz), 3.47 (1H, dd, *J* = 9.5 and 6.5 Hz), 2.49 (2H, dd, *J* = 6.5 and 4.0 Hz), 2.35 (1H, br s), 2.16 (2H, s), 0.11 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 141.1, 139.8, 130.5, 130.3, 130.1, 129.8, 129.7, 126.3, 105.9, 87.7, 75.4, 74.7, 70.8, 28.3, 27.0, 0.0; HRMS (ESI+) calc. for $C_{21}H_{26}O_2NaSi$ $[M+Na]^+$ 361.1594, found 361.1592.

General procedure B: Semihydrogenation (11a–d, 12a). A suspension of Pd / $CaCO_3$ (5 wt% Pd, 5.0 mol%) in toluene (10.0 mL / mmol substrate) was placed under a hydrogen atmosphere. A solution of alkyne (1.0 equiv.) and quinoline (20-50 mol%) in toluene or cyclohexene (1.0 mL / mmol substrate) were added *via* syringe. The solution was stirred vigorously under H_2 (balloon) until complete as monitored by TLC (visualised with vanillin). The mixture was filtered through Celite and concentrated to give the crude product, which was purified *via* column chromatography.

*(Z)-1-(Benzyldimethylsilyl)-5-(benzyloxy)pent-1-en-3-ol (**11a**).* Prepared following general procedure B with Pd / $CaCO_3$ (60 mg, 0.028 mmol) in toluene (3.0 mL), and alkyne **7a** (200 mg, 0.59 mmol) and quinoline (14.0 µL, 0.12 mmol, 20 mol%) in toluene (0.6 mL), with a 1 h reaction time. Purification *via* column chromatography (5% Et_2O / petroleum ether) gave **11a** (154 mg, 0.45 mmol, 77%) as a clear oil. R_f 0.12 (10% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3482, 2593, 1600, 1493, 1248, 1097, 831, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42-7.27 (5H, m), 7.20 (2H, t, *J* = 7.5 Hz), 7.07 (1H, t, *J* = 7.5 Hz), 7.01 (2H, d, *J* = 7.0 Hz), 6.31 (1H, dd, *J* = 14.5 and 8.5 Hz), 5.60 (1H, dd, *J* = 14.5 and 1.0 Hz), 4.51 (2H, d, *J* = 1.5 Hz), 4.28 (1H, td, *J* = 8.5 and 4.0 Hz), 3.65 (1H, ddd, *J* = 9.5, 6.5 and 5.0 Hz), 3.57 (1H, ddd, *J* = 9.5, 7.5 and 5.0 Hz), 2.44 (1H, d, *J* = 3.0 Hz), 2.18 (2H, s), 1.80 (1H, dtd, *J* = 14.5, 7.5 and 5.0 Hz), 1.67 (1H, dddd, *J* = 14.5, 6.5, 5.0 and 4.0 Hz), 0.14 (3H, s), 0.13 (3H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 151.0, 140.1, 138.2, 128.9, 128.6, 128.4, 128.3, 127.8, 127.8, 124.3, 73.4, 71.6, 68.3, 36.8, 27.0, −1.2, −1.2.; HRMS (ESI+) calc. for $C_{21}H_{28}O_2NaSi$ $[M+Na]^+$ 363.1751, found 363.1751.

*(Z)-1-(Benzyldimethylsilyl)-5-(benzyloxy)pent-1-en-3-yl acetate (**11b**).* Prepared following general procedure B with Pd / $CaCO_3$ (839 mg, 5 wt% Pd, 0.39 mmol) in toluene (70 mL), and alkyne **7b** (3.00 g, 7.89 mmol) and quinoline (0.185 mL, 1.58 mmol, 20 mol%) in toluene (10 mL), with a 2 h reaction time. Purification *via* column chromatography (5% Et_2O / petroleum ether) gave **11b** (2.57 g, 6.71 mmol, 85%) as a clear oil. R_f 0.39 (20% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2956, 1737, 1239, 832, 699; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-6.94 (10H, m), 6.20 (1H, dd, *J* = 14.5 and 9.5 Hz), 5.69 (1H, d, *J* = 14.5 Hz), 5.58-5.50 (1H, m), 4.50 (1H, d, *J* = 12.0 Hz), 4.44 (1H, d, *J* = 12.0 Hz), 3.50-3.44 (2H, m), 2.22 (1H, d, *J* = 13.5 Hz), 2.18 (1H, d, *J* = 13.5 Hz), 2.00 (3H, s), 1.97-1.88 (1H, m), 1.84-1.74 (1H,

m), 0.16 (3H, s), 0.14 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.3, 145.9, 139.9, 138.5, 131.6, 128.5, 128.4, 128.3, 128.4, 127.8, 127.7, 124.4, 73.1, 72.2, 66.2, 35.3, 26.5, 21.4 – 1.8 (2C); HRMS (ESI+) calc. for $C_{23}H_{30}O_3NaSi$ $[M+Na]^+$ 405.1856, found 405.1856.

*(Z)-Benzyl(5-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy) pent-1-en-1-yl)dimethylsilane (**11c**).* Prepared following general procedure B with Pd / $CaCO_3$ (35 mg, 0.017 mmol) in toluene (1.5 mL), and alkyne **7c** (150 mg, 0.33 mmol) and quinoline (8.0 µL, 0.068 mmol, 20 mol%) in toluene (1.8 mL), with a 2 h reaction time. Purification *via* column chromatography (1% Et_2O / petroleum ether) gave **11c** (101 mg, 0.22 mmol, 67%) as a clear oil. R_f 0.34 (4% Et_2O / petroleum ether / Et_2O); IR (thin film, ν_{max} / cm^{-1}) 2955, 1250, 1048, 1030, 697; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-6.95 (10H, m), 6.29 (1H, dd, *J* = 14.5 and 8.5 Hz), 5.45 (1H, d, *J* = 14.5 Hz), 4.53-4.43 (3H, m), 3.64-3.46 (2H, m), 2.16 (2H, s), 1.76-1.65 (2H, m), 0.87 (9H, s), 0.11 (3H, s), 0.09 (3H, s), 0.03 (3H, s), 0.02 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 153.2, 139.9, 138.8, 128.4, 128.4, 128.3, 127.6, 127.5, 125.9, 124.2, 73.0, 70.2, 66.7, 39.0, 26.8, 26.0, 18.3, –1.5, –1.7, –3.9, –4.5; HRMS (ESI+) calc. for $C_{27}H_{42}O_2Si_2Na$ $[M+Na]^+$ 477.2616, found: 477.2614.

*(Z)-Benzyl(5-(benzyloxy)-3-((4-methoxybenzyl)oxy)pent-1-en-1-yl)dimethylsilane (**11d**).* Prepared following general procedure B with Pd / $CaCO_3$ (23 mg, 0.011 mmol) in toluene (1.0 mL), and alkyne **7d** (100 mg, 0.22 mmol) and quinoline (5 µL, 0.042 mmol, 20 mol%) in toluene (1.2 mL), with a 2 h reaction time. Purification *via* column chromatography (10% Et_2O / petroleum ether) gave **11d** (89 mg, 0.19 mmol, 88%) as a clear oil. R_f 0.45 (25% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2954, 1613, 1247, 1036, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-6.80 (14H, m), 6.28 (1H, dd, *J* = 14.5 and 9.5 Hz), 5.74 (1H, d, *J* = 14.5 Hz), 4.54-4.42 (5H, m), 3.77 (3H, s), 3.68-3.51 (2H, m), 2.15 (2H, s), 1.94-1.82 (1H, m), 1.80-1.67 (1H, m), 0.09 (3H, s), 0.08 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 150.3, 139.9, 138.8, 130.7, 129.3, 128.5, 128.4, 128.4, 128.3, 127.7, 127.6, 124.3, 113.9, 75.9, 73.0, 70.1, 66.6, 55.4, 36.3, 26.8, –1.4, –1.5; HRMS (ESI+) calc. for $C_{29}H_{36}O_3SiNa$ $[M+Na]^+$ 483.2326, found: 483.2324.

*(Z)-5-(Benzyldimethylsilyl)-1-(benzyloxy)pent-4-en-2-ol (**12a**).* Prepared following general procedure B with Pd / $CaCO_3$ (1.15 g, 0.54 mmol) in toluene (100 mL), and alkyne **8a** (3.67 g, 10.8 mmol) and quinoline (0.64 mL, 5.4 mmol, 50 mol%) in cyclohexene (10 mL), with a 1.5 h reaction time. Purification *via* column chromatography (40% Et_2O / petroleum ether) gave **12a** (3.78 g, 10.8 mmol, *Z*:*E*, 6:1, 99%) as a clear oil. R_f 0.40 (20% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3444, 2895, 1493, 1095, 830; ^1H NMR (400 MHz, $CDCl_3$) δ (6:1 *Z*/*E*-mixture, major isomer reported) 7.42-6.98 (10H, m), 6.39 (1H, dt, *J* = 14.0 and 7.5 Hz), 5.63 (1H, dt, *J* = 14.0 and 1.0 Hz), 4.56 (2H, s), 3.92-3.79 (1H, m), 3.48 (1H, dd, *J* = 9.5 and 3.5 Hz), 3.34 (1H, dd, *J* = 9.5 and 7.5 Hz), 2.41-2.19 (2H, m), 2.36 (1H, d, *J* = 3.5 Hz), 2.18 (2H, s), 0.13 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 145.0, 140.0, 138.0, 130.1, 128.6, 128.3, 128.2 (3C), 127.9, 127.8, 124.1, 74.0, 73.5, 70.2, 37.4, 26.7, – 1.5, –1.6; HRMS (ESI+) calc. for $C_{21}H_{28}O_2NaSi$ $[M+Na]^+$ 363.1751, found 363.1756.

*(Z)-5-(Benzyldimethylsilyl)-1-(benzyloxy)pent-4-en-2-yl acetate (**12b**).* To a solution of **12a** (205 mg, 0.61 mmol, *Z*:*E*, 6:1, 1.0 equiv.), acetic anhydride (0.12 mL, 1.22 mmol, 2.0 equiv.) and Et_3N (0.25 mL, 1.83 mmol, 3.0 equiv.) in CH_2Cl_2 (4 mL) was added a crystal of 4-dimethylaminopyridine. After stirring for 30 min, water (10 mL) was added, the organic phase separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (10% Et_2O / petroleum ether) gave **12b** (219 mg, 0.58 mmol, *Z*:*E*, 6:1, 95%) as a clear oil. R_f 0.40 (20% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3026, 1738, 1236, 905, 698; ^1H NMR (400 MHz, $CDCl_3$) δ (6:1 *Z*/*E*-mixture, major isomer reported) 7.39-6.95 (10H, m), 6.27 (1H, dt, *J* = 14.0 and 7.5 Hz), 5.60 (1H, dt, *J* = 14.0 and 1.5 Hz), 5.13-5.03 (1H, m), 4.56 (1H, d, *J* = 12.0 Hz), 4.50 (1H, d, *J* = 12.0 Hz), 3.52-3.48 (2H, m), 2.41-2.35 (2H, m), 2.16 (2H, s), 2.05 (3H, s), 0.11 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 170.7, 143.9, 140.0, 138.1, 130.5, 128.5, 128.3, 128.3, 127.8, 127.7, 124.2, 73.3, 72.2, 70.8, 35.1, 26.7, 21.3, – 1.6; HRMS (ESI+) calc. for $C_{23}H_{30}O_3NaSi$ $[M+Na]^+$ 405.1856, found 405.1863.

*(Z)-Benzyl(5-(benzyloxy)-4-((tert-butyldimethylsilyl)oxy) pent-1-en-1-yl)dimethylsilane (**12c**).* To a solution of *tert*-butyldimethylsilyl chloride (186 mg, 1.23 mmol, 2.1 equiv.) in CH_2Cl_2 (1.2 mL) was added imidazole (88 mg, 1.3 mmol, 2.2 equiv.). After stirring for 10 min, alcohol **12a** (200 mg, 0.587 mmol, *Z*:*E*, 6:1, 1.0 equiv.) was added and the mixture was stirred overnight. The mixture was then diluted with CH_2Cl_2 (5 mL), and NH_4Cl (5 mL sat., aq.) was added. The organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 5 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (2% Et_2O / petroleum ether) gave **12c** (239 mg, 0.53 mmol, *Z*:*E*, 6:1, 90%) as a colourless oil. R_f 0.63 (4% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2955, 1602, 1453, 1250, 698; ^1H NMR (400 MHz, $CDCl_3$) δ (6:1 *Z*/*E* mixture, major isomer reported) 7.36-6.94 (10H, m), 6.40 (1H, dt, *J* = 14.0 and 7.5 Hz), 5.55 (1H, dd, *J* = 14.0 and 1.5 Hz), 4.51 (2H, s), 3.89-3.82 (1H, m), 3.41-3.31 (2H, m), 2.41-2.18 (2H, m), 2.16 (2H, s), 0.88 (9H, s), 0.09 (6H, s), 0.04 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.3, 140.3, 128.9, 128.4 (2C), 128.2, 127.7 (2C) 127.6, 124.1, 74.7, 73.4, 71.6, 38.9, 26.8, 26.0, 18.3, –1.6, –4.3, –4.5; HRMS (ESI+) calc. for $C_{27}H_{42}O_2Si_2Na$ $[M+Na]^+$ 477.2616, found 477.2614.

*(Z)-Benzyl(5-(benzyloxy)-4-((4-methoxybenzyl)oxy)pent-1-en-1-yl)dimethylsilane (**12d**).* Prepared following general procedure A with **12a** (200 mg, 0.59 mmol, *Z*:*E* 6:1), toluene (3.7 mL), 4-methoxybenzyl 2,2,2-trichloroacetimidate (249 mg, 0.88 mmol) and scandium (III) triflate (43 mg, 87 µmol). Purification *via* column chromatography (10% Et_2O / petroleum ether) gave **12d** (195 mg, 0.42 mmol, 72%) as a colourless oil. R_f 0.73 (30% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2953, 1611, 1246, 1207, 1035, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30-6.73 (14H, m), 6.31 (1H, dt, *J* = 14.0 and 7.5 Hz), 5.49 (1H, dt, *J* = 14.0 and 1.5 Hz), 4.52 (1H, d, *J* = 11.5

Hz), 4.46 (2H, s), 4.44 (1H, d, *J* = 11.5 Hz), 3.72 (3H, s), 3.56-3.49 (1H, m), 3.47-3.37 (m, 2H), 2.28 (2H, ddd, *J* = 7.5, 6.0 and 1.5 Hz), 2.08 (2H, s), 0.01 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 145.6, 140.2, 138.5, 130.9, 129.5, 129.3, 128.5, 128.4, 128.2, 127.7, 124.1, 113.8, 77.8, 73.5, 72.5, 71.8, 55.4, 36.1, 26.7, –1.6 (2C); HRMS (ESI+) calc. for $C_{29}H_{36}O_3SiNa$ $[M+Na]^+$ 483.2326, found 483.2326.

General procedure C: Fluoride Promoted Debenzylation / Cyclization. To a solution of benzyldimethylalkenylsilane (1.0 equiv.) in THF (5.0 mL mmol^{-1} substrate) was added TBAF•$3H_2O$ (1.0 M in THF, 0.25-1.0 equiv.). After stirring for 15 min (or until complete as judged by TLC), the mixture was diluted with Et_2O (15 mL mmol^{-1} substrate), and HCl (1 M, aq., 5 mL mmol^{-1} substrate) was added. The organic phase was separated and the aqueous phase extracted with Et_2O (x 2, 15 mL mmol^{-1}). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. 6-Membered siloxanes were purified *via* **rapid** flash column chromatography through a short column of silica gel (0.2-0.4 g of silica gel / mmol substrate). 5-Membered siloxanes are **extremely** unstable towards silica gel, but generally required no further purification and were used directly.

General procedure D: K_2CO_3 / MeOH Promoted Debenzylation / Cyclization. To a solution of the acetate (1.0 equiv.) in MeOH (3.0 mL / mmol substrate) was added K_2CO_3 (1.5 equiv.), and the resulting mixture was stirred vigorously. Upon completion (1-3 h, as judeged by TLC), the mixture was diluted with Et_2O (10 mL mmol^{-1} substrate), and NH_4Cl (sat., aq., 5 mL mmol^{-1}) was added. The organic phase was separated, and the aqueous phase extracted Et_2O (x 2, 10 mL mmol^{-1}). The combined organic phases were dried ($MgSO_4$), filtered and concentrated.

General procedure E: KOTMS Promoted Debenzylation / Cyclization. To a round-bottomed flask charged with $KOSiMe_3$ (1.3 equiv.) was added a solution of vinylsilane (1.0 equiv.) in THF (5.0 mL / mmol substrate). After stirring for 1 h, the mixture was diluted with Et_2O (15 mL mmol^{-1} substrate), and HCl (1 M, aq. 5 mL mmol^{-1} substrate) was added. The organic phase was separated, and the aqueous phase extracted with Et_2O (x 2, 15 mL mmol^{-1}). The combined organic phases were dried ($MgSO_4$), filtered and concentrated.

*5-(2-(Benzyloxy)ethyl)-2,2-dimethyl-2,5-dihydro-1,2-oxasilole (**13**).* Prepared using general procedure C, with vinylsilane **11c** (20 mg, 0.044 mmol) in THF (0.3 mL) and TBAF•$3H_2O$ (44 µL, 1.0 M in THF, 1.0 equiv.), and a 15 min reaction time. **13** (11 mg, 0.044 mmol, 99%) was obtained as a clear oil which required no further purification.

Also prepared using general procedure D, with vinylsilane **11b** (534 mg, 1.34 mmol) in MeOH (4.5 mL) and K_2CO_3 (278 mg, 2.01 mmol), and a 3 h reaction time. **13** (334 mg, 1.34 mmol, 99%) was obtained as a clear oil which required no further purification.

Also prepared using general procedure E, with vinylsilane **11a** (20 mg, 0.059 mmol) in THF (0.3 mL) and $KOSiMe_3$ (10 mg, 0.077 mmol), and a 1 h reaction time. **13** (15 mg, 0.059 mmol, 99%) was obtained as a clear oil which required no further purification. IR (thin film, ν_{max} / cm^{-1}) 2858, 1251, 1097, 853, 788; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.25 (5H, m), 6.86 (1H, dd, *J* = 10.5 and 1.5 Hz), 6.03 (1H, dd, *J* = 10.5 and 2.0 Hz), 4.87-4.80 (1H, m), 4.54 (1H, d, *J* = 12.0 Hz), 4.49 (1H, d, *J* = 12.0 Hz), 3.70-3.58 (2H, m), 2.02-1.91 (1H, m), 1.76-1.66 (1H, m), 0.25 (3H, s), 0.24 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 152.9, 137.9, 127.8, 127.1, 126.9, 126.1, 79.7, 72.5, 66.6, 37.0, 0.9, 0.0; HRMS (ESI+) calc. for $C_{14}H_{21}O_2Si$ $[M+H]^+$ 249.1305, found 249.1306.

*6-((Benzyloxy)methyl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasiline (**14**).* Prepared using general procedure C, with vinylsilane **12a** (6.13 g, 18.0 mmol) in THF (90 mL) and TBAF•$3H_2O$ (4.5 mL, 1.0 M in THF, 0.25 equiv.), and a 15 min reaction time. Purification *via* rapid column chromatography (5% Et_2O / petroleum ether) gave **14** (3.40 g, 13.2 mmol, 74%) as a colourless oil.

Also prepared using general procedure D, with vinylsilane **12b** (50 mg, 0.13 mmol) in MeOH (0.4 mL) and K_2CO_3 (27.0 mg, 0.20 mmol), and a 3 h reaction time. Purification *via* rapid column chromatography (5% Et_2O / petroleum ether) gave **14** (41 mg, 0.12 mmol, 93%) as a colourless oil.

Also prepared using general procedure E, with vinylsilane **12a** (164 mg, 0.48 mmol) in THF (2.4 mL) and $KOSiMe_3$ (80 mg, 0.62 mmol), and a 1 h reaction time. Purification *via* rapid column chromatography (5% Et_2O / petroleum ether) gave **14** (85 mg, 0.34 mmol, 71%) as a colourless oil. R_f 0.29 (5% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2859, 1355, 1129, 843, 789; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.13 (5H, m), 6.72-6.65 (1H, m), 5.79-5.71 (1H, m), 4.52 (1H, d, *J* = 12.0 Hz), 4.47 (1H, d, *J* = 12.0 Hz), 4.10-4.00 (1H, m), 3.46 (1H, dd, *J* = 9.5 and 5.5 Hz), 3.34 (1H, dd, *J* = 9.5 and 5.5 Hz), 2.26-1.99 (m, 2H), 0.11 (s, 3H), 0.10 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 146.8, 138.5, 128.5, 127.8, 127.7, 127.3, 74.6, 73.5, 70.5, 33.4, –0.1, –0.4; HRMS (ESI+) calc. for $C_{14}H_{21}O_2Si$ $[M+H]^+$ 249.1305, found 249.1307.

General procedure F: General Fluoride Promoted Cross-Coupling Procedure. To a vial containing the cyclic siloxane (1.0-1.2 equiv.), halide (1.0-1.2 equiv.) and $Pd(dba)_2$ (5.0 mol%) or $[allylPdCl]_2$ (2.5 mol%) was added TBAF•$3H_2O$ (1.0 M in THF, 2.0-3.0 equiv.). The resulting dark brown solution was stirred at room temperature. Upon completion (5 min to 16 h, as judged by TLC), the crude mixture was purified directly *via* column chromatography.

*(Z)-5-(Benzyloxy)-1-phenylpent-1-en-3-ol (**26a**).* Prepared following general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), iodobenzene (**25a**) (24 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (3.0 mg, 5.0 µmol) and TBAF•$3H_2O$ (0.2 mL, 1.0 M in THF, 0.20 mmol, 2.0 equiv.), with a 5 min reaction time. Purification *via* column chromatography (15% EtOAc / petroleum ether) gave **26a** (27 mg, 0.098 mmol, 98%) as a yellow oil. R_f 0.27 (20% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3432, 2860, 1452, 1028, 697; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.13 (10H, m), 6.48 (1H, d, *J* = 11.5 Hz), 5.66 (1H, dd, *J* = 11.5 and 9.0 Hz, *H*2), 4.83-4.74 (1H, m), 4.46 (2H, s), 3.73-3.64 (1H, m), 3.64-3.55 (1H, m), 2.76 (1H, br s), 2.01-1.89 (1H, m), 1.87-1.77 (1H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.0, 136.6, 134.0, 128.9, 128.5, 128.3, 127.7, 127.6, 127.2, 73.3, 68.5, 67.2, 36.9; HRMS

(ESI+) calc. for $C_{18}H_{20}O_2Na$ $[M+Na]^+$ 291.1356, found 291.1356.

*(Z)-1-(Benzyloxy)-5-phenylpent-4-en-2-ol (**27a**).* Prepared following general procedure F with **14** (25 mg, 0.10 mmol, 1.0 equiv.), iodobenzene (**25a**) (24 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (3.0 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.2 mL, 1.0 M in THF, 0.20 mmol, 2.0 equiv.), with a 15 min reaction time. Purification *via* column chromatography (15% EtOAc / petroleum ether) gave **27a** (27 mg, 0.10 mmol, 99%) as a yellow oil. R_f 0.25 (20% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3405, 2862, 1099, 737, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.22 (10H, m) 6.58 (1H, dt, *J* = 11.5 and 1.5 Hz), 5.77 (1H, dt, *J* = 11.5 and 7.5 Hz), 4.55 (2H, s), 4.02-3.91 (1H, m), 3.54 (1H, dd, *J* = 9.5 and 3.5 Hz), 3.40 (1H, dd, *J* = 9.5 and 7.5 Hz), 2.61-2.51 (3H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.9, 137.3, 131.2, 128.8, 128.5, 128.3, 127.9, 127.8, 127.7, 126.8, 74.0, 73.4, 70.5, 32.5; HRMS (ESI+) calc. for $C_{18}H_{20}O_2Na$ $[M+Na]^+$ 291.1356, found 291.1356.

(Z)-1-(((5-(Benzyloxy)-1-phenylpent-1-en-3-yl)oxy)methyl)-4-methoxybenzene (**26b**), and 1-(((5-(benzyloxy)pent-1-en-3-yl)oxy)methyl)-4-methoxybenzene (**26b-desilylation**). Prepared following general procedure F with **11d** (46 mg, 0.10 mmol, 1.0 equiv.), iodobenzene (**25a**) (24 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (3.0 mg, 5.0 μmol) and TBAF•$3H_2O$ (0.2 mL, 1.0 M in THF, 0.20 mmol, 2.0 equiv.), with a 30 min reaction time. Purification via column chromatography (15% EtOAc / petroleum ether) gave **26b** (15 mg, 0.038 mmol, Z:E 3:1, 38%) and **26b-desilylation** (15 mg, 0.048 mmol, 48%) as colourless oils. **26b**: R_f 0.39 (25% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2925, 1612, 1454, 1035, 698; ^1H NMR (400 MHz, $CDCl_3$) δ (3:1 Z/E mixture, major isomer reported) 7.41-6.67 (15H, m), 5.64 (1H, dd, J = 11.5 and 9.0 Hz), 4.64 (1H, td, J = 9.0 and 4.5 Hz), 4.48-4.37 (3H, m), 4.09 (1H, d, J = 11.3 Hz), 3.73 (3H, s), 3.69-3.52 (2H, m), 2.08-1.84 (2H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 133.5, 132.4, 130.8, 129.8, 129.6, 129.1, 128.8, 128.4, 127.9, 127.7, 127.5, 127.2, 113.9, 113.7, 73.1, 70.8, 69.9, 67.0, 55.3, 35.9; HRMS (ESI+) calc. for $C_{26}H_{28}O_3Na$ $[M+Na]^+$ 411.1931, found 411.1930. **26b-desilylation**: R_f 0.70 (25% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2933, 2860, 1613, 1513, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-6.83 (9H, m), 5.80-5.70 (1H, m), 5.26-5.20 (2H, m), 4.52 (1H, d, J = 11.5 Hz), 4.27 (1H, d, J = 11.5 Hz), 4.01-3.90 (1H, m), 3.79 (3H, s), 3.64-3.48 (2H, m), 1.97-1.87 (1H, m), 1.86-1.76 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 139.0, 131.0, 129.9, 129.5, 128.5, 127.8, 127.7, 117.2, 113.9, 77.3, 73.1, 70.1, 66.8, 55.4, 36.0; HRMS (ESI+) calc. for $C_{20}H_{24}O_3Na$ $[M+Na]^+$ 335.1618, found: 335.1617.

*(Z)-1-(((1-(Benzyloxy)-5-phenylpent-4-en-2-yl)oxy)methyl)-4-methoxybenzene (**27b**).* Prepared following general procedure F with **12d** (24 mg, 0.052 mmol, 1.0 equiv.), iodobenzene (**25a**) (13 mg, 0.063 mmol, 1.2 equiv.), $Pd(dba)_2$ (1.5 mg, 2.6 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.1 mL, 1.0 M in THF, 0.10 mmol, 2.0 equiv.), with a 30 min reaction time. Purification *via* column chromatography (15% EtOAc / petroleum ether) gave **27b** (19 mg, 0.049 mmol, 94%) as a yellow oil. R_f 0.38 (10% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2902, 2860, 1613, 1495, 1208, 698; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-6.14 (12H, m), 6.86-6.79 (2H, m), 6.47 (1H, dt, *J* = 11.5 and 1.5 Hz), 5.70 (1H, dt, *J* = 11.5 and 7.5 Hz), 4.57 (1H, d, *J* = 11.5 Hz), 4.51 (1H, d, *J* = 11.5 Hz), 4.48 (2H, s), 3.76 (3H, s), 3.68 (1H, quint., *J* = 5.5 Hz), 3.55-3.46 (2H, m), 2.65-2.56 (2H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 138.5, 137.5, 130.9, 130.8, 129.5, 128.9, 128.5, 128.3 (2C), 127.7 (2C) 126.8, 113.9, 77.7, 73.5, 72.5, 71.7, 55.4, 31.1; HRMS (ESI+) calc. for $C_{26}H_{28}O_3Na$ $[M+Na]^+$ 411.1931, found 411.1933.

*(4Z,6E)-1-(Benzyloxy)-7-phenylhepta-4,6-dien-3-ol (**26c**).* From (*E*)-iodostyrene, **25b**: Prepared following general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), (*E*)-iodostyrene (**25b**)[29] (28 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 45 min reaction time. Purification *via* column chromatography (20% EtOAc / petroleum ether) gave **26c** (23 mg, 0.078 mmol, 78%) as a yellow oil.

From (*E*)-bromostyrene, **25c**: Prepared following general procedure F with **13** (50 mg, 0.20 mmol, 1.0 equiv.), (*E*)-bromostyrene (**25c**)[30] (44 mg, 0.24 mmol, 1.2 equiv.), $Pd(dba)_2$ (6.0 mg, 0.010 mmol, 5.0 mol%) and TBAF•$3H_2O$ (0.60 mL, 1.0 M in THF, 0.60 mmol, 3.0 equiv.), with a 15 min reaction time. Purification *via* column chromatography (20% EtOAc / petroleum ether) gave **27b** (46 mg, 0.16 mmol, 78%) as a yellow oil. R_f 0.25 (20% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3403, 2861, 1453, 1094, 742; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.12 (10H, m), 7.03 (1H, ddd, *J* = 15.5, 11.5 and 1.0 Hz), 6.50 (1H, d, *J* = 15.5 Hz), 6.19-6.11 (1H, m), 5.50-5.40 (1H, m), 4.96-4.85 (1H, m), 4.45 (2H, s), 3.69-3.61 (1H, m), 3.61-3.52 (1H, m), 2.70 (1H, br s), 2.01-1.88 (1H, m), 1.78-1.69 (1H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.0, 137.1, 134.2, 133.7, 130.0, 128.6, 128.5, 127.8, 127.7, 127.6, 126.6, 123.8, 73.3, 68.1, 67.2, 37.1; HRMS (ESI+) calc. for $C_{20}H_{22}O_2Na$ $[M+Na]^+$ 317.1512, found 317.1512.

*(4Z,6E)-1-(Benzyloxy)-7-phenylhepta-4,6-dien-2-ol (**27c**).* From (*E*)-iodostyrene, **25b**: Prepared following general procedure F with **14** (25 mg, 0.10 mmol, 1.0 equiv.), (*E*)-iodostyrene[29] (**25b**) (28 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 16 h reaction time. Purification *via* column chromatography (20% EtOAc / petroleum ether) gave **27c** (22 mg, 0.075 mmol, 75%) as a yellow oil.

From (*E*)-bromostyrene, **25c**: Prepared following general procedure F with **14** (25 mg, 0.10 mmol, 1.0 equiv.), (*E*)-bromostyrene[30] (**25c**) (22 mg, 0.12 mmol, 1.2 equiv.), $[allylPdCl]_2$ (0.9 mg, 2.5 μmol, 2.5 mol%) and TBAF•$3H_2O$ (0.30 mL, 1 M in THF, 0.30 mmol, 3.0 equiv.), with a 5 h reaction time. Purification *via* column chromatography (20% EtOAc / petroleum ether) gave **27c** (18 mg, 0.068 mmol, 68%) as a yellow oil. R_f 0.19 (20% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3437, 2859, 1595, 1092, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46-7.19 (10H, m), 7.06(1H, dd, *J* = 15.5 and 11.0 Hz), 6.57 (1H, d, *J* = 15.5 Hz), 6.50 (1H, t, *J* = 11.0 Hz), 5.56 (1H, dt, *J* = 11.0 and 8.0 Hz), 4.57 (2H, s), 3.99-3.89 (1H, m), 3.57 (1H, dd, *J* = 9.5 and 3.5 Hz), 3.44 (1H, dd, *J* = 9.5 and 7.5 Hz), 2.58-2.50 (2H, m), 2.41 (1H, br s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.9, 137.4,

133.2, 131.4, 128.6, 128.5, 127.8, 127.7, 127.6, 127.4, 126.5, 124.0, 73.7, 73.5, 70.3, 32.1; HRMS (ESI+) calc. for $C_{20}H_{22}O_2Na$ $[M+Na]^+$ 317.1512, found 317.1501.

*(E)-1-(((3-Iodoallyl)oxy)methyl)-4-methoxybenzene (**25d**).* Prepared following general procedure A using (*E*)-3-iodoprop-2-en-1-ol[31] (320 mg, 1.74 mmol), scandium(III) triflate (128 mg, 0.26 mmol), toluene (9 mL), and 4-methoxybenzyl 2,2,2-trichloroacetimidate (0.54 mL, 2.61 mmol). Purification *via* column chromatography (2.5% → 5% Et_2O / petroleum ether) gave **25d** (346 mg, 1.14 mmol, 65%) as a colourless oil. R_f 0.35 (5% Et_2O / petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 (2H, d, *J* = 8.5 Hz), 6.89 (2H, d, *J* = 8.5 Hz), 6.65 (1H, dt, *J* = 14.5 and 5.5 Hz), 6.39 (1H, dt, *J* = 14.5 and 1.5 Hz), 4.45 (2H, s), 3.92 (2H, dd, *J* = 5.5 and 1.5 Hz), 3.81 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 142.5, 129.8, 129.4, 113.9, 78.8, 72.0, 71.5, 55.3. Spectroscopic data in agreement with the literature.[32]

*(E)-1-(((3-Bromoallyl)oxy)methyl)-4-methoxybenzene (**25e**).* Prepared following general procedure A with (*E*)-3-bromoprop-2-en-1-ol[33] (1.00 g, 7.30 mmol), scandium(III) triflate (539 mg, 1.10 mmol), 4-methoxybenzyl 2,2,2-trichloroacetimidate (2.3 mL, 11 mmol) and toluene (46 mL). Purification *via* column chromatography (2%→4% Et_2O / petroleum ether) gave **25e** (1.10 g, 4.28 mmol, 59%) as a colourless oil. R_f 0.56 (30% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2837, 1613, 1248, 1103, 820; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.30-6.84 (4H, m), 6.40-6.27 (2H, m), 4.45 (2H, s), 3.95 (2H, d, *J* = 5.0 Hz), 3.81 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) *δ* 159.5, 134.4, 129.9, 129.6, 114.0, 108.7, 72.1, 69.5, 55.4; HRMS (CI+) calc. for $C_{11}H_{17}BrNO_2$ $[M+NH_4]^+$ 274.044, found 274.044.

*(4Z,6E)-1-(Benzyloxy)-8-((4-methoxybenzyl)oxy)octa-4,6-dien-3-ol (**26d**).* **From vinyl iodide 25d**: Prepared using general procedure F with **13** (30 mg, 0.12 mmol, 1.2 equiv.), vinyl iodide **25d** (30 mg, 0.10 mmol, 1.0 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 15 min reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **26d** (27 mg, 0.073 mmol, 73%) as a yellow oil.

From vinyl bromide 25e: Prepared using general procedure F with **13** (30 mg, 0.12 mmol, 1.2 equiv.), vinyl bromide **25e** (26 mg, 0.10 mmol, 1.0 equiv.), $[allylPdCl]_2$ (0.9 mg, 2.5 μmol, 2.5 mol%) and TBAF•$3H_2O$ (0.30 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 3 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **26d** (21 mg, 0.056 mmol, 57%) as a yellow oil. R_f 0.15 (30% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3430, 2854, 1513, 1247, 1096, 1033; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32-7.16 (7H, m), 6.80 (2H, d, *J* = 8.5 Hz), 6.50 (1H, dq, *J* = 15.0, 11.0 and 1.0 Hz), 5.98 (1H, t, *J* = 11.0 Hz), 5.75 (1H, dt, *J* = 15.0 and 6.0 Hz), 5.38 (1H, dd, *J* = 11.0 and 9.0 Hz), 4.80-4.71 (1H, m), 4.44 (2H, s), 4.36 (2H, s), 3.95 (2H, dd, *J* = 6.0 and 1.0 Hz), 3.73 (3H, s), 3.66-3.59 (1H, m), 3.58-3.50 (1H, m), 2.64 (1H, br s), 1.93-1.81 (1H, m), 1.74-1.65 (1H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 138.0, 133.6, 131.8, 130.3, 129.5, 129.1, 128.5, 128.4, 127.7, 127.6, 127.4, 113.9, 113.8, 133.7, 73.3, 72.0, 70.1, 68.2, 67.1, 55.3, 36.9; HRMS (ESI+) calc. for $C_{23}H_{28}O_4Na$ $[M+Na]^+$ 391.1880, found 391.1867.

*(4Z,6E)-1-(benzyloxy)-8-((4-methoxybenzyl)oxy)octa-4,6-dien-2-ol (**27d**).* **From vinyl iodide 25d**: Prepared using general procedure F with **14** (30 mg, 0.12 mmol, 1.2 equiv.), vinyl iodide **25d** (30 mg, 0.10 mmol, 1.0 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 16 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **27d** (24 mg, 0.065 mmol, 65%) as a yellow oil.

From vinyl bromide 25e: Prepared using general procedure F with **14** (30 mg, 0.12 mmol, 1.2 equiv.), vinyl bromide **25e** (26 mg, 0.10 mmol, 1.0 equiv.), $[allylPdCl]_2$ (0.9 mg, 2.5 μmol, 2.5 mol%) and TBAF•$3H_2O$ (0.30 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 3 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **27d** (22 mg, 0.060 mmol, 60%) as a yellow oil. R_f 0.19 (30% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3433, 2856, 1513, 1247, 989; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.25 (7H, m), 6.87 (2H, d, *J* = 8.5 Hz), 6.56-6.47 (1H, m), 6.11 (1H, t, *J* = 11.0 Hz), 5.80 (1H, dt, *J* = 12.5 and 6.0 Hz), 5.47 (1H, dt, *J* = 11.0 and 7.5 Hz), 4.54 (2H, s), 4.43 (2H, s), 4.03 (2H, d, *J* = 6.0 Hz), 3.91-3.83 (1H, m), 3.78 (3H, s), 3.51 (1H, dd, *J* = 9.5 and 3.5 Hz), 3.37 (1H, dd, *J* = 9.5 and 7.5 Hz), 2.45-2.33 (3H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 138.0, 130.7, 130.4, 130.3, 129.5, 128.5, 127.8, 127.7, 127.6, 127.1, 113.8, 73.8, 73.4, 71.9, 70.3, 70.2, 55.3, 31.8; HRMS (ESI+) calc. for $C_{23}H_{28}O_4Na$ $[M+Na]^+$ 391.1879, found 391.1873.

*(E)-1-(((3-Iodo-2-methylallyl)oxy)methyl)-4-methoxybenzene (**25f**).* Prepared following general procedure A with (*E*)-3-iodo-2-methylprop-2-en-1-ol[34] (352 mg, 1.78 mmol), scandium(III) triflate (131 mg, 0.26 mmol), toluene (9 mL) and 4-methoxybenzyl 2,2,2-trichloroacetimidate (0.55 mL, 2.67 mmol). Purification *via* column chromatography (2.5%→5% Et_2O / petroleum ether) gave **25f** (420 mg, 1.32 mmol, 74%) as a clear oil. IR (thin film, ν_{max} / cm^{-1}) 2835, 1612, 1513, 1247, 1035; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.25 (2H, d, *J* = 8.5 Hz), 6.89 (2H, d, *J* = 8.5 Hz), 6.28-6.25 (1H, m), 4.41 (2H, s), 3.97 (2H, d, *J* = 1.0 Hz), 3.81 (3H, s) 1.85 (3H, d, *J* = 1.0 Hz); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 145.0, 130.0, 129.4, 113.9, 78.6, 73.7, 71.7, 55.3, 21.6; HRMS (Cl+) calc. for $C_{12}H_{19}INO_2$ $[M+NH_4]^+$ 336.0460, found 336.0459. NMR spectroscopic data in agreement with the literature.[35]

*(4Z,6E)-1-(Benzyloxy)-8-((4-methoxybenzyl)oxy)-7-methylocta-4,6-dien-3-ol (**26e**).* Prepared using general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), vinyl iodide **25f** (38 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 1 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **26e** (32 mg, 0.084 mmol, 84%) as a yellow oil. R_f 0.20 (30% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3425, 2856, 1513, 1247, 1033; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.23 (7H, m), 6.88 (2H, d, *J* = 8.5 Hz), 6.38-6.25 (2H, m), 5.48 (1H, dd, *J* = 10.5, and 8.5 Hz), 4.89-4.81 (1H, m), 4.52 (2H, s), 4.39 (2H, s), 3.93 (2H, s), 3.80 (3H, s), 3.73-3.66 (1H, m), 3.66-3.58 (1H, m), 2.73 (1H,

br s), 1.99-1.89 (1H, m), 1.82-1.70 (1H, m), 1.79 (3H, s); ^{13}C NMR{^{1}H} (101 MHz, $CDCl_3$) δ 159.2, 138.0, 137.0, 133.2, 130.4, 129.4, 128.5, 127.7, 127.6, 125.0, 121.3, 113.8, 75.5, 73.3, 71.6, 68.3, 67.0, 55.3, 36.9, 14.2; HRMS (ESI+) calc. for $C_{24}H_{30}O_4Na$ $[M+Na]^+$ 405.1946, found 405.19272.

*(4Z,6E)-1-(Benzyloxy)-8-((4-methoxybenzyl)oxy)-7-methylocta-4,6-dien-2-ol (**27e**).* Prepared using general procedure F with **14** (25 mg, 0.10 mmol, 1.0 equiv.), vinyl iodide **25f** (38 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 µmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 16 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **27e** (27 mg, 0.073 mmol, 73%) as a yellow oil. R_f 0.23 (30% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3446, 2856, 1513, 1247, 1034; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.28 (7H, m), 6.87 (2H, d, *J* = 8.5 Hz), 6.40-6.26 (2H, m), 5.55-5.45 (1H, m), 4.54 (2H, s), 4.39 (2H, s), 3.93 (2H, s), 3.93-3.83 (1H, m), 3.79 (3H, s), 3.52 (1H, dd, *J* = 9.5 and 3.5 Hz), 3.38 (1H, dd, *J* = 9.5 and 7.5 Hz), 2.44-2.38 (2H, m), 2.37 (1H, d, *J* = 3.5 Hz), 1.78 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ_C 159.2, 138.0, 135.8, 130.5, 129.4, 128.5, 127.8, 127.7, 126.6, 126.5, 121.7, 113.8, 75.7, 73.9, 73.4, 70.3, 55.3, 31.7, 14.3; HRMS (ESI+) calc. for $C_{24}H_{30}O_4Na$ $[M+Na]^+$ 405.2036, found 405.2028.

(2E,4E)-5-Iodopenta-2,4-dienal and (2E,4Z)-5-Iodopenta-2,4-dienal. To a solution of triphenylphosphine (10.6 g, 40.4 mmol, 1.1 equiv.) in CH_2Cl_2 (200 mL) at 0 °C was added iodine (10.25 g, 41.7 mmol, 1.1 equiv.), followed by glutaconaldehyde potassium salt (5.00 g, 36.7 mmol, 1.0 equiv.).[36] The mixture was stirred in the dark for 72 h, then $NaHCO_3$ (100 mL, 5% w/v, aq.) was added. The organic phase was separated, and the aqueous phase extracted with Et_2O (3 × 150 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated. Purification twice by column chromatography (40% Et_2O / petroleum ether; 2% Et_2O / petroleum ether) gave (2*E*,4*Z*)-5-iodopenta-2,4-dienal (1.92 g, 9.18 mmol, 25%), and (2*E*,4*E*)-5-iodopenta-2,4-dienal (2.18 g, 10.3 mmol 28%) as orange solids. (2*E*,4*Z*)-5-iodopenta-2,4-dienal: R_f 0.32 (25% Et_2O / petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (1H, d, *J* = 8.0 Hz), 7.33-7.18 (1H, m), 7.08-6.99 (2H, m), 6.37 (1H, dd, *J* = 15.5 and 8.0 Hz); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 193.7, 150.0, 136.8, 135.1, 95.2. (2*E*,4*E*)-5-iodopenta-2,4-dienal: R_f 0.24 (25% Et_2O / petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (1H, d, *J* = 8.0 Hz), 7.31 (1H, ddd, *J* = 14.5, 11.0 and 1.0 Hz), 7.15 (1H, dt, *J* = 14.5 and 1.0 Hz), 6.97 (1H, ddd, *J* = 15.5, 11.0 and 1.0 Hz), 6.14 (1H, ddt, *J* = 15.5, 8.0 and 1.0 Hz); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 193.4, 149.7, 143.3, 131.3, 92.3. Spectroscopic data in agreement with the literature.[26b]

*1-((((2E,4E)-5-Iodopenta-2,4-dien-1-yl)oxy)methyl)-4-methoxybenzene (**25g**).* To a solution of (2*E*,4*E*)-5-iodopenta-2,4-dienal (500 mg, 2.40 mmol, 1.0 equiv., prepared as described above) in CH_2Cl_2 (6.0 mL) at –78 °C was added DIBALH (3.6 mL, 1.0 M in cyclohexane, 3.6 mmol, 1.5 equiv.) dropwise. After stirring for 1 h, the reaction was quenched by sequential addition of water (0.15 mL), NaOH (0.15 mL, 15% w/v, aq.), and water (0.36 mL). The mixture was warmed to room temperature, then $MgSO_4$ was added. The resulting mixture was stirred for 15 min, filtered, and concentrated. Purification *via* column chromatography (50% EtOAc / petroleum ether) gave (2*E*,4*E*)-5-iodopenta-2,4-dien-1-ol (382 mg, 1.82 mmol, 76%) as a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (1H, dd, *J* = 14.5 and 11.0 Hz), 6.35 (1H, d, *J* = 14.5 Hz), 6.20 (1H, ddt, *J* = 15.5, 11.0 and 1.5 Hz), 5.86 (1H, dt, *J* = 15.5 and 5.5 Hz), 4.16 (2H, app. t, *J* = 5.0 Hz), 1.43 (1H, t, *J* = 6.0 Hz); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.6, 133.2, 130.7, 79.6, 62.9. Spectroscopic data in agreement with the literature.[16] To a solution of (2*E*,4*E*)-5-iodopenta-2,4-dien-1-ol (370 mg, 1.76 mmol, 1.0 equiv.) and scandium(III) triflate (130 mg, 264 µmol, 0.15 equiv.) in toluene (11 mL) was added 4-methoxybenzyl 2,2,2-trichloroacetimidate (0.55 mL, 2.7 mmol, 1.5 equiv.). After stirring for 1 h, $NaHCO_3$ (20 mL, sat., aq.) was added, and the mixture was diluted with Et_2O (20 mL). The organic phase separated, and the aqueous phase extracted with Et_2O (2 × 20 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (7% Et_2O / petroleum ether) gave **25g** (476 mg, 1.44 mmol, 82%) as a colourless oil. R_f 0.70 (30% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2836, 1612, 1512, 1174, 820; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.24 (2H, m), 7.04 (1H, dt, *J* = 14.5 and 11.0 Hz), 6.92-6.86 (2H, m), 6.34 (1H, d, *J* = 14.5 Hz), 6.20 (1H, dd, *J* = 15.5 and 11.0 Hz), 5.81 (1H, dt, *J* = 15.5 and 6.0 Hz), 4.45 (2H, s), 4.08-3.90 (2H, m), 3.81 (3H, s); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.4, 144.7, 132.0, 131.0, 130.3, 129.5, 114.0, 79.5, 72.2, 69.6, 55.4; HRMS (ESI+) calc. for $C_{13}H_{15}O_2INa$ $[M+Na]^+$ 353.0009, found 353.0009.

*1-((((2E,4E)-5-Bromopenta-2,4-dien-1-yl)oxy)methyl)-4-methoxybenzene (**25h**).* To a solution of triphenylphosphine (4.29 g, 16.4 mmol, 1.1 equiv.) in CH_2Cl_2 (80 mL) at 0 °C was added bromine (0.82 mL, 16 mmol, 1.1 equiv.), followed by glutaconaldehyde potassium salt (2.00 g, 14.7 mmol, 1.0 equiv.).[36] The mixture was stirred in the dark for 16 h, then $NaHCO_3$ (50 mL, 5% w/v, aq.) was added. The organic phase was separated, and the aqueous phase extracted with Et_2O (70 mL). The combined organic phases were washed with brine (50 mL), dried ($MgSO_4$), filtered and concentrated. Purification twice by column chromatography (40% Et_2O / petroleum ether; 2% Et_2O / petroleum ether) gave (2*E*,4*Z*)-5-Bromopenta-2,4-dienal (520 mg, 3.23 mmol, 22%) and (2*E*,4*E*)-5-Bromopenta-2,4-dienal (690 mg, 4.26 mmol, 29%) as brown solids. Spectroscopic data was in agreement with the literature.[26b] To a solution of the thus prepared (2*E*,4*E*)-5-bromopenta-2,4-dienal (680 mg, 4.22 mmol, 1.0 equiv.) in CH_2Cl_2 (11.0 mL) at –78 °C was added DIBALH (6.4 mL, 1.0 M in cyclohexane, 6.4 mmol, 1.5 equiv.) dropwise. After stirring for 1 h, the reaction was quenched by sequential addition of water (0.26 mL), NaOH (0.26 mL, 15% w/v, aq.), and water (0.64 mL). The mixture was warmed to room temperature, then $MgSO_4$ was added. The mixture was stirred for 15 min, filtered, and concentrated. Purification *via* column chromatography (50% EtOAc / petroleum ether) gave (2*E*,4*E*)-5-Bromopenta-2,4-dien-1-ol (492 mg, 3.00 mmol, 71%) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (1H, dd, *J* = 13.5 and 11.0 Hz), 6.33 (1H, dt, *J* = 13.5 and 1.0 Hz), 6.20

(1H, ddt, *J* = 15.5, 11.0 and 1.5 Hz), 5.87 (1H, dtt, *J* = 15.5, 5.5 and 1.0 Hz), 4.17 (app. t, 2H, *J* = 4.0 Hz), 1.49 (1H, t, *J* = 5.0 Hz); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ_C 136.8, 133.4, 128.3, 109.2, 63.0. Spectroscopic data in agreement with the literature.[37] Following general procedure B, (2*E*,4*E*)-5-bromopenta-2,4-dien-1-ol (468 mg, 2.87 mmol), scandium(III) triflate (215 mg, 437 μmol), 4-methoxybenzyl 2,2,2-trichloroacetimidate (0.91 mL, 4.4 mmol) and toluene (19 mL) afforded **25h** (478 mg, 1.00 mmol, 59%) as a yellow oil after purification *via* column chromatography (2%→4% Et_2O / petroleum ether). R_f 0.19 (4% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2836, 1612, 1585, 1512, 736; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-6.85 (4H, m), 6.72 (1H, ddd, *J* = 13.5, 11.0 and 1.0 Hz), 6.35-6.26 (1H, m), 6.24-6.16 (1H, m), 5.85-5.78 (1H, m), 4.44 (s, 2H), 4.03-3.96 (m, 2H), 3.80 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.4, 137.0, 131.2, 130.2, 129.5, 114.0, 109.1, 72.2, 69.7, 55.4; HRMS (CI+) calc. for $C_{13}H_{15}O_2Br$ $[M+H]^+$ 283.0331, found 283.0326.

*(4Z,6E,8E)-1-(Benzyloxy)-10-((4-methoxybenzyl)oxy)deca-4,6,8-trien-3-ol (**26f**).* **From iododiene 25g**: Prepared using general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), **25g** (40 mg, 0.10 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 16 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **26f** (32 mg, 0.081 mmol, 81%) as a yellow oil.

From bromodiene **25h**: Prepared using general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), **25h** (34 mg, 0.12 mmol, 1.2 equiv.), $[allylPdCl]_2$ (0.9 mg, 2.5 μmol, 2.5 mol%) and TBAF•$3H_2O$ (0.30 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 3 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **26f** (23 mg, 0.058 mmol, 58%) as a yellow oil. R_f 0.20 (30% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3428, 2861, 151, 1248, 1095; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.20 (7H, m), 6.89 (2H, d, *J* = 8.5 Hz), 6.89-6.44 (1H, m), 6.30-6.19 (2H, m), 6.10-6.01 (1H, m), 5.81 (1H, dt, *J* = 14.0 and 6.0 Hz), 5.44 (1H, dd, *J* = 10.5 and 9.0 Hz), 4.88-4.77 (1H, m), 4.50 (2H, s), 4.43 (2H, s), 4.03 (2H, d, *J* = 6.0 Hz), 3.79 (3H, s), 3.71-3.65 (1H, m), 3.63-3.55 (1H, m), 2.65 (1H, br s), 1.99-1.88 (1H, m), 1.80-1.70 (1H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 138.0, 133.8, 133.7, 132.5, 130.3, 129.6, 129.4, 128.5, 127.8, 127.7, 127.6, 113.8, 73.3, 71.8, 70.1, 68.2, 67.2, 55.3, 36.9; HRMS (ESI+) calc. for $C_{25}H_{30}O_4Na$ $[M+Na]^+$ 417.1911, found 417.1927.

*(4Z,6E,8E)-1-(Benzyloxy)-10-((4-methoxybenzyl)oxy)deca-4,6,8-trien-2-ol (**27f**).* **From iododiene 25g**: Prepared using general procedure F with **14** (25 mg, 0.10 mmol, 1.0 equiv.), **25g** (40 mg, 0.10 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 16 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **27f** (25 mg, 0.063 mmol, 63%) as a yellow oil.

From bromodiene 25h: Prepared using general procedure F with **14** (25 mg, 0.10 mmol, 1.0 equiv.), **25h** (34 mg, 0.12 mmol, 1.2 equiv.), $[allylPdCl]_2$ (0.9 mg, 2.5 μmol, 2.5 mol%) and TBAF•$3H_2O$ (0.30 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 3 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **27f** (21 mg, 0.053 mmol, 53%) as a yellow oil. R_f 0.17 (30% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3443, 2856, 1513, 1247, 944; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39-7.25 (7H, m), 6.89 (2H, d, *J* = 8.5 Hz), 6.89 (1H, dd, *J* = 14.0 and 11.5 Hz), 6.35-6.10 (3H, m), 5.82 (1H, dt, *J* = 14.5 and 6.0 Hz), 5.50 (1H, dt, *J* = 10.5 and 8.0 Hz), 4.55 (2H, s), 4.45 (2H, s), 4.05 (2H, d, *J* = 6.0 Hz), 3.93-3.85 (1H, m), 3.81 (3H, s), 3.53 (1H, dd, *J* = 9.5 and 3.5 Hz), 3.39 (1H, dd, *J* = 9.5 and 7.0 Hz), 2.47-2.40 (2H, m), 2.37 (1H, d, *J* = 4.0 Hz); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.2, 137.9, 132.8, 132.7, 131.0, 130.4, 130.2, 129.4, 128.5, 128.0, 127.8, 127.7, 127.4, 113.8, 73.7, 73.4, 71.8, 70.2, 70.1, 55.3, 31.9; HRMS (ESI+) calc. for $C_{25}H_{30}O_4Na$ $[M+Na]^+$ 417.2036, found 417.2045.

*(2E,4Z)-5-Iodopenta-2,4-dien-1-ol (**25i**).* To a solution of (2*E*,4*Z*)-5-iodopenta-2,4-dienal (100 mg, 0.481 mmol, 1.0 equiv., prepared as described above) in CH_2Cl_2 (1.2 mL) at –78 °C was added DIBALH (0.72 mL, 1.0 M in cyclohexane, 0.72 mmol, 1.5 equiv.) dropwise. After stirring for 1 h, the reaction was quenched by sequential addition of water (0.03 mL), an aqueous solution of NaOH (0.03 mL, 15% w/v, aq.), and water (0.07 mL). The mixture was warmed to room temperature, and $MgSO_4$ was added. The mixture was stirred for 15 min, filtered, and concentrated. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **25i** (81 mg, 0.385 mmol, 80%) as a light yellow oil. R_f 0.17 (30% EtOAc / petroleum ether); ^1H NMR (400 MHz, $CDCl_3$) δ 6.76 (1H, dd, *J* = 10.0 and 7.5 Hz), 6.50-6.40 (1H, m), 6.30 (1H, d, *J* = 7.5 Hz), 6.12 (1H, dt, *J* = 15.5 and 5.5 Hz), 4.25 (2H, d, *J* = 5.0 Hz), 1.52 (1H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 137.7, 137.2, 130.9, 82.9, 63.3. Spectroscopic data in agreement with the literature.[12a]

*(2E,4Z,6Z)-10-(Benzyloxy)deca-2,4,6-triene-1,8-diol (**26g**).* Prepared using general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), vinyl iodide **25i** (25 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 4 h reaction time. Purification *via* column chromatography (50% EtOAc / petroleum ether) gave **26g** (14 mg, 0.051 mmol, 52%) as a yellow oil. R_f 0.22 (50% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3383, 2923, 1679, 1617, 1096, 1076, 699; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.11 (5H, m), 6.62-6.53 (1H, m), 6.40-6.32 (1H, m), 6.17-6.04 (1H, m), 5.96-5.85 (1H, m), 5.75 (1H, dt, *J* = 15.0 and 6.0 Hz), 5.42-3.44 (1H, m), 4.74-4.67 (1H, m), 4.36 (s, 2H), 4.08 (2H, dd, *J* = 6.0 and 1.5 Hz), 3.58-3.42 (2H, m), 2.62 (1H, s), 1.86-1.73 (1H, m), 1.70-1.40 (2H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 138.1, 134.6, 134.3, 130.1, 128.6, 127.9, 127.8, 125.9, 124.4, 124.2, 73.5, 68.4, 67.1, 63.5, 37.0; HRMS (ESI+) calc. for $C_{17}H_{22}O_3Na$ $[M+Na]^+$ 297.1461, found 297.1461.

*(4Z,6Z)-1-(Benzyloxy)-7-cyclohexylhepta-4,6-dien-3-ol (**26h**).* Prepared using general procedure F with **13** (25 mg, 0.10 mmol, 1.0 equiv.), vinyl iodide **25j**[38] (27 mg, 0.12 mmol, 1.2 equiv.), $Pd(dba)_2$ (2.9 mg, 5.0 μmol, 5.0 mol%) and TBAF•$3H_2O$ (0.3 mL, 1.0 M in THF, 0.30 mmol, 3.0 equiv.), with a 2 h reaction time. Purification *via* column

chromatography (25% EtOAc / petroleum ether) gave **26h** (14 mg, 0.051 mmol, 51%) as a yellow oil. R_f 0.27 (25% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3398, 2922, 1449, 1259, 1098, 1075, 697; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40-7.22 (5H, m), 6.33 (1H, app. t, J = 11.5 Hz), 6.15 (1H, app. t, J = 11.5 Hz), 5.49-5.38 (1H, m), 5.41-5.32 (1H, m), 4.87-4.78 (1H, m), 4.51 (2H, s), 3.72-3.58 (2H, m), 2.60 (s, 1H), 2.52-2.35 (1H, m), 1.99-1.87 (m, 1H), 1.82-1.01 (m, 10H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 140.3, 138.2, 133.0, 128.6, 127.8, 127.8, 125.0, 121.3, 73.4, 68.4, 67.0, 37.0, 36.6, 33.3, 33.2, 26.1, 26.0, 25.9; HRMS (ESI+) calc. for $C_{20}H_{28}O_2Na$ $[M+Na]^+$ 323.1982, found 323.1981.

*Ethyl 7-(benzyldimethylsilyl)-5-oxohept-6-ynoate (**36**).* To a solution of benzyldimethylsilylacetylene (177 mg, 1.02 mmol, 1.1 equiv.) in THF (1.0 mL) at –78 °C was added a solution of *n*-BuLi (0.50 mL, 2.1 M in Et_2O, 23.9 mmol, 1.15 equiv.) dropwise *via* syringe. The resulting mixture was stirred for 10 min, then a solution of $ZnCl_2$ (1.20 mL, 0.86 M in THF, 1.03 mmol, 1.1 equiv.) was added. After stirring at –78 °C for 10 min, the cooling bath was removed and the reaction was allowed to warm to 0 °C, then stirred for a further 30 min. Ethyl 5-chloro-5-oxopentanoate (**30**) (0.14 mL, 0.90 mmol, 1.0 equiv.) was added, and the reaction was stirred for 1 h at 0 °C, then allowed to warm to room temperature followed by further stirring for 1 h. The mixture was diluted with Et_2O (20 mL), and quenched by addition of NH_4Cl (5.0 mL, sat., aq.). The organic phase was separated, and the aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. Purification of the residue *via* column chromatography (15% Et_2O / petroleum ether) gave **36** (146 mg, 0.46 mmol, 52%) as a colourless oil. R_f 0.15 (10% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2963, 1732, 1676, 1112, 842; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.02 (5H, m), 4.14 (2H, q, J = 7.0 Hz), 2.63 (2H, t, J = 7.0 Hz), 2.26 (2H, t, J = 7.5 Hz), 2.26 (1H, s), 1.97 (2H, q, J = 7.0 Hz), 1.26 (3H, t, J = 7.0 Hz), 0.20 (6H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 186.7, 173.0, 138.0, 128.5, 128.4, 124.9, 103.0, 96.7, 60.6, 44.4, 33.2, 25.5, 19.1, 14.4, –2.6; HRMS (ESI+) calc. for $C_{18}H_{24}O_3Si$ $[M+H]^+$ 317.1574, found 317.1573.

*Ethyl (S)-5-acetoxy-7-(benzyldimethylsilyl)hept-6-ynoate (**37**).* To a degassed solution of **36** (100 mg, 0.32 mmol, 1.0 equiv.) in isopropyl alcohol (4.0 mL) under argon was added a solution of (1*S*,2*S*)-(+)-*N*-tosyl-1,2-diphenylethane-1,2-diamine[η^6-1-isopropyl-4-methylbenzene)-ruthenium(II) (4.6 mg, 6.0 μmol, 2.0 mol%) in CH_2Cl_2 (0.1 mL). The mixture was stirred for 1 h, then concentrated to give ethyl (*S*)-7-(benzyldimethylsilyl)-5-hydroxyhept-6-ynoate. This was redissolved in CH_2Cl_2 (2.0 mL), and acetic anhydride (0.07 mL, 0.64 mmol, 2.0 equiv.), Et_3N (0.14 mL, 0.96 mmol, 3.0 equiv.) and a crystal of 4-dimethylaminopyridine were added. After stirring for 1 h, NH_4Cl (5.0 mL sat., aq.) was added. The organic phase was separated, and the aqueous phase extracted with CH_2Cl_2 (2 × 5.0 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated. The residue was purified *via* column chromatography (15% → 25% Et_2O / petroleum ether) to give **37** (107 mg, 0.30 mmol, 94%) as a colourless oil. $[\alpha]_D^{20}$ –5.8 (*c* 0.1, $CHCl_3$); 99% *ee* (CHIRALPAK IB, 0.5% IPA / hexane, 1.3 mL/min, t_R (5*R*) 6.8 min, t_R (5*S*) 7.6 min); R_f 0.40 (50% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2962, 1736, 1372, 1231, 1159, 1022, 840; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.01 (5H, m), 5.42-5.34 (1H, m), 4.14 (2H, q, J = 7.0 Hz), 2.38-2.30 (2H, m), 2.20 (1H, s), 2.09 (3H, s), 1.82-1.73 (2H, m), 1.26 (3H, t, J = 7.0 Hz), 0.14 (3H, s), 0.13 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.2, 169.9, 138.8, 128.5, 128.3, 124.5, 103.7, 89.2, 63.9, 60.5, 34.1, 33.8, 26.1, 21.2, 20.6, 14.4, –2.1; HRMS (ESI+) calc. for $C_{20}H_{28}O_4SiNa$ $[M+Na]^+$ 383.1649, found 383.1653.

*Ethyl (S)-4-(2,2-dimethyl-2,5-dihydro-1,2-oxasilol-5-yl)butanoate (**34**).* Ethyl (*S*,*Z*)-5-acetoxy-7-(benzyldimethylsilyl) hept-6-enoate was prepared using general procedure B with Pd / $CaCO_3$ (691 mg, 0.32 mmol) in toluene (30 mL), and **32** (2.34 g, 6.49 mmol) and quinoline (0.38 mL, 3.24 mmol, 50 mol%) in toluene (3.0 mL) and cyclohexene (3.30 mL), with a 30 min reaction time. Purification via column chromatography (15% Et_2O / petroleum ether) gave ethyl (*S*,*Z*)-5-acetoxy-7-(benzyldimethylsilyl)hept-6-enoate (1.93 g, 5.32 mmol, 82%) as a clear oil. $[\alpha]_D^{20}$ –7.2 (c 1.0, $CHCl_3$); R_f 0.45 (50% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2957, 1734, 1494, 1370, 833; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.02 (5H, m), 6.19 (1H, dd, J = 14.5 and 9.0 Hz), 5.69 (1H, dd, J = 14.5 and 1.0 Hz), 5.38-5.28 (1H, m), 4.14 (2H, q, J = 7.0 Hz), 2.35-2.22 (2H, m), 2.19 (2H, d, J = 3.0 Hz), 2.04 (3H, s), 1.71-1.40 (4H, m), 1.26 (3H, t, J = 7.0 Hz), 0.16 (3H, t, J = 3.0 Hz), 0.15 (3H, t, J = 3.0 Hz); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.3, 170.3, 145.9, 139.8, 131.7, 128.4, 128.3, 124.2, 74.2, 60.5, 34.4, 34.1, 26.5, 21.4, 20.7, 14.4, –1.6, –1.7; HRMS (ESI+) calc. for $C_{20}H_{34}O_4SiN$ $[M+NH_4]^+$ 380.2251, found 380.2261. Using general procedure C, a solution of this product (339 mg, 0.93 mmol) in THF (4.5 mL) and TBAF•$3H_2O$ (0.65 mL, 1.0 M in THF, 1.05 equiv.), with a 30 min reaction time, gave **34** (185 mg, 0.81 mmol, 87%) as a colourless oil which required no further purification; $[\alpha]_D^{20}$ +48.9 (c 1.0, $CHCl_3$); R_f 0.45 (50% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 2959, 1734, 1250, 1030, 853; ^1H NMR (400 MHz, $CDCl_3$) δ 6.81 (1H, dd, J = 10.5 and 1.5 Hz), 6.04 (1H, dd, J = 10.5 and 2.0 Hz), 4.71 (1H, ddt, J = 6.5, 4.0 and 2.0 Hz), 4.10 (2H, q, J = 7.0 Hz), 2.36 (2H, t, J = 7.0 Hz), 1.84-1.59 (3H, m), 1.46 (1H, dddd, J = 12.5, 10.0, 6.5 and 5.5 Hz), 1.24 (3H, t, J = 7.0 Hz), 0.25 (3H, s), 0.23 (3H, s); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 173.7, 153.2, 127.3, 82.5, 60.3, 36.5, 34.4, 20.8, 14.4, 1.5, 0.7; HRMS (ESI+) calc. for $C_{11}H_{21}O_3SiN$ $[M+H]^+$ 229.1255, found 229.1256.

(1*E*,3*E*)-1-Iodotrideca-1,3-dien-5-ol ((±)-**38**). To a solution of triphenylphosphine (2.58 g, 9.8 mmol, 1.1 equiv.) in CH_2Cl_2 (50 mL) at 0 °C, was added iodine (2.50 g, 9.8 mmol, 1.1 equiv.), followed by glutaconaldehyde potassium salt[36] (1.22 g, 9.8 mmol, 1.0 equiv.). The reaction was stirred in the dark for 72 h, then $NaHCO_3$ (100 mL, 5% w/v, aq.) was added. The organic phase was separated, and the aqueous phase extracted with Et_2O (3 × 150 mL). The combined organic phases were washed with brine (100 mL), dried ($MgSO_4$), filtered and concentrated. Purification by column chromatography (30% Et_2O / petroleum ether) gave a mixture of (2*E*,4*Z*)-5-iodopenta-2,4-

dienal and (2*E*,4*E*)-5-iodopenta-2,4-dienal (2.18 g, 10.3 mmol, 28%) as a pale yellow oil.[26b] To a suspension of magnesium turnings (389 mg, 16.0 mmol, 2.0 equiv.) in THF (3.0 mL) at 0 °C was added 1-bromooctane (2.1 mL, 12.0 mmol, 1.0 equiv.) and THF (25 ml). The mixture was stirred for 1 h, then cooled to −40 °C. To this was added dropwise a solution of the above prepared (2*E*,4*Z*)-5-iodopenta-2,4-dienal and (2*E*,4*E*)-5-iodopenta-2,4-dienal (2.18 g, 10.3 mmol). The mixture was stirred for 15 minutes, then the cooling bath was removed and the reaction was warmed to room temperature. The reaction was then quenched by addition of NH_4Cl (20 mL, sat., aq.). The organic phase was separated, and the aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic phases were washed with brine (20 mL), dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (30% Et_2O / petroleum ether) gave a 1.2:1 mixture of (1*E*,3*E*)-1-iodotrideca-1,3-dien-5-ol (±)-**38** and (1*Z*,3*E*)-1-iodotrideca-1,3-dien-5-ol as an orange oil (1.27 g, 3.9 mmol). This oil was dissolved in pentane (5 mL), and stored in the freezer (−20 °C) overnight. The resulting white crystals of (±)-**38** (409 mg, 1.27 mmol, 14%, *E*:*Z* 10:1) were collected by filtration. R_f 0.51 (50% Et_2O / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3430, 2923, 1682, 1464, 979; ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 (1H, ddd, J = 14.5, 4.0 and 0.5 Hz), 6.33 (1H, d, J = 14.5 Hz), 6.19-6.11 (1H, ddd, J = 15.5, 4.5 and 0.5 Hz), 5.73 (1H, dd, J = 15.5 and 6.5 Hz), 4.15-4.08 (1H, m), 1.60-1.49 (2H, m), 1.43-1.19 (12H, m), 0.91-0.85 (3H, m); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.7, 137.4, 129.9, 79.4, 72.3, 37.3, 32.0, 29.7, 29.4, 25.5, 22.8, 14.3.

*(5R,1E,3E)-1-iodotrideca-1,3-dien-5-ol (**(R)-38**).* DMSO (0.88 mL, 12.4 mmol, 4.0 equiv.) was added dropwise to a solution of oxalyl chloride (0.53 mL, 6.2 mmol, 2.0 equiv.) in CH_2Cl_2 (20.0 mL) at −78 °C. After stirring for 30 min, a solution of (±)-**38** (1.00 g, 3.1 mmol, 1.0 eq.) in CH_2Cl_2 (1.0 mL) was added dropwise, and the mixture was stirred for further 30 min. Triethylamine (2.6 mL, 18.6 mmol, 6.0 equiv.) was added dropwise, and the mixture allowed to warm to room temperature over 1 h. The reaction was quenched by addition of water (20 mL), and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phases were washed with brine (30 mL), dried ($MgSO_4$), filtered and concentrated. Filtration through silica gel (4% Et_2O / petroleum ether eluent) afforded crude (1*E*,3*E*)-1-iodotrideca-1,3-dien-5-one (0.70 g, 2.19 mmol, 71%) as a waxy colourless solid, which was used directly in the next transformation. R_f 0.48 (10% Et_2O / petroleum ether); ^1H NMR (400 MHz, C_6D_6) δ 6.75-6.58 (2H, m), 6.19-6.08 (1H, m), 5.74-5.62 (1H, m), 2.14 (2H, t, J = 7.5 Hz), 1.66-1.54 (2H, m), 1.34-1.18 (10H, m), 0.90 (3H, t, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (101 MHz, C_6D_6) δ 198.5, 143.7, 139.6, 129.5, 89.6, 41.5, 32.3, 29.9, 29.7, 29.6, 24.4, 23.1, 14.4. To a solution of this ketone (0.70 g, 2.20 mmol, 1.0 equiv.) and (*S*)-(−)-2-methyl-CBS-oxazaborolidine (0.22 mL, 1.0 M in toluene, 0.22 mmol, 0.1 equiv.) in THF (5.5 mL) at −40 °C was added dropwise a solution of BH_3•THF complex (2.4 mL, 1.0 M in THF, 2.4 mmol, 1.2 equiv.). After stirring at for 2 h −20 °C, the reaction was warmed to −10 °C and stirred for a further 1 h. The reaction was then quenched by addition of MeOH (3 mL), and allowed to warm to room temperature. NH_4Cl (5 mL, sat., aq.) was added, the aqueous phase was extracted with Et_2O (3 × 5 mL), and the combined organic phases were washed with brine (10 mL), dried ($MgSO_4$), filtered and concentrated. Purification *via* column chromatography (10% Et_2O / petroleum ether) gave (*R*)-**38** (231 mg, 0.72 mmol, 33% over two steps) as an orange solid. The solid was recrystallized from pentane (0.5 mL) (overnight, −20 °C freezer), and the crystals washed with cold pentane, to give (*R*)-**33** (63 mg, 27% recovery, 20.4% *ee*). The mother liquor was evaporated to dryness to give (*R*)-**38** (120 mg, 90.4% *ee*, 52% recovery, 0.37 mmol, 12% over 2 steps and recrystallisation) as a colourless solid. 90.4% *ee* (CHIRALPAK IC, 10% IPA/hexane, 0.7 mL/min, t_R (5*R*) 6.8 min, t_R (5*S*) 7.6 min); m.p. 36 °C; Spectroscopic data identical to that of (±)-**38**.

*Ethyl (5S,6Z,8E,10E,12R)-5,12-dihydroxyicosa-6,8,10-trienoate (**39**).* Prepared following general procedure F with **34** (71 mg, 0.31 mmol, 1.0 equiv.), (*R*)-**38** (120 mg, 0.37 mmol, 1.2 equiv.), $Pd(dba)_2$ (9.0 mg, 15.7 µmol, 5.0 mol%) and TBAF•$3H_2O$ (0.93 mL, 1.0 M in THF, 0.93 mmol, 3.0 equiv.), with a 2 h reaction time. Purification *via* column chromatography (30% EtOAc / petroleum ether) gave **39** (83 mg, 0.23 mmol, 73%) as a yellow oil. $[\alpha]_D^{20}$ +1.8 (*c* 0.6, $CHCl_3$); R_f 0.29 (40% EtOAc / petroleum ether); IR (thin film, ν_{max} / cm^{-1}) 3369, 2926, 2360, 1734, 1463; ^1H NMR (400 MHz, $CDCl_3$) δ 6.49 (1H, dd, J = 14.0 and 11.5 Hz), 6.32-6.19 (2H, m), 6.08 (1H, app. t, J = 11.0 Hz), 5.75 (1H, dd, J = 14.5 and 7.0 Hz), 5.42 (1H, app. t, J = 10.0 Hz), 4.63-4.54 (1H, m), 4.20-4.07 (3H, m), 2.33 (2H, t, J = 7.0 Hz), 1.81-1.43 (6H, m), 1.48-1.17 (15H, m), 0.87 (1H, t, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 173.6, 137.7, 134.1, 133.7, 130.2, 130.1, 122.4, 72.7, 67.6, 60.4, 37.3, 36.8, 34.1, 31.9, 29.6, 29.5, 29.3, 25.4, 22.7, 20.8, 14.3, 14.1; HRMS (ESI+) calc. for $C_{22}H_{38}O_4Na$ $[M+Na]^+$ 389.2673, found 389.2666.

*Leukotriene B_3 (**33**).* To a solution of **39** (66 mg, 0.18 mmol, 1.0 equiv.) in isopropanol (9 mL) and water (4.5 mL) was added LiOH (17 mg, 0.71 mmol, 4.0 eq.). After stirring for 2 h, the mixture was acidified with HCl (1 M, aq.), and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated to give leukotriene B_3 (60 mg, 0.18 mmol, 99%) as a colourless oil. $[\alpha]_D^{20}$ +15.4 (*c* 1.0, $CHCl_3$); IR (thin film, ν_{max} / cm^{-1}) 3408, 2925, 2340, 1734, 970; ^1H NMR (500 MHz, CD_3OD) δ 6.55 (1H, dd, J = 14.0 and 12.0 Hz), 6.33-6.20 (2H, m), 6.08 (1H, app. t, J = 11.0 Hz), 5.72 (1H, dd, J = 14.5 and 7.0 Hz), 5.37 (1H, app. t, J = 10.0 Hz), 4.62-4.52 (1H, m), 4.12-4.03 (1H, m), 2.34-2.24 (2H, m), 1.76-1.17 (18H, m), 0.90 (1H, t, J = 7.0 Hz); $^{13}C\{^1H\}$ NMR (125 MHz, CD_3OD) δ 178.3, 138.6, 135.1(2), 131.2, 130.6, 128.6, 73.2, 68.2, 38.4, 38.1, 33.0, 30.7,30.6, 30.4, 26.9, 26.6, 23.7, 22.3, 14.4; HRMS (ESI−) calc. for $C_{20}H_{33}O_4$ $[M-H]^-$ 337.2384, found 337.2386. Spectroscopic data in agreement with that reported by Kobayashi *et al*.[19]

SUPPORTING INFORMATION

Supporting Information (Siloxane equilibria NMR spectra, ECC DOSY NMR experiments, copies of ^1H and ^{13}C NMR

spectra) is available free of charge on the ACS Publications website (PDF).

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