

PAPER

View Article Online
View Journal | View Issue



Cite this: *Org. Biomol. Chem.*, 2020, **18**, 2297

Diastereoselective synthesis of trisubstituted olefins using a silicon-tether ring-closing metathesis strategy†

Stéphane Wittmann,‡ Alexander F. Tiniakos and Joëlle Prunet *

The diastereoselective synthesis of trisubstituted olefins with concomitant C–C bond formation is still a difficult challenge, and olefin metathesis reactions for the formation of such alkenes are usually not high yielding or/and diastereoselective. Herein we report an efficient and diastereoselective synthesis of trisubstituted olefins flanked by an allylic alcohol, by a silicon-tether ring-closing metathesis strategy. Both *E*- and *Z*-trisubstituted alkenes were synthesised, depending on the method employed to cleave the silicon tether. Furthermore, this methodology features a novel Peterson olefination for the synthesis of allyldimethylsilanes. These versatile intermediates were also converted into the corresponding allylchlorodimethylsilanes, which are not easily accessible in high yields by other methods.

Received 30th November 2019,
Accepted 4th March 2020

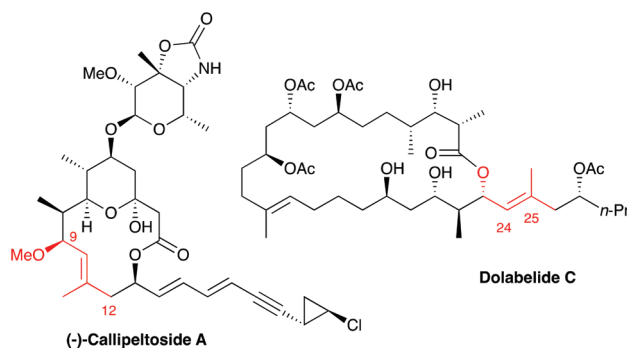
DOI: 10.1039/c9ob02563d

rsc.li/obc

Introduction

The trisubstituted *E* olefin motif with a methyl substituent is present in numerous polyketide natural products. Among these, callipeltoside **A**¹ and dolabelide **C**² possess another common feature: an allylic alkoxy group on the lone substituent of the trisubstituted olefin (highlighted in red in Scheme 1). During our previous approaches to the synthesis of dolabelide **C**,³ we had envisaged appending the side chain by a cross-metathesis (CM) reaction between an allylic alcohol and a *gem*-disubstituted olefin to form the C24–C25 trisubstituted olefin. Unfortunately, all attempts to perform CM between diverse allylic alcohols (protected or not) and the required *gem*-disubstituted olefin for dolabelide **C** led to dimerisation of the allylic alcohol partner.⁴ Silicon-tether ring-closing metathesis (RCM) reactions with O–Si–O linkages have been widely used for the formation of alkenes, when the corresponding CM reactions are not high yielding or/and diastereoselective.⁵ Previous works by Kobayashi *et al.*⁶ and Evans *et al.*⁷ illustrate the use of such linkage for the formation of *E* and *Z* trisubstituted olefins, respectively, *via* eight-membered rings (Scheme 2).

However, there are much fewer examples of RCM reactions with O–Si–C tethers. The reported formations of trisubstituted olefins from allyl silanes lead to bicyclic products,⁸ and the others focus on vinyl silanes.⁹ We propose a strategy for an efficient and diastereoselective synthesis of trisubstituted olefins flanked by an allylic alcohol, which involves a RCM reaction with a O–Si–C tether. In our preliminary communication,¹⁰ the metathesis precursors **C** were prepared by dehydrogenative coupling of allylic alcohols **A** and allyldimethylsilanes **B**, and the metathesis products **D** were converted into the *E* olefin (Scheme 2). Herein, we report our preliminary attempts to synthesise compounds **C** and a synthesis of versatile allylchlorodimethylsilanes from silanes **B**. Furthermore, the *Z* olefin isomer can also be accessed by choosing the appropriate method to cleave the tether (Scheme 2).



Scheme 1 Structures of callipeltoside **A** and dolabelide **C**, highlighting the trisubstituted olefin motif, adapted from ref. 10.

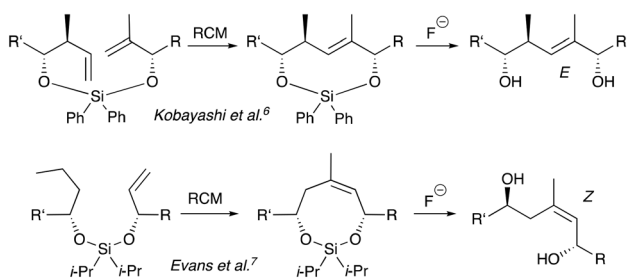
WestCHEM, School of Chemistry, University of Glasgow, Joseph Black Building, University Avenue, Glasgow G12 8QQ, UK. E-mail: joelle.prunet@glasgow.ac.uk

†Electronic supplementary information (ESI) available. See DOI: 10.1039/c9ob02563d

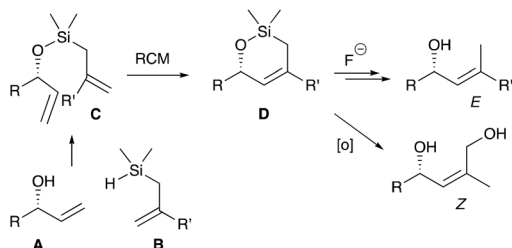
‡Present address: Institut de Chimie Moléculaire et des Matériaux d'Orsay, CNRS UMR 8182, Université Paris-Sud, Université Paris-Saclay, Bâtiment 420, 91405 Orsay cedex, France.



Previous work: O-Si-O tether



Our work: O-Si-C tether



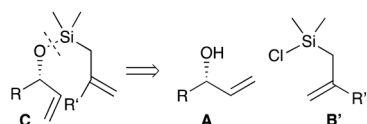
Scheme 2 Differences between previous RCM with silicon tethers leading to trisubstituted olefins in previous works and our work.

Results and discussion

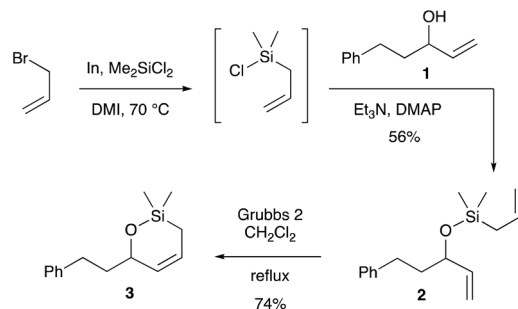
The preparation of the RCM substrates **C** we first envisioned is shown in Scheme 3: it would entail silyl ether formation between allylic alcohols **A** and allylchlorodimethylsilanes **B'**.

The first issue to address was the preparation of compounds **B'**. Allylchlorodimethylsilanes can be prepared by reaction of the corresponding allyl Grignard reagents with dichlorodimethylsilane, but the yields are usually low. For example, allylchlorodimethylsilane was synthesised in 44% yield¹¹ using this method, and the methallyl derivative in 39% yield.¹² Organoindium derivatives have been reported to favour mono-addition of allyl nucleophiles, thus leading to better yields of allylchlorosilanes.¹³ As a preliminary trial, allylbromide, when treated with indium and dichlorodimethylsilane in 1,3-dimethyl-2-imidazolidinone (DMI), led to allylchlorodimethylsilane, which was not isolated but directly reacted with alcohol **1** in the presence of triethylamine and DMAP to furnish the desired silyl ether **2** in 56% yield (Scheme 4). RCM reaction of compound **2** with Grubbs 2 catalyst proceeded smoothly¹⁴ to furnish cyclic silyl ether **3** in 74% yield, thus validating our strategy.

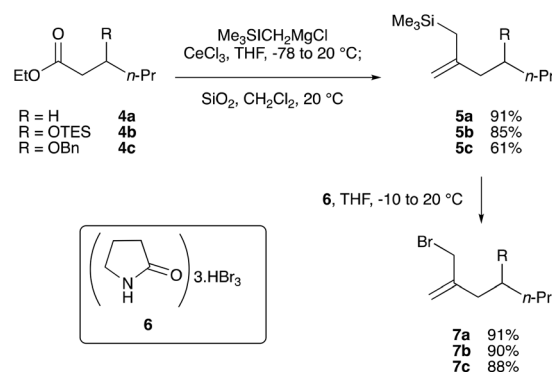
We then prepared several allylic bromides with a *gem*-disubstituted olefin, which are models or racemic versions of the



Scheme 3 First route for the preparation of RCM substrates **C**.



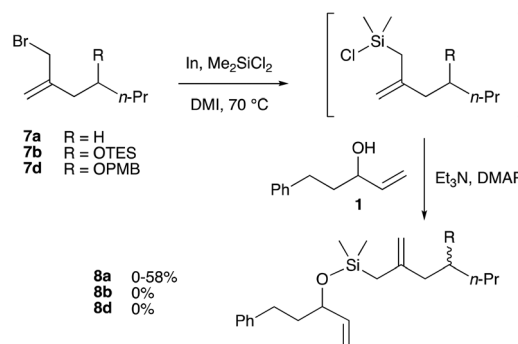
Scheme 4 First attempt at allylchlorosilane formation using indium, followed by silicon-tether RCM reaction.



Scheme 5 Preparation of allylic bromides by a Peterson olefination/bromination sequence.

side chain of dolabelide **C**, by a known method.¹⁵ Esters **4a-c**¹⁰ were subjected to trimethylsilylmethylmagnesium chloride in the presence of anhydrous cerium trichloride, and the resulting β -hydroxysilanes were stirred with silica gel in dichloromethane to furnish trimethylsilyl enol ethers **5a-c** in 61–91% yield (Scheme 5). Bromination of the Peterson olefination products **5a-c** was performed with pyrrolidone hydrotribromide **6** in THF to give the allylic bromides **7a-c** in 88–91% yield.

The allylchlorodimethylsilane formed *in situ* from **7a** and dichlorodimethylsilane in the presence of indium, was treated with alcohol **1** to furnish silyl ether **8a** in 58% yield (Scheme 6). Unfortunately, this reaction was not reproducible,



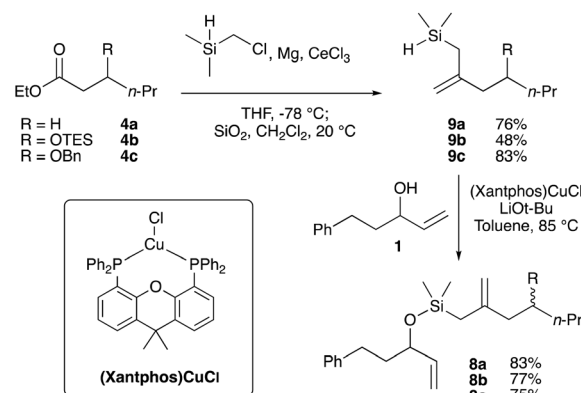
Scheme 6 Synthesis of RCM precursors using indium.



and variable yields were obtained after further attempts. Moreover, compounds **8b** and **8d** could not be prepared by this method. These poor results might be due to the additional steric hindrance present in **7b** and **7d**¹⁶ (R = OTES and OPMB, respectively), which renders the indium derivatives less reactive.¹⁷ When magnesium was employed instead of indium with compound **7b**, silyl ether **8b** was produced in only 4% yield, along with several side-products resulting from the cleavage of the triethylsilyl ether. The same reaction was tried on the PMB derivative **7d**; however, in this case, only the Würtz coupling product was obtained. This Barbier-type reaction was also attempted with zinc,^{16,18} but the desired silyl ethers **8a,b**, **d** were never observed.

Inspired by a report from Maruoka and coworkers who described the preparation of bromosilanes from the corresponding silanes,¹⁹ we converted allylic bromides **7a–c** into silanes **9a–c** in 81–86% yield, by reaction of the Grignard reagents derived from **7a–c** with chlorodimethylsilane (Scheme 7). It was found that slow addition of a solution of the bromide compound to a solution of 3.5 equivalents of magnesium and 1 equivalent of chlorodimethylsilane was necessary to reduce the formation of the Würtz coupling products. Maruoka *et al.* used bromine for the conversion of the silanes to the bromosilanes, but these conditions are not compatible with the alkene present in **9a–c**. Several chlorination conditions were employed – CuCl₂, catalytic CuI;²⁰ FeCl₃, acetyl chloride²¹ – without success. Finally, the use of hexachloroethane and catalytic palladium dichloride furnished the chlorosilane intermediates, which were treated with allylic alcohol **1** in the presence of triethylamine and DMAP to give the desired chlorosilanes **8a–c** in 47–77% yield.²²

At this point, we were satisfied to have found a reliable method for the synthesis of RCM precursors **8a–c** *via* the chlorosilanes, but the overall sequence was too long to be practical, so we sought to shorten the route in two different ways. Silyl ethers **8a–c** could be prepared directly from silanes **9a–c** by a copper-catalysed dehydrogenative coupling,²³ bypassing one step and the need to deal with sensitive chlorosilanes. Furthermore, we envisioned a novel Peterson olefination for the synthesis of allyldimethylsilanes **9a–c** from esters **4a–c**, which would proceed in an analogous fashion as the for-

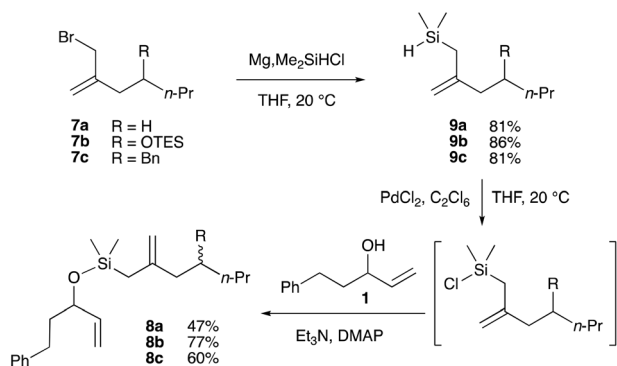


Scheme 8 Synthesis of RCM precursors by Peterson olefination and dehydrogenative coupling, adapted from ref. 10, showing an improved yield of **9c**.

mation of allyltrimethylsilanes **5a–c** (Scheme 5). As previously reported in our communication,¹⁰ both steps proceeded uneventfully (Scheme 8). It is worth noting that this new olefination reaction provides an easy access to allyldimethylsilanes, but also to the corresponding chlorosilanes (see Scheme 7).

RCM reactions of silyl ethers **8a–c** in the presence of the Grubbs 2 catalyst in refluxing dichloromethane gave the cyclic products **10a–c** in 63–94% yield. These cyclic silyl ethers are unstable on silica gel, and the yield of **10a** could be improved from 63% (ref. 10) to 83% simply by performing the purification by a quick filtration through a silica plug instead of a column chromatography. As previously reported, direct cleavage was attempted on **10b** with diverse fluoride sources and Lewis acids, but without success, leading to isomerisation product **13b'** or elimination products **14b** and **14b'** (see Table 1 for structures of these compounds).¹⁰ We thus resorted to a two-step process, starting with cleavage of the silicon–oxygen bond with methyllithium to give allyltrimethylsilanes **11a–c** (Scheme 9).

Removal of the trimethylsilyl group was then optimised on compound **11b** (Table 1). Employing Lewis acids such as BF₃·OEt₂ or Sc(OTf)₃ (entries 1 and 2) only led to elimination product **14b'**, with the TES group still in place. When **11b** was treated with TBAF under mild conditions (entry 3), the starting compound was recovered in full. Product **12b**, resulting from direct protodesilylation of the TMS group was obtained under more forcing conditions (entry 4), along with isomerisation product **13b** and elimination product **14b**; in all those compounds, the TES group had been removed. In order to reduce the amount of elimination product and favor the reprotonation, water was added to the reaction mixture (entry 5); in this case, the desired olefin **12b** was produced in 35% yield, along with 35% of the isomerised olefin **13b**. Although these conditions were not ideal, they were applied to **11a** and **11c**, for which the TMS removal would not be disrupted by the TES group cleavage. The desired products were obtained in 68% and 64% yields, respectively, along with 28% of the corresponding isomerisation product in each case (Scheme 9).

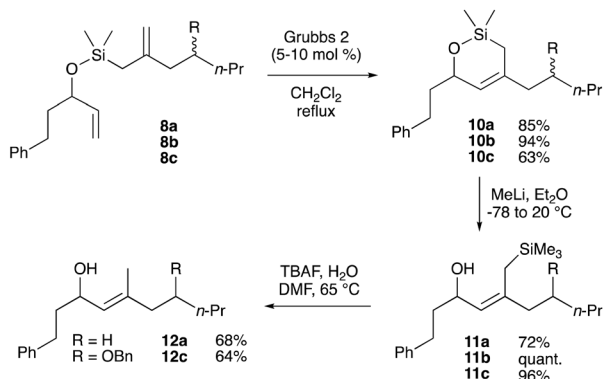


Scheme 7 Synthesis of RCM precursors *via* silanes.



Table 1 Optimisation of trimethylsilyl group removal

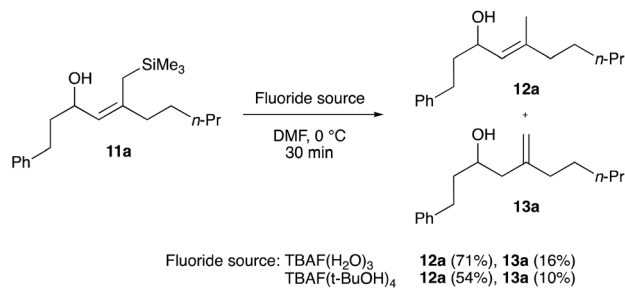
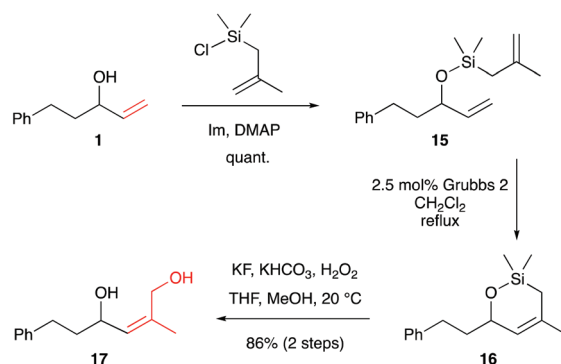
Entry	Conditions	Yield (%)				
		11b	12b	13b	14b	14b'
1	BF ₃ ·OEt ₂ Et ₂ O, −78 °C					100 ^a
2	Sc(OTf) ₃ Toluene, 20 °C					100 ^a
3	TBAF (3 equiv.) THF, −10 °C	100				
4	TBAF (6 equiv.) DMF, 65 °C		25	17	27	
5	TBAF (6 equiv.) H ₂ O (6 equiv.) DMF, 65 °C		35	35		

^a Conversion.**Scheme 9** RCM reaction and tether cleavage.¹⁰

Trimethylsilyl group removal was further optimised on compound **11a** by varying the fluoride source (Scheme 10). When using solid TBAF hydrate, the reaction was complete after 30 min at low temperature, and the amount of isomerised product **13a** was reduced. With TBAF(*t*-BuOH)₄, the amount of isomerised product was further decreased, but the yield of the desired product **12a** was only moderate.

As previously reported in our communication,¹⁰ this new synthetic route was applied to the synthesis of the C16–C30 fragment of dolabelide C.

We then reasoned that this methodology could also be employed for the construction of *Z*-trisubstituted olefins, if the silyl substituent was used to extend the chain (Scheme 11). Alcohol **1** was reacted with known methallyldimethyl-

**Scheme 10** Influence of fluoride source in trimethylsilyl group removal.**Scheme 11** Formation of *Z*-trisubstituted olefins by silicon-tether RCM.

chlorosilane¹² in the presence of imidazole and DMAP to furnish silyl ether **15** in quantitative yield.²⁴ Ring-closing metathesis of **15** with the Grubbs 2 catalyst gave cyclic silyl ether **16**, which was subjected without purification to Tamao–Fleming oxidation, and diol **17** was obtained in excellent yield for the two steps. In this manner, a terminal alkene (in red in **1**) can be converted into a *Z*-trisubstituted olefin (in red in **17**) in three high yielding steps, and the primary alcohol is a convenient handle for subsequent elongation of the chain.

Conclusions

In conclusion, we have developed a new methodology for the construction of *E*-trisubstituted olefins flanked by an allylic alcohol, featuring a silicon-tether ring-closing metathesis reaction. In the course of synthesising the metathesis substrates, we designed a novel Peterson olefination reaction that enabled direct access to allyldimethylsilanes. These allylsilanes are versatile intermediates that can be converted into the corresponding chlorosilanes, which are otherwise difficult to obtain in good yields. This methodology was applied to the synthesis of the C16–C30 fragment of dolabelide C, showcasing its practical aspect. Furthermore, *Z*-trisubstituted olefins could also be prepared when Tamao–Fleming oxidation was used to cleave the silicon tether.



Experimental section

General methods

Unless otherwise noted all reactions were carried out under an argon atmosphere. The glassware used was flame-dried under vacuum (~0.6 mbar) using a heat gun. Air- and moisture-sensitive liquids and solutions were transferred *via* syringe or stainless steel cannula flushed with argon prior to use. Unless otherwise noted all reagents were obtained from commercial suppliers and used without further purification. All reactions were stirred with a magnetic stirrer. Temperatures refer to bath temperatures. Reaction solvents were collected from an in-house solvent purification system (THF, CH₂Cl₂, Et₂O, CH₃CN). Dry ethanol, dry methanol and dry DMF were used from commercial bottles. NMR spectra were recorded on a Bruker DPX-400 spectrometer (¹H NMR at 400 MHz and ¹³C NMR at 100 MHz) or a Bruker DPX-500 spectrometer (¹H NMR at 500 MHz and ¹³C NMR at 126 MHz). Chemical shifts are reported in ppm. ¹H NMR spectra were recorded with CDCl₃ as the solvent using residual CHCl₃ (δ = 7.26) as internal standard, and for ¹³C NMR spectra the chemical shifts are reported relative to the central resonance of CDCl₃ (δ = 77.16). Signals in NMR spectra are described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), septet (sept), multiplet (m), broad (br) or combination of these, which refers to the spin-spin coupling pattern observed. Spin-spin coupling constants reported are uncorrected. Two-dimensional (COSY, HSQC, HMBC, NOESY) NMR spectroscopy was used where appropriate to assist the assignment of signals in the ¹H and ¹³C NMR spectra. IR spectra were obtained employing a Shimadzu FTIR-8400 instrument with a Golden Gate™ attachment that uses a type IIa diamond as a single reflection element so that the IR spectrum of the compound (solid or liquid) could be detected directly (thin layer). High resolution mass spectra were recorded under ESI and CI conditions by the analytical services at the University of Glasgow. Flash chromatography was executed under forced flow conditions, using the indicated solvent system and EMD Guduran silica gel 60 as solid support. Thin layer chromatography (TLC) was carried out on Merck silica gel 60 covered aluminum sheets, and monitored by UV-light or by staining with a solution of anisaldehyde or potassium permanganate.

2,2-Dimethyl-6-phenethyl-3,6-dihydro-2H-1,2-oxasiline 3

Allyl bromide (0.70 g, 5.8 mmol, 1.8 equiv.) was added to a stirred solution of indium (0.44 g, 3.8 mmol, 1.2 equiv.) in DMI (7.5 mL) at room temperature under argon. The mixture was stirred for 2 h at room temperature under argon. Dichlorodimethylsilane (0.48 g, 3.8 mmol, 1.2 equiv.) was added to the mixture and the reaction was stirred for 3 h at 70 °C under argon. The mixture was allowed to cool down and was added dropwise to a stirred solution of **1** (0.50 g, 3.1 mmol), triethylamine (0.78 g, 7.7 mmol, 2.5 equiv.) and DMAP (0.19 g, 1.5 mmol, 0.50 equiv.) in THF (10 mL) at 0 °C under argon. The reaction mixture was stirred overnight at room temperature under argon. The reaction mixture was then

quenched with a saturated aqueous solution of sodium hydrogen carbonate (10 mL) and extracted with ether (3 × 10 mL). The ether extracts were combined and washed with brine (2 × 20 mL), dried (MgSO₄), filtered and concentrated *in vacuo* to deliver a yellow oil. Purification by column chromatography on silica gel (petroleum ether–ether 99/1) gave silyl ether **2** (0.29 g, 56%) as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ 7.30–7.26 (m, 2H), 7.20–7.16 (m, 3H), 5.89–5.74 (m, 2H), 5.18 (ddd, *J* = 17.1, 1.5, 1.4 Hz, 1H), 5.08 (ddd, *J* = 10.4, 1.5, 1.3 Hz, 1H), 4.92–4.84 (m, 2H), 4.14 (m, 1H), 2.73–2.57 (m, 2H), 1.89–1.74 (m, 2H), 1.63 (d, *J* = 8.1 Hz, 2H), 0.13 (s, 3H), 0.12 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 142.3, 141.3, 134.3, 128.5, 128.5, 125.9, 114.5, 113.8, 73.7, 39.6, 31.8, 25.2, −1.5, −1.7. IR (neat, cm^{−1}) 3078, 3027, 2949, 2915, 2860, 1631, 1605, 1497, 1454, 1422, 1252, 1083, 1030.

To a solution of silane **2** (0.15 g, 0.58 mmol) in dichloromethane (11 mL) was added second-generation Grubbs' catalyst (25 mg, 0.030 mmol, 5.0 mol%) under argon. The solution was stirred at 45 °C (reflux) for 2 h and monitored by TLC. The reaction mixture was then concentrated *in vacuo*. Purification of the crude compound by column chromatography on silica gel (petroleum ether–ether 98/2) gave the product **3** (99 mg, 74%) as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.26 (m, 2H), 7.22–7.16 (m, 3H), 5.91–5.85 (m, 1H), 5.57 (dq, *J* = 10.8, 2.2 Hz, 1H), 4.45–4.39 (m, 1H), 2.81–2.66 (m, 2H), 1.91–1.75 (m, 2H), 1.30 (ddt, *J* = 17.5, 4.7, 2.2 Hz, 1H), 1.20 (dddd, *J* = 17.5, 5.6, 2.7, 2.2 Hz, 1H), 0.21 (s, 3H), 0.18 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 142.6, 132.5, 128.7, 128.4, 125.8, 124.4, 71.6, 40.0, 31.5, 12.4, 0.57, −0.5. IR (neat, cm^{−1}) 3026, 2958, 2936, 2877, 1642, 1604, 1497, 1454, 1257, 1030. HRMS (EI, *m/z*) calcd for (C₁₄H₂₀OSi)⁺ 232.1283, found 232.1280.

Trimethyl(2-methyleneheptyl)silane 5a

Cerium(III) chloride heptahydrate (27.8 g, 74.5 mmol, 3.50 equiv.) was added to a 500 mL three-necked round-bottomed flask and dried under vacuum at 120 °C for 2 h, 140 °C for 2 h and then at 160 °C for 2 h. The flask was allowed to cool down and was purged with argon for 10 min, and dry THF (200 mL) was added. The mixture was stirred for 20 h at room temperature under argon to give the cerium(III) chloride–THF complex as a white precipitate. A trimethylsilylmethylmagnesium chloride solution (1.30 M in THF, 57.0 mL, 74.5 mmol, 3.50 equiv.) was added dropwise at −78 °C under argon. The gray suspension was stirred for 30 min, and then ethyl caproate (3.07 g, 21.3 mmol) in dry THF (15 mL) was added at −78 °C. The reaction was stirred at −78 °C for 2 h, the flask was then removed from the cold bath, and the mixture was stirred at room temperature for 15 h. The reaction mixture was cooled to 0 °C, a saturated aqueous solution of ammonium chloride (200 mL) was added at 0 °C, and the mixture was stirred for 20 min. Water was added, and the mixture was extracted with ether (3 × 150 mL). The combined ether extracts were washed with water and brine (2 × 300 mL), then dried (Na₂SO₄), filtered and concentrated *in vacuo* to give a yellow oil. The oil was then stirred overnight with silica in dichloromethane. Filtration, followed by concentration *in vacuo* gave the allylic silane **5a**



(3.59 g, 91%) as a clear oil. ^1H NMR (400 MHz, CDCl_3) δ 4.58–4.57 (m, 1H), 4.51–4.49 (m, 1H), 1.94 (t, J = 7.6 Hz, 2H), 1.52 (d, J = 1.0 Hz, 2H), 1.47–1.39 (m, 2H), 1.35–1.22 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H), 0.01 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 148.2, 106.8, 38.4, 31.8, 27.7, 27.0, 22.8, 14.2, –1.1. IR (neat, cm^{-1}) 2956, 2929, 2861, 1633, 1467, 1418, 1248, 1157. HRMS (CI, m/z) calcd for $(\text{C}_{11}\text{H}_{25}\text{Si})^+$ 185.1726, found 185.1722.

Triethyl(2-((trimethylsilyl)methyl)hept-1-en-4-yloxy)silane 5b

The crude silane **5b** was obtained from the corresponding ester **4b** (4.94 g, 18.0 mmol) according to the procedure described above for silane **5a**. The crude oil was purified by column chromatography on silica gel (petroleum ether–ether 98/2) and the resulting oil was stirred overnight with silica in dichloromethane. The mixture was then filtered and concentrated *in vacuo* to give the allylic silane **5b** (4.81 g, 85%) as a clear oil. ^1H NMR (400 MHz, CDCl_3) δ 4.61–4.59 (m, 1H), 4.56–4.54 (m, 1H), 3.82–3.76 (m, 1H), 2.14 (ddd, J = 13.6, 5.8, 0.8 Hz, 1H), 2.06 (ddd, J = 13.6, 7.1, 0.5 Hz, 1H), 1.52 (s, 2H), 1.51–1.26 (m, 4H), 0.96 (t, J = 8.1 Hz, 9H), 0.89 (t, J = 7.1 Hz, 3H), 0.60 (q, J = 7.8 Hz, 6H), 0.02 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.7, 109.8, 71.3, 46.8, 39.5, 27.3, 18.8, 14.4, 7.1, 5.3, –1.2. IR (neat, cm^{-1}) 2955, 2910, 2876, 1634, 1458, 1416, 1248, 1099, 1074, 1040, 1005. HRMS (ESI, m/z) calcd for $(\text{C}_{17}\text{H}_{38}\text{OSi}_2\text{Na})^+$ 337.2353, found 337.2327.

(4-(Benzoyloxy)-2-methyleneheptyl)trimethylsilane 5c

Cerium(III) chloride heptahydrate (21.3 g, 57.1 mmol, 3.50 equiv.) was dried under vacuum at 120 °C for 2 h, 140 °C for 2 h and then at 160 °C for 2 h. The flask was allowed to cool down to room temperature and was purged with argon for 10 min, and dry THF (190 mL) was added. The mixture was stirred for 20 h at room temperature under argon to give the cerium(III) chloride–THF complex as a white precipitate. To a stirred solution of magnesium (1.4 g, 57 mmol, 3.5 equiv.) and 1,2-dibromoethane (3 drops) in THF (48 mL) at 65 °C was added slowly a solution of chloromethyltrimethylsilane (8.0 mL, 58 mmol, 3.5 equiv.) in THF (12 mL). The solution was then stirred for 2 h at room temperature. The above solution was then added dropwise (over 1 h) at –78 °C to the cerium. The gray suspension was stirred for 30 min, and then ester **4c** (4.09 g, 16.3 mmol) in dry THF (20 mL) was added at –78 °C. The reaction was stirred at –78 °C for 2 h, the flask was then removed from the cold bath, and the mixture was stirred at room temperature for 15 h. A saturated aqueous solution of ammonium chloride (200 mL) was added at 0 °C, and the mixture was stirred for 20 min. Water was added, and the mixture was extracted with diethyl ether (3 × 200 mL). The combined ether extracts were washed with water and brine (2 × 300 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to give a yellow oil. The oil was stirred one day with silica gel in dichloromethane. The mixture was then filtered and concentrated *in vacuo* and the resulting crude oil was purified by column chromatography on silica gel (petroleum ether–ether 98/2) to give the allylic silane **5c** (2.90 g, 61%) as a clear

oil. ^1H NMR (500 MHz, CDCl_3) δ 7.37–7.26 (m, 5H), 4.68–4.66 (m, 1H), 4.61–4.59 (m, 1H), 4.57 (d, J = 11.5 Hz, 1H), 4.50 (d, J = 11.5 Hz, 1H), 3.57–3.51 (m, 1H), 2.33 (dd, J = 14.0, 6.2 Hz, 1H), 2.09 (dd, J = 14.0, 6.6 Hz, 1H), 1.55 (d, J = 2.6 Hz, 2H), 1.53–1.47 (m, 3H), 1.40–1.32 (m, 1H), 0.91 (t, J = 7.1 Hz, 3H), 0.03 (s, 9H). ^{13}C NMR (126 MHz, CDCl_3) δ 144.8, 139.2, 128.4, 127.9, 127.5, 109.8, 77.9, 71.2, 43.3, 36.6, 27.2, 18.9, 14.4, –1.1. IR (neat, cm^{-1}) 2957, 2934, 2872, 1497, 1454, 1248, 1090, 1069, 1028. HRMS (ESI, m/z) calcd for $(\text{C}_{18}\text{H}_{30}\text{OSiNa})^+$ 313.1958, found 313.1949.

2-(Bromomethyl)hept-1-ene 7a²⁵

Pyrrolidone hydrotribromide (4.1 g, 7.8 mmol, 1.0 equiv.) was added to a stirred solution of the allylic silane **5a** (1.44 g, 7.82 mmol) and pyridine (4.1 mL, 51 mmol, 6.5 equiv.) in dry THF (322 mL) at –10 °C under argon. The mixture was stirred for 2 h and allowed to warm to room temperature during this period. A saturated aqueous solution of sodium thiosulfate (250 mL) was added and the resulting mixture was stirred for 5 min. The mixture was extracted with ether (3 × 200 mL). The ether extracts were combined and washed with a saturated aqueous solution of copper sulfate (2 × 300 mL) and brine (2 × 300 mL), then dried (Na_2SO_4), filtered and concentrated *in vacuo* to deliver a yellow oil. Purification by column chromatography on silica gel (petroleum ether–ether 99/1) gave the bromide **7a** (1.36 g, 91%) as a clear oil. Obtained data in accordance with previously reported data.²⁵

(2-(Bromomethyl)hept-1-en-4-yloxy)triethylsilane 7b

Bromide **7b** (2.35 g, 92%) was obtained as a clear oil according to the procedure for bromination described above from the corresponding allylic silane **5b** (2.50 g, 7.95 mmol). ^1H NMR (400 MHz, CDCl_3) δ 5.24–5.23 (m, 1H), 4.99–4.98 (m, 1H), 4.06 (dd, J = 10.0, 0.9 Hz, 1H), 3.99 (dd, J = 10.0, 0.9 Hz, 1H), 3.83 (app quint, J = 5.9 Hz, 1H), 2.40 (ddd, J = 14.1, 5.9, 1.0 Hz, 1H), 2.34 (ddd, J = 14.1, 5.9, 1.0 Hz, 1H), 1.45–1.27 (m, 4H), 0.96 (t, J = 8.0 Hz, 9H), 0.90 (t, J = 7.0 Hz, 3H), 0.60 (q, J = 8.0 Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.2, 117.9, 71.0, 41.2, 39.4, 37.6, 18.8, 14.4, 7.1, 5.2. IR (neat, cm^{-1}) 2957, 2936, 2913, 2876, 1458, 1414, 1377, 1238, 1209, 1105, 1074, 1040, 1005. HRMS (CI, m/z) calcd for $(\text{C}_{14}\text{H}_{30}^{79}\text{BrOSi})^+$ 321.1249, found 321.1248.

((2-(Bromomethyl)hept-1-en-4-yl)oxy)methylbenzene 7c

Bromide **7c** (2.61 g, 88%) was obtained as a clear oil according to the procedure for bromination described above from the corresponding allylic silane **5c** (2.90 g, 10.0 mmol). (Purification by column chromatography on silica gel (petroleum ether–ether 98/2).) ^1H NMR (500 MHz, CDCl_3) δ 7.37–7.25 (m, 5H), 5.25 (s, 1H), 5.04 (s, 1H), 4.57 (d, J = 11.5 Hz, 1H), 4.53 (d, J = 11.5 Hz, 1H), 4.03 (d, J = 10.0 Hz, 1H), 3.98 (d, J = 10.0 Hz, 1H), 3.59 (app quint, J = 5.8 Hz, 1H), 2.51 (dd, J = 14.7, 5.6 Hz, 1H), 2.46 (dd, J = 14.7, 6.6 Hz, 1H), 1.62–1.35 (m, 4H), 0.92 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 143.1, 138.8, 128.5, 127.9, 127.7, 117.8, 77.4, 71.1, 37.9, 37.5, 36.3, 18.8, 14.3. IR (neat, cm^{-1}) 2957, 2932, 2870, 1497, 1454,



1352, 1209, 1067, 1028. HRMS (ESI, m/z) calcd for $(C_{15}H_{21}O^{79}BrNa)^+$ 319.0668, found 319.0660.

1-((2-(Bromomethyl)hept-1-en-4-yloxy)methyl)-4-methoxybenzene **7d**

A solution of bromide **7b** (0.99 g, 3.1 mmol) in 5/95 HF/CH₃CN (20 mL) was stirred for 2 h at room temperature. A saturated aqueous solution of calcium chloride (40 mL) was added to the reaction mixture. The mixture was extracted with diethyl ether (3 × 20 mL) and the combined organic layers were washed with a saturated aqueous solution of sodium bicarbonate (20 mL), brine (50 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo* to give the alcohol as a clear oil (0.63 g, 98%), which was used without further purification. To a stirred solution of sodium hydride (48.0 mg, 1.14 mmol) in diethyl ether (2 mL) was added dropwise a solution of 4-methoxybenzyl alcohol (1.10 g, 7.56 mmol) in diethyl ether (2 mL). The mixture was stirred for 20 min at room temperature. Freshly distilled trichloroacetonitrile (0.800 mL, 7.56 mmol) was then added dropwise at 0 °C and the resulting mixture was stirred for 1 h and the temperature was allowed to warm up during this period. The solution was then concentrated *in vacuo* and the crude oil was washed with a solution of pentane (5 mL) and methanol (0.6 mL), filtered and concentrated *in vacuo*. This process washing/filtration/concentration was repeated three times to give 4-methoxybenzyl trichloroacetimidate (1.9 g, 89%) as a clear oil. To a stirred solution of the alcohol (717 mg, 3.46 mmol) in dichloromethane (7.5 mL) was added the previously formed 4-methoxybenzyl trichloroacetimidate in dichloromethane (0.5 mL), followed by camphorsulfonic acid (81 mg, 0.35 mmol). The mixture was then stirred for one day at room temperature. A saturated aqueous solution of sodium bicarbonate (15 mL) was then added. The mixture was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with brine (30 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography (dry column) on silica gel (petroleum ether–ether 9/1) gave the protected alcohol **7d** (962 mg, 85%) as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ 7.26 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 5.24 (s, 1H), 5.03–5.02 (m, 1H), 4.49 (d, J = 11.1 Hz, 1H), 4.45 (d, J = 11.1 Hz, 1H), 4.02 (dd, J = 10.0, 0.8 Hz, 1H), 3.97 (d, J = 10.0, 0.8 Hz, 1H), 3.80 (s, 3H), 3.58–3.53 (m, 1H), 2.51–2.41 (m, 2H), 1.58–1.32 (m, 4H), 0.91 (t, J = 7.2 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 159.3, 143.1, 130.9, 129.5, 117.8, 113.9, 77.0, 70.7, 55.4, 37.8, 37.6, 36.3, 18.8, 14.3. IR (neat, cm^{−1}) 2955, 2934, 2870, 1613, 1512, 1464, 1302, 1244, 1209, 1173, 1034. HRMS (ESI, m/z) calcd for $(C_{16}H_{23}^{79}BrO_2Na)^+$ 349.0774, found 349.0764.

Dimethyl(2-methyleneheptyl)silane **9a**¹⁰

To a stirred solution of magnesium (150 mg, 6.22 mmol, 3.30 equiv.) and chlorodimethylsilane (0.210 mL, 1.86 mmol, 1.00 equiv.) in THF (1 mL) was added dropwise (over 1 h) at room temperature a solution of bromide **7a** (355 mg, 1.86 mmol) in THF (1.8 mL). The reaction mixture was stirred at room temperature

for 2 h. A saturated aqueous solution of ammonium chloride (5 mL) was then added and the mixture was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine (20 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo* to deliver silane **9a** (257 mg, 81%) as a clear oil. ¹H NMR (400 MHz, CDCl₃) δ 4.61–4.60 (m, 1H), 4.56–4.54 (m, 1H), 3.90 (non, J = 3.5 Hz, 1H), 1.98 (t, J = 7.6 Hz, 2H), 1.59 (dd, J = 3.5, 1.0 Hz, 2H), 1.47–1.40 (m, 2H), 1.35–1.24 (m, 4H), 0.89 (t, J = 7.1 Hz, 3H), 0.09 (d, J = 3.5 Hz, 6H). Obtained data in accordance with previously reported data.¹⁰

(2-((Dimethylsilyl)methyl)hept-1-en-4-yloxy)triethylsilane **9b**¹⁰

Hydrosilane **9b** (804 mg, 86%) was obtained as a clear oil from the corresponding bromide **7b** (999 mg, 3.11 mmol) according to the procedure described above for hydrosilane **9a**. In this case, the reaction time was increased to 5 h. (Purification by column chromatography on silica gel (petroleum ether).) ¹H NMR (400 MHz, CDCl₃) δ 4.64–4.62 (m, 1H), 4.62–4.60 (m, 1H), 3.91 (non, J = 3.6 Hz, 1H), 3.83–3.77 (m, 1H), 2.19 (ddd, J = 13.6, 5.8, 1.1 Hz, 1H), 2.11 (ddd, J = 13.6, 7.2, 0.9 Hz, 1H), 1.62–1.57 (m, 2H), 1.51–1.25 (m, 4H), 0.96 (t, J = 8.0 Hz, 9H), 0.89 (t, J = 6.9 Hz, 3H), 0.60 (q, J = 8.0 Hz, 6H), 0.10 (d, J = 3.6 Hz, 3H), 0.09 (d, J = 3.6 Hz, 3H). Obtained data in accordance with previously reported data.¹⁰

(4-(Benzlyoxy)-2-methyleneheptyl)dimethylsilane **9c**¹⁰

Hydrosilane **9c** (1.95 g, 81%) was obtained as a clear oil from the corresponding bromide **7c** (2.59 g, 8.71 mmol) according to the procedure described above for hydrosilane **9a**. In this case, the reaction time was increased to 5 h. (Purification by column chromatography on silica gel (petroleum ether–ether 97/3).) ¹H NMR (400 MHz, CDCl₃) δ 7.37–7.24 (m, 5H), 4.70–4.69 (m, 1H), 4.66–4.65 (m, 1H), 4.57 (d, J = 11.5 Hz, 1H), 4.49 (d, J = 11.5 Hz, 1H), 3.93 (non, J = 3.6 Hz, 1H), 3.58–3.52 (m, 1H), 2.37 (ddd, J = 14.1, 6.1, 1.2 Hz, 1H), 2.14 (ddd, J = 14.1, 6.5, 1.0 Hz, 1H), 1.66–1.57 (m, 2H), 1.53–1.31 (m, 4H), 0.90 (t, J = 7.1 Hz, 3H), 0.10 (d, J = 3.6 Hz, 3H), 0.09 (d, J = 3.6 Hz, 3H). Obtained data in accordance with previously reported data.¹⁰

Dimethyl(2-methyleneheptyl)(5-phenylpent-1-en-3-yloxy)silane **8a**¹⁰

To a stirred solution of silane **9a** (36 mg, 0.21 mmol, 1.2 equiv.) in THF (0.05 mL) were added palladium dichloride (0.40 mg, 0.0020 mmol, 1.2 mol%) and hexachloroethane (25 mg, 0.10 mmol, 0.60 equiv.). The reaction mixture was stirred for 1 h at room temperature. The reaction mixture was then added to a stirred solution of alcohol **1** (28 mg, 0.18 mmol), triethylamine (0.060 mL, 0.44 mmol, 2.5 equiv.) and DMAP (11 mg, 0.090 mmol, 0.50 equiv.) in THF (0.4 mL) at 0 °C. The reaction mixture was stirred for 1 h at room temperature. A saturated aqueous solution of sodium bicarbonate (3 mL) was added and the mixture was extracted with ether (3 × 3 mL). The combined organic layers were washed with brine (10 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo* to deliver an oil. Purification by column chromatography on



silica gel (petroleum ether–ether 99.5/0.5) gave the silane **8a** (27 mg, 47%) as a clear oil. ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.27 (m, 2H), 7.20–7.17 (m, 3H), 5.84 (ddd, $J = 17.0, 10.3, 6.3$ Hz, 1H), 5.17 (dt, $J = 17.0, 1.7$ Hz, 1H), 5.08 (ddd, $J = 10.3, 1.7, 1.1$ Hz, 1H), 4.62–4.61 (m, 1H), 4.57–4.56 (m, 1H), 4.16–4.10 (m, 1H), 2.72–2.57 (m, 2H), 1.99 (t, $J = 7.7$ Hz, 2H), 1.88–1.74 (m, 2H), 1.63 (s, 2H), 1.47–1.39 (m, 2H), 1.35–1.24 (m, 4H), 0.89 (t, $J = 7.0$ Hz, 3H), 0.13 (s, 3H), 0.12 (s, 3H). Obtained data in accordance with previously reported data.¹⁰

3,3-Diethyl-9,9-dimethyl-7-methylene-11-phenethyl-5-propyl-4,10-dioxa-3,9-disilatrdec-12-ene **8b**¹⁰

Silane **8b** (490 mg, 77%) was obtained as a clear oil and as a 1 : 1 mixture of diastereomers from the corresponding silane **9b** and alcohol **1** (224 mg, 1.38 mmol) according to the procedure described above for silane **8a**. (Purification by column chromatography on silica gel (petroleum ether–ether 99.5/0.5).) ^1H NMR (400 MHz, CDCl_3) δ 7.30–7.26 (m, 2H), 7.19–7.15 (m, 3H), 5.83 (ddd, $J = 17.0, 10.3, 6.3$ Hz, 1H), 5.16 (dt, $J = 17.0, 1.5$ Hz, 1H), 5.07 (ddd, $J = 10.3, 1.8, 1.1$ Hz, 1H), 4.66–4.62 (m, 2H), 4.12 (app q, $J = 6.3$ Hz, 1H), 3.82–3.77 (m, 1H), 2.72–2.56 (m, 2H), 2.22–2.08 (m, 2H), 1.88–1.75 (m, 2H), 1.67–1.59 (m, 2H), 1.50–1.26 (m, 4H), 0.95 (t, $J = 7.9$ Hz, 9H), 0.89 (t, $J = 6.8$ Hz, 3H), 0.60 (q, $J = 7.9$ Hz, 6H), 0.15–0.11 (m, 6H). Obtained data in accordance with previously reported data.¹⁰

(4-(Benzoyloxy)-2-methyleneheptyl)dimethyl((5-phenylpent-1-en-3-yl)oxy)silane **8c**¹⁰

Silane **8c** (1.85 g, 60%) was obtained as a clear oil and as a 1 : 1 mixture of diastereomers from the corresponding silane **9c** and alcohol **1** (1.14 g, 7.06 mmol) according to the procedure described above for silane **8a**. (Purification by column chromatography on silica gel (petroleum ether–ether 99/1).) ^1H NMR (400 MHz, CDCl_3) δ 7.37–7.26 (m, 7H), 7.20–7.17 (m, 3H), 5.85 (dddd, $J = 17.0, 10.3, 6.4, 1.7$ Hz, 1H), 5.18 (ddt, $J = 17.0, 3.0, 1.5$ Hz, 1H), 5.11–5.07 (m, 1H), 4.75–4.72 (m, 1H), 4.71–4.68 (m, 1H), 4.59 (d, $J = 11.5$ Hz, 1H), 4.51 (d, $J = 11.5$ Hz, 1H), 4.14 (q, $J = 6.4$ Hz, 1H), 3.58 (quint, $J = 6.1$ Hz, 1H), 2.73–2.58 (m, 2H), 2.45–2.38 (m, 1H), 2.21–2.15 (m, 1H), 1.90–1.77 (m, 2H), 1.72–1.64 (m, 2H), 1.56–1.33 (m, 4H), 0.92 (t, $J = 6.9$ Hz, 3H), 0.16 (s, 3H), 0.15 (s, 3H). Obtained data in accordance with previously reported data.¹⁰

(Z)-1-Phenyl-7-(triethylsilyloxy)-5-((trimethylsilyl)methyl)dec-4-en-3-ol **11b**

To a stirred solution of oxysilane **10b** (351 mg, 0.810 mmol) in diethyl ether (30 mL) at -78°C was added dropwise methyl-lithium (1.6 M solution in diethyl ether, 1.5 mL, 2.4 mmol, 3.0 equiv.). The reaction was stirred 1 h at -78°C and was allowed to warm up to room temperature for 1 h. The mixture was quenched by addition of a saturated aqueous solution of ammonium chloride (50 mL) and was extracted with diethyl ether (3 \times 30 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by filtration through a silica plug gave allylic alcohol **11b** (364 mg,

quant.) as a clear oil and as a 1 : 1 mixture of diastereomers. ^1H NMR (500 MHz, CDCl_3) δ 7.29–7.16 (m, 5H), 5.14 (d, 1H, $J = 8.9$ Hz), 4.27–4.20 (m, 1H), 3.82–3.76 (m, 1H), 2.81–2.63 (m, 2H), 2.15–2.10 (m, 1H), 2.04 (td, $J = 13.6, 6.9$ Hz, 1H), 1.92–1.83 (m, 1H), 1.78–1.69 (m, 1H), 1.64 (d, 0.5H, $J = 13.4$ Hz), 1.57–1.52 (m, 1H), 1.55 (d, 0.5H, $J = 13.4$ Hz), 1.49–1.28 (m, 4H), 1.19 (d, 0.5H, $J = 3.6$ Hz), 1.18 (d, 0.5H, $J = 3.7$ Hz), 0.96 (t, 4.5H, $J = 7.9$ Hz), 0.96 (t, 4.5H, $J = 7.9$ Hz), 0.89 (t, 3H, $J = 6.8$ Hz), 0.60 (q, 6H, $J = 7.9$ Hz), 0.01 (s, 4.5H), 0.00 (s, 4.5H). ^{13}C NMR (126 MHz, CDCl_3) δ 142.3, 139.0, 138.6, 128.6, 128.5, 127.4, 127.1, 125.9, 71.9, 71.4, 68.2, 68.1, 47.4, 47.0, 39.5, 39.4, 32.1, 32.0, 23.0, 22.5, 18.8, 18.5, 14.5, 14.4, 7.1, 5.3, $-0.6, -0.7$. IR (neat, cm^{-1}) 3421, 2955, 2935, 2876, 1496, 1456, 1415, 1249, 1156, 1124, 1101, 1039, 1006. HRMS (ESI, m/z) calcd for $(\text{C}_{26}\text{H}_{48}\text{O}_2\text{Si}_2\text{Na})^+$ 471.3085, found 471.3095.

(E)-5-Methyl-1-phenyldec-4-ene-3,7-diol **12b** and 5-methylene-1-phenyldecane-3,7-diol **13b**¹⁰

To a stirred solution of allylic silane **11b** (35.9 mg, 0.080 mmol) in DMF (1.7 mL) were added water (9 μL , 0.47 mmol, 6.0 equiv.) and tetrabutylammonium fluoride (1.0 M solution in THF, 0.48 mL, 0.48 mmol, 6.0 equiv.). The solution was stirred at 65°C for 1 h and was then quenched by addition of a saturated aqueous solution of ammonium chloride (2 mL). The mixture was then extracted with diethyl ether (3 \times 2 mL) and the combined organic layers were washed with brine (3 \times 5 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether–ethyl acetate 4/6) gave alcohol **12b** (7.3 mg, 35%) as a clear oil and alcohol **13b** (7.3 mg, 35%) as a clear oil (1 : 1 mixtures of diastereomers). **12b**: ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.26 (m, 2H), 7.20–7.16 (m, 3H), 5.35–5.31 (m, 1H), 4.44–4.38 (m, 1H), 3.76–3.69 (m, 1H), 2.75–2.62 (m, 2H), 2.21 (dd, $J = 13.5, 3.3$ Hz, 1H), 2.06 (ddd, $J = 13.5, 9.3, 0.8$ Hz, 1H), 1.99–1.90 (m, 1H), 1.82–1.73 (m, 1H), 1.69 (d, $J = 1.2$ Hz, 3H), 1.51–1.41 (m, 4H), 0.94 (t, $J = 7.1$ Hz, 3H). **13b**: ^1H NMR (400 MHz, CDCl_3) δ 7.31–7.17 (m, 5H), 5.01 (s, 1H), 4.99 (s, 1H), 3.82–3.71 (m, 2H), 2.86–2.79 (m, 1H), 2.75–2.66 (m, 1H), 2.34–2.02 (m, 4H), 1.85–1.76 (m, 2H), 1.50–1.34 (m, 4H), 0.96–0.92 (m, 3H). Obtained data in accordance with previously reported data.¹⁰

(E)-5-Methyl-1-phenyldec-4-en-3-ol **12a** and 5-methylene-1-phenyldecane-3-ol **13a**¹⁰

To a stirred solution of allylic silane **11a** (38.0 mg, 0.12 mmol) in DMF (2.5 mL) at 0°C were added TBAF(H_2O)₃ (99.0 mg, 0.315 mmol, 2.50 equiv.). The solution was then stirred at 0°C for 30 min and was then quenched by addition of a saturated aqueous solution of ammonium chloride (3 mL). The mixture was then extracted with diethyl ether (3 \times 5 mL) and the combined organic layers were washed with brine (3 \times 5 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether : ether 3 : 2) gave alcohol **12a** (22.0 mg, 71%) as a clear oil and alcohol **13a** (5.0 mg, 16%) as a clear oil. Following the same procedure **12a** and **13a** were prepared in 54% and 10% yield respectively



using TBAF(*t*-BuOH)₄ (133 mg, 0.24 mmol, 2 equiv.). **12a**: ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.27 (m, 2H), 7.24–7.14 (m, 3H), 5.23 (ddd, *J* = 8.7, 2.5, 1.2 Hz, 1H), 4.40 (dtd, *J* = 9.9, 6.6, 3.5 Hz, 1H), 2.69–2.67 (m, 2H), 2.00 (m, 2H), 1.98–1.89 (m, 1H), 1.82–1.72 (m, 1H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.48–1.39 (m, 2H), 1.37–1.25 (m, 5H), 0.90 (s, 3H). **13a**: ¹H NMR (400 MHz, CDCl₃) δ 7.32–7.28 (m, 2H), 7.24–7.17 (m, 3H), 4.90 (m, 1H), 4.84 (s, 1H), 3.79–3.68 (m, 1H), 2.92–2.80 (m, 1H), 2.71 (dt, *J* = 13.8, 8.1 Hz, 1H), 2.28 (dd, *J* = 13.5, 3.3 Hz, 1H), 2.11 (dd, *J* = 13.8, 9.4 Hz, 1H), 2.01 (t, *J* = 7.7 Hz, 2H), 1.84–1.74 (m, 3H), 1.46–1.26 (m, 6H), 0.90 (t, *J* = 7.0 Hz, 3H). Obtained data in accordance with previously reported data.¹⁰

Chlorodimethyl(2-methylallyl)silane¹²

To a 3-neck flask fitted with a reflux condenser was added pre-dried magnesium turnings (4.86 g, 200 mmol, 2.00 equiv.), diethyl ether (230 mL) and 3 drops of 1,2-dibromoethane. Then, a mixture of dimethyldichlorosilane (12.1 mL, 100 mmol) and 3-chloro-2-methyl-1-propene (14.7 mL, 150 mmol, 1.50 equiv.) in diethyl ether (20 mL) was added dropwise over 4 h, maintaining gentle reflux. The reaction mixture was stirred for a further 12 h at room temperature at which point a white precipitate had formed. After filtering off the white solid, the filtrate was concentrated at 20 °C, 250 mbar. The crude product was then purified by vacuum distillation at 50 °C, 20 mbar furnishing chlorodimethyl(2-methylallyl)silane (4.99 g, 34 mmol, 34%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 4.60 (s, 1H), 4.50 (s, 1H), 1.73 (m, 3H), 1.57 (s, 2H), 0.10 (2s, 6H). Obtained data in accordance with previously reported data.¹²

Dimethyl(7-methylallyl)((5-phenylpent-1-en-3-yl)oxy)silane 15

To a stirred solution of allylic alcohol **1** (500 mg, 3.08 mmol) and chlorodimethyl(2-methylallyl)silane (687 mg, 4.62 mmol, 1.50 equiv.) in dichloromethane (6 mL) at 0 °C was added imidazole (630 mg, 9.25 mmol, 3.00 equiv.) and DMAP (10 mg, 0.08 mmol, 0.025 equiv.). The reaction mixture was then left to warm to room temperature and stirred for further 2 h. Then, water (5 mL) was added and the mixture was extracted with diethyl ether (3 × 5 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether:ether 99:1) gave **15** (845 mg, 3.08 mmol, quant.) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.31–7.28 (m, 3H), 7.21–7.18 (m, 2H), 5.85 (ddt, *J* = 16.9, 10.3, 6.4 Hz, 1H), 5.19 (dd, *J* = 17.1, 0.9 Hz, 1H), 5.10 (dd, *J* = 10.3, 0.8 Hz, 1H), 4.64 (s, 1H), 4.55 (s, 1H), 4.18–4.14 (m, 1H), 2.73–2.60 (m, 2H), 1.90–1.80 (m, 2H), 1.78 (s, 3H), 1.66 (s, 2H), 0.16 (s, 3H), 0.15 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 142.8, 142.2, 141.2, 128.4, 128.3, 125.7, 114.4, 108.9, 73.6, 39.5, 31.6, 28.9, 25.3, −1.1, −1.4. IR (neat, cm^{−1}) 2959, 2914, 2940, 1638, 1454, 1252, 1078. HRMS (ESI, *m/z*) calcd for (C₁₇H₂₈OSiNa)⁺ 297.1651, found 297.1637.

5,8,8-Trimethyl-3-phenethyl-3,9-dihydro-2H-8,9-oxasiline 16

Diene **15** (260 mg, 0.95 mmol) and Grubbs II (20.0 mg, 0.024 mmol, 0.025 equiv.) in degassed dichloromethane

(9.5 mL) were refluxed for 2 h. The solvent was then removed by concentrating *in vacuo*. Petroleum ether (5 mL) and diethyl ether (5 mL) were then added and the diethyl ether was removed by concentrating *in vacuo*. The resultant solution that had specs of dark solid was passed through a plug of silica and rinsed with petroleum ether, thus giving the desired silacycle **16** as colorless oil that was immediately used in the next step with no further purification. ¹H NMR (400 MHz, CDCl₃) δ 7.30–7.25 (m, 2H), 7.24–7.14 (m, 3H), 5.35–5.34 (m, 1H), 5.19 (ddd, *J* = 9.1, 4.5, 2.2 Hz, 1H), 2.80–2.64 (m, 2H), 1.89–1.73 (m, 5H), 1.27–1.11 (m, 2H), 0.19 (s, 3H), 0.16 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 142.6, 132.4, 128.5, 128.2, 126.0, 125.6, 71.4, 40.2, 31.4, 28.2, 17.6, 0.3, −0.8. IR (neat, cm^{−1}) 3028, 2959, 1715, 1454, 1250, 1140, 1030. HRMS (ESI, *m/z*) calcd for (C₁₅H₂₂OSiNa)⁺ 269.1338, found 269.1328.

(Z)-2-Methyl-6-phenylhex-2-ene-1,4-diol 17

The above silacycle **16** was dissolved in a mixture of MeOH (9.5 mL) and THF (9.5 mL), then KF (275 mg, 4.75 mmol, 5.00 equiv.) and KHCO₃ (219 mg, 2.19 mmol, 2.30 equiv.) were added followed by the dropwise addition of a 30% aqueous solution of H₂O₂ (4.6 mL, 35 mmol, 37 equiv.). The reaction mixture was left to stir at room temperature for 16 h and was quenched with a saturated aqueous solution of sodium thiosulfate (20 mL). NaCl was then added until the mixture became saturated followed by extraction of the product with ethyl acetate (5 × 20 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (petroleum ether: ether 1:1) gave diol **17** (168 mg, 0.81 mmol, 86% over 2 steps) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.30–7.26 (m, 2H), 7.22–7.15 (m, 3H), 5.40 (d, *J* = 8.3 Hz, 1H), 4.46–4.41 (m, 1H), 4.22 (d, *J* = 12.3 Hz, 1H), 4.00 (d, *J* = 12.3 Hz, 1H), 2.74–2.63 (m, 2H), 2.04–1.90 (m, 3H), 1.83 (m, 3H), 1.81–1.76 (m, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 141.7, 138.7, 130.9, 128.4, 128.4, 125.9, 67.3, 62.1, 39.1, 31.7, 21.8. IR (neat, cm^{−1}) 3024, 2920, 2851, 1724, 1601, 1493, 1454, 1373, 1261, 1072. HRMS (ESI, *m/z*) calcd for (C₁₃H₁₈OSiNa)⁺ 269.1199, found 269.1190.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support for this work was provided by the University of Glasgow and the EPSRC (Doctoral Training Allocation for A. F. T. EP/M508056/1).

References

- 1 A. Zampella, M. V. D'Auria, L. Minale, C. Debitus and C. Roussakis, *J. Am. Chem. Soc.*, 1996, **118**, 11085.



- 2 K. Suenaga, T. Nagoya, T. Shibata, H. Kigoshi and K. Yamada, *J. Nat. Prod.*, 1997, **60**, 155.
- 3 (a) A. Vincent and J. Prunet, *Synlett*, 2006, 2269; (b) L. Grimaud, R. de Mesmay and J. Prunet, *Org. Lett.*, 2002, **4**, 419; (c) L. Grimaud, D. Rotulo, R. Ros-Perez, L. Guitry-Azam and J. Prunet, *Tetrahedron Lett.*, 2002, **43**, 7477; (d) D. Rotulo-Sims and J. Prunet, *Org. Lett.*, 2007, **9**, 4147.
- 4 M.-G. Braun, A. Vincent, M. Boumediene and J. Prunet, *J. Org. Chem.*, 2011, **76**, 4921.
- 5 (a) P. A. Evans, *Metathesis in Natural Product Synthesis*, ed. J. Cossy, S. Arseniyadis and C. Meyer, Wiley, New York, 2010, p. 225; (b) A. Čusak, *Chem. – Eur. J.*, 2012, **18**, 5800; (c) J. H. Jun, S. Javed, C. N. Ndi and P. R. Hanson, *Synthesis of Heterocycles by Metathesis Reactions*, ed. J. Prunet, Springer, 2017, p. 319.
- 6 R. Matsui, K. Seto, Y. Sato, T. Suzuki, A. Nakazaki and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2011, **50**, 680.
- 7 P. A. Evans, A. Čusak, A. Grisin, M. J. Lawler and M. Pink, *Synthesis*, 2016, **48**, 2402.
- 8 (a) F. Li and M. J. Miller, *J. Org. Chem.*, 2006, **71**, 5221; (b) J. C. Tung, W. Chen, B. C. Noll, R. E. Taylor, S. C. Fields, W. H. Dent III and F. R. Green, *Synthesis*, 2007, 2388.
- 9 See for example: C. Rodríguez-Esrich, F. Urpí and J. Vilarrasa, *Org. Lett.*, 2008, **10**, 5191.
- 10 For a preliminary account of this work, see: A. F. Tiniakos, S. Wittmann, A. Audic and J. Prunet, *Org. Lett.*, 2019, **21**, 589, <https://pubs.acs.org/doi/10.1021/acs.orglett.8b03552>. Further permissions related to the material excerpted should be directed to the ACS.
- 11 A. Meijere, D. Faber, U. Heinecke, R. Walsh, T. Müller and Y. Apeloig, *Eur. J. Org. Chem.*, 2001, 663.
- 12 A. Fürstner and D. Voigtländer, *Synthesis*, 2000, 959.
- 13 Z. Li, C. Yang, H. Zheng, H. Qiu and G. Lai, *J. Organomet. Chem.*, 2008, **693**, 3771.
- 14 C. Meyer and J. Cossy, *Tetrahedron Lett.*, 1997, **38**, 7861.
- 15 J. S. Clark, C. A. Baxter, A. G. Dossetter, S. Poigny, J. L. Castro and W. G. Whittingham, *J. Org. Chem.*, 2008, **73**, 1040.
- 16 Compound **7d** was obtained by cleavage of the silyl ether of **7b** followed by reprotection of the resulting alcohol as its *p*-methoxybenzyl ether, see Experimental section for details.
- 17 J. Legros, F. Meyer, M. Coliboeuf, B. Crousse, D. Bonnet-Delpont and J.-P. Bégué, *J. Org. Chem.*, 2003, **68**, 6444.
- 18 Y. Zhang, X. Jia and J.-X. Wang, *Eur. J. Org. Chem.*, 2009, 2983.
- 19 A. Shibato, Y. Itagaki, E. Tayama, Y. Hokke, N. Asao and K. Maruoka, *Tetrahedron*, 2000, **56**, 5373.
- 20 A. Kunai and J. Ohshita, *J. Organomet. Chem.*, 2003, **686**, 3.
- 21 R. Savelle, W. Zawartka and R. Leino, *Organometallics*, 2012, **31**, 3199.
- 22 P. Pongkittiphan, E. A. Theodorakis and W. Chavasiri, *Tetrahedron Lett.*, 2009, **50**, 5080.
- 23 H. Ito, A. Watanabe and M. Sawamura, *Org. Lett.*, 2005, **7**, 1869.
- 24 Methallyldimethylsilane was too volatile to be isolated in good yield from the Peterson olefination.
- 25 L. E. Overman and D. Lesuisse, *Tetrahedron Lett.*, 1985, **26**, 4167.

