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Synthesis of Solandelactone F, Constanolactone A, Advanced Intermediate Towards Solandelactone E from a Common Synthetic Intermediate

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Abstract: The stereoselective synthesis of solandelactone F, constanolactone A and an advanced intermediate towards solandelactone E, from a common synthetic intermediate, is disclosed. The propargylic sulfide stereocenter is created stereoselectively via carbon-carbon bond formation in the reaction of α-chloro sulfides with alkynylzinc reagents via 1,2-asymmetric induction by a β-siloxy group. The characteristic 1,4-diol motif of the natural products is introduced by a [2,3] sigmatropic rearrangement of an allylic sulfoxide or by Mislow-Evans-Braverman rearrangement of a propargylic sulfoxide followed by stereoselective reduction of the ensuing α, β-unsaturated ketone. Unlike earlier reports, the C11/C9 carbinol center is created with excellent stereocontrol and derivatives of natural products differing at C14/C12 can be readily obtained. Catalytic asymmetric protocols and substrate-controlled asymmetric induction is utilized for the efficient introduction of the stereogenic centers.

Introduction

The marine environment is a source of a multitude of new compounds belonging to unique structural classes. In 1996, Shin and co-workers isolated solandelactones E (**1**) and F (**2**) from the hydroid *Solanderia secunda*, near the Jaeju island in Korea.[1] Solandelactones constitute the family of oxygenated fatty acids, oxylipins that include constanolactones A (**3**) and B (**4**),[2] halicholactone (**5**) and neohalicholactone (**6**)[3], (Figure 1).

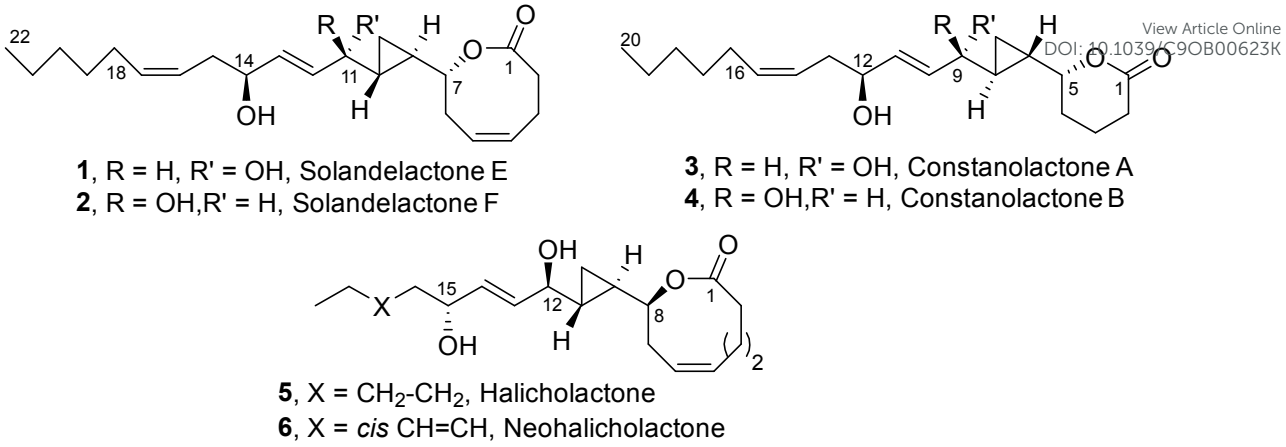

Figure 1. Oxylipins isolated from marine organisms.

The structural features common to oxylipins include a long alkyl chain incorporating a 2-ene-1,4-diol moiety and a lactone ring attached to a *trans*-cyclopropane ring. While solandelactones, halicholactone and neohalicholactone possess a (*R*,*R*)-disubstituted cyclopropane motif, constanolactones are endowed with the reversed (*S*,*S*)-configuration. Another difference is that while the lactone oxygen and the remote carbinol in the alkyl chain have the same configuration in solandelactones and constanolactones, it is reversed in halicholactones and neohalicholactones. The oxylipins display inhibitory activity against 5-lipoxygenase[3] and farnesyl transferase,[4] found in cancer cells. Their unique structural features and limited availability from natural sources have attracted the attention of synthetic chemists. Martin and co-workers reported the first, linear stereoselective synthesis of solandelactone E and F thereby correcting the original incorrect absolute configuration assignment at C11.[5] Subsequently, White[6] and Pietruszka[7] disclosed the synthesis of solandelactones A-H exploiting the Nozaki-Hiyama-Kishi reaction. The same strategy was adopted in many syntheses of halicholactones[8] and constanolactones[9] to create the C-11 carbinol stereocenter which unfortunately, proceeded with poor stereocontrol (dr 2:1). Recently, Aggarwal and co-workers reported a stereoselective synthesis of solandelactones E and F through a lithiation-borylation-allylation sequence.[10]

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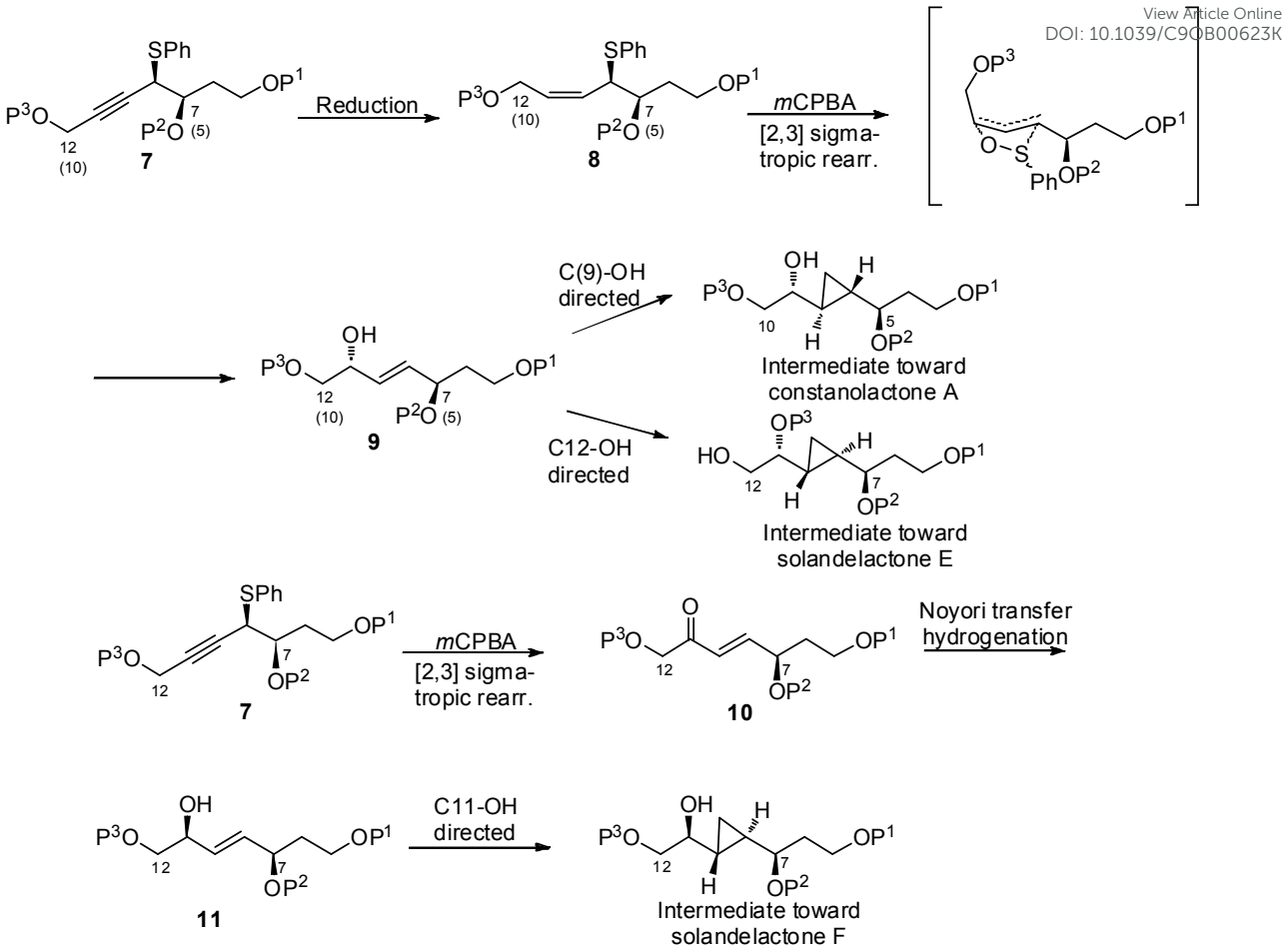
The main challenges to be overcome in any new synthetic proposal towards oxylipins includes the creation of the C11 carbinol with perfect stereocontrol and the cyclopropane ring with the correct absolute stereochemistry. Our unique strategy for the synthesis of solandelactones E, F and constanolactone A with stereocontrol at C11/C9 (natural product numbering respectively) relied on taking advantage of a new methodology[11] developed for the stereocontrolled synthesis of 1,4-diols from β-siloxy propargylic sulfides. The method comprised of the stereoselective preparation of propargylic sulfide **7**, its semihydrogenation to sulfide **8**, oxidation to sulfoxide and Mislow-Evans rearrangement to afford tetrol derivative **9**. Cyclopropanation following Furukawa's protocol,[12] directed by the newly created C9-carbinol (constanolactone numbering), would serve to secure the (*S*,*S*)-configuration of the cyclopropane ring as present in constanolactone A. Alternately, homoallylic C12-hydroxy (solandelactone numbering) directed cyclopropanation following Charette's report[13] would deliver the (*R*,*R*)-cyclopropane configuration present in solandelactone E. Oxidation of sulfide **7** followed by [2,3] sigmatropic shift would furnish unsaturated ketone **10** that on asymmetric reduction would afford alcohol **11**, the epimer of compound **9**. Cyclopropanation following Furukawa's protocol directed by the secondary hydroxyl would serve to introduce the (*R*,*R*)-cyclopropane configuration of solandelactone F. Thus, a common synthon was envisioned to access solandelactones E, F and constanolactone A, Scheme 1.



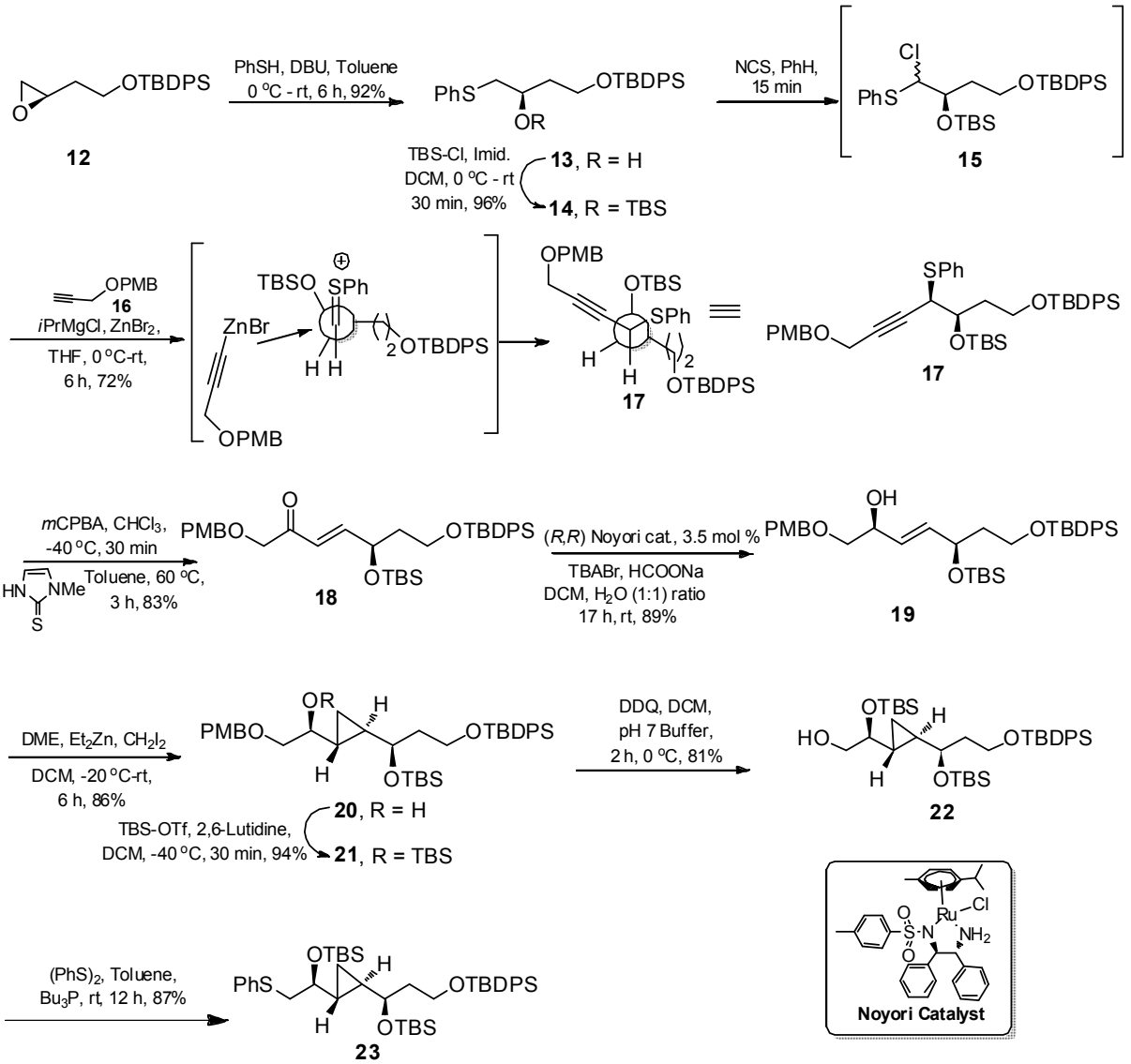
Scheme 1. Strategy for the synthesis of solandelactones E, F and constanolactones A from a common intermediate **7**.

Results and discussion

Synthesis of Solandelactone F

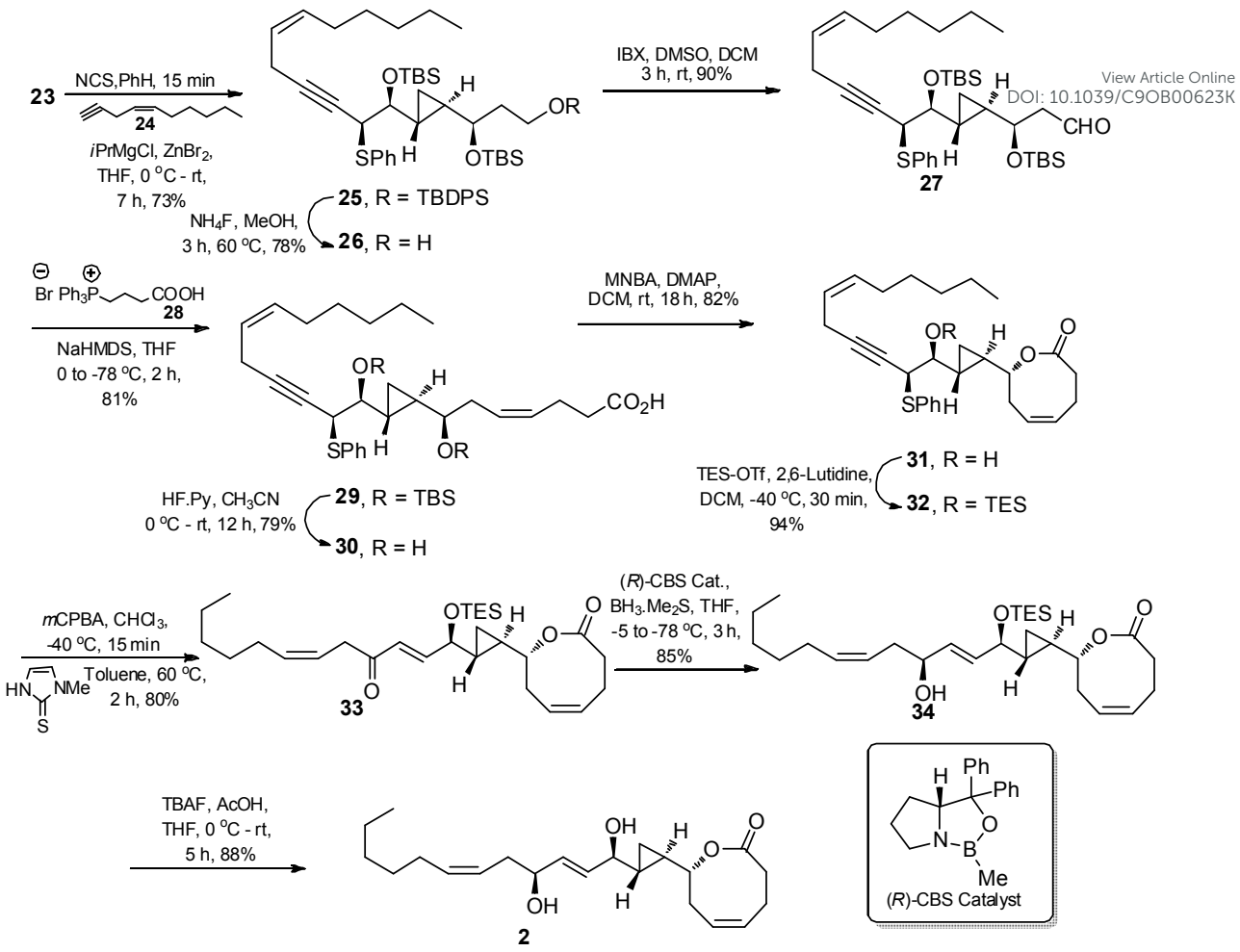
The synthesis of solandelactone F began from the known epoxide **12**[14] which on reaction with thiophenol in the presence of catalytic amount of DBU afforded the hydroxy sulfide **13**. Protection under standard conditions furnished silyl ether **14**. Propargylic sulfide **17** was prepared stereoselectively by reaction of the α-chloro sulfide **15**, obtained by treatment of sulfide **14** with *N*-chlorosuccinimide (NCS), with the alkynylzinc bromide prepared from propargyl ether **16**.[11] The configuration of the newly created stereocenter in compound **17** was unambiguously established by comparison of the ^{1}H NMR spectra of the diastereomeric mandelate esters derived from allylic alcohol **36** (vide infra). Selective

oxidation of the sulfide with *m*CPBA at low temperature afforded an epimeric mixture of sulfoxides which without isolation was subjected to Mislow-Evans-Braverman rearrangement[15] in the presence of *N*-methyl thioimidazole[16] to furnish α,β-unsaturated ketone **18**. Stereoselective transfer hydrogenation using (*R*,*R*)-TsDPEN-[RuCl(cymene)] in aqueous media[17] afforded allyl alcohol **19** (dr 96:4, 89%). Hydroxy directed cyclopropanation following Furukawa's protocol cleanly furnished the cyclopropane derivative **20**. Protection of the carbinol as its silyl ether **21** followed by deprotection of the PMB ether[18] afforded alcohol **22**. Following Hata's protocol,[19] alcohol **22** was converted to sulfide **23** (Scheme 2) setting the stage for further C-C bond (C12-C13) formation.



Scheme 2. Synthesis of sulfide **23**.

Treatment of sulfide **23** with NCS followed by reaction of the ensuing chloro sulfide with alkynylzinc bromide prepared from enyne **24**[20] afforded propargylic sulfide **25** stereoselectively.[11] The two choices available for further progress towards the target were a) creation of the C14 carbinol stereocenter and b) construction of the lactone ring by Wittig olefination of an aldehyde, derived eventually from the primary silyl ether **25**. To avoid the extra obligatory step of protecting the C14 hydroxyl during the oxidation of the primary hydroxyl to an aldehyde, the first option was not exercised. Proceeding, the primary silyl ether in compound **25** was selectively deprotected using ammonium fluoride[21] in methanol to yield alcohol **26**. Oxidation with IBX[22] afforded the aldehyde **27** which was subjected to homologation with the ylide generated from phosphonium salt **28**[23] to afford unsaturated acid **29**. Deprotection of the TBS ethers using HF-pyridine[24] afforded the seco acid **30** which on lactonization using Shiina's protocol[25] afforded the sulfide **31**. The C11-hydroxy group was protected as its TES ether **32** and the sulfide transformed into unsaturated ketone **33** following the two step one-pot protocol discussed above.[26] Reduction of the unsaturated ketone using (*R*)-CBS reagent[27] yielded alcohol **34** (dr >95:<5, 85%). Deprotection of the TES ether using TBAF buffered with acetic acid furnished solandelactone F (**2**), Scheme 3 with physical constants in good agreement with reported data.[10b] The overall yield is 4.05%.

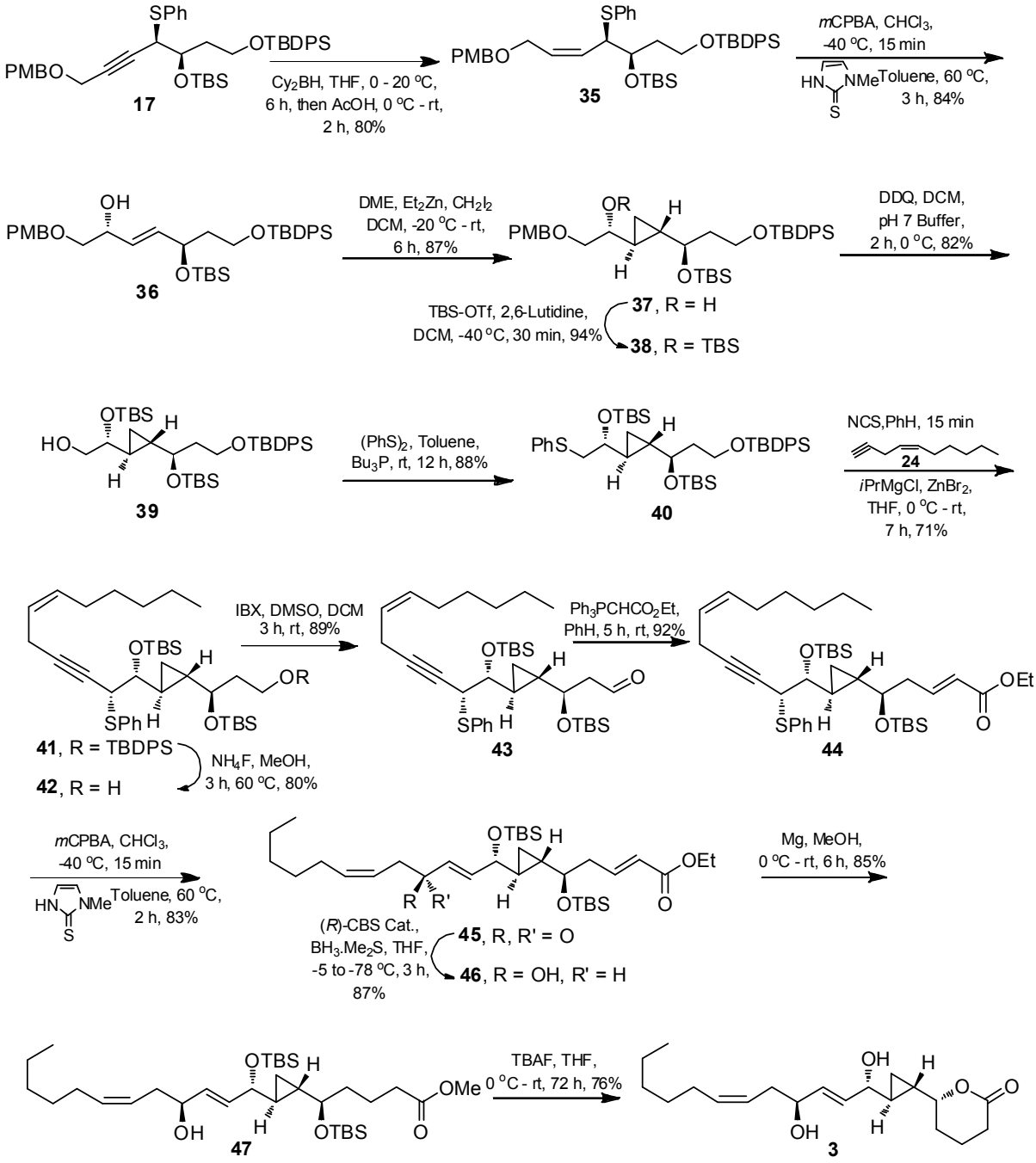


Scheme 3. Synthesis of solandelactone F.

Synthesis of constanolactone A

The synthesis of constanolactone A began from propargylic sulfide **17** which on semihydrogenation using dicyclohexylborane afforded allylic sulfide **35**. Oxidation of the sulfide followed by rearrangement furnished the allyl alcohol **36**.[28] Cyclopropanation proceeded stereoselectively to furnish alcohol **37** which was protected as its silyl ether **38**. Deprotection of the PMB ether afforded primary alcohol **39** which was readily converted to sulfide **40**. Propargyl sulfide **41** was obtained stereoselectively[11] by reaction of the derived chloro sulfide and alkynylzinc bromide. Selective deprotection of the silyl ether followed by oxidation of the resulting alcohol **42** afforded aldehyde **43**. Wittig olefination afforded the *trans*-ester **44** selectively. Unsaturated ketone **45** was obtained cleanly by the one-pot oxidation-rearrangement sequence. Reduction using (*R*)-CBS reagent furnished alcohol **46**.

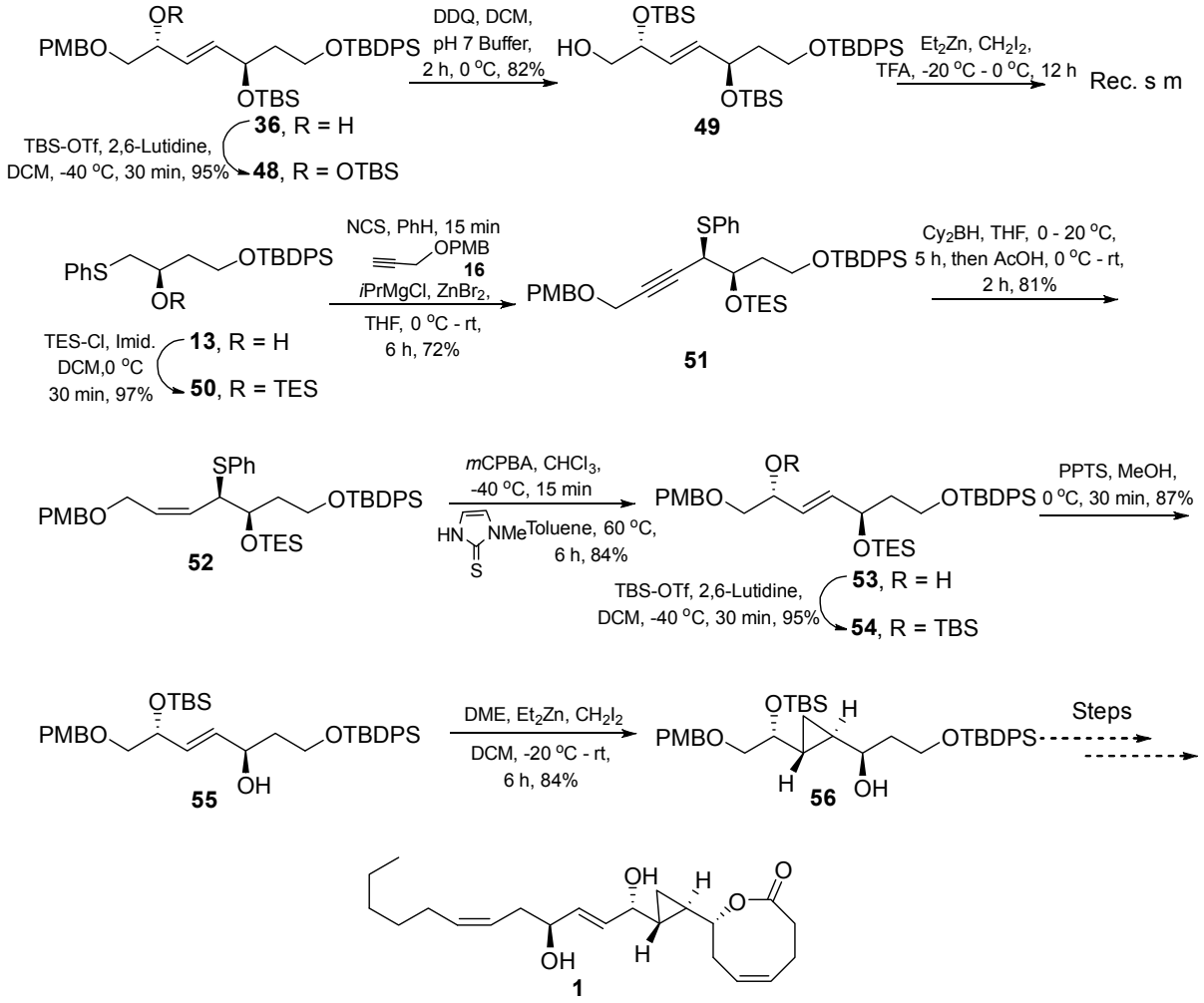
Conjugate reduction of the unsaturated ester using Mg/MeOH[29] yielded compound **47**. TBAF promoted desilylation resulted in concomitant cyclization to furnish constanolactone A (**3**), (Scheme 4) with physical characteristics in good agreement with literature data.[2b] The overall yield is 5.47%.



Scheme 4. Synthesis of constanolactone A.

Synthesis of an intermediate towards Solandelactone E

The creation of (*R*,*R*)-cyclopropane ring of solandelactone E was envisioned using homoallylic hydroxyl directed cyclopropanation of compound **49**, *anti* to the C11-silyl ether, based on the precedent of Charette.[13] Alcohol **36** was protected as its silyl ether **48** and the PMB ether was deprotected to furnish the requisite alcohol **49**. Cyclopropanation using Shi's protocol[30] as disclosed by Charette and co-workers returned unreacted starting material along with minor quantities of desilylated alcohol. Extended periods of time, excess reagents or elevated temperatures were of no avail.[31] Having been unsuccessful in using the homoallylic alcohol to direct cyclopropanation, we turned to the C-7 hydroxy group directed cyclopropanation to create the desired configuration. Towards this objective, alcohol **13** was protected as its TES ether **50**. Further reaction with NCS and alkynylzinc bromide afforded propargylic sulfide **51** stereoselectively.[11]



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Scheme 5. Synthesis of an advanced intermediate towards solandelactone E.

Semihydrogenation using dicyclohexylborane afforded sulfide **52** which was transformed into alcohol **53**. Protection of the hydroxyl as its TBS ether afforded compound **54** which on selective deprotection of the TES ether using PPTS yielded alcohol **55**. Cyclopropanation using Furukawa's protocol proceeded cleanly to furnish alcohol **56**, which is a key intermediate that can be elaborated to solandelactone E following an identical sequence of reactions delineated for the synthesis of the epimer solandelactone F, from compound **20**, Scheme 5. The alcohol **56** possesses the correct absolute configuration of the C11 carbinol and the cyclopropane ring for elaboration to solandelactone E.

Conclusions

A highly stereoselective route to solandelactone E, F and constanolactone A is disclosed. The stereogenic centers are created by catalytic asymmetric reactions and substrate-controlled asymmetric induction. The potential of α-chloro sulfides for stereoselective carbon-carbon bond formation is elegantly demonstrated. The propargyl/allyl sulfides have been utilized for 1,4-diol synthesis in an iterative fashion to create the carbinol stereocenters of oxylipins. The disclosed route permits to vary the configuration of C11 and C14 carbinols at will by appropriate choice of Noyori/CBS catalysts. Attempted use of a homoallylic alcohol to direct cyclopropanation *anti* to the existing allyl silyl ether based on Charette's precedent did not bear fruit.

Experimental

General Information

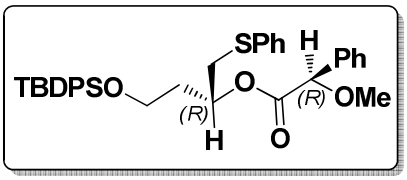
Dry reactions were performed under an inert atmosphere using nitrogen. All glassware apparatus used for reactions were thoroughly oven-dried. Anhydrous solvents were distilled prior to use: THF from Na and benzophenone; CH_2Cl_2 and toluene from CaH_2; MeOH from Mg cake; $CHCl_3$ from P_2O_5; acetone from $KMnO_4$ and K_2CO_3. Commercial reagents were

used without purification. Column chromatography was carried out by using silica gel (100−200 mesh). Analytical thin-layer chromatography (TLC) was run on silica gel 60 F254 precoated plates (250 μm thickness). Optical rotations $[\alpha]_D$ were measured on a polarimeter and are given in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were recorded neat or in KBr (as mentioned) and reported in wavenumbers (cm^{-1}). Mass spectral data were obtained using MS (EI) ESI and HRMS mass spectrometers. High-resolution mass spectra (HRMS; ESI+) were obtained using either a TOF or a double-focusing spectrometer. ^{1}H NMR spectra were recorded at 300, 400, or 500 MHz and ^{13}C NMR spectra at 75, 100, or 125 MHz in $CDCl_3$ with the residual solvent signal as an internal standard unless mentioned otherwise; chemical shifts are in ppm downfield from tetramethylsilane, and coupling constants (J) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

(*R*)-4-((*tert*-Butyldiphenylsilyl)oxy)-1-(phenylthio)butan-2-ol (13): To a stirred mixture of DBU (0.75 mL, 5 mmol) and thiophenol (5.6 mL, 54.5 mmol) in toluene (20 mL) cooled at 0 °C was added a solution of epoxide **12** (16.14 g, 49.5 mmol) in toluene (50 mL). The resulting reaction mixture was stirred at rt for 6 h and quenched by the addition of 0.5 N HCl (20 mL). The layers were separated and the aq layer extracted with EtOAc (2x30 mL). The combined organic layers were washed with 1 N NaOH (30 mL), brine (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The resulting compound was purified by silica gel column chromatography using 10% EtOAc/hexanes as the eluent to afford compound **13** (19.86 g, 45.6 mmol) in 92% yield as an oil. TLC: R_f 0.3 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ = -3.4 (*c* 1.05, $CHCl_3$); IR (neat): 3478, 3069, 2931, 2857, 1585, 1427, 1109, 703, 505 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.61 (m, 4H), 7.44–7.34 (m, 8H), 7.31–7.23 (m, 2H), 7.22–7.14 (m, 1H), 4.07–3.97 (m, 1H), 3.92–3.77 (m, 2H), 3.40 (s, 1H), 3.12–2.97 (m, 2H), 1.90–1.71 (m, 2H), 1.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

135.7, 135.3, 132.9, 132.8, 129.6, 129.3, 128.8, 127.6, 126.0, 68.7, 62.0, 41.0, 37.4, 26.7, 18.9; MS (ESI-TOF) *m/z*: 459 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{26}H_{32}NaO_2SSi$ 459.1784; found 459.1782.

(*R*)-(*R*)-4-((*tert*-Butyldiphenylsilyl)oxy)-1-(phenylthio)butan-2-yl2-methoxy-2-phenyl acetate:



To a solution of alcohol **13** (15 mg, 0.034 mmol) in dichloromethane (0.5 mL) cooled at 0 ^oC was added (*R*)-methoxyphenylacetic acid (6.8 mg, 0.041 mmol), DMAP (1 mg, 20 mol%) and EDC.HCl (9.8 mg, 0.051 mmol). The reaction mixture was stirred at rt for 2 h. After complete consumption of starting material, the reaction mixture was diluted with dichloromethane (2 mL) and H_2O (2 mL). The layers were separated and the aq layer was extracted with dichloromethane (2x5 mL). The combined organic layers were sequentially washed with satd aq $NaHCO_3$ (5 mL), 1 N HCl (5 mL), H_2O (2x5 mL), brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford the corresponding ester in 89% yield as a liquid. The crude product was characterised by ^1H NMR spectroscopy. TLC: R_f 0.4 (10% EtOAc/hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 7.63–7.53 (m, 4H), 7.48–7.11 (m, 16H), 5.31–5.20 (m, 1H), 4.68 (s, 1H), 3.67–3.55 (m, 2H), 3.38 (s, 3H), 3.08 (dd, *J* = 13.7, 6.1 Hz, 1H), 2.89 (dd, *J* = 13.7, 6.6 Hz, 1H), 2.11–1.96 (m, 1H), 1.89–1.74 (m, 1H), 0.97 (s, 9H).

(*R*)-(*S*)-4-((*tert*-Butyldiphenylsilyl)oxy)-1-(phenylthio)butan-2-yl 2-methoxy-2-phenyl acetate:

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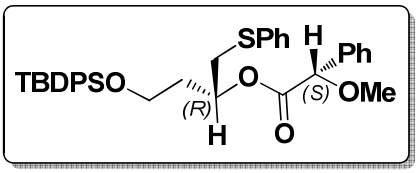

Alcohol **13** (15 mg, 0.034 mmol) was reacted with (*S*)-methoxyphenylacetic acid (6.8 mg, 0.041 mmol) as described above to furnish the corresponding ester in 92% yield as a liquid. The crude product was characterised by ^{1}H NMR spectroscopy. TLC: R_f 0.35 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55–7.48 (m, 4H), 7.44–7.37 (m, 4H), 7.37–7.29 (m, 6H), 7.29–7.16 (m, 6H), 5.31–5.23 (m, 1H), 4.53 (s, 1H), 3.44–3.36 (m, 1H), 3.34 (s, 3H), 3.32–3.24 (m, 1H), 3.20 (dd, *J* = 14.0, 6.2 Hz, 1H), 3.10 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.94–1.83 (m, 1H), 1.76–1.66 (m, 1H), 0.93 (s, 9H).

Note: The configuration of alcohol **13** was unambiguously assigned by comparison of the ^{1}H NMR spectra of the mandelate esters. In agreement with the assignment of '*R*' configuration for the carbinol **13**, the C*H*$_2$OTBDPS appeared downfield in the '*R*' ester while the C*H*$_2$SPh appeared downfield in the '*S*' ester.

(*R*)-2,2,3,3,10,10-Hexamethyl-9,9-diphenyl-5-((phenylthio)methyl)-4,8-dioxa-3,9-disila undecane (14): To a solution of alcohol **13** (19 g, 43.75 mmol) in anhydrous dichloromethane (40 mL) cooled at 0 °C was added imidazole (6.25 g, 91.9 mmol) followed by TBS-Cl (6.92 g, 45.9 mmol). The reaction mixture was allowed to warm to rt and stirred for 30 min. The reaction mixture was quenched by the addition of water (30 mL) and diluted with dichloromethane (30 mL). The layers were separated, the organic layer was washed with water (30 mL), brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 2% EtOAc/hexane (v/v) to give the pure silyl ether **14** (23.1 g, 42 mmol) in 96% yield as a gummy oil. TLC: R_f 0.5 (2% EtOAc/hexane); $[\alpha]^{20}_D$ = +21.6 (*c* 1.0, $CHCl_3$); IR (neat): 3068, 2954, 2857, 1585, 1470, 1253, 1108, 701, 503 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.67–7.63 (m, 4H), 7.42–7.32 (m, 8H), 7.27–7.22 (m, 2H), 7.18–7.13 (m, 1H), 4.12–4.04 (m, 1H), 3.74 (t, J = 6.2 Hz, 2H), 3.05–3.00 (m, 2H), 2.0-1.91 (m, 1H), 1.79–1.69 (m, 1H), 1.03 (s, 9H), 0.84 (s, 9H), 0.03 (s, 3H), -0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 135.54, 135.52, 133.78, 133.73, 129.5, 129.3, 128.7, 127.6, 125.8, 68.6, 60.3, 41.2, 39.1, 26.8, 25.8, 19.1, 18.0, -4.4, -4.7; MS (ESI-TOF) *m/z*: 573 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{32}H_{46}NaO_2SSi_2$ 573.2649; found 573.2656.

(*R*)-5-((*R*)-4-((4-Methoxybenzyl)oxy)-1-(phenylthio)but-2-yn-1-yl)-2,2,3,3,10,10-hexa methyl -9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (17): To a solution of alkyne **16** (3.52 g, 20 mmol) in anhydrous THF (10 mL) cooled at 0 °C was added ^{i}PrMgCl·LiCl (1.5 M in THF, 14.6 mL, 22 mmol) and the mixture stirred for 30 min at the same temperature. To the so generated Grignard reagent was added a solution of $ZnBr_2$ (1.5 M in THF, 20 mL, 30 mmol) at 0 °C and the mixture stirred for 30 min. Separately, in another round-bottom flask, the chloro sulfide **15** was prepared by adding a solution of sulfide **14** (5.50 g, 10 mmol) in anhydrous benzene (50 mL) to NCS (1.33 g, 10 mmol) in anhydrous benzene (50 mL) and stirring for 15 min. To the organozinc reagent maintained at 0 °C was added a solution of chloro sulfide in benzene. The reaction mixture was stirred gradually allowing it to attain rt, and stirred further for a period of 6 h when TLC examination indicated complete consumption of the chloro sulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of satd aq NH_4Cl solution (20 mL). It was allowed to warm to rt and diluted with Et_2O (20 mL). The layers were separated and the aq layer was extracted with Et_2O (3×20 mL). The combined organic layers were washed with H_2O (30 mL), brine (20 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to afford a crude compound that was purified by column chromatography using 5% EtOAc/hexane (v/v) as the eluent to give the pure product **17** (5.22 g, 7.2 mmol) in 72% yield as a colorless liquid. TLC: R_f 0.3 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = -20.1 (c 0.85, $CHCl_3$); IR (neat): 3066, 2932, 2857,

1612, 1512, 1249, 1084, 701, 504 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.69–7.65 (m, 4H), 7.51–7.48 (m, 2H), 7.44–7.34 (m, 6H), 7.30–7.20 (m, 5H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.45 (s, 2H), 4.19–4.11 (m, 3H), 4.07 (dt, *J* = 3.7, 1.7 Hz, 1H), 3.81–3.77 (m, 5H), 2.19–2.11 (m, 1H), 1.96–1.88 (m, 1H), 1.05 (s, 9H), 0.86 (s, 9H), 0.01 (s, 3H), -0.03 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 135.54, 135.51, 134.6, 133.8, 133.7, 132.4, 129.7, 129.55, 129.52, 128.9, 127.6, 127.5, 127.4, 113.7, 84.0, 81.5, 70.5, 70.4, 60.3, 56.9, 55.1, 46.2, 36.1, 26.8, 25.7, 19.1, 18.0, -4.68, -4.70; MS (ESI-TOF) *m/z*: 747 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{56}NaO_4SSi_2$ 747.3330; found 747.3342.

(*R*,*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)-1-((4-methoxy benzyl) oxy)hept-3-en-2-one (18): To a solution of sulfide **17** (20.95 g, 29 mmol) in dichloromethane (20 mL) cooled at -40 °C was added *m*CPBA (7.15 g, 29 mmol) and the reaction mixture stirred at the same temperature for 30 min. Toluene (50 mL) and 2-mercapto-1-methyl-imidazole (3.97 g, 34.8 mmol) were added. The reaction mixture was stirred at 60 °C for 3 h and then quenched by the addition of satd aq $NaHCO_3$ (30 mL). The mixture was diluted with dichloromethane (30 mL) and the layers were separated. The combined organic layers were washed successively with water (50 mL), brine (30 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to furnish the crude compound which was purified by column chromatography using 5% EtOAc/hexanes (v/v) as the eluent to afford the product **18** (15.16 g, 24 mmol) in 83% yield as a liquid. TLC: R_f 0.1 (5% EtOAc/hexanes); $[\alpha]^{20}_D$ = +13.2 (*c* 0.6, $CHCl_3$); IR (neat): 3070, 2954, 2857, 1695, 1629, 1513, 1251, 1108, 704, 505 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.66–7.62 (m, 4H), 7.44–7.34 (m, 6H), 7.29–7.25 (m, 2H), 6.92 (dd, *J* = 15.8, 4.7 Hz, 1H), 6.89–6.86 (m, 2H), 6.44 (dd, *J* = 15.8, 1.6 Hz, 1H), 4.59–4.55 (m, 1H), 4.52 (s, 2H), 4.17 (d, *J* = 16.8 Hz, 1H), 4.14 (d, *J* = 16.8 Hz, 1H) 3.80 (s, 3H), 3.78–3.74 (m, 1H), 3.71–3.65 (m, 1H), 1.77–1.71 (m, 2H), 1.04 (s, 9H), 0.87 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

197.1, 159.3, 150.0, 135.4, 133.5, 129.6, 129.55, 129.5, 129.2, 127.6, 127.57, 123.6, 113.8, 73.8, 72.8, 68.8, 59.8, 55.1, 40.2, 26.8, 25.7, 19.0, 18.1, -4.6, -5.1; MS (ESI-TOF) *m/z*: 655 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{37}H_{52}NaO_5Si_2$ 655.3245; found 655.3239.

(*2S,5R,E*)-5-((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)-1-((4-methoxy benzyl)oxy)hept-3-en-2-ol (19): To a solution of ketone **18** (13.90 g, 22 mmol) in a 1:1 mixture of dichloromethane (110 mL) and water (110 mL) were added HCO_2Na (14.96 g, 220 mmol), *n*-Bu_4NBr (1.41 g, 4.4 mmol) and (*R,R*)-TsDPEN catalyst (350 mg, 2.5 mol%). The biphasic reaction mixture was vigorously stirred for 12 h, an additional 1 mol% of catalyst was added and the reaction mixture was stirred for an additional 5 h. The layers were separated and the aq layer was extracted with dichloromethane (2x30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford the crude compound which was purified by column chromatography using 10% EtOAc/hexanes (v/v) as the eluent to furnish the alcohol **19** (dr 9.6:0.4) in 89% yield as a clear liquid. TLC: R_f 0.2 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ = +9.6 (*c* 1.0, $CHCl_3$); IR (neat): 3451, 3069, 2931, 2857, 1612, 1513, 1250, 1106, 704, 505 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.43–7.32 (m, 6H), 7.28–7.22 (m, 2H), 6.92–6.86 (m, 2H), 5.74 (ddd, *J* = 15.6, 6.0, 0.9 Hz, 1H), 5.54 (ddd, *J* = 15.6, 5.7, 0.8 Hz, 1H), 4.48 (s, 2H), 4.38 (q, *J* = 6.2 Hz, 1H), 4.33–4.24 (m, 1H), 3.82–3.69 (m, 4H), 3.70–3.60 (m, 1H), 3.44 (dd, *J* = 9.4, 3.3 Hz, 1H), 3.29 (dd, *J* = 9.4, 8.3 Hz, 1H), 2.36 (d, *J* = 2.9 Hz, 1H), 1.82–1.62 (m, 2H), 1.04 (s, 9H), 0.86 (s, 9H), 0.02 (d, *J* = 3.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 135.3, 135.1, 133.7, 129.7, 129.4, 129.2, 127.9, 127.4, 113.6, 73.9, 72.7, 70.4, 69.6, 60.2, 54.9, 40.9, 26.7, 25.8, 19.0, 18.0, -4.3, -5.0; MS (ESI-TOF) *m/z*: 657 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{37}H_{54}NaO_5Si_2$ 657.3402; found 657.3416.

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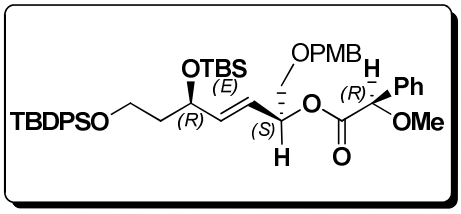
(*R*)-((2*S*,5*R*,*E*)-5-(*tert*-Butyldimethylsilyloxy)-7-(*tert*-butyldiphenylsilyloxy)-1-(4-methoxybenzyloxy)hept-3-en-2-yl) 2-methoxy-2-phenylacetate:



To a solution of alcohol **19** (15 mg, 0.023 mmol) in dichloromethane (0.5 mL) cooled at 0 ^{o}C was added (*R*)-methoxyphenylacetic acid (4.8 mg, 0.028 mmol), DMAP (1 mg, 20 mol%), and EDC.HCl (8.8 mg, 0.046 mmol). The reaction mixture was stirred at rt for 2 h. After complete consumption of starting material, the reaction mixture was diluted with dichloromethane (2 mL) and H_2O (2 mL). The layers were separated and the aq layer was extracted with dichloromethane (2×5 mL). The combined organic layers were sequentially washed with satd aq $NaHCO_3$ (10 mL), 1 N HCl (10 mL), H_2O (10 mL), brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure to afford the corresponding ester in 91% yield as a liquid. The crude product was characterised by ^{1}H NMR spectroscopy. TLC: R_f 0.3 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.60 (m, 4H), 7.44–7.33 (m, 8H), 7.31–7.24 (m, 3H), 7.22–7.18 (m, 2H), 6.89–6.84 (m, 2H), 5.50 (ddd, *J*= 7.2, 5.7, 4.1,1H), 5.41 (dd, *J* = 15.6, 5.8 Hz, 1H), 5.33 (dd, *J* = 15.5, 5.7 Hz, 1H), 4.77 (s, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.40 (d, *J* = 11.6 Hz, 1H), 4.18 (q, *J* = 6.2 Hz, 1H), 3.80 (s, 3H), 3.65 (dt, *J* = 10.3, 6.2 Hz, 1H), 3.53 (dt, *J* = 10.3, 6.2 Hz, 1H), 3.49 (dd, *J* = 10.8, 7.1 Hz, 1H), 3.44 (dd, *J* = 10.8, 4.1 Hz, 1H), 3.39 (s, 3H), 1.68–1.40 (m, 2H), 1.03 (s, 9H), 0.80 (s, 9H), -0.07 (s, 3H), -0.11 (s, 3H).

(*S*)-((2*S*,5*R*,*E*)-5-(*tert*-Butyldimethylsilyloxy)-7-(*tert*-butyldiphenylsilyloxy)-1-(4-methoxy benzyloxy)hept-3-en-2-yl) 2-methoxy-2-phenylacetate:

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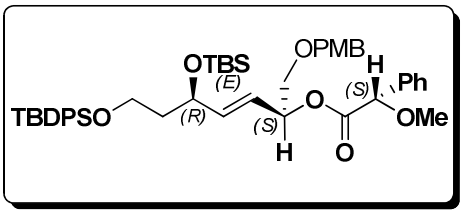

Alcohol **19** (15 mg, 0.023 mmol) was reacted with (*S*)-methoxyphenylacetic acid (4.8 mg, 0.028 mmol) as described above to furnish the corresponding ester in 88% yield as a liquid. The crude product was characterised by ^{1}H NMR spectroscopy. TLC: R_f 0.35 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64–7.59 (m, 4H), 7.44–7.40 (m, 2H), 7.40–7.31 (m, 6H), 7.29–7.26 (m, 3H), 7.07–7.02 (m, 2H), 6.81–6.76 (m, 2H), 5.66 (dd, *J* = 15.0, 6.2 Hz, 1H), 5.53 (dd, *J* = 15.0, 6.2 Hz, 1H), 5.51–5.44 (m, 1H), 4.74 (s, 1H), 4.31 (q, *J* = 6.2 Hz, 1H), 4.26 (d, *J* = 11.6 Hz, 1H), 4.21 (d, *J* = 11.6 Hz, 1H), 3.78 (s, 3H), 3.70 (dt, *J* = 10.3, 6.0 Hz, 1H), 3.60 (dt, *J* = 10.4, 6.1 Hz, 1H), 3.40 (s, 3H), 3.38 (dd, *J* = 10.7, 4.0 Hz, 1H), 3.34 (dd, *J* = 10.7, 4.0 Hz, 1H), 1.71–1.52 (m, 2H), 1.04 (s, 9H), 0.83 (s, 9H), -0.02 (s, 3H), -0.05 (s, 3H).

Note: The configuration of alcohol **19** was unambiguously assigned by comparison of the ^{1}H NMR spectra of mandelate esters. Thus, supporting the '*S*' configuration of the carbinol **19**, the C*H*$_2$OPMB appeared downfield in the '*R*' ester while C*H*OTBS appeared downfield in the '*S*' ester.

(*S*)-1-((*1R,2R*)-2-((*R*)-2,2,3,3,10,10-Hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecan-5-yl)cyclopropyl)-2-((4-methoxybenzyl)oxy)ethanol (20): To a stirred solution of Et_2Zn (1.0 M in hexanes, 10 mL, 10 mmol) in a mixture of dichloromethane (15 mL) and 1,2-dimethoxyethane (1 mL, 10 mmol) cooled at -20 °C, was added CH_2I_2 (1.61 mL, 20 mmol) over a 15-20 min period while maintaining the internal temperature between -8 °C and -15 °C. After the addition was completed, the resulting white suspension was stirred for 40 min at -20°C. A solution of alcohol **19** (3.17 g, 5 mmol) in dichloromethane (10 mL) was added via cannula under argon over a 5-6 min period. The cooling bath was removed and the clear

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reaction mixture was allowed to warm to rt and stirred for 6 h at the same temperature. The reaction was quenched with satd aq NH_4Cl (15 mL) and extracted with dichloromethane (2x10 mL). The organic layer was sequentially washed with aq 10% HCl (10 mL), satd aq $NaHCO_3$ (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was concentrated under reduced pressure to afford the crude product which was purified by flash chromatography using 12% EtOAc/petroleum ether (v/v) to give pure cyclopropyl alcohol **20** (2.79 g, 4.3 mmol) in 86% yield as a colouress oil. TLC: R_f 0.1 (10% EtOAc/hexane); $[\alpha]^{20}_D$ = -2.2 (*c* 0.55, $CHCl_3$); IR (neat): 3450, 3066, 2935, 2858, 1613, 1513, 1466, 1249, 1103, 832, 703, 502 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.45–7.34 (m, 6H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.46 (s, 2H), 3.79 (s, 3H), 3.78–3.70 (m, 2H), 3.53 (dd, *J* = 9.4, 3.0 Hz, 1H), 3.42–3.33 (m, 2H), 3.21–3.14 (m, 1H), 2.32 (s, 1H), 1.74–1.67 (m, 2H), 1.04 (s, 9H), 0.83 (s, 9H), 0.81–0.69 (m, 2H), 0.58–0.53 (m, 2H), 0.03 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 135.5, 133.9, 133.8, 129.9, 129.56, 129.52, 129.3, 127.5, 113.8, 73.9, 73.7, 73.0, 71.4, 60.6, 55.2, 40.7, 26.8, 25.8, 22.3, 19.1, 18.4, 18.0, 8.7, -3.9, -4.7; MS (ESI-TOF) *m/z*: 671 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{38}H_{56}NaO_5Si_2$ 671.3564; found 671.3563.

(*R*)-5-((1*R*,2*R*)-2-((*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-((4-methoxybenzyl)oxy)ethyl) cyclopropyl)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (21):

To a solution of alcohol **20** (4.9 g, 7.6 mmol) in anhydrous dichloromethane (15 mL) cooled at -40 °C was added 2,6-lutidine (1.84 mL, 16 mmol) followed by TBSOTf (1.9 mL, 8.32 mmol). The reaction mixture was stirred at the same temperature for 30 min, quenched by the addition of water (10 mL) and diluted with dichloromethane (15 mL). The layers were separated, the organic layer was washed with water (20 mL), brine (20 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 2% EtOAc/hexane (v/v) to give pure

silyl ether **21** (5.4 g, 7.1 mmol) in 94% yield as a gummy oil. TLC: R_f 0.2 (2% EtOAc/hexane); $[\alpha]^{20}_D$ = -8.8 (*c* 0.25, $CHCl_3$); IR (neat): 3068, 2953, 2891, 1613, 1513, 1467, 1250, 1102, 833, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.42–7.33 (m, 6H), 7.24 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 3.79 (s, 3H), 3.77–3.69 (m, 2H), 3.42–3.36 (m, 3H), 3.36–3.29 (m, 1H), 1.79–1.66 (m, 2H), 1.03 (s, 9H), 0.87 (s, 9H), 0.83 (s, 9H), 0.81–0.76 (m, 2H), 0.52–0.46 (m, 1H), 0.46–0.40 (m, 1H), 0.07 (s, 3H), 0.03 (s, 6H), -0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 135.5, 134.0, 133.9, 130.5, 129.5, 129.4, 129.1, 127.6, 113.6, 75.1, 73.2, 72.9, 72.3, 60.8, 55.1, 40.8, 26.8, 25.9, 25.8, 22.1, 19.9, 19.1, 18.2, 18.10, 8.5, -3.8, -4.3, -4.4, -4.6; MS (ESI-TOF) *m/z*: 785 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{44}H_{70}O_5NaSi_3$ 785.4429; found 785.4429.

(*S*)-2-((*tert*-Butyldimethylsilyl)oxy)-2-((1*R*,2*R*)-2-((*R*)-2,2,3,3,10,10-hexamethyl-9,9-di phenyl -4,8-dioxa-3,9-disilaundecan-5-yl)cyclopropyl)ethanol (22): To a solution of the compound **21** (4.96 g, 6.5 mmol) in a mixture of dichloromethane (20 mL) and pH 7 phosphate buffer (2 mL) cooled at 0 ^oC was added DDQ (1.77 g, 7.8 mmol). The reaction mixture was stirred for 2 h at the same temperature and then quenched by the addition of satd aq $NaHCO_3$ (10 mL), diluted with dichloromethane (10 mL) and stirred for 30 min. The layers were separated, the organic layer was washed with water (10 mL), brine (15 mL) and dried over Na_2SO_4. The solvent was concentrated under reduced pressure and crude residue was purified by flash column chromatography using 5% EtOAc/hexane (v/v) as the eluent to afford alcohol **22** (3.4 g, 5.2 mmol) in 81% yield as a clear, colorless liquid. TLC: R_f 0.3 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = -0.5 (*c* 0.65, $CHCl_3$); IR (neat): 3483, 3068, 2929, 2857, 1730, 1466, 1254, 1103, 834, 772, 702 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.68–7.63 (m, 4H), 7.44–7.35 (m, 6H), 3.78–3.70 (m, 2H), 3.54 (dd, *J* = 10.9, 3.3 Hz, 1H), 3.45 (dd, *J* = 10.9, 6.7 Hz, 1H), 3.42–3.36 (m, 1H), 3.16–3.10 (m, 1H), 1.94 (s, 1H), 1.76–1.69 (m, 2H), 1.04 (s,

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9H), 0.90 (s, 9H), 0.83 (s, 9H), 0.80–0.67 (m, 2H), 0.58–0.52 (m, 1H), 0.51–0.45 (m, 1H), 0.09 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 133.9, 129.6, 129.5, 127.6, 127.5, 76.2, 71.6, 66.9, 60.6, 40.6, 26.8, 25.8, 22.4, 19.1, 18.1, 9.9, -3.9, -4.0, -4.6, -4.7; MS (ESI-TOF) *m/z*: 665 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{36}H_{62}O_4NaSi_3$ 665.3854; found 665.3856.

(*R*)-5-((1*R*,2*R*)-2-((*S*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-(phenylthio)ethyl)cyclopropyl)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (23): To a solution of alcohol **22** (2.90 g, 4.5 mmol) in toluene (9 mL) at rt was added diphenyldisulfide (1 g, 5 mmol) followed by tri-*n*-butylphosphine (1.35 mL, 5.4 mmol). The reaction mixture was stirred at ambient temperature for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel using 2% EtOAc/hexane (v/v) as the eluent to afford sulfide **23** as colorless oil (2.88 g, 3.9 mmol) in 87% yield. TLC: R_f 0.3 (2% EtOAc/hexane); $[\alpha]^{20}_D$ = -12.4 (*c* 0.25, $CHCl_3$); IR (neat): 3070, 2930, 2857, 1585, 1468, 1253, 1106, 835, 774 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.63 (m, 4H), 7.44–7.33 (m, 6H), 7.32–7.28 (m, 2H), 7.27–7.22 (m, 2H), 7.15 (tt, *J* = 8.6, 1.3 Hz, 1H), 3.79–3.72 (m, 2H), 3.43 (q, *J* = 6.7 Hz, 1H), 3.36 (q, *J* = 6.1 Hz, 1H), 3.05–3.02 (m, 2H), 1.81–1.71 (m, 2H), 1.05 (s, 9H), 1.00–0.90 (m, 1H), 0.88 (s, 9H), 0.86–0.77 (m, 10H), 0.52–0.44 (m, 2H), 0.05 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 135.5, 134.0, 133.9, 129.6, 129.5, 128.83, 128.81, 127.6, 127.5, 125.6, 73.3, 71.5, 60.8, 41.6, 40.9, 26.9, 25.9, 25.8, 22.8, 21.9, 19.1, 18.13, 18.10, 8.9, -3.9, -4.2, -4.4, -4.6; MS (ESI-TOF) *m/z*: 757 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{42}H_{66}O_3NaSSi_3$ 757.3938; found 757.3948.

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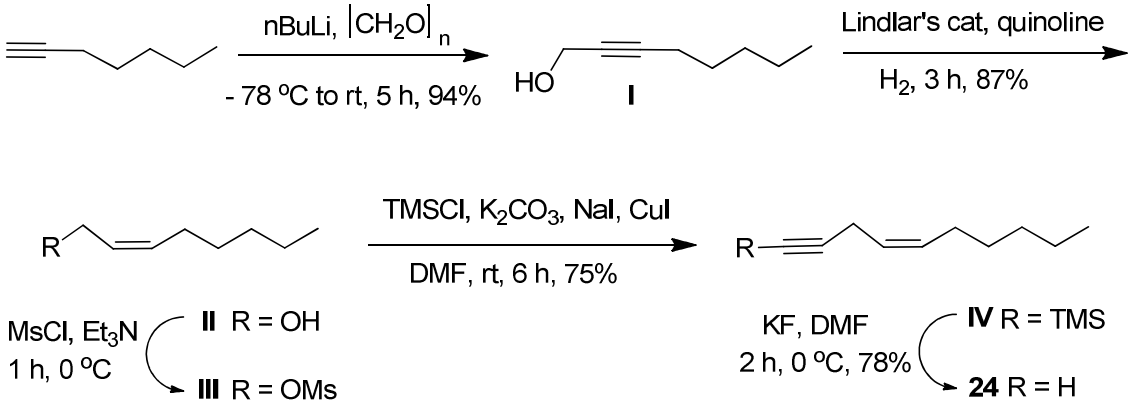
(*Z*)-Dec-4-en-1-yne (24):



Oct-2-yn-1-ol (I): To a stirred solution of 1-heptyne (1.44 g, 15 mmol) in anhydrous THF (30 mL) cooled at –78 °C was added *n*BuLi (2.5 M/hexanes, 6 mL, 15 mmol) dropwise. After stirring for 1 h, paraformaldehyde (496 mg, 16.5 mmol) was added to the reaction mixture, stirring continued for an additional 2 h at the same temperature and then gradually warmed to rt over 3 h. The reaction mixture was quenched with satd aq NH_4Cl solution (50 mL) and extracted with diethyl ether (3x20 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford the crude product. Purification by the flash column chromatography using 20% EtOAc/Hexane (v/v) as the eluent affored oct-2-yn-1-ol **I** (1.78 g, 14.1 mmol) in 94% yield as a yellow oil. TLC: R_f 0.1 (20% EtOAc/Hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.20 (t, J = 2.1 Hz, 2H), 2.50 (bs, 1H), 2.16 (tt, J = 7.1, 2.1 Hz, 2H), 1.52–1.41 (m, 2H), 1.37–1.20 (m, 4H), 0.85 (t, J = 7.0 Hz, 3H).

Oct-2-en-1-ol (II): To a solution of the above alkynol **I** (1.76 g, 14 mmol) in hexane (14 mL) was added Lindlar's catalyst (88 mg, 5 wt%), quinoline (18 μL) and the mixture stirred under H_2 atmosphere for 3 h. The catalyst was filtered using a Celite pad. The filtrate was evaporated under reduced pressure and the residue was purified by the flash column chromatography using 20% EtOAc/Hexane (v/v) as the eluent to give oct-2-en-1-ol **II** (1.56 g, 12.2 mmol) in 87% yield as a colorless oil. TLC: R_f 0.2 (20% EtOAc/Hexanes); ^{1}H NMR

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(400 MHz, $CDCl_3$) δ 5.64–5.50 (m, 2H), 4.20 (d, *J* = 6.3 Hz, 2H), 2.07 (q, *J* = 6.6 Hz, 2H), 1.62 (bs, 1H) 1.42–1.23 (m, 6H), 0.89 (t, *J* = 6.9 Hz, 3H).

1-Trimethylsilyl-deca-4(*Z*)-en-1-yne (IV): To a solution of oct-2-en-1-ol **II** (1.53 g, 12 mmol) in anhydrous dichloromethane (25 mL) cooled at 0 ^oC was added Et_3N (3.7 mL, 26.4 mmol) followed by MsCl (1 mL, 13.2 mmol) and the mixture stirred at the same temperature for 1 h. After completion the reaction mixture was quenched with water (20 mL) and extracted with dichloromethane (3x20 mL). The combined organic extracts were washed with 1N HCl (30 mL), water (30 mL), brine (30 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure to afford the crude mesylate **III** which was used in the next step without further purification.

To a solution of trimethylsilylacetylene (1.8 mL, 13.2 mmol) in anhydrous DMF (6 mL), successively K_2CO_3 (3.32 g, 24 mmol), NaI (3.6 g, 24 mmol), CuI (2.3 g, 12 mmol) and the solution of the crude mesylate **III** in DMF (6 mL) were added. The yellow-green suspension was vigorously stirred at room temperature for 6 h, then quenched with satd aq NH_4Cl (15 mL) and diluted with diethylether (20 mL). The layers were separated and the organic layer was washed with H_2O (3x10 mL), brine (20 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure at low temperature to afford a crude compound that was purified by column chromatography using pentane as the eluent to give 1-trimethylsilyl-deca-4(*Z*)-en-1-yne **IV** (1.87 g, 9 mmol) in addition to the product of S_N2' displacement in a 5:1 ratio in 75% combined yield. TLC: R_f 0.8 (hexane); ^1H NMR (500 MHz, $CDCl_3$, the signals for the minor isomer is denoted with an asterisk) δ 5.78–5.71 (m, 1H)*, 5.70–5.64 (m, 1H), 5.42–5.35 (m, 1H), 5.28 (dt, *J* = 17, 1.5 Hz, 1H)*, 5.07 (dt, *J* = 10, 1.4 Hz, 1H)*, 3.09–3.04 (m, 1H)*, 2.97–2.93 (m, 2H), 2.04–1.98 (m, 2H), 1.40–1.34 (m, 6H)*, 1.33–1.23 (m, 6H), 0.88 (t, *J* = 7.1, 6H), 0.16 (s, 18H).

Compound 24: To a stirred solution of 1-trimethylsilyl-deca-4(*Z*)-en-1-yne **IV** (1.04 g, 3 mmole) in anhydrous dimethylformamide (5 mL) was added potassium fluoride dihydrate (940 mg, 10 mmole) at 0 ^{o}C. The reaction mixture was stirred for 2 h at the same temperature, quenched by the addition water (10 mL) and diluted with diethyl ether (15 mL). The layers were separated, the organic layer was washed with water (2x10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was concentrated under reduced pressure (water bath temperature < 30 ^{o}C) and the crude residue was distilled. The fraction collected at 105 ^{o}C/2 Torr afforded the pure desilylated compound **24** (530 mg, 3.9 mmole) in 78% yield as a clear, colorless oil. TLC: R_f 0.8 (Hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53–5.39 (m, 2H), 2.96–2.92 (m, 2H), 2.04 (q, *J* = 7.1 Hz, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.41–1.24 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H).

(*R*)-5-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (25): To a solution of alkyne **24** (408 mg, 3 mmol) in anhydrous THF (1.5 mL) cooled at 0 °C was added ^{i}PrMgCl·LiCl (1.5 M in THF, 2.2 mL, 3.3 mmol) and the mixture stirred for 30 min at the same temperature. To the so generated Grignard reagent was added a solution of $ZnBr_2$ (1.5 M in THF, 3 mL, 4.5 mmol) at 0 °C and the mixture stirred for 30 min. Separately, in another round-bottom flask, the chloro sulfide was prepared by adding a solution of sulfide **23** (735 mg, 1 mmol) in anhydrous benzene (5 mL) to NCS (134 mg, 1 mmol) in anhydrous benzene (5 mL) and stirring for 15 min. To the organozinc reagent maintained at 0 °C was added a solution of chloro sulfide in benzene. The reaction mixture was stirred gradually allowing it to attain rt and stirred further for a period of 7 h when TLC examination indicated complete consumption of the chloro sulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of satd aq NH_4Cl solution (10 mL). It was allowed to warm to rt and diluted with Et_2O (10 mL). The layers were separated and the aq

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layer was extracted with Et_2O (3×10 mL). The combined organic layers were washed with H_2O (15 mL), brine (15 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to afford a crude compound that was purified by column chromatography using 2% EtOAc/hexane (v/v) as the eluent to give the pure product **25** (630 mg, 0.73 mmol) in 73% yield as a light yellow color gummy liquid. TLC: R_f 0.5 (2% EtOAc/hexane); $[\alpha]^{20}_D$ = +27.6 (*c* 0.8, $CHCl_3$); IR (neat): 3067, 2930, 2857, 1585, 1467, 1252, 1103, 835, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.65–7.60 (m, 4H), 7.46–7.42 (m, 2H), 7.39–7.29 (m, 7H), 7.23–7.15 (m, 2H), 5.40–5.33 (m, 1H), 5.32–5.25 (m, 1H), 3.93–3.90 (m, 1H), 3.71 (t, *J* = 6.9 Hz, 2H), 3.47 (td, *J* = 7.0, 4.7 Hz, 1H), 3.35 (dd, *J* = 7.1, 3.8 Hz, 1H), 2.86 (d, *J* = 6.8 Hz, 2H), 1.94 (q, *J* = 7.1 Hz, 2H), 1.89–1.81 (m, 1H), 1.75–1.67 (m, 1H), 1.33–1.18 (m, 6H), 1.01 (s, 9H), 0.89–0.84 (m, 12H), 0.81–0.78 (m, 11H), 0.57–0.52 (m, 1H), 0.52–0.47 (m, 1H), 0.05 (s, 3H), 0.03 (s, 3H), -0.1 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 134.04, 134.01, 131.8, 131.4, 129.4, 128.6, 127.6, 127.5, 126.8, 124.0, 83.9, 78.2, 77.2, 71.2, 60.8, 47.2, 40.9, 31.4, 29.0, 27.0, 26.9, 25.9, 25.8, 23.0, 22.5, 20.0, 19.1, 18.2, 18.0, 17.4, 14.0, 9.4, -3.9, -4.0, -4.5, -4.6; MS (ESI-TOF) *m/z*: 891 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{52}H_{80}NaO_3SSi_3$ 891.5034; found 891.5031.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-3-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-1-((*tert*-butyldimethylsilyl) oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)propan-1-ol (26): A solution of compound **25** (364 mg, 0.42 mmol) and NH_4F (78 mg, 2.1 mmol) in MeOH (1.5 mL) was stirred in an oil bath at 60 °C for 3 h. The reaction mixture was quenched by the addition of water (1 mL). MeOH was evaporated under reduced pressure and to the residue was added Et_2O (5 mL). The layers were separated and the organic layer was washed with water (5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 5% EtOAc/hexane (v/v) to give the pure alcohol **26** (208 mg, 0.33 mmol) in 78% yield as a

gummy oil. TLC: R_f 0.2 (5% EtOAc/hexanes); $[\alpha]^{20}_D$ = +29.6 (*c* 0.5, $CHCl_3$); IR (neat): 3444, 2929, 2857, 1655, 1466, 1253, 1085, 836, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.49–7.44 (m, 2H), 7.32–7.26 (m, 2H), 7.25–7.19 (m, 1H), 5.47–5.39 (m, 1H), 5.38–5.30 (m, 1H), 3.93 (dt, *J* = 5.7, 2.3 Hz, 1H), 3.86–3.77 (m, 1H), 3.67–3.57 (m, 1H), 3.48–3.41 (m, 1H), 3.38 (dd, *J* = 7.3, 3.4 Hz, 1H), 2.93 (d, *J* = 6.8 Hz, 2H), 2.26 (s, 1H), 2.00 (q, *J* = 6.8 Hz, 2H), 1.86 (ddd, *J* = 12.7, 8.6, 4.7 Hz, 1H), 1.77–1.67 (m, 1H), 1.39–1.17 (m, 6H), 1.01–0.94 (m, 1H), 0.93–0.81 (m, 22H), 0.65 (t, *J* = 6.8 Hz, 2H), 0.10 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 131.6, 131.3, 128.7, 126.8, 123.9, 84.0, 78.2, 77.2, 74.7, 60.4, 47.3, 39.2, 31.4, 29.0, 27.0, 25.85, 25.80, 22.5, 22.3, 20.1, 18.1, 17.9, 17.4, 14.0, 10.6, -3.9, -4.1, -4.5, -4.7; MS (ESI-TOF) *m/z*: 653 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{36}H_{62}NaO_3SSi_2$ 653.3856; found 653.3857.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-3-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-1-((*tert*-butyldimethylsilyl) oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)propanal (27): To a stirred solution of 2-iodoxybenzoic acid (130 mg, 0.46 mmol) in anhydrous DMSO (0.6 mL) cooled at 0 ^0C was added a solution of alcohol **26** (195 mg, 0.31 mmol) in anhydrous dichloromethane (1.5 mL) and the reaction mixture stirred for a period of 3 h at rt. After completion of the reaction, the mixture was filtered on a small Celite pad and the filtrate was diluted with dichloromethane (10 mL), washed with water (5 mL), brine (5 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the residue which was purified by column chromatography using 3% EtOAc/hexane (v/v) to give the pure aldehyde **27** (177 mg, 0.28 mmol) in 90% yield as a gummy liquid. TLC: R_f 0.7 (5% EtOAc/hexanes); $[\alpha]^{20}_D$ = +13.0 (*c* 0.7, $CHCl_3$); IR (neat): 3014, 2956, 2857, 2714, 1726, 1467, 1254, 1091, 836, 775 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 9.78 (t, *J* = 2.4 Hz, 1H), 7.50–7.44 (m, 2H), 7.32–7.20 (m, 3H), 5.46–5.38 (m, 1H), 5.36–5.28 (m, 1H), 3.96–3.92 (m, 1H), 3.76–3.70 (m, 1H), 3.34 (dd, *J* = 7.4, 3.8 Hz, 1H), 2.92 (d, *J* = 6.6 Hz, 2H), 2.69-2.63 (m, 1H), 2.63-2.56 (m, 1H),

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1.99 (q, *J* = 6.7 Hz, 2H), 1.37–1.21 (m, 6H), 1.10–1.0 (m, 1H), 0.99–0.75 (m, 22H), 0.68–0.59 (m, 2H), 0.10 (s, 3H), 0.07 (s, 3H), 0.03 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.0, 135.3, 131.7, 131.6, 128.8, 127.0, 123.9, 84.4, 77.7, 77.2, 70.8, 51.8, 47.2, 31.4, 29.0, 27.0, 25.78, 25.76, 23.1, 22.5, 20.1, 18.1, 17.9, 17.4, 14.0, 10.0, -4.0, -4.1, -4.6, -4.7; MS (ESI-TOF) *m/z*: 651 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{36}H_{60}NaO_3SSi_2$ 651.3699; found 651.3704.

4-(Bromotriphenylphosphoranyl)butanoic acid (28): A mixture of 4-bromocarboxylic acid (1.84 g, 11 mmol) and triphenylphosphine (2.88 g, 11 mmol) was heated at 80 ^{o}C for 24 h under argon. The mixture was allowed to cool at rt. The residue was washed with anhydrous ether (3x20 mL) and dried under vacuo to afford the pure phosphonium salt **28** as a white solid (4.2 g) in 90% yield. Mp 242 ^{o}C.^{1}H NMR (400 MHz, D_2O) δ 7.84–7.78 (m, 3H), 7.77–7.69 (m, 6H), 7.69–7.61 (m, 6H), 3.35–3.23 (m, 2H), 2.53 (t, *J* = 6.6 Hz, 2H), 1.98–1.85 (m, 2H); ^{13}C NMR (101 MHz, D_2O) δ 179.2, 137.6, 136.1, 132.6, 120.5, 36.2, 23.3, 20.0.

(*R*,*Z*)-7-((*tert*-Butyldimethylsilyl)oxy)-7-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-1-((*tert*-butyldimethylsilyl)oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)hept-4-enoic acid (29): To a stirred suspension of phosphonium salt **28** (347 mg, 0.81 mmol) in anhydrous THF (0.8 mL) cooled at 0 ^{o}C and maintained under an Ar atmosphere was added NaHMDS (1 M in THF, 1.6 mL, 1.62 mmol) and the reaction mixture was stirred for 1 h at the same temperature. The resulting ylide was cooled to -78 °C and the solution of aldehyde **27** (170 mg, 0.27 mmol) in anhydrous THF (1 mL) was added slowly and the mixture stirred further for a period of 1 h at the same temperature. After completion of the reaction as monitored by TLC, the mixture was quenched with satd aq NH_4Cl solution (5 mL), acidified with 1 N HCl solution (2 mL) to pH=4 and was extracted with EtOAc (2x5 mL). The combined organic layers were dried over Na_2SO_4, concentrated and the crude product was purified by silica gel column chromatography using 20% EtOAc/hexane as the eluent to afford compound **29** (153 mg,

0.22 mmol) in 81% yield as a colorless oil. TLC: R_f 0.1 (20% EtOAc/hexane). The acid was characterized as its methyl ester obtained by reaction with ethereal diazomethane. $[\alpha]^{20}_D$ = +27.2 (*c* 0.25, $CHCl_3$); IR (neat): 3010, 2956, 2856, 1741, 1466, 1256, 1088, 835, 774 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.39 (m, 2H), 7.23–7.17 (m, 2H), 7.17–7.11 (m, 1H), 5.45–5.21 (m, 4H), 3.89–3.86 (m, 1H), 3.59 (s, 3H), 3.35–3.27 (m, 2H), 2.84 (d, *J* = 6.8 Hz, 2H), 2.29–2.18 (m, 6H), 1.92 (q, *J* = 6.7 Hz, 2H), 1.31–1.14 (m, 6H), 0.88–0.77 (m, 23H), 0.58–0.51 (m, 1H), 0.48–0.41 (m, 1H), -0.01 (s, 3H), -0.03 (s, 3H) -0.04 (s, 3H) -0.05 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 135.6, 131.6, 131.5, 128.7, 128.6, 127.7, 126.8, 124.0, 83.9, 78.1, 77.1, 73.2, 51.4, 47.1, 36.1, 34.0, 31.4, 29.0, 27.0, 25.87, 25.83, 22.9, 22.6, 22.5, 19.8, 18.2, 18.1, 17.4, 14.0, 8.3, -4.0, -4.1, -4.4, -4.5; MS (ESI-TOF) *m/z*: 735 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{41}H_{68}NaO_4SSi_2$ 735.4275; found 735.4267.

(*R*,*Z*)-7-Hydroxy-7-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-1-hydroxy-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)hept-4-enoic acid (30): To a solution of compound **29** (140 mg, 0.2 mmol) in anhydrous CH_3CN (1.25 mL) cooled at 0 °C was added HF.pyridine (~70% HF, 30 μL) and the reaction mixture stirred at rt for a period of 12 h. The reaction was cooled at 0 °C and quenched by the dropwise addition of satd aq $NaHCO_3$ solution (1 mL) and warmed to rt with stirring. The reaction mixture was extracted with dichloromethane (3x2 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford the crude product. Purification by the flash column chromatography using 60% EtOAc/Hexane (v/v) as the eluent affored compound **30** (78 mg, 0.16 mmol) in 79% yield. TLC: R_f 0.1 (60% EtOAc/Hexanes). The acid was characterized as its methyl ester, prepared by reaction with ethereal diazomethane. $[\alpha]^{20}_D$ = +2.0 (*c* 0.2, $CHCl_3$); IR (neat): 3448, 2924, 2854, 1735, 1438, 1249, 1164, 1029, 744 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.48–7.43 (m, 2H), 7.26–7.21 (m, 3H), 5.48–5.33 (m, 3H), 5.29–5.20 (m, 1H), 3.77 (dt, *J* = 6.9, 2.3 Hz, 1H), 3.58 (s, 3H), 3.17-3.09 (m, 2H), 2.86 (d, *J* = 6.8

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Hz, 2H), 2.63 (s, 1H), 2.39–2.22 (m, 6H), 1.92 (q, *J* = 7.1 Hz, 2H), 1.31–1.14 (m, 6H), 1.13–1.06 (m, 1H), 1.05–0.98 (m, 1H), 0.81 (t, *J* = 7.0 Hz, 3H), 0.62–0.52 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 133.6, 132.4, 131.9, 130.4, 128.8, 128.1, 127.1, 123.5, 85.8, 76.5, 73.9, 73.5, 51.6, 47.4, 35.0, 33.6, 31.4, 28.9, 27.1, 22.9, 22.7, 22.5, 19.4, 17.3, 14.0, 6.5; MS (ESI-TOF) *m/z*: 507 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{29}H_{40}O_4SNa$ 507.2545; found 507.2539.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-1-Hydroxy-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)-3,4,7,8-tetrahydro-2H-oxocin-2-one (31): A solution of hydroxy acid **30** (65 mg, 0.14 mmol) in dichloromethane (40 mL) was added using a mechanically driven syringe to the solution of 2-methyl-6-nitrobenzoic anhydride (72 mg, 0.21 mmol) and DMAP (34 mg, 0.28 mmol) in dichloromethane (100 mL) over a period of 16 h. After addition was complete, the reaction mixture was stirred further for a period of 2 h at rt. The reaction mixture was concentrated to 20 mL by evaporation of the solvent under reduced pressure and then satd aq $NaHCO_3$ (20 mL) was added at 0 °C. The layers were separated and the aq layer was extracted with dichloromethane (3x20 mL). The combined organic layers were washed with water (20 mL), brine (20 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to afford a crude compound that was purified by column chromatography using 10% EtOAc/hexane (v/v) as the eluent to afford the pure product **31** (50 mg, 0.11 mmol) in 82% yield as a gummy liquid. TLC: R_f 0.2 (10% EtOAc/hexane); $[\alpha]^{20}_D$ = +5.20 (*c* 0.25, $CHCl_3$); IR (neat): 3453, 3015, 2925, 2856, 1741, 1460, 1216, 1056, 734 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.51 (m, 2H), 7.34–7.30 (m, 3H), 5.81–5.70 (m, 2H), 5.49–5.43 (m, 1H), 5.36–5.29 (m, 1H), 4.03 (ddd, *J* = 9.9, 7.8, 1.7 Hz, 1H), 3.81 (dt, *J* = 7.0, 2.3 Hz, 1H), 3.19 (td, *J* = 6.5, 2.4 Hz, 1H), 2.94 (dt, *J* = 6.9, 1.7 Hz, 2H), 2.88–2.79 (m, 1H), 2.72 (ddd, *J* = 13.3, 5.8, 3.0 Hz, 1H), 2.65–2.55 (m, 1H), 2.34–2.25 (m, 2H), 2.14–2.07 (m, 1H), 2.00 (q, *J* = 7.0 Hz, 2H), 1.38–1.18 (m, 6H), 0.91–0.82 (m, 5H), 0.75–0.70 (m,

2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 133.8, 132.6, 132.2, 132.0, 128.8, 128.3, 128.2, 123.5, 86.1, 81.0, 76.4, 73.7, 47.6, 37.7, 34.3, 31.4, 29.0, 27.1, 24.4, 22.5, 20.6, 20.5, 17.3, 14.0, 7.5; MS (ESI-TOF) *m/z*: 453 $[M + H]^+$. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{37}O_3S$ 453.2463; found 453.2466.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*S*,2*R*,*Z*)-2-(Phenylthio)-1-((triethylsilyl)oxy)dodec-6-en-3-yn-1-yl) cyclopropyl)-3,4,7,8-tetrahydro-2H-oxocin-2-one (32): To a solution of alcohol **31** (32 mg, 0.07 mmol) in anhydrous dichloromethane (0.5 mL) cooled at -40 °C was added 2,6- lutidine (18 µL, 0.15 mmol) followed by TESOTf (24 µL, 0.10 mmol). The reaction mixture was stirred at the same temperature for 30 min, quenched by the addition of water (5 mL), diluted with dichloromethane (5 mL). The layers were separated and the organic layer was washed with water (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 2% ethyl acetate/hexane (v/v) to give pure silyl ether **32** (37 mg, 0.065 mmol) in 94% yield as a gummy oil. TLC: R_f 0.2 (2% EtOAc/hexanes); $[\alpha]^{20}_D$ = -4.4 (*c* 0.25, $CHCl_3$); IR (neat): 3011, 2926, 2855, 1731, 1249, 1039, 744cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53–7.46 (m, 2H), 7.33–7.21 (m, 3H), 5.82–5.67 (m, 2H), 5.48–5.39 (m, 1H), 5.38–5.28 (m, 1H), 4.02–3.95 (m, 1H), 3.95–3.91 (m, 1H), 3.38 (dd, *J* = 7.3, 3.9 Hz, 1H), 2.94 (dt, *J* = 6.9, 1.7 Hz, 2H), 2.89–2.77 (m, 1H), 2.71 (ddd, *J* = 13.2, 5.5, 3.1 Hz, 1H), 2.65–2.55 (m, 1H), 2.35–2.24 (m, 2H), 2.15–2.06 (m, 1H), 2.00 (q, *J* = 7.0 Hz, 2H), 1.45–1.13 (m, 6H), 1.00–0.81 (m, 14H), 0.78–0.65 (m, 2H), 0.56 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 135.3, 132.5, 132.1, 131.7, 128.8, 128.4, 127.2, 123.9, 84.9, 81.5, 77.5, 76.5, 47.7, 37.7, 34.2, 31.4, 29.0, 27.1, 24.4, 22.5, 21.5, 20.3, 17.4, 14.0, 9.4, 6.8, 5.1; MS (ESI-TOF) *m/z*: 589 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{50}O_3SNaSi$ 589.3148; found 589.3143.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((*R*,2*E*,6*Z*)-4-Oxo-1-((triethylsilyl)oxy)dodeca-2,6-dien-1-yl) cyclopropyl) -3,4,7,8-tetrahydro-2H-oxocin-2-one (33): To a solution of compound **32** (28

mg, 0.05 mmol) in dichloromethane (0.5 mL) cooled at -40 °C was added *m*CPBA (12 mg, 0.05 mmol) and the reaction mixture stirred at the same temperature for 15 min. Toluene (1 mL) and 2-mercapto-1-methyl-imidazole (8 mg, 0.075 mmol) were added. The reaction mixture was stirred at 60 °C for 2 h and then quenched by the addition of satd aq $NaHCO_3$ (3 mL). The mixture was diluted with dichloromethane (5 mL), the layers were separated and the aq layer was extracted with dichloromethane. The combined organic layers were washed successively with water (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to furnish the crude compound which was purified by column chromatography using 5% EtOAc/hexanes (v/v) as the eluent to afford the product **33** (19 mg, 0.04 mmol) in 80% yield as a liquid. TLC: R_f 0.3 (5% EtOAc/hexanes); $[\alpha]^{20}_D$ = +2.3 (*c* 0.35, $CHCl_3$); IR (neat): 3013, 2925, 2854, 1742, 1682, 1459, 1260, 1091, 1020, 800 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 6.79 (dd, *J* = 15.7, 5.2 Hz, 1H), 6.27 (dd, *J* = 15.7, 1.4 Hz, 1H), 5.83–5.67 (m, 2H), 5.66–5.51 (m, 2H), 4.05–3.96 (m, 2H), 3.31 (dt, *J* = 6.9, 1.7 Hz, 2H), 2.90–2.78 (m, 1H), 2.72 (ddd, *J* = 13.3, 5.8, 3.0 Hz, 1H), 2.62–2.51 (m, 1H), 2.29 (ddd, *J* = 13.3, 11.8, 4.8 Hz, 1H), 2.21–2.08 (m, 2H), 2.08–2.01 (m, 2H), 1.42–1.21 (m, 6H), 1.12–1.01 (m, 1H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.91–0.83 (m, 4H), 0.76–0.66 (m, 2H), 0.59 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (101 MHz, CDC_3) δ 198.1, 176.7, 147.4, 133.9, 132.8, 128.0, 127.5, 121.0, 80.5, 72.8, 39.8, 37.7, 34.2, 31.5, 29.0, 27.5, 24.4, 23.1, 22.5, 19.3, 13.9, 8.7, 6.7, 4.9; MS (ESI-TOF) *m/z*: 497 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{28}H_{46}O_4SiNa$ 497.3063; found 497.3083.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*R*,2*E*,4*S*,6*Z*)-4-Hydroxy-1-((triethylsilyl)oxy)dodeca-2,6-dien-1-yl) cyclopropyl)-3,4,7,8-tetrahydro-2H-oxocin-2-one (34): A solution of (*R*)-(-)-2-methyl-CBS-oxazaborolidine (14 µL, 1 M solution in toluene, 0.0135 mmol) in THF (0.2 mL) was treated with BH_3·DMS (15 µL, 0.135 mmol) at -5 ºC. After 1 h the reaction mixture was cooled to –78 ºC. A solution of enone **33** (13 mg, 0.027 mmol) in THF (0.3 mL) was then

added slowly and stirred for 2 h at the same temperature. After completion of reaction, satd aq NH_4Cl solution (2 mL) was added. The aq layer was extracted with EtOAc (3x2 mL), the combined organic layers were dried over Na_2SO_4 and concentrated. Purification of the residue by column chromatography using 10% EtOAc/hexane (v/v) furnished pure alcohol **34** (11 mg, 0.023 mmol) in 85% yield as a gummy oil. TLC: R_f 0.2 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ = –17.0 (*c* 0.1, $CHCl_3$); IR (neat): 3451, 2930, 2842, 1740, 1462, 1370, 1225, 1085, 1019, 703 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 5.82–5.71 (m, 2H), 5.71–5.63 (m, 2H), 5.60–5.53 (m, 1H), 5.41–5.33 (m, 1H), 4.18–4.11 (m, 1H), 4.00–3.95 (m, 1H), 3.83 (t, *J* = 5.6 Hz, 1H), 2.89–2.80 (m, 1H), 2.72 (ddd, *J* = 13.4, 5.8, 3.2 Hz, 1H), 2.61–2.52 (m, 1H), 2.37–2.24 (m, 3H), 2.24–2.17 (m, 1H), 2.15–2.08 (m, 1H), 2.08–1.99 (m, 2H), 1.40–1.20 (m, 6H), 1.05–0.98 (m, 1H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.91–0.82 (m, 4H), 0.70–0.65 (m, 2H), 0.58 (q, *J* = 8.2 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.9, 133.7, 132.8, 132.7, 132.1, 128.2, 124.2, 81.3, 73.7, 71.6, 37.7, 35.3, 34.3, 31.5, 29.3, 27.4, 24.4, 24.0, 22.5, 19.2, 14.0, 8.8, 6.8, 4.9; MS (ESI-TOF) *m/z*: 499 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{28}H_{48}O_4SiNa$ 499.3220; found 499.3202.

(*R*,*Z*)-8-((1*R*,2*R*)-2-((1*R*,2*E*,4*S*,6*Z*)-1,4-Dihydroxydodeca-2,6-dien-1-yl)cyclopropyl)-3,4,7,8-tetrahydro-2H-oxocin-2-one (2): To a stirred solution of compound **34** (6 mg, 0.0125 mmol) in anhydrous THF (0.3 mL) was added TBAF buffered with AcOH (62 µL, 1 M in THF, 0.062 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 5 h and then concentrated in vacuo. The residue was purified by silica gel column chromatography using 50% EtOAc/petroleum ether (v/v) to give pure hydroxy compound **2** (3.9 mg, 0.011 mmol) in 88% yield as a viscous oil. TLC: R_f 0.2 (50% EtOAc/hexane). $[\alpha]^{20}_D$ = +2.3 (*c* 0.05, $CHCl_3$); IR (neat): 3462, 2927, 2853, 1745, 1459, 1326, 1260, 1091, 1020, 800 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.83–5.68 (m, 4H), 5.63–5.52 (m, 1H), 5.42–5.32 (m, 1H), 4.21–4.16 (m, 1H), 4.00 (ddd, *J* = 10.0, 8.2, 1.8 Hz, 1H), 3.70–3.63 (m, 1H), 2.90–

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2.78 (m, 1H), 2.73 (ddd, *J* = 13.2, 5.9, 3.0 Hz, 1H), 2.58 (ddd, *J* = 14.0, 10.5, 6.1 Hz, 1H), 2.36–2.25 (m, 3H), 2.23–2.17 (m, 1H), 2.16–2.09 (m, 1H), 2.08–2.01 (m, 2H), 1.39–1.22 (m, 6H), 1.07–0.98 (m, 2H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.81–0.75 (m, 1H), 0.74–0.67 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 134.0, 133.6, 132.8, 131.7, 128.0, 124.0, 80.7, 74.9, 71.5, 37.7, 35.3, 34.3, 31.5, 29.3, 27.4, 24.4, 23.6, 22.6, 19.8, 14.0, 9.0; MS (ESI-TOF) *m/z*: 385 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{22}H_{34}O_4Na$ 385.2355; found 385.2345.

(*R*)-5-((*R*,*Z*)-4-((4-Methoxybenzyl)oxy)-1-(phenylthio)but-2-en-1-yl)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (35): A suspension of dicyclohexylborane (8 mmol) was prepared by dropwise addition of cyclohexene (1.64 mL, 16 mmol) to a solution of borane-dimethylsulfide complex (10.5 M, 0.76 mL, 8 mmol) in anhydrous THF (3 mL), maintaining the temperature at 0-5 °C. The resulting mixture was warmed to 20 °C, stirred for 1 h, then cooled to 0 °C and then the solution of alkyne **17** (2.9 g, 4 mmol) in anhydrous THF (10 mL) was added slowly. The mixture was warmed to 20 °C over 3 h and stirred for an additional 2 h. Glacial acetic acid (0.46 mL, 8 mmol) was then added dropwise at 0 °C, the resulting solution was stirred for 2 h at rt and then made basic by slow addition of satd aq $NaHCO_3$ (10 mL). The resulting mixture was diluted with water (10 mL) and extracted with Et_2O (3x15 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel using 3% EtOAc/Hexane as the eluent to give alkene **35** (2.32 g, 3.2 mmol) in 80% yield as a gummy liquid. TLC: R_f 0.2 (5% EtOAc/Hexanes); $[\alpha]^{20}_D$ = +56.8 (*c* 0.25, $CHCl_3$); IR (neat): 3065, 2935, 2867, 1613, 1513, 1250, 1106, 830, 702 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.63 (m, 4H), 7.44–7.33 (m, 8H), 7.24–7.19 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 2H), 6.85–6.81 (d, *J* = 8.6 Hz, 2H), 5.66–5.57 (m, 2H), 4.18 (d, *J* = 11.3 Hz, 1H), 4.14 (d, *J* = 11.3 Hz, 1H), 4.08 (dt, *J* = 7.5, 4.1 Hz, 1H), 3.90 (dd, *J* = 9.3, 3.6 Hz, 1H), 3.81–3.76 (m, 4H), 3.74 (t,

J = 6.4 Hz, 2H), 3.60 (dd, *J* = 12.7, 5.2 Hz, 1H), 2.16–2.08 (m, 1H), 1.80–1.71 (m, 1H), 1.04 (s, 9H), 0.84 (s, 9H), 0.01 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 135.6, 135.5, 134.7, 133.8, 133.7, 130.3, 129.9, 129.6, 129.5, 129.3, 128.8, 127.6, 127.4, 113.7, 71.8, 71.3, 65.8, 60.7, 55.2, 53.4, 36.8, 26.9, 25.8, 19.1, 18.1, -4.3, -4.6; MS (ESI-TOF) *m/z*: 749 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{58}O_4Si_2SNa$ 749.3492; found 749.3465.

(2*R*,5*R*,*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)-1-((4-methoxy benzyl) oxy) hept-3-en-2-ol (36): Following the procedure detailed for the preparation of compound **18** from sulfide **17**, sulfide **35** (1.91 g, 2.63 mmol) was treated with *m*CPBA (648 mg, 2.63 mmol) followed by 2-mercapto-1-methyl-imidazole (362 mg, 3.16 mmol) to afford alcohol **36** (1.4 g, 2.21 mmol) in 84% yield as a colourless liquid. TLC: R_f 0.2 (10% EtOAc/Hexanes); $[\alpha]^{20}_D$ = +7.10 (*c* 1.0, $CHCl_3$); IR (neat): 3452, 3065, 2935, 2858, 1613, 1513, 1466, 1250, 1106, 830, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.61 (m, 4H), 7.43–7.31 (m, 6H), 7.27–7.21 (m, 2H), 6.90–6.84 (m, 2H), 5.72 (ddd, *J* = 15.5, 6.1, 1.2 Hz, 1H), 5.54 (ddd, *J* = 15.5, 6.0, 1.0 Hz, 1H), 4.47 (s, 2H), 4.37 (q, *J* = 6.2 Hz, 1H), 4.31–4.24 (m, 1H), 3.79 (s, 3H), 3.76–3.70 (m, 1H), 3.69–3.61 (m, 1H), 3.45 (dd, *J* = 9.5, 3.2 Hz, 1H), 3.28 (dd, *J* = 9.5, 8.2 Hz, 1H), 2.34 (bs, 1H), 1.78–1.61 (m, 2H), 1.03 (s, 9H), 0.84 (s, 9H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 135.5, 135.4, 133.8, 129.8, 129.4, 129.3, 127.8, 127.5, 113.7, 73.9, 72.9, 70.7, 69.6, 60.3, 55.1, 41.0, 26.8, 25.8, 19.1, 18.1, -4.3, -4.9; MS (ESI-TOF) *m/z*: 657 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{37}H_{54}NaO_5Si_2$ 657.3407; found 657.3406.

(*R*)-(2*R*,5*R*,*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)-1-((4methoxy benzyl)oxy)hept-3-en-2-yl 2-methoxy-2-phenylacetate:

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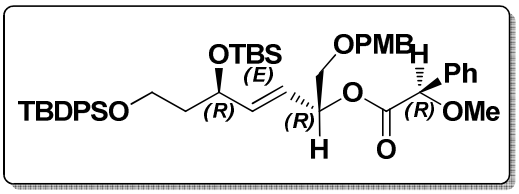
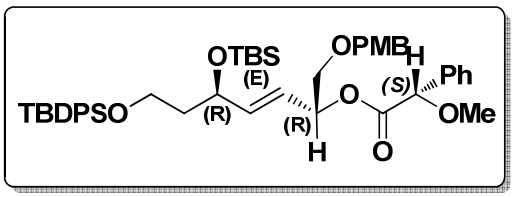


Following the procedure detailed earlier for the preparation of '*R*' mandelate ester from alcohol **19**, alcohol **36** (15 mg, 0.023 mmol) was reacted with (*R*)-methoxyphenylacetic acid (4.8 mg, 0.028 mmol) to furnish the corresponding ester in 89% yield as a liquid. The crude product was characterised by ^{1}H NMR spectroscopy. TLC: R_f 0.25 (10% EtOAc/Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.61 (m, 4H), 7.48–7.33 (m, 8H), 7.33–7.27 (m, 3H), 7.09–7.04 (m, 2H), 6.84–-6.79 (m, 2H), 5.72 (dd, *J* = 15.2, 5.6 Hz, 1H), 5.60–5.50 (m, 2H), 4.77 (s, 1H), 4.35 (q, *J* = 5.8 Hz, 1H), 4.28 (d, *J* = 11.6 Hz, 1H), 4.23 (d, *J* = 11.6 Hz, 1H), 3.79 (s, 3H), 3.77–3.70 (m, 1H), 3.66–3.59 (m, 1H), 3.45–3.35 (m, 5H), 1.73–1.57 (m, 2H), 1.05 (s, 9H), 0.84 (s, 9H), -0.01 (s, 3H), -0.04 (s, 3H).

(*S*)-(2*R*,5*R*,*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)-1-((4-methoxy benzyl)oxy)hept-3-en-2-yl 2-methoxy-2-phenylacetate:



Following the procedure detailed for the preparation of the *'S'* mandelate ester from alcohol **19**, alcohol **36** (15 mg, 0.023 mmol) was reacted with (*S*)-methoxyphenylacetic acid (4.8 mg, 0.028 mmol) to give the corresponding ester in 85% yield as a liquid. The crude product was characterised by ^{1}H NMR spectroscopy. TLC: R_f 0.3 (10% EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64–7.57 (m, 4H), 7.43–7.31 (m, 8H), 7.29–7.21 (m, 3H), 7.21–7.09 (m, 2H), 6.85–6.79 (m, 2H), 5.52–5.46 (m, 1H), 5.43–5.38 (m, 2H), 4.73 (s, 1H), 4.44 (d, *J* = 11.6 Hz, 1H), 4.37 (d, *J* = 11.6 Hz, 1H), 4.24–4.18 (m, 1H), 3.79 (s, 3H), 3.65 (dt, *J* = 10.3,

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6.5 Hz, 1H), 3.56–3.49 (m, 1H), 3.48–3.40 (m, 2H), 3.38 (s, 3H), 1.61–1.38 (m, 2H), 1.03 (s, 9H), 0.80 (s, 9H), -0.08 (s, 3H), -0.14 (s, 3H).

Note: The configuration of alcohol **36** was unambiguously assigned by comparison of the ^{1}H NMR spectra of the mandelate esters. Thus, supporting the '*R*' configuration of the carbinol **36**, the olefinic protons and C*H*OTBS appeared downfield in '*R*' ester**,** while CH_2OPMB appeared downfield in '*S*' ester.

(*R*)-1-((1*S*,2*S*)-2-((*R*)-2,2,3,3,10,10-Hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecan-5-yl)cyclopropyl)-2-((4-methoxybenzyl)oxy)ethanol (37): Following the procedure detailed for the preparation of compound **20** from alcohol **19**, alcohol **36** (887 mg, 1.4 mmol) was treated with 1,2-dimethoxyethane (DME) (0.3 mL, 2.8 mmol), Et_2Zn (1.0 M in hexanes, 0.28 mL, 2.8 mmol) and CH_2I_2 (0.34 mL, 4.2 mmol) to furnish cyclopropyl alcohol **37** (778 mg, 1.2 mmol) in 87% yield as a colourless oil. TLC: R_f 0.15 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ = +2.67 (*c* 0.15, $CHCl_3$); IR (neat): 3451, 3001, 2929, 2856, 1612, 1513, 1249, 1101, 831, 702 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70–7.64 (m, 4H), 7.46–7.36 (m, 6H), 7.28–7.23 (m, 2H), 6.90–6.86 (m, 2H), 4.48 (d, *J* = 11.4 Hz, 1H), 4.45 (d, *J* = 11.4 Hz, 1H), 3.81 (s, 3H), 3.80–3.71 (m, 2H), 3.59 (dd, *J* = 9.5, 2.7 Hz, 1H), 3.40 (t, *J* = 9.0 Hz, 2H), 3.15 (td, *J* = 8.2, 2.5 Hz, 1H), 2.37 (s, 1H), 1.89–1.80 (m, 1H), 1.75–1.67 (m, 1H), 1.05 (s, 9H), 0.86 (s, 9H), 0.83–0.76 (m, 2H), 0.58–0.49 (m, 2H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 135.5, 133.8, 130.0, 129.6, 129.5, 129.4, 127.6, 113.8, 74.2, 74.0, 73.0, 71.4, 60.6, 55.2, 41.1, 26.8, 25.8, 22.0, 19.1, 18.3, 18.0, 7.4, -4.3, -4.5; MS (ESI-TOF) *m/z*: 671 [M + Na]$^+$. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{38}H_{56}NaO_5Si_2$ 671.3564; found 671.3567.

(*R*)-5-((1*S*,2*S*)-2-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-((4-methoxybenzyl)oxy)ethyl)cyclopropyl)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (38): Following the procedure detailed for the preparation of compound **21** from alcohol **20**,

alcohol **37** (460 mg, 0.71 mmol) was treated with 2,6-lutidine (0.2 mL, 1.56 mmol) and TBSOTf (0.18 mL, 0.78 mmol) to afford silyl ether **38** (512 mg, 0.67 mmol) in 94% yield as a gummy oil. TLC: R_f 0.3 (2% EtOAc/Hexane); $[\alpha]^{20}_D$ = +11.0 (*c* 0.2, $CHCl_3$); IR (neat): 3068, 2953, 2857, 1466, 1250, 1039, 834, 704 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.62 (m, 4H), 7.43–7.33 (m, 6H), 7.24–7.21 (m, 2H), 6.86–6.82 (m, 2H), 4.44 (d, *J* = 11.6 Hz, 1H), 4.40 (d, *J* = 11.6 Hz, 1H), 3.78 (s, 3H), 3.74 (t, *J* = 6.5 Hz, 2H), 3.49–3.42 (m, 2H), 3.40–3.33 (m, 2H), 1.82–1.67 (m, 2H), 1.03 (s, 9H), 0.92–0.76 (m, 20H), 0.43 (dt, *J* = 8.7, 4.9 Hz, 1H), 0.30 (dt, *J* = 8.5, 4.9 Hz, 1H), 0.02 (s, 9H), -0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 135.5, 134.0, 130.7, 129.52, 129.51, 129.1, 127.6, 113.6, 77.0, 75.4, 72.8, 71.5, 60.7, 55.2, 41.0, 26.9, 25.9, 21.5, 20.0, 19.2, 18.2, 18.0, 6.2, -4.1, -4.3, -4.5, -4.6; MS (ESI-TOF) *m/z*: 785 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{44}H_{70}O_5NaSi_3$ 785.4429; found 785.4419.

(*R*)-2-((*tert*-Butyldimethylsilyl)oxy)-2-((1*S*,2*S*)-2-((*R*)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecan-5-yl)cyclopropyl)ethanol (39): Following the procedure detailed for the preparation of alcohol **22** from compound **21**, compound **38** (472 mg, 0.62 mmol) was treated DDQ (170 mg, 0.75 mmol) to give alcohol **39** (315 mg, 0.5 mmol) in 82% yield as a liquid. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ = +5.8 (*c* 0.5, $CHCl_3$); IR (neat): 3485, 3070, 2931, 2858, 1467, 1254, 1105, 834, 703 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.62 (m, 4H), 7.46–7.34 (m, 6H), 3.82–3.71 (m, 2H), 3.53 (d, *J* = 4.6 Hz, 2H), 3.31 (td, *J* = 7.8, 4.6 Hz, 1H), 3.02 (dt, *J* = 8.3, 6.2 Hz, 1H), 2.53 (s, 1H), 1.96–1.85 (m, 1H), 1.77–1.67 (m, 1H), 1.04 (s, 9H), 0.95–0.79 (m, 19H), 0.74–0.65 (m, 1H), 0.51–0.39 (m, 2H), 0.07 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 133.8, 129.6, 127.6, 76.4, 73.0, 67.6, 60.4, 41.1, 26.8, 25.8, 22.3, 20.1, 19.1, 18.1, 17.9, 8.5, -4.1, -4.2, -4.62; MS (ESI-TOF) *m/z*: 665 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{36}H_{62}O_4NaSi_3$ 665.3854; found 665.3862.

(*R*)-5-((1*S*,2*S*)-2-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-(phenylthio)ethyl)cyclopropyl)-2,2, 3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (40): Following the procedure detailed for the preparation of sulfide **23** from alcohol **22**, alcohol **39** (250 mg, 0.39 mmol) was treated with diphenyldisulfide (93 mg, 0.43 mmol) followed by tri-*n*-butylphosphine (0.12 mL, 0.47 mmol) to afford sulfide **40** (252 mg, 0.34 mmol) in 88% yield as a colourless oil. TLC: R_f 0.3 (2% EtOAc/Hexane); $[\alpha]^{20}_D$ = +14.1 (*c* 0.85, $CHCl_3$); IR (neat): 3068, 2927, 2856, 1467, 1254, 1101, 834, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.63 (m, 4H), 7.45–7.34 (m, 6H), 7.33–7.28 (m, 2H), 7.26–7.20 (m, 2H), 7.16–7.10 (m, 1H), 3.75 (t, *J* = 6.5 Hz, 2H), 3.43 (q, *J* = 6.1 Hz, 1H), 3.37 (dd, *J* = 13.0, 6.1 Hz, 1H), 3.11–3.01 (m, 2H), 1.85–1.68 (m, 2H), 1.05 (s, 9H), 0.92–0.75 (m, 20H), 0.47 (dt, *J* = 8.8, 4.6 Hz, 1H), 0.32 (dt, *J* = 8.6, 4.7 Hz, 1H), 0.02 (s, 3H), 0.01 (s, 3H), -0.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2, 135.5, 133.9, 129.5, 128.8, 128.7, 127.6, 125.6, 72.8, 71.7, 60.7, 41.6, 40.9, 26.8, 25.8, 22.2, 19.1, 18.1, 18.0, 7.0, -4.1, -4.3, -4.4, -4.6; MS (ESI-TOF) *m/z*: 757 [M + Na]$^+$. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{42}H_{66}O_3NaSSi_3$ 757.3938; found 757.3936.

(*R*)-5-((1*S*,2*S*)-2-((1*R*,2*S*,*Z*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)-2,2,3,3,10,10-hexamethyl-9,9-diphenyl-4,8-dioxa-3,9-disilaundecane (41): Following the procedure detailed for the preparation of compound **25** from sulfide **23**, sulfide **40** (206 mg, 0.28 mmol) was treated with NCS (38 mg, 0.28 mmol) in anhydrous benzene (3 mL) and further reacted with the alkynylzinc bromide, prepared from alkyne **24** (113 mg, 0.84 mmol) in anhydrous THF (0.5 mL), ^{i}PrMgCl·LiCl (1.5 M in THF, 0.6 mL, 0.87 mmol) and $ZnBr_2$ (1.5 M in THF, 0.75 mL, 1.12 mmol), at 0 °C to furnish sulfide **41** (175 mg, 0.2 mmol) in 71% yield as a colourless liquid. TLC: R_f 0.3 (2% EtOAc/Hexane); $[\alpha]^{20}_D$ = -22.0 (*c* 0.4, $CHCl_3$); IR (neat): 3018, 2927, 2857, 1465, 1254, 1097, 771 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.47–7.42 (m, 2H), 7.42–

7.32 (m, 6H), 7.27–7.20 (m, 2H), 7.20–7.15 (m, 1H), 5.45–5.37 (m, 1H), 5.36–5.28 (m, 1H), 3.90 (dt, J = 4.2, 2.3 Hz, 1H), 3.71 (t, J = 6.6 Hz, 2H), 3.62 (t, J = 4.3 Hz, 1H), 3.51 (q, J = 6.1 Hz, 1H), 2.93-2.88 (m, 2H), 1.98 (q, J = 6.8 Hz, 2H), 1.73 (q, J = 6.3 Hz, 2H), 1.38–1.20 (m, 6H), 1.04 (s, 9H), 0.91–0.83 (m, 14H), 0.82 (s, 9H), 0.60 (dt, J = 8.9, 4.7 Hz, 1H), 0.41 (dt, J = 8.8, 4.9 Hz, 1H), 0.02 (s, 3H), 0.01 (s, 3H), -0.01 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 135.6, 134.0, 131.4, 129.5, 128.6, 127.6, 126.7, 124.1, 84.1, 78.0, 74.9, 70.7, 60.8, 47.1, 40.7, 31.5, 29.0, 27.1, 26.9, 25.9, 25.8, 22.5, 21.4, 19.5, 19.2, 18.2, 18.0, 17.4, 14.1, 6.5, -4.1, -4.2, -4.4, -4.6; MS (ESI-TOF) *m/z*: 891 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{52}H_{80}NaO_3Si_3S$ 891.5034; found 891.5023.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-3-((1*S*,2*S*)-2-((1*R*,2*S*,*Z*)-1-((*tert*-butyldimethylsilyl) oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)propan-1-ol (42): Following the procedure detailed for the preparation of alcohol **26** from compound **25**, compound **41** (152 mg, 0.175 mmol) was treated with NH_4F (32 mg, 0.875 mmol) in MeOH (1.5 mL) at 60 °C for 3 h to give alcohol **42** (88 mg, 0.14 mmol) in 80% yield as a gummy oil. TLC: R_f 0.2 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ = -32.7 (*c* 0.22, $CHCl_3$); IR (neat): 3447, 2929, 2857, 1467, 1253, 1083, 837 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.45 (m, 2H), 7.30–7.24 (m, 2H), 7.24–7.18 (m, 1H), 5.45–5.36 (m, 1H), 5.36–5.28 (m, 1H), 3.98–3.82 (m, 2H), 3.79–3.65 (m, 2H), 3.52 (q, J = 5.7 Hz, 1H), 2.91 (d, J = 6.6 Hz, 2H), 2.28 (bs, 1H), 1.98 (q, J = 7.0 Hz, 2H), 1.89–1.78 (m, 1H), 1.72–1.61 (m, 1H), 1.40–1.19 (m, 6H), 1.07–0.98 (m, 1H), 0.93–0.80 (m, 22H), 0.72 (dt, J = 9.0, 4.6 Hz, 1H), 0.36 (dt, J = 9.1, 4.7 Hz, 1H), 0.06 (s, 3H), 0.05 (s, 3H), 0.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 131.6, 131.5, 128.7, 126.9, 124.0, 84.4, 77.6, 73.7, 73.6, 60.2, 47.1, 38.6, 31.4, 29.0, 27.1, 25.84, 25.80, 22.5, 20.3, 20.1, 18.2, 17.9, 17.4, 14.0, 5.8, -4.1, -4.3, -4.4, -4.7; MS (ESI-TOF) *m/z*: 653 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{36}H_{62}NaO_3Si_2S$: 653.3856; found: 653.3840.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-3-((1*S*,2*S*)-2-((1*R*,2*S*,*Z*)-1-((*tert*-butyldimethylsilyl)oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)propanal (43): Following the procedure detailed for the preparation of aldehyde **27** from alcohol **26**, alcohol **42** (75 mg, 0.12 mmol) was treated with 2-iodoxybenzoic acid (50 mg, 0.18 mmol) in anhydrous DMSO and dichloromethane to afford aldehyde **43** (64 mg, 0.1 mmol) in 89% yield as a colourless oil. TLC: R_f 0.5 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ = -35.0 (*c* 0.6, $CHCl_3$); IR (neat): 2928, 2857, 1725, 1467, 1254, 1091, 837 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 9.78 (t, *J* = 2.3 Hz, 1H), 7.50–7.45 (m, 2H), 7.32–7.26 (m, 2H), 7.25–7.20 (m, 1H), 5.46–5.38 (m, 1H), 5.38–5.30 (m, 1H), 3.92 (dt, *J* = 4.0, 2.3 Hz, 1H), 3.89 (q, *J* = 5.9 Hz, 1H), 3.65 (t, *J* = 4.6 Hz, 1H), 2.95–2.91 (m, 2H), 2.68–2.54 (m, 2H), 1.99 (q, *J* = 7.0 Hz, 2H), 1.44–1.21 (m, 6H), 1.11–1.02 (m, 1H), 0.93–0.81 (m, 22H), 0.70 (dt, *J* = 8.8, 4.8 Hz, 1H), 0.47 (dt, *J* = 8.9, 4.9 Hz, 1H), 0.06 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.9, 135.3, 131.6, 131.5, 128.7, 127.0, 123.9, 84.5, 77.4, 74.3, 69.3, 51.7, 47.1, 31.4, 29.0, 27.1, 25.8, 25.7, 22.5, 21.4, 19.5, 18.1, 17.9, 17.4, 14.0, 6.3, -4.3, -4.5, -4.7; MS (ESI-TOF) *m/z*: 651 [M + Na]$^+$. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{36}H_{60}NaO_3Si_2S$ 651.3699; found 651.3673.

(*R*,*E*)-Ethyl5-((*tert*-butyldimethylsilyl)oxy)-5-((1*S*,2*S*)-2-((1*R*,2*S*,*Z*)-1-((*tert*-butyl dimethylsilyl)oxy)-2-(phenylthio)dodec-6-en-3-yn-1-yl)cyclopropyl)pent-2-enoate (44): To a stirred solution of aldehyde **43** (55 mg, 0.087 mmol) in anhydrous benzene (0.5 mL) was added (carbethoxymethylene)triphenylphosphorane (36 mg, 0.1 mmol) in portions at rt. After stirring the reaction mixture for 5 h, the solvent was evaporated and the residue was purified by column chromatography using 2% EtOAc/Hexanes (v/v) as the eluent to furnish the product **44** (56 mg, 0.08 mmol) in 92% yield as a liquid. TLC: R_f 0.5 (5% EtOAc/Hexanes); $[\alpha]^{20}_D$ = -43.2 (*c* 0.5, $CHCl_3$); IR (neat): 3130, 2929, 2856, 1721, 1467, 1257, 1067, 772 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.51–7.45 (m, 2H), 7.31–7.25 (m, 2H),

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7.24–7.19 (m, 1H), 6.99 (dt, *J* = 15.6, 7.7 Hz, 1H), 5.79 (dt, *J* = 15.6, 1.3 Hz, 1H), 5.46–5.38 (m, 1H), 5.37–5.29 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.92 (dt, *J* = 4.4, 2.3 Hz, 1H), 3.69 (t, *J* = 4.4 Hz, 1H), 3.41 (q, *J* = 5.8 Hz, 1H), 2.94–2.90 (m, 2H), 2.46–2.32 (m, 2H), 1.99 (q, *J* = 6.9 Hz, 2H), 1.40–1.22 (m, 9H), 0.99–0.82 (m, 23H), 0.68 (dt, *J* = 8.9, 5.0 Hz, 1H), 0.41 (dt, *J* = 8.9, 4.9 Hz, 1H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 146.0, 135.6, 131.55, 131.51, 128.7, 126.8, 124.0, 123.2, 84.3, 77.7, 74.3, 73.1, 60.1, 47.1, 40.8, 31.4, 29.0, 27.1, 25.8, 22.5, 21.2, 19.6, 18.2, 18.0, 17.4, 14.2, 14.0, 6.3, -4.2, -4.3, -4.4, -4.6; MS (ESI-TOF) *m/z*: 721 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{40}H_{66}NaO_4SSi_2$ 721.4118; found 721.4125.

(*R*,*E*)-Ethyl5-((*tert*-butyldimethylsilyl)oxy)-5-((1*S*,2*S*)-2-((*S*,2*E*,6*Z*)-1-((*tert*-butyl dimethylsilyl)oxy)-4-oxododeca-2,6-dien-1-yl)cyclopropyl)pent-2-enoate (45): Following the procedure detailed for the preparation of enone **33** from sulfide **32**, sulfide **44** (49 mg, 0.07 mmol) was treated with *m*CPBA (17 mg, 0.07 mmol) followed by 2-mercapto-1-methyl-imidazole (12 mg, 0.1 mmol) to afford enone **45** (35 mg, 0.058 mmol) in 83% yield as a gummy liquid. TLC: R_f 0.4 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ = +1.2 (*c* 0.25, $CHCl_3$); IR (neat): 2928, 2857, 1722, 1657, 1464, 1260, 1087, 801 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (dt, *J* = 15.6, 7.7 Hz, 1H), 6.81 (dd, *J* = 15.6, 5.0 Hz, 1H), 6.25 (dd, *J* = 15.6, 1.5 Hz, 1H), 5.85 (d, *J* = 15.6 Hz, 1H), 5.65–5.50 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.00 (td, *J* = 5.1, 1.3 Hz, 1H), 3.38 (q, *J* = 5.6 Hz, 1H), 3.33–3.27 (m, 2H), 2.44–2.37 (m, 2H), 2.04 (q, *J* = 6.9 Hz, 2H), 1.41–1.19 (m, 9H), 1.00–0.79 (m, 23H), 0.55 (dt, *J* = 8.6, 5.0 Hz, 1H), 0.38 (dt, *J* = 8.5, 5.1 Hz, 1H), 0.04 (s, 3H), 0.00 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.3, 166.3, 148.3, 145.4, 133.8, 126.9, 123.4, 120.8, 72.8, 72.5, 60.1, 41.1, 39.8, 31.4, 29.0, 27.5, 25.8, 22.5, 21.8, 21.5, 18.2, 18.0, 14.3, 14.0, 6.3, -4.3, -4.5, -4.6, -4.7; MS (ESI-TOF) *m/z*: 629 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{62}NaO_5Si_2$ 629.4033; found 629.4039.

(*R*,*E*)-Ethyl5-((*tert*-butyldimethylsilyl)oxy)-5-((1*S*,2*S*)-2-((1*S*,2*E*,4*S*,6*Z*)-1-((*tert*-butyl dimethylsilyl)oxy)-4-hydroxydodeca-2,6-dien-1-yl)cyclopropyl)pent-2-enoate (46): Following the procedure detailed for the preparation of alcohol **34** from enone **33**, enone **45** (29 mg, 0.047 mmol) was treated with (*R*)-(-)-2-methyl-CBS-oxazaborolidine (24 µL, 1 M solution in toluene, 0.0235 mmol) and BH_3·DMS (25 µL, 0.235 mmol) at 0 to -78 ºC to give alcohol **46** (25 mg, 0.041 mmol) in 87% yield as a colourless oil. TLC: R_f 0.2 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ = +3.5 (*c* 0.2, $CHCl_3$); IR (neat): 3428, 2925, 2855, 1723, 1461, 1258, 1079, 836 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (dt, *J* = 15.6, 7.7 Hz, 1H), 5.85 (d, *J* = 15.6 Hz, 1H), 5.72 (dd, *J* = 15.4, 5.9 Hz, 1H), 5.63 (dd, *J* = 15.4, 5.9 Hz, 1H), 5.59–5.50 (m, 1H), 5.43–5.34 (m, 1H), 4.22–4.06 (m, 3H), 3.84–3.74 (m, 1H), 3.50–3.41 (m, 1H), 2.40 (t, *J* = 6.2 Hz, 2H), 2.38–2.21 (m, 2H), 2.04 (q, *J* = 7.0 Hz, 2H), 1.90 (s, 1H), 1.40–1.20 (m, 9H), 0.98–0.81 (m, 23H), 0.50 (dt, *J* = 8.7, 4.7 Hz, 1H), 0.37 (dt, *J* = 8.7, 4.9 Hz, 1H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 145.8, 133.8, 133.3, 131.7, 124.50, 123.3, 74.1, 72.4, 71.9, 60.2, 41.2, 35.3, 31.5, 29.3, 27.4, 25.9, 25.8, 22.5, 22.4, 21.3, 18.2, 18.0, 14.3, 14.0, 6.4, -4.2, -4.3, -4.6; MS (ESI-TOF) *m/z*: 631 [M + Na]$^+$. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{34}H_{64}NaO_5Si_2$ 631.4190; found 631.4199.

(*R*)-Methyl5-((*tert*-butyldimethylsilyl)oxy)-5-((1*S*,2*S*)-2-((1*S*,2*E*,4*S*,6*Z*)-1-((*tert*-butyl dimethylsilyl)oxy)-4-hydroxydodeca-2,6-dien-1-yl)cyclopropyl)pentanoate (47): To a stirred solution of compound **46** (20 mg, 0.032 mmol) in anhydrous methanol (2 mL) was added magnesium turnings (8 mg, 0.32 mmol) under nitrogen at 0 ^oC, stirring was continued 6 h at rt. 1 N HCl (1 mL) was added carefully until excess magnesium dissolved and the reaction mixture was extracted with ether (3x5 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to furnish the crude compound which was purified by column

chromatography using 12% EtOAc/Hexanes (v/v) as the eluent to afford the product **47** (16 mg, 0.027 mmol) in 85% yield as a gummy liquid. TLC: R_f 0.2 (10% EtOAc/hexanes); $[\alpha]^{20}_D$ = +5.6 (*c* 0.5, $CHCl_3$); IR (neat): 3451, 2960, 2855, 1739, 1259, 1024, 771 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (ddd, *J* = 15.4, 6.0, 0.9 Hz, 1H), 5.62 (ddd, *J* = 15.4, 6.2, 0.7 Hz, 1H), 5.58–5.50 (m, 1H), 5.43–5.34 (m, 1H), 4.14 (q, *J* = 6.2 Hz, 1H), 3.76 (t, *J* = 6.1 Hz, 1H), 3.67 (s, 3H), 3.33 (q, *J* = 5.6 Hz, 1H), 2.39–2.20 (m, 4H), 2.04 (q, *J* = 7.0 Hz, 2H), 1.93 (bs, 1H), 1.76–1.65 (m, 2H), 1.55–1.46 (m, 2H), 1.40–1.19 (m, 6H), 0.95–0.73 (m, 23H), 0.51–0.43 (dt, *J* = 8.5, 4.8 Hz, 1H), 0.37 (dt, *J* = 8.7, 4.9 Hz, 1H), 0.03 (s, 3H), 0.01 (s, 3H), -0.01 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 133.9, 133.2, 131.6, 124.5, 74.6, 72.9, 71.9, 51.5, 37.5, 35.2, 34.3, 31.5, 29.3, 27.4, 25.9, 22.5, 22.3, 21.2, 20.5, 18.2, 18.1, 14.0, 6.6, -4.2, -4.5; MS (ESI-TOF) *m/z*: 619 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{33}H_{64}NaO_5Si_2$ 619.4190; found 619.4191.

(*R*)-6-((1*S*,2*S*)-2-((1*S*,2*E*,4*S*,6*Z*)-1,4-Dihydroxydodeca-2,6-dien-1-yl)cyclopropyl)tetra hydro-2H-pyran-2-one (3): To a stirred solution of compound **47** (14 mg, 0.0235 mmol) in anhydrous THF (0.2 mL) was added TBAF (0.12 mL, 1 M in THF, 0.117 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 72 h and then concentrated in vacuo. The residue was purified by silica gel column chromatography using 75% EtOAc/Hexane (v/v) to afford lactonised compound **3** (6 mg, 0.0178 mmol) in 76% yield as a viscous oil. TLC: R_f 0.1 (70% EtOAc/Hexane); $[\alpha]^{20}_D$ = -3.5 (*c* 0.1, $CHCl_3$); IR (neat): 3417, 2924, 2856, 1730, 1459, 1263, 1039, 768 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 5.91–5.73 (m, 2H), 5.62–5.51 (m, 1H), 5.44–5.35 (m, 1H), 4.24–4.09 (m, 1H), 3.83–3.67 (m, 2H), 2.56 (dt, *J* = 17.8, 6.5 Hz, 1H), 2.45 (ddd, *J* = 17.8, 8.4, 7.0 Hz, 1H), 2.39–2.26 (m, 2H), 2.11–1.89 (m, 5H), 1.88–1.74 (m, 1H), 1.72–1.52 (m, 1H), 1.38–1.23 (m, 6H), 1.20–1.11 (m, 1H), 1.07–0.97 (m, 1H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.74 (dt, *J* = 8.6, 5.4 Hz, 1H), 0.61 (dt, *J* = 8.6, 5.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 133.8, 133.4, 131.5, 124.4, 83.7, 74.2, 71.6, 35.0, 31.5,

29.5, 29.3, 27.8, 27.4, 23.0, 22.5, 20.2, 18.4, 14.0, 7.5; MS (ESI-TOF) *m/z*: 359 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{32}O_4Na$ 359.2198; found 359.2186.

(5*R*,8*R*,*E*)-8-((*tert*-Butyldimethylsilyl)oxy)-5-(((4-methoxybenzyl)oxy)methyl)-2,2,3,3,13,13-hexamethyl-12,12-diphenyl-4,11-dioxa-3,12-disilatetradec-6-ene (48): Following the procedure detailed for the preparation of compound **21** from alcohol **20**, alcohol **36** (545 mg, 0.86 mmol) was treated with 2,6-lutidine (0.22 mL, 1.90 mmol) and TBSOTf (0.20 mL, 0.95 mmol) to give silyl ether **48** (613 mg, 0.82 mmol) in 95% yield as a gummy oil. TLC: R_f 0.5 (2% EtOAc/Hexane); $[\alpha]^{20}_D$ = +10.1 (*c* 0.8, $CHCl_3$); IR (neat): 3071, 2928, 2857, 1513, 1467, 1251, 1087, 834, 777, 704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.60 (m, 4H), 7.42–7.29 (m, 6H), 7.25–7.18 (m, 2H), 6.86–6.80 (m, 2H), 5.66 (dd, *J* = 15.5, 6.1 Hz, 1H), 5.57 (dd, *J* = 15.5, 5.2 Hz, 1H), 4.43 (s, 2H), 4.36 (q, *J* = 6.1 Hz, 1H), 4.29 (q, *J* = 5.2 Hz, 1H), 3.79–3.69 (m, 4H), 3.69–3.60 (m, 1H), 3.36–3.27 (m, 2H), 1.80–1.59 (m, 2H), 1.03 (s, 9H), 0.87 (s, 9H), 0.83 (s, 9H), 0.03 (s, 3H), 0.01 (s, 6H), -0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 135.5, 134.0, 133.9, 130.6, 129.7, 129.5, 129.1, 127.6, 113.6, 75.0, 72.9, 72.1, 69.8, 60.5, 55.2, 41.2, 26.8, 25.9, 19.2, 18.3, 18.2, -4.3, -4.6, -4.7, -4.9; MS (ESI-TOF) *m/z*: 771 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{68}O_5NaSi_3$ 771.4272; found 771.4265.

(2*R*,5*R*,*E*)-2,5-bis((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)hept-3-en-1-ol (49): Following the procedure detailed for the preparation of alcohol **22** from compound **21**, compound **48** (456 mg, 0.61 mmol) was treated DDQ (207 mg, 0.91 mmol) to furnish alcohol **49** (314 mg, 0.50 mmol) in 82% yield as a colourless liquid. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ = -2.8 (*c* 0.25, $CHCl_3$); IR (neat): 3454, 3070, 2954, 2888, 1468, 1254, 1088, 834, 777, 703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.63 (m, 4H), 7.46–7.34 (m, 6H), 5.66 (ddd, *J* = 15.5, 6.2, 0.9 Hz, 1H), 5.52 (ddd, *J* = 15.5, 6.1, 0.9 Hz, 1H), 4.38 (q, *J* = 6.1 Hz, 1H), 4.23–4.16 (m, 1H), 3.76 (dt, *J* = 10.3, 6.4 Hz, 1H), 3.67 (dt, *J* = 10.3, 6.1 Hz,

1H), 3.52–3.44 (m, 1H), 3.43–3.35 (m, 1H), 1.91 (s, 1H), 1.81–1.62 (m, 2H), 1.06 (s, 9H), 0.91 (s, 9H), 0.86 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 133.8, 129.6, 129.5, 128.8, 127.6, 73.7, 69.6, 66.9, 60.4, 41.1, 26.8, 25.8, 19.2, 18.2, -4.2, -4.3, -4.8, -4.9; MS (ESI-TOF) *m/z*: 651 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{60}O_4NaSi_3$ 651.3697; found 651.3688.

(*R*)-9,9-Diethyl-2,2-dimethyl-3,3-diphenyl-7-((phenylthio)methyl)-4,8-dioxa-3,9-disilaundecane (50): To a solution of alcohol **13** (545 mg, 1.25 mmol) in anhydrous dichloromethane (3 mL) cooled at 0 °C was added imidazole (187 mg, 2.75 mmol) followed by TES-Cl (0.23 mL, 1.37 mmol). The reaction mixture was allowed to warm to rt and stirred for 30 min, then quenched by the addition of water (5 mL) and diluted with dichloromethane (5 mL). The layers were separated, the organic layer was washed with water (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 2% EtOAc/Hexane (v/v) to give the pure silyl ether **50** (671 mg, 1.22 mmol) in 97% yield as a gummy oil. TLC: R_f 0.5 (2% EtOAc/Hexane); $[\alpha]^{20}_D$ = +18.3 (*c* 0.6, $CHCl_3$); IR (neat): 3069, 2955, 2878, 1584, 1470, 1253, 1108, 1086, 736, 701 cm^{-1}.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.44–7.39 (m, 2H), 7.39–7.32 (m, 6H), 7.27–7.22 (m, 2H), 7.18–7.14 (m, 1H), 4.13–4.06 (m, 1H), 3.78–3.70 (m, 2H), 3.04 (dd, *J* = 13.1, 5.6 Hz, 1H), 3.01 (dd, *J* = 13.1, 6.4 Hz, 1H), 2.00–1.92 (m, 1H), 1.77–1.70 (m, 1H), 1.03 (s, 9H), 0.90 (t, *J* = 7.9 Hz, 9H), 0.58–0.51 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.9, 135.5, 135.4, 133.7, 133.6, 129.5, 129.3, 128.7, 127.6, 125.8, 68.5, 60.3, 41.3, 39.2, 26.8, 19.0, 6.8, 4.9; MS (ESI-TOF) *m/z*: 573 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{32}H_{46}NaO_2SSi_2$ 573.2655; found 573.2657.

(*R*)-9,9-Diethyl-7-((*R*)-4-((4-methoxybenzyl)oxy)-1-(phenylthio)but-2-yn-1-yl)-2,2-dimethyl -3,3-diphenyl-4,8-dioxa-3,9-disilaundecane (51): Following the procedure detailed for the preparation of compound **17** from sulfide **14**, sulfide **50** (528 mg, 0.96 mmol)

was treated with NCS (128 mg, 0.96 mmol) in anhydrous benzene (10 mL) and further reacted with the alkynylzinc bromide, prepared from alkyne **16** (338 mg, 1.92 mmol) in anhydrous THF (1 mL), ^{i}PrMgCl·LiCl (1.5 M in THF, 1.3 mL, 2 mmol) and $ZnBr_2$ (1.5 M in THF, 2 mL, 2.9 mmol), at 0 °C to furnish propargylic sulfide **51** (500 mg, 0.69 mmol) in 72% yield as a colorless liquid. TLC: R_f 0.3 (5% EtOAc/Hexane); $[\alpha]^{20}_D$ = -17.0 (*c* 0.7, $CHCl_3$); IR (neat): 3068, 2955, 2878, 1612, 1512, 1247, 1107, 1085, 737, 703 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73–7.66 (m, 4H), 7.54–7.49 (m, 2H), 7.45–7.33 (m, 6H), 7.30–7.19 (m, 5H), 6.87–6.81 (m, 2H), 4.44 (s, 2H), 4.22–4.16 (m, 1H), 4.15–4.12 (m, 2H), 4.07 (dd, *J* = 4.1, 1.9 Hz, 1H), 3.84–3.75 (m, 5H), 2.21–2.12 (m, 1H), 1.96–1.87 (m, 1H), 1.06 (s, 9H), 0.89 (t, *J* = 7.9 Hz, 9H), 0.54 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 135.56, 135.52, 134.5, 133.8, 133.7, 132.5, 129.8, 129.5, 128.9, 127.6, 127.57, 127.5, 113.7, 84.0, 81.6, 70.6, 70.5, 60.3, 56.9, 55.1, 46.4, 36.4, 26.8, 19.1, 6.8, 4.9; MS (ESI-TOF) *m/z*: 747 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{43}H_{57}O_4SSi_2$ 725.3516; found 725.3497.

(*R*)-9,9-Diethyl-7-((*R*,*Z*)-4-((4-methoxybenzyl)oxy)-1-(phenylthio)but-2-en-1-yl)-2,2-dimethyl-3,3-diphenyl-4,8-dioxa-3,9-disilaundecane (52): Following the procedure detailed for the preparation of alkene **35** from alkyne **17**, alkyne **51** (456 mg, 0.63 mmol) was treated with dicyclohexylborane (1.26 mmol) followed by AcOH (70 µL, 1.26 mmol) to afford alkene **52** (370 mg, 0.51 mmol) in 81% yield as a colourless oil. TLC: R_f 0.4 (5% EtOAc/Hexanes); $[\alpha]^{20}_D$ = +64.3 (*c* 0.35, $CHCl_3$); IR (neat): 3066, 2953, 2876, 1612, 1513, 1466, 1246, 1103, 737, 702 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.64 (m, 4H), 7.44–7.34 (m, 8H), 7.23–7.19 (m, 3H), 7.16–7.13 (m, 2H), 6.85–6.82 (m, 2H), 5.65–5.58 (m, 2H), 4.18 (d, *J* = 11.4 Hz, 1H), 4.15 (d, *J* = 11.4 Hz, 1H), 4.11 (dt, *J* = 8.2, 4.2 Hz, 1H), 3.89 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.79 (s, 3H), 3.77–3.72 (m, 3H), 3.58 (dd, *J* = 12.5, 4.2 Hz, 1H), 2.13–2.05 (m, 1H), 1.77–1.69 (m, 1H), 1.05 (s, 9H), 0.90 (t, *J* = 7.9 Hz, 9H), 0.58–0.51 (m, 6H);

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.1, 135.6, 135.5, 134.6, 133.9, 133.8, 133.7, 130.3, 130.0, 129.6, 129.5, 129.3, 128.9, 128.7, 127.6, 127.5, 113.7, 71.8, 71.3, 65.7, 60.7, 55.2, 53.7, 37.1, 26.8, 19.1, 6.9, 5.1; MS (ESI-TOF) *m/z*: 749 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{58}O_4Si_2SNa$ 749.3492; found 749.3484.

(2*R*,5*R*,*E*)-7-((*tert*-Butyldiphenylsilyl)oxy)-1-((4-methoxybenzyl)oxy)-5-((triethylsilyl)oxy)hept-3-en-2-ol (53): Following the procedure detailed for the preparation of compound **18** from sulfide **17**, sulfide **52** (320 mg, 0.44 mmol) was treated with *m*CPBA (108 mg, 0.44 mmol) followed by 2-mercapto-1-methyl-imidazole (76 mg, 0.66 mmol) to afford alcohol **53** (235 mg, 0.37 mmol) in 84% yield as a liquid. TLC: R_f 0.3 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ = +6.25 (*c* 0.8, $CHCl_3$); IR (neat): 3451, 3074, 2926, 2860, 1613, 1512, 1463, 1247, 1104, 738, 704 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.44–7.33 (m, 6H), 7.27–7.23 (m, 2H), 6.90–6.86 (m, 2H), 5.74 (ddd, *J* = 15.5, 6.4, 1.0 Hz, 1H), 5.57 (ddd, *J* = 15.5, 6.2, 1.0 Hz, 1H), 4.48 (s, 2H), 4.39 (q, *J* = 6.2 Hz, 1H), 4.32–4.26 (m, 1H), 3.80 (s, 3H), 3.75 (dt, *J* = 10.2, 6.3 Hz, 1H), 3.65 (dt, *J* = 10.2, 6.2 Hz, 1H), 3.46 (dd, *J* = 9.4, 3.2 Hz, 1H), 3.29 (dd, *J* = 9.4, 8.4 Hz, 1H), 2.36 (bs, 1H), 1.81–1.72 (m, 1H), 1.71–1.64 (m, 1H), 1.04 (s, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.57 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 135.5, 133.8, 129.8, 129.5, 129.3, 127.9, 127.5, 113.8, 73.8, 72.9, 70.7, 69.5, 60.2, 55.1, 41.0, 26.8, 19.1, 6.8, 4.8; MS (ESI-TOF) *m/z*: 657 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{37}H_{54}NaO_5Si_2$ 657.3407; found 657.3383.

(5*R*,8*R*,*E*)-5-(((4-Methoxybenzyl)oxy)methyl)-2,2,3,3,13,13-hexamethyl-12,12-diphenyl-8-((triethylsilyl)oxy)-4,11-dioxa-3,12-disilatetradec-6-ene (54): Following the procedure detailed for the preparation of compound **21** from alcohol **20**, alcohol **53** (120 mg, 0.19 mmol) was treated with 2,6-lutidine (48 μL, 0.42 mmol) and TBSOTf (46 μL, 0.20 mmol) to yield silyl ether **54** (134 mg, 0.18 mmol) in 95% yield as a gummy oil. TLC: R_f 0.3 (2% EtOAc/Hexane); $[\alpha]^{20}_D$ = +7.12 (*c* 0.8, $CHCl_3$); IR (neat): 3070, 2958, 2857, 1513, 1467,

1251, 1087, 835, 704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.60 (m, 4H), 7.41–7.30 (m, 6H), 7.24–7.19 (m, 2H), 6.86–6.80 (m, 2H), 5.66 (ddd, *J* = 15.5, 6.2, 0.8 Hz, 1H), 5.57 (dd, *J* = 15.5, 5.4 Hz, 1H), 4.42 (s, 2H), 4.37 (q, *J* = 6.2 Hz, 1H), 4.28 (q, *J* = 5.4 Hz, 1H), 3.77 (s, 3H), 3.75–3.69 (m, 1H), 3.68–3.58 (m, 1H), 3.35–3.28 (m, 2H), 1.80–1.69 (m, 1H), 1.68–1.58 (m, 1H), 1.02 (s, 9H), 0.89 (t, *J* = 7.9 Hz, 9H), 0.86 (s, 9H), 0.54 (q, *J* = 7.9 Hz, 6H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 135.5, 134.0, 130.6, 129.8, 129.5, 129.1, 127.6, 113.6, 74.9, 72.9, 72.1, 69.6, 60.4, 55.2, 41.3, 26.8, 25.8, 19.2, 18.3, 6.9, 4.9, -4.6, -4.7; MS (ESI-TOF) *m/z*: 771 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{68}O_5NaSi_3$ 771.4272; found 771.4265.

(7*R*,10*R*,*E*)-10-(((4-Methoxybenzyl)oxy)methyl)-2,2,12,12,13,13-hexamethyl-3,3-diphenyl -4,11-dioxa-3,12-disilatetradec-8-en-7-ol (55): To a stirred solution of disilylated compound **54** (112 mg, 0.15 mmol) in MeOH (1.5 mL) was added pyridinium p-toluenesulfonate (PPTS) (2 mg, 2.5 mol %) at 0 °C. The reaction mixture was stirred at the same temperature for 30 min, then quenched with satd aq $NaHCO_3$ (2 mL) and diluted with dichloromethane (5 mL). The organic layer was separated and the aq layer was extracted with dichloromethane (3x5 mL). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by flash column chromatography (10% EtOAc/Hexane) gave alcohol **55** (82 mg, 0.13 mmol) in 87% yield. TLC R_f 0.25 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ = -3.14 (*c* 0.35, $CHCl_3$); IR (neat): 3450, 2940, 2858, 1613, 1465, 1249, 1103, 829, 701 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.63–7.59 (m, 4H), 7.40–7.28 (m, 6H), 7.21–7.16 (m, 2H), 6.82–6.77 (m, 2H), 5.75–5.65 (m, 2H), 4.45–4.36 (m, 3H), 4.32–4.25 (m, 1H), 3.86–3.74 (m, 2H), 3.73 (s, 3H), 3.36–3.28 (m, 2H), 1.74–1.66 (m, 2H), 0.99 (s, 9H), 0.83 (s, 9H), -0.01 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 135.5, 133.1, 133.0, 130.5, 130.3, 129.8, 129.1, 127.7, 113.7, 74.8, 72.9,

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72.0, 71.3, 62.6, 55.2, 38.6, 26.8, 25.9, 19.0, 18.3, -4.6, -4.7; MS (ESI-TOF) *m/z*: 657 [M + Na]$^+$. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{37}H_{54}O_5NaSi_2$ 657.3407; found 657.3381.

(*R*)-1-((1*R*,2*R*)-2-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)-2-((4-methoxybenzyl)oxy)ethyl) cyclo propyl)-3-((*tert*-butyldiphenylsilyl)oxy)propan-1-ol (56): Following the procedure detailed for the preparation of compound **20** from alcohol **19**, alcohol **55** (63 mg, 0.1 mmol) was treated with 1,2-dimethoxyethane (DME) (21 µL, 0.2 mmol), Et_2Zn (1.0 M in hexanes, 0.2 mL, 0.2 mmol) and CH_2I_2 (32 µL, 0.4 mmol) to furnish cyclopropyl alcohol **56** (55 mg, 0.08 mmol) in 84% yield as a colouress oil. TLC: R_f 0.2 (10% EtOAc/Hexane); $[\alpha]^{20}_D$ = -2.0 (*c* 0.35, $CHCl_3$); IR (neat): 3450, 2930, 2857, 1612, 1513, 1464, 1249, 1098, 831, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.65 (m, 4H), 7.46–7.36 (m, 6H), 7.24–7.21 (m, 2H), 6.86–6.82 (m, 2H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 3.91–3.80 (m, 2H), 3.77 (s, 3H), 3.47 (q, *J* = 5.5 Hz, 1H), 3.40 (d, *J* = 5.5 Hz, 2H), 3.28–3.21 (m, 2H), 1.85–1.78 (m, 2H), 1.04 (s, 9H), 0.88–0.84 (m, 11H), 0.60–0.54 (m, 2H), 0.01 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.0, 135.56, 135.53, 133.1, 133.0, 130.4, 129.8, 129.2, 127.7, 113.6, 75.6, 75.0, 73.0, 72.5, 63.5, 55.2, 38.4, 26.8, 25.8, 21.6, 19.6, 19.0, 18.1, 7.3, -4.3, -4.6; MS (ESI-TOF) *m/z*: 671 [M + Na]$^+$. HRMS (ESI-TOF) *m/z*: [M + Na]$^+$ calcd for $C_{38}H_{56}NaO_5Si_2$ 671.3564; found 671.3552.

(But-3-en-1-yloxy) (*tert*-butyl)diphenylsilane (V): To a solution of the homoallylic alcohol (17 g, 236 mmol) in anhydrous dichloromethane (230 mL) cooled at 0 °C was added imidazole (33.70 g, 495 mmol) and then TBDPSCl (64.5 mL, 248 mmol). The reaction mixture was allowed to warm to rt and stirred for 5 h. The reaction mixture was quenched by the addition of water (100 mL) and diluted with dichloromethane (50 mL). The layers were separated and the organic layer was washed with water (50 mL), brine (50 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography on silica gel using petroleum ether as the

eluent to give pure silyl ether **V** (71 g, 229 mmol) in 97% yield as a colorless oil. TLC: R_f 0.5 (hexane); IR (neat): 3070, 2933, 2896, 2860, 1468, 1427, 1386, 1105, 701, 504 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.70–7.65 (m, 4H), 7.43–7.35 (m, 6H), 5.89–5.78 (m, 1H), 5.09–4.98 (m, 2H), 3.71 (t, J = 6.7 Hz, 2H), 2.36–2.28 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.5, 135.2, 133.8, 129.5, 127.6, 116.4, 63.4, 37.2, 26.9, 19.2; MS (ESI-TOF) *m/z*: 311 $[M + H]^+$. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{27}OSi$ 311.1825; found 311.1828.

***tert*-Butyl(2-(oxiran-2-yl)ethoxy)diphenylsilane (VI):** To a solution of the silyl ether **V** (70.37 g, 227 mmol) in dichloromethane (450 mL) cooled at 0 ^oC was added *m*CPBA (56 g, 227 mmol, 70%). The mixture was stirred at 0 ^oC for l h and further at rt for 6 h. Satd aq Na_2SO_3 (50 mL) solution was added and stirred for 15 min. The layers were separated and the aq layer was extracted with dichloromethane (2x100 mL). The combined organic layers were washed with satd aq $NaHCO_3$ (2x100 mL), brine (50 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to give the crude epoxide which was purified by column chromatography using 5% EtOAc/petroleum ether (v/v) to give the title compound **VI** (69.56 g, 213.4 mmol) in 94% yield as a colorless liquid. TLC: R_f 0.2 (5% EtOAc/hexane). IR (neat): 3070, 2960, 2858, 1426, 1260, 1107, 703, 504 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.61–7.57 (m, 4H), 7.37–7.28 (m, 6H), 3.79–3.70 (m, 2H), 3.04–2.99 (m, 1H), 2.69 (dd, J = 5.0, 4.1 Hz, 1H), 2.43 (dd, J = 5.1, 2.7 Hz, 1H), 1.72–1.67 (m, 2H), 0.98 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.4, 133.6, 133.5, 129.6, 127.6, 60.8, 49.9, 47.1, 35.6, 26.7, 19.1; MS (ESI-TOF) *m/z*: 349 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{20}H_{26}NaO_2Si$ 349.1594; found 349.1607.

(*R*)-*tert*-Butyl(2-(oxiran-2-yl)ethoxy)diphenylsilane (12): The catalyst *(R,R)*-salen-Co (302 mg, 0.5 mmol) was dissolved in dichloromethane (5 mL) and treated with acetic acid (285 µL, 5 mmol). The solution was allowed to stir at rt open to air for 30 min over which time the

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color changed from orange-red to dark brown. The solution was concentrated in vacuo to leave a crude brown solid, which was dissolved in THF (5 mL), and then racemic epoxide **VI** (16.8 g, 50 mmol) was added to the solution. The reaction mixture was cooled at 0 °C and H_2O (495 μL, 27.5 mmol) was added dropwise over a 5 min period. The reaction mixture was allowed to warm to rt and stirred for 40 h. Direct purification by flash chromatography on silica gel using 5% EtOAc/hexane provided the enantioenriched epoxide **12** (7.66 g, 47%, >99% ee). $[\alpha]^{20}_D$ = +3.5 (*c* 1.0, $CHCl_3$).

(5*R*,8*R*,*E*)-8-((*tert*-Butyldimethylsilyl)oxy)-3,3-diethyl-5-(((4-methoxybenzyl)oxy)methyl) -13,13-dimethyl-12,12-diphenyl-4,11-dioxa-3,12-disilatetradec-6-ene (VII): To a solution of alcohol **36** (494 mg, 0.78 mmol) in anhydrous dichloromethane (1.5 mL) cooled at -40 °C was added 2,6-lutidine (0.2 mL, 1.72 mmol) followed by TESOTf (0.19 mL, 0.86 mmol). The reaction mixture was stirred at the same temperature for 30 min, quenched by the addition of water (5 mL), diluted with dichloromethane (5 mL). The layers were separated and the organic layer was washed with water (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 2% EtOAc/hexane (v/v) to give pure silyl ether **VII** (542 mg, 0.72 mmol) in 93% yield as a gummy oil. TLC: R_f 0.5 (2% EtOAc/hexane); IR (neat): 3074, 2927, 2856, 1513, 1464, 1250, 1088, 830, 704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.60 (m, 4H), 7.42–7.29 (m, 6H), 7.24–7.17 (m, 2H), 6.85–6.80 (m, 2H), 5.66 (dd, *J* = 15.5, 5.8 Hz, 1H), 5.57 (dd, *J* = 15.5, 5.2 Hz, 1H), 4.42 (s, 2H), 4.36 (q, *J* = 5.9 Hz, 1H), 4.27 (q, *J* = 5.4 Hz, 1H), 3.76 (s, 3H), 3.75–3.69 (m, 1H), 3.69–3.60 (m, 1H), 3.38–3.25 (m, 2H), 1.78–1.59 (m, 2H), 1.02 (s, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.82 (s, 9H), 0.56 (q, *J* = 8.1 Hz, 6H), -0.01 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 135.5, 134.1, 134.0, 130.5, 129.9, 129.5, 129.1, 127.6, 113.6, 74.9, 72.9, 71.8, 69.8, 60.5, 55.2, 41.2, 26.8,

25.8, 19.2, 18.2, 6.8, 4.9, -4.3, -4.9; MS (ESI-TOF) *m/z*: 771 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{68}O_5NaSi_3$ 771.4272; found 771.4243.

(2*R*,5*R*,*E*)-5-((*tert*-Butyldimethylsilyl)oxy)-7-((*tert*-butyldiphenylsilyl)oxy)-2-((triethylsilyl) oxy)hept-3-en-1-ol (VIII): To a solution of the compound **VII** (411 mg, 0.55 mmol) in a mixture of dichloromethane (2 mL) and pH 7 phosphate buffer (0.2 mL) cooled at 0 ^oC was added DDQ (150 mg, 0.66 mmol). The reaction mixture was stirred for 1.5 h at the same temperature and then quenched by the addition of satd aq $NaHCO_3$ (5 mL), diluted with dichloromethane (5 mL) and stirred for 30 min. The layers were separated, organic layer was washed with water (10 mL), brine (10 mL) and dried over Na_2SO_4. The solvent was concentrated under reduced pressure and crude residue was purified by flash column chromatography using 5% EtOAc/hexane (v/v) as the eluent to give alcohol **VIII** (282 mg, 0.45 mmol) in 82% yield as a gummy liquid. TLC: R_f 0.3 (5% EtOAc/hexane); IR (neat): 3452, 3069, 2932, 2858, 1467, 1253, 1089, 834, 776, 703 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69–7.62 (m, 4H), 7.45–7.33 (m, 6H), 5.67 (ddd, *J* = 15.5, 6.3, 0.9 Hz, 1H), 5.53 (ddd, *J* = 15.5, 6.4, 0.9 Hz, 1H), 4.38 (q, *J* = 6.2 Hz, 1H), 4.24–4.14 (m, 1H), 3.76 (dt, *J* = 10.3, 6.5 Hz, 1H), 3.66 (dt, *J* = 10.3, 6.0 Hz, 1H), 3.51–3.43 (m, 1H), 3.43–3.35 (m, 1H), 1.95 (s, 1H), 1.80–1.60 (m, 2H), 1.05 (s, 9H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.86 (s, 9H), 0.60 (q, *J* = 8.0 Hz, 6H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 135.5, 133.9, 129.5, 128.9, 127.6, 73.6, 69.6, 66.9, 60.3, 41.0, 26.8, 25.8, 19.2, 18.2, 6.8, 4.9, -4.3, -4.9; MS (ESI-TOF) *m/z*: 651 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{60}O_4NaSi_3$ 651.3697; found 651.3685.

(5*R*,8*R*,*E*)-3,3-Diethyl-5-(((4-methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-8-((triethylsilyl)oxy)-4,11-dioxa-3,12-disilatetradec-6-ene (IX): Following the procedure detailed above, alcohol **53** (476 mg, 0.75 mmol) was treated with 2,6-lutidine (0.19 mL, 1.65 mmol) and TESOTf (0.18 mL, 0.825 mmol) to furnish disilyl ether **IX** (531 mg,

0.71 mmol) in 94% yield as a gummy oil. TLC: R_f 0.5 (2% EtOAc/hexane); IR (neat): 3074, 2954, 2878, 1513, 1463, 1246, 1088, 737, 705 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$) δ 7.68–7.62 (m, 4H), 7.43–7.33 (m, 6H), 7.25–7.21 (m, 2H), 6.87–6.83 (m, 2H), 5.68 (ddd, *J* = 15.5, 6.2, 0.8 Hz, 1H), 5.61 (dd, *J* = 15.5, 5.6 Hz, 1H), 4.46 (d, *J* = 11.6 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 4.39 (q, *J* = 6.2 Hz, 1H), 4.29 (q, *J* = 5.6 Hz, 1H), 3.79 (s, 3H), 3.78–3.73 (m, 1H), 3.67 (dt, *J* = 10.2, 6.1 Hz, 1H), 3.39–3.27 (m, 2H), 1.82–1.72 (m, 1H), 1.71–1.61 (m, 1H), 1.05 (s, 9H), 0.96–0.88 (m, 18H), 0.62–0.52 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 135.5, 134.0, 133.9, 130.5, 129.9, 129.5, 129.1, 127.5, 113.6, 74.9, 72.9, 71.9, 69.6, 60.4, 55.2, 41.2, 26.8, 19.2, 6.87, 6.83, 4.9; MS (ESI-TOF) *m/z*: 771 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{43}H_{68}O_5NaSi_3$ 771.4272; found 771.4262.

(2*R*,5*R*,*E*)-7-((*tert*-Butyldiphenylsilyl)oxy)-2,5-bis((triethylsilyl)oxy)hept-3-en-1-ol (X): Following the procedure detailed above, compound **IX** (471 mg, 0.63 mmol) was treated DDQ (172 mg, 0.76 mmol) to give alcohol **X** (314 mg, 0.50 mmol) in 80% yield as a colourless liquid. TLC: R_f 0.25 (5% EtOAc/hexane); IR (neat): 3449, 3068, 2955, 2877, 1464, 1238, 1089, 738, 703 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.70–7.62 (m, 4H), 7.46–7.32 (m, 6H), 5.68 (dd, *J* = 15.5, 6.3 Hz, 1H), 5.54 (dd, *J* = 15.6, 6.2 Hz, 1H), 4.39 (q, *J* = 6.2 Hz, 1H), 4.24–4.14 (m, 1H), 3.82–3.72 (m, 1H), 3.71–3.60 (m, 1H), 3.54–3.34 (m, 2H), 1.96 (s, 1H), 1.84–1.61 (m, 2H), 1.05 (s, 9H), 1.00–0.87 (m, 18H), 0.67–0.50 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 133.9, 129.5, 129.1, 127.6, 73.6, 69.5, 66.9, 60.3, 41.2, 26.8, 19.2, 6.8, 6.7, 4.94, 4.90; MS (ESI-TOF) *m/z*: 651 $[M + Na]^+$. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{35}H_{60}O_4NaSi_3$ 651.3697; found 651.3677.

Supporting Information

^1H and ^{13}C NMR spectroscopic characterization data. This material is available free of charge via the internet at http://

Conflict of Interest

The authors declare no conflict of interest.

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TOC Graphics:

Propargylic/allylic sulfides, obtained using α-chloro sulfides, are utilized for 1,4-diol synthesis in a iterative manner to create the carbinol stereocenters.