JOC The Journal of Organic Chemistry

Article

Convergent Synthesis of the Dihydropyran Core Containing C1-C15 Subunit of Sorangicin A Employing Gold(I)-Catalyzed Cyclization of an Allenic Alcohol

Sadagopan Raghavan, and Satyanarayana Nyalata

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b01743 • Publication Date (Web): 10 Oct 2016

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Convergent Synthesis of the Dihydropyran Core Containing C1-C15 Subunit of Sorangicin A Employing Gold(I)-Catalyzed Cyclization of an Allenic Alcohol

Sadagopan Raghavan* and Satyanarayana Nyalata

Natural Product Chemistry Division, Indian Institute of Chemical Technology, Hyderabad, India

sraghavan@iict.res.in

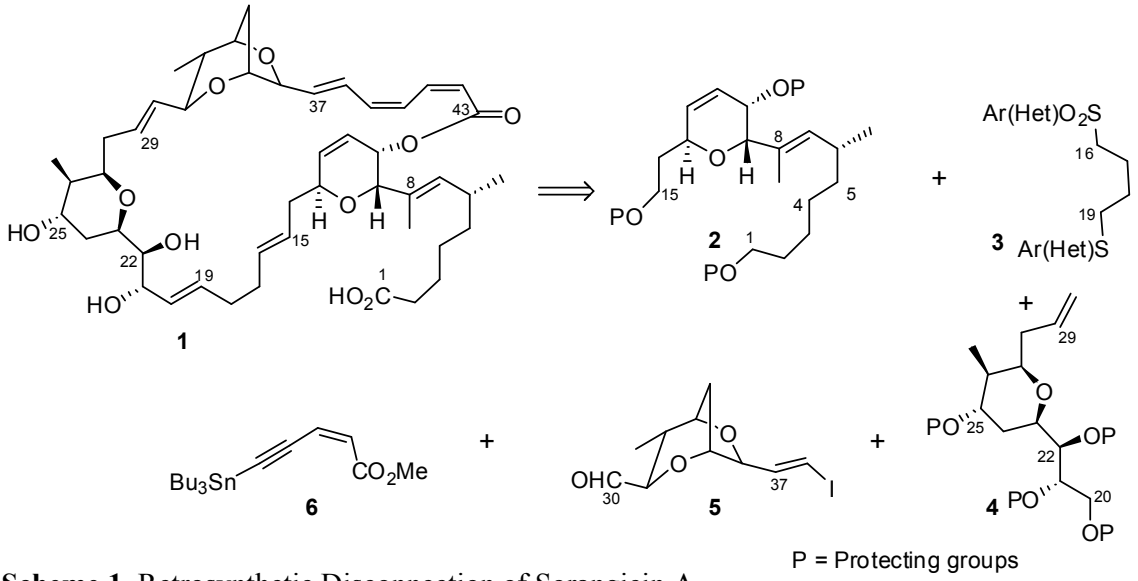
Abstract: A convergent route to the C1-C15 subunit of sorangicin A is disclosed. The key steps include carbon-carbon bond formation using an α-chlorosulfide, regioselective hydrozirconation of an internal alkyne for the preparation of a trisubstituted iodo alkene, allene formation using Myers-Movassaghi protocol, stereoselective reduction of allylic and propargylic ketones using Noyori's catalyst and gold(I)-catalyzed cyclization of a β-hydroxy allene to construct the dihydropyran ring.

INTRODUCTION

The isolation and structure elucidation of sorangicin A **1**, obtained from a fermentation broth of myxobacteria *Sorangium cellulosum* (strain So ce 12)[1] was reported by Jansen and co-workers in 1985. Sorangicin A displayed potent antibiotic activity against both Gram-positive and Gram-negative bacteria at concentrations of 0.01-0.3 and 3-25 μg/mL respectively. The mechanism of action involves inhibition of DNA-dependant RNA polymerase (RNAP) of bacteria, without affecting eukaryotic cells.[2] Sorangicin A displayed activity against rifampicin resistant microbes, too.

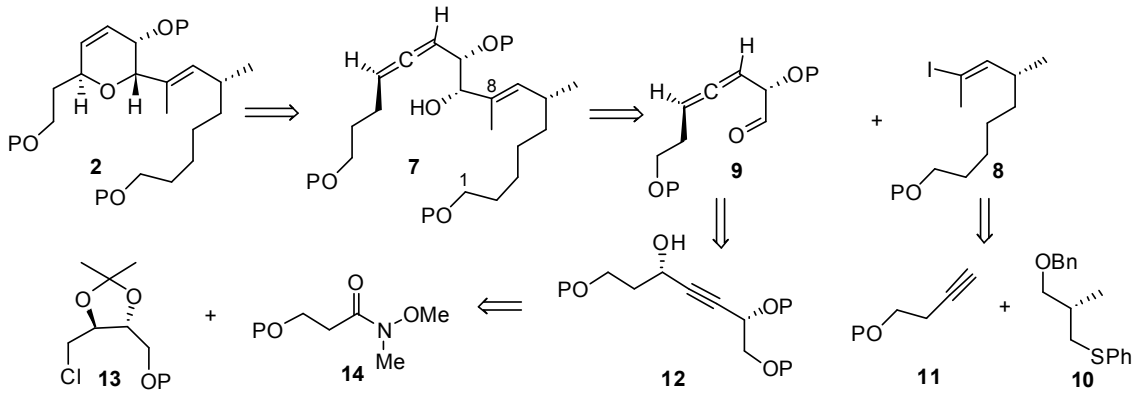
The structure assigned to sorangicin A was based on extensive NMR experiments and mass spectrometry.[3] Structurally, sorangicin A is comprised of C1-C8 side chain with a carboxyl group, attached to an unsaturated 31-membered macrocyclic lactone, possessing 15 stereocenters. A dioxabicyclo[3.2.1]octane, (*Z*,*Z*,*E*) trienoate linkage and di- and tetrahydropyran ring systems are contained in the macrocyclic ring.

The challenging structure, potent antibiotic activity and novel mechanism of action has led to widespread interest in sorangicin A among synthetic chemists. Smith and co-workers reported the first and only total synthesis of sorangicin A in 2009.[4] Crimmins and co-workers have reported a formal synthesis[5] and many groups have reported the synthesis of subunits.[6] By a retrosynthetic disconnection, sorangicin A was envisioned to be obtained by the union of fragments **2**-**6**, Scheme 1.



Scheme 1. Retrosynthetic Disconnection of Sorangicin A.

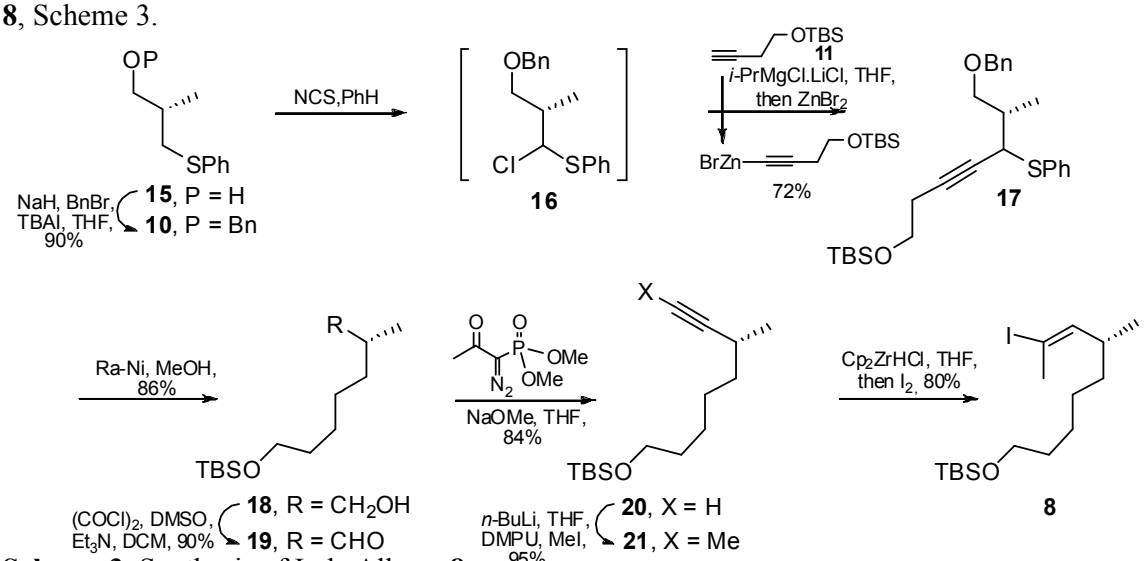
Herein, we disclose a highly stereoselective route to the C1-C15 subunit **2**, of sorangicin, utilizing an α-chlorosulfide intermediate for the C4-C5 bond formation and gold-catalyzed 6-*endo* cyclization of a β-hydroxy allene to construct the dihydropyran core. The fragment **2** can be derived from β-hydroxy allene **7**, which in turn can be obtained from the union of a suitable nucleophile derived from iodoalkene **8** and allenic aldehyde **9**. The iodo alkene **8** can be obtained from sulfide **10** and alkyne **11**. The aldehyde **9** was envisioned to be obtained from propargylic alcohol **12** which in turn can be traced to chloro acetonide **13** and Weinreb amide **14**, Scheme 2.



Scheme 2. Retrosynthetic Analysis of Subunit 2.

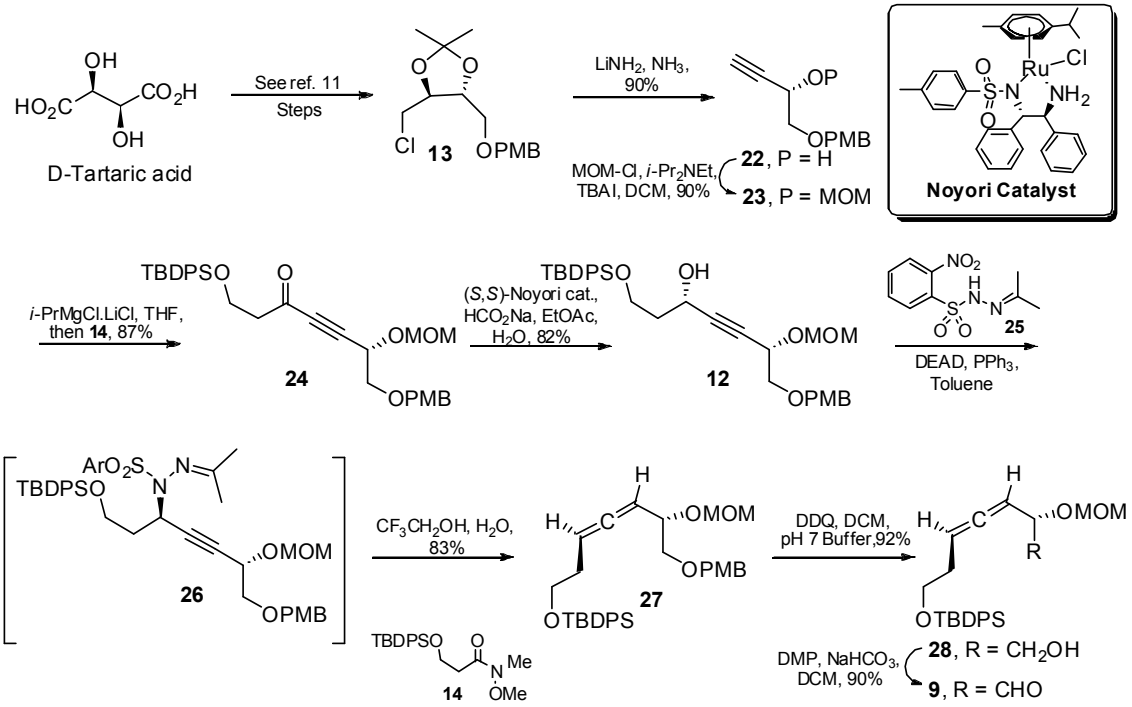
RESULTS AND DISCUSSION

The synthesis began with the known sulfide **15**,[7] prepared from methallyl alcohol by a chemoenzymatic route, which was converted readily into its benzyl ether **10**. Treatment of **10** with *N*-chlorosuccinimide yielded the α-chlorosulfide **16**, which without isolation was reacted with the alkynylzinc reagent prepared from **11**, to furnish propargylic sulfide **17** as an inconsequential mixture of diastereomers (4.5:5.5).[8] One-pot reduction and hydrogenolysis furnished alcohol **18**. Oxidation using the Swern protocol[9] yielded aldehyde **19**, which on subjecting to the Ohira-Bestman protocol[10] afforded the alkyne **20**. Methylation of the lithio acetylide furnished alkyne **21** that on reaction with an excess of Cp_2ZrHCl in THF at 50 ^oC[11] followed by quenching the resulting vinylzirconium species with iodine yielded iodo alkene **8**, Scheme 3.



Scheme 3. Synthesis of Iodo Alkene **8**.

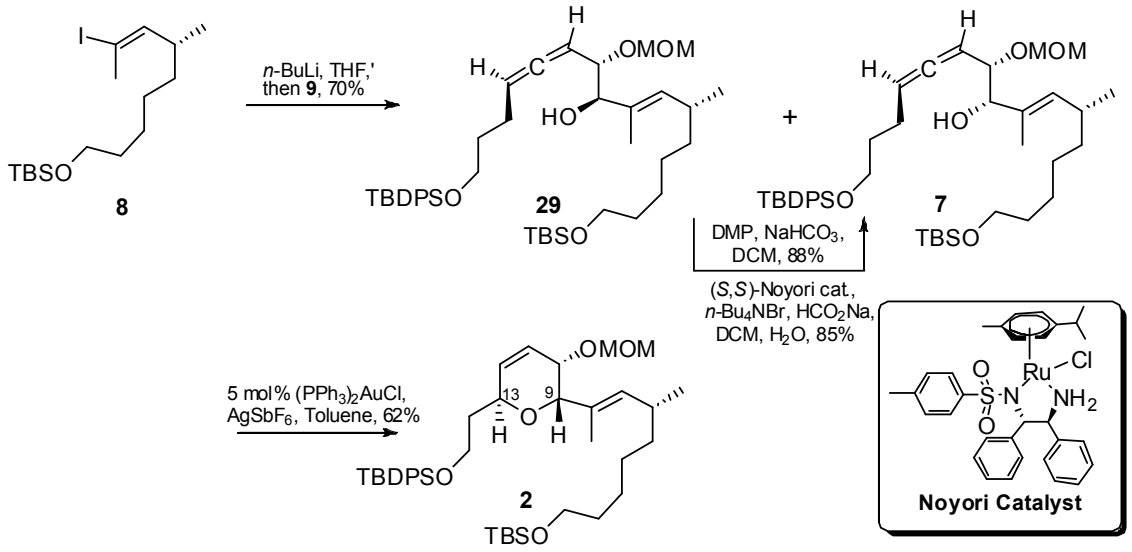
The synthesis of aldehyde 9 commenced with (D)-tartaric acid which was transformed by a known sequence of four straight forward reactions[12] into chloroacetonide 13. Alkynol 22, obtained by treatment of 13 with $LiNH_2$,[13] was protected using standard conditions as its MOM-ether 23. Reaction of the lithium acetylide derived from 23 with the Weinreb amide 14,[14] furnished the ketone 24. Stereoselective reduction of the propargylic ketone using the Noyori protocol[15] afforded alcohol 12 (82%, 99% de). Alcohol 12 was converted to allene 27 using Myers-Movassaghi's protocol.[16] Thus reaction of 12 with hydrazone 25 under Mitsunobu conditions[17] yielded hydrazone derivative 26 that on treatment with aq trifluroethanol led to diazene formation and further rearrangement to afford allene 27. Deprotection of the PMB-ether using DDQ[18] furnished the alcohol 28 that on oxidation using Dess-Martin periodinane[19] furnished aldehyde 9, Scheme 4.



Scheme 4. Synthesis of Aldehyde **9**.

The reaction of alkenyllithium derived from iodoalkene **8** with aldehyde **9** required lots of experimentation. Attempted reaction of the aldehyde **9** with the alkenyllithium derived from **8** at -78 ^oC led to the competitive isomerization of the allenic aldehyde into a *E*,*Z*-mixture of diene aldehydes which further reacted to afford a complex mixture of products.

The situation was no better using the less basic organomagnesium or organozinc reagents prepared by transmetalation. Also trials involving inverse addition of alkenyllithium to aldehyde afforded a complex mixture of products. Finally it was found that soon after addition of the aldehyde to the alkenyllithium at -78 ^{o}C, warming to 0 ^{o}C and maintaining for 10 minutes led to a separable mixture of alcohols **7** and **29** in a 4:6 ratio and in 70% combined yield.[20] In an effort to improve the diastereoselectivity in favour of the desired carbinol **7**, the solution of an equimolar mixture of $ZnCl_2$ and aldehyde **9** was added to the alkenyllithium at -78 ^{o}C, warmed immediately to 0 ^{o}C and quenched after 10 min. The selectivity of **7**:**29** improved only slightly from 4:6 to 7:3 though at the cost of the yield (60%). The alcohol **29** was oxidized using Dess-Martin periodinane and reduced using Noyori catalyst[21] to furnish alcohol **7** (9:1 dr). The key transformation of the allenic alcohol to dihydropyran proceeded cleanly using $AuCl(PPh_3)_2$ in the presence of $AgSbF_6$ in toluene to furnish the dihydropyran derivative **2**.[22] The structure of compound **2** was supported by NOE studies that revealed NOE between C10H and C14H and absence of any NOE between C9H and C13H, Scheme 5.



Scheme 5. Synthesis of the C1-C15 Subunit **2**.

CONCLUSION

In conclusion we have devised a highly stereoselective route to the C1-C15 subunit of sorangicin A comprising the *trans*-2,6-dihydropyran core. The key features of the route include the use of α-chlorosulfide for C-C bond formation, regioselective hydrozirconation of an internal alkene, Myers-Movassaghi protocol for allene formation, Noyori reduction for the creation of C9 and C13 carbinol stereocenters and gold-catalyzed cyclization for the preparation of dihydropyran core. The synthesis of the other subunits are in progress and would be reported in due course.

EXPERIMENTAL SECTION

Dry reactions were performed under an inert atmosphere using argon or 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. ^1H 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.

(*S*)-2-Methyl-3-(phenylthio)propan-1-ol 15: AIBN (2.56 g, 15.62 mmol) was added to a solution of methallyl alcohol (5.18 g, 72 mmol) in thiophenol (376 mL) at rt. The mixture was heated to 80 ^{o}C and stirred for 12 h. The mixture was cooled to rt. After dilution with Et_2O (400 mL), the solution was washed successively with aq 5% NaOH solution (400 mL), brine (2×400 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography using 20% EtOAc/hexanes (v/v) as the eluent to afford the racemic alcohol **15** (11.6 g, 63.7 mmol) in 88% yield as a liquid; TLC: R_f 0.25 (20% EtOAc/hexane); IR (neat): 3356, 2958, 2954, 2873, 1477, 1030, 739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.33 (m, 2H), 7.30-7.25 (m, 2H), 7.19-7.15 (m, 1H), 3.63 (dd, *J* = 10.8, 5.5 Hz, 1H), 3.60 (dd, *J* = 10.8, 6.1 Hz, 1H), 3.07 (dd, *J* = 13.0, 6.4 Hz, 1H), 2.84 (dd, *J* = 13.0, 6.9 Hz, 1H), 2.00-1.90 (m, 1H), 1.63 (brs, 1H), 1.05 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.5, 128.5, 128.4, 125.4, 66.0, 36.8, 35.1, 16.0; MS (ESI): *m/z* 183 $[M+H]^+$.

To a stirred solution of (±)-alcohol **15** (11.61 g, 63.8 mmol) in anhydrous chloroform (90 mL) cooled at 0 °C was added vinyl acetate (16.3 g, 255 mmol) and *Pseudomonas fluorescens* Amano Lipase (PFL) (0.7 g). The resulting solution was then stirred at 0 °C for 5 h. Monitoring by HPLC using a chiral column revealed the absence of (*R*)-**15**. (HPLC: ee = 99.0%, Chiralpak IC column, mobile phase: hexane/isopropanol 98/02, flow rate: 1 mL min^{-1}, temperature = 25 °C, detection: UV 220 nm, retention time (*S*)-isomer = 25.47 min, (*R*)-isomer 23.76 min). The resulting reaction mixture was filtered through a pad of Celite, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to yield the crude product. Purification of the crude residue by column chromatography using 20% EtOAc/hexane (v/v) as the eluent afforded alcohol **15** (5.22 g, 28.71 mmol) in 45% yield as a colorless liquid; TLC: R_f 0.25 (20% EtOAc/hexane). $[\alpha]^{20}_D$ = +15.45 (*c* 1.0, $CHCl_3$); MS (ESI): *m/z* 183 $[M+H]^+$. HRMS (ESI): calcd for $C_{10}H_{15}OS$: 183.0838, found: 183.0834.

(*S*)-(3-(Benzyloxy)-2-methylpropyl)(phenyl)sulfane 10: To a suspension of NaH (60% in Nujol, 1.83 g, 45.7 mmol) in anhydrous THF (40 mL) cooled at 0 ^{o}C was added the solution of alcohol **15** (5.2 g, 28.54 mmol) in anhydrous THF (90 mL). After the mixture was stirred for 30 min, benzyl bromide (3.4 mL, 28.54 mmol) and TBAI (1.77 g, 4.81 mmol) were added and the reaction mixture was stirred at rt for 2 h. After dilution with Et_2O (50 mL), the reaction mixture was cooled to 0 ^{o}C and treated with aq satd NH_4Cl solution (50 mL). The aq phase was extracted with Et_2O (2×50 mL) and the combined organic extracts were washed with brine (2×50 mL), dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography using 0.5-1% EtOAc/hexane (v/v) as the eluent to afford the compound **10** (6.98 g, 25.7 mmol) in 90% yield as a colourless liquid; TLC: R_f 0.4 (hexane); $[\alpha]^{20}_D$ = –9.74 (*c* 1.0, $CHCl_3$); IR (neat): 3060, 2856, 1477, 1364, 1094, 737 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36-7.30 (m, 6H), 7.29-7.22 (m, 3H), 7.16-7.12 (m, 1H), 4.49 (d, *J* = 12.4 Hz, 1H), 4.46 (d, *J* = 12.4 Hz, 1H), 3.43 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.42 (dd, *J* = 10.5, 5.6 Hz, 1H), 3.15 (dd, *J* = 13.0, 5.8 Hz, 1H), 2.79 (dd, *J* = 13.0, 7.5 Hz, 1H), 2.12-2.02 (m, 1H), 1.06 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.3, 137.0, 128.5, 128.4, 128.0, 127.2, 127.1, 125.2, 73.7, 72.7, 37.1, 33.6, 16.5; MS (ESI): *m/z* 273 $[M+H]^+$. HRMS (ESI): calcd for $C_{17}H_{21}OS$: 273.1308, found: 273.1322.

(((6*S*)-7-(Benzyloxy)-6-methyl-5-(phenylthio)hept-3-yn-1-yl)oxy)(*tert*-butyl) dimethylsilane 17: To a solution of (but-3-yn-1-yloxy)(*tert*-butyl)dimethylsilane (**11**) (10.5 g, 57.1 mmol) in anhydrous THF (57 mL) cooled at –10 °C was added *i*-PrMgCl·LiCl (1.5 M in THF, 38.1 mL, 57.1 mmol) and stirred for 30 min at the same temperature. To the generated Grignard reagent, a solution of $ZnBr_2$ (1.5 M in THF, 41.9 mL, 62.8 mmol) was added at 0 °C and stirred for 30 min. Separately in another rb flask the chlorosulfide **16** was prepared by adding a solution of sulfide **10** (7.76 g, 28.5 mmol) in anhydrous benzene (145 mL) to NCS (3.81 g, 28.5 mmol) in anhydrous benzene (140 mL) and stirring for 45 min. To

the organozinc reagent maintained at 0 °C was added a solution of chlorosulfide (28.5 mmol) in benzene (285 mL). 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 chlorosulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of aq sat NH_4Cl solution (50mL). It was allowed to warm to rt and diluted with Et_2O (80 mL). The layers were separated and the aq layer was extracted with Et_2O (3×80 mL). The combined organic layers were washed with H_2O (100 mL), brine (100 mL), dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure to afford a crude compound which was purified by column chromatography using 1-2% EtOAc/hexanes (v/v) as the eluent to afford the pure product **17** as a 4.5:5.5 mixture of diastereomers at the newly created stereocentre (8.35 g, 18.39 mmol) in 72% yield as a light yellow liquid. TLC: R_f 0.2 (1% EtOAc/hexane); $[\alpha]^{20}_D$ = +15.26 (*c* 1.0, $CHCl_3$); IR (neat): 3061, 2930, 1472, 1253, 1102, 836 cm^{-1}; ^1H NMR (diastereomers with 0.9:1 ratio and the minor isomer denoted with asterisk, 500 MHz, $CDCl_3$): δ 7.50-7.45 (m, 4H), 7.35-7.20 (m, 16H), 4.47 (s, 2H)*, 4.46 (s, 2H), 4.25 (dt, *J* = 4.3, 2.1 Hz, 1H)*, 4.02 (dt, *J* = 4.9, 2.3 Hz, 1H), 3.69 (dd, *J* = 9.3, 6.4 Hz, 1H)*, 3.63 (t, *J* = 7.3 Hz, 2H)*, 3.62 (t, *J* = 7.3 Hz, 2H), 3.48 (dd, *J* = 9.3, 5.2 Hz, 1H), 3.46 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.41 (dd, *J* = 9.3, 5.3 Hz, 1H)*, 2.40-2.36 (m, 4H), 2.23-2.11 (m, 2H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H)*, 0.89 (s, 9H)*, 0.88 (s, 9H), 0.05 (s, 12H); ^{13}C NMR (diastereomers with 0.9:1 ratio and the minor isomer denoted with asterisk, 100 MHz, $CDCl_3$): δ 138.35, 138.30*, 135.1, 134.9*, 132.0*, 131.5, 128.62*, 128.60, 128.57, 128.16, 128.13*, 127.39*, 127.31, 126.9, 126.8*, 82.9*, 82.0, 79.8*, 77.6, 72.9, 72.8, 72.3*, 61.8, 42.7*, 41.3, 38.3, 37.2*, 25.8, 23.1, 18.1, 14.7, 12.6*, –5.3; MS (ESI): *m/z* 477 $[M+Na]^+$. HRMS (ESI): calcd for $C_{27}H_{38}NaO_2SSi$: 477.2254, found: 477.2266.

(*R*)-7-((*tert*-Butyldimethylsilyl)oxy)-2-methylheptan-1-ol 18: To a solution of compound **17** (8.3 g, 18.3 mmol) in methanol (152 mL) was added freshly prepared W2 Raney-Nickel

(suspension in methanol, 32 g) and the above mixture was stirred for 16 h under hydrogen atmosphere. The reaction mixture was filtered through a pad of Celite and washed with methanol (2×30 mL). The combined organic layers were concentrated under reduced pressure, and the residue was purified by column chromatography using 10-12% EtOAc/hexanes (v/v) as the eluent to afford the pure product **18** (4.1 g, 15.7 mmol) in 86% yield as a colourless liquid. TLC: R_f 0.15 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = +4.80 (*c* 1.0, $CHCl_3$); IR (neat): 3352, 2930, 1466, 1253, 1100, 836 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.60 (t, *J* = 6.6 Hz, 2H), 3.51 (dd, *J* = 10.5, 5.7 Hz, 1H), 3.41 (dd, *J* = 10.5, 6.5 Hz, 1H), 1.66-1.56 (m, 2H), 1.56-1.47 (m, 2H), 1.45-1.36 (m, 1H), 1.36-1.23 (m, 3H), 1.16-1.04 (m, 1H), 0.91 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 67.9, 63.1, 35.5, 33.0, 32.6, 26.6, 26.0, 25.8, 18.2, 16.4, –5.3; MS (ESI): *m/z* 261 $[M+H]^+$. HRMS (ESI): calcd for $C_{14}H_{33}O_2Si$: 261.2244, found: 261.2235.

(*R*)-7((*tert*-Butyldimethylsilyl)oxy)-2-methylheptanal 19: Dimethylsulfoxide (4.42 mL, 62.4 mmol) was added drop wise to a solution of oxalyl chloride (2.72 mL, 31.2 mmol) in anhydrous dichloromethane (142 mL) cooled at –78 ^oC and the solution was maintained under a nitrogen atmosphere. After 0.5 h a solution of alcohol **18** (4.06 g, 15.6 mmol) in anhydrous dichloromethane (16 mL) was added dropwise. After a further 45 min, triethylamine (17.4 mL, 124.8 mmol) was added and the mixture was warmed to rt over 1 h. Water (100 mL) was added and the layers were separated. The aq phase was extracted with dichloromethane (3x100 mL). The combined organic extracts were washed with water (80 mL), brine (80 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a yellow colour liquid. The residue was purified by column chromatography using 5-8 % EtOAc/hexanes (v/v) as the eluent to afford the pure aldehyde **19** (3.66 g, 14.1 mmol) in 90% yield as a colourless liquid. TLC: R_f 0.25 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = –7.04 (*c* 1.0, $CHCl_3$); IR (neat): 2932, 2858, 1708, 1466, 1253, 1100, 835, 775 cm^{-1}; ^1H NMR (400

MHz, $CDCl_3$): δ 9.61 (d, *J* = 2 Hz, 1H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.37-2.27 (m, 1H), 1.77-1.64 (m, 1H), 1.56-1.45 (m, 2H), 1.42-1.28 (m, 5H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205, 62.9, 46.1, 32.5, 30.4, 26.8, 25.8, 25.7, 18.2, 13.2, –5.3; MS (ESI): *m/z* 259 $[M+H]^+$. HRMS (ESI): calcd for $C_{14}H_{31}O_2Si$: 259.2087, found: 259.2073.

(*R*)-*tert*-Butyldimethyl((6-methyloct-7-yn-1-yl)oxy)silane 20: To a solution of Ohira-Bestman reagent (5.4 g, 28 mmol) in anhydrous THF (40 mL) cooled at –78 °C was added NaOMe (5.4 M in MeOH, 4.66 mL, 25.2 mmol) diluted with anhydrous THF (24 mL) over a period of 10 min. A solution of aldehyde **19** (3.6 g, 14 mmol) in anhydrous THF (24 mL) was added to the above solution at –78 °C and the reaction mixture was warmed to 0 °C and stirred for a further 30 min. The mixture was quenched with aq sat Rochelle-salt solution (30 mL). The layers were separated and the aq layer was extracted with Et_2O (3x25 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography using hexanes as the eluent to afford the pure product **20** (2.99 g, 11.76 mmol) in 84% yield as a clear colourless liquid. TLC: R_f 0.3 (hexane); $[\alpha]^{20}_D$ = –11.26 (*c* 1.0, $CHCl_3$); IR (neat): 3311, 2932, 2113, 1253, 1100, 837 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.60 (t, *J* = 6.5 Hz, 2H), 2.46-2.37 (m, 1H), 2.03 (d, *J* = 2.4 Hz, 1H), 1.56-1.48 (m, 3H), 1.48-1.38 (m, 3H), 1.38-1.28 (m, 2H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 89.1, 68.0, 63.1, 36.7, 32.7, 27.0, 25.9, 25.6, 20.9, 18.3, –5.2; MS (ESI): *m/z* 255 $[M+H]^+$. HRMS (ESI): calcd for $C_{15}H_{31}OSi$: 255.2138, found: 255.2133.

Note!!: The amount of base has to be less than the amount of the Ohira-Bestman reagent in order to avoid epimerisation of the aldehyde.

(*R*)-*tert*-Butyldimethyl((6-methylnon-7-yn-1-yl)oxy)silane 21: To a solution of **20 (**2.95 g 11.65 mmol) in anhydrous THF (58 mL) cooled at –78 °C was added *n*-BuLi (2.5 M in Hexane, 14 mL, 35.0 mmol). Stirring was continued for 1 h at –78 °C and then additionally for 15 min without dry ice bath. The lithium acetylide solution was again cooled down to –78 °C and treated with methyl iodide (4.4 mL, 70 mmol) and freshly distilled DMPU (4.2 mL, 35.0 mmol). The reaction mixture was stirred at –78 °C for 2 h and warmed to rt and stirred for 12 h. The reaction was quenched with aq sat NH_4Cl (40 mL). The layers were separated and the aq layer was extracted with Et_2O (3×60 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure the crude product was purified by flash column chromatography using 1% EtOAc/hexanes (v/v) as the eluent to afford methylated product **21** (2.97 g, 11.1 mmol) in 95% yield as a colourless liquid. TLC: R_f 0.3 (hexane); $[\alpha]^{20}_D$ = –14.34 (*c* 1.0, $CHCl_3$); IR (neat): 2930, 2859, 1253, 1100, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.60 (t, *J* = 6.5 Hz, 2H), 2.39-2.30 (m, 1H), 1.79 (d, *J* = 2.4 Hz, 3H), 1.56-1.49 (m, 2H), 1.49-1.41 (m, 1H), 1.41-1.24 (m, 5H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 83.9, 75.3, 63.1, 37.2, 32.7, 27.1, 25.9, 25.8, 25.6, 21.4, 18.3, 3.4, –5.2; MS (ESI): *m/z* 269 $[M+H]^+$. HRMS (ESI): calcd for $C_{16}H_{33}OSi$: 269.2295, found: 269.2285.

(*R,E*)-*tert*-Butyl((8-iodo-6-methylnon-7-en-1-yl)oxy)dimethylsilane 8: To a solution of Cp_2ZrHC1 (5.62 g, 21.8 mmol) in anhydrous THF (24 mL) was added the solution of alkyne **21** (2.92 g, 10 mmol) in anhydrous THF (30 mL) and the mixture was stirred at 50 °C under nitrogen atmosphere in the absence of light for 50 min resulting in a blood-red reaction mixture. This reaction mixture was cooled to rt and stirred for 5 min when it turned to an orange yellow solution. A solution of iodine (5.6 g, 21.8 mmol) in THF (22.0 mL) was added via a cannula and this reaction mixture was stirred for 30 min at –78 °C. The temperature was raised to 0 °C and stirring was continued for 1h. The reaction was quenched with aq sat

$Na_2S_2O_3$ (20 mL). The organic layer was separated and the aq layer was extracted with ethyl acetate (4×40 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography using 0.5% EtOAc/hexanes (v/v) as the eluent to afford pure product **8** (3.45 g, 8.7 mmol) in 80% yield as a yellow colour liquid. TLC: R_f 0.42 (hexane); $[\alpha]^{20}_D = -19.08$ (*c* 1.0, $CHCl_3$); IR (neat): 2929, 2857, 1463, 1252, 1099, 835, 774 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.93 (dq, *J* = 9.7, 1.4 Hz, 1H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.41-2.33 (m, 1H), 2.36 (d, *J* = 1.5 Hz, 3H), 1.54-1.46 (m, 2H), 1.35-1.19 (m, 6H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.4, 92.3, 63.1, 36.9, 35.6, 32.7, 27.7, 27.1, 25.9, 25.8, 20.4, 18.3, –5.2; MS (ESI): *m/z* 397 $[M+H]^+$. HRMS (ESI): calcd for $C_{16}H_{34}OISi$: 397.1418, found: 397.1400.

Preparation of Chloroacetonide 13: The chloroacetonide was prepared in a four step sequence from (D)-tartaric acid.

(4*S*,5*S*)-Dimethyl-2,2-dimethyl-1,3-dioxolane-4,5-dicarboxylate I: In a 50 mL, one-necked, rb flask fitted with a reflux condenser and a magnetic stirring bar under nitrogen, a mixture of D-tartaric acid (3.0 g, 20 mmol), 2,2-dimethoxypropane (5.67 mL, 46 mmol), methanol (1.2 mL) and *p*-toluenesulfonic acid monohydrate (12 mg, 0.06 mmol) was warmed to 102 ^oC with occasional swirling until a dark-red homogeneous solution is obtained. Additional 2,2-dimethoxypropane (2.8 mL, 22.88 mmol) and cyclohexane (13.5 mL) are added and the flask was fitted with a 30-cm Vigreux column and a variable reflux distilling head. The mixture was heated to reflux with internal stirring and the acetone–cyclohexane and methanol–cyclohexane azeotropes are slowly removed. Additional 2,2-dimethoxypropane (0.18 mL, 1.44 mmol) was added and the mixture was heated under reflux for 15 min. After the mixture was cooled it to rt, anhydrous potassium carbonate (27 mg, 0.2 mmol) was added and the mixture was stirred until the reddish colour had abated. Volatile

material was removed under reduced pressure (water aspirator) and the residue was fractionally distilled under vacuum to afford the product **I** (3.8 g, 17.6 mmol) in 88% yield as a pale-yellow oil, bp 94–101 °C (0.5 mm Hg). TLC: R_f 0.25 (15% EtOAc/hexane); $[\alpha]^{20}_D$ = +44.93 (*c* 1.0, $CHCl_3$); [$^{lit.12d}[\alpha]^{20}_D$ = +48.8^O (*c* 1.0, MeOH)]; IR (neat): 2995, 2355, 1757, 1214, 1110, 859 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.80 (s, 2H), 3.82 (s, 6H), 1.48 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.4, 113.1, 76.3, 52.0, 25.6; MS (ESI): *m/z* 241 $[M+Na]^+$. HRMS (ESI): calcd for $C_9H_{14}O_6Na$: 241.0682, found: 241.0667.

((4*R*,5*R*)-2,2-Dimethyl-1,3-dioxolane-4,5-diyl)dimethanol II: To a suspension of $LiAlH_4$ (1.7 g, 43.8 mmol) in anhydrous THF (45 mL) cooled at 0 °C was added a solution of compound **I** (3.82 g, 17.5 mmol) in anhydrous THF (18 mL) dropwise over a period of 30 min. The reaction mixture was stirred for an additional 30 min at 0 °C and it was warmed to rt and stirred for 2 h. The reaction mixture was diluted with ether (60 mL) and quenched with ice pieces. The reaction mixture was stirred at room temperature for 1 h, and the resulting reaction mixture was filtered through a pad of Celite, and the filter cake was washed with EtOAc (3×100 mL) and MeOH (200 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography using 60-70% EtOAc/hehane (v/v) as the eluent to afford diol **II** (2.55 g, 15.75 mmol) in 90% yield as a colourless liquid. TLC: R_f 0.25 (60% EtOAc/hexane); $[\alpha]^{20}_D$ = +6.21 (*c* 1.0, $CHCl_3$); IR (neat): 3404, 2935, 2882, 1377, 1217, 1056, 844 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.00-3.95 (m, 2H), 3.77 (ddd, *J* = 11.7, 2.6, 1.4 Hz, 2H), 3.70 (ddd, *J* = 11.7, 2.4, 1.2 Hz, 2H), 2.83-2.66 (brs, 2H), 1.41 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 108.5, 77.8, 61.5, 26.2; MS (ESI): *m/z* 185 $[M+Na]^+$. HRMS (ESI): calcd for $C_7H_{14}O_4Na$: 185.0784, found: 185.0776.

((4*R*,5*R*)-5-(((4-Methoxybenzyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol III: To a solution of diol **II** (2.53 g, 15.6 mmol) in anhydrous benzene (26 mL) maintained

under nitrogen was added 4-methoxybenzyl chloride (1.5 mL, 14.51 mmol) and KOH (0.84 g, 14.98 mmol). The reaction mixture was refluxed for 9 h and then filtered. The solvent was removed under reduced pressure, and the crude product was purified by flash column chromatography using 30-40% EtOAc/hexane (v/v) as the eluent to afford alcohol **III (**3.6 g, 12.8 mmol) in 82% yield as a colourless oil. TLC: R_f 0.28 (30% EtOAc/hexane); $[\alpha]^{20}_D$ = –9.94 (*c* 1.0, $CHCl_3$); [$^{lit.\ 12b}[\alpha]^{23}_D$ = –8.44 (*c* 1.08, $CHCl_3$)]; IR (neat): 3454, 2932, 1612, 1513, 1375, 1248, 1082, 843 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* =8.7 Hz, 2H), 4.53 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 4.02 (ddd, *J* = 8.2, 5.9, 5.2 Hz, 1H), 3.91 (dt, *J* = 8.2, 4.4 Hz, 1H), 3.80 (s, 3H), 3.75 (dt, *J* = 11.6, 4.3 Hz, 1H), 3.70-3.64 (m, 2H), 3.51 (dd, *J* = 9.8, 5.9 Hz, 1H), 2.33 (dd, *J* = 7.6, 4.0 Hz, 1H), 1.41 (s, 3H), 1.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.7, 129.2, 128.8, 113.3, 108.8, 79.0, 76.2, 72.6, 69.6, 61.9, 54.6, 26.4; MS (ESI): *m/z* 305 $[M+Na]^+$. HRMS (ESI): calcd for $C_{15}H_{23}O_5$: 283.1530, found: 283.1533

(4*S*,5*R*)-4-(Chloromethyl)-5-(((4-methoxybenzyl)oxy)methyl)-2,2-dimethyl-1,3-dioxolane 13: To a stirred solution of **III** (3.58 g, 12.7 mmol) in CCl_4 (64 mL) was added triphenyl phosphine (6.7 g, 25.4 mmol) at rt and the mixture was heated at reflux for 12 h. The reaction mixture was cooled to 0 °C, diluted with hexanes (64 mL) and stirred for 30 min. The precipitate was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography using 3% EtOAc/hexane (v/v) as the eluent to afford compound **13** (3.24 g, 10.79 mmol) in 85% yield as a colourless liquid. TLC : R_f 0.25 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = –1.13 (*c* 1.0, $CHCl_3$); IR (neat): 2989, 2865, 1610, 1513, 1248, 1084, 828 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.52 (s, 2H), 4.08-4.05 (m, 2H), 3.81 (s, 3H), 3.69-3.56 (m, 4H), 1.44 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.7, 129.3, 128.6, 113.1, 109.2, 77.6, 77.2, 72.5, 69.5,

54.4, 43.9, 26.5, 26.4; MS (ESI): *m/z* 323 $[M+Na]^+$. HRMS (ESI): calcd for $C_{15}H_{21}O_4ClNa$: 323.1020, found: 323.1001.

(*S*)-1-((4-Methoxybenzyl)oxy)but-3-yn-2-ol 22: To freshly prepared $LiNH_2$ (prepared in situ by dissolving lithium metal (65 mg atom) in liq NH_3 (160 mL) at –33 °C was added the solution of chloride **13** (2.2 g, 10.7 mmol**)** in anhydrous THF (11 mL) during 3 min. After 30 min, solid NH_4Cl (11 g) was added and ammonia was warmed to rt to evaporate. The residue was partitioned between water (50 mL) and ether (50 mL). The organic layer was separated and the aq layer was extracted with Et_2O (2×50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography using 20-25% EtOAc/hexanes (v/v) as the eluent to afford pure product **22**, (1.98 g, 9.63 mmol) in 90% yield as a colourless liquid. TLC: R_f 0.2 (20% EtOAc/hexane); $[\alpha]^{20}_D$ = +4.66 (*c* 1.0, $CHCl_3$); IR (neat): 3412, 3284, 2909, 2115, 1512, 1246, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.56 (d, *J* = 11.6 Hz, 1H), 4.54-4.51 (m, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 3.80 (s, 3H), 3.62 (dd, *J* = 9.9, 3.7 Hz, 1H), 3.55 (dd, *J* = 9.9, 7.2 Hz, 1H), 2.74-2.70 (brs, 1H), 2.45 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.7, 129.2, 129.0, 113.3, 81.9, 73.3, 72.7, 72.4, 60.7, 54.7; MS (ESI): *m/z* 229 $[M+Na]^+$. HRMS (ESI): calcd for $C_{12}H_{14}O_3Na$: 229.0835, found: 229.0821.

(*S*)-1-Methoxy-4-(((2-(methoxymethoxy)but-3-yn-1-yl)oxy)methyl)benzene 23: To a cooled (0 ^oC) solution of compound **22** (1.96 g, 9.53 mmol) and *i*-Pr_2NEt (4.9 mL, 28.6 mmol) in anhydrous dichloromethane (48 mL) was added MOM-Cl (1.1 mL, 14.3 mmol) slowly followed by TBAI (0.35 g, 0.95 mmol) and the mixture was stirred for 6 h at rt. After completion of the reaction as monitored by TLC, H_2O (20 mL) was added and the reaction mixture was extracted with dichloromethane (3×30 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give a crude residue, which was purified

by column chromatography using 10% EtOAc/hexane (v/v) as the eluent to afford compound **23** (2.14 g, 8.58 mmol) in 90% yield as a light yellow liquid. TLC: R_f 0.3 (10% EtOAc/hexane); $[\alpha]^{20}_D$ = +49.67 (*c* 1.0, $CHCl_3$); IR (neat): 3281, 2897, 2114, 1512, 1247, 1030, 822 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 4.93 (d, *J* = 6.8 Hz, 1H) 4.68 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.53 (td, *J* = 6.6, 2.1 Hz, 1H), 3.80 (s, 3H), 3.67-3.64 (m, 2H), 3.40 (s, 3H), 2.44 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 129.6, 129.0, 113.5, 94.0, 79.8, 74.3, 72.7, 71.7, 64.8, 55.3, 54.8; MS (ESI): *m/z* 273 $[M+Na]^+$. HRMS (ESI): calcd for $C_{14}H_{18}O_4Na$: 273.1097, found: 273.1080.

3-((*tert*-Butyldiphenylsilyl)oxy)-*N*-methoxy-*N*-methylpropanamide 14: Mono TBDPS protected 1,3-propane diol (6.2 g, 20 mmol) was dissolved in acetone (80 mL) and cooled at 0 ^oC. Jones reagent (12.5 mL) (prepared by dissolution of 26.72 g CrO_3 in 23 mL of conc. H_2SO_4 and dilution to 100 mL with H_2O) was added slowly. The reaction mixture was stirred at the same temperature for 10 min, then the acetone was removed in vacuo. Ethyl acetate (100 mL) was added and this solution was washed several times with H_2O and once with brine. The solution was dried over anhydrous Na_2SO_4 and was then evaporated in vacuo to afford the corresponding acid (6.2 g, 19 mmol) in 95% yield as viscous oil which was used in the next step without further purification. A solution of the acid (6.2 g, 19 mmol) in CH_2Cl_2 (95 mL) was cooled to 0 °C in a flame-dried flask. 1,1'-Carbonyl diimidazole (3.7 g, 22.8 mmol) was added to the reaction mixture at this temperature. After stirring for 30 min, *N*,*O*-dimethyl hydroxylamine hydrochloride (2.2 g, 22.8 mmol) was added and the reaction was warmed to rt. After 4 h the salts were filtered through a cotton plug and the filtrate was washed with aq HCl (1 M, 50 mL) and brine (50 mL). The organic layer was dried with anhydrous Na_2SO_4 and concentrated to obtain Weinreb amide **14** (6.22 g, 16.7 mmol) in 88% yield as a light yellow oil. TLC: R_f 0.2 (15% EtOAc/hexane); IR (neat): 3070, 2933, 2757,

1664, 1426, 1109, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70-7.66 (m, 4H), 7.45-7.35 (m, 6H), 4.01 (t, *J* = 6.7 Hz, 2H), 3.66 (s, 3H), 3.18 (s, 3H), 2.71 (t, *J* = 6.7 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.0, 135.3, 133.4, 129.4, 127.4, 61.0, 59.9, 34.7, 31.7, 26.6, 18.9; MS (ESI): *m/z* 394 $[M+Na]^+$. HRMS (ESI): calcd for $C_{21}H_{30}NO_3Si$: 372.1989, found: 372.1996.

(*S*)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxa-12-silatetradec-6yn-8-one 24: To a stirred solution of alkyne **23** (2.12 g, 8.49 mmol) in THF (28 mL) was added *i*-PrMgCl (2.0 M in THF, 4.24 mL, 8.5 mmol) at 0 ^oC under nitrogen atmosphere. After stirring at the same temperature for 1 h, the mixture was transferred to the solution of Weinreb amide **14** (2.4 g, 6.53 mmol) in THF (38 mL) via cannula at 0 ^oC under nitrogen atmosphere. Then the mixture was warmed to rt and stirred for 8 h. The reaction was quenched by adding aq sat NH_4Cl (30 mL) and the reaction mixture was diluted with EtOAc (25 mL). After separation of the two layers, the aq layer was extracted with EtOAc (3×25 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography using 15% EtOAc/hexane (v/v) as the eluent to afford compound **24** (3.18 g, 5.68 mmol) in 87% yield as a pale yellow liquid. TLC: R_f 0.4 (15% EtOAc/hexane); $[\alpha]^{20}_D$ = + 42.09 (*c* 1.0, $CHCl_3$); IR (neat): 3069, 2933, 2213, 1680, 1248, 1107, 1031, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68-7.63 (m, 4H), 7.45-7.35 (m, 6H), 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.86 (d, *J* = 6.8 Hz, 1H), 4.66 (d, *J* = 6.8 Hz, 1H), 4.65 (d, *J* = 6.1 Hz, 1H), 4.56 (d, *J* = 11.8 Hz, 1H), 4.51 (d, *J* = 11.8 Hz, 1H), 4.00 (t, *J* = 6.1 Hz, 2H), 3.80 (s, 3H), 3.69-3.63 (m, 2H), 3.39 (s, 3H), 2.78 (t, *J* = 6.1 Hz, 2H), 1.02 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.3, 159.2, 135.4, 133.1, 129.6, 129.5, 129.2, 127.6, 113.7, 94.7, 87.8, 84.4, 73.0, 71.0, 65.1, 59.0, 55.6, 55.1, 48.0, 26.6, 19.0; MS (ESI): *m/z* 578 $[M+NH_4]^+$. HRMS (ESI): calcd for $C_{33}H_{44}O_6NSi$: 578.2932, found: 578.2951.

(5*S*,8*S*)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxa-12-silatetradec-6-yn-8-ol 12: A solution of compound **24** (4.1 g, 7.23 mmol) in ethyl acetate (144 mL) was added to a suspension of [(*S*,*S*)-TsDPEN]Ru-(*p*-cymene)Cl (91mg, 0.144 mmol), sodium formate (9.0 g, 115.6 mmol) and 1-butyl-3-methylimidazolium tetrafluoroborate (163 mg, 0.72 mmol) in water (144 mL). The reaction mixture was stirred for 12 h at rt. The phases were separated and the aq phase was extracted with ethyl acetate (2×100 mL). The combined organic layers were washed with brine (40 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product obtained was purified by column chromatography using 20-25% EtOAc/hexane (v/v) as the eluent to afford compound **12** (3.33 g, 5.93 mmol) in 82% yield as liquid. TLC : R_f 0.25 (20% EtOAc/hexane); $[\alpha]^{20}_D$ = +45.45 (*c* 1.0, $CHCl_3$); IR (neat): 3448, 3070, 2932, 2116, 1513, 1248, 1107, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.70-7.64 (m, 4H), 7.46-7.37 (m, 6H), 7.26 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.91 (d, *J* = 6.7 Hz, 1H), 4.75-4.70 (m, 1H), 4.65 (d, *J* = 6.7 Hz, 1H), 4.59 (ddd, *J* = 6.8, 4.5, 1.5 Hz, 1H), 4.56 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.01 (ddd, *J* = 11.9, 7.9, 3.9 Hz, 1H), 3.84-3.78 (m, 4H), 3.66-3.60 (m, 2H), 3.38 (s, 3H), 3.29 (d, *J* = 5.2 Hz, 1H), 2.05-1.98 (m, 1H), 1.94-1.85 (m, 1H), 1.04 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.1, 135.4, 132.8, 129.8, 129.7, 129.1, 127.7, 113.6, 94.2, 86.9, 80.7, 72.8, 72.0, 65.2, 61.5, 61.1, 55.5, 55.1, 38.8, 26.6, 18.9; MS (ESI): *m/z* 580 $[M+NH_4]^+$. HRMS (ESI): calcd for $C_{33}H_{46}O_6NSi$: 580.3088, found: 580.3103.

(*S*)-(5*S*,8*S*)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxa-12-silatetradec-6-yn-8-yl-2-methoxy-2-phenylacetate IV: To a solution of the alcohol **12** (14 mg, 0.025 mmol) in anhydrous CH_2Cl_2 (2 mL) were added (*S*)-*O*-methyl mandelic acid (4.2 mg, 0.025 mmol), DCC (6.2 mg, 0.03 mmol) and a few crystals of DMAP and the mixture was stirred for 45 min. The solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel using 10-12%

EtOAc/hexane (v/v) as the eluent to afford a esters **IV** (14.5 mg, 0.02 mmol) in 82% yield as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69-7.54 (m, 4H), 7.45-7.33 (m, 9H), 7.32-7.27 (m, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.72 (td, *J* = 7.6, 1.2 Hz, 1H), 4.71 (s, 1H), 4.7 (d, *J* = 6.7 Hz, 1H), 4.53 (d, *J* = 6.7 Hz, 1H), 4.51-4.41 (m, 3H), 3.80 (s, 3H), 3.75-3.62 (m, 2H), 3.49 (dd, *J* = 10.7, 7.4 Hz, 1H), 3.44 (dd, *J* = 10.7, 4.0 Hz, 1H), 3.39 (s, 3H), 3.31 (s, 3H), 2.10-1.90 (m, 2H), 1.02 (s, 9H).

(*R*)-(5*S*,8*S*)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxa-12-silatetradec-6-yn-8-yl-2-methoxy-2-phenylacetate V: To a solution of the alcohol **12** (14 mg, 0.025 mmol) in anhydrous CH_2Cl_2 (2 mL) were added (*R*)-*O*-methyl mandelic acid (4.2 mg, 0.025 mmol), DCC (6.2 mg, 0.03 mmol) and a few crystals of DMAP and the mixture was stirred for 45 min. The solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel using 10-12% EtOAc/hexane (v/v) as the eluent to afford a esters **V** (14 mg, 0.02 mmol) in 80% yield as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73-7.67 (m, 2H), 7.59-7.50 (m, 4H), 7.44-7.32 (m, 8H), 7.29-7.23 (m, 4H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.71 (t, *J* = 7.6 Hz, 1H), 4.82 (d, *J* = 6.7 Hz, 1H), 4.74 (s, 1H), 4.60 (d, *J* = 6.7 Hz, 1H), 4.55-4.47 (m, 3H), 4.26-4.17 (m, 2H), 3.79 (s, 3H), 3.60-3.53 (m, 2H), 3.44-3.33 (m, 8H), 1.96-1.82 (m, 2H), 0.98 (s, 9H).

(5*S*,7*S*)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxa-12-silatetradeca-6,7-diene 27: DEAD (1.1 mL, 7.1 mmol) was added dropwise to a solution containing the mixture of *N*-isopropylidene-*N'*-2-nitrobenzenesulfonylhydrazine (**25**)(1.83 g, 7.14 mmol), alcohol **12** (3.32 g, 5.9 mmol) and triphenylphosphine (1.87 g, 7.14 mmol) in anhydrous toluene (137 mL) cooled at 0 °C under nitrogen atmosphere. After 5 min, the reaction mixture was warmed to rt. After 20 min a mixture of trifluoroethanol and water (1:1, 67.5 mL) was added to the reaction mixture to enable formation of the allylic diazene intermediate. After 3 h, the reaction mixture was partitioned between diethyl ether (60 mL)

and water (60 mL) and the aq layer was extracted with diethyl ether (2×100 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using 5% EtOAc/hexane (v/v) as the eluent to afford allene **27** (2.67 g, 4.9 mmol) in 83% yield as a colourless liquid. TLC: R_f 0.3 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = +79.84 (*c* 1.0, $CHCl_3$); IR (neat): 3069, 2932, 1964, 1513, 1248, 1152, 1107, 1033, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.45-7.35 (m, 6H), 7.26 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.25 (qd, *J* = 7.3, 1.5 Hz, 1H), 5.10-5.03 (m, 1H), 4.74 (d, *J* = 6.7 Hz, 1H), 4.60 (d, *J* = 6.7 Hz, 1H), 4.50 (s, 2H), 4.31-4.24 (m, 1H), 3.80 (s, 3H), 3.73 (td, *J* = 6.8, 1.7 Hz, 2H), 3.55-3.51 (m, 2H), 3.35 (s, 3H), 2.29 (qd, *J* = 6.8, 2.7 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.2, 158.9, 135.3, 133.6, 130.1, 129.4, 129.0, 127.4, 113.5, 94.0, 88.9, 73.4, 72.7, 72.5, 63.3, 55.1, 55.0, 32.0, 26.7, 19.0; MS (ESI): *m/z* 569 $[M+Na]^+$. HRMS (ESI): calcd for $C_{33}H_{42}O_5Na$ Si: 569.2693, found: 569.2701.

(2*S*,4*S*)-7-((*tert*-Butyldiphenylsilyl)oxy)-2-(methoxymethoxy)hepta-3,4-dien-1-ol 28: To a solution of the PMB ether **27** (2.65 g, 4.85 mmol) in a mixture of dichloromethane (30 mL) and pH 7 phosphate buffer (3 mL) was added DDQ (1.65 g, 7.28 mmol). The reaction mixture was stirred for 1.5 h at ambient temperature and then diluted with Et_2O (20 mL). The organic solution was washed with water (2×10 mL) and sat aq $NaHCO_3$ (15 mL). The combined aq layers were extracted with Et_2O (2×25 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography using 20-25% EtOAc/hexane (v/v) as the eluent to afford alcohol **28** (1.9 g, 4.46 mmol) in 92% yield as a clear, colourless liquid. TLC: R_f 0.25 (20% EtOAc/hexane); $[\alpha]^{20}_D$ = +81.49 (*c* 1.0, $CHCl_3$); IR (neat): 3450, 3070, 2931, 1964, 1427, 1106, 1030, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29-7.64 (m, 4H), 7.45-7.35 (m, 6H), 5.28 (qd, *J* = 7.1, 1.6 Hz, 1H), 5.07-5.01 (m, 1H), 4.75 (d, *J* = 6.7

Hz, 1H), 4.61 (d, *J* = 6.7 Hz, 1H), 4.13 (tdd, *J* = 7.2, 3.7, 1.6 Hz, 1H), 3.73 (td, *J* = 6.7, 0.8 Hz, 2H), 3.69-3.54 (m, 2H), 3.37 (s, 3H), 2.35 (dd, *J* = 8.3, 4.7 Hz, 1H), 2.29 (qd, *J* = 6.7, 2.8 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.2, 135.4, 133.6, 129.5, 127.5, 94.5, 89.3, 88.4, 76.4, 65.4, 63.2, 55.4, 32.0, 26.7, 19.1; MS (ESI): *m/z* 449 $[M+Na]^+$. HRMS (ESI): calcd for $C_{25}H_{34}O_4NaSi$: 449.2118, found: 449.2096.

(2*S*,4S)-7-((*tert*-Butyldiphenylsilyl)oxy)-2-(methoxymethoxy)hepta-3,4-dienal 9: To a solution of alcohol **28** (1.87 g, 4.4 mmol) in dichloromethane (44 mL) was added sodium bicarbonate (5.55 g, 66 mmol) and Dess-Martin periodinane (2.8 g, 6.6 mmol). The mixture was stirred at ambient temperature for 1.5 h and then quenched with aq sat $Na_2S_2O_3$ (20 mL). After stirring for an additional 10 min, the mixture was then diluted with Et_2O (20 mL) and aq sat NH_4Cl (20 mL). The layers were separated and the aq layer was extracted with Et_2O (2×20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography using 20% EtOAc/Hexane (v/v) as the eluent to afford compound **9 (**1.68 g, 3.96 mmol) in 90% yield, as a colourless liquid. TLC: R_f 0.4 (20% EtOAc/hexane); $[\alpha]^{20}_D$ = +49.24 (*c* 1.0, $CHCl_3$); IR (neat): 3070, 2932, 2858, 1964, 1734, 1427, 1108, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (d, *J* = 1.3 Hz, 1H), 7.68-7.63 (m, 4H), 7.45-7.35 (m, 6H), 5.41 (qd, *J* = 7.1, 1.9 Hz, 1H), 5.10-5.03 (m 1H), 4.76 (d, *J* = 6.7 Hz, 1H), 4.66 (d, *J* = 6.7 Hz, 1H), 4.46 (dt, *J* = 7.2, 1.7 Hz, 1H), 3.73 (td, *J* = 6.6, 1.6 Hz, 2H), 3.37 (s, 3H), 2.31 (qd, *J* = 6.6, 2.7 Hz, 2H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.6, 198.1, 135.4, 133.6, 129.5, 127.6, 94.9, 90.7, 85.4, 79.3, 63.1, 55.7, 31.8, 26.7, 19.1; MS (ESI): *m/z* 447 $[M+Na]^+$. HRMS (ESI): calcd for $C_{25}H_{32}O_4SiNa$: 447.1962, found: 447.1965.

(8*S*,10*S*,11*R*,14*R*,*E*)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxa-3,21-disilatricosa-7,8,12-trien-11-ol 29 and **(8*S*,10*S*,11*S*,14*R*,*E*)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxa-3,21-**

disilatricosa-7,8,12-trien-11-ol 7: *n*-BuLi (2.5 M in Hexane, 0.96 mL, 2.4 mmol) was added dropwise to a stirred solution of vinyl iodide **8** (990 mg, 2.5 mmol) in Et_2O (17 mL) cooled at –78 °C. The reaction mixture was stirred at –78 °C for 20 min and at 0 °C for 10 min before being re-cooled to –78 °C. A solution of aldehyde **9** (424 mg, 1.0 mmol) in Et_2O (7 mL) was added dropwise and the reaction mixture was warmed to 0 ^oC immediately and stirred at 0 °C for 20 min. The reaction was quenched with aq sat NH_4Cl (5 mL). The organic layer was separated and the aq layer was extracted with Et_2O (4×8 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purification by flash column chromatography using 10% EtOAc/Hexane (v/v) as the eluent to afford alcohol **7** (194 mg, 0.28 mmol) in 28% yield and alcohol **29** (291 mg, 0.42 mmol) in 42% yield as a separable mixture of diastereomers (dr = 1:1.5 respectively).

Compound 29: TLC: R_f 0.3 (10% EtOAc/hexane); IR (neat): 3469, 3070, 2930, 1964, 1467, 1253, 1104, 704 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.68-7.63 (m, 4H), 7.44-7.35 (m, 6H), 5.27 (d, *J* = 9.6 Hz, 1H), 5.20 (q, *J* = 6.7 Hz, 1H), 5.04-4.99 (m, 1H), 4.71 (d, *J* = 6.6 Hz, 1H), 4.51 (d, *J* = 6.6 Hz, 1H), 4.12 (dd, *J* = 8.4, 5.0 Hz, 1H), 4.09-4.07 (m, 1H), 3.73 (t, *J* = 6.7 Hz, 2H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.32 (s, 3H), 2.42-2.33 (m, 1H), 2.29 (qd, *J* = 6.7, 2.4 Hz, 2H), 1.61 (d, *J* = 1.2 Hz, 3H), 1.51-1.44 (m, 2H), 1.33-1.19 (m, 6H), 1.04 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.4, 135.5, 134.3, 133.7, 131.1, 129.5, 127.5, 93.7, 88.3, 87.3, 78.0, 76.7, 63.4, 63.2, 55.5, 37.4, 32.8, 32.2, 31.9, 27.2, 26.8, 25.9, 20.9, 20.8, 19.1, 18.3, 13.0, –5.2; MS (ESI): *m/z* 717 $[M+Na]^+$. HRMS (ESI): calcd for $C_{41}H_{66}O_5Si_2Na$: 717.4341, found: 717.4347.

Compound 7: TLC: R_f 0.25 (10% EtOAc/hexane); $[\alpha]^{20}_D$ = +84.07 (*c* 0.6, $CHCl_3$); IR (neat): 3452, 2926, 2856, 1964, 1463, 1102, 1028, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.68-7.64 (m, 4H), 7.44-7.35 (m, 6H), 5.22-5.14 (m, 2H), 4.87-4.82 (m, 1H), 4.75 (d, *J* = 6.5

Hz, 1H), 4.54 (d, *J* = 6.5 Hz, 1H), 4.03 (t, *J* = 8.2 Hz, 1H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.72 (t, *J* = 6.8 Hz, 2H), 3.56 (t, *J* = 6.5 Hz, 2H), 3.36 (s, 3H), 2.40-2.32 (m, 1H), 2.28 (qd, *J* = 6.8, 2.7 Hz, 2H), 1.60 (d, *J* = 1.2 Hz, 3H), 1.50-1.43 (m, 2H), 1.33-1.21 (m, 5H), 1.21-1.14 (m, 1H), 1.04 (s, 9H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.9, 136.8, 135.5, 133.7, 131.3, 129.5, 127.5, 94.1, 88.53, 88.50, 80.5, 77.7, 63.3, 63.2, 55.7, 37.4, 32.8, 32.1, 31.9, 29.6, 27.1, 26.7, 25.9, 20.8, 19.1, 18.3, 12.0, –5.2; MS (ESI): *m/z* 717 $[M+Na]^+$. HRMS (ESI): calcd for $C_{41}H_{66}O_5Si_2Na$: 717.4341, found: 717.4356.

Mandelate esters of the mixtutre of alcohols 7 and **29 (VI):** To a solution of the mixture of alcohols **7** and **29** (16 mg, 0.023 mmol) in anhydrous CH_2Cl_2 (2 mL) were added (*R*)-*O*-methyl mandelic acid (4 mg, 0.023 mmol), DCC (6 mg, 0.028 mmol) and a few crystals of DMAP were added and the mixture was stirred for 45 min. The solvent was removed under vacuum and the residue was purified by flash column chromatography on silica gel using 5-7% EtOAc/hexane (v/v) as the eluent to afford esters **VI** (15.5 mg, 0.018 mmol) in 80% yield as a colourless oil. The data for the ester of alcohol **29** is denoted with an asterisk. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68-7.62 (m, 8H), 7.46-7.29 (m, 22H), 5.24 (d, *J* = 9.2 Hz, 1H)*, 5.20-5.10 (m, 4H), 5.06 (d, *J* = 9.5 Hz, 1H), 4.82-4.74 (m, 4H), 4.65 (d, *J* = 6.7 Hz,1H), 4.45 (d, *J* = 6.7 Hz, 1H), 4.39 (d, *J* = 6.7 Hz, 1H)*, 4.20 (d, *J* = 6.7 Hz, 1H)*, 4.19 (t, *J* = 7.2 Hz, 1H), 4.10 (t, *J* = 8 Hz, 1H) *, 3.74-3.66 (m, 4H), 3.55 (t, *J* = 6.6 Hz, 2H)*, 3.54 (t, *J* = 6.6 Hz, 2H), 3.42 (s, 3H), 3.41 (s, 3H)*, 3.40 (s, 3H)*, 3.30 (s, 3H), 2.30-2.21 (m, 4H), 1.97-1.90 (m, 2H), 1.74-1.67 (m, 4H), 1.66-1.56 (m, 8H), 1.55 (d, *J* = 1.2 Hz, 3H)*, 1.46-1.38 (m, 4H), 1.29 (d, *J* = 1.2 Hz, 3H), 1.04 (s, 9H), 1.03 (s, 9H)*, 0.89 (s, 9H)*, 0.88 (brs, 12H), 0.77 (d, *J* = 6.6 Hz, 3H)*, 0.02 (s, 12H).

(8*S*,10*S*,14*R*,*E*)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxa-3,21-disilatricosa-7,8,12-trien-11-one VII: To a solution of alcohol **29** (278 mg,

0.4 mmol) in dichloromethane (8 mL) was added sodium bicarbonate (504 mg, 6 mmol) and Dess-Martin periodinane (254 mg, 0.6 mmol). The mixture was stirred for 1.5 h at ambient temperature and then quenched with aq sat $Na_2S_2O_3$ (5 mL). After stirring for an additional 10 min, the mixture was then diluted with Et_2O (5 mL) and aq sat NH_4Cl (5 mL). The layers were separated and the aq layer was extracted with Et_2O (2×5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography using 5-8% EtOAc/Hexane (v/v) as the eluent to afford compound **VII (**243 mg, 0.35 mmol) in 88% yield as light yellow liquid. TLC: R_f 0.15 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = +109.76 (*c* 0.33, $CHCl_3$); IR (neat): 2930, 2858, 1964, 1680, 1466, 1105, 1033, 704; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68-7.63 (m, 4H), 7.45-7.35 (m, 6H), 6.43 (dq, *J* = 9.7, 1.2 Hz, 1H), 5.32-5.23 (m, 2H), 5.19-5.13 (m, 1H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.58 (d, *J* = 6.8 Hz, 1H), 3.72 (td, *J* = 6.6, 0.6 Hz, 2H), 3.58 (t, *J* = 6.5 Hz, 2H), 3.33 (s, 3H), 2.59-2.52 (m, 1H), 2.30 (qd, *J* = 6.7, 2.6 Hz, 2H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.52-1.45 (m, 2H), 1.43-1.34 (m, 1H), 1.34-1.21 (m, 5H), 1.04 (s, 9H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.2, 197.4, 150.3, 135.4, 133.7, 133.6, 129.5, 127.6, 94.3, 89.9, 89.0, 75.0, 63.2, 63.1, 55.8, 36.7, 33.5, 32.7, 31.9, 27.2, 26.7, 25.9, 25.8, 20.0, 19.1, 18.3, 11.8, –5.2; MS (ESI): *m/z* 715 $[M+Na]^+$. HRMS (ESI): calcd for $C_{41}H_{64}O_5Si_2Na$: 715.4184, found: 715.4181.

(8*S*,10*S*,11*S*,14*R*,*E*)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxa-3,21-disilatricosa-7,8,12-trien-11-ol 7: To a solution of ketone **VII** (235 mg, 0.34 mmol) in 1:1 mixture of dichloromethane/water (1.8 mL) were added sodium formate (231 mg, 3.4 mmol) and *n*-Bu_4NBr (32.8 mg, 0.102 mmol). The biphasic reaction mixture was vigorously stirred and *(S,S)*-Noyori catalyst (5.4 mg, 2.5 mol%) was added. After stirring for 15 h, an additional 1 mol% of catalyst was added and the reaction mixture was stirred for an additional 12 h. The layers were separated and the aq layer was extracted

with dichloromethane (2×5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under the reduced pressure to afford a separable mixture of alcohol **7** and **29** (200 mg, 0.289 mmol) in 85% combined yield as 9:1 mixture of isomers respectively.

***tert*-Butyl(2-((2*S*,5*S*,6*S*)-6-((*R*,*E*)-9-((*tert*-butyldimethylsilyl)oxy)-4-methylnon-2-en-2-yl)-5-(methoxymethoxy)-5,6-dihydro-*2H*-pyran-2-yl)ethoxy)diphenylsilane 2:** To a solution of the allene **7** (160 mg, 0.23 mmol) in anhydrous toluene (3 mL) under nitrogen was added $(PPh_3)_2AuCl$ (5.9 mg, 5 mol%) and $AgSbF_6$ (4.1 mg, 5 mol%) The mixture was stirred at rt for 6 h. The mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography using 5-6% EtOAc/Hexane (v/v) as the eluent to afford compound **2** (99 mg, 0.14 mmol) in 62% yield as a light yellow liquid. TLC: R_f 0.3 (5% EtOAc/hexane); $[\alpha]^{20}_D$ = +35.08 (*c* 0.22, $CHCl_3$); IR (neat): 2927, 2856, 1741, 1636, 1103, 1041, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69-7.64 (m, 4H), 7.44-7.33 (m, 6H), 6.04-5.94 (m, 2H), 5.36 (dt, *J*=9.5, 1.2 Hz, 1H), 4.72-4.66 (m, 2H), 4.58 (d, *J* = 6.8 Hz, 1H), 3.99 (s, 1H), 3.89 (dd, *J* = 5.0, 2.2 Hz, 1H), 3.88-3.83 (m, 1H), 3.73-3.67 (m, 1H), 3.57 (t, *J* = 6.6 Hz, 2H), 3.35 (s, 3H), 2.43-2.35 (m, 1H), 1.92-1.81 (m, 1H), 1.75-1.65 (m, 4H), 1.51-1.40 (m, 2H), 1.34-1.17 (m, 6H), 1.04 (s, 9H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.5, 134.1, 133.9, 132.4, 130.0, 129.5, 127.6, 124.4, 95.7, 74.0, 70.0, 68.7, 63.3, 60.4, 55.4, 37.4, 34.4, 32.8, 31.8, 29.6, 27.3, 26.8, 25.9, 20.9, 19.2, 18.3, 13.8, –5.2; MS (ESI): *m/z* 717 $[M+Na]^+$. HRMS (ESI): calcd for $C_{41}H_{66}O_5Si_2Na$: 717.4341 found: 717.4354.

Supporting Information

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

ACKNOWLEDGEMENT

N. Satyanarayana is thankful to Council of Scientific and Industrial Research (CSIR)-New Delhi for fellowship. S. R is grateful to the Department of Science and Technology, New Delhi for funding the project (EMR/2014/000753) and CSIR, New Delhi for funding under the XII five year plan programme entitled ORIGIN (CSC-108).

REFERENCES

(1) Jansen, R.; Wray, V.; Irschik, H.; Reichenbach, H.; Hofle, G. *Tetrahedron Lett*. **1985**, *26*, 6031.

(2) Irschik, H.; Jansen, R.; Gerth, K.; Hofle, G.; Reichenbach, H. *J. Antibiot.* **1987**, *40*, 7.

(3) Jansen, R.; Irschik, H.; Reichenbach, H.; Schomburg, D.; Wray, V.; Hofle, G. *Liebigs Ann. Chem*. **1989**, 111.

(4) Smith, A. B., III; Dong, S.; Brenneman, J. B.; Fox, R. J. *J. Am. Chem. Soc.* **2009**, *131*, 12109 and references cited therein.

(5) Crimmins, M. T.; Haley, M. W.; O'Bryan, E. A. *Org. Lett*. **2011**, *13*, 4712 and references cited therein.

(6) (a) Smith, A. B., III; Dong, S. *Org. Lett.* **2009,** *11*, 1099 and references cited therein. (b) Lee, K.; Kim, H.; Hong, J. *Eur. J. Org. Chem.* **2012**, 1025. (c) Sridhar, Y.; Srihari, P. *Org. Biomol. Chem*. **2013**, *11*, 4640 and references cited therein. (d) Michaelis, L.; Schinzer, D. *Synlett*. **2014**, *25*, 951 and references cited therein

(7) Raghavan, S.; Rajendar, S. *Org. Biomol. Chem.* **2016**, *14*, 131. Addition of thiophenol to methallyl alcohol in the presence of catalytic amount of AIBN yielded the racemic alcohol **15**, which was resolved using Amano lipase to furnish the (*S*)-alcohol in 45% yield and 99% ee.

(8) (a) Dilworth, B. M.; McKervey, M. A. *Tetrahedron*. **1986**, *42*, 3731. (b) Raghavan, S.; Vinoth Kumar, V.; Raju Chowhan, L. Synlett 2010, 1807.

(9) Mancuso, A. J.; Brownfain, D. S.; Swern, D. *J. Org. Chem.***1979**, *44*, 4148 and references cited therein

(10) (a) Ohira, S.; *Synth. Commun*. **1989**, *19*, 561. (b) Muller, S, J.; Liepold, B.; Roth, G. J.; Bestmann, H, J. *Synlett*. **1996**, 521.

(11) Panek, S. J.; Hu, T. *J. Org. Chem.* **1997,** *62,* 4912.

(12) (a) Kim, B. M.; Bae, S. J.; So, S. M.; Yoo, H. T.; Chang, S. K.; Lee, J. H.; Kang, J. *Org. Lett*. **2001**, *3*, 2349. (b) Roulland, E. *Angew. Chem. Int. Ed.* **2008**, *47*, 3762. (c) Lo, H. J.; Chang, Y. K.; Yan, T. H. *Org. Lett*. **2012**, *14*, 5896. (d) Li, B.; Yang, X.; Yang , K.; Fu, E. *Synth. Commun*. **2005**, *35*, 2603.

(13) Yadav, J. S.; Chander, M. C.; Joshi, B. V. *Tetrahedron Lett.* **1988**, *29*, 2737.

(14) The amide **14** was prepared by Jones oxidation of the mono-protected silyl ether of 1,3-propanediol followed by treatment of the resulting acid with carbonyldiimidazole and *N*,*O*-dimethylhydroxylamine hydrochloride. For related preparation, see: Ng, S.M.; Bader, S.J.; Snaper, M. L. *J. Am. Chem. Soc.* **2006**, *128*, 7315.

(15) (a) Rodriguez, A. R.; Spur, B. W. *Tetrahedron Lett*. **2012**, *53*, 1912. (b) Matsumara, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738.

(16) (a) Myers, A. G.; Zheng, B. *J. Am. Chem. Soc.* **1996**, *118*, 4492. (b) Movassaghi, M.; Ahmad, O. K. *J. Org. Chem.* **2007**, *72*, 1838.

(17) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett*. **1995**, *36*, 6373 and references cited therein.

(18) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett*. **1982,** *23,* 885.

(19) Meyer, S. D.; Schreiber, S. *J. Org. Chem.* **1994**, *59*, 7549 and references cited therein.

(20) Attemted reaction of aldehyde **9** with the alkenylzinc species, obtained from **21** by reaction with Schwartz reagent followed by transmetalation with diethylzinc**,** did not furnish any desired product, instead a complex mixture of products resulted. For transmetalation of

alkenylzirconium to alkenylzinc species and addition to aldehyde, see: Wipf, P.; Xu, W. *Tetrahedron Lett.* **1994**, *35*, 5197.

(21) (a) Peach, P.; Cross, D. J.; Kenny, J. A.; Mann, I.; Houson, I.; Campbell, L.; Walsgroveb, T.; Willsa, M. *Tetrahedron*. **2006**, *62*, 1864. (b) Nicolaou, K. C.; Adsool, V. A.; Hale, C. R. H. *Angew. Chem. Int. Ed.* **2011**, *50*, 5149.

(22) Gockel, B.; Krause. N. *Org. Lett*. **2006**, *8*, 4485.

TOC Graphics