

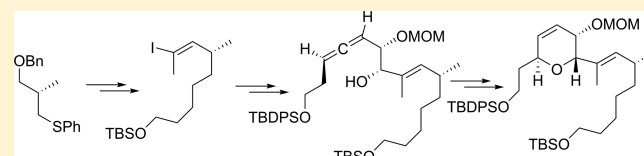
Convergent Synthesis of the Dihydropyran Core Containing the C1–C15 Subunit of Sorangicin A Employing Gold(I)-Catalyzed Cyclization of an Allenic Alcohol

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S Supporting Information

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 -chloro sulfide, regioselective hydrozirconation of an internal alkyne for the preparation of a trisubstituted iodoalkene, allene formation using the 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 displays potent antibiotic activity against both Gram-positive and Gram-negative bacteria at concentrations of 0.01–0.3 and 3–25 $\mu\text{g}/\text{mL}$, respectively. The mechanism of action involves inhibition of DNA-dependent RNA polymerase (RNAP) of bacteria without affecting eukaryotic cells.² Sorangicin A displayed activity against rifampicin-resistant microbes as well.

The structure assigned to sorangicin A was based on extensive NMR experiments and mass spectrometry.³ Structurally, sorangicin A is composed of a 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.

Herein, we disclose a highly stereoselective route to the C1–C15 subunit **2** of sorangicin, utilizing an α -chloro sulfide intermediate for the C4–C5 bond formation and gold-catalyzed 6-*endo* cyclization of a β -hydroxy allene to construct the dihydropyran core. 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 iodoalkene **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 chloroacetone **13** and Weinreb amide **14**, Scheme 2.

RESULTS AND DISCUSSION

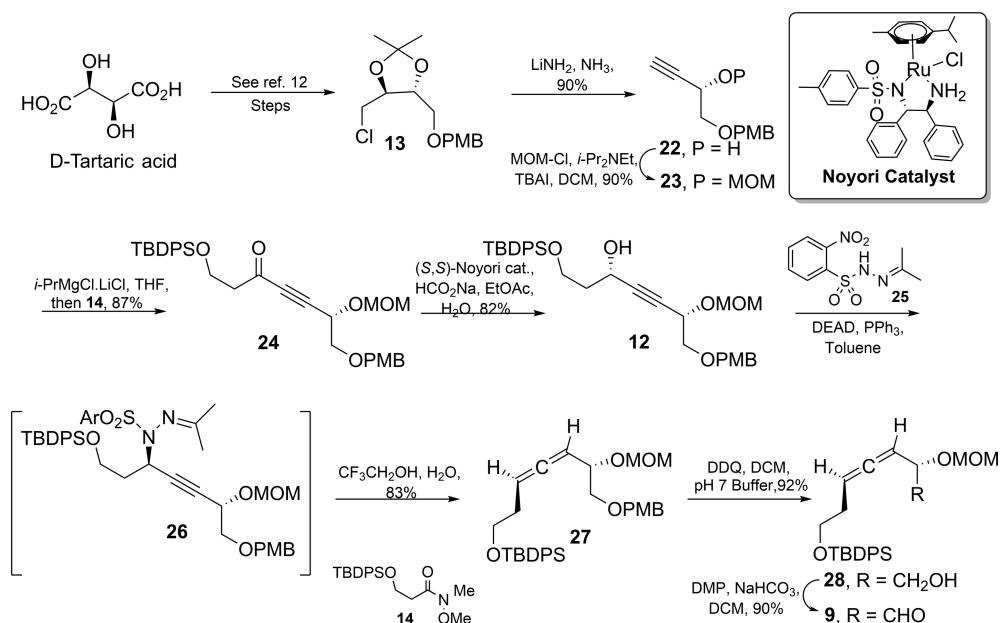
The synthesis began with the known sulfide **15**,⁷ prepared from methallyl alcohol by a chemoenzymatic route, which was converted readily into its benzyl ether **10**. Treatment of **10** with *N*-chlorosuccinimide yielded the α -chloro sulfide **16**, which without isolation was reacted with the alkynylzinc 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 protocol⁹ yielded aldehyde **19**, which on being subjected to the Ohira–Bestman protocol¹⁰ 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 °C¹¹ followed by quenching of the resulting vinylzirconium species with iodine yielded iodoalkene **8**, Scheme 3.

The synthesis of aldehyde **9** commenced with *D*-tartaric acid, which was transformed by a known sequence of four straightforward reactions¹² into chloroacetone **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 acetylide derived from **23** with the Weinreb amide **14**¹⁴ furnished the ketone **24**. Stereoselective reduction of the propargylic ketone using the Noyori protocol¹⁵ afforded alcohol **12** (82%, 99% de). Alcohol **12** was converted to allene **27** using the Myers–Movassaghi protocol.¹⁶ Thus, reaction of **12** with hydrazone **25** under Mitsunobu conditions¹⁷ yielded hydrazone derivative **26** that on treatment with aqueous trifluoroethanol led to diazene formation and further rearrange-

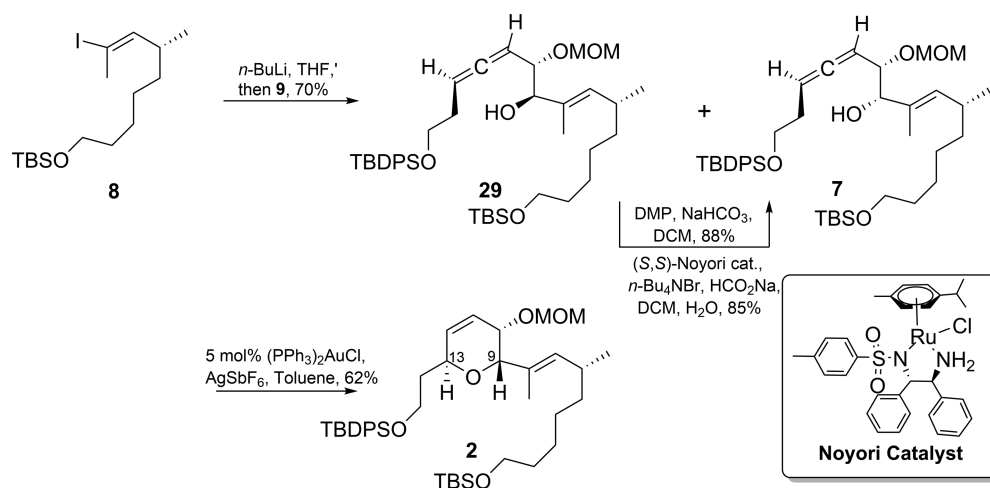
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Scheme 4. Synthesis of Aldehyde 9



Scheme 5. Synthesis of the C1–C15 Subunit 2



equimolar mixture of ZnCl_2 and aldehyde **9** was added to the alkenyllithium at -78°C , warmed immediately to 0°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 catalyst²¹ to furnish alcohol **7** (9:1 dr). The key transformation of the allenic alcohol to dihydropyran proceeded cleanly using $\text{AuCl}(\text{PPh}_3)_2$ 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*.

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 -chloro sulfide 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 the dihydropyran core. Syntheses of the other subunits are in progress and will 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 ; and 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 pre-coated plates (250 μm thickness). Optical rotations $[\alpha]_D$ were measured on a polarimeter and are given in units of $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$. 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 °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) and 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, 2873, 1477, 1030, 739 cm^{-1} ; ^1H 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 $[\text{M} + \text{H}]^+$.

To a stirred solution of (\pm)-alcohol **15** (11.61 g, 63.8 mmol) in anhydrous chloroform (90 mL) cooled at 0 °C were 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/2-propanol 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); $[\alpha]_D^{20} = +15.45$ (c 1.0, CHCl_3); MS (ESI) m/z 183 $[\text{M} + \text{H}]^+$; HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{15}\text{OS}$ 183.0838, found 183.0834.

(S)-3-(Benzyloxy)-2-methylpropylphenylsulfane (10). To a suspension of NaH (60% in Nujol, 1.83 g, 45.7 mmol) in anhydrous THF (40 mL) cooled at 0 °C was added a 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 °C and treated with aq satd NH_4Cl solution (50 mL). The aqueous 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 colorless liquid; TLC R_f 0.4 (hexane); $[\alpha]_D^{20} = -9.74$ (c 1.0, CHCl_3); IR (neat) 3060, 2856, 1477, 1364, 1094, 737 cm^{-1} ; ^1H 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 $[\text{M} + \text{H}]^+$; HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{21}\text{OS}$ 273.1308, found 273.1322.

((6S)-7-(Benzyloxy)-6-methyl-5-(phenylthio)hept-3-yn-1-yl)-oxy)tert-butyltrimethylsilane (17). To a solution of (but-3-yn-1-yl)oxy)tert-butyltrimethylsilane (**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 the mixture stirred for 30 min at the same temperature. To the generated Grignard reagent was added a

solution of ZnBr_2 (1.5 M in THF, 41.9 mL, 62.8 mmol) at 0 °C and the mixture stirred for 30 min. Separately, in another round-bottom (rb) flask, the chloro sulfide **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 chloro sulfide (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 chloro sulfide. The reaction mixture was cooled to 0 °C and quenched by the addition of aq satd NH_4Cl solution (50 mL). It was allowed to warm to rt and diluted with Et_2O (80 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (3×80 mL). The combined organic layers were washed with H_2O (100 mL) and brine (100 mL) and dried over anhydrous Na_2SO_4 , and the solvent was evaporated under reduced pressure to afford a crude compound that 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 stereocenter (8.35 g, 18.39 mmol) in 72% yield as a light yellow liquid; TLC R_f 0.2 (1% EtOAc/hexane); $[\alpha]_D^{20} = +15.26$ (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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{38}\text{NaO}_2\text{Si}$ 477.2254, found 477.2266.

(R)-7-((tert-Butyldimethylsilyloxy)-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 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 colorless liquid; TLC R_f 0.15 (5% EtOAc/hexane); $[\alpha]_D^{20} = +4.80$ (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 $[\text{M} + \text{H}]^+$; HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{33}\text{O}_2\text{Si}$ 261.2244, found 261.2235.

(R)-7-((tert-Butyldimethylsilyloxy)-2-methylheptanal (19). Dimethyl sulfoxide (4.42 mL, 62.4 mmol) was added dropwise to a solution of oxalyl chloride (2.72 mL, 31.2 mmol) in anhydrous dichloromethane (142 mL) cooled at –78 °C, 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 aqueous phase was extracted with dichloromethane (3×100 mL). The combined organic extracts were washed with water (80 mL) and brine (80 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure to give a yellow 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 colorless liquid: TLC R_f 0.25 (5% EtOAc/hexane); $[\alpha]_D^{20} = -7.04$ (c 1.0, CHCl₃); IR (neat) 2932, 2858, 1708, 1466, 1253, 1100, 835, 775 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₄H₃₁O₂Si 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 satd Rochelle salt solution (30 mL). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 25 mL). The combined organic extracts were dried over anhydrous Na₂SO₄, 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 colorless liquid: TLC R_f 0.3 (hexane); $[\alpha]_D^{20} = -11.26$ (c 1.0, CHCl₃); IR (neat) 3311, 2932, 2113, 1253, 1100, 837 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₅H₃₁O₂Si 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 epimerization 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 a dry ice bath. The lithium acetylide solution was again cooled 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, warmed to rt, and stirred for 12 h. The reaction was quenched with aq satd NH₄Cl (40 mL). The layers were separated, and the aqueous layer was extracted with Et₂O (3 × 60 mL). The combined organic extracts were dried over anhydrous Na₂SO₄. 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 colorless liquid: TLC R_f 0.3 (hexane); $[\alpha]_D^{20} = -14.34$ (c 1.0, CHCl₃); IR (neat) 2930, 2859, 1253, 1100, 836 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₆H₃₃O₂Si 269.2295, found 269.2285.

(R,E)-tert-Butyl((8-iodo-6-methylnon-7-en-1-yl)oxy)dimethylsilane (8). To a solution of Cp₂ZrHCl (5.62 g, 21.8 mmol) in anhydrous THF (24 mL) was added a 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 an orange yellow color. A solution of iodine (5.6 g, 21.8 mmol) in THF (22.0 mL) was added via a cannula, and the reaction mixture was stirred for 30 min at -78 °C. The temperature was warmed to 0 °C, and stirring was continued for 1 h. The reaction was quenched with aq satd Na₂S₂O₃ (20 mL). The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (4 × 40 mL). The combined organic layers

were dried over anhydrous Na₂SO₄, 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 color liquid: TLC R_f 0.42 (hexane); $[\alpha]_D^{20} = -19.08$ (c 1.0, CHCl₃); IR (neat) 2929, 2857, 1463, 1252, 1099, 835, 774 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₆H₃₄O₂Si 397.1418, found 397.1400.

Preparation of Chloroacetone 13. The chloroacetone was prepared in a four-step sequence from D-tartaric acid.

(4S,5S)-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 °C with occasional swirling until a dark-red homogeneous solution was obtained. Additional 2,2-dimethoxypropane (2.8 mL, 22.88 mmol) and cyclohexane (13.5 mL) were 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 were 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 color 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 mmHg); TLC R_f 0.25 (15% EtOAc/hexane); $[\alpha]_D^{20} = +44.93$ (c 1.0, CHCl₃) [lit.^{12b} $[\alpha]_D^{20} = +48.8$ (c 1.0, MeOH)]; IR (neat) 2995, 2355, 1757, 1214, 1110, 859 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.80 (s, 2H), 3.82 (s, 6H), 1.48 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 169.4, 113.1, 76.3, 52.0, 25.6; MS (ESI) m/z 241 [M + Na]⁺; HRMS (ESI) calcd for C₉H₁₄O₆Na 241.0682, found 241.0667.

((4R,5R)-2,2-Dimethyl-1,3-dioxolane-4,5-diol)dimethanol (II). To a suspension of LiAlH₄ (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, 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, 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 Na₂SO₄, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography using 60–70% EtOAc/hexane (v/v) as the eluent to afford diol **II** (2.55 g, 15.75 mmol) in 90% yield as a colorless liquid: TLC R_f 0.25 (60% EtOAc/hexane); $[\alpha]_D^{20} = +6.21$ (c 1.0, CHCl₃); IR (neat) 3404, 2935, 2882, 1377, 1217, 1056, 844 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) δ 108.5, 77.8, 61.5, 26.2; MS (ESI) m/z 185 [M + Na]⁺; HRMS (ESI) calcd for C₇H₁₄O₄Na 185.0784, found 185.0776.

((4R,5R)-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 were 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 colorless oil: TLC R_f 0.28 (30% EtOAc/hexane); $[\alpha]_D^{20} = -9.94$ (c 1.0, CHCl₃); [lit.^{12b} $[\alpha]_D^{23} =$

–8.44 (*c* 1.08, CHCl₃); IR (neat) 3454, 2932, 1612, 1513, 1375, 1248, 1082, 843 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₁₅H₂₃O₅ 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 CCl₄ (64 mL) was added triphenylphosphine (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 colorless liquid: TLC *R_f* 0.25 (5% EtOAc/hexane); [α]_D²⁰ = –1.13 (*c* 1.0, CHCl₃); IR (neat) 2989, 2865, 1610, 1513, 1248, 1084, 828 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₁₅H₂₁O₄ClNa 323.1020, found 323.1001.

(*S*)-1-((4-Methoxybenzyl)oxy)but-3-yn-2-ol (**22**). To freshly prepared LiNH₂ (prepared in situ by dissolving lithium metal (65 mg atom) in liq NH₃ (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 NH₄Cl (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 aqueous layer was extracted with Et₂O (2 × 50 mL). The combined organic layers were dried over anhydrous Na₂SO₄, 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 colorless liquid: TLC *R_f* 0.2 (20% EtOAc/hexane); [α]_D²⁰ = +4.66 (*c* 1.0, CHCl₃); IR (neat) 3412, 3284, 2909, 2115, 1512, 1246, 1030 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₁₂H₁₄O₃Na 229.0835, found 229.0821.

(*S*)-1-Methoxy-4-(((2-(methoxymethoxy)but-3-yn-1-yl)oxy)methyl)benzene (**23**). To a cooled (0 °C) solution of compound **22** (1.96 g, 9.53 mmol) and *i*-Pr₂NEt (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, H₂O (20 mL) was added, and the reaction mixture was extracted with dichloromethane (3 × 30 mL) and dried over anhydrous Na₂SO₄. 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); [α]_D²⁰ = +49.67 (*c* 1.0, CHCl₃); IR (neat) 3281, 2897, 2114, 1512, 1247, 1030, 822 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₄H₁₈O₄Na 273.1097, found 273.1080.

3-((*tert*-Butyldiphenylsilyloxy)-*N*-methoxy-*N*-methylpropanamide (**14**). Mono-TBDPS-protected 1,3-propanediol (6.2 g, 20 mmol) was dissolved in acetone (80 mL) and cooled at 0 °C. Jones reagent (12.5 mL) (prepared by dissolution of 26.72 g CrO₃ in 23 mL of concd H₂SO₄ and dilution to 100 mL with H₂O) was added slowly. The reaction mixture was stirred at the same temperature for 10 min, and then the acetone was removed in vacuo. Ethyl acetate (100 mL) was added, and this solution was washed several times with H₂O and once with brine. The solution was dried over anhydrous Na₂SO₄ and was then evaporated in vacuo to afford the corresponding acid (6.2 g, 19 mmol) in 95% yield as a viscous oil which was used in the next step without further purification. A solution of the acid (6.2 g, 19 mmol) in CH₂Cl₂ (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 the mixture was stirred 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 Na₂SO₄ 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, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) 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 C₂₁H₃₀NO₃Si 372.1989, found 372.1996.

(*S*)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxa-12-silatetradec-6-yn-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 °C under nitrogen atmosphere. After being stirred 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 °C under nitrogen atmosphere. Then the mixture was warmed to rt and stirred for 8 h. The reaction was quenched by addition of aq satd NH₄Cl (30 mL), and the reaction mixture was diluted with EtOAc (25 mL). After separation of the two layers, the aqueous layer was extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na₂SO₄, 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); [α]_D²⁰ = +42.09 (*c* 1.0, CHCl₃); IR (neat) 3069, 2933, 2213, 1680, 1248, 1107, 1031, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 + NH₄]⁺; HRMS (ESI) calcd for C₃₃H₄₄O₆NSi 578.2932, found 578.2951.

(*S*,*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 (91 mg, 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 aqueous phase was extracted with ethyl acetate (2 × 100 mL). The combined organic layers were washed with brine (40 mL), dried over anhydrous Na₂SO₄, 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); [α]_D²⁰ = +45.45 (*c* 1.0, CHCl₃); 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 $[\text{M}+\text{NH}_4]^+$. HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{46}\text{O}_6\text{NSi}$ 580.3088, found 580.3103.

(S)-(5S,8S)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxo-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 ester IV (14.5 mg, 0.02 mmol) in 82% yield as a colorless oil: ^1H 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)-(5S,8S)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxo-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 esters V (14 mg, 0.02 mmol) in 80% yield as a colorless oil: ^1H 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).

(5S,7S)-5-(((4-Methoxybenzyl)oxy)methyl)-13,13-dimethyl-12,12-diphenyl-2,4,11-trioxo-12-silatetradeca-6,7-diene (27). DEAD (1.1 mL, 7.1 mmol) was added dropwise to a solution containing a 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 aqueous layer was extracted with diethyl ether (2 \times 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 colorless liquid: TLC R_f 0.3 (5% EtOAc/hexane); $[\alpha]_D^{20} = +79.84$ (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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{42}\text{O}_3\text{Si}$ 569.2693, found 569.2701.

(2S,4S)-7-((tert-Butyldiphenylsilyloxy)-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 \times 10 mL) and sat aq NaHCO_3 (15 mL). The combined aqueous layers were extracted with Et_2O (2 \times 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, colorless liquid: TLC R_f 0.25 (20% EtOAc/hexane); $[\alpha]_D^{20} = +81.49$ (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 (td, $J = 7.2, 3.7, 1.6$ 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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{34}\text{O}_4\text{NaSi}$ 449.2118, found 449.2096.

(2S,4S)-7-((tert-Butyldiphenylsilyloxy)-2-(methoxymethoxy)hepta-3,4-dienal (9). To a solution of alcohol 28 (1.87 g, 4.4 mmol) in dichloromethane (44 mL) were 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 satd $\text{Na}_2\text{S}_2\text{O}_3$ (20 mL). After being stirred for an additional 10 min, the mixture was diluted with Et_2O (20 mL) and aq satd NH_4Cl (20 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (2 \times 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 colorless liquid: TLC R_f 0.4 (20% EtOAc/hexane); $[\alpha]_D^{20} = +49.24$ (c 1.0, CHCl_3); IR (neat) 3070, 2932, 2858, 1964, 1734, 1427, 1108, 704 cm^{-1} ; ^1H 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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{32}\text{O}_4\text{SiNa}$ 447.1962, found 447.1965.

(8S,10S,11R,14R,E)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxo-3,21-disilatricos-7,8,12-trien-11-ol (29) and (8S,10S,11S,14R,E)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxo-3,21-disilatricos-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 recooled 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 °C immediately and stirred at 0 °C for 20 min. The reaction was quenched with aq satd NH_4Cl (5 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (4 \times 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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{41}\text{H}_{66}\text{O}_5\text{Si}_2\text{Na}$ 717.4341, found 717.4347.

Compound 7: TLC R_f 0.25 (10% EtOAc/hexane); $[\alpha]_{\text{D}}^{20} = +84.07$ (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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{41}\text{H}_{66}\text{O}_5\text{Si}_2\text{Na}$ 717.4341, found 717.4356.

Mandelate Esters of the Mixture 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*-methylmandelic acid (4 mg, 0.023 mmol), DCC (6 mg, 0.028 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 5–7% EtOAc/hexane (v/v) as the eluent to afford esters VI (15.5 mg, 0.018 mmol) in 80% yield as a colorless oil. The data for the ester of alcohol 29 is denoted with an asterisk: ^1H 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).

(8S,10S,14R,E)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxo-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) were 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 satd $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL). After being stirred for an additional 10 min, the mixture was diluted with Et_2O (5 mL) and aq satd NH_4Cl (5 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (2 \times 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); $[\alpha]_{\text{D}}^{20} = +109.76$ (c 0.33, CHCl_3); IR (neat) 2930, 2858, 1964, 1680, 1466, 1105, 1033, 704; ^1H 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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{41}\text{H}_{64}\text{O}_5\text{Si}_2\text{Na}$ 715.4184, found 715.4181.

(8S,10S,11S,14R,E)-10-(Methoxymethoxy)-2,2,12,14,21,21,22,22-octamethyl-3,3-diphenyl-4,20-dioxo-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 the mixture was stirred 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 aqueous layer was extracted with dichloromethane (2 \times 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , filtered, and concentrated under 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-((2S,5S,6S)-6-((*R,E*)-9-((*tert*-butyldimethylsilyloxy)-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 were added $(\text{PPh}_3)_2\text{AuCl}$ (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); $[\alpha]_{\text{D}}^{20} = +35.08$ (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 $[\text{M} + \text{Na}]^+$; HRMS (ESI) calcd for $\text{C}_{41}\text{H}_{66}\text{O}_5\text{Si}_2\text{Na}$ 717.4341, found 717.4354.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01743.

HPLC chromatogram, ^1H and ^{13}C NMR spectroscopic characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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■ 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**, *1989*, 111.
- (4) Smith, A. B., III; Dong, S.; Brenneeman, 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**, *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 acatalytic 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.; Kumar, V.; Chowhan, L. *Synlett* **2010**, *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) Müller, S. J.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, *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 monoprotected 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.; Snapper, M. L. *J. Am. Chem. Soc.* **2006**, *128*, 7315.
- (15) (a) Rodriguez, A. R.; Spur, B. W. *Tetrahedron Lett.* **2012**, *53*, 1912. (b) Matsumura, 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) Attempted 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.; Walsgrove, T.; Wills, 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.