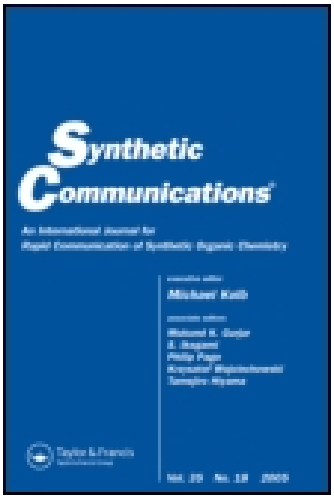

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Synthetic Studies toward C3-C9 Segment of Soraphen $A_{1\alpha}$

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Synthetic Studies toward C3-C9 Segment of Soraphen $A_{1\alpha}$

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Abstract: The ring-closure metathesis of the diene (2S,3R,4S)-1-(*tert*-butyldiphenylsilyloxy)-2,4-dimethylhex-5-en-3-yl acrylate produced the dihydropyrone with the correct stereochemistry for Soraphen $A_{1\alpha}$ synthesis. The C2,C3 stereocenters were introduced by the addition of the (Z)-crotyl-n-butylstannane to the β-alkoxyaldehyde(S)-3-(benzyloxy)-2-methylpropanal in presence of $TiCl_4$ as a chelating catalyst to give the desired anti,syn homoallyic alcohol (2S,3R,4S)-1-(*tert*-butyldiphenylsilyloxy)-2,4-dimethylhex-5-en-3-ol.

Keywords: Soraphen $A_{1\alpha}$, ring-closure metathesis, (Z)-crotyl-n-butylstannane

INTRODUCTION

Soraphen A **1** is a macrolide isolated from myxobacterium *Sorangium cellulosum,* which exhibits potent antifungal activity against various pathogenic plant fungi.[1,2] Soraphen A has highly efficient and specific inhibitory action on acetyl CoA carboxylase. The structure was well defined by X-ray crystallographic study. This 18-membered macrolide with an unsubstituted phenyl ring has received considerable attention as a synthetic target. Numerous synthetic studies have been reported.[3] The only total synthesis of Soraphen A was reported by Giese in 1999.[3b] We reported the synthesis of C11–C17 fragment **2** of Soraphen A.[4] See Fig. 1.

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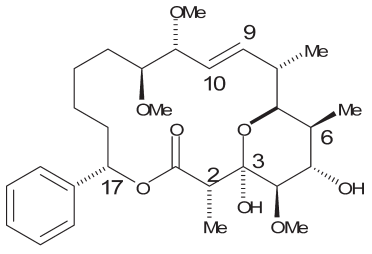


Soraphen $A_{1\alpha}$

Figure 1. Soraphen $A_{1\alpha}$.

RESULTS AND DISCUSSION

Our design for the synthesis of C1-C9 fragment of Soraphen $A_{1\alpha}$ was essentially based on the Lewis acid–catalyzed diene-aldehyde cycloaddition (LACDAC) reaction[5] of diene **3** with aldehyde[6] **4** (Fig. 2). It was anticipated that this would establish the C6 and C7 stereocenters of the dihydropyran ring.

However, because of problems in obtaining the correct stereochemistry at C6, C7 of Soraphen $A_{1\alpha}$, our focus was shifted to an alternative route for the preparation of the vital dihydropyrone with the correct stereochemistry for Soraphen $A_{1\alpha}$ (Fig. 3).

The key step in this route is a ring-closing metathesis[7] of the acylate ester **5**. The requisite 2(S),4(S)-dimethyl-hex-5-en-3(R)-ol **7a**,**b** was prepared by the chelation-controlled addition of (Z)-crotyl-n-butylstannane to the β-alkoxy aldehydes **4a** or **b** using titanium tetrachloride.

Reaction of crotyl bromide and tributyltin chloride in the presence of zinc powder in the mixed cosolvent tetrahydrofuran (THF) and saturated NH_4Cl gave but-2-enyl-tributyl-stannane **8**[8] as mixture of (Z/E isomers 8:1) in

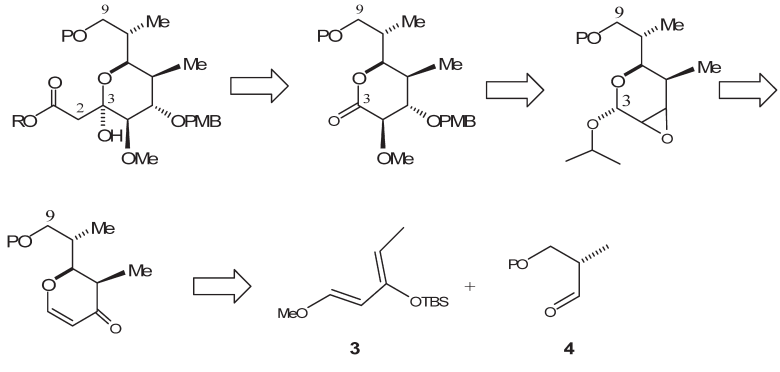


Figure 2. C3-C9 Soraphen $A_{1\alpha}$ segment synthesis.

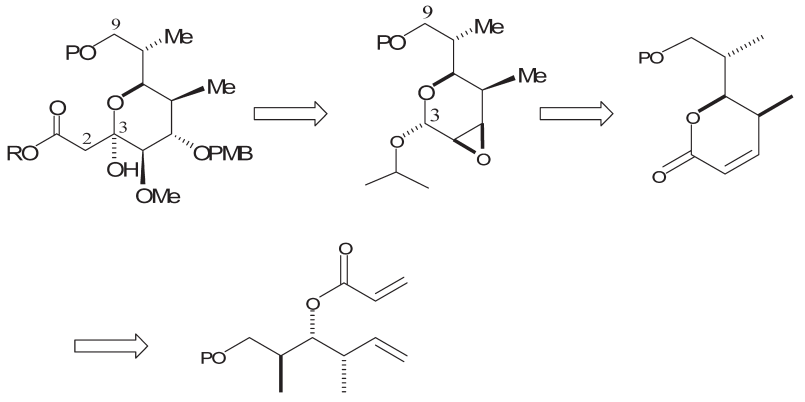
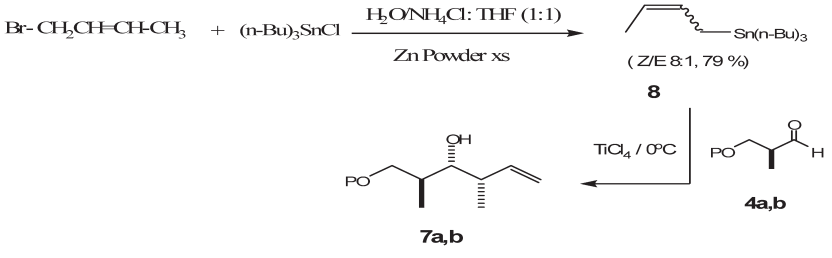


Figure 3. Retero synthesis of C3-C9 soraphen $A_{1\alpha}$ segment.

79% yield (Scheme 1). Addition of (*Z*)-crotyltri-*n*-butylstannane **8** to the β-alkoxyaldehydes **4a** or **b** in the presence of $TiCl_4$ gave the desired *anti*,*syn* homoallylic alcohol **7a** or **b**[8] in good yields.



Scheme 1. a, P = TBDPS; b, P = Bn.

The stereochemistry of this product is the result of two factors: attack of the crotyl stannane occurs on the *re*-face of the chelated aldehyde **4** because of the steric hindrance of the α-methyl group on approach to the *si*-face (Fig. 4).

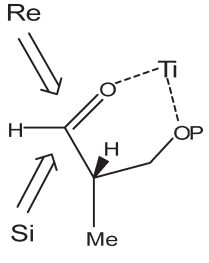


Figure 4. Selective facial approach to chelated aldehydes **4**.

The C3,C4 erythro stereochemistry is due to approach of the *si*-face of the crotyl stannane (i.e., **A**) in comparison to approach of the *re*-face of this reagent (i.e., **B**, Fig. 5).

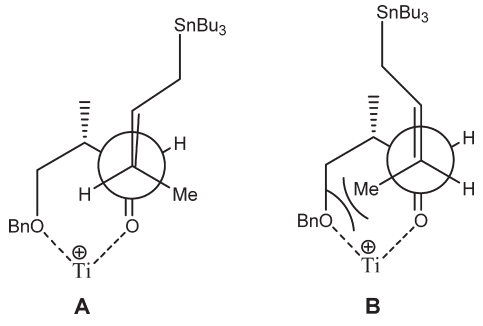
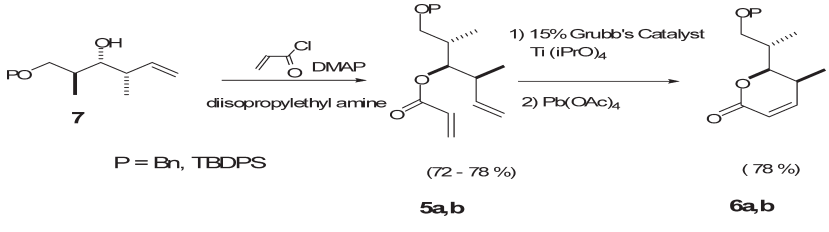


Figure 5. Chelation-controlled addition of β-alkoxy aldehydes to (Z)-crotyl-n-butylstannane.

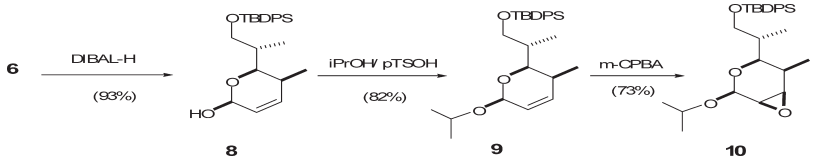
The produced alcohols **7a** or **b** were subjected to reaction with acryloyl chloride in the presence of diisopropylethylamine in anhydrous dichloromethane to afford acryloate ester **5a** or **b** in good yields (Scheme 2). The produced terminal dienes **5a** or **b** were subjected to ring-closing metathesis (RCM) using 15% Grubbs's catalyst[7] in anhydrous dichloromethane. The reaction mixture was then treated with lead tetracetate to remove the colored ruthenium by-products[9] to afford the unsaturated lactones **6a** or **b** in good yields.



Scheme 2.

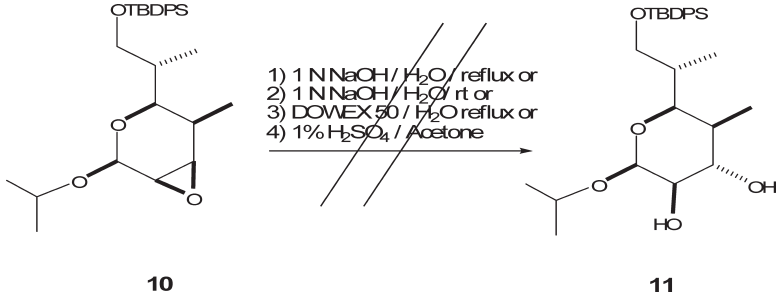
Dihydropyrone **6a** was subjected to reduction using diisobutylaluminum hydride (DIBAL) in anhydrous dichloromethane to afford lactols **8** (93%) (Scheme 3). The produced lactol **8** was treated with p-toluenesulfonic acid using isopropyl alcohol in the presence of a catalytic amount of p-toluenesulfonic acid to afford the (1S)-*tert*-butyl-[(5S,6R)-2-(6-isopropoxy-3-methyl-3,6-dihydro-2H-pyran-2-yl)-propoxy]-diphenylsilane **9** (82%) via mixed acetalization. The epoxidation of **9** was carried out with

m-chloroperoxybenzoic acid (CPBA) in anhydrous dichloromethane to give *tert*-butyl-[(2S,5R,6S)-2-(2-isopropoxy-5-methyl-3,7-dioxa-bicyclo[4.1.0]-hept-4-yl)-propoxy]-diphenylsilane **10** (73%).



Scheme 3.

All attempts for the diaxial cleavage of the epoxides **10** to get the target C3-C9 1,2-diaxial diol fragment **11** were unsuccessful (Scheme 4).



Scheme 4.

EXPERIMENTAL

General Data

Unless otherwise noted, reactions were carried out in oven-dried glassware. Spectrograde solvents were used without purification with the exception of tetrahydrofuran, which was distilled from sodium benzophenone ketyl, and CH_2Cl_2, which was distilled from P_2O_5. Anhydrous toluene was purchased from the Aldrich Chemical Co. Elemental analyses were obtained from Midwest Microlabs, Ltd., Indianapolis, and high-resolution mass spectral (HRMS) determinations were made at the Washington University Resource for Biomedical and Bio-organic Mass Spectrometry. Melting points were determined for samples in open capillaries and are uncorrected. All ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 300 MHz and 75 MHz respectively. All chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane signal. All IR spectral data were collected on a Nicolet Magna IR 560 spectrophotometer. Optical rotations were measured on a Perkin-Elmer

polarimeter 341 at 589 nm and 20 °C. Thin-layer chromatography (TLC) was performed on Merck Kiesegel 60 F254 and detected by one of the following methods: ultraviolet visualization, iodine, or vanillin solution [vanillin (8 g), sulfuric acid (2.5 mL, 96 wt%), ethanol (100 mL)]. Most iron complexes were stored refrigerated at less than 4 °C.

But-2-enyl-tributyl-stannane (8)

In an oven-dried two-necked round-bottom flask equipped with a magnetic stir bar and a condenser, Tributyltin chloride (4.17 g, 12.8 mmol) was added to saturated aqueous NH_4Cl (25 mL) and THF (25 mL). An excess amount of zinc powder (2 g, 2 eq) was added to the reaction mixture. The mixture was stirred at room temperature for 5 min before crotyl bromide (5.0 g, 3.7 mmol, 2 eq) was slowly added over a period of 30 min using a pressure, relief dropping funnel. The reaction mixture was stirred at room temperature for an additional 45 min after addition was completed. The reaction mixture was then extracted with petroleum ether (40–60 °C, 3 × 100 mL). The combined organic layer were dried ($MgSO_4$), and the solvent was evaporated under reduced pressure to give a crude oil, which was found to be mixture of Z- and E- isomers (8:1). The spectroscopic data of this product was consistent with the literature values.[8]

1-Benzyloxy-2(S),4(S)-dimethyl-hex-5-en-3(R)-ol (7a)

Titanium tetrachloride (1.07 g, 5.67 mmol) was added dropwise via a syringe to a solution of (R)-3-benzyloxy-2-methylpropanal **8** (1.08 g, 5.78 mmol) in dry CH_2Cl_2 (60 mL) at −85 °C. The color of the reaction mixture turned bright yellow. After stirring the solution at −85 °C for 10 min, tributylcrotyl-stannane (2.0 g, 5.8 mmol) was slowly added via a syringe down the side walls of the reaction flask. The reaction mixture became colorless. After completion of the addition, the reaction mixture was stirred at −85 °C for 5 min before being quenched by addition of a saturated aqueous solution of $NaHCO_3$ (10 mL). The resulting mixture was warmed to room temperature with stirring. The mixture was then diluted with ether (100 mL); the layers were separated, and the aqueous layer was extracted with ether (3 × 50 mL). The combined ethereal layer were washed with water and brine (10 mL each) and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (ethyl acetate/hexanes = 1:19) to afford pure alcohol **7a** as a colorless oil (2.78, 89%). ^{1}H NMR ($CDCl_3$) δ 7.37–7.27 (m, 5H), 5.85 (ddd, J = 17.4, 9.7, 7.3 Hz, 1H), 4.94–5.06 (m, 2H), 4.51 (s, 2H), 3.66 (dd, J = 9.7, 4.6 Hz, 1H), 3.40 (m, 1H), 3.16 (d, J = 4.5 Hz, 1H), 2.31 (m, 1H), 1.96 (m, 1H), 1.04 (d, J = 7.6 Hz, 3H), 0.96 (d, J = 7.6 Hz, 3H). The signal for OH was not observed. ^{13}C NMR ($CDCl_3$) δ 142.3, 138.2, 128.4, 128.1, 127.7, 114.4,

78.70, 74.40, 73.5, 41.15, 38.0, 14.6, 13.6. The spectroscopic data of this product were consistent with the literature values.[10]

1-(*tert*-Butyl-diphenyl-silanyloxy)-2(S),4(S)-dimethyl-hex-5-en-3(R)-ol (7b)

To a solution of (S)-3-(*tert*-butyl-diphenylsilyloxy)-2-methyl-propionaldehyde, (3.0 g, 10 mmol) in dry CH_2Cl_2, (50 mL) at $-85\,^{\circ}C$ under nitrogen, titanium tetrachloride (1.8 mL, 9.5 mmol) was added dropwise via a syringe (mixture turned bright yellow upon addition). The reaction mixture was stirred at $-85\,^{\circ}C$ for 10 min before tributyl crotyl stannane **8** (3.35 g, 9.67 mmol) was slowly added over a 10-min period via a syringe down the side walls of the round-bottom flask. The reaction mixture turned clear during addition. Upon completion of the addition, the reaction was quenched by addition of a saturated solution of $NaHCO_3$ (10 mL). The solution was warmed to room temperature with stirring. The reaction mixture was diluted with ether (100 mL), the layers were separated, and the aqueous layer was extracted with ether (3×20 mL). The combined ethereal extracts were washed with brine (10 mL) and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The resultant crude yellow oil was purified by column chromatography (ethyl acetate/hexanes = 1:10) to afford 1-(*tert*-butyldiphenylsilyloxy)-2(S),4(S)-dimethyl-hex-5-en-3(R)-ol as a colorless oil (3.4 g, 93%). $R_f = 0.28$ (ethyl acetate/hexanes 1:5); ^1H NMR ($CDCl_3$) δ 7.70–7.66 (m, 4H), 7.45–7.37 (m, 6H), 5.62 (ddd, $J = 17.0$, 9.9, 7.0 Hz, 1H), 5.05 (dd, $J = 17.0$, 1.2 Hz, 1H), 4.96 (dd, 10.0, 1.8 Hz, 1H), 3.78 (dd, $J = 9.9$, 3.5 Hz, 1H), 3.68–3.62 (m, 2H), 2.95 (d, $J = 3$ Hz, 1H), 2.32 (bs, 1H), 1.81 (m, 1H), 1.12 (d, $J = 7.0$ Hz, 3H), 1.07 (s, 9H), 0.98 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR δ 141.8, 135.6, 133.3, 133.1, 129.7, 127.6, 115.3, 76.1, 68.4, 41.7, 36.7, 26.8, 19.1, 16.7, 9.5; IR (CH_2Cl_2) ν 3512, 1647, 1590 cm^{-1}.

4(R)-Acroyloxy-6-benzyloxy-3(S),5(S)-dimethyl-1-hexane (5a)

A solution of 1-benzyloxy-2(S),4(S)-dimethyl-hex-5-en-3(R)-ol **7a** (0.43 g, 1.8 mmol) in dry CH_2Cl_2 (7 mL) and a catalytic amount of DMAP (10 mg) were added to an oven-dried round-bottom flask equipped with a magnetic stirbar. The reaction mixture was cooled to $-78\,^{\circ}C$ and then diisopropylethylamine (Hunig's base) (1.0 mL, 5.7 mmol) was added dropwise via a syringe immediately followed by acryloyl chloride (0.21 g, 2.3 mmol). The reaction mixture was stirred at $-78\,^{\circ}C$ for 2 h. The reaction was diluted with CH_2Cl_2 (25 mL) and quenched by addition of brine solution (10 mL). The reaction mixture was warmed to room temperature with stirring. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was

evaporated under reduced pressure. The resultant crude oil was purified by column chromatography (ethyl acetate/hexanes = 1:4) to afford (**5a**) as a colorless oil (0.50 g, 95%). $R_f = 0.18$ (ethyl acetate/hexanes = 1:4); $[\alpha]_D = +23$ (c = 0.01 $CHCl_3$). Elemental analysis: calculated: C, 74.97; H, 8.39; O, 16.64; found C, 74.95; H, 8.37; O, 16.65. ^{1}H NMR ($CDCl_3$) δ 7.32 (s, 5H), 6.37 (dd, $J = 17.6$, 1.7 Hz, 1H), 6.10 (dd, $J = 17.6$, 10.5 Hz, 1H), 5.82 (dd, $J = 9.9$, 1.2 Hz, 1H), 5.76–5.70 (m, 1H), 5.09–4.90 (m, 2H), 4.46 (s, 2H), 3.55 (dd, $J = 8.8$, 4.7 Hz, 1H), 3.48 (m, 1H), 3.26 (dd, $J = 9.4$, 7.6 Hz, 1H), 2.56 (m, 1H), 2.17 (m, 1H), 1.01 (d, $J = 7.3$ Hz, 3H), 0.99 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 166.2, 140.3, 138.5, 130.8, 128.6, 128.4, 127.7, 127.6, 115.3, 78.3, 73.2, 71.8, 39.5, 35.7, 12.8, 10.1.

4(R)-Acryloxy-6-[(*tert*-butyldiphenylsilyloxy]-3(S),5(S)-dimethyl-1-hexane (5b)

A solution of 1-(*tert*-butyl-diphenylsilyloxy)-2(S),4(S)-dimethyl-hex-5-en-3(R)-ol **7b** (1.3 g, 3.4 mmol) in anhydrous CH_2Cl_2 (25 mL) and a catalytic amount of DMAP (25 mg) was added to an oven-dried round-bottom flask equipped with a magnetic stirbar. The reaction mixture was cooled to −78 °C (dry ice/acetone). The solution was stirred at −78 °C for 5 min before diisopropylethyl amine (0.83 g, 6.4 mmol) was added dropwise, followed by slow addition of acryloyl chloride (0.61 g, 6.7 mmol). The reaction mixture was stirred for 2 h, diluted with CH_2Cl_2 (30 mL), and quenched with brine (5 mL). The reaction mixture was quickly warmed to room temperature. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with brine and dried (MgSO4), and the solvent evaporated under reduced pressure. The resultant crude oil was purified by column chromatography (ethyl acetate/hexanes = 1:9) to afford pure product as a colorless oil (1.17 g, 79%), $R_f = 0.73$ (ethyl acetate/hexanes = 1:4), Elemental analysis: calculated: C, 74.27; H, 8.31; O, 10.99; found: C, 74.28; H, 8.30; O, 11.00. ^{1}H NMR ($CDCl_3$) δ 7.71–7.64 (m, 4H), 7.43–7.32 (m, 6H), 6.38 (dd, $J = 15.8$, 1.2 Hz, 1H), 6.10 (dd, $J = 17.0$, 11.1 Hz, 1H), 5.82 (dd, $J = 11.7$, 1.2 Hz, 1H), 5.17 (dd, $J = 7.6$, 3.5 Hz, 1H), 5.10–4.98 (m, 2H), 3.53–3.37 (m, 3H), 2.58–2.47 (m, 1H), 2.10–1.98 (m, 1H), 1.02 (s, 9H), 0.98 (d, $J = 5.8$ Hz, 3H), 0.89 (d, $J = 7.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 165.6, 139.3, 135.4, 133.8, 129.9, 128.9, 128.7, 128.1, 127.5, 115.2, 76.6, 66.3, 37.6, 27.1, 19.2, 17.3, 11.7.

(5S,6R)-6-[(1S)-2-Benzyloxy-1-methyl-ethyl]-5-methyl-5,6-dihydro-pyran-2-one (6a)

To an oven-dried round-bottom flask equipped with a magnetic stirbar under nitrogen atmosphere, a solution of 4(R)-acroyloxy-6-benzyloxy-3(S),

5(S)-dimethyl-1-hexane **5a** (0.5 g, 1.7 mmol) in CH_2Cl_2 (50 mL) was added followed by addition of titanium(IV) isopropoxide (0.15 g, 0.52 mmol). The reaction mixture was heated to reflux for 1 h and then cooled to room temperature. A solution of Grubbs's catalyst (0.21 g, 0.25 mmol) in dry CH_2Cl_2 (5 mL) was added in three portions over a 1- h period. The reaction mixture was heated at reflux for 18 h before cooling to room temperature. Lead tetracetate (0.9 g) was added, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was filtered through a pad of silica gel and the filter bed was washed with CH_2Cl_2 (100 mL). The filtrate was concentrated under reduced pressure, and the crude product was purified by column chromatography (ethyl acetate/hexanes = 1:4) to afford the product as a colorless oil (0.35 g, 78%). $R_f = 0.19$ (ethyl acetate/hexanes = 1:4); $[\alpha]_D = +21$ (c = 0.1, CH_2Cl_2). Elemental analysis: calculated: C, 73.82; H, 7.74; O, 18.44; found: C, 73.82; H, 7.74; O, 18.45. ^{1}H NMR ($CDCl_3$) δ 7.35–7.30 (m, 5H), 6.66 (dd, $J = 9.9$, 2.9 Hz, 1H), 5.94 (dd, $J = 9.9$, 2.3 Hz, 1H), 4.51 (s, 2H), 4.31 (dd, $J = 10.5$, 2.9 Hz, 1H), 3.71 (dd, $J = 9.4$, 7.0 Hz, 1H), 3.39 (dd, $J = 9.4$, 5.8 Hz, 1H), 2.90–2.84 (m, 1H), 2.46–2.40 (m, 1H), 1.09 (d, $J = 7.0$ Hz, 3H), 1.03 (d, $J = 7.0$ Hz, 3H).

(5S,6R)-6-[(1S)-2-(*tert*-Butyl-diphenylsilanyloxy)-1-methyl-ethyl]-5-methyl-5,6-dihydro-pyran-2-one (6b)

To an oven-dried round-bottom flask equipped with a magnetic stirbar under nitrogen atmosphere, a solution of 4(R)-acryloxy-6-[(*tert*-butyl diphenylsilyloxy]-3(S),5(S0-dimethyl-1-hexane **5b** (1.5 g, 4.1 mmol) in CH_2Cl_2 (150 mL) was added followed by addition of titanium(IV) isopropoxide (0.34 g, 1.23 mmol). The reaction mixture was heated to reflux for 1 h and cooled to room temperature. A solution of Grubbs's catalyst (0.5 g, 0.6 mmol) in dry CH_2Cl_2 (5 mL) was added in three portions over a 1- h period. The reaction mixture was heated at reflux overnight before cooling to room temperature. Lead tetracetate (2.7 g, 1.5 eq) was added, and the reaction mixture was stirred at room temperature overnight. The reaction mixture was filtered through a pad of silica gel, and the filter bed was washed with CH_2Cl_2 (250 mL). The filtrate was concentrated under reduced pressure, and the crude product was purified by column chromatography (ethyl acetate/hexanes = 1:4) to afford the product as a colorless oil (1.09 g, 78%). $R_f = 0.21$ (ethyl acetate/hexanes = 1:4); $[\alpha]_D = +18$ (c = 0.7 MeOH). Elemental analysis: calculated: C, 73.49; H, 7.89; O, 11.75; found: C, 73.48; H, 7.88; O, 11.76. ^{1}H NMR ($CDCl_3$) δ 7.67–7.61 (m, 4H), 7.48–7.36 (m, 5H), 6.90 (dd, $J = 9.3$, 6.4 Hz, 1H), 5.9 (d, $J = 9.4$ Hz, 1H), 4.28 (dd, $J = 9.9$, 2.9 Hz, 1H), 3.59 (dd, $J = 4.7$, 1.8 Hz, 2H), 2.34 (m, 1H), 2.19–1.98 (m, 1H), 1.20 (d, $J = 6.4$ Hz, 3H), 1.05 (s, 9H), 0.92 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 165.2, 152.2, 135.8, 133.7, 130.0, 127.9, 120.0, 82.5, 65.4, 36.8, 31.3, 27.2, 19.7, 14.3, 11.9.

(5S,6R)-6-[(1S)-2-(*tert*-Butyl-diphenylsilanyloxy)-1-methyl-ethyl]-5-methyl-5,6-dihydro-2H-pyran-2-ol (8)

A solution of diisobutyl aluminum hydride (DIBAL-H) (1.53 mL, 1 M in hexanes) was added slowly via a syringe to a solution of (5S,6R)-6-[(1S)-2-(*tert*-butyl-diphenylsilyloxy)-1-methyl-ethyl]-5-methyl-5,6-dihydro-pyran-2-one **6b** (0.52 g, 1.3 mmol) in dry CH_2Cl_2 (15 mL) at −78 °C. After completion of addition, the reaction mixture was stirred at −78 °C under nitrogen for 1 h before quenching by addition of 10% aqueous sodium potassium tartrate (5 mL). The resulting solution was warmed to room temperature with stirring, and stirring was continued for an extra hour. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were washed with brine (10 mL) and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The resultant crude product was purified by column chromatography (ethyl acetate/hexanes = 1:4) to afford the alcohol as a colorless oil (0.45 g, 89%), $[\alpha]_D = +11$ (c = 0.07, CH_2Cl_2); $R_f = 0.16$ (ethyl acetate/hexanes 1:4). Elemental analysis: found: C, 73.13; H, 8.35; O, 11.69; calculated: C, 73.14; H, 8.36; O, 11.71. ^{1}H NMR ($CDCl_3$) δ 7.70–7.64 (m, 4H), 7.50–7.42 (m, 6H), 5.74–5.66 (m, 1H), 4.90 (m, 1H), 3.82–3.78 (m, 1H), 3.60 (d, $J = 7.8$ Hz, 2H), 3.25–3.20 (m, 1H), 2.40–2.32 (m, 1H), 2.0–1.78 (br m, 2H), 1.06 (s, 9H), 0.97 (d, $J = 7.0$ Hz, 3H), 0.79 (d, $J = 6.4$ Hz, 3H).

(1S)-*tert*-Butyl-[(5S,6R)-2-(6-isopropoxy-3-methyl-3,6-dihydro-2H-pyran-2-yl)-propoxy]-diphenyl-silane (9)

Camphorsulphonic acid (10 mg) was added to a solution of (5S,6R)-6-[(1S)-2-(*tert*-butyl-diphenylsilanyloxy)-1-methyl-ethyl]-5-methyl-5,6-dihydro-2H-pyran-2-ol **8** (0.42 g, 1.0 mmol) in isopropyl alcohol (10 mL). The reaction mixture was stirred at room temperature. The reaction was monitored by thin-layer chromatography (TLC). After 3 h, the reaction was quenched by addition of a few drops of triethyl amine. The solvent was evaporated under reduced pressure, and the resultant crude product was purified by column chromatography (ethyl acetate/hexanes = 1:10) to afford (1S)-*tert*-butyl-[(5S,6R)-2-(6-isopropoxy-3-methyl-3,6-dihydro-2H-pyran-2-yl)-propoxy]-diphenylsilane **9** as a colorless oil (0.36 g, 79%). $R_f = 0.65$ (ethyl acetate/hexanes = 1:4); $[\alpha]_D = +13$ (c = 0.12, CH_2Cl_2). Elemental analysis: calculated: C, 74.29; H, 8.91; O, 10.60; found: C, 74.31; H, 8.93; O, 10.62. ^{1}H NMR ($CDCl_3$) δ 7.70–7.67 (m, 4H), 7.46–7.38 (m, 6H), 5.98 (dd, $J = 10.5$, 9.3 Hz, 1H), 5.58 (dd, $J = 10.3$, 3.5 Hz, 1H), 5.03 (d, $J = 2.9$ Hz, 1H), 3.81 (dd, $J = 9.9$, 2.3 Hz, 1H), 3.50 (m, 2H), 3.18 (m, 1H), 2.32 (m, 1H), 2.10 (m, 1H), 1.16 (d, $J = 5.9$ Hz, 6H), 1.02 (s, 9H), 0.91 (d, $J = 7.0$ Hz, 3H), 0.79 (d, $J = 7.0$ Hz, 3H).

tert-Butyl-[(2S,5R,6S)-2-(2-isopropoxy-5-methyl-3,7-dioxa-bicyclo[4.1.0]hept-4-yl)-propoxy]-diphenyl-silane (10)

m-Chloroperbenzoic acid (80–85%, 0.23 g, 1.23 mmol) was added to a stirred solution of (1S)-*tert*-butyl-[(5S,6R)-2-(6-isopropoxy-3-methyl-3,6-dihydro-2H-pyran-2-yl)-propoxy]-diphenyl-silane **9** (0.30 g, 0.66 mmol) in CH_2Cl_2 (15 mL). The reaction was stirred at room temperature overnight and then quenched by addition of saturated aqueous solution of sodium thiosulphate (2 mL) followed by a saturated solution of $NaHCO_3$ (2 mL). The resultant mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The resultant crude product was purified by column chromatography (ethyl acetate/hexanes = 1:4) to afford *tert*-butyl-[(2S,5R, 6S)-2-(2-isopropoxy-5-methyl-3,7-dioxa-bicyclo[4.1.0]hept-4-yl)-propoxy]-diphenyl-silane **10** as colorless oil (0.22 g, 73%). $R_f = 0.83$ (ethyl acetate/hexanes = 1:4); $[\alpha]_D = +21$ (c = 0.12, CH_2Cl_2). Elemental analysis: calculated: C, 71.75; H, 8.60; O, 13.65; found: C, 71.77; H, 6.62; O, 13.67. ^{1}H NMR ($CDCl_3$) δ 7.70–7.67 (m, 4H), 4.92 (d, $J = 3.0$ Hz, 1H), 3.89 (dd, $J = 9.4$, 3.5 Hz, 1H), 3.75 (dd, $J = 10.5$, 2.9 Hz, 1H), 3.70 (dd, $J = 9.9$, 3.5 Hz, 1H), 3.60–3.48 (m, 3H), 1.85–1.92 (m, 1H), 1.15 (d, $J = 5.8$ Hz, 6H), 1.04 (s, 9H), 0.87 (d, $J = 7.0$ Hz, 3H), 0.82 (d, $J = 7.0$ Hz, 3H).

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