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Studies Directed Towards the Total Synthesis of (–)-Dictyostatin

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The stereoselective synthesis of the three major fragments (C1–C9, C10–C17, and C19–C26) of an antimitotic marine macrolide, (–)-dictyostatin, has been achieved with a desymmetrization strategy and Oppolzer *syn* and *anti* aldol protocols as the key reactions. Takai olefination and Sonogashira coupling reactions were successfully utilized to establish the 2*Z*,4*E*-dienoate portion of the C1–C9 fragment and Stille coupling for the *Z*-diene core of C19–C26.

Introduction

Scarce, biologically potent marine macrolides with intricate structural features are always attractive synthetic targets to organic chemists. Natural products of marine origin are generally obtained in minute quantities that are insufficient for detailed biological activity studies.[1] For instance, dictyostatin, a polyketide antimitotic marine macrolide, was first isolated in 1994 by Pettit et al.[2] from the marine sponge *Spongia* sp. off the coast of Maldives and later by Wright and co-workers[3] from *Corralistidae* sponges. Although it was isolated in 1994, due to its low availability, its complete stereochemical structure was not known for a further decade. In 2004, Paterson and Wright and co-workers proposed structure **1** for dictyostatin (Figure 1) on the basis of extensive high-field NMR experiments, Murata *J*-based configuration analysis, and molecular modeling,[4] and it was finally confirmed by total synthesis.[5] The 22-membered macrolide is an efficient inhibitor of human cancer cell growth at low concentrations with the same mode of action as taxol, which promotes tubulin polymerization and prevents mitosis from proceeding beyond the G2/M phase of the cell cycle.[3]

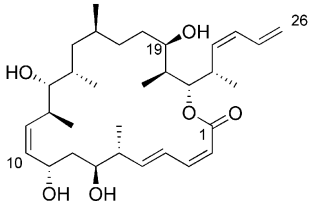

Figure 1. Structure of (–)-dictyostatin (**1**).

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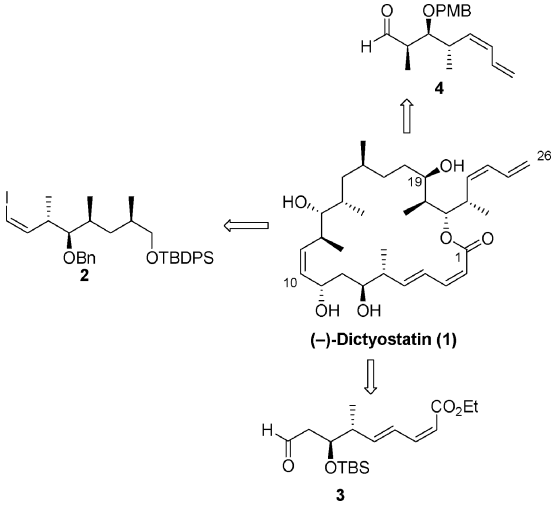
Interesting structural features combined with the important biological activity of dictyostatin has attracted several research groups to attempt its total synthesis,[6] as well as the synthesis of its analogues[7] and crucial intermediates.[8] Herein, we report our efforts, en route to (–)-dictyostatin (**1**), at a highly stereoselective synthesis of the key intermediates (C1–C9, C10–C17, and C19–C26) of **1** (Scheme 1), comprising nine of its eleven stereocentres and including a *cis*-1,2-disubstituted olefin, a 2*Z*,4*E*-dienoate, and a terminal *Z*-diene core.

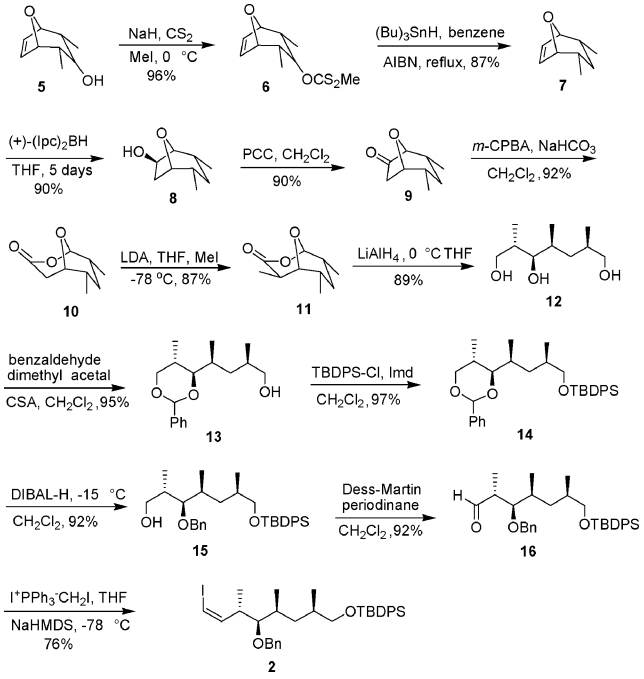


Scheme 1. Retrosynthetic analysis of **1**.

Results and Discussion

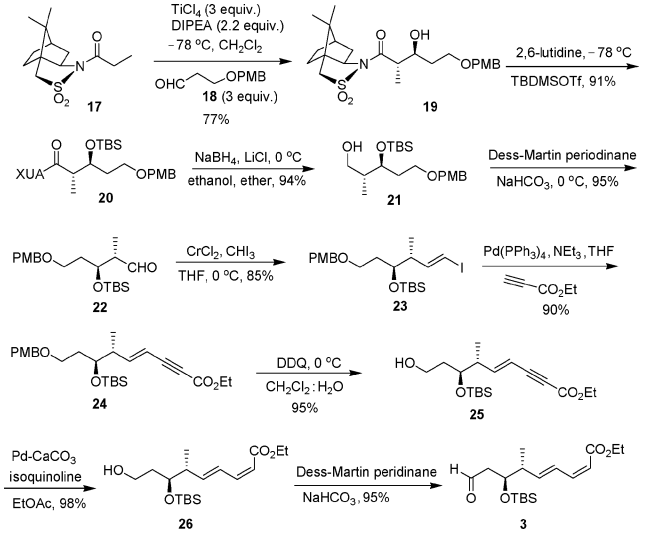
As depicted in Scheme 2, the construction of the C10–C17 segment was initiated with the preparation of xanthate **6** from bicyclic alcohol **5**[9] using NaH, CS_2, and MeI at 0 °C (96%) followed by exposure of xanthate **6** to Barton–McCombie[10] conditions (Bu_3SnH, cat. AIBN in benzene) to afford the deoxygenated symmetric volatile bicyclic olefin **7** (87%). The bicyclic olefin **7** was subjected to the key de-

symmetrization reaction using the chiral hydroboration reaction of Brown et al.[11] [(+)-Ipc_2BH, THF, 0 °C, NaOH, H_2O_2] to afford the required alcohol **8** with good enantio- and regioselectivity (90% yield). Alcohol **8** was oxidized with PCC[12] to furnish the corresponding ketone **9** (90%). The ketone **9** was further oxidized to yield lactone **10** (92%) under Bayer–Villiger conditions[13] (*m*-CPBA, $NaHCO_3$, CH_2Cl_2). The so-formed bicyclic lactone was then subjected to enolization using LDA in THF at –78 °C followed by treatment with MeI to furnish the methylated lactone **11** as a single diastereomer (87%). The alkylation was totally stereocontrolled by the substrate and occurs only from the *exo* face. Reductive ring-opening of the lactone **11** using excess $LiAlH_4$ resulted in the triol **12** (89%), the key intermediate in our desymmetrization strategy with four chiral centers. The 1,3-diol functionality in triol **12** was protected as the benzylidene acetal using benzaldehyde dimethyl acetal and catalytic CSA in CH_2Cl_2 at 0 °C to afford **13** (95%) and the free hydroxy group was silylated with TBDPS-Cl to furnish the fully protected triol **14**. Subsequent regioselective reductive ring-opening of the benzylidene acetal using DIBAL-H[14] at –15 °C in CH_2Cl_2 led to alcohol **15** (92%). Oxidation of the alcohol with Dess–Martin periodinane[15] in the presence of $NaHCO_3$ at 0 °C produced aldehyde **16** without any epimerization. The key intermediate *Z*-vinyl iodide **2** was obtained from aldehyde **16** using Stork's protocol.[16]



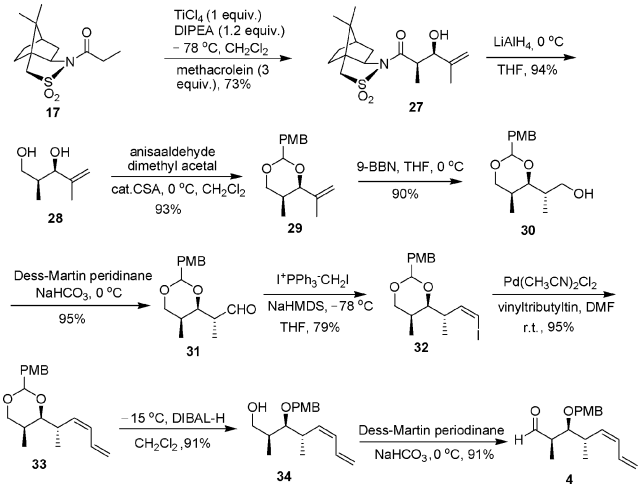
Scheme 2. Synthesis of the C10–C17 segment **2**.

The construction of the C1–C9 fragment (Scheme 3) was initiated with the installation of *anti* centers in **3** by employing the Oppolzer *anti* aldol protocol.[17] Thus, treatment of *N*-propionylsultam **17** with $TiCl_4$ (1 equiv.) and DIPEA (1.2 equiv.) at –78 °C followed by the addition of aldehyde **18** in CH_2Cl_2 produced the *anti* product along with the *syn* isomer in minor quantities. These two isomers were readily separated by column chromatography on silica gel and yielded *anti* aldol compound **19** (9:1 *anti*/*syn*; 77%). The hydroxy group of **19** was silylated using TBDMSOTf[18] and 2,6-lutidine to give **20** (91%). The reductive cleavage of the chiral auxiliary was achieved with $LiBH_4$ (generated in situ) in diethyl ether to yield alcohol **21** (94%). This alcohol was oxidized with Dess–Martin periodinane to give aldehyde **22** (95%). Takai olefination[19] of aldehyde **22** provided *E*-vinyl iodide **23** (*E*/*Z* = 20:1, 85% yield). The *E*-vinyl iodide **23** was then subjected to Pd-mediated cross-coupling under Sonogashira reaction conditions[20] using [Pd-$(PPh_3)_4$], catalytic CuI, and NEt_3 followed by ethyl propiolate to furnish **24** in 90% yield. The oxidative removal of the PMB ether with DDQ in CH_2Cl_2/H_2O (19:1) gave alcohol **25** (95%). The dienoate precursor **25** was treated with the Lindlar catalyst (Pd–$CaCO_3$ poisoned with Pb) in the presence of isoquinoline in benzene to give dienoate **26** (98%). Oxidation of the hydroxy group in the dienoate with Dess–Martin periodinane led to the construction of the C1–C9 fragment (**3**) in 95% yield. The ^1H and ^{13}C NMR data of aldehyde **3** were identical to the reported data.[6b]



Scheme 3. Synthesis of the C1–C9 segment **3**.

As outlined in Scheme 4, the synthesis of the C19–C26 fragment was initiated with the Oppolzer *syn* aldol reaction[17] between *N*-propionylsultam **17** and methacrolein using $TiCl_4$ (3 equiv.) and DIPEA (2.2 equiv.) at –78 °C to afford a diastereomeric mixture of *syn* and *anti* products. These two isomers were easily separated by column chromatography on silica gel to obtain the *syn* isomer **27** with good selectivity (95:5 *syn*/*anti*; 73%). Reductive removal of the chiral auxiliary using $LiAlH_4$ furnished diol **28** (94%). This diol was protected as its PMB acetal with anisaldehyde dimethyl acetal and catalytic CSA to give **29** in 93% yield.



Scheme 4. Synthesis of the C19–C26 segment **4**.

At this juncture, the methyl center was installed by hydroboration of the unsymmetrical double bond in **29** with 9-BBN[21] in THF at 0 °C to afford the 1,2-*anti* isomer **30** with 86% *de*. The alcohol **30** was oxidized using Dess–Martin periodinane to give aldehyde **31** and subsequently elaborated to the (*Z*)-vinyl iodide **32** using Stork's protocol. The diene precursor **32** was subjected to Stille cross-coupling[22] with vinyltributyltin in the presence of $[Pd(CH_3CN)_2Cl_2]$ in DMF at room temperature for 15 min to obtain the *Z*-diene **33** in 95% yield. Regioselective reductive ring-opening of the PMB acetal with DIBAL-H in CH_2Cl_2 at –15 °C furnished the alcohol **34** (91%). The primary alcohol of **34** was oxidized with Dess–Martin periodinane reagent to afford aldehyde **4**[23] in 91% yield, thus, completing the synthesis of the C19–C26 segment of (–)-dictyostatin.

Conclusions

We have synthesized, en route to the total synthesis, three major segments of (–)-dictyostatin in a highly stereoselective manner. By using a desymmetrization approach and Oppolzer *syn* and *anti* aldol protocols, the requisite stereocenters were achieved. Takai olefination and Sonogashira and Stille cross-coupling reactions were used in the construction of the two diene systems. Attempts to couple these fragments en route to the total synthesis of (–)-dictyostatin are in progress.

Experimental Section

General: Unless otherwise mentioned, all reactions were carried out under an inert atmosphere of argon or nitrogen using standard syringe, septa, and cannula techniques. Commercial reagents were used without further purification. All solvents were purified by standard techniques. Infrared (IR) spectra were recorded with a Perkin–Elmer 683 spectrometer with NaCl optics. Spectra were calibrated against the polystyrene absorption at 1610 cm^{-1}. Samples were scanned neat, in KBr wafers or in chloroform as a thin film. Optical rotations were obtained with a Jasco DIP-360 digital polarimeter. NMR spectra were recorded in $CDCl_3$ with a Varian Gemini 200, Bruker 300, or Varian Unity 400 NMR spectrometer. Column chromatographic separations were carried out on silica gel (60–120 mesh). Mass spectra were obtained on a Finnigan MAT1020B or micromass VG 70-70H spectrometer operating at 70 eV using a direct inlet system.

***O*-(2,4-Dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-yl) *S*-Methyl Carbonodithioate (6):** Alcohol **5**[9] (8 g, 51.9 mmol) in THF (20 mL) was added to a suspension of NaH (4.98 g, 103 mmol) in THF (20 mL) under nitrogen at 0 °C. The reaction mixture was heated at 60 °C for 30 min. After cooling the reaction mixture again to 0 °C, CS_2 (4.7 mL, 77.9 mmol) was added and the reaction mixture was stirred for 30 min. MeI (4.8 mL, 77.9 mmol) was added and the reaction mixture was stirred at room temperature for 6 h. After complete consumption of the starting material (confirmed by TLC), the reaction mixture was cooled to 0 °C and quenched with aqueous ammonium chloride solution, extracted with EtOAc (3 × 50 mL), dried with anhydrous Na_2SO_4, evaporated under reduced pressure, and purified by silica gel column chromatography using 5% EtOAc/hexane to furnish the xanthate **6** (12.09 g, 96%) as a colorless liquid. IR (KBr): $\tilde{\nu}$ = 2964, 2933, 2880, 1628, 1220, 1159, 1049, 935 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.4 (s, 2 H, 6-H, 7-H), 6.29 (t, J = 4.9 Hz, 1 H, 3-H), 4.48 (d, J = 3.0 Hz, 2 H, 1-H, 5-H), 2.54 (s, 3 H, SMe), 2.50–2.42 (m, 2 H, 2-H, 4-H), 0.84 (d, J = 7.3 Hz, 6 H, 2 Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 217.0, 133.7 (2 C), 82.5, 81.5 (2 C), 37.3 (2 C), 18.7, 12.1 (2 C) ppm.

2,4-Dimethyl-8-oxabicyclo[3.2.1]oct-6-ene (7): $(Bu)_3SnH$ (14.9 mL, 56.5 mmol) followed by a catalytic amount of AIBN were added to a stirred solution of xanthate **6** (11.5 g, 47.1 mmol) in benzene (20 mL) and the reaction mixture was heated at reflux in the presence of the light of an incandescent lamp for 6 h. The residue was purified on a silica gel column using 5% EtOAc in hexane as eluent. The column fractions were distilled to remove the solvent and finally the compound was distilled at atmospheric pressure by maintaining the receiver at –78 °C to obtain the olefin **7** as a light-yellow oil (5.85 g, 87%). IR (KBr): $\tilde{\nu}$ = 2955, 2924, 2853, 1660, 1458, 1045, 940 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.16 (s, 2 H, 6-H, 7-H), 4.46 (d, J = 3.3 Hz, 2 H, 1-H, 5-H), 1.91–1.79 (m, 2 H, 2-H, 4-H), 1.60–1.52 (m, 1 H, 3-H), 0.91 (m, 1 H, 3′-H), 0.71 (d, J = 7.1 Hz, 6 H, 2 Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 130.2 (2 C), 82.9 (2 C), 34.2, 30.3 (2 C), 17.2 (2 C) ppm.

(6*R*)-2,4-Dimethyl-8-oxabicyclo[3.2.1]octan-6-ol (8): Olefin **7** (5.5 g, 39.8 mmol) predissolved in THF (10 mL) was added to the white crystals of (+)-Ipc_2BH [generated in situ from (–)-α-pinene] in THF (3 mL) at –20 °C. The reaction was stirred at the same temperature for 1 h and kept in the refrigerator for 5 d at –20 °C. After this, the trialkylborane was treated with 3 N sodium hydroxide (50 mL) and 30% hydrogen peroxide (12.5 mL) and stirred at 25 °C for 5 h. The reaction mixture was extracted with diethyl ether (3 × 50 mL), dried (Na_2SO_4), and evaporated. The residue was purified by silica gel chromatography (hexane/ethyl acetate, 9:1, used as eluent) to remove the olefin and (–)-α-pinene alcohol and then eluted with hexane/ethyl acetate (1:1) mixture to give the alcohol as a colorless liquid (5.58 g, 90%). $[a]_D^{25}$ = +4.3 (c = 2.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3408, 2950, 2877, 1458, 1046 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.21 (m, 2 H, 1-H, 5-H), 3.85 (d, J = 3.39 Hz, 1 H, 6-H), 2.67 (br., 1 H, OH), 2.16 (m, 1 H, 7-H), 1.89–1.77 (m, 2 H, 2-H, 4-H), 1.71–1.63 (m, 1 H, 7′-H), 1.59–1.51 (m, 1 H, 3-H), 0.88 (d, J = 6.9 Hz, 3 H, 4-Me), 0.72 (d, J = 6.9 Hz, 3 H, 2-Me), 0.63–0.51 (m, 1 H, 3′-H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 87.3, 79.8, 71.4, 36.6, 34, 33.5, 32.7, 17.2, 17.0 ppm. MS (EI): m/z = 157.1 [M +

H]$^+$. HRMS: calcd. for $C_9H_{17}O_2$ [M + H]$^+$ 157.1228; found 157.1224.

2,4-Dimethyl-8-oxabicyclo[3.2.1]octan-6-one (9): Pyridinium chlorochromate (PCC; 10.38 g, 48.0 mmol) was added to a solution of alcohol **8** (5 g, 32.0 mmol) in dichloromethane (50 mL) at room temperature. After stirring the reaction mixture for 3 h, 2-propanol (10 mL) was added and the solvent was removed under reduced pressure, the residue was filtered and washed with diethyl ether. The organic layer was washed with 1 N HCl (20 mL), water, and brine, dried (Na_2SO_4) and removal of solvent afforded a gummy material, which was purified by silica gel column chromatography using 20% EtOAc/hexane as eluent to afford the ketone **9** (4.43 g, 90% yield) as a light-yellow liquid. $[\alpha]_D^{25}$ = –17.1 (*c* = 1.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2955, 2860, 1756, 1155, 1040 cm 4.41 (dd, *J* = 7.5, 3.0 Hz, 1 H, 5-H), 3.65 (d, *J* = 3.7 Hz, 1 H, 1-H), 2.45 (dd, *J* = 18.1, 8.3 Hz, 1 H, 7-H), 2.20 (m, 1 H, 4-H), 2.16 (d, *J* = 18.1 Hz, 1 H, 7′-H), 1.97 (m, 1 H, 2-H), 1.72 (m, 1 H, 3-H), 1.42 (m, 1 H, 3′-H), 0.90 (d, *J* = 6.7 Hz, 3 H, 4-Me), 0.83 (d, *J* = 6.7 Hz, 3 H, 2-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 215.1, 80.1, 78.2, 37.5, 34.2, 33.4, 33.1, 17, 15.4 ppm. MS (EI): *m*/*z* = 155.1 [M + H]$^+$. HRMS: calcd. for $C_9H_{15}O_2$ [M + H]$^+$ 155.1047; found 155.1063.

6,8-Dimethyl-2,9-dioxabicyclo[3.3.1]nonan-3-one (10): Ketone **9** (3.5 g, 22.7 mmol) in CH_2Cl_2 (15 mL) was added to a suspension of $NaHCO_3$ (3.8 g, 45.4 mmol) in CH_2Cl_2 (20 mL) followed by *m*-CPBA (7.8 g, 45.4 mmol) and the mixture was stirred at ambient temperature for 10 h. The reaction mixture was diluted with dichloromethane (25 mL) and the CH_2Cl_2 layer was washed with a solution of sodium metabisulfite followed by a 5% $NaHCO_3$ solution and water, extracted with CH_2Cl_2 (2 × 30 mL), dried with Na_2SO_4, concentrated under reduced pressure, and the residue purified by silica gel column chromatography using hexane/ethyl acetate (8:2) as eluent to afford the lactone **10** (3.55 g, 92%) as an oil. $[\alpha]_D^{25}$ = +49.8 (*c* = 1.1, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2962, 1743, 1226, 1190, 1121, 968 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.48 (d, *J* = 2.2 Hz, 1 H, 1-H), 4.11 (dd, *J* = 7.7, 4.3 Hz, 1 H, 5-H), 2.83 (dd, *J* = 18.3, 7.8 Hz, 1 H, 4-H), 2.54 (d, *J* = 18.3 Hz, 1 H, 4′-H), 2.15 (m, 1 H, 8-H), 1.98 (m, 1 H, 6-H), 1.63 (m, 1 H, 7-H), 1.14 (m, 1 H, 7′-H), 0.98 (d, *J* = 6.9 Hz, 3 H, 8-Me), 0.90 (d, *J* = 6.9 Hz, 3 H, 6-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 167.0, 100.5, 70.7, 35.3, 32.6, 29.4, 28.5, 16.6, 5.7 ppm. MS (EI): *m*/*z* = 171.1 [M + H]$^+$. HRMS: calcd. for $C_9H_{15}O_3$ [M + H]$^+$ 171.1021; found 171.1016.

(4*R*)-4,6,8-Trimethyl-2,9-dioxabicyclo[3.3.1]nonan-3-one (11): LDA [905 mg, 8.3 mmol, generated in situ from *n*BuLi (5.2 mL) and diisopropylamine (1.75 mL)] was added to a solution of lactone **10** (0.95 g, 5.5 mmol) in THF (15 mL) at –78 °C. The lithium enolate thus generated was alkylated with methyl iodide (0.53 mL, 8.37 mmol) whilst stirring the reaction mixture for 2 h at the same temperature. Then the reaction mixture was quenched with a saturated ammonium chloride solution. The mixture was extracted with diethyl ether (3 × 15 mL) and removal of the solvent gave the methylated lactone. Purification by silica gel column chromatography using 15% EtOAc/hexane as eluent afforded compound **11** (0.9 g, 87%) as a colorless oil. $[\alpha]_D^{25}$ = +35.5 (*c* = 2.6, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2963, 2928, 1736, 1459, 1227, 1180, 1138, 965 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.43 (d, *J* = 2.3 Hz, 1 H, 1-H), 3.69 (d, *J* = 4.68 Hz, 1 H, 5-H), 2.54 (q, *J* = 7.03 Hz, 1 H, 4-H), 2.11 (m, 1 H, 8-H), 1.97 (m, 1 H, 6-H), 1.64 (m, 1 H, 7-H), 1.47 (d, *J* = 7.8 Hz, 3 H, 4′-Me), 1.10 (m, 1 H, 7′-H), 1.0 (d, *J* = 7.03 Hz, 3 H, 8-Me), 0.90 (d, *J* = 7.03 Hz, 3 H, 6-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 171.6, 101.1, 77.8, 35.7, 33.9, 33, 30.1, 19.6, 16.7, 16.1 ppm. MS (EI): *m*/*z* = 185.1 [M + H]$^+$. HRMS: calcd. for $C_{10}H_{17}O_3$ [M + H]$^+$ 185.1177; found 185.1180.

(2*S*,3*R*,4*S*,6*R*)-2,4,6-Trimethylheptane-1,3,7-triol (12): A solution of lactone **11** (0.85 g, 4.61 mmol) in THF (15 mL) was added to an ice-cooled suspension of $LiAlH_4$ (0.526 g, 13.8 mmol) in THF (10 mL) under nitrogen and the reaction mixture was stirred for 5 h at room temperature. It was then cooled to 0 °C and quenched with a saturated solution of Na_2SO_4 by portionwise addition and stirred at room temperature for 4 h. The white precipitate was filtered off through a pad of Celite, washed with ethyl acetate, dried with Na_2SO_4, concentrated, and purified by chromatography on silica gel (1:1 EtOAc/hexane) to afford the triol **12** (0.776 g, 89%) as a viscous colorless liquid. $[\alpha]_D^{25}$ = +29.6 (*c* = 2.05, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3339, 2961, 2923, 1722, 1461, 1278, 1027, 981 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.74–3.60 (m, 2 H, 1-H), 3.50 (m, 2 H, 7-H), 3.40 (dd, *J* = 10.1, 6.9 Hz, 1 H, 3-H), 1.88 (m, 1 H, 2-H), 1.75 (m, 2 H, 4-H, 6-H), 1.67–1.58 (m, 1 H, 5-H), 1.03–0.94 (m, 1 H, 5′-H), 0.89 (m, 6 H, 2′-Me, 4′-Me), 0.80 (d, *J* = 6.7 Hz, 3 H, 6′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 76.7, 68.3, 68.2, 37.1, 37, 32.3, 31.9, 16.8, 13.5, 13.4 ppm. MS (EI): *m*/*z* = 191.1 [M + H]$^+$. HRMS: calcd. for $C_{10}H_{23}O_3$ [M + H]$^+$ 191.1647; found 191.1648.

(2*R*,4*S*)-2-Methyl-4-[(5*S*)-5-methyl-2-phenyl-1,3-dioxan-4-yl]pentan-1-ol (13): Benzaldehyde dimethyl acetal (0.148 mL, 0.98 mmol) and a catalytic amount of azeotropically dried CSA were added to a stirred solution of triol **12** (125 mg, 0.65 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The reactionmixture was stirred at room temperature for 5 h. After the starting material was completely consumed (monitored by TLC), the reaction was quenched with aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 10 mL). The organic layer was dried with anhydrous Na_2SO_4, evaporated, and purified on silica gel (5% EtOAc/hexane) to furnish the protected diol **13** (172 mg, 95%) as a colorless liquid. $[\alpha]_D^{25}$ = +8.2 (*c* = 0.65, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3419, 3035, 2961, 2927, 2874, 1718, 1458, 1157, 1070, 752, 699 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (m, 2 H, Ph-H), 7.35 (m, 3 H, Ph-H), 5.47 (s, 1 H, Ph-CH), 4.11 (dd, *J* = 11.1, 4.7 Hz, 1 H, 3-H), 3.53 (m, 2 H, 1-H), 3.42 (m, 2 H, 7-H), 2.13–2.02 (m, 1 H, 2-H), 1.96–1.86 (m, 1 H, 4-H), 1.81–1.70 (m, 1 H, 6-H), 1.68–1.59 (m, 1 H, 5-H), 1.55 (br., 1 H, OH), 1.17–1.07 (m, 1 H, 5′-H), 1.00 (d, *J* = 6.7 Hz, 3 H, 2′-Me), 0.97 (d, *J* = 6.7 Hz, 3 H, 4′-Me), 0.77 (d, *J* = 6.7 Hz, 3 H, 6′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.9, 128.5, 128, 126.1, 101.1, 84.2, 73.2, 68.4, 37, 32.9, 30.7, 30.6, 17.2, 14.2, 12.1 ppm. MS (EI): *m*/*z* = 301.0 [M + Na]$^+$. HRMS: calcd. for $C_{17}H_{26}O_3Na$ [M + Na]$^+$ 301.1774; found 301.1762.

***tert*-Butyl{(2*R*,4*S*)-2-methyl-4-[(5*S*)-5-methyl-2-phenyl-1,3-dioxan-4-yl]pentyloxy}diphenylsilane (14):** Imidazole (88 mg, 1.2 mmol) followed by TBDPS-Cl (0.168 mL, 0.64 mmol) were added to a stirred solution of alcohol **13** (120 mg, 0.4 mmol) in CH_2Cl_2 at 0 °C. The reaction mixture was stirred at room temperature for 30 min. The reaction was quenched with aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 15 mL), dried with Na_2SO_4, evaporated, and purified on silica gel (5% EtOAc/hexane) to furnish the silyl ether **14** (214 mg, 97%) as an oily colorless liquid. $[\alpha]_D^{25}$ = +20.7 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2927, 2856, 2359, 1648, 1546, 1398, 1108, 1024, 755 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (m, 4 H, Ph-H), 7.46–7.30 (m, 11 H, Ph-H), 5.41 (s, 1 H, Ph-CH), 4.10 (dd, *J* = 11.1, 4.7 Hz, 1 H, 3-H), 3.48 (m, 3 H, 1-H, 7-H), 3.32 (dd, *J* = 1.8, 10.0 Hz, 1 H, 7-H), 2.08 (m, 1 H, 2-H), 1.81 (m, 2 H, 4-H, 6-H), 1.64 (m, 1 H, 5-H), 1.10 (m, 1 H, 5′-H), 1.03 (s, 9 H, $SiMe_3$), 0.94 (m, 6 H, 2′-Me, 4′-Me), 0.71 (d, *J* = 6.6 Hz, 3 H, 6′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 139.0, 135.5, 134.0, 129.4, 128.4,

128.0, 127.5, 126.0, 100.9, 84.6, 73.2, 69.0, 37.1, 33.0, 30.6, 30.6, 26.8, 19.2, 17.4, 13.8, 12.0 ppm. MS (EI): *m*/*z* = 539.0 [M + Na]$^+$. HRMS: calcd. for $C_{33}H_{45}O_3Si$ [M + H]$^+$ 517.3132; found 517.3136.

(2*S*,4*S*,6*R*)-3-(Benzyloxy)-7-(*tert*-butyldiphenylsilyloxy)-2,4,6-trimethylheptan-1-ol (15): DIBAL-H (0.866 mL, 1.22 mmol, 20% of DIBAL-H in toluene) was slowly added to a solution of compound **14** (210 mg, 0.407 mmol) in CH_2Cl_2 at –15 °C and the reaction mixture was stirred at the same temperature while monitoring the progress of reaction by TLC. After consumption of all the starting material, the reaction mixture was quenched with a saturated aqueous potassium sodium tartrate solution and stirred at room temperature for 1 h. The reaction mixture was extracted with CH_2Cl_2 (3 × 15 mL), concentrated under reduced pressure, and purified by silica gel column chromatography to afford alcohol **15** (194 mg, 92%) as a colorless liquid. $[\alpha]_D^{25}$ = –6.5 (*c* = 2.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3443, 2917, 2849, 1215, 1110, 757 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (m, 4 H, Ph-H), 7.38 (m, 6 H, Ph-H), 7.29 (m, 5 H, Ph-H), 4.59 (d, *J* = 10.9 Hz, 1 H, Ph-CH), 4.53 (d, *J* = 10.9 Hz, 1 H, Ph-CH), 3.61 (d, *J* = 5.0 Hz, 2 H, 1-H), 3.47 (m, 2 H, 7-H), 3.23 (dd, *J* = 8.1, 2.8 Hz, 1 H, 3-H), 1.90 (m, 1 H, 2-H), 1.80 (m, 2 H, 4-H, 6-H), 1.62 (m, 1 H, 5-H), 1.02–1.06 (m, 10 H, $SiMe_3$, 5′-H), 0.97 (d, *J* = 6.6 Hz, 3 H, 2′-Me), 0.95 (d, *J* = 6.7 Hz, 3 H, 4′-Me), 0.89 (d, *J* = 6.9 Hz, 3 H, 6′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.2, 135.58, 135.55, 133.8, 129.5, 128.3, 127.6, 127.5, 87.7, 75.1, 68.7, 66.7, 38.4, 37.8, 33.3, 33.2, 26.8, 19.2, 17.8, 15.3, 14.8 ppm. MS (EI): *m*/*z* = 541.0 [M + Na]$^+$. HRMS: calcd. for $C_{33}H_{46}O_3SiNa$ [M + Na]$^+$ 541.3108; found 541.3110.

(2*R*,4*S*,6*R*)-3-(Benzyloxy)-7-(*tert*-butyldiphenylsilyloxy)-2,4,6-trimethylheptanal (16): A solution of alcohol **15** (100 mg, 0.19 mmol) in CH_2Cl_2 (3 mL) was added to a suspension of Dess–Martin periodinane (122 mg, 0.28 mmol) and $NaHCO_3$ (32 mg, 0.38 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. Afterwards, the reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with a saturated aqueous $NaHCO_3$ solution (3 × 10 mL). The combined organic layers were dried with Na_2SO_4, evaporated in vacuo, and purified by column chromatography over silica gel (10% EtOAc/hexane) to afford aldehyde **16** (91 mg, 92%) as a slightly yellow oil. $[\alpha]_D^{25}$ = –14.8 (*c* = 0.55, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2927, 2856, 2364, 1708, 1462, 1108, 701 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.77 (d, *J* = 2.2 Hz, 1 H, CHO), 7.66–7.63 (m, 5 H, Ph-H), 7.42–7.35 (m, 5 H, Ph-H), 7.29–7.22 (m, 5 H, Ph-H), 4.55–4.43 (ABq, *J* = 11.3 Hz, 2 H, Ph-CH_2), 3.52–3.41 (m, 3 H, 3-H, 7-H), 2.68 (ddq, *J* = 6.7, 2.2, 1.8 Hz, 1 H, 2-H), 1.84–1.72 (m, 1 H, 4-H), 1.63–1.54 (m, 2 H, 5-H, 6-H), 1.30 (m, 1 H, 5′-H), 1.04–1.0 (m, 12 H, $SiMe_3$, 2′-Me), 0.96–0.92 (m, 6 H, 4′-Me, 6′-Me) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 204.7, 135.5, 135.4, 133.7, 129.4, 128.2, 127.52, 127.5, 127.4, 83.8, 74.2, 68.5, 49.2, 37.8, 33.3, 33.0, 26.9, 19.3, 18.0, 14.8, 11.8 ppm. MS (EI): *m*/*z* = 539.1 [M + Na]$^+$. HRMS: calcd. for $C_{33}H_{48}O_3NSi$ [M + NH_4]$^+$ 534.3398; found 534.3398.

(2*R*,4*S*,5*R*,6*S*,*Z*)-5-(Benzyloxy)-8-iodo-2,4,6-trimethyloct-7-enyloxy)*tert*-butyldiphenylsilane (2): A suspension of (iodomethyl)triphenylphosphonium iodide (205 mg, 0.38 mmol) in THF (10 mL) was treated with NaHMDS (1 M in THF, 0.310 mL, 0.31 mmol) and the resulting solution was stirred for 20 min at room temperature. The resulting dark-red solution was cooled to –78 °C and HMPA (0.04 mL, 0.23 mmol) was added followed by aldehyde **16** (80 mg, 0.15 mmol) in THF (10 mL) at –78 °C. The reaction mixture was stirred for an additional 1 h at the same temperature. Then it was diluted with hexane (10 mL), filtered through Celite, concentrated in vacuo, and purified on silica gel (5% EtOAc/hexane) to afford vinyl iodide **2** (75 mg, 76%) as a colorless liquid. $[\alpha]_D^{25}$ = +5.4 (*c* = 0.6, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3067, 2926, 1645, 1259, 1107, 1075, 700 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67–7.64 (m, 5 H, Ph-H), 7.41–7.35 (m, 5 H, Ph-H), 7.30–7.23 (m, 5 H, Ph-H), 6.25 (dd, *J* = 8.8, 7.3 Hz, 1 H, 7-H), 6.06 (d, *J* = 7.3 Hz, 1 H, 8-H), 4.52 (s, 2 H, Ph-CH_2), 3.53 (dd, *J* = 9.8, 4.9 Hz, 1 H, 1-H), 3.35 (dd, *J* = 9.8, 7.3 Hz, 1 H, 1′-H), 3.12 (t, *J* = 4.7 Hz, 1 H, 5-H), 2.84–2.72 (m, 1 H, 6-H), 1.81–1.62 (m, 2 H, 2-H, 4-H), 1.48–1.39 (ddd, *J* = 13.2, 7.5, 5.0 Hz, 1 H, 3-H), 1.28 (m, 1 H, 3′-H), 1.04 (s, 9 H, $SiMe_3$), 1.01 (d, *J* = 6.7 Hz, 3 H, 6′-Me), 0.98 (d, *J* = 6.6 Hz, 3 H, 4′-Me), 0.92 (d, *J* = 6.7 Hz, 3 H, 2′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 143.7, 135.6, 129.4, 128.1, 127.5, 127.4, 127.2, 86.4, 81.5, 74.4, 68.8, 42.5, 37.8, 33.9, 33.3, 29.6, 26.8, 18.3, 17.3, 15.8 ppm. MS (EI): *m*/*z* = 663.0 [M + Na]$^+$. HRMS: calcd. for $C_{34}H_{49}INO_2Si$ [M + NH_4]$^+$ 658.2572; found 658.2578.

***N*-[(2*S*,3*S*)-3-Hydroxy-5-(4-methoxybenzyloxy)-2-methylpentanoyl]-bornane-10,2-sultam (19):** Titanium tetrachloride (1.5 mL, 13.8 mmol) was added dropwise to a 0.2 M solution of (*R*)-*N*-propionylbornane-10,2-sultam[18] (**17**; 1.25 g, 4.6 mmol) in CH_2Cl_2 at –78 °C under nitrogen. Diisopropylethylamine (1.75 mL, 10.1 mmol) was added very slowly to the resulting yellow slurry to give a deep-red solution, which was stirred at –78 °C. After 1.5 h, aldehyde **18** (2.6 g, 13.8 mmol) was added slowly over a period of 15 min and the mixture was stirred at –78 °C for an additional 1.5 h. The reaction was quenched with aqueous NH_4Cl and the mixture was warmed to ambient temperature. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3 × 50 mL), dried with anhydrous Na_2SO_4, evaporated under reduced pressure, and purified on silica gel using 20% EtOAc/hexane as eluent to furnish the *anti* aldol product **19** (2.94 g, 77%) as a colorless oil. $[\alpha]_D^{25}$ = –20.9 (*c* = 2.3, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3485, 2929, 2362, 1692, 1513, 1459, 1329, 1245, 1129 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.7 Hz, 2 H, Ph-H), 6.87 (d, *J* = 8.7 Hz, 2 H, Ph-H), 4.44 (dd, *J* = 16.3, 11.3 Hz, 2 H, Ph-CH_2), 3.90 (m, 2 H, 2-H, HC-N), 3.80 (s, 3 H, Ph-OMe), 3.72–3.58 (m, 2 H, 5-H), 3.50 (ABq, *J* = 13.7 Hz, 2 H, CH_2-SO_2), 3.22 (m, 1 H, 3-H), 3.09 (d, *J* = 7.1 Hz, 1 H, OH), 2.17–2.02 (m, 2 H, 4-H), 1.97–1.84 (m, 4 H), 1.43–1.25 (m, 3 H), 1.17 (m, 6 H, 2 Me), 0.96 (s, 3 H, Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 175.1, 159.1, 130.0, 129.3, 113.7, 74.1, 72.9, 67.6, 65.3, 55.2, 53.1, 48.2, 47.6, 45.3, 44.6, 38.4, 34.0, 32.8, 26.4, 20.7, 19.8, 13.7 ppm. MS (EI): *m*/*z* = 488.0 [M + Na]$^+$. HRMS: calcd. for $C_{24}H_{35}O_6NSNa$ [M + Na]$^+$ 488.2082; found 488.2079.

***N*-[(2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)-2-methylpentanoyl]bornane-10,2-sultam (20):** 2,6-Lutidine (0.878 mL, 7.5 mmol) followed by TBS-OTf (1.3 mL, 5.6 mmol) were added to a solution of alcohol **19** (1.75 g, 8.7 mmol) in CH_2Cl_2 (30 mL) at –78 °C and the reaction mixture was stirred at –78 °C for 30 min. The reaction mixture was quenched with saturated NH_4Cl and extracted with CH_2Cl_2 (3 × 30 mL), dried with anhydrous Na_2SO_4, and evaporated under reduced pressure to yield a white solid, which on purification over silica gel (10% EtOAc/hexane) afforded the TBS-substituted product **20** (1.97 g, 91%) as a white crystalline solid. $[\alpha]_D^{25}$ = –15.2 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2956, 2929, 1694, 1513, 1331, 1248, 1212, 1134, 1060 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.85 (d, *J* = 8.6 Hz, 2 H, Ph-H), 4.35 (s, 2 H, Ph-CH_2), 4.30 (m, 1 H, 3-H), 3.86 (t, *J* = 5.5 Hz, 1 H, HC-N), 3.78 (s, 3 H, Ph-OMe), 3.48 (m, 2 H, H_2C-SO_2), 3.43 (d, *J* = 6.2 Hz, 2 H, 5-H), 3.34 (m, 1 H, 2-H), 1.96–1.76 (m, 4 H), 1.63 (m, 2 H, 4-H), 1.41–1.24 (m, 3 H), 1.13 (d, *J* = 6.9 Hz, 3 H, 2′-Me), 1.01 (s, 3 H, Me) 0.89 (s, 3 H, Me), 0.86 (s, 9 H, $SiMe_3$), 0.11 (s, 3 H, SiMe), 0.05 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 173.5, 158.9, 130.7, 129.1, 113.5, 72.4, 69.3, 66.1, 65.1, 55.1, 53, 47.9, 47.5, 46.4, 44.5,

38.4, 32.7, 32.2, 26.3, 25.8, 20.5, 19.7, 17.9, 9.3, –4.4, –5.4 ppm. MS (EI): *m*/*z* = 602.0 [M + Na]$^+$. HRMS: calcd. for $C_{30}H_{49}NO_6NaSiS$ [M + Na]$^+$ 602.2947; found 602.2959.

(2*R*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)-2-methylpentan-1-ol (21): LiCl (660 mg, 15.5 mmol) and $NaBH_4$ (590 mg, 15.5 mmol) at 0 °C were placed in a 100 mL round-bottomed flask equipped with a magnetic bar. Ethanol (30 mL) was added and the suspension was stirred at room temperature for 1 h to generate $LiBH_4$ as a white suspension The suspension was cooled to 0 °C and aldol compound **20** (1.8 g, 3.1 mmol) was added in diethyl ether (20 mL). The reaction mixture was stirred for 2 h. Afterwards the volatiles were removed in vacuo, the residue was quenched with aqueous NH_4Cl solution, extracted with EtOAc (3 × 30 mL), dried with anhydrous Na_2SO_4, evaporated, and purified on silica gel (20% EtOAc/hexane) to furnish **21** (1.06 g, 94%) as an oily liquid. $[\alpha]_D^{25}$ = –2.6 (*c* = 0.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3443, 3015, 2955, 2927, 1250, 1216, 1082, 758 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.89 (d, *J* = 8.6 Hz, 2 H, Ph-H), 4.46–4.37 (ABq, *J* = 11.5 Hz, 2 H, Ph-CH_2), 3.88 (dd, *J* = 10.1, 5.8 Hz, 1 H, 1-H), 3.80 (s, 3 H, Ph-OMe), 3.75–3.70 (dd, *J* = 10.9, 3.9 Hz, 1 H, 1′-H), 3.54–3.47 (m, 3 H, 3-H, 5-H), 1.88–1.81 (q, *J* = 6.4 Hz, 2 H, 4-H), 1.79–1.72 (m, 1 H, 2-H), 0.99 (d, *J* = 7.1 Hz, 3 H, 2′-Me), 0.88 (s, 9 H, $SiMe_3$), 0.08 (s, 3 H, SiMe), 0.07 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.1, 130.3, 129.2, 113.7, 74, 72.6, 66.4, 65.2, 55.2, 38.9, 34.4, 25.8, 17.9, 13.9, –4.5, –4.6 ppm. MS (EI): *m*/*z* = 391.0 [M + Na]$^+$. HRMS: calcd. for $C_{20}H_{36}O_4NaSi$ [M + Na]$^+$ 391.2280; found 391.2295.

(2*S*,3*S*)-3-(*tert*-Butyldimethylsilyloxy)-5-(4-methoxybenzyloxy)-2-methylpentanal (22): A solution of alcohol **21** (500 mg, 1.35 mmol) in CH_2Cl_2 (10 mL) was added to a suspension of Dess–Martin periodinane (690 mg, 1.63 mmol) and $NaHCO_3$ (230 mg, 2.7 mmol) in CH_2Cl_2 (10 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was then diluted with CH_2Cl_2 (15 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 15 mL). The combined organic layers were dried with Na_2SO_4, evaporated in vacuo, and purification by silica gel column chromatography (10% EtOAc/hexane) afforded aldehyde **22** (472 mg, 95%) as a yellow oil. $[\alpha]_D^{25}$ = +21.1 (*c* = 1.6, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2930, 2856, 1710, 1250, 1102, 770 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.72 (d, *J* = 2.0 Hz, 1 H, CHO), 7.25 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.88 (d, *J* = 8.6 Hz, 2 H, Ph-H), 4.41 (dd, *J* = 15.1, 11.5 Hz, 2 H, Ph-CH_2), 4.15 (td, *J* = 6.4, 5.09 Hz, 1 H, 3-H), 3.81 (s, 3 H, Ph-OMe), 3.52 (t, *J* = 6.4 Hz, 2 H, 5-H), 2.52 (m, 1 H, 2-H), 1.79 (m, 2 H, 4-H), 1.10, (d, *J* = 6.9 Hz, 3 H, 2′-Me), 0.87 (s, 9 H, $SiMe_3$), 0.06 (s, 6 H, $SiMe_2$) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 204.6, 159.1, 130.3, 129.2, 113.7, 72.6, 70.4, 65.9, 55.2, 51.6, 34.6, 25.7, 18.0, 10.0, –4.6, –4.4 ppm. MS (EI): *m*/*z* = 389.0 [M + Na]$^+$. HRMS: calcd. for $C_{20}H_{34}O_4NaSi$ [M + Na]$^+$ 389.2119; found 389.2121.

***tert*-Butyl[(3*S*,4*R*,*E*)-6-Iodo-1-(4-methoxybenzyloxy)-4-methylhex-5-en-3-yloxy]dimethylsilane (23):** Anhydrous (flame-dried under argon) $CrCl_2$ (1.1 g, 8.4 mmol, 10 equiv.) in THF (10 mL) was stirred for 30 min at room temperature, generating a creamy gray-green suspension. CHI_3 (667 mg, 1.69 mmol, 2 equiv.) in THF at 0 °C was then added to this mixture followed by aldehyde **22** (310 mg, 0.84 mmol, 1 equiv.) in THF at 0 °C. The resulting dark-red mixture was stirred for 3 h at the same temperature. After completion of the reaction (confirmed by TLC) the reaction mixture was filtered through Celite and the residue washed with diethyl ether. The filtrate was then washed with saturated aqueous solution of sodium thiosulfate and brine solution. The organic layer was dried with Na_2SO_4 and concentrated in vacuo to afford the crude *trans*-vinyl iodide, which was purified by silica gel column chromatography (hexane/EtOAc = 95:5) to give *trans*-vinyl iodide **23** (352 mg, 85%) as a colorless oil. $[\alpha]_D^{25}$ = +15.1 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2954, 2929, 1612, 1249, 1096, 835 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.84 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.44 (dd, *J* = 14.5, 8.1 Hz, 1 H, 5-H), 5.95 (dd, *J* = 14.5, 0.75 Hz, 1 H, 6-H), 4.37 (dd, *J* = 19.0, 11.5 Hz, 2 H, Ph-CH_2), 3.80 (s, 3 H, Ph-OMe), 3.72 (td, *J* = 6.0, 4.1 Hz, 1 H, 3-H), 3.42 (t, *J* = 6.4 Hz, 2 H, 1-H), 2.30 (m, 1 H, 4-H), 1.65 (q, *J* = 6.4 Hz, 2 H, 2-H), 1.00 (d, *J* = 6.9 Hz, 3 H, 4′-Me), 0.88 (s, 9 H, $SiMe_3$), 0.04 (s, 3 H, SiMe), 0.03 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.2, 148.3, 130.4, 129.2, 113.7, 75.3, 72.6, 72.0, 66.3, 55.1, 46.1, 34.0, 26.0, 18.2, 15.2, –4.24, –4.29 ppm. MS (EI): *m*/*z* = 513.0 [M + Na]$^+$. HRMS: calcd. for $C_{21}H_{35}O_3NaSi$ [M + Na]$^+$ 513.1292; found 513.1294.

Ethyl (6*R*,7*S*,*E*)-7-(*tert*-Butyldimethylsilyloxy)-9-(4-methoxybenzyloxy)-6-methylnon-4-en-2-ynoate (24): CuI (26.4 mg, 0.13 mmol) and tetrakis(triphenylphosphane)palladium (80 mg, 0.069 mmol) were added to a solution of vinyl iodide **23** (340 mg, 0.69 mmol) in NEt_3 (2 mL). The reaction mixture was stirred for 30 min at room temperature, after which a solution of ethyl propionate (0.141 mL, 1.3 mmol, 2 equiv.) in THF was added dropwise over 10 min. After 2 h, the volatiles were removed in vacuo and purified by silica gel column chromatography (10% EtOAc/hexane) to obtain the enynoate compound **24** (287 mg, 90%) as a colorless oil. $[\alpha]_D^{25}$ = +40.5 (*c* = 0.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2954, 2930, 2210, 1708, 1614, 1252, 1097 cm^{-1}. ^{1}H NMR (300 MHz, CDCl3): δ = 7.26 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.89 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.49 (dd, *J* = 16.0, 8.1 Hz, 1 H, 5-H), 5.54 (dd, *J* = 16.0, 0.94 Hz, 1 H, 4-H), 4.41 (dd, *J* = 21.1, 11.5 Hz, 2 H, Ph-CH_2), 4.25 (q, *J* = 7.0 Hz, 2 H, CH_3-CH_2-CO_2), 3.80 (s, 3 H, Ph-OMe), 3.76 (m, 1 H, 7-H), 3.44 (t, *J* = 6.4 Hz, 2 H, 9-H), 2.38 (m, 1 H, 6-H), 1.65 (m, 2 H, 8-H), 1.31 (t, *J* = 7.1 Hz, 3 H, CH_3-CH_2-CO_2), 1.03 (d, *J* = 6.9 Hz, 3 H, 6′-Me), 0.88 (s, 9 H, $SiMe_3$), 0.04 (s, 3 H, SiMe), 0.03 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.1, 154.1, 153.8, 130.4, 129.2, 113.7, 107.2, 85.4, 79.7, 72.5, 72.2, 66.3, 61.8, 55.2, 43.3, 34.3, 25.8, 18, 15.2, 14, –4.4 ppm. MS (EI): *m*/*z* = 483.0 [M + Na]$^+$. HRMS: calcd. for $C_{26}H_{40}NaO_5Si$ [M + Na]$^+$ 483.2537; found 483.2538.

Ethyl (6*R*,7*S*,*E*)-7-(*tert*-Butyldimethylsilyloxy)-9-hydroxy-6-methylnon-4-en-2-ynoate (25): DDQ (153 mg, 0.67 mmol) was added portionwise to a solution of PMB ether **24** (260 mg, 0.56 mmol) in a mixture of CH_2Cl_2 and water (5:1, 15 mL) at 0 °C under vigorous stirring. After completion (confirmed by TLC), the reaction mixture was quenched with a saturated $NaHCO_3$ solution and extracted with CH_2Cl_2 (3 × 15 mL), dried with anhydrous Na_2SO_4, and concentrated under reduced pressure to yield a viscous oil, which was purified by silica gel column chromatography (15% EtOAc/hexane) to afford the alcohol **25** (182 mg, 95%) as a colorless oil. $[\alpha]_D^{25}$ = +15.5 (*c* = 0.8, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3019, 2925, 2212, 1702, 1465, 1215, 758 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.47 (dd, *J* = 16.0, 8.1 Hz, 1 H, 5-H), 5.60 (dd, *J* = 16.0, 1.3 Hz, 1 H, 4-H), 4.25 (q, *J* = 7.1 Hz, 2 H, CH_3-CH_2-CO_2), 3.81 (td, *J* = 4.7, 2.2 Hz, 1 H, 7-H), 3.71 (m, 2 H, 9-H), 2.50 (m, 1 H, 6-H), 1.83 (br., 1 H, OH), 1.67 (m, 2 H, 8-H), 1.32 (t, *J* = 7.1 Hz, 3 H, CH_3-CH_2-CO_2), 1.05 (d, *J* = 6.7 Hz, 3 H, 6′-Me), 0.90 (s, 9 H, $SiMe_3$), 0.09 (s, 3 H, SiMe), 0.07 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 154.05, 153.6, 107.4, 85.1, 79.9, 73.2, 61.8, 59.7, 43.2, 35.7, 25.8, 17.9, 14.6, 14.03, –4.5, –4.4 ppm. MS (EI): *m*/*z* = 341.1 [M + H]$^+$. HRMS: calcd. for $C_{18}H_{33}O_4Si$ [M + H]$^+$ 341.2143; found 341.2152.

Ethyl (2*Z*,4*E*,6*R*,7*S*)-7-(*tert*-Butyldimethylsilyloxy)-9-hydroxy-6-methylnona-2,4-dienoate (26): Isoquinoline (0.2 mL) followed by

the $Pd/CaCO_3$ catalyst poisoned with Pb (30 mg) were added to a solution of alcohol **25** (125 mg, 0.36 mmol) in benzene (10 mL) under hydrogen. The reaction mixture was stirred at room temperature for 15 min, washed with a 0.8 M HCl solution (2 × 5 mL) to remove isoquinoline from the reaction mixture, extracted with diethyl ether (3 × 10 mL), dried with Na_2SO_4, and the solvents evaporated in vacuo. The crude product was purified by silica gel column chromatography (20% EtOAc/hexane) to furnish the dienoate **26** (122 mg, 98%) as yellow oil. $[\alpha]_D^{25}$ = –5.1 (*c* = 0.5, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3020, 2928, 2361, 1710, 1640, 1463, 1253, 1215, 763 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39 (dd, *J* = 15.4, 11.3 Hz, 1 H, 3-H), 6.54 (t, *J* = 11.3 Hz, 1 H, 4-H), 5.99 (dd, *J* = 15.4, 7.7 Hz, 1 H, 2-H), 5.59 (d, *J* = 11.3 Hz, 1 H, 5-H), 4.18 (q, *J* = 7.1 Hz, 2 H, CH_3-CH_2-CO_2), 3.86 (m, 1 H, 7-H), 3.72 (m, 2 H, 9-H), 2.54 (m, 1 H, 6-H),1.83 (s, 1 H, OH), 1.68 (m, 2 H, 8-H), 1.30 (t, *J* = 7.1 Hz, 3 H, CH_3-CH_2-CO_2), 1.07 (d, *J* = 6.9 Hz, 3 H, 6′-Me), 0.90 (s, 9 H, $SiMe_3$), 0.09 (s, 3 H, SiMe), 0.07 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 166.5, 146.7, 145.04, 126.9, 116.2, 73.8, 59.8, 60.1, 42.6, 35.3, 25.8, 18.01, 14.6, 14.2, –4.5, –4.3 ppm. MS (EI): *m*/*z* = 343.1 $[M + H]^+$. HRMS: calcd. for $C_{18}H_{35}O_4Si$ $[M + H]^+$ 343.2299; found 343.2289.

Ethyl (2*Z*,4*E*,6*R*,7*S*)-7-(*tert*-Butyldimethylsilyloxy)-6-methyl-9-oxonona-2,4-dienoate (3): A solution of alcohol **26** (100 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) was added to a suspension of Dess–Martin periodinane (148 mg, 0.35 mmol) and $NaHCO_3$ (49 mg, 0.58 mmol) in CH_2Cl_2 (5 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with aqueous $NaHCO_3$ solution (2 × 10 mL). The organic layer was dried with Na_2SO_4, evaporated under reduced pressure, and the crude product was purified by silica gel column chromatography (10% EtOAc/hexane) to yield aldehyde **3** (94.4 mg, 95%) as slightly yellow oil. $[\alpha]_D^{25}$ = +4.7 (*c* = 0.45, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2957, 2932, 2857, 1715, 1638, 1465, 1254, 1184, 1090, 1028 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.77 (s, 1 H, CHO), 7.39 (dd, *J* = 15.4, 11.3 Hz, 1 H, 3-H), 6.54 (t, *J* = 11.3 Hz, 1 H, 4-H), 5.96 (dd, *J* = 15.4, 7.9 Hz, 1 H, 2-H), 5.62 (d, *J* = 11.3 Hz, 1 H, 5-H), 4.19 (m, 3 H, CH_3-CH_2-CO_2, 7-H), 2.50 (m, 3 H, 6-H, 8-H), 1.30 (t, *J* = 7.1 Hz, 3 H, CH_3-CH_2-CO_2), 1.09 (d, *J* = 6.9 Hz, 3 H, 6′-Me), 0.87 (s, 9 H, $SiMe_3$), 0.08 (s, 3 H, SiMe), 0.04 (s, 3 H, SiMe) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.6, 166.4, 144.6, 145.2, 127.6, 116.7, 70.9, 59.9, 48.2, 43.3, 25.7, 18.0, 14.9, 14.2, –4.6, –4.5 ppm. MS (EI): *m*/*z* = 341.0 $[M + H]^+$. HRMS: calcd. for $C_{18}H_{36}NO_4Si$ $[M + NH_4]^+$ 358.2408; found 358.2410.

***N*-[(2*R*,3*R*)-3-Hydroxy-2,4-dimethylpent-4-enoyl]bornane-10,2-sultam (27):** Titanium tetrachloride (2 mL, 18.4 mmol) was added dropwise to a 0.2 M solution of (*R*)-*N*-propionylbornane-10,2-sultam[18] (**17**; 5 g, 18.4 mmol) in CH_2Cl_2 at –78 °C under nitrogen. To the resulting yellow slurry, diisopropylethylamine (3.82 mL, 22.1 mmol) was added slowly and the resulting deep-red solution was stirred at –78 °C. After 1.5 h, methacrolein (4.5 mL, 55.3 mmol) was added slowly and the mixture was stirred at –78 °C for an additional 1.5 h. The reaction was quenched with aqueous NH_4Cl and the mixture was warmed to ambient temperature. The reaction mixture was then diluted with water and extracted with CH_2Cl_2 (3 × 50 mL), dried with Na_2SO_4, and evaporated under reduced pressure to yield the crude *syn* aldol product, which on purification by silica gel column chromatography (15% EtOAc/hexane) gave the *syn* aldol product **27** (6.4 g, 73%) as a white solid. $[\alpha]_D^{25}$ = –81.3 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3505, 2961, 2885, 2360, 1676, 1455, 1331, 1270, 1214, 1132, 1062 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.15 (s, 1 H, 5-H), 4.97 (s, 1 H, 5′-H), 4.42 (s, 1 H, 3-H), 3.91 (t, *J* = 6.4 Hz, 1 H, HC-N), 3.56–3.44 (m, 3 H, H_2C-SO_2, OH), 3.27 (dq, *J* = 7.1, 2.4 Hz, 1 H, 2-H), 2.07 (m, 2 H), 1.91 (m, 3 H), 1.72 (s, 3 H, 4-Me), 1.45–1.29 (m, 2 H), 1.20 (d, *J* = 7.1 Hz, 3 H, 2′-Me), 1.15 (s, 3 H, Me), 0.98 (s, 3 H, Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 177, 142.9, 111.9, 72.8, 64.9, 52.9, 48.3, 47.7, 44.5, 41.4, 38.2, 32.7, 26.3, 20.7, 19.8, 19.4, 10.9 ppm. MS (EI): *m*/*z* = 364.1 $[M + Na]^+$. HRMS: calcd. for $C_{17}H_{27}NO_4NaS$ $[M + Na]^+$ 364.1558; found 364.1556.

(2*S*,3*R*)-2,4-Dimethylpent-4-ene-1,3-diol (28): The *syn* aldol **27** (3.37gr, 9.87 mmol) in THF (15 mL) was added to a suspension of $LiAlH_4$ (570 mg, 14.8 mmol) in THF (15 mL) under nitrogen at 0 °C and the mixture was stirred for 3 h at room temperature. Then it was quenched with saturated aqueous Na_2SO_4 at 0 °C. The solids were filtered, washed with diethyl ether, the filtrate dried with Na_2SO_4, evaporated under reduced pressure, and purified by silica gel column chromatography (20% EtOAc/hexane) to afford diol **28** (1.19 g, 94%) as a colorless oil. $[\alpha]_D^{25}$ = +12.6 (*c* = 0.8, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3416, 2918, 1650, 1216, 1021 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.01 (s, 1 H, 5-H), 4.93 (s, 1 H, 5′-H), 4.25 (d, *J* = 1.8 Hz, 1 H, 3-H), 3.71 (m, 2 H, 1-H), 2.62 (br., 2 H, OH), 1.90 (m, 1 H, 2-H), 1.72 (s, 3 H, 4-Me), 0.90 (d, *J* = 7.0 Hz, 3 H, 2′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 146.1, 110.4, 76.8, 66.6, 37.1, 19.2, 9.7 ppm. MS (EI): *m*/*z* = 131.1 $[M + H]^+$. HRMS: calcd. for $C_7H_{14}O_2Na$ $[M + Na]^+$ 153.1894; found 153.1991.

(4*R*,5*S*)-2-(4-Methoxyphenyl)-5-methyl-4-(prop-1-en-2-yl)-1,3-dioxane (29): Anisaldehyde dimethyl acetal (2.15 mL, 12.6 mmol) and a catalytic amount of azeotropically dried CSA were added to a stirred solution of diol **28** (1.1 g, 8.4 mmol) in CH_2Cl_2 at 0 °C. The reaction mixture was stirred at room temperature for 5 h. It was then quenched with aqueous $NaHCO_3$, extracted with CH_2Cl_2 (3 × 20 mL), dried with anhydrous Na_2SO_4, evaporated, and purified on silica gel using 5% EtOAc/hexane as eluent to furnish the protected diol **29** (1.93 g, 93%) as an oily liquid. $[\alpha]_D^{25}$ = +17.5 (*c* = 3.1, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2963, 2924, 1650, 1616, 1516, 1247, 1117, 826 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.90 (d, *J* = 8.6 Hz, 2 H, Ph-H), 5.52 (s, 1 H, Ph-CH), 5.10 (d, *J* = 1.5 Hz, 1 H, 5-H), 4.92 (d, *J* = 1.5 Hz, 1 H, 5′-H), 4.32 (d, *J* = 1.7 Hz, 1 H, 3-H), 4.14–4.02 (m, 2 H, 1-H), 3.80 (s, 3 H, Ph-OMe), 1.78 (m, 1 H, 2-H), 1.70 (s, 3 H, 4-Me), 1.07 (d, *J* = 6.9 Hz, 3 H, 2′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.8, 142.2, 131.5, 127.4, 113.5, 110.4, 101.4, 81.3, 73.2, 55.2, 30.4, 19, 11.0 ppm. MS (EI): *m*/*z* = 249.1 $[M + H]^+$. HRMS: calcd. for $C_{15}H_{20}O_3Na$ $[M + Na]^+$ 271.1312; found 271.1316.

(*S*)-2-[(4*S*,5*S*)-2-(4-Methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]propan-1-ol (30): A solution of olefin **29** (1.73 g, 6.9 mmol) in THF (15 mL) at 0 °C was treated with 9-BBN (1.7 g, 13.9 mmol) in THF. The reaction mixture was stirred at room temperature for 12 h. It was then quenched with 3 N NaOH (1.4 g) and 30% aqueous H_2O_2 (2.2 mL) and stirred for 6 h at room temperature. The reaction mixture was extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with brine, dried with anhydrous Na_2SO_4, concentrated in vacuo, and purified by silica gel column chromatography (20% EtOAc/hexane) to afford alcohol **30** (1.66 g, 90%) as a colorless oil. $[\alpha]_D^{25}$ = –8.8 (*c* = 0.35, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3445, 3018, 2961, 1615, 1518, 1250, 1215, 1033, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.87 (d, *J* = 8.6 Hz, 2 H, Ph-H), 5.48 (s, 1 H, Ph-CH), 4.05 (m, 2 H, 5-H), 3.79 (s, 4 H, Ph-OMe, 3-H), 3.7–3.58 (m, 2 H, 1-H), 1.99 (m, 1 H, 2-H), 1.67 (m, 1 H, 4-H), 1.21 (d, *J* = 6.9 Hz, 3 H, 4′-Me), 0.83 (d, *J* = 6.9 Hz, 3 H, 2′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 160.0, 131.0, 127.3, 113.7, 101.7, 85.2, 73.9, 67.9, 55.2, 36.6, 29.9, 11.9, 10.9 ppm. MS (EI): *m*/*z* = 289.2 $[M + Na]^+$. HRMS: calcd. for $C_{15}H_{22}O_4Na$ $[M + Na]^+$ 289.1415; found 289.1407.

(*R*)-2-[(4*R*,5*S*)-2-(4-Methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]propanal (31): A solution of alcohol **30** (510 mg, 1.9 mmol) in CH_2Cl_2 (10 mL) was added to a suspension of Dess–Martin periodinane (1.05 g, 2.5 mmol) and $NaHCO_3$ (322 mg, 3.84 mmol) in CH_2Cl_2 (15 mL) at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. The suspension was diluted with hexane and the solvents were evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (10% EtOAc/hexane) to yield aldehyde **31** (408 mg, 95%) as a slightly yellow oil. $[\alpha]_D^{25}$ = –30.2 (*c* = 1.2, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2918, 2849, 1725, 1615, 1516, 1248, 1165, 1030, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.84 (d, *J* = 2.2 Hz, 1 H, CHO), 7.39 (d, *J* = 8.8 Hz, 2 H, Ph-H), 6.88 (d, *J* = 8.8 Hz, 2 H, Ph-H), 5.48 (s, 1 H, Ph-CH), 4.11 (m, 3 H, 3-H, 5-H), 3.79 (s, 3 H, Ph-OMe), 2.63 (m, 1 H, 2-H), 1.66 (m, 1 H, 4-H), 1.22 (d, *J* = 6.9 Hz, 3 H, 4′-Me), 1.01 (d, *J* = 7.1 Hz, 3 H, 2′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 204.1, 159.8, 130.6, 127.2, 113.4, 100.8, 81.5, 72.7, 55.2, 47.3, 30.2, 11.9, 7.0 ppm. MS (EI): *m*/*z* = 265.1 $[M + H]^+$. HRMS: calcd. for $C_{15}H_{21}O_4$ $[M + H]^+$ 265.1434; found 265.1436.

(4*S*,5*S*)-4-[(*S*,*Z*)-4-Iodobut-3-en-2-yl]-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (32): A suspension of (iodomethyl)triphenylphosphonium iodide (1.03 g, 1.98 mmol) in THF (10 mL) was treated with NaHMDS (1 M in THF, 1.98 mL, 1.98 mmol) and the resulting solution was stirred for 20 min at room temperature. The resulting dark-red solution was cooled to –78 °C and to it was added HMPA (0.276 mL, 1.59 mmol) followed by aldehyde **31** (350 mg, 1.32 mmol) in THF (10 mL). After stirring for 30 min at –78 °C the reaction mixture was warmed to room temperature and stirred for an additional 1 h. The reaction mixture was diluted with hexane (10 mL), filtered through Celite, concentrated in vacuo, and purified by silica gel column chromatography (5% EtOAc/hexane) to afford vinyl iodide **32** (405 mg, 79%). $[\alpha]_D^{25}$ = +84.6 (*c* = 0.9, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2960, 2362, 1646, 1615, 1395, 1248, 1078, 1024 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.7 Hz, 2 H, Ph-H), 6.88 (d, *J* = 8.8 Hz, 2 H, Ph-H), 6.22 (d, *J* = 7.4 Hz, 1 H, 6-H), 6.15 (dd, *J* = 7.9, 7.4 Hz, 1 H, 5-H), 5.42 (s, 1 H, Ph-CH), 4.09–4.04 (dd, *J* = 11.2, 2.4 Hz, 1 H, 1-H), 4.03–3.99 (dd, *J* = 11.2, 1.5 Hz, 1 H, 1′-H), 3.80–3.75 (m, 4 H, Ph-OMe, 3-H), 2.83–2.70 (m, 1 H, 4-H), 1.73–1.65 (m, 1 H, 2-H), 1.22 (d, *J* = 6.9 Hz, 3 H, 2′-Me), 0.99 (d, *J* = 6.9 Hz, 3 H, 4′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.7, 144.0, 131.3, 127.2, 113.4, 101.4, 82.6, 82.1, 73.8, 55.2, 41.4, 30.1, 14.5, 11.2 ppm. MS (EI): *m*/*z* = 389.0 $[M + H]^+$. HRMS: calcd. for $C_{16}H_{21}IO_3$ $[M + Na]^+$ 411.1535; found 411.1546.

(4*S*,5*S*)-4-[(*S*,*Z*)-Hexa-3,5-dien-2-yl]-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (33): Bis(acetonitrile)palladium(II) chloride (33 mg, 0.12 mmol) followed by vinyltributyltin (0.282 mL, 0.96 mmol) were added to a degassed and stirred solution of vinyl iodide **32** (250 mg, 0.64 mmol) in dry DMF (4 mL) and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with water (15 mL) and extracted with diethyl ether (3 × 15 mL). The combined organic layers were dried with Na_2SO_4, evaporated under reduced pressure, and purified by silica gel column chromatography (15% EtOAc/hexane) to afford the diene (175 mg, 95%) as an oily colorless liquid. $[\alpha]_D^{25}$ = –26.8 (*c* = 0.55, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2963, 2933, 2876, 1690, 1614, 1517, 1250, 1031 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.8 Hz, 2 H, Ph-H), 6.85 (d, *J* = 8.8 Hz, 2 H, Ph-H), 6.70 (dt, *J* = 16.9, 10.7 Hz, 1 H, 7-H), 6.07 (t, *J* = 10.7 Hz, 1 H, 6-H), 5.42 (s, 1 H, Ph-CH), 5.39 (t, *J* = 10.1 Hz, 1 H, 5-H), 5.20 (d, *J* = 16.9 Hz, 1 H, 8-H), 5.10 (d, *J* = 10.2 Hz, 1 H, 8′-H), 4.08 (m, 2 H, 1-H), 3.78 (s, 3 H, Ph-OMe), 3.60 (dd, *J* = 9.4, 1.8 Hz, 1 H, 3-H), 2.90 (m, 1 H, 4-H), 1.71 (m, 1 H, 2-H), 1.20 (d, *J* = 6.7 Hz, 3 H, 2′-Me), 0.97 (d, *J* = 6.9 Hz, 3 H, 4′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.5, 135.7, 132.9, 131.4, 129.5, 127.1, 117.0, 113.3, 101.2, 83.2, 73.8, 55.2, 34.0, 29.9, 15.9, 11.0 ppm. MS (EI): *m*/*z* = 289.0 $[M + H]^+$. HRMS: calcd. for $C_{18}H_{24}O_3Na$ $[M + Na]^+$ 311.1617; found 311.1624.

(2*S*,3*S*,4*S*,*Z*)-3-(4-Methoxybenzyloxy)-2,4-dimethylocta-5,7-dien-1-ol (34): DIBAL-H (1.1 mL, 1.56 mmol, 20% of DIBAL-H in toluene) was added slowly to a solution of diene **33** (150 mg, 0.52 mmol) in CH_2Cl_2 at –15 °C and the reaction mixture was stirred at the same temperature while monitoring the progress of reaction by TLC. After consumption of all the starting material, the reaction mixture was quenched with a saturated aqueous potassium sodium tartrate solution and stirred vigorously at room temperature for 1 h. The reaction mixture was extracted with CH_2Cl_2 (3 × 15 mL), concentrated under reduced pressure, and purified by silica gel column chromatography to afford alcohol **34** (137 mg, 91%) as a colorless liquid. $[\alpha]_D^{25}$ = +42.7 (*c* = 0.55, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3421, 2926, 1612, 1513, 1247, 1033 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.87 (d, *J* = 8.6 Hz, 2 H, Ph-H), 6.69 (dt, *J* = 16.9, 10.7 Hz, 1 H, 7-H), 6.03 (t, *J* = 10.7 Hz, 1 H, 6-H), 5.54 (t, *J* = 10.3 Hz, 1 H, 5-H), 5.22 (d, *J* = 16.9 Hz, 1 H, 8-H), 5.12 (d, *J* = 10.2 Hz, 1 H, 8′-H), 4.55 (d, *J* = 10.7 Hz, 1 H, Ph-CH), 4.47 (d, *J* = 10.7 Hz, 1 H, Ph-CH), 3.79 (s, 3 H, Ph-OMe), 3.63–3.50 (m, 2 H, 1-H), 3.40 (dd, *J* = 5.8, 4.3 Hz, 1 H, 3-H), 2.93–3.05 (ddq, *J* = 9.8, 6.7, 6.6 Hz, 1 H, 4-H), 1.90–2.02 (m, 1 H, 2-H), 1.63 (br. s, 1 H, OH), 1.03 (d, *J* = 6.7 Hz, 3 H, 4-Me), 0.96 (d, *J* = 6.9 Hz, 3 H, 2-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.1, 135.3, 132.4, 130.9, 129.5, 129.0, 117.4, 113.6, 84.2, 73.8, 66.1, 55.2, 37.6, 35.0, 18.5, 11.5 ppm. MS (EI): *m*/*z* = 313.1 $[M + Na]^+$. HRMS: calcd. for $C_{18}H_{26}O_3Na$ $[M + Na]^+$ 313.1779; found 313.1770.

(2*R*,3*S*,4*S*,*Z*)-3-(4-Methoxybenzyloxy)-2,4-dimethylocta-5,7-dienal (4): A solution of alcohol **34** (100 mg, 0.34 mmol) in CH_2Cl_2 (5 mL) was added to a suspension of Dess–Martin periodinane (219 mg, 0.51 mmol) and $NaHCO_3$ (86 mg, 1.03 mmol) in CH_2Cl_2 (10 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. It was then diluted with CH_2Cl_2 (10 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 10 mL). The combined organic layers were dried with Na_2SO_4, evaporated in vacuo, and purified by silica gel column chromatography (10% EtOAc/hexane) to afford aldehyde **4** as a slightly yellow oil (90 mg, 91%). $[\alpha]_D^{25}$ = +31.5 (*c* = 0.65, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 2925, 2854, 1709, 1610, 1512, 1252, 1032, 758 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 9.69 (d, *J* = 1.13 Hz, 1 H, CHO), 7.23 (d, *J* = 8.7 Hz, 2 H, Ph-H), 6.87 (d, *J* = 8.7 Hz, 2 H, Ph-H), 6.55 (ddd, *J* = 16.8, 10.9, 0.9 Hz, 1 H, 7-H), 6.04 (t, *J* = 10.9 Hz, 1 H, 6-H), 5.44 (t, *J* = 10.5 Hz, 1 H, 5-H), 5.23 (dd, *J* = 16.8, 1.8 Hz, 1 H, 8-H), 5.12 (d, *J* = 10.2 Hz, 1 H, 8′-H), 4.50 (d, *J* = 10.7 Hz, 1 H, Ph-CH), 4.44 (d, *J* = 10.7 Hz, 1 H, Ph-CH), 3.79 (s, 3 H, Ph-OMe), 3.70 (t, *J* = 5.0 Hz, 1 H, 3-H), 3.02–2.90 (m, 1 H, 4-H), 2.63–2.54 (ddq, *J* = 6.9, 5.0, 1.1 Hz, 1 H, 2-H), 1.17 (d, *J* = 6.9 Hz, 3 H, 4′-Me), 1.07 (d, *J* = 6.9 Hz, 3 H, 2′-Me) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 204.1, 159.2, 133.7, 132.1, 130.3, 130.1, 129.4, 118.0, 113.7, 81.9, 73.5, 55.2, 49.4, 35.5, 18.2, 9.1 ppm. MS (EI): *m*/*z* = 311.0 $[M + Na]^+$. HRMS: calcd. for $C_{18}H_{24}O_3Na$ $[M + Na]^+$ 311.1623; found 311.1631.

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