Supplimentary Information

Asymmetric Total Synthesis of Stagonolide F

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Experimental Procedures and spectral data of compounds

4.1. *Tert*-butyl (hex-5-enyloxy) dimethylsilane (4): To a cooled (0 °C) solution of 5-hexen-1-ol **3** (5 g, 50 mmol) in dry CH₂Cl₂ (60 mL) was added imidazole (6.8 g, 100 mmol) and *tert*-butyl dimethyl silyl chloride (8.25 g, 55.0 mmol) under N₂ atmosphere and stirred for 3 h at r.t. After completion of the reaction, the reaction mixture was diluted with H₂O and extracted into CH₂Cl₂ (2 × 50 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography (Hexane: EtOAc 9.5:0.5) to obtain pure compound **4** (9.9 g, 93%) as colorless liquid. IR (neat): 2932, 2859, 1254, 1102, 836, 773 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): 5.89-5.74 (*m*, 1 H), 5.06-4.91 (*m*, 2 H), 3.61 (*t*, *J* = 6.2 Hz, 2 H), 2.11-2.01 (*m*, 2 H), 1.60-1.36 (*m*, 4 H), 0.89 (*s*, 9 H), 0.04 (*s*, 6 H). ¹³C-NMR (75 MHz, CDCl₃): 138.8, 114.3, 63.0, 33.5, 32.3, 25.9, 25.2, 18.3, -5.3. ESI-MS: 429 [M+2]⁺.

4.2. (*S*)-6-(*Tert*-butyldimethylsilyloxy) hexane-1, 2-diol (5): To a cooled (0 °C) solution of compound **4** (5 g, 23.36 mmol) in *tert*-butanol: water (30: 30 mL) ADD-mix- α (32.7 g) was added and stirred at the same temperature for 36 h. After completion of the reaction, sodium sulfite (12 g) was added and stirred for 30 min. The reaction mixture was filtered on celite and the organic layer was extracted into EtOAc (3 × 40 mL). The combined organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. The crude residue was purified by column chromatography (Hexane: EtOAc 7:3) to obtain pure compound **5** (5.15 g, 89%) as colorless liquid. $[\alpha]_D^{25} = -0.4$ (*c* = 1, CHCl₃). IR (neat): 3389, 2931, 2862, 1258, 1073, 1048 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): 3.73-3.65 (*m*, 1 H), 3.61 (*t*, *J* = 6.0 Hz, 2 H), 3.46-3.35 (*m*, 1 H), 3.32-3.30 (*m*, 1 H), 1.6-1.37 (*m*, 6 H), 0.88 (*s*, 9 H), 0.04 (*s*, 6 H). ¹³C NMR (75 MHz, CDCl₃): 71.7, 67.1, 63.0, 32.5, 32.2, 25.6, 21.6; 17.9, -3.6. ESI-MS: 249 [M+1]⁺.

4.3. (*S*)-*Tert*-butyl dimethyl (4-(oxiran-2-yl)butoxy) silane (6): To a cooled (0 °C) solution of compound **5** (3.0 g, 12.09 mmol), dibutyltin oxide (catalytic), and Et₃N (3.33 mL, 24.18 mmol) in dry CH₂Cl₂ was added *p*-toluene sulfonyl chloride (2.3 g, 12.09 mmol) under N₂ atmosphere and stirred for 4 h at r.t. After completion of the reaction, the reaction mixture was diluted with saturated NaHCO₃ solution and extracted into CH₂Cl₂ (2 × 20 mL). The organic extract was washed with H₂O, brine, and dried over Na₂SO₄ and the solvent was removed under

reduced pressure. The residue was purified by column chromatography (Hexane: EtOAc 9:1) to obtain pure compound 4.3 g, 90% as yellow liquid. To a stirred solution of monotosylate derivative (4.0 g, 9.95 mmol) in dry MeOH (15 mL) was added K₂CO₃ (2.88 g, 20.89 mmol) under nitrogen atmosphere and stirred for 2 h at r.t. After completion of the reaction, MeOH was removed under reduced pressure and diluted with H₂O (10 mL) and extracted into CH₂Cl₂ (2 × 10 mL). The combining organic extracts were washed with H₂O, brine solution and dried over Na₂SO₄. The crude residue was purified by column chromatography (Hexane: EtOAc 8:2) to afford pure compound **6** (2.1 g, 92%) as colorless liquid. $[\alpha]_D^{25} = -5.2$ ($c = 0.28$, CHCl₃). IR (neat): 2952, 2931, 1254, 1219, 1100 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): 3.61 (*t*, $J = 6.0$ Hz, 2 H), 2.95-2.86 (*m*, 1 H), 2.74 (*t*, $J = 5.2$ Hz, 1 H), 2.46 (*dd*, $J = 3.0, 5.2$ Hz, 1 H), 1.62-1.45 (*m*, 6 H), 0.88 (*s*, 9 H), 0.04 (*s*, 6 H). ¹³C-NMR (75 MHz, CDCl₃): 62.8, 52.2, 46.9, 32.5, 32.2, 25.9, 22.2, 18.3, -5.3. HRMS (ESI): m/z [M+1]⁺ calcd for C₁₂H₂₆O₂Si = 231.1775, found = 231.1780.

4.4. (S)-7-(Tert-butyl dimethyl silyloxy) hept-1-en-3-ol (7): To a cooled (-20 °C) stirred solution of trimethylsulfoniumiodide (7.09 g, 34.7 mmol) in dry THF (15 mL) was added *n*-BuLi (31.25 mL, 1.6 M, 50.4 mmol) under N₂ atmosphere and stirred for 1 h. A solution of epoxide **6** (2.0 g, 8.69 mmol) in THF was added and a cloudy suspension was formed. The stirring was continued for another 1 h at -20 °C. The reaction mixture was warmed to 0 °C and quenched with saturated aqueous NH₄Cl (20 mL). The two phases were separated and the aqueous phase was extracted into EtOAc (3 × 20 mL). The combined organic layer was washed with H₂O (2 × 20 mL), brine, and dried over Na₂SO₄ and concentrated under reduced pressure. The residual oil was purified by column chromatography (Hexane: EtOAc 8:2) to furnish the allylic alcohol **7** (1.7 g, 81%) as a colorless oil. $[\alpha]_D^{25} = -10.4$ ($c = 0.4$, CHCl₃). IR (neat): 3155, 2923, 2852, 1221, 1051, 818, 772 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): 5.98-5.77 (*m*, 1 H), 5.16 (*dd*, $J = 4.4, 11.6$ Hz, 2 H), 4.19-4.05 (*m*, 1 H), 3.61 (*t*, $J = 6.2$ Hz, 2 H), 1.63-1.30 (*m*, 6 H), 0.88 (*s*, 9 H), 0.04 (*s*, 6 H). ¹³C NMR (75 MHz, CDCl₃): 141.1, 114.5, 73.1, 63.0, 36.6, 32.5, 25.9, 21.6, 18.3, -5.3. HRMS (ESI): m/z [M+Na]⁺ calcd for C₁₃H₂₈O₂NaSi = 267.1751, found = 267.1754.

4.5. (S) - 11, 11, 12, 12-Tetramethyl-5-vinyl-2, 4, 10-trioxa-11-silatridecane (8): To a cooled (0 °C) solution of compound **7** (1.5 g, 6.14 mmol) and DIPEA (3.96 mL, 30.7 mmol) in dry CH₂Cl₂ (20 mL) was added MOM-Cl (0.94 mL, 12.29 mmol) slowly and stirred for 6 h at r.t.

After completion of the reaction as monitored by TLC, H₂O was added, and the reaction mixture was extracted into CH₂Cl₂ (3 × 20 mL), and dried over Na₂SO₄. The solvent was removed in *vacuum* to give a crude residue, which was purified by column chromatography (Hexane: EtOAc 8.5:1.5) to afford compound **8** (1.61 g, 91%) as a colorless oil. $[\alpha]_D^{25} = -21.6$ ($c = 1.1$, CHCl₃). IR (neat): 2933, 2859, 1255, 1099, 1038, 837, 774 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): 5.70-5.61 (*m*, 1 H), 5.18 (*dd*, $J = 4.4, 11.6$ Hz, 2 H), 4.70 (*d*, $J = 6.7$ Hz, 1 H), 4.53 (*d*, $J = 6.7$ Hz, 1 H), 4.02-3.92 (*m*, 1 H), 3.60 (*t*, $J = 6.2$ Hz, 2 H), 3.37 (*s*, 3 H), 1.67-1.32 (*m*, 6 H), 0.88 (*s*, 9 H), 0.04 (*s*, 6 H). ¹³C NMR (75 MHz, CDCl₃): 138.3, 117.1, 93.6, 77.2, 63.0, 55.3, 35.1, 32.6, 25.9, 21.7, 18.3, -5.3. HRMS (ESI): m/z $[M+1]^+$ calcd for C₁₅H₃₃O₃Si = 289.2193, found = 289.2189.

4.6. (S)-5-(Methoxy methoxy) hept-6-en-1-ol (9): To a stirred solution of silyl ether **8** (1.5 g, 5.20 mmol) in methanol (20 mL) was added catalytic amount of PTSA and stirred for 1 h at r.t. After completion of the reaction, methanol was removed, diluted with H₂O (10 mL) and extracted into ether (3 × 20 mL). The combining ether extracts was dried over Na₂SO₄ and evaporated under reduced pressure. The residue was purified by column chromatography (Hexane: EtOAc 7:3) to afford pure product **9** (0.85 g, 94%) as a colorless liquid. $[\alpha]_D^{25} = -27.7$ ($c = 0.4$, CHCl₃). IR (neat): 3425, 2933, 1219, 1037, 772 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): 5.70-5.62 (*m*, 1 H), 5.18 (*dd*, $J = 4.5, 10.1$ Hz, 2 H), 4.70 (*d*, $J = 6.4$ Hz, 1 H), 4.53 (*d*, $J = 6.7$ Hz, 1 H), 4.01-3.92 (*m*, 1 H), 3.64 (*t*, $J = 6.4$ Hz, 2 H), 3.37 (*s*, 3 H), 1.74-1.36 (*m*, 6 H). ¹³C NMR (75 MHz, CDCl₃): 138.1, 117.1, 93.6, 77.2, 62.5, 55.3, 35.0, 32.4, 21.4. HRMS (ESI): m/z $[M+Na]^+$ calcd for C₉H₁₈O₃Na = 197.1148, found = 197.1150.

4.7. (S)-5-(Methoxy methoxy) hept-6-enoic acid (10): To a solution of the compound **9** (0.8 g, 4.59 mmol) in 1:1 acetonitrile-water solution (20 mL) was added [bis (acetoxymethyl)-iodo benzene] BAIB (4.44 g, 13.79 mmol), 2, 2, 6, 6-tetramethyl-1-piperidinyloxy (TEMPO) (0.21 g, 1.37 mmol) and stirred for 3 h at r.t. After completion of the reaction noticed by TLC, the reaction mixture was quenched with hypo and extracted into EtOAc (2 × 10 mL). The combining extracts was dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography (Hexane: EtOAc 6:4) to obtain pure compound **10** (0.76 g, 88%) as colorless liquid. $[\alpha]_D^{25} = -28.6$ ($c = 0.5$, CHCl₃). IR (neat): 2938, 2826, 1709, 1645, 1150, 1032, 771 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): 5.71-5.62 (*m*, 1 H), 5.20 (*dd*, $J = 6.0, 10.1$ Hz, 2

H), 4.70 (*d*, *J* = 6.7 Hz, 1 H), 4.53 (*d*, *J* = 6.7 Hz, 1 H), 4.03-3.97 (*m*, 1 H), 3.37 (*s*, 3 H), 2.39 (*t*, *J* = 7.1 Hz, 2 H), 1.81-1.52 (*m*, 6 H). ¹³C NMR (75 MHz, CDCl₃): 179.4, 137.8, 117.6, 93.6, 76.8, 55.4, 34.5, 33.8, 20.6. HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₉H₁₈O₄Na = 211.0941, found = 211.10944.

4.8. (S)- ((R)-Pent-4-en-2-yl) 5-(methoxy methoxy) hept-6-enoate (13): To a cooled (0 °C) solution of the compound **10** (0.3 g, 1.59 mmol) in dry CH₂Cl₂ (5 mL) was added DCC (0.49 g, 2.38 mmol), DMAP (0.038 g, 0.318 mmol) under N₂ atmosphere and stirred for 0.5 h. The alcohol **11** (0.27 g, 3.19 mmol) in CH₂Cl₂ was added to the above reaction mass and stirred for 4 h at r.t. After completion of the reaction as noticed by TLC, the reaction mixture was diluted with H₂O (15 mL) and extracted into CH₂Cl₂ (2 × 10 mL). The combining extracts was dried over Na₂SO₄ and concentrated under reduced pressure. The crude residue was purified by column chromatography (Hexane: EtOAc 9:1) to obtain pure compound **13** (0.32 g, 80%) as liquid. [α]_D²⁵ = - 5.9 (*c* = 0.6, CHCl₃). IR (neat): 2979, 2936, 1733, 1643, 1034, 772 cm⁻¹. ¹H NMR (300 MHz, CDCl₃): 5.78-5.59 (*m*, 2 H), 5.22-5.15 (*m*, 2 H), 5.09-5.02 (*m*, 2 H), 4.98-4.92 (*m*, 1 H), 4.68 (*d*, *J* = 6.7 Hz, 1 H), 4.51 (*d*, *J* = 6.7 Hz, 1 H), 4.00-3.95 (*m*, 1 H), 3.35 (*s*, 3 H), 2.35-2.21 (*m*, 4 H), 1.78-1.47 (*m*, 4 H), 1.19 (*d*, *J* = 6.4 Hz, 3 H). ¹³C NMR (75 MHz, CDCl₃): 172.8, 137.9, 133.6, 117.5, 117.3, 93.6, 76.7, 69.7, 55.3, 40.2, 34.6, 34.2, 20.8, 19.4. HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₁₄H₂₄O₄Na = 279.1567, found = 279.1569.

^1H and ^{13}C NMR spectral copies of compounds

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 4

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 5

^{13}C NMR (300 MHz, CDCl_3) Spectrum of Compound 5

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 6

¹H NMR (300 MHz, CDCl₃) Spectrum of Compound 7

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 7

16

17

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 9

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 9

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 10

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 10

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 12

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 12

25

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 14

B CHINNA BABU
YVL-AZ-2
13C IN CDCL3

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 14

^1H NMR (300 MHz, CDCl_3) Spectrum of Compound 1

^{13}C NMR (75 MHz, CDCl_3) Spectrum of Compound 1