Supporting Information for

Total synthesis of (+)-aspicilin from d-mannitol

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Experimental Section

General

Reactions were conducted under N₂ in anhydrous solvents such as CH₂Cl₂, THF, and EtOAc. All reactions were monitored by TLC (silica-coated glass plates and visualizing under UV light). Yield refers to chromatographically and spectroscopically (¹H, ¹³C NMR) pure product. Air sensitive reagents were transferred by syringe or double-ended needle. Evaporation of solvents was performed at reduced pressure using Buchi rotary evaporator. ¹H and ¹³C NMR spectra of samples in CDCl₃ were recorded on Varian FT-200 MHz (Gemini) and Bruker UXNMR FT-300 MHz (Avance) spectrometers. Chemical shifts (δ) are reported relative to TMS (δ = 0.0) as an internal standard. Mass spectra were recorded in EI conditions at 70 eV on LC-MSD (Agilent technologies) spectrometers. All high resolution spectra were recorded on QSTAR XL hybrid ms/ms system (Applied Biosystems/ MDS scienx, foster city, USA), equipped with ESI source. Column chromatography was performed on silica gel (60–120 mesh) supplied by Acme Chemical Co., India. TLC was performed on Merck 60 F-254 silica gel plates. Optical rotations were measured with JASCO DIP-370 Polarimeter at 25 °C.
(1R,2S,3R)-2,3-di(benzyloxy)-1-[(1,1,1-triethylsilyl)oxy]methyl-4-pentenyl)oxy] (triethyl)silane (9)

To a stirred solution of diol 8 (0.89 g, 2.71 mmol) and imidazole (0.38 g, 6 mmol) in DCM (15 mL) at 0 °C was added chlorotriethylsilane (0.89 mL, 6 mmol) slowly in dropwise manner. After 6h, the reaction mixture was quenched with ice cold water and extracted with DCM, dried over Na₂SO₄ and concentrated under vacuo. The crude product was purified by column chromatography (10% EtOAc/hexane) to give 9 (1.28 g, 85%).

\[ \alpha \]̅\(_{D}^{25} +2.8 \ (c \ 0.5, \ CHCl_3); \]

\(^1\)H NMR (300 MHz, CDCl₃): \( \delta \) 7.33-7.18 (m, 10H), 5.9-5.78 (m, 1H), 5.34-5.27 (m, 2H), 4.73 (s, 2H), 4.6-4.35 (ABq, \( J = 12.0 \) Hz, 2H), 4.04-3.98 (m, 1H), 3.93-3.88 (m, 1H), 3.82-3.76 (dd, \( J = 5.3, 9.8 \) Hz, 1H), 3.56 -3.49 (m, 2H), 0.96-0.89 (m, 18H), 0.61-0.51 (m, 12H);

\(^{13}\)C NMR (75 MHz, CDCl₃): \( \delta \) 139.2, 138.6, 135.9, 128.1, 128.0, 127.8, 127.7, 127.2, 127.1, 118.3, 85.6, 81.5, 75.1, 74.1, 70.7, 64, 6.9, 6.7, 4.9, 4.3;

IR(neat): \( \nu \) 2954, 2877, 1457, 1413, 1238, 1088 cm\(^{-1}\);

ESI-MS: \( m/z \): 579 [M+Na]⁺;

HRMS \( m/z \) calcd for C\(_{32}\)H\(_{52}\)O\(_4\)NaSi\(_2\) [M+Na]⁺: 579.3301, found, 579.3301.

(2S,3S,4R)-3,4-di(benzyloxy)-2-[(1,1,1-triethylsilyl)oxy]-5-hexenal (2)

To a -78 °C cooled solution of oxalyl chloride (1.1 mL, 11.5 mmol) in CH₂Cl₂ (20 mL) was added DMSO (0.8 mL, 11.5 mmol) in a dropwise manner. After 15 min, di-TES ether 9 (1.28 g, 2.3 mmol) in CH₂Cl₂ (8 mL) was added to the above mixture and allowed to stir at -78 °C for 20 min and then at -40 °C for another 20 min. The resulting mixture was again cooled to -78 °C and then treated with Et₃N (1.9 mL, 13.78 mmol). The mixture was allowed to warm to room temperature and diluted with CH₂Cl₂ and then washed with ice-cold water and followed by brine solution. Removal of the solvent followed by purification on silica gel column chromatography (5% EtOAc/hexane) gave the pure aldehyde 2 (1.0 g, 80%).

\[ \alpha \]̅\(_{D}^{25} -1.6 \ (c \ 1, \ CHCl_3);

\(^1\)H NMR (300 MHz, CDCl₃): \( \delta \) 9.55 (s, 1H), 7.30-7.16 (m, 10H), 5.81-5.67 (m, 1H), 5.34-5.26 (m, 2H), 4.66 (s, 2H), 4.56-4.29 (ABq, \( J = 11.7 \) Hz, 2H), 4.19-4.16 (m, 1H), 4.03-3.98 (m, 1H), 3.73-3.69 (dd, \( J = 6.9, 2.4 \) Hz, 1H), 0.89-0.82 (m, 9H), 0.56-0.47 (m,
6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 203.1, 138.2, 135.1, 128.2, 128.1, 127.8, 127.7, 127.5, 127.4, 120.0, 85.1, 80.8, 78.4, 74.1, 70.8, 29.6, 6.6, 4.6;
IR (neat): $\nu$ 2924, 2877, 1733, 1458, 1082 cm$^{-1}$;
ESI-MS: $m/z$: 441 [M+H]$^+$;
HRMS $m/z$ calcld for C$_{26}$H$_{36}$O$_4$NaSi [M+Na]$^+$: 463.2280, found, 463.2280.

2-[10-(benzyloxy)decyl]oxirane (11)
To a stirred solution of olefin (4.0 g, 14.6 mmol) obtained from 10 in dry CH$_2$Cl$_2$ (50 mL) was added NaHCO$_3$ (1.47 g, 17.5 mmol), followed by m-CPBA (3.02 g, 17.5 mmol). The resulting mixture was allowed to stir at 25 ºC for 2h. The reaction mixture was diluted with water (50 mL) and extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layers were washed with brine (2 × 100 mL) and dried over anhydrous Na$_2$SO$_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (5% EtOAc/hexane) to afford pure product 11 (3.56 g, 84%) as a colorless oil.

(R)-2-[10-(benzyloxy)decyl]oxirane (12)
A mixture of (R,R)-(-)-N,N'-bis(3,5-di-tert-butylsalicylidene)-1,2-cyclohexanediaminocobalt (36.0 mg, 0.06 mmol), toluene (0.13 mL) and AcOH (0.014 mL, 0.241 mmol) was stirred in open air for 1 h at 25 ºC. The solvent was removed by rotary evaporator under reduced pressure and the brown residue was dried under reduced pressure. The oxirane 11 (3.5 g, 12.05 mmol) was added in one portion, and the mixture was cooled in ice-bath and water (0.12 mL, 6.6 mmol) was added slowly at 0 ºC. The resulting mixture was allowed to stir for 24 h at 25 ºC. The product 12 was purified by column chromatography (10% EtOAc/hexane) in 45% (1.57 g) yield.

[$\alpha$]$^25_D$ +2.3 (c 0.5, CHCl$_3$); >98% ee.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.31-7.27 (m, 5H), 4.46 (s, 2H), 3.42 (t, $J$ = 6.0 Hz, 2H), 2.86-2.80 (m, 1H), 2.70-2.66 (m, 1H), 2.41-2.39 (dd, $J$ = 5.3, 2.3 Hz, 1H), 1.63-1.53 (m, 2H), 1.42-1.25 (m, 16H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 138.6, 128.2, 127.5, 127.3, 72.7, 70.4, 52.3, 47.0, 32.4, 29.7, 29.4, 29.3, 26.1, 25.8;
IR (neat): $\nu$ 2927, 2854, 1637, 1355, 1258, 1104, 771 cm$^{-1}$;
ESI-MS: $m/z$: 313 [M+Na]$^+$;

(S)-11-[1-(tert-butyl)-1,1-dimethylsilyl]oxydodecan-1-ol (15)
A solution of benzyl ether (440 mg, 1.5 mmol) obtained from 14 was added to sodium (52.5 mg, 7.5 mmol) in liq. NH₃ (10 mL) in dry THF (6 mL). The mixture was stirred for 5 min and quenched with solid NH₄Cl. Ammonia was allowed to evaporate and the residual mixture was taken in diethyl ether (20 mL) and washed with water (24 mL), brine solution (14 mL) and dried over anhydrous Na₂SO₄. Removal of the solvent followed by purification on column chromatography (30% EtOAc/hexane) gave the pure alcohol 15 (303 mg, 94%) as a colourless liquid.

\[ \alpha_{25}^D +4.8 \ (c \ 0.5, \ CHCl_3) ; \]

\(^1\)H NMR (300 MHz, CDCl₃): \( \delta \) 3.79-3.7 (m, 1H), 3.61 (t, \( J = 3.6 \) Hz, 2H), 1.62-1.5 (m, 2H), 1.37-1.25 (m, 17H), 1.10 (d, \( J = 6.0 \) Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H).;

\(^{13}\)C NMR (75 MHz, CDCl₃): \( \delta \) 68.7, 62.8, 39.7, 32.7, 29.6, 29.5, 29.4, 25.8, 25.7, 23.7, 18.1, -4.4, -4.7; IR (neat): \( \nu \) 3346, 2928, 2856, 1465, 1371, 1254 cm\(^{-1}\).

ESI-MS: \( m/z \): 317 [M+H]\(^+\);

**tert-butyl(dimethyl)[((1S)-1-methyl-10-undecenyl]oxysilane (16)**

To a solution of iodo compound (0.513g, 1.2 mmol) obtained from 15 in THF was added \( t \)-BuOK (0.26 g, 2.4 mmol) in small portions at 0 °C. The mixture was stirred for 6h and quenched with cold water and then extracted with ethyl acetate (3 x 20 mL) followed by washed with brain solution. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (5% EtOAc/hexane) to give 16 (0.345g, 96%) as colourless oil.

\[ \alpha_{25}^D +4.2 \ (c \ 0.75, \ CHCl_3) ; \]

\(^1\)H NMR (300 MHz, CDCl₃): \( \delta \) 5.83-5.7 (m, 1H), 5.0-4.88 (m, 2H), 3.8-3.71 (m, 1H), 2.04 (q, \( J = 6.8 \) Hz, 2H), 1.4-1.25 (m, 14H), 1.11 (d, \( J = 6.0 \) Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); \(^{13}\)C NMR (75 MHz, CDCl₃): \( \delta \) 139.2, 114.0, 68.6, 39.7, 33.8, 29.7, 29.6, 29.4, 29.1, 28.9, 25.9, 25.8, 23.8, 18.1, -4.4, -4.7; IR (neat): \( \nu \) 321 [M+Na]\(^+\);

**((S)-1-methyl-10-undecenyl-2-(diethoxyphosphoryl)acetate (3)**

To a stirred solution of alcohol (0.184 g, 1 mmol) obtained from 16 in dichloromethane (3 mL) at 0 °C was added dicyclohexylcarbodimide (0.226 g, 1.1 mmol) and catalytic...
amount of DMAP. After 10 min, a solution of acid (0.21 g, 1.1 mmol) in dichloromethane (3 mL) was added at 0 °C. Then the reaction mixture was stirred at room temperature for 10 h and then diluted with diethyl ether. The resulting precipitate was filtered through Celite™ pad and the filtrate was washed with water, brine solution and dried over anhydrous sodium sulfate. The crude product was purified by column chromatography (30% EtOAc/hexanes) to give ester 3 (0.32 g, 88%).

$\left[\alpha\right]_{D}^{25} +2.8 \ (c \ 0.6, \ \text{CHCl}_3);$

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 5.81-5.67 (m, 1H), 4.96-4.83 (m, 3H), 4.18-4.04 (m, 4H), 2.91 (d, $J_{H,P} = 21.5$ Hz, 2H), 2.0-1.92 (m, 2H), 1.34-1.14 (m, 23H);

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 165.3 (d, $J_{C-P} = 6.0$ Hz, PCH$_2$C=O), 139.1, 114.1, 72.6, 62.9, 62.8, 35.8, 34.5 ($J_{C-P} = 134$ Hz, PCH$_2$C=O), 29.7, 29.5, 29.4, 29.4, 29.1, 28.9, 25.2, 19.8, 16.3, 16.2;

IR (neat): $\nu$ 2927, 1733, 1640, 1580, 1457, 1272, 1119, 1027 cm$^{-1}$;

ESI-MS: $m/z$ 385 [M+Na]$^+$;

HRMS: $m/z$: calcd for C$_{18}$H$_{35}$O$_5$NaP [M+Na]$^+$: 385.2119, found, 385.2123.

(S)-1-methyl-10-undecenyl(2$E$,4$R$,5$S$,6$R$)-5,6-di(benzyloxy)-4-[(1,1,1-triethylsilyl) oxy]-2,7-octadienoate (17)

To a stirred solution of phosphonate 3 (0.33g, 0.91 mmol) and LiCl (0.05g, 1.1 mmol) mmol) in dry CH$_3$CN was added DBU (0.15 mL, 1.1 mmol) in a dropwise manner. After 15 min, aldehyde 2 was added in dry CH$_3$CN to the above reaction mixture and stirred for 30 min at 25 °C. Then the mixture was diluted with ether (10 mL) followed by water (10 mL) and the layers were separated. The combined organic layers were dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. The crude product was purified by column chromatography (10% EtOAc/hexanes) to give the product 17 (0.477g, 80% yield) as a colourless oil.

$[\alpha]_{D}^{25} +2.2 \ (c \ 1.1, \ \text{CHCl}_3);$

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.27-7.15 (m, 10H), 6.96 (dd, $J = 15.6$, 5.8 Hz, 1H), 5.95 (dd, $J = 15.6$, 1.5 Hz, 1H), 5.85-5.65 (m, 2H), 5.3-5.19 (m, 2H), 4.95-4.82 (m, 3H), 4.69-4.28 (m, 5H), 3.89 (dd, $J = 7.5$, 5.8 Hz, 1H), 3.48 (dd, $J = 5.6$, 3.9 Hz, 1H), 1.99-1.91 (m, 2H), 1.32-1.13 (m, 17H), 0.88-0.81 (m, 9H), 0.53-0.45 (m, 6H).
\( ^{13}\text{C} \text{NMR (75MHz, CDCl}_3\):} \ \delta 165.9, 147.3, 139.1, 138.5, 138.3, 135.5, 128.2, 128.1, 128.0, 127.8, 127.4, 122.5, 118.9, 114.1, 85.8, 81.0, 74.8, 72.5, 70.9, 70.7, 35.9, 33.7, 29.5, 29.4, 29.1, 28.9, 25.3, 20.0, 6.7, 4.8; \\
\text{IR (neat): } \nu 2924, 2854, 1717, 1633, 1260, 1085, 1020 \text{ cm}^{-1}; \\
\text{ESI-MS: } m/z: 666 \left[\text{M+NH}_4\right]^+; \\
\text{HRMS: } m/z: \text{calcd for } C_{40}H_{64}NO_5Si[M+NH_4]^+: 666.4553, \text{found, 666.4557}; \\
\text{(5R,6S,7R,18S)-6,7-di(benzyloxy)-18-methyl-5-[(1,1,1-triethylsilyl)oxy]-1-oxa-3-cyclooctadecen-2-one (19)} \\
\text{A mixture of compound } 18 \text{ (100 mg, 0.16 mmol) and 5\% Pd on BaSO}_4 \text{ (40 mg) in ethyl acetate (6 mL) was stirred under hydrogen atmosphere at 18 °C for 1h. The resulting mixture was then filtered through a short pad of Celite}^{TM} \text{ which was washed with ethyl acetate (10 mL). The combined filtrates were concentrated under reduced pressure to afford the product as colourless oil which was purified by chromatography (5 \% EtOAc/hexanes). Concentration of the appropriate fractions (R}_f 0.6 \text{ gave the compound } 19 \text{ (95 mg, 95\%).} \\
\text{[\alpha]^{25}_D} +2.3 \text{ (c 0.75, CHCl}_3\); \\
\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_3\):} \ \delta 7.34-7.14 \text{ (m,10H), 7.02 (dd, } J = 15.8, 7.5 \text{ Hz, 1H), 5.88} \\
\text{ (d, } J = 15.6 \text{ Hz, 1H), 4.98-4.85} \text{ (m, 2H), 4.71-4.62} \text{ (m, 2H), 4.43-4.35} \text{ (m, 2H), 3.62} \text{ (dd,}
\text{ } J = 7.9, 1.5 \text{ Hz, 1H), 3.30-3.23} \text{ (m, 1H), 1.52-1.08} \text{ (m, 23H), 0.88} \text{ (t, } J = 7.9 \text{ Hz, 9H),}
\text{ 0.57-0.49} \text{ (m, 6H);} \ \text{\textsuperscript{13}C NMR (75 MHz, CDCl}_3\):} \ \delta 165.7, 146.4, 139.0, 138.7, 128.2,
\text{ 128.1, 127.8, 127.5, 127.3, 122.7, 86.8, 78.5, 75.1, 74.4, 73.5, 70.9, 35.2, 31.4,}
\text{ 28.1, 27.9, 27.2, 26.7, 26.4, 25.8, 24.8, 23.1, 20.3, 6.8, 4.8;}
\text{IR (neat): } \nu 2926, 2854, 1717, 1445, 1260, 1072 \text{ cm}^{-1}; \\
\text{ESI-MS: } m/z: 640 \left[\text{M+NH}_4\right]^+; \\
\text{HRMS: } m/z: \text{calcd for } C_{38}H_{58}O_5NaSi [M+Na]^+: 645.3951, \text{found, 645.3971.}