Supporting Information
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A Concise Total Synthesis of 2-epi-(−)-Pachastrissamine via a Three-Component Tandem Cross-Metathesis/Intramolecular $S_N2'$ Substitution/Cross-Metathesis Sequence

Dongjo Lee*

Department of Pharmacology, College of Medicine, Dankook University, San#29, Anseo-dong, Dongnam-gu, Cheonan-si, Chungnam 330-714, Republic of Korea

drlee21@dankook.ac.kr

Part A (S1–S7)
Experimental Procedures and Product Characterization

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I. Materials and Methods

General Methods: Except as otherwise indicated, reactions were carried out under an argon atmosphere in flame- or oven-dried glassware. In aqueous work-up, all organic solutions were dried over sodium sulfate or magnesium sulfate, and filtered prior to rotary evaporation at water aspirator pressure. Reactions were monitored by thin layer chromatography (TLC) with 0.25-mm E. Merck precoated silica gel plates (Kieselgel 60F$_{254}$, Merck). Spots were detected by viewing under a UV light, colorizing with charring after dipping in anisaldehyde solution with acetic acid and sulfuric acid and
MeOH, or in KMnO₄ solution with sulfuric acid and ethanol, or ceric ammonium molybdate solution with sulfuric acid and ethanol. Silica gel for flash chromatography (particle size 0.040-0.063 mm) was supplied by E. Merck. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted.

**Materials:** Commercial reagents and solvents were used as received with the following exceptions. All solvents were freshly purified and dried by standard techniques just before use. Dichloromethane (CH₂Cl₂), toluene (PhMe) were distilled from calcium hydride (CaH₂).

**Instrumentation:** ¹H and ¹³C spectra were recorded on a Bruker AMX-500 (500 MHz) and a Bruker advance 400 (400 MHz) spectrometer. Chemical shifts are reported as δ value relative to internal chloroform (δ 7.26 for ¹H and δ 77.0 for ¹³C). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constant in Hz, and assignment. Infrared (IR) spectra were measured on a Perkin-Elmer 1600 FT-IR spectrometer referenced to a polystyrene standard. Data are represented as follows: frequency of the absorption (cm⁻¹), intensity of absorption (s = strong, m = medium, w = weak, br = broad), and assignment (where appropriate). High resolution mass spectra were recorded by the mass spectrometry staff at the Seoul National University national center for inter-university research facilities using JEOL JMS-700 (FAB or CI). High resolution values are calculated to four decimal places from the molecular formula, all found values being within a tolerance of 5 ppm. Optical rotations were measured using a Jasco P-2000 in a cell of 1 dm path length (l).
II. Experimental Procedures

Tandem Olefin Cross-Metathesis/$S_N2'$ Substitution

To a solution of the known olefin (+)-8 (21.5 mg, 0.150 mmol) in CH$_2$Cl$_2$ (1.5 mL) were added CH$_2$=CHCH$_2$Cl (0.25 mL, 3.004 mmol) and Grubbs second-generation catalyst 11 (IMesH$_2$)(PC$_3$)(Cl)$_2$Ru=CHPh, Grubbs II) (12.8 mg, 0.015 mmol) under N$_2$ atmosphere at room temperature. The reaction mixture was heated to reflux for 4 h under N$_2$ atmosphere, and an additional amount of Grubbs second-generation catalyst 11 (IMesH$_2$)(PC$_3$)(Cl)$_2$Ru=CHPh, Grubbs II) (12.8 mg, 0.015 mmol) was added. The reaction mixture was stirred at 45 °C for additional 12 h under N$_2$ atmosphere, then cooled to room temperature and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel, using hexanes/acetone (1:1) as elutant, provided a 10:1 mixture of (-)-7a and (-)-7b (14.4 mg, 62% isolated yield, 77% Based On Recovered Starting Material).

To a solution of the known olefin (+)-8 (29.9 mg, 0.209 mmol) in CH$_2$Cl$_2$ (1.74 mL) were added CH$_2$=CHCH$_2$Cl (0.34 mL, 4.178 mmol) and Grubbs second-generation catalyst 11 (IMesH$_2$)(PC$_3$)(Cl)$_2$Ru=CHPh, Grubbs II) (35.5 mg, 0.042 mmol) under N$_2$ atmosphere at room temperature. The reaction mixture was stirred at 45 °C for 2 h under N$_2$ atmosphere, then diluted with toluene (PhMe) (1.74 mL) was added. The reaction mixture was stirred at 100 °C for additional 12 h under N$_2$ atmosphere, then cooled to room temperature and concentrated in vacuo. Purification of the residue by flash
chromatography on silica gel, using hexanes/acetone (1:1) as eluant, provided a 2.3:1 mixture of (−)-7a and (−)-7b (13.9 mg, 43% isolated yield, 61% Based On Recovered Starting Material).

(3aR,6S,6aR)-6-vinyltetrahydrofuro[3,4-d]oxazol-2(3H)-one (−)-7a

[α]D25 −147.4 (c 0.30, CHCl3);

1H NMR (500 MHz, CDCl3): δ 6.15 (br, 1−NH), 5.77 (ddd, J = 17.2, 10.7, 4.6 Hz, 1H), 5.39 (d, J = 17.4 Hz, 1H), 5.30 (d, J = 10.7 Hz, 1H), 4.93 (d, J = 7.8 Hz, 1H), 4.69 (d, J = 2.1 Hz, 1H), 4.38−4.39 (m, 1H), 3.88−3.94 (m, 2H);

13C NMR (75 MHz, CDCl3): δ 158.9, 132.9, 118.0, 84.3, 83.9, 73.0, 56.7;

IR (Neat): 3309, 1754, 1408, 1211, 1047, 944, 768 (cm−1);

HRMS (FAB) found 156.0668 [(M+H)+]; calcd for C7H10NO: 156.0661.

(3aR,6R,6aR)-6-vinyltetrahydrofuro[3,4-d]oxazol-2(3H)-one (−)-7b

[α]D25 −108.2 (c 0.37, CHCl3);

1H NMR (500 MHz, CDCl3): δ 6.37 (br, 1−NH), 5.98 (ddd, J = 17.4, 10.6, 6.9 Hz, 1H), 5.47 (d, J = 17.3 Hz, 1H), 5.40 (d, J = 10.5 Hz, 1H), 5.00 (dd, J = 7.4, 3.8 Hz, 1H), 4.42 (dd, J = 7.4, 4.1 Hz, 1H), 4.01−4.08 (m, 2H), 3.60 (dd, J = 10.5, 4.0 Hz, 1H);

13C NMR (75 MHz, CDCl3): δ 159.2, 130.6, 120.4, 83.9, 81.6, 73.5, 57.3;

IR (Neat): 3300, 1746, 1415, 1084, 773, 694 (cm−1);

HRMS (Cl) found 156.0662 [(M+H)+]; calcd for C7H10NO: 156.0661.

(3aR,6S,6aR)-6-((E)-tetradec-1-en-1-yl)tetrahydrofuro[3,4-d]oxazol-2(3H)-one (−)-6

To a solution of (−)-7 (9.70 mg, 0.063 mmol) in CH2Cl2 (2 mL) were added 1-tetradecene (0.48 mL, 1.876 mmol) and Grubbs’ second-generation catalyst 11 (IMesH2(PCy3)(Cl)2Ru=CHPh, Grubbs II) (10.60 mg, 0.013 mmol) at room temperature. The reaction mixture was stirred at 45 °C for 2 h under N2 atmosphere, then cooled to room temperature and concentrated in vacuo. Purification of the residue
by flash chromatography on silica gel, using hexanes/EtOAc (1:1) as eluant, provided (−)-6 (17.19 mg, 85%, E/Z = 10:1).

To a solution of (+)-8 (33.30 mg, 0.233 mmol) in CH₂Cl₂ (2 mL) were added CH₃=CHCH₂Cl (0.38 mL, 4.653 mmol) and Grubbs second-generation catalyst 11 (IMesH₂)(PCy₃)(Cl)₂Ru=CHPh, Grubbs II) (10.0 mg, 0.023 mmol) at room temperature. The reaction mixture was stirred at 45 °C for 2 h under N₂ atmosphere, and an additional amount of Grubbs second-generation catalyst (IMesH₂)(PCy₃)(Cl)₂Ru=CHPh, Grubbs II) (10.0 mg, 0.023 mmol) was added. The reaction mixture was heated to reflux for 12 h under N₂ atmosphere. 1-Tetradecene (1.18 mL, 4.653 mmol) and Grubbs second-generation catalyst (IMesH₂)(PCy₃)(Cl)₂Ru=CHPh, Grubbs II) (10.0 mg, 0.023 mmol) were added to the resulting mixture. The reaction mixture was stirred at 45 °C for 2 h under N₂ atmosphere, then cooled to room temperature and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel, using hexanes/EtOAc (1:1) as eluant, provided (−)-6 (33.86 mg, 45%).

[α]D⁰ +80.4 (c 0.70, CHCl₃);

¹H NMR (CDCl₃, 500 MHz): δ 6.23 (br, 1-NH), 5.80 (ddd, J = 14.7, 6.5, 6.5 Hz, 1H), 5.36 (dd, J = 15.6, 5.7 Hz, 1H), 4.87 (d, J = 7.9 Hz, 1H), 4.61 (d, J = 5.1 Hz, 1H), 4.37 (t, J = 5.6 Hz, 1H), 3.92 (dd, J = 10.2, 4.7 Hz, 1H), 3.84 (d, J = 10.2 Hz, 1H), 2.0 (dt, J = 14.0, 7.0 Hz, 2H), 1.37 (t, J = 6.7 Hz, 2H), 1.20–1.31 (m, 18H), 0.88 (t, J = 6.7 Hz, 3H);

¹³C NMR (CDCl₃, 75 MHz): δ 159.1, 135.5, 124.2, 84.3, 84.2, 72.8, 56.7, 32.3, 31.9, 29.6, 29.4, 29.3, 29.1, 28.8, 22.7, 14.1;

IR (Neat): 3269, 2922, 2851, 1713, 1468, 1248, 1062, 956, 764 (cm⁻¹);

HRMS (FAB) Found 324.2546 [(M+H)⁺]; calcd for C₁₉H₃₄NO₃: 324.2539.

(3aR,6S,6aR)-6-tetradecyltetrahydrofuro[3,4-d]oxazol-2(3H)-one (−)-5
To a solution of (−)-6 (6.30 mg, 0.063 mmol) in EtOAc (2 mL) were added 10% Pd/C (12 mg) at room temperature. The reaction mixture was stirred under H₂ atmosphere for 4.5 h, then filtered through a pad of Celite and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel, using hexanes/EtOAc (1:1) as eluant, provided (−)-5 (4.70 mg, 74%).

[α]²⁵_D –40.1 (c 0.34, CHCl₃);

¹H NMR (CDCl₃, 500 MHz): 6 5.70 (br, 1-NH), 4.71 (dd, J = 8.1, 2.5 Hz, 1H), 4.34–4.37 (m, 1H), 4.05–4.09 (m, 1H), 3.94 (dd, J = 10.2, 5.0 Hz, 1H), 3.77 (dd, J = 10.2, 2.6 Hz, 1H), 1.26–1.54 (m, 26H), 0.88 (t, J = 6.8 Hz, 3H);

¹³C NMR (CDCl₃, 75 MHz): δ 158.7, 84.2, 84.0, 72.6, 56.3, 31.9, 30.6, 29.68, 29.67, 29.64, 29.62, 29.52, 29.46, 29.35, 29.29, 25.4, 22.7, 14.1;

IR (Neat): 3262, 2920, 2849, 1759, 1726, 1468, 1212, 1079, 1053, 720 (cm⁻¹);

HRMS [FAB] Found 326.2687 [(M+H)⁺; calc for C₁₉H₃₆NO₃: 326.2695].

(2R,3S,4S)-4-amino-2-tetradecyltetrahydropyran-3-ol (2-epi(−)-Pachastrissamine 2)

To a solution of (−)-5 (3.80 mg, 0.0117 mmol) in EtOH (0.5 mL) was added an aqueous KOH solution (1.0 M in H₂O, 0.5 mL) at room temperature. The reaction mixture was heated to reflux for 12 h under N₂ atmosphere and cooled to room temperature, then concentrated and dried with MeOH (1 mL x 3) and toluene (1 mL x 3) in azeotrope. Purification of the residue by flash column chromatography on silica gel, using CH₂Cl₂/MeOH/NH₄OH (100:10:1) as eluant, provided (−)-2 (2.52 mg, 72%).

[α]²⁵_D –9.6 (c 0.2, MeOH);

¹H NMR (500 MHz, CDCl₃): δ 4.13 (dd, J = 8.9, 6.5 Hz, 1H), 3.58–3.63 (m, 2H), 3.47–3.48 (m, 1H), 3.40 (dd, J = 8.8, 6.9 Hz, 1H), 1.25–1.73 (m, 29H), 0.88 (t, J = 6.8 Hz, 3H);

S6
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 85.2, 74.8, 73.2, 52.6, 33.7, 31.9, 29.68, 29.66, 29.65, 29.59, 29.55, 29.4, 25.9, 22.7, 14.1;
 IR (Neat): 3341, 3282, 3073, 2954, 2921, 2850, 1470, 1036, 759 (cm$^{-1}$);
 HRMS (Cl) Found 300.2900 [(M+H)$^+$; calcd for C$_{19}$H$_{38}$NO$_2$: 300.2903].

III. References

A Concise Total Synthesis of 2-epi-(−)-Pachastrissamine via a Three-Component Tandem Cross-Metathesis/Intramolecular $S_N2'$ Substitution/Cross-Metathesis Sequence

Dongjoo Lee*

Department of Pharmacology, College of Medicine, Dankook University, San#29, Anseo-dong, Dongnam-gu, Cheonan-si, Chungnam 330-714, Republic of Korea

drlee21@dankook.ac.kr

Part B (S1-S14)
Copies of $^1$H, $^{13}$C NMR and Other Spectra
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Yellow-small (400MHz)

(75 MHz $^{13}$C NMR, CDCl$_3$)