Supporting Information

Total Synthesis of (*R*)-Telomestatin

Takayuki Doi,^{*,a} Masahito Yoshida,^a Kazuo Shin-ya,^{b,c}
and Takashi Takahashi^{*,a}

^a*Department of Applied Chemistry, Tokyo Institute of Technology,
2-12-1 Ookayama, Meguro, Tokyo 152-8552, Japan
email: doit@apc.titech.ac.jp, ttak@apc.titech.ac.jp*

^b*Institute of Molecular and Cellular Biosciences, The University of Tokyo,
1-1-1 Yayoi, Bunkyo-ku, Tokyo 113-0032, Japan.*

^c*National Institute of Advanced Industrial Science and Technology (AIST),
Biological Information Research Center (BIRC),
Protein Network Team, Low M.W. Chemical Laboratory,
AIST Tokyo Waterfront Bio-IT Research Building,
2-42 Aomi, Koto-ku, Tokyo 135-0064, Japan*

General Techniques

NMR spectra were recorded on a JEOL Model ECP-400 (400 MHz for ^1H , 100 MHz for ^{13}C) or a Varial 500 MHz NMR instrument in the indicated solvent. Chemical shifts are reported in units parts per million (ppm) relative to chloroform (7.26 ppm for ^1H) or chloroform-*d* (77.1 ppm for ^{13}C), dichloromethane (5.32 ppm for ^1H) or dichloromethane-*d*₂ (53.5 ppm for ^{13}C), DMSO (2.49 ppm for ^1H) or DMSO-*d*₆ (39.7 ppm for ^{13}C), CH_3CN (1.931 ppm for ^1H) when internal standard is not indicated. Multiplicities are reported by using the following abbreviations: s; singlet, d; doublet, t; triplet, q; quartet, m; multiplet, br; broad, *J*; coupling constants in Hertz.

IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrophotometer. Only the strongest and/or structurally important absorption is reported as the IR data given in cm^{-1} .

Optical rotations were measured with a JASCO P-1020 polarimeter.

All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light, visualized by *p*-anisaldehyde solution.

Merck silica gel or Chlomatorex NH-silica gel was used for column chromatography.

Mass spectra were obtained on AppliedBioSystems Mariner TK3500 Biospectrometry Workstation (ESI-TOF) mass spectrometers. HRMS (ESI-TOF) were calibrated with angiotensin I (SIGMA), bradykinin (SIGMA), and neurotensin (SIGMA) as an internal standard.

Analytical HPLC (UV 254 nm) was performed on Hewlett Packard HP-1100 series system eluted with $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CH}_3\text{CO}_2\text{H}$ (70:30:0.1). (Senshu Pak PEGASIL-ODS, 5 μm , 4.6 x 250 mm, 1 mL/min).

Preparative reversed-phase HPLC (UV 254 nm) was performed on Gilson 215 system with $\text{CH}_3\text{CN}-\text{H}_2\text{O}-\text{CF}_3\text{CO}_2\text{H}$ (70:30:0.1) The column was Senshu Pak PEGASIL-ODS, 5 μm , 20 x 250 mm.

Experimental Section

Preparation of *N*-Boc-Cys(*S*-*t*Bu)-Thr-OMe (2). To a solution of *N*-Boc-Cys(*S*-*t*Bu)-OH (15.0 g, 54.1 mmol) in CH₂Cl₂ (162 mL, 3.0 mL/mmol) was added H-Thr-OMe•HCl (10.0 g, 59.5 mmol), HOBt (8.8 g, 70.3 mmol) and DIEA (12.0 mL, 70.3 mmol) at room temperature and the mixture was cooled to 0 °C. To a mixture was added EDCI•HCl (11.4 g, 59.5 mmol) at the same temperature and stirred at room temperature. After being stirred at the same temperature for 1 h, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 4% MeOH in CHCl₃ to afford *N*-Boc-Cys(*S*-*t*Bu)-Thr-OMe (2) (20.5 g, 52.5 mmol, 97%) as a colorless oil. $[\alpha]_D^{26}$ -8.6 (c = 0.76, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.21 (brd, *J* = 7.73 Hz, 1H, *NH*), 5.57 (brd, *J* = 7.73 Hz, 1H, BocNH), 4.51 (brd, *J* = 7.73 Hz, 1H, d), 4.24 (m, 2H, b and e), 3.67 (s, 3H, g), 2.84 (m, 2H, c), 1.34 (s, 9H, a), 1.22 (s, 9H, h), 1.09 (d, *J* = 6.28 Hz, 3H, f). ¹³C NMR (100 MHz, CDCl₃) δ 171.2, 170.9, 155.4, 80.1, 67.9, 57.4, 54.2, 52.4, 42.4, 30.7, 30.4, 28.1, 19.7. FT-IR (solid) 3334, 2975, 1667, 1514, 1367, 1165, 1020, 757 cm⁻¹. HRMS (ESI-TOF) calcd. for C₁₇H₃₃N₂O₆S [M+H]⁺ 393.2054 found 393.2067.

Preparation of oxazole 3. To a solution of *N*-Boc-Thr-OH (15.0 g, 57.8 mmol) in CH₂Cl₂ (174 mL, 3.0 mL/mmol) was added H-Ser-OMe•HCl (10.8 g, 69.3 mmol), HOBt (8.6 g, 63.5 mmol) and DIEA (11.8 mL, 67 mmol) at room temperature, and then cooled to 0 °C. To the mixture was added EDCI•HCl (11.6 g, 60.7 mmol) at the same temperature and the mixture was stirred at room temperature. After being stirred at the same temperature for 1 h, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of dipeptide in CH₂Cl₂ (174 mL, 3.0 mL/mmol) was added a solution of DAST (9.2 mL, 69.3 mmol) in CH₂Cl₂ at -78 °C under argon. After being stirred at the same temperature for 1 h, the mixture was poured into saturated aqueous NaHCO₃ at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of oxazoline in CH₂Cl₂ (174 mL, 3.0 mL/mmol) was added DBU (22.4 mL, 174 mmol) at 0 °C under argon. To the mixture was slowly added BrCCl₃ (17.1 mL, 174 mmol) at the same temperature. After being stirred at room temperature for 3 h, the mixture was poured into 3 M HCl at 0 °C. The aqueous layer was extracted with twice ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO₃, brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 20% ethyl acetate in hexane to afford oxazole **i** (11.8 g, 34.6 mmol, 60% in 3 steps) as a white powder. $[\alpha]_D^{28}$ -56 (c = 0.84, CHCl₃). ¹H NMR (400 MHz, DMSO-*d*₆, 80 °C) δ 8.75 (s, 1H, g), 4.52 (d, *J* = 8.21 Hz, 1H, f), 4.23 (dq, *J*_{d,e} = 6.28 Hz, *J*_{d,f} = 8.21 Hz, 1H, d),

3.82 (s, 3H, h), 1.60 (s, 6H, b and c), 1.28 (d, $J = 6.28$ Hz, 3H, e), 1.23 (brs, 9H, a). ^{13}C NMR (100 MHz, DMSO- d_6 , 80 °C) δ 162.0, 160.5, 144.8, 132.3, 93.9, 79.3, 74.1, 60.6, 51.2, 27.3, 17.2. FT-IR (solid) 3100, 2982, 1705, 1585, 1393, 1260, 1134, 1106, 856, 774, 516 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{16}\text{H}_{24}\text{N}_5\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 363.1527 found 363.1524.

To a solution of oxazole **i** (7.4 g, 21.7 mmol) in 1,4-dioxane (10 mL) was added 4 M HCl/1,4-dioxane (30 mL) at 0 °C under argon. After being stirred at room temperature for 1.5 h, the solvent was removed under reduced pressure. The crude **3** was used for the next reaction without further purification.

Preparation of oxazole 4a. To a solution of *N*-Boc-Ser-OH (13.0 g, 53.0 mmol) in CH_2Cl_2 (159 mL, 3.0 mL/mmol) was added H-Ser-OMe•HCl (9.1 g, 58.3 mmol), HOBT (8.6 g, 63.6 mmol) and DIEA (12.0 mL, 68.9 mmol) at room temperature, and the mixture was cooled to 0 °C. To the mixture was added EDCI•HCl (11.2 g, 58.3 mmol) at the same temperature and stirred at room temperature. After being stirred at the same temperature for 1 h, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of dipeptide in CH_2Cl_2 (159 mL, 3.0 mL/mmol) was added a solution of DAST (8.4 mL, 63.6 mmol) in CH_2Cl_2 at -78 °C under argon. After being stirred at the same temperature for 1 h, the mixture was poured into saturated aqueous NaHCO_3 at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of oxazoline in CH_2Cl_2 (159 mL, 3.0 mL/mmol) was added DBU (24 mL, 159 mmol) at 0 °C under argon. To the mixture was slowly added BrCCl_3 (15.6 mL, 159 mmol) at the same temperature. After being stirred at room temperature for 3 h, the mixture was poured into 3 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 20% ethyl acetate in hexane to afford **ii** (11.5 g, 35.5 mmol, 67% in 3 steps) as a yellow powder. $[\alpha]_D^{27} -82$ ($c = 0.59$, CHCl_3). ^1H NMR (400 MHz, DMSO- d_6 , 80 °C) δ 8.71 (s, 1H, f), 5.08 (dd, $J_{d',e} = 2.89$ Hz, $J_{d,e} = 6.76$ Hz, 1H, e), 4.27 (dd, $J_{d,e} = 6.76$ Hz, $J_{d,d'} = 9.42$ Hz, 1H, d), 4.02 (dd, $J_{d',e} = 2.89$ Hz, $J_{d,d'} = 9.42$ Hz, 1H, d'), 3.81 (s, 3H, g), 1.63 (s, 3H, b or c), 1.52 (s, 3H, b or c), 1.31 (bs, 9H, a). ^{13}C NMR (100 MHz, DMSO- d_6 , 80 °C) δ 163.3, 160.5, 144.7, 132.2, 93.7, 78.7, 66.3, 54.1, 51.2, 27.4. FT-IR (solid) 3137, 2991, 1738, 1586, 1439, 1367, 1247, 852, 802, 657, 555 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_6$ $[\text{M}+\text{H}]^+$ 327.1551 found 327.1558.

To a solution of methyl ester **ii** (6.0 g, 18.4 mmol) in MeOH (37 mL, 2.0 mL/mmol), THF (37 mL, 2.0 mL/mmol) and H_2O (9.2 mL, 0.5 mL/mmol) was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (1.04 g, 25.0 mmol) at 0 °C. After being stirred at the same temperature for 3 h, the mixture was acidified with 3 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was recrystallized with hexane/ CH_2Cl_2 to afford **4a** (5.5 g, 17.5 mmol, 95%) as a white powder.

$[\alpha]_D^{27} -70$ ($c = 0.63$, CHCl_3). ^1H NMR (400 MHz, $\text{DMSO}-d_6$, 80°C) δ 8.59 (s, 1H, f), 5.07 (dd, $J_{d',e} = 3.38$ Hz, $J_{d,d'} = 6.76$ Hz, 1H, e), 4.26 (dd, $J_{d,e} = 6.76$ Hz, $J_{d,d'} = 9.18$ Hz, 1H, d), 4.01 (dd, $J_{d',e} = 3.38$ Hz, $J_{d,d'} = 9.18$ Hz, 1H, d'), 1.63 (s, 3H, b or c), 1.52 (s, 3H, b or c), 1.31 (brs, 9H, a). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 80°C) δ 163.0, 161.3, 144.2, 133.3, 93.7, 79.4, 78.7, 66.4, 54.1, 27.8. FT-IR (solid) 3129, 2982, 1691, 1365, 1166, 1094, 852, 768, 695, 553 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{14}\text{H}_{20}\text{N}_5\text{O}_6\text{Na}$ $[\text{M}+\text{H}]^+$ 335.1214 found 335.1210.

Benzyl ester 4b. To a solution of carboxylic acid **4a** (5.0 g, 15.7 mmol) in DMF (47.1 mL, 3.0 mL/mmol) was added K_2CO_3 (4.3 g, 31.4 mmol) at room temperature under argon, and then cooled to 0°C . To the mixture was added BnBr (2.1 mL, 17.3 mmol) at the same temperature. After being stirred at room temperature for 12 h, the mixture was filtered through a pad of Celite. The filtrate was diluted with ethyl acetate and H_2O , and the aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 13% ethyl acetate in hexane to afford benzyl ester **4b** (6.0 g, 14.9 mmol, 95%) as a yellow powder. $[\alpha]_D^{27} -69$ ($c = 0.73$, CHCl_3). ^1H NMR (400 MHz, $\text{DMSO}-d_6$, 80°C) δ 8.76 (s, 1H, f), 7.32-7.43 (m, 5H, h), 5.33 (s, 2H, g), 5.08 (dd, $J_{d',e} = 2.89$ Hz, $J_{d,e} = 6.28$ Hz, 1H, e), 4.26 (dd, $J_{d,e} = 6.28$ Hz, $J_{d,d'} = 9.18$ Hz, 1H, d), 4.03 (dd, $J_{d',e} = 2.89$ Hz, $J_{d,d'} = 9.18$ Hz, 1H, d'), 1.63 (s, 3H, b or c), 1.52 (s, 3H, b or c), 1.31 (brs, 9H, a). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 80°C) δ 163.4, 160.0, 144.9, 135.5, 132.2, 128.0, 127.6, 127.4, 93.7, 79.4, 78.7, 66.3, 65.4, 54.1, 27.4. FT-IR (solid) 3107, 2974, 1696, 1586, 1457, 1377, 1100, 982, 849, 753, 699 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{21}\text{H}_{26}\text{N}_5\text{O}_6\text{Na}$ $[\text{M}+\text{Na}]^+$ 425.1683 found 425.1699.

Methyloxazole 5. To a solution of *N*-Boc-Cys(*S*-*t*Bu)-Thr-OMe (**2**) (15.0 g, 38.2 mmol) in CH_2Cl_2 (191 mL, 5.0 mL/mmol) was added DIEA (19.5 mL, 114.6 mmol) and DMSO (13.6 mL, 191 mmol) at room temperature under argon, and then cooled to 0°C . To the mixture was added $\text{SO}_3\cdot\text{Py}$ (14.0 g, 87.9 mmol) at the same temperature. After being stirred at the same temperature for 2 h, the mixture was poured into 1 M HCl at 0°C . The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by short-pad column chromatography on flash silica gel with 40% ethyl acetate in hexane to afford ketone.

To a solution of PPh_3 (22.0 g, 84.0 mmol) in THF (343 mL, 9.0 mL/mmol) was added I_2 (9.7 g, 76.4 mmol) and NEt_3 (26.6 mL, 191 mmol) at room temperature under argon, and the mixture was cooled to -78°C . To the mixture was added dropwise a solution of the above ketone in THF (38.0 mL, 1.0 mL/mmol) at the same temperature, and then the mixture was allowed to warm up to room temperature. After being stirred at the same temperature for 2.5 h, the mixture was concentrated in vacuo. The residue was diluted with ethyl acetate and H_2O . The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 12% ethyl acetate in hexane to afford methyloxazole **5** (10.4 g, 27.9 mmol, 73% in 2 steps) as a

colorless oil. $[\alpha]_D^{26} -24$ ($c = 0.49$, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 5.48 (m, 1H, BocNH), 5.10 (m, 1H, b), 3.90 (s, 3H, e), 3.05 (m, 2H, c), 2.61 (s, 3H, d), 1.44 (s, 9H, a), 1.29 (s, 9H, f). ^{13}C NMR (100 MHz, CDCl_3) δ 162.6, 161.0, 156.6, 154.9, 127.5, 80.2, 52.0, 42.8, 32.5, 30.9, 28.3, 12.0. FT-IR (KBr) 3358, 2962, 1701, 1611, 1516, 1150, 1096, 985, 885, 606 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{17}\text{H}_{29}\text{N}_2\text{O}_5\text{S}$ $[\text{M}+\text{H}]^+$ 373.1792 found 373.1808.

Acid 6. To a solution of methyl ester **5** (7.0 g, 18.8 mmol) in MeOH (18.8 mL, 1.0 mL/mmol), THF (18.8 mL, 1.0 mL/mmol) and H_2O (5.6 mL, 0.3 mL/mmol) was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (1.0 M, 1.8 g, 43.2 mmol) at 0 °C. After being stirred at the same temperature for 3 h, the mixture was acidified with 3 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 4% methanol in CHCl_3 to afford acid **6** (6.7 g, 18.8 mmol, quant.) as a pale pink powder. $[\alpha]_D^{28} -28$ ($c = 0.91$, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 6.37 (m, 1H, BocNH), 5.12 (m, 1H, b), 3.07 (brs, 2H, c), 2.65 (s, 3H, d), 1.42 (s, 9H, a), 1.30 (s, 9H, e). ^{13}C NMR (100 MHz, CDCl_3) δ 165.1, 162.4, 157.3, 155.3, 127.3, 80.1, 49.2, 42.8, 32.5, 30.9, 28.3, 12.0. FT-IR (solid) 3312, 2972, 1706, 1514, 1366, 1163, 1101, 757, 589 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{16}\text{H}_{26}\text{N}_2\text{O}_5\text{SNa}$ $[\text{M}+\text{Na}]^+$ 381.1455 found 381.1456.

Amide 7. To a solution of crude **3** in CH_2Cl_2 (83.5 mL, 5.0 mL/mmol) was added carboxylic acid **6** (6.0 g, 16.7 mmol) and DIEA (14.2 mL, 83.5 mmol) at room temperature under argon, and the mixture was cooled to 0 °C. To the mixture was added PyBroP (10.9 g, 23.4 mmol) at the same temperature. After being stirred at room temperature for 1.5 h, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 50% ethyl acetate in hexane to afford amide **7** (10.9 g, 20.2 mmol, 93%) as a pale yellow powder. $[\alpha]_D^{29} -30$ ($c = 0.71$, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 8.20 (s, 1H, h), 7.98 (brd, $J = 8.70$ Hz, 1H, NH), 5.68 (brs, 1H, BocNH), 5.28 (dd, $J = 3.87, 8.94$ Hz, 1H, e), 5.00 (brs, 1H, b), 4.56 (m, 1H, f), 3.88 (s, 3H, i), 2.94 (m, 2H, c), 2.57 (s, 3H, d), 1.44 (s, 9H, a), 1.31 (s, 9H, j), 1.26 (d, $J = 6.76$ Hz, 3H, g). ^{13}C NMR (100 MHz, CDCl_3) δ 163.9, 162.3, 161.4, 159.9, 154.9, 154.0, 144.1, 133.0, 128.6, 80.1, 67.6, 52.3, 52.2, 49.1, 42.8, 32.1, 30.9, 28.3, 19.3, 11.7. FT-IR (solid) 3398, 2974, 1707, 1664, 1509, 1366, 1156, 1112, 844, 711 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{36}\text{N}_4\text{O}_8\text{SNa}$ $[\text{M}+\text{Na}]^+$ 563.2146 found 563.2136.

Tris-oxazole 8. To a solution of amide **7** (2.8 g, 5.18 mmol) in THF (52 mL, 10 mL/mmol) was added the Burgess reagent (1.48 g, 6.22 mmol) at room temperature under argon, and the mixture was warmed up to 70 °C. After being stirred at the same temperature for 8 h, the mixture was diluted with H_2O at 0 °C. The aqueous layer was extracted

twice with ethyl acetate. The organic layer was washed with brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of the oxazoline in CH_2Cl_2 (20.8 mL, 4.0 mL/mmol) was added DBU (3.9 mL, 25.9 mmol) at 0 °C under argon. To the mixture was added a solution of BrCCl_3 (2.54 mL, 25.9 mmol) in CH_2Cl_2 (5.2 mL, 1.0 mL/mmol) at the same temperature. After being stirred at room temperature for 8 h, the mixture was poured into 3 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 25% ethyl acetate in CHCl_3 to afford tris-oxazole **8** (2.1 g, 3.94 mmol, 75% in 2 steps) as a yellow powder. $[\alpha]_D^{29} -24$ ($c = 0.79$, CHCl_3). ^1H NMR (400 MHz, CDCl_3) δ 8.30 (s, 1H, f), 5.51 (brs, 1H, BocNH), 5.14 (brs, 1H, b), 3.91 (s, 3H, g), 3.10 (m, 2H, c), 2.80 (s, 3H, e), 2.71 (s, 3H, d), 1.45 (s, 9H, a), 1.30 (s, 9H, h). ^{13}C NMR (100 MHz, CDCl_3) δ 161.9, 161.6, 156.8, 154.9, 154.8, 151.0, 150.9, 143.4, 134.2, 125.5, 124.8, 80.2, 52.1, 49.1, 42.8, 32.6, 30.9, 28.3, 11.9. FT-IR (solid) 3343, 2962, 1689, 1515, 1324, 1276, 1161, 1043, 884, 758, 670 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{24}\text{H}_{32}\text{N}_4\text{O}_7\text{SNa}$ $[\text{M}+\text{Na}]^+$ 543.1884 found 543.1910.

Amide 9. To a solution of oxazole **4b** (4.0 g, 9.98 mmol) in 1,4-dioxane (10 mL) was added 4 M HCl/ethyl acetate (30 mL) at 0 °C under argon. After being stirred at room temperature for 1.5 h, the solvent was removed under reduced pressure. The residue was used for the next reaction without further purification.

To a solution of the residue in CH_2Cl_2 (24.9 mL, 3.0 mL/mmol) was added carboxylic acid **4a** (2.6 g, 8.32 mmol) and DIEA (8.5 mL, 49.9 mmol) at room temperature under argon and the mixture was cooled to 0 °C. To the mixture was added PyBroP (5.0 g, 10.8 mmol) at the same temperature. After being stirred at room temperature for 1.5 h, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 50% ethyl acetate in hexane to afford amide **9** (3.9 g, 6.99 mmol, 84%) as a pale yellow powder. $[\alpha]_D^{25} -48$ ($c = 0.74$, CHCl_3). ^1H NMR (400 MHz, $\text{DMSO}-d_6$, 80 °C) δ 8.74 (s, 1H, i), 8.56 (s, 1H, f), 8.17 (d, $J = 8.21$ Hz, 1H, NH), 7.32-7.43 (m, 5H, k), 5.32 (s, 2H, j), 5.22 (dt, $J_{g,h} = 5.31$ Hz, $J_{NH,h} = 8.21$ Hz, 1H, h), 5.09 (dd, $J_{d',e} = 2.89$ Hz, $J_{d,e} = 6.76$ Hz, e), 4.28 (dd, $J_{d,e} = 6.76$ Hz, $J_{d,d'} = 9.18$ Hz, 1H, d), 4.06 (dd, $J_{d',e} = 2.89$ Hz, $J_{d,d'} = 9.18$ Hz, 1H, d'), 3.91 (d, $J = 5.31$ Hz, 2H, g), 1.64 (s, 3H, b or c), 1.53 (s, 3H, b or c), 1.32 (brs, 9H, a). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$, 80 °C) δ 162.7, 160.0, 159.3, 145.2, 141.7, 135.5, 135.2, 132.1, 128.0, 127.7, 127.6, 93.7, 78.7, 66.3, 65.5, 61.3, 54.2, 49.0, 27.5. FT-IR (solid) 3397, 2982, 1688, 1599, 1368, 1252, 1114, 841, 771, 558 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{27}\text{H}_{32}\text{N}_4\text{O}_8\text{Na}$ $[\text{M}+\text{Na}]^+$ 579.2062 found 579.2060.

Tris-oxazole 10. To a solution of amide **9** (3.0 g, 5.39 mmol) in CH₂Cl₂ (16.0 mL, 3.0 mL/mmol) was added a solution of DAST (853 μ L, 6.46 mmol) in CH₂Cl₂ (5.39 mL, 1.0 mL/mmol) at –78 °C under argon. After being stirred at the same temperature for 1 h, the mixture was poured into saturated aqueous NaHCO₃ at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of oxazoline in CH₂Cl₂ (21.6 mL, 4.0 mL/mmol) was added DBU (4.0 mL, 27.0 mmol) at 0 °C under argon. To the mixture was added a solution of BrCCl₃ (2.6 mL, 27.0 mmol) in CH₂Cl₂ (5.4 mL, 1.0 mL/mmol) at the same temperature. After being stirred at room temperature for 8 h, the mixture was poured into 3 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 20% ethyl acetate in CHCl₃ to afford tris-oxazole **10** (2.1 g, 3.83 mmol, 71% in 2 steps) as a yellow powder. $[\alpha]_D^{28}$ –57 (*c* = 0.74, CHCl₃). ¹H NMR (400 MHz, DMSO-*d*₆, 80 °C) δ 8.95 (s, 1H, h), 8.92 (s, 1H, g), 8.86 (s, 1H, f), 7.33–7.47 (m, 5H, j), 5.36 (s, 2H, i), 5.15 (dd, $J_{d',e}$ = 2.89 Hz, $J_{d,e}$ = 6.28 Hz, 1H, e), 4.31 (dd, $J_{d,e}$ = 6.28 Hz, $J_{d,d'}$ = 9.18 Hz, 1H, d), 4.08 (dd, $J_{d',e}$ = 2.89 Hz, $J_{d,d'}$ = 9.18 Hz, 1H, d'), 1.67 (s, 3H, b or c), 1.54 (s, 3H, b or c), 1.32 (brs, 9H, a). ¹³C NMR (100 MHz, DMSO-*d*₆, 80 °C) δ 164.1, 159.8, 155.3, 154.6, 145.2, 140.4, 135.4, 133.1, 129.6, 128.8, 128.0, 127.7, 127.6, 93.8, 79.5, 78.7, 66.4, 65.7, 54.1, 27.4. FT-IR (solid) 3135, 2976, 1702, 1364, 1142, 1094, 974, 725, 555 cm^{–1}. HRMS (ESI-TOF) calcd. for C₂₇H₂₈N₄O₈Na [M+Na]⁺ 559.1799 found 559.1816.

Acid 11. To 10% Pd/C (100 mg, 20 wt%) was added ethyl acetate (10 mL, 2.0 mL/100 mg) and MeOH (10 mL, 2.0 mL/100 mg) under argon. The reaction vessel was purged with H₂ three times. A solution of benzyl ester **10** (500 mg, 0.93 mmol) in ethyl acetate (10 mL, 2.0 mL/100 mg) and MeOH (10 mL, 2.0 mL/100 mg) was added at room temperature. After being stirred for 1.5 h, the mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification. $[\alpha]_D^{26}$ –69 (*c* = 0.75, CHCl₃). ¹H NMR (400 MHz, DMSO-*d*₆, 80 °C) δ 8.90 (s, 1H, h), 8.85 (s, 1H, g), 8.74 (s, 1H, f), 5.15 (dd, $J_{d',e}$ = 2.89 Hz, $J_{d,e}$ = 6.29 Hz, e), 4.30 (dd, $J_{d,e}$ = 6.29 Hz, $J_{d,d'}$ = 9.18 Hz, 1H, d), 4.08 (dd, $J_{d',e}$ = 2.89 Hz, $J_{d,d'}$ = 9.18 Hz, 1H, d'), 1.67 (s, 3H, b or c), 1.54 (s, 3H, b or c), 1.32 (brs, 9H, a). FT-IR (solid) 3137, 2930, 1690, 1366, 1248, 1168, 1093, 724, 592 cm^{–1}.

Amide 12. To a solution of tris-oxazole methyl ester **8** (404 mg, 0.777 mmol) in 1,4-dioxane (5.0 mL) was added 4 M HCl/1,4-dioxane (15 mL) at 0 °C under argon. After being stirred at room temperature for 1.5 h, the mixture was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of the residue in CH₂Cl₂ (3.9 mL, 5.0 mL/mmol) was added a solution of carboxylic acid **11** (0.932 mmol) in DMF (7.8 mL, 10 mL/mmol) and DIEA (1.2 mL, 6.99 mmol) at room temperature under argon and the

mixture was cooled to 0 °C. To the mixture was added PyBroP (545 mg, 1.17 mmol) at the same temperature. After being stirred at room temperature for 1.5 h, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 20% ethyl acetate in CHCl₃ to afford amide **12** (561 mg, 0.66 mmol, 85% in 2 steps) as a pale yellow powder. $[\alpha]_D^{28}$ -20 (c = 0.65, CHCl₃). ¹H NMR (400 MHz, DMSO-*d*₆, 80 °C) δ 8.91 (s, 1H, m), 8.85 (s, 1H, h), 8.82 (s, 1H, g), 8.75 (d, *J* = 7.24 Hz, 1H, *NH*), 8.73 (s, 1H, f), 5.37 (dt, *J*_{NH,j} = 7.24 Hz, *J*_{ij} = 7.73 Hz, 1H, j), 5.15 (dd, *J*_{d',e} = 2.41 Hz, *J*_{d,e} = 6.52 Hz, 1H, e), 4.31 (dd, *J*_{d,e} = 6.52 Hz, *J*_{d,d'} = 9.42 Hz, 1H, d), 4.08 (dd, *J*_{d',e} = 2.41 Hz, *J*_{d,d'} = 9.42 Hz, 1H, d'), 3.86 (s, 3H, n), 3.29 (dd, *J*_{ij} = 7.73 Hz, *J*_{i,i'} = 13.5 Hz, 1H, i), 3.23 (dd, *J*_{ij} = 7.73 Hz, *J*_{i,i'} = 13.5 Hz, 1H, i'), 2.73 (s, 3H, l), 2.67 (s, 3H, k), 1.66 (s, 3H, b or c), 1.54 (s, 3H, b or c), 1.32 (brs, 18H, a and o). ¹³C NMR (100 MHz, DMSO-*d*₆, 80 °C) δ 164.1, 160.9, 160.5, 159.1, 155.5, 155.3, 154.0, 153.9, 150.4, 150.3, 144.4, 142.1, 140.4, 140.2, 136.2, 133.0, 129.7, 128.8, 124.5, 123.6, 93.8, 78.7, 66.4, 54.2, 51.3, 47.4, 42.1, 30.4, 30.2, 27.5, 10.9, 10.8. FT-IR (solid) 3304, 3137, 2975, 1705, 1657, 1365, 1154, 1097, 755, 724 cm⁻¹. HRMS (ESI-TOF) calcd. for C₃₉H₄₄N₈O₁₂SNa [M+Na]⁺ 871.2692 found 871.2675.

Macrolactam 13. To a solution of amide **12** (561 mg, 0.66 mmol) in 1,4-dioxane (10 mL) was added 4 M HCl/1,4-dioxane (30 mL) at 0 °C under argon. After being stirred at room temperature for 1.5 h, the mixture was concentrated in vacuo. The residue was used for the next reaction without further purification.

To a solution of the residue in MeOH (35 mL, 53 mL/mmol), THF (35 mL, 53 mL/mmol) and H₂O (5.0 mL, 7.6 mL/mmol) was added LiOH•H₂O (0.1 M, 315 mg, 7.5 mmol) at 0 °C, and the mixture was warmed up to room temperature. After being stirred at the same temperature for 1 h, the mixture was acidified with 4 M HCl/1,4-dioxane at 0 °C, and the solvent was removed under reduced pressure. The residue was dried under reduced pressure for 12 h and used for the next reaction without further purification.

To a solution of DPPA (4.3 mL, 19.8 mmol), HOBT (2.7 g, 19.8 mmol), DIEA (4.5 mL, 26.4 mmol), DMAP (81 mg, 0.66 mmol) in CH₂Cl₂ (110 mL) and DMF (70 mL) was added a solution of the residue in DMF (40 mL) dropwisely at room temperature under argon. After being stirred at room temperature for 3 d, the mixture was poured into 1 M HCl at 0 °C. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 3 M HCl, saturated aqueous NaHCO₃ and brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 4% MeOH in CHCl₃, and by GPC eluted with CHCl₃ to afford macrolactam **13** (214 mg, 0.32 mmol, 48% in 3 steps) as a white powder. $[\alpha]_D^{28}$ -6.7 (c = 0.70, CHCl₃). ¹H NMR (400 MHz, CD₂Cl₂) δ 8.53 (d, *J* = 7.28 Hz, 1H, Ser-NH), 8.45 (d, *J* = 7.25 Hz, 1H, Cys-NH), 8.31 (s, 1H, c), 8.29 (s, 1H, c), 8.27 (s, 1H, c), 8.24 (s, 1H, c), 5.40-5.55 (m, 2H, a and d), 4.17 (dd, *J* = 3.86 Hz, *J*_{b,b'} = 11.3 Hz, 1H, b), 4.00 (dd, *J* = 4.83 Hz, *J*_{b,b'} = 11.3 Hz, 1H, b'), 3.24 (dd, *J* = 5.79 Hz, *J*_{g,g'} = 13.5 Hz, 1H, e), 3.15 (dd, *J* = 4.34 Hz, *J*_{g,g'} = 13.5 Hz, 1H, e'),

2.73 (s, 3H, f), 2.68 (s, 3H, f), 1.23 (s, 9H, g). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 161.3, 159.8, 159.5, 156.7, 156.5, 155.7, 151.5, 141.8, 141.0, 140.4, 139.1, 137.4, 137.3, 131.4, 130.8, 128.7, 126.0, 125.0, 104.0, 77.9, 48.8, 42.8, 32.7, 30.9, 12.1. FT-IR (solid) 3362, 3120, 2938, 1665, 1581, 1499, 1180, 1100, 1065, 914, 768, 726, 582 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{30}\text{H}_{28}\text{N}_8\text{O}_9\text{SNa}$ $[\text{M}+\text{Na}]^+$ 699.1592 found 699.1577.

Dehydration of 13. To a solution of macrolactam **13** (200 mg, 0.295 mmol) and DBU (663 μL , 4.43 mmol) in CH_2Cl_2 (8.9 mL, 30 mL/mmol) was added MsCl (171 mL, 2.21 mmol) at 0 $^\circ\text{C}$ under argon. After being stirred at the same temperature for 3 h, the mixture was poured into H_2O at 0 $^\circ\text{C}$. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed with 1 M HCl , saturated aqueous NaHCO_3 and brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 3% MeOH in CHCl_3 to afford dehydroamide **14** (179 mg, 0.271 mmol, 92%) as a white powder. $[\alpha]_D^{26}$ -3.2 ($c = 0.39$, CHCl_3). ^1H NMR (400 MHz, CD_2Cl_2) δ 9.55 (brs, 1H, $\Delta\text{-NH}$), 8.45 (d, $J = 6.28$ Hz, 1H, Cys-NH), 8.34 (s, 1H, c), 8.28 (s, 1H, c), 8.27 (s, 1H, c), 8.22 (s, 1H, c), 6.75 (s, 1H, a), 5.84 (s, 1H, b), 5.41 (m, 1H, d), 3.27 (dd, $J = 5.80$ Hz, $J_{\text{g,g'}} = 13.0$ Hz, 1H, e), 3.16 (dd, $J = 3.87$ Hz, $J_{\text{g,g'}} = 13.0$ Hz, 1H, e'), 2.75 (s, 3H, f), 2.69 (s, 3H, f), 1.22 (s, 9H, g). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 161.3, 159.8, 159.5, 156.7, 156.5, 155.7, 155.0, 151.7, 151.5, 141.8, 141.0, 140.4, 139.1, 137.4, 137.3, 131.4, 130.8, 128.7, 126.0, 125.0, 104.0, 77.9, 48.8, 42.8, 32.7, 30.9, 12.1. FT-IR (solid) 3362, 3120, 2938, 1665, 1581, 1499, 1180, 1100, 1065, 914, 768, 726, 582 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{30}\text{H}_{26}\text{N}_8\text{O}_8\text{SNa}$ $[\text{M}+\text{Na}]^+$ 681.1487 found 681.1498.

14

Oxazoline formation for 14. A suspension of dehydroamide **14** (80 mg, 0.121 mmol) and pulverized activated MS 4A in dry CH_2Cl_2 (8.0 mL, 0.1 mL/mg) and dry MeOH (1.0 mL) was stirred at room temperature for 15 min under argon to remove a trace amount of water. A solution of *N*-bromosuccinimide (NBS) (22 mg, 0.127 mmol) in dry CH_2Cl_2 (0.8 mL, 0.01 mL/mg) was added to the reaction mixture at 0 $^\circ\text{C}$ under argon. After being stirred at the same temperature for 1 h, the mixture was filtered through a pad of Celite. The filtrate was treated with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ at 0 $^\circ\text{C}$. The aqueous layer was extracted twice with ethyl acetate. The organic layer was washed brine, dried over MgSO_4 , and filtered. The filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 2% MeOH in CHCl_3 to afford bromide **iii** (84 mg, 0.109 mmol, 90%, diastereomer mixture) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 8.89 (d, $J = 3.3$ Hz, 1H, Ala-NH), 8.62 (d, $J = 6.93$ Hz, 1H, Cys-NH), 8.34 (s, 2H, c and c), 8.24 (s, 1H, c), 8.20 (s, 1H, c), 5.34 (dd, $J = 6.93, 12.2$ Hz, 1H, d), 5.16, 5.08 (each d, $J = 10.1$ Hz, 1H, a), 4.05, 4.40 (each d, $J = 10.1$ Hz, 1H, a), 3.14-3.22 (m, 5H, b and e), 2.74 (s, 3H, f), 2.69 (s, 3H, f), 1.26 (s, 9H, g). FT-IR (solid) 3147, 2934, 1710, 1638, 1592, 1496, 1360, 1157, 915 cm^{-1} . HRMS (ESI-TOF) calcd. for $\text{C}_{31}\text{H}_{29}\text{BrN}_8\text{O}_9\text{SNa}$ $[\text{M}+\text{Na}]^+$ 791.0854 found 791.0857.

iii

To a solution of bromide **iii** (36 mg, 0.047 mmol) in 1,4-dioxane (3.6 mL, 0.1 mL/mg) was added K_2CO_3 (19 mg, 0.14 mmol) at 0 $^\circ\text{C}$ under argon and the mixture was warmed up to 60 $^\circ\text{C}$. After being stirred at the same temperature

for 6 h, the mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuo. The residue was purified by column chromatography on flash silica gel with 15% MeOH in CHCl₃ to afford oxazoline **15** (26 mg, 0.037 mmol, 79%, 1:1 diastereomer mixture) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 9.08, 8.73 (each brd, *J* = 7.73 Hz, 1H, *NH*), 8.26 x 2, 8.23, 8.22, 8.17, 8.16, 8.09, 8.08 (each s, 4H, c), 5.42-5.52 (m, 1H, d), 4.56-4.70 (m, 2H, a), 3.45, 3.43 (each s, 3H, b), 3.13-3.26 (m, 2H, e), 2.70, 2.68, 2.66 x 2 (each s, 6H, f), 1.32, 1.26 (each s, 9H, g). FT-IR (neat) 3550, 3139, 2965, 1666, 1591, 1502, 1365, 1157, 1062, 842, 752, 722 cm⁻¹. HRMS (ESI-TOF) calcd. for C₃₁H₂₈N₈O₉SNa [M+Na]⁺ 711.1592 found 711.1576.

Hepta-oxazole 16. A suspension of oxazoline **15** (56 mg, 0.081 mmol) and pulverized activated MS 5A in dry toluene (5.6 mL, 0.1 mL/mg) was stirred at room temperature for 1 h under argon to remove a trace amount of water. To the mixture was added camphorsulfonic acid (94 mg, 0.41 mmol, 5 equiv) (azeotroped with toluene) at room temperature under argon. After being stirred at 70 °C for 14 h, the mixture was filtered through a pad of Celite. The filtrate was treated with saturated aqueous NaHCO₃ at 0 °C. The aqueous layer was extracted with ethyl acetate and CHCl₃. The combined organic layer was washed with brine, dried over MgSO₄, and filtered. The filtrate was concentrated in vacuo. The residue was used for the next reaction without further purification. ¹H NMR (400 MHz, CDCl₃) δ 8.61 (brd, *J* = 6.76 Hz, 1H, *NH*), 8.34 (s, 1H, a), 8.23 (s, 2H, a), 8.18 (s, 1H, a), 8.09 (s, 1H, aa), 5.43 (dd, *J* = 5.31, 6.76 Hz, 1H, b), 3.21 (d, *J* = 5.31 Hz, 2H, c), 2.75 (s, 3H, d), 2.70 (s, 3H, d), 1.25 (s, 9H, e). FT-IR (solid) 3132, 2925, 1661, 1593, 1500, 1364, 1104, 802, 718 cm⁻¹. HRMS (ESI-TOF) calcd. for C₃₀H₂₄N₈O₈SNa [M+Na]⁺ 679.1330 found 679.1339.

Telomestatin (1). To a solution of triphenylphosphine oxide (20 mg, 0.072 mmol) in dry CH₂Cl₂ (0.75 mL) was added Tf₂O (6.1 μL, 0.036 mmol) at 0 °C under argon and the mixture was stirred at the same temperature for 30 min. To the mixture was added a solution of **16** (4.0 mg, 0.006 mmol) and anisole (3.9 μL, 0.036 mmol) in dry CH₂Cl₂ (0.75 mL) at room temperature under argon. After being stirred at the same temperature for 3.5 h, the mixture was poured into saturated aqueous NaHCO₃ at 0 °C. The aqueous layer was extracted twice with 10% MeOH in CHCl₃. The organic layer was washed with brine, dried over Na₂SO₄, and filtered. The filtrate was concentrated in vacuo. The residue was purified by short-pad silica gel column chromatography eluted with 33% MeOH in CHCl₃. Further purification was carried out using preparative reversed-phase Analytical HPLC (ODS) eluted with CH₃CN-H₂O-TFA (70:30:0.1) to afford telomestatin (**1**) (0.7 mg, 1.2 μmol, 20%) as a white yellowish solid. HPLC *t_R* = 5.3 min (5.3 min for a mixture of synthetic **1** and natural product). UV λ_{max} 262 nm. CD (MeOH, *c* = 2.2 x 10⁻⁵ M) Δε 39,000. ¹H NMR (500 MHz, CH₃CN:H₂O = 1:1) δ 8.61 (s, 1H, a), 8.55 (s, 1H, a), 8.46 (s, 2H, a), 8.43 (s, 1H, a), 5.90 (t, 1H, *J* = 10 Hz, b), 4.15 (dd, 1H, *J* = 10, 10 Hz, c), 3.73 (dd, 1H, *J* = 10, 10 Hz, c), 2.65 (s, 3H, d), 2.60 (s, 3H, d). HRMS (ESI-TOF) calcd. for C₂₆H₁₄N₈O₇SNa [M+Na]⁺ 605.0598 found 605.0599.

¹H NMR of telomestatin (1)
(CH₃CN : H₂O = 1 : 1)

UV spectrum of synthetic telomestatin

CD spectra of synthetic and natural telomestatins