Supporting Information

An Aldol Approach to the Total Synthesis of Pamamycin 621 A

Guo-Bao Ren and Yikang Wu*

State Key Laboratory of Bioorganic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 45 Lingling Road, Shanghai 200032, China

E-mail: yikangwu@mail.sioc.ac.cn

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**General Information.** THF was distilled over Na/Ph2CO under an argon atmosphere before use. Toluene was distilled in turn from Red-Al and LiAlH4 under nitrogen atmosphere before use. CH2Cl2 and MeCN were distilled over CaH2 before use. PE (chromatography solvent) stands for petroleum ether (b.p. 60-90 °C). DPPA refers to diphenylphosphoryl azide ((PhO)2P(O)N3). DEAD stands for diethyl azodicarboxylate.

**Scheme S1. Outline of the route to epoxide 9 (cf ref. 1).**

Conversion of 24 into 25a. **Method A** Aq. F3CCO2H (50% w/w, 0.25 mL) was added to a solution of 24 (69 mg, 76.9 μmol) in CH2Cl2 (1.5 mL) and MeOH (1.5 mL) stirred at ambient temperature. The stirring was then continued at the same temperature for 4 h. Aq. sat. NaHCO3 was added. The mixture was extracted with Et2O. The organic phase was washed with water and brine before being dried over Na2SO4. The solvent was removed by rotary evaporation. The residue was dissolved in THF (1 mL) and MeOH (0.5 mL). 10% Pd-C (65 mg) was added. The mixture was stirred under H2 (1 atm) at ambient temperature. When the reaction was complete as shown by TLC (ca. 24 h), the solids were filtered off. The filtrate and washings were concentrated on a rotary evaporator. The residue was dissolved in 2,6-lutidine (1 mL) and was heated at 120°C (bath) for 2 h. After cooling to ambient temperature, the solvent was removed by rotary evaporation. The residue was chromatographed (1:1 EtOAc/PE) on silica gel to give 25a as a colorless oil (41 mg, 71.2 μmol, 93%): [α]D26 −61.9 (c 0.90, CHCl3). 1H NMR (300 MHz, CDCl3) δ 7.38-7.27 (m, 5H), 5.43 (dd, J = 2.6, 8.7 Hz, 1H), 4.71-4.65 (m, 3H), 4.24 (dd, J = 2.8, 8.7 Hz, 1H), 4.16 (dt, J = 3.0, 7.7 Hz, 1H), 3.99-3.85 (m, 3H), 3.84-3.79 (m, 2H), 3.74-3.68 (m, 1H), 3.38 (s, 3H), 3.31 (m, 1H), 2.00-1.81 (m, 6H), 1.68-1.60 (m, 5H), 1.53-1.47 (m, 3H), 1.38-1.34 (m, 2H), 1.08 (d, J = 6.2 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H), 0.90 (d, J = 7.2 Hz, 3H), 0.79 (d, J = 7.1 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 174.9, 153.4, 139.5, 129.2, 128.6, 125.7, 95.8, 82.0, 81.4, 81.1, 75.9, 75.3, 72.9, 69.9, 57.8, 55.5, 42.4, 41.5, 40.1, 38.4, 37.5, 31.7, 29.2, 29.1, 27.1, 18.3, 14.2, 13.9, 11.6, 9.9; FT-IR (film) 3502, 2961, 2934, 1784, 1705, 1041, 703 cm−1. ESI-MS m/z 598.3 ([M+Na]+). ESI-HRMS calcd for C32H49NO8Na ([M+Na]+) 598.3350; found: 598.3356.

**Method B** A mixture of 24 (9.0 mg, 10 μmol), 10% Pd-C (9 mg) in MeOH (1.5 mL) was stirred under H2 (1 atm) for 2 h. The catalyst was filtered off. The filtrate and washings were concentrated on a rotary evaporator. To the residue 2,6-lutidine (1 mL) was added. The mixture was heated at 120°C (bath) for 2 h. Aq. sat. CuSO4 (5 mL) was added. After stirring for 10 min, the mixture was extracted with Et2O (3 ×10 mL). The combined organic phases were washed with water and brine before being dried over anhydrous Na2SO4. Removal of the solvent on a rotary evaporator and column chromatography (2:3 EtOAc/PE) on silica gel gave 25a as a colorless oil (5.0 mg, 8.6 μmol, 86%).
Conversion of 24 into 25b. A mixture of 24 (15 mg, 16.7 μmol), 10% Pd-C (15 mg), and CSA (1 mg, 4.3 μmol) in MeOH (1 mL) was stirred at ambient temperature under a H₂ (1 atm) atmosphere for 48 h. The solid was filtered off. The combined filtrate and washings were concentrated on a rotary evaporator. The residue was chromatographed on silica gel (1:1 EtOAc/PE) to afford 25b as a colorless oil (6.0 mg, 11.3 μmol, 68%): [α]D25 −67.7 (c 0.60, CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.27 (m, 5H), 5.45 (dd, J = 2.6, 8.7 Hz, 1H), 4.73 (t, J = 8.6 Hz, 1H), 4.22 (dd, J = 2.8, 8.6 Hz, 1H), 4.19-4.07 (m, 2H), 4.02-3.91 (m, 2H), 3.88-3.78 (m, 3H), 3.34 (br s, 1H), 3.27 (br s, 1H), 2.60-2.52 (m, 1H), 1.86-1.70 (m, 3H), 1.47-1.25 (m, 9H), 1.08 (d, J = 7.0 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 174.9, 153.6, 139.5, 129.2, 128.6, 125.7, 100.4, 74.5, 74.1, 69.8, 57.8, 42.6, 41.3, 40.7, 39.6, 37.6, 30.6, 29.7, 29.0, 26.0, 19.0, 14.3, 14.2, 12.0, 9.1; FT-IR (film) 3543, 2957, 1780, 1705, 1456, 1384, 1098, 737 cm⁻¹. ESI-MS m/z 554.5 ([M+Na]+); ESI-HRMS calcd for C₂₃H₄₂O₇Na ([M+Na]+) 554.3088; found: 554.3093. All these data were fully consistent with those for a sample obtained by removal of the MOM protecting group in 25a.

Conversion of 25a into 5. LiOH (1 M, 0.17 mL, 0.17 mmol) and H₂O₂ (30%, 79 μL, 0.695 mmol) were added dropwise in turn to a solution of 25a (50 mg, 86.9 μmol) in THF (6 mL) and H₂O (2 mL) stirred at 0°C. After completion of the addition, the mixture was stirred at ambient temperature for 4 h. Aq. sat. Na₂SO₃ was added. The stirring was continued for another 0.5 h before the mixture was extracted with EtOAc, washed with water and brine, and dried over anhydrous Na₂SO₄. Removal of the solvent on a rotary evaporator and column chromatography (1:30 MeOH/CH₂Cl₂) on silica gel gave acid 5 as a colorless oil (35 mg, 81.4 μmol, 94%): [α]D25 −10.2 (c 3.20, CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 4.76 (d, J = 7.2 Hz, 1H), 4.68 (d, J = 7.2 Hz, 1H), 4.27-4.18 (m, 1H), 4.02-3.86 (m, 3H), 3.84-3.70 (m, 2H), 3.41 (s, 3H), 2.51 (m, 1H), 2.05-1.94 (m, 4H), 1.90-1.72 (m, 2H), 1.68-1.55 (m, 4H), 1.53-1.42 (m, 3H), 1.40-1.25 (m, 3H), 1.14 (d, J = 7.0 Hz, 3H), 0.92 (t, J = 7.1 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H), 0.78 (d, J = 6.8 Hz, 3H); ¹³C NMR (75 MHz, CHCl₃) δ 177.2, 95.8, 81.5, 81.4, 80.4, 75.4, 75.3, 71.6, 55.3, 44.5, 41.5, 40.4, 37.9, 37.5, 31.5, 29.5, 29.1, 26.5, 18.3, 14.2, 13.7, 11.4, 9.4; FT-IR (film) 3493, 2961, 2936, 2877, 1736, 1098, 1039 cm⁻¹. ESI-MS m/z 453.2 ([M+Na]+); ESI-HRMS calcd for C₂₃H₃₃O₇Na ([M+Na]+) 453.2823; found: 453.2820.

Hydrogenation of 30 (30'). A solution of 30 (143 mg, 0.321 mmol), 10% Pd-C (70 mg) and Et₃N (89 μL, 0.642 mmol) in EtOAc (5 mL) was stirred at ambient temperature under H₂ (1 atm) atmosphere for 48 h. The solid was filtered off. The filtrate was concentrated on a rotary evaporator. The residue was chromatographed on silica gel (1:1 PE/EtOAc) to afford 30' (138 mg, 0.309 mmol, 96%) as a colorless oil: [α]D25 −28.1 (c 1.15, CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.27 (m, 5H), 5.44 (dd, J = 8.7, 3.8 Hz, 1H), 4.69 (t, J = 8.8 Hz, 1H), 4.24 (dd, J = 9.1, 3.7 Hz, 1H), 3.93 (q, 1H), 3.72 (m, 1H), 3.64 (m, 1H), 3.21 (m, 1H), 2.76 (d, J = 7.3 Hz, 1H), 1.55-1.33 (m, 9H), 1.30 (s, 3H), 1.29 (s, 3H), 1.18 (d, J = 6.7 Hz, 1H), 0.92 (t, J = 6.8 Hz, 1H), 0.78 (d, J = 6.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 176.3, 153.7, 138.8, 129.1, 128.6, 125.7, 100.4, 74.5, 74.1, 69.8, 68.8, 57.8, 43.4, 40.1, 36.7, 31.1, 26.5, 25.0, 23.7, 19.1, 14.2, 13.9, 11.8; FT-IR (film) 3543, 2957, 1780, 1705, 1456, 1384.
Mesylation of 30' (30''). MsCl (57 μL, 0.711 mmol) was added to a solution of 30' (106 mg, 0.237 mmol) and NEt₃ (99 μL, 0.711 mmol) in CH₂Cl₂ (3 mL) stirred at ambient temperature under N₂ atmosphere. When the reaction was complete as shown by TLC, aq saturated NaHCO₃ was added. The mixture was extracted with Et₂O. The organic phase was washed with water and brine before being dried over anhydrous Na₂SO₄. Removal of the solvent and chromatography on silica gel (4:1 PE/EtOAc) gave 30'' (121 mg, 0.230 mmol, 97%) as a colorless oil: [α]D²⁵ +24.1 (c 2.05, CHCl₃). 1H NMR (300 MHz, CDCl₃) δ 7.38-7.25 (m, 5H), 5.40 (dd, J = 4.1, 8.9 Hz, 1H), 4.88 (dt, J = 10.0, 4.0 Hz, 1H), 4.71 (t, J = 9.0 Hz, 1H), 4.27 (dd, J = 4.1, 9.2 Hz, 1H), 4.22-4.14 (m, 1H), 3.70-3.62 (m, 1H), 3.21-3.12 (m, 1H), 2.00 (s, 3H), 1.88-1.76 (m, 2H), 1.56 (m, 1H), 1.50-1.41 (m, 5H), 1.34 (m, 1H), 1.27 (s, 3H), 1.25 (s, 3H), 1.16 (d, J = 7.0 Hz, 3H), 0.88 (t, J = 7.1 Hz, 3H), 0.80 (d, J = 6.8 Hz, 3H); 13C NMR (75 MHz, CDCl₃) δ 174.0, 153.0, 139.3, 129.3, 129.0, 126.3, 100.3, 84.2, 74.5, 69.8, 68.9, 57.7, 40.5, 40.0, 36.6 (2C's), 28.1, 24.9, 23.7, 23.4, 19.1, 14.0, 13.9, 11.8; FT-IR (film): 2959, 2874, 1783, 1704, 1457, 1383, 1356, 1174, 918, 760, 702 cm⁻¹. ESI-MS m/z 548.2 ([M+Na]+); ESI-HRMS calcd for C₂₆H₃₉NO₈SNa ([M+Na]+) 548.2289; found 548.2280.

Hydrolysis of 30'' (31). Aq. HCl (1 N, 0.68 mmol, 0.68 mL) was added to a solution of 30'' (356 mg, 0.678 mmol) in THF (5 mL) and MeOH (2.5 mL) stirred at ambient temperature. When the reaction was complete as shown by TLC, aq. saturated NaHCO₃ was added. The mixture was extracted with EtOAc. The organic phase was washed in turn with water and brine before being dried over anhydrous Na₂SO₄. Removal of the solvent and chromatography on silica gel (1:1 PE/EtOAc) gave 31 (294 mg, 0.606 mmol, 89%) as a colorless oil: [α]D²⁵ +14.0 (c 1.60, CHCl₃); 1H NMR (300MHz, CDCl₃) δ 7.43-7.27 (m, 5H), 5.42 (dd, J = 4.0, 8.9 Hz, 1H), 4.94 (dt, J = 10.0, 4.3 Hz, 1H), 4.74 (t, J = 8.8 Hz, 1H), 4.30 (dd, J = 4.1, 8.9 Hz, 1H), 4.27-4.21 (m, 1H), 3.85 (m, 1H), 3.66 (m, 1H), 3.04 (br, 1H), 2.40 (br, 1H), 2.09 (s, 3H), 1.94-1.90 (m, 1H), 1.68-1.34 (m, 8H), 1.22 (d, J = 6.9 Hz, 3H), 0.97-0.89 (m, 6H); 13C NMR (75 MHz, CDCl₃) δ 173.9, 153.1, 139.3, 129.3, 128.9, 126.3, 84.2, 75.7, 72.3, 69.8, 57.7, 41.6, 40.7, 37.7, 36.7, 28.0, 26.7, 18.8, 14.1, 13.8, 11.9; FT-IR (film) 3401, 2959, 1782, 1705, 1458, 1387, 1174, 707 cm⁻¹. ESI-MS m/z 508.4 ([M+Na]+). ESI-HRMS calcd for C₂₃H₃₅NO₈SNa ([M+Na]+) 508.1976; found 508.1976.

Conversion of 31 into 6. Method A A solution of 31 (71 mg, 0.146 mmol) in 2,6-lutidine (2 mL) was stirred at 120 °C (bath) under argon atmosphere for 3 h. Removal of the solvent by rotary evaporation left a residue (d.r. = 10:1 by 1H NMR), which on column chromatography on silica gel (1:4 EtOAc/PE) gave enantiopure 6 (51 mg, 0.131 mmol, 90%) as a colorless oil: [α]D²⁵ −24.7 (c 2.40, CHCl₃). 1H NMR (300 MHz, CDCl₃) δ 7.38-7.27 (m, 5H), 5.42 (dd, J = 4.1, 8.8 Hz, 1H), 4.68 (t, J = 8.9 Hz, 1H), 4.26 (dd, J = 4.2, 9.0 Hz, 1H), 4.04-3.84 (m, 3H), 3.52 (q, J = 6.0 Hz, 1H), 1.80-1.61 (m, 4H), 1.59-1.30 (m, 5H), 1.24 (d, J = 6.7 Hz, 3H), 0.92 (t, J = 6.9 Hz, 3H), 0.87 (d, J = 6.9 Hz, 3H); 13C NMR (75 MHz, CDCl₃) δ 174.3, 153.1, 139.3, 129.3, 129.3, 125.8, 80.7, 80.1, 73.8, 69.6, 57.6, 42.7, 40.1, 37.2, 28.9, 27.2, 18.8, 14.2, 13.7, 11.7; FT-IR (film) 3521, 2959, 1780, 1704, 1456, 1384, 1202, 977, 700 cm⁻¹. ESI-MS m/z 412.1 ([M+Na]+). ESI-HRMS calcd for C₂₂H₂₉NO₃SNa ([M+Na]+) 412.1670; found 412.1670.
Method B Use pyridine instead of 2,6-lutidine and heating at 110 °C (bath) for 2 h gave enantiopure 6 in 62% yield after the same work-up (d.r. = 95:5 for the crude product mixture by 1H NMR) and chromatography as mentioned above.

**Coupling of 5 and 6 leading to the intermediate ester “5+6”.** 2,4,6-Trichlorobenzoyl chloride (26 μL, 0.172 mmol) was added to a mixture of acid 5 (37 mg, 86.0 μmol), alcohol 6 (48 mg, 123 μmol), DMAP (52 mg, 0.43 mmol) and powered/activated 4Å molecular sieves (200 mg) in dry CH2Cl2 (2 mL) stirred at ambient temperature under an argon atmosphere. When the reaction was complete as shown by TLC, EtOAc was added. The mixture was filtered through Celite. The filtrate was washed in turn with aq. sat. NaHCO3, water and brine, and dried over anhydrous Na2SO4. Removal of the solvent by rotary evaporation and column chromatography (1:2 EtOAc/PE) on silica gel gave the intermediate ester “5+6” as a colorless oil (59 mg, 73.6 μmol, 86%): [α]D26 −27.4 (c 1.70, CHCl3). 1H NMR (300 MHz, CDCl3) δ 7.36-7.25 (m, 5H), 5.41 (dd, J = 4.4, 8.7 Hz, 1H), 4.83 (m, 1H), 4.69-4.62 (m, 3H), 4.22 (dd, J = 4.3, 8.9 Hz, 1H), 1.98-1.84 (m, 4H), 1.82-1.65 (m, 5H), 1.63-1.45 (m, 9H), 1.44-1.31 (m, 5H), 1.28-1.15 (m, 2H), 1.21 (d, J = 6.3 Hz, 3H), 1.08 (d, J = 7.1 Hz, 3H), 0.92-0.82 (m, 12H), 0.75 (d, J = 6.8 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 174.7, 174.5, 153.4, 138.9, 129.1, 128.6, 125.8, 95.8, 82.2, 81.7, 80.2, 79.8, 77.2, 75.9, 75.8, 75.4, 72.0, 69.6, 57.7, 55.5, 45.0, 42.9, 41.5, 41.4, 40.1, 37.7, 37.4, 32.0, 31.7, 29.5, 29.24, 29.16, 28.3, 26.4, 18.8, 18.3, 14.2, 14.0, 13.9, 13.2, 12.1, 10.3, 9.5; FT-IR (film) 3500, 2962, 2876, 1782, 1728, 1457, 1382, 1041, 700 cm−1. ESI-MS m/z 824.4 ([M+Na]+). ESI-HRMS calcd for C45H71NO11Na ([M + Na]+) 824.4919; found: 824.4921.

Removal of chiral auxiliary in “5+6” leading to 32. Aq. LiOH (1 M, 0.18 mL, 0.18 mmol) and H2O2 (30%, 68 μL, 0.60 mmol) were added dropwise in turn to a solution of the intermediate ester “5+6” (60 mg, 74.9 μmol) in THF (6 mL) and H2O (2 mL) stirred at 0°C. The stirring was continued at ambient temperature for 2 h. Aq. saturated Na2SO3 was added. The mixture was stirred for another 0.5 h before being extracted with EtOAc, washed with water and brine, and dried over anhydrous Na2SO4. Removal of the solvent on a rotary evaporator and column chromatography on silica gel (eluting with initially 1:70 then 1:20 MeOH/CH2Cl2) gave acid 32 (46 mg, 70.0 μmol, 94%) as a colorless oil: [α]D24 −8.1 (c 0.30, CHCl3). 1H NMR (300 MHz, CDCl3) δ 4.93-4.88 (m, 1H), 4.70 (d, J = 12.3 Hz, 1H), 4.66 (d, J = 12.3 Hz, 1H), 4.15-4.08 (m, 1H), 4.00-3.88 (m, 4H), 3.82-3.69 (m, 3H), 3.38 (s, 3H), 2.71-2.60 (m, 1H), 2.60-2.49 (m, 1H), 2.04-1.92 (m, 6H), 1.90-1.70 (m, 4H), 1.68-1.47 (m, 10H), 1.45-1.28 (m, 5H), 1.20 (d, J = 7.0 Hz, 3H), 1.11 (d, J = 7.1 Hz, 3H), 0.96 (d, J = 6.7 Hz, 3H), 0.94-0.86 (m, 9H), 0.77 (d, J = 6.7 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 176.7, 174.5, 153.4, 138.9, 129.1, 128.6, 125.8, 95.8, 82.2, 81.7, 80.2, 79.8, 77.2, 75.9, 75.8, 75.4, 72.0, 69.6, 57.7, 55.5, 45.0, 42.9, 41.5, 41.4, 40.1, 37.7, 37.4, 32.0, 31.7, 29.5, 29.24, 29.16, 28.3, 26.4, 18.8, 18.3, 14.2, 14.0, 13.9, 13.2, 12.1, 10.3, 9.5; FT-IR (film) 3496, 2962, 2876, 1732, 1728, 1457, 1382, 1041, 700 cm−1. ESI-MS m/z 679.4 ([M+Na]+). ESI-HRMS calcd for C36H64O10Na ([M + Na]+) 679.4392; found: 679.4385.
Macrolactonization of 32 giving 32’. NEt₃ (0.10 mL, 0.74 mmol) and 2,4,6-trichlorobenzoyl chloride (114 μL, 0.617 mmol) were added in turn to a solution of acid 32 (8.1 mg, 12.3 μmol) and DMAP (75 mg, 0.617 mmol) in dry toluene (12.5 mL) stirred at ambient temperature under argon atmosphere (balloon). The stirring was continued at ambient temperature for 24 h and 120 °C (bath temperature) for another 24 h. The mixture was then cooled to ambient temperature. Aq. sat. NaHCO₃ was introduced, followed by EtOAc. The phases were separated. The organic layer was washed with water and brine before being dried over NaSO₄. Removal of the solvent by rotary evaporation and column chromatography (1:7 EtOAc/PE) on silica gel gave lactone 32’ as a colorless oil (5.2 mg, 8.1 μmol, 66%): [α]D⁰₂⁵ = -2.5 (c 0.26, CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 4.00-4.93 (m, 1H), 4.78-4.72 (m, 1H), 4.68 (d, J = 8.6 Hz, 1H), 4.67 (d, J = 8.6 Hz, 1H), 4.20-4.10 (m, 1H), 4.01-4.38 (m, 4H), 3.78-3.66 (m, 2H), 3.38 (s, 3H), 2.62-2.58 (m, 1H), 2.41-2.35 (m, 1H), 1.98-1.89 (m, 1H), 1.82-1.72 (m, 1H), 1.70-1.55 (m, 6H), 1.52-1.35 (m, 7H), 1.30-1.24 (m, 4H), 1.09 (d, J = 7.5 Hz, 3H), 1.06 (d, J = 7.4 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H), 0.93-0.85 (m, 9H), 0.93 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.8, 95.8, 81.7, 81.2, 78.8, 78.7, 77.2, 76.3, 75.8, 75.3, 75.1, 55.6, 46.4, 42.0, 41.4, 41.2, 39.6, 37.4, 33.5, 31.9, 29.8, 29.6, 28.7, 28.2, 27.7, 27.3, 18.2, 17.7, 14.5, 14.2 (2C’s), 11.9, 10.4, 9.9, ( & 9.2, as seen in HMQC); FT-IR (film) 2959, 2874, 1738, 1732, 1041 cm⁻¹. ESI-MS m/z 661.4 ([M+Na]+). ESI-HRMS calcd for C₃₆H₆₂O₉Na ([M+Na]+) 661.4286; found 661.4273.

Removal the MOM in 32’ leading to 32''. Aq. HBr (10%, 13.6 μL, 17.3 μmol) was added to a solution of 32’ (5.2 mg, 8.15 μmol) in MeCN (1 mL) stirred at ambient temperature. When the reaction was complete as shown by TLC, aq. saturated NaHCO₃ was added. The mixture was extracted with Et₂O. The phases were separated. The organic phase was washed in turn with water and brine, dried over anhydrous NaSO₄. Removal of the solvent by rotary evaporation and column chromatography on silica gel (1:4 EtOAc/PE) gave alcohol 32'' (4.7 mg, 7.91 μmol, 97%) as a colorless oil: [α]D²⁴ = +11.3 (c 0.32, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.93 (dd, J = 7.0, 2.8 Hz, 1H), 4.77 (dt, J = 7.8, 4.7 Hz, 1H), 4.15-4.04 (m, 3H), 3.95 (m, 1H), 3.87-3.80 (m, 2H), 3.74 (m, 1H), 3.21 (br s, 1H), 2.62 (dq, J = 2.4, 6.9 Hz, 1H), 2.39 (m, 1H), 2.05-1.83 (m, 6H), 1.82-1.72 (m, 5H), 1.72-1.25 (m, 1H), 1.10 (d, J = 6.9 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H), 0.95-0.87 (m, 12H), 0.86 (d, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 173.7, 173.5, 81.7, 81.6, 78.6, 78.1, 77.2, 76.3, 76.2, 68.4, 46.7, 41.7, 17.7, 14.2, 10.7, 9.7, 8.8; FT-IR (film) 3516, 2960, 2928, 2873, 1735, 1461, 1236, 1067, 803 cm⁻¹. ESI-MS m/z 617.1 ([M+Na]⁺). ESI-HRMS calcd for C₃₄H₅₈O₈Na ([M+Na]⁺) 617.4024; found 617.4030.

Conversion of 32'' into 33. DPPA (5.7 μL, 33.7 μmol) was added to a solution of the above obtained alcohol 32'' (9.1 mg, 15.3 μmol), PPh₃ (8.0 mg, 30.6 μmol) and DEAD (5.2 μL, 33.7 μmol) in dry THF (1 mL) stirred at ambient temperature. After
1 h, another portion of Ph3P (8.0 mg, 30.6 µmol), DEAD (5.2 µL, 33.7 µmol) and DPPA (5.7 µL, 33.7 µmol) were added in turn. When the reaction was complete as shown by TLC, the solvent was removed by rotary evaporation. The residue was chromatographed on silica gel (1:12 EtOAc/PE) to give azide 33 (8.7 mg, 14.0 µmol, 92%) as a colorless oil: [α]D25 +6.2 (c 0.41, CHCl3). 1H NMR (300 MHz, CDCl3) δ 4.95 (t, J = 4.5 Hz, 1H), 4.76 (dt, J = 7.0, 5.2 Hz, 1H), 4.18-4.10 (m, 1H), 4.05-3.82 (m, 4H), 3.77 (dt, J = 6.8, 6.3 Hz, 1H), 3.44-3.34 (m, 1H), 2.60 (m, 1H), 2.38 (dq, J = 7.3, 6.8 Hz, 1H), 2.02-1.85 (m, 5H), 1.84-1.73 (m, 5H), 1.69-1.52 (m, 6H), 1.50-1.31 (m, 6H), 1.30-1.25 (m, 3H), 1.10 (d, J = 7.1 Hz, 3H), 1.08 (d, J = 7.2 Hz, 3H), 0.97-0.83 (m, 15H); 13C NMR δ 173.7, 173.6, 81.7, 81.5, 78.8, 78.7, 77.4, 76.1, 75.8, 75.4, 60.2, 46.5, 42.1, 41.2, 40.3, 39.7, 38.6, 36.3, 33.7, 31.5, 29.9, 28.8, 28.2, 27.6, 27.5, 19.3, 17.8, 14.6, 14.3, 13.9, 12.0, 10.4, 10.0, 9.2; FT-IR (film) 2960, 2871, 2170, 2103, 1738, 1732, 1261, 1011, 967, 800 cm⁻¹. ESI-MS m/z 637.5 ([M+NH4]+) 642.5 ([M+Na]+). ESI-HRMS calcd for C34H57N3O7Na ([M+Na]+) 642.4089; found: 642.4084.

Conversion of 33 into Pamamycin 621A (1). A solution of azide 33 (8.1 mg, 13.1 µmol) and n-Bu3SnH (0.5 mL) in dry toluene (1 mL) were stirred at 120°C under argon atmosphere for 2 h. Removal of the solvent, and the residue was dissolved in dry MeCN (1 mL) and the buffer (1 mL, with the stock solution prepared from 1.84 g of NaOAc, 1.3 g of HOAc, 5 mL of H2O, and 7 mL of 37% aq. HCHO). The stirring was continued at ambient temperature for 0.5 h before NaBH3CN (10 mg) was added in two portions. When the reaction was complete as shown by TLC, aq. saturated NaHCO3 was added. The mixture was extracted with CH2Cl2. The organic phase was washed in turn with water and brine, dried over anhydrous Na2SO4. Removal of the solvent and chromatography on silica gel (0.5:1:6 NEt3/EtOAc/PE) gave Pamamycin-621A (1), 7.5 mg, 12.0 µmol) as a colorless oil: [α]D27 +5.4 (c 0.40, CH2Cl2) (lit.2 [α]D25 +5.1 (c 1.3, CH2Cl2)). FT-IR (film) 2924, 2854, 1786, 1736, 1460, 1094, 801 cm⁻¹. ESI-MS m/z 622.1 ([M+H]+). ESI- HRMS calcd for C36H63NNaO7 ([M+Na]+) 644.4497; found: 644.4470. For 1H and 13C NMR data listing, see the Tables on next page.

Reference for Supporting Information section

**Table 1.** Comparison of the $^1$H NMR data (all acquired in CDCl$_3$) of 1.

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$^a$Spectra/data were kindly provided by Prof. Peter Metz.

**Table 2.** Comparison of the $^{13}$C NMR data (all acquired in CDCl$_3$) of 1.

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$^a$Authentic spectra/data were kindly provided by Prof. Peter Metz. $^b$Broadened (difficult to detect).
S 9

300 MHz, CDCl3
10 MHz, CDCl₃
S 12  
75 MHz, CDCl₃
75 MHz, CDCl3
300 MHz, CDCl$_3$
100 MHz, CDCl3
75 MHz, CDCl3
HMQC (Partial) of 32' shown the 9.2 ppm carbon that is broadened in 13C NMR
S 24

400 MHz, CDCl3
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HMQC spectrum of 33
$\text{CDCl}_3$, $\delta_{\text{acetone}}$
100 MHz, CDCl₃
(Kindly provided by Prof. Metz)

PK 25 in CDCl3

Pamamycin 621A (1)

(This work)
(Kindly provided by Prof. Metz)

(This work)
S 34

75 MHz, CDCl3

rgb=16-84

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Sample directory:
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Acq. time 1.500 sec
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DECOUPLE H1, 300.0294698 MHz
Power 40 dB
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DATA PROCESSING
FT size 4096
Total time 11677 hr, 15 min, 24 sec
S 37
300 MHz, CDCl3