

**Synthesis of the Entire Carbon Framework of the Kedarcidin Chromophore
Aglycon**

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General Experimental Techniques. All reactions were performed in flame-dried or oven-dried glassware under a positive-pressure of nitrogen or argon. Air and moisture sensitive compounds were introduced via syringe or stainless steel cannula through a rubber septum. To minimize decomposition, extreme care was taken in the handling and isolation of sensitive compounds, especially for nine-membered cyclic diyne products. In such cases, homogenously-deactivated silica gel – previously prepared 36–48 h prior, by the addition of 6% (vol/wt) water to neutral silica (preferably Kanto Chem. Co. Silica Gel 60N, 0.040–0.050 mm) – was used for flash column chromatography, and the product was eluted through as quick as deemed possible (typically between 10–20 minutes): The combination of dry positive N₂-flow and N₂-saturated solvents (via N₂-bubbling) as eluents were also used in chromatographic purification techniques, and solvents were removed below 25 °C and products were always handled under N₂.

Physical Data. Melting points were recorded on a Yanagimoto micro-melting point apparatus. NMR spectra were recorded on a Varian Gemini-200, Varian Mercury-200, Varian INOVA-500, JEOL α -500, and Bruker AM-600 instruments and referenced to residual undeuterated solvent molecules. The following multiplicity-abbreviations are used: s=singlet; d=doublet; t=triplet; q=quintet; m=multiplet; br=broad. FT-IR spectra were recorded on a Perkin-Elmer 1600 series FT-IR spectrophotometer. Optical rotations were recorded on a JASCO DIP-370 polarimeter. High-resolution mass spectra (HRMS) were recorded on a JEOL HX-110A mass spectrometer and on a PerSeptive BioSystems Mariner™ (ESI-TOF MS with double-calibration allowing 4-decimal points of accuracy). HRMS of the mesylate **18** was definitively recorded on a

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Bruker Daltonics ApexIII 7T, Fourier-Transform-Ion-Cyclotron (FT-ICR) mass spectrometer. Matrix assisted laser desorption ionization mass spectra (MALDI-TOFMS) were recorded on a PerSeptive Biosystems Voyager DE STR mass spectrometer using α -cyano-4-hydroxy cinnamic acid (α -CHCA) as the matrix, and all compounds were doubly calibrated with α -CHCA dimer and clipped adrenocorticotrophic hormone (ACTH, 18-19 clip) for accuracy.

Chromatography. Analytical thin layer chromatography (TLC) was performed using 0.25 mm E. Merck Silica gel (60F-254) plates. Reaction components were visualized by illumination with ultraviolet light (254 nm) and by staining with 6% ethanolic *p*-anisaldehyde (includes 6% conc. sulfuric acid and 1% acetic acid), 8% ethanolic phosphomolybdic acid, or ceric ammonium molybdate in 10% sulfuric acid. E. Merck silica gel 60 (partical size 0.040-0.063 mm) or Kanto Chem. Co. Silica Gel 60N(partical size 0.040–0.050 mm) was used for flash column chromatography.

Solvents and Reagents. Solvents were distilled and/or stored over MS4A prior to use. Tetrahydrofuran (THF) was distilled from sodium metal/benzophenone ketyl. Dichloromethane, 1,2-dichloroethane, benzene, toluene, triethylamine, *N,N*-diisopropylethylamine, hexamethyldisilazane, and pyridine were distilled from calcium hydride. Dimethyl sulfoxide (DMSO) and *N,N*-dimethylformamide (DMF) were distilled from calcium hydride at reduced pressure. Dry methanol was purchased from Kanto Chem. Co. Diethylether (Et₂O) was dried over MS4A. Methanesulfonyl chloride was distilled at reduced pressure. IBX and Dess-Martin periodinane were prepared according to the procedures by Santagostino¹ and Ireland² *et al.* Tris(dibenzylideneacetone)dipalladium(chloroform) was prepared according to the procedure by Ishii *et al.*³ Copper(I) iodide was purified according to the *Inorganic Syntheses* procedure.⁴ Zn(BH₄)₂ was prepared in Et₂O solution according to the procedure by Nakata *et al.*⁵ All other reagents were used as obtained from commercial sources or were purified according to standard procedures.⁶

All compounds given below bear the same formula numbers as used in the main text, and the carbon numbering follows that for the kedarcidin chromophore.

References

- 1 Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.
- 2 Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.
- 3 Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253.
- 4 Kauffman, G. B.; Fang, L. Y. *Inorg. Synth.* **1983**, *22*, 101.
- 5 Nakata, T.; Tani, T.; Hatozaki, M.; Oishi, T. *Chem. Pharm. Bull.* **1984**, *32*, 1411.
- 6 Perrin, D. D.; Amarego, W. L. *Purification of Laboratory Chemicals*, 3rd ed.;

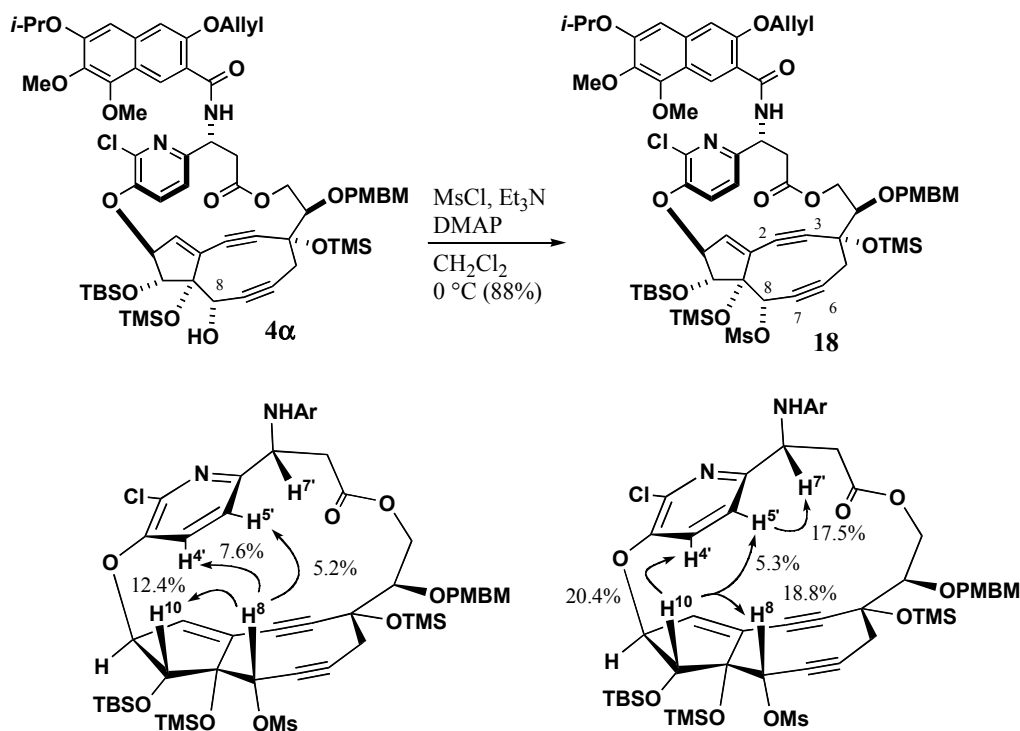
NOE experiments on **18** (the mesylate of **4α**)

Figure 2. NOE experiments on **18** (600 MHz, CD₂Cl₂, -27 °C).

A solution of **4α** (22.2 mg, 18.3 μmol) and Et₃N (77 μL, 549 μmol) in CH₂Cl₂ (1.5 mL) was treated with MsCl (21.2 μL, 274 μmol) and DMAP (0.2 mg, 1.83 μmol) at 0 °C, and the mixture was stirred at 0 °C for 45 min. The reaction mixture was diluted with ethyl acetate (20 mL), and then treated with sat. NaHCO₃ (aq.) (3 mL) at 0 °C. The water layer was extracted with ethyl acetate (5 mL x 3), and the combined organic layers washed with brine (3 mL), and then dried over Na₂SO₄. After removal of the solvent, the crude product was purified by flash column chromatography (hexane/EtOAc = 1:0 to 1.5:1) to give **18** (20.7 mg, 16.0 μmol, 88%).

18: colorless powder: [α]_D²⁹ 117.1 (c 0.42, CH₂Cl₂); ¹H NMR (500 MHz, C₆D₆, rt) δ 0.18 (9H, s, TMS), 0.35 (9H, s, TMS), 0.54 (3H, s, TBS), 0.57 (3H, s, TBS), 1.08 (9H, s, TBS), 1.23 (3H, d, *J* = 6.0 Hz, H11'' or H12''), 1.24 (3H, d, *J* = 6.0 Hz, H11'' or H12''), 2.48 (3H, s, Ms), 2.50 (1H, ddd, *J* = 17.0, 3.0, 1.5 Hz, H5), 2.69 (1H, dd, *J* = 15.0, 11.0 Hz, H8'), 3.16 (1H, dd, *J* = 17.0, 1.5 Hz, H5), 3.39 (1H, dd, *J* = 15.0, 5.5 Hz, H8'), 3.46 (3H, s, PMBM), 3.75 (3H, s, H13''), 3.84 (3H, s, H14''), 4.15 (1H, dd, *J* = 12.0, 2.0 Hz, H14), 4.21-4.24 (1H, m, H13), 4.27-4.33 (2H, m, CH₂=CH-CH₂-), 4.30 (1H, dd, *J* = 12.0, 5.5 Hz, H14), 4.37 (1H, d, *J* = 11.0 Hz, PMBM), 4.42 (1H,

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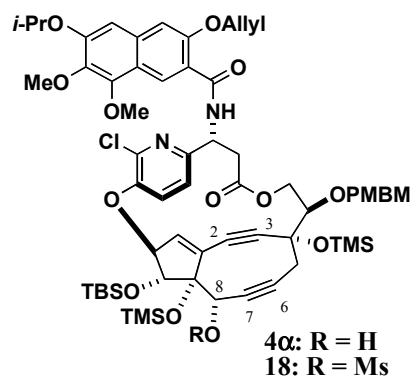
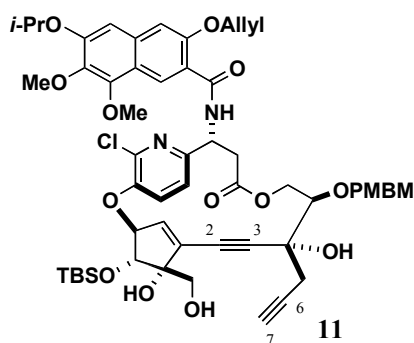
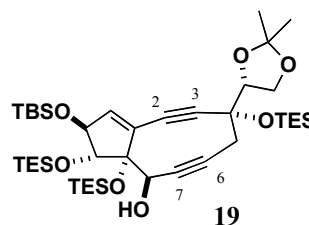
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heptet, $J = 6.0$ Hz, H10''), 4.64 (1H, d, $J = 11.0$ Hz, PMBM), 4.74 (1H, d, $J = 6.5$ Hz, PMBM), 4.84 (1H, d, $J = 2.0$ Hz, H10), 4.91 (1H, d, $J = 6.5$ Hz, PMBM), 4.91 (1H, t, $J = 2.0$ Hz, H8), 5.21 (1H, ddd, $J = 10.0, 2.0, 1.0$ Hz, CH₂=CH-CH₂-), 5.54 (1H, ddd, $J = 17.0, 2.0, 1.0$ Hz, CH₂=CH-CH₂-), 5.52 (1H, t, $J = 2.5$ Hz, H11), 6.02 (1H, ddd, $J = 11.0, 8.0, 5.5$ Hz, H7'), 6.23 (1H, dddd, $J = 17.0, 10.0, 6.0, 6.0$ Hz, CH₂=CH-CH₂-), 6.48 (1H, d, $J = 2.5$ Hz, H12), 6.76 (1H, s, H5''), 6.82 (1H, s, H4''), 6.93 (2H, d, $J = 9.0$ Hz, PMBM), 7.09 (1H, d, $J = 8.0$ Hz, H5'), 7.29 (2H, d, $J = 9.0$ Hz, PMBM), 7.66 (1H, d, $J = 8.0$ Hz, H4'), 9.19 (1H, d, $J = 8.0$ Hz, NH), 9.74 (1H, s, H1''); ¹H NMR (500 MHz, CD₂Cl₂, -20 °C) δ 0.16 (9H, s, TMS), 0.17 (9H, s, TMS), 0.21 (3H, s, TBS), 0.35 (3H, s, TBS), 0.97 (9H, s, TBS), 1.42 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 1.43 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 2.40 (1H, ddd, $J = 17.0, 2.5, 1.5$ Hz, H5), 2.56 (1H, dd, $J = 15.0, 11.5$ Hz, H8'), 2.98 (1H, dd, $J = 17.0, 2.0$ Hz, H5), 3.16 (1H, dd, $J = 15.0, 5.0$ Hz, H8'), 3.23 (3H, s, Ms), 3.69 (3H, s, PMBM), 3.78 (1H, dd, $J = 12.5, 1.0$ Hz, H14), 3.86 (3H, s, H13''), 3.94 (1H, brddd, $J = 5.0, 1.5, 1.0$ Hz, H13), 4.03 (3H, s, H14''), 4.10 (1H, dd, $J = 12.5, 5.0$ Hz, H14), 4.34 (1H, d, $J = 11.5$ Hz, PMBM), 4.43 (1H, d, $J = 2.5$ Hz, H10), 4.47 (1H, dd, $J = 3.5, 2.0$ Hz, H8), 4.53 (1H, d, $J = 11.5$ Hz, PMBM), 4.71 (1H, heptet, $J = 6.0$ Hz, H10''), 4.73-4.76 (2H, m, CH₂=CH-CH₂-), 4.73 (1H, d, $J = 7.0$ Hz, PMBM), 4.78 (1H, d, $J = 7.0$ Hz, PMBM), 5.37 (1H, t, $J = 2.5$ Hz, H11), 5.38 (1H, brdd, $J = 10.0, 1.0$ Hz, CH₂=CH-CH₂-), 5.47 (1H, dd, $J = 17.5, 2.0, 1.0$ Hz, CH₂=CH-CH₂-), 5.58 (1H, ddd, $J = 11.5, 7.5, 5.0$ Hz, H7'), 6.34 (1H, dddd, $J = 17.5, 10.0, 6.0, 6.0$ Hz, CH₂=CH-CH₂-), 6.39 (1H, d, $J = 2.0$ Hz, H12), 6.83 (1H, s, H5''), 6.84 (2H, d, $J = 8.5$ Hz, PMBM), 7.08 (1H, s, H4''), 7.20 (2H, d, $J = 8.5$ Hz, PMBM), 7.31 (1H, d, $J = 8.0$ Hz, H5'), 7.50 (1H, d, $J = 8.0$ Hz, H4'), 8.81 (1H, s, H1''), 9.02 (1H, d, $J = 7.5$ Hz, NH); ¹³C NMR (150 MHz, CD₂Cl₂, -27 °C) δ -5.37 (TBS), -4.47 (TBS), 1.04 (3C, TMS), 2.01 (3C, TMS), 18.18 (TBS), 21.55 (C11'' or C12''), 21.57 (C11'' or C12''), 25.80 (3C, TBS), 31.70 (C5), 38.91 (Ms), 40.41 (C8'), 51.21 (C7'), 55.11 (PMBM), 60.92 (C13''), 61.76 (C14''), 66.88 (CH₂=CH-CH₂-), 68.75 (C14), 70.18 (PMBM), 70.23 (C8), 76.11 (C10''), 77.44 (C4), 78.56 (C10), 80.51 (C13), 84.24 (C9), 88.55 (C6), 92.03 (C2), 93.12 (C7), 94.98 (PMBM), 95.21 (C11), 99.48 (C2), 101.97 (C4''), 106.17 (C5''), 113.41 (2C, PMBM), 118.12 (C2''), 118.67 (C8a''), 119.27 (CH₂=CH-CH₂-), 124.43 (C5'), 127.59 (C1''), 129.33 (PMBM), 129.44 (2C, PMBM), 132.28 (C4a''), 132.53 (CH₂=CH-CH₂-), 133.31 (C4''), 133.56 (C1), 137.83 (C12), 139.77 (C7''), 146.46 (C2'), 147.65 (C3'), 149.02 (C8''), 153.56 (C6''), 153.98 (C3''), 154.62 (C6'), 158.95 (PMBM), 164.05 (C9''), 170.65 (C9'); FT-IR (film) ν 2930, 1734, 1618, 1560, 1515, 1447, 1368, 1249, 1177, 1125, 1033, 845 cm⁻¹; FT-ICR-HRMS (ESI), calcd. for C₆₃H₈₄ClN₂O₁₇SSi (M+H)⁺: 1291.4482; found: 1291.4484.

Comparison of ^{13}C -NMR shifts

Table 2. ^{13}C NMR chemical shift / ppm
 (18: 150 MHz, CD_2Cl_2 , -27 °C; 4 α : 125 MHz, CD_2Cl_2 ;
 19: 150 MHz, CDCl_3 ; 11: 125 MHz, CD_2Cl_2)

	18	4 α	19	11
C-2	92.03	90.12	90.73	81.51
C-3	99.48	100.14	97.85	94.62
C-6	88.55	89.25	89.63	78.96
C-7	93.12	92.87	93.75	71.72

Energy minimized model structure of the simplified β -alcohol (20)

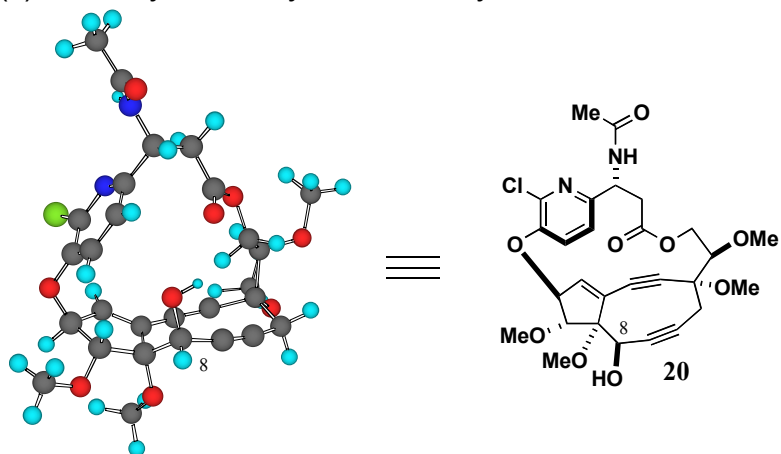
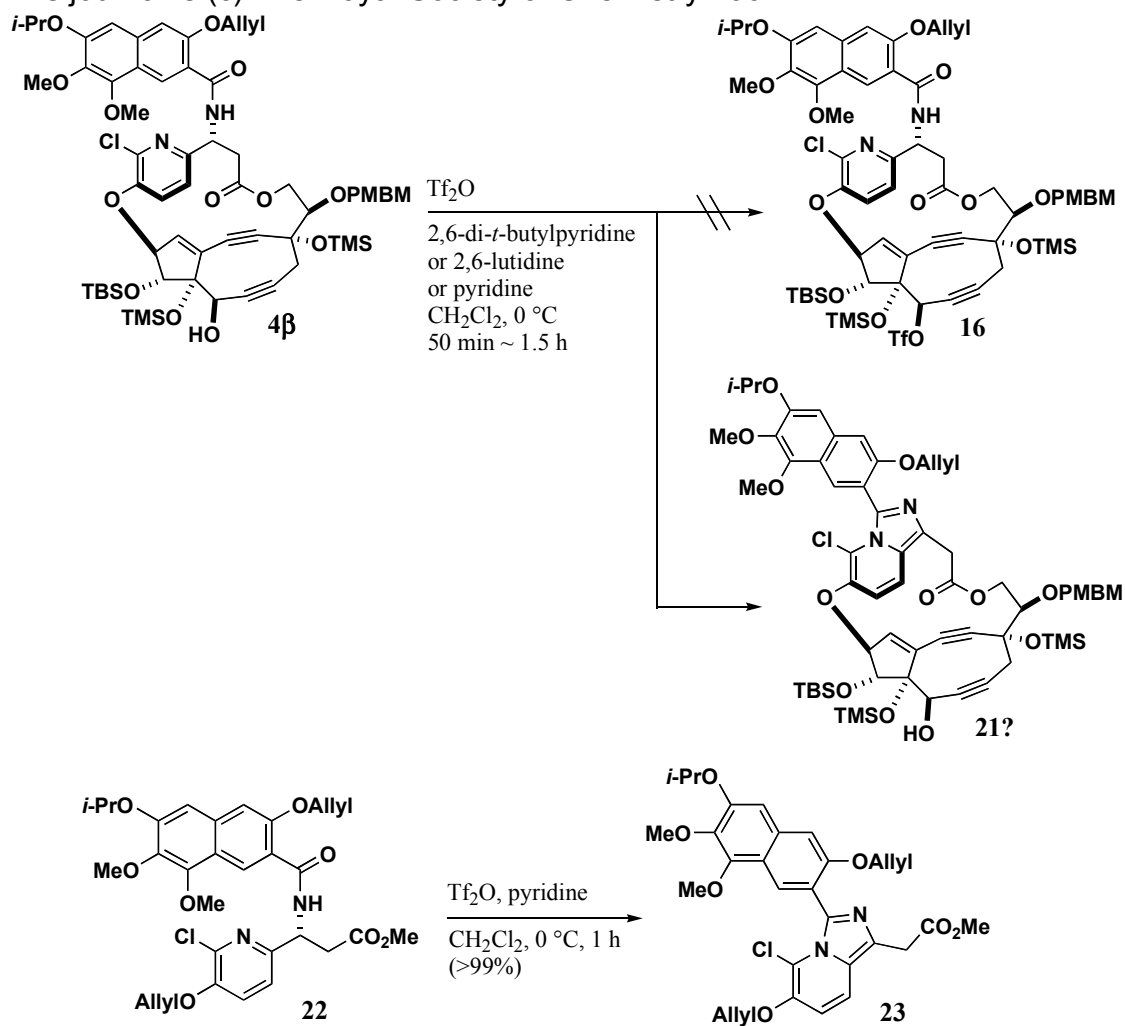


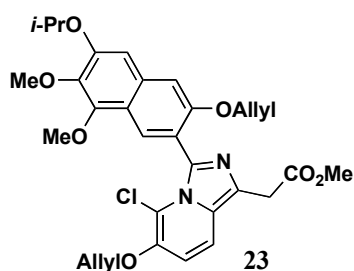
Figure 3. Energy minimized structure of **20** (MM2*, Macromodel ver 6.0).

Attempted triflate formation of the β -alcohol (**4 β**)

When the β -alcohol **4 β** was treated with Tf_2O in the presence of various bases such as 2,6-di-*t*-butyl pyridine, 2,6-lutidine or pyridine at 0 °C (below -30 °C, no reaction occurred.), a product formed, but was found to be unstable on silica gel. Although this product could not be isolated in pure form, we conclude that the product was in fact the imidazo[1,5-*a*]pyridine derivative **21** instead of the desired triflate **16** on the basis of the following results: (1) The amide proton disappeared in the ^1H NMR of the crude product; (2) The MALDI-TOFMS of the crude product showed $m/z = 1195.1$, which corresponds to $(\text{M}+\text{H})^+$ of **21** [calcd. for $\text{C}_{62}\text{H}_{80}\text{ClN}_2\text{O}_{14}\text{Si}_3$ $(\text{M}+\text{H})^+$: 1195.5]; and (3) a subsequent model study on **22**, whereby the secondary amide appears to react with Tf_2O (Scheme 5).



Scheme 5. Unexpected imidazo[1,5-a]pyridine formation: a model study.



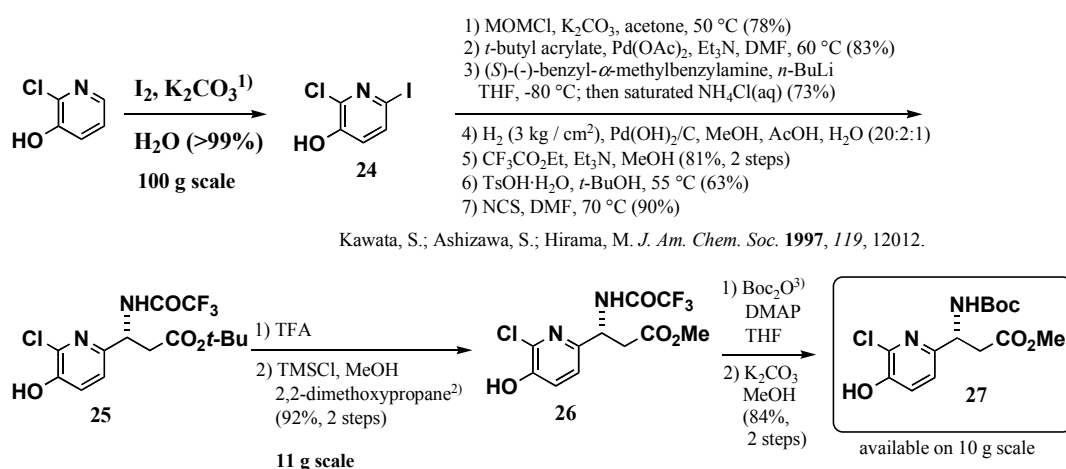
23. To a solution of **22** (4.0 mg, 6.677 μmol) and pyridine (16.2 μL , 0.2003 mmol) in CH_2Cl_2 (0.3 mL) was added Tf_2O (16.8 μL , 0.1002 mmol) at 0 °C. After being stirred at 0 °C for 1 h, the reaction mixture was diluted with EtOAc (10 mL) and quenched with sat. NaHCO_3 (aq.) (2.5 mL) at 0 °C. The layers were separated, and the aqueous phase was extracted with EtOAc. The combined organic extracts were washed with brine, dried over Na_2SO_4 , and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 3:1 to 1:1) to give **23** (3.9 mg, 6.677 μmol , >99%).

23: yellow amorphous oil; ^1H NMR (500 MHz, CDCl_3) δ 1.46 (3H, d, J = 6.0

Hz, H11'' or H12''), 1.47 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 3.73 (3H, s, OMe), 3.92 (3H, s, H13''), 3.99 (1H, d, $J = 16.0$ Hz, H8'), 4.03 (1H, d, $J = 16.0$ Hz, H8'), 4.05 (3H, s, H14''), 4.51-4.56 (4H, m, CH₂=CH-CH₂- x 2), 4.71 (1H, heptet, $J = 6.0$ Hz, H10''), 4.99-5.07 (2H, m, CH₂=CH-CH₂-), 5.23-5.27 (1H, m, CH₂=CH-CH₂-), 5.33-5.40 (1H, m, CH₂=CH-CH₂-), 5.85 (1H, ddt, $J = 17.5, 11.0, 5.0$ Hz, CH₂=CH-CH₂-), 6.00 (1H, ddt, $J = 18.0, 10.5, 5.5$ Hz, CH₂=CH-CH₂-), 6.72 (1H, d, $J = 10.0$ Hz, H4'), 6.86 (1H, s, H5''), 6.94 (1H, s, H4''), 7.43 (1H, d, $J = 10.0$ Hz, H5'), 8.21 (1H, s, H1''); ¹³C NMR (125 MHz, CDCl₃) δ 22.14, 22.30, 34.18, 52.30, 61.16, 61.71, 68.72, 70.73, 73.02, 103.52, 104.91, 113.93, 115.99, 116.46, 116.57, 118.52, 118.66, 121.54, 125.69, 126.00, 128.99, 132.68, 133.07, 133.12, 136.28, 140.04, 143.68, 149.01, 152.54, 156.18, 171.56; FT-IR (film) ν 2978, 2934, 1740, 1629, 1550, 1479, 1442, 1397, 1307, 1244, 1189, 1125, 1030, 984, 927, 852, 784 cm⁻¹; HRMS (EI, 70 eV), calcd. for C₃₁H₃₃ClN₂O₇ (M⁺): 580.1976; found: 580.1990.

New practical synthesis of ansamacrolide (5)

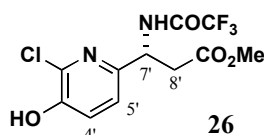
1. Synthesis of the azatyrosine moiety (27)



1) Wishka, D. G.; Graber, D. R.; Seest, E. P.; Dolak, L. A.; Han, F.; Watt, W.; Morris, J. *J. Org. Chem.* **1998**, *62*, 7851.

2) Rodriguez, A.; Nomen, M.; Spur, B. W.; Godfroid, J. *J. Tetrahedron Lett.* **1998**, *39*, 8563.

3) Burk, M. J.; Allen, J. G. *J. Org. Chem.* **1997**, *62*, 7054.



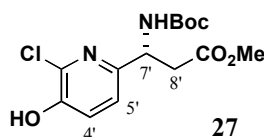
The *t*-butyl ester **25** (10.72 g, 29.07 mmol) was dissolved in TFA (73 mL) at 0 °C. The colorless suspension was stirred at room temperature for 3.5 h to give a clear solution. The mixture was diluted with CHCl₃, then concentrated and the residue was diluted with Et₂O (400 mL), washed with water (45 mL) and then with brine (20 mL). The water layer was extracted with Et₂O (50 mL x 4), and the combined organic

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extracts were dried over Na_2SO_4 , concentrated and dried under high vacuum to give a yellow amorphous (14.72 g). To a solution of the product (14.72 g) in 2,2-dimethoxypropane (58 mL) was added MeOH (12.5 mL, 0.3086 mol) and TMSCl (370 μL , 2.907 mmol), and the reaction mixture was stirred at room temperature for 47 h. After removal of the solvent, the residue was diluted with EtOAc (400 mL) and then treated with water (60 mL). The aqueous layer was separated and extracted with EtOAc (80 mL x 3). The combined organic layers were dried over Na_2SO_4 and concentrated, and the crude product was purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1 to 1.5:1) to give **26** (8.76 g, 26.82 mmol, 92% for 2 steps).

26: colorless powder; mp 115-116 °C (hexane/EtOAc = 5/1); $[\alpha]_{\text{D}}^{28}$ 105.1 (c 0.88, CHCl_3); ^1H NMR (200 MHz, CDCl_3) δ 2.86 (1H, dd, $J = 16.2, 6.8$ Hz, $\text{H8}'$), 3.08 (1H, dd, $J = 16.2, 5.0$ Hz, $\text{H8}'$), 1.42 (3H, s, OMe), 5.42 (1H, ddd, $J = 7.8, 6.8, 5.0$ Hz, $\text{H7}'$), 7.26 (1H, d, $J = 7.8$ Hz, $\text{H5}'$), 7.33 (1H, d, $J = 7.8$ Hz, $\text{H4}'$), 7.82 (1H, d, $J = 7.8$ Hz, NH); ^{13}C NMR (50 MHz, CDCl_3) δ 38.22, 49.88, 52.14, 115.73 ($J_{\text{F}} = 286$ Hz), 122.72, 124.77, 137.49, 148.06, 148.49, 156.68 ($J_{\text{F}} = 37.2$ Hz), 171.34; FT-IR (KBr) ν 3294, 3028, 2960, 2062, 1717, 1570, 1464, 1441, 1410, 1373, 1294, 1212, 1183, 1085, 1046, 839, 760, 671 cm^{-1} ; HRMS (EI, 70 eV), calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_4\text{F}_3\text{Cl}$ (M^+): 326.0281; found: 326.0277.

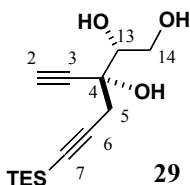
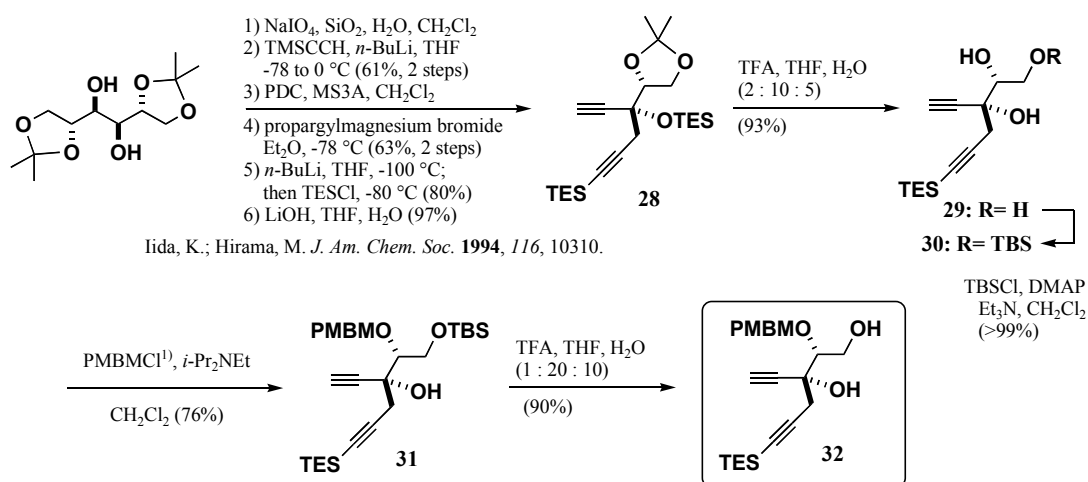


To a solution of the trifluoroacetamide **26** (8.68 g, 26.57 mmol) and Boc_2O (15.7 mL, 66.42 mmol) in THF (88.6 mL) was added DMAP (324.6 mg, 2.657 mmol), and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with EtOAc (450 mL) and then quenched with sat. NH_4Cl (aq.) (80 mL) and water (30 mL). The water layer was separated, and extracted with EtOAc (70 mL x 3). The combined organic extracts were washed with brine (50 mL) and dried over Na_2SO_4 , then concentrated. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt 10:1 to 4:1) to give colorless oil. To a solution of this oil in MeOH (116 mL) was added K_2CO_3 (4.82 g, 34.9 mmol). After stirring at room temperature for 3.3 h, the reaction mixture was poured into 10% KHSO_4 (aq.) (190 mL), extracted with EtOAc (500 mL + 100 mL x 4), and the extracts were washed with brine (40 mL), dried over Na_2SO_4 , and concentrated. The crude product was purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1 to 2:1) to give the Boc-tyrosine **27** (7.34 g, 22.20 mmol, 84 % for 2 steps).

27: colorless powder: mp 131-133 °C (hexane/EtOAc = 2/1); $[\alpha]_{\text{D}}^{21}$ 36.9 (c

0.224, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 1.44 (9H, s, Boc), 2.84 (1H, dd, *J* = 16.5, 6.5 Hz, H8'), 3.02 (1H, dd, *J* = 16.5, 5.0 Hz, H8'), 3.63 (3H, s, OMe), 5.10 (1H, ddd, *J* = 8.5, 6.5, 5.0 Hz, H7'), 5.60 (1H, s, OH), 5.69 (1H, d, *J* = 8.5 Hz, NH), 7.25 (2H, brs, H4', H5'); ¹³C NMR (50 MHz, CDCl₃) δ 28.59 (3C), 39.56, 51.21, 52.04, 80.29, 122.44, 124.57, 137.41, 147.53, 151.54, 155.48, 171.96; FT-IR (KBr) ν 3234, 2976, 1740, 1683, 1566, 1487, 1437, 1419, 1368, 1300, 1229, 1165, 1083, 1027, 991, 899, 851, 775 cm⁻¹; HRMS (EI, 70 eV), calcd. for C₁₄H₁₉N₂O₅Cl (M⁺): 330.0983; found: 330.0982.

2. Synthesis of the acetylenic moiety (32)



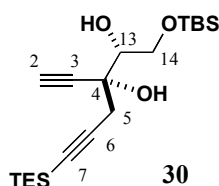
28 (16.24 g, 38.41 mmol) dissolved in THF (115 mL) and water (56.5 mL) was treated with TFA (22.6 mL) at 0 °C, and the reaction mixture was stirred for 72 h at room temperature. The reaction mixture was neutralized by the drop-wise addition of Et₃N (41 mL) at 0 °C. The mixture was diluted with EtOAc (300 mL) and then treated with sat. NaHCO₃ (aq.) (50 mL). After stirring for 0.5 h at room temperature, NaCl was added to the mixture until NaCl was insoluble. The organic phase was separated, and the water layer was extracted with EtOAc (100 mL x 2). The combined organic extracts were washed with brine (60 mL), dried over Na₂SO₄, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 5:1 to 2:1) to give **29** (9.60 g, 35.76 mmol, 93%).

29: yellow oil; [α]_D²⁶ 34.1 (c 0.208, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ

Supplementary Material (ESI) for Chemical Communications

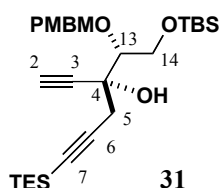
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0.61 (6H, q, $J = 8.0$ Hz, TES), 0.10 (9H, t, $J = 8.0$ Hz, TES), 2.09 (1H, dd, $J = 7.0, 5.0$ Hz, C14-OH), 2.57 (1H, s, H2), 2.65 (1H, d, $J = 6.5$ Hz, C13-OH), 2.80 (1H, d, $J = 16.5$ Hz, H4), 2.85 (1H, d, $J = 16.5$ Hz, H4), 3.07 (1H, s, C4-OH), 3.83 (1H, dt, $J = 6.5, 4.0$ Hz, H13), 3.89 (1H, ddd, $J = 11.5, 5.0, 4.0$ Hz, H14), 3.94 (1H, ddd, $J = 11.5, 7.0, 4.0$ Hz, H14); ^{13}C NMR (50 MHz, CDCl_3) δ 4.86 (3C), 7.94 (3C), 31.54, 63.20, 71.86, 75.09, 75.56, 83.64, 87.40, 102.12; FT-IR (neat) ν 3314, 2958, 2916, 2878, 2180, 2116, 1638, 1460, 1417, 1238, 1071, 1019, 891, 729 cm^{-1} ; HRMS (EI, 70 eV), calcd. for $\text{C}_{14}\text{H}_{24}\text{O}_3\text{Si}$ (M^+): 268.1495; found: 268.1500.



To a solution of **29** (9.60 g, 35.76 mmol) and Et_3N (7.5 mL, 53.6 mmol) in CH_2Cl_2 (72 mL) was added TBSCl (5.50 g, 36.5 mmol) and DMAP (430.0 mg, 3.52 mmol) at 0 °C. After stirring for 12 h at room temperature, the reaction mixture was diluted with hexane/EtOAc (2.8/1) (350 mL) and washed with water (100 mL). The water layer was extracted with hexane/EtOAc (2.8/1) (100 mL x 2), and the combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 , and concentrated. The crude product was purified by flash column chromatography on silica gel (hexane/EtOAc = 25:1 to 4.4:1) to give **30** (13.69 g, 35.76 mmol, >99%).

30: colorless oil; $[\alpha]_{\text{D}}^{29}$ 19.5 (c 1.12, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.11 (6H, s, TBS), 0.60 (6H, q, $J = 8.0$ Hz, TES), 0.91 (9H, s, TBS), 0.99 (9H, t, $J = 8.0$ Hz, TES), 2.51 (1H, s, H2), 2.71 (1H, d, $J = 4.5$ Hz, C13-OH), 2.80 (1H, d, $J = 16.5$ Hz, H4), 2.87 (1H, d, $J = 16.5$ Hz, H4), 3.60 (1H, s, C4-OH), 3.86 (1H, ddd, $J = 8.0, 6.0, 4.5$ Hz, H13), 3.86 (1H, ddd, $J = 13.0, 6.0$ Hz, H14), 3.97 (1H, dd, $J = 13.0, 8.0$ Hz, H14); ^{13}C NMR (50 MHz, CDCl_3) δ -5.02 (2C), 4.88 (3C), 7.94 (3C), 18.67, 26.28 (3C), 32.10, 64.25, 72.08, 74.42 (2C), 83.77, 86.96, 102.40; FT-IR (neat) ν 3444, 3314, 2958, 2878, 2180, 1464, 1417, 1363, 1257, 1062, 1007, 839, 779, 727, 669 cm^{-1} ; HRMS (EI, 70 eV), calcd. for $\text{C}_{20}\text{H}_{38}\text{O}_3\text{Si}_2$ (M^+): 382.2359; found: 382.2355.

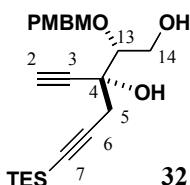


To a solution of **30** (3.12 g, 8.15 mmol) and *i*- Pr_2NEt (6.0 mL, 34.40 mmol) in

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CH₂Cl₂ (8 mL) was added a solution of freshly prepared PMBMCl (4.326 g, 22.93 mmol) in CH₂Cl₂ (12 mL) via cannula over 10 min. After stirring for 26.5 h at room temperature, the reaction mixture was diluted with Et₂O (200 mL) and quenched by sat. NaHCO₃ (20 mL) at 0 °C. The aqueous layer was separated and extracted with Et₂O (50 mL x 2), and the combined organic phase was dried over MgSO₄ and then concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 1:0 to 18:1) to give **31** (3.31 g, 6.21 mmol, 76%).

31: colorless oil; $[\alpha]_D^{29}$ 18.8 (c 1.01, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.07 (3H, s, TBS), 0.09 (3H, s, TBS), 0.59 (6H, q, *J* = 8.5 Hz, TES), 0.89 (9H, s, TBS), 0.99 (9H, t, *J* = 8.5 Hz, TES), 2.52 (1H, s, H2), 2.82 (1H, d, *J* = 16.5 Hz, H4), 2.86 (1H, d, *J* = 16.5 Hz, H4), 3.81 (3H, s, PMBM), 3.93 (1H, dd, *J* = 7.5, 5.0 Hz, H13), 4.00 (1H, dd, *J* = 10.0, 5.0 Hz, H14), 4.10 (1H, dd, *J* = 10.0, 7.5 Hz, H14), 4.47 (1H, s, OH), 4.54 (1H, d, *J* = 12.0 Hz, PMBM), 4.61 (1H, d, *J* = 12.0 Hz, PMBM), 4.89 (1H, d, *J* = 7.0 Hz, PMBM), 4.97 (1H, d, *J* = 7.0 Hz, PMBM), 6.88 (2H, d, *J* = 8.0 Hz, PMBM), 7.26 (2H, d, *J* = 8.0 Hz, PMBM); ¹³C NMR(50 MHz, CDCl₃) δ -5.52, -5.46, 4.58 (3C), 7.62 (3C), 18.25, 25.90 (3C), 31.45, 55.41, 64.40, 69.84, 72.60, 73.75, 79.39, 84.19, 85.77, 95.94, 102.72, 113.99 (2C), 129.50 (2C), 129.79, 159.44; FT-IR (neat) ν 3443, 3309, 2955, 2361, 2176, 1726, 1613, 1515, 1464, 1414, 1383, 1362, 1302, 1250, 1172, 1105, 1084, 1036, 837, 779, 737, 668 cm⁻¹; HRMS (EI, 70 eV), calcd. for C₂₉H₄₈O₅Si₂ (M⁺): 532.3040; found: 532.3044.

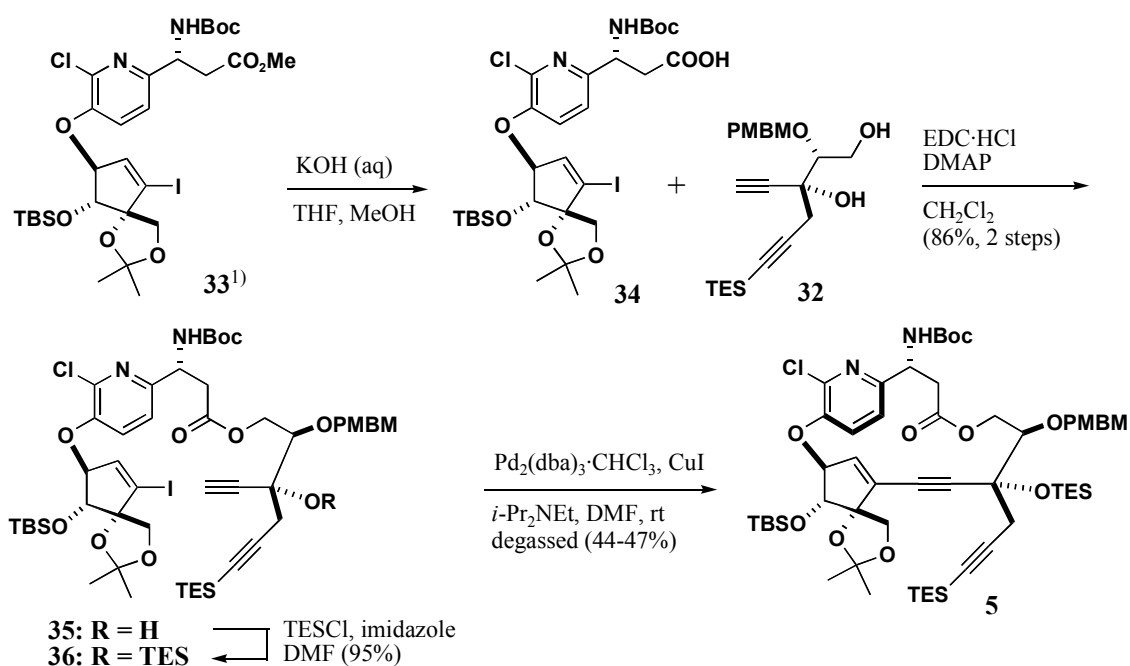


31 (2.026 g, 3.801 mmol) dissolved in THF (24 mL) and water (12 mL) was treated with TFA (1.2 mL) at 0 °C, and the reaction mixture was stirred for 4.5 h at room temperature. Sat. NaHCO₃ (aq.) (14 mL) was added dropwise to the solution at 0 °C. After stirring vigorously for 0.5 h at room temperature, the mixture was extracted with EtOAc (100 mL x 3). The combined organic extracts were dried over MgSO₄ and then concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc = 7:1 to 3:1) to give **32** (1.457 g, 3.481 mmol, 92%).

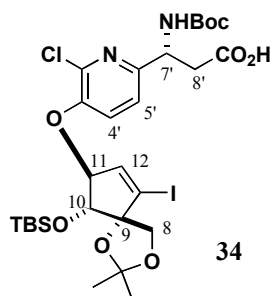
32: colorless oil; $[\alpha]_D^{27}$ 43.4 (c 1.00, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.60 (6H, q, *J* = 7.5 Hz, TES), 0.99 (9H, t, *J* = 7.5 Hz, TES), 2.54 (1H, s, H2), 2.80 (1H, d, *J* = 17.0 Hz, H5), 2.86 (1H, d, *J* = 17.0 Hz, H5), 3.00 (1H, dd, *J* = 8.5, 4.0 Hz, C14-OH), 3.12 (1H, s, C4-OH), 3.79 (1H, dd, *J* = 6.5, 3.5 Hz, H13), 3.81 (3H, s, PMBM), 3.85 (1H, ddd, *J* = 12.0, 6.5, 4.0 Hz, H14), 4.04 (1H, ddd, *J* = 12.0, 8.5, 3.5 Hz, H14),

4.57 (1H, d, $J = 11.5$ Hz, PMBM), 4.69 (1H, d, $J = 11.5$ Hz, PMBM), 4.86 (1H, d, $J = 6.5$ Hz, PMBM), 4.96 (1H, d, $J = 6.5$ Hz, PMBM), 6.89 (2H, d, $J = 8.5$ Hz, PMBM), 7.27 (2H, d, $J = 8.5$ Hz, PMBM); ^{13}C NMR (125 MHz, CDCl_3) δ 4.57 (3C), 7.51 (3C), 31.64, 55.36, 62.68, 70.29, 71.19, 74.13, 83.45, 84.05, 86.87, 95.94, 101.86, 114.13 (2C), 129.29, 129.66 (2C), 159.66; FT-IR (neat) ν 3401, 3306, 2954, 2874, 2177, 1736, 1613, 1587, 1515, 1463, 1415, 1382, 1250, 1171, 1037, 919, 885, 835, 727, 663 cm^{-1} ; HRMS (EI, 70 eV), calcd. for $\text{C}_{23}\text{H}_{34}\text{O}_5\text{Si}$ (M^+): 418.2176; found: 418.2175.

3. Transformation to the ansamacrolide (5)



1) Koyama, Y.; Lear, M. J.; Yoshimura, F.; Ohahsi, I.; Mashimo, T.; Hirma, M. *Org. Lett.* **2005**, *7*, 267.



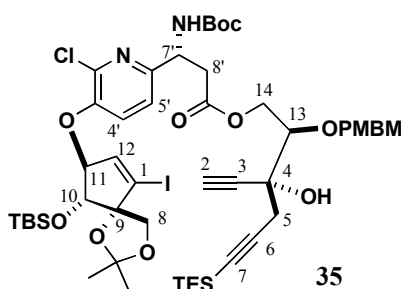
A solution of **33** (5.54 g, 7.495 mmol) in THF (41.6 mL) and MeOH (20.8 mL) was cooled to 0 °C. A 0.5 M aqueous solution of KOH (27.0 mL, 13.5 mmol) was added dropwise over 3 min. The reaction mixture was stirred at 0 °C for 10 min and then for a further 2.5 h at room temperature. After diluting with Et_2O (400 mL) and washing with 5% KHSO_4 (aq.) (85 mL), the layers were separated, and the aqueous fraction was extracted with Et_2O (100 mL x 4). The combined organic extracts were

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washed with brine (35 mL), dried over Na₂SO₄, and then concentrated. The crude product (5.58 g, >99%) was used directly in the next reaction, but purified by flash column chromatography over silica gel eluting with 100:5 = CHCl₃:MeOH for characterization.

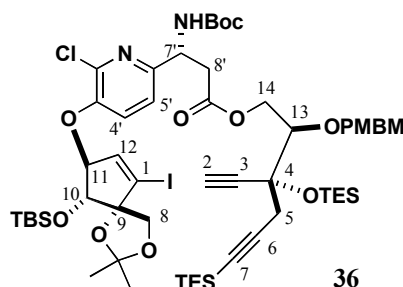
34: colorless oil; $[\alpha]_D^{27}$ 122.4 (c 0.608, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.08 (3H, s, TBS), 0.18 (3H, s, TBS), 0.88 (9H, s, TBS), 1.43 (9H, s, Boc), 1.46 (3H, s, acetonide), 1.59 (1H, s, acetonide), 2.93 (1H, dd, *J* = 16.5, 7.0 Hz, H8'), 3.08 (1H, dd, *J* = 16.5, 3.5 Hz, H8'), 3.96 (1H, d, *J* = 9.5 Hz, H8), 4.12 (1H, d, *J* = 9.5 Hz, H8), 4.23 (1H, d, *J* = 5.0 Hz, H10), 5.12 (1H, ddd, *J* = 8.5, 7.0, 3.5 Hz, H7'), 5.18 (1H, dd, *J* = 5.0, 1.5 Hz, H11), 6.39 (1H, d, *J* = 1.5 Hz, H12), 7.14 (1H, d, *J* = 8.5 Hz, H4'), 7.29 (1H, d, *J* = 8.5 Hz, H5'); ¹³C NMR (50 MHz, CDCl₃) δ -4.36(2C), 18.34, 25.95(3C), 26.24, 27.94, 28.49(3C), 39.18, 50.80, 71.00, 76.98, 80.29, 85.79, 90.65, 107.34, 111.71, 121.19, 121.65, 139.42, 140.36, 148.77, 151.55, 155.41, 175.10; FT-IR (film) ν 2930, 1714, 1563, 1505, 1455, 1371, 1254, 1167, 1089, 974, 840, 758 cm⁻¹; HRMS (EI, 70 eV), calcd. for C₂₈H₄₁ClIN₂O₈Si (M-H)⁺: 723.1362; found: 723.1358.



To a solution of the crude carboxylic acid **34** (5.58 g, 7.495 mmol) and the alcohol **32** (2.99 g, 7.143 mmol) in CH₂Cl₂ (94 mL) was added EDC·HCl (2.16 g, 11.24 mmol) at 0 °C. After being stirred at 0 °C for 5 min, to the reaction mixture was added a solution of DMAP (91.8 mg, 0.7514 mmol) in CH₂Cl₂ (2 mL) at 0 °C. The reaction mixture was then stirred at room temperature for 13 h. After dilution of Et₂O (400 mL) and washing with sat. NH₄Cl (aq.) (85 mL), the layers were separated, and the aqueous layers extracted with Et₂O (60 mL x 4). The combined organic extracts were dried over Na₂SO₄, concentrated, and the crude product purified by flash column chromatography on silica gel (hexane/EtOAc = 1:0 to 4:1) to give **35** (7.22 g, 6.415 mmol, 86% for 2 steps).

35: white amorphous; $[\alpha]_D^{29}$ 94.9 (c 0.958, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ 0.11 (3H, s, TBS), 0.20 (3H, s, TBS), 0.59 (6H, q, *J* = 8.0 Hz, TES), 0.90 (9H, s, TBS), 0.98 (6H, q, *J* = 8.0 Hz, TES), 1.44 (9H, s, Boc), 1.47 (3H, s, acetonide), 1.60 (3H, s, acetonide), 2.54 (1H, s, H2), 2.81 (1H, d, *J* = 17.0 Hz, H5), 2.82 (1H, dd, *J* = 16.4, 6.5 Hz, H8'), 2.83 (1H, d, *J* = 17.0 Hz, H5), 3.04 (1H, dd, *J* = 16.4, 5.4 Hz, H8'),

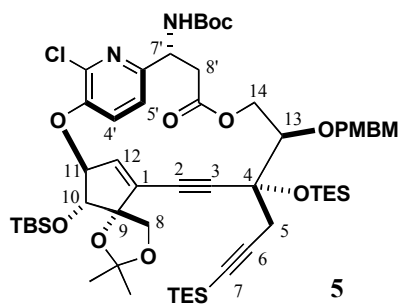
3.27 (1H, s, OH), 3.80 (3H, s, PMBM), 3.97 (1H, d, $J = 9.3$ Hz, H8), 4.00 (1H, dd, $J = 6.5, 3.2$ Hz, H13), 4.12 (1H, d, $J = 9.3$ Hz, H8), 4.22 (1H, d, $J = 4.9$ Hz, H10), 4.32 (1H, dd, $J = 12.0, 6.5$ Hz, H14), 4.54 (1H, dd, $J = 12.0, 3.2$ Hz, H14), 4.60 (2H, s, PMBM), 4.86 (1H, d, $J = 7.0$ Hz, PMBM), 4.88 (1H, d, $J = 7.0$ Hz, PMBM), 5.09 (1H, ddd, $J = 9.1, 6.5, 5.1$ Hz, H7'), 5.11 (1H, dd, $J = 4.9, 1.4$ Hz, H11), 5.77 (1H, d, $J = 9.1$ Hz, NH), 6.39 (1H, d, $J = 1.4$ Hz, H12), 6.87 (2H, d, $J = 8.7$ Hz, PMBM), 7.10 (1H, d, $J = 8.5$ Hz, H4'), 7.24 (1H, d, $J = 8.5$ Hz, H5'), 7.26 (2H, d, $J = 8.7$ Hz, PMBM); ^{13}C NMR (150 MHz, CDCl_3) δ -4.47 (TBS), -4.52 (TBS), 4.35 (3C, TES), 7.47 (3C, TES), 18.18 (TBS), 25.80 (3C, TBS), 26.11 (acetone), 27.79 (acetone), 28.36 (3C, Boc), 31.29 (C5), 39.06 (C8'), 50.78 (C7'), 55.28 (PMBM), 64.54 (C14), 69.84 (PMBM), 70.52 (C4), 70.82 (C8), 74.23 (C2), 77.21 (C10), 79.27 (C13), 79.91 (Boc), 82.99 (C3), 85.55 (C11), 86.96 (C6), 90.40 (C1), 95.09 (PMBM), 101.54 (C7), 107.38 (C9), 111.47 (acetone), 113.86 (2C, PMBM), 120.80 (C4'), 121.09 (C5'), 129.42 (PMBM), 129.44 (2C, PMBM), 139.10 (C12), 140.02 (C6'), 148.43 (C3'), 151.59 (C2'), 155.17 (Boc), 159.31 (PMBM), 171.11 (C9'); FT-IR (film) ν 3435, 2955, 2981, 1717, 1615, 1560, 1515, 1455, 1369, 1287, 1250, 1169, 1089, 1034, 897, 840, 780, 739, 668 cm^{-1} ; MS (ESI), calcd for $\text{C}_{51}\text{H}_{75}\text{ClIN}_2\text{O}_{12}\text{Si}_2$ ($\text{M}+\text{H}$) $^+$ 1125.3592, found 1125.3605.



To a solution of **35** (5.010 g, 4.451 mmol) and imidazole (1.1 g, 16.15 mmol) in DMF (22 mL) was added TESCl (1.1 mL, 6.676 mmol) at 0 °C. After stirring for 15 h at room temperature, the reaction mixture was diluted with Et_2O (300 mL) and then quenched with sat. NaHCO_3 (aq.) (30 mL) and water (15 mL). The mixture was then extracted with Et_2O (50 mL x4), the organic layers were combined and then washed with brine (20 mL), dried over MgSO_4 and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/ EtOAc = 12:1 to 5:1) to give **36** (5.215 g, 4.206 mmol, 95%).

36: white amorphous; $[\alpha]_{\text{D}}^{28}$ 86.9 (c 0.276, CHCl_3); ^1H NMR (600 MHz, CDCl_3) δ 0.11 (3H, s, TBS), 0.20 (3H, s, TBS), 0.57 (6H, q, $J = 7.9$ Hz, TES), 0.71 (6H, q, $J = 7.9$ Hz, TES), 0.90 (9H, s, TBS), 0.95 (9H, t, $J = 7.9$ Hz, TES), 0.97 (9H, t, $J = 7.9$ Hz, TES), 1.44 (9H, s, Boc), 1.47 (3H, s, acetone), 1.60 (3H, s, acetone), 2.56 (1H, s, H2), 2.75 (1H, d, $J = 17.2$ Hz, H4), 2.79 (1H, dd, $J = 16.6, 6.0$ Hz, H8'), 2.90

(1H, d, $J = 17.2$ Hz, H4), 3.04 (1H, dd, $J = 16.6, 4.7$ Hz, H8'), 3.80 (3H, s, PMBM), 3.97 (1H, d, $J = 9.3$ Hz, H8), 4.07 (1H, dd, $J = 7.3, 2.5$ Hz, H13), 4.12 (1H, d, $J = 9.3$ Hz, H8), 4.22 (1H, d, $J = 4.9$ Hz, H10), 4.32 (1H, dd, $J = 11.8, 7.3$ Hz, H14), 4.49 (1H, dd, $J = 11.8, 2.5$ Hz, H14), 4.56 (1H, d, $J = 11.7$ Hz, PMBM), 4.66 (1H, d, $J = 11.7$ Hz, PMBM), 4.86 (1H, d, $J = 6.7$ Hz, PMBM), 4.91 (1H, d, $J = 6.7$ Hz, PMBM), 5.07 (1H, ddd, $J = 8.7, 6.0, 4.7$ Hz, H7'), 5.10 (1H, dd, $J = 4.9, 1.4$ Hz, H11), 5.81 (1H, d, $J = 8.7$ Hz, NH), 6.39 (1H, d, $J = 1.4$ Hz, H12), 6.87 (2H, d, $J = 8.7$ Hz, PMBM), 7.07 (1H, d, $J = 8.5$ Hz, H4'), 7.24 (1H, d, $J = 8.5$ Hz, H5'), 7.27 (2H, d, $J = 8.7$ Hz, PMBM); ^{13}C NMR (150 MHz, CDCl_3) δ -4.55 (TBS), -4.48 (TBS), 4.33 (3C, TES), 5.91 (3C, TES), 6.94 (3C, TES), 7.42 (3C, TES), 18.17 (TBS), 25.79 (3C, TBS), 26.11 (acetonide), 27.79 (acetonide), 28.35 (3H, Boc), 32.19 (C5), 38.62 (C8'), 50.76 (C7'), 55.25 (PMBM), 65.18 (C14), 69.49 (PMBM), 70.82 (C8), 71.90 (C4), 75.60 (C2), 76.79 (C10), 79.04 (C13), 79.73 (Boc), 83.61 (C3), 85.47 (C11), 86.07 (C6), 90.43 (C1), 95.26 (PMBM), 102.22 (C7), 107.28 (C9), 111.45 (acetonide), 113.73 (2C, PMBM), 120.72 (C4'), 120.91 (C5'), 129.19 (2C, PMBM), 129.96 (PMBM), 139.16 (C12), 139.93 (C2'), 148.28 (C3'), 151.94 (C6'), 155.19 (Boc), 159.09 (PMBM), 171.22 (C9'); FT-IR (film) ν 3436, 3307, 2955, 1736, 1612, 1560, 1515, 1456, 1368, 1245, 1152, 1106, 1039, 922, 840, 780, 741, 668 cm^{-1} ; MS (ESI), calcd for $\text{C}_{57}\text{H}_{89}\text{ClIN}_2\text{O}_{12}\text{Si}_3$ ($\text{M}+\text{H}$) $^+$ 1239.4457, found 1239.4465.



A solution of **36** (372.9 mg, 0.3009 mmol) and *i*-Pr₂NEt (1.87 mL, 10.72 mmol) in DMF (300 mL) was degassed by freeze-pump-thaw cycle (three times). After addition of CuI (114.5 mg, 0.6012 mmol), the mixture was vigorously stirred at room temperature in the dark for 0.5 h, producing a colorless solution. Pd₂(dba)₃·CHCl₃ (155.7 mg, 0.1504 mmol) was added to the resulting solution, after which the reaction mixture was stirred at room temperature for 1 h in the dark, diluted with Et₂O (450 mL) and then quenched with sat. NH₄Cl (aq.) (50 mL) and water (40 mL) at 0 °C. The mixture was vigorously stirred at room temperature until the aqueous phase turned into dark blue (ca. 1 h). After being diluted with Et₂O (800 mL), the layers were separated, and the organic phase was washed with water (60 mL x 4). The aqueous layers were

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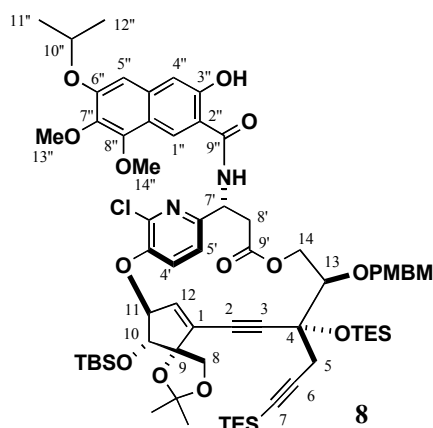
extracted with Et₂O (100 mL x 3), and the combined organic extracts were washed with brine (80 mL), dried over MgSO₄ and then concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 20:1 to 8:1) to give **5** (158.7 mg, 0.1427 mmol, 47%).

5. (1.4 gram scale). A solution of **36** (668.3 mg, 0.5393 mmol) and *i*-Pr₂NEt (3.35 mL, 19.17 mmol) in DMF (270 mL) was degassed by freeze-pump-thaw cycle (two times). After addition of CuI (209 mg, 1.097 mmol), the mixture was vigorously stirred at room temperature in the dark for 0.5 h, producing a colorless solution. Pd₂(dba)₃·CHCl₃ (307 mg, 0.2966 mmol) was added to the resulting solution, after which the reaction mixture was stirred at room temperature for 35 min in the dark, diluted with Et₂O (400 mL) and then quenched with sat. NH₄Cl (aq.) (80 mL) and water (40 mL) at 0 °C in a sequential manner. The mixture was vigorously stirred at room temperature until the aqueous phase turned into dark blue (ca. 1 h). A second batch of **36** (695.7 mg, 0.5614 mmol) was processed in parallel in an identical manner, and the reaction batches were combined and diluted with Et₂O (500 mL x 3). After the layers were separated, the organic phase was washed with water (100 mL x 4) and brine (100 mL). Then, the aqueous layers were extracted with Et₂O (150 mL x 4), dried over Na₂SO₄ and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 20:1 to 8:1) to give **5** (532.0 mg, 0.4784 mmol, 44%).

5: colorless oil; $[\alpha]_D^{30}$ 99.3 (c 0.550, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.22 (3H, s, TBS), 0.25 (3H, s, TBS), 0.62 (6H, q, *J* = 8.0 Hz, TES), 0.62 (6H, q, *J* = 8.0 Hz, TES), 0.89 (9H, t, *J* = 8.0 Hz, TES), 0.98 (9H, s, TBS), 0.99 (9H, t, *J* = 8.0 Hz, TES), 1.44 (9H, s, Boc), 1.45 (3H, s, acetonide), 1.48 (3H, s, acetonide), 2.49 (1H, d, *J* = 16.5 Hz, H5), 2.51 (1H, dd, *J* = 14.0, 11.5, H8a'), 2.82-2.89 (1H, m, H8b'), 2.85 (1H, d, *J* = 16.5 Hz, H5), 3.82 (3H, s, PMBM), 3.94-3.98 (2H, m, H13, H14), 3.95 (1H, d, *J* = 9.0 Hz, H8), 4.06 (1H, d, *J* = 3.5 Hz, H10), 4.19 (1H, d, *J* = 9.0 Hz, H8), 4.21 (1H, dd, *J* = 12.5, 6.5 Hz, H14), 4.41 (1H, d, *J* = 11.5 Hz, PMBM), 4.59 (1H, d, *J* = 11.5 Hz, PMBM), 4.77 (1H, d, *J* = 6.5 Hz, PMBM), 4.88 (1H, d, *J* = 6.5 Hz, PMBM), 5.10-5.18 (1H, m, H7'), 5.44 (1H, dd, *J* = 3.5, 2.0 Hz, H11), 5.52 (1H, d, *J* = 8.0 Hz, NH), 5.79 (1H, d, *J* = 2.0 Hz, H12) 6.89 (2H, d, *J* = 8.5 Hz, PMBM), 7.06 (1H, brs, H4'), 7.06 (1H, brs, H5'), 7.25 (2H, d, *J* = 8.5 Hz, PMBM); ¹³C NMR (125 MHz, CDCl₃) δ -4.36 (TBS), -4.26 (TBS), 4.18 (3C, TES), 5.85 (3C, TES), 6.89 (3C, TES), 7.60 (3C, TES), 18.29 (TBS), 25.87 (3C, TBS), 26.37 (acetonide), 26.66 (acetonide), 28.15 (C5), 28.31 (3C, Boc), 41.27 (C8'), 51.81 (C7'), 55.28 (PMBM), 68.47 (C14), 68.82 (PMBM), 70.12 (C8), 73.82 (C4), 79.89 (Boc), 81.84 (C10), 82.39 (C2), 83.56 (C13), 85.75 (C6), 88.39 (C9), 88.90 (C11), 95.38 (PMBM), 95.82 (C3), 101.78 (C7), 110.84 (acetonide), 113.81 (2C, PMBM), 122.89 (C5'), 129.33 (2C, PMBM), 129.76 (PMBM), 131.84 (C1), 132.32 (C4'), 139.70 (C12), 146.85 (C2'), 148.18 (C3'), 154.55 (C6'), 154.73

(Boc), 159.23 (PMBM), 169.88 (C9'); FT-IR (film) ν 3436, 2928, 2868, 1734, 1718, 1654, 1617, 1560, 1514, 1464, 1380, 1298, 1250, 1081, 1008, 885, 838, 778, 727 cm^{-1} ; MS (ESI), calcd for $\text{C}_{57}\text{H}_{88}\text{ClN}_2\text{O}_{12}\text{Si}_3$ (M+H)⁺ 1111.5334, found 1111.5339.

Synthesis of 8 from 5



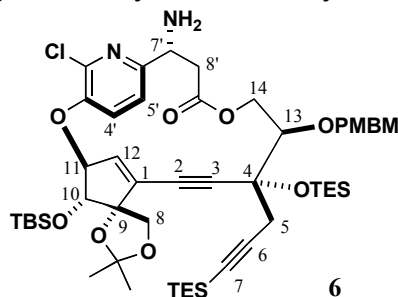
(1) To a solution of **5** (316.2 mg, 0.2844 mmol) and 2,6-lutidine (225 μL , 1.932 mmol) in CH_2Cl_2 (5.7 mL) was added TBSOTf (325 μL , 1.415 mmol) at $-50\text{ }^\circ\text{C}$. The reaction mixture was stirred at $-50\text{ }^\circ\text{C}$ for 0.5 h and then at $0\text{ }^\circ\text{C}$ for 5.5 h. The product solution was diluted with Et_2O (20 mL) and then quenched with sat. NH_4Cl (aq.) (5 mL) at $0\text{ }^\circ\text{C}$. The aqueous fraction was extracted with Et_2O (7 mL x 3), and the combined organic extracts washed with brine (3 mL), dried over Na_2SO_4 , and then concentrated in high vacuum to give an *O*-silylcarbamate (475.8 mg). This product was used directly in the next reaction without further purification: (2) The crude *O*-silylcarbamate (475.8 mg) was dissolved in CH_2Cl_2 (9.4 mL), and the mixture was stirred at room temperature in the dark for 16.5 h in the presence of silica gel (2.27 g). The slurry was poured onto a silica-gel column and flash chromatography was performed by eluting with 1% Et_3N in CHCl_3 . The fractions containing product were combined and then concentrated to give amine **6** (323.3 mg). This product was used directly in the next reaction: (3) The amine **6** (323.3 mg, 0.2844 mmol), acid **7** (87.1

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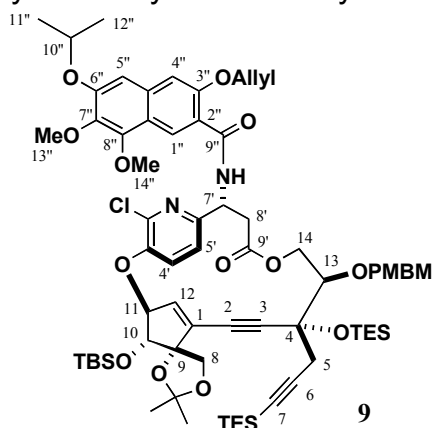
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mg, 0.2844 mmol) and HOAt (131.5 mg, 0.9661 mmol) were dissolved in CH₂Cl₂ (9.4 mL), and the solution was cooled to 0 °C. EDC·HCl (162.9 mg, 0.8497 mmol) was added, and the reaction mixture stirred at 0 °C for 17 h, after which the reaction was diluted with Et₂O (20 mL) and then quenched with sat. NH₄Cl (aq.) (3 mL) and water (2 mL) at 0 °C. The layers were separated, and the aqueous phase was extracted with Et₂O (10 mL x 4). The combined organic extracts were dried over MgSO₄ and concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:0 to 5:1) to give **8** (324.8 mg, 0.2498 mmol, 88% for 3 steps).

8: white amorphous; $[\alpha]_D^{24}$ 114.5 (c 0.406, CHCl₃); ¹H NMR (600 MHz, CDCl₃) δ 0.23 (3H, s, TBS), 0.27 (3H, s, TBS), 0.65 (6H, q, *J* = 7.9 Hz, TES), 0.66 (6H, q, *J* = 7.9 Hz, TES), 0.90 (9H, t, *J* = 7.9 Hz, TES), 0.99 (9H, s, TBS), 1.02 (9H, t, *J* = 7.9 Hz, TES), 1.46 (6H, d, *J* = 6.1 Hz, H11''), 1.47 (3H, s, acetonide), 1.50 (3H, s, acetonide), 2.51 (1H, d, *J* = 16.6 Hz, H5), 2.60 (1H, dd, *J* = 14.4, 11.5 Hz, H8'), 2.89 (1H, d, *J* = 16.6 Hz, H5), 3.01 (1H, dd, *J* = 14.4, 4.9 Hz, H8'), 3.70 (3H, s, PMBM), 3.91 (3H, s, H13''), 3.97 (1H, d, *J* = 6.5 Hz, H13), 3.99 (1H, d, *J* = 8.6 Hz, H8), 4.02 (1H, d, *J* = 12.5 Hz, H14), 4.09 (1H, d, *J* = 3.9 Hz, H10), 4.14 (3H, s, H14''), 4.22 (1H, d, *J* = 8.6 Hz, H8), 4.27 (1H, dd, *J* = 12.5, 6.5 Hz, H14), 4.43 (1H, d, *J* = 11.5 Hz, PMBM), 4.59 (1H, d, *J* = 11.5 Hz, PMBM), 4.73 (1H, heptet, *J* = 6.1 Hz, H10''), 4.79 (1H, d, *J* = 6.7 Hz, PMBM), 4.89 (1H, d, *J* = 6.7 Hz, PMBM), 5.48 (1H, dd, *J* = 3.9, 2.2 Hz, H11), 5.63 (1H, ddd, *J* = 11.5, 7.9, 4.9 Hz, H7'), 5.79 (1H, d, *J* = 2.2 Hz, H12), 6.72 (1H, s, H5''), 6.87 (2H, d, *J* = 8.6 Hz, PMBM), 7.10 (1H, s, H4''), 7.12 (1H, d, *J* = 8.0 Hz, H4'), 7.18 (1H, d, *J* = 8.0 Hz, H5'), 7.24 (2H, d, *J* = 8.6 Hz, PMBM), 7.65 (1H, d, *J* = 7.9 Hz, NH), 8.23 (1H, s, H1''), 11.73 (1H, s, OH); ¹³C NMR (150 MHz, CDCl₃) δ -4.37 (TBS), -4.27 (TBS), 4.18 (3C, TES), 5.86 (3C, TES), 6.90 (3C, TES), 7.65 (3C, TES), 18.30 (TBS), 21.90 (2C, C11'', C12''), 25.86 (9C, TBS), 26.38 (acetonide), 26.63 (acetonide), 28.18 (C5), 40.88 (C8'), 50.46 (C7'), 55.17 (PMBM), 61.05 (C13''), 61.57 (C14''), 68.63 (C13), 68.77 (PMBM), 70.13 (C8), 70.60 (C10''), 73.79 (C4), 81.88 (C10), 82.33 (C2), 83.55 (C13), 85.78 (C6), 88.47 (C9), 88.95 (C11), 95.46 (PMBM), 95.88 (C3), 101.75 (C7), 101.89 (C5''), 110.82 (C4''), 110.90 (acetonide), 113.62 (C2''), 117.44 (C8a'') 113.78 (2C, PMBM), 121.27 (C1''), 123.02 (C5'), 129.16 (2C, PMBM), 129.70 (PMBM), 132.07 (C1), 132.68 (C4'), 135.24 (C4a''), 139.29 (C7''), 139.50 (C12), 146.91 (C2'), 148.55 (C8''), 148.69 (C3'), 153.42 (C6'), 154.08 (C6''), 157.23 (C3''), 159.20 (PMBM), 169.31 (C9''), 169.69 (C9'); FT-IR (film) ν 3339, 2948, 2868, 1735, 1654, 1618, 1515, 1465, 1384, 1301, 1248, 1082, 1008, 885, 838, 778, 729, 703 cm⁻¹; MS (ESI), calcd. for C₆₈H₉₆ClN₂O₁₅Si₃ (M+H)⁺: 1299.5807; found: 1299.5798.



6: Pale yellow oil; $[\alpha]_D^{21}$ 97.9 (c 0.362, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.22 (3H, s, TBS), 0.26 (3H, s, TBS), 0.60-0.66 (12H, m, TES), 0.89 (9H, t, $J = 7.5$ Hz, TES), 0.98 (9H, s, TBS), 0.99 (9H, t, $J = 8.5$ Hz, TES), 1.45 (3H, s, acetonide), 1.48 (3H, s, acetonide), 2.17 (2H, brs, NH_2), 2.48 (1H, d, $J = 16.5$ Hz, H5), 2.56 (1H, dd, $J = 14.0, 12.0$ Hz, H8'), 2.70 (1H, dd, $J = 14.0, 4.5$ Hz, H8'), 2.86 (1H, d, $J = 16.5$ Hz, H5), 3.82 (3H, s, PMBM), 3.90 (1H, d, $J = 12.0$ Hz, H14), 3.95 (1H, d, $J = 9.0$ Hz, H8), 3.96 (1H, d, $J = 6.0$ Hz, H13), 4.05 (1H, d, $J = 4.5$ Hz, H10), 4.19 (1H, d, $J = 9.0$ Hz, H8), 4.24 (1H, dd, $J = 12.0, 6.0$ Hz, H14), 4.31 (1H, dd, $J = 12.0, 4.5$ Hz, H7'), 4.41 (1H, d, $J = 11.5$ Hz, PMBM), 4.59 (1H, d, $J = 11.5$ Hz, PMBM), 4.78 (1H, d, $J = 6.5$ Hz, PMBM), 4.88 (1H, d, $J = 6.5$ Hz, PMBM), 5.44 (1H, dd, $J = 4.5, 2.0$ Hz, H11), 5.84 (1H, d, $J = 2.0$ Hz, H12), 6.90 (2H, d, $J = 8.5$ Hz, PMBM), 6.95 (1H, d, $J = 8.0$ Hz, H4'), 7.03 (1H, d, $J = 8.0$ Hz, H5'), 7.25 (2H, d, $J = 8.5$ Hz, PMBM); ^{13}C NMR (50 MHz, CDCl_3) δ -4.21 (TBS), -4.09 (TBS), 4.31 (3C, TES), 6.00 (3C, TES), 7.06 (3C, TES), 7.80 (3C, TES), 18.44 (TBS), 26.02 (3C, TBS), 26.50 (acetonide), 26.81 (acetonide), 28.22 (C5), 44.41 (C8'), 53.66 (C7'), 55.45 (PMBM), 68.52 (PMBM), 69.02 (C14), 70.22 (C8), 73.94 (C4), 82.03 (C10), 82.71 (C2), 83.87 (C13), 85.76 (C6), 88.46 (C9), 88.94 (C11), 95.62 (C3), 95.91 (PMBM), 101.98 (C7), 110.97 (acetonide), 113.96 (2C, PMBM), 122.19 (C5'), 129.47 (2C, PMBM), 129.90 (PMBM), 131.77 (C1), 132.29 (C4'), 140.18 (C12), 147.29 (C2'), 147.99 (C3'), 158.66 (C6'), 159.35 (PMBM), 170.93 (C9'); FT-IR (film) ν 3547, 2954, 1734, 1515, 1448, 1250, 1079, 1033, 839, 739 cm^{-1} ; MALDI-TOFMS, calcd for $\text{C}_{52}\text{H}_{79}\text{ClN}_2\text{O}_{10}\text{Si}_3\text{Na}$ ($\text{M}+\text{Na}$) $^+$ 1033.4629, found 1033.4916.



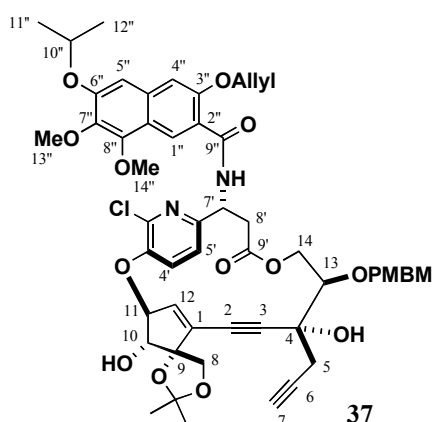
To a suspension of **8** (173.5 mg, 0.1334 mmol) and Cs_2CO_3 (100.0 mg, 0.3069 mmol) in DMF (1.8 mL) was added allyl bromide (24.8 μL , 0.2669 mmol) at 0 °C. After stirring for 2 h at 0 °C, the reaction mixtures was diluted with EtOAc (25 mL) and quenched with sat. NH_4Cl (aq.) (3 mL) and then water (1 mL) at 0 °C. The water layer was extracted with EtOAc (4 mL x 4), and the combined organic layers were washed with brine (3 mL), dried over MgSO_4 , and then concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:0 to 4:1) to give **9** (179.6 mg, 0.1334 mmol, >99%).

9: white amorphous; $[\alpha]_{\text{D}}^{28}$ 118.7 (c 0.826, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.23 (3H, s, TBS), 0.27 (3H, s, TBS), 0.64 (6H, q, $J = 8.0$ Hz, TES), 0.66 (6H, q, $J = 8.5$ Hz, TES), 0.85 (9H, t, $J = 7.5$ Hz, TES), 0.99 (9H, s, TBS), 1.01 (9H, t, $J = 8.0$ Hz, TES), 1.45 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 1.46 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 1.46 (3H, s, acetonide), 1.50 (3H, s, acetonide), 2.52 (1H, d, $J = 16.5$ Hz, H5), 2.63 (1H, dd, $J = 14.5, 11.0$ Hz, H8'), 2.86 (1H, d, $J = 16.5$ Hz, H5), 3.15 (1H, dd, $J = 14.5, 5.0$ Hz, H8'), 3.68 (3H, s, PMBM), 3.91 (3H, s, H13''), 3.97 (1H, d, $J = 7.0$ Hz, H13), 3.97 (1H, d, $J = 9.0$ Hz, H8), 4.01 (1H, d, $J = 12.5$ Hz, H14), 4.06 (3H, s, H14''), 4.07 (1H, d, $J = 4.5$ Hz, H10), 4.22 (1H, d, $J = 9.0$ Hz, H8), 4.23 (1H, dd, $J = 12.5, 7.0$ Hz, H14), 4.41 (1H, d, $J = 11.5$ Hz, PMBM), 4.58 (1H, d, $J = 11.5$ Hz, PMBM), 4.71 (1H, heptet, $J = 6.0$ Hz, H10''), 4.77 (1H, d, $J = 6.5$ Hz, PMBM), 4.79-4.82 (2H, m, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 4.88 (1H, d, $J = 6.5$ Hz, PMBM), 5.39 (1H, dd, $J = 10.0, 1.5, 1.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.46 (1H, dd, $J = 4.5, 2.5$ Hz, H11), 5.47 (1H, ddd, $J = 17.0, 1.5, 1.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.72 (1H, ddd, $J = 11.0, 7.5, 5.0$ Hz, H7'), 5.84 (1H, d, $J = 2.5$ Hz, H12), 6.32 (1H, dddd, $J = 17.0, 10.0, 5.5, 5.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 6.80 (1H, s, H5''), 6.84 (2H, d, $J = 8.5$ Hz, PMBM), 7.04 (1H, s, H4''), 7.10 (1H, d, $J = 8.5$ Hz, H4'), 7.18 (1H, d, $J = 8.5$ Hz, H5'), 7.23 (2H, d, $J = 8.5$ Hz, PMBM), 8.94 (1H, s, H1''), 9.06 (1H, d, $J = 7.5$ Hz, NH); ^{13}C NMR (50MHz, CDCl_3) δ -4.20 (TBS), -4.11 (TBS), 4.32 (3C, TES), 5.87 (3C, TES), 7.05 (3C, TES), 7.80 (3C, TES), 18.44 (TBS), 22.10 (2C, C11'', C12''), 26.02 (3C, TBS), 26.49 (acetonide), 26.82 (acetonide), 28.26 (C5), 41.12 (C8'), 51.51 (C7'), 55.28 (PMBM), 61.17 (C13''), 61.78 (C14''), 68.54

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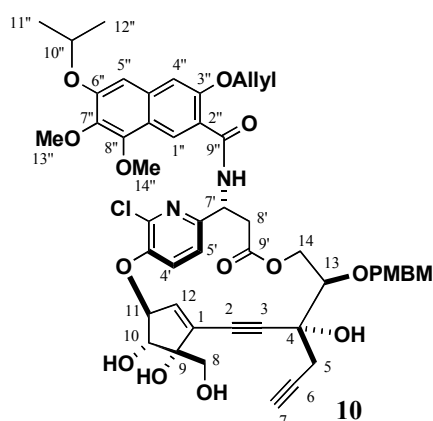
(C14), 68.90 (PMBM), 70.19 (C8), 70.36 (CH₂=CH-CH₂-), 70.79 (C10''), 73.96 (C4), 82.00 (C10), 82.49 (C2), 83.76 (C13), 85.89 (C6), 88.47 (C9), 89.05 (C11), 95.44 (PMBM), 96.00 (C3), 101.91 (C7), 102.86 (C5''), 106.80 (acetonide), 110.96 (C4''), 113.90 (2C, PMBM), 118.96 (CH₂=CH-CH₂-), 119.33 (C8a''), 119.61 (C2''), 123.39 (C5'), 128.36 (C1''), 129.54 (2C, PMBM), 129.75 (PMBM), 131.87 (CH₂=CH-CH₂-), 132.52 (C4a''), 132.68 (C4'), 133.77 (C1), 139.87 (C12), 140.32 (C7''), 147.00 (C2'), 148.29 (C3'), 149.57 (C8''), 153.80 (C6''), 154.32 (C3''), 154.74 (C6'), 159.32 (PMBM), 164.64 (C9''), 170.21 (C9'); FT-IR (film) ν 3392, 1735, 1654, 1619, 1515, 1448, 1383, 1251, 1112, 839, 758 cm⁻¹; MS (ESI), calcd. for C₇₁H₁₀₀ClN₂O₁₅Si₃ (M+H)⁺: 1339.6120; found: 1339.6131.



To a solution of **9** (729.1 mg, 0.5440 mmol) in THF (9.2 mL) was added TBAF (1.0 M solution in THF, 1.75 mL, 1.75 mmol) at 0 °C, and the resulting solution was stirred at 0 °C for 2 h. Further TBAF (1.0 M solution in THF, 217 μ L, 0.217 mmol) was added at 0 °C and stirring was continued for 1.5 h at 0 °C. The reaction mixtures was diluted with EtOAc (50 mL) and then quenched by the sequential addition of sat. NH₄Cl (aq.) (3 mL) and water (3 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (10 mL x 4). The combined organic extracts were washed with brine (6 mL), dried over Na₂SO₄, and concentrated. The residue was filtered through a short pad of silica gel, eluted with EtOAc, and the fractions containing the product were combined and concentrated. The crude product was then purified by flash column chromatography on silica gel (hexane/EtOAc = 5:1 to 0:1) to give **37** (533.0 mg, 0.5344 mmol, 98%).

37: white powder; mp 80-81 °C (hexane/EtOAc); $[\alpha]_D^{27}$ 190.7 (c 0.254, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 1.35 (3H, d, *J* = 6.5 Hz, H11'' or H12''), 1.36 (3H, d, *J* = 6.0 Hz, H11'' or H12''), 1.41 (3H, s, acetonide), 1.43 (3H, s, acetonide), 1.99 (1H, t, *J* = 2.5 Hz, H7), 2.34 (1H, dd, *J* = 16.5, 2.5 Hz, H5), 2.57 (1H, dd, *J* = 14.5, 11.5 Hz, H8'), 2.59 (1H, dd, *J* = 16.5, 2.5 Hz, H5), 2.93 (1H, d, *J* = 3.5 Hz, C10-OH), 3.15 (1H, dd, *J* = 14.5, 5.0 Hz, H8'), 3.49 (1H, s, C4-OH), 3.64 (3H, s, PMBM), 3.81

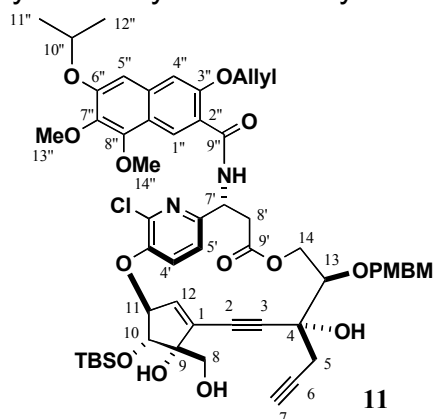
(3H, s, H13''), 3.88 (1H, d, $J = 9.0$ Hz, H8), 3.92-3.99 (3H, m, H13, H14), 3.96 (3H, s, H14''), 4.02 (1H, d, $J = 9.0$ Hz, H8), 4.08 (1H, ddd, $J = 3.5, 1.0, 1.0$ Hz, H10), 4.43 (1H, d, $J = 11.0$ Hz, PMBM), 4.45 (1H, d, $J = 11.0$ Hz, PMBM), 4.60 (1H, heptet, $J = 6.5$ Hz, H10''), 4.66 (1H, d, $J = 7.0$ Hz, PMBM), 4.66-4.71 (2H, m, CH₂=CH-CH₂-), 4.83 (1H, d, $J = 7.0$ Hz, PMBM), 5.29 (1H, dd, $J = 10.5, 3.0, 1.5$ Hz, CH₂=CH-CH₂-), 5.37 (1H, ddd, $J = 17.5, 3.0, 1.5$ Hz, CH₂=CH-CH₂-), 5.41 (1H, dd, $J = 2.5, 1.0$ Hz, H11), 5.61 (1H, ddd, $J = 11.5, 8.0, 5.0$ Hz, H7'), 6.06 (1H, dd, $J = 2.5, 1.0$ Hz, H12), 6.20 (1H, dddd, $J = 17.5, 10.5, 5.5, 5.5$ Hz, CH₂=CH-CH₂-), 6.70 (1H, s, H5''), 6.76 (2H, d, $J = 8.5$ Hz, PMBM), 6.94 (1H, s, H4''), 7.01 (1H, d, $J = 8.0$ Hz, H4'), 7.13 (2H, d, $J = 8.5$ Hz, PMBM), 7.14 (1H, d, $J = 8.0$ Hz, H5'), 8.84 (1H, s, H1''), 8.96 (1H, d, $J = 8.0$ Hz, NH); ¹³C NMR (50 MHz, CDCl₃) δ 22.09 (2C, C11'', C12''), 26.03 (acetonide), 26.69 (acetonide), 31.71 (C5), 40.81 (C8'), 51.23 (C7'), 55.36 (PMBM), 61.19 (C13''), 61.81 (C14''), 67.77 (C14), 70.08 (C8), 70.36 (CH₂=CH-CH₂-), 70.81 (PMBM), 71.10 (C10''), 72.05 (2C, C6, C7), 72.25 (C4), 78.59 (C10), 79.27 (C2), 79.41 (C9), 82.78 (C13), 89.56 (C11), 94.76 (C3), 95.89 (PMBM), 102.85 (C5''), 106.79 (C4''), 111.75 (acetonide), 114.08 (2C, PMBM), 118.96 (C8a''), 119.44 (CH₂=CH-CH₂-), 123.51 (C2''), 128.36 (C5'), 128.95 (C1''), 129.55 (PMBM), 129.80 (2C, PMBM), 132.51 (C4a''), 132.58 (CH₂=CH-CH₂-), 133.09 (C4'), 133.81 (C1), 140.01 (C12), 140.35 (C7''), 146.11 (C2'), 148.42 (C3'), 149.55 (C8''), 153.86 (C6''), 154.27 (C3''), 154.38 (C6'), 159.61 (PMBM), 164.76 (C9''), 170.27 (C9'); FT-IR (film) ν 3510, 2934, 1734, 1653, 1617, 1559, 1515, 1449, 1395, 1301, 1247, 1079, 1030, 858, 821 cm⁻¹; MS (ESI), calcd. for C₅₃H₅₈ClN₂O₁₅ (M+H)⁺: 997.3526; found: 997.3536.



The diol **37** (455.5 mg, 0.457 mmol) dissolved in THF (13.4 mL) and H₂O (6.7 mL) was treated with TFA (2.7 mL, 34.8 mmol), and the solution was stirred at 50 °C for 9.5 h. After cooling to 0 °C, the reaction mixture was neutralized by dropwise addition of Et₃N (9.7 mL, 69.6 mmol) over 10 min. The resulting mixture was diluted with EtOAc (40 mL) and treated with sat. NaHCO₃ (11 mL) at 0 °C. After stirring for

0.5 h at room temperature, the mixture was extracted with EtOAc (10 mL x 4). The combined organic layers were washed with brine, dried over Na₂SO₄, and filtered. After removal of the solvent, the crude product was purified by flash column chromatography on silica gel deactivated by 6 wt % of H₂O (hexane/EtOAc = 1:1 to 1:4) to give **10** (312.0 mg, 0.326 mmol, 71%).

10: colorless powder; mp 106-107 °C (hexane/EtOAc); [α]_D²⁹ 99.7 (c 0.13, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 1.45 (3H, d, *J* = 6.5 Hz, H11'' or H12''), 1.46 (3H, d, *J* = 6.5 Hz, H11'' or H12''), 2.17 (3H, t, *J* = 2.5 Hz, H7), 2.23 (1H, dd, *J* = 7.5, 5.0 Hz, C8-OH), 2.52 (1H, dd, *J* = 16.5, 2.5 Hz, H5), 2.64 (1H, dd, *J* = 16.5, 2.5 Hz, H5), 2.74 (1H, dd, *J* = 15.0, 11.5 Hz, H8'), 3.13 (1H, d, *J* = 7.0 Hz, C10-OH), 3.23 (1H, dd, *J* = 15.0, 5.0 Hz, H8'), 3.38 (1H, s, C4-OH), 3.60 (1H, dd, *J* = 11.5, 7.5 Hz, H8), 3.74 (1H, s, C9-OH), 3.74 (1H, dd, *J* = 11.5, 5.0 Hz, H8), 3.76 (3H, s, PMBM), 3.91 (3H, s, H13''), 4.00-4.04 (1H, m, H13), 4.07 (3H, s, H14''), 4.13-4.17 (2H, m, H14), 4.40 (1H, dd, *J* = 7.0, 3.0 Hz, H10), 4.55 (1H, d, *J* = 11.5 Hz, PMBM), 4.58 (1H, d, *J* = 11.5 Hz, PMBM), 4.71 (1H, heptet, *J* = 6.5 Hz, H10''), 4.77 (1H, d, *J* = 7.5 Hz, PMBM), 4.75-4.81 (2H, m, CH₂=CH-CH₂-), 4.94 (1H, d, *J* = 7.5 Hz, PMBM), 5.40 (1H, ddd, *J* = 11.0, 2.0, 1.0 Hz, CH₂=CH-CH₂-), 5.47 (1H, ddd, *J* = 17.5, 3.0, 1.0 Hz, CH₂=CH-CH₂-), 5.50 (1H, dd, *J* = 3.0, 2.5 Hz, H11), 5.70 (1H, ddd, *J* = 11.5, 8.0, 5.0 Hz, H7'), 6.14 (1H, d, *J* = 2.5 Hz, H12), 6.30 (1H, dddd, *J* = 17.5, 11.0, 5.5, 5.5 Hz, CH₂=CH-CH₂-), 6.80 (1H, s, H5''), 6.87 (2H, d, *J* = 9.0 Hz, PMBM), 7.04 (1H, s, H4''), 7.24 (2H, d, *J* = 9.0 Hz, PMBM), 7.27 (1H, d, *J* = 8.5 Hz, H4'), 7.34 (1H, d, *J* = 8.5 Hz, H5'), 8.93 (1H, s, H1''), 9.03 (1H, d, *J* = 8.0 Hz, NH); ¹³C NMR (50 MHz, CDCl₃) δ 22.09 (2C, C11'', C12''), 26.64 (C5), 40.60 (C8'), 51.18 (C7'), 55.33 (PMBM), 61.21 (C13''), 61.88 (C14''), 65.16 (C8), 68.27 (C14), 69.93 (PMBM), 70.41 (CH₂=CH-CH₂-), 70.82 (C10''), 72.08 (2C, C7, C6), 72.55 (C4), 79.16 (C10), 80.36 (C2), 81.68 (C9), 83.32 (C13), 92.21 (C11), 95.00 (C3), 95.76 (PMBM), 102.88 (C5''), 106.82 (C4''), 114.03 (2C, PMBM), 118.89 (CH₂=CH-CH₂-), 119.11 (C8a''), 119.62 (C2''), 123.71 (C5'), 128.28 (C1''), 129.07 (PMBM), 129.79 (2C, PMBM), 132.42 (CH₂=CH-CH₂-), 133.06 (C4a''), 133.89 (C4'), 134.16 (C1), 139.35 (C12), 140.36 (C7''), 146.85 (C2'), 148.12 (C3'), 149.46 (C8''), 153.94 (C6''), 154.25 (2C, C3'', C6'), 159.53 (PMBM), 165.02 (C9''), 170.64 (C9'); FT-IR (film) ν 3508, 2934, 1733, 1640, 1616, 1515, 1448, 1396, 1302, 1248, 1113, 1031, 856, 823 cm⁻¹; MS (ESI), calcd. for C₅₀H₅₄ClN₂O₁₅ (M+H)⁺: 957.3213; found: 957.3228.



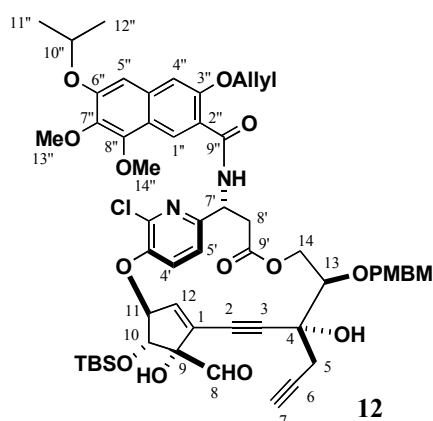
To a solution of **10** (339.4 mg, 0.3545 mmol) and Et₃N (0.4 mL, 2.870 mmol) in ClCH₂CH₂Cl (17 mL) was added TBSCl (248.0 mg, 1.645 mmol) and DMAP (6.2 mg, 0.05075 mmol), and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was diluted with EtOAc (60 mL) and then quenched by addition of sat. NaHCO₃ (aq.) (10 mL). The layers were separated, and the aqueous phase was extracted with EtOAc (10 mL x 4). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, and then concentrated. The residue was purified by flash column chromatography on silica gel (hexane/EtOAc = 4:1 to 1:1.2) to give **11** (324.4 mg, 0.3027 mmol, 85%).

11: colorless powder; $[\alpha]_D^{28}$ 108.6 (c 0.046, CH₂Cl₂); ¹H NMR (600 MHz, C₆D₆) δ 0.21 (3H, s, TBS), 0.25 (3H, s, TBS), 0.92 (9H, s, TBS), 1.22 (6H, d, *J* = 6.0 Hz, H11'', H12''), 1.97 (1H, t, *J* = 2.6 Hz, H7), 2.59 (1H, dd, *J* = 16.6, 2.6 Hz, H5), 2.64 (1H, dd, *J* = 16.6, 2.6 Hz, H5), 2.63-2.66 (1H, m, C8-OH), 2.76 (1H, dd, *J* = 15.1, 11.1 Hz, H8'), 3.31 (1H, dd, *J* = 15.1, 4.5 Hz, H8'), 3.33 (3H, s, PMBM), 3.49 (1H, s, C4-OH), 3.70 (1H, s, C9-OH), 3.75 (3H, s, H13''), 3.86 (brd, *J* = 11.8 Hz, H8), 3.90 (3H, s, H14''), 4.01 (brdd, *J* = 11.8, 4.0 Hz, H8), 4.13 (1H, dd, *J* = 5.8, 1.3 Hz, H13), 4.24 (1H, dd, *J* = 12.2, 5.8 Hz, H14), 4.44 (1H, dd, *J* = 12.2, 1.3 Hz, H14), 4.35 (1H, d, *J* = 11.4 Hz, PMBM), 4.35-4.41 (2H, m, CH₂=CH-CH₂-), 4.40 (1H, d, *J* = 11.4 Hz, PMBM), 4.41 (1H, heptet, *J* = 6.0 Hz, H10''), 4.59 (1H, d, *J* = 6.8 Hz, PMBM), 4.79 (1H, d, *J* = 6.8 Hz, PMBM), 4.87 (1H, d, *J* = 2.6 Hz, H10), 5.27 (1H, ddd, *J* = 10.5, 3.3, 1.3 Hz, CH₂=CH-CH₂-), 5.29 (1H, ddd, *J* = 16.5, 3.3, 1.3 Hz, CH₂=CH-CH₂-), 5.44 (1H, t, *J* = 2.6 Hz, H11), 6.07 (1H, ddd, *J* = 11.1, 7.6, 4.5 Hz, H7'), 6.08 (1H, d, *J* = 2.6 Hz, H12), 6.31 (1H, dddd, *J* = 16.5, 10.5, 5.3, 5.3 Hz, CH₂=CH-CH₂-), 6.75 (1H, s, H5''), 6.80 (2H, d, *J* = 8.6 Hz, PMBM), 6.85 (1H, s, H4''), 7.09 (1H, d, *J* = 8.1 Hz, H5'), 7.17 (2H, d, *J* = 8.6 Hz, PMBM), 7.29 (1H, d, *J* = 8.1 Hz, H4'), 9.34 (1H, d, *J* = 7.6 Hz, NH), 9.70 (1H, s, H1''); ¹³C NMR (150 MHz, C₆D₆) δ -4.61 (TBS), -4.11 (TBS), 18.47 (TBS), 26.14 (3C, TBS), 22.24 (2C, C11'', C12''), 27.22 (C5), 41.47 (C8'), 52.05 (C7'), 55.10 (PMBM), 61.03 (C13''), 61.72 (C14''), 65.12 (C8), 68.86 (C14), 69.95 (PMBM), 70.57 (CH₂=CH-CH₂-), 71.03 (C10''), 72.67 (C7), 72.77 (C4),

Supplementary Material (ESI) for Chemical Communications

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79.77 (C6), 78.88 (C10), 81.26 (C2), 82.31 (C9), 84.00 (C13), 93.24 (C11), 95.90 (C3), 96.04 (PMBM), 103.85 (C5''), 107.40 (C4''), 114.46 (2C, PMBM), 119.16 (CH₂=CH-CH₂-), 120.16 (C8a''), 120.90 (C2''), 124.12 (C5'), 129.39 (C1''), 130.06 (PMBM), 130.08 (2C, PMBM), 133.44 (CH₂=CH-CH₂-), 134.47 (C4a''), 134.64 (C4'), 135.42 (C1), 138.51 (C12), 141.37 (C7''), 147.16 (C2'), 148.73 (C3'), 150.56 (C8''), 154.66 (C6''), 155.07 (C3''), 155.41 (C6'), 160.20 (PMBM), 164.94 (C9''), 170.92 (C9'); ¹³C NMR (125 MHz, CD₂Cl₂); δ -5.17 (TBS), -4.69 (TBS), 18.01 (TBS), 21.75 (C11'' or C12''), 21.76 (C11'' or C12''), 25.55 (3C, TBS), 26.70 (C5), 40.65 (C8'), 51.17 (C7'), 55.21 (PMBM), 60.90 (C13''), 61.64 (C14''), 64.46 (C8), 67.66 (C14), 69.98 (PMBM), 70.33 (CH₂=CH-CH₂-), 70.74 (C10''), 71.72 (C7), 71.95 (C4), 77.95 (C10), 78.96 (C6), 80.20 (C2), 81.51 (C9), 83.45 (C13), 92.42 (C11), 94.62 (C3), 95.96 (PMBM), 102.79 (C5''), 106.81 (C4''), 113.82 (2C, PMBM), 118.70 (CH₂=CH-CH₂-), 118.98 (C8a''), 119.58 (C2''), 123.32 (C5'), 127.71 (C1''), 129.19 (PMBM), 129.65 (2C, PMBM), 132.75 (CH₂=CH-CH₂-), 133.72 (C4a''), 133.94 (C4'), 134.10 (C1), 138.64 (C12), 140.27 (C7''), 146.57 (C2'), 148.09 (C3'), 149.24 (C8''), 153.85 (C6''), 154.21 (C3''), 154.52 (C6'), 159.55 (PMBM), 164.31 (C9''), 170.27 (C9'); FT-IR (film) ν 3509, 2933, 2281, 1734, 1654, 1617, 1560, 1515, 1449, 1396, 1302, 1248, 1114, 854, 783 cm⁻¹; MS (ESI), calcd. for C₅₆H₆₈ClN₂O₁₅Si (M+H)⁺: 1071.4078; found: 1071.4080.

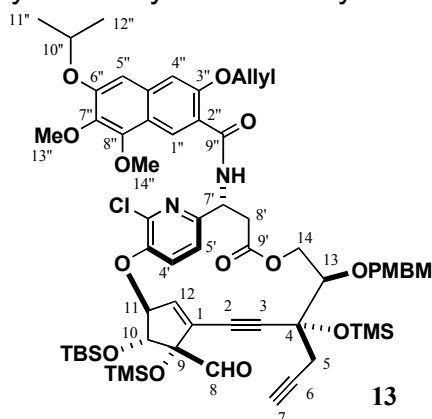


IBX-oxidation procedure. To a solution of **11** (23.5 mg, 21.9 μmol) in CH₂Cl₂ (1.5 mL) was added powdered and activated MS4A (120 mg), and the suspension was stirred at room temperature for 10 min. IBX (0.5 M DMSO solution, 440 μL, 0.220 mmol) was added to the suspension, and the reaction mixture was vigorously stirred at room temperature for 9 h. The mixture was then diluted with dry Et₂O (ca. 35 mL), and filtered through a pad of Celite eluting with Et₂O. The resulting solution was washed with water (3 mL x 3), brine (3 mL x 2), and then dried over MgSO₄. After solvent exchange from Et₂O to benzene by azeotropic removal of benzene (40 mL x 4), the product solution was concentrated, azeotroped with dry

toluene (3 mL x 3), and then dried under high vacuum to give **12** (23.0 mg, 21.9 μmol). This highly hygroscopic aldehyde was silylated without hesitation.

SO₃·pyridine oxidation. To a solution of **11** (40.4 mg, 37.7 μmol) and Et₃N (80 μL , 0.574 mmol) in DMSO-CH₂Cl₂ (3 : 10, 2.2 mL) was added SO₃·pyridine (40.8 mg, 0.256 mmol) and the mixture was stirred at room temperature. Further SO₃·pyridine (40.8 mg, 0.256 mmol) and Et₃N (80 μL , 0.574 mmol) were added twice at 3 h intervals. After stirring at room temperature for a total of 9 h, the mixture was diluted with dry Et₂O (ca. 80 mL) and then quenched with water 5 mL. The mixture was washed with water (4 mL x 3), brine (5 mL x 3), and then dried over Na₂SO₄. After solvent exchange from Et₂O to benzene by azeotropic removal of benzene (40 mL x 4), the product solution was concentrated, azeotroped with dry toluene (3 mL x 3), and dried under high vacuum to give **16** (41.3 mg). This highly hygroscopic aldehyde **12** was silylated without hesitation.

12: white solid; $[\alpha]_{\text{D}}^{22}$ 79.2 (c 0.082, benzene); ¹H NMR (500 MHz, C₆D₆) δ 0.06 (3H, s, TBS), 0.12 (3H, s, TBS), 0.86 (9H, s, TBS), 1.23 (6H, d, J = 6.0 Hz, H11''), 1.81 (1H, t, J = 2.0 Hz, H7), 2.29 (1H, dd, J = 16.5, 2.0 Hz, H5), 2.48 (1H, dd, J = 16.5, 2.0 Hz, H5), 2.65 (1H, dd, J = 15.0, 11.5 Hz, H8'), 3.30 (3H, s, PMBM), 3.39 (1H, dd, J = 15.0, 5.0 Hz, H8'), 3.75 (3H, s, H13''), 3.85 (3H, s, H14''), 4.07 (1H, dd, J = 5.0, 1.5 Hz, H13), 4.17 (1H, dd, J = 12.0, 1.5 Hz, H14), 4.24 (1H, dd, J = 12.0, 5.0 Hz, H14), 4.30 (1H, d, J = 9.0 Hz, PMBM), 4.41 (1H, d, J = 9.0 Hz, PMBM), 4.42 (1H, heptet, J = 6.0 Hz, H10''), 4.39-4.43 (2H, m, CH₂=CH-CH₂-), 4.48 (1H, d, J = 7.0 Hz, PMBM), 4.67 (1H, d, J = 7.0 Hz, PMBM), 4.86 (1H, d, J = 2.5 Hz, H10), 5.27 (1H, ddd, J = 11.0, 3.0, 1.5 Hz, CH₂=CH-CH₂-), 5.30 (1H, ddd, J = 17.5, 3.0, 1.5 Hz, CH₂=CH-CH₂-), 5.37 (1H, t, J = 2.5 Hz, H11), 5.93 (1H, d, J = 2.5 Hz, H12), 6.11 (1H, ddd, J = 11.5, 8.0, 5.0 Hz, H7'), 6.34 (1H, ddd, J = 17.5, 11.0, 6.0 Hz, CH₂=CH-CH₂-), 6.77 (1H, s, H5''), 6.79 (2H, d, J = 8.5 Hz, PMBM), 6.87 (1H, s, H4''), 6.96 (1H, d, J = 7.5 Hz, H4'), 7.13 (2H, d, J = 8.5 Hz, PMBM), 7.28 (1H, d, J = 7.5 Hz, H5'), 9.36 (1H, d, J = 8.0 Hz, NH), 9.79 (1H, s, H1''), 9.97 (1H, s, CHO); FT-IR (film) ν 3529, 2928, 1735, 1685, 1654, 1647, 1617, 1560, 1541, 1449, 1395, 1300, 1248, 1114, 1031, 853 cm⁻¹; MALDI-TOFMS, calcd. for C₅₆H₆₅ClN₂O₁₅SiNa (M+Na)⁺: 1091.3741; found: 1091.3748.



To a solution of the crude aldehyde **12** (41.3 mg, 37.7 μmol) and 2,6-lutidine (131 μL , 1.13 mmol) in CH_2Cl_2 (2.5 mL) was added TMSOTf (132 μL , 0.565 mmol) at $-78\text{ }^\circ\text{C}$. The reaction mixture was stirred at $-70\text{ }^\circ\text{C}$ for 3.5 h. The mixture was diluted with dry Et_2O (15 mL) at $-70\text{ }^\circ\text{C}$, and then quenched with sat. NaHCO_3 (aq.) (4 mL) at $-70\text{ }^\circ\text{C}$. The layers were separated, and the aqueous phase extracted with Et_2O (10 mL x 3). The combined organic extracts were washed with brine (5 mL), dried over Na_2SO_4 , and concentrated. After solvent exchange from Et_2O to benzene by azeotropic removal of benzene (20 mL x 3), the product solution was concentrated, azeotroped with dry toluene (3 mL x 3), and then dried under high vacuum to give **13** (46.9 mg, 37.7 μmol). This silylated aldehyde **13** was used immediately in the next reaction without further purification.

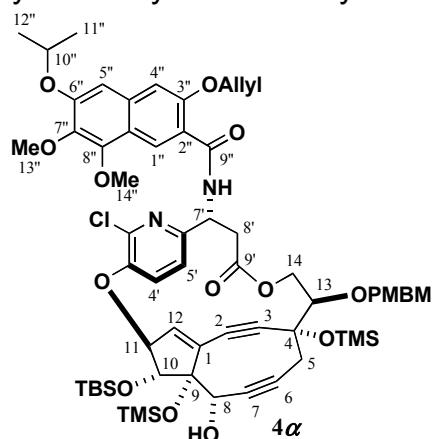
13: white solid; $[\alpha]_{\text{D}}^{22}$ 65.1 (c 0.685, benzene); ^1H NMR (500 MHz, C_6D_6) δ 0.17 (9H, s, TMS), 0.20 (3H, s, TBS), 0.25 (3H, s, TBS), 0.30 (9H, s, TMS), 1.04 (9H, s, TBS), 1.22 (3H, d, $J = 6.5$ Hz, H11'' or H12''), 1.23 (3H, d, $J = 6.5$ Hz, H11'' or H12''), 1.85 (1H, t, $J = 2.5$ Hz, H7), 2.50 (1H, dd, $J = 16.5, 2.5$ Hz, H5), 2.59 (1H, dd, $J = 16.5, 2.5$ Hz, H5), 2.74 (1H, dd, $J = 14.0, 11.0$ Hz, H8'), 3.30 (1H, dd, $J = 14.0, 5.0$ Hz, H8'), 3.36 (3H, s, PMBM), 3.75 (3H, s, H13''), 3.84 (3H, s, H14''), 4.07 (1H, dd, $J = 11.5, 1.0$ Hz, H14), 4.16 (1H, dd, $J = 6.5, 1.0$ Hz, H13), 4.36 (1H, d, $J = 11.0$ Hz, PMBM), 4.41 (1H, heptet, $J = 6.5$ Hz, H10''), 4.61 (1H, d, $J = 11.0$ Hz, PMBM), 4.71 (1H, d, $J = 7.0$ Hz, PMBM), 4.91 (1H, d, $J = 7.0$ Hz, PMBM), 5.00 (1H, d, $J = 4.5$ Hz, H10), 5.21 (1H, ddd, $J = 10.0, 3.0, 1.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.26 (1H, ddd, $J = 17.5, 3.0, 1.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.61 (1H, dd, $J = 4.5, 2.0$ Hz, H11), 6.08 (1H, ddd, $J = 11.0, 7.5, 5.0$ Hz, H7'), 6.18 (1H, d, $J = 2.0$ Hz, H12), 6.27 (1H, dddd, $J = 17.5, 10.0, 6.0, 6.0$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 6.76 (1H, s, H5''), 6.84 (1H, s, H4''), 6.85 (2H, d, $J = 8.5$ Hz, PMBM), 6.88 (1H, d, $J = 8.0$ Hz, H5'), 7.26 (2H, d, $J = 8.5$ Hz, PMBM), 7.27 (1H, d, $J = 8.0$ Hz, H4'), 9.29 (1H, d, $J = 7.5$ Hz, NH), 9.78 (1H, s, H1''), 9.80 (1H, s, CHO); ^{13}C NMR (125 MHz, C_6D_6) δ -4.30 (TBS), -4.18 (TBS), 1.87 (3C, TMS), 2.57 (3C, TMS), 18.59 (TBS), 22.06 (2C, C11'', C12''), 26.20 (3C, TBS), 27.75 (C5), 41.73 (C8'),

Supplementary Material (ESI) for Chemical Communications

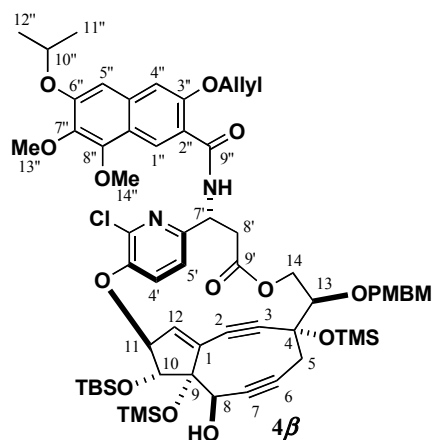
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52.13 (C7'), 54.90 (PMBM), 60.78 (C13''), 61.39 (C14''), 67.99 (C14), 69.32 (PMBM), 70.34 (CH₂=CH-CH₂-), 70.91 (C10''), 72.35 (C7), 74.79 (C9), 79.40 (C10), 79.61 (C6), 82.63 (C2), 83.21 (C13), 88.93 (C4), 92.24 (C11), 95.51 (C3), 96.91 (PMBM), 103.87 (C5''), 107.30 (C4''), 114.29 (PMBM), 118.75 (CH₂=CH-CH₂-), 120.09 (C8a''), 121.15 (C2''), 123.63 (C5'), 129.17 (C1''), 129.66 (2C, PMBM), 130.23 (PMBM), 131.41 (C4a''), 133.26 (CH₂=CH-CH₂-), 133.54 (C1), 134.15 (C4'), 141.25 (C12), 141.59 (C7''), 146.92 (C2'), 148.10 (C3'), 150.35 (C8''), 154.35 (C6''), 154.88 (C3''), 155.76 (C6'), 159.95 (PMBM), 164.39 (C9''), 170.32 (C9'), 201.28 (C9); FT-IR (film) ν 2927, 1734, 1653, 1617, 1559, 1515, 1448, 1395, 1250, 1122, 1032, 845 cm⁻¹; MALDI-TOFMS, calcd. for C₆₂H₈₁ClN₂O₁₅Si₃Na (M+Na)⁺: 1235.4531; found: 1235.4544.

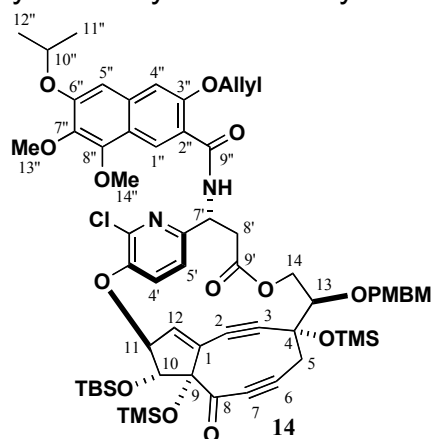
Nine-membered cyclization of 13. Anhydrous CeCl₃ (711.1 mg, 2.883 mmol, purchased from Aldrich) was dried at 90 °C under high vacuum for 2 h with vigorous stirring to afford a fine white powder of anhydrous CeCl₃. After introduction of Ar into the flask, the resulting CeCl₃ is pre-cooled to 0 °C. Freshly distilled THF (40 mL), pre-cooled to 0 °C, was added to the powder of CeCl₃ in one portion over an ice-water bath with vigorous stirring, and the resulting mixture was stirred at room temperature for 20 h within a tightly-sealed flask under a positive pressure of Ar. To a separate solution of HN(TMS)₂ (578 mL, 2.739 mmol) in THF (23 mL) was added *n*-BuLi (1.57 M hexane solution, 1.74 mL, 2.739 mmol) dropwise at 0 °C. The resulting solution of LiN(TMS)₂ was stirred at 0 °C for 0.5 h and then added to the suspension of CeCl₃ at -45 °C via cannula. The mixture was allowed to warm to -25 °C over 70 min with fast, but smooth stirring. To the mixture of CeCl₃ and LiN(TMS)₂ was added a solution of the crude aldehyde **13** (76.1 mg, 60.37 μ mol) in THF (10 mL) dropwise at -25 °C. After stirring at -25 °C for 25 h, the reaction mixture was quenched with aqueous phosphate buffer (pH 7, 22 mL) at -25 °C, and then diluted with EtOAc (130 mL). The precipitate which formed was filtered through a pad of Celite and then washed with EtOAc. The filtrate was washed with brine (15 mL x 2) and the aqueous layer was extracted with EtOAc (25 mL x 2). The combined organic extracts were dried over Na₂SO₄, filtered, then concentrated, and the resulting residue was purified by flash column chromatography on deactivated silica gel (see page 1) (hexane/EtOAc = 5:1 to 2.5:1) to give **4 α** (26.3 mg, 21.66 μ mol, 35.9% for 3 steps) and **4 β** (8.2 mg, 6.75 μ mol, 11.2% for 3 steps).



4 α : colorless powder; $[\alpha]_D^{29}$ 125.3 (c 0.965, CH₂Cl₂); ¹H NMR (500 MHz, C₆D₆) δ 0.18 (9H, s, TMS), 0.25 (3H, s, TBS), 0.28 (3H, s, TMS), 0.31 (9H, s, TMS), 1.04 (9H, s, TBS), 1.22 (3H, d, J = 6.5 Hz, H11'' or H12''), 1.23 (3H, d, J = 6.5 Hz, H11'' or H12''), 2.43 (1H, ddd, J = 17.0, 3.5, 1.0 Hz, H5), 2.57 (1H, d, J = 12.0 Hz, OH), 2.63 (1H, dd, J = 14.0, 11.5 Hz, H8'), 3.17 (1H, dd, J = 17.0, 2.0 Hz, H5), 3.30 (1H, dd, J = 14.0, 5.5 Hz, H8'), 3.47 (3H, s, PMBM), 3.75 (3H, s, H13''), 3.84 (3H, s, H14''), 4.13 (1H, brdt, J = 12.0, 2.0 Hz, H8), 4.23 (1H, brd, J = 5.0, H13), 4.33 (1H, dd, J = 11.5, 5.5 Hz, H14), 4.37 (1H, d, J = 11.5 Hz, PMBM), 4.36-4.43 (2H, m, CH₂=CH-CH₂-), 4.42 (1H, heptet, J = 6.5 Hz, H10''), 4.45 (1H, dd, J = 11.5, 4.5 Hz, H14), 4.52 (1H, d, J = 2.5 Hz, H10), 4.66 (1H, d, J = 11.5 Hz, PMBM), 4.74 (1H, d, J = 6.5 Hz, PMBM), 4.93 (1H, d, J = 6.5 Hz, PMBM), 5.20 (1H, ddd, J = 10.0, 3.0, 1.5 Hz, CH₂=CH-CH₂-), 5.25 (1H, ddd, J = 17.0, 3.0, 1.5 Hz, CH₂=CH-CH₂-), 5.44 (1H, t, J = 2.5 Hz, H11), 6.03 (1H, ddd, J = 11.5, 8.0, 5.5 Hz, H7'), 6.38 (1H, d, J = 2.5 Hz, H12), 6.75 (1H, s, H5''), 6.82 (1H, d, J = 8.5 Hz, H4'), 6.83 (1H, s, H4''), 6.92 (2H, d, J = 8.0 Hz, PMBM), 7.16 (2H, d, J = 8.0 Hz, PMBM), 7.31 (1H, d, J = 8.5 Hz, H5'), 9.22 (1H, d, J = 8.0 Hz, NH), 9.74 (1H, s, H1''); ¹³C NMR (125 MHz, CD₂Cl₂, rt) δ -4.85 (TBS), -4.27 (TBS), 1.24 (3C, TMS), 2.19 (3C, TMS), 18.39 (TBS), 21.85 (2C, C11'', C12''), 25.95 (3C, TBS), 29.95 (C5), 41.05 (C8'), 51.49 (C7'), 55.27 (PMBM), 60.95 (C13''), 61.67 (C14''), 67.23 (C8), 69.15 (C14), 69.62 (CH₂=CH-CH₂-), 70.44 (PMBM), 70.90 (C10''), 78.45 (C4), 80.70 (C13), 82.06 (C10), 87.12 (C9), 89.25 (C6), 90.12 (C2), 92.87 (C7), 94.79 (PMBM), 95.53 (C11), 100.40 (C3), 103.02 (C4''), 106.96 (C5''), 113.83 (2C, PMBM), 118.89 (C2''), 118.98 (CH₂=CH-CH₂-), 119.80 (C8a''), 123.83 (C5'), 127.84 (C1''), 129.37 (2C, PMBM), 129.99 (PMBM), 132.83 (CH₂=CH-CH₂-), 132.88 (C4'), 133.41 (C4a''), 133.80 (C1), 137.66 (C12), 140.44 (C7''), 146.97 (C2'), 147.98 (C3'), 149.35 (C8''), 153.96 (C6''), 154.31 (C3''), 155.11 (C6'), 159.45 (PMBM), 164.35 (C9''), 170.44 (C9'); FT-IR (film) ν 3385, 2926, 2854, 1735, 1654, 1618, 1515, 1448, 1396, 1249, 1123, 1034, 843 cm⁻¹; MALDI-TOFMS, calcd. for C₆₂H₈₁ClN₂O₁₇Si₃Na (M+Na)⁺: 1235.4531; found: 1235.4443 HRMS (ESI), calcd. for C₆₂H₈₂ClN₂O₁₇Si₃ (M+H)⁺: 1213.4712; found: 1213.4734.



4β. colorless solid: $[\alpha]_D^{28}$ 109.2 (c 0.405, CH_2Cl_2); ^1H NMR (500 MHz, C_6D_6) δ 0.17 (9H, s, TMS), 0.23 (3H, s, TBS), 0.27 (9H, s, TMS), 0.30 (3H, s, TBS), 1.07 (9H, s, TBS), 1.22 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 1.23 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 2.35 (1H, d, $J = 17.5$ Hz, H5), 2.78 (1H, dd, $J = 16.5, 11.0$ Hz, H8'), 3.14 (1H, d, $J = 17.5$ Hz, H5), 3.33 (1H, dd, $J = 16.5, 5.0$ Hz, H8'), 3.45 (3H, s, PMBM), 3.75 (3H, s, H13''), 3.85 (3H, s, H14''), 4.10 (1H, brs, H8), 4.18-4.21 (1H, m, H13), 4.26 (1H, dd, $J = 11.5, 4.0$ Hz, H14), 4.32 (1H, dd, $J = 11.5, 5.0$ Hz, H14), 4.42 (1H, d, $J = 11.5$ Hz, PMBM), 4.42 (1H, heptet, $J = 6.0$ Hz, H10''), 4.36-4.44 (2H, m, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 4.59 (1H, d, $J = 11.5$ Hz, PMBM), 4.76 (1H, d, $J = 7.0$ Hz, PMBM), 4.93 (1H, d, $J = 7.0$ Hz, PMBM), 5.10 (1H, d, $J = 3.5$ Hz, H10), 5.20-5.26 (2H, m, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.45 (1H, dd, $J = 3.5, 2.5$ Hz, H11), 5.98 (1H, ddd, $J = 11.0, 7.5, 5.0$ Hz, H7'), 6.23 (1H, dddd, $J = 17.0, 10.0, 6.0, 6.0$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 6.61 (1H, d, $J = 2.5$ Hz, H12), 6.76 (1H, s, H5''), 6.82 (1H, s, H4''), 6.90 (2H, d, $J = 9.0$ Hz, PMBM), 6.99 (1H, d, $J = 8.0$ Hz, H5'), 7.28 (2H, d, $J = 9.0$ Hz, PMBM), 7.38 (1H, d, $J = 8.0$ Hz, H4'), 9.22 (1H, d, $J = 8.5$ Hz, NH), 9.77 (1H, s, H1''); FT-IR (film) ν 3538, 2921, 2851, 1735, 1654, 1618, 1560, 1515, 1497, 1449, 1396, 1250, 1123, 1035, 843 cm^{-1} ; HRMS (ESI), calcd. for $\text{C}_{62}\text{H}_{82}\text{ClN}_2\text{O}_{15}\text{Si}_3$ ($\text{M}+\text{H}$) $^+$: 1213.4712; found: 1213.4720.



To a suspension of **4a** (18.2 mg, 15.0 μmol) and dry NaHCO_3 (35 mg, 0.417 mmol) in degassed CH_2Cl_2 (1.0 mL) was added Dess-Martin periodinane (63.6 mg, 0.150 mmol), and the reaction mixture was stirred at room temperature for 1.5 h. The reaction mixture was diluted with degassed EtOAc (15 mL), and sat. NaHCO_3 (aq.) (1 mL) and sat. $\text{Na}_2\text{S}_2\text{O}_3$ (aq.) (1 mL) was added. The mixture was stirred rapidly for 5 min until both phases were clear. The layers were separated and the aqueous layer was extracted with degassed EtOAc (5 mL x 2). The combined organic extracts were washed with brine (2 mL), dried over Na_2SO_4 , and concentrated. To minimize the decomposition of **14**, the evaporator should be substituted with inert gas (N_2). The crude product was purified by flash column chromatography on silica gel (hexane/EtOAc = 1:0 to 3:1) using a dry nitrogen flow to give **14** (16.8 mg, 13.9 μmol , 93%).

14: yellow oil; $[\alpha]_{\text{D}}^{28}$ 83.4 (c 0.885, CH_2Cl_2); ^1H NMR (500 MHz, C_6D_6) δ 0.16 (9H, s, TMS), 0.29 (3H, s, TBS), 0.31 (9H, s, TMS), 0.39 (3H, s, TBS), 1.07 (9H, s, TBS), 1.22 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 1.23 (3H, d, $J = 6.0$ Hz, H11'' or H12''), 2.43 (1H, dd, $J = 18.0, 1.0$ Hz, H5), 2.58 (1H, dd, $J = 14.0, 10.5$ Hz, H8'), 3.16 (1H, d, $J = 18.0$ Hz, H5), 3.30 (1H, dd, $J = 14.0, 5.0$ Hz, H8'), 3.49 (3H, s, PMBM), 3.75 (3H, s, H13''), 3.84 (3H, s, H14''), 3.99 (1H, dd, $J = 11.5, 2.0$ Hz, H14), 4.16-4.19 (1H, m, H13), 4.23 (1H, dd, $J = 11.5, 4.5$ Hz, H14), 4.33-4.37 (2H, m, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 4.54 (1H, d, $J = 11.5$ Hz, PMBM), 4.41 (1H, heptet, $J = 6.0$ Hz, H10''), 4.63 (1H, d, $J = 11.5$ Hz, PMBM), 4.68 (1H, d, $J = 7.0$ Hz, PMBM), 4.84 (1H, d, $J = 7.0$ Hz, PMBM), 5.21 (1H, ddd, $J = 10.5, 3.0, 1.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.26 (1H, ddd, $J = 17.0, 3.0, 1.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 5.44 (1H, t, $J = 2.5$ Hz, H11), 5.50 (1H, d, $J = 3.0$ Hz, H10), 5.95 (1H, ddd, $J = 10.5, 7.5, 5.0$ Hz, H7'), 6.25 (1H, d, $J = 2.5$ Hz, H12), 6.26 (1H, dddd, $J = 17.0, 10.5, 5.5, 5.5$ Hz, $\text{CH}_2=\text{CH}-\text{CH}_2-$), 6.65 (1H, d, $J = 8.5$ Hz, H5'), 6.75 (1H, s, H5''), 6.84 (1H, s, H4''), 6.96 (2H, d, $J = 9.0$ Hz, PMBM), 7.21 (1H, d, $J = 8.5$ Hz, H4'), 7.31 (2H, d, $J = 9.0$ Hz, PMBM), 9.29 (1H, d, $J = 7.5$ Hz, NH), 9.74 (1H, s, H1''); ^{13}C NMR (125 MHz, CD_2Cl_2 , rt) δ -4.67, -4.13, 1.22 (3C), 2.26 (3C), 18.43, 21.85, 21.84, 26.05 (3C), 30.97, 41.26, 51.53, 55.30, 60.95, 61.67, 66.74, 69.34, 70.42, 70.90, 75.30, 77.50, 81.80, 89.81, 92.08, 92.60, 93.58, 95.45, 99.38, 102.89, 103.01, 106.99,

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113.86 (2C), 118.86 (2C), 119.86, 123.18, 127.82, 129.42 (2C), 129.81, 131.85, 132.95, 133.38, 133.78, 138.73, 140.42, 146.86, 147.89, 149.34, 153.94, 154.32, 154.88, 159.50, 164.35, 170.14, 181.40; FT-IR (film) ν 3556, 2925, 1734, 1684, 1653, 1617, 1559, 1507, 1457, 1251, 1122, 846 cm^{-1} ; MALDI-TOFMS, calcd. for $\text{C}_{62}\text{H}_{79}\text{ClN}_2\text{O}_{17}\text{Si}_3\text{Na}$ ($\text{M}+\text{Na}$)⁺: 1233.4375; found: 1233.4378.

Reduction of 14. To a solution of **14** (2.1 mg, 1.73 mmol) in Et_2O (0.35 mL) was added freshly prepared $\text{Zn}(\text{BH}_4)_2$ (0.35 M solution in Et_2O , 25 mL, 71.4 mmol) at $-30\text{ }^\circ\text{C}$. After being stirred at $-30\text{ }^\circ\text{C}$ for 1 h, further $\text{Zn}(\text{BH}_4)_2$ (0.35 M solution in Et_2O , 50 mL, 142.9 mmol) were added at $-30\text{ }^\circ\text{C}$, and the reaction mixture was stirred at $-30\text{ }^\circ\text{C}$ for 2 h. The reaction mixture was quenched by addition of 40 mg of silica gel at $-30\text{ }^\circ\text{C}$, and the mixture was stirred at $-30\text{ }^\circ\text{C}$ for 3 min. The resulting slurry was purified by flash column chromatography on silica gel (hexane/ EtOAc = 1:0 to 2:1) to give **4 β** (1.2 mg, 0.988 mmol, 57%).