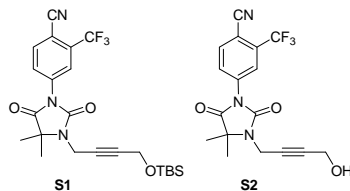
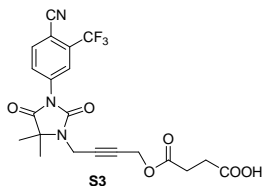


Supplementary Information

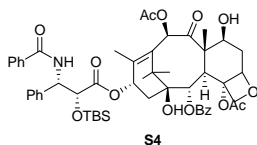


To the solution of cyanonilutamide¹ **4** in DMF (8.5 mL) was added NaH (60% in mineral oil, 134 mg, 3.34 mmol) under argon at room temperature. After stirring for 15 minutes at ambient temperature, the mixture was treated dropwise with a solution of tert-butyl(4-iodobut-2-ynoxy)dimethylsilane (1.01 g, 3.34 mmol) in anhydrous DMF (8.5 mL). The mixture was stirred at room temperature for 3 hours. Then the solution was poured into saturated brine and extracted with ethyl acetate (3x 100 mL). The combined organic extracts were washed with water and saturated brine, and dried over Na₂SO₄. After filtration, the solution was concentrated and the residue was purified by flash chromatography (30% ethyl acetate in hexane) to give TBS ether **S1** (1.05 g, 81.5%) as a white solid.

To TBS ether **S1** (885 mg, 1.88 mmol) was added the solution of HCl in ethanol (1%, 60 mL) at room temperature. After stirring for 15 minutes, the mixture was treated with saturated NaHCO₃ solution carefully and extracted with ethyl acetate (3x 150 mL). The combined organic phase was then washed with saturated brine, dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (50% ethyl acetate in hexane) to afford a white solid **S2** (543 mg, 81.4%): ¹H NMR (500 MHz, CDCl₃) δ 8.14 (1H, d, *J* = 2.1 Hz), 7.99 (1H, dd, *J* = 8.4, 2.1 Hz), 7.92 (1H, d, *J* = 8.4 Hz), 4.27 (4H, m), 1.62 (6H, s); ¹³C NMR (500 MHz, CDCl₃) δ 174.4, 152.5, 136.3, 135.4, 133.7, 128.0, 123.2, 123.1, 115.0, 108.8, 100.0, 82.6, 80.0, 62.2, 51.1, 29.3, 23.3; HRMS (ESI+) calcd for C₁₇H₁₈F₃N₄O₃ [M+NH₄]⁺ 383.1331, found 383.1311.

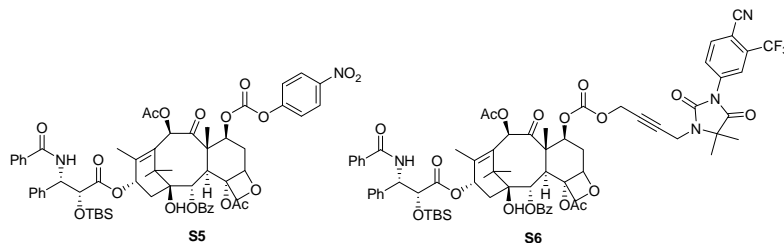


To the solution of compound **S2** (61mg, 0.167 mmol) in DCM (1.6 mL) was added succinic anhydride (50 mg, 0.5 mmol) and DMAP (62 mg, 0.5 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. After filtration and rotary evaporation, the residue was then purified by flash chromatography (70% ethyl acetate in hexane) to afford **S3** as a white solid (70 mg, 90%): ¹H NMR (500 MHz, CDCl₃) δ 8.12 (1H, d, *J* = 2.1 Hz), 7.98 (1H, dd, *J* = 8.4, 2.1 Hz), 7.92 (1H, d, *J* = 8.4 Hz), 4.69 (2H, t, *J* = 1.9 Hz), 4.26 (2H, t, *J* = 1.9 Hz), 2.70 – 2.61 (4H, m), 1.61 (6H, s); ¹³C NMR (500 MHz, CDCl₃) δ 176.6, 174.4, 171.4, 152.7, 136.3, 135.4, 133.6, 128.2, 123.3, 123.3, 115.0, 108.7, 81.1, 78.5, 62.3, 52.3, 29.2, 28.7, 23.2; HRMS (APCI+) calcd for C₂₁H₁₉F₃N₃O₆ [M+H]⁺ 466.1226, found 466.1243.



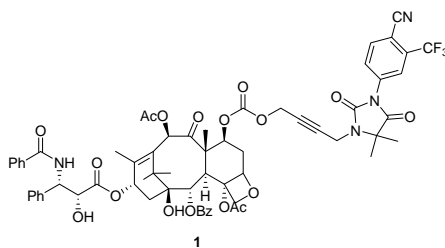
To solution of paclitaxel (55.4 mg, 0.065 mmol) in DMF (0.5 mL) was added imidazole (22.1

mg, 0.325 mmol) and TBSCl (98 mg, 0.65 mmol) successively at room temperature. The mixture was stirred overnight at 60 °C, then treated with saturated NaHCO₃ solution, and extracted with ethyl acetate (3x 10 mL). The combined organic layers were washed with water and saturated brine, dried over Na₂SO₄, vacuum filtered, and concentrated. The resulting residue was purified by flash chromatography (50% ethyl acetate in hexane) to give a white solid **S4** (58 mg, 92.3%).

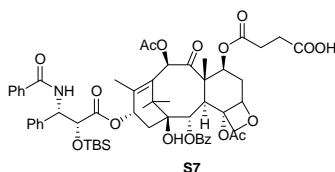


Bis(4-nitrophenyl) carbonate (20 mg, 0.063 mmol) and DMAP (11 mg, 0.063 mmol) was added to the solution of compound **S4** (20 mg, 0.21 mmol) in DCM (0.1 mL). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 10 mL), washed with saturated brine, and dried over Na₂SO₄. The extract was then vacuum filtered and concentrated. The residue was purified by flash chromatography (30% ethyl acetate in hexane) to give a white solid **S5** (16 mg, 67%).

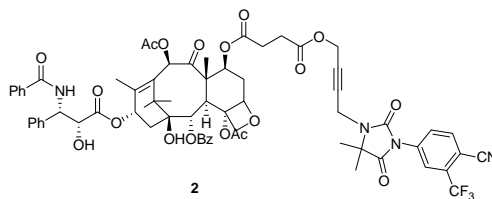
Then compound **S5** (16 mg, 0.014 mmol), compound **S2** (15 mg, 0.042 mmol) and DMAP (5 mg, 0.042 mmol) was dissolved in DCM (0.1 mL). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 10 mL), washed with saturated brine, and dried over Na₂SO₄, followed by vacuum filtration and rotary evaporation. The residue was then purified by flash chromatography (50% ethyl acetate in hexane) to afford **S6** as a white solid (15.7 mg, 82%): ¹H NMR (500 MHz, CDCl₃) δ 8.12 (3H, m), 7.99 (1H, dd, *J* = 9.0, 2.2 Hz), 7.91 (1H, d, *J* = 8.4 Hz), 7.74 (2H, dd, *J* = 8.1, 1.4 Hz), 7.60 (1H, t, *J* = 7.4 Hz), 7.50 (3H, dd, *J* = 14.2, 7.7 Hz), 7.44 – 7.36 (4H, m), 7.34 – 7.30 (3H, m), 7.08 (1H, d, *J* = 9.0 Hz), 6.31 (1H, s), 6.25 (1H, t, *J* = 9.0 Hz), 5.73 (1H, d, *J* = 9.0 Hz), 5.69 (1H, d, *J* = 6.9 Hz), 5.51 (1H, dd, *J* = 10.6, 7.1 Hz), 4.97 (1H, d, *J* = 8.4 Hz), 4.91 (1H, d, *J* = 15.8 Hz), 4.67 (2H, m), 4.34 (1H, d, *J* = 8.6 Hz), 4.28 (2H, d, *J* = 1.4 Hz), 4.19 (1H, d, *J* = 8.5 Hz), 3.95 (1H, d, *J* = 6.9 Hz), 2.64 – 2.54 (1H, m), 2.57 (3H, s), 2.40 (1H, dd, *J* = 15.3, 9.6 Hz), 2.20 – 2.12 (1H, m), 2.14 (3H, s), 2.03 – 1.95 (1H, m), 1.97 (3H, s), 1.81 (3H, s), 1.61 (6H, s), 1.21 (3H, s), 1.15 (3H, s), 0.79 (9H, s), -0.04 (3H, s), -0.30 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 201.6, 174.4, 171.6, 170.2, 169.2, 167.21, 167.0, 153.7, 152.4, 141.1, 138.3, 136.3, 135.4, 134.1, 133.7, 132.8, 132.0, 130.3, 129.1, 128.9, 128.9, 128.1, 128.1, 127.1, 126.5, 123.2, 123.2, 115.6, 115.1, 108.6, 83.9, 81.6, 81.0, 78.8, 78.4, 76.5, 76.0, 75.4, 75.2, 74.5, 71.4, 64.5, 62.2, 56.1, 55.9, 55.8, 46.9, 43.4, 35.7, 33.4, 29.2, 26.5, 25.6, 23.3, 23.1, 21.6, 20.9, 18.2, 14.7, 10.8, -5.1, -5.7; HRMS (FAB⁺) calcd for C₇₁H₇₈F₃N₄O₁₈Si [M+H]⁺ 1359.5033, found 1359.5117.



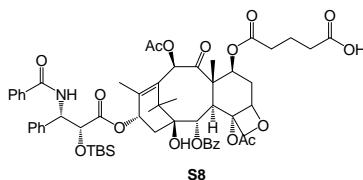
To the solution of compound **S6** (15.7 mg, 0.012 mmol) in THF (1 mL) was added HF-pyridine (0.2 mL) at 0 °C. The mixture was stirred at room temperature and the reaction was monitored by TLC. When the reaction completed, saturated NaHCO₃ solution was added to the reaction mixture. The mixture was then extracted with ethyl acetate (3× 15 mL), washed with saturated brine, and dried over Na₂SO₄. After filtration and rotary evaporation, the residue was then purified by flash chromatography (50% ethyl acetate in hexane) to afford compound **1** (12.9 mg, 86.4%) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 2.0 Hz), 8.11 (2H, dd, *J* = 8.0, 1.5 Hz), 7.99 (1H, dd, *J* = 8.5, 2.0 Hz), 7.92 (1H, d, *J* = 8.5 Hz), 7.75 (2H, dd, *J* = 8.5, 1.5 Hz), 7.62 (1H, tt, *J* = 7.5, 1.5 Hz), 7.52 – 7.40 (9H, m), 7.35 (1H, tt, *J* = 7.5, 1.5 Hz), 7.01 (1H, d, *J* = 9.0 Hz), 6.28 (1H, s), 6.18 (1H, t, *J* = 9.0 Hz), 5.79 (1H, dd, *J* = 9.0, 2.5 Hz), 5.66 (1H, d, *J* = 7.0 Hz), 5.46 (1H, dd, *J* = 9.0, 2.5 Hz), 4.93 (1H, d, *J* = 7.0 Hz), 4.91 (1H, dt, *J* = 16.0, 2.0 Hz), 4.79 (1H, dd, *J* = 4.0, 2.5 Hz), 4.67 (1H, dt, *J* = 16.0, 2.0 Hz), 4.32 (1H, d, *J* = 8.0 Hz), 4.28 (2H, t, *J* = 2.0 Hz), 4.17 (1H, d, *J* = 8.5 Hz), 3.91 (1H, d, *J* = 6.5 Hz), 3.54 (1H, broad s), 2.58 (1H, ddd, *J* = 15.0, 10.0, 7.5 Hz), 2.38 (3H, s), 2.33 (1H, d, *J* = 9.5 Hz), 2.32 (1H, d, *J* = 9.0 Hz), 2.15 (3H, s), 1.97 (1H, ddd, *J* = 14.5, 10.5, 2.0 Hz), 1.84 (3H, d, *J* = 1.0 Hz), 1.80 (3H, s), 1.71 (1H, broad s), 1.61 (6H, s), 1.21 (3H, s), 1.16 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 201.6, 174.4, 172.7, 170.6, 169.2, 167.1, 166.9, 153.7, 152.4, 140.6, 138.0, 136.3, 135.4, 133.9, 133.7, 133.0, 132.1, 130.3, 129.1, 128.9, 128.8, 128.5, 128.1, 127.2, 127.1, 123.2, 123.2, 115.1, 108.6, 83.8, 81.7, 81.0, 78.6, 78.3, 76.5, 76.1, 75.4, 74.3, 73.2, 72.3, 64.5, 62.2, 56.3, 55.9, 55.0, 47.0, 43.3, 35.6, 33.5, 29.3, 26.6, 23.3, 22.6, 21.0, 20.9, 14.7, 10.7; HRMS (FAB+) calcd for C₆₅H₆₄F₃N₄O₁₈ [M+H]⁺ 1245.4168, found 1245.4193.



To paclitaxel analog **S4** (18.7 mg, 0.02 mmol) in DCM (0.2 mL) was added succinic anhydride (7.1 mg, 0.06 mmol) and DMAP (7.8 mg, 0.06 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3X 10 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (60% ethyl acetate in hexane) to afford a white solid **S7** (21.4 mg, 100%): ¹H NMR (500 MHz, CDCl₃) δ 8.12 (2H, d, *J* = 8.1 Hz), 7.74 (2H, d, *J* = 7.8 Hz), 7.61 (1H, t, *J* = 7.5 Hz), 7.54 – 7.47 (3H, m), 7.44 – 7.36 (4H, m), 7.33 – 7.30 (3H, m), 7.08 (1H, d, *J* = 8.9 Hz), 6.25 (1H, t, *J* = 9.2 Hz), 6.22 (1H, s), 5.72 (1H, dd, *J* = 9.1, 1.7 Hz), 5.69 (1H, d, *J* = 7 Hz), 5.62 (1H, dd, *J* = 10.5, 7.2 Hz), 4.97 (1H, d, *J* = 9.5 Hz), 4.66 (1H, d, *J* = 2.2 Hz), 4.33 (1H, d, *J* = 8.5 Hz), 4.20 (1H, d, *J* = 8.5 Hz), 3.95 (1H, d, *J* = 6.9 Hz), 2.72 – 2.64 (1H, m), 2.64 – 2.57 (4H, m), 2.56 (3H, s), 2.40 (1H, dd, *J* = 15.4, 9.6 Hz), 2.17 (1H, d, *J* = 9.2 Hz), 2.14 (3H, s), 1.96 (3H, s), 1.85 (1H, t, *J* = 13.0 Hz), 1.80 (3H, s), 1.20 (3H, s), 1.15 (3H, s), 0.79 (9H, s), -0.04 (3H, s), -0.31 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ_C 202.0, 171.6, 171.2, 170.0, 169.3, 167.1, 167.0, 141.1, 138.3, 134.2, 133.8, 132.7, 131.9, 130.3, 129.2, 128.9, 128.8, 128.1, 127.1, 126.5, 88.6, 84.1, 81.1, 78.7, 77.3, 75.4, 75.2, 74.6, 71.8, 71.4, 56.1, 55.7, 46.9, 43.4, 35.7, 33.3, 26.5, 25.6, 23.1, 21.5, 20.8, 18.2, 14.7, 10.9, -5.1, -5.7; HRMS (APCI+) calcd for C₅₇H₆₉NO₁₇SiNa [M+Na]⁺ 1090.4233, found 1090.4229.

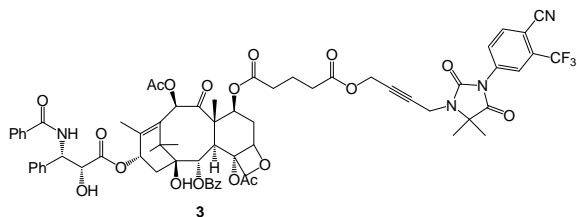


To the solution of white solid **S7** (21.4 mg, 0.02 mmol), compound **S2** (21.4 mg, 0.06 mmol) and DMAP (7 mg, 0.06 mmol) in DCM (1 mL) was added EDCI (11.5 mg, 0.06 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. Without purification, the residue (19.4 mg) was dissolved in THF (1 mL) and HF-pyridine (0.23 mL) was added at 0 °C. The mixture was stirred at room temperature until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture. The mixture was then extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (50% ethyl acetate in hexane) to give compound **2** (14 mg, 53.8% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.12 (1H, d, *J* = 2.0 Hz), 8.10 (2H, dd, *J* = 8.0, 1.5 Hz), 7.97 (1H, dd, *J* = 8.0, 2.0 Hz), 7.89 (1H, d, *J* = 8.0 Hz), 7.76 (2H, dd, *J* = 8.5, 1.5 Hz), 7.62 (1H, tt, *J* = 7.5, 1.5 Hz), 7.52 – 7.40 (9H, m), 7.34 (1H, tt, *J* = 7.0, 1.5 Hz), 7.04 (1H, d, *J* = 9.0 Hz), 6.16 (1H, s), 6.16 (1H, t, *J* = 9.0 Hz), 5.79 (1H, dd, *J* = 9.0, 2.5 Hz), 5.66 (1H, d, *J* = 7.0 Hz), 5.56 (1H, dd, *J* = 10.8, 7.0 Hz), 4.92 (1H, d, *J* = 10.0 Hz), 4.79 (1H, d, *J* = 3.0 Hz), 4.67 (2H, d, *J* = 3.5 Hz), 4.30 (1H, d, *J* = 8.5 Hz), 4.27 (2H, d, *J* = 2.0 Hz), 4.17 (1H, d, *J* = 8.5 Hz), 3.90 (1H, d, *J* = 7.0 Hz), 3.61 (1H, d, *J* = 5.0 Hz), 2.73 – 2.65 (1H, m), 2.66 – 2.54 (4H, m), 2.36 (3H, s), 2.33 (1H, d, *J* = 9.0 Hz), 2.32 (1H, d, *J* = 9.0 Hz), 2.15 (3H, s), 1.86 – 1.79 (1H, m), 1.81 (3H, s), 1.80 (3H, s), 1.61 (6H, d, *J* = 2.5 Hz), 1.20 (3H, s), 1.13 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 202.0, 174.4, 172.6, 171.9, 171.3, 170.6, 169.2, 167.0, 152.5, 140.6, 138.2, 136.4, 135.5, 133.9, 133.8, 133.0, 132.1, 130.4, 129.1, 128.9, 128.7, 128.3, 127.3, 123.1, 115.0, 108.6, 83.9, 81.2, 80.9, 78.9, 78.7, 76.6, 75.5, 74.4, 73.3, 72.2, 71.9, 62.3, 56.2, 55.0, 52.1, 47.1, 43.5, 35.8, 33.5, 29.2, 29.1, 28.8, 26.7, 23.2, 22.6, 20.9, 14.8, 10.9; HRMS (FAB⁺) calcd for C₆₈H₆₈F₃N₄O₁₉ [M+H]⁺ 1301.4430, found 1301.4403.

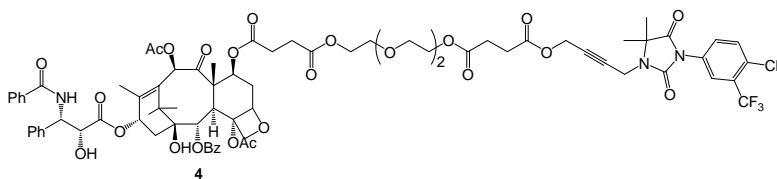


To paclitaxel analog **S4** (18 mg, 0.019 mmol) in DCM (1 mL) was added glutaric anhydride (6.5 mg, 0.057 mmol) and DMAP (7 mg, 0.057 mmol). The mixture was stirred at room temperature for 2 days. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄, followed by vacuum filtration and rotary evaporation. The residue was then purified by flash chromatography (60% ethyl acetate in hexane) to afford a white solid **S8** (10 mg, 48.7%): ¹H NMR (500 MHz, CDCl₃) δ 8.12 (2H, dd, *J* = 8.5, 1.4 Hz), 7.74 (2H, dd, *J* = 8.5, 1.4 Hz), 7.61 (1H, tt, *J* = 7.4, 1.9 Hz), 7.54 – 7.47 (3H, m), 7.44 – 7.36 (4H, m), 7.34 – 7.29 (3H, m), 7.09 (1H, d, *J* = 8.9 Hz), 6.26 (1H, s), 6.25 (1H, t, *J* = 9.7 Hz), 5.73 (1H, dd, *J* = 8.9, 1.8 Hz), 5.69 (1H, d, *J* = 7 Hz), 5.61 (1H, dd, *J* = 10.6, 7.1 Hz),

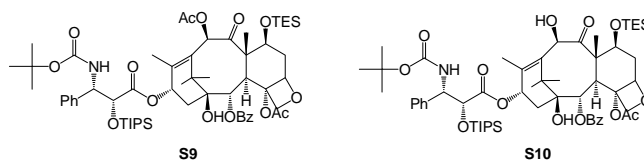
4.97 (1H, dd, $J = 9.3, 1.2$ Hz), 4.67 (1H, d, $J = 2.1$ Hz), 4.33 (1H, d, $J = 8.5$ Hz), 4.21 (1H, d, $J = 8.5$ Hz), 3.96 (1H, d, $J = 7.0$ Hz), 2.62 – 2.55 (1H, m), 2.57 (3H, s), 2.45 – 2.26 (5H, m), 2.19 – 2.15 (1H, m), 2.14 (3H, s), 1.97 (3H, d, $J = 1.1$ Hz), 1.93 – 1.81 (3H, m), 1.20 (3H, s), 1.15 (3H, s), 0.79 (9H, s), -0.03 (3H, s), -0.31 (3H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 202.1, 176.9, 172.2, 171.6, 170.0, 169.2, 167.2, 167.0, 141.0, 138.3, 134.2, 133.8, 132.8, 131.9, 130.3, 129.2, 128.9, 128.9, 128.8, 128.1, 127.1, 126.5, 84.1, 81.1, 78.7, 77.3, 76.5, 75.3, 75.2, 74.6, 71.4, 56.1, 55.8, 46.9, 43.4, 35.7, 33.5, 33.0, 32.7, 26.5, 25.6, 23.1, 21.5, 20.8, 19.5, 18.2, 14.7, 11.0, -5.1, -5.7; HRMS (APCI+) calcd for $\text{C}_{58}\text{H}_{71}\text{NO}_{17}\text{SiNa}$ $[\text{M}+\text{Na}]^+$ 1104.4389, found 1104.4384.



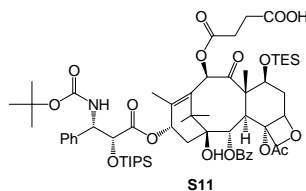
To the solution of compound **S2** (10 mg, 0.01 mmol), compound **S8** (11 mg, 0.03 mmol) and DMAP (4 mg, 0.03 mmol) in DCM (1 mL) was added EDCI (6 mg, 0.03 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na_2SO_4 . Then the mixture was filtered, concentrated and vacuum dried. Without purification, the residue (12.3 mg) was dissolved in THF (1 mL) and HF-pyridine (0.2 mL) was added at 0 °C. The mixture was stirred at room temperature and the reaction was monitored by TLC. When starting material was completely consumed, saturated NaHCO_3 solution was added to the reaction mixture carefully. The mixture was then extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na_2SO_4 . After filtration and rotary evaporation, the residue was then purified by flash chromatography (50% ethyl acetate in hexane) to give compound **3** (10.2 mg, 77.6% for two steps) as a white solid: ^1H NMR (500 MHz, CDCl_3) δ 8.13 (1H, d, $J = 2.0$ Hz), 8.10 (2H, d, $J = 8.0$ Hz), 7.99 (1H, dd, $J = 8.5, 2.0$ Hz), 7.92 (1H, d, $J = 8.5$ Hz), 7.76 (2H, d, $J = 8.0$ Hz), 7.62 (1H, t, $J = 7.5$ Hz), 7.52 – 7.47 (5H, m), 7.43 – 7.39 (4H, m), 7.34 (1H, t, $J = 7.0$ Hz), 7.05 (1H, d, $J = 8.5$ Hz), 6.19 (1H, s), 6.16 (1H, t, $J = 9.0$ Hz), 5.79 (1H, dd, $J = 9.0, 2.0$ Hz), 5.65 (1H, d, $J = 6.0$ Hz), 5.54 (1H, dd, $J = 10.0, 8.0$ Hz), 4.92 (1H, d, $J = 8.5$ Hz), 4.79 (1H, d, $J = 3.0$ Hz), 4.66 (2H, s), 4.31 (1H, d, $J = 8.5$ Hz), 4.28 (2H, s), 4.17 (1H, d, $J = 8.5$ Hz), 3.90 (1H, d, $J = 7.5$ Hz), 3.61 (1H, d, $J = 5.0$ Hz), 2.57 (1H, ddd, $J = 14.5, 9.5, 8.0$ Hz), 2.45 – 2.36 (4H, m), 2.37 (3H, s), 2.32 (1H, s), 2.31 (1H, s), 2.14 (3H, s), 1.94 – 1.87 (2H, m), 1.85 – 1.78 (1H, m), 1.82 (3H, d, $J = 0.8$ Hz), 1.79 (3H, s), 1.61 (6H, s), 1.19 (3H, s), 1.15 (3H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 202.0, 174.4, 172.5, 172.3, 172.0, 170.6, 169.0, 167.1, 152.5, 140.7, 138.2, 136.4, 135.5, 133.9, 133.8, 133.0, 132.0, 130.3, 129.2, 128.9, 128.5, 128.1, 127.2, 123.2, 115.1, 108.6, 84.0, 81.1, 80.9, 78.8, 78.6, 76.6, 75.4, 74.4, 73.3, 72.2, 71.6, 62.2, 56.3, 55.0, 52.0, 47.0, 43.3, 35.6, 33.6, 33.1, 29.3, 26.6, 23.3, 22.7, 20.9, 19.6, 14.8, 10.9; HRMS (FAB+) calcd for $\text{C}_{69}\text{H}_{70}\text{F}_3\text{N}_4\text{O}_{19}$ $[\text{M}+\text{H}]^+$ 1315.4586, found 1315.4564.



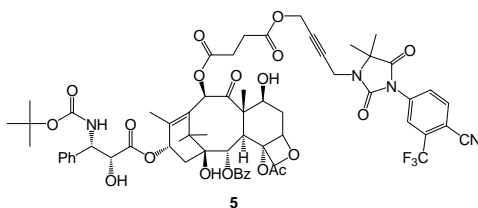
To the solution of paclitaxel analog **S7** (24 mg, 0.02 mmol), compound **S13** (20 mg, 0.034 mmol) and DMAP (8 mg, 0.06 mmol) in DCM (0.6 mL) was added EDCI (12 mg, 0.06 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 10 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. After purified by flash chromatography (60% ethyl acetate in hexane), the product (14 mg, 0.0085 mmol) was dissolved in THF (0.6 mL) and HF-pyridine (0.14 mL) was added at 0 °C. The mixture was stirred at room temperature until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture. The mixture was then extracted with ethyl acetate (3x 10 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (70% ethyl acetate in hexane) to give compound **4** (7 mg, 22.8% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 2.0 Hz), 8.10 (2H, dd, *J* = 8.0, 1.5 Hz), 7.98 (1H, dd, *J* = 8.5, 2.0 Hz), 7.91 (1H, d, *J* = 8.5 Hz), 7.76 (2H, dd, *J* = 8.0, 1.5 Hz), 7.61 (1H, tt, *J* = 7.5, 1.5 Hz), 7.52 – 7.46 (5H, m), 7.43 – 7.38 (4H, m), 7.34 (1H, tt, *J* = 7.5, 2.0 Hz), 7.08 (1H, d, *J* = 9.0 Hz), 6.17 (1H, s), 6.16 (1H, dt, *J* = 9.0, 1.5 Hz), 5.79 (1H, dd, *J* = 8.5, 2.5 Hz), 5.65 (1H, d, *J* = 7.0 Hz), 5.55 (1H, dd, *J* = 10.5, 7.5 Hz), 4.92 (1H, dd, *J* = 9.0, 1.0 Hz), 4.79 (1H, d, *J* = 2.5 Hz), 4.68 (2H, d, *J* = 2.0 Hz), 4.30 (1H, d, *J* = 9.0 Hz), 4.27 (2H, d, *J* = 2.0 Hz), 4.25 – 4.21 (4H, m), 4.17 (1H, d, *J* = 9.0 Hz), 3.89 (1H, d, *J* = 7.0 Hz), 3.70 – 3.67 (4H, m), 3.64 (4H, s), 2.71 – 2.54 (9H, m), 2.36 (3H, s), 2.35 – 2.28 (2H, m), 2.15 (3H, s), 1.86 – 1.79 (1H, m), 1.81 (3H, d, *J* = 1.0 Hz), 1.79 (3H, s), 1.61 (6H, d, *J* = 2.5 Hz), 1.19 (3H, s), 1.15 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 201.9, 174.4, 172.6, 172.5, 172.2, 171.6, 170.4, 169.1, 167.1, 167.0, 152.4, 140.5, 138.1, 136.3, 135.4, 133.9, 133.8, 133.0, 132.0, 130.2, 129.1, 128.8, 128.4, 128.1, 127.2, 127.1, 123.2, 115.1, 108.6, 84.0, 81.1, 78.6, 76.5, 75.4, 74.3, 73.3, 72.2, 71.6, 70.6, 69.2, 69.1, 64.0, 63.8, 62.2, 56.2, 55.0, 52.3, 47.1, 43.3, 35.6, 33.4, 29.2, 28.9, 28.8, 26.6, 23.3, 22.6, 20.9, 14.7, 10.9; HRMS (MALDI⁺) calcd for C₇₈H₈₃F₃N₄O₂₅Na [M+Na]⁺ 1555.5196, found 1555.4937.



To the solution of docetaxel analog **S9**² (310 mg, 0.277 mmol) in ethanol (20 mL) was added hydrazine monohydrate (4.8 mL). The mixture was stirred at room temperature overnight. After the addition of saturated NH₄Cl solution, the mixture was extracted with ethyl acetate (3x 100 mL), washed with saturated brine, and dried over Na₂SO₄, followed by vacuum filtration and rotary evaporation. The residue was then purified by flash chromatography (15% ethyl acetate in hexane) to afford white solid **S10** (253 mg, 84.8%).

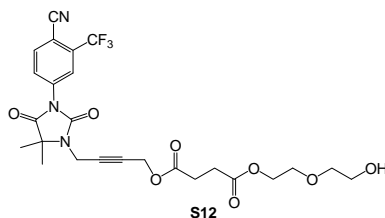


To the solution of docetaxel analog **S10** (36 mg, 0.033 mmol) in toluene (2 mL) was added succinic anhydride (15 mg, 0.1 mmol) and DMAP (13 mg, 0.1 mmol). The mixture was stirred at 85-90 °C for 24 hours. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and aqueous HCl solution (0.2%) was added carefully. The aqueous layer was then extracted with ethyl acetate (3x 30 mL). The combined organic phase was washed with saturated brine and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was purified by flash chromatography (60% ethyl acetate in hexane) to afford white solid **S11** (16 mg, 41%): ¹H NMR (500 MHz, CDCl₃) δ 8.11 (2H, d, *J* = 7.5 Hz), 7.57 (1H, t, *J* = 7.5 Hz), 7.47 (2H, t, *J* = 7.9 Hz), 7.36 (2H, t, *J* = 7.8 Hz), 7.30 – 7.25 (3H, m), 6.48 (1H, s), 6.25 (1H, t, *J* = 8.9 Hz), 5.69 (1H, d, *J* = 7.1 Hz), 5.40 (1H, d, *J* = 9.8 Hz), 5.30 (1H, d, *J* = 9.8 Hz), 4.94 (1H, dd, *J* = 9.4, 1.6 Hz), 4.80 (1H, s), 4.47 (1H, dd, *J* = 10.7, 6.7 Hz), 4.31 (1H, d, *J* = 8.3 Hz), 4.17 (1H, d, *J* = 8.5 Hz), 3.83 (1H, d, *J* = 7.1 Hz), 2.89 – 2.79 (1H, m), 2.79 – 2.71 (3H, m), 2.56 – 2.49 (1H, m), 2.51 (3H, s), 2.35 (1H, dd, *J* = 15.5, 9.3 Hz), 2.24 – 2.16 (1H, m), 2.00 (3H, s), 1.89 (1H, ddd, *J* = 13.9, 10.5, 2.1 Hz), 1.68 (3H, s), 1.67 (1H, broad s), 1.29 (9H, s), 1.21 (6H, s), 0.94 – 0.84 (30H, m), 0.63 – 0.50 (6H, m); ¹³C NMR (500 MHz, CDCl₃) δ 201.7, 175.4, 171.8, 170.4, 167.2, 155.4, 141.0, 133.7, 133.2, 130.3, 129.3, 128.8, 128.7, 127.8, 126.5, 84.3, 81.2, 80.3, 79.0, 77.3, 76.6, 76.0, 75.4, 75.0, 72.3, 71.6, 58.5, 46.8, 43.4, 37.3, 35.5, 29.1, 28.7, 28.2, 26.5, 23.1, 21.6, 17.9, 17.9, 14.4, 12.6, 10.2, 6.9, 5.4; HRMS (APCI+) calcd for C₆₂H₉₁NO₁₇Si₂Na [M+Na]⁺ 1200.5723, found 1200.5710.



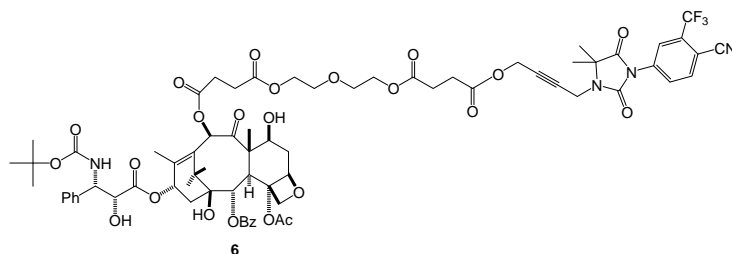
To the solution of docetaxel analog **S11** (22 mg, 0.019 mmol), compound **S2** (22.3 mg, 0.057 mmol) and DMAP (7 mg, 0.057 mmol) in DCM (1 mL) was added EDCI (11 mg, 0.057 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. Without purification, the residue (28 mg) was dissolved in THF (1 mL) and HF-pyridine (0.3 mL) was added at 0 °C. The mixture was stirred at room temperature until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture. The mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (50% ethyl acetate in hexane) to give compound **5** (13.3 mg, 55.8% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 2.0 Hz), 8.10 (2H, d, *J* = 7.5 Hz), 7.99 (1H, dd, *J* = 8.0, 2.0 Hz), 7.90 (1H, d, *J* = 8.0 Hz), 7.61 (1H, tt, *J* = 7.5, 1.0 Hz), 7.50 (2H, t, *J* = 8.0 Hz), 7.42 – 7.35 (4H, m), 7.32 (1H, tt, *J* = 7.0, 1.0 Hz), 6.29 (1H, s), 6.22 (1H, t, *J* = 8.5 Hz), 5.65 (1H, d, *J* =

7.0 Hz), 5.35 (1H, d, $J = 9.5$ Hz), 5.25 (1H, d, $J = 8.0$ Hz), 4.93 (1H, dd, $J = 9.0, 1.5$ Hz), 4.71 (2H, s), 4.61 (1H, d, $J = 1.0$ Hz), 4.38 (1H, dd, $J = 11.0, 6.5$ Hz), 4.29 (1H, d, $J = 8.0$ Hz), 4.29 (2H, s), 4.15 (1H, d, $J = 8.0$ Hz), 3.78 (1H, d, $J = 7.0$ Hz), 3.32 (1H, s), 2.91 – 2.83 (2H, m), 2.83 – 2.66 (2H, m), 2.51 (1H, ddd, $J = 15.5, 10.0, 7.0$ Hz), 2.43 (1H, broad s), 2.37 (3H, s), 2.35 – 2.20 (2H, m), 1.89 – 1.81 (1H, m), 1.84 (3H, s), 1.66 (3H, s), 1.62 (6H, s), 1.33 (9H, s), 1.25 (3H, s), 1.13 (3H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 203.5, 174.5, 172.4, 171.3, 170.2, 167.2, 155.5, 152.4, 142.6, 138.3, 136.3, 135.4, 133.9, 132.9, 130.3, 129.1, 129.0, 128.8, 128.2, 128.1, 126.8, 123.2, 115.0, 108.8, 84.5, 81.2, 80.4, 79.2, 78.6, 76.5, 76.0, 75.0, 73.9, 72.5, 72.3, 62.3, 58.8, 56.3, 52.5, 45.7, 43.3, 35.8, 35.6, 29.2, 29.0, 28.9, 28.3, 26.9, 23.3, 22.8, 22.1, 15.0, 9.7; HRMS (FAB+) calcd for $\text{C}_{64}\text{H}_{70}\text{F}_3\text{N}_4\text{O}_{19}$ $[\text{M}+\text{H}]^+$ 1255.4586, found 1255.4573.

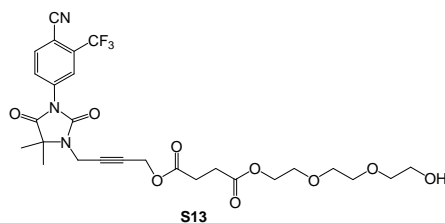


Di (ethylene glycol) (1 mL, 10.51 mmol) and pyridine (0.85 mL, 10.51 mmol) were dissolved in DCM (8 mL) and the solution of TBSCl (1.58 g, 10.51 mmol) in DCM (4 mL) was added at 0 °C. The mixture was stirred at room temperature overnight. The reaction solution was concentrated and purified by flash chromatography (50% ethyl acetate in hexane) to give TBS ether as colorless oil (900 mg, 37.2%).

To the solution of this colorless liquid (44 mg, 0.2 mmol), compound **S3** (31 mg, 0.067 mmol) and DMAP (25 mg, 0.2 mmol) in DCM (4 mL) was added EDCI (40 mg, 0.2 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, and dried over Na_2SO_4 . Then the mixture was filtered and rotary evaporated. Without purification, the residue (25 mg) was dissolved in the solution of HCl in ethanol (1%, 1.2 mL) at room temperature. After stirring for 15 minutes, the mixture was treated with saturated NaHCO_3 solution carefully and extracted with ethyl acetate (3x 15 mL). The combined organic phase was then washed with saturated brine, dried over Na_2SO_4 , vacuum filtered, and rotary evaporated. The residue was purified by flash chromatography (50% ethyl acetate in hexane) to afford compound **S12** (19 mg, 51.3% for two steps) as a white solid: ^1H NMR (400 MHz, CDCl_3) δ 8.15 (1H, d, $J = 1.8$ Hz), 8.00 (1H, dd, $J = 8.2, 1.8$ Hz), 7.93 (1H, d, $J = 8.2$ Hz), 4.70 (2H, t, $J = 2.0$ Hz), 4.29 – 4.25 (2H, m), 3.76 – 3.68 (4H, m), 3.62 – 3.58 (2H, m), 2.67 (4H, s), 1.62 (6H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 174.4, 172.1, 171.7, 152.4, 136.3, 135.4, 133.9, 133.6, 128.1, 123.2, 123.2, 115.0, 108.6, 100.0, 81.1, 78.5, 72.4, 69.1, 63.8, 62.2, 61.8, 52.4, 29.2, 28.9, 28.9, 23.3; HRMS (ESI+) calcd for $\text{C}_{25}\text{H}_{26}\text{F}_3\text{N}_3\text{O}_8$ M^+ 553.1672, found 553.1684.



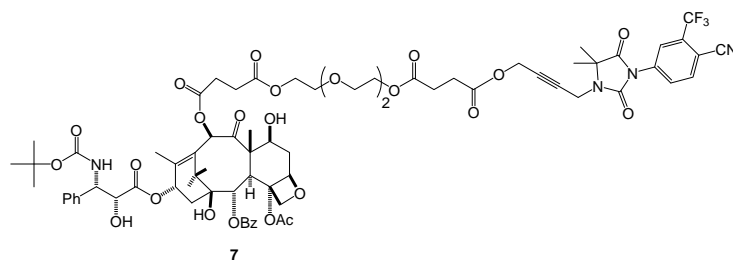
To the solution of docetaxel analog **S11** (20 mg, 0.017 mmol), compound **S12** (11 mg, 0.0204 mmol) and DMAP (6.7 mg, 0.051 mmol) in DCM (0.5 mL) was added EDCI (10 mg, 0.051 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 10 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. After purified by flash chromatography (40% ethyl acetate in hexane), the product (14.5 mg, 0.0085 mmol) was dissolved in pyridine (0.5 mL) and CH₃CN (0.25 mL). HF-pyridine (0.063 mL) was added to the solution at room temperature. The mixture was stirred at 62 °C until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture dropwise. The mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (70% ethyl acetate in hexane) to give compound **6** (10.2 mg, 40.8% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 1.5 Hz), 8.10 (2H, d, *J* = 7.5 Hz), 7.99 (1H, dd, *J* = 8.5, 2.0 Hz), 7.91 (1H, d, *J* = 8.5 Hz), 7.61 (1H, tt, *J* = 7.5, 1.5 Hz), 7.49 (2H, t, *J* = 7.5 Hz), 7.42 – 7.35 (4H, m), 7.32 (1H, tt, *J* = 7.0, 1.5 Hz), 6.30 (1H, s), 6.22 (1H, t, *J* = 8.5 Hz), 5.65 (1H, d, *J* = 7.0 Hz), 5.36 (1H, d, *J* = 10.0 Hz), 5.25 (1H, d, *J* = 9.0 Hz), 4.93 (1H, dd, *J* = 9.5, 2.0 Hz), 4.69 (2H, t, *J* = 2.0 Hz), 4.61 (1H, m), 4.39 (1H, dd, *J* = 11.0, 7.0 Hz), 4.29 (1H, d, *J* = 8.5 Hz), 4.27 (2H, t, *J* = 2.5 Hz), 4.27 – 4.23 (4H, m), 4.16 (1H, d, *J* = 8.5 Hz), 3.78 (1H, d, *J* = 7.5 Hz), 3.71 – 3.67 (4H, m), 3.34 (1H, broad s), 2.85 (2H, dt, *J* = 6.5, 2.5 Hz), 2.81 – 2.68 (2H, m), 2.68 – 2.65 (4H, m), 2.53 (1H, ddd, *J* = 15.0, 9.5, 6.5 Hz), 2.47 (1H, broad s), 2.37 (3H, s), 2.37 – 2.22 (2H, m), 1.89 – 1.82 (1H, m), 1.84 (3H, s), 1.72 (1H, broad s), 1.66 (3H, s), 1.61 (6H, s), 1.33 (9H, s), 1.25 (3H, s), 1.13 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 203.6, 174.4, 173.1, 172.5, 172.2, 172.0, 171.6, 170.3, 167.1, 155.5, 152.4, 142.7, 138.4, 136.3, 135.4, 133.8, 133.0, 130.3, 129.2, 129.0, 128.8, 128.2, 128.1, 126.8, 123.2, 115.0, 108.6, 84.5, 81.2, 81.1, 80.4, 79.1, 78.6, 76.5, 75.9, 75.0, 73.7, 72.5, 72.2, 69.0, 63.9, 62.2, 58.6, 56.3, 52.3, 45.7, 43.3, 35.8, 35.6, 29.2, 29.1, 29.0, 28.9, 28.8, 28.2, 26.8, 23.2, 22.7, 22.0, 14.9, 9.6; HRMS (FAB+) calcd for C₇₂H₈₂F₃N₄O₂₄ [M+H]⁺ 1443.5271, found 1443.5204.



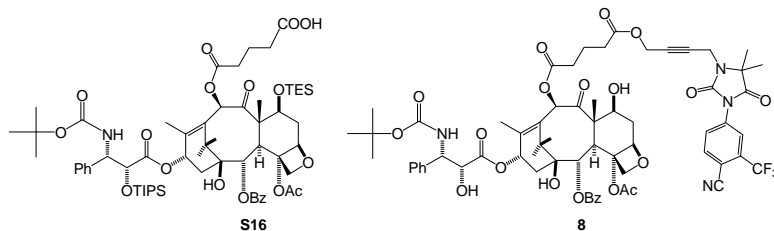
Tri (ethylene glycol) (1 mL, 7.5 mmol) and pyridine (0.61 mL, 7.5 mmol) were dissolved in DCM (6 mL) and the solution of TBSCl (1.1 g, 7.5 mmol) in DCM (3 mL) was added at 0 °C. The mixture was stirred at room temperature overnight. The reaction solution was concentrated and purified by flash chromatography (50% ethyl acetate in hexane) to give TBS ether as colorless oil (800 mg, 38.9%).

To the solution of this colorless liquid (50 mg, 0.181 mmol), compound **S3** (28 mg, 0.061 mmol) and DMAP (25 mg, 0.2 mmol) in DCM (4 mL) was added EDCI (40 mg, 0.2 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. Without purification, the residue (20 mg) was dissolved in the solution of HCl in ethanol (1%, 0.9 mL) at room temperature. After stirring

for 15 minutes, the mixture was treated with saturated NaHCO_3 solution carefully and extracted with ethyl acetate (3X 15 mL). The combined organic phase was then washed with saturated brine, dried over Na_2SO_4 , vacuum filtered, and rotary evaporated. The residue was purified by flash chromatography (60% ethyl acetate in hexane) to afford compound **S13** (11 mg, 30.2% for two steps) as a white solid: ^1H NMR (400 MHz, CDCl_3) δ 8.15 (1H, d, J = 1.5 Hz), 8.00 (1H, dd, J = 8.6, 1.9 Hz), 7.93 (1H, d, J = 8.4 Hz), 4.70 (2H, t, J = 1.8 Hz), 4.28 (2H, t, J = 1.8 Hz), 4.23 (4H, t, J = 4.7 Hz), 3.75 – 3.64 (8H, m), 3.64 – 3.59 (2H, m), 2.69 – 2.65 (4H, m), 1.62 (6H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 174.4, 172.2, 171.6, 152.4, 136.3, 135.4, 133.9, 133.6, 128.8, 123.2, 123.2, 115.0, 108.6, 100.0, 81.06, 78.6, 72.5, 70.7, 70.4, 69.1, 63.9, 62.2, 61.9, 52.3, 29.2, 28.9, 28.8, 23.3; HRMS (ESI+) calcd for $\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_3\text{O}_9$ M^+ 597.1934, found 597.1954.

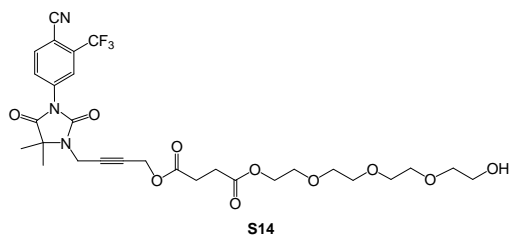


To the solution of docetaxel analog **S11** (20 mg, 0.017 mmol), compound **S13** (15 mg, 0.026 mmol) and DMAP (6.2 mg, 0.051 mmol) in DCM (0.8 mL) was added EDCI (10 mg, 0.051 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na_2SO_4 . Then the mixture was vacuum filtered and rotary evaporated. After purified by flash chromatography (50% ethyl acetate in hexane), the product (12 mg, 0.007 mmol) was dissolved in pyridine (0.4 mL) and CH_3CN (0.2 mL). HF-pyridine (0.052 mL) was added to the solution at room temperature. The mixture was stirred at 62 °C until the completion of the reaction (monitored by TLC). Then saturated NaHCO_3 solution was added to the reaction mixture dropwise. The mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na_2SO_4 . After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (70% ethyl acetate in hexane) to give compound **7** (8.2 mg, 34.5% for two steps) as a white solid: ^1H NMR (500 MHz, CDCl_3) δ 8.13 (1H, d, J = 2.0 Hz), 8.10 (2H, d, J = 7.0 Hz), 7.99 (1H, dd, J = 8.5, 2.0 Hz), 7.91 (1H, d, J = 8.5 Hz), 7.61 (1H, tt, J = 7.0, 1.5 Hz), 7.49 (2H, t, J = 7.5 Hz), 7.42 – 7.35 (4H, m), 7.32 (1H, tt, J = 7.0, 1.5 Hz), 6.29 (1H, s), 6.22 (1H, t, J = 9.0 Hz), 5.65 (1H, d, J = 7.0 Hz), 5.37 (1H, d, J = 9.0 Hz), 5.25 (1H, d, J = 8.5 Hz), 4.93 (1H, dd, J = 9.0, 1.5 Hz), 4.68 (2H, t, J = 2.0 Hz), 4.61 (1H, broad s), 4.38 (1H, dd, J = 4.5, 3.5 Hz), 4.29 (1H, d, J = 8.5 Hz), 4.27 (2H, t, J = 2.0 Hz), 4.27 – 4.22 (4H, m), 4.16 (1H, d, J = 8.5 Hz), 3.78 (1H, d, J = 7.0 Hz), 3.71 – 3.67 (4H, m), 3.65 (4H, s), 3.36 (1H, broad s), 2.85 (2H, dt, J = 7.0, 2.0 Hz), 2.81 – 2.67 (2H, m), 2.68 – 2.63 (4H, m), 2.52 (1H, ddd, J = 15.0, 10.0, 6.5 Hz), 2.48 (1H, broad s), 2.37 (3H, s), 2.28 (2H, m), 1.90 – 1.81 (1H, m), 1.84 (3H, s), 1.73 (1H, broad s), 1.66 (3H, s), 1.61 (6H, s), 1.33 (9H, s), 1.25 (3H, s), 1.13 (3H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 203.7, 174.4, 173.1, 172.6, 172.2, 172.1, 171.6, 170.3, 167.1, 155.5, 152.4, 142.6, 138.4, 136.3, 135.4, 133.8, 133.0, 130.3, 129.2, 129.0, 128.8, 128.2, 128.1, 126.8, 123.2, 115.0, 108.6, 84.5, 81.2, 81.1, 80.4, 79.1, 78.6, 76.5, 75.9, 75.0, 73.7, 72.5, 72.2, 70.6, 69.2, 64.0, 62.2, 58.6, 56.3, 52.3, 45.7, 43.2, 35.7, 35.6, 29.2, 29.1, 28.9, 28.8, 28.2, 26.8, 23.3, 22.7, 22.0, 14.9, 9.6; HRMS (FAB+) calcd for $\text{C}_{74}\text{H}_{86}\text{F}_3\text{N}_4\text{O}_{25}$ $[\text{M}+\text{H}]^+$ 1487.5533, found 1487.5585.



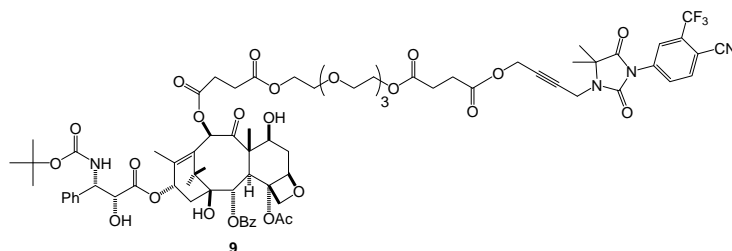
To the solution of docetaxel analog **S10** (87 mg, 0.082 mmol) in toluene (5 mL) was added glutaric anhydride (28 mg, 0.246 mmol) and DMAP (30 mg, 0.246 mmol). The mixture was stirred at 85-90 °C for 5 days. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and aqueous HCl solution (0.2%) was added carefully. The aqueous layer was then extracted with ethyl acetate (3x 20 mL). The combined organic phase was washed with saturated brine and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was purified by flash chromatography (40% ethyl acetate in hexane) to afford white solid **S16** (38 mg, 39%).

To the solution of docetaxel analog **S16** (38 mg, 0.032 mmol), compound **S2** (34 mg, 0.096 mmol) and DMAP (12 mg, 0.096 mmol) in DCM (1.7 mL) was added EDCI (19 mg, 0.096 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. Without purification, the residue was dissolved in pyridine (1.6 mL) and CH₃CN (0.8 mL). HF-pyridine (0.23 mL) was added to the solution at room temperature. The mixture was stirred at 62 °C until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture dropwise. The mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (50% ethyl acetate in hexane) to give compound **8** (20.4 mg, 53.6% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 2.0 Hz), 8.10 (2H, d, *J* = 7.5 Hz), 7.99 (1H, dd, *J* = 8.5, 2.0 Hz), 7.90 (1H, d, *J* = 8.5 Hz), 7.61 (1H, tt, *J* = 7.5, 1.5 Hz), 7.50 (2H, t, *J* = 8.0 Hz), 7.42 – 7.35 (4H, m), 7.32 (1H, tt, *J* = 7.0, 1.5 Hz), 6.30 (1H, s), 6.23 (1H, t, *J* = 3.5 Hz), 5.66 (1H, d, *J* = 7.5 Hz), 5.35 (1H, d, *J* = 9.5 Hz), 5.25 (1H, d, *J* = 8.0 Hz), 4.94 (1H, dd, *J* = 9.5, 2.0 Hz), 4.69 (2H, t, *J* = 2.0 Hz), 4.62 (1H, s), 4.43 – 4.37 (1H, m), 4.30 (1H, d, *J* = 9.0 Hz), 4.29 (2H, t, *J* = 2 Hz), 4.16 (1H, d, *J* = 9.0 Hz), 3.79 (1H, d, *J* = 7.0 Hz), 3.34 (1H, d, *J* = 3.5 Hz), 2.65 – 2.50 (4H, m), 2.46 (1H, d, *J* = 4.5 Hz), 2.37 (3H, s), 2.34 – 2.22 (2H, m), 2.04 (2H, tt, *J* = 7, 7 Hz), 1.90 – 1.83 (1H, m), 1.84 (3H, d, *J* = 1.0 Hz), 1.66 (3H, s), 1.63 (6H, s), 1.33 (9H, s), 1.25 (3H, s), 1.13 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 203.7, 174.4, 173.0, 172.2, 170.3, 167.1, 155.5, 152.4, 142.3, 138.2, 136.3, 135.4, 133.9, 133.8, 132.9, 130.3, 129.2, 129.0, 128.8, 128.2, 128.1, 126.8, 123.2, 123.1, 115.0, 108.6, 84.4, 81.1, 81.0, 79.1, 78.7, 76.5, 75.7, 75.0, 73.8, 72.4, 72.3, 62.2, 58.7, 56.3, 52.1, 45.7, 43.3, 35.7, 35.5, 33.1, 32.8, 29.2, 28.2, 26.8, 23.3, 22.7, 22.0, 20.0, 14.9, 9.7; HRMS (FAB⁺) calcd for C₆₅H₇₂F₃N₄O₁₉ [M+H]⁺ 1269.4743, found 1269.4652.



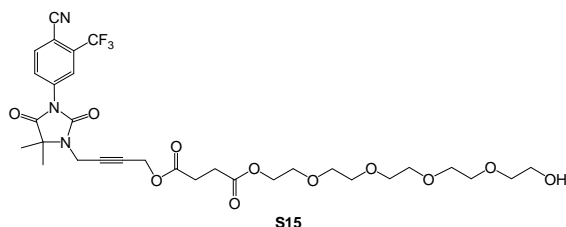
Tetra (ethylene glycol) (1 mL, 5.8 mmol) and pyridine (0.47 mL, 5.8 mmol) were dissolved in DCM (4.6 mL) and the solution of TBSCl (0.873 g, 5.8 mmol) in DCM (2.3 mL) was added at 0 °C. The mixture was stirred at room temperature overnight. The reaction solution was concentrated and purified by flash chromatography (50% ethyl acetate in hexane) to give TBS ether as colorless oil (717 mg, 40%).

To the solution of this colorless liquid (70 mg, 0.225 mmol), compound **S3** (34 mg, 0.075 mmol) and DMAP (28 mg, 0.225 mmol) in DCM (4 mL) was added EDCI (44 mg, 0.225 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. Without purification, the residue was dissolved in the solution of HCl in ethanol (1%, 7.2 mL) at room temperature. After stirring for 15 minutes, the mixture was treated with saturated NaHCO₃ solution carefully and extracted with ethyl acetate (3x 20 mL). The combined organic phase was then washed with saturated brine, dried over Na₂SO₄, vacuum filtered, and rotary evaporated. The residue was purified by flash chromatography (5% methanol in DCM) to afford compound **S14** (19.5 mg, 40.6% for two steps) as a white solid.



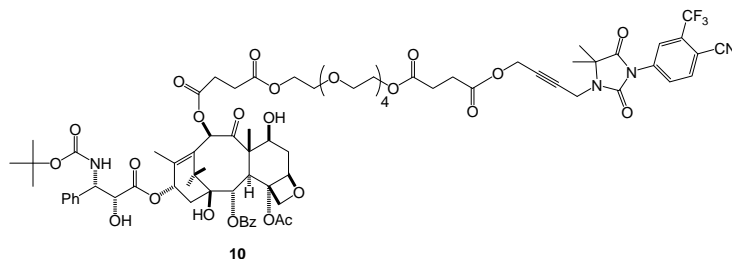
To the solution of docetaxel analog **S11** (22 mg, 0.019 mmol), compound **S14** (10 mg, 0.0156 mmol) and DMAP (6 mg, 0.047 mmol) in DCM (0.5 mL) was added EDCI (10 mg, 0.05 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. After purified by flash chromatography (60% ethyl acetate in hexane), the product (16 mg, 0.009 mmol) was dissolved in pyridine (0.5 mL) and CH₃CN (0.25 mL). HF-pyridine (0.068 mL) was added to the solution at room temperature. The mixture was stirred at 62 °C until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture dropwise. The mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (70% ethyl acetate in hexane) to give compound **9** (8.4 mg, 35.2% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 1.5 Hz), 8.09 (2H, d, *J* = 8.0 Hz), 7.98 (1H, dd, *J* = 8.5, 1.5 Hz), 7.91 (1H, d, *J* = 8.5 Hz), 7.60 (1H, t, *J* = 7.5 Hz), 7.49 (2H, t, *J* = 7.5 Hz), 7.41 – 7.35 (4H, m), 7.31 (1H, tt, *J* = 7.0, 1.5 Hz), 6.29 (1H, s),

6.22 (1H, t, $J = 8.5$ Hz), 5.65 (1H, d, $J = 7.0$ Hz), 5.37 (1H, d, $J = 9.5$ Hz), 5.25 (1H, d, $J = 9.0$ Hz), 4.93 (1H, dd, $J = 9.0, 1.5$ Hz), 4.68 (2H, t, $J = 2.0$ Hz), 4.61 (1H, broad s), 4.38 (1H, dd, $J = 10.5, 7.0$ Hz), 4.29 (1H, d, $J = 8.0$ Hz), 4.27 (2H, t, $J = 2.0$ Hz), 4.27 – 4.21 (4H, m), 4.15 (1H, d, $J = 8.0$ Hz), 3.78 (1H, d, $J = 7.5$ Hz), 3.71 – 3.67 (4H, m), 3.65 (4H, s), 3.65 (4H, s), 2.85 (2H, dt, $J = 7.5, 1.5$ Hz), 2.81 – 2.67 (2H, m), 2.68 – 2.64 (4H, m), 2.53 (1H, ddd, $J = 15.0, 9.5, 7.0$ Hz), 2.47 (1H, broad s), 2.37 (3H, s), 2.36 – 2.21 (2H, m), 1.89 – 1.82 (1H, m), 1.84 (3H, s), 1.70 (1H, broad s), 1.65 (3H, s), 1.61 (6H, s), 1.32 (9H, s), 1.24 (3H, s), 1.13 (3H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 203.6, 174.4, 173.1, 172.6, 172.2, 172.1, 171.6, 170.3, 167.2, 155.5, 152.4, 142.6, 138.3, 136.3, 135.4, 133.8, 133.0, 130.3, 129.2, 129.0, 128.8, 128.2, 128.1, 126.8, 123.2, 123.1, 115.0, 108.6, 84.5, 81.1, 80.3, 79.1, 78.6, 76.5, 75.9, 75.0, 73.7, 72.5, 72.2, 70.7, 69.1, 64.0, 62.2, 58.6, 56.2, 52.3, 45.7, 43.3, 35.7, 35.5, 29.2, 29.1, 28.9, 28.8, 28.2, 26.8, 23.3, 22.7, 22.0, 14.9, 9.6; HRMS (FAB+) calcd for $\text{C}_{76}\text{H}_{90}\text{F}_3\text{N}_4\text{O}_{26}$ $[\text{M}+\text{H}]^+$ 1531.5795, found 1531.5819.



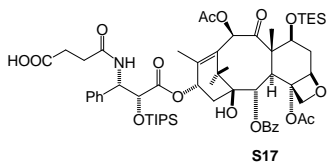
Penta(ethylene glycol) (2 mL, 9.5 mmol) and pyridine (0.767 mL, 9.5 mmol) were dissolved in DCM (7.5 mL) and the solution of TBSCl (1.43 g, 9.5 mmol) in DCM (3.8 mL) was added at 0 °C. The mixture was stirred at room temperature overnight. The reaction solution was concentrated and purified by flash chromatography (70% ethyl acetate in hexane) to give TBS ether as colorless oil (1.426 mg, 43%).

To the solution of this colorless liquid (90 mg, 0.257 mmol), compound **S3** (39 mg, 0.086 mmol) and DMAP (32 mg, 0.257 mmol) in DCM (4.6 mL) was added EDCI (50 mg, 0.257 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, and dried over Na_2SO_4 . Then the mixture was vacuum filtered and rotary evaporated. Without purification, the residue was dissolved in the solution of HCl in ethanol (1%, 8.2 mL) at room temperature. After stirring for 15 minutes, the mixture was treated with saturated NaHCO_3 solution carefully and extracted with ethyl acetate (3x 25 mL). The combined organic phase was then washed with saturated brine, dried over Na_2SO_4 , vacuum filtered, and rotary evaporated. The residue was purified by flash chromatography (5% methanol in DCM) to afford compound **S15** (18.8 mg, 31.9% for two steps) as a white solid.



To the solution of docetaxel analog **S11** (23 mg, 0.02 mmol), compound **S15** (11 mg, 0.0161 mmol) and DMAP (6 mg, 0.05 mmol) in DCM (0.5 mL) was added EDCI (10 mg, 0.05 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture

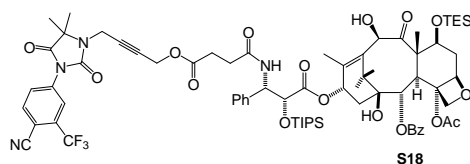
was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. Then the mixture was vacuum filtered and rotary evaporated. After purified by flash chromatography (70% ethyl acetate in hexane), the product (17 mg, 0.0092 mmol) was dissolved in pyridine (0.52 mL) and CH₃CN (0.26 mL). HF-pyridine (0.071 mL) was added to the solution at room temperature. The mixture was stirred at 62 °C until the completion of the reaction (monitored by TLC). Then saturated NaHCO₃ solution was added to the reaction mixture dropwise. The mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na₂SO₄. After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (70% ethyl acetate in hexane) to give compound **10** (9.5 mg, 37.5% for two steps) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.13 (1H, d, *J* = 2.0 Hz), 8.09 (2H, d, *J* = 8.0 Hz), 7.98 (1H, dd, *J* = 8.5, 2.0 Hz), 7.91 (1H, d, *J* = 8.5 Hz), 7.60 (1H, tt, *J* = 7.5, 1.5 Hz), 7.49 (2H, t, *J* = 8.0 Hz), 7.42 – 7.35 (4H, m), 7.31 (1H, tt, *J* = 7.5, 1.5 Hz), 6.29 (1H, s), 6.22 (1H, t, *J* = 8.0 Hz), 5.65 (1H, d, *J* = 6.5 Hz), 5.38 (1H, d, *J* = 8.5 Hz), 5.25 (1H, d, *J* = 8.0 Hz), 4.93 (1H, dd, *J* = 9.5, 1.5 Hz), 4.68 (2H, t, *J* = 2.0 Hz), 4.62 (1H, broad s), 4.38 (1H, dd, *J* = 11.0, 7.0 Hz), 4.29 (1H, d, *J* = 8.5 Hz), 4.27 (2H, t, *J* = 2.0 Hz), 4.26 – 4.21 (4H, m), 4.15 (1H, d, *J* = 8.0 Hz), 3.78 (1H, d, *J* = 7.0 Hz), 3.71 – 3.67 (4H, m), 3.65 (4H, s), 3.65 (4H, s), 3.64 (4H, s), 2.84 (2H, dt, *J* = 6.5, 1.5 Hz), 2.80 – 2.67 (2H, m), 2.66 – 2.63 (4H, m), 2.52 (1H, ddd, *J* = 14.5, 9.0, 6.0 Hz), 2.48 (1H, broad s), 2.37 (3H, s), 2.22 – 2.36 (2H, m), 1.90 – 1.83 (1H, m), 1.84 (3H, s), 1.71 (1H, broad s), 1.65 (3H, s), 1.61 (6H, s), 1.32 (9H, s), 1.24 (3H, s), 1.13 (3H, s); ¹³C NMR (500 MHz, CDCl₃) δ 203.6, 174.4, 173.1, 172.6, 172.2, 172.1, 171.6, 170.3, 167.1, 155.5, 152.4, 142.7, 138.4, 136.3, 135.4, 133.8, 132.9, 130.3, 129.2, 129.0, 128.8, 128.2, 128.1, 126.8, 123.2, 123.1, 115.1, 108.7, 84.5, 81.1, 80.3, 79.1, 78.6, 76.5, 75.9, 75.0, 73.7, 72.4, 72.2, 70.7, 70.6, 69.1, 64.1, 64.0, 62.2, 60.5, 58.6, 56.2, 52.3, 45.7, 43.3, 35.7, 35.6, 29.2, 29.1, 28.9, 28.8, 28.2, 26.8, 23.3, 22.7, 22.0, 14.9, 9.6; HRMS (FAB+) calcd for C₇₈H₉₄F₃N₄O₂₇ [M+H]⁺ 1575.6058, found 1575.5980.



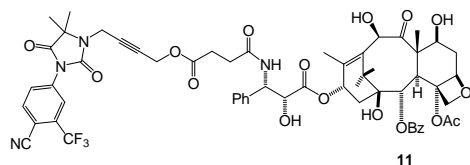
To the solution of docetaxel derivative **S9** (105 mg, 0.094 mmol) in DCM (1 mL) was added TFA (0.48 mL) dropwise at 0 °C. The mixture was stirred at 0 °C until the completion of the reaction (monitored by TLC). After careful addition of saturated NaHCO₃ solution, the mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, dried over Na₂SO₄, vacuum filtered and rotary evaporated. The residue was then purified by flash chromatography (40% ethyl acetate in hexane) to give primary amine as a white solid (65 mg, 68%).

This amine (65 mg, 0.064 mmol) was dissolved in DCM (1 mL). Succinic anhydride (20 mg, 0.192 mmol) and DMAP (24 mg, 0.192 mmol) was added successively. The mixture was then stirred at room temperature overnight. After addition of water, the mixture was extracted with ethyl acetate (3X 20 mL), washed with saturated brine, dried over Na₂SO₄, vacuum filtered and rotary evaporated. The residue was then purified by flash chromatography (40% ethyl acetate in hexane) to give compound **S17** (31 mg, 43.8%) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.07 (2H, d, *J* = 7.5 Hz), 7.54 (1H, t, *J* = 7.3 Hz), 7.46 (2H, t, *J* = 7.7 Hz), 7.35 (2H, t, *J* = 7.6 Hz), 7.28 (1H, d, *J* = 7.3 Hz), 7.24 (3H, d, *J* = 7.8 Hz), 6.42 (1H, s), 6.41 (1H, d, *J* = 10.0 Hz), 6.33 (1H,

t, $J = 9.0$ Hz), 5.69 (1H, d, $J = 7.2$ Hz), 5.56 (1H, d, $J = 9.0$ Hz), 4.91 (1H, d, $J = 8.5$ Hz), 4.82 (1H, d, $J = 1.8$ Hz), 4.46 (1H, dd, $J = 10.5, 6.7$ Hz), 4.23 (2H, dd, $J = 17.9, 8.5$ Hz), 3.80 (1H, d, $J = 7.1$ Hz), 2.56 – 2.44 (3H, m), 2.49 (3H, s), 2.42 – 2.35 (1H, m), 2.32 – 2.23 (2H, m), 2.20 – 2.13 (1H, m), 2.17 (3H, s), 2.01 (3H, s), 1.92 – 1.84 (1H, m), 1.69 (3H, s), 1.23 (3H, s), 1.21 (3H, s), 0.89 (30H, m), 0.80 – 0.46 (6H, m); ^{13}C NMR (500 MHz, CDCl_3) δ 201.8, 175.4, 171.6, 171.2, 170.2, 169.5, 167.0, 140.2, 138.1, 133.7, 133.5, 130.3, 129.5, 128.8, 128.0, 126.42, 84.3, 81.2, 79.1, 76.6, 75.6, 75.1, 75.0, 72.3, 71.5, 58.4, 55.7, 46.7, 43.5, 37.2, 35.7, 30.1, 28.3, 26.8, 23.1, 22.0, 21.0, 17.9, 17.9, 14.2, 12.5, 10.3, 6.8, 5.4; HRMS (ESI⁺) calcd for $\text{C}_{59}\text{H}_{86}\text{NO}_{16}\text{Si}_2$ $[\text{M}+\text{H}]^+$ 1120.5485, found 1120.5470.



Compound **S17** (31 mg, 0.028 mmol) was dissolved in ethanol (2.6 mL) and hydrazine monohydrate (0.29 mL) was added. The mixture was stirred at room temperature overnight. After the addition of saturated NH_4Cl solution, the mixture was extracted with ethyl acetate (3x 25 mL), washed with saturated brine, and dried over Na_2SO_4 , followed by vacuum filtration and rotary evaporation. The residue was then purified by flash chromatography (50% ethyl acetate in hexane) to give **S18** (12 mg, 40%) as white solid.



To the solution of compound **S18** (12 mg, 0.011 mmol), compound **S2** (12 mg, 0.034 mmol) and DMAP (4.2 mg, 0.034 mmol) in DCM (0.6 mL) was added EDCI (6.6 mg, 0.034 mmol). The mixture was stirred at room temperature overnight. After the addition of water, the mixture was extracted with ethyl acetate (3x 15 mL), washed with saturated brine, and dried over Na_2SO_4 . Then the mixture was vacuum filtered and rotary evaporated. After purified by flash chromatography (50% ethyl acetate in hexane), the product (15 mg, 0.011 mmol) was dissolved in pyridine (0.6 mL) and CH_3CN (0.3 mL). HF-pyridine (0.081 mL) was added to the solution at room temperature. The mixture was stirred at 62 °C until the completion of the reaction (monitored by TLC). Then saturated NaHCO_3 solution was added to the reaction mixture dropwise. The mixture was extracted with ethyl acetate (3x 20 mL), washed with saturated brine, and dried over Na_2SO_4 . After vacuum filtration and rotary evaporation, the residue was then purified by flash chromatography (100% ethyl acetate) to give compound **11** (8.7 mg, 68.5% for two steps) as a white solid: ^1H NMR (500 MHz, CDCl_3) δ 8.11 (d, 1H, $J = 2.5$ Hz), 8.09 (2H, dd, $J = 8.5, 1.0$ Hz), 7.96 (1H, dd, $J = 8.5, 2.5$ Hz), 7.89 (1H, d, $J = 8.5$ Hz), 7.60 (1H, tt, $J = 7.5, 1.5$ Hz), 7.50 (2H, t, $J = 7.5$ Hz), 7.41 – 7.33 (4H, m), 7.32 (1H, tt, $J = 6.5, 2.0$ Hz), 6.52 (1H, d, $J = 9.0$ Hz), 6.22 (1H, dt, $J = 9.0, 1.5$ Hz), 5.67 (1H, d, $J = 7.0$ Hz), 5.56 (1H, dd, $J = 9.0, 2.5$ Hz), 5.19 (1H, s), 4.91 (1H, dd, $J = 9.5, 2.0$ Hz), 4.65 (1H, d, $J = 2.0$ Hz), 4.53 (1H, dt, $J = 16.0, 2.0$ Hz), 4.32 (1H, dt, $J = 16.0, 2.0$ Hz), 4.27 (1H, d, $J = 9.0$ Hz), 4.23 – 4.20 (3H, m), 4.20 (1H, d, $J = 8.5$ Hz), 3.88 (1H, d, $J = 6.5$ Hz), 3.49 (1H, broad s), 2.71 – 2.64 (1H, m), 2.59 – 2.42 (4H, m), 2.34 (3H, s), 2.26 (2H, dd, J

= 9.0, 6.5 Hz), 2.11 (1H, broad s), 1.87 – 1.79 (1H, m), 1.83 (3H, d, J = 0.5 Hz), 1.74 (3H, s), 1.57 (6H, s), 1.24 (3H, s), 1.12 (3H, s); ^{13}C NMR (500 MHz, CDCl_3) δ 211.4, 174.3, 172.8, 172.4, 170.8, 170.3, 166.9, 152.4, 138.3, 138.0, 136.3, 136.2, 135.4, 133.8, 130.3, 129.4, 129.0, 128.8, 128.3, 128.1, 126.9, 123.2, 123.1, 115.0, 108.6, 84.2, 81.2, 81.1, 78.7, 78.3, 76.7, 74.9, 74.6, 73.2, 72.8, 72.1, 62.2, 57.7, 54.6, 52.4, 46.5, 43.2, 37.0, 36.0, 30.4, 29.1, 29.0, 26.6, 23.2, 22.7, 20.9, 14.4, 10.0; HRMS (FAB+) calcd for $\text{C}_{59}\text{H}_{62}\text{F}_3\text{N}_4\text{O}_{17}$ $[\text{M}+\text{H}]^+$ 1155.4062, found 1155.5883.

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