Supporting Information

Experimental Section

2’’-3’’-di-*O*-Benzyletopside (2β). An oven-dried 500mL three-necked flask equipped with mechanical stirrer, thermometer and N_2 inlet was charged with **3** (9.0 g, 22.5 mmol) and **4** (10.53 g, 27.2 mmol) and 200 mL of anhydrous acetonitrile. With stirring, the mixture was cooled to –13^{o}C. BF_3-etherate (4.45 mL, 33.7 mmol) was added in one portion. The solution was stirred at –10^{o}C for 5 h (precipitation was noted after approximately 10 min.) and the reaction was quenched by addition of pyridine (8.22 mL, 102 mmol) and the mixture concentrated under vacuum to a volume of 70 mL. Dichloromethane (100 mL) was added and the solution washed three times with water (100 mL) and the organic layer was concentrated to 70 mL and acetonitrile added (100 mL). The solution was concentrated to 80 mL. This was repeated and the solution heated to 65-70^{o}C and then slowly cooled to 20^{o}C and stirred for 1 h. The slurry was cooled to 0^{o}C and stirred 2 h. The product was collected by filtration, washed with cold acetonitrile (50 mL) and the wet-cake dissolved in dichloromethane (150 mL). The solution was concentrated to 100 mL and methanol (300 mL) was added. The dichloromethane was removed by distillation at atmospheric pressure maintaining the volume at 325 mL by addition of methanol. The slurry was cooled to 20^{o}C and stirred for 1 h then to 0^{o}C and stirred two hours. The solid was collected by filtration and dried under vacuum at 45^{o}C to afford **2**β (14.08 g, 81.9%): mp 167-169^{o}C; IR 3400, 2938, 1774 cm^{-1}; ^{1}H NMR (360 MHz, $CDCl_3$) δ 7.36-7.19 (m, 8H), 7.01-6.98 (m, 2H), 6.82 (s, 1H), 6.55 (s, 1H), 6.24 (s, 2H), 5.97-5.89 (dd, 2H J=1.2, 28.2 Hz), 5.44 (s, 1H), 4.90-4.85 (m, 2H), 4.78-4.71 (m, 3H), 4.59-4.50 (m, 3H), 4.38 (t, 1H, J=9 Hz), 4.23-4.14 (m, 2H), 3.74 (s, 6H), 3.65 (t, 1H, J=9 Hz), 3.55 (t, 1H J=10.2 Hz), 3.47-3.34 (m, 2H), 3.32-3.27 (m, 1H), 3.25-3.19 (dd, 1H J=5.2, 14 Hz), 2.92-2.82 (m, 1H), 1.38 (d, 3H, J-5 Hz); ^{13}C NMR ($CDCl_3$) δ 174.88, 148.69, 147.05, 146.40, 138.50, 137.78, 134.01, 132.54, 130.62, 128.56, 128.29, 128.21, 128.09, 127.87, 127.71, 127.63, 110.61, 109.17, 107.81, 102.29, 101.54, 99.54, 81.67, 80.96, 75.39, 75.05, 73.48, 68.21, 67.89, 65.96, 56.44, 56.39, 43.74, 41.31, 37.47, 20.43; MS *m/z* (rel. int.) 786 (MNH_4^+, 32), 769 (MH^+, 6), 383 (91), 261 (59), 229 (100); Anal. Calc’d. for $C_{43}H_{44}O_{13}$: C, 67.17; H, 5.77. Found C, 67.13; H, 5.75.

Etoposide (1). To a solution of **2**β (20 g, 26.01 mmol) in THF (150 mL) was added 5% Pd on C (2.5 g 50% water-wet) in THF (50 mL) and the mixture hydrogenated 50 psi and room temperature for 4 h. The catalyst was filtered on a Buchner funnel containing a 0.45 μ filter and Celite-521 and washed with warm THF(2 x 200 mL) at 55^{o}C. The combined filtrate was concentrated to approximately 50 mL. Water (300 mL) and 10% $NaHSO_3$ (3 mL) were added and the mixture stirred at room temperature for 30 min then at 3^{o}C for 30 min. The slurry was filtered, washed with cold water (2 x 25 mL) and dried under vacuum to afford etoposide **1** (14.83 g, 96.8%) as a white crystalline solid with physical and spectral properties consistent with those reported previously (ref. 2a and 2s) and an HPLC purity of 100 %.