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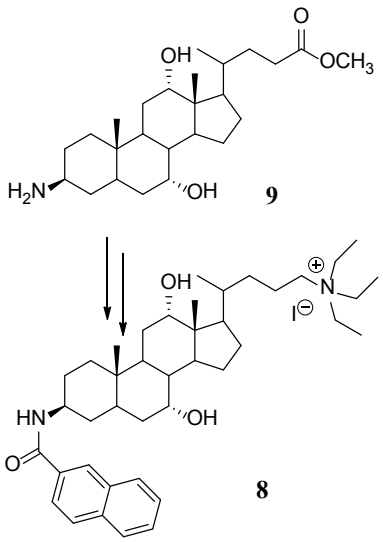
Supporting Information

Synthesis



The compound **9** (0.035 mol, 14.2 g) was dissolved under N_2 atmosphere in dried $CHCl_3$ (120 ml) at 0°C. Then 161 mmol (22.0 ml) of dried TEA was added, maintaining the temperature. 2-naphthoyl chloride (0.0319 mol, 6.08 g) was dissolved in $CHCl_3$ (40 ml) under N_2 atmosphere, and the solution was added dropwise to the previous one at 0°C. The solution was stirred at room temperature for 12 hours, concentrated in rotavapor and product **10** was purified on silica gel column using CH_2Cl_2:MeOH (20:1) as eluent and dried under vacuum overnight at 50 ºC. R_f=0.30. Yield: 70%.

^{1}H NMR (300 MHz, DMSO-d_6, δ/ppm) of **10:** 8.39 (s, 1H, NHCO); 8.02-7.55 (m, 7H, H naphthalene); 4.13 (s, 1H, H12); 3.83 (s, 1H, H7); 3.66 (s, 1H, H3); 3.58 (s, 3H, OCH_3); 2.35-1.19 (m, H bile salt skeleton and lateral chain); 0.95-0.93 (d, *J* = 6.24 Hz, 3H, H21); 0.91 (s, 3H, H19); 0.61 (s, 3H, H18).

^{13}C NMR (75 MHz, DMSO-d_6, δ/ppm) of **10:** 174.41 ($COCH_3$); 167.14 (CONH); 134.72-125.31 (C naphthalene); 71.96 (C12); 67.16 (C7); 51.70; 46.90; 46.66; 42.13; 37.26; 35.63; 35.48; 35.22; 34.05; 31.73; 31.51; 31.32; 29.48; 27.84; 26.86; 25.11; 23.51; 23.40; 17.71; 13.01.

The compound **10** (17.9 mmol, 10.3 g) in MeOH/KOH/ (350 ml, 1M) was refluxed for 1 hour, concentrated and the solid obtained was suspended in water (500 ml) and then acidified to pH=1 with HCl 37%. After filtration, the solid obtained was washed with water to neutrality, and dried in a vacuum oven at 60 ºC, obtaining the product **11**. Yield: 100%.

^{1}H NMR (300 MHz, DMSO-d_6, δ/ppm) of **11:** 8.39 (s, 1H, NHCO); 8.02-7.55 (m, 7H, H naphthalene); 4.13 (s, 1H, H12); 3.83 (s, 1H, H7); 3.66 (s, 1H, H3); 2.35-1.19 (m, H bile salt skeleton and lateral chain); 0.95-0.93 (d, *J* = 6.24 Hz, 3H, H21); 0.91 (s, 3H, H19); 0.61 (s, 3H, H18).

^{13}C NMR (75 MHz, DMSO-d_6, δ /ppm) of **11:** 175.25 (COOH); 167.14 (CONH); 134.72-125.31 (C naphthalene); 71.96 (C12); 67.16 (C7); 46.90; 46.66; 42.13; 37.26; 35.63; 35.48; 35.22; 34.05; 31.73; 31.51; 31.32; 29.48; 27.84; 26.86; 25.11; 23.51; 23.40; 17.71; 13.01.

For subsequent steps, the hydroxyl groups of compound **11** were protected. The intermediate **11** (0.0178 mol, 10 g) was dissolved in formic acid (150 ml) and heated for 4 hours at 55ºC. The compound **12** was precipitated in cold water, filtered and washed until all the formic acid was removed. The product was used without further purification for the next step and only was dried in vacumm for one day at 50 ºC Yield: 96%.

^{1}H NMR (300 MHz, DMSO-d_6, δ/ppm) of **12:** 8.38 (s, 1H, NHCO); 8.31(s, 1H, COH); 8.26 (s, 1H, COH); 8.02-7.55 (m, 7H, H naphthalene); 5.13 (s, 1H); 4.93 (s, 1H); 4.12 (s, 1H); 2.35-1.19 (m, H bile salt skeleton and lateral chain); 0.98 (s, 3H, H19); 0.80-0.78 (d, *J* = 6.24 Hz, 3H, H21); 0.74 (s, 3H, H18).

^{13}C NMR (75 MHz, DMSO-d_6, δ /ppm) of **12:** 175.25 (COOH); 167.14 (CONH); 162.43 (COH); 134.72-125.31 (C naphthalene); 75.56 (C7); 71.65 (C12); 47.65; 46.30; 45.47; 43.49; 37.79; 36.40; 35.02; 34.92; 33.29; 31.72; 31.47; 31.34; 31.21; 28.77; 27.32; 26.29; 24.93; 23.01; 22.95; 18.01; 12.53.

The alcohol **13** was obtained by the reduction of **12**. In a three neck bottom flask provide with a pressure-equalization funnel, a stirring bar and under nitrogen atmosphere, TEA (0.0222 mol, 3 ml) was added to a solution of **12** (0.017 mol, 10.5 g) in dried THF (60 ml), and then ethyl chloroformiate (0.0222 mol, 2.15 ml) was added dropwise. The suspension obtained was stirred for 2 hours at room temperature, cooled to -10 °C and $NaBH_4$ (0.0814 mol, 3 g) was added. Then CH_3OH (75 ml) was added dropwise. Stirring was maintained for 30 min at 0 °C and 30 min at room

temperature. The mixture was diluted with water (150 ml), acidified with HCl (0.2 M, 75 ml) and extracted with ethyl acetate (initially with 90 ml and then with 4×25 ml). The organic phase was washed with water (2×20 ml) and the compound was purified on silica gel column using CH_2Cl_2:MeOH (10:1) as eluent. R_f=0.53. Yield:70%.

^{1}H NMR (300 MHz, DMSO-d_6, δ/ppm) of **13:** 8.38 (s, 1H, NHCO); 8.31(s, 1H, COH); 8.26 (s, 1H, COH); 8.02-7.55 (m, 7H, H naphthalene); 5.14 (s, 1H); 4.92 (s, 1H); 4.12 (s, 1H); 3.38-3.33 (m, 2H); 2.35-1.19 (m, H bile salt skeleton and lateral chain); 0.98 (s, 3H, H19); 0.82-0.79 (d, *J* = 6.24 Hz, 3H, H21); 0.74 (s, 3H, H18).

^{13}C NMR (75 MHz, DMSO-d_6, δ /ppm) of **13:** 167.14 (CONH); 162.43 (COH); 134.72-125.31 (C naphthalene); 75.62 (C7); 71.58 (C12); 62.00; 47.82; 46.31; 45.42; 43.50; 37.81; 36.41; 35.15; 35.02; 33.29; 32.31; 31.73; 31.35; 29.83; 28.78; 27.46; 26.30; 24.94; 23.00; 22.95; 18.42; 12.53.

Transformation of **13** into the iodide derivative **14** was carried out as follows. To a solution of triphenylphosphine (0.0162 mol, 4.16 g) and imidazole (0.0162 mol, 1.13 g) in dichloromethane (60 ml) at 0 °C, iodine (0.0162 mol, 4.16 g) was added in portions over 20 min. The product **13** (0.0106 mol, 6.39 g) in dichloromethane (50 ml) was added and warmed to room temperature. After 48 h, the reaction mixture was diluted with $CHCl_3$ (150 ml), washed with 10% aq. sodium thiosulphate solution (3×25 ml), and water (3×25 ml). The organic phase was dried over anhydrous Na_2SO_4 filtered, concentrated under vacuum, and the crude-product was purified on silica gel column using CH_2Cl_2:MeOH (6:4) as eluent. R_f=0.77. Yield: 81%.

^{1}H NMR (300 MHz, DMSO-d_6, δ/ppm) of **14:** 8.38 (s, 1H, NHCO); 8.31(s, 1H, COH); 8.26 (s, 1H, COH); 8.02-7.55 (m, 7H, H naphthalene); 5.13 (s, 1H); 4.92 (s, 1H); 4.12 (s, 1H); 3.27-3.18 (m, 2H); 2.35-1.19 (m, H bile salt skeleton and lateral chain); 0.98 (s, 3H, H19); 0.82-0.79 (d, *J* = 6.24 Hz, 3H, H21); 0.74 (s, 3H, H18).

^{13}C NMR (75 MHz, DMSO-d_6, δ /ppm) of **14:** 167.28 (CONH); 162.34 (COH); 134.72-125.31 (C naphthalene); 75.62 (C7); 71.58 (C12); 47.82; 46.31; 45.42; 43.50; 37.81; 36.41; 35.15; 35.02; 33.29; 32.31; 31.73; 31.35; 29.83; 28.78; 27.46; 26.30; 24.94; 23.00; 22.95; 18.42; 12.53; 9.93.

The iodide derivative **15** was obtained by de-protection of **14**. To a solution of **14** (2.2 g, 3.9 mmol) in $CHCl_3$/MeOH (5:4, 18 ml), K_2CO_3 was added (1.56 g) and the mixture stirred at room temperature. After 8 h, the reaction mixture was filtered and the solid washed with $CHCl_3$. The solvent was removed in vacuum. Water (30 ml) was added to the residue, and the solution was extracted with $CHCl_3$ (3×20 ml). The organic phase was consecutively washed with water (2×20 ml), HCl (2 M, 2×20 ml), and brine (2×20 ml) and dried over anhydrous Na_2SO_4. The crude product obtained after evaporation of the solvent was purified on a silica gel column by using CH_2Cl_2:MeOH (25:1) as eluent. The solid obtained was dried in vacuum overnight at 55 ºC. R_f=0.15. Yield: 55%.

^{1}H NMR (300 MHz, DMSO-d_6, δ/ppm) of **15:** 8.38 (s, 1H, NHCO); 8.02-7.55 (m, 7H, H naphthalene); 4.13 (s, 1H); 3.80 (s, 1H); 3.67 (s, 1H); 3.29-3.17 (m, 2H); 2.35-1.19 (m, H bile salt skeleton and lateral chain); 0.97-0.94 (d, *J* = 6.24 Hz, 3H, H21); 0.92 (s, 3H, H19); 0.62 (s, 3H, H18).

^{13}C NMR (75 MHz, DMSO-d_6, δ /ppm) of **15:** 167.13 (CONH); 134.72-125.31 (C naphthalene); 71.92 (C7); 67.19 (C12); 46.99; 46.65; 42.14; 37.25; 37.12; 35.64; 35.49; 35.32; 35.21; 34.05; 31.73; 30.67; 29.50; 28.00; 26.89; 26.86; 25.11; 23.51; 23.41; 18.17;13.07;10.22.

The last step corresponds to the transformation of the iodide derivative **15** into the ammonium one **8**. TEA (0.01004 mol, 1.4 ml) was added dropwise on a suspension of **15** (7.6×10^{-4} mol, 0.5 g) in acetonitrile (8.5 ml) and the mixture was refluxed for 24 h under N_2 atmosphere. After concentration in rotavapor to dryness and purification on silica gel column using CH_2Cl_2:MeOH (7:3) as eluent, **8** was obtained as a white powder. This solid was dried in vacuum overnight at 70 ºC. R_f=0.34. Yield: 50%.