Supporting Information for the World Wide Web Edition

Synthesis of Side-chain Elongated Bile Salts. Melting points were determined on a Kofler micro hot stage and are uncorrected. NMR spectra were recorded at ambient temperature in $CDCl_3$ or CD_3OD with a 5 mm probe operating at 300 MHz (^1H) or 75 MHz (^{13}C). For ^1H NMR and ^{13}C NMR spectra, the internal references were TMS (δ 0.00) and $CDCl_3$ (δ 77.00) respectively. IR spectra were recorded as films on a AgCl plate. Solvents were used either as purchased or dried and purified by standard methodology. M-H-W laboratories, Phoenix AZ, carried out elemental analyses. Flash chromatography was performed using silica gel (32-63 μm) purchased from Scientific Adsorbents, Atlanta, GA.

(3α,5β,7α,12α)-3,7,12- Tris(formyloxy)cholan-24-ol (3a): Cholic acid (1 g; 2.45 mmol) was converted to the triformate **2a** using a catalytic amount of perchloric acid in formic acid as previously reported to afford colorless crystals (1.13 g, 94%)(*1*). The triformate **2a** (1 g; 2.03 mmol) was dissolved in anhydrous THF (20 ml) and cooled to 0 °C. Triethylamine (1 mL) was then added followed by ethylchloroformate (0.6 mL) causing the solution to become milky. This milky solution was stirred for an additional 1.5 hours at 0 °C under nitrogen. Sodium borohydride (0.5 g) dissolved in water (10 mL) was then carefully added over 1 min causing the evolution of copious amounts of gas. This was then allowed to stir for 1 hour. The reaction was then carefully quenched by the addition of 1M HCl (10 mL) causing another large evolution of gas. The mixture was

then transferred to a separatory funnel with the aid of ethyl acetate (20 mL), the organic layer washed with 1M HCl (3 × 20 mL), dried (Na_2SO_4) and the solvent was removed *in vacuo* to afford a colorless gum which was chromatographed the same day on silica gel (eluted with 50:50 EtOAc:Hexanes) to yield a white solid (0.80 g, 82%). mp 87-91 °C; TLC R*f* 0.04 (4:1 EtOAc:Hexanes); IR ($CHCl_3$, cm^{-1}) 1718, 3446; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 0.76 (s, 3H), 0.86 (d, 3H, *J* = 6.6 Hz), 0.95 (s, 3H), 3.60(t, 2H, *J* = 6.0 Hz), 4.72 (m, 1H), 5.08 (d, 1H, *J* = 2.1 Hz), 5.28 (s, 1H), 8.03 (s, 1H), 8.11 (s, 1H), 8.17 (s, 1H); ^{13}C NMR ($CDCl_3$) 12.06, 17.75, 22.24, 22.71, 25.47, 26.51, 27.19, 28.49, 29.18, 31.27, 31.51, 34.20, 34.38, 34.44, 34.91, 37.66, 40.74, 42.90, 44.92, 47.31, 63.22, 70.66, 73.68, 75.32, 160.46, 160.50, 160.51; Anal. Calcd. for $C_{27}H_{42}O_7$; C, 67.76; H, 8.84; Found: C, 67.72; H, 8.76

(3α,5β,7α)-3,7- Bis(formyloxy)cholan-24-ol (3b): Chenodeoxycholic acid (1 g; 2.54 mmol) was converted to the diformate **2b** as above to afford colorless crystals (1.05 g, 92%). The diformate **2b** (1 g; 2.23 mmol) was further converted to the C-24 alcohol and chromatographed the same day on silica gel (eluted with 30:70 EtOAc:Hexanes) to yield a white solid (0.79 g, 82%). mp 65-67 °C; TLC R*f* 0.09 (4:1 EtOAc:Hexanes); IR ($CHCl_3$, cm^{-1}) 1721, 3446; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 0.66 (s, 3H), 0.93 (d, 3H, *J* = 6.3 Hz), 0.96 (s, 3H), 3.61 (t, 2H, *J* = 6.0 Hz), 4.73 (m, 1H), 5.04 (d, 1H, *J* = 3.0 Hz), 8.03 (s, 1H), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$) 11.68, 18.60, 20.59, 22.60, 23.45, 26.70, 28.04, 29.30, 31.45, 31.76, 33.97, 34.55, 34.74, 34.75, 35.47, 37.87, 39.41, 40.95, 42.62, 50.08, 55.90, 63.45, 71.38, 74.01, 160.66, 160.67; Anal. Calcd. for $C_{26}H_{42}O_5$; C, 71.85; H, 9.74; Found: C, 71.77; H, 9.38

(3α,5β,12α)-3,12- Bis(formyloxy)cholan-24-ol (3c): Deoxycholic acid (1 g; 2.54 mmol) was converted to the diformate **2c** as above to afford a colorless crystals (1.11 g, 97%). The diformate **2c** (1 g; 2.23 mmol) was further converted to the C-24 alcohol and chromatographed the same day on silica gel (30:70 EtOAc:Hexanes) to yield a white solid (0.76 g, 78%). mp 68-69 °C; TLC R*f* 0.09 (4:1 EtOAc:Hexanes); IR ($CHCl_3$, cm^{-1}) 1721, 3406; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 0.75 (s, 3H), 0.85 (d, 3H, *J* = 6.3 Hz), 0.93 (s, 3H), 3.60 (t, 2H, *J* = 6.6 Hz), 4.84 (m, 1H), 5.26 (s, 1H), 8.04 (s, 1H), 8.14 (s, 1H); ^{13}C NMR ($CDCl_3$) 12.28, 17.78, 22.88, 23.41, 25.72, 25.87, 26.43, 26.75, 27.42, 29.27, 31.60, 32.08, 33.9, 34.18, 34.64, 35.02, 35.58, 41.71, 44.95, 47.51, 49.23, 63.33, 74.07, 76.07, 160.54, 160.61; Anal. Calcd. for $C_{26}H_{42}O_5$; C, 71.85; H, 9.74; Found: C, 71.83; H, 9.55

(3α,5β,7α,12α)-3,7,12-Tris(formyloxy)cholan-24-al (4a): The alcohol **3a** (0.75 g; 1.57 mmol) was dissolved in CH_2Cl_2 followed by the addition of pyridinium chlorochromate (0.51 g; 2.36 mmol). The reaction was carefully followed by TLC until the reaction was complete (~2 hours). The reaction was then transferred to a silica gel column (poured in 10:90 EtOAc:Hexanes) and eluted (25:75 EtOAc:Hexanes) to afford a colorless solid (0.65 g, 87%). mp 141-142 °C; TLC R*f* 0.11 (4:1 EtOAc:Hexanes); IR ($CHCl_3$, cm^{-1}) 1718, 1721; ^{1}H NMR (300 MHz, $CDCl_3$, δ) 0.76 (s, 3H), 0.85 (d, 3H, *J* = 6.3 Hz), 0.95 (s, 3H), 4.72 (m, 1H), 5.08 (d, 1H, *J* = 1.2 Hz), 5.28 (s, 1H), 8.03 (s, 1H), 8.11 (s, 1H), 8.17 (s, 1H), 9.76 (t, 1H, *J* = 1.5 Hz) ; ^{13}C NMR ($CDCl_3$) 12.09, 17.54, 22.27, 22.73, 25.50, 26.54, 27.17, 27.61, 28.51, 31.28, 34.25, 34.41, 34.47, 34.69, 37.69, 40.75, 40.76,

42.93, 44.99, 47.27, 70.61, 73.68, 75.19, 160.41, 160.48, 160.49, 202.55; Anal. Calcd. for $C_{27}H_{40}O_7$; C, 68.04; H, 8.46; Found: C, 67.84; H, 8.21

(3α,5β,7α)-3,7-Bis(formyloxy)cholan-24-al (4b): The alcohol **3b** (0.75 g; 1.73 mmol) was converted to the aldehyde as above, transferred to a silica gel column (poured in 10:90 EtOAc:Hexanes) and eluted (20:80 EtOAc:Hexanes) to afford a colorless solid (0.63 g, 84%). mp 121-123 °C; TLC R*f* 0.31 (4:1 EtOAc:Hexanes); IR ($CHCl_3$, cm^{-1}) 1717, 1721; ^1H NMR (300 MHz, $CDCl_3$, δ) 0.67 (s, 3H), 0.93 (d, 3H, *J* = 6.6 Hz), 0.96 (s, 3H), 4.78 (m, 1H), 5.04 (d, 1H, *J* = 3.0 Hz), 8.03 (s, 1H), 8.08 (s, 1H), 9.76 (t, 1H, *J* = 1.8 Hz); ^{13}C NMR ($CDCl_3$) 11.71, 18.35, 20.59, 22.62, 23.47, 26.72, 27.87, 28.02, 31.45, 33.95, 34.55, 34.76, 34.77, 35.25, 37.87, 39.38, 40.85, 40.94, 42.70, 50.09, 55.74, 71.32, 74.00, 160.68, 160.69, 203.02; Anal. Calcd. for $C_{26}H_{40}O_5$; C, 72.19; H, 9.32; Found: C, 72.35; H, 9.27

(3α,5β,12α)-3,12-Bis(formyloxy)cholan-24-al (4c): The alcohol **3c** (0.75 g; 1.73 mmol) was converted to the aldehyde as above, transferred to a silica gel column (poured in 10:90 EtOAc:Hexanes) and eluted (20:80 EtOAc:Hexanes) to afford a colorless solid (0.64 g, 86%). mp 98-103 °C; TLC R*f* 0.31 (4:1 EtOAc:Hexanes); IR ($CHCl_3$, cm^{-1}) 1716, 1721; ^1H NMR (300 MHz, $CDCl_3$, δ) 0.75 (s, 3H), 0.83 (d, 3H, *J* = 6.6 Hz), 0.93 (s, 3H), 4.83 (m, 1H), 5.25 (s, 1H), 8.03 (s, 1H), 8.14 (s, 1H), 9.76 (t, 1H, *J* = 1.8 Hz); ^{13}C NMR ($CDCl_3$) 12.07, 17.29, 22.67, 23.18, 25.47, 25.66, 26.20, 26.52, 27.16, 27.45, 31.85, 33.76, 33.93, 34.41, 34.52, 35.34, 40.57, 41.47, 44.76, 47.16, 49.00, 73.74, 75.62,

160.22, 160.34, 202.37; Anal. Calcd. for $C_{26}H_{40}O_5$; C, 72.19; H, 9.32; Found: C, 72.44; H, 9.67

(3α,5β,7α,12α)-3,7,12-Tris(formyloxy)-27-norcholest-24-en-26-oic acid ethyl ester (5a): Aldehyde **4a** (0.5 g; 1.05 mmol) was dissolved in benzene (20 mL) followed by the addition of (carboethoxymethylene)triphenylphosphorane (1.83 g; 5.25 mmol). The reaction was allowed to stir for 2 hours at room temperature then transferred directly to a silica gel column and eluted (25:75 EtOAc:Hexanes). The colorless residue was crystallized from ethyl acetate over several days to afford a white solid (0.55 g, 96%) which was a mixture of *E* and *Z* double bond isomers as identified by NMR (~20:1 *E:Z* by ^{1}H NMR). The mixture was not further characterized.

(3α,5β,7α)-3,7-Bis(formyloxy)-27-norcholest-24-en-26-oic acid ethyl ester (5b): Aldehyde **4b** (0.5 g; 1.16 mmol) was converted to the α,β-unsaturated ester as above and chromatographed on silica gel (15:85 EtOAc:Hexanes) to afford a white solid (0.53 g, 92%) which was a mixture of *E* and *Z* double bond isomers as identified by NMR (~20:1 *E:Z* by ^{1}H NMR). The mixture was not further characterized.

(3α,5β,12α)-3,12-bis(formyloxy)-27-norcholest-24-en-26-oic acid ethyl ester (5c): Aldehyde **4c** (0.5 g; 1.16 mmol) was converted to the α,β-unsaturated ester as above and chromatographed on silica gel (15:85 EtOAc:Hexanes) to afford a white solid (0.54 g, 93%) which was a mixture of *E* and *Z* double bond isomers as identified by NMR (~20:1 E:Z by ^{1}H NMR). The mixture was not further characterized.

(3α,5β,7α,12α)-3,7,12-Trihydroxy-27-norcholestan-26-oic acid (6a): The α,β-unsaturated ester **5a** (0.50 g; 0.91 mmol) was dissolved in 100% EtOH (20 mL). Pd/C (50 mg; 10% Pd content) was added and the mixture was hydrogenated on a Parr apparatus (45 psi) overnight. The Pd/C was then filtered through a pad of celite, half of the solvent was removed *in vacuo,* followed by the dropwise addition of 10% KOH (10 mL) being careful to maintain a clear solution. The reaction was then refluxed overnight, cooled, and very carefully quenched using 0.5 M HCl until the pH was acidic. The resultant precipitate was crystallized from ethanol and water to afford a fluffy solid (350 mg, 88%). mp 191 °C; TLC R*f* 0.24 (1:9:90 AcOH:MeOH:CH_2Cl_2); IR ($CHCl_3$, cm^{-1}) 1715, 2798, 3445; ^1H NMR (300 MHz, CD_3OD, δ) 0.71 (s, 3H), 0.91 (s, 3H), 1.12 (d, 3H, *J* = 6.3 Hz), 3.33 (m, 1H), 3.81 (s, 1H), 3.97 (s, 1H); ^{13}C NMR (CD_3OD) 12.34, 17.36, 22.63, 22.64, 22.83, 25.05, 25.11, 26.23, 27.44, 28.60, 30.43, 33.79, 34.40, 34.41, 34.90, 35.30, 35.31, 35.33, 41.38, 41.56, 45.73, 46.17, 66.30, 70.49, 71.06, 174.53; Anal. Calcd. for $C_{26}H_{44}O_5$; C, 71.52; H, 10.16; Found: C, 71.41; H, 10.43

(3α,5β,7α)-3,7-Dihydroxy-27-norcholestan-26-oic acid (6b): The α,β-unsaturated ester **5b** (0.50 g; 0.99 mmol) was hydrogenated and saponified as above and crystallized from ethyl acetate to afford a white solid (360 mg, 86%). mp 190-191 °C; TLC R*f* 0.32 (1:99 AcOH:EtOAc); IR ($CHCl_3$, cm^{-1}) 1715, 2796, 3452; ^1H NMR (300 MHz, CD_3OD, δ) 0.69 (s, 3H), 0.88 (s, 3H), 1.00 (d, 3H, *J* = 6.3 Hz), 3.37 (m, 1H), 3.88 (s, 1H); ^{13}C NMR (CD_3OD) 12.28, 18.32, 21.23, 22.56, 23.90, 25.36, 28.43, 31.85, 33.31, 33.86, 34.76,

34.85, 35.21, 35.27, 35.72, 38.32, 38.35, 40.38, 41.27, 41.91, 41.99, 50.01, 55.66, 66.21, 71.58, 174.48; Anal. Calcd. for $C_{26}H_{44}O_4$; C, 74.24; H, 10.54; Found: C, 74.38; H, 10.65

(3α,5β,12α)-3,12-Dihydroxy-27-norcholestan-26-oic acid (6c): The α,β-unsaturated ester **5c** (0.50 g; 0.99 mmol) was hydrogenated and saponified as above and crystallized from ethanol and water to afford a white solid (360 mg, 86%). mp 185-187 °C; TLC R*f* 0.32 (1:99 AcOH:EtOAc); IR ($CHCl_3$, cm^{-1}) 1718, 2790, 3440; ^1H NMR (300 MHz, CD_3OD, δ) 0.71 (s, 3H), 0.91 (s, 3H), 1.04 (d, 3H, *J* = 6.3 Hz), 3.28 (m, 1H), 3.82 (s, 1H); ^{13}C NMR (CD_3OD) 11.64, 18.54, 20.30, 22.72, 23.18, 25.00, 27.96, 30.59, 32.32, 33.76, 34.76, 34.85, 35.21, 35.22, 35.36, 38.71, 38.99, 40.38, 41.47, 41.92, 41.93, 50.03, 55.74, 66.21, 70.38, 174.48; Anal. Calcd. for $C_{26}H_{44}O_4$; C, 74.24; H, 10.54; Found: C, 74.42; H, 10.78

References:

1. Tserng, K. Y., and Klein, P. D. (1977) *Steroids 29*, 635-48.