SUPPLEMENTARY INFORMATION

SYNTHESIS OF ISOMERIC DIMERS OF DEOXYCHOLIC ACID DERIVATIVES

LINKED BY 1,2,3-TRIAZOLE

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EXPERIMENTAL

Melting point values were determined on a Kofler hot-stage apparatus (Boetius). Infrared (IR) spectra were recorded with a Bruker FS 113V or a Bruker IFS 66v/S FT-IR spectrophotometers for solutions in chloroform or as KBr pellets. ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded using a Varian Gemini 300 VT spectrometer (300 and 75.5 MHz, respectively) or a Varian Gemini 400 MHz (402.6 and 101.2 MHz, respectively) operating in the Fourier transform mode using solutions in deuteriochloroform. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane as the internal standard. Electron impact (ionization energy of 70 eV) mass spectra were recorded using a Waters/Micromass ZQ ES spectrometer. High resolution ESI-MS spectra were performed on a Bruker microQToF mass spectrometer. The solvents were dried and distilled according to standard procedures. Reaction progress and purity of the compounds were monitored by TLC using pre-coated aluminum-backed silica plates (E. Merck, no. 5554) and visualized with 10% H_2SO_4 after heating. Silica gel 60 (E. Merck 70–230 mesh, no. 7734) was used for flash chromatography.

Reduction of acid 3 to 3 α ,12 α -diacetoxy-5 β -cholan-24-ol (4, C₂₈H₄₆O₅)

To 3 g acid **3** (6.3 mmol) dissolved in 51 cm³ anhydrous tetrahydrofuran 5.7 cm³ triethylamine (42.0 mmol) and 1.5 cm³ ethylchloroformate (16.0 mmol) was added. The mixture was stirred at room temperature for 3 h. Then, 3.62 g sodium borohydride (95.1 mmol) dissolved in 21 cm³ H₂O was added and the mixture was stirred for 44 h. After addition of 75 cm³ HCl (1N) stirring was continued for another 0.5 h. The product was extracted with ethyl acetate, the organic layer was washed with NaHCO₃ (5%) and brine, dried with anhydrous magnesium sulfate. After evaporation of the solvent the product was chromatographed on silica gel column with chloroform/ethyl acetate mixture (25:1) as an eluent giving 2.91 g compound **4** (82%) as a solid. M.p.: 157–160 °C; R_f = 0.57 (toluene–ethyl acetate 1:1); ¹H NMR (400 MHz, CDCl₃): δ = 5.09 (s, 1H, 12 β -H), 4.70 (m, 1H, 3 β -H), 3.61 (bs, 2H, 24-CH₂O), 2.10 (s, 3H, 12-OCOCH₃), 2.04 (s, 3H, 3-OCOCH₃), 0.91 (s, 3H, 19-CH₃), 0.82 (d, J = 6.6 Hz, 3H, 21-CH₃), 0.73 (s, 3H, 18-CH₃) ppm (in accordance with data in Ref. 26); FT-IR (CHCl₃): $\bar{\nu}$ = 3626, 3493, 2944, 2870, 1718, 1449, 1256, 1195, 1161, 1052 cm⁻¹; EI-MS (70 eV): m/z = 402.2 (5%), 342.2 (100%), 315.3 (18%), 255.2 (61%), 42.8 (83%).

Propargyl 3 α ,12 α -diacetoxy-5 β -cholan-24-oate (6, C₃₁H₄₆O₆)

To 328 mg acid **3** (0.689 mmol) dissolved in 2.9 cm³ methylene chloride 0.06 cm³ propargylic alcohol (1.034 mmol) and 8.4 mg 4-dimethylaminopyridine (0.069 mmol) was added and the solution was stirred at room temperature for 0.5 h. Then, 156.4 mg *N,N'*-dicyclohexylcarbodiimide (0.758 mmol) was added and the mixture was stirred for additional

0.5 h. The precipitate was filtered off and the solvent was evaporated. The crude product was chromatographed on silica gel with chloroform/ethyl acetate mixture (110:1) as an eluent giving 288.4 mg of pure compound **6** (81%) as a colorless thick oil; $R_f = 0.58$ (toluene–ethyl acetate 5:1); ^1H NMR (400 MHz, CDCl_3): $\delta = 5.08$ (t, $J = 2.4$ Hz, 1H, $12\beta\text{-H}$), 4.71 (m, 1H, $3\beta\text{-H}$), 4.67 (dd, $J = 2.4$ Hz, $J = 0.8$ Hz, 2H, $\text{COOCH}_2\text{C}\equiv\text{C}$), 2.47 (t, $J = 2.4$ Hz, 1H, $\text{C}\equiv\text{CH}$), 2.11 (s, 3H, 12-OCOCH_3), 2.04 (s, 3H, 3-OCOCH_3), 0.91 (s, 3H, 19-CH_3), 0.80 (d, $J = 6.4$ Hz, 3H, 21-CH_3), 0.72 (s, 3H, 18-CH_3) ppm; FT–IR (CHCl_3): $\bar{\nu} = 3308, 2947, 2871, 2132, 1727, 1449, 1255, 1195, 1161, 1027\text{ cm}^{-1}$; EI–MS (70 eV): $m/z = 454.4$ (2%), 394.2 (43%), 315.2 (15%), 255.2 (47%), 42.8 (100%); ES HR–MS: calcd for $\text{C}_{31}\text{H}_{46}\text{O}_6\text{Na}$ 537.3192, found 537.3207.

3 α ,12 α -diacetoxy-5 β -cholan-24-yl propiolate (7, $\text{C}_{31}\text{H}_{46}\text{O}_6$)

To 350 mg compound **4** (0.756 mmol) dissolved in 1.5 cm^3 methylene chloride 10.4 mg DMAP (0.086 mmol) and 0.07 cm^3 propiolic acid (1.134 mmol) was added and the solution was stirred at room temperature for 0.5 h. Then, 171.5 mg N,N' -dicyclohexylcarbodiimide (0.832 mmol) was added and the mixture was stirred for additional 0.5 h. The precipitate was filtered off and the solvent was evaporated. The crude product was chromatographed on silica gel with chloroform/ethyl acetate mixture (120:1) as an eluent giving 243.3 mg of pure compound **7** (62%) as a colorless oil. $R_f = 0.63$ (toluene–ethyl acetate 5:1); ^1H NMR (400 MHz, CDCl_3): $\delta = 5.09$ (t, $J = 2.8$ Hz, 1H, $12\beta\text{-H}$), 4.70 (m, 1H, $3\beta\text{-H}$), 4.16 (m, 2H, $24\text{-CH}_2\text{O}$), 2.88 (s, 1H, $\text{C}\equiv\text{CH}$), 2.11 (s, 3H, 12-OCOCH_3), 2.04 (s, 3H, 3-OCOCH_3), 0.91 (s, 3H, 19-CH_3), 0.81 (d, 3H, $J = 6.7$ Hz, 21-CH_3), 0.73 (s, 3H, 18-CH_3) ppm; FT–IR (CHCl_3): $\bar{\nu} = 3301, 2951, 2870, 2123, 1715, 1449, 1380, 1196, 1028\text{ cm}^{-1}$; EI–

MS (70 eV): m/z = 454.4 (2%), 394.2 (100%), 340.3 (18%), 315.3 (18%), 255.1 (83%), 42.8 (83%); ES HR-MS: calcd for $C_{31}H_{46}O_6Na$ 537.3192, found 537.3229.

compound 5

compound 5

compound 6

compound 6

compound 7

compound 7

compound 8

compound 8

compound 9

compound 9