

Electronic Supplementary information

Synthesis and anti-cancer evaluation of steroidal diglycoside-pyrazoline hybrids

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Spectral data of Steroidal diglycosides 3b-k:

Compound (3b). ^1H NMR (400 MHz, CDCl_3) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1 α), 1.15 (m, 1H, H-5 α), 1.20 (m, 1H, H-6 α), 1.23 (d, 6H, J = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4 β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9 α), 1.41 (m, 1H, H-15 α), 1.52 (m, 1H, H-2 β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4 α), 1.68 (m, 1H, H-6 β), 1.75 (m, 1H, H-1 β), 1.78 (m, 1H, H-11 α), 1.85 (m, 1H, H-2 α), 1.88 (m, 1H, H-7 α), 1.90 (m, 1H, H-15 β), 2.04 (m, 1H, H-11 β), 2.05 (m, 1H, H-16 α), 2.08 (m, 1H, H-7 β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16 β), 2.38 (s, 3H, Me), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17 α), 3.20 (dd, 2H, J = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3 α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, J = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, J = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12 α), 6.52 (s, 1H, NH), 6.84 (m, 1H, Ar-H), 7.06 (m, 3H, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. ^{13}C NMR (100 MHz, CDCl_3 , 25 °C): δ = 13.05, 18.10, 25.06, 25.90, 29.94, 32.15, 35.20, 36.52, 36.84, 36.95, 37.32, 39.05, 41.45, 46.35, 48.72, 52.22, 55.61, 58.01, 59.72, 69.10, 78.02, 78.41, 79.46, 79.62, 83.20, 87.12, 97.22, 101.32, 123.82, 126.74, 127.82, 129.62, 130.36, 130.44, 145.30, 161.64, 131.04, 134.42, 155.92, 167.72 ppm. MS (EI, 70 eV): m/z (%) = 875 [$\text{M} + \text{H}$] $^+$. EA calcd (%) for $\text{C}_{50}\text{H}_{70}\text{N}_2\text{O}_{11}$ (874.50): calcd. C 68.62, H 8.06, N 3.20; found C 68.60, H 8.13, N 3.22.

Compound (3c). ^1H NMR (400 MHz, CDCl_3) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1 α), 1.15 (m, 1H, H-5 α), 1.20 (m, 1H, H-6 α), 1.23 (d, 6H, J = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4 β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9 α), 1.41 (m, 1H, H-15 α), 1.52 (m, 1H, H-2 β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4 α), 1.68 (m, 1H, H-6 β), 1.75 (m, 1H, H-1 β), 1.78 (m, 1H, H-11 α), 1.85 (m, 1H, H-2 α), 1.88 (m, 1H, H-7 α), 1.90 (m, 1H, H-15 β), 2.04 (m, 1H, H-11 β), 2.05 (m, 1H, H-16 α), 2.08 (m, 1H, H-7 β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16 β), 2.37 (s, 3H, Me), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17 α), 3.20 (dd, 2H, J = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3 α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, J = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, J = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12 α), 6.52 (s, 1H, NH), 7.54-7.65 (m, 3H, Ar-H), 7.80 (dd, 4H, J = 6.3 Hz, Ar-H), 8.10

(d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 875 [M + H]⁺. EA calcd (%) for C₅₀H₇₀N₂O₁₁ (874.50): calcd. C 68.62, H 8.06, N 3.20; found C 68.60, H 8.13, N 3.22.

Compound (3d). ¹H NMR (400 MHz, CDCl₃) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1α), 1.15 (m, 1H, H-5α), 1.20 (m, 1H, H-6α), 1.23 (d, 6H, J = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9α), 1.41 (m, 1H, H-15α), 1.52 (m, 1H, H-2β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4α), 1.68 (m, 1H, H-6β), 1.75 (m, 1H, H-1β), 1.78 (m, 1H, H-11α), 1.85 (m, 1H, H-2α), 1.88 (m, 1H, H-7α), 1.90 (m, 1H, H-15β), 2.04 (m, 1H, H-11β), 2.05 (m, 1H, H-16α), 2.08 (m, 1H, H-7β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17α), 3.20 (dd, 2H, J = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, J = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, J = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12α), 5.32 (s, 1H, OH), 6.52 (s, 1H, NH), 6.86 (m, 1H, Ar-H), 7.13 (m, 3H, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 877 [M + H]⁺. EA calcd (%) for C₄₉H₆₈N₂O₁₂ (876.48): calcd. C 67.10, H 7.81, N 3.19; found C 67.14, H 7.80, N 3.20.

Compound (3e). ¹H NMR (400 MHz, CDCl₃) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1α), 1.15 (m, 1H, H-5α), 1.20 (m, 1H, H-6α), 1.23 (d, 6H, J = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9α), 1.41 (m, 1H, H-15α), 1.52 (m, 1H, H-2β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4α), 1.68 (m, 1H, H-6β), 1.75 (m, 1H, H-1β), 1.78 (m, 1H, H-11α), 1.85 (m, 1H, H-2α), 1.88 (m, 1H, H-7α), 1.90 (m, 1H, H-15β), 2.04 (m, 1H, H-11β), 2.05 (m, 1H, H-16α), 2.08 (m, 1H, H-7β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17α), 3.20 (dd, 2H, J = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.65 (s, 3H, OMe), 3.68 (m, 1H, H-3α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, J = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, J = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12α), 6.52 (s, 1H, NH), 6.85-6.93 (m, 2H, Ar-H), 7.24-7.33 (m, 2H, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 891 [M + H]⁺. EA calcd (%) for C₅₀H₇₀N₂O₁₂ (890.49): calcd. C 67.39, H 7.92, N 3.14; found C 67.38, H

7.90, N 3.12.

Compound (3f). ^1H NMR (400 MHz, CDCl_3) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1 α), 1.15 (m, 1H, H-5 α), 1.20 (m, 1H, H-6 α), 1.23 (d, 6H, J = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4 β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9 α), 1.41 (m, 1H, H-15 α), 1.52 (m, 1H, H-2 β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4 α), 1.68 (m, 1H, H-6 β), 1.75 (m, 1H, H-1 β), 1.78 (m, 1H, H-11 α), 1.85 (m, 1H, H-2 α), 1.88 (m, 1H, H-7 α), 1.90 (m, 1H, H-15 β), 2.04 (m, 1H, H-11 β), 2.05 (m, 1H, H-16 α), 2.08 (m, 1H, H-7 β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16 β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17 α), 3.20 (dd, 2H, J = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.63 (s, 3H, OMe), 3.68 (m, 1H, H-3 α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, J = 9.5, 2.0 Hz, H-1''), 4.91 (dd, 1H, J = 9.5, 2.0 Hz, H-1'), 4.88 (t, 1H, H-22), 4.95 (dd, 1H, H-12 α), 6.52 (s, 1H, NH), 6.82 (d, 2H, J = 8.1 Hz, Ar-H), 7.05 (d, 2H, J = 8.1 Hz, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 891 [M + H] $^+$. EA calcd (%) for $\text{C}_{50}\text{H}_{70}\text{N}_2\text{O}_{12}$ (890.49): calcd. C 67.39, H 7.92, N 3.14; found C 67.38, H 7.90, N 3.12.

Compound (3g). ^1H NMR (400 MHz, CDCl_3) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1 α), 1.15 (m, 1H, H-5 α), 1.20 (m, 1H, H-6 α), 1.23 (d, 6H, J = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4 β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9 α), 1.41 (m, 1H, H-15 α), 1.52 (m, 1H, H-2 β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4 α), 1.68 (m, 1H, H-6 β), 1.75 (m, 1H, H-1 β), 1.78 (m, 1H, H-11 α), 1.85 (m, 1H, H-2 α), 1.88 (m, 1H, H-7 α), 1.90 (m, 1H, H-15 β), 2.04 (m, 1H, H-11 β), 2.05 (m, 1H, H-16 α), 2.08 (m, 1H, H-7 β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16 β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17 α), 3.20 (dd, 2H, J = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3 α), 3.74 (s, 6H, OMe), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, J = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, J = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12 α), 6.52 (s, 1H, NH), 6.64-6.78 (m, 3H, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 921 [M + H] $^+$. EA calcd (%) for $\text{C}_{51}\text{H}_{72}\text{N}_2\text{O}_{13}$ (920.49): calcd. C 66.50, H 7.88, N 3.04; found C 66.48, H 7.86, N 2.99.

Compound (3h). ¹H NMR (400 MHz, CDCl₃) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1α), 1.15 (m, 1H, H-5α), 1.20 (m, 1H, H-6α), 1.23 (d, 6H, *J* = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9α), 1.41 (m, 1H, H-15α), 1.52 (m, 1H, H-2β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4α), 1.68 (m, 1H, H-6β), 1.75 (m, 1H, H-1β), 1.78 (m, 1H, H-11α), 1.85 (m, 1H, H-2α), 1.88 (m, 1H, H-7α), 1.90 (m, 1H, H-15β), 2.04 (m, 1H, H-11β), 2.05 (m, 1H, H-16α), 2.08 (m, 1H, H-7β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17α), 3.20 (dd, 2H, *J* = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, *J* = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, *J* = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12α), 6.52 (s, 1H, NH), 6.80-6.91 (m, 2H, Ar-H), 7.30-7.34 (m, 2H, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): *m/z* (%) = 879 [M + H]⁺. EA calcd (%) for C₄₉H₆₇FN₂O₁₁ (879.47): calcd. C 66.95, H 7.68, N 3.19; found C 66.91, H 7.70, N 3.20.

Compound (3i). ¹H NMR (400 MHz, CDCl₃) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1α), 1.15 (m, 1H, H-5α), 1.20 (m, 1H, H-6α), 1.23 (d, 6H, *J* = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9α), 1.41 (m, 1H, H-15α), 1.52 (m, 1H, H-2β), 1.60 (m, 2H, H-2'a & H-2''a), 1.65 (m, 1H, H-4α), 1.68 (m, 1H, H-6β), 1.75 (m, 1H, H-1β), 1.78 (m, 1H, H-11α), 1.85 (m, 1H, H-2α), 1.88 (m, 1H, H-7α), 1.90 (m, 1H, H-15β), 2.04 (m, 1H, H-11β), 2.05 (m, 1H, H-16α), 2.08 (m, 1H, H-7β), 2.10 (m, 2H, H-2'b & H-2''b), 2.16 (m, 1H, H-16β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17α), 3.20 (dd, 2H, *J* = 9.5, 3.0 Hz, H-4' & H-4''), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3α), 3.84 (m, 2H, H-5' & H-5''), 3.88 (q, 2H, H-3' & H-3''), 4.81 (dd, 1H, *J* = 9.5, 2.0 Hz, H-1''), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, *J* = 9.5, 2.0 Hz, H-1'), 4.95 (dd, 1H, H-12α), 6.52 (s, 1H, NH), 7.09 (d, 2H, *J* = 8.4), 7.37 (d, 2H, *J* = 8.4), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): *m/z* (%) = 895 [M + H]⁺. EA calcd (%) for C₄₉H₆₇ClN₂O₁₁ (894.44): calcd. C 65.72, H 7.54, N 3.13; found C 65.70, H 7.53, N 3.12.

Compound (3j). ¹H NMR (400 MHz, CDCl₃) δ = 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1α), 1.15 (m, 1H, H-5α), 1.20 (m, 1H, H-6α), 1.23 (d, 6H, *J* = 6.4 Hz, Me-6' & Me-6''), 1.30 (m, 1H, H-4β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9α), 1.41 (m, 1H, H-15α), 1.52

(m, 1H, H-2 β), 1.60 (m, 2H, H-2`a & H-2``a), 1.65 (m, 1H, H-4 α), 1.68 (m, 1H, H-6 β), 1.75 (m, 1H, H-1 β), 1.78 (m, 1H, H-11 α), 1.85 (m, 1H, H-2 α), 1.88 (m, 1H, H-7 α), 1.90 (m, 1H, H-15 β), 2.04 (m, 1H, H-11 β), 2.05 (m, 1H, H-16 α), 2.08 (m, 1H, H-7 β), 2.10 (m, 2H, H-2`b & H-2``b), 2.16 (m, 1H, H-16 β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17 α), 3.20 (dd, 2H, $J = 9.5, 3.0$ Hz, H-4` & H-4``), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3 α), 3.84 (m, 2H, H-5` & H-5``), 3.88 (q, 2H, H-3` & H-3``), 4.81 (dd, 1H, $J = 9.5, 2.0$ Hz, H-1``), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, $J = 9.5, 2.0$ Hz, H-1`), 4.95 (dd, 1H, H-12 α), 6.52 (s, 1H, NH), 6.28 (m, 2H, Ar-H), 7.30 (s, 1H, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 851 [M + H]⁺. EA calcd (%) for C₄₇H₆₆N₂O₁₂ (850.46): calcd. C 66.33, H 7.82, N 3.29; found C 66.32, H 7.80, N 3.31.

Compound (3k). ¹H NMR (400 MHz, CDCl₃) $\delta =$ 1.01 (s, 3H, Me-19), 1.04 (m, 1H, H-1 α), 1.15 (m, 1H, H-5 α), 1.20 (m, 1H, H-6 α), 1.23 (d, 6H, $J = 6.4$ Hz, Me-6` & Me-6``), 1.30 (m, 1H, H-4 β), 1.32 (s, 3H, Me-18), 1.37 (m, 1H, H-9 α), 1.41 (m, 1H, H-15 α), 1.52 (m, 1H, H-2 β), 1.60 (m, 2H, H-2`a & H-2``a), 1.65 (m, 1H, H-4 α), 1.68 (m, 1H, H-6 β), 1.75 (m, 1H, H-1 β), 1.78 (m, 1H, H-11 α), 1.85 (m, 1H, H-2 α), 1.88 (m, 1H, H-7 α), 1.90 (m, 1H, H-15 β), 2.04 (m, 1H, H-11 β), 2.05 (m, 1H, H-16 α), 2.08 (m, 1H, H-7 β), 2.10 (m, 2H, H-2`b & H-2``b), 2.16 (m, 1H, H-16 β), 2.79 (m, 2H, H-21), 3.10 (q, 1H, H-17 α), 3.20 (dd, 2H, $J = 9.5, 3.0$ Hz, H-4` & H-4``), 3.45 (s, 6H, OMe), 3.68 (m, 1H, H-3 α), 3.84 (m, 2H, H-5` & H-5``), 3.88 (q, 2H, H-3` & H-3``), 4.81 (dd, 1H, $J = 9.5, 2.0$ Hz, H-1``), 4.88 (t, 1H, H-22), 4.91 (dd, 1H, $J = 9.5, 2.0$ Hz, H-1`), 4.95 (dd, 1H, H-12 α), 6.52 (s, 1H, NH), 6.82 (d, 2H, $J = 7.2$ Hz, Ar-H), 7.54-7.65 (m, 3H, Ar-H), 7.86 (d, 2H, $J = 7.2$ Hz, Ar-H), 8.10 (d, 2H, Ar-H) ppm. MS (EI, 70 eV): m/z (%) = 906 [M + H]⁺. EA calcd (%) for C₄₉H₆₇N₃O₁₃ (905.47): calcd. C 64.95, H 7.45, N 4.64; found C 64.98, H 7.42, N 4.63.