Electronic Supplementary Material

Discovery of novel ursolic acid derivatives as effective antimicrobial agents through a ROS-mediated apoptosis mechanism

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Contents

1.General synthetic process for intermediates and target compounds

1.1. Synthesis of the intermediates 1.

Weight the ursolic acid (5.00 g, 10.95 mmol) in a round-bottomed flask, and added into a solution of 20 mL of dimethylformamide containing K_2CO_3 (3.03 g, 21.90 mmol) and epibromohydrin (1.80 g, 13.14 mmol) to stir at room temperature until the ursolic acid was reacted completely. After that, 60 mL of ethyl acetate was added into the mixture. The organic layer was washed by water and a saturated solution of ammonium chloride, dried with sodium sulfate, and followed by the removal of the solvent under a vacuum. Finally, the desired product was purified by a silica gel using CH_2Cl_2 and CH_3OH (V:V = 100:1) as the eluent to afford the intermediate **1**.

1.2. Synthesis of the intermediates 2.

Weight the intermediate **1** (1 g, 1.95 mmol) in a pressure bottle, and added into a solution of 10 mL of *N*, *N*- dimethylformamide containing sodium azide (0.25 g, 3.90 mmol) and NH_4Cl (0.21 g, 3.90 mmol) for reaction at 60 ℃ until the intermediate **1** was reacted completely. After that, 30 mL of dichloromethane was added into the mixture. The organic layer was washed by water and a saturated solution of ammonium chloride, dried with sodium sulfate, and followed by the removal of the solvent under a vacuum. Finally, the desired product was purified by a silica gel using CH_2Cl_2 and CH_3OH (V:V = 100:1) as the eluent to afford the intermediate **2**.

1.3. Synthesis of the intermediates 3.

Weight the intermediate **1** (1 g, 0.95 mmol) in a pressure bottle, and added into a solution of 5 mL of isopropanol containing piperazine (0.50 g, 5.85 mmol) for reaction at 60 ℃until the intermediate **1** was reacted completely. After that, 30 mL of dichloromethane was added into the mixture. The organic layer was washed by water, dried with sodium sulfate, and followed by the removal of the solvent under a vacuum. Finally, the desired product was purified by a silica gel using CH_2Cl_2 and CH_3OH (V:V = 40:1 - 20:1) as the eluent to afford the intermediate **3**.

1.4. Synthesis of the target compounds A1-A22.

The synthesis of target compounds **A1-A22** is the same as that of intermediate **3**.

1.5. Synthesis of the target compounds B1-B10.

The target compounds **B1-B10** were synthesized with reference to the methods reported in the literature with minor modifications (Clements et al. 2019). Add 3-bromopropyne to the corresponding amine in a garden-bottom flask containing 5 mL of dichloromethane solution at a 1 equivalents:1.5 equivalents feeding ratio. After reacting for 1h, weigh the intermediate **2** (0.30 g, 0.54 mmol) in the above garden-bottom flask, and added triethylamine (0.07 g, 0.65 mmol) and CuI (0.02 g, 0.11 mmol) at room temperature until the intermediate **2** was reacted completely. After that, 20 mL of dichloromethane was added into the mixture. The organic layer was washed by water, dried with sodium sulfate, and followed by the removal of the solvent under a vacuum. Finally, the desired product was purified by a silica gel using CH_2Cl_2 and CH_3OH (V:V = 40:1 - 10:1) as the eluent to afford the target compound **B1-B10**.

1.6. Synthesis of the target compounds C1-C6.

Weight the intermediate **3** (0.3 g, 0.50 mmol) in a garden-bottom flask, and added into a solution of 5 mL of dichloromethane containing corresponding sulfonyl chloride (0.11 g, 0.60 mmol) and triethylamine (0.06 g, 0.60 mmol) at room temperature until the intermediate **3** was reacted completely. After that, 20 mL of dichloromethane was added into the mixture. The organic layer was washed by water, dried with sodium sulfate, and followed by the removal of the solvent under a vacuum. Finally, the desired product was purified by a silica gel using CH_2Cl_2 and CH_3OH (V:V = 100:1) as the eluent to afford the target compound **C1-C6**.

2.Characterization data of all intermediates and target compounds

3-(oxiran-1-yl) -2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (1)

White solid, yield 70.3%, m. p. 84.3-86.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (s, 1H, 12-CH=C), 4.35–4.26 (m, 1H, 1′a-O<u>CH$_2$</u>CH), 3.86–3.75 (m, 1H, 1′b-O<u>CH$_2$</u>CH), 3.22–3.10 (m, 2H, 2′-OCH+3-<u>CH</u>OH), 2.82–2.76 (m, 1H, 3′a-CH_2O), 2.64–2.57 (m, 1H, 3′b-CH_2O), 2.21 (dd, J = 11.1, 5.6 Hz, 1H, 18-H), 2.04–1.72 (m, 4H, 11-H+2-H),

1.71–1.42 (m, 11H, 16-H+9-H+22-H+20-H+6-H+1-H+19-H), 1.38–1.20 (m, 4H, 21-H+7-H), 1.10–0.98 (m, 2H, 15-H), 1.05 (s, 3H, 27-CH_3), 0.95 (s, 3H, 23-CH_3), 0.91 (d, *J* = 6.0 Hz, 3H, 30-CH_3), 0.88 (s, 3H, 25-CH_3), 0.83 (d, *J* = 6.5 Hz, 3H, 29-CH_3), 0.74 (s, 3H, 26-CH_3), 0.72 (d, *J* = 1.5 Hz, 3H, 24-CH_3), 0.68 (d, *J* = 11.3 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.6, 138.2, 125.9, 79.2, 65.2, 64.9, 55.5, 53.1, 49.7, 48.5, 47.8, 45.0, 42.3, 39.8, 39.3, 39.1, 39.0,38.9, 37.2, 36.9, 33.3, 30.9, 28.4, 28.2, 27.5, 24.4, 23.8, 23.6, 21.4, 18.6, 17.3, 17.2, 15.9, 15.7; HRMS (ESI): m/z calcd for $C_{33}H_{53}O_4^+$: 513.3938; found: 513.3928.

3-azido-2-hydroxypropyl-3β-hydroxy-urs-12-en-28-oate (2)

White solid, yield 89.3%, m. p. 93.6-94.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.24 (d, *J* = 3.3 Hz, 1H, 12-CH=C), 4.19–3.93 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.42–3.30 (m, 2H, 3′-N_3CH_2), 3.20 (dd, *J* = 10.9, 4.5 Hz, 1H, 3-$\underline{CH}$OH), 2.20 (d, *J* = 11.2 Hz, 1H, 18-H), 2.07–1.72 (m, 4H, 11-H+2-H), 1.71–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.37 (ddd, *J* = 29.7, 24.2, 12.9 Hz, 5H, 6b-H+21-H+7-H), 1.15 – 1.00 (m, 5H, 15H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.94 (d, *J* = 6.0 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, *J* = 7.0 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H) ; ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.7, 138.8, 125.6, 79.0, 69.1, 65.5, 55.2, 53.4, 53.3, 53.0, 48.5, 47.5, 42.2, 39.5, 39.1, 38.8, 38.6, 37.0, 36.8, 33.0, 30.6, 28.2, 27.9, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.2, 17.0, 15.7, 15.5; HRMS (ESI): m/z calcd for $C_{33}H_{54}O_4N_3^+$: 556.4109; found: 556.4099.

3-(Piperazine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (3) (A1)

White solid, yield 66.7 %, m. p. 115.9-117.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.24 (dd, *J* = 8.2, 3.7 Hz, 1H, 12-CH=C), 4.11–3.87 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, *J* = 10.9, 4.7 Hz, 1H, 3-$\underline{CH}$OH), 3.04–2.85 (m, 4H, 4′-NCH_2), 2.71–2.37 (m, 6H, 3′-N$\underline{CH_2}$CH+5′-NCH_2), 2.22 (d, *J* = 11.2 Hz, 1H, 18-H), 2.07–1.74 (m, 4H, 11-H+2-H), 1.72–1.44 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.41–1.23 (m, 5H, 6b-H+21-H+7-H), 1.12–1.00 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, *J* = 2.6 Hz, 3H, 24-CH_3), 0.69 (s, 1H,

5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 138.9, 125.8, 79.3, 66.6, 65.4, 61.4, 55.5, 54.0, 53.2, 48.6, 47.8, 45.9, 42.4, 39.9, 39.4, 39.2, 39.1, 38.9, 37.3, 37.0, 33.3, 30.9, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{37}H_{63}O_4N_2^+$: 599.4782; found: 599.4778.

3-(4-Methyl piperazine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A2)

White solid, yield 52.1 %, m. p. 86.1-87.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (q, J = 3.6 Hz, 1H, 12-CH=C), 4.09–3.86 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, J = 10.9, 4.6 Hz, 1H, 3-$\underline{CH}$OH), 2.80–2.27 (m, 10H, 4′-NCH_2+3′-N$\underline{CH_2}$CH+5′-NCH_2), 2.31 (s, 3H, 6′-NCH_3), 2.22 (d, J = 11.2 Hz, 1H, 18-H), 2.06–1.75 (m, 4H, 11-H+2-H), 1.72–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.40–1.21 (m, 5H, 6b-H+21-H+7-H), 1.11–1.00 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, J = 6.2 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, J = 2.6 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 138.7, 125.8, 79.3, 66.6, 65.4, 60.6, 55.5, 55.3, 53.2, 48.6, 47.8, 46.2, 42.4, 39.8, 39.4, 39.1, 39.0, 38.9, 37.3, 37.1, 33.3, 30.9, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 15.9, 15.8; HRMS (ESI): m/z calcd for $C_{38}H_{65}O_4N_2^+$: 613.4939; found: 613.4932.

3-(4-Ethyl piperazine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A3)

White solid, yield 50.0 %, m. p. 85.3-87.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (q, J = 3.6 Hz, 1H, 12-CH=C), 4.08–3.84 (m, 3H, 1′-O$\underline{CH_2}$CH+2'-$\underline{CH}$OH), 3.20 (dd, J = 10.9, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 2.78–2.28 (m, 12H, 4′-NCH_2+3′-N$\underline{CH_2}$CH+5′-NCH_2+6′-N$\underline{CH_2}CH_3$), 2.22 (d, J = 11.2 Hz, 1H, 18-H), 2.04–1.81 (m, 4H, 11-H+2-H), 1.75–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.40–1.20 (m, 5H, 6b-H+21-H+7-H), 1.11–0.99 (m, 2H, 15-H), 1.08 (t, J = 7.0 Hz, 3H, 7′-$NCH_2\underline{CH_3}$), 1.07 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, J = 6.2 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.84 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, J = 2.6 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 138.6, 125.8, 79.3, 66.6, 65.4, 60.7, 55.5, 53.1, 52.6, 48.6, 47.9, 42.4, 39.9, 39.4, 39.2, 39.1, 38.9, 37.3, 37.0, 33.3, 31.0, 28.5, 28.3, 27.6, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0,

15.8, 12.3; HRMS (ESI): m/z calcd for $C_{39}H_{67}O_4N_2^+$: 627.5095; found: 627.5090.

3-(4-Isopropyl piperazine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A4)

White solid, yield 55.7 %, m. p. 91.5-93.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (q, J = 3.6 Hz, 1H, 12-CH=C), 4.08–3.84 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.19 (dd, J = 10.7, 4.6 Hz, 1H, 3-$\underline{CH}$OH), 2.76–2.29 (m, 11H, 4′-NCH_2+3′-N$\underline{CH_2}$CH+5′-NCH_2+6′-N$\underline{CH}(CH_3)_2$), 2.21 (d, J = 11.2 Hz, 1H, 18-H), 2.04–1.75 (m, 4H, 11-H+2-H), 1.71–1.44 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.42–1.17 (m, 5H, 6b-H+21-H+7-H), 1.10–0.98 (m, 2H, 15-H), 1.06 (s, 3H, 27-CH_3), 1.04 (d, J = 6.5 Hz, 6H, 7′-NCH($\underline{CH_3}$)$_2$), 0.97 (s, 3H, 23-CH_3), 0.92 (d, J = 6.1 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.73 (d, J = 2.6 Hz, 3H, 24-CH_3), 0.68 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 138.6, 125.8, 79.3, 66.6, 65.3, 60.7, 55.5, 54.8, 53.9, 53.2, 49.0, 48.6, 47.8, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 33.3, 30.9, 28.5, 28.3, 27.5, 24.5, 23.9, 23.6, 21.5, 18.9, 18.6, 17.4, 17.3, 15.9, 15.8; HRMS (ESI): m/z calcd for $C_{40}H_{69}O_4N_2^+$: 641.5252; found: 641.5246.

3-(4-Tert-butyl piperazine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A5)

White solid, yield 58.8 %, m. p. 103.9-105.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (q, J = 3.6 Hz, 1H, 12-CH=C), 4.07–3.85 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, J = 10.8, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 2.73–2.28 (m, 10H, 4′-NCH_2+3′-N$\underline{CH_2}$CH+5′-NCH_2), 2.21 (d, J = 11.2 Hz, 1H, 18-H), 2.05–1.78 (m, 4H, 11-H+2-H), 1.71–1.44 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.39–1.21 (m, 5H, 6b-H+21-H+7-H), 1.12–0.99 (m, 2H, 15-H), 1.07 (s, 12H, 27-CH_3+7′-NC$(CH_3)_3$) 0.97 (s, 3H, 23-CH_3), 0.93 (d, J = 6.2 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, J = 2.9 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 138.6, 125.8, 79.3, 66.6, 65.3, 60.6, 55.5, 54.2, 53.2, 48.6, 47.9, 46.0, 42.4, 39.9, 39.4, 39.2, 39.1, 38.9, 37.3, 37.0, 33.3, 31.0, 28.5, 28.3, 27.6, 26.1, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{41}H_{71}O_4N_2^+$: 655.5408; found: 655.541.

3-(4-Acetyl piperazine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A6)

White solid, yield 58.3 %, m. p. 104.8-106.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.23 (dd, J = 7.7, 3.8 Hz, 1H, 12-CH=C), 4.13–3.90 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.72–3.43 (m, 4H, 5′-NCH_2), 3.20 (dd, J = 10.8, 4.5 Hz, 1H, 3-$\underline{CH}$OH), 2.69–2.56 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.55–2.37 (m, 4H, 4′-NCH_2), 2.21 (d, J = 11.2 Hz, 1H, 18-H), 2.09 (s, 3H, 7′-$COCH_3$), 2.05–1.74 (m, 4H, 11-H+2-H), 1.71–1.45 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.39–1.21 (m, 5H, 6b-H+21-H+7-H), 1.12–0.99 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, J = 6.2 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, J = 2.5 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 169.3, 138.7, 125.8, 79.3, 66.6, 65.7, 60.7, 55.5, 53.8, 53.3, 53.2, 48.6, 47.8, 46.4, 42.4, 41.5, 39.9, 39.4, 39.2, 39.1, 38.9, 37.3, 37.1, 33.3, 30.9, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{39}H_{65}O_5N_2^+$: 641.4888; found: 641.4882.

3-(4-Morpholine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A7)

White solid, yield 72.7 %, m. p. 85.5-87.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (dd, J = 8.4, 3.6 Hz, 1H, 12-CH=C), 4.12–3.87 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.78–3.64 (m, 4H, 5′-OCH_2), 3.20 (dd, J = 10.3, 5.0 Hz, 1H, 3-$\underline{CH}$OH), 2.66–2.58 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.50–2.29 (m, 4H, 4′-NCH_2), 2.22 (d, J = 11.3 Hz, 1H, 18-H), 2.07–1.77 (m, 4H, 11-H+2-H), 1.69–1.44 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.40–1.26 (m, 5H, 6b-H+21-H+7-H), 1.12–1.00 (m, 2H, 15-H), 1.08 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, J = 6.1 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.74 (d, J = 2.5 Hz, 3H, 24-CH_3), 0.71 (d, J = 11.4 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 138.7, 125.8, 79.3, 67.3, 66.6, 65.4, 61.3, 55.5, 54.1, 53.2, 48.6, 47.9, 42.4, 39.9, 39.4, 39.2, 39.1, 39.0, 37.3, 37.1, 33.3, 31.0, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{37}H_{62}O_5N^+$: 600.4623; found: 600.4619.

3-(Piperidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A8)

White solid, yield 93.1 %, m. p. 95.5-97.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (dd,

J = 7.3, 3.5 Hz, 1H, 12-CH=C), 4.08–3.89 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, *J* = 10.8, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 2.67–2.55 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.46–2.29 (m, 4H, 4′-NCH_2), 2.22 (d, *J* = 11.2 Hz, 1H, 18-H), 2.04–1.74 (m, 4H, 11-H+2-H), 1.72–1.44 (m, 16H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+5′-$NCH_2\underline{CH_2}$+6′-$NCH_2CH_2\underline{CH_2}$), 1.40–1.22 (m, 5H, 6b-H+21-H+7-H), 1.11–1.00 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (d, *J* = 2.1 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.6, 125.8, 79.3, 66.6, 65.1, 61.4, 55.5, 55.1, 53.1, 48.5, 47.9, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 33.3, 31.0, 28.5, 28.3, 27.5, 26.1, 24.5, 24.3, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{38}H_{64}O_4N^+$: 598.4830; found: 598.4825.

3-(2-Methylpiperidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A9)

White solid, yield 61.5 %, m. p. 85.1-86.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.24 (q, *J* = 3.5 Hz, 1H, 12-CH=C), 4.12–3.82 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, *J* = 10.8, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 3.01–2.31 (m, 4H, 3′-N$\underline{CH_2}$CH+8′-N$\underline{CH_2}CH_2$), 2.22 (d, *J* = 11.4 Hz, 1H, 18-H), 2.19–2.07 (m, 1H, 4′-N$\underline{CH}CH_3$), 2.05–1.74 (m, 4H, 11-H+2-H), 1.71–1.46 (m, 14H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+5′-NCH$\underline{CH_2}$+7′-NCH_2), 1.39–1.23 (m, 7H, 6b-H+21-H+7-H+6′-$NCH_2CH_2\underline{CH_2}$), 1.10–1.00 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 1.05 (d, *J* = 3.0 Hz, 3H, 9′-NCH$\underline{CH_3}$), 0.97 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.0 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.74 (s, 3H, 24-CH_3), 0.71 (d, *J* = 11.3 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.6, 125.8, 79.3, 66.8, 66.6, 64.8, 55.5, 53.2, 52.8, 48.5, 47.8, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 34.9, 33.3, 31.0, 28.5, 28.3, 27.5, 26.3, 24.6, 24.0, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 16.0, 15.7; HRMS (ESI): m/z calcd for $C_{39}H_{66}O_4N^+$: 612.4986; found: 612.4980.

3-(3-Methylpiperidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A10)

white solid, yield 65.5 %, m. p. 88.9-90.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.24 (q, *J* = 3.5 Hz, 1H, 12-CH=C), 4.07–3.83 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, *J* = 10.8, 4.9 Hz, 1H, 3-$\underline{CH}$OH), 2.91–2.62 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.41–2.11 (m, 3H,

8′-N$\underline{CH_2}CH_2$+4′a-$\underline{CH_2}$CH), 2.23 (d, *J* = 11.4 Hz, 1H, 18-H), 2.05–1.76 (m, 5H, 11-H+2-H+4′b-$\underline{CH_2}$CH), 1.74–1.45 (m, 15H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+5′-NCH$_2\underline{CH}$+6′-NCH$_2$CH$_2\underline{CH_2}$+7′-NCH$_2\underline{CH_2}$), 1.42–1.20 (m, 5H, 6b-H+21-H+7-H), 1.11–1.00 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.86 (d, *J* = 4.2 Hz, 3H, 9′-CH$\underline{CH_3}$), 0.85 (d, *J* = 6.3 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.74 (s, 3H, 24-CH_3), 0.71 (d, *J* = 11.3 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.6, 125.8, 79.3, 66.8, 65.2, 63.7, 61.0, 55.8, 55.5, 53.2, 48.6, 47.9, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 33.3, 33.1, 31.5, 31.0, 28.5, 28.3, 27.5, 25.8, 24.5, 23.9, 23.6, 21.5, 19.8, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{39}H_{66}O_4N^+$: 612.4986; found: 612.4984.

3-(4-Methylpiperidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A11)

white solid, yield 50.0 %, m. p. 89.5-91.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.27–5.22 (m, 1H, 12-CH=C), 4.08–3.83 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.21 (dd, *J* = 10.8, 4.9 Hz, 1H, 3-$\underline{CH}$OH), 2.96–2.72 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.44–2.16 (m, 5H, 4′-N$\underline{CH_2}$CH$_2$+18-H), 2.04–1.78 (m, 5H, 11-H+2-H+6′-$\underline{CH}$CH$_3$), 1.71–1.46 (m, 12H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+5a′-NCH$_2\underline{CH_2}$), 1.39–1.22 (m, 7H, 6b-H+21-H+7-H+5b′-NCH$_2\underline{CH_2}$), 1.11–1.01 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.91 (d, *J* = 7.8 Hz, 3H, 7′-CH$\underline{CH_3}$), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.74 (d, *J* = 2.1 Hz, 3H, 24-CH_3), 0.71 (d, *J* = 11.4 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.6, 125.9, 79.4, 67.0, 66.8, 65.3, 60.9, 56.0, 55.6, 53.2, 52.9, 48.5, 47.9, 42.4, 39.9, 39.4, 39.2, 39.1, 39.0, 37.3, 37.0, 34.9, 34.5, 33.3, 31.0, 28.5, 28.3, 27.6, 24.6, 23.9, 23.6, 22.2, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{39}H_{66}O_4N^+$: 612.4986; found: 612.4982.

(3S)-piperidine-3-carboxylate-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A12)

White solid, yield 83.1 %, m. p. 72.1-73.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.23 (d, J = 3.1 Hz, 1H, 12-CH=C), 4.17–4.09 (m, 2H, 10′-OCH_2CH_3), 4.07–3.91 (m, 3H,

1′-OCH_2CH+2′-CHOH), 3.25–3.09 (m, 2H, 3-CHOH+5′-$CHCOOCH_2$), 2.97–2.30 (m, 6H, 3′-NCH_2CH+4′-NCH2+8′-NCH_2), 2.21 (d, J = 11.2 Hz, 1H, 18-H), 2.05–1.82 (m, 4H, 11-H+2-H), 1.79–1.44 (m, 14H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+6′-N $CH_2CH_2CH_2$+7′-NCH_2CH_2), 1.41–1.17 (m, 5H, 6b-H+21-H+7-H), 1.24 (t, J = 7.1 Hz, 3H, 11′-OCH_2CH_3), 1.11–0.99 (m, 2H, 15-H), 1.06 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.92 (d, J = 6.2 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.73 (d, J = 1.6 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 173.7, 138.6, 125.8, 79.3, 66.4, 65.3, 61.0, 55.5, 54.9, 53.2, 48.5, 47.8, 42.4, 41.5, 39.8, 39.4, 39.1, 39.0, 39.8, 37.3, 37.0, 33.3, 30.9, 28.5, 28.3, 27.5, 26.7, 24.5, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8, 14.5; HRMS (ESI): m/z calcd for $C_{41}H_{68}O_6N^+$: 670.5041; found: 612.5034.

(3R)-piperidine-3-carboxylate-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A13)

White solid, yield 77.1 %, m. p. 76.4-78.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.26 (d, *J* = 2.9 Hz, 1H, 12-CH=C), 4.23–4.12 (m, 3H, 10′-O<u>CH_2</u>CH_3+2′-<u>CH</u>OH), 4.10–3.98 (m, 2H, 1′-O<u>CH_2</u>CH), 3.28–3.15 (m, 2H, 3-<u>CH</u>OH+5′-<u>CH</u>$COOCH_2$), 3.14–2.29 (m, 6H, 3′-N<u>CH_2</u>CH+4′-NCH_2+8′-NCH_2), 2.24 (d, *J* = 11.2 Hz, 1H, 18-H), 2.07–1.46 (m, 18H,11-H+2-H+16-H+9-H+22-H+20-H+6a-H+1-H+19-H+6′-NCH_2CH_2<u>CH_2</u>+7′-NC H_2<u>CH_2</u>), 1.43–1.26 (m, 5H, 6b-H+21-H+7-H), 1.28 (t, *J* = 7.1 Hz, 3H, 11′-OCH_2<u>CH_3</u>), 1.14–1.02 (m, 2H, 15-H), 1.10 (s, 3H, 27-CH_3), 1.00 (s, 3H, 23-CH_3), 0.96 (d, *J* = 6.1 Hz, 3H, 30-CH_3), 0.93 (s, 3H, 25-CH_3), 0.88 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.80 (s, 3H, 26-CH_3), 0.75 (s, 3H, 24-CH_3), 0.72 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.7, 173.1, 138.7, 125.8, 79.3, 66.2, 65.1, 61.3, 55.5, 54.9, 53.2, 48.6, 47.8, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.1, 33.3, 30.9, 28.5, 28.3, 27.5, 26.4, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8, 14.5. HRMS (ESI): m/z calcd for $C_{41}H_{68}O_6N^+$: 670.5041; found: 612.5034.

3-(Pyrrolidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A14)

White solid, yield 67.0 %, m. p. 94.6-96.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (q, *J* = 3.6 Hz, 1H, 12-CH=C), 4.12–3.84 (m, 3H, 1′-O<u>CH_2</u>CH+2′-<u>CH</u>OH), 3.21 (dd, *J* = 10.9, 4.8 Hz, 1H, 3-<u>CH</u>OH), 2.75–2.32 (m, 6H, 3′-N<u>CH_2</u>CH+4′-NCH_2), 2.24 (d, *J* =

11.3 Hz, 1H, 18-H), 2.07–1.76 (m, 8H, 11-H+2-H+5′-$NCH_2\underline{CH_2}$), 1.70–1.47 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.40–1.24 (m, 5H, 6b-H+21-H+7-H), 1.12–1.00 (m, 2H, 15-H), 1.08 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.94 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.91 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.78 (s, 3H, 26-CH_3), 0.75 (d, *J* = 1.1 Hz, 3H, 24-CH_3), 0.71 (d, *J* = 11.1 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.7, 125.8, 79.4, 67.4, 67.0, 58.8, 55.6, 54.5, 53.2, 48.6, 47.9, 42.4, 39.9, 39.4, 39.2, 39.1, 39.0, 37.3, 37.0, 33.4, 31.0, 28.5, 28.3, 27.6, 24.6, 24.0, 23.6, 21.5, 18.7, 17.5, 17.4, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{37}H_{62}O_4N^+$: 584.4673; found: 584.4670.

3-(R-3-hydroxy-pyrrolidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A15)

white solid, yield 43.1 %, m. p. 98.7-100.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.23 (d, *J* = 3.3 Hz, 1H, 12-CH=C), 4.37 (dd, *J* = 11.7, 5.7 Hz, 1H, 5′-$\underline{CH}$OH), 4.11–3.88 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, *J* = 10.8, 4.7 Hz, 1H, 3-$\underline{CH}$OH), 3.12–2.91 (m, 2H, 7′-N$\underline{CH_2}CH_2$), 2.81–2.66 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.61–2.34 (m, 2H, 4′-N$\underline{CH_2}$CH), 2.25–2.13 (m, 2H, 6a′-$NCH_2\underline{CH_2}$+18-H), 2.06–1.73 (m, 5H, 11-H+2-H+6b′-$NCH_2\underline{CH_2}$), 1.72–1.43 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.39–1.20 (m, 5H, 6b-H+21-H+7-H), 1.13–0.99 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.1 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.73 (s, 3H, 24-CH_3), 0.70 (d, *J* = 11.5 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.7, 125.8, 79.3, 71.4, 67.3, 66.7, 63.8, 63.2, 58.8, 55.5, 53.6, 53.2, 52.8, 48.6, 47.8, 42.4, 39.8, 39.4, 39.1, 39.0, 38.9, 37.3, 37.1, 35.1, 33.3, 30.9, 28.5, 28.3, 27.5, 24.5, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{37}H_{62}O_5N^+$: 600.4623; found: 600.4621.

3-(S-3-hydroxy-pyrrolidine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A16)

White solid, yield 54.3 %, m. p. 98.4-99.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.23 (d, *J* = 3.3 Hz, 1H, 12-CH=C), 4.37 (dd, *J* = 11.6, 5.7 Hz, 1H, 5′-$\underline{CH}$OH), 4.11–3.87 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (dd, *J* = 10.7, 4.7 Hz, 1H, 3-$\underline{CH}$OH), 3.11–2.88 (m,

2H, 7′-N$\underline{CH_2}CH_2$), 2.80–2.63 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.59–2.30 (m, 2H, 4′-N$\underline{CH_2}$CH), 2.26–2.14 (m, 2H, 6a′-NCH$_2\underline{CH_2}$+18-H), 2.06–1.73 (m, 5H, 11-H+2-H+6b′-NCH$_2\underline{CH_2}$), 1.72–1.43 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.41–1.18 (m, 5H, 6b-H+21-H+7-H), 1.13–0.99 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.1 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.73 (s, 3H, 24-CH_3), 0.70 (d, *J* = 11.4 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.8, 125.9, 79.3, 71.6, 67.5, 66.8, 63.8, 63.3, 58.9, 55.5, 53.4, 53.3, 52.8, 48.6, 47.9, 42.4, 39.9, 39.4, 39.2, 39.1, 39.0, 37.3, 37.0, 35.3, 33.4, 31.0, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{37}H_{62}O_5N^+$: 600.4623; found: 600.4609.

3-(Dimethylamino-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A17)

White solid, yield 72.1 %, m. p. 143.9-144.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.25 (dd, *J* = 6.9, 3.3 Hz, 1H, 12-CH=C), 4.12–3.87 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.21 (dd, *J* = 10.9, 4.7 Hz, 1H, 3-$\underline{CH}$OH), 2.52–2.26 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.33 (s, 6H, 4′-NCH_3), 2.23 (d, *J* = 11.6 Hz, 1H, 18-H), 2.07–1.76 (m, 4H, 11-H+2-H), 1.73–1.45 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.42–1.19 (m, 5H, 6b-H+21-H+7-H), 1.12–0.99 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.1 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.74 (s, 3H, 24-CH_3), 0.70 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.7, 125.8, 79.3, 66.7, 66.0, 62.0, 55.5, 53.2, 48.6, 47.9, 45.8, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 33.3, 31.0, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{35}H_{60}O_4N^+$: 558.4517; found: 558.4504.

3-(Diethylamine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A18)

White solid, yield 76.1 %, m. p. 93.8-95.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.23 (t, *J* = 3.3 Hz, 1H, 12-CH=C), 4.29–3.98 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.21 (dd, *J* = 11.0, 4.4 Hz, 1H, 3-$\underline{CH}$OH), 3.09–2.49 (m, 6H, 4′-N$\underline{CH_2}CH_3$+3′-N$\underline{CH_2}$CH), 2.20 (d, *J* = 11.2 Hz, 1H, 18-H), 2.06–1.72 (m, 4H, 11-H+2-H), 1.71–1.45 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.42–1.19 (m, 11H, 6b-H+21-H+7-H+5′-NCH$_2\underline{CH_3}$), 1.12–1.00 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3),

0.94 (d, *J* = 6.0 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (s, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.6, 138.7, 125.9, 79.3, 65.9, 65.2, 57.1, 55.5, 53.2, 48.6, 47.8, 42.4, 39.8, 39.4, 39.2, 39.1, 38.9, 37.3, 37.1, 33.3, 30.9, 28.5, 28.3, 27.5, 24.6, 23.9, 23.6, 21.5, 18.6, 17.5, 17.4, 16.0, 15.8, 10.2; HRMS (ESI): m/z calcd for $C_{37}H_{64}O_4N^+$: 586.4830; found: 586.4828.

3-(1-Methyl-propargylamine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A19)

White solid, yield 84.6 %, m. p. 74.2-75.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.24 (dd, *J* = 7.6, 3.6 Hz, 1H, 12-CH=C), 4.11–3.89 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.55–3.42 (m, 2H, 5′-N$\underline{CH_2}$C≡CH), 3.20 (dd, *J* = 11.0, 4.6 Hz, 1H, 3-$\underline{CH}$OH), 2.67–2.47 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.44 (s, 3H, 4′-NCH_3), 2.29 (t, *J* = 2.4 Hz, 1H, 7′-C≡CH), 2.22 (d, *J* = 11.2 Hz, 1H, 18-H), 2.05–1.75 (m, 4H, 11-H+2-H), 1.70–1.45 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.40–1.19 (m, 5H, 6b-H+21-H+7-H), 1.11–0.99 (m, 2H, 15-H), 1.07 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.1 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.73 (s, 3H, 24-CH_3), 0.70 (d, *J* = 11.2 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.7, 138.7, 125.8, 79.3, 74.8, 66.5, 66.0,, 58.2, 55.5, 53.1, 48.6, 47.8, 46.3, 42.4, 41.9, 39.8, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 33.3, 30.9, 28.5, 28.3, 27.5, 24.5, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{37}H_{60}O_4N^+$: 582.4517; found: 582.512.

3-(Diallylamine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A20)

White solid, yield 88.7 %, m. p. 69.8-71.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 5.86–5.73 (m, 2H, 5′-$\underline{CH}$=CH_2), 5.23 (q, *J* = 3.5 Hz, 1H, 12-CH=C), 5.20–5.12 (m, 4H, 6′-CH=$\underline{CH_2}$), 4.13–3.79 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.30–2.97 (m, 5H, 3-$\underline{CH}$OH+4′-CH_2), 2.58–2.29 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.21 (d, *J* = 11.3 Hz, 1H, 18-H), 2.05–1.77 (m, 4H, 11-H+2-H), 1.69–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.41–1.21 (m, 5H, 6b-H+21-H+7-H), 1.10–1.00 (m, 2H, 15-H), 1.06 (s, 3H, 27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.92 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.90 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.73 (s, 3H,

24-CH_3), 0.70 (d, *J* = 10.5 Hz, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.7, 138.7, 135.3, 125.8, 118.5, 79.3, 66.5, 66.0, 57.3, 55.7, 55.5, 53.2, 48.5, 47.9, 42.4, 39.9, 39.4, 39.1, 39.0, 38.9, 37.3, 37.0, 33.3, 30.9, 28.5, 28.3, 27.5, 24.5, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{39}H_{64}O_4N^+$: 610.4830; found: 610.4827.

3-(1-Methyl-Benzylamine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A21)

White solid, yield 68.5 %, m. p. 76.9-78.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.35–7.23 (m, 5H, Phenyl-H), 5.22 (dd, *J* = 8.1, 3.7 Hz, 1H, 12-CH=C), 4.16–3.86 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.73–3.46 (m, 2H, 5′-NCH_2), 3.20 (dd, *J* = 10.8, 4.7 Hz, 1H, 3-$\underline{CH}$OH), 2.61–2.33 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.27 (s, 3H, 4′-NCH_3), 2.20 (d, *J* = 11.2 Hz, 1H, 18-H), 2.04–1.74 (m, 4H, 11-H+2-H), 1.65–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.39–1.22 (m, 5H, 6b-H+21-H+7-H), 1.11–1.01 (m, 2H, 15-H), 1.06 (s, 3H, 27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, *J* = 5.6 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.73 (s, 3H, 24-CH_3), 0.69 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.8, 138.6, 138.2, 129.4, 128.7, 127.7, 125.8, 66.5, 66.0, 62.8, 59.6, 55.5, 53.2, 48.5, 47.8, 42.5, 42.4, 39.8, 39.4, 39.1, 39.0, 39.8, 37.3, 37.0, 33.3, 30.9, 28.5, 28.3, 27.5, 24.5, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 16.0, 15.8; HRMS (ESI): m/z calcd for $C_{41}H_{64}O_4N^+$: 634.4830; found: 634.4824.

3-(1-Ethyl-Benzylamine-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (A22)

White solid, yield 72.7 %, m. p. 76.9-78.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.33–7.16 (m, 5H, Phenyl-H), 5.18 (dd, *J* = 8.2, 3.8 Hz, 1H, 12-CH=C), 4.07–3.80 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.73–3.46 (m, 2H, 6′-NCH_2), 3.17 (dd, *J* = 10.8, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 2.67–2.40 (m, 4H, 3′-N$\underline{CH_2}$CH+4′-N$\underline{CH_2}CH_3$), 2.17 (d, *J* = 13.4 Hz, 1H, 18-H), 1.99–1.77 (m, 4H, 11-H+2-H), 1.63–1.45 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.33–1.21 (m, 5H, 6b-H+21-H+7-H), 1.07–1.00 (m, 2H, 15-H), 1.03 (s, 3H, 27-CH_3), 1.02 (t, *J* = 7.1 Hz, 3H, 5′-$NCH_2\underline{CH_3}$), 0.94 (s, 3H, 23-CH_3), 0.90 (d, *J* = 5.9 Hz, 3H, 30-CH_3), 0.86 (s, 3H, 25-CH_3), 0.81 (d, *J* = 6.1 Hz, 3H, 29-CH_3), 0.74

(s, 3H, 26-CH_3), 0.69 (s, 3H, 24-CH_3), 0.66 (s, 1H, 5-H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 138.9, 138.6, 129.2, 128.7, 127.5, 125.9, 79.3, 66.6, 66.0, 58.5, 56.0, 55.5, 53.2, 48.5, 47.8, 42.4, 39.8, 39.4, 39.1, 39.0 , 38.9, 37.2, 36.9, 33.3, 30.9, 28.5, 28.3, 27.5, 24.5, 23.9, 23.6, 21.5, 18.6, 17.4, 17.3, 15.9, 15.7, 12.1; HRMS (ESI): m/z calcd for $C_{42}H_{66}O_4N^+$: 648.4986; found: 648.4982.

3-(4-((4-methyl piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B1)

Yellow solid, yield 44.3%, m. p. 89.2-90.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 0.8 Hz, 1H, triazole-H), 5.25 (q, J = 3.3 Hz, 1H, 12-CH=C), 4.55–4.49 (m, 1H, 1′a-OCH_2CH), 4.33–4.25 (m, 1H, 2′-CHOH), 4.25–4.19 (m, 1H, 1′b-OCH_2CH), 4.12–4.05 (m, 1H, 3′a-NCH_2CH), 4.02–3.92 (m, 1H, 3′b-NCH_2CH), 3.69 (s, 2H, 5′-NCH_2C), 3.18 (dd, J = 10.9, 4.9 Hz, 1H, 3-CHOH), 2.72–2.34 (m, 8H, 6′-NCH_2+7′-NCH_2), 2.29 (s, 3H, 8′-NCH_3), 2.20 (d, J = 11.3 Hz, 1H, 18-H), 2.06–1.72 (m, 4H, 11-H+2-H), 1.69–1.44 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19 -H), 1.39–1.24 (m, 5H, 6b-H+21-H+7-H), 1.12–0.99 (m, 5H, 15-H+27-CH_3), 0.96 (s, 3H, 23-CH_3), 0.93 (d, J = 6.3 Hz, 3H, 30-CH_3), 0.89 (d, J = 1.6 Hz, 3H, 25-CH_3), 0.84 (d, J = 6.5 Hz, 3H, 29-CH_3), 0.75 (s, 3H, 26-CH_3), 0.71 (d, J = 3.6 Hz, 3H, 24-CH_3), 0.68 (s, 1H, 5-H).^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5, 143.4, 138.5, 125.6, 125.5, 124.4, 78.9, 68.5, 65.4, 55.1, 54.6, 53.4, 53.1, 52.9, 52.8, 52.1, 48.4, 47.4, 45.6, 42.1, 39.5, 39.0, 38.8, 38.7, 38.5, 36.9, 36.8, 32.9, 30.5, 28.1, 27.9, 27.1, 24.2, 23.5, 23.2, 21.1, 18.2, 17.1, 16.9, 15.6, 15.4; HRMS (ESI): m/z calcd for $C_{41}H_{68}O_4N_5^+$: 694.5266; found: 694.5275.

3-(4-((4-ethyl piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B2)

Yellow solid, yield 43.0%, m. p. 80.3-81.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 0.9 Hz, 1H, triazole-H), 5.28–5.24 (m, 1H, 12-CH=C), 4.59–4.51 (m, 1H, 1′a-OCH_2CH), 4.35–4.28 (m, 1H, 2′-CHOH), 4.28–4.22 (m, 1H, 1′b-OCH_2CH), 4.14–4.06 (m, 1H, 3′a-NCH_2CH), 4.02–3.98 (m, 1H, 3′b-NCH_2CH), 3.85–3.76 (m, 2H, 5′-NCH_2C), 3.20 (dd, J = 11.1, 4.8 Hz, 1H, 3-CHOH), 2.82–2.72 (m, 10H, 6′-NCH_2+7′-NCH_2+8′-NCH_2CH_3), 2.22 (d, J = 11.2 Hz, 1H, 18-H), 2.07–1.74 (m, 4H,

11-H+2-H), 1.68–1.45 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.37–1.28 (m, 5H, 6b-H+21-H+7-H), 1.09 (d, *J* = 15.0 Hz, 5H, 15-H+27-CH_3), 0.99 (d, *J* = 14.9 Hz, 6H, 23-CH_3+9′-$NCH_2\underline{CH_3}$), 0.94 (d, *J* = 6.3 Hz, 3H, 30-CH_3), 0.90 (d, *J* = 2.7 Hz, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.72 (d, *J* = 4.0 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.5, 138.5, 125.7, 125.1, 79.0, 68.3, 68.2, 65.4, 55.2, 53.5, 52.9, 52.2, 51.4, 48.8, 48.4, 47.5, 42.1, 39.51, 39.1, 38.8, 38.8, 38.6, 37.0, 36.8, 33.0, 30.6, 29.7, 28.2, 28.0, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.2, 17.0, 15.7, 15.5, 9.7; HRMS (ESI): m/z calcd for $C_{42}H_{70}O_4N_5^+$: 708.5422; found: 708.5419.

3-(4-((4-acetyl piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B3)

Yellow solid, yield 64.0%, m. p. 90.8-92.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.63 (d, *J* = 0.8 Hz, 1H, triazole-H), 5.24 (q, *J* = 3.5 Hz, 1H, 12-CH=C), 4.55–4.49 (m, 1H, 1′a-O$\underline{CH_2}$CH), 4.36–4.27 (m, 1H, 2′-$\underline{CH}$OH), 4.27–4.20 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.13–4.04 (m, 1H, 3′a-N$\underline{CH_2}$CH), 3.99–3.96 (m, 1H, 3′b-N$\underline{CH_2}$CH), 3.67 (s, 2H, 5′-N$\underline{CH_2}$C), 3.60–3.55 (m, 2H, 7′a-NCH_2), 3.45–3.42 (m, 2H, 7′b-NCH_2), 3.18 (dd, *J* = 11.0, 4.7 Hz, 1H, 3-$\underline{CH}$OH), 2.53–2.48 (m, 2H, 6′a-N$\underline{CH_2}$), 2.44 (t, *J* = 5.0 Hz, 2H, 6′b-N$\underline{CH_2}$), 2.19 (d, *J* = 11.2 Hz, 1H, 18-H), 2.04 (s, 3H, 9′-NCO$\underline{CH_3}$), 2.02–1.71 (m, 4H, 11-H+2-H), 1.69–1.44 (m, 11H, 16-H+9-H+22-H+20-H+6-H+1-H+19-H), 1.38–1.26 (m, 4H, 21-H+7-H), 1.13–1.00 (m, 5H, 15-H+27-CH_3), 0.96 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.88 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.75 (s, 3H, 26-CH_3), 0.71 (d, *J* = 4.5 Hz, 3H, 24-CH_3), 0.68 (s, 1H, 5-H). ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 177.7, 169.1, 143.6, 138.7, 125.7, 124.4, 80.0, 68.6, 65.5, 55.2, 53.0, 52.9, 52.4, 48.5, 47.5, 46.2, 42.2, 41.3, 39.6, 39.1, 38.9, 38.8, 38.7, 37.0, 36.9, 33.1, 30.6, 28.2, 28.0, 27.2, 24.3, 23.6, 23.4, 21.4, 21.2, 18.4, 17.3, 17.1, 15.8, 15.5; HRMS (ESI): m/z calcd for $C_{42}H_{68}O_5N_5^+$: 722.5215; found: 722.5220.

3-(4-((4-formyl piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B4)

Yellow solid, yield 46.6%, m. p. 87.6-89.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.97 (s, 1H, 8′-NCO$\underline{H}$), 7.63 (d, *J* = 1.6 Hz, 1H, triazole-H), 5.24 (dd, *J* = 7.1, 3.6 Hz, 1H,

12-CH=C), 4.56–4.48 (m, 1H, 1′a-O$\underline{CH_2}$CH), 4.36–4.28 (m, 1H, 2′-$\underline{CH}$OH), 4.28–4.20 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.15–4.04 (m, 1H, 3′a-N$\underline{CH_2}$CH), 4.01–3.95 (m, 1H, 3′b-N$\underline{CH_2}$CH), 3.69 (s, 2H, 5′-N$\underline{CH_2}$C), 3.55–3.50 (m, 2H, 7′a-NCH$_2$), 3.38–3.34 (m, 2H, 7′b-NCH$_2$), 3.19 (dd, *J* = 11.1, 4.5 Hz, 1H, 3-$\underline{CH}$OH), 2.54–2.50 (m, 2H, 6′a-NCH$_2$), 2.45 (t, *J* = 5.1 Hz, 2H, 6′b-NCH$_2$), 2.20 (d, *J* = 11.1 Hz, 1H, 18-H), 2.08–1.81 (m, 4H, 11-H+2-H), 1.71–1.48 (m, 11H, 16-H+9-H+22-H+20-H+6-H+1-H+19-H), 1.36–1.27 (m, 4H, 21-H+7-H), 1.14–1.01 (m, 5H, 15-H+27-CH$_3$), 0.96 (s, 3H, 23-CH$_3$), 0.93 (d, *J* = 6.2 Hz, 3H, 30-CH$_3$), 0.89 (s, 3H, 25-CH$_3$), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH$_3$), 0.76 (s, 3H, 26-CH$_3$), 0.71 (d, *J* = 5.3 Hz, 3H, 24-CH$_3$), 0.69 (s, 1H, 5-H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 177.7, 160.9, 143.7, 138.8, 125.6, 124.4, 79.0, 68.7, 65.6, 55.2, 53.5, 53.2, 53.1, 52.1, 48.6, 47.5, 45.6, 42.2, 39.9, 39.6, 39.1, 38.9, 38.8, 38.7, 37.0, 36.9, 33.0, 30.6, 28.2, 28.0, 27.2, 24.3, 23.7, 23.4, 21.2, 18.4, 17.3, 17.3, 17.1, 15.8, 15.6; HRMS (ESI): m/z calcd for $C_{41}H_{66}O_5N_5^+$: 708.5058; found: 708.5043.

3-(4-((4-phenyl piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B5)

Yellow solid, yield 51.4%, m. p. 96.2-97.6 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (d, *J* = 1.2 Hz, 1H, triazole-H), 7.24 (dd, *J* = 8.7, 7.3 Hz, 2H, phenyl-H), 6.90 (d, *J* = 7.8 Hz, 2H, phenyl-H), 6.84 (t, *J* = 7.2 Hz, 1H, phenyl-H), 5.25 (dd, *J* = 6.3, 3.1 Hz, 1H, 12-CH=C), 4.56–4.50 (m, 1H, 1′a-O$\underline{CH_2}$CH), 4.37–4.28 (m, 1H, 2′-$\underline{CH}$OH), 4.28–4.24 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.14–4.6 (m, 1H, 3′a-N$\underline{CH_2}$CH), 4.01–3.97 (m, 1H, 3′b-N$\underline{CH_2}$CH), 3.72 (s, 2H, 5′-N$\underline{CH_2}$C), 3.22–3.15 (m, 5H, 3-$\underline{CH}$OH+7′-N$\underline{CH_2}$), 2.67 (d, *J* = 4.3 Hz, 4H, 6′-NCH$_2$), 2.21 (d, *J* = 11.1 Hz, 1H, 18-H), 2.06–1.73 (m, 4H, 11-H+2-H), 1.70–1.45 (m, 11H, 16-H+9-H+22-H+20-H+6-H+1-H+19-H), 1.37–1.26 (m, 4H, 21-H+7-H), 1.14–0.99 (m, 5H, 15-H+27-CH$_3$), 0.97 (s, 3H, 23-CH$_3$), 0.94 (d, *J* = 6.2 Hz, 3H, 30-CH$_3$), 0.89 (s, 3H, 25-CH$_3$), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH$_3$), 0.75 (s, 3H, 26-CH$_3$), 0.72 (d, *J* = 5.1 Hz, 3H, 24-CH$_3$), 0.68 (s, 1H, 5-H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 177.8, 177.7, 151.2, 138.7, 129.2, 125.3, 124.4, 119.9, 116.2, 79.0, 68.8, 65.5, 55.2, 53.2, 53.0, 52.9, 49.1, 48.5, 47.5, 42.2, 39.5, 39.1, 38.9, 38.8, 38.6, 37.0, 36.8, 33.0, 30.6, 28.1, 27.9, 27.2, 24.3, 23.6, 23.6, 23.3, 21.2, 18.3, 17.2, 17.0,

15.7, 15.5; HRMS (ESI): m/z calcd for $C_{46}H_{70}O_4N_5^+$: 756.5422; found: 756.5427.

3-(4-((4-(4-fluorophenyl)piperazin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxy propyl-3*β*-hydroxy-urs-12-en-28-oate (B6)

Yellow solid, yield 44.2%, m. p. 111.2-112.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 1.6 Hz, 1H, triazole-H), 6.93 (dd, J = 11.7, 5.8 Hz, 2H, phenyl-H), 6.84 (dd, J = 9.2, 4.6 Hz, 2H, phenyl-H), 5.25 (d, J = 2.7 Hz, 1H, 1H, 12-CH=C), 4.56–4.50 (m, 1H, 1′a-O$\underline{CH_2}$CH), 4.39–4.31 (m, 1H, 2′-$\underline{CH}$OH), 4.30–4.22 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.14–4.06 (m, 1H, 3′a-N$\underline{CH_2}$CH), 4.01–3.97 (m, 1H, 3′b-N$\underline{CH_2}$CH), 3.73 (s, 2H, 5′-N$\underline{CH_2}$C), 3.19 (dd, J = 11.0, 4.6 Hz, 1H, 3-$\underline{CH}$OH), 3.14–3.07 (m, 4H, 7′-N$\underline{CH_2}$), 2.72–2.64 (m, 4H, 6′-NCH_2), 2.21 (d, J = 11.1 Hz, 1H, 18-H), 2.06–1.75 (m, 4H, 11-H+2-H), 1.71–1.45 (m, 11H, 16-H+9-H+22-H+20-H+6-H+1-H+19-H), 1.39–1.26 (m, 4H, 21-H+7-H), 1.14–1.01 (m, 5H, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.94 (d, J = 6.1 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.85 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.72 (d, J = 4.6 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 157.2 (d, $^1J_{C\text{-}F}$ = 238.9 Hz),147.8, 143.8 (d, $^4J_{C\text{-}F}$ = 1.6 Hz), 138.6, 125.6, 124.4, 117.9 (d, $^3J_{C\text{-}F}$ = 7.5 Hz),, 115.6 (d, $^2J_{C\text{-}F}$ = 22.1 Hz), 79.0, 68.8, 68.6, 65.5, 55.1, 53.1, 53.0, 52.9, 50.0, 48.5, 47.5, 42.2, 39.5, 39.1, 38.9, 38.7, 38.6, 36.9, 36.8, 33.0, 30.6, 28.1, 27.9, 27.2, 24.3, 23.6, 23.6, 23.3, 21.2, 18.3, 17.2, 17.2, 17.0, 15.7, 15.5.^{19}F NMR (376 MHz, $CDCl_3$) δ -124.30; HRMS (ESI): m/z calcd for $C_{46}H_{69}O_4N_5F^+$: 774.5328; found: 774.5334.

3-(4-(piperidin-1-ylmethyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B7)

Yellow solid, yield 48.8%, m. p. 89.7-91.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H, triazole-H), 5.26 (d, J = 3.7 Hz, 1H, 12-CH=C), 4.60–4.52 (m, 1H, 1′a-O$\underline{CH_2}$CH), 4.39–4.29 (m, 1H, 2′-$\underline{CH}$OH), 4.28–4.21 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.13–4.07 (m, 1H, 3′a-N$\underline{CH_2}$CH), 4.04–3.95 (m, 1H, 3′b-N$\underline{CH_2}$CH), 3.89 (s, 2H, 5′-N$\underline{CH_2}$C), 3.20 (dd, J = 10.9, 4.6 Hz, 1H, 3-$\underline{CH}$OH), 2.75 (s, 4H, 6′-NCH_2), 2.21 (d, J = 11.1 Hz, 1H, 18-H), 2.05–1.87 (m, 4H, 11-H+2-H), 1.75–1.41 (m, 17H, 16-H+9-H+22-H+20-H+6-H+1-H +19-H+7′-N$CH_2\underline{CH_2}CH_2$+8′-N$CH_2CH_2\underline{CH_2}$), 1.39–1.27 (m, 4H, 21-H+7-H), 1.14–0.99 (m, 5H, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, J = 6.2 Hz, 3H, 30-CH_3),

0.89 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.72 (d, *J* = 2.1 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.5, 138.5, 126.4, 125.7, 79.0, 68.4, 68.3, 65.4, 55.2, 53.8, 53.3, 52.9, 52.9, 48.4, 48.4, 47.5, 42.1, 39.5, 39.07, 38.8, 38.8, 38.6, 37.0, 36.7, 33.0, 30.6, 28.2, 27.9, 27.2, 24.3, 23.6, 23.3, 23.1, 21.2, 18.3, 17.2, 17.0, 15.7, 15.5; HRMS (ESI): m/z calcd for $C_{41}H_{67}O_4N_4^+$: 679.5154; found: 679.5134.

3-(4-((2-methyl piperidin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B8)

Yellow solid, yield 68.9%, m. p. 120.1-121.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.64 (s, 1H, triazole-H), 5.25 (d, *J* = 3.0 Hz, 1H, 12-CH=C), 4.58–4.47 (m, 1H, 1′a-O$\underline{CH_2}$CH), 4.38–4.30 (m, 1H, 2′-$\underline{CH}$OH), 4.30–4.21 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.16–4.04 (m, 1H, 3′a-N$\underline{CH_2}$CH), 3.99 (d, *J* = 11.7 Hz, 1H, 3′b-N$\underline{CH_2}$CH), 3.94 (s, 1H, 5′a-N$\underline{CH_2}$C), 3.74 (d, *J* = 13.9 Hz, 1H, 5′b-N$\underline{CH_2}$C), 3.19 (dd, *J* = 11.0, 4.7 Hz, 1H, 1H, 3-$\underline{CH}$OH), 2.83 (s, 1H, 6′-N$\underline{CH}CH_3$), 2.27 (d, *J* = 50.6 Hz, 2H, 6′-N$\underline{CH_2}CH_2$CH), 2.20 (s, 1H, 18-H), 2.06–1.76 (m, 4H, 11-H+2-H), 1.70–1.47 (m, 16H,16-H+9-H+22-H+20-H+6a-H+1-H+19-H+7′a-N$\underline{CH_2}CH_2CH_2$+7′b-NCH$\underline{CH_2}CH_2$H+8′-NCH$_2$CH$_2$$\underline{CH_2}$), 1.38–1.28 (m, 5H, 6b-H+21-H+7-H), 1.14–1.04 (m, 5H, 15-H+27-CH_3), 0.97 (s, 6H, 23-CH_3+6′-NCH$\underline{CH_3}$), 0.94 (d, *J* = 6.2 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.72 (d, *J* = 3.8 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H). ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 177.6, 138.7, 138.6, 125.7, 125.6, 79.0, 68.6, 65.5, 56.2, 55.3, 53.2, 52.7, 48.9, 48.5, 47.6, 42.2, 39.6, 39.1, 38.9, 38.8, 38.7, 37.0, 36.9, 34.3, 33.0, 30.6, 29.8, 28.2, 28.0, 27.3, 25.8, 24.3, 23.8, 23.6, 23.4, 21.2, 19.4, 18.4, 17.3, 17.1, 15.7, 15.6; HRMS (ESI): m/z calcd for $C_{42}H_{69}O_4N_4^+$: 693.5313; found: 693.5320.

3-(4-((3-methyl piperidin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B9)

Yellow solid, yield 51.9%, m. p. 98.7-100.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.01 (s, 1H, triazole-H), 5.26 (d, *J* = 3.6 Hz, 1H, 12-CH=C), 4.56 (t, *J* = 13.0 Hz, 1H, 1′a-O$\underline{CH_2}$CH), 4.31 (d, *J* = 16.0 Hz, 1H, 2′-$\underline{CH}$OH), 4.28–4.20 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.09 (dd, *J* = 16.3, 8.5 Hz, 1H, 3′a-N$\underline{CH_2}$CH), 4.04–3.95 (m, 1H, 3′b-N$\underline{CH_2}$CH), 3.87

(s, 2H, 5′-N$\underline{CH_2}$C), 3.20 (dd, *J* = 10.9, 4.5 Hz, 1H, 3-$\underline{CH}$OH), 3.09 (d, *J* = 28.9 Hz, 2H, 6′-N$\underline{CH_2}CH_2CH_2$), 2.21 (d, *J* = 11.0 Hz, 1H, 18-H), 2.08–1.74 (m, 8H, 11-H+2-H+6′-N$\underline{CH_2}CH_2CH$+8′$CH_2CH_2\underline{CH_2}$), 1.72–1.42 (m, 13H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+7′-N$CH_2\underline{CH}CH_3$+7′-N$CH_2\underline{CH_2}CH_2$), 1.40–1.25 (m, 5H, 6b-H+21-H+7-H), 1.15–1.02 (m, 5H, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.1 Hz, 3H, 4′-N$CH_2CH\underline{CH_3}$), 0.89 (s, 3H, 30-CH_3), 0.87 (d, *J* = 5.6 Hz, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.72 (d, *J* = 2.0 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 177.5, 138.5, 125.7, 125.6, 79.0, 68.4, 68.4, 65.4, 55.2, 53.5, 53.3, 52.9, 48.4, 47.5, 42.1, 39.5, 39.1, 38.8, 38.8, 38.6, 37.0, 36.8, 33.0, 31.9, 30.6, 29.7, 28.2, 28.0, 27.9, 27.2, 24.2, 23.6, 23.6, 23.3, 21.2, 19.4, 18.3, 17.2, 17.2, 17.0, 15.7, 15.5; HRMS (ESI): m/z calcd for $C_{42}H_{69}O_4N_4^+$: 693.5313; found: 693.5294.

3-(4-((4-methyl piperidin-1-yl)methyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (B10)

Yellow solid, yield 44.4%, m. p. 110.9-112.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.73 (s, 1H, triazole-H), 5.25 (d, *J* = 3.4 Hz, 1H, 12-CH=C), 4.56–4.50 (m, 1′a-O$\underline{CH_2}$CH), 4.35–4.28 (m, 1H, 2′-$\underline{CH}$OH), 4.27–4.23 (m, 1H, 1′b-O$\underline{CH_2}$CH), 4.11–4.07 (m, 3′a-N$\underline{CH_2}$CH), 4.02–3.96 (m, 3′b-N$\underline{CH_2}$CH), 3.68 (s, 2H, 5′-N$\underline{CH_2}$C), 3.19 (dd, *J* = 11.0, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 2.95 (d, *J* = 10.5 Hz, 2H, 6′a-N$\underline{CH_2}CH_2CH$), 2.21 (d, *J* = 11.2 Hz, 1H, 18-H), 2.11 (s, 6′b-N$\underline{CH_2}CH_2CH$), 2.06–1.73 (m, 4H, 11-H+2-H), 1.70–1.45 (m, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H+7′-N$CH_2\underline{CH_2}CH$), 1.39–1.27 (m, 6H, 6b-H+21-H+7-H+8′-N$CH_2CH_2\underline{CH}$), 1.13–1.01 (m, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.94 (d, *J* = 6.2 Hz, 3H, 9′-N$CH_2CH_2CH\underline{CH_3}$), 0.90 (d, *J* = 6.4 Hz, 3H, 30-CH_3), 0.89 (d, *J* = 1.0 Hz, 3H, 25-CH_3), 0.85 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.72 (d, *J* = 3.2 Hz, 3H, 24-CH_3), 0.69 (s, 1H, 5-H). ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 177.6, 143.6, 138.7, 125.7, 124.9, 79.0, 68.6, 65.5, 55.3, 53.8, 53.5, 53.2, 53.0, 48.5, 47.6, 42.2, 39.6, 39.1, 38.9, 38.8, 38.7, 37.0, 36.9, 33.7, 33.1, 30.7, 30.4, 28.2, 28.0, 27.3, 24.3, 23.6, 23.4, 21.8, 21.2, 18.4, 17.3, 17.1, 15.7, 15.6; HRMS (ESI): m/z calcd for $C_{42}H_{69}O_4N_4^+$: 693.5313; found: 693.5317.

3-(4-tosyl piperazin-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (C1)

Yellow solid, yield 79.7%, m. p. 116.9-118.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.1 Hz, 2H, phenyl-H), 7.32 (d, J = 8.1 Hz, 2H, phenyl-H), 5.20 (d, J = 4.1 Hz, 1H, 12-CH=C), 4.04–3.83 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.19 (dd, J = 10.7, 4.3 Hz, 1H, 3-$\underline{CH}$OH), 2.97 (d, J = 27.4 Hz, 4H, 5′-NCH_2), 2.66 (s, 2H, 4′a-NCH_2), 2.54–2.47 (m, 2H, 4′b-NCH_2), 2.43 (s, 3H, phenyl-CH_3), 2.40–2.33 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.18 (d, J = 11.3 Hz, 1H, 18-H), 2.02–1.74 (m, 4H, 11-H+2-H), 1.69–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.43–1.25 (m, 5H, 6b-H+21-H+7-H), 1.12–1.01 (m, 5H, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.92 (d, J = 5.7 Hz, 3H, 30-CH_3), 0.88 (s, 3H, 25-CH_3), 0.83 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.69 (s, 4H, 24-CH_3+5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 143.9, 138.6, 138.4, 132.1, 129.8, 127.9, 125.5, 125.4, 79.0, 66.3, 65.4, 60.3, 60.0, 55.2, 53.5, 52.9, 52.4, 48.3, 47.5, 46.1, 42.1, 39.5, 39.1, 38.8, 38.6, 36.9, 36.7, 33.0, 30.6, 28.2, 27.9, 27.2, 24.2, 23.6, 23.3, 21.6, 21.2, 18.3, 17.1, 17.0, 15.7, 15.5. HRMS (ESI): m/z calcd for $C_{44}H_{69}O_6N_2S^+$: 753.4871; found: 753.4866.

3-(4-((2-fluorophenyl)sulfonyl)piperazin-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (C2)

Yellow solid, yield 85.1%, m. p. 118.2-120.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.79 (m, 1H, phenyl-H), 7.62–7.55 (m, 1H, phenyl-H), 7.29 (dd, J = 7.7, 0.9 Hz, 1H, phenyl-H), 7.25–7.18 (m, 1H, phenyl-H), 5.21 (dd, J = 8.3, 3.7 Hz, 1H, 12-CH=C), 4.08–3.82 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.26–3.15 (m, 5H, 3-$\underline{CH}$OH+5′-NCH_2), 2.68 (dd, J = 9.2, 4.4 Hz, 2H, 4′a-NCH_2), 2.55–2.47 (m, 2H, 4′b-NCH_2), 2.46–2.35 (m, 2H, 3′-NCH), 2.19 (d, J = 11.3 Hz, 1H, 18-H), 2.03–1.73 (m, 4H, 11-H+2-H), 1.71–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.37–1.29 (m, 5H, 6b-H+21-H+7-H), 1.13–1.00 (m, 5H, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.92 (d, J = 6.0 Hz, 3H, 30-CH_3), 0.88 (s, 3H, 25-CH_3), 0.83 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.76 (s, 3H, 26-CH_3), 0.70 (d, J = 1.5 Hz, 3H, 24-CH_3), 0.68 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 159.0 (d, $^{1}J_{C\text{-}F}$ = 256.1 Hz), 138.5 (d, $^{3}J_{C\text{-}F}$ = 18.7 Hz), 135.2 (d, $^{5}J_{C\text{-}F}$ = 8.3 Hz), 131.3, 125.4, 124.8 (d, $^{4}J_{C\text{-}F}$ = 14.6 Hz), 124.5 (d, $^{6}J_{C\text{-}F}$ = 3.9 Hz), 117.4 (d, $^{2}J_{C\text{-}F}$ = 22.0 Hz)., 79.0, 66.3, 65.5, 60.1, 55.2, 53.5, 52.9, 52.7, 48.3, 47.5, 45.8, 42.1, 39.5, 39.1, 38.7, 38.6, 37.0, 36.7, 33.0, 30.6, 28.2,

27.9, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.1, 17.0, 15.7, 15.5. ^{19}F NMR (377 MHz, $CDCl_3$) δ -107.13. HRMS (ESI): m/z calcd for $C_{43}H_{66}O_6N_2FS^+$: 757.4620; found: 757.4612.

3-(4-((3-chlorophenyl)sulfonyl)piperazin-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (C3)

Yellow solid, yield 78.5%, m. p. 112.1-113.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H, phenyl-H), 7.61 (dd, *J* = 16.6, 7.9 Hz, 2H, phenyl-H), 7.49 (t, *J* = 7.9 Hz, 1H, phenyl-H), 5.21 (s, 1H, 12-CH=C), 4.09–3.81 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.20 (d, *J* = 6.6 Hz, 1H, 3-$\underline{CH}$OH), 3.06 (s, 4H, 5′-NCH_2), 2.69 (d, *J* = 4.6 Hz, 2H, 4′a-NCH_2), 2.51 (dd, *J* = 15.0, 9.8 Hz, 2H, 4′b-NCH_2), 2.46–2.33 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.19 (d, *J* = 11.1 Hz, 1H, 18-H), 2.04–1.77 (m, 4H, 11-H+2-H), 1.74–1.51 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.34 (dd, *J* = 19.6, 12.1 Hz, 5H, 6b-H+21-H+7-H), 1.09 (d, *J* = 21.2 Hz, 5H, 15-H+27-CH_3), 0.97 (s, 3H, 23-CH_3), 0.93 (d, *J* = 5.4 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.3 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.71 (s, 4H, 24-CH_3+5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 138.7, 137.1, 135.5, 133.2, 130.5, 127.8, 125.9, 125.5, 79.0, 66.2, 65.5, 60.0, 55.2, 52.9, 52.4, 48.4, 47.5, 46.0, 42.1, 39.5, 39.1, 38.8, 38.8, 38.6, 37.0, 36.8, 33.0, 30.6, 28.2, 28.0, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.1, 17.0, 15.7, 15.5; HRMS (ESI): m/z calcd for $C_{43}H_{66}O_6N_2ClS^+$: 773.4325; found: 773.4307.

3-(4-((4-bromophenyl)sulfonyl)piperazin-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (C4)

Yellow solid, yield 54.9%, m. p. 106.4-107.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.6 Hz, 2H, phenyl-H), 7.61 (d, *J* = 8.4 Hz, 2H, phenyl-H), 5.21 (d, *J* = 4.4 Hz, 1H, 12-CH=C), 4.08–3.84 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.23–3.17 (m, 1H, 3-$\underline{CH}$OH), 3.04 (s, 4H, 5′-NCH_2), 2.68 (d, *J* = 2.8 Hz, 2H, 4′a-NCH_2), 2.56–2.49 (m, 2H, 4′b-NCH_2), 2.46–2.34 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.19 (d, *J* = 11.3 Hz, 1H, 18-H), 1.98–1.71 (m, 4H, 11-H+2-H), 1.66–1.48 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.37–1.28 (m, 12.1, 6.0 Hz, 5H, 6b-H+21-H+7-H), 1.10–1.00 (m, 5H, 15-H+27-CH_3), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 6.1 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.71 (s, 3H,

24-CH_3), 0.65 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 138.7, 138.5, 134.4, 132.5, 129.3, 128.2, 125.5, 125.4, 79.0, 66.3, 65.6, 60.3, 55.2, 52.9, 52.4, 48.3, 47.5, 46.0, 42.1, 39.5, 39.1, 38.8, 38.6, 37.0, 36.7, 33.0, 30.6, 29.7, 28.2, 27.9, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.2, 17.0, 15.7, 15.5; HRMS (ESI): m/z calcd for $C_{43}H_{65}O_6N_2BrS^+$: 817.3819; found: 817.3805.

3-(4-((4-cyanophenyl)sulfonyl)piperazin-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (C5)

Yellow solid, yield 81.3%, m. p. 125.9-127.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 4H, phenyl-H), 5.24–5.18 (m, 1H, 12-CH=C), 4.09–3.83 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-$\underline{CH}$OH), 3.21 (d, *J* = 7.4 Hz, 1H, 3-$\underline{CH}$OH), 3.08 (s, 4H, 5′-NCH_2), 2.70 (s, 2H, 4′a-NCH_2), 2.59–2.51 (m, 2H, 4′b-NCH_2), 2.50–2.35 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.18 (d, *J* = 11.2 Hz, 1H, 18-H), 2.06–1.75 (m, 4H, 11-H+2-H), 1.65–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.37–1.26 (m, 14.7, 8.3 Hz, 5H, 6b-H+21-H+7-H), 1.07 (s, 3H, 27-CH_3), 1.02 (s, 2H, 15-H), 0.98 (s, 3H, 23-CH_3), 0.93 (d, *J* = 5.8 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.84 (d, *J* = 6.4 Hz, 3H, 29-CH_3), 0.77 (s, 3H, 26-CH_3), 0.72 (s, 1H, 5-H), 0.70 (d, *J* = 2.1 Hz, 3H, 24-CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.6, 140.0, 138.7, 138.5, 133.1, 128.4, 125.6, 125.4, 117.3, 116.8, 79.0, 66.3, 65.7, 60.3, 60.1, 55.2, 53.6, 52.9, 52.5, 48.4, 47.5, 46.1, 42.2, 39.6, 39.1, 38.9, 38.8, 38.6, 37.0, 36.8, 33.0, 30.6, 28.2, 28.0, 27.2, 24.3, 23.6, 23.3, 21.2, 18.3, 17.2, 17.1, 15.8, 15.6; HRMS (ESI): m/z calcd for $C_{44}H_{65}O_6N_3S^+$: 764.4667; found: 764.4643.

3-(4-(N,N-dimethylsulfamoyl)piperazin-1-yl)-2-hydroxypropyl-3*β*-hydroxy-urs-12-en-28-oate (C6)

Yellow solid, yield 71.2%, m. p. 105.7-107.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.22 (dd, *J* = 8.2, 3.7 Hz, 1H, 12-CH=C), 4.10–3.86 (m, 3H, 1′-O$\underline{CH_2}$CH+2′-CHOH), 3.26 (d, J = 3.1 Hz, 3H, 5′a-NCH_2CH_2), 3.18 (dd, J = 10.8, 4.8 Hz, 1H, 3-$\underline{CH}$OH), 3.08 (s, 1H, 5′b-NCH_2CH_2), 2.81 (s, 6H, 6′-NCH_3CH_3), 2.69–2.61 (m, 2H, 4′a-NCH_2), 2.50–2.45 (m, 2H, 4′b-NCH_2), 2.43–2.36 (m, 2H, 3′-N$\underline{CH_2}$CH), 2.20 (d, *J* = 11.2 Hz, 1H, 18-H), 2.05–1.77 (m, 4H, 11-H+2-H), 1.71–1.46 (m, 10H, 16-H+9-H+22-H+20-H+6a-H+1-H+19-H), 1.45–1.25 (m, 5H, 6b-H+21-H+7-H), 1.13–0.99 (m, 5H, 15-H+27-C

H_3), 0.96 (s, 3H, 23-CH_3), 0.92 (d, J = 6.1 Hz, 3H, 30-CH_3), 0.89 (s, 3H, 25-CH_3), 0.83 (d, J = 6.4 Hz, 3H, 29-CH_3), 0.75 (s, 3H, 26-CH_3), 0.72 (d, J = 2.4 Hz, 3H, 24-CH_3), 0.68 (s, 1H, 5-H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.5, 138.6, 125.5, 78.9, 66.3, 65.5, 60.2, 55.2, 53.5, 52.9, 52.8, 48.3, 47.5, 46.3, 42.1, 39.5, 39.1, 38.8, 38.7, 38.6, 38.3, 37.0, 36.8, 36.7, 33.0, 30.6, 28.2, 27.9, 27.2, 24.2, 23.6, 23.3, 21.2, 18.3, 17.1, 17.0, 15.7, 15.5. HRMS (ESI): m/z calcd for $C_{39}H_{68}O_6N_3S^+$: 706.4823; found: 706.4813.

3.Result of cell membrane permeability (Figure S1)

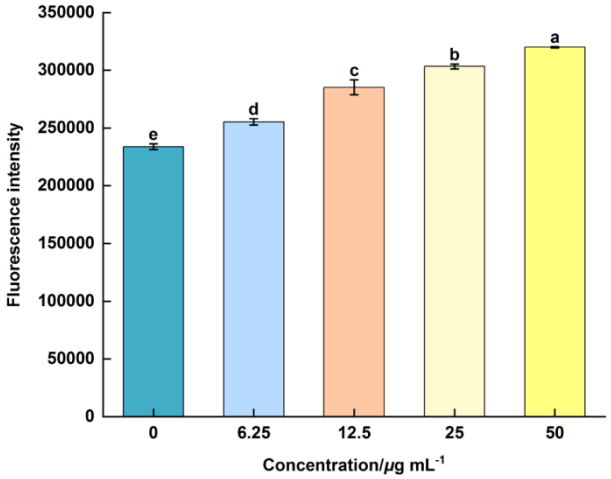

Figure S1. Cell membrane permeability of *Xoo* cells after incubation with different dosages of molecule **A17**.

4.*In vivo* antimicrobial bioassay of citrus canker (Figure S2)

In vivo assay of compound **A16** against citrus ulcer bacteria was evaluated using the previously reported methods (Liu et al. 2020). TC was used as the positive control. Two-year-old citrus was selected for this experiment. Two 3 × 3 rectangular wounds were punctured on the left and right side of the citrus leaf using a disposable sterile syringe, respectively. For the protective test, filter paper soaked in 200 μg mL^{-1} of compound **A16** solution or TC solution for 1 h was evenly applied to the wound. After 24 h, the filter paper containing the drug was discarded and a new filter paper soaked

in Xac suspension (OD_{595} = 0.01) was applied to the above wound for 24 h. For the curative assay, the relevant operations are reversed, with inoculation followed by the application of the agent. After that, so the treatment groups were incubated in a climatic chamber (95% RH) at 28 °C for 16 h of light and 25 °C for 8 h of darkness. Loss of chlorophyll content was used 14 d after inoculation to assess its protective and therapeutic activity. Chlorophyll content was determined by the spectrophotometric method (Zhao et al. 2013). Samples from different treatment groups were weighed and ground to 0.1 g and then immersed in 10 mL (85% acetone: 85% ethanol = 1:1) for 2 h in the dark. Absorbance was measured at 663nm and 645nm respectively. The control efficiencies I were calculated by the following equation:

$$\text{Control efficiency (\%)} = (C - T)/ C \times 100$$

In the equation, C and T are the mean chlorophyll loss content in the negative control and treatment groups, respectively.

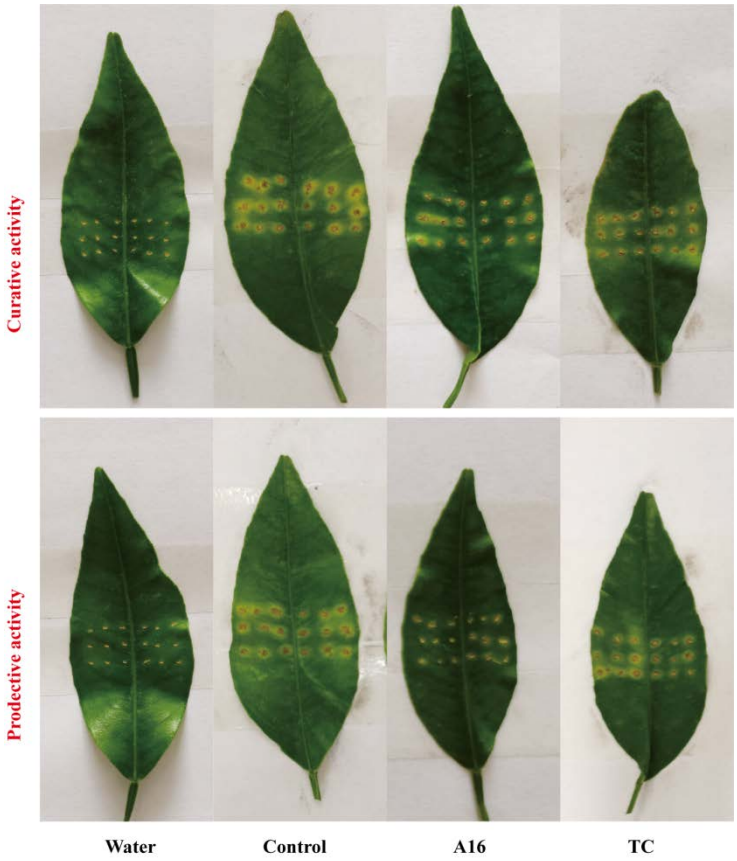

Figure S2. Control efficacies of compound **A16** and **TC** towards citrus bacterial canker at 200 μg mL^{-1}.

5.References

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