Supporting Information

Efficient Access to 2-Isobetulinic Acid, 2-Isooleanolic Acid and 2-Isoursolic Acid

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**General Experimental** All commercially available solvents and reagents were used without further purification. Melting points are uncorrected. $^1$H NMR and $^{13}$C NMR spectra were recorded at 300 and 75 MHz respectively. Chemical shifts are reported as δ values from an internal tetramethylsilane standard. Low- and high-resolution mass spectra (LRMS and HRMS) were given with electron impact mode. Infrared spectra were recorded in KBr.


![Chemical Structure](image)

To a solution of 28-O-trityl-lup-20(29)-en-28-ol-3-one (10)\(^1\) (1.14 g, 1.67 mmol) in tert-butyl alcohol (80 mL), was added potassium tert-butoxide (2.07 g, 18.4 mmol). The reaction mixture was stirred under air at 30 °C for 10 h. After the solvent was removed *in vacuo*, 1 N HCl (25 mL) was added. The mixture was extracted with ethyl acetate (3×35 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* to give crude diketone 11. Crude diketone 11 was used for the next reaction without further purification. To a solution of the above diketone 11 in tetrahydrofuran (25 mL) and ethanol (5 mL) was added sodium borohydride (176 mg, 4.65 mmol) at 0 °C. The reaction mixture was then warmed to room temperature and stirred for 1 h. The reaction was quenched with 1 N HCl (25 mL), and then the organic solvents were evaporated. The residue was extracted with ethyl acetate (3×30 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (petroleum ether-ethyl acetate, 8:1) to give diol 12 as a white solid (798 mg, 68% for two steps). Mp 199-201 °C; IR (KBr) 3592, 3440, 3062, 2948, 2871, 1709, 1643, 1483, 1364, 1374, 1314, 1218, 1061, 992, 888, 638 cm\(^{-1}\); $^1$H NMR (CDCl\(_3\)) δ 0.53 (s, 3 H), 0.88 (s, 3 H), 0.96 (s, 6 H), 1.07 (s, 3 H), 1.63 (s, 3 H), 2.04–2.23 (m, 6 H), 2.90
and 3.13 (d, $J = 8.8$ Hz, each 1 H), 3.15 (d, $J = 3.4$ Hz, 1 H), 4.02–4.03 (m, 1 H), 4.51 and 4.58 (d, $J = 2.0$ Hz, each 1 H), 7.46–7.50 (m, 6 H), 7.26–7.32 (m, 6 H), 7.21–7.24 (m, 3 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.7, 15.9, 17.0, 17.1, 18.1, 19.1, 20.9, 25.2, 26.8, 29.7, 29.9, 30.2, 34.1, 35.2, 36.8, 37.2, 38.1, 40.7, 42.6, 44.4, 47.6, 47.7, 48.9, 50.8, 55.2, 59.6, 71.2, 78.4, 85.9, 109.3, 126.8, 127.7, 128.8, 144.5, 150.8; ESI-MS m/z: 723.5 [M+Na]$^+$; Anal. Calcd for C$_{49}$H$_{64}$O$_3$: C 83.95, H 9.20, Found: C 83.50, H 9.10.

**28-O-trityl-lup-20(29)-en-28-ol-2-one (13).**

![Structure of 28-O-trityl-lup-20(29)-en-28-ol-2-one (13)](image)

To a solution of diol 12 (500 mg, 0.713 mmol) in pyridine (3 mL) was added portionwise p-toluenesulfonyl chloride (190 mg, 1 mmol). The reaction mixture was stirred at 30 °C for 12 h. After the diol 12 was consumed completely (monitored by TLC), the reaction temperature was raised to 60 °C, and the reaction was kept at this temperature for another 12 h. After cooling to room temperature, 1 N HCl (25 mL) was added into the reaction mixture. The mixture was extracted with ethyl acetate (3×30 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether-ethyl acetate, 80:1) to give 13 as a white solid (308 mg, 63%), together with 10 (171 mg, 35%) as a minor product. For 13: Mp 228-230 °C; IR (KBr) 3397, 3062, 2950, 1707, 1644, 1600, 1484, 1452, 1379, 1268, 1215, 1157, 1062, 994, 890, 761, 701, 638, 552, 477 cm$^{-1}$; $^1$H NMR (CDCl$_3$) $\delta$ 0.50 (s, 3 H), 0.76 (s, 3 H), 0.85 (s, 3 H), 0.93 (s, 3 H), 1.03 (s, 3 H), 1.63 (s, 3 H), 1.82–1.87 (m, 1 H), 2.09–2.32 (m, 6 H), 2.90 and 3.11 (d, $J = 8.8$ Hz, each 1 H), 4.52 and 4.58 (d, $J = 2.0$ Hz, each 1 H), 7.46–7.49 (m, 6 H), 7.25-7.32 (m, 6 H), 7.19-7.24 (m, 3 H); $^{13}$C NMR (CDCl$_3$) $\delta$ 14.7, 15.5, 17.1, 19.0, 19.1, 20.9, 23.1, 25.0, 27.0, 29.6, 29.7, 29.9, 30.1, 33.3, 33.7, 35.2, 37.2, 39.0, 40.0, 42.6, 42.9, 47.6, 47.7, 48.8, 50.0, 55.6, 56.0, 56.5, 59.6, 85.9, 109.5, 126.8, 127.7, 128.8, 144.5, 150.6, 212.2; ESI-MS m/z:
721.4 [M+K]+; Anal. Calcd for C_{49}H_{62}O_2·0.75 H_2O: C 84.50, H 9.18, Found: C 84.52, H 9.15. For 10: \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \( \delta \) 0.54 (s, 3 H), 0.85 (s, 3 H), 0.88 (s, 3 H), 1.01 (s, 3 H), 1.03 (s, 3 H), 1.63 (s, 3 H), 2.18–2.39 (m, 3 H), 2.92 and 3.12 (d, \( J = 8.8 \) Hz, each 1 H), 4.47 and 4.55 (d, \( J = 2.1 \) Hz, each 1 H), 7.22–7.33 (m, 9 H), 7.48-7.50 (m, 6 H); ESI-MS: 721.4 [M+K]+. The spectrum data was in agreement with the data reported in reference 1.

If the reaction was terminated without raising the reaction temperature to 60 °C, tosylate 12b could be isolated as a white solid. For 12b: Mp 103-105 °C; \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}) \( \delta \) 0.45 (s, 3 H), 0.65 (s, 3 H), 0.83 (s, 3 H), 0.94 (s, 3 H), 1.01 (s, 3 H), 1.57 (s, 3 H), 2.38 (s, 3 H), 2.06–2.10 (m, 3 H), 2.82 and 3.05 (d, \( J = 8.8 \) Hz, each 1 H), 3.82 (brs, 1 H), 4.09 (d, \( J = 3.3 \) Hz, 1 H), 4.47 and 4.55 (s, each 1 H), 7.21–7.45 (m, 17 H), 7.80-7.83 (m, 2 H); \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}) \( \delta \) 14.5, 15.7, 16.6, 17.6, 17.7, 18.8, 20.5, 21.2, 24.8, 26.4, 28.8, 29.4, 29.8, 33.7, 34.7, 36.6, 36.8, 38.0, 38.6, 42.3, 42.4, 44.4, 47.2, 47.3, 48.4, 49.8, 54.9, 67.8, 85.5, 90.2, 109.8, 125.6, 127.0, 127.4, 127.7, 127.9, 128.1, 128.3, 129.9, 130.0, 130.2, 134.3, 144.1, 144.4, 150.0; ESI-MS m/z: 872.4 [M+NH\textsubscript{4}]\textsuperscript{+}; HRMS Calcd for C_{56}H_{70}O_5S+Na [M+Na]+: 877.48417, found: 877.48362.

\textbf{28-O-trityl-2β-hydroxylup-20(29)-en-28-ol (14) and 28-O-trityl-2α-hydroxylup-20(29)-en-28-ol (14a).}

To a solution of ketone 13 (1 g, 1.46 mmol) in tetrahydrofuran (15 mL) and ethanol (3 mL) was added sodium borohydride (0.08 g, 2.11 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 1 h. The reaction was quenched with 1 N HCl (25 mL), and the organic solvents were evaporated \textit{in vacuo}. The residue was extracted with ethyl acetate (3×30 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate,
filtered and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether-ethyl acetate, 25:1) to give 2β-hydroxy isomer 14 (885 mg, 89%) and 2α-hydroxy isomer 14a (100 mg, 10%). For 14: a white solid. Mp 143-146 °C; IR (KBr) 3417, 3063, 2945, 2870, 1708, 1645, 1455, 1378, 1213, 1157, 1064, 768, 703 cm⁻¹; ¹H NMR (CDCl₃) δ 0.52 (s, 3 H), 0.89 (s, 3 H), 0.90 (s, 3 H), 0.98 (s, 3 H), 1.01 (s, 3 H), 1.64 (s, 3 H), 1.82-1.87 (m, 1 H), 2.17-2.20 (m, 3 H), 2.90 and 3.14 (d, J = 8.8 Hz, each 1 H), 3.99-4.02 (m, 1 H), 4.52 and 4.58 (d, J = 2.1 Hz, each 1 H), 7.47-7.49 (m, 6 H), 7.25-7.32 (m, 6 H), 7.22-7.24 (m, 3 H); ¹³C NMR (CDCl₃) δ 14.7, 15.7, 19.1, 19.7, 21.2, 24.8, 25.3, 26.8, 29.9, 30.1, 32.5, 32.8, 33.6, 35.2, 37.4, 38.2, 40.8, 42.5, 46.3, 47.6, 47.7, 48.2, 48.9, 50.8, 52.7, 59.6, 67.5, 85.8, 109.3, 126.8, 127.7, 128.8, 144.5, 150.8; ESI-MS m/z: 723.4 [M+K]⁺; Anal. Calcd for C₄₉H₆₄O₂·0.5 H₂O: C 84.79, H 9.44, Found: C 84.71, H 9.69. For 14a: a white solid. Mp 167-171 °C; IR (KBr) 3366, 3063, 2943, 2868, 1645, 1600, 1454, 1379, 1260, 1217, 1152, 1064, 1037, 888, 803, 768, 703, 637 cm⁻¹; ¹H NMR (CDCl₃) δ 0.50 (s, 3 H), 0.79 (s, 3 H), 0.82 (s, 3 H), 0.89 (s, 3 H), 0.90 (s, 3 H), 1.63 (s, 3 H), 1.95-1.98 (m, 1 H), 2.12-2.23 (m, 3 H), 2.90 and 3.12 (d, J = 8.8 Hz, each 1 H), 3.79-3.87 (m, 1 H), 4.52 and 4.57 (d, J = 2.1 Hz, each 1 H), 7.46-7.49 (m, 6 H), 7.25-7.32 (m, 6 H), 7.19-7.24 (m, 3 H); ¹³C NMR (CDCl₃) δ 14.7, 15.7, 17.1, 18.4, 19.1, 20.7, 22.4, 25.1, 26.9, 29.9, 30.1, 33.4, 34.0, 34.9, 35.2, 37.2, 39.2, 40.8, 42.5, 47.6, 47.8, 48.9, 49.7, 50.3, 51.2, 55.8, 59.6, 65.3, 85.8, 109.4, 126.8, 127.7, 128.8, 144.5, 150.7; ESI-MS m/z: 723.4 [M+K]⁺; Anal. Calcd for C₄₉H₆₄O₂·0.5 H₂O: C 84.79, H 9.44, Found: C 84.54, H 9.44.

2β-Hydroxylup-20(29)-en-28-ol (2-Isobetulin) (5).

![2β-Hydroxylup-20(29)-en-28-ol (2-Isobetulin) (5).](image)

To a solution of 14 (50 mg, 0.073 mmol) in absolute ethanol (5 mL) was added PPTS (54.8 mg, 0.219 mmol). The reaction mixture was stirred at 70 °C for 8 h. After cooling to room temperature, the solvent
was evaporated in vacuo. Ice water (20 mL) was added to the residue, and extracted with ethyl acetate (3×30 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether-ethyl acetate, 8:1) to give 2-isobetulin (5) as a white solid (32 mg, 99%). Mp 192-195 °C; IR (KBr) 3742, 3359, 2931, 2867, 2372, 1708, 1643, 1457, 1374, 1029, 881, 703, 465 cm⁻¹; ¹H NMR (CDCl₃) δ 0.93 (s, 3 H), 0.98 (s, 6 H), 1.03 (s, 3 H), 1.06 (s, 3 H), 1.71 (s, 3 H), 1.92-1.98 (m, 3 H), 2.35-2.44 (m, 1 H), 3.34 and 3.80 (d, J = 10.8 Hz, each 1 H), 4.00-4.11 (m, 1 H), 4.60 and 4.70 (d, J = 1.8 Hz, each 1 H); ¹³C NMR (CDCl₃) δ 14.1, 14.8, 15.9, 19.2, 19.8, 21.4, 22.7, 24.8, 25.5, 27.1, 29.3, 29.4, 29.7, 29.7, 29.9, 31.9, 32.6, 32.9, 33.8, 34.0, 37.6, 38.3, 41.2, 42.9, 46.5, 47.8, 47.9, 48.4, 48.9, 51.0, 52.9, 60.6, 67.5, 109.3, 150.5; ESI-MS m/z: 465.4 [M+Na]⁺; Anal. Calcd for C₃₀H₅₀O₂·0.5 H₂O: C 79.77, H 11.38, Found: C 80.17, H 11.63.


To a solution of compound 14 (1.2 g, 1.75 mmol) in dry pyridine was added Ac₂O (1 mL), and the reaction mixture was stirred overnight at room temperature. After cooling to 0 °C, 1 N HCl (25 mL) was added into the mixture. The mixture was extracted with ethyl acetate (3×30 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was used for next reaction without further purification. The crude residue was dissolved in absolute ethanol (50 mL) and then PPTS (1.75 mg, 7 mmol) was added. The reaction mixture was stirred at 70 °C for 8 h. After cooling to room temperature, the solvent was evaporated in vacuo. Ice water (50 mL) was added to the residue, and extracted with ethyl acetate (3×50 mL). The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was
purified by column chromatography (petroleum ether-ethyl acetate, 15:1) to give 2β-O-acetyl-lup-20(29)-en-28-ol (15) as a white solid (684 mg, 80% from 14). Mp 86-88 °C; IR (KBr) 2868, 1735, 1610, 1509, 1374, 1249, 1225, 1028 cm⁻¹; ¹H NMR (CDCl₃) δ 0.92 (s, 3 H), 0.95 (s, 3 H), 0.97 (s, 3 H), 1.02 (s, 3 H), 1.04 (s, 3 H), 1.67 (s, 3 H), 2.0 (s, 3 H), 2.34–2.43 (m, 1 H), 3.33 and 3.80 (d, J = 10.5 Hz, each 1 H), 4.58 and 4.67 (brs, each 1 H), 5.03–5.06 (m, 1 H); ¹³C NMR (CDCl₃) δ 14.8, 16.0, 18.6, 18.9, 19.1, 21.3, 24.0, 25.4, 27.1, 29.3, 29.9, 32.7, 32.9, 33.9, 34.0, 37.5, 37.8, 41.2, 43.0, 43.1, 44.3, 47.9, 48.9, 51.0, 53.8, 58.4, 60.7, 70.7, 109.7, 150.4; ESI-MS m/z: 507.5 [M+Na]⁺; Anal. Calcd for C₃₂H₅₀O₄·0.2 H₂O: C 78.70, H 10.81, Found: C 79.18, H 10.41.

**2β-O-acetyl-lup-20(29)-en-28-aldehyde (16).**

To a solution of compound 15 (100 mg, 0.206 mmol) in CH₂Cl₂ was added PCC (88.81 mg, 0.412 mmol), and the reaction mixture was stirred at room temperature for 40 min. Silica gel was poured into the mixture and the solvent was evaporated under reduced pressure to dryness. The residue was directly used for purification by column chromatography on silica gel (petroleum ether-ethyl acetate, 19:1) to give 2β-O-acetyl-lup-20(29)-en-28-aldehyde (16) as a white solid (91.7 mg, 92%). Mp 143-145 °C; ¹H NMR (CDCl₃) δ 0.91 (s, 3 H), 0.92 (s, 3 H), 0.95 (s, 3 H), 0.97 (s, 3 H), 1.04 (s, 3 H), 1.69 (s, 3 H), 2.00 (s, 3 H), 2.82-2.88 (m, 1 H), 4.62, 4.75 (brs, each 1 H), 5.04-5.06 (m, 1 H), 9.68 (s, 1 H); ¹³C NMR (CDCl₃) δ 14.2, 15.8, 18.5, 18.7, 19.0, 21.1, 21.5, 23.9, 25.6, 28.7, 29.2, 29.9, 32.6, 32.8, 33.2, 33.9, 37.7, 38.8, 41.0, 42.7, 42.9, 44.2, 47.5, 48.1, 51.0, 53.6, 59.3, 70.6, 110.2, 149.7, 170.6, 206.7; ESI-MS m/z: 987.6 [2M+Na]⁺; HRMS Calcd for C₃₂H₅₀O₃: 482.3760, found: 482.3764.

**2β-O-acetyl-lup-20(29)-en-28-oic acid (17).**

![2β-O-acetyl-lup-20(29)-en-28-oic acid (17).](image)
Compound 16 (60 mg, 0.124 mmol) was dissolved in 5 mL of tert-butyl alcohol, 1 mL of distilled THF and 1.5 mL of 2-methyl-2-betene. The solution was stirred and cooled in an ice-bath. Then 3 mL of freshly prepared aqueous solution of NaH₂PO₄/NaClO₂ (0.15 g/0.15 g) was slowly added to the mixture, and the resulting mixture was stirred for 15 min. The mixture was then warmed to room temperature. and stirred for 1 h. The mixture was then poured into 5 mL of a saturated solution of NH₄Cl and extracted with CH₂Cl₂. The combined extract was washed with saturated sodium bicarbonate solution and brine, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The crude product was purified by column chromatography (petroleum ether-ethyl acetate, 12:1) to give 2β-O-acetyl-lup-20(29)-en-28-oic acid (17) as a white solid (53.3 mg, 86%). Mp 166-167 °C; ¹H NMR (CDCl₃) δ 0.91 (s, 3 H), 0.94 (s, 6 H), 0.98 (s, 3 H), 1.05 (s, 3 H), 1.69 (s, 3 H), 2.00 (s, 3 H), 2.13-2.29 (m, 2 H), 2.98-3.01 (m, 1 H), 4.61 and 4.74 (s, each 1 H), 5.04-5.07 (m, 1 H); ¹³C NMR (CDCl₃) δ 14.7, 16.0, 18.5, 18.8, 19.4, 21.2, 21.6, 23.9, 25.6, 29.6, 30.6, 32.2, 32.7, 32.9, 33.9, 37.1, 37.8, 38.6, 40.9, 42.6, 43.0, 44.2, 47.0, 49.3, 51.0, 53.8, 56.4, 70.7, 109.7, 150.3, 170.5, 181.6; ESI-MS m/z: 497.3 [M-H]⁻; Anal. Calcd for C₃₂H₅₀O₄·0.2 H₂O: C 76.51, H 10.11, Found: C 76.3, H 9.96.

2β-Hydroxylup-20(29)-en-28-oic acid (2-Isobetulinic acid) (6).

Method A. Compound 17 (50 mg, 0.1 mmol) was dissolved in 5 mL of MeOH, then 1 mL of 4 N NaOH was added dropwise. The reaction mixture was stirred at 40 °C for 2 h. The mixture was diluted in CH₂Cl₂ and washed with 10% HCl and brine. The organic layer was dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (petroleum ether-ethyl acetate, 4:1) to give 2-isobetulinic acid (6) as a white solid (44 mg, 96%). Mp 259-261 °C; IR (KBr) 3455, 2942, 2868, 1686, 1451, 1375, 1235, 1187, 1043 cm⁻¹; ¹H
Method B. To a 50 °C warm mixture of butyl acetate (1.6 mL), aqueous phosphate buffer (0.67 M, pH 7.6, 0.86 mL), 2-isobetulin (5) (100 mg, 0.226 mmol), 4-acetamido-TEMPO (3.42 mg, 0.016 mmol) and Bu₄NBr·H₂O (3.6 mg, 0.011 mmol), were added slowly an aqueous solution of NaClO₂ (25%, 0.135 mL, 0.452 mmol) and NaClO (purchased from Alfa Aesar, 5%, 2 µL) within 5 min. Stirring at this temperature was continued and some additional NaClO was added portionwise and very slowly until completion of the reaction (monitored by TLC). After cooling to room temperature, water was added and the pH value adjusted to 8 by the addition of 2 N NaOH (0.1 mL). After extraction of the mixture with butyl acetate (20 mL), the organic layer was separated, washed with water and brine, dried over sodium sulfate, filtered and concentrated in vacuo. The crude product was purified by column chromatography (methylene chloride/ethyl acetate, 200:1) to give 2-isobetulinic acid (6) as a white solid (29 mg, 28%).

Benzyl-2-oxo-olean-12-en-28-oic acid (22).

Following the procedure for preparation of 13, treatment of benzyl-2β,3β-dihydroxyolean-12-en-28-oic acid (20)² (2 g, 3.55 mmol) with p-toluene sulfonyl chloride in pyridine afforded ketone 22 as a white solid (1.3 g, 67%). Mp 160-162 °C; IR (KBr) 3383, 2947, 2391, 1737, 1706, 1460, 1382, 1308, 1271, 1160, 1124, 1072, 1026, 729, 696 cm⁻¹; ¹H NMR (CDCl₃) δ 0.59 (s, 3 H), 0.88 (s, 6 H), 0.90 (s, 3 H), 0.92
(s, 3 H), 1.05 (s, 3 H), 1.16 (s, 3 H), 2.92 (dd, J = 4.0 Hz, 14.1 Hz, 1 H), 5.04 (d, J = 12.5 Hz, 1 H), 5.06 (d, J = 12.5 Hz, 1 H), 5.23 (t, J = 3.2 Hz, 1 H), 7.26-7.36 (m, 5 H); $^{13}$C NMR (CDCl$_3$) δ 16.4, 16.6, 19.1, 23.1, 23.3, 23.6, 25.8, 27.6, 30.7, 32.3, 32.4, 33.1, 33.5, 33.9, 39.2, 39.8, 41.4, 41.9, 42.8, 45.9, 46.8, 47.3, 55.6, 55.7, 56.4, 66.0, 122.1, 127.9, 128.0, 128.4, 136.4, 143.8, 177.3, 211.8; ESI-MS m/z: 583.2 [M+K]$^+$; HRMS Calcd for C$_{37}$H$_{53}$O$_3$ [M+H]$^+$: 545.3916, found: 545.4010.

**Benzyl-2-oxo-urs-12-en-28-oic acid (23).**

![Structure of Benzyl-2-oxo-urs-12-en-28-oic acid (23).](image)

Following the procedure for preparation of 13, treatment of benzyl-2β,3β-dihydroxyurs-12-en-28-oic acid (21)$^2$ (2.5 g, 4.44 mmol) with p-toluene sulfonyl chloride in pyridine afforded ketone 23 as a white solid (1.5 g, 62%). Mp 183-186 °C; $^1$H NMR (CDCl$_3$) δ 0.61 (s, 3 H), 0.86 (s, 3 H), 0.88 (s, 3 H), 0.89 (s, 3 H), 0.95 (s, 3 H), 1.06 (s, 3 H), 1.11 (s, 3 H), 4.97 (d, J = 12.4 Hz, 1 H), 5.10 (d, J = 12.4 Hz, 1 H), 5.23 (t, J = 3.3 Hz, 1 H), 7.28-7.35 (m, 5 H); $^{13}$C NMR (CDCl$_3$) δ 16.5, 16.7, 17.0, 19.0, 21.1, 23.2, 23.3, 23.5, 24.2, 27.9, 30.6, 32.7, 33.5, 36.6, 38.8, 39.1, 39.2, 40.0, 42.2, 42.8, 47.1, 48.1, 52.9, 55.5, 55.8, 56.3, 66.0, 125.2, 127.9, 128.2, 128.4, 136.3, 138.2, 177.1, 211.8; ESI-MS m/z: 583.2 [M+K]$^+$; HRMS Calcd for C$_{37}$H$_{53}$O$_3$ [M+H]$^+$: 545.3916, found: 545.3991.

**Benzyl-2β-hydroxyolean-12-en-28-oic acid (24) and benzyl-2α-hydroxyolean-12-en-28-oic acid (24a).**

![Structure of Benzyl-2β-hydroxyolean-12-en-28-oic acid (24) and benzyl-2α-hydroxyolean-12-en-28-oic acid (24a).](image)

Following the procedure for preparation of 14, reduction of ketone 22 (120 mg, 0.22 mmol) with NaBH$_4$ afforded alcohol 24 (91 mg, 76%) and 2α-hydroxy isomer 24a (6 mg, 5%). For 24: a white solid. Mp
160-163 °C; IR (KBr) 3592, 3439, 2706, 1728, 1647, 1462, 1384, 1259, 1205, 1170, 1122, 1075, 1031, 817, 740, 697, 470 cm⁻¹; ¹H NMR (CDCl₃) δ 0.63 (s, 3 H), 0.86 (s, 3 H), 0.93 (s, 6 H), 1.01 (s, 3 H), 1.13 (s, 3 H), 1.16 (s, 3 H), 2.92 (m, 1 H), 4.08 (brs, 1 H), 5.07 (d, J = 12.5 Hz, 1 H), 5.10 (d, J = 12.5 Hz, 1 H), 5.32 (brs, 1 H), 7.26-7.34 (m, 5 H); ¹³C NMR (CDCl₃) δ 16.8, 18.5, 19.0, 23.1, 23.4, 23.6, 24.6, 25.9, 27.5, 29.7, 30.7, 32.4, 32.5, 32.6, 33.1, 33.9, 37.8, 39.6, 41.5, 41.9, 45.9, 46.6, 46.8, 47.2, 48.0, 53.5, 65.9, 67.6, 122.8, 127.9, 128.0, 128.4, 136.5, 143.7, 177.4; ESI-MS m/z: 569.2 [M+Na]⁺; Anal. Calcd for C₃₇H₅₄O₃: C 81.27, H 9.95; Found: C 81.31, H 9.64. For 24a: a white solid. Mp 184-186 °C; ¹H NMR (CDCl₃) δ 0.61 (s, 3 H), 0.85 (s, 3 H), 0.90 (s, 6 H), 0.92 (s, 3 H), 0.93 (s, 3 H), 1.13 (s, 3 H), 2.92 (dd, J=4.1 Hz, 13.7 Hz, 1 H), 3.84–3.92 (m, 1 H), 5.02–5.12 (m, 2 H), 5.32 (t, J=3.2 Hz, 1 H), 7.26-7.35 (m, 5 H); ¹³C NMR (CDCl₃) δ 16.4, 17.0, 18.4, 22.6, 23.1, 23.5, 23.7, 25.9, 27.6, 29.7, 30.7, 32.4, 32.7, 33.1, 33.5, 33.9, 39.0, 39.5, 41.4, 41.8, 45.9, 46.8, 49.5, 51.2, 55.7, 65.1, 65.9, 122.5, 127.9, 128.0, 128.4, 136.5, 143.7, 177.4; ESI-MS m/z: 569.2 [M+Na]⁺; Anal. Calcd for C₃₇H₅₄O₃: C 81.27, H 9.95; Found: C 81.29, H 9.70.

Benzyl-2β-hydroxyurs-12-en-28-oic acid (25).

Following the procedure for preparation of 14, reduction of ketone 23 (0.3 g, 0.55 mmol) with NaBH₄ afforded alcohol 25 as a white solid (0.23 g, 77%). Mp 189-191 °C; ¹H NMR (CDCl₃) δ 0.65 (s, 3 H), 0.85 (s, 3 H), 0.93 (s, 3 H), 0.94 (s, 3 H), 1.01 (s, 3 H), 1.07 (s, 3 H), 2.27 (d, J = 11.3 Hz, 1 H), 4.06-4.10 (m, 1 H), 4.97 (d, J = 12.5 Hz, 1 H), 5.10 (d, J = 12.5 Hz, 1 H), 5.26 (t, J = 3.6 Hz, 1 H), 7.28-7.36 (m, 5 H); ¹³C NMR (CDCl₃) δ 16.9, 17.0, 18.7, 19.0, 23.4, 23.6, 24.3, 24.7, 27.9, 29.6, 29.7, 30.7, 32.7, 32.9, 33.1, 36.7, 37.8, 38.9, 39.1, 39.9, 42.3, 46.6, 47.6, 48.1, 48.2, 53.1, 53.5, 66.0, 67.6, 126.0, 127.9, 128.2, 128.4, 136.4, 138.1, 177.2; ESI-MS m/z: 569.4 [M+Na]⁺; Anal. Calcd for C₃₇H₅₄O₃: C 81.27, H 9.95; Found: C
2β-Hydroxyolean-12-en-28-oic acid (2-Isooleanolic acid) (7).

A mixture of benzyl ester 24 (60 mg, 0.11 mmol) and 10% Pd/C (6 mg) in THF (4 mL) was stirred at room temperature under H₂ atmospheric pressure for 5 h. The reaction mixture was filtered through Celite and the insoluble substance was washed with THF. The filtrate was concentrated in vacuo to give 2-isoooleanolic acid (7) (46 mg, 92%) as a white solid. Mp 240-243 °C; IR (KBr) 3437, 2928, 2861, 1694, 1465, 1384, 1269, 1031 cm⁻¹; ¹H NMR (C₅D₅N) δ 0.94 (s, 3 H), 0.96 (s, 3 H), 1.00 (s, 3 H), 1.05 (s, 3 H), 1.20 (s, 3 H), 1.29 (s, 3 H), 1.39 (s, 3 H), 3.24 (dd, J = 4.2 Hz, 13.8 Hz, 1 H), 4.33-4.36 (m, 1 H), 5.50 (t, J = 3.3 Hz, 1 H); ¹³C NMR (C₅D₅N) δ 23.8, 23.9, 24.7, 26.2, 28.3, 31.0, 33.0, 33.2, 33.3, 33.8, 34.3, 38.1, 40.1, 42.1, 42.4, 46.5, 46.7, 47.4, 47.6, 48.5, 54.8, 66.9, 122.8, 144.8, 180.1; ESI-MS m/z: 479.3 [M+Na]⁺; Anal. Calcd for C₃₀H₄₈O₃·0.75 H₂O: C 76.63, H 10.61, Found: C 76.69, H 10.26.

2β-Hydroxyurs-12-en-28-oic acid (2-Isoursolic acid) (8).

Following the procedure for preparation of 7, hydrogenolysis of benzyl ester 25 (110 mg, 0.20 mmol) afforded 2-isoursolic acid (8) as a white solid (90 mg, 98%). Mp 256-258 °C; ¹H NMR (C₅D₅N) δ 0.79 (s, 3 H), 0.85 (s, 3 H), 0.87 (s, 3 H), 0.92 (s, 3 H), 0.93 (s, 3 H), 0.99 (s, 3 H), 1.25 (s, 3 H), 4.08 (brs, 1 H), 5.28 (brs, 1 H); ¹³C NMR (C₅D₅N) δ 17.6, 18.4, 19.3, 21.4, 23.9, 24.0, 24.8, 25.1, 28.7, 31.2, 33.0, 33.5, 33.8, 37.5, 38.0, 39.5, 39.6, 40.4, 42.9, 47.7, 47.8, 48.2, 48.6, 53.8, 54.8, 66.9, 126.0, 139.3, 179.9; ESI-MS m/z: 455.3 [M-H]⁻; Anal. Calcd for C₃₀H₄₈O₃·0.5 H₂O: C 77.37, H 10.60, Found: C 77.17, H
References:

