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REDUCTION OF 2,3-*Seco*-28-OXO-19β,28-EPOXY-18α-OLEAN-2,3-DICARBOXYLIC ACID AND ITS CYCLIC ANHYDRIDE

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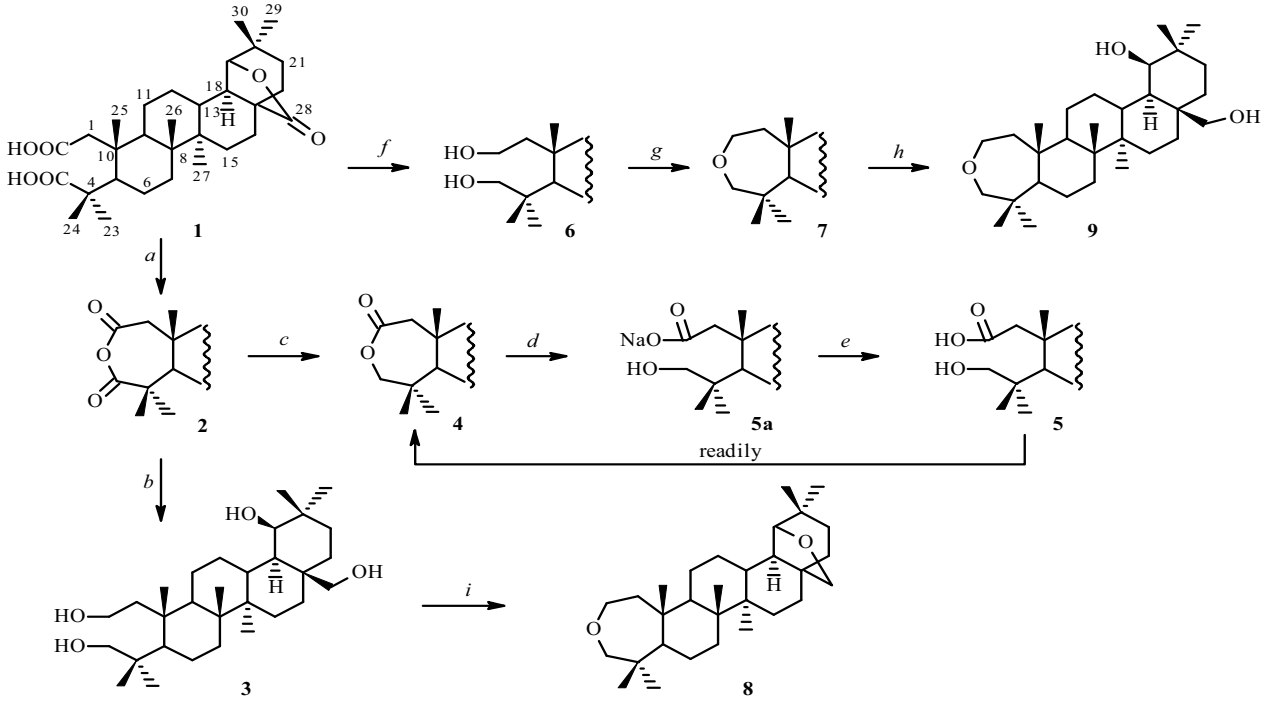
Reduced derivatives of 2,3-seco-28-oxo-19β,28-epoxy-18α-olean-2,3-dicarboxylic acid and its cyclic anhydride were prepared. Reduction of the starting 2,3-secodicarboxylic acid by $NaBH_4$–I_2 produced the 2,3-seco-2,3-dihydroxy derivative. Reaction of the starting anhydride with $LiAlH_4$ gave the 2,3-seco-2,3,19β,28-tetrahydroxy derivative. Cyclization using acidic reagents of the 2,3-seco-2,3-hydroxy- and 2,3-seco-2,3,19β,28-tetrahydroxy derivatives gave the corresponding cyclic ethers containing an oxepane ring. The anhydride ring was reduced by $NaBH_4$ to the corresponding ε-lactone, the structure of which was confirmed by an x-ray crystal structure.

Keywords: 2,3-*seco*-28-oxo-19β,28-epoxy-18α-olean-2,3-dicarboxylic acid, 2,3-secotriterpenoids, polyhydroxytriterpenoids, reduction, ε-lactone, oxepanes.

A-Secotriterpenoids are widely distributed in the plant world and are assumed to play a role in the plant protective system [1]. Semi-synthetic A-*seco*-derivatives of triterpenoids exhibit various types of biological activity, in particular, they inhibit HIV-1 proteases [2] and have cytotoxic and antitumor activity [3-5]. Herein we report the preparation of derivatives of a 2,3-*seco*-2,3-dicarboxylic acid (**1**) in order to expand the array of semi-synthetic triterpenoids and to discover among them compounds with high biological activity. Starting material **1** was readily obtained in high yield from allobetulin [6].



1, **2**, **3**, **4**, **5**, **5a**, **6**, **7**, **8**, **9**

a. $(COCl)_2/CH_2Cl_2$; *b*. $LiAlH_4/(CH_2Cl_2–Et_2O)$; *c*. $NaBH_4$/*i*-PrOH; *d*. NaOH/(MeOH–THF–H_2O); *e*. acetate buffer; *f*. $NaBH_4$–I_2/THF 40°C; *g*. $AlCl_3/SiO_2/CH_2Cl_2$; *h*. $LiAlH_4/(CH_2Cl_2–Et_2O)$; *i*. H_2SO_4 over SiO_2 (3%)/CH_2Cl_2

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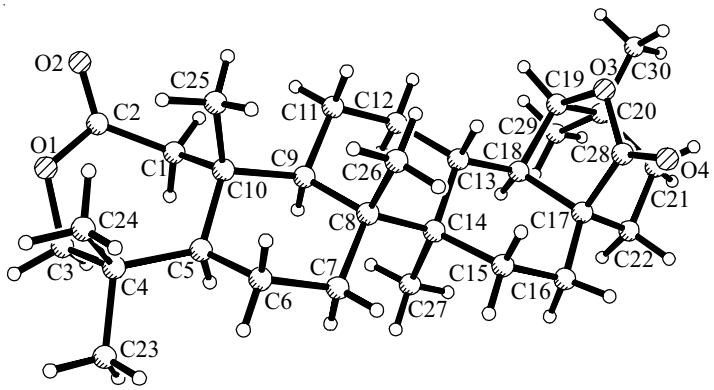

Fig. 1. Molecular structure of **4** from an XSA.

Reaction of **1** with two equivalents of oxalylchloride produced the seven-membered cyclic anhydride **2** in 90% yield, which was reduced by $LiAlH_4$ to the corresponding polyhydroxy derivative **3** in 67% yield. Reaction of **2** with $NaBH_4$ in isopropanol occurred selectively to form a lactone **4** in 96% yield. Reduction of the 3-carbonyl that was vicinal to the *gem*-dimethyl group agreed well with the literature on the reduction of asymmetric cyclic anhydrides [7, 8]. Several protons and C atoms appeared as broadened or very broad resonances at the temperature (+28°C) at which the PMR and ^{13}C NMR spectra were recorded. These were mainly resonances of the seven-membered ring and the substituents on it and the six-membered ring adjoined to it. Thus, resonances for the C-4 methyls were observed in the PMR spectrum as a very broad singlet at 0.90-0.98 ppm; the C-1 and C-3 protons, as broad resonances. Resonances for C-1, C-3–C-7, C-10, and C-23 appeared in the ^{13}C NMR spectrum as variously broadened resonances. The resonance for the $C^{24}H_3$ methyl group could not be found.

Apparently this pattern is related to readily occurring conformational oscillations of the seven-membered ring. It can be assumed that the difference in chemical shifts were greatest for the C-24 resonances of the conformers compared with the other C atoms involved in the exchange. Therefore, they were still in the coalescence range in spectra recorded at the aforementioned temperature. Figure 1 shows the molecular structure of **4** from an x-ray structure analysis (XSA). The six-membered rings had the chair conformation; the five-membered, an envelope with C-18 deviating by 0.692(4) Å. The seven-membered lactone ring had the chair conformation. The fragment C1-C2-O1-C3-O2 was planar within ±0.040(3) Å. A similar lactone ring in a triterpenoid was reported [9]. However, the atomic coordinates are not listed in the Cambridge Crystallographic Database so the structures cannot be compared. As an example, the chair conformation was observed for the seven-membered lactone ring in (1*R**,7*S**)-1-hydroxy-4-oxabicyclo[5.4.0]undecan-3-one [10]. Several weak C–H…O bonds are noteworthy among the intermolecular interactions in the crystal of **4**: (C-24)–H…O-2 (H…O 2.58 Å, C–H…O 145°), (C-29)–H…O-4 (2.60 Å, 171°), (C-18) –H…O-4 (2.63Å, 164°).

The seven-membered lactone ring of **4** was opened by bases to the corresponding acid salt **5a**. Compound **4** was completely converted to the corresponding salt, which was isolated in 87% yield, by the action of a 12-fold excess of NaOH in MeOH:THF:H_2O and refluxing for 1.5 h. However, producing the acid from this salt was exceedingly problematical. Thus, treatment of the reaction mixture with conc. HCl until the pH was 5 formed a precipitate consisting according to PMR data of mainly starting lactone **4** with traces of acid **5**. Diluting the same reaction mixture with acetate buffer at pH 5.0–5.5 formed a precipitate consisting according to PMR data of 30% lactone **4** and 70% acid **5** (characteristic resonances at 2.54 and 2.63, 2H-1, AB system, ^2J = 14.0; 3.39, and 3.72, 2H-3, AB system ^2J = 11.4). Moreover, the PMR spectrum recorded after storing the tube for 2 d at –8°C showed 20% acid **5** and 80% lactone **4**.

Selective reduction of both carboxylic acids in **1** was achieved using $NaBH_4$–I_2, which generated BH_3–THF *in situ* [1]. This was used earlier for selective reduction of different carboxylic acids [12]. The optimum conditions for this reaction were a three-fold excess of I_2 and heating at 40°C for 6 h. This practically completely converted starting **1** to the diol **6**, which was isolated in 73% yield. Carrying out the reaction at room temperature gave a low conversion of the starting compound that was probably due to the formation of insoluble intermediates [12]. Increasing the reaction time produced in the reaction mixture the product of further reduction, tetraol **3**. The carboxylic groups in **1** were inert to reduction by $NaBH_4$–Br_2–THF although according to the literature [13] replacing I_2 by Br_2 accelerated the reduction in the case of malonic acid derivatives.

TABLE 1. ^{13}C NMR Spectra ($CDCl_3$ + DMSO-d_6) of **1** and **3**–**9**[a]

C atom	**1** (4:1)	**3** (5:1)	**4** ($CDCl_3$)	**5a** (5:1)	**6** (5:1)	**7** ($CDCl_3$)	**8** ($CDCl_3$)	**9** (5:1)
1	41.96 t	40.84 t	46.4 very br.	47.59 t	40.89 t	40.65 t	40.58 t	39.42 t
2	173.04 s	57.76 t	174.39 s	179.44 s	57.80 t	66.76 t	66.80 t	66.05 t
3	181.46 s	71.36 t	77.59 br.t	72.20 t	71.29 t	77.43 t	77.39 t	76.48 t
4	45.91 s	40.06 s	39.97 br.s	40.23 s	39.98 s	39.90 s	39.94 s	39.42 s
5	47.43 d	44.75 d	~ 61 very br.	43.98 d	44.68 d	59.25 d	59.32 d	58.68 d
6	20.57 t	20.84 t	19.79 br.t	20.50 t	20.60 t	20.81 t	20.94 t	20.43 t
7	32.17 t	32.87 t	33.40 br.t	32.48 t	32.55 t	33.64 t	33.88 t	33.36 t
8	39.88 s	40.29 s	41.35 s	39.70 s	39.64 s	40.86 s	40.96 s	40.94 s
9	42.13 d	41.99 d	47.92 d	43.37 d	42.90 d	48.20 d	48.08 d	46.52 d
10	41.60 s	41.60 s	37.95 br.s	42.09 s	41.66 s	41.98 s	42.00 s	41.28 s
11	21.37 t	20.90 t	21.82 t	21.61 t	20.81 t	22.40 t	22.55 t	21.88 t
12	26.06 t	23.93 t	26.33 t	25.84 t	25.96 t	26.76 t	26.74 t	24.11 t
13	35.85 d	32.23 d	35.98 d	35.74 d	35.69 d	36.21 d	34.38 d	32.28 d
14	39.82 s	42.12 s	40.17 s	39.59 s	39.56 s	40.02 s	40.83 s	41.95 s
15	27.43 t	26.27 t	27.54 t	27.20 t	27.21 t	27.63 t	26.27 t	26.12 t
16	25.10 t	34.33 t	25.38 t	24.99 t	24.94 t	25.49 t	26.24 t	34.35 t
17	45.61 s	37.24 s	45.88 s	45.44 s	45.47 s	45.97 s	41.36 s	37.19 s
18	46.04 d	41.27 d	46.38 d	45.98 d	45.89 d	46.48 d	46.59d	41.20 d
19	85.36 d	72.99 d	85.56 d	85.20 d	85.21 d	85.63 d	87.65 d	72.94 d
20	33.09 s	34.84 s	33.37 s	32.89 s	32.93 s	33.40 s	36.14 s	34.75 s
21	31.93 t	30.65 t	32.17 t	31.78 t	31.77 t	32.21 t	32.64 t	30.58 t
22	31.39 t	33.75 t	31.75 t	31.30 t	31.25 t	31.80 t	36.64 t	33.72 t
23	26.63[a] q	25.51[a] q	28.52 br.q	28.10 q	25.63[a] q	28.41 q	28.42 q	27.79 q
24	23.93[a] q	24.42[a] q	Not found	23.07 q	24.26[a] q	21.02 q	21.06 q	20.65 q
25	19.76 q	19.99 q	19.37 q	19.75 q	20.23 q	14.10 q	14.09 q	13.31 q
26	15.17 q	15.63 q	16.12 q	15.06 q	15.26 q	16.24 q	16.45 q	16.05 q
27	13.28 q	14.08 q	13.15 q	13.13 q	12.95 q	13.18 q	13.08 q	13.91 q
28	179.30 s	63.94 t	179.40 s	179.11 s	179.19 s	179.66 s	71.20 t	63.93 t
29	28.36 q	28.06 q	28.55 q	28.14 q	28.19 q	28.62 q	28.69 q	27.94 q
30	23.47 q	25.51 q	23.72 q	23.34 q	23.32 q	23.80 q	24.43 q	25.40 q

[a]Chemical shifts of resonances marked with the same letters may be interchangeable within the same column.

Diol **6** cyclized to form oxepane **7** in CH_2Cl_2 containing $AlCl_3$ and silica gel. The reaction occurred under rather mild conditions with stirring at room temperature for 15 h to give 73% yield. Apparently the $AlCl_3$ played a dual role. It generated HCl upon reaction with H_2O adsorbed to the surface of the silica gel and/or surface SiOH groups and also acted as a Lewis acid to facilitate intramolecular nucleophilic substitution and form the oxepane ring [14]. This was indicated by the fact that the reaction did not occur with $AlCl_3$ that was adsorbed beforehand on the surface of activated silica gel and was rinsed and dried to remove HCl. Sulfuric acid adsorbed to the silica gel surface was synthetically a more convenient reagent for this reaction [15]. It was used successfully to produce allobetulin [16]. Thus, tetraol **3** gave the corresponding derivative **8** in 81% yield upon refluxing in CH_2Cl_2 for 15 h if H_2SO_4 was used.

Compound **7** was reduced by $LiAlH_4$ to the corresponding diol (**9**) in 97% yield.

EXPERIMENTAL

IR spectra were recorded in KBr on a Vector 22 instrument. Mass spectra (ionizing electron energy 70 eV) were recorded in a Thermo Electron DFS instrument. Melting points were measured on a Kofler stage and Mettler Toledo FP 900 instrument (in this instance the heating rate is given). Acetate buffer was prepared by mixing NaOAc (5.444 g) and AcOH (1.1 mL) in H_2O (200 mL). PMR and ^{13}C NMR spectra were recorded from $CDCl_3$ or $CDCl_3$ + DMSO-d_6 (4:1 or 5:1 ratio by volume) solutions on a Bruker DRX-500 spectrometer (operating frequency 500.13 MHz for ^1H and 125.76 MHz for ^{13}C). The internal standards were $CHCl_3$ (δ_H 7.24 ppm, δ_C 76.90 ppm) or DMSO resonances (δ_H 2.50 ppm, δ_C 39.50 ppm). Proton

resonances in PMR spectra were assigned using ^1H–^1H double resonance spectra and two-dimensional homonuclear ^1H–^1H correlation spectra (^1H–^1H COSY). The multiplicities of resonances in ^{13}C NMR spectra were determined from spectra recorded with J-modulation (JMOD) and with off-resonance irradiation of protons. Resonances were assigned using 2D heteronuclear correlation spectroscopy ^{13}C–^1H COSY ($^1J_{C,H}$ = 135 Hz) and COLOC ($^{2,3}J_{C,H}$ = 10 Hz). Resonances of most protons in PMR spectra appeared as overlapping multiplets. Therefore, accurate chemical shifts and SSCC were found only for certain resonances that appeared separately. Analytical data of all compounds agreed with those calculated.

2,3-*Seco*-28-oxo-19β,28-epoxy-18α-olean-2,3-dicarboxylic Acid (1). Compound **1** was prepared by the literature method [6], mp 280–283°C (lit [17] dec. temp. 283–284°C). IR spectrum (ν, cm^{-1}): 1762 (lactone), 1698 (COOH).

PMR spectrum ($CDCl_3$ + DMSO-d_6, 4:1, δ, ppm, J/Hz): 0.79 (3H, s, CH_3-27), 0.80 (3H, s, CH_3-26), 0.83 (3H, s, CH_3-25), 0.86 (3H, s, CH_3-30), 0.91 (3H, s, CH_3-29), 1.12 and 1.14 (3H each, s, CH_3-23, CH_3-24), 1.21 (1H, ddd, $J_{13a,12a}$ = 12.5, $J_{13a,18a}$ = 11.4, $J_{13a,12e}$ = 2.8, H-13a), 1.54 (1H, br.d, $J_{12e,12a}$ = 12.5, H-12e), 1.69 (1H, br.d, $J_{16e,16a}$ = 14.0, H-16e), 1.73 (1H, d, $J_{18a,13a}$ = 11.4, H-18a), 2.31 and 2.43 (1H each, d, ^2J = 17.8, AB system, H-1), 2.34 (1H, br.d, $J_{5a,6a}$ = 11, H-5a), 2.39 (1H, br.d, $J_{9a,11a}$, H-9a), 3.82 (1H, s, H-19e). Resonances of other protons were observed as overlapping multiplets in the regions 0.85–0.96 (H-12a), 1.03–1.17 (H-11, 2H-15), and 1.24–1.52 (10H). Table 1 gives the ^{13}C NMR spectrum.

2,3-*Seco*-28-oxo-19β,28-epoxy-18α-olean-2,3-anhydride (2). A solution of **1** (1.043 g, 2.08 mmol) in CH_2Cl_2 (50 mL) was treated with oxalylchloride (0.4 mL, 4.6 mmol) and left for 1 d closed with a $CaCl_2$ tube. The solvent and unreacted oxalylchloride were distilled off. The solid was placed on a filter, washed with hexane:Et_2O (1:1, 10 mL), and dried in a desiccator over NaOH in vacuo (oil pump) to afford a colorless powder (0.908 g, 90%). The analytical data have been published [18].

2,3-*Seco*-18α-olean-2,3,19β,28β-tetraol (3). A solution of cyclic anhydride **2** (1.079 g, 2.23 mmol) in CH_2Cl_2 (40 mL) was stirred, treated with $LiAlH_4$ (1.055 g, 27.81 mmol) in Et_2O (50 mL), and stirred for 1 d. The excess of the reagent was carefully destroyed by H_2O. The precipitate was filtered off and washed with EtOH (3 × 5 mL). The filtrate was evaporated and purified by column chromatography over silica gel (Et_2O in CH_2Cl_2 gradient then EtOH in CH_2Cl_2 gradient) to afford the product (0.718 g, 67%), mp 226.0°C (1°/min). IR spectrum (ν, cm^{-1}): 3383 (OH).

PMR spectrum ($CDCl_3$ + DMSO-d_6, 5:1, δ, ppm, J/Hz): 0.81 and 0.97 (3H each, s, CH_3-23, CH_3-24), 0.84 (12H, s, CH_3-25, CH_3-27, CH_3-29, CH_3-30), 0.96 (3H, s, CH_3-26), 0.83–0.91 (2H, m, H-12a, H-15), 0.92 (1H, dm, $J_{21e,21a}$ = 14.1, 3J < 4.5, H-21e), 1.06 (1H, ddd, $J_{16a,16e}$ = $J_{16a,15a}$ = 13.6, $J_{16a,15e}$ = 4.1, H-16a), 1.09 (1H, ddd, $J_{22a,22e}$ = $J_{22a,21a}$ = 14.1, $J_{22a,21e}$ = 4.3, H-22a), 1.17 (1H, m, H-11a), 1.23 (2H, m, H-6, H-7), 1.36 (1H, ddd, $J_{16e,16a}$ = 13.6, $J_{16e,15a}$ = 4.2, $J_{16e,15e}$ = 2.9, H-16e), 1.66 (1H, m, H-12e), 1.68 (1H, m, H-1), 1.77 (1H, m, H-1′), 1.80 (1H, ddd, $J_{21a,21e}$ = $J_{21a,22a}$ = 14.1, $J_{21a,22e}$ = 4.2, H-21a), 1.91 (1H, ddd, $J_{13a,18a}$ = $J_{13a,12a}$ = 11.7, $J_{13a,12e}$ = 3.6, H-13a), 3.13 (1H, br.s, H-19e), 3.22 and 3.98 (1H each, d, ^2J = 11.6, H-28), 3.29 and 3.30 (1H each, d, ^2J = 11.1, AB system, H-3), 3.45 (1H, ddd, $J_{2,2'}$ = 10.2, $J_{2,1'}$ = 9.0, $J_{2,1}$ = 6.1, H-2), 3.69 (1H, ddd, $J_{2',2}$ = 10.2, $J_{2',1}$ = 9.4, $J_{2',1'}$ = 5.3, H-2′). Resonances of other protons appeared in the region 1.38–1.57 ppm (8H). Table 1 gives the ^{13}C NMR spectrum.

2,3-*Seco*-2,28-dioxo-2,3:19β,28-diepoxy-18α-oleane (4). A mixture of cyclic anhydride **2** (0.494 g, 1.02 mmol) and $NaBH_4$ (0.129 g, 3.41 mmol) was treated with isopropanol (10 mL) and stirred for 5 h closed with a $CaCl_2$ tube. The mixture was decomposed by conc. HCl and treated with CH_2Cl_2 (60 mL). The precipitate was filtered off. The solvent was distilled off. The product was purified by column chromatography over silica gel (CH_2Cl_2:Et_2O, 9:1) to afford **4** (0.460 g, 96%) as colorless crystals that sublimed without melting at >250°C and decomposed in a capillary at 358–360°C and 352°C (5°/min). IR spectrum (ν, cm^{-1}): 1765 (five-membered lactone), 1737 (seven-membered lactone).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.82 (3H, s, CH_3-27), 0.90 (9H, s, CH_3-25, CH_3-26, CH_3-30), 0.97 (3H, s, CH_3-29), 0.99 (1H, m, H-12a), 1.16 (1H, ddd, ^2J = 13.3, $J_{15e,16a}$ = 4.5, $J_{15e,16e}$ = 2.5, H-15e), 1.61 (1H, m, H-11e), 1.67 (1H, dm, ^2J = 13.0, H-12e), 1.77 (1H, d, $J_{18,13}$ = 11.1, H-18), 1.82 (1H, dm, ^2J = 13.7, H-16e), 2.39 and 2.78 (v.br, 1H each, H-1), 3.69 and 4.08 (v.br.d, 1H each, H-3), 3.90 (1H, s, H-19). Resonances of other protons were observed as overlapping multiplets in the region 1.18–1.60. Table 1 gives the ^{13}C NMR spectrum.

Unit-cell constants and intensities of 2815 independent reflections were measured on a Bruker P4 diffractometer (Mo K_α-radiation, graphite monochromator, θ/2θ-scanning, 2θ ≤ 53°, 297 K). The crystals were monoclinic, a = 6.5957(4), b = 12.8975(9), c = 15.438(1) Å, β = 99.351(4)°, V = 1295.85(15) $Å^3$, Z = 2 ($C_{30}H_{46}O_4$), d_{calcd} = 1.206 g/cm^3, space group $P2_1$, size 0.2 × 0.5 × 0.8 mm. Absorption corrections were made analytically using the crystal faces. The structure was solved by direct methods and refined by anisotropic least-squares methods for nonhydrogen atoms. Hydrogen atoms were placed geometrically and refined using a rider model. The final refinement parameters were wR_2 = 0.1358, S = 1.059 (all reflections),

R_1 = 0.0488 [for 2419 $I > 2\sigma(I)$]. All calculations were performed using the SHELX-97 program set [19]. Atomic coordinates and geometric parameters were deposited in the Cambridge Crystallographic Data Centre (CCDC 757536).

Sodium Salt of 2,3-*Seco*-3-hydroxy-28-oxo-19β,28-epoxy-18α-olean-2-carboxylic Acid (5a). A suspension of dilactone **4** (0.315 g, 0.67 mmol) and NaOH (0.328 g, 8.20 mmol) in MeOH:THF:H_2O (15:7.5:1 mL, respectively) was refluxed for 1.5 h and cooled. The precipitate was filtered off. The filtrate was evaporated and treated with CH_2Cl_2 (30 mL). The precipitate was filtered off. The solution was again evaporated to afford **5a** (0.288 g, 87%). IR spectrum (ν, cm^{-1}): 3420 (OH), 1779 (five-membered lactone), 1567 (CO_2^-) 1392 (CO_2^-).

PMR spectrum ($CDCl_3$ + DMSO-d_6, 5:1, δ, ppm, J/Hz): 0.77 (3H, s, CH_3-27), 0.83 (6H, s, CH_3-25, CH_3-26), 0.88 (6H, s, CH_3-24, CH_3-30), 0.92 (3H, s, CH_3-23), 0.94 (3H, s, CH_3-29), 0.95–1.12 (2H, m, H-12a, H-11a), 1.54 (1H, dm, ^2J = 12.5, H-12e), 1.73 (1H, dm, ^2J = 13.7, H-16e), 1.74 (1H, d, $J_{18,13}$ = 11.0, H-18), 1.88 (1H, br.d, $^2J \sim 11$, H-11e), 1.94–2.02 (2H, m, H-5, H-9), 2.31 and 2.42 (1H each, d, ^2J = 13.8, AB system, H-1), 3.12 (1H, d, ^2J = 11.3, H-3), 3.61 (1H, br.d, ^2J = 11.3, H-3′), 3.86 (1H, s, H-19). Resonances of other protons were observed as overlapping multiplets in the region 1.11-1.51. Table 1 gives the ^{13}C NMR spectrum. $C_{30}H_{47}NaO_5 \cdot H_2O$.

2,3-*Seco*-28-oxo-19β,28-epoxy-18α-olean-2,3-diol (6). A suspension of $NaBH_4$ (0.967 g, 25.57 mmol) in THF (5 mL) was stirred and treated dropwise with a solution of I_2 (0.779 g, 3.07 mmol) in THF (4 mL) at a rate such that the temperature stayed below 40°C. After the iodine color disappeared, a solution of **1** (0.500 g, 1.00 mmol) in THF (5 mL) was added dropwise. The mixture was held at 40°C, stirred for 6 h, and treated with MeOH (2 mL). The precipitate was filtered off and washed with THF (8 mL). The filtrate was treated with MeOH (1 mL) and left overnight. The solvent was distilled off. The resulting solid was dissolved in refluxing MeOH (20 mL) and reprecipitated by adding H_2O (40 mL). The precipitate was filtered off, washed with H_2O, and dried in a desiccator in vacuo (oil pump) over anhydrous NaOH to afford a colorless powder (0.347 g, 73%), mp 247–249°C. IR spectrum (ν, cm^{-1}): 3505 (OH), 1754 (lactone).

PMR spectrum ($CDCl_3$ + DMSO-d_6, 5:1, δ, ppm, J/Hz): 0.76 (3H, s, CH_3-27), 0.82 (3H, s, CH_3-26), 0.84 (3H, s, CH_3-25), 0.84 and 0.96 (3H each, s, CH_3-23, CH_3-24), 0.88 (3H, s, CH_3-30), 0.93 (3H, s, CH_3-29), 0.91 (1H, m, H-12a), 1.67 and 1.80 (1H each, m, H-1), 1.72 (1H, dm, ^2J = 14.0, H-16e), 1.75 (1H, d, $J_{18,13}$ = 11.2, H-18), 3.29 and 3.32 (1H each, d, ^2J = 11.0, AB system, H-3), 3.46 and 3.70 (1H each, m, H-2), 3.85 (1H, s, H-19). Resonances of other protons were observed as overlapping multiplets in the region 1.05–1.62. Table 1 gives the ^{13}C NMR spectrum. Found: *m/z* 456.3591 $[M - H_2O]^+$, $C_{30}H_{48}O_3$, calcd: 456.3598.

2,3-*Seco*-28-oxo-2,3:19β,28-diepoxy-18α-oleane (7). Diol **6** (0.467 g, 0.98 mmol), $AlCl_3$ (0.260 g, 2.00 mmol), silica gel (1 g), and CH_2Cl_2 (8 mL) were mixed in a flat-bottomed flask, stirred on a magnetic stirrer for 15 h closed with a $CaCl_2$ tube, and treated with H_2O (0.5 mL). The precipitate was filtered off on a glass filter and washed with CH_2Cl_2 (3 × 10 mL) and THF (2 × 10 mL). The solvent was distilled off. The product was purified by column chromatography over silica gel (CH_2Cl_2:Et_2O, 50:1) to afford a colorless powder (0.328 g, 73%), mp 341.3°C (2°/min). IR spectrum (ν, cm^{-1}): 1763 (lactone).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.80 (3H, s, CH_3-23), 0.83 (3H, s, CH_3-27), 0.86 (3H, s, CH_3-24), 0.92 (3H, s, CH_3-30), 0.95 (3H, s, CH_3-26), 1.00 (3H, s, CH_3-29), 1.01 (3H, s, CH_3-25), 0.81 (1H, m, H-5), 0.93 (1H, m, H-12a), 1.56 (1H, dm, ^2J = 12.0, H-11e), 1.66 (1H, dm, ^2J = 13.0, H-12e), 1.76 (1H, ddd, ^2J = 13.8, $J_{1,2}$ = 4.5, $J_{1,2'}$ = 1.1, H-1), 1.79 (1H, d, $J_{18,13}$ = 11.2, H-18), 1.84 (1H, ddd, ^2J = 14.0, $J_{16e,15a}$ = 4.0, $J_{16e,15e}$ = 3.3, H-16e), 3.24 and 3.43 (1H each, d, ^2J = 12.7, AB system, H-3), 3.66 (1H, ddd, ^2J = 12.0, $J_{2,1'}$ = 12.0, $J_{2,1}$ = 4.5, H-2), 3.73 (1H, ddd, ^2J = 12.0, $J_{2',1'}$ = 6.5, $J_{2',1}$ = 1.1, H-2′), 3.91 (1H, s, H-19). Resonances of other protons were observed as overlapping multiplets in the regions 1.16-1.30 (1H-7, 1H-9, 1H-11a, 2H-15) and 1.32-1.53 (1H-1′, 1H-7′, 2H-6, 1H-13, 1H-16a, 2H-21, 2H-22). Table 1 gives the ^{13}C NMR spectrum.

2,3-*Seco*-2,3:19β,28-diepoxy-18α-oleane (8). Tetraol **3** (0.222 g, 0.46 mmol), H_2SO_4/SiO_2 (0.222 g, 3%), and CH_2Cl_2 (5 mL) were mixed in a flat-bottomed flask, stirred vigorously, refluxed for 14 h, and evaporated to dryness. The residue was chromatographed over silica gel (CH_2Cl_2 eluent) to afford colorless crystals (0.165 g, 81%), mp 236.1°C (1°/min). The IR spectrum lacked characteristic bands.

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 0.77 (3H, s, CH_3-30), 0.81 (3H, s, CH_3-23), 0.82 (1H, m, H-5), 0.87 (6H, s, CH_3-24, CH_3-27), 0.91 (3H, s, CH_3-29), 0.85-0.92 (1H, m, H-12a), 1.02 (6H, s, CH_3-25, CH_3-26), 1.11 (1H, ddd, ^2J = 13.0, $J_{15e,16a}$ = 4.3, $J_{15e,16e}$ = 2.5, H-15e), 1.66 (1H, dm, ^2J = 13.1, H-12e), 1.78 (1H, ddd, ^2J = 15.0, $J_{1',2}$ = 4.6, $J_{1',2'}$ = 1.1, H-1′), 3.24 (1H, d, ^2J = 12.6, H-3), 3.41 (1H, d, ^2J = 7.8, H-28), 3.44 (1H, d, ^2J = 12.6, H-3′), 3.51 (1H, br.s, H-19), 3.67 (1H, ddd, $J_{2,1}$ = 12.5, ^2J = 12.0, $J_{2,1'}$ = 4.6, H-2), 3.73 (1H, ddd, ^2J = 12.0, $J_{2',1}$ = 6.8, $J_{2',1'}$ = 1.1, H-2′), 3.75 (1H, dd, ^2J = 7.8, J = 1.5, H-28′). Resonances of other protons were observed as overlapping multiplets in the region 1.16-1.56. Table 1 gives the ^{13}C NMR spectrum.

2,3-*Seco*-2,3-epoxy-18α-olean-19β,28β-diol (9). A suspension of $LiAlH_4$ (0.090 g, 2.37 mmol) in Et_2O (15 mL) was stirred vigorously, treated with a solution of **7** (0.328 g, 0.72 mmol) in CH_2Cl_2 (7 mL), refluxed without admitting moisture ($CaCl_2$ tube) for 8 h, treated with H_2O (0.1 mL) and then NaOH solution (15%, 0.1 mL), H_2O (0.3 mL), and CH_2Cl_2 (50 mL). The precipitate was filtered off. The solvent was distilled off to afford a white powder (0.323 g, 97%), mp 235.1°C (5°/min). IR spectrum (ν, cm^{-1}): 3420 (OH).

PMR spectrum ($CDCl_3$ + DMSO-d_6, 5:1, δ, ppm, J/Hz)*: 0.74 (3H, s, CH_3-23), 0.81 (6H, s, CH_3-24, CH_3-30), 0.84 (3H, s, CH_3-29), 0.85 (3H, s, CH_3-27), 0.95 (3H, s, CH_3-25), 1.02 (3H, s, CH_3-26), 0.75 (1H, m, H-5), 0.84 (1H, m, H-15), 0.90 (1H, m, H-12a), 0.93 (1H, m, H-21e), 1.05-1.15 (2H, m, H-16a, H-22a), 1.44-1.54 (4H, m, H-11e, H-15′, H-18, H-22e), 1.69 (1H, dm, ^2J = 13.0, H-12e), 1.72 (1H, dd, ^2J = 14.0, $J_{1,2}$ = 4.6, H-1), 1.82 (1H, ddd, $^2J = J_{21a,22a} = 13.5$, $J_{21a,22e} = 4.1$, H-21a), 1.95 (1H, ddd, $J_{13,12a} = 13$, $J_{13,18} = 11.2$, $J_{13,12e} = 3.7$, H-13), 3.13 (1H, d, $J_{19,18} = 2.0$, H-19), 3.15 and 3.39 (1H each, d, ^2J = 12.5, H-3), 3.23 and 4.01 (1H each, d, ^2J = 11.4, H-28), 3.59 (1H, ddd, $^2J = J_{2,1'} = 12.1$, $J_{2,1} = 4.6$, H-2), 3.65 (1H, dd, ^2J = 12.1, $J_{2',1'} = 6.5$, H-2′). Resonances of other protons were observed as overlapping multiplets in the region 1.16–1.43. Table 1 gives the ^{13}C NMR spectrum.

*The PMR spectrum of **9** recorded in DMSO-d_6 also showed resonances for OH groups as a broad triplet at 3.98 (J ~ 4, 28-OH) and a broad doublet at 4.15 (J = 4.5, 19-OH).

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REFERENCES

1. W. J. Baas, *Phytochemistry*, **24**, 1875 (1985).
2. Y. Wei, C.-M. Maa, and M. Hattori, *Eur. J. Med. Chem.*, **44**, 4112 (2009).
3. M. Urban, J. Sarek, J. Klinot, G. Korinkova, and M. Hajduch, *J. Nat. Prod.*, **67**, 1100 (2004).
4. M. Urban J. Sarek, I. Tislerova, P. Dzubak, and M. Hajduch, *Bioorg. Med. Chem.*, **13**, 5527 (2005).
5. C. Moiteiro, F. Justino, R. Tavares, M. J. Marcelo-Curto, M. H. Florencio, M. S. J. Nascimento, M. Pedro, F. Cerqueira, and M. M. M. Pinto, *J. Nat. Prod.*, **64**, 1273 (2001).
6. L. Ruzicka, G. P. Frame, H. M. Leicester, M. Liguori, and H. Brungger, *Helv. Chim. Acta*, **17**, 426 (1934).
7. J. Seyden-Penne, *Reductions. The Alumino- and Borohydrides in Organic Synthesis*, Wiley-VCH, New York, 1997, p. 92.
8. D. M. Bailey and R. E. Johnson, *J. Org. Chem.*, **35**, 10, 3574 (1970).
9. S. Brewis, T. G. Halsall, H. R. Harrison, and O. J. R. Hodder, *J. Chem. Soc. D: Chem. Commun.*, 891 (1970).
10. G. A. Molander, J. B. Etter, L. S. Harring, and P.-J. Thorel, *J. Am. Chem. Soc.*, **113**, 8036 (1991).
11. M. Periasamy and M. Thirumalaikumar, *J. Organomet. Chem.*, **609**, 137 (2000).
12. J. V. B. Kanth and M. Periasamy, *J. Org. Chem.*, **56**, 5964 (1991).
13. M. Tudge, H. Mashima, C. Savarin, G. Humphrey, and I. Davies, *Tetrahedron Lett.*, **49**, 1041 (2008).
14. A. R. Katritzky and C. W. Rees, *Comprehensive Heterocyclic Chemistry*, Elsevier, 1997, **7**, 577.
15. F. Chavez, S. Subrez, and M. A. Diaz, *Synth. Commun.*, **24**, 16, 2325 (1994).
16. T.-S. Li, J.-X. Wang, and X.-J. Zheng, *J. Chem. Soc. Perkin Trans. 1*, 3957 (1998).
17. O. Dischendorfer and O. Polak, *Monatsh. Chem.*, **51**, 43 (1929).
18. A. V. Shernyukov, I. Ya. Mainagashev, D. V. Korchagina, Yu. V. Gatilov, N. F. Salakhutdinov, and G. A. Tolstikov, *Dokl. Akad. Nauk*, **429**, 3, 339 (2009); A. V. Shernyukov, I. Ya. Mainagashev, D. V. Korchagina, Yu. V. Gatilov, N. F. Salakhutdinov, and G. A. Tolstikov, *Dokl. Chem.*, **429**, 286 (2009).
19. G. M. Sheldrick, *SHELX-97. Programs for Crystal Structure Analysis (Release 97-2)*, University of Gottingen, Germany, 1997.