Partial Synthesis of Krukovines A and B, Triterpene Ketones Isolated from the Brazilian Medicinal Plant *Maytenus krukovii*

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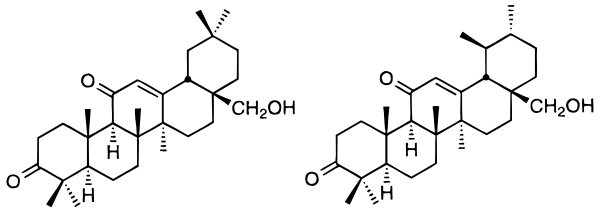
Krukovines A (**1**) and B (**2**), triterpene ketones isolated from the Brazilian medicinal plant "chuchuhuasi" (*Maytenus krukovii*), were synthesized in eight steps from the commercially available oleanolic acid and ursolic acid, respectively.

Many oleanane and ursane triterpenoids are reported to have interesting biological, pharmacological, and medicinal activities similar to those of retinoids and steroids. These include antiinflammatory activity, suppression of tumor promotion, suppression of immunoglobulin synthesis, protection of the liver against toxic injury, induction of collagen synthesis, and induction of differentiation in leukemia or teratocarcinoma cells.[1] Therefore, it is important to supply those triterpenoids with novel structures in sufficient amounts for biological testing. And, in this regard, synthesis rather than isolation from natural sources is more efficient and economical.

Recently, the new triterpene ketones krukovines A and B were isolated from the Brazilian medicinal plant *Maytenus krukovii* A. C. Smith (Celastraceae) (local name "chuchuhuasi"), which is used for the treatment of skin cancer. These interesting compounds were determined to be **1** and **2** based on spectral data.[2] In this paper, we wish to describe the first synthesis of krukovines A and B from the commercially available oleanolic acid and ursolic acid, respectively. Our work confirms the structures proposed for these compounds.



1 **2**

Krukovines A and B have a hydroxymethyl group at C-17 and two carbonyl groups at C-3 and C-11. On the other hand, oleanolic acid and ursolic acid (starting materials) have a carboxyl group at C-17 and a hydroxyl group at C-3. Therefore, the order of protection, deprotection, reduction, and oxidation is very important. Consequently, we adopted the route as shown in Scheme 1.

Methyl 3-[(*tert*-butyldimethylsilyl)oxy]olean-12-en-28-oate (**5**) was prepared in 98% yield with *tert*-butylchlorodimethylsilane and imidazole in DMF[3] from methyl oleanolate (**4**) derived from oleanolic acid (**3**) as reported.[4] $LiAlH_4$ reduction of **5** gave alcohol **6** in 90% yield. Acetylation of **6** with Ac_2O in pyridine gave acetate **7** in 94% yield. Although desilylation of **7** with tetra-*n*-butylammonium fluoride[3] did not give a good result, desilylation of **7** with hydrofluoric acid in MeCN[5] gave hydroxy acetate **8** in 91% yield. Jones' oxidation of **8** gave keto acetate **9** in 98% yield. Allyllic oxidation[6] of **9** gave the α,β-unsaturated ketone **10** in 41% yield. Alkaline hydrolysis of **10** with KOH in MeOH (at room temperature, 30 min) gave krukovine A (**1**) in quantitative yield. Interestingly, reflux conditions gave **1** in only 52% yield because of decomposition of **10**. Similarly, krukovine B (**2**) was synthesized from ursolic acid (**11**) according to the same method. The yields of each step are described in the Experimental Section. ^{1}H- and ^{13}C-NMR spectra of our synthetic krukovines A and B were identical with those of authentic krukovines A and B, respectively. Our synthesis not only confirms the structures proposed for krukovines A and B, but also provides sufficient material for biological testing.

Experimental Section

General Experimental Procedures. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-181 digital polarimeter, and $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. UV and IR spectra were recorded on a Perkin-Elmer Lambda 9 UV/vis/NIR spectrophotometer and a Perkin-Elmer 600 series FTIR spectrophotometer, respectively. ^{1}H- (300 MHz) and ^{13}C- (75 MHz) NMR spectra were recorded on a Varian XL-300 Fourier transform spectrometer. The chemical shifts are reported in δ (ppm) using the δ 7.27 signal of C*H*Cl$_3$ (^{1}H NMR) and δ 77.30 signal of *C*DCl$_3$ (^{13}C NMR) as an internal standard. LRMS and HRMS were obtained on a VG Analytical ZAB 2SE high-field mass spectrometer. The standard workup method was as follows: an organic extract was washed with saturated aqueous $NaHCO_3$ solution (three times) and then with saturated aqueous NaCl solution (three times), dried over anhydrous $MgSO_4$, and filtered.

Methyl 3-[(*tert*-Butyldimethylsilyl)oxy]olean-12-en-28-oate (5). To a stirred solution of methyl oleanolate (**4**) (600 mg, 1.3 mmol) in anhydrous DMF (3 mL) were added *tert*-butylchlorodimethylsilane (378 mg, 2.5 mmol) and imidazole (342 mg, 5.0 mmol). The mixture was stirred at room temperature overnight. It was diluted with a mixture of CH_2Cl_2 and Et_2O (1:2). After the mixture was washed with 5% aqueous HCl (three times), it was worked up according to the standard method. The filtrate was evaporated *in vacuo* to give a residue (839 mg). The residue was subjected to flash column chromatography on Si gel [hexane−EtOAc (7:

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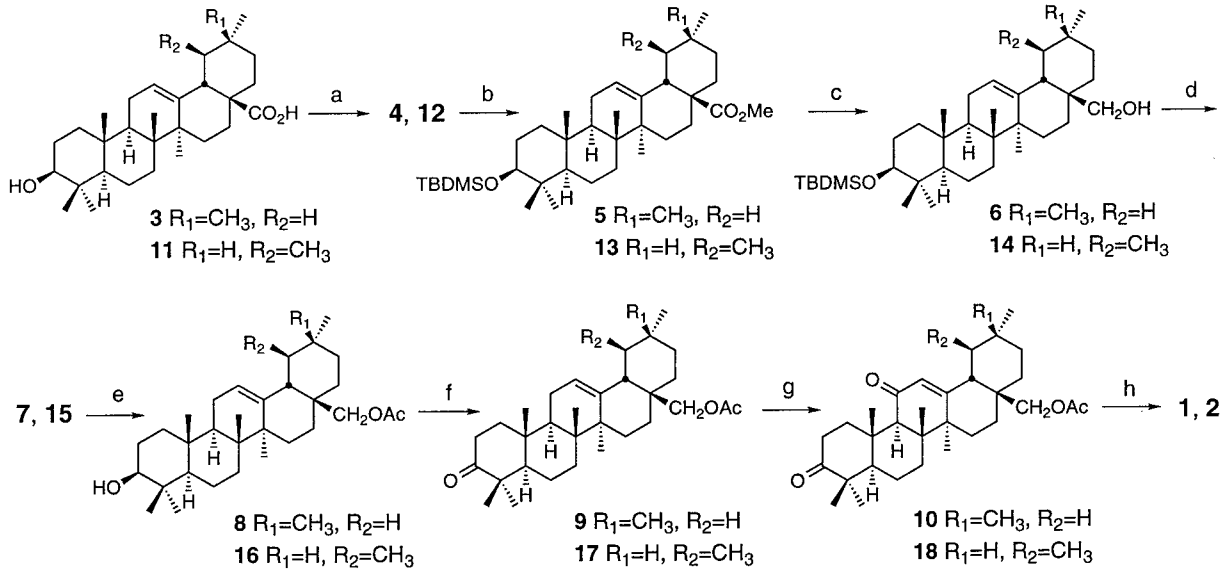
Scheme 1[a]



[a] Key: (a) CH_2N_2/Et_2O/THF; (b) TBDMSCl/imid/DMF; (c) LAH/THF; (d) Ac_2O/pyr; (e) 48% HF/CH_3CN (1:9); (f) Jones; (g) CrO_3/pyr/CH_2Cl_2; (h) KOH/MeOH.

1)] to give the title compound as an amorphous solid (728 mg, yield: 98%): IR (KBr) ν_{max} 2949, 1727, 1472, 1386, 1361, 1254, 1201, 1163, 1099, 1073, 1033, 1004 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.29 (1H, t, J = 3.4 Hz, H-12), 3.63 (3H, s, CO_2CH_3), 3.19 (1H, dd, J = 11.0, 4.8 Hz, H-3), 1.13, 0.93 (each 3H, s, t-CH_3), 0.91 (6H, s, t-CH_3 × 2), 0.89 [9H, s, SiC(CH_3)$_3$], 0.87, 0.75, 0.72 (each 3H, s, t-CH_3), 0.039 [6H, s, Si(CH_3)$_2$]; FABMS (NBA) m/z 585 $[M + H]^+$ (38), 583 (47), 527 (45), 453 (100), 393 (33); HRFABMS m/z 585.4706 $[M + H]^+$ (calcd for $C_{37}H_{64}O_3Si$ + H, 585.4703).

Methyl 3-[(*tert*-Butyldimethylsilyl)oxy]urs-12-en-28-oate (13). The title compound was prepared from methyl ursolate (**12**)[7] (100 mg, 0.21 mmol) according to the same method as for **5** to give an amorphous solid (102 mg, yield: 83%): IR (KBr) ν_{max} 2950, 1727, 1461, 1388, 1359, 1254, 1199, 1142, 1098, 1076, 1004 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.25 (1H, t, J = 3.5 Hz, H-12), 3.61 (3H, s, CO_2CH_3), 3.19 (1H, dd, J = 11.4, 4.8 Hz, H-3), 2.23 (1H, d, J = 11.0 Hz, H-18), 1.08 (3H, s, t-CH_3), 0.96 (3H, br s, H_3-30), 0.92, 0.91 (each 3H, s, t-CH_3), 0.89 [9H, s, SiC(CH_3)$_3$], 0.86 (3H, d, J = 6.0 Hz, H_3-29), 0.75, 0.74 (each 3H, s, t-CH_3), 0.037 [6H, s, Si(CH_3)$_2$]; CIMS (NH_3) m/z 603 $[M + NH_4]^+$, 586 $[M + H]^+$.

3-[(*tert*-Butyldimethylsilyl)oxy]olean-12-en-28-ol (6). To a stirred solution of methyl 3-[(*tert*-butyldimethylsilyl)oxy]urs-12-en-28-oate (**5**) (681 mg, 1.2 mmol) in anhydrous THF (43 mL) was added $LiAlH_4$ (390 mg, 10 mmol) under nitrogen atmosphere at room temperature. The slurry was stirred at room temperature overnight. To the mixture were added H_2O (0.9 mL), 40% aqueous NaOH solution (0.3 mL), and H_2O (0.9 mL), successively. After an insoluble matter was removed by filtration through Celite, the filtrate was evaporated *in vacuo* to give a residue (723 mg). The residue was subjected to flash column chromatography [hexane−EtOAc (6:1)] to give the title compound as an amorphous solid (585 mg, yield: 90%): IR (KBr) ν_{max} 3435, 2950, 1463, 1387, 1361, 1255, 1103, 1077, 1005 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.20 (1H, t, J = 3.5 Hz, H-12), 3.56 (1H, d, J = 10.9 Hz, H-28a), 3.22 (1H, d, J = 10.9 Hz, H-28b), 3.19 (1H, dd, J = 11.2, 4.9 Hz, H-3), 1.17, 0.94, 0.93, 0.91 (each 3H, s, t-CH_3), 0.89 [12H, s, SiC(CH_3)$_3$ and t-CH_3], 0.88, 0.76 (each 3H, s, t-CH_3), 0.042 [6H, s, Si(CH_3)$_2$]; FABMS (NBA) m/z 557 $[M + H]^+$ (9), 556 $[M]^+$ (14), 499 (9), 425 (25), 203 (100); HRFABMS m/z 557.4772 $[M + H]^+$ (calcd for $C_{36}H_{64}O_2Si$ + H, 557.4754).

3-[(*tert*-Butyldimethylsilyl)oxy]urs-12-en-28-ol (14). The title compound was prepared from methyl 3-[(*tert*-butyldimethylsilyl)oxy]urs-12-en-28-oate (**13**) (88 mg, 0.15 mmol) according to the same method as for **6** to give an amorphous solid (74 mg, yield: 89%): IR (KBr) ν_{max} 3456, 2929, 1461, 1387, 1254, 1101, 1069, 1023, 1004 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.14 (1H, t, J = 3.5 Hz, H-12), 3.54 (1H, d, J = 11.0 Hz, H-28a), 3.205 (1H, d, J = 11.0 Hz, H-28b), 3.197 (1H, dd, J = 11.2, 4.9 Hz, H-3), 1.11, 0.99, 0.95 (each 3H, s, t-CH_3), 0.94 (3H, br s, H_3-30), 0.92 (3H, s, t-CH_3), 0.90 [9H, s, SiC(CH_3)$_3$], 0.81 (3H, d, J = 5.9 Hz, H_3-29), 0.76 (3H, s, t-CH_3), 0.04 [6H, s, Si(CH_3)$_2$]; CIMS (NH_3) m/z 558 $[M + H]^+$.

3-[(*tert*-Butyldimethylsilyl)oxy]olean-12-en-28-yl Acetate (7). A mixture of 3-[(*tert*-butyldimethylsilyl)oxy]olean-12-en-28-ol (**6**) (569 mg, 1.0 mmol), Ac_2O (2.8 mL), and pyridine (5.6 mL) was kept at room temperature overnight. After MeOH was added to the mixture to decompose the excess Ac_2O in an ice bath, it was evaporated *in vacuo* to give the title compound as an amorphous solid (576 mg, yield: 94%): IR (KBr) ν_{max} 2950, 1745, 1463, 1386, 1361, 1250, 1230, 1102, 1077, 1042, 1004 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.21 (1H, t, J = 3.5 Hz, H-12), 4.04 (1H, d, J = 11.0 Hz, H-28a), 3.71 (1H, d, J = 11.0 Hz, H-28b), 3.19 (1H, dd, J = 11.1, 4.8 Hz, H-3), 2.06 (3H, s, OCOCH_3), 1.16, 0.95, 0.93, 0.91 (each 3H, s, t-CH_3), 0.89 [12H, s, SiC(CH_3)$_3$ and t-CH_3], 0.88, 0.76 (each 3H, s, t-CH_3), 0.041 [6H, s, Si(CH_3)$_2$]; FABMS (NBA) m/z 599 $[M + H]^+$ (9), 598 $[M]^+$ (15), 539 (18), 467 (25), 407 (30), 203 (100); HRFABMS m/z 599.4883 $[M + H]^+$ (calcd for $C_{38}H_{66}O_3Si$ + H, 599.4859).

3-[(*tert*-Butyldimethylsilyl)oxy]urs-12-en-28-yl Acetate (15). The title compound was prepared from 3-[(*tert*-butyldimethylsilyl)oxy]urs-12-en-28-ol (**14**) (400

mg, 0.72 mmol) according to the same method as for **7** to give an amorphous solid (414 mg, yield: 96%): IR (KBr) ν_{max} 2929, 1743, 1460, 1387, 1360, 1231, 1101, 1069, 1033, 1003 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.14 (1H, t, J = 3.5 Hz, H-12), 4.07 (1H, d, J = 11.0 Hz, H-28a), 3.63 (1H, d, J = 11.0 Hz, H-28b), 3.19 (1H, dd, J = 11.4, 4.8 Hz, H-3), 2.05 (3H, s, OCOCH_3), 1.10, 0.99, 0.94 (6H, s, *t*-CH_3 and H_3-30), 0.91 (3H, s, *t*-CH_3), 0.90 [9H, s, SiC(CH_3)$_3$], 0.82 (3H, d, J = 6.0 Hz, H_3-29), 0.76 (3H, s, *t*-CH_3), 0.039 [6H, s, Si(CH_3)$_2$]; CIMS (NH_3) m/z 617 [M + NH_4]$^+$.

3-Hydroxyolean-12-en-28-yl Acetate (8). To a mixture of 3-[(*tert*-butyldimethylsilyl)oxy]olean-12-en-28-yl acetate (**7**) (485 mg, 0.81 mmol) was added a solution of 48% HF in MeCN (1:9) (11 mL). The slurry was stirred at room temperature overnight. It was diluted with a mixture of CH_2Cl_2 and Et_2O (1:2). After the mixture was washed with H_2O (twice), it was worked up according to the standard method. The filtrate was evaporated *in vacuo* to give a crystalline solid (390 mg). The solid was subjected to flash column chromatography [hexane−EtOAc (2.5:1)] to give the title compound as crystals (357 mg, yield 91%): mp 192−193 °C; IR (KBr) ν_{max} 3496, 2942, 1717, 1465, 1433, 1386, 1364, 1266, 1234, 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.21 (1H, t, J = 3.5 Hz, H-12), 4.04 (1H, d, J = 11.0 Hz, H-28a), 3.71 (1H, d, J = 11.0 Hz, H-28b), 3.23 (1H, dd, J = 10.7, 5.1 Hz, H-3), 2.06 (3H, s, OCOCH_3), 1.17, 1.00, 0.95, 0.93, 0.90, 0.88, 0.80 (each 3H, s, *t*-CH_3); FABMS (NBA) m/z 485 [M + H]$^+$ (15), 484 [M]$^+$ (28), 425 (24), 407 (25), 307 (12), 203 (100); HRFABMS m/z 485.3930 [M + H]$^+$ (calcd for $C_{32}H_{52}O_3$ + H, 485.3995).

3-Hydroxyurs-12-en-28-yl Acetate (16). The title compound was prepared from 3-[(*tert*-butyldimethylsilyl)oxy]urs-12-en-28-yl acetate (**15**) (367 mg, 0.61 mmol) according to the same method as for **8** to give crystals (246 mg, yield 83%): mp 177−178 °C; IR (KBr) ν_{max} 3552, 2922, 1726, 1454, 1384, 1258, 1050, 1039 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.15 (1H, t, J = 3.7 Hz, H-12), 4.07 (1H, d, J = 11.0 Hz, H-28a), 3.63 (1H, d, J = 11.0 Hz, H-28b), 3.23 (1H, dd, J = 10.6, 5.0 Hz, H-3), 2.05 (3H, s, OCOCH_3), 1.11, 1.002, 0.996, 0.95 (each 3H, s, *t*-CH_3), 0.94 (3H, br s, H_3-30), 0.82 (3H, d, J = 5.7 Hz, H_3-29), 0.80 (3H, s, *t*-CH_3); CIMS (NH_3) m/z 503 [M + NH_4]$^+$, 485 [M + H]$^+$.

3-Oxoolean-12-en-28-yl Acetate (9). To a stirred solution of 3-hydroxyolean-12-en-28-yl acetate (**8**) (342 mg, 0.71 mmol) in Me_2CO (28 mL) was added Jones' reagent dropwise until it had a pale brown color. The mixture was stirred at room temperature for 15 min. After most of Me_2CO was evaporated *in vacuo*, H_2O was added to the concentrated mixture. The aqueous mixture was extracted with CH_2Cl_2 (three times). The extract was worked up according to the standard method. The filtrate was evaporated *in vacuo* to give the title compound as an amorphous solid (334 mg, yield: 98%): IR (KBr) ν_{max} 2948, 1741, 1706, 1459, 1384, 1362, 1232, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.23 (1H, t, J = 3.5 Hz, H-12), 4.04 (1H, d, J = 11.0 Hz, H-28a), 3.72 (1H, d, J = 11.0 Hz, H-28b), 2.57 (1H, m, H-2β), 2.36 (1H, m, H-2α), 2.07 (3H, s, OCOCH_3), 1.18, 1.10, 1.07, 1.06, 1.01, 0.90, 0.88 (each 3H, s, *t*-CH_3); FABMS (NBA) m/z 483 [M + H]$^+$ (82), 482 [M]$^+$ (44), 423 (65), 307 (73), 289 (47), 203 (100); HRFABMS m/z 483.3825 [M + H]$^+$ (calcd for $C_{32}H_{50}O_3$ + H, 483.3838).

3-Oxours-12-en-28-yl Acetate (17). The title compound was prepared from 3-hydroxyurs-12-en-28-yl acetate (**16**) (217 mg, 0.45 mmol) according to the same method as for **9** to give an amorphous solid (212 mg, yield: 98%): IR (KBr) ν_{max} 2926, 1740, 1706, 1460, 1384, 1360, 1231, 1032 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.17 (1H, t, J = 3.7 Hz, H-12), 4.07 (1H, d, J = 11.0 Hz, H-28a), 3.64 (1H, d, J = 11.0 Hz, H-28b), 2.56 (1H, m, H-2β), 2.38 (1H, m, H-2α), 2.06 (3H, s, OCOCH_3), 1.11, 1.10, 1.08, 1.06, 1.05 (each 3H, s, *t*-CH_3), 0.94 (3H, br s, H_3-30), 0.82 (3H, d, J = 6.3 Hz, H_3-29); CIMS (NH_3) m/z 501 [M + NH_4]$^+$, 484 [M + H]$^+$; HRFABMS m/z 483.3830 [M + H]$^+$ (calcd for $C_{32}H_{50}O_3$ + H, 483.3838).

3,11-Dioxoolean-12-en-28-yl Acetate (10). To a stirred mixture of chromium trioxide (3.72 g, 37 mmol), dry pyridine (6.0 mL, 74 mmol), and CH_2Cl_2 (25 mL) was added a solution of 3-oxoolean-12-en-28-yl acetate (**9**) (310 mg, 0.64 mmol) in CH_2Cl_2 (12 mL). The mixture was stirred at room temperature for 8.5 h. The brown solution was decanted from the residue, which was washed with Et_2O several times. After the combined organic extract was washed with 5% aqueous NaOH solution (three times) and 5% aqueous HCl (three times), it was worked up according to the standard method. The filtrate was evaporated *in vacuo* to give a residue (223 mg). The residue was subjected to flash column chromatography [hexane−EtOAc (4:1)] to give the title compound as an amorphous solid (130 mg, yield: 41%): UV (EtOH) λ_{max} (log ϵ) 248 (4.11); IR (KBr) ν_{max} 2950, 1742, 1705, 1659, 1619, 1462, 1386, 1364, 1231, 1043, 1001 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.62 (1H, s, H-12), 3.96 (1H, d, J = 11.2 Hz, H-28a), 3.71 (1H, d, J = 11.2 Hz, H-28b), 2.96 (1H, ddd, J = 13.7, 7.1, 4.2 Hz, H-1β), 2.64 (1H, ddd, J = 15.9, 11.2, 7.1, H-2β), 2.42 (1H, s, H-9), 2.35 (1H, ddd, J = 15.9, 6.5, 4.2 Hz, H-2α), 2.27 (1H, dd, J = 13.7, 3.7 Hz, H-18), 2.07 (3H, s, OCOCH_3), 2.02 (1H, ddd, J = 13.9, 13.9, 4.4 Hz), 1.39, 1.26, 1.16, 1.09, 1.06, 0.92, 0.90 (each 3H, s, *t*-CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 217.4 (C-3), 199.5 (C-11), 171.3 (O*C*OCH$_3$), 169.3 (C-13), 128.7 (C-12), 70.4 (C-28), 61.3, 55.7, 48.1, 45.5, 45.1, 43.7, 42.9, 40.1, 37.0, 36.1, 34.5, 34.0, 33.1, 32.3, 31.2, 31.1, 26.6, 26.2, 23.7, 23.6, 22.3, 21.7, 21.2, 19.0, 18.7, 15.9; FABMS (NBA) m/z 497 [M + H]$^+$ (100), 479 (7), 436 (9), 307 (27), 289 (17); HRFABMS m/z 497.3645 [M + H]$^+$ (calcd for $C_{32}H_{48}O_4$ + H, 497.3631).

3,11-Dioxours-12-en-28-yl Acetate (18). The title compound was prepared from 3-oxours-12-en-28-yl acetate (**17**) (100 mg, 0.21 mmol) according to the same method as for **10** to give an amorphous solid (39 mg, yield: 38%): UV (EtOH) λ_{max} (log ϵ) 247 (4.03) nm; IR (KBr) ν_{max} 2930, 1740, 1704, 1657, 1617, 1460, 1386, 1364, 1238, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.56 (1H, s, H-12), 3.97 (1H, d, J = 11.2 Hz, H-28a), 3.63 (1H, d, J = 11.2 Hz, H-28b), 2.93 (1H, ddd, J = 13.4, 7.0, 3.9 Hz, H-1β), 2.66 (1H, ddd, J = 15.9, 11.5, 7.0 Hz, H-2β), 2.41 (1H, s, H-9), 2.35 (1H, ddd, J = 15.9, 6.2, 3.9 Hz, H-2α), 2.06 (3H, s, OCOCH_3), 2.06 (1H, ddd, J = 13.7, 13.7, 4.8 Hz), 1.83 (1H, ddd, J = 13.7, 13.7, 5.1 Hz), 1.33, 1.30, 1.20, 1.10, 1.07 (each 3H, s, *t*-CH_3), 0.97 (3H, br s, H_3-30), 0.83 (3H, d, J = 6.3 Hz, H_3-29); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 217.3 (C-3), 199.0 (C-11), 171.3 (O*C*OCH$_3$), 163.5 (C-13), 131.0 (C-12), 70.7 (C-

28), 61.1, 55.8, 54.3, 48.1, 45.2, 43.9, 40.1, 39.3, 39.2, 37.5, 36.9, 35.3, 34.5, 32.4, 30.4, 26.9, 26.5, 23.3, 21.8, 21.3, 21.2, 20.9, 19.0, 18.5, 17.6, 16.0; CIMS (NH_3) *m/z* 515 $[M + NH_4]^+$, 498 $[M + H]^+$; HRFABMS *m/z* 497.3642 $[M + H]^+$ (calcd for $C_{32}H_{48}O_4 + H$, 497.3631).

28-Hydroxyolean-12-ene-3,11-dione (Krukovine A) (1). A mixture of 3,11-dioxoolean-12-en-28-yl acetate (**10**) (72 mg, 0.14 mmol), KOH (420 mg), and MeOH (4.2 mL) was stirred at room temperature for 30 min. After the mixture was acidified with 5% aqueous HCl, it was extracted with a mixture of CH_2Cl_2 and Et_2O (1:2) (three times). The extract was worked up according to the standard method. The filtrate was evaporated *in vacuo* to afford the crude title compound (66 mg, yield: quantitative) as a crystalline solid. It was recrystallized from MeOH to give the title compound (39 mg) as colorless crystals: mp 233−235 °C; $[\alpha]^{22}_D$ +90.2° (*c* 0.18, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 251 (4.17) nm; IR (KBr) ν_{max} 3438, 2946, 2856, 1703, 1652, 1611, 1458, 1385, 1365, 1259, 1208, 1110, 1064, 1002 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.61 (1H, s, H-12), 3.49 (1H, d, J = 11.0 Hz, H-28a), 3.24 (1H, d, J = 11.0 Hz, H-28b), 2.95 (1H, ddd, J = 13.7, 7.1, 4.2 Hz, H-1β), 2.63 (1H, ddd, J = 15.9, 11.1, 7.1, H-2β), 2.44 (1H, s, H-9), 2.36 (1H, ddd, J = 15.9, 6.6, 4.2 Hz, H-2α), 2.18 (1H, dd, J = 13.4, 4.0 Hz, H-18), 1.96 (1H, ddd, J = 13.7, 13.7, 4.4 Hz), 1.40, 1.26, 1.15, 1.11, 1.07, 0.92, 0.90 (each 3H, s, *t*-CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 217.5 (C-3), 199.7 (C-11), 170.3 (C-13), 128.4 (C-12), 69.9 (C-28), 61.3, 55.7, 48.1, 45.5, 45.2, 43.8, 43.0, 40.0, 37.3, 37.0, 34.5, 34.1, 33.2, 32.3, 31.3, 30.9, 26.7, 26.1, 23.7, 23.6, 21.8, 21.7, 19.1, 18.7, 16.0; FABMS (NBA) *m/z* 455 $[M + H]^+$ (100), 437 (12), 391 (8), 307 (66), 289 (37), 220 (18); HRFABMS *m/z* 455.3521 $[M + H]^+$ (calcd for $C_{30}H_{46}O_3 + H$, 455.3525).

28-Hydroxyurs-12-ene-3,11-dione (Krukovine B) (2). The title compound was prepared from 3,11-dioxours-12-en-28-yl acetate (**18**) (30 mg, 0.60 mmol) according to the same method as for **1** to afford a crystalline solid (27 mg, yield: 98%). It was recrystallized from MeOH to give the title compound (19 mg) as colorless crystals: mp 250−251 °C; $[\alpha]^{22}_D$ +95.2° (*c* 0.10, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 251 (3.96) nm; IR (KBr) ν_{max} 3415, 2979, 2954, 2931, 2873, 2860, 1706, 1633, 1458, 1386, 1316, 1276, 1210, 1136, 1106, 1060, 1048, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.56 (1H, s, H-12), 3.47 (1H, d, J = 11.2 Hz, H-28a), 3.18 (1H, d, J = 11.2 Hz, H-28b), 2.92 (1H, ddd, J = 13.4, 7.1, 3.9 Hz, H-1β), 2.66 (1H, ddd, J = 15.9, 11.2, 7.1 Hz, H-2β), 2.42 (1H, s, H-9), 2.36 (1H, ddd, J = 15.9, 6.4, 3.9 Hz, H-2α), 2.01 (1H, ddd, J = 13.7, 13.7, 4.6 Hz), 1.86 (1H, ddd, J = 13.7, 13.7, 3.8 Hz), 1.33, 1.30, 1.19, 1.10, 1.07 (each 3H, s, *t*-CH_3), 0.97 (3H, br s, H_3-30), 0.82 (3H, d, J = 6.3 Hz, H_3-29); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 217.4 (C-3), 199.2 (C-11), 164.5 (C-13), 130.7 (C-12), 70.0 (C-28), 61.0, 55.7, 54.3, 48.1, 45.2, 44.0, 40.1, 39.5, 39.3, 38.7, 36.8, 35.1, 34.5, 32.4, 30.5, 26.9, 26.6, 22.9, 21.8, 21.4, 20.8, 19.1, 18.5, 17.7, 16.1; EIMS (70 eV) *m/z* 454 $[M]^+$ (56), 439 (16), 426 (24), 289 (100), 248 (74); HREIMS *m/z* 454.3473 $[M]^+$ (calcd for $C_{30}H_{46}O_3$, 454.3447).

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