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Synthesis of Olean-18(19)-ene Derivatives from Betulin

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Abstract—The rare olean-18(19)-ene triterpenoids moradiol and moronic acid were synthesized from betulin, and their antiviral properties were investigated.

Key words: antiviral activity, betulin, lupane and oleanane type triterpenoids, moronic acid, X-ray analysis

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INTRODUCTION

Publications appeared in the middle of the 20th century describing the isolation and structure elucidation of triterpenoids of the olean-18(19)-ene series, morolic acid (**I**) and its derivatives, from the tree *Mora excelsa* [1]. Later, moronic acid (**II**), an oxo derivative of morolic acid, had been isolated from plants of the species *Rhus javanica* [2], *Brazilian propolis* [3], and from the above ground parts of the medicinal plant *Phoradendron reichenbachianum (mistletoe*, *Loranthaceae*) [4]. It has been shown in [5] that the pot liquor of the roots of *Ozoroa mucronata* containing moronic acid as an active component is used in African folk medicine for the treatment of intestinal dyspepsia, dysentery, and diarrhea. Antiviral activity toward herpes simplex HSV-1 (EC_{50} 3.9 μM, therapeutic index, TI = 10.3–16.3) [2] and HIV-1 (EC_{50} < 0.1 μM, TI > 186) [6] have been found for moronic acid. Morolic acid derivatives, in particular amide of 3',3'-dimethylsuccinylmorolic acid with *L*-leucine, are new prospective anti-HIV agents [7, 8]. 3,21-Dioxoolean-18(19)-enoic acid isolated from the plant *Acacia aulacocarpa* became the first natural nonprotein inhibitor of Tie2 kinase [9]. At the same time, the content of morolic and moronic acids in natural sources is extremely low [2–4]; therefore, the development of methods of synthesis of the olean-18(19)-ene derivatives from available raw materials is topical.

RESULTS AND DISCUSSION

Betulin (**III**), a triterpenoid of the lupane series easily accessible from the birch bark [10, 11], was the starting subject in this study. Separate steps of moronic acid (**II**) synthesis from 28-oxobetulone (**IV**) have been given in [1, 12–15]; spectral data are absent for (**V**), (**VIII**), (**X**), (**XI**), and (**XIII**).

The transformation of betulin (**III**) in 28-oxobetulone (**IV**) was carried out in three steps in accordance with our method [16, 17]. The reduction of lactone (**IV**) by two equiv of lithium aluminum hydride in a CH_2Cl_2/Et_2O mixture proceeded with the formation of oleanane-3β,19β,28-triol (**V**) in a 60% yield (scheme). The choice of this solvent system was due to the good solubility of lactone (**IV**) in it and an increased yield of triol (**V**) in comparison with the data in [13]. The complete reduction followed from the data of the ^{13}C NMR spectrum, in which the signals of C3, C19, and C28 atoms were observed at δ 78.9, 74.6, and 64.6 ppm, respectively. The use of 1 equiv of $LiAlH_4$ in the reaction with (**IV**) led to the obtainment of 28-oxoallobetulin (**VI**); the structure if its acetate (**VII**) was confirmed by X-ray analysis (Figs. 1, 2).

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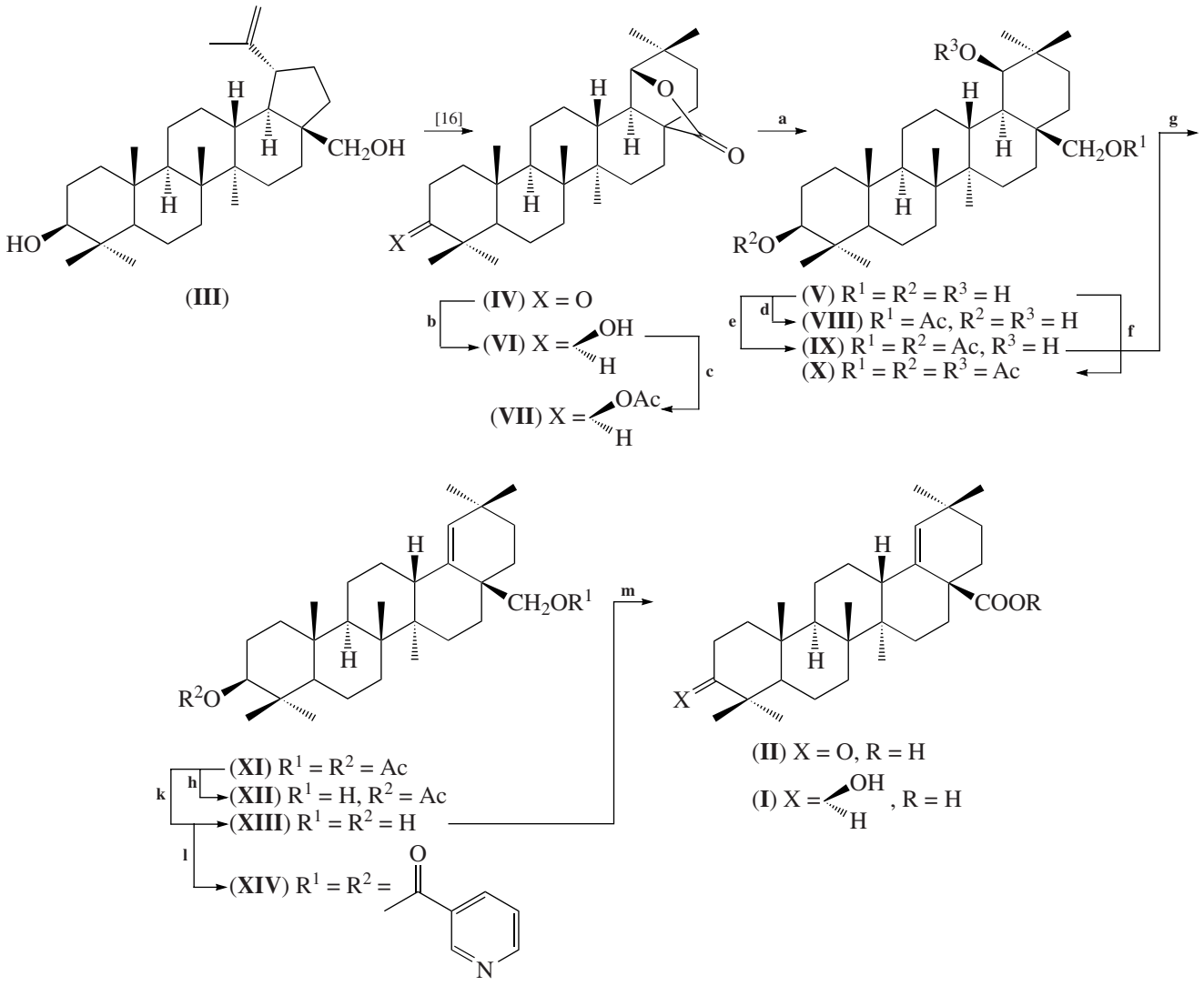

Reagents and conditions: a. 2 equiv $LiAlH_4$, boiling, 3 h; b. 1 equiv $LiAlH_4$, 25°C, 2 h; c. Ac_2O/pyridine; d. AcOH, 100°C, 1 h; e. Ac_2O/pyridine, 100°C, 2.5 h; f. Ac_2O/pyridine, boiling, 3 h; g. $POCl_3$/pyridine; h. 0.1 N NaOH/MeOH; k. 5% KOH/MeOH; l. $C_6H_4NCOCl \cdot HCl$/pyridine; m. Jones reagent.

Scheme.

The different reactivity of triol (**V**) hydroxy groups allowed us to achieve a regioselective actetylation. For example, under conditions similar to betulin acylation [18], the reflux of (**V**) in glacial acetic acid led to 28-acetoxyoleane-3β,19β-diol (**VIII**) with a 95% yield. The interaction of triol (**V**) with acetic anhydride in pyridine under heating on a water bath for 2.5 h resulted in 3β,28-diacetoxyoleanan-19β-ol (**IX**), the structure of which was established by X-ray analysis [19]. The acetylation of (**V**) with acetic anhydride under more drastic conditions, reflux on a sand bath, allowed the obtainment of 3β,19β,28-triacetoxyoleanane (**X**).

Dehydration of (**IX**) in the presence of $POCl_3$ in pyridine resulted in 3β,28-diacetoxyoleanan-18(19)-ene (**XI**) with a 87% yield. The signals of carbon atoms at 18,19-double bond in its ^{13}C NMR spectrum were observed at 134.4 and 139.3 ppm. A selective saponification of diacetate (**XI**) with 0.1 N NaOH solution in methanol led to 3β-acetoxy-28-hydroxy-18(19)-ene (**XII**). The boiling of diacetate (**XI**) in 5% KOH/MeOH helped to achieve an exhaustive deacetylation with the formation of 3β,28-dihydroxyolean-18(19)-ene (**XII**). The acetylation of moradiol (**XIII**) with nicotinic acid chloride led to (**XIV**), an analogue of betulin dinicotinate of the 18(19)-oleanene type (a prospective hepatoprotector and anti HIV agent) [20].

Moronic acid (**II**) was obtained by moradiol oxidation with the Jones reagent in acetone, similar to the

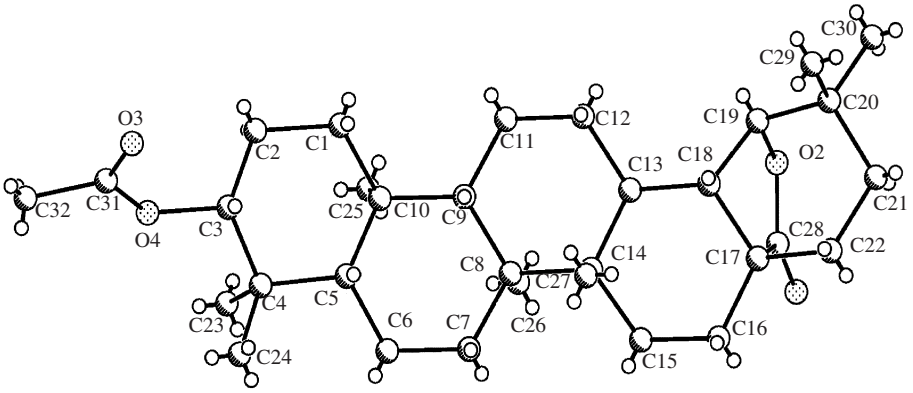

Fig. 1. Structure of 3β-*O*-acetyl-19β,28-epoxy-28-oxo-18α-oleanane (**VII**) according to the data of X-ray analysis.

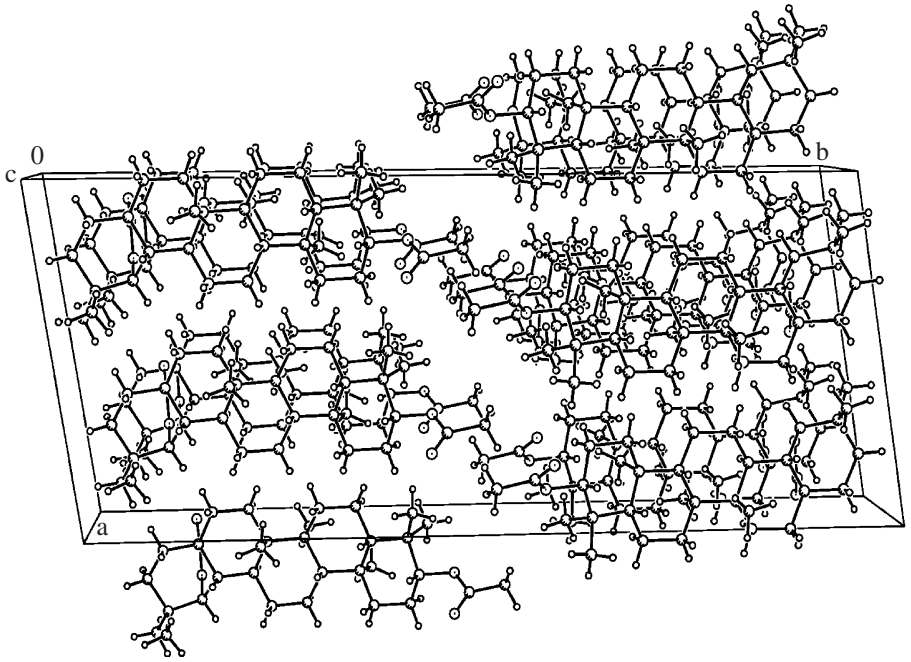

Fig. 2. The spatial packing of 3β-*O*-acetyl-19β,28-epoxy-28-oxo-18α-oleanane (**VII**) according to the data of X-ray analysis.

synthesis of betulonic acid from betulin [16]. Physicochemical constants and spectral characteristics of the obtained acid (**II**) coincided with published data for natural triterpenoid [5, 21]. The total yield of moronic acid (**II**) from lactone (**IV**) was 34%. The availability and cheapness of betulin make this the recommended preparative method for the obtainment of triterpenoids of the olean-18(19)-ene series and their synthetic derivatives.

We had previously established the possibility of inhibition of influenza virus A reproduction by triterpenoids of lupane and oleanane series [16, 22–24]. Hence, we studied the antiviral properties of compounds (**IX**) and (**XI**) on the cell culture with the virus A/Rostock/34 (H7N1). The two substances practically did not affect the virus reproduction at nontoxic concentrations (less than 183.5 and 23.7 μM, respectively). The value of average effective concentration (EC_{50}) of compound (**XI**) cannot be calculated based on the data obtained (> 23.7 μM)—it was 505.3 μM for (**IX**).

EXPERIMENTAL

TLC was carried out on Silufol sheets (Chemapol, Czechia) in a 20 : 1 chloroform–methanol solvent system under detection with a 5% phosphor–tungstic acid

solution in ethanol (2–3 min at 100–120°C). ^{1}H and ^{13}C NMR spectra (δ, ppm, spin-coupling constants, Hz) were registered on a Bruker AM-300 spectrometer (Germany, 300 and 75.5 MHz, respectively) in $CDCl_3$, $SiMe_4$ was an internal standard. Optical rotation was measured on a Perkin-Elmer 241 MC polarimeter in a cuvette of 1 dm length. Mps were determined on a Boetius microscopic table. For ozonization, an Ozone-2K ozonizer (Russia) was used. Column chromatography was carried out on a neutral Al_2O_3 (Reakhim). Betulin (**III**) was obtained by a procedure in [20], and 28-oxoallobetulone (**IV**) synthesized according to [17]. Nicotinic acid chloride hydrochloride was prepared by [25].

Oleanan-3β,19β,28-triol (V). $LiAlH_4$ (80 mg, 2 mmol) preliminarily dissolved in 50 ml of dry diethyl ether was added to a solution of 28-oxoallobetulon (**IV**) (0.46 g, 1 mmol) in dry CH_2Cl_2 (50 ml) at room temperature. The reaction mixture was refluxed for 3 h, surplus $LiAlH_4$ excess was precipitated with 5 ml H_2O, the precipitate was filtered off, the organic layer was washed with water (3 × 20 ml), dried with Na_2SO_4, and evaporated in the vacuum of a water jet pump. The following results were observed: the yield of white (**V**) was 0.28 g (60%); R_f 0.30; mp 283–284°C (EtOH), $[\alpha]_D^{20}$ + 23.0° (*c* 1.00, $CHCl_3$) (lit. [13]: mp 296–298°C, $[\alpha]_D^{20}$ + 24°); ^{1}H NMR: 0.76, 0.85, 0.93, 0.95, 0.99, 1.04 (21 H, 6 s, 7CH_3), 1.20–2.00 (27 H, m, CH_2, CH), 3.18–3.23 (1 H, m, H3), 3.35 (1 H, br s, H19), 3.45 and 4.15 (1 H each, two d, *J* 12, H28); ^{13}C NMR: 14.6, 15.3, 15.8, 16.0, 18.3, 20.9, 24.4, 25.8, 26.7, 27.3, 27.9, 27.9, 27.9, 30.7, 32.5, 33.9, 34.5, 35.2, 37.1, 37.7, 38.7, 38.9, 39.8, 41.0, 42.3, 50.1, 55.3, 64.6 (C28), 74.6 (C19), 78.9 (C3). Found, %: C 78.52; H 11.48. $C_{30}H_{52}O_3$ (M_r 460.738). Calculated, %: C 78.21; H 11.38.

3β-Acetoxy-19β,28-epoxy-28-oxo-18α-oleanane (VII) was obtained from 28-oxoallobetulone (**IV**) (0.47 g, 1 mmol) similarly to (**V**) at room temperature with the use of equimolar quantity (40 mg) of $LiAlH_4$. The resulting (**VI**) was further boiled for 3 h in a mixture of 10 ml Ac_2O and 15 ml of dry pyridine, the solution was poured out in 50 ml of 5% HCl, and the precipitate was filtered, washed, dried, and crystallized from EtOH to give (**VII**). The following results were observed: a yield of 0.36 g (76%), R_f 0.56; mp 302–303°C, $[\alpha]_D^{20}$ + 23.4° (*c* 1.00, $CHCl_3$) (lit. [15]: mp 360°C, $[\alpha]_D^{20}$ + 54.3°); ^{1}H NMR: 0.86, 0.93, 0.94, 1.01, 1.05 (15 H, 5 s, 5CH_3), 1.15–2.00 (30 H, m, CH_2, CH), 2.03 (3 H, s, OAc), 3.80 (1 H, s, H19), 4.60 (1 H, br s, H3); ^{13}C NMR: 13.6, 15.3, 15.5, 16.4, 18.1, 21.0, 21.2, 24.0, 25.5, 26.9, 27.3, 27.8, 27.9, 29.1, 31.9, 32.3, 33.5, 33.7, 35.9, 37.2, 38.8, 38.9, 39.8, 40.5, 46.1, 46.7, 51.3, 55.5, 81.2 (C3), 85.9 (C19), 171.2, 179.8 (C28). Found, %: C 76.81; H 10.23. $C_{32}H_{50}O_4$ (M_r 498.743). Calculated, %: C 77.06; H 10.10.

X-ray analysis of 3β-acetoxy-19β,28-epoxy-28-oxo-18α-oleanane (VII). Colorless prism-like crystals ($C_{32}H_{50}O_4$, *M* 498.72) monoclinic, at 120 K *a* 13.255(3) Å, *b* 6.424(1) Å, *c* 32.500(7) Å, β 98.937(4), *V* 2734(1) Å^3, spatial group *C*2, *Z*4, d_{calc} 1.212 g/cm^{-3}. An experimental set of 8182 reflections was obtained on a diffractometer Bruker SMART CCD area detector at 120 K (λMo-K_α irradiation, $2\theta_{max}$ 54.0°) from a monocrystal with the size 0.30 × 0.13 × 0.10 mm. After the averaging of equivalent reflections, 3256 independent reflections (R_{int} 0.1603) were obtained which are used for the calculation and refinement of structure. Absorption (μ 0.077 mm^{-1}) was not taken into account. The structure is solved by a direct method, all nonhydrogen atoms were localized from subtractive syntheses of electronic density and refined by F_{hkl}^2 in anisotropic approximation. All hydrogen atoms were placed in geometrically calculated positions and taken into account at refinement in a rider model with U(H) = 1.2 U(C), where U(C) is the equivalent temperature factor of carbon atom to which the corresponding H atom is bound. The final value of error factors are as follows: *R*1 = 0.0560 (calculated from F_{hkl} for 2028 reflections with $I > 2\sigma(I)$), wR2 = 0.1569 (calculated from F_{hkl}^2 for all 3256 reflections), and GOF = 1.014, 325 refined parameters. All the calculations were carried out using the program set SHELXTL PLUS 5. Coordinates of atoms and temperature factors are deposited in the Cambridge bank of the structural data (CCDC 640543) http://www.ccdc.cam.ac.uk/products/csd/request/.

28-Acetoxyoleanane-3β,19β-diol (VIII). A solution of (**V**) (0.46 g, 1 mmol) in 15 ml of glacial AcOH was heated at 100°C with a reflux condenser for 1 h. The reaction mixture was poured out in 50 ml of cold water; the precipitate was filtered, washed, dried, and chromatographed on a column eluted by chloroform. The following results were observed: the yield of (**VIII**) was 0.44 g (95%); R_f 0.60; mp 211–212°C ($CHCl_3$–MeOH), $[\alpha]_D^{20}$ + 20° (*c* 1.00, $CHCl_3$)); ^{1}H NMR: 0.76, 0.83, 0.92, 0.98, 0.99, 1.05 (21 H, 6 s, 7CH_3), 1.20–1.90 (24 H, m, CH_2, CH), 2.03 (3 H, s, OAc), 3.15–3.25 (1 H, m, H3), 3.30 (1 H, br s, H19), 3.75 (2 H, t, *J* 6, C19O<u>H</u>), 4.30 and 4.60 (2 H, two d, *J* 12, H28); ^{13}C NMR: 14.6, 15.3, 15.8, 16.0, 18.2, 20.8, 20.9, 24.5, 25.6, 26.3, 27.3, 27.7, 27.9, 29.4, 31.3, 31.6, 32.6, 33.6, 35.2, 36.9, 37.1, 38.7, 38.8, 41.0, 42.0, 42.6, 50.1, 55.4, 62.5 (C28), 74.4 (C19), 78.9 (C3), 171.2. Found, %: C 76.13, H 10.68. $C_{32}H_{54}O_4$ (M_r 502.775). Calculated, %: C 76.45, H 10.83.

3β,28-Diacetoxyoleanan-19β-ol (IX). A solution of (**V**) (0.46 g, 1 mmol) in 15 ml of dry pyridine and 10 ml of Ac_2O was heated on a water bath for 2.5 h. The reaction mixture was poured out in 50 ml of 5% HCl solution; the precipitate was filtered, washed, dried, and chromatographed on a Al_2O_3 column eluted with chlo-

roform. The following results were observed: the yield of (**IX**) was 0.43 g (93%); R_f 0.85; mp 245–246°C ($CHCl_3$–MeOH), $[\alpha]_D^{20}$ + 22° (*c* 1.00, $CHCl_3$) (lit. [13]: mp 240–242.5°C, $[\alpha]_D^{20}$ + 22°); ^{1}H NMR: 0.73, 0.84, 0.90, 0.95, 1.03 (21 H, 5 s, 7 CH_3), 1.20–1.80 (25 H, m, CH_2, CH), 2.02 and 2.03 (6 H, 2 s, 2 OAc), 3.30 (1 H, br s, H19), 4.30 and 4.60 (2 H, two d, *J* 12, H28), 4.45–4.50 (1 H, m, H3); ^{13}C NMR: 14.6, 15.8, 16.1, 16.4, 18.1, 20.7, 21.0, 21.2, 23.6, 24.4, 25.5, 26.3, 27.7, 27.8, 29.3, 31.3, 31.5, 32.4, 33.7, 35.1, 37.0, 37.7, 38.3, 40.9, 41.9, 42.5, 42.9, 50.0, 55.4, 62.5 (C28), 74.4 (C19), 80.9 (C3), 170.9, 171.3. Found, %: C 75.20, H 10.56. $C_{34}H_{56}O_5$ (M_r 544.811). Calculated, %: C 74.96, H 10.36.

3β,19β,28-Triacetoxyoleanane (X). A solution of (**V**) (0.46 g, 1 mmol) in dry pyridine (15 ml) and Ac_2O (10 ml) was refluxed on a sand bath for 3 h and the product (**X**) was isolated as described in the above experiment. The following results were observed: a yield of 0.43 g (93%); R_f 0.95; mp 216–217°C ($CHCl_3$–MeOH), $[\alpha]_D^{20}$ + 24.5° (*c* 1.00, $CHCl_3$). (lit. [13]: mp 242–244°C); ^{1}H NMR: 0.80, 0.83, 0.93, 0.98, 1.00 (21 H, 5 s, 7CH_3), 1.10–1.70 (24 H, m, CH_2, CH), 2.03, 2.05, and 2.09 (9 H, 3 s, 3 OAc), 4.25 and 4.53 (2 H, two d, *J* 11, H28), 4.47 (1 H, dd, *J* 4, 11, H3), 4.76 (1 H, s, H19); ^{13}C NMR: 14.8, 15.7, 16.0, 16.4, 18.1, 20.7, 21.0, 21.2, 21.3, 23.6, 24.1, 25.3, 26.1, 27.7, 27.8, 30.1, 31.3, 31.4, 32.8, 33.7, 35.2, 37.0, 37.1, 37.7, 38.3, 40.9, 42.1, 42.2, 50.0, 55.4, 61.8 (C28), 76.4 (C19), 80.8 (C3), 170.3, 170.9, 171.3. Found, %: C 73.80, H 9.64. $C_{36}H_{58}O_6$ (M_r 586.848). Calculated, %: C 73.68, H 9.96.

3β,28-Diacetoxyolean-18(19)-ene (XI). Phosphorus oxychloride (2.2 ml) was added dropwise to a solution of (**IX**) (0.54 g, 1 mmol) in dry pyridine (20 ml), and the reaction mixture was refluxed for 3 h. The cooled reaction mixture was carefully poured out on 50 g of ice, a precipitate was filtered, washed with water, dried, and chromatographed on a column eluted with benzene. The following results were observed: the yield of compound (**XI**) was 0.47 g (87%); R_f 0.90; mp 272–273°C ($CHCl_3$–MeOH), $[\alpha]_D^{20}$ + 26.5° (*c* 1.00, $CHCl_3$) (lit. [1]: mp 273°C; $[\alpha]_D^{20}$ + 23°; ^{1}H NMR: 0.76, 0.83, 0.83, 0.90, 0.95, 0.96, 1.04 (21 H, 6 s, 7CH_3), 1.10–1.90 (23 H, m, CH_2, CH), 2.00 and 2.01 (6 H, 2 s, 2 OAc), 3.45 and 3.60 (1 H each, two d, *J* 10.7, H28), 4.43 (1 H, dd, *J* 6, 9, H3), 5.05 (1 H, br s, H19). ^{13}C NMR: 14.9, 16.3, 16.6, 16.9, 18.5, 21.4, 21.4, 24.0, 25.5, 26.6, 27.7, 28.0, 29.9, 30.7, 31.5, 31.8, 32.5, 33.6, 34.9, 37.5, 38.1, 39.0, 39.1, 39.9, 41.2, 43.4, 51.4, 55.9, 65.5 (C28), 81.1 (C3), 134.4 (C18), 139.3 (C19), 171.0, 171.2. Found, %: C 77.95, H 10.61. $C_{34}H_{54}O_4$ (M_r 526.797). Calculated, %: C 77.52, H 10.33.

3β-Acetoxy-28-hydroxyolean-18(19)-ene (XII). A 0.1 N NaOH/MeOH (10 ml) was added to (**XI**) (0.52 g, 1 mmol) in benzene (15 ml). The solution was kept for 16 h at room temperature and neutralized by a cation exchanger KU-2-8 (H^+-form). The product was chromatographed on a column eluted with benzene. The following results were observed: the yield of (**XII**) was 0.37 g (72%); R_f 0.65; mp 232–233°C ($CHCl_3$–MeOH); $[\alpha]_D^{20}$ + 7° (*c* 1.00, $CHCl_3$) (lit. [1]: mp 282–283°C; $[\alpha]_D^{20}$ + 5°; ^{1}H NMR: 0.77, 0.80, 0.88, 0.93, 0.94, 1.04 (21 H, 6 s, 7CH_3), 1.20–1.70 (25 H, m, CH_2, CH), 2.00 (3 H, s, OAc), 3.45 and 3.55 (1 H each, two d, *J* 10.7, H28), 4.55 (1 H, dd, *J* 9.2, 6.1, H3); ^{13}C NMR: 14.8, 16.3, 16.6, 16.9, 18.5, 21.4, 21.4, 24.0, 26.6, 27.7, 28.0, 29.8, 30.7, 31.5, 31.8, 32.5, 33.6, 34.9, 37.5, 38.1, 39.0, 39.1, 39.9, 41.2, 43.5, 51.4, 55.8, 65.4 (C28), 81.1 (C3), 134.3 (C18), 139.3 (C19), 171.0. Found, %: C 79.59, H 11.15. $C_{32}H_{52}O$ (M_r 484.760). Calculated, %: C 79.29, H 10.81.

3β,28-Dihydroxyolean-18(19)-ene (moradiol) (XIII). A solution of (**XI**) (0.51 g, 1 mmol) in benzene (50 ml) and 5% KOH/MeOH (30 ml) was refluxed for 5 h. The reaction mixture was neutralized with 5% HCl and poured out in 200 ml of water. The precipitate was filtered, washed with water, dried, and chromatographed on column eluted with benzene. The following results were observed: a yield of (**XIII**) 0.46 g (90%); R_f 0.43; mp 248–249°C ($CHCl_3$–MeOH), $[\alpha]_D^{20}$ –17° (*c* 1.00, $CHCl_3$) (lit. [1]: mp 220°C, $[\alpha]_D^{20}$ –11°); ^{1}H NMR: 0.77, 0.78, 0.88, 0.95, 0.98, 1.06 (21 H, 6 s, 7CH_3), 1.10–1.85 (25 H, m, CH_2, CH), 3.21 (1 H, dd, *J* 5.5, 11, H3), 3.47 and 3.65 (2 H, two d, *J* 11, H28), 5.15 (1 H, s, H19); ^{13}C NMR: 14.8, 15.6, 16.1, 16.6, 18.2, 20.9, 25.3, 26.2, 27.4, 27.9, 29.8, 30.4, 30.9, 31.3, 31.7, 32.5, 33.3, 34.6, 37.2, 38.6, 38.9, 39.5, 40.8, 43.5, 51.4, 55.8, 65.4 (C28), 78.9 (C3), 134.5 (C19), 138.6 (C18). Found, %: C 81.02, H 11.45. $C_{30}H_{50}O_2$ (M_r 442.723). Calculated, %: C 81.39, H 11.38.

3β,28-Di-*O*-nicotinoyllolean-18(19)-ene (XIV). A freshly prepared nicotinic acid chloride hydrochloride (0.43 g, 3 mmol) was added under stirring and cooling (0–5°C) to a solution of (**XIII**) (0.44 g, 1 mmol) in a mixture of anhydrous pyridine (5 ml) and tributylamine (5 ml). The mixture was allowed to warm to room temperature and additionally stirred for 4 h. The reaction mixture was poured out in 50 ml of cold water, acidified with HCl, and extracted with chloroform. The extract was washed with water and 5% HCl, then again with water, dried with Na_2SO_4, and evaporated in a vacuum. The following results were observed: the yield of (**XIV**)

was 0.39 g (90%); R_f 0.45; mp 135–138°C ($CHCl_3$–MeOH); ^{1}H NMR: 0.79, 0.91, 0.95, 0.99, 1.08 (21 H, 6 s, 7CH_3), 1.10–1.80 (23 H, m, CH_2, CH), 4.25 and 4.45 (2 H, two d, *J* 11, H28), 4.75 (1 H, m, H3), 5.13 (1 H, s, H19), 7.25 and 7.35 (2 H, two dd, *J* 3.8, 4.7, H5'), 8.20 and 8.28 (2 H, two ddd, *J* 4.7, 1.6, 1.7, H4'), 8.65 and 8.70 (2 H, two t, *J* 4.1, H6'), 9.14 and 9.18 (2 H, two dd, *J* 1.8, 5.9, H2'); ^{13}C NMR: 14.7, 15.2, 16.1, 16.7, 18.1, 21.0, 25.3, 26.2, 27.4, 28.0, 29.3, 30.7, 30.8, 31.4, 32.2, 32.7, 33.5, 37.2, 38.0, 38.2, 38.6, 38.9, 40.8, 43.2, 51.0, 55.6, 65.8 (C28), 82.3 (C3), 123.2, 123.2, 126.3, 126.7, 133.9 (C19), 136.9, 136.9, 137.8 (C18), 150.9, 150.9, 153.2, 153.3, 164.9, 165.0. Found, %: C 77.48, H 8.34, N 4.04. $C_{42}H_{56}N_2O_4$ (M_r 652.914). Calculated, %: C 77.2, H 8.64, N 4.29.

3-Oxoolean-18(19)-en-28-oic (moronic) acid (II). A freshly prepared Jones reagent (6.25 ml) was added to a solution of (**XIII**) (0.46 g, 1 mmol) in 30 ml of acetone. The reaction mixture was stirred for 4 h at 0°C, 2.5 ml MeOH was added, the solvent was evaporated in a vacuum, and the residue was diluted with 50 ml of water. The precipitate was filtered, washed with water, dried, and chromatographed on a column with the crushed activated charcoal, and eluting with benzene. The following results were observed: a yield of (**II**) 0.36 g (78%); R_f 0.46; mp 213–214°C (EtOH), $[\alpha]_D^{20}$ + 33° (*c* 1.00, $CHCl_3$) (lit. mp 210–212°C, $[\alpha]_D^{20}$ + 29° [5]; mp 222°C, $[\alpha]_D^{20}$ + 29° [21]); ^{1}H NMR: 0.78, 0.93, 0.97, 1.00, 1.02, 1.05, 1.08 (21 H, 7 s, 7CH_3), 1.10–2.20 (23 H, m, CH_2, CH), 2.50–2.55 (1 H, m, H2), 5.10 (1 H, s, H19); ^{13}C NMR: 14.7, 15.7, 16.4, 19.5, 20.8, 21.4, 25.9, 26.7, 29.0, 29.2, 30.2, 31.9, 33.1, 33.3, 33.4, 33.6, 33.9, 36.8, 39.7, 40.4, 41.3, 42.4, 47.1, 47.8, 50.3, 54.7, 133.3 (C19), 136.4 (C18), 181.9 (C28), 218.3 (C3). Found, %: C 79.40, H 10.56. $C_{30}H_{46}O_3$ (M_r 454.690). Calculated, %: C 79.25, H 10.20.

The antiviral properties of (IX) and (XI) were investigated with an influenza virus on a fibroblast culture of hen embryos by the method of plaque reduction of A/FPV/Rostock/34 (H7N1) as described earlier [24]. The substances under study were preliminarily dissolved in 10% ethanol and then twofold successive serial dilutions were prepared on the support medium 199 (Sigma Chemical Co.). As a quantitative criterion of the observable antiviral action, a decrease in the virus titer was determined in comparison with the control. The 50% effective concentrations (EC_{50}) of the researched substances under study were also calculated. The maximal tolerable concentrations of the compounds were determined after the incubation with a not infected cell culture for 72 h at 37°C.

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