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Synthesis, Structure, and Acylation of Dihydroquinopimaric Acid Hydroxy Derivatives

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Abstract—Reduction conditions of methyl dihydroquinopimarate with sodium borohydride and lithium aluminum hydride were established. As a result of the reduction 14β-hydroxy, 17α-hydroxy, 14β,17α-dihydroxy, and 14β,17α,21α-trihydroxy derivatives were obtained. The structure of methyl esters of 14β-acetoxy- and 17α-hydroxydihydroquinopimaric acid was established by XRD and NMR methods. Mono-, di-, and triacylates were obtained from the diterpene alcohols.

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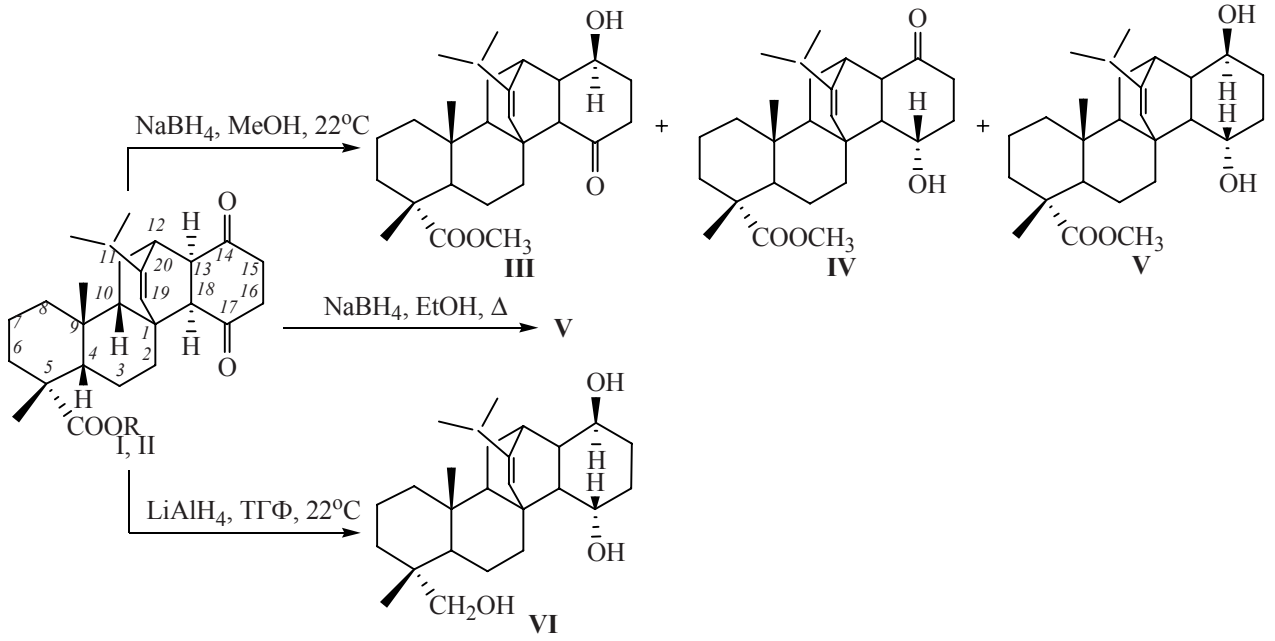
Resin acids and their derivatives have found medicinal and industrial use [1, 2]. Proceeding from levopimaric acid, the main metabolite of the galipot of the pine *Pinus Silvestris,* various diene adducts have been obtained [3] whose modification at the functional groups is attractive for introducing various pharmacophoric moieties. The quinopimaric acid, the adduct of levopimaric acid and p-benzoquinone, was involved mainly into reactions proceeding with the changes in the framework (retrodiene reaction and thermal cleavage [4, 5], conversion into a

Scheme 1.



R = H (**I**), CH_3 (**II**).

cyclopentanonepimaric acid [6] etc.). The publications on the synthetic transformations of dihydroquinopimaric acid (**I**) are virtually absent. Here we report on the reduction of the carbonyl (C^{14}, C^{17}) and carboxy (C^{21}) groups of the dihydroquinopimaric acid and on the acylation of alcohols thus obtained.

The reduction of methyl dihydroquinopimarate (**II**) with sodium borohydride in methanol at room temperature occurred with the complete conversion of the initial compound leading to the formation of a mixture of hydroxy derivatives **III–V** (Scheme 1). The precipitate formed in the course of the reaction was alcohol **III**. On subjecting the mother liquor to column chromatography the alcohols **III–V** were obtained in the individual state. The overall yield of ketoalcohol **III** was 51%, compounds **IV** and **V** were obtained in 15 and 24% yields respectively. The structures of ketol **IV** (Fig. 1) and ketol acetate **VII** (Fig. 2) were established by XRD analysis. The data obtained showed that ketol **III** was 14β-hydroxy isomer, and ketol **IV** was 17α-hydroxy isomer.

The assignment of carbon and proton signals in the NMR spectra of methyl 14β-hydroxy-14-deoxodihydroquinopimarate (**III**) was performed with the use of calculations by additive schemes, by interpretation of the ^{13}C NMR spectrum recorded with the modulation of the CH-coupling constants, and by registering 2D CH-correlation spectra. According to the map of the proton-carbon spectrum the protons H^{13}, H^{18}, H^{16} belonging to atoms C^{13}, C^{18}, C^{16} with the chemical shifts δ 48.0, 61.9, and 36.6 ppm respectively appeared as a multiplet in the region δ 2.00–2.51 ppm, and two protons $H^{15a,\varepsilon}$ at the atom C^{15} (δ 36.2 ppm), gave rise to a multiplet in the region δ 1.72–1.90 ppm. The signals from protons H^{12} and H^{19} attached to the atoms C^{12} and C^{19} with the chemical shifts δ 35.1 and 124.1 ppm respectively were observed as broadened signals at δ 2.68 and 5.55 ppm. The signal of proton H^{14} (C^{14}, δ 68.2 ppm) appeared at δ 3.90 ppm as a doublet of triplets ($J_{14,15a}$ 5.0, $J_{14,15\varepsilon}$ 9.5, $J_{14,13}$ 4.8 Hz) due to coupling with protons $H^{15a,\varepsilon}$ and H^{13}.

The characteristic signals in the NMR spectra of methyl 17α-hydroxy-17-deoxodihydroquinopimarate (**IV**) are broadened signals of atom C^{17} at δ 64.8 ppm and of proton H^{17} at δ 4.16 ppm.

In reaction of methyl dihydroquinopimarate (**II**) with sodium borohydride in ethanol at boiling only 14β,17α-diol **V** was obtained in 86% yield (after recrystallization from methanol). The NMR spectra of diol **V** contain the characteristic broadened signals of protons H^{14} and H^{17} at δ 3.85 and 4.16 ppm (the corresponding signals of atoms C^{14} and C^{17} appear at δ 67.9 and 65.0 ppm).

After the reduction of dihydroquinopimaric acid (**I**) with $LiAlH_4$ in anhydrous THF at room temperature 14β,17α,21α-triol **VI** was isolated in 82% yield (on recrystallization from acetone) (Scheme 1). The exhaustive reduction was confirmed by the signals of atoms C^{14}, C^{17}, and C^{21} at δ 67.9, 64.9, and 71.9 ppm in the ^{13}C NMR spectrum. In the ^{1}H NMR spectrum the broadened signals of protons H^{14} and H^{17} were observed at δ 3.83 and 4.11 ppm, the signals of protons H^{21} appeared as doublets at δ 3.10 and 3.40 ppm.

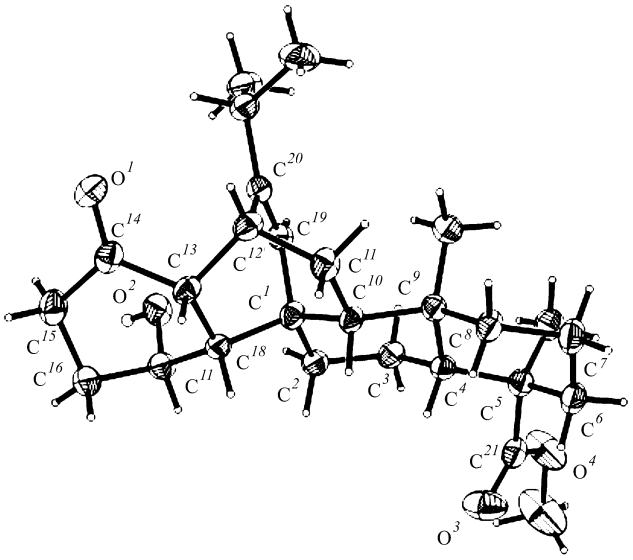


Fig. 1. Structure of methyl 17α-hydroxy-17-deoxodihydroquinopimarate (**IV**).

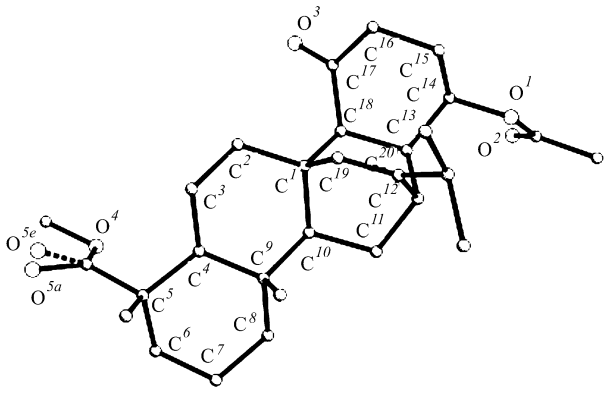


Fig. 2. Structure of methyl 14β-acetoxy-14-deoxodihydroquinopimarate (**VII**).

Alcohols **III, V**, and **VI** were acylated with acid anhydrides and chlorides (Scheme 2). By reactions with acid anhydrides in pyridine we obtained acetates **VII, XII**, and **XV**, hemisuccinates **VIII, XIII**, and **XVI**, and hemiphthalate **IX** in 67–87% yields. After the purification by the column chromatography of the products of reactions between alcohols **III, V**, and **VI** with aromatic acid chlorides we isolated 14β-O-cinnamate **X** and nicotinates **XI, XIV**, and **XVII** in 65–71% yields.

In the ^{13}C NMR spectra of acylates the characteristic signals are those of the carbonyl atoms $C^{1'}$, $C^{1''}$, $C^{1'''}$ at δ 169.9–178.2 ppm. In the ^{1}H NMR spectrum of hemisuccinate **VIII** the protons $H^{2'}$, $H^{3'}$ gave rise to a characteristic multiplet at δ 2.42–2.60 ppm. In the NMR spectra of compounds **IX–XI** the signals of the aromatic substituent were located at δ_C 123–152 ppm and δ_H 7.26–9.22 ppm. In the spectra of 14,17-disubstituted and 14,17,21-trisubstituted acylates the signals of atoms C^{14}, C^{17}, C^{21} appeared downfield with respect to the chemical shifts of these atoms in the spectra of initial alcohols.

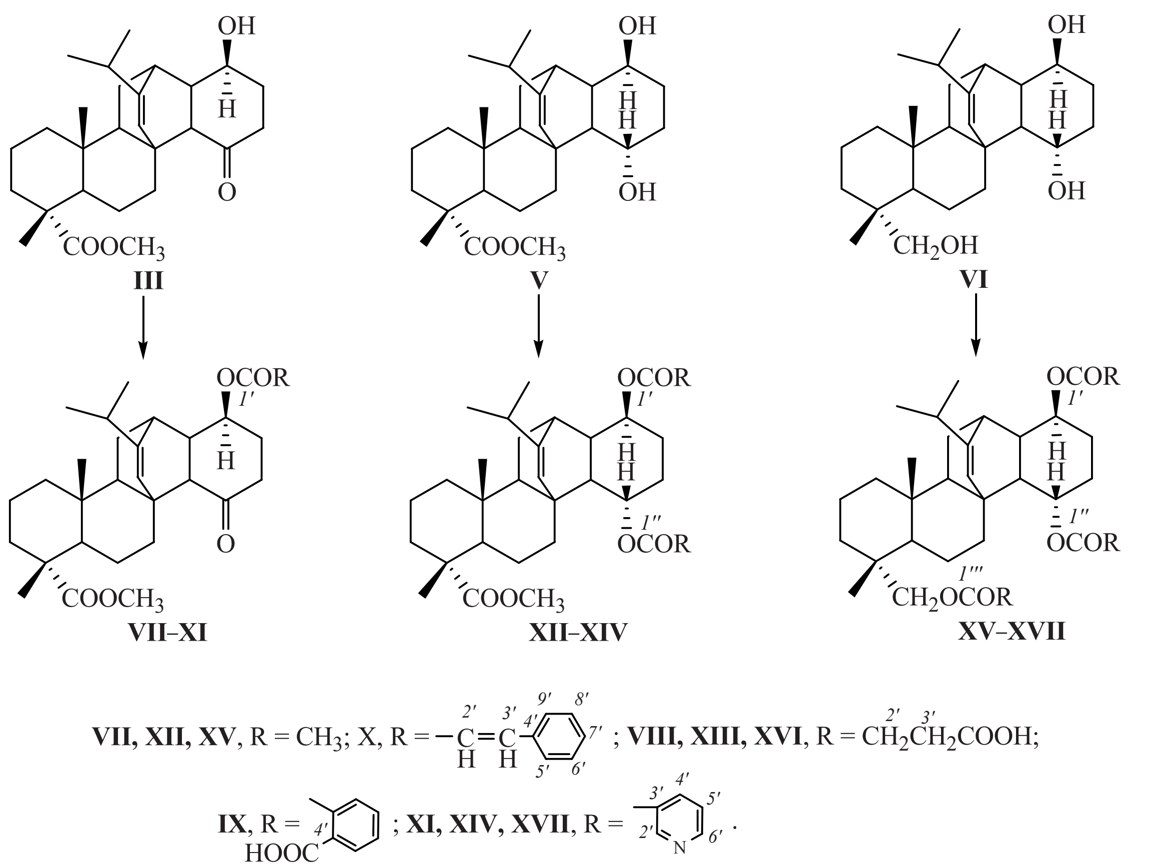
Hence we developed methods of preparation of 14β-hydroxy, 17α-hydroxy, 14β,17α-dihydroxy, and 14β,17α,21α-trihydroxy derivatives of dihydroquinopimaric acid and of their acylation.

EXPERIMENTAL

^{13}C and ^{1}H NMR spectra were registered on a spectrometer Bruker AM-300 (75.5 and 300 MHz respectively), internal reference TMS. The optical rotation was measured on a polarimeter Perkin-Elmer MC-241 from solutions in $CHCl_3$. Melting points were measured on a Boëtius heating block. TLC analysis was performed on Silufol plates (Chemapol, Czechia), eluent chloroform–acetone, 20:1. The spots were visualized by 10% ethanol solution of phosphotungstic acid followed by heating at 100–120°C for 2–3 min. Dihydroquinopimaric acid (**I**) and methyl dihydroquinopimarate (**II**), chlorides of nicotinic and cinnamic acids were prepared by published procedures [7, 8].

Reduction of methyl dihydroquinopimarate (**II**). To a solution of 1 mmol (0.43 g) of compound **II** in 10 ml of MeOH was added by portions 2.5 mmol (0.1 g) of $NaBH_4$. The reaction mixture was stirred at room

Scheme 2.



temperature for 2 h. Compound **III** precipitated in the course of the process was filtered off, dried, and crystallized from methanol. The mother liquor containing a mixture of three compounds was poured into 20 ml of 5% aqueous HCl, the precipitate was filtered off, washed with water, deried, and subjected to column chromatography on Al_2O_3 (eluent chloroform–acetone, 20:1). Compounds **III, IV**, and **V** were obtained in the individual state.

Methyl 14-hydroxy-20-isopropyl-5,9-dimethyl-17-oxopentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-5-carboxylate (III). Overall yield 0.2 g (51%) (the precipitate formed in the course of the reaction and that isolated from the mother liquor), mp 182–185°C, $[\alpha]_D^{20}$ +52.4° (*C* 0.01, $CHCl_3$) (mp 190–192°C, α_D^{20} +27° [7]). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.61 s (3H, CH_3), 0.85–1.00 m (1H, H^{3e}), 1.04 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.08 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.13 s (3H, CH_3), 1.14–1.25 m (1H, H^{3a}), 1.29–1.70 m (12H, H^{2a,e}, H^{4}, H^{7a,}, H^{6a,e}, H^{8a,e}, H^{10}, H^{11a,e}), 1.72–1.90 m (2H, H^{15a,e}), 2.00–2.51 m [5H, H^{13}, H^{18}, H^{16a,e}, $CH(CH_3)_2$, $J_{13,18}$ 11.1, $J_{18,13}$ 10.8 Hz], 2.68 br.s (1H, H^{12}), 3.40 br.s (1H, OH), 3.90 d.t (1H, H^{14}, $J_{14,15a}$ 5.0, $J_{14,15e}$ 9.5, $J_{14,13a}$ 4.8 Hz), 3.65 s (3H, $COOCH_3$), 5.55 br.s (1H, H^{19}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 212.9 (C^{17}), 179.3 (C^{21}), 147.1 (C^{20}), 125.2 (C^{19}), 68.5 (C^{14}), 61.9 (C^{18}), 55.0 (C^{4}), 51.9 ($COOCH_3$), 49.4 (C^{10}), 48.0 (C^{13}), 47.1 (C^{5}), 40.4 (C^{9}), 38.1 (C^{8}), 37.7 (C^{6}), 36.6 (C^{16}), 36.2 (C^{15}), 35.1 (C^{12}), 34.9 (C^{2}), 33.0 [$CH(CH_3)_2$], 30.2 (C^{1}), 27.4 (C^{11}), 21.9 (C^{3}), 21.5 (CH_3), 19.6 (CH_3), 17.0 (C^{7}), 16.8 (CH_3), 15.7 (CH_3). Found, %: C 75.32; H 9.01. $C_{27}H_{40}O_4$. Calculated, %: C 75.66; H 9.41.

Methyl 17-hydroxy-20-isopropyl-5,9-dimethyl-14-oxopentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-5-carboxylate (IV). Yield 0.1 g (24%), mp 166–168°C (165–166°C [6]), $[\alpha]_D^{20}$ –45.8° (*C* 0.01, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.61 s (3H, CH_3), 0.80–1.06 m (2H), 1.08 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.11 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.17 s (3H, CH_3), 1.35–2.00 m (12H), 2.01–2.66 m (7H), 3.40 br.s (1H, OH), 3.22 br.s (1H), 3.68 s (3H, $COOCH_3$), 4.16 br.s (1H, H^{17}), 5.55 br.s (1H, H^{19}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 211.6 (C^{14}), 179.3 (C^{21}), 154.0 (C^{20}), 122.9 (C^{19}), 64.8 (C^{17}), 56.7, 55.6, 51.9 ($COOCH_3$), 51.6, 49.6, 47.1 (C^{5}), 40.2, 37.9, 37.6, 36.8, 34.5, 34.3, 32.8, 32.7, 27.9, 27.7, 21.8, 21.0, 19.7, 16.9, 16.7, 15.7. Found, %: C 75.32; H 9.01. $C_{27}H_{40}O_4$. Calculated, %: C 75.66; H 9.41.

X-ray diffraction analysis of compound IV. Colorless plate crystals $C_{27}H_{40}O_4$ (*M* 428.59) rhombic, at 120 K *a* 9.626(2), *b* 9.839(2), *c* 24.867(6) Å, *V* 2355.3(9) Å^3, space group $P2_12_12_1$, *Z* 4, d_{calc} 1.209 g/cm^3. Experimental set of 17709 reflections was obtained on a diffractometer Bruker SMART CCD area detector at 120 K (λMOK_α radiation, $2\theta_{max}$ 58.0°) from a single crystal of dimensions 0.50 × 0.35 × 0.25 mm. After averaging the equivalent reflections 6184 independent reflections were obtained (R_{int} 0.0594) that were used for solving and refining the structure. The extinction (μ 0.079 mm^{-1}) was not taken into account. The structure was solved by the direct method, all nonhydrogen atoms were localized in the difference synthesis of the electron density and refined by F_{hkl}^2 in anisotropic approximation; all hydrogen atoms were placed in the geometrically calculated positions and taken into account in the refining in the *rider* model with U(H) = 1.2U(C) where U(C) is the equivalent thermal factor of the carbon atom linked to the corresponding hydrogen atom. Final values of divergence factors: R_1 0.0525 [calculated by F_{hkl} for 3556 reflections with $I > 2\sigma(I)$], wR_2 0.0789 [calculated by F_{hkl} for all 6184 reflections], *GOOF* 0.999, 280 refined parameters. All calculations were performed using programs package SHELXTL PLUS 5. The structure was registered in Cambridge Crystallographic Data Center (CCDC 630828).

Methyl 14,17-dihydroxy-20-isopropyl-5,9-dimethylpentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-5-carboxylate (V). *a*. Yield 0.06 g (15%), mp 202–204°C (238–245°C [6]), $[\alpha]_D^{20}$ –5.0° (*C* 0.67, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.63 s (3H, CH_3), 0.75–1.00 m (2H), 1.04 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.08 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.17 s (3H, CH_3), 1.18–1.78 m (12H), 1.92–2.17 m (7H), 2.58 m (1H), 3.50 m (2H, OH), 3.58 s (3H, $COOCH_3$), 3.85 br.s (1H, H^{14}), 4.12 br.s (1H, H^{17}), 5.50 br.s (1H, H^{19}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 179.5 (C^{21}), 152.3 (C^{20}), 122.4 (C^{19}), 67.9 (C^{14}), 65.0 (C^{17}), 56.0, 52.9, 51.8 ($COOCH_3$), 49.6, 47.2 (C^{5}), 46.0, 39.8, 39.4, 38.3, 37.6, 36.9, 34.7, 32.7, 30.6, 26.2, 25.5, 21.9, 21.3, 19.7, 17.0, 16.8, 15.8. Found, %: C 75.42; H 9.21. $C_{27}H_{42}O_4$. Calculated, %: C 75.31; H 9.83.

b. To a solution of 1 mmol (0.43 g) of methyl dihydroquinopimarate (**II**) in 10 ml of EtOH was added by portions 2.5 mmol (0.1 g) of $NaBH_4$. The reaction mixture was boiled for 4 h, poured into 20 ml of 5% aqueous HCl, the precipitate was filtered off, washed with water, dried, and recrystallized from methanol. Yield 0.42 g (86%), mp 204–205°C.

5-Hydroxymethyl-20-isopropyl-5,9-dimethylpentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-14,17-

diol (VI). To a dispersion of 3 mmol (0.1 g) of $LiAlH_4$ in 15 ml of anhydrous THF was added dropwise at stirring a solution of 1 mmol (0.41 g) of compound **I** in anhydrous THF. The reaction mixture was stirred for 4 h, then at cooling was dropwise added 7 ml of H_2O and 7.5 ml of 20% solution of H_2SO_4. The organic phase was separated, the water phase was extracted with chloroform (3 × 10 ml), the combined organic solutions were washed with cold water (3 × 30 ml), dried with $CaCl_2$, and evaporated in a vacuum. The residue was recrystallized from acetone. Yield 0.32 g (82%), mp 178–180°C (209–210°C [9, 10]), $[\alpha]_D^{20}$ +28° (*C* 0.01, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.60 s (3H, CH_3), 0.75 s (3H, CH_3), 0.78–0.90 m (2H), 1.02 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.04 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.07–1.51 m (12H), 1.50–2.18 m (7H), 2.51 br.s (1H), 3.03 br.s (3H, OH), 3.10 d (1H, H^{21}, *J* 10.8 Hz), 3.40 d (1H, H^{21}, *J* 11.0 Hz), 3.83 br.s (1H, H^{14}), 4.11 br.s (1H, H^{17}), 5.51 br.s (1H, H^{19}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 151.7 (C^{20}), 122.7 (C^{19}), 71.8 (C^{21}), 67.9 (C^{14}), 64.9 (C^{17}), 55.9, 52.9, 48.0, 45.9, 39.4, 39.5, 39.4, 37.9, 37.2, 36.8, 35.3, 34.8, 32.6, 26.1, 25.5 (C^5), 21.3, 20.3, 18.9, 17.8, 16.0, 16.7. Found, %: C 76.98; H 9.35. $C_{26}H_{42}O_3$. Calculated, %: C 77.56; H 10.51.

Acylation of compounds III, V, and VI. To 1 mmol of compound **III, V**, or **VI** in 10–15 ml of pyridine was added 0.3, 0.6, or 0.9 ml of Ac_2O respectively, and the mixture was left standing for 15 h. Then the reaction mixture was poured into 50 ml of 5% solution of HCl, cooled to 0°C, the precipitate was filtered off, washed with water, dried, and crystallized from methanol.

20-Isopropyl-5,9-dimethyl-5-methoxycarbonyl-17-oxopentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-14-yl acetate (VII). Yield 0.40 g (87%), mp 209–210°C, $[\alpha]_D^{20}$ +39.0° (*c* 0.01, $CHCl_3$) (mp 217–220°C, $[\alpha]_D^{20}$ +45.5° [7]). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.61 s (3H, CH_3), 0.85–1.00 m (2H, $H^{3a,e}$), 1.04 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.08 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.16 s (3H, CH_3), 1.26–1.99 m (12H, $H^{2a,e}$, H^4, $H^{7a,e}$, $H^{6a,e}$, $H^{8a,e}$, H^{10}, $H^{11a,e}$), 2.08–2.19 m (2H, $H^{15a,e}$), 2.05 s (3H, $H^{2'}$), 2.18–2.48 m [5H, $CH(CH_3)_2$, H^{13}, H^{18}, $H^{16a,e}$], 2.68 br.s (1H, H^{12}), 3.65 s (3H, $COOCH_3$), 4.92 s (1H, H^{14}, $J_{14,15a}$ 5.2, $J_{14,15e}$ 10.3, $J_{14,13}$ 4.9 Hz), 5.55 s (1H, H^{19}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 211.5 (C^{17}), 179.2 (C^{21}), 170.2 ($C^{1'}$), 147.6 (C^{20}), 124.1 (C^{19}), 70.7 (C^{14}), 61.9 (C^{18}), 54.8 (C^4), 51.9 ($COOCH_3$), 47.1 (C^5), 49.3 (C^{10}), 44.5 (C^{13}), 40.3 (C^8), 38.1 (C^9), 37.8 (C^6), 36.6 (C^{16}), 36.1 (C^{15}), 35.1 (C^{12}), 35.0 (C^2), 33.0 [$CH(CH_3)_2$], 30.0 (C^1), 23.8 (C^{11}), 21.8 (C^3), 21.4 ($C^{2'}$), 21.2 (CH_3), 19.6 (CH_3), 16.8 (CH_3), 17.0 (C^7), 15.7 (CH_3). Found, %: C 73.98; H 8.45. $C_{29}H_{42}O_5$. Calculated, %: C 74.01; H 8.99.

X-ray diffraction analysis of compound VII. Colorless plate crystals, $C_{29}H_{43}O_5$ (*M* 471.63) rhombic, at 120 K *a* 7.1304(7), *b* 14.0189(1), *c* 25.733(3) Å, *V* 2572.3(5) Å^3, space group $P2_12_12_1$, *Z* 4, d_{calc} 1.218 g/cm^3. Experimental set of 19877 reflections was obtained on a diffractometer Bruker SMART CCD area detector at 120 K (λMOK_α radiation, $2\theta_{max}$ 60.16°) from a single crystal of dimensions 0.6 × 0.4 × 0.1 mm. After averaging the equivalent reflections 7384 independent reflections were obtained (R_{int} 0.0864) that were used for solving and refining the structure. The extinction (μ 0.081 mm^{-1}) was not taken into account. The structure was solved by the direct method, all nonhydrogen atoms were localized in the difference synthesis of the electron density and refined by F_{hkl}^2 in anisotropic approximation; all hydrogen atoms were placed in the geometrically calculated positions and taken into account in the refining in the *rider* model with *U*(H) = 1.2*U*(C) where *U*(C) is the equivalent thermal factor of the carbon atom linked to the corresponding hydrogen atom. Final values of divergence factors: R_1 0.0667 [calculated by F_{hkl} for 4993 reflections with $I > 2\sigma(I)$], wR_2 0.1067 (calculated by F_{hkl}^2 for all 7384 reflections), *GOOF* 1.024, 306 refined parameters. All calculations were performed using programs package SHELXTL PLUS. The structure was registered in Cambridge Crystallographic Data Center (CCDC 630827).

Methyl 14,17-diacetoxy-20-isopropyl-5,9-dimethylpentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-5-carboxylate (XII). Yield 0.42 g (81%), mp 209–210°C, $[\alpha]_D^{20}$ –2.5° (*c* 0.67, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.63 s (3H, CH_3), 0.81–0.95 m (2H), 1.02 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.08 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.16 s (3H, CH_3), 1.26–1.99 m (12H), 1.73 s (3H, $H^{2'}$), 2.08–2.19 m (2H), 2.01 s (3H, $H^{2''}$), 2.15–2.41 m (5H), 2.48 br.s (1H, H^{12}), 3.65 s (3H, $COOCH_3$), 4.67 br.s (1H, H^{14}), 4.87 br.s (1H, H^{17}), 5.55 s (1H, H^{19}). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 179.1 (C^{21}), 170.4 ($C^{1'}$), 170.1 ($C^{1''}$), 144.4 (C^{20}), 124.6 (C^{19}), 69.5 (C^{14}), 67.4 (C^{17}), 56.0, 50.0, 49.6, 49.4, 46.9, 42.9, 40.2, 38.0, 37.5, 36.6, 36.3, 34.5, 32.5, 30.4 (C^5), 23.8, 22.9, 21.8, 21.5 ($C^{2'}$), 21.2 ($C^{2''}$), 21.2, 19.6, 16.9, 16.6, 15.7. Found, %: C 72.34; H 9.01. $C_{31}H_{46}O_6$. Calculated, %: C 72.54; H 8.99.

14,17-Diacetoxy-20-isopropyl-5,9-dimethylpentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-5-ylmethyl acetate (XV). Yield 0.45 g (85%), mp 68–70°C,

$[\alpha]_D^{20}$ +14.0° (*C* 0.01, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.50 s (3H, CH_3), 0.81–0.98 m (2H), 0.85 s (3H, CH_3), 0.95 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.05 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.20–1.71 m (12H), 1.78 s (3H, H*2′*), 1.87 s (3H, H*2″*), 1.89 s (3H, H*2‴*), 1.92–2.28 m (7H), 2.50 br.s (1H), 3.25 d (1H, H*21*, *J* 10.8 Hz), 4.01 d (1H, H*21*, *J* 10.9 Hz), 4.67 br.s (1H, H*14*), 4.87 br.s (1H, H*17*), 5.40 br.s (1H, H*19*). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 171.2 (C*1′*), 170.6 (C*1″*), 169.9 (C*1‴*), 148.7 (C*20*), 123.6 (C*19*), 73.6 (C*21*), 71.3 (C*17*), 67.9 (C*14*), 55.8, 53.0, 48.1, 45.9, 35.2, 39.5, 38.9, 38.8, 38.0, 37.1, 32.6, 34.4, 30.8 (C*5*), 26.0, 25.5, 25.1 (C*2′*), 23.0 (C*2″*), 22.6 (C*2‴*), 21.2, 20.4, 19.0, 17.9, 17.3, 16.1. Found, %: C 71.81; H 8.65. $C_{32}H_{48}O_6$. Calculated, %: C 72.69; H 9.15.

Compounds VIII, IX, XIII, and XVI. To a solution of 1 mmol of compound **III, V**, or **VI** in anhydrous pyridine was added 2 mmol (0.2 g), 4, or 6 mmol of succinic anhydride, or 5 mmol (0.9 g) of phthalic anhydride and a catalytic quantity of DMAP. The mixture was boiled for 12 h, the reaction mixture was poured into 20 ml of 5% solution of HCl, the precipitate was filtered off, washed with water, dried, and subjected to column chromatography on Al_2O_3, eluent chloroform.

3-(20-Isopropyl-5,9-dimethyl-5-methoxycarbonyl-17-oxopentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-14-yl-(oxycarbonyl)propanoic acid (VIII). Yield 0.40 g (75%), mp 93–95°C, $[\alpha]_D^{20}$ +34.0° (*c* 0.01, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.55 s (3H, CH_3), 0.66–0.95 m (2H), 1.01 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.03 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.15 s (3H, CH_3), 1.21–2.21 m (12H), 2.21–2.42 m (7H), 2.42–2.60 m (4H, H*2′*, H*3′*), 2.67 br.s (1H), 3.51 s (3H, $COOCH_3$), 4.81 d.t (1H, H*14*, $J_{14,13}$ 4.7, $J_{13,15a}$ 5.1, $J_{14,15e}$ 9.3 Hz), 5.49 br.s (1H, H*19*), 9.05 br.s (1H, COOH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 209.3 (C*17*), 178.5 (C*21*), 174.8 (C*1′*), 170.8 (C*4′*), 147.1 (C*20*), 124.9 (C*19*), 71.3 (C*14*), 61.6, 54.6, 55.2, 51.8, 47.3, 45.2 (C*5*), 45.0, 38.6, 38.1, 37.2, 35.9, 35.8, 35.6, 33.3, 30.7, 29.2 (C*2′*), 29.0 (C*3′*), 24.3, 22.3, 21.9, 19.9, 17.5, 17.3, 16.1. Found, %: C 69.82; H 7.54. $C_{31}H_{44}O_7$. Calculated, %: C 70.43; H 8.39.

2-(20-Isopropyl-5,9-dimethyl-5-methoxycarbonyl-17-oxopentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-14-yl-(oxycarbonyl)benzoic acid (IX). Yield 0.44 g (76%), mp 145–148°C, $[\alpha]_D^{20}$ +35.0° (*c* 0.01, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.58 s (3H, CH_3), 0.81–0.89 m (2H), 0.92 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.01 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.15 s (3H, CH_3), 1.25–1.83 m (12H), 1.87–2.50 m (6H), 2.62–2.76 m (2H), 3.62 s (3H, $COOCH_3$), 5.56 br.s (1H, H*19*), 5.16 d.t (1H, H*14*, $J_{14,13}$ 5.0, $J_{14,15a}$ 5.2, $J_{14,15e}$ 9.0 Hz), 6.75 br.s (1H, COOH), 7.50–7.71 m (3H, H*3′*, H*5′*, H*6′*), 7.90 d (1H, H*8′*, J_{gem} 6.1 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 212.1 (C*17*), 179.1 (C*21*), 170.9 (C*1′*), 166.8 (C*4′*), 147.6 (C*20*), 32.7 (C*3′*), 131.6 (C*2′*), 130.7 (C*5′*), 130.6 (C*7′*), 129.4 (C*8′*), 128.6 (C*6′*), 123.8 (C*19*), 72.1 (C*14*), 61.8, 54.5, 53.3, 51.7, 49.1, 46.9 (C*5*), 40.2, 37.8, 37.5, 36.4, 36.1, 34.9, 34.8, 32.6, 29.8, 23.4, 21.6, 21.1, 19.1, 16.8, 16.6, 15.5. Found, %: C 72.89; H 7.69. $C_{35}H_{44}O_7$. Calculated, %: C 72.18; H 7.09.

3,3'-{(20-Isopropyl-5,9-dimethyl-5-methyloxycarbonylpentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-14,17-diylbis(oxycarbonyl)}-dipropanoic acid (XIII). Yield 0.43 g (68%), mp 93–95°C, $[\alpha]_D^{20}$ –4.5° (*c* 0.67, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.35 s (3H, CH_3), 0.38–0.58 m (2H), 0.75 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 0.80 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 0.85 s (3H, CH_3), 0.91–1.48 m (12H), 1.51–1.98 m (7H), 2.07 br.s (1H), 2.02–2.40 m (8H, H*1′*, H*2′*, H*1″*, H*2″*), 3.33 s (3H, $COOCH_3$), 4.71 br.s (2H, H*14*, H*17*), 5.19 br.s (1H, H*19*), 9.15 br.s (2H, 2COOH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 179.5 (C*21*), 177.3 (C*1′*), 177.2 (C*1″*), 171.9 (C*4′*), 171.6 (C*4″*), 145.6 (C*20*), 124.6 (C*19*), 70.2 (C*14*), 68.1 (C*17*), 56.0, 53.3, 51.8, 49.6, 49.4, 47.0 (C*5*), 42.8, 40.2, 38.0, 37.6, 36.6, 36.3, 35.1, 32.9, 30.7 (C*2″*), 29.2 (C*2′*), 28.8 (C*3′*), 28.6 (C*3″*), 23.7, 22.6, 21.6, 21.0, 19.3, 16.9, 16.6, 15.8. Found, %: C 66.05; H 8.09. $C_{35}H_{50}O_{10}$. Calculated, %: C 66.65; H 7.99.

3,3'-{20-Isopropyl-5-(3-carboxypropanoyloxymethyl)-5,9-dimethylpentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-14,17-diylbis(oxycarbonyl)}dipropanoic acid (XVI). Yield 0.47 g (67%), mp 98–100°C, $[\alpha]_D^{20}$ –1.5° (*C* 0.005, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.60 s (3H, CH_3), 0.85 s (3H, CH_3), 0.91–1.03 m (2H), 1.04 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.08 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.20–1.69 m (12H), 1.70–2.19 m (7H), 2.48 br.s (1H), 2.55–2.78 m (12H, $3CH_2CH_2$), 3.70 d (1H, H*21*, *J* 11.0 Hz), 3.85 d (1H, H*21*, *J* 10.9 Hz), 5.09–5.19 m (2H, H*14*, H*17*), 5.49 br.s (1H, H*19*), 8.05 br.s (3H, 3COOH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 178.0 (C*1′*), 178.1 (C*1″*), 178.2 (C*1‴*), 171.7 (C*4′*), 171.8 (C*4″*), 171.9 (C*4‴*), 144.4 (C*20*), 124.8 (C*19*), 73.3 (C*21*), 70.3 (C*17*), 68.4 (C*14*), 60.1, 55.1, 49.9, 49.2, 43.1, 40.1, 38.7, 38.1, 36.1, 35.8, 35.5, 32.6 (C*5*), 30.5, 29.1 and 29.0 (CH_2CH_2), 28.9 and 28.8 (CH_2CH_2), 28.7 and 28.6 (CH_2CH_2), 29.2, 23.9, 21.3, 19.6, 19.7, 17.8, 15.8, 15.0. Found, %: C 67.55; H 7.01. $C_{38}H_{54}O_{12}$. Calculated, %: C 67.94; H 7.74.

Compounds X, XI, XIV, and XVII. To a solution of 1 mmol of compound **III, V**, or **VI** in 15 ml of anhydrous

pyridine was added 2, 4, or 6 mmol of nicotinoyl chloride or 2 mmol of cinnamic anhydride respectively, and the mixture was boiled for 6 h, the reaction mixture was poured into 20 ml of 5% solution of HCl, the precipitate was filtered off, washed with cold water, dried, and subjected to column chromatography on Al_2O_3, eluent chloroform.

Methyl 20-isopropyl-5,9-dimethyl-17-oxo-14-cinnamoyloxypentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-5-carboxylate (X). Yield 0.36 g (67%), mp 109–110°C, $[\alpha]_D^{20}$ +24° (*c* 0.01, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.63 s (3H, CH_3), 0.89–1.08 m (2H), 1.09 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.13 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.15 s (3H, CH_3), 1.19–1.79 m (12H), 1.91–2.50 m (6H), 2.78 d.t (1H, H^{1a}, J_1 4.4, J_2 3.7, J_3 13.4 Hz), 3.20 br.s (1H), 3.67 s (3H, H^{21}), 5.10 d.t (1H, H^1, $J_{14,13}$ 5, $J_{14,15a}$ 4.7, $J_{14,15e}$ 9.5 Hz), 5.61 br.s (1H, H^{19}), 6.41 d (1H, H$^{2'}$, *J* 15.9 Hz), 6.83 d (1H, H$^{3'}$, *J* 15.4 Hz), 7.26–7.81 m (5H, H$^{5'}$, H$^{6'}$, H$^{7'}$, H$^{8'}$, H$^{9'}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 211.0 (C^{17}), 179.2 (C^{21}), 171.9 (C$^{1'}$), 147.2 (C^{20}), 145.2 (C$^{3'}$), 142.1 (C$^{4'}$), 130.3 (C$^{9'}$), 129.3 (C$^{5'}$), 128.3 (C$^{6'}$), 128.1 (C$^{8'}$), 127.6 (C$^{7'}$), 124.3 (C^{19}), 117.9 (C$^{2'}$),70.6 (C^{14}), 61.8, 54.6, 51.8, 49.4, 47.1, 45.1 (C^5), 40.2, 38.2, 37.8, 36.6, 35.9, 35.5, 35.2, 32.9, 31.9, 30.2, 21.3, 20.0, 19.6, 17.0, 16.8, 15.7. Found, %: C 76.99; H 7.53. $C_{36}H_{46}O_5$. Calculated, %: C 77.39; H 8.30.

Methyl 20-isopropyl-5,9-dimethyl-17-oxo-14-nicotinoyloxypentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-5-carboxylate (XI). Yield 0.38 g (70%), mp 117–118°C, $[\alpha]_D^{20}$ +3.0° (*c* 0.67, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.58 s (3H, CH_3), 0.71–0.85 m (2H), 0.89 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.00 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.10 s (3H, CH_3), 1.25–1.83 m (12H), 1.97–2.50 m (6H), 2.65–2.75 m (2H), 3.63 s (3H, $COOCH_3$), 5.55 br.s (1H, H^{19}), 5.26 d.t (1H, H^1, $J_{14,13}$ 5.0, $J_{14,15a}$ 5.2, $J_{14,15e}$ 8.9 Hz), 7.42–7.49 m (1H, H$^{5'}$), 8.09 d (1H, H$^{4'}$, *J* 7.8 Hz), 8.75 d (1H, H$^{6'}$, *J* 3.9 Hz), 9.22 br.s (1H, H$^{2'}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 210.1 (C^{17}), 178.6 (C^{21}), 163.7 (C$^{1'}$), 152.8 (C$^{6'}$), 150.1 (C$^{2'}$), 146.2 (C^{19}), 136.9 (C$^{4'}$), 125.7 (C$^{3'}$), 124.2 (C^{20}), 123.2 (C$^{5'}$), 71.3 (C^{14}), 61.2, 54.0, 51.4, 49.0, 46.6, 45.1 (C^5), 39.7, 37.8, 37.3, 36.2, 35.4, 35.3, 34.7, 32.4, 29.9, 24.0, 21.5, 20.8, 19.0, 16.8, 16.4, 15.3. Found, %: C 73.54; H 8.03; N 2.51. $C_{33}H_{43}NO_5$. Calculated, %: C 74.27; H 8.12; N 2.62.

Methyl 20-isopropyl-5,9-dimethyl-14,17-bis-(nicotinoyloxy)pentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]-icos-19-ene-5-carboxylate (XIV). Yield 0.47 g (71%), mp 100–102°C, $[\alpha]_D^{20}$ –10.5° (*c* 0.67, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.61 s (3H, CH_3), 0.80 s (3H, CH_3), 0.81–1.03 m (2H), 1.09 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.11 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.12–1.98 m (12H), 2.10 s (3H, $COOCH_3$), 2.12–2.72 m (6H), 3.38 d.t (1H, H^{13}, J_1 4.4, J_2 3.7, J_3 13.4 Hz), 3.85–4.15 m (1H, H^{18}), 5.50 br.s (2H, H^{14}, H^{17}), 5.63 br.s (1H, H^{19}), 7.23–7.39 m (2H, H$^{5'}$, H$^{5''}$), 8.09–8.22 m (2H, H$^{4'}$ H$^{4''}$), 8.69–8.71 m (2H, H$^{6'}$, H$^{6''}$), 9.02–9.22 m (2H, H$^{2'}$, H$^{2''}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 178.0 (C^{21}), 164.7 (C$^{1'}$), 164.5 (C$^{1''}$), 153.2 (C$^{6'}$), 153.1 (C$^{6''}$), 150.6 (C$^{2'}$), 150.5 (C$^{4''}$), 145.2 (C^{19}), 136.9 (C$^{4''}$), 136.7 (C$^{2''}$), 128.1 (C^{20}), 126.2 (C$^{3'}$), 126.1 (C$^{3''}$), 123.2 (C$^{5'}$), 123.1 (C$^{5''}$), 70.8 (C^{14}), 70.3 (C^4), 56.5, 51.7, 49.7, 49.4, 46.9, 43.0 (C^5), 41.0, 39.3, 38.2, 36.7, 36.4, 35.9, 35.0, 32.6, 30.7, 29.6, 23.9, 23.1, 21.3, 19.3, 16.8, 15.1. Found, %: C 72.99; H 7.53; N 4.01. $C_{39}H_{48}N_2O_6$. Calculated, %: C 73.1; H 7.55; N 4.37.

{20-Isopropyl-5,9-dimethyl-14,17-bis(nicotinoyloxy)pentacyclo[10.6.2^{1,10}.0^{4,9}.0^{13,18}]icos-19-ene-5-ylmethyl} nicotinoate (XVII). Yield 0.48 g (65%), mp 107–109°C, $[\alpha]_D^{20}$ +16° (*c* 0.01, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.60 s (3H, CH_3), 0.75 s (3H, CH_3), 0.80–0.93 m (2H), 1.09 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.10 d [3H, $CH(CH_3)_2$, *J* 6.9 Hz], 1.15–1.95 m (12H), 2.12–2.75 m (6H), 3.45 br.s (1H, H^{13}), 3.70 d (1H, H^{21}, *J* 10.9 Hz), 3.85 d (1H, H^{21}, *J* 10.8 Hz), 3.81–4.15 m (1H, H^{18}), 5.46 br.s (2H, H^{14}, H^{17}), 5.61 br.s (1H, H^{19}), 7.19–7.39 m (3H, H$^{5'}$, H$^{5''}$, H$^{5'''}$), 8.09–8.32 m (3H, H$^{4'}$, H$^{4''}$, H$^{4'''}$), 8.62–8.69 m (3H, H$^{6'}$, H$^{6''}$, H$^{6'''}$), 9.02–9.22 m (3H, H$^{2'}$, H$^{2''}$, H$^{2'''}$). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 164.8 (C$^{1'}$), 164.6 (C$^{1''}$), 164.4 (C$^{1'''}$), 153.2 (C$^{6'}$), 153.1 (C$^{6''}$), 153.0 (C$^{6'''}$), 150.6 (C$^{4'}$), 150.5 (C$^{4''}$), 150.4 (C$^{4'''}$), 147.2 (C^{19}), 136.9 (C$^{2'}$), 136.8 (C$^{2''}$), 136.7 (C$^{2'''}$), 128.0 (C^{20}), 126.2 (C$^{3'}$), 126.1 (C$^{3''}$), 126.0 (C$^{3'''}$), 123.2(C$^{5'}$), 123.1 (C$^{5''}$), 123.0 (C$^{5'''}$), 73.6 (C^{21}), 70.9 (C^{14}), 70.5 (C^{17}), 65.6, 56.4, 49.6, 49.3, 42.9 (C^5), 40.9, 39.1, 38.4, 38.1, 36.6, 36.3, 34.9, 32.5, 30.7, 29.6, 23.8, 22.9, 20.9, 19.3, 16.8, 15.0. Found, %: C 72.99; H 7.53, N 5.80. $C_{44}H_{51}N_3O_6$. Calculated, %: C 73.1; H 7.55, N 5.85.

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REFERENCES

1. Onoda, Y., Magaribuchi, T., and Tamaki, H., *Jpn. J. Pharmacol*., 1989, vol. 51, p. 65.
2. Seebacher, W., Ньfner, A., Haslinger, E. and Weis, R., *Monatsh. Chem*., 1998, vol. 129, p. 697.
3. Galin, F.Z., Flekhter, O.B., and Tret'yakova, E.V., *Khimiya i komp'yuternoe modelirovanie. Butlerovskie soobshcheniya* (Chemistry and Computer Modeling, Butlerov Communications), 2004, vol. 5, no. 2, p. 1.
4. Tolstikov, G.A., Shul'ts, E.E., Mukhametyanova, T.Sh., Sultanova, V.S., and Spirikhin, L.V., *Zh. Org. Khim.,* 1992, vol. 28, p. 1310.
5. Tolstikov, G.A., Shul'ts, E.E., Mukhametyanova, T.Sh., Baikova, I.P., and Spirikhin, L.V., *Zh. Org. Khim.,* 1993, vol. 29, p. 698.
6. Tret'yakova, E.V., Flekhter, O.B., Galin, F.Z., Spirikhin, L.V., and Tolstikov, G.A., *Zh. Org. Khim.,* 2003, vol. 39, p. 1811.
7. Herz, W., Blackstone, R.C., and Nair, M.G., *J. Org. Chem*., 1967, vol. 32, p. 2992.
8. Baltina, L.A., Serdyuk, N.G., Kondratenko, R.M., Tolstikov, G.A., and Vasil'eva, E.V., *Zh. Org. Khim.,* 2003, vol. 39, p. 2040.
9. Sandermann, W. and Striesow, K., *Chem. Ber.,* 1957, vol. 90, nos. 3–5, p. 693.
10. Tolstikov, G.A. and Potapov, V.M., *Izv. Akad. Nauk KazSSR, Ser. Khim*., 1969, no. 2, p. 43.