

Synthetic Transformations of Higher Terpenoids: XII.* Transformation of Lambertianic Acid into 14,16-Epoxyabietane Diterpenoids

S. V. Chernov, E. E. Shul'ts, M. M. Shakirov, and G. A. Tolstikov

Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences,
pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia
e-mail: schultz@nioch.nsc.ru

Received January 9, 2005

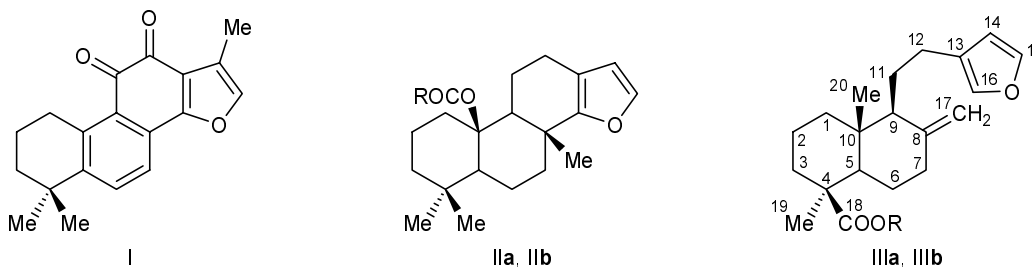
Abstract—Hydroxylation of lambertianic acid with potassium permanganate in alkaline medium afforded 15,16-epoxy-8 α ,17-dihydroxy-13(16),14-labdadienoic acid which was oxidized with periodic acid to the corresponding 8 α -hydroxy aldehyde, and the latter underwent smooth cyclization in acid medium to give diterpenoid of the 14,16-epoxyabietane series.

DOI: 10.1134/S1070428006010064

Diterpenoids containing a furan ring and structural-related fragments constitute a group of metabolites possessing valuable biological activity. Compounds exhibiting antiviral, cytostatic, immune regulating, psychotropic, and other properties have been reported. Such compounds are widespread in the plant kingdom [2]. The rhizome *Salvia miltiorrhiza* Bunge (Labiatae) also known as Tanshen or Danshen contains diterpenoid quinones which possess cardiotropic activity. A typical representative of these metabolites is tanshinone IIA (**I**) which acts as an effective vasodilator for heart coronary vessels. Danshen is widely used in the traditional Chinese medicine to treat coronary heart diseases; its alcohol extract contains no less than 30 quinones of the 14,16-epoxyabietane series [3, 4]. The synthesis of tanshindiols was reported in [5]. Marginatafuran diterpenoids like **II** were isolated from

dorid nudibranch *Cadlina luteomerginata* [6–8]. In the present article we describe the synthesis of furanoditerpenoids of that type via transformations of lambertianic acid (**IIIa**).

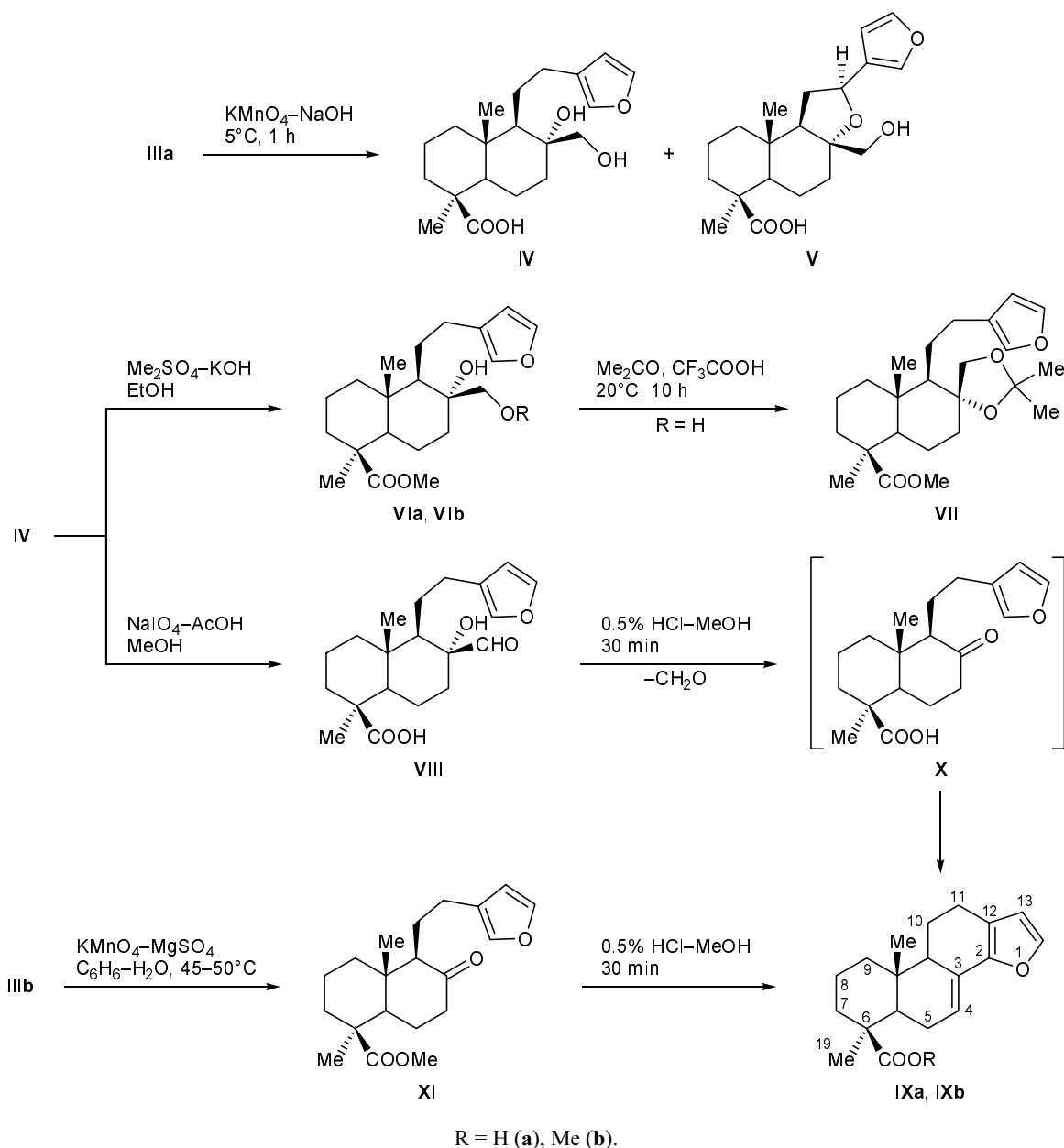
We found that hydroxylation of lambertianic acid (**IIIa**) with potassium permanganate in aqueous alkali gives 59% of 8,17-dihydroxy acid **IV** (Scheme 1). We also isolated 8,12-epoxy acid **V** as by-product (yield 5.5%); its methyl ester was described by us previously [9]. Methylation of **IV** with excess dimethyl sulfate involved both carboxy and primary hydroxy group to afford a mixture of esters **VIa** and **VIb** at a ratio of 1:1. Ester **VIa** was smoothly converted into dioxolane **VII** by treatment with acetone in the presence of trifluoroacetic acid. By oxidation of dihydroxy acid **IV** with sodium periodate we synthesized hydroxy aldehyde **VIII** in 77% yield, and the latter was treated with



R = H (a), Me (b).

* For communication XI, see [1].

Scheme 1.



dilute (0.5%) hydrochloric acid in methanol to obtain the target acid of the phenanthro[1,2-*b*]furan series (compound **IXa**, yield 74%). Presumably, the transformation of aldehyde **VIII** into **IX** involves intermediate formation of oxo acid **X** which undergoes fast intramolecular ring closure. An analogous transformation was observed when a solution of **VIII** in chloroform was kept in an NMR ampule. After 12 h, signal from the aldehyde proton disappeared from the ^1H NMR spectrum, and the singlets from C^{19}H_3 and C^{20}H_3 changed their position (δ 1.27 and 0.60 ppm, respectively; hereinafter, the atom numbering in the

labdane skeleton of compounds **III–VIII**, **X**, and **XI** corresponds to that shown above for **IIIa**, **IIIb**).

As might be expected, 8-oxo-17-norlambertianic acid methyl ester (**XI**), which was synthesized by us previously by oxidation of lambertianic acid methyl ester (**IIIb**) with KMnO_4 under neutral conditions [9], underwent analogous intramolecular ring closure to give ester **IXb** on treatment with hydrochloric acid in methanol. Compound **IXb** was identical to the product obtained by methylation of acid **IXa**. It should be noted that cleavage of α -hydroxy aldehydes to ketones was observed previously in the steroid series [10].

Facile cyclization of 8-oxo derivatives attracts interest from the viewpoint of comparison with the cyclization of lambertianic acid methyl ester (**IIIb**), which occurs under strongly acidic conditions and is characterized by a poor yield [11].

The structure of the newly synthesized compounds was determined on the basis of their spectral data. The presence of a chromophoric conjugated triene system in molecules **IXa** and **IXb** follows from the UV spectra which display absorption bands with their maxima at λ 255, 268, and 282 nm. The formation of polycyclic phenanthro[1,2-*b*]furan skeleton leads to considerable changes ($\Delta\delta_c \sim 5$ ppm) in the chemical shifts of the bridgehead carbon atoms C^{5a} and C^{9a} (which are common for the A and B rings) in the ¹³C NMR spectra. In the ¹H NMR spectra of **IXa** and **IXb**, the 9b-H and 11-H signals were displaced downfield relative to the corresponding signals (9-H and 12-H) from the labdane system.

The stereochemical configuration of compounds **IV** and **VI** as 8 α -hydroxy isomers was established on the basis of the NOESY spectra. β -Orientation of the hydroxymethyl group on C⁸ unambiguously follows from the NOEs observed for the 17-H protons (δ 3.15 and 3.65 ppm) on 10-CH₃ (δ 0.53 ppm) and 11-H (δ 1.31 and 1.60 ppm) in the spectrum of **VIb**. The (8*R*,12*S*)-configuration of epoxy labdanoid **V** was also deduced from the NOESY data. We observed NOE on the diastereotopic 17-H protons (δ , ppm: 3.44 d and 3.73 d.d) on irradiation of protons of the 10-CH₃ group (δ 0.64 ppm). In addition, the C²⁰H₃ protons showed NOE on the axial proton on C² and pseudoaxial proton on C¹¹. Irradiation at a resonance frequency corresponding to 17-H (δ 3.44 ppm) gave a response on the second 17-H proton, both protons on C¹¹, and protons of the angular methyl group. No response on 11-H was observed upon irradiation of the second 17-H proton (δ 3.73 ppm), but strong responses were observed on the pseudoaxial 6-H proton and C²⁰H₃ protons. Both 11-H protons showed NOE on 12-H, while 12-H gave NOE only on 11-H. These data unambiguously confirm the steric structure assumed for compound **V**.

EXPERIMENTAL

The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT-8200 high-resolution mass spectrometer (vaporizer temperature 190–250°C). The NMR spectra were recorded on Bruker AC-200 (200.13 MHz for ¹H and 50.32 MHz for ¹³C) and Bruker DRX-500 spectrometers (500.13 MHz for ¹H

and 125.76 MHz for ¹³C) from solutions in CDCl₃, CD₃OD, or CCl₄. Signals in the NMR spectra were assigned using various proton–proton and carbon–proton shift correlation techniques (COSY, COLOC, CORRD), as well as ¹H NMR 2D-NOESY spectroscopy (for compounds **V** and **VIb**). The IR spectra were measured in KBr on a Vector-22 instrument. The UV spectra were recorded on an HP 8453 UV-Vis spectrophotometer from solutions in ethanol ($c = 10^{-4}$ M). The optical rotations $[\alpha]_D$ were measured in chloroform or ethanol at room temperature (20–23°C) using a WXQ-4 polarimeter. The progress of reactions was monitored by TLC on Silufol UV-254 plates. The products were isolated by column chromatography on silica gel or aluminum oxide.

(1*S*,4*aS*,5*R*,6*R*,8*aS*)-5-[2-(3-Furyl)ethyl]-6-hydroxy-6-hydroxymethyl-1,4*a*-dimethylperhydronaphthalene-1-carboxylic acid [(8*R*)-15,16-epoxy-8,17-dihydroxy-13(16),14-labdadien-18-oic acid] (IV**) and (2*S*,3*aR*,5*aS*,6*S*,9*aS*,9*bR*)-2-(3-furyl)-3a-hydroxymethyl-6,9*a*-dimethylperhydronaphtho[2,1-*b*]furan-6-carboxylic acid [8*a*,12*a*:15,16-diepoxy-17-hydroxy-13(16),14-labdadien-18-oic acid] (**V**).** Lambertianic acid (**IIIa**), 6.3 g (20 mmol), was dissolved on heating in 200 ml of distilled water containing 3 g (75 mmol) of sodium hydroxide, the solution was cooled to 5°C, 50 g of ice was added, and a cold solution of 4.1 g (26 mmol) of potassium permanganate in 100 ml of water was added over a period of 30 min under stirring. The mixture was kept for 1 h at 0–5°C, the precipitate of MnO₂ was filtered off and washed with hot water (2 × 20 ml), and the filtrate was acidified with acetic acid. The precipitate was filtered off, washed with cold water, and dried. We thus isolated 5.0 g of a mixture of dihydroxy acid **IV** and epoxy acid **V** as a colorless powder. Recrystallization from ethyl acetate gave 0.38 g (5.5%) of compound **V**. The mother liquor was evaporated, and the residue was recrystallized from petroleum ether–*tert*-butyl methyl ether. Yield of **IV** 4.1 g (59%), mp 192–194°C (from petroleum ether–*t*-BuOMe), $[\alpha]_D^{20} = +42^\circ$ ($c = 5.2$, ethanol). IR spectrum, ν , cm⁻¹: 787, 874, 973, 1023, 1042, 1094, 1157, 1500, 1696, 3200, 3337, 3441, 3515. ¹H NMR spectrum (CD₃OD), δ , ppm (*J*, Hz): 0.75 s (3H, C²⁰H₃), 1.01–1.10 m (3H, 1-H, 3-H, 5-H), 1.14 s (3H, C¹⁹H₃), 1.20 m (1H, 7-H), 1.31–1.48 m (3H, 2-H, 9-H, 11-H), 1.73–1.92 m (5H, 1-H, 2-H, 6-H, 11-H), 2.13 m (1H, 3-H, ²*J* = 13.2), 2.21 m (1H, 7-H, ²*J* = 14.0), 2.43 m (1H, 12-H, ²*J* = 14.6), 2.60 m (1H, 12-H, ²*J* = 14.6), 3.48 d and 3.69 d (2H, 17-H, *J* = 7.1), 6.28 d.d (1H, 14-H, *J* = 2.6, 1.0), 7.22 d (1H,

16-H, $J = 1.0$), 7.32 d (1H, 15-H, $J = 2.6$). ^{13}C NMR spectrum, δ_{C} , ppm: 13.87 (C^{20}), 19.56 (C^2), 21.93 (C^6), 26.40 (C^{11}), 28.66 (C^{12}), 29.21 (C^{19}), 38.06, 38.35 (C^3 , C^7), 40.46 (C^1), 41.23 (C^{10}), 44.03 (C^4), 56.00 (C^5), 60.13 (C^9), 62.70 (C^{17}), 75.57 (C^8), 111.41 (C^{14}), 126.23 (C^{13}), 139.03 (C^{16}), 142.97 (C^{15}), 180.79 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 350 [M]⁺ (1.6), 332 [$M - 18$] (11), 319 (10), 273 (17), 161 (22), 147 (34), 121 (57), 109 (30), 96 (24), 81 (100), 55 (45), 43 (32), 41 (41), 31 (60). Found: [M]⁺ 350.20869. $\text{C}_{20}\text{H}_{30}\text{O}_5$. Calculated: M 350.20931.

Compound **V**. mp 232–234°C (from MeOH), $[\alpha]_{\text{D}}^{20} = +12^\circ$ ($c = 3.1$, EtOH). ^1H NMR spectrum (CD_3OD), δ , ppm (J , Hz): 0.84 s (3H, C^{20}H_3), 1.13 d.d.d (1H, 3-H, $J = 13.5, 13.2, 4.3$), 1.15 d.d.d (1H, 1-H, $J = 13.0, 11.9, 3.8$), 1.20 m (1H, 7-H, $^2J = 12.4$), 1.25 s (3H, C^{19}H_3), 1.26 m (1H, 5-H), 1.50 m (1H, 2-H, $^2J = 14.2$), 1.61 m (1H, 1-H, $J = 13.0, 4.2, 2.8, 1.5$), 1.87 m (1H, 11-H), 1.92 m (1H, 9-H), 1.96–2.06 m (3H, 2-H, 6-H), 2.17–2.24 m (2H, 3-H, 11-H), 2.37 d.d.d (1H, 7-H, $J = 12.4, 7.0, 3.5$), 3.44 d.d (1H, 17-H, $J = 10.9, 2.0$), 3.73 d (1H, 17-H, $J = 10.9$), 5.06 d.d (1H, 12-H, $J = 9.0, 6.6, 1.1$), 6.49 d.d (1H, 14-H, $J = 2.0, 1.0$), 7.47 m (1H, 15-H, $J = 2.0, 1.7$), 7.57 d.d (1H, 15-H, $J = 1.7, 1.0$). ^{13}C NMR spectrum, δ_{C} , ppm: 14.14 (C^{20}), 20.18 (C^2), 23.21 (C^6), 29.34 (C^{19}), 31.74 (C^{11}), 35.92 (C^7), 38.18 (C^3), 39.49 (C^3), 41.49 (C^1), 44.54 (C^4), 58.22 (C^5), 62.52 (C^9), 63.57 (C^{17}), 74.77 (C^{12}), 84.46 (C^8), 109.99 (C^{14}), 129.68 (C^{13}), 140.64 (C^{15}), 144.77 (C^{16}), 180.90 (C^{18}). Found, %: C 67.24; H 7.51. $\text{C}_{20}\text{H}_{28}\text{O}_5$. Calculated, %: C 67.04; H 7.89.

Methyl (1S,4aS,5R,6R,8aS)-5-[2-(3-furyl)ethyl]-6-hydroxy-6-hydroxymethyl-1,4a-dimethylperhydronaphthalene-1-carboxylate [methyl (8R)-15,16-epoxy-8,17-dihydroxy-13(16),14-labdadien-18-oate] (VIa) and methyl (1S,4aS,5R,6R,8aS)-5-[2-(3-furyl)ethyl]6-hydroxy-6-methoxymethyl-1,4a-dimethylperhydronaphthalene-1-carboxylate [methyl (8R)-15,16-epoxy-8-hydroxy-17-methoxy-13(16),14-labdadien-18-oate] (VIb). To a solution of 6.0 g (17.1 mmol) of dihydroxy acid **IV** in 20 ml of ethanol we added a 40% aqueous solution of potassium hydroxide to pH 9 (about 1 ml). The mixture was heated to 50–55°C, and 5 ml (6.6 g, 51 mmol) of dimethyl sulfate was added dropwise under stirring. The mixture was stirred for 15 min, 2 ml of 40% aqueous potassium hydroxide was added to decompose excess dimethyl sulfate, and the mixture was stirred for 15 min, poured into water, and extracted with *tert*-butyl methyl ether. The extract was washed with water

and evaporated, and the residue was subjected to chromatography on aluminum oxide using petroleum ether–*tert*-butyl methyl ether (3:1 to 1:1) as eluent to isolate (in the order of elution) 2.8 g (44%) of compound **VIb** and 3.0 g (49%) of **VIa**.

Compound **VIa**. Oily substance, $[\alpha]_{\text{D}}^{20} = +30^\circ$ ($c = 5.9$, chloroform). ^1H NMR spectrum (CCl_4), δ , ppm (J , Hz): 0.51 s (3H, C^{20}H_3), 0.90–1.02 m (2H, 1-H, 3-H), 1.12 s (3H, C^{19}H_3), 1.08–1.22 m (3H, 5-H, 7-H, 9-H), 1.36 m (2H, 2-H, 11-H), 1.58–1.82 m (5H, 1-H, 2-H, 6-H, 11-H), 2.08–2.13 m (2H, 3-H, 7-H), 2.36 m (1H, 12-H, $^2J = 14.2$), 2.54 m (1H, 12-H, $^2J = 14.2$), 3.35 d.d (1H, 17-H, $^2J = 8.0, J = 1.2$), 3.52 d (1H, 17-H, $J = 8.0$), 3.58 s (3H, OCH_3), 6.18 d.d (1H, 14-H, $J = 2.6, 1.0$), 7.14 d (1H, 16-H, $J = 1.0$), 7.23 d.d (1H, 15-H, $J = 2.6, 1.0$). Mass spectrum, m/z (I_{rel} , %): 364 [M]⁺ (4.1), 346 [$M - 18$] (20), 315 (16), 273 (16), 264 (16), 255 (20), 161 (30), 147 (39), 135 (27), 121 (84), 95 (56), 81 (100), 73 (84), 55 (57), 41 (67). $\text{C}_{21}\text{H}_{32}\text{O}_5$.

Compound **VIb**. Oily substance. ^1H NMR spectrum ($\text{CDCl}_3\text{-CCl}_4$), δ , ppm (J , Hz): 0.53 s (3H, C^{20}H_3), 0.90–1.05 m (2H, 1-H, 3-H), 1.09 s (3H, C^{19}H_3), 1.07–1.12 m (2H, 5-H, 7-H), 1.22 d.d (1H, 9-H, $J = 12.2, 3.0$), 1.31 m (1H, 11-H, $^2J = 12.9$), 1.38 m (1H, 2-H, $^2J = 13.6$), 1.55–1.80 m (5H, 1-H, 2-H, 6-H, 11-H), 2.08–2.13 m (2H, 3-H, 7-H), 2.36 m (1H, 12-H, $^2J = 14.2$), 2.53 m (1H, 12-H, $^2J = 14.2$), 3.15 d.d (1H, 17-H, $^2J = 8.2, J = 1.2$), 3.48 s (3H, OCH_3), 3.65 d (1H, 17-H, $J = 8.2$), 3.68 s (3H, OCH_3), 6.19 d.d (1H, 14-H, $J = 2.6, 1.0$), 7.14 d (1H, 16-H, $J = 1.0$), 7.23 d (1H, 15-H, $J = 2.6$). ^{13}C NMR spectrum, δ_{C} , ppm: 13.34 (C^{20}), 19.04 (C^2), 21.48 (C^6), 26.05 (C^{11}), 27.98 (C^{12}), 28.65 (C^{19}), 37.79 (C^3), 38.51 (C^7), 38.96 (C^1), 39.67 (C^{10}), 43.56 (C^4), 50.81 (OCH_3), 56.51 (C^5), 58.43 (OCH_3), 58.98 (C^9), 73.35 (C^{17}), 74.00 (C^8), 110.92 (C^{14}), 125.46 (C^{13}), 138.30 (C^{16}), 141.98 (C^{15}), 176.47 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 378 [M]⁺ (3), 349 (11), 331 (24), 271 (20), 173 (25), 161 (21), 147 (28), 135 (21), 121 (100), 107 (42), 95 (53), 81 (77), 67 (37), 55 (68). Found: [M]⁺ 378.20079. $\text{C}_{22}\text{H}_{34}\text{O}_5$. Calculated: M 378.20422.

Methyl (1S,4aS,5R,6R,8aS)-9-[2-(3-furyl)ethyl]-2',2',4,10-tetramethylperhydrospiro[naphthalene-8,5'-1,3-dioxolane]-4-carboxylate (VII). Trifluoroacetic acid, 0.1 ml, was added to a solution of 0.35 g (1 mmol) of diol **VIa** in 5 ml of acetone. After 10 h, the mixture was diluted with water and extracted with *tert*-butyl methyl ether. The extract was washed with a 3% solution of NaHCO_3 and water and evaporated, and the residue was subjected to column chromatog-

raphy using petroleum ether–*tert*-butyl methyl ether (4:1) as eluent. Yield 0.27 g (76%), $[\alpha]_{\text{D}}^{20} = +10^{\circ}$ ($c = 8.2$, chloroform). ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 0.43 s (3H, C^{20}H_3), 0.92–1.0 m (2H, 1-H, 3-H), 1.10 d.d (1H, 5-H, $J = 12.4, 2.8$), 1.12 s (3H, C^{19}H_3), 1.27 s and 1.35 s [3H each, $\text{C}(\text{CH}_3)_2$], 1.25–1.42 m (4H, 2-H, 7-H, 9-H, 11-H), 1.55 m (1H, 11-H), 1.68 m (2H, 1-H, 6-H), 1.74 d.d.t (1H, 2-H, $^2J = 13.9, J = 3.7$), 1.86 d.d.d (1H, 6-H, $J = 14.4, 6.6, 3.3$), 2.04 d.t (1H, 7-H, $^2J = 12.7, J = 3.4, 3.4$), 2.10 m (1H, 3-H, $^2J = 13.3$), 2.30 m (1H, 12-H, $^2J = 14.3, 12.1, 5.4, 0.9$), 2.54 m (1H, 12-H, $^2J = 14.3$), 3.61 d.d (1H, 4'-H, $J = 8.4, 1.7$), 3.71 d (1H, 4'-H, $J = 8.4$), 6.16 d.d (1H, 14-H, $J = 1.8, 0.9$), 7.11 m (1H, 16-H, $J = 1.5, 1.0, 0.9$), 7.22 d.d (1H, 15-H, $J = 1.5, 1.0$). ^{13}C NMR spectrum, δ_{C} , ppm: 12.36 (C^{20}), 18.94 (C^2), 21.90 (C^6), 26.42 (C^{11}), 28.02 (C^{12}), 26.70, 28.51 ($2'\text{-CH}_3$), 28.54 (C^{19}), 37.70 (C^3), 38.83 (C^1), 39.34 (C^{10}), 39.54 (C^7), 43.55 (C^4), 50.95 (CH_3), 55.76 (C^5), 56.40 (C^9), 68.28 (C^4), 84.85 (C^8), 106.59 (C^2), 110.71 (C^{14}), 125.27 (C^{13}), 138.23 (C^{16}), 142.27 (C^{15}), 176.91 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 404 [M] $^+$ (0.8), 357 (1.1), 346 (4), 269 (6), 147 (10), 135 (12), 127 (22), 121 (31), 117 (100), 84 (22), 81 (21), 73 (34), 57 (24), 47 (19), 41 (41). $\text{C}_{24}\text{H}_{36}\text{O}_5$.

(1S,4aS,5R,6R,8aS)-6-Formyl-5-[2-(3-furyl)ethyl]-6-hydroxy-1,4a-dimethylperhydronaphthalene-1-carboxylic acid [(8R)-15,16-epoxy-8-hydroxy-17-oxo-13(16),14-labdadien-18-oic acid] (VIII). Acetic acid, 1 ml, was added to a solution of 3.0 g (8.5 mmol) of acid IV in 20 ml of methanol, and a solution of 1.9 g (8.8 mmol) of NaIO_4 in 3 ml of hot water (90–95°C) was then added dropwise under stirring. After 10 min, the mixture was poured into water and extracted with methylene chloride (3×10 ml). The extract was washed with a 3% solution of NaHCO_3 and water and evaporated, and the residue was recrystallized from petroleum ether–*tert*-butyl methyl ether. Yield 2.3 g (77%), mp 171–173°C, $[\alpha]_{\text{D}}^{20} = +37^{\circ}$ ($c = 8.4$, chloroform). ^1H NMR spectrum ($\text{CDCl}_3\text{-CCl}_4$), δ , ppm (J , Hz): 0.64 s (3H, C^{20}H_3), 1.05–1.25 m (4H, 1-H, 3-H, 5-H, 7-H), 1.27 s (3H, C^{19}H_3), 1.40–1.90 m (7H, 1-H, 2-H, 6-H, 9-H, 11-H), 1.96–2.08 m (3H, 3-H, 7-H, 11-H), 2.21 m (1H, 12-H), 2.32 m (1H, 12-H), 6.06 d.d (1H, 14-H, $J = 2.0, 1.2$), 7.07 d.d (1H, 16-H, $J = 1.6, 1.2$), 7.28 d (1H, 15-H, $J = 2.0, 1.2$), 9.32 s (1H, CHO), 10.5 br.s (1H, OH). ^{13}C NMR spectrum, δ_{C} , ppm: 13.37 (C^{20}), 19.65 (C^2), 22.27 (C^6), 24.16 (C^{11}), 25.99 (C^{12}), 28.97 (C^{19}), 37.74 (C^7), 39.44 (C^3), 42.47 (C^1), 43.40 (C^{10}), 44.18 (C^4), 55.09 (C^5), 61.68 (C^9), 82.00 (C^8), 110.82 (C^{14}), 124.58 (C^{13}), 138.75

(C^{16}), 142.53 (C^{15}), 183.33 (C^{18}), 209.50 (C^{17}). Mass spectrum, m/z (I_{rel} , %): 318 [$M - 30$] (10), 224 (23), 209 (100), 163 (17), 121 (35), 107 (28), 95 (31), 91 (33), 81 (79), 55 (70), 41 (80). $\text{C}_{20}\text{H}_{28}\text{O}_5$.

6,9a-Dimethyl-5,5a,6,7,8,9,9a,9b,10,11-decahydrophenanthro[1,2-*b*]furan-6-carboxylic acid (IXa). Hydroxy aldehyde VIII, 2.0 g (5.7 mmol), was dissolved in 8 ml of methanol, 0.3 ml of 10% hydrochloric acid was added, and the mixture was kept for 30 min at 0°C. The precipitate was filtered off and washed with 50% aqueous methanol. Yield 1.4 g (74%), mp 225–227°C (from petroleum ether–*t*-BuOMe). IR spectrum, ν , cm^{-1} : 733, 816, 833, 884, 893, 964, 977, 1024, 1102, 1500, 1686. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 0.76 s (3H, C^{17}H_3), 1.04–1.14 m (2H, 7-H, 9-H), 1.27 s (3H, C^{16}H_3), 1.37 d.q (1H, 10-H, $J = 12.3, 12.2, 4.0, 2.8$), 1.48–1.56 m (2H, 5a-H, 8-H), 1.87–1.98 m (3H, 8-H, 9-H, 10-H), 2.02 d.d (1H, 9b-H, $J = 12.3, 5.1$), 2.18 d.d.t (1H, 7-H, $J = 13.5, 3.2, 2.2$), 2.36–2.45 m (2H, 5-H, 11-H), 2.52 m (1H, 11-H, $^2J = 16.0, J = 5.2, 3.0$), 2.68 m (1H, 5-H, $^2J = 14.2$), 5.96 quint (1H, 4-H, $J = 2.8, 2.7$), 6.17 d (1H, 13-H, $J = 1.8$), 7.19 d (1H, 14-H, $J = 1.8$). ^{13}C NMR spectrum, δ_{C} , ppm: 12.53 (C^{17}), 19.50 (C^8), 22.32 (C^{11}), 23.78 (C^{10}), 23.92 (C^5), 28.65 (C^{16}), 35.21 (C^{9a}), 38.11 (C^7), 39.25 (C^9), 43.80 (C^6), 49.85 (C^{9b}), 51.03 and 51.09 ($\text{C}^{5a}, \text{OCH}_3$), 110.60 (C^{13}), 115.09 (C^4), 118.37 (C^3), 125.76 (C^{12}), 140.75 (C^{14}), 150.02 (C^2), 177.49 (C^{15}). Mass spectrum, m/z (I_{rel} , %): 300 [M] $^+$ (100), 254 (99), 239 (77), 183 (50), 146 (40), 134 (76), 131 (40), 115 (24), 91 (44), 77 (26), 55 (38), 43 (37), 41 (43). Found: [M] $^+$ 300.17364. $\text{C}_{19}\text{N}_{24}\text{O}_3$. Calculated: M 300.17253.

Methyl 6,9a-dimethyl-5,5a,6,7,8,9,9a,9b,10,11-decahydrophenanthro[1,2-*b*]furan-6-carboxylate (IXb) was synthesized in a similar way from 0.6 g (1.9 mmol) of ketone XI. Yield 0.51 g (82%), mp 125–128°C (from petroleum ether–acetone), $[\alpha]_{\text{D}}^{20} = -7^{\circ}$ ($c = 3.6$, chloroform). IR spectrum, ν , cm^{-1} : 696, 883, 986, 1575, 1610 ($\text{C}=\text{C}$), 1093, 1127, 1148 ($\text{C}-\text{O}-\text{C}$), 1248, 1718 ($\text{C}=\text{O}$). UV spectrum, λ_{max} , nm ($\log \epsilon$): 255 (4.44), 268 (4.85), 282 (4.13). ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 0.66 s (3H, C^{17}H_3), 1.06 m (1H, 7-H, $^2J = 13.4$), 1.08 m (1H, 9-H, $^2J = 14.0$), 1.20 s (3H, C^{16}H_3), 1.35 d.d.d.d (1H, 10-H, $J = 12.9, 12.4, 4.9, 2.9$), 1.48 m (2H, 5a-H, 8-H), 1.85–1.95 m (3H, 8-H, 9-H, 10-H), 2.00 d.d (1H, 9b-H, $J = 12.9, 6.1$), 2.16 d.d.t (1H, 7-H, $J = 13.4, 3.2, 2.0$), 2.36–2.45 m (2H, 5-H, 11-H), 2.53 m (1H, 11-H, $^2J = 15.9, 4.9, 2.9$), 2.57 m (1H, 5-H), 3.63 s (3H, OCH_3), 5.96 q (1H,

4-H, $J = 2.7, 2.8$), 6.17 d (1H, 13-H, $J = 2.0$), 7.18 d (1H, 15-H, $J = 2.0$). ^{13}C NMR spectrum, δ_{C} , ppm: 12.53 (C^{17}), 19.50 (C^8), 22.32 (C^{11}), 23.78 (C^{10}), 23.92 (C^5), 28.65 (C^{16}), 35.21 (C^{9a}), 38.11 (C^7), 39.25 (C^9), 43.80 (C^6), 49.85 (C^{9b}), 51.03 and 51.09 (C^{5a} , OCH_3), 110.60 (C^{13}), 115.09 (C^4), 118.37 (C^3), 125.76 (C^{12}), 140.75 (C^{14}), 150.02 (C^2), 177.49 (C^{15}). Mass spectrum, m/z (I_{rel} , %): 314 [M] $^+$ (50), 254 (100), 239 (58), 183 (31), 146 (13), 121 (23), 91 (12), 81 (13), 55 (15), 43 (11), 41 (13). Found: [M] $^+$ 314.18897. $\text{C}_{20}\text{H}_{26}\text{O}_3$. Calculated: M 314.18818. Compound **IXb** was also obtained by methylation of acid **IXa** with dimethyl sulfate according to the procedure described above for compound **IV**.

This study was performed under financial support by the Russian Foundation for Basic Research (project no. 03–03–33093) and by the President of the Russian Federation (program for support of leading scientific schools, project no. NSh 1488.3-03).

REFERENCES

1. Kharitonov, Yu.V., Shul'ts, E.E., Shakirov, M.M., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2005, vol. 41, p. 1145.
2. Faulkner, D.J., *Nat. Prod. Rep.*, 2002, vol. 19, no. 1, p. 1.
3. Hson Mou Chang, Kwok Ping Cheng, Tai Francis Choang, Hak Fun Chow, Kuk Ying Chui, Po Ming Hon, Fan Wah Lau Tan, Yun Yang, Zeng Pei Zhong, Chi Ming Lee, Hing Leung Sham, Chun Fei Chan, Yu Xin Cui, and Wong, H.N.C., *J. Org. Chem.*, 1990, vol. 55, p. 3537.
4. Thomson, R.H., *Naturally Occuring Quinones IV: Recent Advances*, London: Blackie Academic & Professional, 1997, 4th ed., p. 694.
5. Lee, J. and Snyder, J.K., *J. Org. Chem.*, 1992, vol. 57, p. 5301.
6. Gustafson, K., Andersen, R.J., He, C.H., and Clardy, J., *Tetrahedron Lett.*, 1985, vol. 26, p. 2521.
7. Faulkner, D.J., Molinski, T.F., Andersen, R.J., Dumdei, E.J., and Dilip de Silva E., *Comp. Biochem. Physiol., Part C: Pharmacol., Toxicol., Endocrinol.*, 1990, vol. 97, no. 2, p. 233.
8. Dumdei, E.J., Kubanek, J., Coleman, J.E., Pika, J., Andersen, R.J., Steiner, J.R., and Clardy, J., *Can. J. Chem.*, 1997, vol. 75, p. 773.
9. Chernov, S.V., Shults, E.E., Shakirov, M.M., Bagrjanskaja, I.Yu., Gatilov, Yu.V., and Tolstikov, G.A., *Arkivoc*, 2003, part XIII, p. 172.
10. Steiger, M. and Reichstein, T., *Helv. Chim. Acta*, 1938, vol. 21, p. 546.
11. Vlad, P.F. and Ungur, N.D., *Khim. Prirodn. Soedin.*, 1984, no. 6, p. 725.