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Synthetic Transformations of Higher Terpenoids: IX.* Nitrogen-Containing Heterocyclic Compounds on the Basis of Lambertianic Acid

S. V. Chernov, E. E. Shul'ts, M. M. Shakirov, I. Yu. Bagryanskaya, Yu. V. Gatilov, 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

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Abstract—Oxidation of lambertianic acid methyl ester and methyl 15,16-epoxy-17-hydroxylabda-13(16)14-dien-18-oate gave 17-nor-8-oxo-, 8,12-epoxy-17-hydroxy-, and 8-formyl-17-norlabdadienoic acid esters which were subjected to reductive amination, and the subsequent intramolecular aminomethylation of 17-nor-8(R)-methylamino- and 17-methylaminolabdadienoates with formaldehyde afforded new polycyclic compounds, furoazocine and furoazonine derivatives.

Terpenoids and alkaloids containing a furan ring as a structural fragment often exhibit valuable biological activity [2, 3]. One of these compounds is lambertianic acid (**Ia**) which is a component of needles and oleoresin of Siberian pine *Pinus sibirica* R. Mayr.; it shows a pronounced stimulating effect [4] and is a precursor of some promising biologically active compounds [1, 5–7]. In the present communication we describe transformations of lambertianic acid (**Ia**) into novel diterpene alkaloids having hexahydro[3,4-*b*]furoazocine and -[3,4-*b*]furoazonine fragments. The key intermediate products in these syntheses were those obtained by oxidation of lambertianic acid methyl ester (**Ib**), namely methyl 15,16-epoxy-17-nor-8-oxolabda-13(16),14-dien-18-oate (**II**), 8,12-epoxy-17-hydroxy labdanoid **III**, and 17-hydroxy-8,17-dihydrolambertianic acid methyl ester (**IV**); the synthesis of the latter was described previously [7].

The oxidation of ester **Ib** with $KMnO_4$ under conditions of phase-transfer catalysis [8] gave a mixture of ketone **II** (21%), (8*R*,12*S*)-epoxy labdanoid **III** (39%), and its 12-epimer **V** (11%) (Scheme 1), which were separated by column chromatography. The reaction was carried out in neutral medium which was maintained by addition of magnesium sulfate. In the absence of the latter, other products were also formed. The structure of compound **II** follows from the spectral data. Its mass spectrum contained the molecular ion peak with *m*/*z* 332 (13%) and fragment ion peaks with *m*/*z* 238 (37%) and 95 (23%), corresponding to decomposition with formation of functionally substituted decalin and furylethyl ions. In the ^{13}C NMR spectrum of **II**, the C^8=O carbonyl carbon atom resonated at δ_C 208.92 ppm, and the C^9 signal was a doublet displaced downfield ($\Delta\delta_C$ 6.7 ppm) relative to the corresponding signal in the spectrum of the initial compound (δ_C 55.04 ppm [9]). The structure and stereochemical configuration of compound **III** were unambiguously proved by the X-ray diffraction data (Fig. 1). The bond lengths in molecule **III** approach the corresponding standard values [10] and coincide within 3σ with those found for diosbulbin B and teucrolivin G [11, 12] as the closest structural analogs deposited to the Cambridge Structural Database [13]. The six-membered rings in **III** adopt a *chair* conformation, and the oxolane fragment exists in a *twist* form; the approximate C_2 symmetry axis passes through the middle of the C^8–C^9 bond and C^{12} atom. The furan ring is planar (the mean-square deviation of atoms is 0.004 Å). Despite the presence of hydroxy and oxo groups in the molecule, no intermolecular hydrogen bonds were detected in crystal.

The structure of isomer **V** was confirmed by the NMR spectra of both **V** and its acetate **VI**. Signals in

* For communication VIII, see [1].

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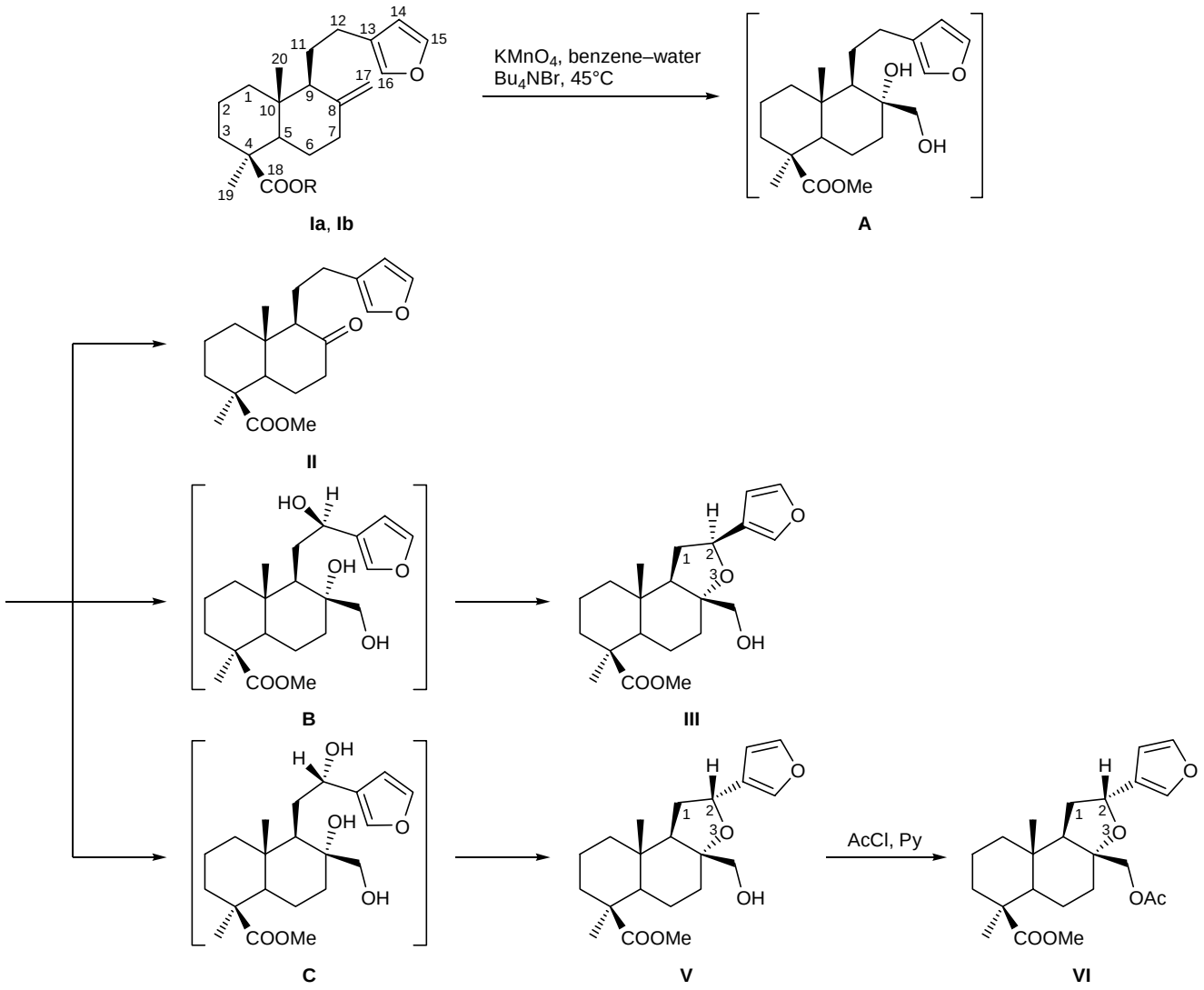
Scheme 1.

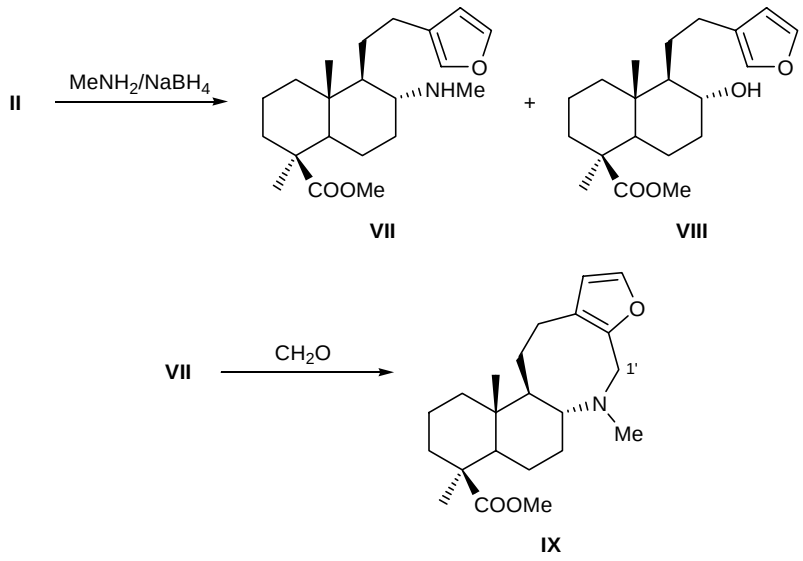


I, R = H (**a**), Me (**b**).

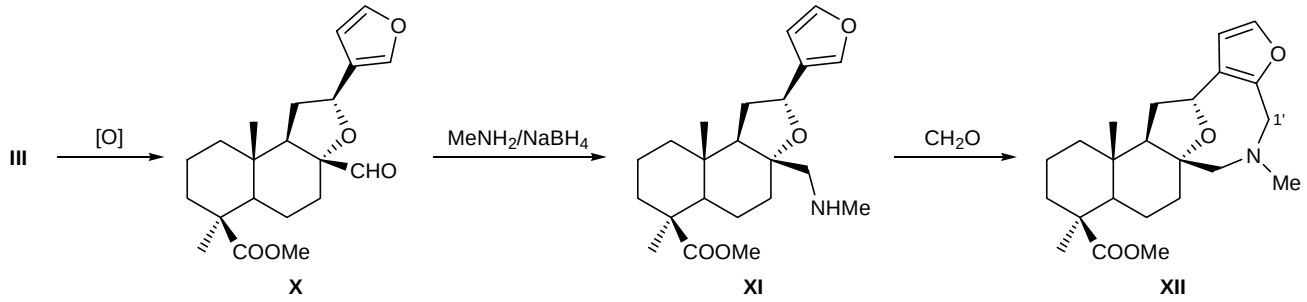
the ^{1}H NMR spectra were assigned using two-dimensional ^{1}H–^{1}H and ^{13}C–^{1}H correlation techniques (COSY, HMBX, and COLOC). The (*8R*,12*R*) configuration of **VI** was determined from the results of NOESY experiments. The β-orientation of the hydroxymethyl group on C^8 unambiguously follows from the presence of NOEs on diastereotopic 17-H protons (δ 3.96 ppm, d, and 4.36 ppm, d.d) and protons of the methoxycarbonyl group on C^4 (δ 3.61 ppm) upon irradiation of protons in the methyl group on C^{10} (δ 0.64 ppm). In addition, the $C^{20}H_3$ protons show NOEs with the axial protons on C^2 and C^6 and pseudoaxial proton on C^{11}. Irradiation of 17-H (δ 3.96 ppm) gives NOEs on the other 17-H proton, axial protons on C^2, C^6, and C^7, and protons of the angular methyl group. Irradiation at a frequency corresponding to the second 17-H proton (δ 4.36 ppm) gives no NOE on 6-H and 7-H, but a strong NOE was observed on the pseudoaxial proton on C^{11}, and a weak effect (as compared to the upfield 17-H), on $C^{20}H_3$. These data are consistent with the assumed steric structure of compounds **V** and **VI**. Insignificant differences in proton chemical shifts for stereoisomeric epoxy labdanoids **III** and **V** should also be noted. The largest differences in the ^{13}C NMR spectra were observed for the C^9, C^{12}, C^{17}, and C^{19} signals.

As shown in Scheme 1, the first step in the oxidation of lambertianic acid methyl ester (**Ia**) is hydroxylation of the exocyclic C^8=C^{17} double bond, which occurs at the less sterically hindered α-side and

Scheme 2.



Scheme 3.



gives intermediate glycol **A**. Further transformations of intermediate **A** follow two pathways. The first of these leads to ketone **II**, while oxidation of the $C^{12}H_2$ methylene group gives isomeric triols **B** and **C** which undergo ring closure to epoxy derivatives **III** and **V**.

Heterocyclic derivatives of lambertianic acid were synthesized via reductive amination of carbonyl compounds and subsequent intramolecular aminomethylation according to Mannich with the use of formaldehyde. Treatment of ketone **II** with $MeNH_2$–$NaBH_4$ afforded 52% of 17-nor-8α-methylamino labdanoid **VII** and 33% of secondary alcohol **VIII** (Scheme 2). Methylamino derivative **VII** reacted with formaldehyde to give hexahydrofuroazocine **IX** whose structure was proved by the X-ray diffraction data (Fig. 2). The six-membered rings in molecule **IX** have a *chair* conformation, and the furan ring is planar within 0.003 Å. The eight-membered nitrogen-containing heteroring adopt a conformation like *twist–boat* in cyclooctane; this conformation is not the most stable for cyclooctanes [14]. We have found neither structures having an analogous tetracyclic skeleton with a cyclooctene fragment nor hexahydrofuro[*b*]azocine derivatives in the Cambridge Structural Database [13]. Among ten

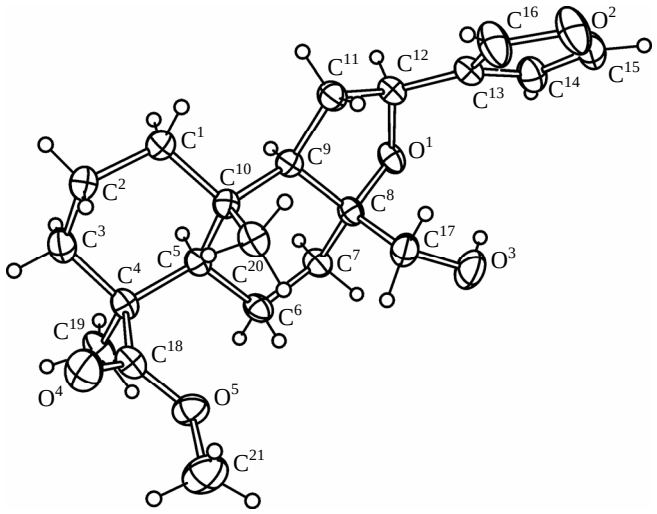
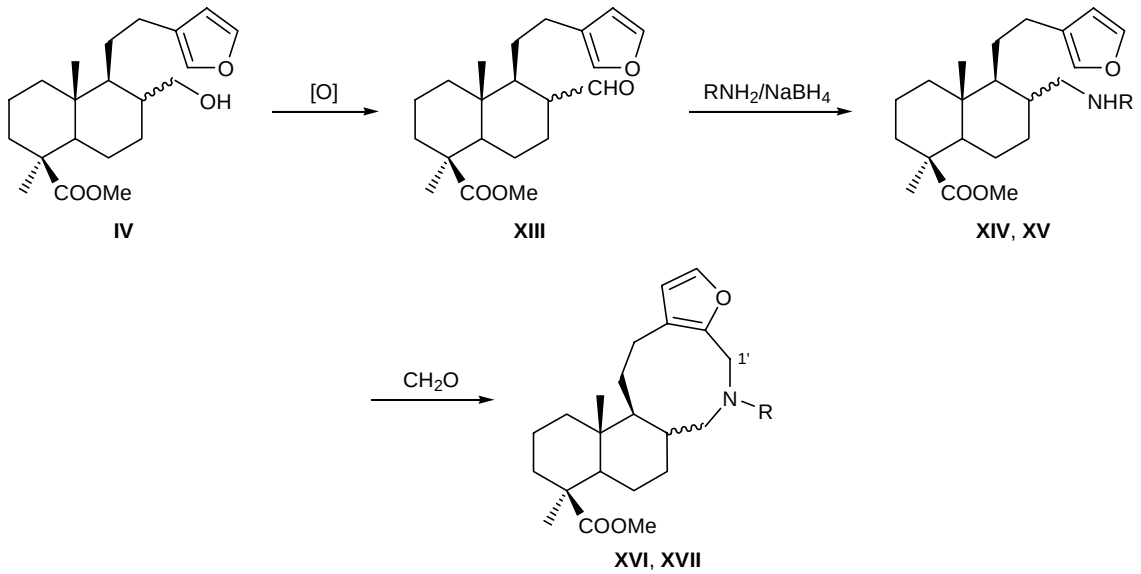


Fig. 1. Structure of the molecule of methyl 8α,12α:15,16-diepoxy-17-hydroxylabda-13(16),14-dien-18-oate (**III**) according to the X-ray diffraction data.

Scheme 4.



IV **XIII** **XIV**, **XV** **XVI**, **XVII**

XIV, **XVI**, R = 2-(3-indolylethyl); **XV**, **XVII**, R = $PhCH_2CH(CO_2Me)$.

structures derived from *cis*-cyclooctene, only 8-methylidene-1,3,3-tris(phenylsulfonyl)cyclooctene [15] had a *twist–boat* conformation of the eight-membered ring. The nitrogen atom in the hexahydroazocine fragment in **IX** has a pyramidal configuration, and it deviates by 0.446 Å from the plane passing through the C^8, $C^{1'}$, and C^{22} atoms. The bond lengths and bond angles in molecule **IX** are similar to the corresponding standard values [10].

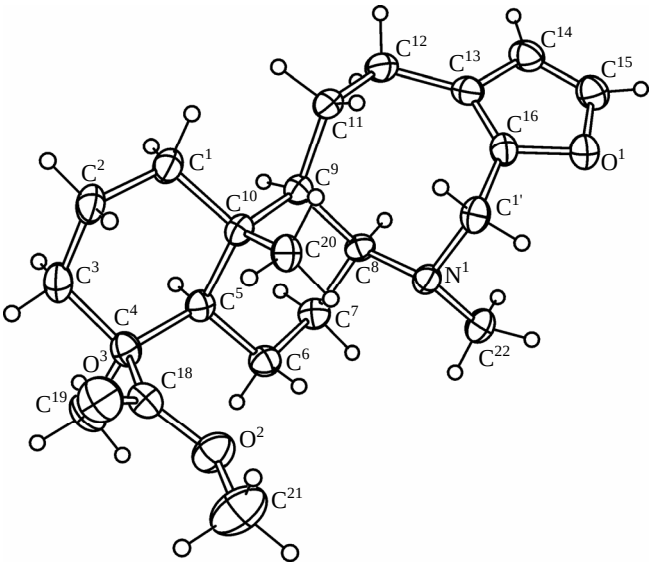


Fig. 2. Structure of the molecule of methyl (1*R*,11*S*,14*S*,19*S*)-10,15,19-trimethyl-7-oxa-10-azatetracyclo[14.4.0.0^{4,8}.0^{1,11}]-nonadeca-4(8),5-diene-15-carboxylate (**IX**) according to the X-ray diffraction data.

By oxidation of 8,12-epoxy-17-hydroxy labdanoid **III** with pyridinium chlorochromate in methylene chloride we obtained aldehyde **X**, and reductive amination of the latter with $MeNH_2$–$NaBH_4$ gave amine **XI** (Scheme 3). As in the preceding case, intramolecular aminomethylation of **XI** by the action of formaldehyde smoothly led to formation of furoazonine **XII**. The structure of **XII** was unambiguously confirmed by the spectral data.

Under analogous conditions, the oxidation of 8-hydroxymethyl labdanoid **IV** [7] yielded a mixture of (8*R*)- and (8*S*)- aldehydes **XIII** at a ratio of 2:1 (according to the signal intensity ratios for methyl protons, protons of the furan ring, and aldehyde protons in the ^{1}H NMR spectra). The subsequent reductive amination of **XIII** with tryptamine or phenylalanine methyl ester and sodium tetrahydridoborate resulted in formation of the corresponding amines **XIV** and **XV** as mixtures of stereoisomers (Scheme 4). The stereoisomers showed considerable differences in the chemical shifts of C^8 and C^9 in the ^{13}C NMR spectra, δ_C, ppm: **XV**, C^8: 40.36 (*S*), 39.68 (*R*); C^9: 52.88 (*S*), 53.41 (*R*). By cyclization in the presence of formaldehyde we obtained furoazonine derivatives **XVI** and **XVII**. Analysis of the ^{1}H NMR spectra showed that the (8*R*)/(8*S*)-isomer ratio intrinsic to aldehydes **XIII** is retained in both amines **XIV** and **XV** and (8*R*,9*R*)- and (8*S*,9*R*)-furoazonines **XVI** and **XVII**. Thus our results indicate that amines with different orientations of the aminomethyl group on C^8 equally readily undergo ring

closure according to Mannich. It should be emphasized that no Pictet–Spengler products were detected in the reaction with tryptamine derivative **XIV**.

We also found reliable criteria for assignment of hexahydrofuroazocine and hexahydrofuroazonine structures on the basis of their ^{1}H and ^{13}C NMR spectra. Distinctive features of the ^{1}H NMR spectrum of hexahydrofuroazocine **IX** are an upfield shift of the NMe signal (δ 2.09 ppm) and downfield shift of the $C^{20}H_3$ signal (δ 0.99 ppm), which are induced by conformation of the hexahydroazocine fragment. The 8-H signal appears as a quartet at δ 2.21 ppm due to coupling with 7-H and 9-H (J = 3.1 Hz). Diastereotopic protons on $C^{1'}$ resonate at δ 3.44 and 4.33 ppm (^2J = 12.2 Hz).

In going to the hexahydrofuroazonine skeleton (nine-membered heteroring; compounds **XVI** and **XVII**), the difference in the chemical shifts of the 1'-H protons becomes smaller [δ 3.42 and 3.58 ppm for (*S*)-**XVI**], and the signal from the angular methyl group shifts upfield (δ 0.68 ppm). In the ^{13}C NMR spectra of compounds **XVI** and **XVII**, the C^{16} signal is located in a weaker field, as compared to initial amines **XIV** and **XV**.

The stereochemical configuration of epoxyfuroazonine **XII** was determined using NOESY technique. Both diastereotopic protons on C^{17} showed appreciable (and comparable) nuclear Overhauser effects on $C^{20}H_3$ (δ 0.57 ppm) and on each other. Irradiation of the downfield 17-H proton (δ 2.49 ppm) gives NOE on the axial 6-H proton (δ 1.85 ppm), while the effect on the downfield 1'-H proton is weak (δ 4.50 ppm). The upfield 17-H proton (δ 2.18 ppm) produces appreciable NOEs on 12-H (δ 5.04 ppm), pseudoaxial 11-H (δ 1.69 ppm), and 9-H (δ 1.50 ppm), while no effect on 1'-H is observed. Characteristically, protons in the furan ring (14-H and 15-H) show NOEs on 12-H and protons of the angular methyl group, respectively.

Thus we have proposed efficient methods for the synthesis of optically active heteropolycyclic compounds, namely furoazocine and furoazonine derivatives, via transformations of lambertianic acid methyl ester.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Vector-22 spectrometer. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT-8200 high-resolution mass spectrometer (vaporizer temperature 190–300°C). The NMR spectra were recorded on Bruker AC-200 (200.13 MHz for ^{1}H and 50.32 MHz for ^{13}C) and Bruker DRX-500 spectrometers (500.13 MHz for ^{1}H and 125.76 MHz for ^{13}C) from solutions in $CDCl_3$, CD_3OD, or CCl_4. Signals in the NMR spectra were assigned using various proton–proton and carbon–proton shift correlation techniques (COSY, COLOC, CORRD), as well as 2D NOESY experiments. X-Ray analysis of single crystals of compounds **III** and **IX** was performed on a Bruker P-4 diffractometer (MoK_α irradiation, graphite monochromator, 2θ/θ scanning in the range 2θ < 50°). The optical rotations ($[\alpha]_{580}$) were measured on a Polamat A polarimeter from solutions in chloroform at room temperature (20–23°C). The progress of reactions was monitored by thin-layer chromatography on Silufol UV-254 plates. The products were isolated by column chromatography on aluminum oxide.

Oxidation of lambertianic acid methyl ester (Ia) with potassium permanganate. A solution of 5 g of $MgSO_4 \cdot 7H_2O$ in 50 ml of water was added to a solution of 3.3 g (10 mmol) of ester **Ib** and 0.1 g of tetrabutylammonium bromide in 20 ml of benzene. The mixture was vigorously stirred at 45–50°C, and a solution of 3.0 g (19 mmol) $KMnO_4$ in 60 ml of water was added over a period of 1 h. When the reaction was complete (TLC), the precipitate of MnO_2 was filtered off and washed with *tert*-butyl methyl ether. The organic phase was separated, the solvent was distilled off, and the residue was subjected to column chromatography using petroleum ether–*tert*-butyl methyl ether (1:1 to 1:3) to isolate (in the order of elution) 0.7 g (21%) of ketone **II**, 1.4 g (39%) of (8*R*,12*S*)-epoxy labdanoid **III**, and 0.4 g (11%) of (8*R*,12*R*)-epoxy labdanoid **V**.

Methyl (1*S*,4a*S*,5R,8a*S*)-5-[2-(3-furyl)ethyl]-1,4a-dimethyl-6-oxoperhydronaphthalene-1-carboxylate [methyl 15,16-epoxy-17-nor-8-oxolabda-13(16),14-dien-18-oate] (II). mp 61–62°C (from petroleum ether), $[\alpha]_{580}^{20}$ = +55° (c = 5.1). IR spectrum, ν, cm^{-1}: 755, 873, 971, 984, 1026, 1066, 1090, 1117, 1502, 1716, 1721. ^{1}H NMR spectrum (CCl_4), δ, ppm: 0.49 s (3H, $C^{20}H_3$), 0.87 d.d.d (1H, 3-H, J = 14.0, 12.5, 3.5 Hz), 1.03 d.d.d (1H, 1-H, J = 14.0, 12.8, 4.8 Hz), 1.21 s (3H, $C^{19}H_3$), 1.23 m (1H, 5-H), 1.56 m (3H, 1-H, 12-H, 7-H), 1.70 m (1H, 11-H), 1.75 d.d.d (1H, 2-H, J = 13.4, 6.7, 3.8 Hz), 1.82 d.d.d (1H, 6-H, J = 14.0, 12.6, 4.6 Hz), 1.92 m (2H, 3-H, 12-H), 2.15 m (3H, 2-H, 6-H, 11-H), 2.36 d.d.d (1H, 7-H, J = 13.6, 12.0, 3.6 Hz), 3.58 s (3H, OCH_3), 3.61 d.d (1H, 9-H,

J = 11.2, 8.6 Hz), 6.15 d (1H, 14-H, *J* = 2.6 Hz), 7.08 d (1H, 16-H, *J* = 1.9 Hz), 7.24 d.d (1H, 15-H, *J* = 1.9, 2.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.14 (C^{20}), 19.71 (C^2), 22.28 (C^6), 23.79 (C^{12}), 25.49 (C^{11}), 29.30 (C^{19}), 38.09 (C^3), 39.48 (C^1), 42.82 (C^7), 43.82 (C^4), 44.15 (C^{10}), 51.02 (OMe), 55.10 (C^5), 61.70 (C^9), 110.78 (C^{14}), 124.59 (C^{13}), 138.67 (C^{15}), 140.20 (C^{16}), 175.94 (C^{18}), 208.92 (C^8). Mass spectrum, *m*/*z* (I_{rel}, %): 332 $[M]^+$ (13), 238 (37), 223 (100), 163 (41), 121 (28), 95 (23). Found: $[M]^+$ 332.19955. Calculated: *M* 332.19875.

Methyl (2*S*,3a*R*,5a*R*,6*S*,9b*S*)-2-(3-furyl)-3a-hydroxymethyl-6,9a-dimethylperhydronaphtho-[2,1-*b*]furan-6-carboxylate [methyl 8*α*,12*α*:15,16-diepoxy-17-hydroxylabda-13(16),14-dien-18-oate] (III). mp 121–123°C (from petroleum ether–acetone), $[\alpha]_{580}^{20}$ = +35° (*c* = 6.6). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.57 s (3H, $C^{20}H_3$), 1.00 d.d.d (1H, 3-H, *J* = 14.0, 12.2, 3.3 Hz), 1.05 d.d.d (1H, 1-H, *J* = 14.1, 10.9, 3.8 Hz), 1.07 m (1H, 7-H, ^2J = 14.8 Hz), 1.13 s (3H, $C^{19}H_3$), 1.16 m (1H, 5-H), 1.43 m (1H, 2-H), 1.49 m (1H, 1-H), 1.73 d.d.d (1H, 6-H, *J* = 14.0, 7.2, 3.8 Hz), 1.78 m (1H, 9-H), 1.86 m (2H, 2-H, 11-H), 1.92 d.d.d (1H, 6-H, *J* = 14.0, 12.6, 3.0 Hz), 2.07 d.d.d (1H, 11-H, *J* = 12.8, 8.0, 1.8 Hz), 2.15 m (1H, 3-H), 2.18 s (1H, OH), 2.30 d.d.d (1H, 7-H, *J* = 14.8, 6.8, 1.9 Hz), 3.30 d (1H, 17-H, *J* = 13.1 Hz), 3.52 d (1H, 17-H, *J* = 13.1 Hz), 3.57 s (3H, OCH_3), 4.95 d (1H, 12-H, *J* = 8.0, 6.2 Hz), 6.35 d (1H, 14-H, *J* = 1.9 Hz), 7.329 d (1H, 16-H, *J* = 1.7 Hz), 7.331 d.d (1H, 15-H, *J* = 1.7, 1.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.88 (C^{20}), 18.66 (C^2), 21.71 (C^6), 28.31 (C^{19}), 30.05 (C^{11}), 34.54 (C^7), 36.60 (C^{10}), 38.09 (C^3), 39.89 (C^1), 43.31 (C^4), 50.95 (OMe), 56.66 (C^5), 60.53 (C^9), 62.38 (C^{17}), 72.68 (C^{12}), 82.66 (C^8) 108.62 (C^{14}), 127.56 (C^{13}), 138.91 (C^{15}), 143.64 (C^{16}), 177.07 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 332 (21) $[M - 30]^+$, 331 (100), 271 (22), 253 (20), 121 (28), 107 (25). $C_{21}N_{30}O_5$.

Methyl (2*R*,3a*R*,5a*S*,6*S*,9a*S*,9bS)-2-(3-furyl)-3a-hydroxymethyl-6,9a-dimethylperhydronaphtho-[2,1-*b*]furan-6-carboxylate [methyl 8*α*,12β:15,16-diepoxy-17-hydroxylabda-13(16),14-dien-18-oate] (V). Oily substance, $[\alpha]_{580}^{20}$ = +12° (*c* = 4.5). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.58 s (3H, $C^{20}H_3$), 0.87 d.d.d (1H, 3-H, *J* = 14.0, 12.1, 3.0 Hz), 1.01 m (1H, 1-H), 1.10 m (1H, 5-H), 1.16 s (3H, $C^{19}H_3$), 1.28 m (1H, 7-H, ^2J = 13.8 Hz), 1.41 m (2H, 1-H, 2-H), 1.70 d.d.d (1H, 6-H, *J* = 14.0, 12.5, 2.8 Hz), 1.83 m (1H, 2-H), 1.90 m (3H, 6-H, 9-H, 11-H), 2.13 m (2H, 3-H, 11-H), 2.40 d.d.d (1H, 7-H, *J* = 13.9, 6.8, 2.2 Hz), 3.40 d (1H, 17-H, *J* = 8.9 Hz), 3.45 d (1H, 17-H, *J* = 8.9 Hz), 3.60 s (3H, OCH_3), 5.01 d.d (1H, 12-H, *J* = 10.1, 7.6 Hz), 6.22 d.d (1H, 14-H, *J* = 1.6, 0.9 Hz), 7.27 d (1H, 16-H, *J* = 1.0 Hz), 7.31 d.d (1H, 15-H, *J* = 1.6, 1.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.61 (C^{20}), 18.70 (C^2), 21.64 (C^6), 26.83 (C^{19}), 30.98 (C^{11}), 34.29 (C^7), 36.44 (C^{10}), 38.20 (C^3), 39.91 (C^1), 43.23 (C^4), 50.69 (OMe), 57.02 (C^5), 58.52 (C^9), 60.52 (C^{17}), 70.90 (C^{12}), 83.15 (C^8) 108.18 (C^{14}), 128.83 (C^{13}), 138.88 (C^{15}), 142.46 (C^{16}), 176.16 (C^{18}). Found, %: C 70.1; H 8.51. $C_{21}H_{30}O_5$. Calculated, %: C 69.61; H 8.29.

Methyl (2*R*,3a*R*,5a*S*,6*S*,9a*S*,9b*S*)-3a-acetoxymethyl-2-(3-furyl)-6,9a-dimethylperhydronaphtho-[2,1-*b*]furan-6-carboxylate (VI). Acetyl chloride, 0.3 ml, was added to a solution of 0.35 g (1 mmol) of compound **V** in 5 ml of benzene and 0.3 ml of pyridine. After 1 h, the mixture was washed with water, the solvent was distilled off, and the residue was subjected to column chromatography to isolate 0.31 g (82%) of acetate **VI**. $[\alpha]_{580}^{20}$ = +25° (*c* = 2.1). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.64 s (3H, $C^{20}H_3$), 0.99 d.d.d (1H, 3-H, *J* = 13.8, 12.6, 3.0 Hz), 1.05 d.d.d (1H, 1-H, *J* = 13.2, 10.5, 2.8 Hz), 1.16 s (3H, $C^{19}H_3$), 1.19 d.d (1H, 5-H, *J* = 12.7, 3.4 Hz), 1.27 d.d.d (1H, 7-H, *J* = 13.8, 12.2, 11.8 Hz), 1.41 d.d.d (1H, 1-H, *J* = 13.2, 5.8, 2.9 Hz), 1.44 d.d.d (1H, 2-H, *J* = 14.2, 10.2, 4.8 Hz), 1.62 d.d (1H, 9-H, *J* = 7.0, 2.5 Hz), 1.67 d.d (1H, 11-H, *J* = 7.0, 7.8 Hz), 1.82 d.d.d (1H, 2-H, *J* = 14.2, 6.9, 2.2 Hz), 1.86 d.d.d (1H, 6-H, *J* = 14.2, 3.6, 2.8 Hz), 1.97 d.d.d (1H, 6-H, *J* = 14.2, 11.8, 6.8 Hz), 2.05 s (3H, Ac), 2.14 d.d (1H, 11-H, *J* = 7.8, .6 Hz), 2.17 d.d.d (1H, 3-H, *J* = 13.8, 5.8, 2.5 Hz), 2.26 d.t (1H, 7-H, *J* = 12.4, 3.4 Hz), 3.61 s (3H, OCH_3), 3.96 d (1H, 17-H, *J* = 11.4 Hz), 4.36 d.d (1H, 17-H, *J* = 11.4, 1.7 Hz), 5.06 d.d (1H, 12-H, *J* = 10.3, 8.3 Hz), 6.22 d.d (1H, 14-H, *J* = 1.8, 0.85 Hz), 7.26 d.t (1H, 16-H, *J* = 1.7, 0.85 Hz), 7.29 d.d (1H, 15-H, *J* = 1.8, 1.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.98 (C^{20}), 18.82 (C^2), 20.93 (CH_3), 21.70 (C^6), 28.59 (C^{19}), 30.96 (C^{11}), 35.21 (C^7), 36.39 (C^{10}), 38.23 (C^3), 40.09 (C^1), 43.41 (C^4), 51.11 (OMe), 57.12 (C^5), 59.58 (C^9), 62.59 (C^{17}), 71.37 (C^{12}), 81.16 (C^8), 108.35 (C^{14}), 128.97 (C^{13}), 138.75 (C^{15}), 143.06 (C^{16}), 170.58 (C=O), 176.71 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 332 $[M - 72]^+$ (22), 331 (100), 271 (24), 253 (20), 121 (22), 107 (25), 81 (22).

Methyl (1*S*,4a*S*,5*R*,6*R*,8a*S*)-5-[2-(3-furyl)ethyl]-1,4a-dimethyl-6-methylaminoperhydronaphthalene-1-carboxylate [methyl (8*R*)-15,16-epoxy-8-methylamino-17-norlabda-13(16),14-dien-18-oate] (VII). A solution of 1 g of methylamine in 10 ml of

methanol was added to a solution of 0.33 g (1 mmol) of compound **II** in 5 ml of methanol. The mixture was left to stand for 18 h at room temperature and cooled to 0°C, and 0.1 g (2.7 mmol) of sodium tetrahydridoborate was added under stirring. When the reaction was complete (TLC), the mixture was diluted with water and extracted with *tert*-butyl methyl ether. The extract was evaporated, and the residue was subjected to column chromatography using petroleum ether–*tert*-butyl methyl ether (1:1 to 1:3) as eluent to isolate first 0.18 g (52%) of amine **VII** and 0.11 g (33%) of alcohol **VIII**. Compound **VII**: mp 65–67°C (from petroleum ether), $[\alpha]_{580}^{20}$ = +21° (*c* = 2.8). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.69 s (3H, $C^{20}H_3$), 0.88 d.d.d (1H, 1-H, *J* = 13.8, 12.6, 3.0 Hz), 0.95 d.d.d (1H, 3-H, *J* = 13.6, 10.5, 2.7 Hz), 1.08 m (2H, 5-H, 11-H), 1.13 s (3H, $C^{19}H_3$), 1.36 d.d.d (1H, 7-H, *J* = 13.7, 6.8, 3.2 Hz), 1.55–1.80 m (6H, 1-H, 2-H, 6-H, 9-H, 12-H), 2.14 d.d.d (1H, 11-H, *J* = 14.2, 12.2, 5.6 Hz), 2.24 m (2H, 3-H, 6-H), 2.31 m (1H, 12-H), 2.33 s (3H, NCH_3), 2.42 m (1H, 7-H), 2.58 d.d (1H, 8-H, *J* = 4.2, 3.8 Hz), 3.60 s (3H, OCH_3), 5.12 s (1H, NH), 6.17 d (1H, 14-H, *J* = 2.6 Hz), 7.12 d (1H, 16-H, *J* = 1.5 Hz), 7.26 d.d (1H, 15-H, *J* = 2.6, 1.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.40 (C^{20}), 18.46 (C^2), 19.10 (C^6), 23.42 (C^{12}), 25.00 (C^{11}), 28.85 (C^{19}), 30.33 (C^7), 35.90 (NMe), 38.41 (C^{10}), 38.30 (C^3), 39.71 (C^1), 43.77 (C^4), 50.95 (OMe), 52.95 (C^9), 56.28 (C^5), 57.46 (C^8), 110.84 (C^{14}), 124.94 (C^{13}), 138.56 (C^{15}), 142.48 (C^{16}), 176.67 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 347 $[M]^+$ (15), 264 (47), 81 (16), 70 (100).

Methyl (1*S*,4a*S*,5*R*,6*R*,8a*S*)-5-[2-(3-furyl)ethyl]-6-hydroxy-1,4a-dimethylperhydronaphthalene-1-carboxylate [methyl (8*R*)-15,16-epoxy-8-hydroxy-17-norlabda-13(16),14-dien-18-oate] (VIII). Oily substance, $[\alpha]_{580}^{20}$ = +47° (*c* = 3.3). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.74 s (3H, $C^{20}H_3$), 0.89 d.d.d (1H, 3-H, *J* = 13.6, 12.4, 3.0 Hz), 0.95 m (1H, 1-H), 1.13 s (3H, $C^{19}H_3$), 1.15 m (2H, 5-H, 11-H), 1.39 d.d.d (1H, 7-H, *J* = 12.9, 6.7, 3.0 Hz), 1.55–1.84 m (6H, 1-H, 2-H, 6-H, 9-H, 12-H), 1.98 d.d.d (1H, 11-H, *J* = 14.0, 12.1, 5.1 Hz), 2.25 m (1H, 3-H), 2.35 m (2H, 6-H, 12-H), 2.47 d.d.d (1H, 7-H, *J* = 14.0, 12.2, 2.6 Hz), 3.60 s (3H, OCH_3), 3.92 d.d (1H, 8-H, *J* = 4.8, 3.0 Hz), 6.16 d (1H, 14-H, *J* = 1.5 Hz), 7.12 d (1H, 16-H, *J* = 1.6 Hz), 7.25 d.d (1H, 15-H, *J* = 1.5, 1.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.22 (C^{20}), 18.21 (C^2), 18.91 (C^6), 23.11 (C^{12}), 24.81 (C^{11}), 28.60 (C^{19}), 35.71 (C^7), 38.09 (C^{10}), 38.24 (C^3), 39.54 (C^1), 43.84 (C^4), 51.03 (OMe), 52.63 (C^9), 56.77 (C^5), 66.94 (C^8), 110.63 (C^{14}), 124.93 (C^{13}), 138.67 (C^{15}), 142.20 (C^{16}), 177.32 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 334 $[M]^+$ (44), 319 (34), 316 (26), 223 (52), 163 (47), 121 (81), 109 (51), 95 (51), 81 (100).

Methyl (1*R*,11*S*,14*S*,19*S*)-10,15,19-trimethyl-7-oxa-10-azatetracyclo[14.4.0.0^{4,8}.0^{1,11}]nonadeca-4(8),5-diene-15-carboxylate (IX). To a solution of 0.35 g (1 mmol) of amine **VII** in 10 ml of benzene we added 0.1 g (3.3 mmol) of powdered paraformaldehyde and 0.14 g (1.2 mmol) of trifluoroacetic acid. The mixture was heated for 15 min under reflux, cooled, and washed with a 3% solution of ammonia. The solvent was removed, and the residue was subjected to column chromatography using petroleum ether–*tert*-butyl methyl ether (1:1) as eluent to isolate 0.25 g (71%) of compound **IX**. mp 133–135°C (from petroleum ether–acetone), $[\alpha]_{580}^{20}$ = +32° (*c* = 3.1). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.97 d.d.d (1H, 3-H, *J* = 13.2, 4.4, 0.9 Hz), 1.00 d.d.d (1H, 1-H, *J* = 13.4, 13.0, 4.3 Hz), 0.99 s (3H, $C^{20}H_3$), 1.16 s (3H, $C^{19}H_3$), 1.18 d.d.d (1H, 7-H, *J* = 12.7, 2.6 Hz), 1.20 m (1H, 5-H), 1.44 m (2H, 2-H, 9-H), 1.61 d.d.d (1H, 6-H, *J* = 14.0, 10.1, 5.4 Hz), 1.70 d.d.d (1H, 1-H, *J* = 13.4, 6.7, 3.5 Hz), 1.84 d.d.d (1H, 2-H, *J* = 14.0, 12.2, 4.6 Hz), 1.87 d.d.d (1H, 12-H, *J* = 18.0, 12.0, 6.2 Hz), 1.95 m (1H, 11-H, ^2J = 12.8 Hz), 2.04 d.d.d (1H, 7-H, *J* = 14.0, 6.7, 3.0 Hz), 2.06 d.d.d. (1H, 6-H, *J* = 14.0, 12.0, 3.6 Hz), 2.09 s (3H, NCH_3), 2.17 d.d.d.d (1H, 3-H, *J* = 13.2, 3.8, 2.9, 1.6 Hz), 2.21 q (1H, 8-H, *J* = 3.1 Hz), 2.40 d.d.d (1H, 12-H, *J* = 12.7, 3.9, 1.4 Hz), 2.76 d.d.d.d (1H, 11-H, *J* = 17.2, 12.8, 2.3, 1.0 Hz), 3.44 d.d.d (1H, 1'-H, *J* = 12.2, 6.5, 1.7 Hz), 3.65 s (3H, OCH_3), 4.33 d (1H, 1'-H, *J* = 12.2 Hz), 6.16 d (1H, 14-H, *J* = 2.8 Hz), 7.21 d (1H, 15-H, *J* = 2.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.05 (C^{20}), 18.81 (C^6), 19.20 (C^2), 24.05 (C^{12}), 24.05 (C^{11}), 28.86 (C^{19}), 32.97 (C^7), 38.11 (C^3), 39.19 (C^{10}), 39.94 (C^1), 43.82 (C^4), 43.74 (NMe), 51.18 (OMe), 51.68 ($C^{1'}$), 55.81 (C^5), 57.75 (C^8), 59.05 (C^9), 111.66 (C^{14}), 121.26 (C^{13}), 140.24 (C^{15}), 146.93 (C^{16}), 178.09 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 359 $[M]^+$ (100), 300 (26), 236 (20), 162 (21), 107 (29), 94 (36), 70 (24). Found: $[M]^+$ 359.24715. $C_{22}H_{33}NO_3$. Calculated: *M* 359.24603.

Methyl (2*R*,3a*R*,5a*S*,6*S*,9a*S*,9b*R*)-3a-formyl-2-(3-furyl)-6,9a-dimethylperhydronaphtho[2,1-*b*]furan-6-carboxylate [methyl 8α,12α:15,16-diepoxy-17-oxolabda-13(16),14-dien-18-oate] (X). To a solution of 0.35 g (1 mmol) of compound **III** in 20 ml of anhydrous methylene chloride we added 0.35 g (1.6 mmol) of pyridinium chlorochromate. The mixture was stirred for 2 h and passed through a short column charged with $A1_2O_3$, and the sorbent was washed with 30 ml of

tert-butyl methyl ether. The eluate was evaporated, and the residue was crystallized from petroleum ether–acetone to isolate 0.27 g (76%) of aldehyde **X**, mp 102–105°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.60 s (3H, $C^{20}H_3$), 0.88 d.d.d (1H, 3-H, *J* = 14.3, 10.2, 3.3 Hz), 0.95 d.d.d (1H, 1-H, *J* = 14.2, 10.8, 3.6 Hz), 1.06 d.d (1H, 5-H, *J* = 11.2, 3.3 Hz), 1.16 s (3H, $C^{19}H_3$), 1.21 m (2H, 2-H, 7-H), 1.50 m (2H, 1-H, 9-H), 1.80–2.08 m (4H, 2-H, 6-H, 11-H), 2.12 m (1H, 3-H), 2.20 d.d.d (1H, 7-H, *J* = 14.3, 6.5, 2.0 Hz), 2.43 d.d.d (1H, 11-H, *J* = 12.6, 8.0, 1.8 Hz), 3.57 s (3H, OCH_3), 5.11 d.d (1H, 12-H, *J* = 8.0, 6.6 Hz), 6.33 d.d (1H, 14-H, *J* = 1.8, 0.8 Hz), 7.30 m (2H, 15-H, 16-H), 9.56 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 13.99 (C^{20}), 18.78 (C^2), 21.58 (C^6), 28.38 (C^{19}), 31.71 (C^7), 32.43 (C^{11}), 37.08 (C^{10}), 38.23 (C^3), 39.59 (C^1), 43.27 (C^4), 50.82 (OMe), 56.27 (C^5), 61.56 (C^9), 74.81 (C^{12}), 84.04 (C^8), 108.66 (C^{14}), 127.58 (C^{13}), 138.80 (C^{15}), 141.60 (C^{16}), 176.19 (C^{18}), 195.66 (C^{17}). Found, %: C 70.25; H 7.53. $C_{21}H_{28}O_5$. Calculated, %: C 70.0; H 7.78.

Methyl (2*R*,3a*R*,5a*S*,6*S*,9a*S*,9b*S*)-2-(3-furyl)-6,9a-dimethyl-3a-methylaminoperhydronaphtho-[2,1-*b*]furan-6-carboxylate [methyl 8α,12α:15,16-diepoxy-17-methylaminolabda-13(16),14-dien-18-oate] (XI). A saturated solution of methylamine in 15 ml of methanol was added to a mixture of 0.36 g (1 mmol) of aldehyde **X** in 5 ml of methanol. The mixture was left to stand for 20 h at room temperature and cooled to 0°C, and 0.1 g (2.7 mmol) of sodium tetrahydridoborate was added under stirring. When the reaction was complete (TLC), the mixture was diluted with water and extracted with *tert*-butyl methyl ether. The extract was washed with water and evaporated, and the residue was subjected to column chromatography using petroleum ether–*tert*-butyl methyl ether (1:2) as eluent. Yield 77%, mp 115–118°C (from petroleum ether–acetone), $[\alpha]_{580}^{20}$ = +29° (*c* = 5.2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.65 s (3H, $C^{20}H_3$), 0.99 m (2H, 1-H, 3-H), 1.08 d.d (1H, 5-H, *J* = 10.9, 3.2 Hz), 1.15 s (3H, $C^{19}H_3$), 1.20 m (2H, 2-H, 7-H), 1.50 m (2H, 1-H, 11-H), 1.60 d.d.d (1H, 9-H, *J* = 10.1, 7.6, 1.2 Hz), 1.63 d.d.d (1H, 6-H, *J* = 12.6, 12.0, 4.0 Hz), 1.86 m (2H, 2-H, 6-H), 2.08 d.d.d (1H, 3-H, *J* = 14.2, 6.6, 3.2 Hz), 2.16 s (3H, NCH_3), 2.18 m (2H, 17-H), 2.44 d.t (1H, 7-H, *J* = 12.6, 12.0. 3.1 Hz), 2.56 d.t (1H, 11-H, *J* = 12.1, 1.8 Hz), 3.61 s (3H, OCH_3), 4.86 d.d (1H, 12-H, *J* = 7.8, 6.8 Hz), 5.62 s (1H, NH), 6.25 d (1H, 14-H, *J* = 1.6 Hz), 7.26 d (1H, 16-H, *J* = 1.3 Hz), 7.32 d.d (1H, 15-H, *J* = 1.6, 1.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.87 (C^{20}), 18.64 (C^2), 21.94 (C^6), 28.30 (C^{19}), 29.71 (C^{11}), 35.65 (C^7), 36.43 (NMe), 36.48 (C^{10}), 38.15 (C^3), 40.23 (C^1), 43.06 (C^4), 50.52 (OMe), 54.14 (C^{17}), 57.14 (C^5), 61.18 (C^9), 71.73 (C^{12}), 82.13 (C^8), 108.65 (C^{14}), 128.47 (C^{13}), 138.04 (C^{15}), 141.50 (C^{16}), 175.87 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 375 $[M]^+$ (1.6), 332 (29), 331 (100), 271 (34), 253 (32), 107 (24), 94 (19). Found: $[M]^+$ 375.24122. $C_{22}H_{33}NO_4$. Calculated: *M* 375.24094.

Methyl (1*R*,10*S*,13*S*,18*S*,19*S*)-8,14,18-trimethyl-5,21-dioxa-8-azapentacyclo[15.3.1.0^{2,6}.0^{10,19}.0^{10,21}]-henicosa-2(6),3-diene-14-carboxylate (XII). To a solution of 0.37 g (1 mmol) of amine **XI** in 10 ml of benzene we added 0.1 g (3.3 mmol) of powdered paraformaldehyde and 0.14 g (1.2 mmol) of trifluoroacetic acid. The mixture was heated for 15 min under reflux, cooled, washed with a 3% solution of ammonia, and evaporated, and the residue was subjected to column chromatography using petroleum ether–*tert*-butyl methyl ether (1:1) as eluent. Yield 0.29 g (77%), mp 186–187°C (from petroleum ether–acetone), $[\alpha]_{580}^{20}$ = +37° (*c* = 2.2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.57 s (3H, $C^{20}H_3$), 0.99 d.d.d (1H, 3-H, *J* = 13.3, 12.7, 3.5 Hz), 1.02 d.d.d (1H, 1-H, *J* = 13.4, 10.8, 3.6 Hz), 1.12 d.d (1H, 5-H, *J* = 13.2, 3.2 Hz), 1.16 s (3H, $C^{19}H_3$), 1.21 d.d.d (1H, 7-H, *J* = 13.3, 4.3, 1.8 Hz), 1.40 m (1H, 2-H), 1.46 m (1H, 1-H, *J* = 14.1 Hz), 1.50 d.d (1H, 9-H, *J* = 13.2, 7.4 Hz), 1.69 d.d.d (1H, 11-H, *J* = 13.2, 11.4, 6.3 Hz), 1.81 m (1H, 2-H), 1.85 m (1H, 6-H), 1.95 d.q (1H, 6-H, *J* = 14.1, 6.0, 3.8, 1.9 Hz), 2.13 m (1H, 3-H), 2.16 m (1H, 11-H), 2.18 d (1H, 17-H, *J* = 13.5 Hz), 2.34 s (3H, NCH_3), 2.36 d.t (1H, 7-H, *J* = 14.0, 6.2, 1.8 Hz), 2.49 d (1H, 17-H, *J* = 13.5 Hz), 3.42 d (1H, 1'-H, *J* = 14.8, 0.6 Hz), 3.60 s (3H, OCH_3), 4.50 d (1H, 1'-H, *J* = 14.8 Hz), 5.04 d.d (1H, 12-H, *J* = 8.2, 6.3 Hz), 6.05 d (1H, 14-H, *J* = 1.9, 0.6 Hz), 7.18 d (1H, 15-H, *J* = 1.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.97 (C^{20}), 18.97 (C^2), 21.95 (C^6), 28.85 (C^{19}), 32.14 (C^{11}), 35.78 (C^7), 36.64 (C^{10}), 38.41 (C^3), 40.27 (C^1), 43.50 (C^4), 47.88 (NMe), 51.09 (OMe), 53.36 ($C^{1'}$), 55.70 (C^{17}), 57.50 (C^5), 62.86 (C^9), 73.38 (C^{12}), 82.10 (C^8), 107.95 (C^{14}), 127.14 (C^{13}), 141.00 (C^{15}), 145.45 (C^{16}), 176.74 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 387 $[M]^+$ (14), 345 (23), 344 (100), 284 (44), 195 (23), 163 (40), 162 (29), 121 (30), 107 (30). Found: $[M]^+$ 387.24004. $C_{23}H_{33}NO_4$. Calculated: *M* 387.24094.

Methyl (1*S*,4a*S*,5*R*,6*RS*,8a*S*)-6-formyl-5-[2-(3-furyl)ethyl]-1,4a-dimethylperhydronaphthalene-1-carboxylate [methyl (8*RS*)-15,16-epoxy-17-oxolabda-13(16),14-dien-18-oate] (XIII). A mixture of

0.35 g (1 mmol) of methyl 15,16-epoxy-17-hydroxylabda-13(16),14-dien-18-oate (**IV**) [7] in 20 ml of dry methylene chloride and 0.35 g (1.6 mmol) of pyridinium chlorochromate was stirred for 2 h. The mixture was then passed through a short column charged with Al_2O_3, the sorbent was washed with 30 ml of *tert*-butyl methyl ether, the eluate was evaporated, and the residue was subjected to column chromatography to isolate 0.3 g (85%) of an oily mixture of (8*R*)- and (8*S*)-aldehydes **XIII** at a ratio of 2:1, $[\alpha]_{580}^{20}$ = +29° (*c* = 5.0). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.49 s and 0.57 s (3H, $C^{20}H_3$, 2:1), 0.88–0.93 m (2H, 1-H, 3-H), 1.05 m (1H, 5-H), 1.07 s and 1.10 s (3H, $C^{19}H_3$, 1:2), 1.20–1.32 m (2H, 7-H, 8-H), 1.40–1.56 m (3H, 1-H, 2-H, 12-H), 1.69–1.85 m (4H, 2-H, 6-H, 9-H, 11-H), 2.01–2.40 m (4H, 3-H, 6-H, 11-H, 12-H), 2.53 m (1H, 7-H), 3.51 s and 3.54 s (3H, OCH_3, 2:1), 6.10 d and 6.17 d (1H, 14-H, 1:2, *J* = 2.5, 1.9 Hz), 7.06 d and 7.11 d (1H, 16-H, 1:2, *J* ≈ 1.9 Hz), 7.19 d.d (*J* = 1.9, 1.5 Hz) and 7.22 d.d (*J* = 2.5, 1.5 Hz) (1H, 15-H, 1:2), 9.39 d and 9.90 d (CHO, *J* ≈ 4.9 Hz, 2:1). ^{13}C NMR spectrum, δ_C, ppm: 12.18 and 13.30 [C^{20}, (*S*) and (*R*)], 19.04 and 19.60 [C^2, (*R*) and (*S*)], 20.15 and 21.48 [C^6, (*R*) and (*S*)], 23.07 (C^{12}), 25.34 (C^{11}), 27.11 (C^7), 28.85 (C^{19}), 37.88 (C^3), 38.49 (C^{10}), 38.66 (C^1), 43.62 (C^4), 46.57 (C^8), 50.86 (OMe), 51.92 (C^5), 56.16 (C^9), 110.63 (C^{14}), 124.24 (C^{13}), 138.22 (C^{15}), 141.80 (C^{16}), 176.96 (C^{18}), 203.94 (C^{17}). Mass spectrum, *m*/*z* (I_{rel}, %): 346 $[M]^+$ (1.04), 332 (18), 163 (21), 147 (32), 121 (52), 109 (33), 95 (42), 82 (100).

Methyl (1*S*,4a*S*,5*R*,6*RS*,8a*S*)-5-[2-(3-furyl)ethyl]-6-[2-(1*H*-3-indolyl)ethylaminomethyl]-1,4a-dimethylperhydronaphthalene-1-carboxylate {methyl (8*RS*)-15,16-epoxy-17-[2-(3-indolyl)ethylamino]-labda-13(16),14-dien-18-oate} (XIV). A mixture of 0.35 g (1 mmol) of aldehyde **XIII**, 0.2 g (1.25 mmol) of tryptamine, and one drop of acetic acid in 10 ml of methylene chloride was kept for 18 h. The solvent was distilled off, 10 ml of methanol was added to the residue, the mixture was cooled to 0°C, and 0.1 g (2.7 mmol) of sodium tetrahydridoborate was added under stirring. When the reaction was complete, the mixture was diluted with water and extracted with chloroform. The extract was washed with water and evaporated, and the residue was subjected to column chromatography using methanol as eluent. Yield 0.33 g (87%), colorless oily substance, $[\alpha]_{580}^{20}$ = +24° (*c* = 4.5). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.57 s and 0.60 s (3H, $C^{20}H_3$, 2:1), 0.99 d.d.d (1H, 3-H, *J* = 13.3, 12.7, 3.5 Hz), 1.02 d.d.d (1H, 1-H, *J* = 13.4, 10.8, 3.6 Hz), 1.12 d.d (1H, 5-H, *J* = 13.2, 3.2 Hz), 1.09 s and 1.14 s (3H, $C^{19}H_3$, 1:2), 1.21 m (1H, 7-H, ^2J = 13.3 Hz), 1.40 m (1H, 2-H), 1.46 m (2H, 1-H, 12-H), 1.50 d.d (1H, 9-H, *J* = 13.2, 7.4 Hz), 1.69 d.d.d (1H, 11-H, *J* = 13.2, 11.4, 6.3 Hz), 1.81 m (1H, 2-H), 1.85 m (1H, 6-H), 1.95 d.q (1H, 6-H, *J* = 14.1, 6.0, 3.8, 1.9 Hz), 2.13 m (1H, 3-H), 2.16 m (2H, 11-H, 12-H), 2.18 d (1H, 17-H, *J* = 13.5 Hz), 2.34 s (3H, NCH_3), 2.36 d.t (1H, 7-H, *J* = 14.0, 6.2, 1.8 Hz), 2.49 d (1H, 17-H, *J* = 13.5 Hz), 3.42 m (2H, CH_2), 3.60 s (3H, OCH_3), 3.61 m (2H, CH_2), 7.00–7.08 m (2H, 2'-H, 5'-H, 6'-H), 6.05 d and 6.10 d (1H, 14-H, *J* = 1.6. 0.7 and 1.9, 0.6 Hz, 1:2), 7.18 m (1H, 15-H, *J* = 1.9 Hz), 7.20 m (1H, 4'-H), 7.42 m (1H, 7'-H), 7.75 s and 7.79 s (NH). ^{13}C NMR spectrum, δ, ppm: 12.10 and 12.32 [C^{20}, (*S*) and (*R*)], 19.29 and 19.48 [C^2, (*R*) and (*S*)], 23.25 and 24.12 [C^6, (*R*) and (*S*)], 27.09 (CH_2), 27.44 (C^{11}), 28.74 (C^{19}), 30.39 (C^{12}), 32.42 (C^7), 38.33 (C^3), 38.62 (C^{10}), 39.08 (C^1), 39.56 and 40.49 [C^8, (*R*) and (*S*)], 43.92 (C^4), 50.11 (C^{17}), 50.86 (OMe), 52.62 and 53.07 [C^9, (*S*) and (*R*)], 53.92 (C^5), 54.32 (CH_2), 110.79 ($C^{7''}$), 110.86 (C^{14}), 113.32 ($C^{3''}$), 117.28 ($C^{4''}$), 118.81 and 119.17 ($C^{5''}$, $C^{6''}$), 121.87 (C^2), 125.10 (C^{4a}), 127.59 (C^{13}), 136.53 (C^{7a}), 138.44 (C^{15}), 142.55 (C^{16}), 176.92 (C^{18}). Found, %: C 76.18; H 8.38; N 5.92. $C_{31}H_{42}N_2O_3$. Calculated, %: C 75.92; H 8.57; N 5.71.

Methyl (1*S*,4a*S*,5*R*,6*RS*,8a*S*)-5-[2-(3-furyl)ethyl]-6-(1-methoxycarbonyl-2-phenylethylaminomethyl)-1,4a-dimethylperhydronaphthalene-1-carboxylate [methyl (8*RS*)-15,16-epoxy-17-(1-methoxycarbonyl-2-phenylethylamino)labda-13(16),14-dien-18-oate] (XV) was synthesized in a similar way from 0.35 g (1 mmol) of aldehyde **XIII** and 0.22 g (1.25 mmol) of phenylalanine methyl ester. Yield 72%, $[\alpha]_{580}^{20}$ = +35° (*c* = 2.9). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.55 s and 0.57 s (3H, $C^{20}H_3$, 2:1), 0.90 m (1H, 1-H), 0.96–1.08 m (2H, 3-H, 5-H), 1.12 s and 1.13 s (3H, $C^{19}H_3$, 1:2), 1.30 m (1H, 7-H), 1.42 m (2H, 2-H, 12-H), 1.56 m (3H, 1-H, 8-H, 9-H), 1.70 m (2H, 6-H, 12-H), 1.85 m (2H, 2-H, 11-H), 1.95 m (1H, 6-H), 2.20 m (4H, 3-H, 7-H, 11-H, 17-H), 2.72 m (1H, 17-H), 2.86 m (2H, CH_2), 3.30 m (1H, CH), 3.55 s and 3.60 s (3H, OCH_3, 1:2), 3.59 s and 3.60 s (3H, OCH_3, 2:1), 5.48 s (1H, NH), 6.10 d.d and 6.14 d.d (1H, 14-H, *J* = 1.0, 1.5 and 1.3, 1.6 Hz), 7.05 m (1H, 15-H), 7.16 m (2H, H_{arom}), 7.18 d and 7.20 d (1H, 16-H, 2:1), 7.25 m (3H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 12.10 and 12.43 [C^{20}, (*S*) and (*R*)], 19.45 and 19.70 [C^2, (*R*) and (*S*)], 23.28 and 23.52 [C^6, (*R*) and (*S*)], 26.58 (C^{11}), 28.85 (C^{19}), 28.58 (C^{12}), 32.63 (C^7), 38.39 (C^3), 38.74 (C^{10}), 39.19 (C^1), 39.68 and 40.36 [C^8, (*R*) and (*S*)], 40.06 (CH_2), 43.98 (C^4), 51.20 (CH_3), 52.09 (C^{17}),

50.95 (OMe), 52.88 and 53.41 [C^9, (*R*) and (*S*)], 56.34 (C^5), 63.77 (CH), 110.92 (C^{14}), 125.23 (C^{13}), 126.60 ($C^{4''}$), 128.29 and 129.24 ($C^{2''}$, $C^{6''}$, $C^{3''}$, $C^{5''}$), 137.53 ($C^{1''}$), 138.36 (C^{15}), 142.33 (C^{16}), 174.73 (C=O), 176.85 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 466 (1.3), 416 (8), 192 (22), 132 (24), 102 (100), 81 (23), 28 (44). Found, %: C 73.51; H 8.33; N 5.65. $C_{31}H_{43}N_2O_5$. Calculated, %: C 73.08; H 8.45; N 5.54.

Methyl (1*R*,12*RS*,15*S*,20*S*)-10-[2-(1*H*-3-indolyl)-ethyl]-16,20-dimethyl-7-oxa-10-azatetracyclo-[15.4.0.0^{4,8}.0^{1,12}]eicosa-4(8),5-diene-16-carboxylate (XVI). To a solution of 0.49 g (1 mmol) of amine **XIV** in 10 ml of benzene we added 0.1 g (3.3 mmol) of paraformaldehyde and 0.14 g (1.22 mmol) of trifluoroacetic acid. The mixture was heated for 15 min under reflux, cooled, washed with a 5% solution of ammonia, and evaporated. The residue was purified by column chromatography followed by recrystallization. Yield 0.37 g (73%), mp 126–130°C (from petroleum ether–acetone), $[\alpha]_{580}^{20}$ = +37° (*c* = 3.4). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.64 s and 0.68 s (3H, $C^{20}H_3$, 1:2), 0.90 m (2H, 1-H, 3-H), 1.08 m (1H, 5-H), 1.18 s and 1.19 s (3H, $C^{19}H_3$, 2:1), 1.22 m (1H, 7-H), 1.40 m (2H, 2-H, 12-H), 1.50 m (3H, 1-H, 8-H, 9-H), 1.79–1.89 m (3H, 2-H, 6-H, 11-H), 2.15 m (4H, 3-H, 6-H, 11-H, 17-H), 2.30 m (3H, 7-H, 17-H), 2.90 m (2H, CH_2), 3.42 d (1H, 1'-H, *J* = 14.8, 0.6 Hz), 3.52 m (2H, CH_2), 3.58 m (1H, 1'-H), 3.64 s and 3.66 s (3H, OCH_3, 2:1), 3.70 m (1H, CH), 6.08 d.d and 6.20 d (1H, 14-H, *J* = 1.7, 1.6 Hz, 2:1), 6.95–7.08 m (3H, 2'-H, 5'-H, 6'-H), 7.10 d and 7.18 d (1H, 15-H, *J* = 1.6, 1.7 Hz), 7.20 m (1H, 4'-H), 7.42 m (1H, 7'-H), 7.75 s and 7.79 s (NH). ^{13}C NMR spectrum, δ_C, ppm: 12.10, 12.51 [C^{20}, (*S*) and (*R*)], 19.38 and 19.52 [C^2, (*R*) and (*S*)], 21.32 and 24.12 [C^6, (*R*) and (*S*)], 23.19 (C^{11}), 27.63 (CH_2), 28.43 (C^{12}), 28.78 (C^{19}), 33.45 (C^7), 37.42 and 38.02 [C^8, (*R*) and (*S*)], 38.32 (C^3), 38.95 (C^{10}), 39.04 (C^1), 44.02 (C^4), 51.16 (C^{17}), 51.02 (OMe), 51.46 (CH_2), 54.56 and 55.29 [C^9, (*S*) and (*R*)], 56.40 (C^5), 108.92 ($C^{3''}$), 110.78 ($C^{7''}$), 110.54 (C^{14}), 117.93 ($C^{4''}$), 119.31, 119.40 ($C^{5''}$, $C^{6''}$), 121.24 (C^2), 125.05 (C^{4a}), 127.31 (C^{13}), 136.05 (C^{7a}), 139.33 (C^{15}), 148.48 (C^{16}), 177.43 (C^{18}). Mass spectrum, *m*/*z* (I_{rel}, %): 502 $[M]^+$ (16), 186 (14), 185 (100), 156 (25), 143 (26). Found: $[M]^+$ 502.31843. $C_{32}H_{42}N_2O_3$. Calculated: *M* 502.31952.

Methyl (1*R*,12*RS*,15*S*,20*S*)-10-(1-methoxycarbonyl-2-phenylethyl)-16,20-dimethyl-7-oxa-10-azatetracyclo[15.4.0.0^{4,8}.0^{1,12}]eicosa-4(8),5-diene-16-carboxylate (XVII) was synthesized in a similar way from amine **XV**. Yield 78%, mp 146–149°C (from petroleum ether–acetone), $[\alpha]_{580}^{20}$ = +29° (*c* = 2.7). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.45 s and 0.50 s (3H, $C^{20}H_3$, 2:1), 0.90 m (2H, 1-H, 3-H), 1.05 m (1H, 5-H), 1.07 s and 1.09 s (3H, $C^{19}H_3$, 1:2), 1.18 m (1H, 7-H), 1.40 m (2H, 9-H, 12-H), 1.57 m (2H, 8-H, 11-H), 1.79 m (4H, 1-H, 2-H, 6-H, 12-H), 2.15 m (4H, 3-H, 6-H, 11-H, 17-H), 2.30 m (2H, 7-H, 17-H), 2.92 m (2H, CH_2), 3.56 s and 3.61 s (3H, OCH_3, 1:2), 3.66 s and 3.68 s (3H, OCH_3), 3.70 m (1H, CH), 3.76 d/3.88 d and 4.0 d/4.02 d (2H, 1'-H, 2:1), 6.09 d.d and 6.14 d (1H, 14-H, *J* = 1.5, 1.6 Hz, 2:1), 7.15 m (3H, H_{arom}), 7.20 m (2H, H_{arom}), 7.13 d and 7.18 d (1H, 15-H, 1:2). ^{13}C NMR spectrum, δ_C, ppm: 12.10 and 12.08 [C^{20}, (*S*) and (*R*)]; 19.17 and 19.56 [C^2, (*R*) and (*S*)]; 23.01 and 23.46 [C^6, (*R*) and (*S*)]; 24.52 (C^{11}); 26.79 (C^{12}); 28.56 (C^{19}); 32.99 (C^7); 35.18 and 35.93 [C^8, (*S*) and (*R*)]; 38.09 (C^3); 38.58 (C^{10}); 39.08 (C^1); 43.87 (C^4); 47.06 (C^{17}); 49.24 (CH_2); 50.97 (CH_3); 51.08 (OMe); 53.18 and 53.92 [C^9, (*S*) and (*R*)]; 55.82 (C^5); 66.91 (CH); 112.09 (C^{14}); 121.64 (C^{13}); 126.31 ($C^{4''}$); 127.96, 128.27, 128.89, 129.57 ($C^{2''}$, $C^{6''}$, $C^{3''}$, $C^{5''}$); 138.36 ($C^{1''}$); 139.06 (C^{15}); 148.58 (C^{16}); 172.95 (C=O); 177.90 (C^{18}). Found, %: C 73.32; H 8.53; N 2.45. $C_{32}H_{43}NO_5$. Calculated, %: C 73.70; H 8.25; N 2.69.

X-Ray analysis of compound III. Rhombic crystals with the following unit cell parameters: *a* = 7.6106(9), *b* = 10.982(1), *c* = 23.079(2) Å; *V* = 1928.9(3) Å^3; space group $P2_12_12_1$; *Z* = 4; $C_{21}H_{30}O_5$; d_{calc} = 1.248 g/cm^3; μ = 0.088 mm^{-1}. Intensities of 1961 independent reflections were measured without correction for absorption. The structure was solved by the direct method using SHELXS-97 program and was refined by the least-squares procedure in full-matrix anisotropic (isotropic for hydrogen atoms) approximation using SHELXL-97 program. The coordinates of all hydrogen atoms were calculated by the difference synthesis. The final refinement was performed with respect to all F^2 to wR_2 = 0.1013, *S* = 1.059; 356 parameters were refined (*R* = 0.0407 for 1542 $F > 4\sigma$).

X-Ray analysis of compound IX. Monoclinic crystals with the following unit cell parameters: *a* = 8.147(1), *b* = 11.044(2), *c* = 11.334(2) Å; β = 100.55(1)°; *V* = 1002.5(3) Å^3; space group $P2_1$; *Z* = 2; d_{calc} = 1.191 g/cm^3, μ = 0.078 mm^{-1}. Intensities of 1828 independent reflections were measured without correction for absorption. The structure was solved by the direct method using SHELXS-97 program and was refined by the least-squares procedure in full-matrix anisotropic (isotropic for hydrogen atoms) approximation using SHELXL-97 program. The coordinates of hydrogen atoms were calculated by the difference synthesis. The final refinement was performed with

respect to all F^2 to $wR_2 = 0.1044$, $S = 1.028$; 368 parameters were refined ($R = 0.0388$ for 1434 $F > 4\sigma$).

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