

Synthetic Transformations of Higher Terpenoids: XIV.* Synthesis of Pyrrololabdanoids from Lambertianic Acid

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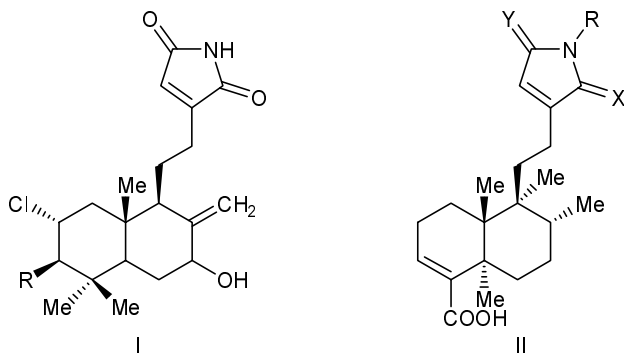
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Abstract—Treatment of lambertianic acid methyl ester with lead tetraacetate gave terpenoid 2,5-diacetoxy-dihydrofuran which reacted with primary amines to yield 3-terpenyl-substituted pyrrol-2(5*H*)-ones; the reaction with hydrazine led to the corresponding pyridazine derivative. The obtained furanoterpenoids underwent oxidative methoxylation by the action of *N*-chlorobenzenesulfonamide or *N*-bromosuccinimide in methanol. 2,5-Dimethoxydihydrofurans thus formed were smoothly converted into 3-substituted furan-2(5*H*)-one in acid medium. Hydrogenation of 2,5-dimethoxydihydrofurans, followed by treatment with amines, gave 1,3-disubstituted pyrroles.

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Diterpene alkaloids containing a pyrrole or pyrrolidine fragment are rare natural metabolites. Nevertheless, some of these compounds were found to exhibit valuable pharmacological properties. For example, labdane diterpenoids lissoclimides **I** isolated from ascidian *Lissoclinum* species are potent cytostatics [2, 3]. Derivatives of clerodane, echinophyllins **II**, are active components of *Echinodorus macrophyllus* which is used in Brazilian traditional medicine for the treatment of hepatitis and rheumatism [4, 5]. Synthesis of analogs of such compounds seems to be an important problem.



I, R = H, Cl; **II**, X = H₂, Y = O; X = O, Y = H₂; R = H, 4-HO-C₆H₄(CH₂)₂, 3-MeO-4-HOC₆H₃CH=CHC(O)NH(CH₂)₄.

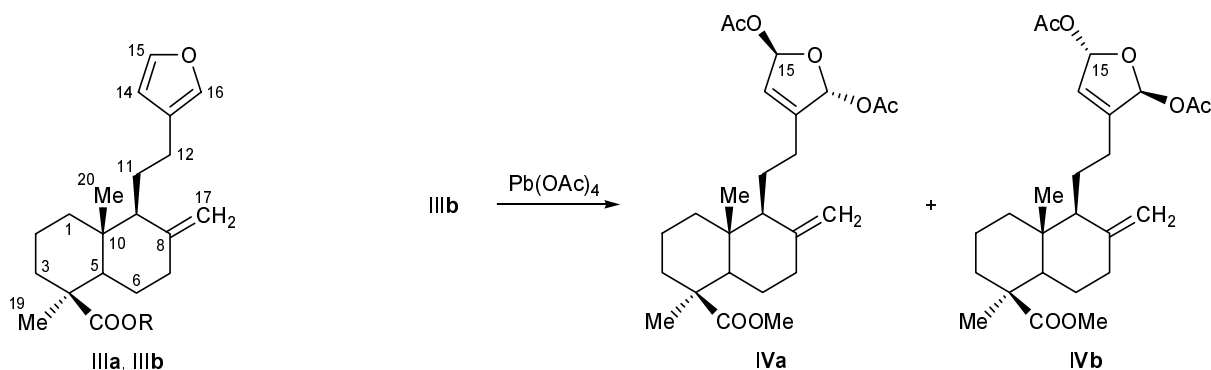
* For communication XIII, see [1].

In the present communication we describe a synthetic approach to labdane diterpenoids containing pyrrole, pyridazine, and furanone fragments. The scheme of synthesis is based on transformations of lambertianic acid (**IIIa**) which is produced by Siberian pine [6]. Treatment of lambertianic acid methyl ester (**IIIb**) with lead tetraacetate gave a mixture of stereoisomeric *trans*-diacetoxy derivatives **IVa** and **IVb** at a ratio of 1:1 (Scheme 1), as followed from the intensity ratio of the singlets from 17-H, 15-H, and 16-H, as well as from the acetoxy protons, in the ¹H NMR spectrum.

The condensation of diacetates **IVa** and **IVb** with hydrazine led to the formation of diterpenoid pyridazine **V**. By reaction of compounds **IVa** and **IVb** with primary amines, such as methylamine, β-alanine methyl ester, *o*-phenylenediamine, and 5-methoxytryptamine, we obtained 3-terpenyl-substituted pyrrol-2(5*H*)-ones **VI–IX** (Scheme 2). Compound **VIIIa** was converted into acetylamino derivative **VIIIb** under standard conditions. 1,4-Disubstituted pyrrol-2(5*H*)-ones attract interest from the viewpoint of development of a new group of antiepileptic agents, GABA agonists related to levetiracetam [7].

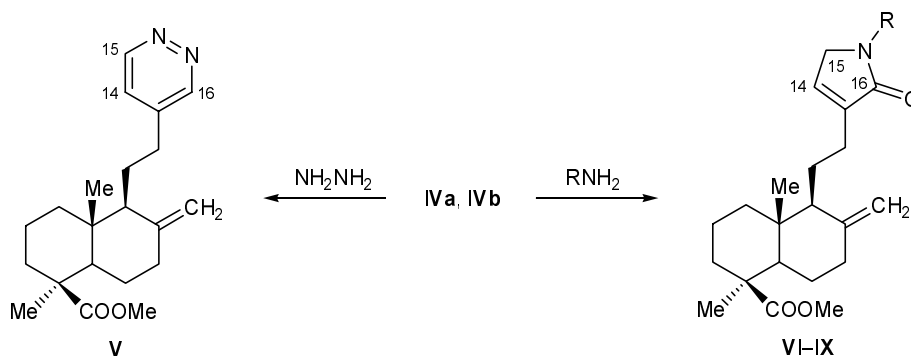
Lambertianic acid methyl ester (**IIIb**) readily underwent oxidative methoxylation by the action of *N*-chlorobenzenesulfonamide in methanol at 0°C. No addition at the double C⁸=C¹⁷ bond occurred under

Scheme 1.



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

Scheme 2.



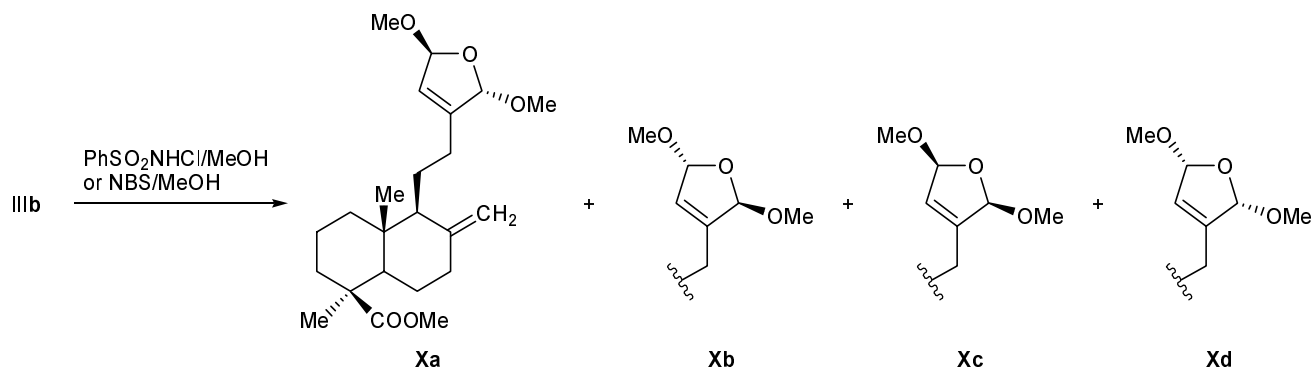
VI, R = CH₃; VII, R = MeOCO(CH₂)₂; VIIIa, R = 2-H₂NC₆H₄; VIIIb, R = 2-AcNHC₆H₄; IX, R = 2-(5-methoxyindol-3-yl)ethyl.

these conditions even in the presence of excess reagent. As a result, the corresponding diastereoisomeric dimethyl acetals **Xa–Xd** were formed (Scheme 3). The same products were obtained by treatment of ester **IIIb** with *N*-bromosuccinimide in methanol. According to the signal intensities of the methoxy protons and 14-H, 15-H, and 16-H** in the ¹H NMR spectra and the GC–

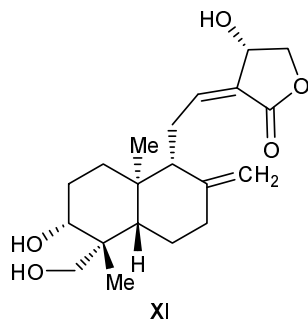
MS data, the stereoisomer ratio was 1:1:1:1. It should be noted that analogous stereochemical results were obtained in the electrochemical or chemical (Br₂/MeOH) methoxylation of 2,5-dimethylfuran [8, 9].

With a view to synthesize structural analogs of natural cytostatics like andrographolide (**XI**) [10] we examined the hydrolysis of acetals **Xa–Xd**. Treatment

Scheme 3.



** The atom numbering accepted for the labdane skeleton is used (see structure **III**).



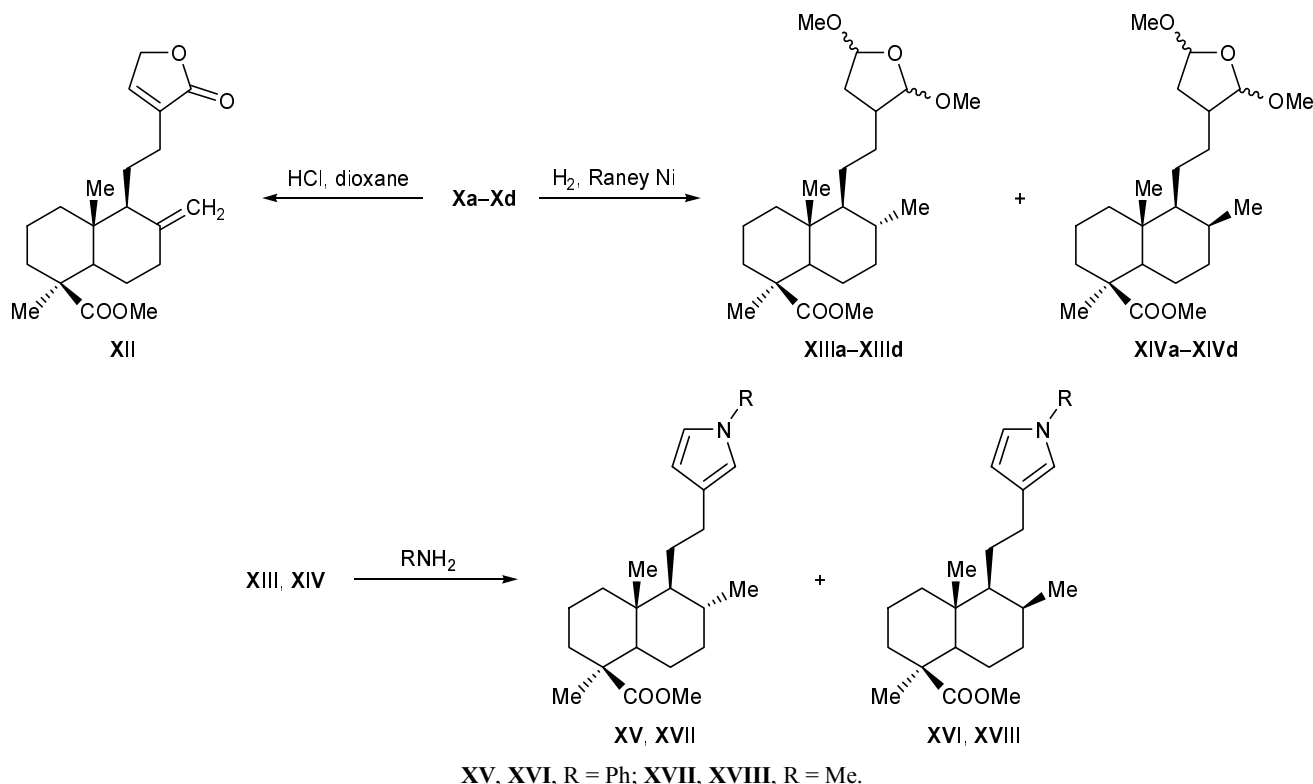
of a mixture of compounds **Xa–Xd** with a solution of hydrogen chloride in dioxane smoothly afforded 3-substituted furan-2(5*H*)-one (but-2-en-4-olide) **XII**. The reaction of **Xa–Xd** with methylamine in acetic acid gave *N*-methylpyrrol-2(5*H*)-one **VI**. The hydrogenation of dimethyl acetals **Xa–Xd** over Raney nickel was accompanied by nonstereoselective reduction of the exocyclic double C=C bond to give tetrahydrofuran derivatives **XIIIa–XIIIId** and **XIVa–XIVd** whose ratio (according to the ^1H NMR data) was 1:1 (stereoisomer ratio 1:1:1:1). By reactions of acetals **XIII** and **XIV** with methylamine and aniline in acetic acid we obtained the corresponding *N*-substituted 15,16-pyrrolo-labdanoids **XV–XVIII** (Scheme 4).

The proposed scheme was also used to synthesize stereochemically pure 8,12-epoxy-15,16-pyrrolo-labda-

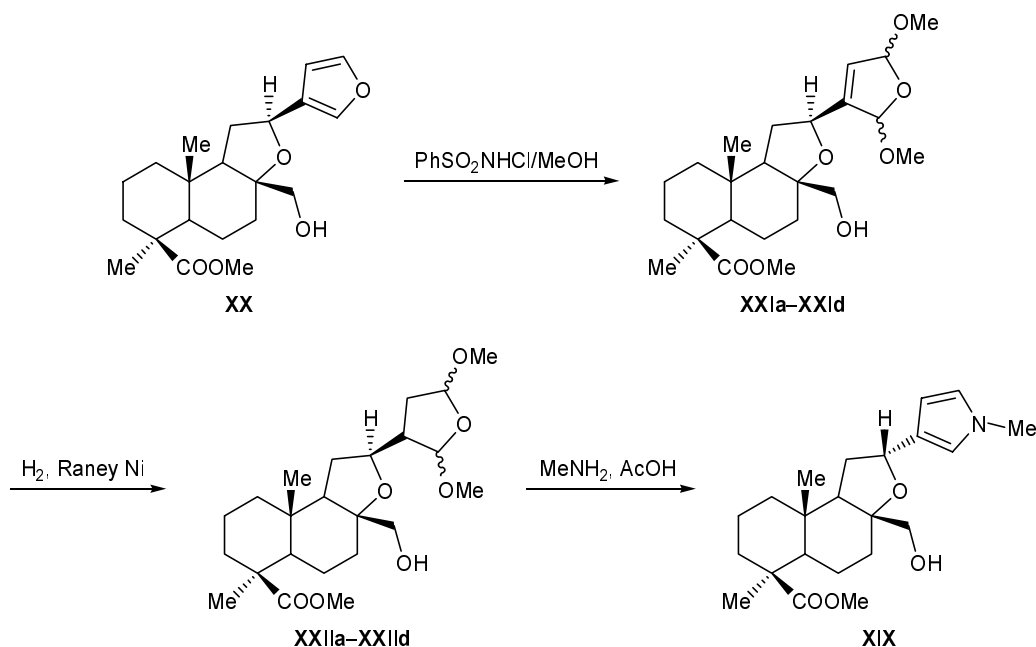
noid **XIX** (Scheme 5). Oxidative methoxylation of compound **XX** [11] gave a mixture of *cis*- and *trans*-acetals **XXIa–XXId** which were hydrogenated over Raney nickel to obtain terpenoid 2,5-dimethoxytetrahydrofurans **XXIIa–XXIIId**. The subsequent treatment of **XXIIa–XXIIId** with methylamine yielded pyrrole derivative **XIX**.

The structure of the newly synthesized compounds was determined on the basis of their spectral parameters. The formation of *trans*-diacetoxy- and *cis,trans*-dimethoxydihydrofurans **IVa**, **IVb**, **Xa–Xd**, and **XXIa–XXId** follows from analysis of the chemical shifts and spin–spin coupling constants of the 15-H and 16-H protons in the ^1H NMR spectra. In the spectra of **IVa** and **IVb**, the 16-H protons resonate as singlets (no coupling with 15-H), while 15-H is coupled with 14-H ($J = 1.2\text{--}1.6$ Hz). Each of the C⁸, C¹¹, C¹², C¹³, C¹⁴, C¹⁵, C¹⁶, and C¹⁷ carbon atoms gives two signals in the ^{13}C NMR spectra. The ^1H NMR spectrum of stereoisomeric acetals **Xa–Xd** contains 4 signals from the methoxy protons. The 16-H signal of *cis* isomers **Xc** and **Xd** is displaced downfield (δ 5.38 ppm) and is coupled with 14-H and 15-H ($J = 1.7$ Hz). Terpenoid tetrahydrofurans **XIIIa–XIIIId** and **XIVa–XIVd** showed in the ^1H NMR spectra doublet signals at δ 0.83, 0.85, 0.89, and 0.91 ppm ($J \approx 7$ Hz)

Scheme 4.



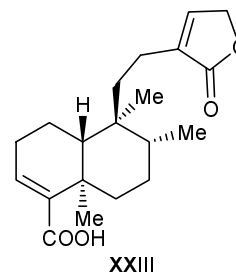
Scheme 5.



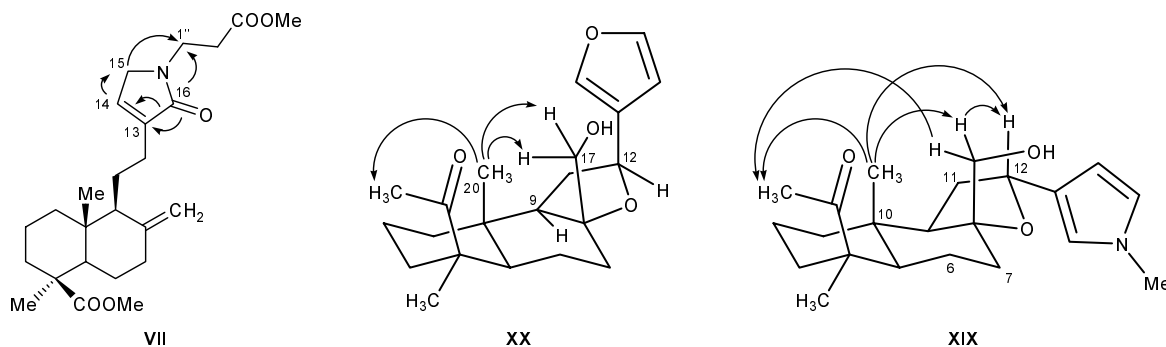
from protons of the C¹⁷H₃ methyl group. All methoxy groups in the spectra of acetals **XIIIa–XIIIId**, **XIVa–XIVd**, **XXIa–XXId**, and **XXIIa–XXIIId** are nonequivalent, and they appear as 8 singlets. Protons in the angular methyl group are also nonequivalent; for example, they resonate at δ 0.49 and 0.51 ppm in the spectrum of **XXIa–XXId**. All carbon atoms in the dihydrofuran ring of **XXIa–XXId** give four signals in the ¹³C NMR spectrum.

The presence of a β -substituted α,β -unsaturated γ -lactam ring on C¹² of the labdane skeleton in molecules **VI–IX** is confirmed by the two-dimensional ¹H–¹H and ¹³C–¹H NMR spectra. In the ¹H–¹H COSY spectrum of **VII**, the olefinic 14-H proton (δ 6.55 ppm) shows couplings with 15-H (δ 3.85 ppm) and 12-H (δ 2.35 ppm), while 15-H (δ 3.85 ppm) is coupled with 14-H and both 12-H protons (δ 2.35 and 2.00 ppm). In the ¹H–¹³C COLOC spectra of **VII** and **IX** we observed cross peaks between 16-H and C¹³ and C¹⁴, as well as between 14-H and C¹⁵. The COLOC spectrum of **VII** revealed interactions of the C¹⁵ and C¹⁶ nuclei with the 1'-H protons in the substituent on the nitrogen, indicating the presence of a pyrrol-2(5*H*)-one fragment. The direct coupling constants between C¹⁴ and 14-H in the ¹³C NMR spectra of **VI–IX** are equal to 173, 175, 172, and 172 Hz, respectively; these values are consistent with those typical of 3-substituted 2,5-dihydropyrroles [12]. The spectral parameters of labdanoid furanone **XII** are in agreement with the assumed structure. The chemical shifts of protons and

carbon nuclei of the butenolide ring in the NMR spectra of compound **XII** almost coincide with those found for naturally occurring 16-oxo-15*H*,16*H*-hardwickic acid (**XXIII**) which has a clerodane skeleton [13].



In the ¹H NMR spectra of terpenoid pyrroles **XV–XVIII**, the signal from the angular C²⁰H₃ methyl group was displaced downfield relative to the corresponding signal in the spectra of **XIII** and **XIV** ($\Delta\delta = 0.18–0.20$ ppm). Protons of the angular methyl group in pyrrololabdanoid **XIX** resonate at δ 0.88 ppm (cf. δ 0.57 ppm for **XX**), while the 12-H proton gives a doublet of doublets at δ 4.51 ppm (cf. δ 4.95 ppm for **XX**) [11]. The observed difference in the chemical shifts of these protons suggests that the transformation of the furan ring into pyrrole is accompanied by change of the configuration at C¹². Therefore, we examined the stereochemical structure of labdanoids **XIX**, **XXI**, and **XXII** using NOESY technique. We found that the NOEs observed in the spectra of compounds **XXI** and **XXII** were analogous to those typical



Characteristic interactions in the ^1H - ^{13}C COLOC spectrum of compound **VII** and in the ^1H - ^1H NOESY spectra of **XIX** and **XX**.

of initial compound **XX** having (8*R*,12*S*)-configuration [14]. The β -orientation of the hydroxymethyl group on C⁸ unambiguously follows from the observation of NOEs on 17-H and C¹⁹H₃ upon irradiation of protons in the C²⁰H₃ group. The 12-H proton showed no NOE on protons of the angular methyl and methoxycarbonyl groups and both 17-H protons (see figure).

The ^1H 2D NOESY spectrum of pyrrololabdan **XIX** displayed interaction between 12-H, on the one hand, and C²⁰H₃ and downfield 17-H (δ 3.93 ppm), on the other, while no response was observed on 9-H. Irradiation of the C²⁰H₃ protons gave responses on 17-H (δ 3.93 ppm), 12-H (δ 4.51 ppm), and protons of the methoxycarbonyl group (δ 3.61 ppm). In addition, NOEs were observed on the axial protons at C², C⁶, and C⁷ and pseudoaxial proton at C¹¹. Irradiation at a frequency corresponding to the 17-H resonance (δ 3.93 ppm) produced NOEs on the second 17-H proton, axial 7-H proton, 12-H, and C¹⁹H₃ and C²⁰H₃ protons. Irradiation of the second 17-H proton (δ 3.38 ppm) gave no response on 12-H, while strong NOEs were observed on the axial 7-H proton and protons of the C¹⁹H₃ group (see figure). These results indicate that compound **XIX** has (8*R*,12*R*)-configuration; this means that the formation of pyrrole ring is accompanied by inversion of the C¹² chiral center.

Thus we have developed a convenient procedure for the transformation of the furan ring in lambertianic acid derivatives into pyrrol-2(5*H*)-one, pyridazine, and furan-2(5*H*)-one fragments. The products formed as a result of this transformation are potential GABA agonists which could exhibit nootropic and anticonvulsant activity.

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 ^1H and ^{13}C NMR spectra were measured on Bruker AC-200 (200.13 and 50.32 MHz for ^1H and ^{13}C , respectively) and Bruker DRX-500 spectrometers (500.13 and 125.76 MHz for ^1H and ^{13}C , respectively) using CDCl₃, CD₃OD, or CCl₄ as solvent. Signals in the NMR spectra were assigned using various proton–proton and carbon–proton shift correlation techniques (COSY, COLOC, CORRD), as well as ^1H 2D NOESY spectra (compounds **IX**, **XIX**, **XXI**, and **XXII**). The IR spectra were recorded 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 specific rotations were measured on a WXQ-4 polarimeter (China) in chloroform or ethanol at 20–23°C.

A mixture of stereoisomeric terpenoid 2,5-dimethoxydihydrofurans **Xa–Xd** was analyzed by gas chromatography–mass spectrometry using a Hewlett–Packard HP 5890 Series II gas chromatograph coupled with an HP 5971 quadrupole mass-selective detector (30-m \times 0.25-mm HP-5 MS quartz capillary column, stationary phase 5% of diphenyl- and 95% of dimethylsiloxane, film thickness 0.25 μm ; oven temperature programming from 50 to 280°C at 4 deg/min, followed by 15 min at 280°C). The stereoisomers were quantitated by the chromatographic peak areas without using correction factors).

The progress of reactions was monitored by TLC on Silufol UV-254 plates. The products were isolated by column chromatography on aluminum oxide.

Methyl 5-[2-(2,5-diacetoxy-2,5-dihydrofuran-3-yl)ethyl]-1,4a-dimethyl-6-methylidenedecahydro-naphthalene-1-carboxylate [methyl 15,16-diacetoxy-15,16-epoxylabda-8(17),13-dien-19-oate] (IVa/IVb). A mixture of 3.31 g (10 mmol) of lambertianic acid methyl ester (**IIIb**) and 4.60 g (11 mmol) of lead tetraacetate in 50 ml of anhydrous benzene was heated to

the boiling point under stirring. At 80°C, lead diacetate began to separate from the solution. The mixture was kept for 10 min at that temperature and cooled, and the precipitate was filtered off and washed with benzene. The filtrate was combined with the washings, passed through a 5-cm layer of aluminum oxide, and evaporated to obtain 3.96 g (89%) of a mixture of diacetates **IVa** and **IVb** as a light yellow oily material. ¹H NMR spectrum (CCl₄), δ, ppm (*J*, Hz): 0.53 s (6H, 2C²⁰H₃); 0.88–1.35 m (7H, 1-H, 2-H, 3-H, 5-H, 7-H, 9-H, 11-H); 1.20 s (6H, 2C¹⁹H₃); 1.50–2.50 m (9H, 1-H, 2-H, 3-H, 6-H, 7-H, 11-H, 12-H); 2.08 s and 2.12 s (6H, 2CH₃); 3.62 s (3H, OCH₃); 4.47 s, 4.52 s, 4.87 s, and 4.89 s (2H, 17-H), 5.77 br.s (1H, 14-H, *J* = 1.6, 1.0); 6.56 s and 6.59 s (1H, 16-H, *J* = 1.0); 6.59 s and 6.82 d (1H, 15-H, *J* = 1.6). ¹³C NMR spectrum, δ_C, ppm: 12.42 (C²⁰); 19.82 (C²); 20.63 (2CH₃); 21.60 (C¹¹); 25.02, 25.10 (C⁶); 26.05 (C¹²); 28.58 (C¹⁹); 38.13, 38.55 (C³, C⁷); 39.10 (C¹); 40.15, 40.22 (C¹⁰); 43.93 (C⁴); 50.61 (CH₃); 55.54, 55.81 (C⁹); 56.16 (C⁵); 99.18, 99.62, 100.74, 101.20 (C¹⁵, C¹⁶); 106.38, 107.37 (C¹⁷); 122.99, 123.39 (C¹⁴); 145.70, 145.88 (C¹³); 147.17, 147.30 (C⁸); 168.11, 168.21, 168.22, 168.28 (MeCO); 175.91 (C¹⁸). Mass spectrum, *m/z* (*I*_{rel.}, %): 448 [M]⁺ (2.3), 388 [M – 60.5], 328 (40), 269 (27), 247 (15), 189 (17), 160 (36), 147 (26), 133 (17), 121 (79), 107 (33), 105 (20), 93 (26), 81 (48), 43 (100). Found: [M]⁺ 448.24732. C₂₅H₃₆O₇. Calculated: *M* 448.24608.

Methyl 1,4a-dimethyl-6-methylidene-5-[2-(pyridazin-4-yl)ethyl]decahydronaphthalene-1-carboxylate (V). A mixture of 0.46 g (1 mmol) of diacetate **IV** and 0.5 ml of hydrazine hydrate in 8 ml of ethanol was heated for 10 min under reflux. The solvent was evaporated to dryness, and the residue was purified by chromatography using petroleum ether–*tert*-butyl methyl ether (1:1) as eluent. Yield 0.23 g (67%), mp 118–120°C (from petroleum ether–acetone), [α]_D²⁰ = +28° (*c* = 9.5, CHCl₃). IR spectrum, ν, cm⁻¹: 755, 776, 810, 853, 872, 980, 1130, 1247, 1551, 1586, 1641, 1716, 2848, 3071, 3415. UV spectrum, λ_{max}, nm (log ε): 250 (3.14), 304 (2.33). ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.48 s (3H, C²⁰H₃), 0.85–1.16 m (2H, 1-H, 3-H), 1.14 s (3H, C¹⁹H₃), 1.22 d.d (1H, 5-H, *J* = 12.5, 3.2), 1.40–2.19 m (10H, 1-H, 2-H, 6-H, 7-H, 9-H, 11-H, 12-H), 2.32–2.50 m (2H, 3-H, 7-H), 2.76 d.d.d (1H, 12-H, ²*J* = 14.2, *J* = 9.7, 4.5), 3.57 s (3H, OCH₃), 4.55 s and 4.91 s (2H, 17-H), 7.22 m (1H, 14-H, *J* = 5.3, 2.5), 8.95 d.d (1H, 16-H, *J* = 2.5, 1.2), 8.98 d.d (1H, 15-H, *J* = 5.3, 1.2). ¹³C NMR spectrum, δ_C, ppm: 12.18 (C²⁰); 19.47 (C²); 23.77, 25.78, and 30.92 (C⁶, C¹¹, C¹²); 28.31 (C¹⁹); 37.71,

38.24, and 38.76 (C¹, C³, C⁷); 39.91 (C¹⁰); 43.73 (C⁴); 50.50 (OCH₃); 54.90 (C⁹); 55.79 (C⁵); 106.37 (C¹⁷); 124.90 (C¹⁴); 141.05 (C¹³); 146.83 (C⁸); 150.19 (C¹⁵); 151.92 (C¹⁶); 176.19 (C¹⁸). Mass spectrum, *m/z* (*I*_{rel.}, %): 342 [M]⁺ (18), 283 (6), 160 (6), 121 (10), 114 (20), 99 (35), 95 (31), 72 (31), 57 (30), 43 (34), 32 (80), 28 (100). Found: [M]⁺ 342.23076. C₂₁H₃₀N₂O₂. Calculated: *M* 342.23071.

Methyl 1,4a-dimethyl-6-methylidene-5-[2-(1-methyl-2-oxo-2,5-dihydro-1H-pyrrol-3-yl)ethyl]decahydronaphthalene-1-carboxylate (VI). *a.* A solution of 0.92 g (2 mmol) of diacetate **IV** in 15 ml of a 10% solution of methylamine in methanol was kept for 1 h. The solvent was evaporated, and the residue was recrystallized from petroleum ether–acetone. Yield 0.47 g (65%), mp 108–110°C.

b. A mixture of 0.22 g of diacetate **VI**, 0.5 ml of 25% aqueous methylamine, 5 ml of acetic acid, and 1 ml of water was heated for 10 min under reflux. The mixture was cooled, diluted with water, and extracted with diethyl ether, the extract was evaporated, and the residue was recrystallized from petroleum ether. Yield 0.12 g (64%), [α]_D²⁰ = +24° (*c* = 2.6, CHCl₃). IR spectrum, ν, cm⁻¹: 816, 882, 986, 1132, 1610, 1692, 1721, 3070, 3424. UV spectrum: λ_{max} 240 nm (log ε 3.26). ¹H NMR spectrum (CDCl₃–CCl₄), δ, ppm (*J*, Hz): 0.43 s (3H, C²⁰H₃), 0.97 d.t (1H, 3-H, *J* = 13.3, 4.0), 1.09 m (1H, 1-H), 1.12 s (3H, C¹⁹H₃), 1.24 d.d (1H, 5-H, *J* = 12.6, 3.1), 1.42–1.53 m (2H, 2-H, 11-H), 1.56 d.d (1H, 9-H, *J* = 11.3, 1.2), 1.66–1.87 m (5H, 1-H, 2-H, 6-H, 7-H, 11-H), 1.94 d.d.d (1H, 6-H, *J* = 13.8, 4.6, 3.1), 1.97–2.04 m (1H, 12-H), 2.07–2.12 m (1H, 3-H), 2.3–2.42 m (2H, 7-H, 12-H), 2.98 s (3H, NCH₃), 3.56 s (3H, OCH₃), 3.77 m (2H, 15-H, *J* = 2.0, 1.7), 4.57 s and 4.81 s (2H, 17-H), 6.53 quint (1H, 14-H, *J* = 1.7). ¹³C NMR spectrum, δ_C, ppm: 12.44 (C²⁰), 19.76 (C²), 21.83 (C¹¹), 25.27 (C¹²), 26.06 (C⁶), 28.69 (C¹⁹), 29.07 (NCH₃), 38.10 (C³), 38.54 (C⁷), 39.02 (C¹), 40.10 (C¹⁰), 44.07 (C⁴), 50.94 (OCH₃), 52.39 (C¹⁵), 55.64 (C⁹), 56.14 (C⁵), 106.75 (C¹⁷), 132.97 (C¹⁴), 140.92 (C¹³), 147.18 (C⁸), 171.27 (C¹⁶), 177.27 (C¹⁸). Mass spectrum, *m/z* (*I*_{rel.}, %): 359 [M]⁺ (18), 300 (10), 284 (14), 192 (13), 180 (14), 124 (19), 111 (100), 81 (14), 55 (10), 31 (24). Found: [M]⁺ 359.23543. C₂₂H₃₃NO₃. Calculated: *M* 359.24603.

Methyl 5-{2-[1-(2-methoxycarbonyl)ethyl]-2-oxo-2,5-dihydro-1H-pyrrol-3-yl}ethyl-1,4a-dimethyl-6-methylidenedeca-hydronaphthalene-1-carboxylate (VII). A mixture of 0.46 g (1 mmol) of diacetate **IV**, 0.3 g of (2 mmol) β-alanine methyl ester hydro-

chloride, and 1 ml of triethylamine in 10 ml of ethanol was heated for 2 h under reflux. The mixture was evaporated under reduced pressure, and the residue was purified by column chromatography using petroleum ether-*tert*-butyl methyl ether (1:1) as eluent. Yield 0.22 g (53%), oily substance, $[\alpha]_D^{20} = +18^\circ$ ($c = 6.9$, CHCl_3). ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 0.46 s (3H, C^{20}H_3), 0.98 t.d (1H, 3-H, $J = 13.4$, 1.7), 1.01 d.d.d (1H, 1-H, $J = 15.2$, 4.4, 1.7), 1.14 s (3H, C^{19}H_3), 1.25 d.d (1H, 5-H, $J = 12.5$, 3.2), 1.45–1.52 m (2H, 2-H, 11-H), 1.57 m (1H, 9-H, $J = 11.1$), 1.68–1.95 m (6H, 1-H, 2-H, 6-H, 7-H, 11-H), 1.97–2.03 m (1H, 12-H, $^2J = 15.1$), 2.12 d.d (1H, 3-H, $J = 13.4$, 4.8, 2.5), 2.35 m (1H, 12-H, $^2J = 15.1$), 2.42 m (1H, 7-H, $^2J = 12.6$), 2.58 t (2H, CH_2 , $J = 6.4$), 3.57 s and 3.64 s (3H each, OCH_3), 3.67 t (2H, NCH_2 , $J = 6.4$), 3.85 br.s (2H, 16-H, halfwidth 12 Hz), 4.58 s and 4.83 s (2H, 17-H), 6.55 t (1H, 14-H, $J = 1.7$, 1.7). ^{13}C NMR spectrum, δ_c , ppm: 12.58 (C^{20}), 19.92 (C^2), 21.94 (C^{11}), 25.36 (C^{12}), 26.19 (C^6), 28.83 (C^{19}), 33.37 (C^{21}), 38.28 (C^{11}), 38.31 (C^3), 38.70 (C^7), 39.18 (C^1), 40.27 (C^{10}), 44.19 (C^4), 50.99 (OCH_3), 51.55 (OCH_3), 51.72 (C^{15}), 55.82 (C^9), 56.34 (C^5), 106.94 (C^{17}), 133.86 (C^{14}), 140.79 (C^{13}), 147.25 (C^8), 171.19 (C^{16}), 172.04 ($\text{C}=\text{O}$), 177.09 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 431 [M] $^+$ (11), 416 (8), 400 (14), 372 (18), 356 (14), 264 (19), 252 (17), 196 (24), 183 (100), 151 (40). Found: [M] $^+$ 431.26701. $\text{C}_{25}\text{H}_{37}\text{NO}_5$. Calculated: M 431.26715.

Methyl 5-{2-[1-(2-aminophenyl)-2-oxo-2,5-dihydro-1H-pyrrol-3-yl]ethyl}-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate (VIIIa). A mixture of 0.46 g (1 mmol) of diacetate IV, 0.3 g (2.8 mmol) of *o*-phenylenediamine, and 0.5 ml of triethylamine in 10 ml of ethanol was heated for 3 h under reflux. The solvent was evaporated, and the residue was purified by chromatography using petroleum ether-*tert*-butyl methyl ether (1:1). Yield 0.25 g (59%), mp 128–130°C (from petroleum ether), $[\alpha]_D^{20} = +21^\circ$ ($c = 2.1$, CHCl_3). ^1H NMR spectrum (CCl_4), δ , ppm (J , Hz): 0.48 s (3H, C^{20}H_3), 0.82–1.06 m (2H, 1-H, 3-H), 1.14 s (3H, C^{19}H_3), 1.22 d.d (1H, 5-H, $J = 12.7$, 3.2), 1.47 m (1H, 2-H), 1.51–1.92 m (8H, 1-H, 2-H, 6-H, 7-H, 9-H, 11-H), 2.01–2.18 m (2H, 3-H, 12-H), 2.39–2.51 m (2H, 7-H, 12-H), 3.55 s (3H, OCH_3), 3.90 br.s (2H, NH_2 , halfwidth 12 Hz), 4.17 m (2H, 15-H), 4.64 s and 4.85 s (2H, 17-H), 6.53–6.68 m (2H, 3'-H, 4'-H), 6.69 t (1H, 14-H, $J = 1.8$, 1.7), 6.87–7.00 m (2H, 5'-H, 6'-H). ^{13}C NMR spectrum, δ_c , ppm: 12.48 (C^{20}), 19.80 (C^2), 21.82 (C^{11}), 25.38 (C^{12}), 26.06 (C^6), 28.65 (C^{19}), 38.15 (C^3), 38.53 (C^7), 39.09 (C^1),

40.15 (C^{10}), 44.04 (C^4), 50.73 (OCH_3), 52.83 (C^{15}), 55.73 (C^9), 56.22 (C^5), 106.94 (C^{17}), 117.87, 118.51 (C^3 , C^5), 125.18 (C^1), 125.73 (C^6), 127.67 (C^4), 135.27 (C^{14}), 140.47 (C^{13}), 142.97 (C^2), 147.16 (C^8), 169.56 (C^{16}), 176.70 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 436 [M] $^+$ (9), 419 (6), 377 (7), 361 (6), 305 (100), 230 (48), 188 (71), 121 (47). Found: [M] $^+$ 436.27208. $\text{C}_{27}\text{H}_{36}\text{N}_2\text{O}_3$. Calculated: M 436.27258.

Methyl 5-{2-[1-(2-acetylaminophenyl)-2-oxo-2,5-dihydro-1H-pyrrol-3-yl]ethyl}-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate (VIIIb). A mixture of 0.3 g (0.69 mmol) of compound VIIIa, 0.10 g of sodium acetate, and 5 ml of acetic anhydride was heated for 2 h at 120–125°C. The solution was cooled and poured onto ice, concentrated aqueous ammonia was added dropwise until alkaline reaction, the mixture was extracted with diethyl ether (2×15 ml), the extract was evaporated, and the residue was purified by chromatography using petroleum ether-diethyl ether (1:2) as eluent. Yield 0.21 g (64%), mp 82–84°C (from petroleum ether-acetone), $[\alpha]_D^{20} = +16^\circ$ ($c = 1.9$, CHCl_3). ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 0.47 s (3H, C^{20}H_3), 0.98 d.t (1H, 3-H, $J = 13.3$, 4.2), 1.06 m (1H, 1-H, $^2J = 15.1$), 1.14 s (3H, C^{19}H_3), 1.25 d.d (1H, 5-H, $J = 12.6$, 3.1), 1.47 m (1H, 2-H), 1.55–1.63 m (2H, 9-H, 11-H), 1.72–1.96 m (6H, 1-H, 2-H, 6-H, 7-H, 11-H), 2.03 s (3H, CH_3), 2.06–2.15 m (2H, 3-H, 12-H), 2.36–2.41 m (1H, 7-H, $J = 12.2$, 4.0, 2.6), 2.44–2.50 m (1H, 12-H), 3.57 s (3H, OCH_3), 4.30 d.d (2H, 15-H, $J = 19.8$, 1.7), 4.61 s and 4.87 s (2H, 17-H), 6.81 t (1H, 14-H, $J = 1.6$), 7.08 d.d (1H, 3'-H, $J = 8.1$, 2.1), 7.10 t (1H, 4'-H, $J = 8.1$, 8.6), 7.27 d.d.d (1H, 5'-H, $J = 8.6$, 8.1, 2.1), 7.74 d.d (1H, 6'-H, $J = 8.1$, 1.3), 8.70 s (1H, NH). ^{13}C NMR spectrum, δ_c , ppm: 12.49 (C^{20}), 19.78 (C^2), 21.90 (C^{11}), 23.97 (CH_3), 25.26 (C^{12}), 26.06 (C^6), 28.68 (C^{19}), 38.10 (C^3), 38.56 (C^7), 39.17 (C^1), 40.18 (C^{10}), 44.04 (C^4), 50.87 (OCH_3), 53.22 (C^{15}), 55.72 (C^9), 56.21 (C^5), 106.83 (C^{17}), 123.97 (C^3), 125.13 (C^5), 126.66, 127.07 (C^4 , C^6), 130.49 (C^1), 132.94 (C^2), 136.11 (C^{14}), 140.31 (C^{13}), 147.11 (C^8), 167.84 ($\text{C}=\text{O}$), 170.59 (C^{16}), 176.76 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 478 [M] $^+$ (44), 419 (8), 377 (8), 361 (8), 269 (10), 230 (100), 189 (21), 188 (99), 119 (29), 107 (17), 93 (19), 57 (23), 43 (36). Found: [M] $^+$ 478.28220. $\text{C}_{29}\text{H}_{38}\text{N}_2\text{O}_4$. Calculated: M 478.28314.

Methyl 5-(2-{1-[2-(5-methoxy-1H-indol-3-yl)ethyl]-2-oxo-2,5-dihydro-1H-pyrrol-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate (IX). Triethylamine, 1 ml, was added to a mixture of 0.92 g (2 mmol) of diacetate IV

and 0.40 g (2.1 mol) of 5-methoxytryptamine in 20 ml of ethanol, and the mixture was heated for 3 h under reflux. The solvent was evaporated, and the residue was purified by chromatography using *tert*-butyl methyl ether as eluent. Yield 0.6 g (60%), mp 85–87°C (from petroleum ether), $[\alpha]_{\text{D}}^{20} = +17.5^\circ$ ($c = 4.1$, CHCl_3). IR spectrum, ν , cm^{-1} : 795, 826, 890, 982, 1032, 1067, 1092, 1155, 1229, 1247, 1500, 1586, 1640, 1666, 1721, 3088, 3250, 3292, 3436. UV spectrum, λ_{max} , nm ($\log \epsilon$): 225 (3.12), 277 (2.46), 295 (2.25), 310 (2.33). ^1H NMR spectrum (CCl_4), δ , ppm (J , Hz): 0.44 s (3H, C^{20}H_3), 0.95 d.t (1H, 1-H, $J = 13.2$, 4.1), 0.96 d.d.d (1H, 3-H, $J = 13.3$, 12.8, 4.2), 1.14 s (3H, C^{19}H_3), 1.21 d.d (1H, 5-H, $J = 12.4$, 3.1), 1.44 m (1H, 2-H), 1.49 m (1H, 11-H), 1.53 d.d (1H, 9-H, $J = 11.1$, 3.2), 1.67 m (1H, 11-H), 1.70 m (1H, 6-H), 1.75 m (1H, 2-H), 1.80 m (1H, 1-H), 1.84 m (1H, 7-H, $^2J = 12.7$), 1.91 m (1H, 6-H), 2.07 m (1H, 12-H), 2.10 m (1H, 3-H, $^2J = 13.3$), 2.35 d.d.d (1H, 7-H, $J = 12.7$, 3.9, 2.5), 2.39 m (1H, 12-H, $^2J = 13.8$), 2.92 t (2H, 2''-H, $J = 7.1$), 3.57 s (3H, OCH_3), 3.64 d.d (2H, 15-H, $J = 18.1$, 1.8), 3.70 d.d (2H, 1''-H, $J = 13.0$, 6.8), 3.76 s (3H, OCH_3), 4.58 s and 4.82 s (2H, 17-H), 6.45 t (1H, 14-H, $J = 1.6$), 6.70 d.d (1H, 6'-H, $J = 8.7$, 2.5), 6.84 d (1H, 2'-H, $J = 2.5$), 6.86 d (1H, 4'-H, $J = 8.0$), 7.11 d (1H, 7'-H, $J = 8.7$), 7.28 d.d.d (1H, 5'-H, $J = 8.7$, 8.0, 2.0), 8.98 br.s (1H, NH, halfwidth 11 Hz). ^{13}C NMR spectrum, δ_{C} , ppm: 12.55 (C^{20}), 19.89 (C^2), 21.99 (C^{11}), 24.75 (C^2), 25.38 (C^{12}), 26.16 (C^6), 28.77 (C^{19}), 38.20 (C^3), 38.65 (C^7), 39.06 (C^1), 40.21 (C^{10}), 42.84 ($\text{C}^{1'}$), 44.12 (C^4), 50.95 (OCH_3), 51.19 (C^{15}), 55.44 (OCH_3), 55.81 (C^9), 56.20 (C^5), 99.96 (C^4), 106.90 (C^{17}), 111.93 and 111.97 (C^6 , C^7), 111.99 (C^3), 122.59 (C^2), 127.64 (C^{7a}), 131.51 (C^{3a}), 133.63 (C^{14}), 140.86 (C^{13}), 147.25 (C^8), 153.76 (C^5), 171.23 (C^{15}), 177.01 (C^{18}). Mass spectrum, m/z (I_{rel} , %): 518 [M]⁺ (22), 459 (4), 346 (3), 254 (12), 173 (100), 160 (59). Found: [M]⁺ 518.32104. $\text{C}_{32}\text{H}_{42}\text{N}_2\text{O}_4$. Calculated: M 518.31444.

Methyl 5-[2-(2,5-dimethoxy-2,5-dihydrofuran-3-yl)ethyl]-1,4a-dimethyl-6-methylidenedecahydro-naphthalene-1-carboxylate (Xa–Xd). *a.* *N*-Chlorobenzenesulfonamide sodium salt, 4.7 g (21 mmol), was added in portions over a period of 10 min to a solution of 3.3 g (10 mmol) of lambertianic acid methyl ester (**IIIb**) and 1.5 ml of acetic acid in 25 ml of methanol under stirring at 0 to 5°C. The mixture was stirred for 30 min at 5°C (TLC), 1–2 ml of a 5% solution of Na_2SO_3 was added to decompose excess *N*-chlorobenzenesulfonamide, 50 ml of water was then added, and the mixture was extracted with *tert*-butyl methyl ether (3 × 15 ml). The extract was washed with a 3% solution

of sodium hydroxide (3 × 10 ml) to remove PhSO_2NH_2 and with water, the solvent was removed, and the residue was subjected to chromatography using petroleum ether–*tert*-butyl methyl ether (1:1) as eluent to isolate 3.5 g (90%) of diastereoisomer mixture **Xa–Xd**.

b. A solution of 1.2 g (3.6 mmol) of ester **IIIb** in 15 ml of methanol was cooled to 0°C, 1.3 g (7.2 mmol) of *N*-bromosuccinimide was added in portions under stirring, the mixture was stirred for 10 min, 1 ml of a 5% solution of Na_2SO_3 and 50 ml of water were added, and the mixture was extracted with diethyl ether (3 × 20 ml). The extract was washed with water and evaporated, and the residue was subjected to chromatography to isolate 1.2 g (85%) of acetal mixture **Xa–Xd**. ^1H NMR spectrum (CCl_4), δ , ppm (J , Hz): 0.47 s (3H, C^{20}H_3); 0.83–1.29 m (3H, 1-H, 3-H, 9-H); 1.14 s (3H, C^{19}H_3); 1.40–2.05 m (10H, 1-H, 2-H, 3-H, 5-H, 6-H, 7-H, 11-H); 2.08–2.25 m (2H, 7-H, 12-H); 2.33–2.40 m (1H, 12-H); 3.23 s, 3.24 s, 3.26 s, and 3.27 s (intensity ratio 1:1:1:1, 6H, OCH_3); 3.52 s (3H, OCH_3); 4.47 s and 4.82 s (2H, 17-H); 5.23 s, 5.27 s, and 5.38 d (1H, 16-H, $J_{\text{cis}} = 1.7$); 5.48 d, 5.50 d, and 5.59 d (2H, 14-H, 15-H, $J = 1.7$, 1.6, 1.6).

Methyl 1,4a-dimethyl-6-methylidene-5-[2-(2-oxo-2,5-dihydrofuran-3-yl)ethyl]decahydronaphthalene-1-carboxylate (XII). Acetal mixture **Xa–Xd**, 0.39 g (1 mmol), was dissolved in 5 ml of dioxane, and 0.5 ml of 20% HCl in dioxane was added. After 30 min, the mixture was treated with 15 ml of a 3% solution of K_2CO_3 and was extracted with *tert*-butyl methyl ether. The extract was washed with water and evaporated, and the residue was recrystallized from petroleum ether. Yield 0.23 g (67%), mp 82–84°C, $[\alpha]_{\text{D}}^{20} = +21.5^\circ$ ($c = 7.1$, CHCl_3). IR spectrum, ν , cm^{-1} : 758, 786, 874, 924, 1003, 1023, 1502, 1642, 1727, 1791, 3081. ^1H NMR spectrum (CCl_4), δ , ppm (J , Hz): 0.39 s (3H, C^{20}H_3), 0.91 d.t (1H, 1-H, $J = 13.3$, 4.3), 0.96 d.d.d (1H, 3-H, $J = 13.2$, 12.8, 4.2), 1.07 s (3H, C^{19}H_3), 1.18 d.d (1H, 5-H, $J = 12.6$, 2.9), 1.40 m (1H, 2-H), 1.47 m (1H, 11-H), 1.53 d.d (1H, 9-H, $J = 11.1$, 3.2), 1.62–1.78 m (4H, 1-H, 2-H, 6-H, 11-H), 1.80 m (1H, 7-H, $^2J = 12.7$), 1.85 m (1H, 6-H), 1.97 m (1H, 12-H), 2.05 m (1H, 3-H, $^2J = 13.2$), 2.29 d.d.d (1H, 7-H, $J = 12.7$, 4.0, 2.6), 2.33 m (1H, 12-H), 3.50 s (3H, OCH_3), 4.47 s and 4.77 s (2H, 17-H), 4.62 d.d (2H, 15-H, $J = 18.0$, 1.6), 6.99 quint (1H, 14-H, $J = 1.6$). ^{13}C NMR spectrum, δ_{C} , ppm: 12.38 (C^{20}), 19.72 (C^2), 21.69 (C^{11}), 24.52 (C^{12}), 25.99 (C^6), 28.59 (C^{19}), 38.04 (C^3), 38.49 (C^7), 39.00 (C^1), 40.08 (C^{10}), 43.98 (C^4), 50.71 (OCH_3), 55.54 (C^9), 56.11 (C^5), 69.48 (C^{15}), 106.66 (C^{17}), 134.60 (C^{14}), 143.23 (C^{13}), 146.99 (C^8),

173.14 (C¹⁶), 176.61 (C¹⁸). Mass spectrum, *m/z* (*I*_{rel.}, %): 346 [M]⁺ (4), 314 (8), 286 (48), 271 (22), 217 (14), 189 (19), 161 (27), 121 (100), 109 (27), 81 (36). Found: [M]⁺ 346.21489. C₂₁H₃₀O₄. Calculated: *M* 346.21439.

Methyl (6*R*)- and (6*S*)-5-[2-(2,5-dimethoxytetrahydrofuran-3-yl)ethyl]-1,4a,6-trimethyldecahydronaphthalene-1-carboxylates XIIIa–XIII d and XIVa–XIV d. A solution of 0.3 g of acetal mixture **Xa–Xd** in 5 ml of methanol was subjected to hydrogenation under atmospheric pressure in the presence of 2 g of Raney nickel. When the reaction was complete (2–3 h), the catalyst was filtered off, the solvent was evaporated, and the residue was subjected to chromatography using petroleum ether–*tert*-butyl methyl ether (1:1) as eluent to isolate 0.29 g (90%) of an oily product. ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.60 s and 0.61 s (3H, C²⁰H₃); 0.83 d, 0.85 d, 0.89 d, and 0.91 d (3H, C¹⁷H₃, *J* = 7); 0.92–1.02 m (2H, 1-H, 3-H); 1.12 s and 1.13 s (3H, C¹⁹H₃); 1.18–1.52 m (4H, 6-H, 9-H, 14-H); 1.58–1.64 m (2H, 7-H, 11-H); 1.79–1.94 m (10H, 1-H, 2-H, 5-H, 6-H, 9-H, 11-H, 12-H, 13-H); 2.02–2.18 m (3H, 3-H, 7-H, 12-H); 3.23 s, 3.24 s, 3.25 s, 3.26 s, 3.27 s, 3.28 s, 3.31 s, and 3.32 s (2×3H, OCH₃); 3.56 s and 3.58 s (3H, OCH₃); 4.58 m, 4.62 d, 4.64 d, 4.74 m, 4.88 m, 4.90 m, 4.91 m, and 4.92 m (2H, 15-H, 16-H). Mass spectrum, *m/z* (*I*_{rel.}, %): 394 [M]⁺ (3), 360 (14), 331 (25), 329 (24), 369 (27), 189 (19), 173 (20), 161 (25), 147 (23), 142 (20), 121 (100), 112 (54), 93 (28). Found: [M]⁺ 394.27010. C₂₃H₃₈O₅. Calculated: *M* 394.27191.

Methyl (6*R*)- and (6*S*)-1,4a,6-trimethyl-5-[2-(1-phenylpyrrol-3-yl)ethyl]decahydronaphthalene-1-carboxylates XV and XVI. A mixture of 0.2 g (0.51 mmol) of 2,5-dimethoxytetrahydrofurans **XIII** and **XIV**, 0.2 g (2.2 mmol) of aniline, 1 ml of water, and 5 ml of acetic acid was heated for 10 min at 90–95°C. When the reaction was complete, the mixture was diluted with water and extracted with *tert*-butyl methyl ether. The extract was washed with water (3×10 ml) and evaporated, and the residue was subjected to chromatography using petroleum ether–*tert*-butyl methyl ether (4:1) as eluent to isolate 0.16 g (78%) of a mixture of isomeric pyrroles **XV** and **XVI**. ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.68 s and 0.79 s (3H, C²⁰H₃), 0.89 m (1H, 3-H), 0.92 m (1H, 1-H), 0.95 d (3H, C¹⁷H₃, *J* = 7.0), 1.18 s and 1.20 s (3H, C¹⁹H₃), 1.21 m (1H, 5-H), 1.32–1.56 m (4H, 2-H, 6-H, 7-H, 9-H), 1.70–1.83 m (2H, 2-H, 11-H), 1.90–2.05 m (2H, 1-H, 6-H), 2.10–2.30 m (3H, 3-H, 11-H,

12-H), 2.50–2.60 m (2H, 7-H, 12-H), 3.62 s and 3.63 s (3H, OCH₃), 6.19 m and 6.22 m (1H, 14-H), 6.88 d and 6.90 d (1H, 15-H, *J* ≈ 2.6), 7.00 m (1H, 16-H), 7.20 m (2H, *o*-H), 7.40 m (3H, *m*-H, *p*-H). ¹³C NMR spectrum, δ_C, ppm: 14.33 and 15.08 (C²⁰), 17.74 and 19.83 (C¹⁷), 18.89 and 19.04 (C²), 19.59 and 20.88 (C⁶), 25.27 and 27.12 (C¹¹), 28.78 and 29.04 (C¹⁹), 29.01 and 29.92 (C¹²), 34.33 and 34.95 (C⁷), 37.17 and 37.84 (C³), 38.16 and 38.32 (C¹), 39.56 and 39.76 (C¹⁰), 43.75 (C⁴), 50.76 (OCH₃), 51.96 (C⁹), 53.52 (C⁵), 57.45 (C⁸), 110.78 and 110.98 (C¹⁴), 115.71 and 115.96 (C¹⁶), 118.57 and 118.60 (C_{arom}), 119.79 and 119.87 (C_{arom}), 124.76 and 124.82 (C¹⁵), 126.59 and 126.76 (C¹³), 129.26 (C_{arom}), 139.36 (C_{arom}), 177.04 (C¹⁸). Found: [M]⁺ 407.28420. C₂₇H₃₇NO₂. Calculated: *M* 407.28241.

Methyl (6*R*)- and (6*S*)-1,4a,6-trimethyl-5-[2-(1-methylpyrrol-3-yl)ethyl]decahydronaphthalene-1-carboxylates XVII and XVIII. Acetal mixture **XIII/XIV**, 0.2 g (0.51 mmol), was dissolved in 5 ml of acetic acid, 0.5 ml of a 25% solution of methylamine and 1 ml of water were added in succession, and the mixture was heated for 15 min at 90°C. The mixture was cooled, diluted with water, and extracted with diethyl ether (3×10 ml). The extract was washed with a 3% solution of ammonia and evaporated, and the residue was subjected to chromatography using petroleum ether–diethyl ether (2:1) as eluent to isolate 0.13 g (74%) of a mixture of pyrroles **XVII** and **XVIII** as an oily substance. ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.57 s and 0.64 s (3H, C²⁰H₃); 0.80–1.0 m (2H, 1-H, 3-H); 0.91 d and 0.93 d (3H, C¹⁷H₃, *J* = 7.0); 1.01–1.09 m (1H, 5-H); 1.15 s and 1.17 s (3H, C¹⁹H₃); 1.45–1.56 m (3H, 2-H, 7-H, 9-H); 1.60–1.99 m (6H, 1-H, 2-H, 6-H, 11-H, 12-H); 2.02–2.20 m (2H, 3-H, 11-H); 2.30–2.50 m (2H, 7-H, 12-H); 3.57 s, 3.59 s, and 3.60 s (2×3H, NCH₃, OCH₃); 5.81 m (1H, 14-H, *J* = 2.7, 2.6, 2.1); 6.24 m (1H, 15-H); 6.36 m (1H, 16-H). ¹³C NMR spectrum, δ_C, ppm: 14.43 and 15.18 (C²⁰), 17.84 and 19.89 (C¹⁷), 19.01 and 19.15 (C²), 19.71 and 21.00 (C⁶), 25.38 and 27.53 (C¹¹), 28.92 and 29.14 (C¹⁹), 29.97 and 30.40 (C¹²), 34.45 and 35.10 (C⁷), 35.82 (NCH₃), 37.24 and 37.99 (C³), 38.32 and 38.66 (C¹), 39.07 and 39.26 (C¹⁰), 43.88 (C⁴), 50.84 (OCH₃), 52.06 (C⁹), 53.67 (C⁵), 57.63 (C⁸), 108.31 and 108.54 (C¹⁴), 118.35 and 118.65 (C¹⁶), 121.14 and 122.04 (C¹⁵), 124.84 and 125.13 (C¹³), 177.11 (C¹⁸). Mass spectrum, *m/z* (*I*_{rel.}, %): 345 [M]⁺ (26), 286 (3), 175 (2), 148 (3), 121 (4), 108 (56), 95 (100), 32 (66). Found: [M]⁺ 345.26689. C₂₂H₃₅NO₂. Calculated: *M* 345.26676.

Methyl 3a-hydroxymethyl-2-(2,5-dimethoxy-2,5-dihydrofuran-3-yl)-6,9a-dimethyldodecahydronaphtho[2,1-*b*]furan-6-carboxylate (XXIa–XXId).

N-Chlorobenzenesulfonamide sodium salt, 0.6 g (2.8 mmol), was added in portions to a solution of 0.5 g (1.4 mmol) of epoxyabdanoid **XX** and 0.1 ml of acetic acid in 15 ml of methanol under stirring at 0 to 5°C. The mixture was stirred for 10 min, a solution of 0.5 g of Na₂SO₃ in 5 ml of water and 50 ml of 1% aqueous sodium hydroxide were added in succession, and the mixture was extracted with diethyl ether (2×15 ml). The extract was washed with a 1% solution of NaOH (2×10 ml) and water and evaporated, and the residue was subjected to chromatography using petroleum ether–diethyl ether (1:1) as eluent to isolate 0.51 g (87%) of a mixture of acetals **XXIa–XXId** as an oily material. ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.49 s and 0.51 s (3H, C²⁰H₃); 0.89–1.03 m (2H, 1-H, 3-H); 1.05–1.07 m (1H, 5-H); 1.07 s (3H, C¹⁹H₃); 1.32–1.44 m (3H, 2-H, 6-H, 7-H); 1.56 m (1H, 9-H); 1.65–1.95 m (5H, 1-H, 2-H, 6-H, 7-H, 11-H); 2.01–2.12 m (1H, 11-H); 2.19–2.26 m (1H, 3-H); 3.10 m (1H, 17-H); 3.21 s, 3.22 s, 3.23 s, 3.24 s, 3.28 s, 3.29 s, 3.30 s, and 3.31 s (2×3H, OCH₃); 3.35–3.43 m (1H, 17-H); 3.52 s (3H, OCH₃); 4.51 m (1H, 12-H); 5.31 m, 5.38 m, 5.40 s, and 5.42 m (1H, 16-H); 5.58 m, 5.65 m, 5.66 m, and 5.69 m (2H); 5.70 m (2H); 5.71 m (2H, 14-H, 15-H). ¹³C NMR spectrum, δ_c, ppm: 12.90, 12.94, 12.99, and 13.02 (C²⁰); 18.76 and 18.82 (C²); 21.85 and 21.92 (C⁶); 28.40 (C¹⁹); 28.94, 28.97, 28.99, and 29.02 (C¹¹); 34.41 and 34.57 (C⁷); 36.58, 36.61, and 36.67 (C³); 38.24 (C¹⁰); 40.15 (C¹); 43.24 (C⁴); 50.85 (OCH₃); 53.22, 53.27, 53.61, 53.75, 53.98, 54.02, 54.12, and 54.23 (15-OCH₃, 16-OCH₃); 56.93 (C⁵); 60.40, 60.44, 60.54, and 60.57 (C⁹); 62.05, 62.06, 62.40, and 62.44 (C⁸); 73.42, 73.58, 73.71, and 73.95 (C¹²); 83.14, 83.21, 83.37, and 83.39 (C¹⁷); 106.01, 106.08, and 106.16 (C¹⁶); 107.45, 107.58, 107.64, and 107.79 (C¹⁵); 124.18, 124.66, 124.84, and 125.55 (C¹⁴); 146.26, 146.41, 146.58, and 146.96 (C¹³); 176.22 (C¹⁸).

Methyl 2-(2,5-dimethoxy-2,5-dihydrofuran-3-yl)-3a-hydroxymethyl-6,9a-dimethyldodecahydronaphtho[2,1-*b*]furan-6-carboxylate (XXIIa–XXIId).

A solution of 0.5 g of stereoisomer mixture **XXIa–XXId** in 10 ml of methanol was subjected to hydrogenation under atmospheric pressure over 2 g of Raney nickel. When the reaction was complete (4 h), the catalyst was filtered off, the solvent was removed from the filtrate, and the residue was purified by chromatography using diethyl ether as eluent to isolate 0.36 g

(72%) of stereoisomer mixture **XXIIa–XXIId** as an oily material. ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.54 s and 0.56 s (3H, C²⁰H₃); 0.92–1.12 m (4H, 1-H, 2-H, 3-H, 5-H); 1.16 s (3H, C¹⁹H₃); 1.36–1.52 m (4H, 6-H, 7-H, 14-H); 1.58–1.64 m (2H, 9-H, 11-H); 1.79–1.94 m (3H, 1-H, 2-H, 6-H); 1.96–2.06 m (1H, 11-H); 2.14–2.20 m (1H, 3-H); 2.26–2.32 m (2H, 7-H, 13-H); 3.21 m (1H, 17-H); 3.30 s, 3.31 s, 3.34 s, 3.35 s, 3.36 s, 3.37 s, 3.42 s, and 3.43 s (2×3H, OCH₃); 3.54 d and 3.59 d (1H, 17-H, *J* = 7.6); 3.60 s (3H, OCH₃); 4.02 m and 4.06 m (1H, 12-H); 4.77 m, 5.04 m, 5.06 m, and 5.08 m (2H, 15-H, 16-H). ¹³C NMR spectrum, δ_c, ppm: 12.88 and 13.02 (C²⁰); 18.80 (C²); 21.79 and 21.94 (C⁶); 28.49 (C¹⁹); 28.74 and 29.13 (C¹¹); 33.57 and 33.72 (C¹⁴); 34.69 and 34.76 (C⁷); 36.64 and 36.72 (C³); 38.29 (C¹⁰); 39.97 and 40.05 (C¹); 43.45 (C⁴); 50.81 and 51.10 (C¹³); 51.99 (OCH₃); 55.32, 55.39, 55.42, 55.54, 55.93, and 55.95 (15-OCH₃, 16-OCH₃); 56.84 and 56.86 (C⁵); 60.51 and 60.54 (C⁹); 62.42 and 62.72 (C⁸); 79.27 and 79.74 (C¹²); 82.54 and 82.67 (C¹⁷); 104.64 and 105.60 (C¹⁶); 107.10 and 108.04 (C¹⁵); 177.13 and 177.16 (C¹⁸).

Methyl 3a-hydroxymethyl-6,9a-dimethyl-2-(1-methylpyrrol-3-yl)dodecahydronaphtho[2,1-*b*]furan-6-carboxylate (XIX).

Acetal mixture **XXIIa–XXIId**, 0.42 g (1 mmol), was dissolved in 10 ml of acetic acid, 1 ml of a 25% solution of methylamine was added dropwise, and 1–2 ml of water was then added until the mixture became turbid. The mixture was heated for 15 min at 85–90°C, cooled, diluted with water, and extracted with diethyl ether (2×15 ml). The extract was washed with a 3% solution of ammonia and evaporated, and the residue was subjected to chromatography using petroleum ether–diethyl ether (1:2). Yield 0.29 g (62%), oily substance, [α]_D²⁰ = +29° (*c* = 2.8, CHCl₃). ¹H NMR spectrum (CDCl₃), δ, ppm (*J*, Hz): 0.88 s (3H, C²⁰H₃), 0.98 t.d (1H, 3-H, *J* = 13.2, 4.2, 0.9), 1.00 d.d.d (1H, 1-H, *J* = 13.5, 4.3, 1.0), 1.17 d.d.d (1H, 5-H, *J* = 12.5, 7.0, 1.7), 1.19 s (3H, C¹⁹H₃), 1.44 d.d.d (1H, 2-H, *J* = 13.5, 12.6, 3.2, 1.0), 1.51 d.d (1H, 9-H, *J* = 9.8, 2.5), 1.56 m (1H, 6-H), 1.73 m (1H, 7-H, ²*J* = 13.8), 1.81 m (1H, 11-H, ²*J* = 15.2), 1.89 m (1H, 6-H), 2.07 d.d.d (1H, 11-H, *J* = 15.2, 12.7, 7.3), 2.20 m (1H, 3-H, ²*J* = 13.2), 3.38 d.d (1H, 17-H, *J* = 11.6, 2.0), 3.61 s and 3.62 s (3H each, NCH₃, OCH₃), 3.93 d (1H, 17-H, *J* = 11.6), 4.51 d.d (1H, 12-H, *J* = 12.7, 2.7), 6.00 m (1H, 14-H, *J* = 2.6, 2.1), 6.44 d (1H, 15-H, *J* = 2.6), 6.50 m (1H, 16-H, *J* = 2.1, 2.7). ¹³C NMR spectrum, δ_c, ppm: 17.03 (C²⁰), 19.23 (C²), 21.27 (C⁶), 27.90 (C¹¹), 28.87 (C¹⁹), 36.06 (CH₃N), 37.26 (C⁷), 37.93 (C³), 39.25 (C¹⁰), 41.33 (C¹), 43.61 (C⁴), 51.14 (OCH₃), 52.77 (C⁹), 56.03 (C⁵),

68.32 (C⁸), 71.36 (C¹²), 73.65 (C¹⁷), 106.83 (C¹⁴), 118.80 (C¹⁶), 121.57 (C¹⁵), 125.77 (C¹³), 177.15 (C=O), 177.09 (C¹⁸). Mass spectrum, m/z (I_{rel} , %): 345 [M]⁺ (26), 286 (3), 175 (2), 148 (3), 121 (4), 108 (56), 95 (100), 32 (66). Found: [M]⁺ 345.26689. C₂₂H₃₃NO₄. Calculated: M 345.26676.

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