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Synthetic Transformations of Higher Terpenoids: XV.* Transformations of Azlactone Derived from 16-Formyllambertianic Acid Methyl Ester

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Abstract—Condensation of 16-formyllambertianic acid methyl ester with hippuric acid gave methyl 15,16-epoxy-16-[(4*Z*)-5-oxo-2-phenyl-4,5-dihydrooxazol-4-ylidenemethyl]labda-8(20),13(16),14-trien-19-oate which underwent ready transformation into 2-benzoylamino-3-(2-furyl)acrylic acid of the labdanoid series. Reactions of the diterpenoid azlactone with amines and α-amino acid esters led to the formation of the corresponding carbamoylvinylbenzamides and *N*-(2-benzoylaminoacryloyl) amino acid esters, and furylacrylic acid hydrazides were formed in reactions with hydrazines. Cyclization of the *N'*-phenylhydrazide by the action of 1 M aqueous sodium hydroxide gave the corresponding 1,2,4-triazin-6-one. By treatment of the azlactone with aqueous ammonia on heating, 4-substituted 2-phenyl-4,5-dihydroimidazol-5-one was obtained.

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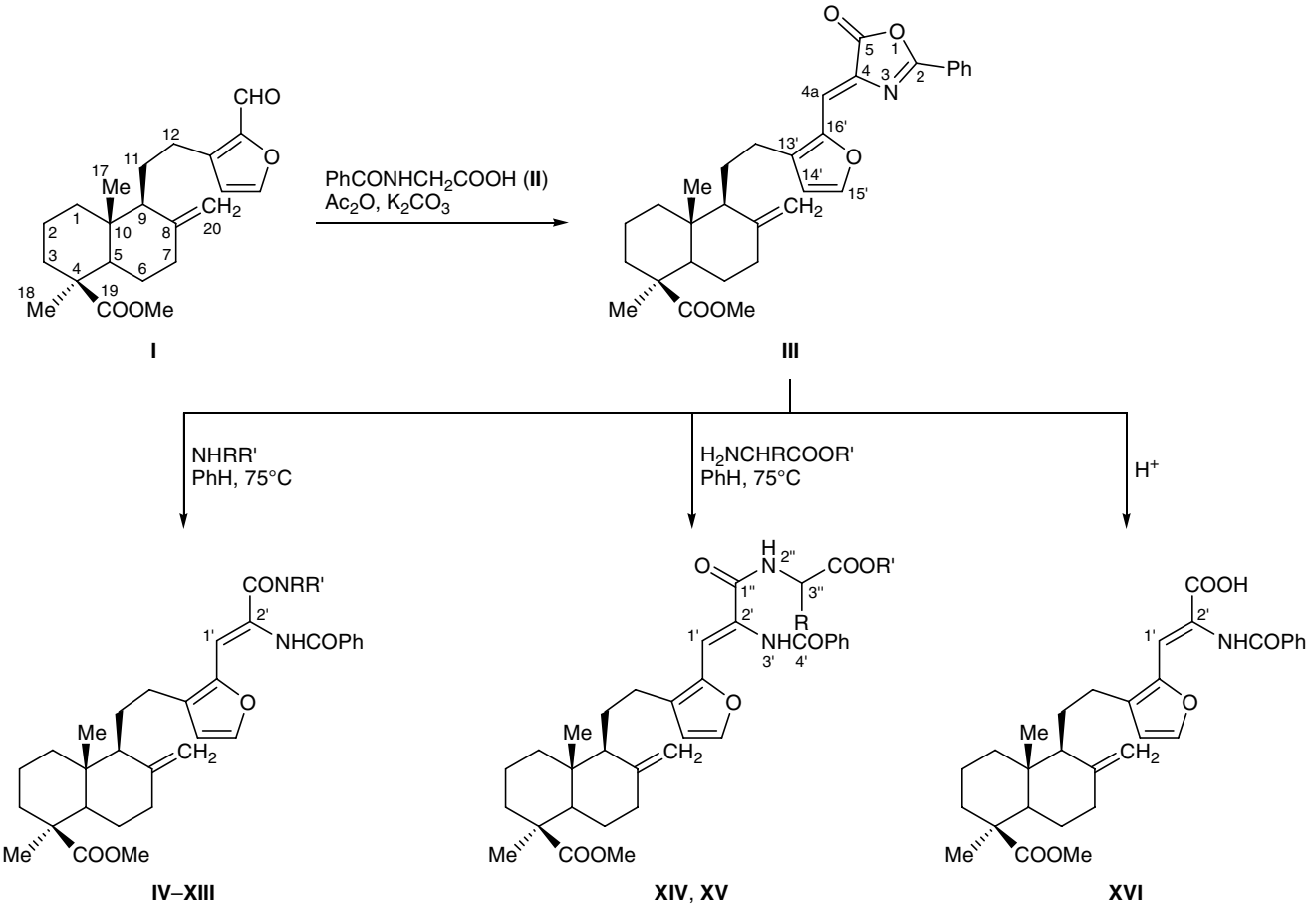
Reactions of aldehydes with acylaminoacetic acids (Erlenmeyer reaction) lead to the formation of oxazol-5(4*H*)-ones [2–4]. From the synthetic viewpoint, these reactions ensure preparation of amino acid derivatives under mild conditions. Aldehyde nature considerably affects the reaction course. Aromatic aldehydes and most heterocyclic aldehydes readily react with hippuric acid to give the corresponding oxazolones in good yields. However, the yields of condensation products from substituted aldehydes are not always satisfactory. Fatty aldehydes difficultly react with hippuric acid, while analogous reactions of terpenoid aldehydes were not studied.

The goal of the present work was to synthesize diterpenoid azlactone from 16-formyllambertianic acid methyl ester (**I**) [5] and study its reactions with nucleophiles. We have found that aldehyde **I** reacts with hippuric acid (**II**) under standard conditions (heating in boiling acetic anhydride in the presence of sodium acetate) [6] to give labdanoid oxazol-5(4*H*)-one **III** in 44% yield (conversion 56%) (Scheme 1). We failed to raise the product yield by increasing the reaction time to 90 min; by contrast, the yield was as poor as 25% as a result of strong tarring. On the other hand, the yield of azlactone **III** increased to 76% when potassium carbonate was used instead of sodium acetate [7]. Compound **III** was formed as a single isomer having *Z* configuration of the double bond.

Azlactone **III** smoothly reacted with primary amines [such as aniline, benzylamines, and phenylethyl(propyl)amines] and 7-aminoheptanoic acid on heating in benzene to give 59–91% of *N*-(1-carbamoylvinyl)benzamides **IV**–**X** (Scheme 1). The lowest yield was observed in the reaction with 3,5,6-trimethoxybenzylamine; extension of the alkyl chain between the benzene ring and amino group increases the product yield. Reactions of compound **III** with secondary amines (piperidine and *N*-methylphenylmethanamine required prolonged heating, and the corresponding terpenoid *N*-(carbamoylvinyl)benzamides **XI** and **XII** were isolated in 73–80% yield. Treatment of **III** with L-proline *tert*-butyl ester smoothly afforded 83% of pyrrolidine-containing labdanoid **XIII**. The NMR spectra of compounds **XI** and **XIII** in $CDCl_3$ revealed conformational isomerism arising from restricted rotation about the amide C–N bond; no such isomerism was observed in DMSO-d_6 [8]. Azlactone **III** readily reacted with α-amino acid (leucine and isoleucine)

* For communication XIV, see [1].

Scheme 1.



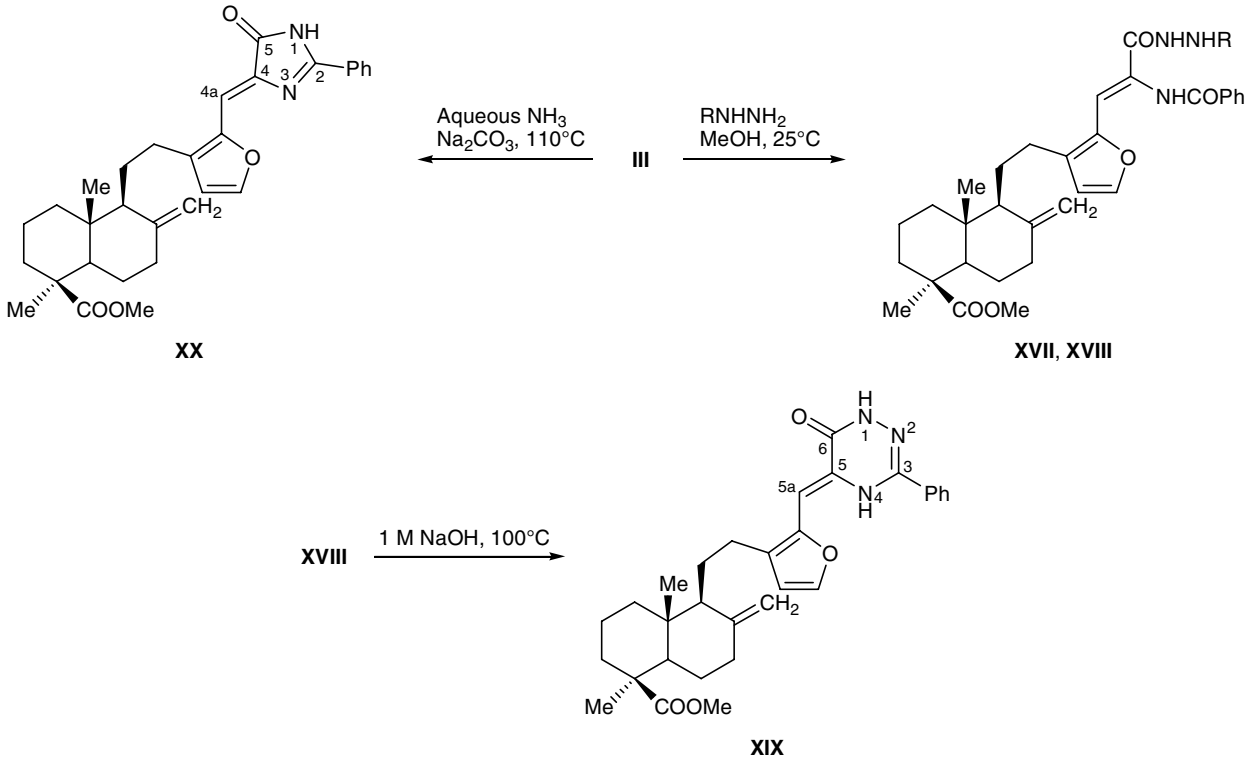
IV–**X**, R′ = H; **IV**, R = Ph; **V**, R = $PhCH_2$; **VI**, R = 4-$HOC_6H_4(CH_2)_2$; **VII**, R = 3,4,5-$(MeO)_3C_6H_2CH_2$; **VIII**, R = 3,5-(*t*-Bu)$_2$-4-$HOC_6H_2(CH_2)_2$; **IX**, R = 3,5-(*t*-Bu)$_2$-4-$HOC_6H_2(CH_2)_3$; **X**, R = $HOCO(CH_2)_6$; **XI**, R = $PhCH_2$, R′ = Me; **XII**, RR′ = $(CH_2)_5$; **XIII**, RR′N = 2-(*tert*-butoxycarbonyl)pyrrolidin-1-yl; **XIV**, R = $MeCH_2CH(Me)$, R′ = Me; **XV**, R = Me_2CHCH_2, R′ = *t*-Bu.

esters, yielding 62–78% of terpenoid *N*-(2-benzoylaminoacryloyl) amino acid esters **XIV** and **XV**. Terpenoid oxazol-5(4*H*)-one **III** undergoes hydrolysis on treatment with a solution of hydrogen chloride in diethyl ether or with 10% alcoholic alkali; the hydrolysis product is individual α-acylamino acid **XVI** with *Z* configuration of the double bond.

Some naturally occurring heterocyclic diterpenoids (e.g., lissoclimides and echinophyllins) exhibit pronounced pharmacological activity [9, 10]. Taking this into account, we made an attempt to obtain nitrogen-containing heterocyclic derivatives via transformations of azlactone **III**. Reactions of **III** with hydrazines on heating in methanol gave the corresponding acrylic acid hydrazides **XVII** and **XVIII** in 77–90% yield (Scheme 2). It is known that hydrazides derived from α,β-unsaturated acids undergo cyclization to 1,2,4-triazin-6-ones [11] or pyrazole derivatives [12]. *N*′-Phenylhydrazide **XVIII** was converted into 3,5-disubstituted 1,2,4-triazin-6-one **XIX** in 80% yield by heating in 1 M aqueous sodium hydroxide for a short time. 4,5-Dihydroimidazol-5-one **XX** of the labdane series was synthesized in 56% yield by heating azlactone **III** with aqueous ammonia in the presence of a base in a sealed ampule. Compounds **XIX** and **XX** were isolated as individual isomers having *Z* configuration of the double bond.

The structure of labdanoids **III**–**XX** was proved by the analytical and spectral data. The ^{1}H NMR spectrum of azlactone **III** contained signals from protons in the diterpene fragment, a signal from the 4a-H olefinic proton, and signals from protons in the phenyl group at δ 7.41 (2H), 7.48 (1H), and 8.07 ppm (2H). The *Z* configuration of the exocyclic double bond was determined on the basis of the $^3J_{CH}$ coupling constant in the ^{13}C NMR spectrum. According to published data [13], the vicinal coupling constant between the carbonyl carbon atom in the oxazolone ring and olefinic H_β proton

Scheme 2.



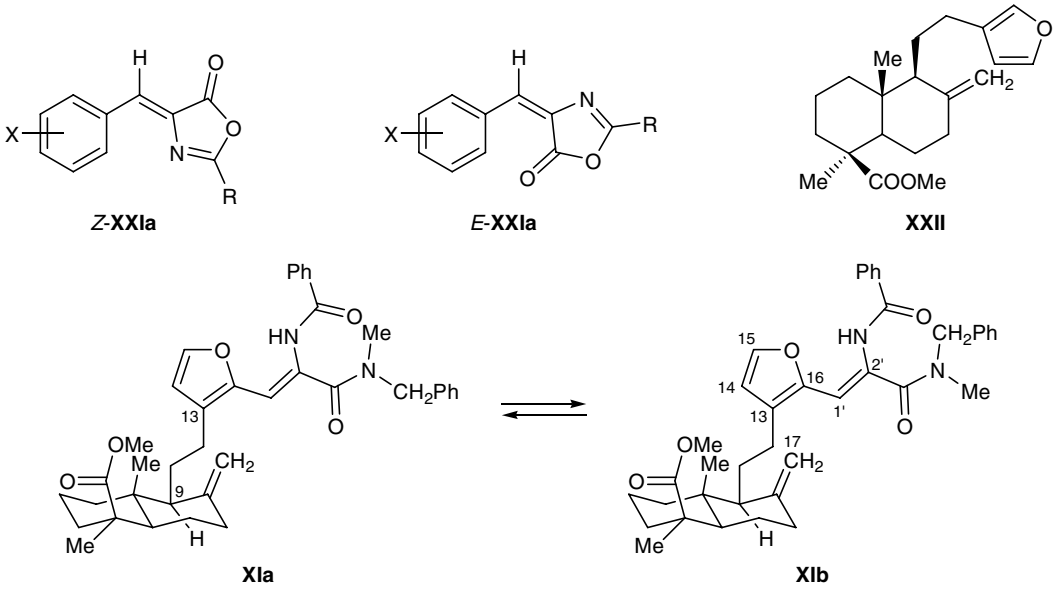
XVII, R = H; **XVIII**, R = Ph.

[^3J(C^5,4a-H)] is 5.5 Hz for *Z* isomers **XXIa** and 12.5 Hz for *E* isomers **XXIb** (Scheme 3). In our case, the $^3J_{CH}$ coupling constant was equal to 5.1 Hz. The oxazolone C=O signal appears as a doublet at δ_C 167.53 ppm due to coupling with 4a-H; therefore, this signal can be readily distinguished from the nearby signals belonging to the C=N carbon atom (a multiplet at δ_C 162.14 ppm due to coupling with *ortho* protons of the phenyl group) and ester carbonyl carbon atom in the terpenoid moiety (δ_C 177.27 ppm). Likewise, we have assigned signals from the carbonyl groups and determined *Z* configuration of the olefinic bond in hydrolysis product **XVI**: ^3J(2′-C, 1′-H) = 5.1 Hz; δ_C 167.60 (COOH), 166.40 ppm (NH**C**OPh).

Introduction of acylaminoacrylic acid fragments into the molecule of lambertianic acid methyl ester (**XXII**) gives rise to additional signals in the ^{1}H NMR spectra of compounds **IV**–**X**, which belong to protons in the amine moiety. The amide proton (CONHR) resonates as a broadened singlet in the region δ 6.7–6.5 ppm, and the NH proton in the benzoylamino group gives a singlet at δ 8.7–8.5 ppm. Signals from the carbonyl carbon nuclei (δ_C 163–170 ppm and 166–167 ppm for **C**ONHR and NH**C**OPh, respectively) are readily distinguished in the ^{13}C NMR spectra. The 1′-H signal in the ^{1}H NMR spectra of **IV**–**X** appears in a stronger field (Δδ = 0.28–0.48 ppm) relative to the corresponding signal of azlactone **III**. Analogous upfield shift of the C$^{1'}$ signal is observed in the ^{13}C NMR spectra (δ_C 110–112 ppm). N,N-Disubstituted amides **XI**–**XIII** characteristically showed in the ^{1}H NMR spectra an upfield shift of the 1′-H signal (Δδ = 1.06–1.25 ppm) as compared to azlactone **III**. Restricted rotation about the amide C–N bond in molecule **XI** (*E*/*Z*-conformer ratio 1 : 1) leads to doubling of signals from the benzylic CH_2 protons (δ 4.71, 4.78 ppm), olefinic 1′-H proton (δ 5.74 s, 5.81 s), and protons in the terpene fragment [δ 6.32, 6.38 (14-H), 7.57, 7.58 (15-H), 4.90, 4.92 and 4.55, 4.57 ppm (17-H)] in the ^{1}H NMR spectrum recorded from a solution in $CDCl_3$. In the ^{13}C NMR spectrum of **XI**, signals from two carbonyl carbon atoms, C$^{1'}$, C$^{2'}$, C^8, C^{16}, and CH_2 (δ_C 32.93, 36.44 ppm) and CH_3 groups (δ_C 50.56, 55.16 ppm) are doubled. In going to DMSO-d_6, no signal doubling is observed, for the conformational equilibrium is completely displaced toward one of the conformers (**XIa** or **XIb**; Scheme 3).

In the IR spectra of hydrazides **XVII** and **XVIII** we observed absorption bands typical of hydrazide and amide groups at 1640–1675, 3059, 3239, and 3431 cm^{-1}.

Scheme 3.



Three NH proton signals in the ^{1}H NMR spectrum of hydrazide **XVIII** are readily distinguished: the hydrazide $CONH_aNH_bPh$ protons resonate as broadened singlets at δ 8.33 (H_a, halfwidth 5 Hz) and 6.26 ppm (H_b, halfwidth 12 Hz), and the N**H**COPh signal is a singlet at δ 8.64 ppm. Singlets at δ 9.07 and 9.09 ppm in the ^{1}H NMR spectra of **XIX** were assigned to protons on N^1 and N^4, respectively, of the 1,2,4-triazin-6-one fragment. Compound **XIX** was identified as 3,5-disubstituted 1,2,4-triazine derivative on the basis of the following data. Its ^{13}C NMR spectrum contained three singlets at δ_C 161.38, 123.96, and 159.49 ppm, which belong to C^6, C^5, and C^3, respectively; they were assigned using two-dimensional ^{13}C–^{1}H correlation technique (COLOC). The C^3 nucleus showed coupling with *ortho* protons in the phenyl substituent, and the C^5 and C^6 nuclei were coupled with 5a-H. The coupling constant ^3J between C^6 and 5a-H is 5.3 Hz, indicating *Z* configuration of the exocyclic double bond. The presence of a triazinone ring in molecule **XIX** is also confirmed by the mass spectrum of this compound, which contains a fragment ion peak with *m*/*z* 187 (I_{rel} 83.5%; phenylmethyldihydrotriazol-1-one).

The structure of imidazolone **XX** follows from the NMR data. Three singlets in the ^{13}C NMR spectrum of **XX** at δ_C 148.01, 158.04, and 174.05 ppm belong, respectively, to the C^4, C^2, and C^5 atoms of the imidazole ring. The C^5 signal in the spectrum recorded without decoupling from protons appears as a doublet ($^3J_{CH}$ = 5.1 Hz) due to coupling with 4a-H; this coupling constant corresponds to *Z* configuration of the exocyclic double C=C bond. The 4a-H signal is located at δ 7.03 ppm (br.s) in the ^{1}H NMR spectrum, i.e., it appears in a weaker field relative to the corresponding signal in the spectrum of **III**; the NH proton resonates as a singlet at δ 11.79 ppm.

Thus, the condensation of 16-formyllambertianic acid methyl ester with hippuric acid gives the corresponding 4,5-dihydrooxazol-5-one derivatives whose subsequent transformations open synthetic routes to new nitrogen-containing derivatives of the labdane series.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Vector-22 spectrometer. The UV spectra were measured on an HP 8453 UV-Vis spectrophotometer from solutions in ethanol with a concentration of about 10^{-4} M. The NMR spectra were obtained from solutions in $CDCl_3$ on Bruker AV-300 (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C), Bruker AM-400 (400.13 MHz for ^{1}H and 100.78 MHz for ^{13}C), and Bruker DRX-500 instruments (500.13 for ^{1}H and 125.76 MHz for ^{13}C). Signals were assigned using various proton–proton and carbon–proton shift correlation techniques (COSY, COLOC, CORRD). The high-resolution mass spectra (electron impact, 70 eV) were run on a Finnigan MAT-8200 mass spectrometer (vaporizer temperature 200–270°C). The melting points were determined using a Kofler hot stage. The optical rotations were measured on a Polamat A polarimeter from solutions in

chloroform or ethanol at room temperature (20–23°C). The progress of reactions was monitored by TLC on Silufol UV-254 plates; spots were visualized by spraying with a 10% aqueous solution of sulfuric acid. Column chromatography was performed on KSK silica gel (grain size 0–70 μm).

16-Formyllambertianic acid methyl ester (**I**) was synthesized from ester **XXII** according to the procedure reported in [5], and compound **XXII** was prepared as described in [14].

Methyl (*Z*)-(1*S*,4a*R*,5*S*)-1,4a-dimethyl-6-methylidene-5-{2-[2-(5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-ylidenemethyl)furan-3-yl]ethyl}decahydronaphthalene-1-carboxylate {III, methyl 15,16-epoxy-16-[(4*Z*)-5-oxo-2-phenyl-4,5-dihydro-1,3-oxazol-4-ylidenemethyl]labda-8(20),13(16),14-trien-19-oate}. *a*. Hippuric acid (**II**), 0.50 g (2.79 mmol), and potassium carbonate, 0.38 g (2.8 mmol), were added under stirring to a solution of 1.00 g (2.8 mmol) of aldehyde **I** in 15 ml of acetic anhydride. The mixture was stirred for 5 h and left overnight, and the precipitate was filtered off, washed with water, dried under reduced pressure, and recrystallized from petroleum ether–diethyl ether (2:1). Yield 1.06 g (76%).

b. Hippuric acid (**II**), 0.50 g (2.8 mmol), and sodium acetate, 0.23 g (2.8 mmol), were added to a solution of 1.00 g (2.8 mmol) of compound **I** in 15 ml of acetic anhydride. The mixture was heated for 1 h under reflux, cooled to room temperature, and passed through 25 g of aluminum oxide. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–diethyl ether (4:1) as eluent to isolate 1.00 g of a mixture of initial compound **I** and product **III**. Recrystallization from petroleum ether–diethyl ether (6:1) gave 0.61 g (44%) of compound **III**. mp 112–115°C, $[\alpha]_D^{20}$ = 1.2° (*c* = 7.7, $CHCl_3$). IR spectrum, ν, cm^{-1}: 702, 780, 883, 983, 1551 (C=C); 1645, 1720, 1759, 1789 (C=O). UV spectrum, λ_{max}, nm (logε): 232 (3.41), 266 (3.75), 392 (4.18), 409 (4.17). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.43 s (3H, $C^{17'}H_3$), 0.82 d.d.d (1H, 1′-H, *J* = 13.5, 13.2, 4.2 Hz), 0.90 t.d (1H, 3′-H, *J* = 13.2, 4.0 Hz), 1.06 s (3H, $C^{18'}H_3$), 1.13 d.d (1H, 5′-H, *J* = 12.4, 3.1 Hz), 1.38 d.m (1H, 2′-H, ^2J = 14.2 Hz), 1.48 d (1H, 9′-H, *J* = 10.8 Hz), 1.60–1.80 m (6H, 7′-H, 2′-H, 6′-H, 11′-H, 1′-H), 1.89 d.m (1H, 6′-H, ^2J = 13.2 Hz), 2.05 d.d.d (1H, 3′-H, *J* = 13.2, 3.3, 1.3 Hz), 2.36 m (1H, 7′-H, ^2J = 12.6 Hz), 2.51 d.d.d (1H, 12′-H, *J* = 14.4, 9.0, 7.7 Hz), 2.66 d.d.d (1H, 12′-H, *J* = 14.4, 7.8, 4.5 Hz), 3.51 s (3H, OCH_3), 4.53 s, 4.92 s (2H, 20′-H), 6.40 d (1H, 14′-H, *J* = 1.8 Hz), 6.92 s (1H, 4a-H), 7.41 m (2H, 3″-H, 5″-H), 7.48 m (1H, 4″-H), 7.68 d (1H, 15′-H, *J* = 1.8 Hz), 8.07 m (2H, 2″-H, 6″-H). ^{13}C NMR spectrum, δ_C, ppm: 12.36 q ($C^{17'}$), 19.54 t ($C^{2'}$), 23.49 t ($C^{12'}$), 23.89 t ($C^{11'}$), 25.90 t ($C^{6'}$), 28.39 q ($C^{18'}$), 37.74 t ($C^{3'}$), 38.19 t ($C^{7'}$), 38.65 t ($C^{1'}$), 39.78 s ($C^{4'}$), 43.87 s ($C^{10'}$), 50.81 q (OCH_3), 54.17 d ($C^{9'}$), 55.77 d ($C^{5'}$), 106.58 t ($C^{20'}$), 113.67 d ($C^{14'}$), 115.00 d (C^{4a}), 125.32 s ($C^{1''}$), 127.86 d ($C^{2''}$, $C^{6''}$), 128.18 s (C^4), 128.49 d ($C^{3''}$, $C^{5''}$), 132.64 d ($C^{4''}$), 137.80 s ($C^{13'}$), 146.80 s ($C^{16'}$), 147.14 s ($C^{8'}$), 147.71 d ($C^{15'}$), 162.14 s (C^2), 167.53 s (C^5), 177.27 s ($C^{19'}$). Found, %: C 74.03; H 7.11; N 2.7. $C_{31}H_{35}NO_5$. Calculated, %: C 74.25; H 6.99; N 2.79.

Methyl (1*S*,4a*R*,5*S*)-5-{2-[2-(2-benzoylamino-3-oxo-3-phenylaminoprop-1-en-1-yl)furan-3-yl]-ethyl}-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate [IV, methyl 16-(2-benzoylamino-3-oxo-3-phenylaminoprop-1-en-1-yl)-15,16-epoxylabda-8(20),13(16),14-trien-19-oate]. Aniline, 0.11 g (1.2 mmol), was added to a solution of 0.50 g (1.0 mmol) of azlactone **III** in 7 ml of benzene, and the mixture was heated for 2 h at 70°C. After cooling, the precipitate was filtered off, washed with diethyl ether, and dried under reduced pressure. Yield 0.49 g (82%), mp 156–159°C, $[\alpha]_D^{20}$ = 14.8° (*c* = 3.1, $CHCl_3$). IR spectrum, ν, cm^{-1}: 700, 754, 891, 1500, 1600, 3075 (C=C); 1722 (C=O); 1638, 1657, 3420 [C(O)NH]. UV spectrum, λ_{max}, nm (logε): 226 (3.89), 326 (4.05). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.45 s (3H, $C^{17}H_3$), 0.91 t.d (1H, 1-H, *J* = 13.5, 3.3 Hz), 0.98 t.d (1H, 3-H, *J* = 13.6, 3.0 Hz), 1.14 s (3H, $C^{18}H_3$), 1.22 d.d (1H, 5-H, *J* = 12.8, 2.6 Hz), 1.45 d.m (1H, 2-H, ^2J = 12.8 Hz), 1.48–1.53 m (2H, 9-H, 11-H), 1.61 m (1H, 11-H), 1.67–1.79 m (3H, 1-H, 6-H, 2-H), 1.85 t.d (1H, 7-H, *J* = 12.8, 3.2 Hz), 1.95 d.m (1H, 6-H, ^2J = 13.2 Hz), 2.11 d.m (1H, 3-H, ^2J = 13.6 Hz), 2.26 m (1H, 12-H, ^2J = 15.5 Hz), 2.38 d.t (1H, 7-H, *J* = 12.8, 2.6 Hz), 2.46 d.d.d (1H, 12-H, *J* = 15.5, 6.6, 4.2 Hz), 3.57 s (3H, OCH_3), 4.52 s and 4.90 s (1H each, 20-H), 6.40 d (1H, 14-H, *J* = 1.8 Hz), 6.85 s (1H, 1′-H), 7.04 t (1H, 4″-H, *J* = 7.6 Hz), 7.24 m (2H, 3″-H, 5″-H), 7.34 d (1H, 15-H, *J* = 1.8 Hz), 7.46 m (2H, 7′-H, 9′-H), 7.55 t (1H, 8′-H, *J* = 8.0 Hz), 7.57 m (2H, 2″-H, 6″-H), 7.95 d (2H, 6′-H, 10′-H, *J* = 7.6 Hz), 8.71 s (1H, 3′-H), 8.80 s (1H, N**H**Ph). ^{13}C NMR spectrum, δ_C, ppm: 12.47 q (C^{17}), 19.73 t (C^2), 23.20 t (C^{12}), 24.14 t (C^{11}), 26.10 t (C^6), 28.60 q (C^{18}), 37.96 t (C^3), 38.46 t (C^7), 38.88 t (C^1), 40.00 s (C^4), 44.11 s (C^{10}), 51.01 q (OCH_3), 54.75 d (C^9), 55.92 d (C^5),

106.53 t (C^{20}), 111.52 d ($C^{1'}$), 112.86 d (C^{14}), 120.07 d ($C^{2''}$, $C^{6''}$), 123.99 d ($C^{4''}$), 126.40 s ($C^{2'}$), 127.44 d ($C^{6'}$, $C^{10'}$), 128.63 d and 128.66 d ($C^{3''}$, $C^{5''}$, $C^{7'}$, $C^{9'}$), 130.52 s (C^{13}), 132.23 d ($C^{8'}$), 132.94 s ($C^{1''}$), 137.98 s ($C^{5'}$), 143.52 d (C^{15}), 146.16 s (C^{16}), 147.49 s (C^{8}), 163.00 s (CONH), 166.00 s ($C^{4'}$), 177.62 s (C^{19}). Found, %: C 74.52; H 7.79; N 4.59. $C_{37}H_{42}N_2O_5$. Calculated, %: C 74.75; H 7.71; N 4.71.

Methyl (1*S*,4a*R*,5*S*)-5-{2-[2-(2-benzoylamino-3-benzylamino-3-oxoprop-1-en-1-yl)furan-3-yl]ethyl}-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate [V, methyl 16-(2-benzoylamino-3-benzylamino-3-oxoprop-1-en-1-yl)-15,16-epoxylabda-8(20),13(16),14-trien-19-oate]. A solution of 0.50 g (1.0 mmol) of azlactone **III** and 0.14 g (1.2 mmol) of benzylamine in 7 ml of benzene was heated for 2 h at 70°C on an oil bath. The solvent was removed under reduced pressure, the residue was treated with 7 ml of diethyl ether, and the precipitate was filtered off, washed with diethyl ether (3×10 ml), and dried under reduced pressure. Yield 0.38 g (62%). Column chromatography of the mother liquor on silica gel (using chloroform as eluent) gave an additional portion, 0.15 g (24%), of compound **V**. mp 98–100°C, $[\alpha]_D^{20}$ = 12.3° (*c* = 5.4, $CHCl_3$). IR spectrum, ν, cm^{-1}: 698, 715, 750, 893, 1516, 1575 (C=C); 1721 (C=O); 1645, 3424 [C(O)NH]. UV spectrum, λ_{max}, nm (logε): 226 (4.08), 317 (4.36). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.45 s (3H, $C^{17}H_3$), 0.93 m (2H, 1-H, 3-H), 1.13 s (3H, $C^{18}H_3$), 1.22 m (1H, 5-H), 1.44 m (1H, 2-H), 1.58 m (2H, 9-H, 11-H), 1.70–1.88 m (5H, 11-H, 1-H, 2-H, 7-H, 6-H), 1.94 m (1H, 6-H), 2.09 m (1H, 3-H), 2.32 m (2H, 7-H, 12-H), 2.53 m (1H, 12-H), 3.57 s (3H, OCH_3), 4.86 s (2H, CH_2), 4.55 s and 4.86 s (1H each, 20-H), 6.32 d (1H, 14-H, *J* = 1.8 Hz), 6.67 s (1H, 1′-H), 7.05 m (4H, 15-H, 4″-H, 3″-H, 5″-H), 7.30 m (5H, NH, 2′-H, 6″-H, 7′-H, 9′-H), 7.41 t (1H, 8′-H, *J* = 7 Hz), 7.75 d (2H, 6′-H, 10′-H), 8.64 s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.48 q (C^{17}), 19.78 t (C^{2}), 23.50 t (C^{12}), 24.26 t (C^{11}), 26.15 t (C^{6}), 28.64 q (C^{18}), 38.03 t (C^{3}), 38.54 t (C^{7}), 38.92 t (C^{1}), 40.07 s (C^{4}), 43.40 t (CH_2), 44.16 s (C^{10}), 50.94 q (OCH_3), 55.16 d (C^{9}), 56.04 d (C^{5}), 106.48 t (C^{20}), 109.00 d ($C^{1'}$), 112.50 d (C^{14}), 127.44 d ($C^{6'}$, $C^{10'}$), 127.47 s ($C^{2'}$), 127.75 d ($C^{2''}$, $C^{6''}$), 128.36 d ($C^{3''}$, $C^{5''}$), 128.36 s ($C^{4''}$), 128.47 d ($C^{7'}$, $C^{9'}$), 130.52 s (C^{13}), 131.39 d ($C^{8'}$), 134.32 s ($C^{5'}$), 134.43 s ($C^{1''}$), 143.30 d (C^{15}), 147.06 s (C^{16}), 147.62 s (C^{8}), 165.29 s ($C^{4'}$), 170.53 s (CONH), 177.61 s (C^{19}). Found, %: C 75.35; H 7.23; N 4.64. $C_{38}H_{44}N_2O_5$. Calculated, %: C 75.00; H 7.24; N 4.64.

Methyl (1*S*,4a*R*,5*S*)-5-[2-(2-{2-benzoylamino-3-[2-(4-hydroxyphenyl)ethylamino]-3-oxoprop-1-en-1-yl}furan-3-yl)ethyl]-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate (VI, methyl 16-{2-benzoylamino-3-[2-(4-hydroxyphenyl)ethylamino]-3-oxoprop-1-en-1-yl}-15,16-epoxylabda-8(20),13(16),14-trien-19-oate). A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.14 g (1.0 mmol) of 2-(4-hydroxyphenyl)ethanamine in 7 ml of benzene was heated for 4 h at 70°C on an oil bath. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform–methanol (100:1) as eluent. The subsequent recrystallization from diethyl ether gave 0.53 g (84%) of compound **VI**, mp 125–128°C, $[\alpha]_D^{20}$ = 13.7° (*c* = 6.5, $CHCl_3$). IR spectrum, ν, cm^{-1}: 712, 828, 893, 1515 (C=C); 1723 (C=O); 1648, 1650, 3423 (CONH); 3347 (OH). UV spectrum, λ_{max}, nm (logε): 225 (3.33), 316 (3.38). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.43 s (3H, $C^{17}H_3$), 0.89 t.d (1H, 1-H, *J* = 13.2, 3.1 Hz), 0.95 t.d (1H, 3-H, *J* = 13.3, 2.6 Hz), 1.10 s (3H, $C^{18}H_3$), 1.21 d (1H, 5-H, *J* = 12.4, 2.2 Hz), 1.42 m (1H, 2-H, ^2J = 12.6 Hz), 1.50 m (2H, 9-H, 11-H), 1.61 m (1H, 11-H), 1.66–1.75 m (3H, 1-H, 6-H, 2-H), 1.84 t.d (1H, 7-H, *J* = 13.2, 3.0 Hz), 1.92 m (1H, 6-H), 2.07 d.m (1H, 3-H, ^2J = 13.3 Hz), 2.27 m (1H, 12-H), 2.35 m (1H, 7-H, ^2J = 12.6 Hz), 2.49 m (1H, 12-H), 2.66 t (2H, CH_2, *J* = 6.3 Hz), 3.45 d.d (2H, C**H**$_2$NH, *J* = 14.1, 6.3 Hz), 3.54 s (3H, OCH_3), 4.51 s and 4.87 s (1H each, 20-H), 6.27 d (1H, 14-H, *J* = 1.8 Hz), 6.63 br.s (1H, CONH), 6.67 m (2H, 3″-H, 5″-H), 6.74 s (1H, 1′-H), 6.86 d (2H, 2″-H, 6″-H, *J* = 7.2 Hz), 7.29 d (1H, 15-H, *J* = 1.8 Hz), 7.38 m (2H, 7′-H, 9′-H), 7.46 t (1H, 8′-H, *J* = 7.1 Hz), 7.83 m (2H, 6′-H, 10′-H), 8.00 br.s (1H, OH), 8.56 s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.37 q (C^{17}), 19.62 t (C^{2}), 23.08 t (C^{12}), 24.02 t (C^{11}), 25.99 t (C^{6}), 28.47 q (C^{18}), 34.34 t (CH_2), 37.79 t (C^{3}), 38.34 t (C^{7}), 38.68 t (C^{1}), 39.89 s (C^{4}), 41.31 t (CH_2N), 44.00 s (C^{10}), 50.96 q (OCH_3), 54.56 d (C^{9}), 55.74 d (C^{5}), 106.44 t (C^{20}), 111.44 d ($C^{1'}$), 112.67 d (C^{14}), 115.41 d ($C^{3''}$, $C^{5''}$), 125.52 s ($C^{2'}$), 127.31 d ($C^{6'}$, $C^{10'}$), 128.48 d ($C^{2''}$, $C^{6''}$), 129.33 s ($C^{1''}$), 129.40 d ($C^{7'}$, $C^{9'}$), 130.19 s (C^{13}), 132.03 d ($C^{8'}$), 132.87 s ($C^{5'}$), 143.38 d (C^{15}), 145.90 s (C^{16}), 147.40 s (C^{8}), 155.14 s ($C^{4''}$), 165.25 s (CONH), 166.53 s ($C^{4'}$), 177.72 s (C^{19}). Found, %: C 73.15; H 7.36; N 4.45. $C_{39}H_{46}N_2O_6$. Calculated, %: C 73.35; H 7.21; N 4.39.

Methyl (1*S*,4a*R*,5*S*)-5-(2-{2-[2-benzoylamino-3-oxo-3-(3,4,5-trimethoxybenzylamino)prop-1-en-1-yl]furan-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate {VII, methyl

16-[2-benzoylamino-3-oxo-3-(3,4,5-trimethoxybenzylamino)prop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate}. A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.22 g (1.1 mmol) of 3,4,5-trimethoxybenzylamine in 7 ml of benzene was heated for 4 h at 70°C on an oil bath. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform as eluent. A fraction containing compound **VII** was evaporated, and the residue was ground with hexane. Yield 41.0 g (59%), mp 78–80°C, $[\alpha]_D^{20}$ = 12.9° (*c* = 3.4, $CHCl_3$). IR spectrum, ν, cm^{-1}: 714, 775, 892, 1508 (C=C); 1721 (C=O); 1638, 1670, 3368, 3410 (CONH). UV spectrum, λ_{max}, nm (log ε): 230 (2.94), 316 (3.28). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.47 s (3H, $C^{17}H_3$), 0.94 m (1H, 1-H), 0.99 m (1H, 3-H), 1.15 s (3H, $C^{18}H_3$), 1.24 d.d (1H, 5-H, *J* = 12.5, 2.8 Hz), 1.46 m (1H, 2-H), 1.56 m (2H, 9-H, 11-H), 1.68–1.81 m (4H, 1-H, 6-H, 2-H, 11-H), 1.86 m (1H, 7-H), 1.96 m (1H, 6-H), 2.13 d.m (1H, 3-H, ^2J = 13.1 Hz), 2.38 m (2H, 12-H, 7-H), 2.60 m (1H, 12-H), 3.58 s (3H, OCH_3), 3.79 s (3H, 4″-OCH_3), 3.84 s (6H, 3″-OCH_3, 5″-OCH_3), 4.51 d (2H, C**H**$_2C_6H_2$, *J* = 6.2 Hz), 4.55 s and 4.89 s (1H each, 20-H), 6.34 d (1H, 14-H, *J* = 1.8 Hz), 6.61 s (2H, 2″-H, 6″-H), 6.70 t (1H, CONH, *J* = 6.1 Hz), 6.88 s (1H, 1′-H), 7.37 d (1H, 15-H, *J* = 1.8 Hz), 7.46 m (2H, 7′-H, 9′-H), 7.54 t (1H, 8′-H, *J* = 7.4 Hz), 7.90 d (2H, 6′-H, 10′-H, *J* = 7.8 Hz), 8.60 br.s (1H, 3'-H). ^{13}C NMR spectrum, δ_C, ppm: 12.49 q (C^{17}), 19.78 t (C^2), 23.37 t (C^{12}), 24.23 t (C^{11}), 26.14 t (C^6), 28.59 q (C^{18}), 38.03 t (C^3), 38.52 t (C^7), 38.98 t (C^1), 40.06 s (C^4), 43.94 t (CH_2), 44.17 s (C^{10}), 50.93 q (OCH_3), 54.94 d (C^9), 56.04 q (3″-OCH_3, 5″-OCH_3), 56.04 d (C^5), 65.64 q (4″-OCH_3), 104.57 d ($C^{2''}$, $C^{6''}$), 106.47 t (C^{20}), 111.03 d ($C^{1'}$), 112.92 d (C^{14}), 126.29 s ($C^{2'}$), 127.31 d ($C^{6'}$, $C^{10'}$), 128.65 d ($C^{7'}$, $C^{9'}$), 130.11 s (C^{13}), 132.16 d ($C^{8'}$), 133.22 s, 133.90 s ($C^{4''}$, $C^{5'}$), 137.08 s ($C^{1''}$), 143.38 d (C^{15}), 146.31 s (C^{16}), 147.60 s (C^8), 153.28 s ($C^{3''}$, $C^{5''}$), 164.83 s (CONH), 166.22 s ($C^{4'}$), 177.52 s (C^{19}). Found, %: C 70.17; H 7.25; N 3.97. $C_{41}H_{50}N_2O_8$. Calculated, %: C 70.49; H 7.16; N 4.01.

Methyl (1*S*,4a*R*,5*S*)-5-[2-(2-{2-benzoylamino-3-[2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethylamino]-3-oxoprop-1-en-1-yl}furan-3-yl)ethyl]-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate (VIII, methyl 16-{2-benzoylamino-3-[2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethylamino]-3-oxoprop-1-en-1-yl}-15,16-epoxylabda-8(20),13(16),14-trien-19-oate). A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.27 g (1.1 mmol) of 2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethylamine in 7 ml of benzene was heated for 6 h at 70°C. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform as eluent, followed by recrystallization from diethyl ether. Yield 0.57 g (76%), mp 91–93°C, $[\alpha]_D^{20}$ = 9.4° (*c* = 1.9, $CHCl_3$). IR spectrum, ν, cm^{-1}: 713, 750, 769, 890, 1515 (C=C); 1722 (C=O); 1578, 1640, 1665 (CONH); 3300, 3426 (OH, NH). UV spectrum, λ_{max}, nm (log ε): 226 (2.89), 316 (3.26). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.48 s (3H, $C^{17}H_3$), 0.94 t.d (1H, 1-H, *J* = 13.3, 3.8 Hz), 0.99 t.d (1H, 3-H, *J* = 13.5, 3.5 Hz), 1.14 s (3H, $C^{18}H_3$), 1.25 d.d (1H, 5-H, *J* = 12.4, 3.0 Hz), 1.37 s (18H, *t*-Bu), 1.48 m (1H, 2-H), 1.56 m (2H, 9-H, 11-H), 1.68–1.80 m (4H, 1-H, 6-H, 2-H, 11-H), 1.87 m (1H, 7-H, ^2J = 12.6 Hz), 1.96 m (1H, 6-H), 2.12 d.m (1H, 3-H, ^2J = 12.6 Hz), 2.33 m (2H, 12-H, 7-H), 2.58 m (1H, 12-H, *J* = 14.2, 6.8, 4.2 Hz), 2.79 t (2H, C**H**$_2C_6H_2$, *J* = 6.2 Hz), 3.58 s (3H, OCH_3), 3.61 m (2H, NHC**H**$_2$), 4.56 s and 4.91 s (1H each, 20-H), 5.07 s (1H, OH), 6.32 d (1H, 14-H, *J* = 1.8 Hz), 6.54 t (1H, CONH, *J* = 5.6 Hz), 6.83 s (1H, 1′-H), 7.00 s (2H, 2″-H, 6″-H), 7.34 d (1H, 15-H, *J* = 1.8 Hz), 7.46 t (2H, 7′-H, 9′-H, *J* = 7.0 Hz), 7.54 t (1H, 8′-H, *J* = 7.0 Hz), 7.91 d (2H, 6′-H, 10′-H, *J* = 7.8 Hz), 8.55 br.s (1H, 3′-H, halfwidth 5.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.44 q (C^{17}), 19.69 t (C^2), 23.21 t (C^{12}), 24.12 t (C^{11}), 26.07 t (C^6), 28.56 q (C^{18}), 30.09 q (CH_3)$_3$, 34.06 s [**C**(CH_3)$_3$], 35.58 t (**C**$H_2C_6H_2$), 37.93 t (C^3), 38.43 t (C^7), 38.86 t (C^1), 39.98 t (CH_2N), 41.56 s (C^4), 44.07 s (C^{10}), 50.96 q (OCH_3), 54.70 d (C^9), 55.90 d (C^5), 106.48 t (C^{20}), 110.72 d ($C^{1'}$), 112.78 d (C^{14}), 125.11 d ($C^{2''}$, $C^{6''}$), 126.31 s ($C^{2'}$), 127.32 d ($C^{6'}$, $C^{10'}$), 128.58 d ($C^{7'}$, $C^{9'}$), 129.33 s and 129.81 s ($C^{5'}$, C^{13}), 132.05 d ($C^{8'}$), 133.19 s ($C^{1''}$), 135.76 s ($C^{3''}$, $C^{5''}$), 143.14 d (C^{15}), 146.24 s (C^{16}), 147.50 s (C^8), 152.10 s ($C^{4''}$), 164.80 s (CONH), 166.22 s ($C^{4'}$), 177.58 s (C^{19}). Found, %: C 74.61; H 8.73; N 3.70. $C_{47}H_{62}N_2O_6$. Calculated, %: C 75.20; H 8.28; N 3.73.

Methyl (1*S*,4a*R*,5*S*)-5-[2-(2-{2-benzoylamino-3-[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylamino]-3-oxoprop-1-en-1-yl}furan-3-yl)ethyl]-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate (IX, methyl 16-{2-benzoylamino-3-[3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylamino]-3-oxoprop-1-en-1-yl}-15,16-epoxylabda-8(20),13(16),-14-trien-19-oate). A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.27 g (1.1 mmol) of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propylamine in 7 ml of benzene was heated for 6 h at 70°C. The solvent was removed under reduced pressure, and the residue was

subjected to chromatography on silica gel using chloroform as eluent, followed by recrystallization from diethyl ether. Yield 0.69 g (91%), mp 85–87°C, $[\alpha]_D^{20}$ = 11.1° (*c* = 3.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 713, 747, 769, 890, 1513 (C=C); 1546, 1580, 1641, 1665 (CONH); 1723 (C=O); 3325, 3400 (OH, NH). UV spectrum, λ_{max}, nm (logε): 226 (2.89), 315 (3.24). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.48 s (3H, $C^{17}H_3$), 0.93 t.d (1H, 1-H, *J* = 13.5, 3.2 Hz), 0.98 t.d (1H, 3-H, *J* = 13.2, 3.0 Hz), 1.14 s (3H, $C^{18}H_3$), 1.25 d.d (1H, 5-H, *J* = 12.8, 2.6 Hz), 1.40 s (18H, *t*-Bu), 1.45 m (1H, 2-H), 1.55 m (2H, 9-H, 11-H), 1.66–1.80 m (4H, 1-H, 7-H, 2-H, 11-H), 1.86 m (3H, $NCH_2C\mathbf{H}_2$, 6-H), 1.96 d.m (1H, 6-H, ^2J = 12.8 Hz), 2.12 d.m (1H, 3-H, ^2J = 13.2 Hz), 2.38 m (2H, 12-H, 7-H), 2.58 m (3H, $C\mathbf{H}_2C_6H_2$, 12-H), 3.41 m (2H, NCH_2), 3.58 s (3H, OCH_3), 4.56 s and 4.92 s (1H each, 20-H), 5.03 s (1H, OH), 6.33 d (1H, 14-H, *J* = 1.8 Hz), 6.52 t (1H, NH, *J* = 6.2 Hz), 6.81 s (1H, 1′-H), 6.97 s (2H, 2″-H, 6″-H), 7.35 d (1H, 15-H, *J* = 1.8 Hz), 7.47 t (2H, 7′-H, 9′-H, *J* = 7.2 Hz), 7.55 t (1H, 8′-H, *J* = 7.2 Hz), 7.93 d (2H, 6′-H, 10′-H, *J* = 7.2 Hz), 8.59 br.s (1H, 3′-H, halfwidth 5.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.50 q (C^{17}), 19.76 t (C^2), 23.27 t (C^{12}), 24.21 t (C^{11}), 26.13 t (C^6), 28.61 q (C^{18}), 30.21 q [$C(\mathbf{C}H_3)_3$], 31.59 t (CH_2), 35.09 t ($\mathbf{C}H_2C_6H_2$), 34.14 s [$\mathbf{C}(CH_3)_3$], 37.99 t (C^3), 38.51 t (C^7), 38.92 t (C^1), 39.69 t (CH_2N), 40.04 s (C^4), 44.13 s (C^{10}), 51.03 q (OCH_3), 54.74 d (C^9), 55.95 d (C^5), 106.55 t (C^{20}), 110.60 d ($C^{1'}$), 112.87 d (C^{14}), 124.76 d ($C^{2''}$, $C^{6''}$), 126.53 s ($C^{2'}$), 127.38 d ($C^{6'}$, $C^{10'}$), 128.65 d ($C^{7'}$, $C^{9'}$), 129.79 s (C^{13}), 132.03 s ($C^{5'}$), 132.14 d ($C^{8'}$), 133.25 s ($C^{1''}$), 135.62 s ($C^{3''}$, $C^{5''}$), 143.17 d (C^{15}), 146.36 s (C^{16}), 147.57 s (C^8), 151.74 s ($C^{4''}$), 164.88 s (CONH), 166.22 s ($C^{4'}$), 177.65 s (C^{19}). Found, %: C 75.32; H 8.63; N 3.62. $C_{48}H_2O_6N_{64}$. Calculated, %: C 75.39; H 8.38, N 3.66.

7-[2-Benzoylamino-3-(3-{2-[(1*S*,4a*R*,5*S*)-5-methoxycarbonyl-5,8a-dimethyl-2-methylidedecahydronaphthalen-1-yl]ethyl}furan-2-yl)prop-2-enoylamino]heptanoic acid (X, methyl 16-[2-benzoylamino-3-(6-carboxyhexylamino)-3-oxoprop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate (X). 7-Aminoheptanoic acid, 0.17 g (1.1 mmol), was added to a solution of 0.50 g (1.0 mmol) of azlactone **III** in 7 ml of benzene, and the mixture was heated for 6 h at 70°C. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform as eluent. The subsequent recrystallization from diethyl ether gave 0.47 g (73%) of compound **X**. mp 106–109°C, $[\alpha]_D^{20}$ = 17.3° (*c* = 2.5, $CHCl_3$). IR spectrum, ν, cm^{-1}: 712, 889, 907, 1522 (C=C); 1572, 1650, 1661 (CONH); 1717 (CO_2Me); 3274, 3300 (OH, NH). UV spectrum, λ_{max}, nm (logε): 227 (3.05), 315 (3.25). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.48 s (3H, $C^{17}H_3$), 0.92 t.d (1H, 1-H, *J* = 13.3, 3.4 Hz), 0.98 t.d (1H, 3-H, *J* = 13.1, 2.9 Hz), 1.14 s (3H, $C^{18}H_3$), 1.24 d.d (1H, 5-H, *J* = 12.6, 2.8 Hz), 1.34 m (4H, 5″-H, 4″-H), 1.45 m (1H, 2-H, ^2J = 12.8 Hz), 1.50–1.62 m (5H, 9-H, 6″-H, 3″-H), 1.66 m (1H, 2-H), 1.70–1.79 m (4H, 1-H, 6-H, 11-H), 1.86 t.d (1H, 7-H, *J* = 12.8, 3.6 Hz), 1.95 d.m (1H, 6-H, ^2J = 12.8 Hz), 2.11 d.m (1H, 3-H, ^2J = 13.1 Hz), 2.28 t (2H, 2″-H, *J* = 7.2 Hz), 2.34 m and 2.37 m (1H each, 12-H, 7-H), 2.56 m (1H, 12-H, *J* = 14.8, 6.6, 4.0 Hz), 3.32 m (2H, 7″-H), 3.57 s (3H, OCH_3), 4.55 s and 4.91 s (1H each, 20-H), 6.30 d (1H, 14-H, *J* = 1.8 Hz), 6.57 t (1H, CONH, *J* = 6.0 Hz), 6.81 s (1H, 1′-H), 7.33 d (1H, 15-H, *J* = 1.8 Hz), 7.46 m (2H, 7′-H, 9′-H), 7.52 t (1H, 8′-H, *J* = 7 Hz), 7.91 m (2H, 6′-H, 10′-H), 8.56 br.s (1H, 3′-H, halfwidth 4.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.47 q (C^{17}), 19.74 t (C^2), 23.26 t (C^{12}), 24.18 t (C^{11}), 24.33 t ($C^{6''}$), 26.11 t (C^6), 26.24 t and 28.44 t ($C^{5''}$, $C^{4''}$), 28.59 q (C^{18}), 29.01 t ($C^{3''}$), 33.72 t ($C^{2''}$), 37.97 t (C^3), 38.50 t (C^7), 38.89 t (C^1), 39.79 t ($C^{7''}$), 40.01 s (C^4), 44.12 s (C^{10}), 51.01 q (OCH_3), 54.74 d (C^9), 55.94 d (C^5), 106.50 t (C^{20}), 110.60 d ($C^{1'}$), 112.82 d (C^{14}), 126.12 s ($C^{2'}$), 127.39 d ($C^{6'}$, $C^{10'}$), 128.61 d ($C^{7'}$, $C^{9'}$), 130.04 s (C^{13}), 132.10 d ($C^{8'}$), 133.21 s ($C^{5'}$), 143.24 d (C^{15}), 146.24 s (C^{16}), 147.56 s (C^8), 164.88 s (CONH), 165.05 s ($C^{4'}$), 177.64 (C^{19}), 178.30 s ($C^{7''}$). Found, %: C 71.02; H 7.59; N 4.29. $C_{38}H_{50}N_2O_7$. Calculated, %: C 70.59; H 7.74; N 4.33.

Methyl (1*S*,4a*R*,5*S*)-5-(2-{2-[2-benzoylamino-3-benzyl(methyl)amino-3-oxoprop-1-en-1-yl]furan-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate {XI, methyl 16-[2-benzoylamino-3-benzyl(methyl)amino-3-oxoprop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate}. A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.15 g (1.2 mmol) of *N*-benzylmethanamine in 7 ml of benzene was heated for 6 h at 70°C. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–diethyl ether (1:1) as eluent. The subsequent recrystallization from petroleum ether gave 0.49 g (80%) of compound **XI**. mp 69–72°C, $[\alpha]_D^{20}$ = 9.9° (*c* = 3.1, $CHCl_3$). IR spectrum, ν, cm^{-1}: 706, 732, 890, 912, 1515 (C=C); 1720 (CO_2Me); 1581, 1646, 1680, 3419 (CONH). UV spectrum, λ_{max}, nm (logε): 226 (3.11), 319 (3.12). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 0.48 s and 0.50 s (3H, $C^{17}H_3$), 0.87 m

(1H, 1-H), 1.02 t.d (1H, 3-H), 1.17 s (3H, $C^{18}H_3$), 1.26 m (1H, 5-H), 1.51 m (3H, 9-H, 11-H, 2-H), 1.71–1.98 m (6H, 1-H, 6-H, 2-H, 11-H, 7-H), 2.14 m (1H, 3-H), 2.37 m (2H, 12-H, 7-H), 2.56 m (1H, 12-H), 3.03 s (3H, NCH_3), 3.62 s (3H, OCH_3), 4.55 s and 4.57 s (1H, 20-H), 4.71 s and 4.78 s (2H, CH_2), 4.90 s and 4.94 s (1H, 20-H), 5.74 s and 5.81 s (1H, 1′-H), 6.32 s and 6.38 s (1H, 14-H), 7.32–7.45 m (4H, 15-H, 3″-H, 4″-H, 5″-H), 7.49 m (2H, 7′-H, 9′-H), 7.53 m (3H, 2″-H, 6″-H, 8′-H), 7.96 d (2H, 6′-H, 10′-H), 9.51 br.s (1H, 3′-H); in DMSO-d_6: 0.30 s (3H, $C^{17}H_3$); 0.79 m (1H, 1-H); 0.89 t.d (1H, 3-H, J = 13.2, 3.0 Hz); 0.99 s (3H, $C^{18}H_3$); 1.16 d.d (1H, 5-H, J = 12.6, 2.8 Hz); 1.28 m and 144 m (3H, 9-H, 11-H, 2-H); 1.56 m, 1.74 t, and 1.80 m (6H, 1-H, 6-H, 2-H, 11-H, 7-H, J = 13 Hz); 1.91 d (1H, 3-H, J = 14 Hz); 2.22 m (2H, 12-H, 7-H); 2.72 m (1H, 12-H); 3.22 s (3H, NCH_3); 3.42 s (3H, OCH_3); 4.45 s (1H, 20-H); 4.51 m (2H, CH_2, J = 7.0 Hz); 4.78 s (1H, 20-H); 5.92 s (1H, 1′-H); 6.39 s (1H, 14-H); 7.16 m and 7.24 m (5H, Ph); 7.42 t (2H, 7′-H, 9′-H, J = 7.2 Hz); 7.49 t (1H, 8′-H, J = 7.2 Hz); 7.62 d (1H, 15-H, J = 1.8 Hz); 7.90 d (2H, 6′-H, 10′-H, J = 7.2 Hz); 9.87 s (1H, 3′-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 12.62 q (C^{17}), 19.90 t (C^2), 23.01 t and 23.22 t (C^{12}), 24.14 t and 24.31 t (C^{11}), 26.26 t (C^6), 28.74 q (C^{18}), 32.93 t and 36.44 t (N**C**H_2Ph), 38.14 t (C^3), 38.65 t (C^7), 39.04 t (C^1), 40.14 s (C^4), 44.28 s (C^{10}), 51.13 q (OCH_3), 50.56 q (NCH_3), 54.62 d and 54.71 d (C^9), 55.16 q (NCH_3), 56.11 d (C^5), 100.77 d and 101.04 d ($C^{1'}$), 106.50 t (C^{20}), 112.94 d (C^{14}), 126.02 s and 126.19 s ($C^{2'}$), 127.02 d ($C^{4''}$), 127.43 d ($C^{6'}$, $C^{10'}$), 127.75 s (C^{13}), 128.26 d ($C^{2''}$, $C^{6''}$), 128.62 d ($C^{3''}$, $C^{5''}$), 128.79 d ($C^{7'}$, $C^{9'}$), 132.21 d ($C^{8'}$), 133.20 s ($C^{5'}$), 136.92 s and 137.12 s ($C^{1''}$), 141.94 d (C^{15}), 146.71 s and 147.10 s (C^{16}), 147.82 s and 147.81 s (C^8), 163.95 s and 164.13 s [**C**ON(CH_3)CH_2Ph], 167.86 s and 168.44 s ($C^{4'}$), 177.69 s (C^{19}). Found, %: C 75.23; H 7.36; N 4.10. $C_{39}H_{46}N_2O_5$. Calculated, %: C 75.24; H 7.36; N 4.50.

Methyl (1*S*,4a*R*,5*S*)-5-{2-[2-(2-benzoylamino-3-oxo-3-piperidinoprop-1-en-1-yl)furan-3-yl]ethyl}-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate [XII, methyl 16-(2-benzoylamino-3-oxo-3-piperidinoprop-1-en-1-yl)-15,16-epoxylabda-8(20),13(16),14-trien-19-oate]. Piperidine, 0.10 g (1.2 mmol), was added to a solution of 0.50 g (1.0 mmol) of azlactone **III** in 7 ml of benzene, and the mixture was heated for 5 h at 70°C. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform as eluent. A fraction containing compound **XII** was evaporated, and the residue was ground with hexane. Yield 0.43 g (73%), mp 89–90°C, $[\alpha]_D^{20}$ = 13.7° (c = 3.3, $CHCl_3$). IR spectrum, ν, cm^{-1}: 707, 853, 889, 1514 (C=C); 1723 (C=O); 1581, 1644, 1683, 3423 (CONH). UV spectrum, λ_{max}, nm (log ε): 227 (4.16), 320 (4.23). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.49 s (3H, $C^{17}H_3$), 0.94 m (1H, 1-H), 1.00 t.d (1H, 3-H, J = 13.3, 3.1 Hz), 1.16 s (3H, $C^{18}H_3$), 1.26 d.d (1H, 5-H, J = 12.6, 2.8 Hz), 1.50 m (1H, 2-H), 1.57–1.82 m (12H, 9-H, 11-H, 1-H, 6-H, 2-H, 3″-H, 4″-H, 4′-H, 5″-H), 1.83 t.d (1H, 7-H, J = 12.6, 3.4 Hz), 1.96 m (1H, 6-H), 2.14 d.m (1H, 3-H, ^2J = 13.3 Hz), 2.31 m (1H, 12-H), 2.11 m (1H, 7-H, ^2J = 12.6 Hz), 2.55 m (1H, 12-H), 3.60 s (3H, OCH_3), 3.60 m (4H, 2″-H, 6″-H), 4.58 s and 4.92 s (1H each, 20-H), 5.67 s (1H, 1′-H), 6.35 d (1H, 14-H, J = 1.8 Hz), 7.47 m (3H, 15-H, 7′-H, 9′-H), 7.52 t (1H, 8′-H, J = 7 Hz), 7.91 d (2H, 6′-H, 10′-H, J = 8 Hz), 9.47 br.s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.50 q (C^{17}), 19.78 t (C^2), 23.15 t (C^{12}), 24.23 t (C^{11}), 24.60 t ($C^{4''}$), 25.18 t and 25.38 t ($C^{3''}$, $C^{5''}$), 26.12 t (C^6), 28.61 q (C^{18}), 38.01 t (C^3), 38.52 t (C^7), 38.97 t (C^1), 40.05 s (C^4), 42.78 t and 48.45 t ($C^{2''}$, $C^{6''}$), 44.16 s (C^{10}), 51.02 q (OCH_3), 54.58 d (C^9), 55.96 d (C^5), 100.12 d ($C^{1'}$), 106.35 t (C^{20}), 112.80 d (C^{14}), 125.55 s ($C^{2'}$), 127.26 d ($C^{6'}$, $C^{10'}$), 127.71 s (C^{13}), 128.62 d ($C^{7'}$, $C^{9'}$), 132.97 d ($C^{8'}$), 133.23 s ($C^{5'}$), 141.68 d (C^{15}), 146.99 s (C^{16}), 147.80 s (C^8), 163.67 s (CONH), 166.21 s ($C^{4'}$), 177.58 s (C^{19}). Found, %: C 73.72; H 7.85; N 4.78. $C_{36}H_{46}N_2O_5$. Calculated, %: C 73.72; H 7.85; N 4.78.

***tret*-Butyl 1-[(2*Z*)-2-benzoylamino-3-(3-{2-[(1*S*,4a*R*,5*S*)-5-methoxycarbonyl-5,8a-dimethyl-2-methylidenedecahydronaphthalen-1-yl]ethyl}furan-2-yl)prop-2-enoyl]pyrrolidine-2-carboxylate (XIII).** A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.20 g (1.2 mmol) of L-proline *tert*-butyl ester in 7 ml of benzene was heated for 5 h at 70°C. The solvent was removed under reduced pressure, and the residue was recrystallized from diethyl ether. Yield 0.56 g (83%), mp 173–175°C, $[\alpha]_D^{20}$ = 17.9° (c = 3.3, $CHCl_3$). IR spectrum, ν, cm^{-1}: 720, 760, 886, 909, 1510 (C=C); 1727 (C=O); 1580, 1638, 1661, 3422, 3510 (CONH). UV spectrum, λ_{max}, nm (log ε): 228 (3.13), 319 (3.22). ^{1}H NMR spectrum, δ, ppm: in $CDCl_3$: 0.48 s (3H, $C^{17}H_3$), 1.00 m (2H, 1-H, 3-H), 1.15 s (3H, $C^{18}H_3$), 1.26 d.d (1H, 5-H), 1.47 s (12H, *t*-Bu, 2-H, 4″-H), 1.57 s (2H, 9-H, 11-H), 1.68–1.90 m (5H, 1-H, 7-H, 2-H, 11-H, 6-H), 1.96 m (3H, 6-H, 3″-H), 2.12 m (1H, 3-H), 2.31 m (1H, 12-H), 2.40 m (1H, 7-H), 2.56 m (1H, 12-H), 3.58 s (3H, OCH_3), 3.79 m (2H, 5″-H),

4.53 s (1H, 20-H), 4.55 m (1H, 2′-H), 4.91 s (1H, 20-H), 5.86 s and 5.94 s (1H, 1′-H), 6.34 d and 6.35 d (1H, 14-H, J = 1.8 Hz), 7.45 m (3H, 15-H, 7′-H, 9′-H), 7.53 m (1H, 8′-H), 7.88 d (2H, 6′-H, 10′-H, J = 7.8 Hz), 9.24 br.s and 9.30 br.s (1H, 3′-H); in DMSO-d_6: 0.31 s (3H, $C^{17}H_3$), 0.87 m (2H, 1-H, 3-H), 0.99 s (3H, $C^{18}H_3$), 1.16 m (1H, 5-H), 1.29 s (9H, *t*-Bu), 1.43 m and 1.49 m (3H, 2-H, 4″-H), 1.58–1.79 m (10H, 1-H, 2-H, 6-H, 7-H, 9-H, 11-H, 3′-H, 3″-H), 1.91 d.m (1H, 3-H, ^2J = 13.2 Hz), 2.05 m (1H, 12-H), 2.19 m and 2.24 m (2H, 7-H, 12-H), 3.22 s (3H, OCH_3), 3.50 m (2H, 5″-H), 4.10 d.d (1H, 2″-H, J = 7, 5 Hz), 4.46 s (1H, 20-H), 4.78 s (1H, 20-H), 6.06 s (1H, 1′-H), 6.40 d (1H, 14-H, J = 1.8 Hz), 7.40 t (2H, 7′-H, 9′-H, J = 7.2 Hz), 7.48 t (1H, 8′-H, J = 7.2 Hz), 7.60 d (1H, 15-H, J = 1.8 Hz), 7.87 d (2H, 6′-H, 10′-H, J = 7.2 Hz), 9.82 s (1H, 3′-H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 12.63 q (C^{17}), 19.76 t (C^2), 23.36 t (C^{12}), 24.42 t (C^{11}), 25.06 t ($C^{4''}$), 26.12 t (C^6), 27.87 q (C^{18}), 28.03 q [$C(\mathbf{C}H_3)_3$], 29.00 t ($C^{3''}$), 37.79 t (C^3), 38.26 t (C^7), 38.63 t (C^1), 40.18 s (C^4), 43.94 s (C^{10}), 49.10 t ($C^{5''}$), 51.31 q (OCH_3), 54.59 d (C^9), 55.39 d (C^5), 59.98 t ($C^{2''}$), 80.40 s [$\mathbf{C}(CH_3)_3$], 106.63 t (C^{20}), 109.27 d ($C^{1'}$), 113.08 d (C^{14}), 126.58 s ($C^{2'}$), 127.41 d (C^{13}), 127.96 s (C^2, $C^{6'}$, $C^{10'}$), 128.81 d ($C^{7'}$, $C^{9'}$), 132.17 d ($C^{8'}$), 133.35 s ($C^{5'}$), 145.82 d (C^{15}), 146.56 s (C^{16}), 147.96 s (C^8), 164.31 s (CONH), 165.87 s ($C^{4'}$), 171.48 s (C=O), 177.71 s (C^{19}). Found, %: C 71.21; H 7.86; N 3.91. $C_{40}H_{52}N_2O_7$. Calculated, %: C 71.42; H 7.73; N 4.17.

Methyl (1*S*,4a*R*,5*S*)-5-(2-{2-[(*Z*)-2-benzoylamino-3-(1-methoxycarbonyl-2-methylbutylamino)-3-oxoprop-1-en-1-yl]furan-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate {XIV, methyl 16-[(*Z*)-2-benzoylamino-3-(1-methoxycarbonyl-2-methylbutylamino)-3-oxoprop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate}. A mixture of 0.35 g (0.64 mmol) of azlactone **III** and 0.12 g (0.77 mmol) of L-isoleucine methyl ester in 7 ml of benzene was heated for 6 h at 70°C. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform–methanol (200:1) as eluent. A fraction containing compound **XIV** was evaporated, and the residue was crystallized from petroleum ether. Yield 0.35 g (78%), mp 57–60°C, $[\alpha]_D^{20}$ = 15.8° (c = 3.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 712, 748, 891, 1511 (C=C); 1273, 1724 (C=O); 1578, 1652, 1673, 3369, 3431 (CONH). UV spectrum, λ_{max}, nm (logε): 227 (3.18), 317 (3.06). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.45 s (3H, $C^{17}H_3$), 0.89 t (3H, 6″-H, J = 7 Hz), 0.93 d (3H, CH_3, J = 7.2 Hz), 0.98 m (2H, 1-H, 3-H), 1.13 s (3H, $C^{18}H_3$), 1.17 m (1H, 5″-H), 1.28 d.d (1H, 5-H, J = 12.6, 2.6 Hz), 1.44 m (2H, 2-H, 5″-H), 1.56 m (1H, 9-H), 1.58 m (1H, 11-H), 1.67–1.81 m (4H, 11-H, 2-H, 1-H, 7-H), 1.86 m (1H, 6-H, J = 12, 4 Hz), 1.94 m (2H, 6-H, 4″-H), 2.10 m (1H, 3-H), 2.38 m (2H, 7-H, 12-H), 2.57 m (1H, 12-H), 3.56 s (3H, OCH_3), 3.68 s (3H, OCH_3), 4.54 s (1H, 20-H), 4.70 d.d (1H, 3″-H, J = 8.2, 4.5 Hz), 4.91 s (1H, 20-H), 6.32 d (1H, 14-H, J = 1.8 Hz), 6.85 s (1H, 1′-H), 6.91 d (1H, 2″-H, J = 5.8 Hz), 7.36 d (1H, 15-H, J = 1.8 Hz), 7.46 t (2H, 7′-H, 9′-H, J = 7.8 Hz), 7.53 t (1H, 8′-H, J = 7.8 Hz), 7.91 d (2H, 10′-H, 6′-H, J = 8 Hz), 8.54 s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 11.46 q ($C^{6''}$), 12.43 q (C^{17}), 15.25 q (CH_3), 19.69 t (C^2), 23.29 t (C^{12}), 24.16 t (C^{11}), 25.03 t ($C^{5''}$), 26.07 t (C^6), 28.55 q (C^{18}), 37.93 t (C^3), 37.99 d ($C^{4''}$), 38.40 t (C^7), 38.85 t (C^1), 39.97 s (C^4), 44.07 s (C^{10}), 50.95 q (OCH_3), 51.86 q (OCH_3), 54.75 d (C^9), 55.89 d (C^5), 56.67 d ($C^{3''}$), 106.45 t (C^{20}), 111.22 d ($C^{1'}$), 112.85 d (C^{14}), 125.86 s ($C^{2'}$), 127.28 d ($C^{10'}$, $C^{6'}$), 128.58 d ($C^{7'}$, $C^{9'}$), 130.18 s (C^{13}), 131.98 d ($C^{8'}$), 133.37 s ($C^{5'}$), 143.30 d (C^{15}), 146.19 s (C^{16}), 147.50 s (C^8), 164.33 s ($C^{1''}$), 166.33 s ($C^{4'}$), 172.20 (C=O), 177.57 s (C^{19}). Found, %: C 70.44; H 7.73; N 4.15. $C_{38}H_{50}N_2O_7$. Calculated, %: C 70.59; H 7.73; N 4.33.

Methyl (1*S*,4a*R*,5*S*)-5-(2-{2-[(*Z*)-2-benzoylamino-3-(1-*tert*-butoxycarbonyl-3-methylbutylamino)-3-oxoprop-1-en-1-yl]furan-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate {XV, methyl 16-[(*Z*)-2-benzoylamino-3-(1-*tert*-butoxycarbonyl-3-methylbutylamino)-3-oxoprop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate (XV). A mixture of 0.50 g (1.0 mmol) of azlactone **III** and 0.17 g (1.2 mmol) of L-leucine *tert*-butyl ester in 7 ml of benzene was heated for 6 h at 70°C. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–diethyl ether (2:1) as eluent. A fraction containing compound **XV** was evaporated, and the residue was recrystallized from petroleum ether. Yield 0.41 g (62%), mp 122–124°C, $[\alpha]_D^{20}$ = 17.8° (c = 3.4, $CHCl_3$). IR spectrum, ν, cm^{-1}: 694, 728, 848, 889, 1518 (C=C); 1725 (C=O); 1553, 1581, 1631–1651, 3262, 3440 (CONH). UV spectrum, λ_{max}, nm (logε): 226 (4.06), 317 (4.26). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.46 s (3H, $C^{17}H_3$), 0.91 d and 0.96 d (6H, CH_3, J = 7.0 Hz), 0.98 m (2H, 1-H, 3-H), 1.13 s (3H, $C^{18}H_3$), 1.24 d.d (1H, 5-H, J = 12.8, 2.8 Hz), 1.42 s [9H, $C(CH_3)_3$], 1.49 m (1H, 2-H), 1.55 m (2H, 9-H, 11-H), 1.57–1.78 m (6H, 11-H, 1-H, 2-H, 6-H,

4″-H), 1.87 m (1H, 7-H), 1.94 d.m (1H, 6-H, ^2J = 13.8 Hz), 2.10 d.m (1H, 3-H, J = 13.6 Hz), 2.38 m (2H, 7-H, 12-H), 2.58 m (1H, 12-H), 3.57 s (3H, OCH_3), 4.57 s (1H, 20-H), 4.62 m (1H, 3″-H), 4.91 s (1H, 20-H), 6.31 d (1H, 14-H, J = 1.8 Hz), 6.76 m (1H, 2″-H), 6.86 s (1H, 1′-H), 7.35 d (1H, 15-H, J = 1.8 Hz), 7.46 t (2H, 7′-H, 9′-H, J = 7.8 Hz), 7.53 t (1H, 8′-H, J = 7.8 Hz), 7.92 d (2H, 6′-H, 10′-H, J = 7.8 Hz), 8.47 s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.46 q (C^{17}), 19.71 t (C^2), 22.16 q and 22.63 q (5″-CH_3), 23.31 t (C^{12}), 24.16 t (C^{11}), 24.72 q ($C^{5''}$), 26.09 t (C^6), 27.82 q [C(**C**H_3)$_3$], 28.59 q (C^{18}), 37.95 t (C^3), 38.44 t (C^7), 38.88 t (C^1), 39.98 s (C^4), 42.07 t ($C^{4''}$), 44.10 s (C^{10}), 50.98 q (OCH_3), 51.67 d ($C^{3''}$), 54.70 d (C^9), 55.92 d (C^5), 81.61 d [**C**(CH_3)$_3$], 106.48 t (C^{20}), 111.51 d ($C^{1'}$), 112.82 d (C^{14}), 125.90 s ($C^{2'}$), 127.34 d ($C^{10'}$, $C^{6'}$), 128.57 d ($C^{7'}$, $C^{9'}$), 130.28 s (C^{13}), 131.97 d ($C^{8'}$), 133.42 s ($C^{5'}$), 143.27 d (C^{15}), 146.22 s (C^{16}), 147.52 s (C^8), 164.16 s ($C^{1''}$), 166.24 s ($C^{4'}$), 171.99 s (C=O), 177.62 s (C^{19}). Found, %: C 71.55; H 8.23; N 4.20. $C_{41}H_{56}N_2O_7$. Calculated, %: C 71.51; H 8.14; N 4.07.

(*Z*)-2-Benzoylamino-3-(3-{2-[(1*S*,4a*R*,5*S*)-5-methoxycarbonyl-5,8a-dimethyl-2-methylidenedecahydronaphthalen-1-yl]ethyl}furan-2-yl)prop-2-enoic acid {XVI, (*Z*)-2-benzoylamino-3-[15,16-epoxy-19-methoxy-19-oxolabda-8(20),13(16),14-trien-16-yl]prop-2-enoic acid}. *a*. A saturated solution of hydrogen chloride in 10 ml of diethyl ether was added to a solution of 0.50 g (1.0 mmol) of compound **III** in 5 ml of diethyl ether, and the mixture was left overnight. The precipitate was filtered off and dried under reduced pressure. Yield 0.45 g (87%).

b. Potassium hydroxide, 0.07 g (1.2 mmol), was added to a solution of 0.50 g (1.0 mmol) of compound **III** in 5 ml of ethanol. The mixture was stirred for 6 h, left to stand overnight, poured onto ice, and extracted with chloroform (3×20 ml). The extracts were combined, washed with cold water (3×20 ml), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was recrystallized from diethyl ether. Yield 0.43 g (82%), mp 211–213°C, $[\alpha]_D^{20}$ = 15.5° (c = 3.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 724, 752, 891, 1510 (C=C); 1572, 1603, 1642, 1665 (CONH); 1693, 1725 (C=O); 3360 (NH, OH). UV spectrum, λ_{max}, nm (log ε): 224 (3.02), 319 (3.22). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.48 s (3H, $C^{17}H_3$), 0.95 t.d (1H, 1-H, J = 13.2, 3.2 Hz), 1.00 t.d (1H, 3-H, J = 13.3, 3.2 Hz), 1.15 s (3H, $C^{18}H_3$), 1.26 d.d (1H, 5-H, J = 12.6, 2.6 Hz), 1.47 d.m (1H, 2-H, J = 13.2 Hz), 1.60 m (2H, 9-H, 11-H), 1.69–1.80 m (4H, 1-H, 6-H, 2-H, 11-H), 1.88 m (1H, 7-H), 1.97 d.m (1H, 6-H, ^2J = 13.1 Hz), 2.12 d.m (1H, 3-H, ^2J = 13.3 Hz), 2.40 m (2H, 12-H, 7-H), 2.64 m (1H, 12-H, J = 14.5, 6.8, 4.2 Hz), 3.58 s (3H, OCH_3), 4.57 s and 4.94 s (2H, 20-H), 6.39 d (1H, 14-H, J = 1.8 Hz), 7.15 s (1H, 1′-H), 7.46 d (1H, 15-H, J = 1.8 Hz), 7.49 t (2H, 7′-H, 9′-H, J = 7.4 Hz), 7.57 t (1H, 8′-H, J = 7.4 Hz), 7.93 d (2H, 6′-H, 10′-H, J = 7.4 Hz), 8.65 br.s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.51 q (C^{17}), 19.76 t (C^2), 23.50 t (C^{12}), 24.24 t (C^{11}), 26.14 t (C^6), 28.63 q (C^{18}), 38.00 t (C^3), 38.48 t (C^7), 38.92 t (C^1), 40.05 s (C^4), 44.15 s (C^{10}), 51.04 q (OCH_3), 54.82 d (C^9), 56.00 d (C^5), 106.61 t (C^{20}), 113.29 d (C^{14}), 115.31 d ($C^{1'}$), 121.78 s ($C^{2'}$), 127.46 d ($C^{6'}$, $C^{10'}$), 128.71 d ($C^{7'}$, $C^{9'}$), 132.31 d ($C^{8'}$), 132.67 s (C^{13}), 133.11 s ($C^{5'}$), 144.34 d (C^{15}), 145.99 s (C^{16}), 147.43 s (C^8), 166.40 s ($C^{4'}$), 167.60 s (C=O), 177.70 s (C^{19}). Mass spectrum, m/z (I_{rel}, %): 501 [M – 18] (3), 275 (6), 315 (6), 252 (6), 239 (10), 121 (12), 105 (100), 77 (23). Found, %: C 75.32; H 8.63; N 3.62. $C_{31}H_{37}NO_6$. Calculated, %: C 75.39; H 8.38; N 3.66.

Methyl (1*S*,4a*R*,5*S*)-5-(2-{2-[(*Z*)-2-benzoylamino-3-hydrazino-3-oxoprop-1-en-1-yl]furan-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate {XVII, methyl 16-[(*Z*)-2-benzoylamino-3-hydrazino-3-oxoprop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate}. Hydrazine hydrate, 0.2 ml, was added dropwise under stirring to a solution of 1.00 g (2.0 mmol) of azlactone **III** in 10 ml of methanol. The mixture was stirred for 5 h and left overnight, the solvent was removed under reduced pressure, and the residue was ground with hexane. Yield 0.96 g (90%), mp 72–75°C, $[\alpha]_D^{20}$ = 2.76° (c = 3.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 713, 750, 888, 1467 (C=C); 1722 (C=O); 1665, 1664, 3309 (CONH, NH_2). UV spectrum, λ_{max}, nm (log ε): 225 (2.99), 318 (3.11), 405 (2.02). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.47 s (3H, $C^{17}H_3$), 0.94 m (2H, 1-H, 3-H), 1.14 s (3H, $C^{18}H_3$), 1.25 d.d (1H, 5-H, J = 12.6, 2.8 Hz), 1.46 m (1H, 2-H), 1.55 m (1H, 9-H), 1.66–1.80 m (5H, 1-H, 6-H, 2-H, 11-H), 1.87 t.d (1H, 7-H, J = 13.0, 3.3 Hz), 1.96 d.m (1H, 6-H, ^2J = 12.6 Hz), 2.12 d.m (1H, 3-H, ^2J = 13.3 Hz), 2.34 m (1H, 12-H), 2.38 m (1H, 7-H), 2.57 m (1H, 12-H), 3.57 s (3H, OCH_3), 3.60 br.s (2H, NH_2), 4.55 s and 4.92 s (1H each, 20-H), 6.33 d (1H, 14-H, J = 1.8 Hz), 6.75 s (1H, 1′-H), 7.32 s (1H, CONH), 7.36 d (1H, 15-H, J = 1.8 Hz), 7.44 t (2H, 7′-H, 9′-H, J = 7.2 Hz), 7.52 t (1H, 8′-H, J = 7.2 Hz), 7.89 d (2H, 6′-H, 10′-H, J = 7.2 Hz), 8.60 br.s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.51 q (C^{17}), 19.74 t (C^2), 23.30 t (C^{12}), 24.16 t (C^{11}), 26.10 t (C^6), 28.66 q (C^{18}), 37.98 t (C^3), 38.38 t (C^7), 38.92 t (C^1),

40.03 s (C^4), 44.12 s (C^{10}), 51.05 q (OCH_3), 54.92 d (C^9), 56.00 d (C^5), 106.06 t (C^{20}), 111.11 d ($C^{1'}$), 113.04 d (C^{14}), 124.43 s ($C^{2'}$), 127.47 d ($C^{6'}$, $C^{10'}$), 129.19 d ($C^{7'}$, $C^{9'}$), 130.48 s (C^{13}), 132.20 s ($C^{5'}$), 133.10 d ($C^{8'}$), 142.78 d (C^{15}), 146.09 s (C^{16}), 147.40 s (C^8), 165.53 s ($C^{4'}$, CONH), 177.56 s (C^{19}). Found, %: C 69.23; H 7.39; N 7.46. $C_{31}H_{39}N_3O_5$. Calculated, %: C 69.79; H 7.31; N 7.88.

Methyl (1*S*,4a*R*,5*S*)-5-(2-{2-[(*Z*)-2-benzoylamino-3-(*N′*-phenylhydrazino)-3-oxoprop-1-en-1-yl]furan-3-yl}ethyl)-1,4a-dimethyl-6-methylidenedecahydronaphthalene-1-carboxylate {XVIII, methyl 16-[(*Z*)-2-benzoylamino-3-(*N′*-phenylhydrazino)-3-oxoprop-1-en-1-yl]-15,16-epoxylabda-8(20),13(16),14-trien-19-oate} (XVIII). Phenylhydrazine, 0.13 g (2.0 mmol), was added dropwise under stirring to a solution of 0.50 g (1.0 mmol) of azlactone **III** in 10 ml of methanol, and the mixture was stirred for 5 h and left overnight. The solvent was removed under reduced pressure, the residue was subjected to chromatography on silica gel using chloroform as eluent, and the product was additionally purified by recrystallization from diethyl ether. Yield 0.47 g (77%), mp 141–144°C, $[\alpha]_D^{20}$ = 5.9° (*c* = 2.2, $CHCl_3$). IR spectrum, ν, cm^{-1}: 692, 760, 899, 1496 (C=C); 1723 (C=O); 1624, 1644, 1664, 3239, 3325, 3431 (CONH, NH). UV spectrum, λ_{max}, nm (log ε): 233 (3.96), 318 (3.96). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.46 s (3H, $C^{17}H_3$), 0.92 t.d (1H, 1-H, *J* = 13.0, 3.0 Hz), 0.97 t.d (1H, 3-H, *J* = 13.1, 3.2 Hz), 1.13 s (3H, $C^{18}H_3$), 1.24 d.d (1H, 5-H, *J* = 12.8, 3.0 Hz), 1.45 d.m (1H, 2-H, ^2J = 13 Hz), 1.55 s (1H, 9-H), 1.60 m (1H, 11-H), 1.67–1.76 m (4H, 1-H, 7-H, 2-H, 11-H), 1.84 m (1H, 7-H), 1.93 m (1H, 6-H), 2.12 d.m (1H, 3-H, ^2J = 13.1 Hz), 2.39 m (2H, 12-H, 7-H), 2.59 m (1H, 12-H), 3.57 s (3H, OCH_3), 4.57 s and 4.93 s (1H each, 20-H), 6.26 br.s (1H, N**H**Ph, halfwidth 12 Hz), 6.35 d (1H, 14-H, *J* = 1.8 Hz), 6.73 t (1H, 4″-H, *J* = 8 Hz), 6.90 m (3H, 1′-H, 2″-H, 6″-H, *J* = 8 Hz), 7.20 t (2H, 3″-H, 5″-H, *J* = 8 Hz), 7.40 d (1H, 15-H, *J* = 1.8 Hz), 7.47 t (2H, 7′-H, 9′-H, *J* = 7.2 Hz), 7.56 t (1H, 8′-H, *J* = 7.2 Hz), 7.93 d (2H, 6′-H, 10′-H, *J* = 7 Hz), 8.33 br.s (1H, CONH, halfwidth 5 Hz), 8.64 s (1H, 3′-H). ^{13}C NMR spectrum, δ_C, ppm: 12.48 q (C^{17}), 19.74 t (C^2), 23.34 t (C^{12}), 24.18 t (C^{11}), 26.11 t (C^6), 28.58 q (C^{18}), 37.98 t (C^3), 38.49 t (C^7), 38.92 t (C^1), 40.03 s (C^4), 44.13 s (C^{10}), 50.97 q (OCH_3), 54.78 d (C^9), 55.98 d (C^5), 106.52 t (C^{20}), 111.85 d ($C^{1'}$), 113.04 d (C^{14}), 113.69 d ($C^{2''}$, $C^{6''}$), 120.89 d ($C^{4''}$), 124.45 s ($C^{2'}$), 127.37 d ($C^{6'}$, $C^{10'}$), 128.69 d and 128.96 d ($C^{7'}$, $C^{9'}$ or $C^{3''}$, $C^{5''}$), 132.34 s (C^{13}), 132.42 d ($C^{8'}$), 133.04 s ($C^{5'}$), 143.83 d (C^{15}), 146.19 s (C^{16}), 147.55 s (C^8), 147.55 s ($C^{1''}$), 165.57 s ($C^{4'}$), 166.65 s (CONH), 177.57 s (C^{19}).

Methyl (1*S*,4a*R*,5*S*)-1,4a-dimethyl-6-methylidene-5-(2-{2-[(*Z*)-6-oxo-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazin-5-ylidenemethyl]furan-3-yl}ethyl)-decahydronaphthalene-1-carboxylate {XIX, methyl 15,16-epoxy-16-[(*Z*)-6-oxo-3-phenyl-1,4,5,6-tetrahydro-1,2,4-triazin-5-ylidenemethyl]labda-8(20),-13(16),14-trien-19-oate}. A mixture of 0.50 g (0.9 mmol) of hydrazide **XVIII** and 10 ml of 1 M aqueous sodium hydroxide was heated for 10 min at 100°C. The mixture was cooled, acidified to pH 1 by adding 1 ml of 6 M hydrochloric acid, and extracted with chloroform (3×25 ml). The extracts were combined, washed with water (3×20 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was subjected to chromatography on silica gel using petroleum ether–chloroform (1:1) as eluent. The product was additionally recrystallized from diethyl ether. Yield 0.19 g (80%), mp 165–168°C, $[\alpha]_D^{20}$ = 17.5° (*c* = 2.8, $CHCl_3$). IR spectrum, ν, cm^{-1}: 692, 770, 892, 1519 (C=C); 1640, 1670 (C=O, C=N); 1724 (C=O); 3202, 3409 (NH). UV spectrum, λ_{max}, nm (log ε): 254 (3.16), 327 (3.22), 340 (3.22); in 1 M NaOH: 285, 320, 405; in 1 M HCl: 251, 326, 340. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.48 s (3H, $C^{17'}H_3$), 1.02 m (1H, 1′-H), 1.06 m (1H, 3′-H), 1.15 s (3H, $C^{18'}H_3$), 1.31 d.d (1H, 5′-H, *J* = 12.0, 2.8 Hz), 1.52 d.m (1H, 2′-H, ^2J = 14 Hz), 1.65 m (2H, 9′-H, 11′-H), 1.73–1.88 m (4H, 1′-H, 6′-H, 2′-H, 11′-H), 1.93 m (1H, 7′-H), 2.02 m (1H, 6′-H), 2.18 d.m (1H, 3′-H, *J* = 13.0 Hz), 2.42 m (1H, 12′-H), 2.47 m (1H, 7′-H), 2.65 m (1H, 12′-H), 3.58 s (3H, OCH_3), 4.59 s and 4.94 s (1H each, 20′-H), 6.33 s (1H, 5a-H), 6.38 d (1H, 14′-H, *J* = 1.8 Hz), 7.46 d (1H, 15′-H, *J* = 1.8 Hz), 7.47 m (3H, 3″-H, 4″-H, 5″-H), 7.73 m (2H, 2″-H, 6″-H), 9.07 s (1H, 1-H), 9.09 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 12.38 q ($C^{17'}$), 19.67 t ($C^{2'}$), 23.19 t ($C^{12'}$), 24.19 t ($C^{11'}$), 26.03 t ($C^{6'}$), 28.52 q ($C^{18'}$), 37.96 t ($C^{3'}$), 38.43 t ($C^{7'}$), 38.88 t ($C^{1'}$), 39.93 s ($C^{4'}$), 44.05 s ($C^{10'}$), 50.87 q (OCH_3), 54.89 d ($C^{9'}$), 55.98 d ($C^{5'}$), 91.36 d (C^{5a}), 106.45 t ($C^{20'}$), 112.96 d ($C^{14'}$), 123.96 s (C^5), 125.11 d ($C^{2''}$, $C^{6''}$), 131.03 d ($C^{3''}$, $C^{5''}$), 130.40 d ($C^{4''}$), 131.03 s ($C^{13'}$), 141.04 d ($C^{15'}$), 141.42 s ($C^{16'}$), 147.40 s ($C^{1''}$), 148.11 s ($C^{8'}$), 159.49 s (C^3), 161.38 s (C^6), 177.53 s ($C^{19'}$). Mass spectrum, *m*/*z* (I_{rel}, %): 515 $[M]^+$ (26), 279 (21), 266 (33), 187 (83), 130 (18), 121 (100), 118 (55), 109 (39), 105 (34), 93 (30), 77 (47), 55 (57), 43 (60). Found: $[M]^+$ 515.27657. $C_{31}H_{37}N_3O_4$. Calculated: *M* 515.27839.

Methyl (1*S*,4a*R*,5*S*)-1,4a-dimethyl-6-methylidene-5-(2-{2-[(*Z*)-5-oxo-2-phenyl-4,5-dihydro-1*H*-imidazol-4-ylidenemethyl]furan-3-yl}ethyl)decahydronaphthalene-1-carboxylate {XX, methyl 15,16-epoxy-16-[(*Z*)-5-oxo-2-phenyl-4,5-dihydro-1*H*-imidazol-4-ylidenemethyl]labda-8(20),13(16),14-trien-19-oate}. A mixture of 0.25 g (0.5 mmol) of compound **III**, 0.06 g (0.6 mmol) of sodium carbonate, and 10 ml of aqueous ammonia was heated for 14 h at 110–115°C in a sealed ampule. The ampule was cooled and opened, and the mixture was poured into 30 ml of water and extracted with methylene chloride (3×30 ml). The extracts were combined, dried over $MgSO_4$, and evaporated under reduced pressure, and the residue was subjected to chromatography on silica gel using chloroform as eluent. Fractions containing compound **XX** were evaporated, and the product was recrystallized from diethyl ether. Yield 0.14 g (56%), mp 208–209°C, $[\alpha]_D^{20}$ = 12.5° (*c* = 1.1, $CHCl_3$). IR spectrum, ν, cm^{-1}: 694, 784, 899, 918, 1500, 1531, 1598, 1631, 3069 (C=C, C=N); 1700, 1722 (C=O); 3120, 3200, 3400, 3427 (NH). UV spectrum, λ_{max}, nm (log ε): 266 (3.94), 407 (4.19), 420 (4.03). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.49 s (3H, $C^{17'}H_3$), 0.85 t.d (1H, 1′-H, *J* = 13.2, 4.2 Hz), 0.94 t.d (1H, 3′-H, *J* = 13.2, 4.0 Hz), 1.10 s (3H, $C^{18'}H_3$), 1.19 d.d (1H, 5′-H, *J* = 12.5, 2.8 Hz), 1.43 d.m (1H, 2′-H, *J* = 14.4 Hz), 1.58 m (1H, 9′-H), 1.69–1.88 m (6H, 1′-H, 6′-H, 2′-H, 11′-H, 7′-H), 1.91 m (1H, 6′-H), 2.09 d.m (1H, 3′-H, ^2J = 12.4 Hz), 2.42 d.d.d (1H, 7′-H, *J* = 12.2, 4.2, 2.5 Hz), 2.68 m and 2.74 m (2H, 12′-H), 3.57 s (3H, OCH_3), 4.65 s and 5.02 s (1H each, 20′-H), 6.43 d (1H, 14-H, *J* = 1.7 Hz), 7.03 br.s (1H, 4a-H), 7.54 m (3H, 3″-H, 5″-H, 4″-H), 7.72 d (1H, 15-H, *J* = 1.7 Hz), 8.19 m (2H, 2″-H, 6″-H), 11.79 s (1H, 1-H). ^{13}C NMR spectrum, δ_C, ppm: 12.64 q ($C^{17'}$), 19.79 t ($C^{2'}$), 23.70 t ($C^{12'}$), 24.16 t ($C^{11'}$), 26.16 t ($C^{6'}$), 28.52 q ($C^{18'}$), 38.00 t ($C^{3'}$), 38.52 t ($C^{7'}$), 38.90 t ($C^{1'}$), 40.01 s ($C^{4'}$), 44.16 s ($C^{10'}$), 51.00 q (OCH_3), 54.26 d ($C^{9'}$), 56.06 d ($C^{5'}$), 106.71 t ($C^{20'}$), 112.70 d (C^{4a}), 113.70 d ($C^{14'}$), 127.24 d ($C^{2''}$, $C^{6''}$), 128.06 s ($C^{1''}$), 128.82 d ($C^{3''}$, $C^{5''}$), 132.00 d ($C^{4''}$), 135.82 s ($C^{13'}$), 137.02 s ($C^{16'}$), 147.39 d ($C^{15'}$), 147.64 s ($C^{8'}$), 148.01 s (C^4), 158.04 s (C^2), 174.05 s (C^5), 177.59 s ($C^{19'}$). Found, %: C 74.61; H 7.11; N 5.41. $C_{31}H_{36}N_2O_4$. Calculated, %: C 74.40; H 7.20; N 5.60.

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REFERENCES

1. Kharitonov, Yu.V., Shul'ts, E.E., Shakirov, M.M., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2006, vol. 42, p. 707.
2. Erlenmeyer, E. and Kunlin, A., *Justus Liebigs Ann. Chem.*, 1901, vol. 316, p. 145.
3. Rao, Y.S. and Filler, R., *Synthesis*, 1975, p. 749.
4. Mukerjee, A.K. and Kumar, P., *Heterocycles*, 1981, vol. 16, p. 1995.
5. Klok, D.A., Shakirov, M.M., Grishko, V.V., and Raldugin, V.A., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 1995, p. 2514.
6. Erlenmeyer, E. and Stadlin, W., *Justus Liebigs Ann. Chem.*, 1904, vol. 337, p. 283.
7. Galat, A., *J. Am. Chem. Soc.*, 1950, vol. 72, p. 4436.
8. Stewart, W.E. and Siddall, T.H., III, *Chem. Rev.*, 1970, vol. 70, p. 517.
9. Kobayashi, J., Sekigichi, M., Shigemori, H., and Ohsaki, A., *Tetrahedron Lett.*, 2000, vol. 41, p. 2939.
10. Uddin, M.J., Kokubo, S., Ueda, K., Suenaga, K., and Uemura, D., *J. Nat. Prod.*, 2001, vol. 64, p. 1169.
11. Nalepa, K. and Slouka, J., *Monatsh. Chem.*, 1967, vol. 98, p. 412.
12. Nalepa, K., *Monatsh. Chem.*, 1967, vol. 98, p. 1230.
13. Prokof'ev, E.P. and Karpeiskaya, E.I., *Tetrahedron Lett.*, 1979, p. 737.
14. Tolstikova, T.G., Sorokina, I.V., Dolgikh, M.P., Kharitonov, Yu.V., Chernov, S.V., Shul'ts, E.E., and Tolstikov, G.A., *Khim.-Farm. Zh.*, 2004, vol. 38, no. 10, p. 13.