ISSN 1070-4280, Russian Journal of Organic Chemistry, 2009, Vol. 45, No. 10, pp. 1456–1463. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © R.V. Shafikov, Ya.R. Urazaeva, S.R. Afon'kina, R.G. Savchenko, L.M. Khalilov, V.N. Odinokov, 2009, published in Zhurnal Organicheskoi Khimii, 2009, Vol. 45, No. 10, pp. 1473–1478.

20-Hydroxyecdysone Oximes and Their Rearrangement into Lactams

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Received April 9, 2009

Abstract—(*E*)-Oximes derived from 20-hydroxyecdysone diacetonides and 7,8-dihydro analog were converted into the corresponding lactams (6-oxo-5a-aza-5a-homo derivatives) via Beckmann rearrangement. 14,15-Anhydro-20-hydroxyecdysone (*Z*)-oxime under analogous conditions (reaction with *p*-toluenesulfonyl chloride in acetone in the presence of Na_2CO_3) gave rise to 20-hydroxyecdisone 20,22-acetonide (*Z*)-*O*-tosyloxime which did not undergo Beckmann rearrangement.

DOI: 10.1134/S1070428009100066

Oximes are widely used in organic synthesis, and they exhibit diverse biological activity [1]. In the recent years, interest in oximes of the steroid series considerably increased [2, 3]. This interest was stimulated primarily by the isolation of steroidal oximes from the marine sponges *Cynachyrella alloclada* and *S. apion* [4]. which, like their synthetic analogs [5], turned out to effectively inhibit aromatase (the key enzyme in the biosynthesis of estrogens) and attracted attention as potential antitumor agents [6]. Ecdysteroid oximes and their chemical properties have been studied poorly. We previously reported on the synthesis of 20-hydroxyecdisone oxime and the corresponding diacetonide [7].

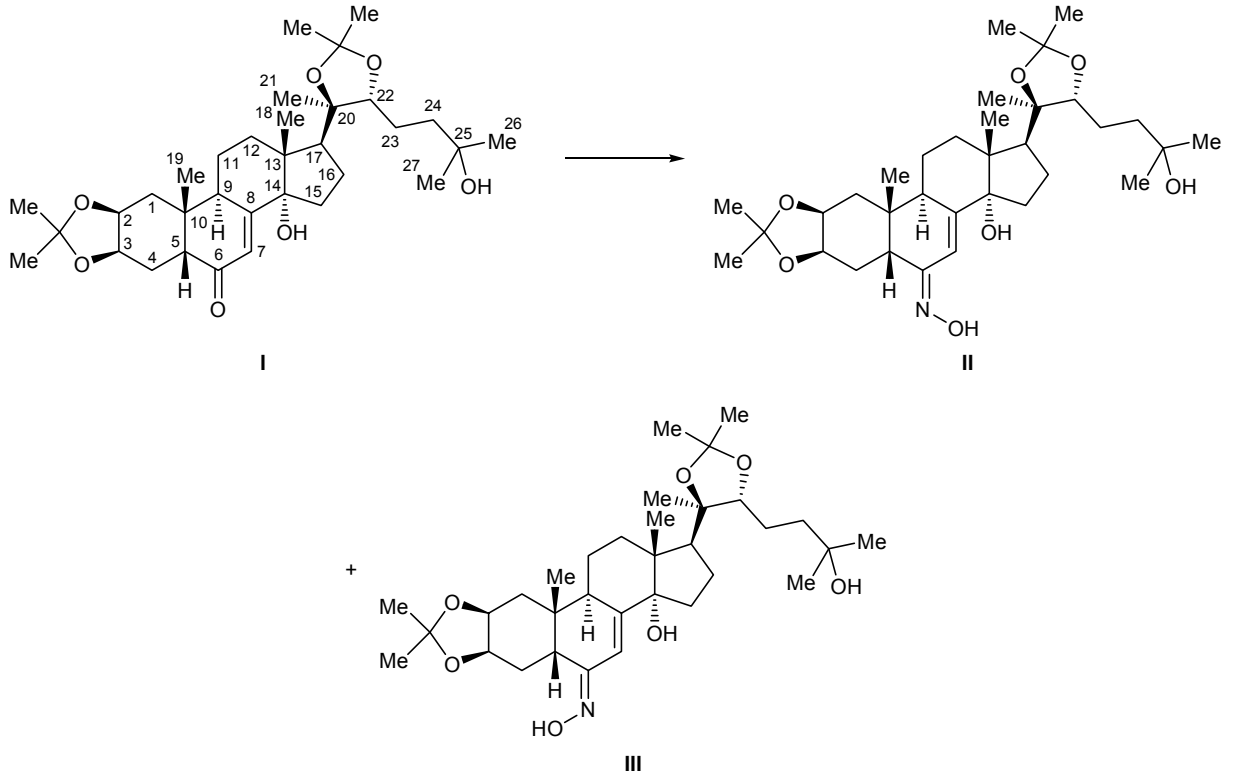
In the present work we succeeded in effecting Beckmann rearrangement of (*E*)-oximes **II** and **V** derived from 20-hydroxyecdysone and its 7,8-dihydro analog with a view to transform the ecdysteroid **B** ring into seven-membered lactam ring, a fragment intrinsic to azabrassinosteroids [8].

By treatment of 20-hydroxyecdysone diacetonide **I** with hydroxylamine hydrochloride in pyridine we obtained a mixture of the corresponding (*E*)- and (*Z*)-oximes **II** and **III** (Scheme 1) [7]. The oximation of 7,8-dihydro-20-hydroxyecdysone diacetonide **IV** under analogous conditions gave (*E*)-oxime **V** (Scheme 2). When the oximation product of 7,8-dihydro analog **IV** was treated with a solution of potassium hydroxide in ethanol, we obtained 14,15-anhydro-7,8-dihydro-20-hydroxyecdysone diacetonide (*E*)-oxime **VI**. An attempt to reduce the latter into 7,8-dihydro-14-deoxy-20-hydroxyecdysone diacetonide oxime by catalytic hydrogenation over Raney nickel resulted in the formation of 7,8-dihydrostachysterone B diacetonide **VII** (Scheme 3). The ^{13}C NMR spectrum of **VII** was fairly similar to the spectrum of 7,8-dihydrostachysterone B 20,22-acetonide [9], and some differences were related to the presence of an additional *O*,*O*′-isopropylidene protective group at positions *2* and *3* of compound **VII**.

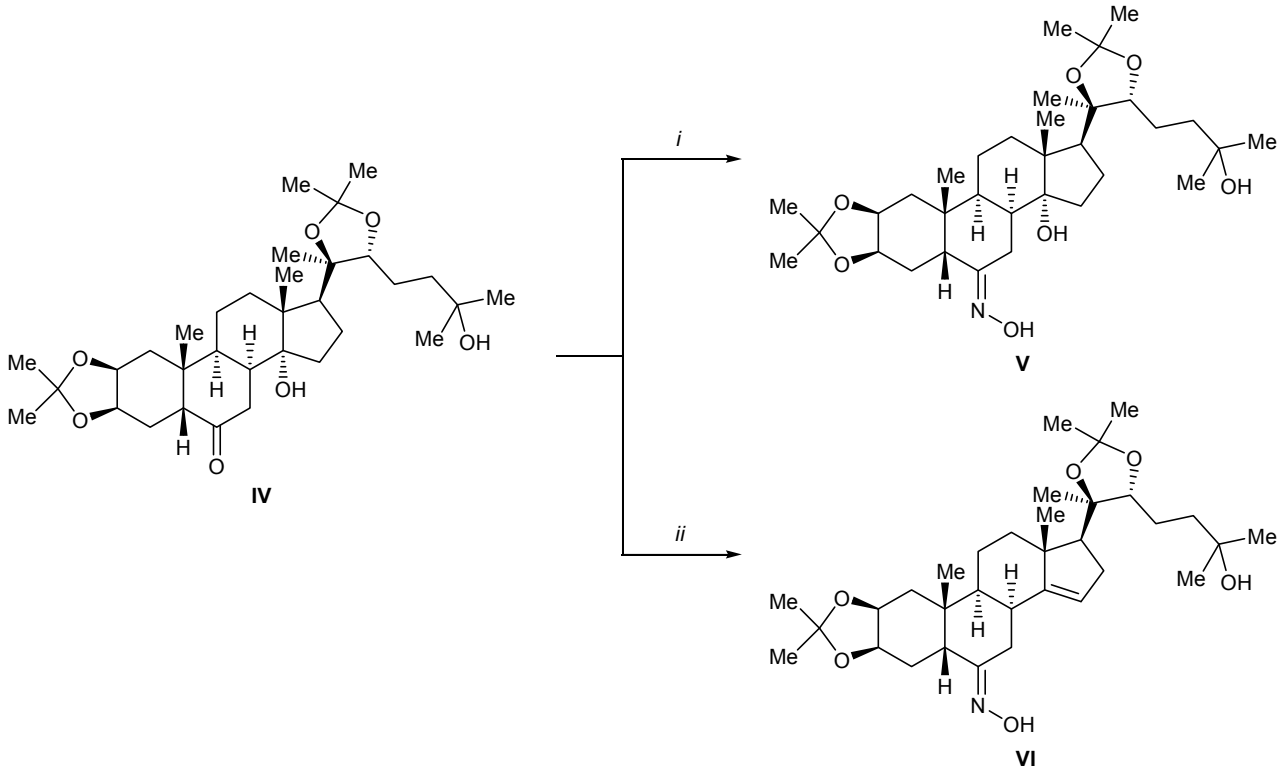
The structure of oximes **V** and **VI** was confirmed by the ^1H and ^{13}C NMR spectra. The signals were assigned using one- (^1H, ^{13}C, APT) and two-dimensional correlation techniques (COSY, HSQC, HMBC). In the ^{13}C NMR spectra of oximes **V** and **VI**, the α-methylene carbon atom (C^7) resonated in a stronger field (δ_C 26.18 and 26.16 ppm, respectively) than the C^5 atom (CH, δ_C 42.28 and 42.48 ppm), indicating their *syn* (C^7) and *anti* (C^5) orientation with respect to the N–OH group. This means that oximes **V** and **VI** have *E* configuration [7, 10].

Oximes of the ecdysteroid series did not undergo Beckmann rearrangement under conditions of acid catalysis. Instead of rearrangement, boron trifluoride–ether complex in methylene chloride promoted deprotection of the hydroxy groups in positions *2* and *3* of

Scheme 1.

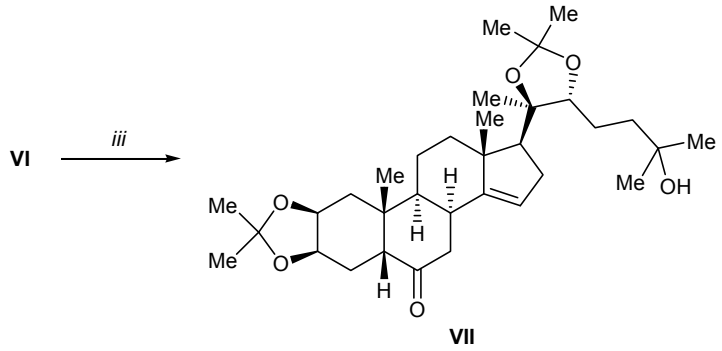


Scheme 2.



i: $NH_2OH \cdot HCl$–pyridine, 70°C; *ii*: (1) $NH_2OH \cdot HCl$–pyridine, 70°C; (2) KOH–EtOH.

Scheme 3.

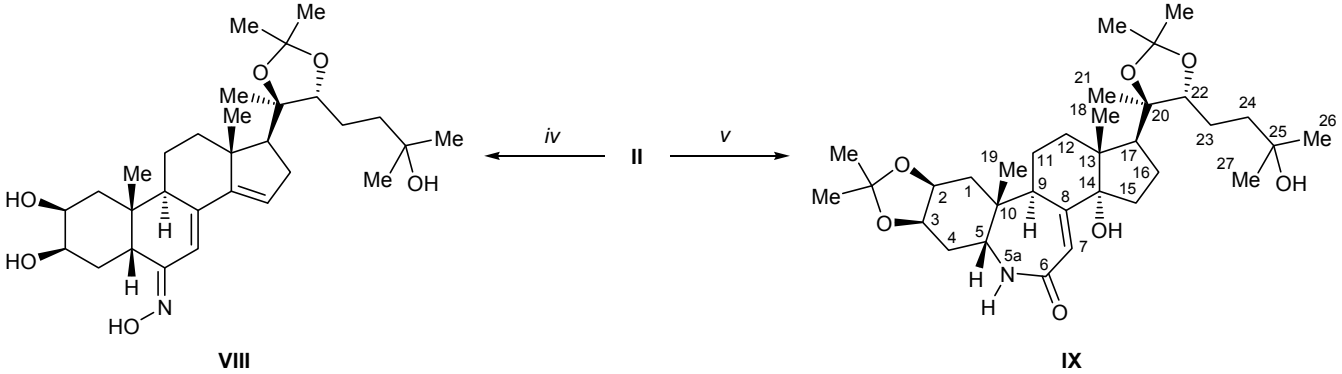


iii: H_2–Raney nickel, 96% EtOH.

(*E*)-oxime **II**, 14,15-dehydration, and *E/Z*-isomerization with formation of 14,15-anhydro-20-hydroxyecdysone 20,22-acetonide (*Z*)-oxime **VIII** (Scheme 4). The ^1H and ^{13}C NMR spectra of compound **VIII** were similar to those of previously described compound **III** [7] (with small differences related to the lack of acetonide protection at C^2 and C^3 in **VIII**). Treatment of oximes **II** and **V** with phosphoric anhydride, phosphorus pentachloride, thionyl chloride, or *p*-toluenesulfonyl chloride resulted in the formation of mixtures of products. We succeeded in effecting rearrangement of oximes **II** and **V** with transformation of the B ring into seven-membered lactam fragment by the action of *p*-toluenesulfonyl chloride in acetone in the presence of sodium carbonate (Schemes 4, 5) [1]. The structure of lactams **IX** and **X** was determined by analysis of their ^1H and ^{13}C NMR spectra. All proton and carbon signals were assigned using one- (^1H, ^{13}C, DEPT 135°) and two-dimensional homo- (COSY, NOESY) and heteronuclear correlation techniques (^{13}C–^1H and ^{15}N–^1H HSQC and HMBC). The transformation of oximes **II** and **V** into the corresponding lactams followed from downfield shift ($\Delta\delta_C$ = 13.2 and 8.6 ppm, respectively) of the signal from C^6 in **IX** and **X**. The existence of a correlation (^{15}N–^1H HMBC) between 5-H (δ 3.26 ppm) and nitrogen nucleus (δ_N 120.1 ppm; this value is typical of nitrogen atom in an amide group [11]) unambiguously indicates that the NHCO group is located between C^5 and C^7 in the B ring of compound **IX**. An additional support is provided by the presence of a cross peak from 7-H (δ 5.85 ppm) and nitrogen atom. Conservation of β-configuration of the 5-H atom in the initial oximes and their rearrangement products **IX** and **X** is ensured by stereospecificity of the Beckmann rearrangement [12].

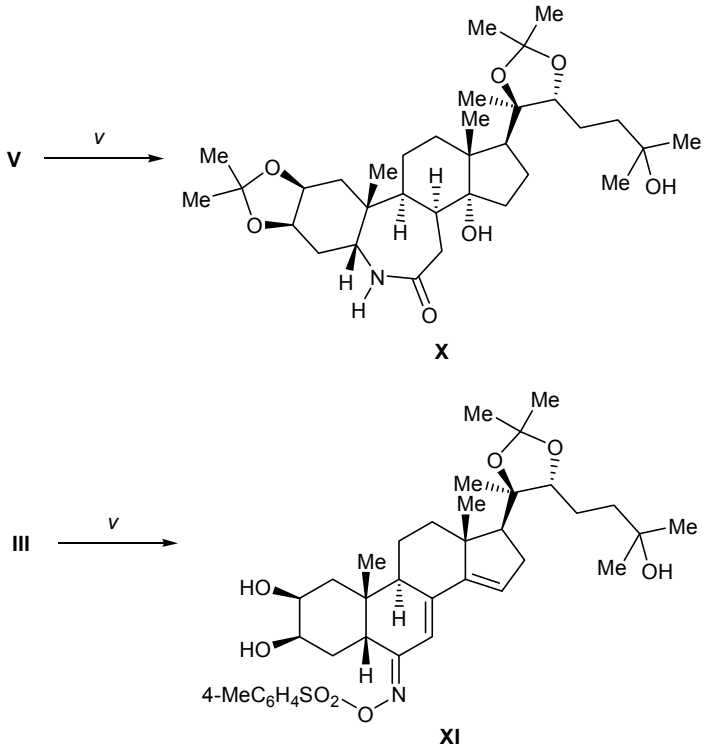
Unlike (*E*)-oximes **II** and **V**, no Beckmann rearrangement occurred with (*Z*)-oxime **III** having a diene fragment. Under analogous conditions, compound **III** was converted into (*Z*)-*O*-tosyloxime **XI** in which the hydroxy groups in positions *2* and *3* were deprotected (Scheme 5). As a result, the C^2 and C^3 signals in the ^{13}C NMR spectrum of **XI** are displaced upfield ($\Delta\delta_C$ = 4.6 ppm), and signal typical of 2,3-*O*-isopropylidene group (δ_C 108.0 ppm) disappears, whereas the signal at

Scheme 4.



iv: $BF_3 \cdot Et_2O$, CH_2Cl_2; *v*: TsCl–Na_2CO_3, Me_2CO.

Scheme 5.



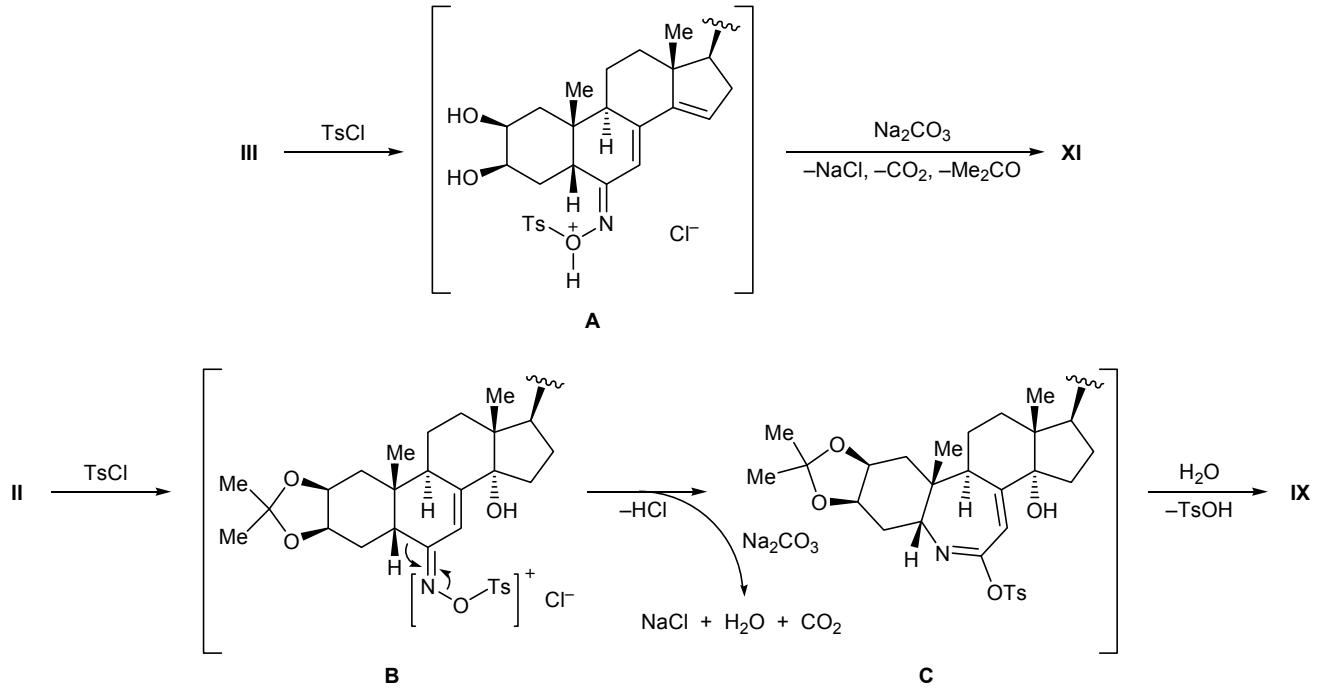
v: $TsCl–Na_2CO_3$, Me_2CO.

δ_C 106.9 ppm from the 20,22-*O*-isopropylidene fragment remains almost unchanged. All signals in the ^1H and ^{13}C NMR spectra of **XI** were assigned using one- (^1H, ^{13}C, DEPT 135°) and two-dimensional correlation techniques (COSY, HSQS, HMBC). Protons in the 18-methyl group (δ 0.98 ppm) gave a cross peak with the carbon signal at δ_C 149.17 ppm in the HMBC spectrum, indicating that the latter belongs to quaternary (DEPT 135°) sp^2-hybridized carbon atom at the double bond (C^{14}). The latter showed a correlation with the signal at δ 6.16 ppm, which was therefore assigned to 7-H. The 7-H proton was coupled (HSQC) with a carbon nuclei resonating at δ_C 113.78 ppm; this signal arises from tertiary (DEPT 135°) sp^2-carbon atom (C^7). Approximately similar chemical shifts of C^5 in compound **XI** (δ_C 37.17 ppm) and initial (*Z*)-oxime **III** (δ_C 37.82 ppm) [7] indicate conservation of *Z* configuration of the oxime moiety. The large vicinal coupling constant (J = 13.2 Hz) for 5-H (δ 3.27 ppm), corresponding to its interaction with the axial 4-H proton suggests axial orientation of 5-H in the A ring, i.e., *cis*-junction of the A and B rings. Aromatic carbon atoms in the *p*-tolylsulfonyl group resonated (DEPT 135°) as singlets at δ 132.64 ($C^{4'}$) and 144.90 ppm ($C^{1'}$) and doublets at δ_C 128.81 ($C^{3'}$, $C^{5'}$) and 129.59 ppm ($C^{2'}$, $C^{6'}$). The most downfield signal in the ^{13}C NMR spectrum of **XI** was located at δ_C 167.17 ppm (DEPT 135°); it was assigned to C^6.

It is known [13, 14] that not oximes themselves but products of their reaction with the acid catalyst undergo Beckmann rearrangement. Stereospecific Beckmann rearrangement always involves that group which is located in the *anti* position with respect to the hydroxy group [12]. The corresponding group in (*Z*)-*O*-tosyloxime **XI** is C^7H with sp^2-hybridized carbon atom, which is not capable of migrating (as in menth-4-en-3-one oxime [15]). Therefore, (*Z*)-*O*-tosyloxime **XI** remains unchanged under the above conditions. Presumably, the stability of oxime **XI** and spatial proximity of the sulfonate group (which forms complex **A** with hydrogen chloride [13]) to the **A** ring promote deprotection of the hydroxy groups on C^2 and C^3 (Scheme 6).

(*E*)-Oxime **II** (or **V**) gives rise to hydrogen chloride complex **B**, and Beckmann rearrangement in (*E*)-*O*-tosyloxime involves migration of C^5H (in the *anti* position with respect to the hydroxy group in the initial oxime) to the nitrogen atom. Complex **B** decomposes with formation of intermediate **C** whose hydrolysis gives lactam **IX** (or **X**), and liberated hydrogen

Scheme 6.



chloride is neutralized with sodium carbonate, thus preventing deprotection of the hydroxy groups in the A ring.

EXPERIMENTAL

The IR spectra were recorded on a Specord 75IR spectrometer from samples dispersed in mineral oil. The UV spectra were measured from solutions in chloroform on a Specord M-40 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker Avance-400 spectrometer at 400.13 and 100.62 MHz, respectively, using $CDCl_3$ as solvent. The ^{1}H and ^{13}C NMR spectra of compound **V** in $CDCl_3$ were recorded on a Bruker AM-300 instrument (300.13 and 75.46 MHz, respectively). Homo- and heteronuclear DEPT-135°, COSY, HSQC, and HMBC experiments were performed on a Bruker Avance-400 spectrometer according to standard procedures. The melting points were determined on a Boetius melting point apparatus. The optical rotations were measured on a Perkin–Elmer 141 polarimeter. Thin-layer chromatography was performed on Silufol plates; spots were visualized by treatment with a solution of vanillin in ethanol acidified with sulfuric acid.

(6*E*)-2,3:20,22-Di-*O*-isopropylidene-7,8α-dihydro-20-hydroxyecdysone oxime (V). Hydroxylamine hydrochloride, 0.39 g (5.6 mmol), was added under stirring to a solution of 0.40 g (0.7 mmol) of compound **IV** (mp 275–277°C; prepared according to the procedure described in [9]) in 6 ml of freshly distilled pyridine, and the mixture was heated for 3 days at 70°C and evaporated on a rotary evaporator. The residue was treated with 20 ml of water, the product was extracted into ethyl acetate (3×30 ml), the extract was dried over $MgSO_4$ and evaporated, and the residue was subjected to column chromatography on silica gel (30 g) using chloroform–methanol (30:1) as eluent. Yield 0.4 g (98%), R_f 0.47 ($CHCl_3$–MeOH, 10:1), mp 90–92°C, $[\alpha]_D^{18}$ = 19.8° (c = 12.7, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.05 s (3H, $C^{18}H_3$), 1.08 s (3H, $C^{21}H_3$), 1.18 s (6H, $C^{26}H_3$, $C^{27}H_3$), 1.21 s (3H, $C^{19}H_3$); 1.27 s, 1.28 s, 1.37 s, and 1.50 s (12H, Me_2C); 1.53–2.17 m (19H, CH, CH_2), 2.32 m (1H, 9-H, $w_{1/2}$ = 20.8 Hz), 3.27 m (1H, 5-H, $w_{1/2}$ = 21.4 Hz), 3.63 m (1H, 22-H, $w_{1/2}$ = 14.0 Hz), 4.23 m (1H, 3-H, $w_{1/2}$ = 13.0 Hz), 4.63 m (1H, 2-H, $w_{1/2}$ = 15.5 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 17.87 t (C^{11}), 18.45 q (C^{18}), 20.91 q (C^{21}), 21.32 t (C^{16}), 23.46 t (C^{23}), 25.89 q (C^{19}), 26.18 t (C^4), 26.18 t (C^7), 26.65 q (C^{26}), 26.65 q (C^{27}), 26.65 q and 29.50 q (20,22-**Me**$_2$C), 28.34 q and 28.90 q (2,3-**Me**$_2$C), 31.28 t (C^{12}), 33.46 t (C^{15}), 36.82 t (C^1), 36.82 s (C^{10}), 41.24 t (C^{24}), 41.48 d (C^9), 41.80 d (C^8), 42.28 d (C^5), 46.74 s (C^{13}), 49.75 d (C^{17}), 70.27 s (C^{25}), 71.46 d (C^3), 73.95 d (C^2), 81.81 d (C^{22}), 84.48 s (C^{20}), 85.53 s (C^{14}), 106.74 s (20,22-Me_2**C**), 107.38 s (2,3-Me_2**C**), 158.57 s (C^6).

(6*E*)-2,3:20,22-Di-*O*-isopropylidene-14,15-anhydro-7,8α-dihydro-20-hydroxyecdysone oxime (VI). Hydroxylamine hydrochloride, 0.29 g (4.0 mmol), was added under stirring to a solution of 0.30 g (0.5 mmol) of diacetonide **IV** in 3 ml of freshly distilled pyridine, and the mixture was heated for 3 days at 70°C. The mixture was cooled to 0°C, a solution of 0.023 g (5.0 mmol) of potassium hydroxide in 2.3 ml of anhydrous ethanol was added, and the mixture was evaporated on a rotary evaporator. The residue was treated with 25 ml of water, the product was extracted into ethyl acetate (3×25 ml), and the extract was dried over $MgSO_4$ and evaporated. Yield 0.07 g (23%), mp 123–125°C, $[\alpha]_D^{20} = -1.4°$ (c = 3.7, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 1.13 s (3H, $C^{18}H_3$), 1.14 s (3H, $C^{21}H_3$), 1.18 s (3H, $C^{19}H_3$), 1.25 m (1H, 9-H), 1.26 s (6H, $C^{26}H_3$, $C^{27}H_3$), 1.29 s and 1.38 s (3H each, 2,3-Me_2C), 1.31 s and 1.50 s (3H each, 20,22-Me_2C), 1.32 m and 2.12 m (2H, 24-H), 1.37 m and 1.56 m (2H, 23-H), 1.51 m and 1.68 m (2H, 7-H), 1.52 m and 1.89 m (2H, 1-H), 1.57–1.77 m (2H, 11-H), 1.62 m and 2.38 m (2H, 4-H), 1.77 m (1H, 17-H), 1.99 d.d (1H, 7α-H, $J_{7\alpha,8}$ = 4.4, $J_{7\alpha,7\beta}$ = 14.8 Hz), 2.07 m and 2.46 m (2H, 16-H), 2.16 m and 2.46 m (2H, 12-H), 2.28 m (1H, 5-H, $w_{1/2}$ = 11.2 Hz), 2.79 m (1H, 8-H, $w_{1/2}$ = 20.4 Hz), 3.13 d.d (1H, 7β-H, $J_{7\beta,7\alpha}$ = 14.8, $J_{7\beta,8}$ = 13.0 Hz), 3.71 m (1H, 22-H, $w_{1/2}$ = 14.3 Hz), 4.25 m (1H, 2-H, $w_{1/2}$ = 13.6 Hz), 4.66 m (1H, 3-H, $w_{1/2}$ = 19.2 Hz), 5.37 m (1H, 15-H, $w_{1/2}$ = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.77 (C^{11}), 21.08 (C^{18}), 21.17 (C^{21}), 23.90 (C^{23}), 26.22 (C^{19}), 26.89 (C^4), 26.16 (C^7), 26.88 (C^{26}), 26.92 (C^{27}), 28.65 and 29.05 (2,3-**Me**$_2$C), 29.11 and 29.87 (20,22-**Me**$_2$C), 30.64 (C^{12}), 30.64 (C^{16}), 33.34 (C^1), 36.05 (C^8), 37.20 (C^{10}), 42.48 (C^5), 42.77 (C^{24}), 47.04 (C^{13}), 48.15 (C^9), 59.65 (C^{17}), 70.56 (C^{25}), 71.80 (C^3), 74.19 (C^2), 81.89 (C^{20}), 83.73 (C^{22}), 107.03 (20,22-Me_2**C**), 107.71 (2,3-Me_2**C**), 122.40 (C^{15}), 152.48 (C^{14}), 158.69 (C^6).

7,8a-Dihydrostachysterone B 2,3:20,22-diacetonide (VII). Gaseous hydrogen was passed at room temperature through a suspension of 0.07 g (0.32 mmol) of (6*E*)-oxime **VI** and 0.7 g of Raney nickel (prepared according to the procedure described in [16] from powdered Ni–Al alloy from Acros Organics) in 4 ml of ethanol until the substrate disappeared completely (~30 h, according to the TLC data). The catalyst was filtered off, the filtrate was evaporated, and the residue was subjected to column chromatography on 5 g of silica gel using chloroform–methanol (30:1) as eluent. Yield 0.04 g (59%), R_f 0.61 ($CHCl_3$–MeOH, 10:1), mp 233–235°C, $[\alpha]_D^{20} = -8.6°$ (c = 2.20, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 1.17 s (3H, $C^{18}H_3$), 1.19 s (3H, $C^{21}H_3$), 1.22 s (6H, $C^{26}H_3$, $C^{27}H_3$), 1.29 s (3H, $C^{19}H_3$); 1.39 s, 1.41 s, and 1.50 s (12H, Me_2C), 1.54–2.23 m (17H, CH, CH_2), 2.48 d.d (1H, 17-H, J = 7.5 Hz), 2.75 t (1H, 7β-H, J = 3.6 Hz), 3.09 d.t (1H, 8-H, J = 18.0, 4.8 Hz), 3.73 m (1H, 22-H, $w_{1/2}$ = 9.9 Hz), 4.22 m (1H, 2-H, $w_{1/2}$ = 9.0 Hz), 4.50 m (1H, 3-H, $w_{1/2}$ = 10.5 Hz), 5.37 m (1H, 15-H, $w_{1/2}$ = 5.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.85 (C^{11}), 20.98 (C^{18}), 21.02 (C^{21}), 23.71 (C^{23}), 25.23 (C^{16}), 25.96 (C^{19}), 26.03 and 28.55 (2,3-**Me**$_2$C), 26.55 and 28.88 (20,22-**Me**$_2$C), 29.05 (C^{27}), 29.66 (C^{26}), 30.47 (C^4), 33.94 (C^1), 37.97 (C^9), 39.82 (C^{10}), 41.29 (C^{24}), 42.32 (C^{12}), 44.57 (C^7), 46.83 (C^{13}), 47.59 (C^8), 50.81 (C^5), 59.40 (C^{17}), 70.31 (C^{25}), 70.94 (C^3), 71.51 (C^2), 81.69 (C^{22}), 83.45 (C^{20}), 106.82 (20,22-Me_2**C**), 107.71 (2,3-Me_2**C**), 122.56 (C^{15}), 150.98 (C^{14}), 211.50 (C^6).

(6*Z*)-20,22-*O*-Isopropylidene-14,15-anhydro-20-hydroxyecdysone oxime (VIII). Freshly distilled boron trifluoride–ether complex, 0.02 ml, was added under stirring to a solution of 0.10 g (0.17 mmol) of (6*E*)-oxime **II** in 3 ml of anhydrous methylene chloride, and the mixture was stirred for 16 h at 20°C. The mixture was cooled to 0°C, 5 ml of water was added under stirring, the product was extracted into ethyl acetate (3×10 ml), the extract was dried over $MgSO_4$, the combined extracts were evaporated under reduced pressure, and the residue was subjected to chromatography on 4 g of silica gel using chloroform–methanol (30:1) as eluent. Yield 0.04 g (45%), R_f 0.43 ($CHCl_3$–MeOH, 10:1), mp 155–157°C, $[\alpha]_D^{20} = -115.0°$ (c = 1.0, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 0.88 s (3H, $C^{19}H_3$), 1.01 s (3H, $C^{18}H_3$), 1.20 s (3H, $C^{21}H_3$), 1.24 s (3H, $C^{26}H_3$), 1.25 s (3H, $C^{27}H_3$), 1.31 s and 1.43 s (6H, 20,22-**Me**$_2$C), 1.52–2.36 m (19H, CH, CH_2), 2.58 m (1H, 9-H, $w_{1/2}$ = 27.0 Hz), 3.21 d.d (1H, 5-H, J = 16.2 Hz), 3.74 m (1H, 22-H, $w_{1/2}$ = 18.6 Hz), 3.74 m (1H, 2-H, $w_{1/2}$ = 18.6 Hz), 4.03 m (1H, 3-H, $w_{1/2}$ = 12.3 Hz), 5.77 br.s (1H, 15-H, $w_{1/2}$ = 7.8 Hz), 6.21 d (1H, 7-H, ^4J = 6.3 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.83 (C^{18}), 20.78 (C^{11}), 21.24 (C^{19}), 23.66 (C^{21}), 23.83 (C^{23}), 26.83 (C^{16}), 28.90 (C^{26}), 29.24 and 29.68 (20,22-**Me**$_2$C), 29.45 (C^{27}), 30.20 (C^{12}), 31.21 (C^4), 35.40 (C^{10}), 36.36 (C^9), 37.97 (C^5), 39.97 (C^1), 41.23 (C^{24}), 47.27 (C^{13}), 57.52 (C^{17}), 67.88 (C^3), 68.20 (C^2), 70.56 (C^{25}), 81.80 (C^{22}), 83.53 (C^{20}), 106.92 (20,22-Me_2**C**), 116.29 (C^7), 123.34 (C^{15}), 140.82 (C^8), 149.64 (C^{14}), 159.64 (C^6).

(20*R*,22*R*)-14α,25-Dihydroxy-2β,3β:20,22-di-*O*-isopropylidene-5a-aza-5a-homo-5β-cholest-7-en-6-one (IX). Oxime **II**, 0.143 g (0.25 mmol), was dis-

solved in 10 ml of freshly distilled acetone, 0.027 g (0.25 mmol) of sodium carbonate and 0.096 g (0.5 mmol) of *p*-toluenesulfonyl chloride were added under stirring, and the mixture was stirred for 24 h at 20°C. The mixture was cooled to 0°C, 6 ml of water was added under stirring, the product was extracted into ethyl acetate (3×20 ml), the combined extracts were dried over $MgSO_4$ and evaporated under reduced pressure, and the residue was subjected to chromatography on 5 g of silica gel using chloroform–methanol (20:1) as eluent. Yield 0.068 g (48%), R_f 0.43 ($CHCl_3$–MeOH, 10:1), mp 165–167°C, $[\alpha]_D^{20}$ = 45.5° (*c* = 3.8, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3420–3280, 2980–2900, 1680, 1620, 1470, 1390, 1230, 1160, 1080, 890. UV spectrum: λ_{max} 259 nm (ε = 11567). ^{1}H NMR spectrum, δ, ppm: 0.80 s (3H, $C^{18}H_3$), 0.98 s (3H, $C^{19}H_3$), 1.11 s (3H, $C^{21}H_3$), 1.20 s and 1.39 s (3H each, 2,3-Me_2C), 1.21 s and 1.46 s (3H each, 20,22-Me_2C), 1.23 s and 1.24 s (3H, $C^{27}H_3$), 1.26 m and 2.17 m (2H, 24-H), 1.40 m and 1.70 m (2H, 12-H), 1.44 m and 2.11 m (2H, 4-H), 1.50 m and 1.70 m (2H, 16-H), 1.56 s and 1.72 s (3H, $C^{26}H_3$), 1.57 m and 1.71 m (2H, 1-H), 1.58 m and 1.64 m (2H, 23-H), 1.80 m and 1.94 m (2H, 15-H), 1.81 m and 2.08 m (2H, 11-H), 2.21 m (1H, 17-H), 2.92 m (1H, 9-H, $w_{1/2}$ = 18.0 Hz), 3.26 m (1H, 5-H, $w_{1/2}$ = 16.8 Hz), 3.64 m (1H, 22-H, $w_{1/2}$ = 13.2 Hz), 4.26 m (1H, 2-H, $w_{1/2}$ = 18.0 Hz), 4.36 m (1H, 3-H, $w_{1/2}$ = 9.0 Hz), 5.85 m (1H, 7-H, $w_{1/2}$ = 16.8 Hz), 6.40 s (1H, NH, *J* = 9.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.10 (C^{18}), 21.07 (C^{11}), 21.76 (C^{21}), 22.25 (C^{19}), 23.15 (C^{16}), 23.55 (C^{23}), 26.33 and 26.88 (2,3-**Me**$_2$C), 28.46 and 28.95 (20,22-**Me**$_2$C), 29.29 (C^{26}), 29.50 (C^{27}), 29.95 (C^{12}), 32.21 (C^{15}), 32.89 (C^4), 38.98 (C^9), 39.65 (C^{10}), 41.35 (C^1), 42.41 (C^{24}), 48.04 (C^{13}), 49.28 (C^{17}), 55.95 (C^5), 70.42 (C^{25}), 71.82 (C^2), 73.99 (C^3), 81.93 (C^{22}), 84.39 (C^{20}), 87.77 (C^{14}), 106.92 (20,22-Me_2**C**), 108.35 (2,3-Me_2**C**), 120.07 (C^7), 154.48 (C^8), 168.78 (C^6). Found, %: C 68.66; H 9.70; N 2.59. $C_{33}H_{53}NO_7$. Calculated, %: C 68.84; H 9.28; N 2.43.

(20*R*,22*R*)-14α,25-Dihydroxy-2β,3β:20,22-di-*O*-isopropylidene-5a-aza-5a-homo-5β,8α-cholestan-6-one (X). Oxime **V**, 0.07 g (0.12 mmol), was dissolved in 5 ml of freshly distilled acetone, 0.013 g (0.12 mmol) of sodium carbonate and 0.046 g (0.24 mmol) of *p*-toluenesulfonyl chloride were added under stirring, and the mixture was stirred for 24 h at 20°C. The mixture was cooled to 0°C, 3 ml of water was added under stirring, the product was extracted into ethyl acetate (3×10 ml), the combined extracts were dried over $MgSO_4$ and evaporated under reduced pressure, and the residue was subjected to chromatography on 3 g of silica gel using chloroform–methanol (20:1) as eluent. Yield 0.015 g (21%), R_f 0.40 ($CHCl_3$–MeOH, 10:1), mp 152–154°C, $[\alpha]_D^{20}$ = 5.2° (*c* = 1.7, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 0.93 s (3H, $C^{18}H_3$), 1.11 s (3H, $C^{21}H_3$), 1.14 s (3H, $C^{19}H_3$), 1.20 m and 2.12 m (2H, 15-H), 1.23 m and 2.11 m (2H, 4-H), 1.24 s (6H, $C^{26}H_3$, $C^{27}H_3$); 1.32 s, 1.41 s, and 1.50 s (12H, 2,3-Me_2C, 20,22-Me_2C); 1.46 m and 1.60 m (2H, 24-H), 1.50 m and 1.65 m (2H, 23-H), 1.53 m and 1.70 m (2H, 25-H), 1.60 m (2H, 11-H), 1.70 m (2H, 12-H), 2.03 m (1H, 17-H), 2.36 m (1H, 9-H, $w_{1/2}$ = 18.0 Hz), 2.55 m (1H, 8-H, $w_{1/2}$ = 36.8 Hz), 2.47 d (1H, 7α-H, $J_{7\alpha,8}$ = 14.0 Hz), 2.75 d.d (1H, 7β-H, $J_{7\beta,7\alpha}$ = 14.0, $J_{7\beta,8}$ = 16.0 Hz), 3.45 m (1H, 5-H, $w_{1/2}$ = 20.8 Hz), 3.66 m (1H, 22-H, $w_{1/2}$ = 14.4 Hz), 4.30–4.39 m (2H, 2-H, 3-H, $w_{1/2}$ = 31.0 Hz), 5.85 m (1H, 7-H, $w_{1/2}$ = 16.8 Hz), 5.67 s (1H, NH, *J* = 29.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 17.17 (C^{18}), 18.27 (C^{11}), 21.05 (C^{16}), 21.49 (C^{21}), 23.56 (C^{23}), 25.57 (C^{19}), 26.81 and 28.96 (2,3-**Me**$_2$C), 28.24 and 29.22 (20,22-**Me**$_2$C), 28.96 (C^{26}), 29.59 (C^{27}), 31.94 (C^{12}), 31.98 (C^4), 32.05 (C^{15}), 36.10 (C^7), 39.90 (C^{10}), 41.17 (C^9), 41.20 (C^1), 41.20 (C^8), 41.40 (C^{24}), 46.62 (C^{13}), 49.81 (C^{17}), 51.03 (C^5), 70.34 (C^{25}), 70.34 (C^2), 72.18 (C^3), 81.90 (C^{22}), 84.39 (C^{20}), 86.14 (C^{14}), 106.95 (20,22-Me_2**C**), 108.41 (2,3-Me_2**C**), 176.13 (C^6).

20,22-*O*-Isopropylidene-14,15-anhydro-20-hydroxyecdysone (*Z*)-*O*-(4-methylphenylsulfonyl)-oxime (XI). Sodium carbonate, 0.019 g (0.18 mmol), and *p*-toluenesulfonyl chloride, 0.069 g (0.36 mmol), were added under stirring to a solution of 0.1 g (0.18 mmol) of oxime **III** (mp 148–150°C; prepared according to the procedure described in [7]*) in 7 ml of freshly distilled acetone, and the mixture was stirred for 24 h at 20°C. The mixture was cooled to 0°C, 5 ml of water was added, the product was extracted into ethyl acetate (3×15 ml), the extract was dried over $MgSO_4$ and evaporated, and the residue was subjected to chromatography on silica gel (4 g) using chloroform–methanol (30:1) as eluent. Yield 0.075 g (59%), R_f 0.51 ($CHCl_3$–MeOH, 10:1), mp 121–123°C, $[\alpha]_D^{20}$ = –95.6° (*c* = 0.63, $CHCl_3$). IR spectrum, ν, cm^{-1}: 3500–3300, 3020–2900, 1600, 1510, 1450, 1380, 1230, 1190. UV spectrum: λ_{max} 300 nm (ε = 15284). ^{1}H NMR spectrum, δ, ppm: 0.79 s (3H, $C^{19}H_3$), 0.98 s (3H, $C^{18}H_3$), 1.18 s (3H, $C^{21}H_3$), 1.23 s (3H, $C^{26}H_3$),

* According to the refined data (HSQC), the C^7 and C^{15} signals, as well as the C^8 and C^{14} signals, in the ^{13}C NMR spectrum of **XI** given in [7] should be swapped.

1.24 s (3H, $C^{27}H_3$), 1.30 s and 1.45 s (6H, 20,22-Me_2C), 1.41 m and 1.87 m (2H, 23-H), 1.42 m and 2.18 m (2H, 12-H), 1.44 m and 1.83 m (2H, 1-H), 1.46 m and 1.61 m (2H, 16-H), 1.52 m and 1.71 m (2H, 24-H), 1.60 m and 1.71 m (2H, 11-H), 1.94 m (1H, 17-H), 2.26 m and 2.57 m (2H, 4-H), 2.36 m (1H, 9-H), 2.44 s (3H, $C^{7'}H_3$), 3.27 d.d (1H, 5-H, $J_{4\alpha,5}$ = 13.2, $J_{4\beta,5}$ = 4.4 Hz), 3.69–3.71 m (1H, 22-H, $w_{1/2}$ = 13.2 Hz), 3.69–3.73 m (1H, 3-H, $w_{1/2}$ = 9.2 Hz), 4.03 m (1H, 2-H, $w_{1/2}$ = 9.2 Hz), 5.81 m (1H, 15-H, $w_{1/2}$ = 6.8 Hz), 6.16 s (1H, 7-H), 7.31 m (2H, 2′-H, 6′-H, $w_{1/2}$ = 8.4 Hz), 7.87 m (2H, 3′-H, 5′-H, $w_{1/2}$ = 8.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.90 (C^{18}), 20.65 (C^{11}), 21.16 (C^{21}), 21.69 ($C^{7'}$), 23.52 (C^{19}), 23.68 (C^{16}), 26.49 (C^{26}), 26.79 and 28.86 (20,22-**Me**$_2$C), 29.19 (C^{27}), 29.63 (C^{12}), 30.95 (C^{23}), 31.32 (C^4), 36.56 (C^{10}), 36.61 (C^1), 37.13 (C^5), 38.06 (C^9), 41.21 (C^{24}), 47.38 (C^{13}), 57.44 (C^{17}), 67.50 (C^2), 67.50 (C^3), 70.46 (C^{25}), 81.73 (C^{22}), 83.39 (C^{20}), 106.99 (20,22-Me_2**C**), 113.47 (C^7), 125.62 (C^{15}), 128.80 ($C^{3'}$, $C^{5'}$), 129.59 ($C^{2'}$, $C^{6'}$), 132.64 ($C^{4'}$), 144.90 ($C^{1'}$), 146.41 (C^8), 149.17 (C^{14}), 167.17 (C^6). Found, %: C 66.08; H 7.80; N 2.03; S 4.24. $C_{37}H_{53}NO_8S$. Calculated, %: C 66.14; H 7.95; N 2.08; S 4.77.

This study was performed under financial support by the Academy of Sciences of Bashkortostan Republic and by the President of the Russian Federation (project no. NSh-6079.2008.3).

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