TRANSFORMED STEROIDS. 171. HETEROCYCLIZATION IN THE 16α,17α-EPIMINOPREGN-5-ENE-3β,21-DIOL-20-ONE SERIES

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The ability of 16α,17α-epimino-20-ketosteroids (I) to form 20,20-acetals and aminals is their known property in their reactions, for example, with acetone [1] or thiocyanates [2, 3]. In the present work, we studied certain characteristics features of the preparation and chemical behavior of these compounds, determined by the presence and participation of a C^{21}-hydroxyl group.

In analogy with C^{21}-unsubstituted ketoaziridine (Ia), which condenses with acetone with the formation of (IIa) [1], aziridine (Ib), even during crystallization from acetone, gives 20-O,N-isopropylidene derivative (IIc). The preparation of the 20-O-methyl analog (IId) of the latter compound requires an acid catalysis in the presence of MeOH. Another possibility of the synthesis of (IId) was also found, i.e., from the 21-O,N-isopropylidene derivative (IV), previously obtained [4] from (Ia) in two stages. This "transacetonation" reaction is irreversible, and proceeds readily in a quantitative yield in a methanolic solution of H_2SO_4 at 20°C. It was used as an alternative to the available [5] and preparatively more acceptable variant of the synthesis of 3,21-diacetate of 16α,17α-epiminopregnenolone (Ic). For

TABLE 1. ^{13}C NMR Spectrum [δ, ppm (J, Hz)] of Steroids (IIb), (IIIb), (VIc, d)

No. of atoms	Compounds			
	(IIb)	(IIIb)	(VIc	(VId)
1	37,36	37.00	36.57	36.99
2	31,47	27.80	27.25	27.82
3	71.76	73.86	73.87	73.83
			(144)	(148)
4	42.44	38.19	37.59	38.16
5	141.12	140.00	139.41	139.76
6	121,43	122,13	121.58	122.06
7	31.76	31.32	32.52	33.40
8	30.46	30.23	30.99	31.47
9	50,66	50,08	49.02	49.24
			(119)	(122)
10	36.86	36,82	36.24	36.61
11	20.66	20,69	19.62	20.34
12	33.90	33.58	32.52	32.95
13	40.51	42.31	42.42	43.06
14	49.36	47.34	54.11	55.4
15	27,13	27.80	31.90	31.57
16	39.78	58.55 d.d	93.66	94,61
	(178,2)	(5 and 176)	(150)	(153)
17	66.09	68.34	83.54	84.4
18	15.32	15.60	13.31	13.66
19	19.41	19.32	18.56	19,37
20	105,91	94.28	98.16	102,48
20-OMe	49,7 q	51.4 q	–	52.67 q
	(140)	(144)	–	(143)
21	64.3	25.6	79.82	79.2
	(143)		(148)	(148)
2′	96.64	200.67	177.72	179.08
2′-CH_3	29,55	–	–	–
	24.31	–	–	–
3-CO	–	170.45	170.9	170.64
3-OCOMe	–	21.41	20.36	21.52

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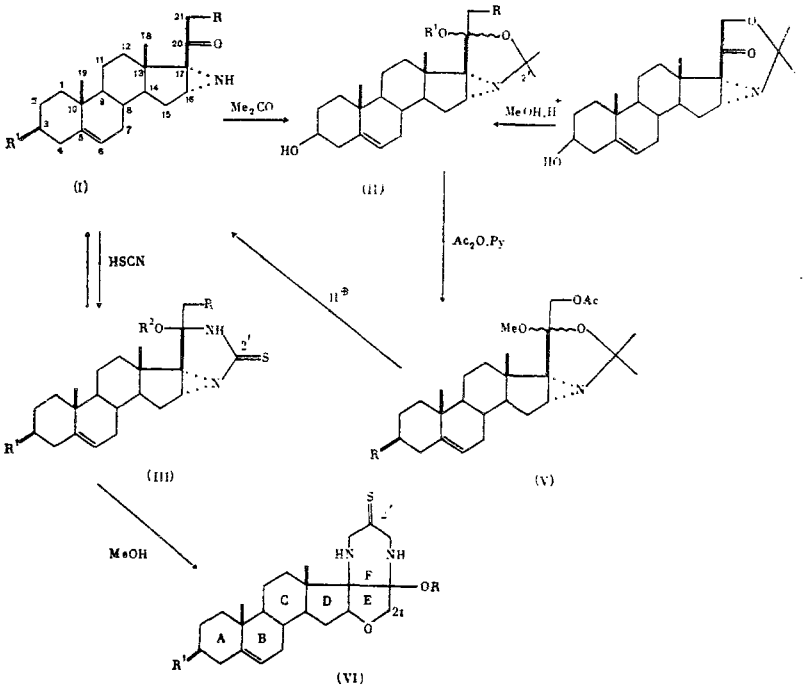
this purpose, compound (IId) was acetylated with Ac_2O in Py, and then the (Va) obtained was hydrolyzed with HCl in a solution of HOAc and MeOH. Unfortunately, we did not succeed in preparing by this method the aziridine (Id) selectively acetylated at C^{21}, since the monoacetylation of the sterically hindered C^{21}-hydroxyl group in (IId) proceeds in low yield. Removal of acetone in (IIc, d), (Va, b) proceeds readily, especially in the case of the semiacetal (IIc), from which (Ib) is regenerated by a simple crystallization from MeOH.



(I) (II) (III) (V) (VI)

R = H, R^1 = OH (Ia, VIa); R = R^1 = OH (Ib); R = R^1 = OAc (Ic); R = OAc, R^1 = OH (Id); R = R^1 = H (IIa); R = H, R^1 = Me (IIb); R = OH, R^1 = H (IIc); R = OH, R^1 = Me (IId); R = R^2 = H, R^1 = OAc (IIIa); R = H, R^1 = OAc, R^2 = Me (IIIb); R = R^1 = OH; R^2 = H (IIIc); R = R^1 = OAc, R^2 = H (IIId); R = OAc (Va); R = OH (Vb); R = Me, R^1 = OH (VIb); R = H, R^1 = OAc (VIc); R = Me, R^1 = OAc (VId).

The structurally identical aminals (IIIa-d) obtained by the condensation of the ketoaziridines (Ia, b) with pyridine or carbethoxyhydrazine thiocyanates in dioxane [3] do not eliminate HSCN on treatment with MeOH. Instead, a brief heating of (IIIc) [3] in MeOH leads to the formation of a heterocyclic structure (VIa). The same reaction in the presence of H_2SO_4 gives the methoxy derivative (VIb), whose precursor is (VIa). The presence of a C^{21} hydroxyl group, an internal nucleophile, is an obligatory structural feature for the occurrence of the very unusual heterocyclization observed, which possibly aids in the cleavage of the aziridine ring at the C^{16}—N bond with stabilization of the C^{16}-carbocation thus formed, through the C^{21}—O-end of the molecule. This supposition is supported by the fact that neither the 21-acetoxy derivative (IIId) nor its 21-unsubstituted analog (IIIa) form aziridine ring-opening products under these conditions. As a matter of fact, heating of (IIIa) in MeOH leads only to the substitution of the C^{20}-hydroxyl group by the methoxyl group, while (IIId) does not react altogether under these conditions.

The structure of compounds (IIc, d) and (IIIa) was confirmed by regeneration from their corresponding aziridines (I) and by physicochemical characteristics. The stereochemistry of the C^{20}-center in compounds (IIa-d) and their acetates (Va-b) has not been established, but an undoubted proof for the proposed stereochemistry of this center* in (III) is the observed ease of isomerization of (IIIc) into (VIa). Examination of the Dreiding models shows

*The configuration of the substituents at the C^{20} atom in compounds (III), (VI) is designated in accordance with the IUPAC nomenclature accepted for C^{20}-substituted pregnanes, and in this case does not coincide with the orientation of the given substituents with respect to the plane of the molecule.

that the observed heterocyclization of (IIc) is possible only when the hydroxymethyl fragment is oriented in the direction of the observer, i.e., toward the C^{16} reaction center. The assignment of the proposed heterocyclic structure to compound (VIa) is based on the following arguments. The observed transformation of (VIa) into (VIb) is characteristic for these types of aminals [1, 2]. The mass spectrum of (VIb) has a molecular peak with m/z 418, differing by 14 units from the molecular peak of (VIa), and shows a fragmentation corresponding to the elimination of MeOH. The acetylation of (VIa), (VIb) by Ac_2O in Py at 20°C for 18-19 h gives only 3-monoacetates (VIc), (VId) (NMR, mass spectra), thus indicating the absence of a free C^{21}-hydroxyl group, and its participation in the cyclization. The conclusion on the opening of the aziridine ring in (VI) was made from comparison of the ^{13}C spectra of compounds (III) and (VI). This comparison was possible only for compounds (IIIb) (VIc, d) which are soluble in $CDCl_3$. In fact, from the data in Table 1 it can be seen that signals of the C^{16} and C^{17} atoms with spectral parameters characteristic for the aziridine ring [6] are absent in the spectra of compounds (VIc, d). Thus, the transition from (IIIb) to (VIc, d) is characterized by a strong shift of signals of the C^{16} and C^{17} atoms to a weak field, which is in particular appreciable for the former atom ($\Delta\delta$ C^{16} = 36 ppm). Increase in δ of the C^{16} atoms in (VIc, d) to 93.66 and 94.61 ppm indicates not only a change in the size of the heterocyclic ring E, but also a change in the nature of the heteroatom, bound to this carbon. From this we concluded that the aziridine ring in (III) opens at the C^{16}—N bond. The most favorable method of neutralization of the electrophilic C^{16} center thus formed is by its β-attack by the C^{21}—O-end of the molecule (the Dreiding models). The values of the chemical shift observed in (VI) of the proton at C^{16} (δ 4.38 ppm), which resonates in the form of the X part of the ABX spectrum, correspond to the proposed structure and the stereochemistry of coupling of the D and E rings. Namely, this character of the C^{16}-proton was observed for all the natural spirostanes with a β-cis-coupling of the D and E rings [7], and also for the known synthetic steroids with a tetrahydropyran ring E with a similar stereochemistry [8]. A further convincing proof for the β-stereochemistry of the substitution at C^{16} atom is the paramagnetic shift of the signal of the C^{18}-methyl group to the 1.23-1.33 ppm region, observed in the spectra of (VIb-d) and characteristic for 16β-substituted pregnanes [8, 9]. In the PMR spectra of (VIb-d) there are two well-separated weak-field signals of the NH protons, characteristic for the NH—CS—NH group [10]. Other physicochemical characteristics, confirming the presence of this group, are the occurrence of a fragmentation in the mass spectra of compounds (VIa-d) with the elimination of this grouping, the UV spectroscopy data (λ_{max} 245-247 nm, log ε 4.26-4.39 [11]). The presence of the NH—CS—NH fragment in (VI) is also confirmed by the $\delta^{13}C$ values of the carbon atom of the C=S group bound to two amine type nitrogen atoms, which are characteristic for thioureas with a cyclic structure [12].

Numerous alternative structures were examined, which are possible during the transformation of (IIIc) in MeOH proceeding with the opening of the aziridine ring both at the C^{16}—N and at the C^{17}—N bonds with different modes of the intramolecular stabilization of the C^{16} or C^{17}-carbocations thus formed (for example, the migration processes $C^{13}Me \rightarrow C^{17}$, $C^{20}(OH) \rightarrow C^{17}$). None of the thus possible structures satisfies the above cited physicochemical characteristics and chemical properties as completely as (VI) can be predicted. We therefore decided that the structure of compound (VId) should be subjected to x-ray diffraction analysis, the results of which will be reported in a separate article (Fig. 1).

EXPERIMENTAL

The melting points were determined on a Koffler block. The IR spectra were recorded

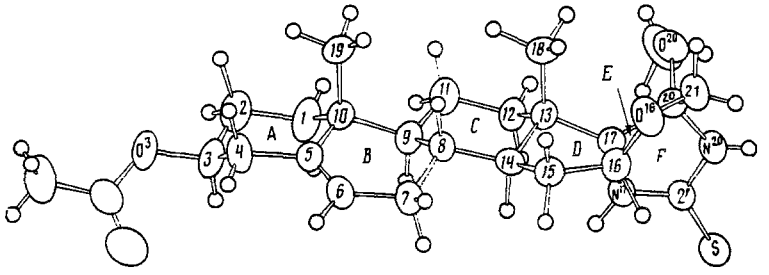


Fig. 1. Structure of molecule of (VI). The nonhydrogen atoms (numerated) are represented as thermal oscillation ellipsoids with p = 0.5.

on a UR-20 spectrophotometer in KBr tablets; the mass spectra were obtained on a Varian MAT CH-6 spectrometer with direct introduction of the sample into the ionic source. The UV spectra were run in EtOH on a Specord UV-VIS spectrophotometer. The ^{13}C NMR spectra (Table 1) were obtained on a Bruker AM-300 spectrometer with a working frequency of 300 MHz. The chemical shifts were measured relative to the $CDCl_3$ signal (δ = 77.1 ppm, solvent). The signals were assigned according to the δ values, the $J_{C,H}$ constants, multiplicity of signals, determined by the spin–echo method modulated by spin–spin interaction with $\tau = 1/J_{C,H}$ = 0.008 sec, 0.004 sec, DJ = 5TJ [13], experiments on a ^{13}C–{^1H} heteronuclear double selective resonance, and comparison with the spectra of the previously studied steroids with 16α, 17α-heterocyclic rings [6]. The PMR spectra were obtained on a Bruker WM-250 spectrometer with a working frequency of 250 MHz. For compound (VId), the chemical shifts of the H^{15} protons (1.48 and 2.20 ppm) were determined from a double resonance spectrum in a differential regime.

16α,17α-Epiminopregn-5-ene-3β,20ξ,21-triol-[16α,17α-N;20]-2',2'-dimethyl-1'3'-oxazine (IIc). A solution of 0.1 g of (Ib) in 10 ml of Me_2CO was held at 20°C for 48 h, and the crystals that separated were filtered off. Yield, 0.09 g of (IIc), mp 169-170°C. IR spectrum (ν, cm^{-1}): 1060, 1235, 1260, 1380, 3350, 3450. PMR spectrum (δ, ppm): 0.89 s (18-Me), 1.03 s (19-Me), 1.3 s and 1.58 s (2'-Me), 3.48 s (OH), 3.55 m (H^3), 3.74 and 3.83 (21-CH_2, AB spectrum, J = 12.8 Hz), 5.32 m (H^6).

20ξ-Methoxy-16α,17α-epiminopregn-5-ene-3β,21-diol-[16α,17α-N;20]-2',2'-dimethyl-1',3'-oxazine (IId). a) A solution of 0.02 g of (Ib) in 5 ml of MeOH and 4 ml of Me_2CO, containing 0.006 ml of H_2SO_4, was held at 20°C for 24 h. The solvent was distilled in vacuo, the residue was diluted with water, the mixture was neutralized with NH_4OH, and the precipitate that separated was filtered off. Yield, 0.025 g of (IId), mp 210-216°C (Me_2CO). IR spectrum (ν, cm^{-1}): 1060, 1375, 1455, 3220, 3500. PMR spectrum (δ, ppm): 0.91 s (18-Me), 1.03 s (19-Me), 1.35 s and 1.54 s (2'-Me), 3.32 s (20-OMe), 3.52 M (H^3), 3.87 (21-CH_2, the AB-part of the ABX spectrum, J = 11.7 Hz), 5.32 m (H^6). Mass spectrum (m/z): 417 M^+, 386 $[M - OMe]^+$, 359 $[M - COCMe_2]^+$, 344 $[M - NH - COCMe_2]^+$.

b) A solution of 0.26 g of (IV) [4] in 100 ml of MeOH, containing 0.27 ml of conc. H_2SO_4 was held at 20°C for 4 h, and then was neutralized with NH_4OH. The solvent was removed in vacuo, the residue was diluted with water, the precipitate that separated was filtered off, and the product obtained was crystallized from Me_2CO. Yield, 0.24 g of (IId), mp 205-210°C. The mother liquor was chromatographed on SiO_2 (TLC, $CHCl_3$–Me_2CO, 2:1) to yield 0.03 g of additional (IId).

3β,21-Diacetoxy-20ξ-methoxy-16α,17α-epiminopregn-5-ene-[16α,17α-N; 20]-2',2'-dimethyl-1',3'-oxazine (Va). A solution of 0.29 g of (IId) in 3.5 ml of Ac_2O and 6 ml of Py was held at 20°C for 16 h. After the usual treatment and crystallization from hexane, 0.22 g of (Va), mp 126-128°C was isolated. IR spectrum (ν, cm^{-1}): 1050, 1250, 1375, 1735. PMR spectrum (δ, ppm): 0.87 s (18-Me), 1.03 s (19-Me), 1.31 s and 1.52 s (2'-Me), 3.3 s (OMe), 4.29 and 4.39 (21-CH_2, AB-spectrum, J = 12.2 Hz), 4.6 m (H^3), 5.36 m (H^6). Mass spectrum (m/z): 501 M^+, 470 $[M - OMe]^+$, 443 $[M - COCMe_2]^+$, 400 $[M - COCH_2OAc]^+$. The mother liquor was chromatographed on SiO_2 (TLC, Et_2O–hexane, 2.5:1) to yield additional 0.1 g of (Va).

21-Acetoxy-20ξ-methoxy-16α,17α-epiminopreg-5-en-3β-ol-[16α,17α-N; 20]-2',2'-dimethyl-1',3'-oxazine (Vb). A 0.07 ml portion of Ac_2O was added to a solution of 0.07 g of (IId) in 11 ml of Py, cooled to 2-10°C. The mixture was held at −10°C for 6 days, while monitoring the course of the reaction chromotographically. It was then evaporated in vacuo by azeotropic distillation with MeOH and hexane, and the dry residue was separated by TLC (SiO_2, benzene–MeOH, 10:1), isolating, together with 0.023 g of (Va), 0.022 g of (Vb), mp 164-169°C (Et_2O–hexane). IR spectrum (ν, cm^{-1}): 1060, 1255, 1385, 1722, 1740, 3500. PMR spectrum (δ, ppm): 0.9 s, (18-Me), 1.023 s (19-Me), 1.32 s and 1.51 s (2'-Me), 2.09 s (21-OAc), 3.29 s (20-Me), 3.52 m (H^3), 4.28 and 4.39 (21-CH_2, AB spectrum, J = 12 Hz), 5.32 m (H^6). Mass spectrum (m/z): 459 M^+, 428 $[M - OMe]^+$, 401 $[M - COMe_2]^+$, 358 $[M - COCH_2 - OAc]^+$.

3,21-Diacetoxy-16α,17α-epiminopregn-5-en-20-one (Ic). A 12-ml portion of a methanolic solution of HCl (10:1) was added to a solution of 0.075 g of (Va) in 6 ml of HOAc, the mixture was held for 2 days at 20°C, and then neutralized with NH_4OH. It was then evaporated in vacuo, the residue was diluted with water, and the precipitate that separated was filtered off, and recrystallized from MeOH. Yield, 0.02 g of (Ic), mp 200-205°C [5]. From the mother liquor, 0.008 g of initial (Va), 0.02 g of (Ic) and 0.006 g of 3β-acetoxy-16α,17α-epiminopregn-5-en-21-ol-20-one, mp 197-202°C, were isolated by TLC (SiO_2, benzene–MeOH, 10:1) [4].

21-Acetoxy-16α,17α-epiminopreg-5-en-3β-ol-20-one (Id). A 2.3-ml portion of a methanolic solution of HCl (10:1) was added to a solution of 0.014 g of (Vb) in 1.2 ml of HOAc. The mixture was held for 3 days at 20°C, neutralized with NH_4OH, and evaporated in vacuo. The residue was diluted with water, the precipitate was filtered off and recrystallized from MeOH. Yield 0.01 g of (Id), mp 148-153°C. IR spectrum (ν, cm^{-1}, KBr): 1052, 1238, 1380, 1438, 1715, 1745, 3400. PMR spectrum (δ, ppm): 0.9 s (18-Me), 1.02 s (19-Me), 1.32 s and 1.52 s (2'-Me), 2.09 s (21-OAc), 3.29 s (20-OMe), 3.52 m (H^3), 4.3 and 3.39 (21-CH_2, AB-spectrum, J = 12 Hz), 5.32 m (H^6). Mass spectrum (m/z): 387 M^+, 372 $[M - NH]^+$, 344 $[M - Ac]^+$, 327 $[M - HOAc]^+$, 312 $[M - NH - HOAc]^+$.

3-Acetoxy-16α,17α-epiminopregn-5-en-20α-ol-[16α,17α-N; 20β]-1',3'-imidazolidine-2'-thione (IIIa). a) A 0.08-g portion of carbethoxyhydrazine thiocyanate [3] was added to a suspension of 0.15 g of (Ib) in 3 ml of dioxane. The reaction mixture was stirred for 5 min at 20°C, and the solvent was then removed in vacuo (20°C, 25 min), the residue was diluted with water, and the precipitate filtered off. Yield, 0.19 g of a product, from which 0.1 g of (IIIa), mp 203-206°C (MeOH) was isolated by TLC (benzene–MeOH, 6:1). IR spectrum (ν, cm^{-1}): 1040, 1100, 1180, 1250, 1380, 1452, 1515, 1736, 3165, 3330. UV spectrum: λ_{max} 266 nm, log ε 4.08. PMR spectrum (δ, ppm): 1.02 s and 1.05 s (18-Me, 19-Me), 1.7 s (21-Me), 2.02 s (3-OAc), 2.81 s (16-H), 3.5 br. s (OH), 4.62 m (H^3), 5.38 m (H^6), 7.92 br. s (NH). Mass spectrum (m/z): 430 M^+, 371 $[M - HSCN]^+$, 356 $[M - HSCN - NH]^+$, 296 $[M - HSCN - NH - HOAc]^+$.

b) A suspension of 0.2 g of (Ib) and 0.08 g of Py·HSCN in 4 ml of dioxane was stirred at 20°C for 1 h 10 min. The solvent was removed in vacuo at 20°C (5 min), the residue was diluted with water, and the precipitate that separated was filtered off and crystallized from MeOH to yield 0.09 g of (IIIa).

On prolonged standing (~3 days) or on heating compound (IIIa) for 6 h in $CHCl_3$, (Ib) is regenerated.

3β-Acetoxy-20α-methoxy-16α,17α-epiminopregn-5-en-[16α,17α-N; 20β]-1',3'-imidazolidine-2'-thione (IIIb). A solution of 0.03 g of (IIIa) in 2 ml of MeOH was boiled for 50 min, was then evaporated in vacuo, and the residue was purified by TLC (benzene–MeOH, 6:1). Yield, 0.028 g of (IIIb), mp 199-201°C ($CHCl_3$–Et_2O). IR spectrum (ν, cm^{-1}): 1040, 1115, 1250, 1380, 1440, 1460, 1505, 1731, 3120-3300. UV spectrum: λ_{max} 266 nm, log ε 4.13. PMR spectrum (δ, ppm): 1.00 s (18-Me, 19-Me), 1.65 s (21-Me), 2.02 s (3-OAc), 3.3 s (20-OMe), 4.6 m (H^3), 5.32 m (H^6), 8.8 br. s (NH). Mass spectrum (m/z): 444 M^+, 412 $[M - MeOH]^+$, 397 $[Me - MeOH - Me]^+$, 352 $[M - MeOH - HOAc]^+$, 337 $[M - MeOH - HOAc - Me]^+$.

16β,21-Epoxypregn-5-ene-3β,20α-diol-[17α,20β-d]-1',3'-imidazolidine-2'-thione (VIa). a) A solution of 0.04 g of (IIIc) [3] in 5 ml of MeOH was boiled for 20 min, the solvent was then distilled off in vacuo, and the residue was crystallized from aqueous MeOH. Yield, 0.038 g of (VIa), mp 291-292°C (dec). IR spectrum (ν, cm^{-1}): 1050, 1335, 1515, 1620 w, 3200-3330, 3400. UV spectrum: λ_{max} 245 nm, log ε 4.29. Mass spectrum (m/z): 404 M^+, 386 $[M - H_2O]^+$, 371 $[M - H_2O - Me]^+$, 368 $[M - 2H_2O]^+$, 330 $[M - NHCSNH_2]$, 314 $[M - HSCN - CH_2OH]^+$.

b) A suspension of 0.005 g of (IIIc) in 2 ml of H_2O and 0.03 ml of 5% HCl was stirred for 50 h at 20°C. The reaction mixture was neutralized with $NaHCO_3$, and the precipitate was filtered off. Yield, 0.005 g of (VIa).

c) A 0.006-ml portion of H_2SO_4 in 1 ml of MeOH was added to a suspension of 0.02 g of (IIIc) in 5 ml of MeOH, and the reaction mixture was stirred for 7 min at 20°C, then evaporated in vacuo, the residue was diluted with water, and the precipitate was filtered off. Yield, 0.019 g of (VIIa).

3β-Acetoxy-16β,21-epoxypregn-5-en-20α-ol-[17α,20β-d]-1',3'-imidazolidine-2'-thione (VIc). A solution of 0.05 g of (VIIa) in 1.5 ml of Py and 0.5 ml of Ac_2O was held for 19 h at 20°C and then was treated in the usual way. Yield, 0.035 g of (VIIc), mp 298-299°C (MeOH). An additional 0.011 g of (VIc) was isolated from the mother liquor by TLC. IR spectrum (ν, cm^{-1}): 1030, 1060, 1130, 1240, 1410, 1460, 1530, 1735, 3250. UV spectrum: λ_{max} 245 nm, log ε 4.29. PMR spectrum (δ, ppm): 1.01 s (19-Me), 1.33 s (18-Me), 2.05 s (3-OAc), 2.59 s (OH), 4.18 and 4.26 (21-CH_2, AB spectrum, J = 10 Hz), 4.38 (H^{16}, the X-part of the ABX-spectrum, J = 4 and 7.5 Hz), 4.62 m (H^3), 5.39 m (H^6), 6.43 s and 6.6 s (2NH). Mass spectrum (m/z): 446 M^+, 428 $[M - H_2O]^+$, 415 $[M - OMe]^+$, 386 $[M - HOAc]^+$, 371 $[M - NH_2CSNH]^+$, 368 $[M - HOAc - H_2O]^+$, 354 $[M - NHCSNH - H_2O]^+$, 341 $[M - NH_2CSNH - CH_2O]^+$, 339.

20α-Methoxy-16β,21-epoxypregn-5-en-3β-ol-[17α,20β-d]-1',3'-imidazolidine-2'-thione (VIb). A solution of 0.18 g of (IIIc) in 45 ml of MeOH, containing 0.05 ml of H_2SO_4 was boiled for 6 h, then evaporated in vacuo, the residue was diluted with water, the mixture was neutralized with $NaHCO_3$, and the precipitate was filtered off, and recrystallized from MeOH. Yield, 0.08 g of (VIb), mp 279-282°C. IR spectrum (ν, cm^{-1}): 1065, 1203, 1230, 1435, 1520, 1635, 3210, 3370-3440. PMR spectrum (δ, ppm): 1.03 s (19-Me), 1.23 s (18-Me), 3.33 s (20-OMe), 3.55 m (H^3), 4.14 and 4.23 (21-CH_2, AB-spectrum, J = 10 Hz), 4.38 (H^{16}, the X-part of the ABX spectrum, J = 4 and 7.5 Hz), 5.35 m (H^6), 7.02 s and 7.4 s (2NH). UV spectrum: λ_{max} 246 nm, log ε 4.26. Mass spectrum (m/z): 418 M^+, 400 $[M - H_2O]^+$, 386 $[M - MeOH]^+$, 370 $[M - H_2O - CH_2O]^+$, 338 $[M - H_2O - MeOH - CH_2O]^+$, 329 $[M - CH_2O - HSCN]^+$, 314 $[M - CH_2O - NHCSNH]^+$, 296 $[M - H_2O - CH_2O - NHCSNH]^+$. Another 0.05 g of (VI) was isolated from the mother liquor by TLC (SiO_2 MeOH–$CHCl_3$ 1:35).

3β-Acetoxy-20α-methoxy-16β,21-epoxypregn-5-ene-[17α,20β-d]-1',3'-imidazolidine-2'-thione (VId). A solution of 0.01 g of (VIIb) in 0.5 ml of Py and 0.1 ml of Ac_2O was held at 20°C for 18 h, was then evaporated in vacuo with heptane, and the residue was purified by TLC (SiO_2, $CHCl_3$) to yield 0.006 g of (VId), mp 276-277°C (dec). IR spectrum (ν, cm^{-1}): 1035, 1075, 1090, 1250, 1260, 1375, 1430, 1520, 1735, 3220, 3370. UV spectrum: λ_{max} 247 nm, log ε 4.39. PMR spectrum (δ, ppm): 1.04 s (19-Me), 1.23 s (18-Me), 2.05 s (3-OAc), 3.32 s (OMe), 4.16 and 4.22 (21-CH_2, AB-spectrum, J = 9.9 Hz), 4.38 (H^{16}, the X-part of the ABX-spectrum, J = 4 and 7.5 Hz), 5.38 m (H^6), 7.15 s and 7.56 s (2NH). Mass spectrum (m/z): 460 M^+, 429 $[M - OMe]^+$, 400 $[M - HOAc]^+$, 385 $[M - NH_2CSNH]^+$, 369 $[M - HOAc - OMe]^+$, 355 $[M - NHCSNH - OMe]^+$, 339 $[M - HOAc - OMe - CH_2O]^+$, 326 $[M - HOAc - NHCSNH]^+$.

CONCLUSIONS

1. The transformation of 21-O,N-isopropylidene derivatives of 16α,17α-epiminopregn-5-ene-2β,21-diol-20-one into 20-O,N-isopropylidene derivatives of 16α,17α-epiminopregn-5-ene-3β,20-diol-20-one was discovered, and, based on this, a new variant of the synthesis of 16α,17α-epiminopregn-5-ene-3β,21-diol-20-one-3',21-diacetate was proposed.

2. A new class of steroids with additional tetrahydrofuran and 1',3-imidazolidine-2'-thione rings E and F, respectively, was synthesized.

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