MODIFIED STEROIDS.

103.* SPLITTING OF THE 17-C—N BOND OF 16,17α-EPIMINO-20-KETOSTEROIDS AND THEIR 20-HYDRAZONES BY REACTION WITH THIOACETIC ACID

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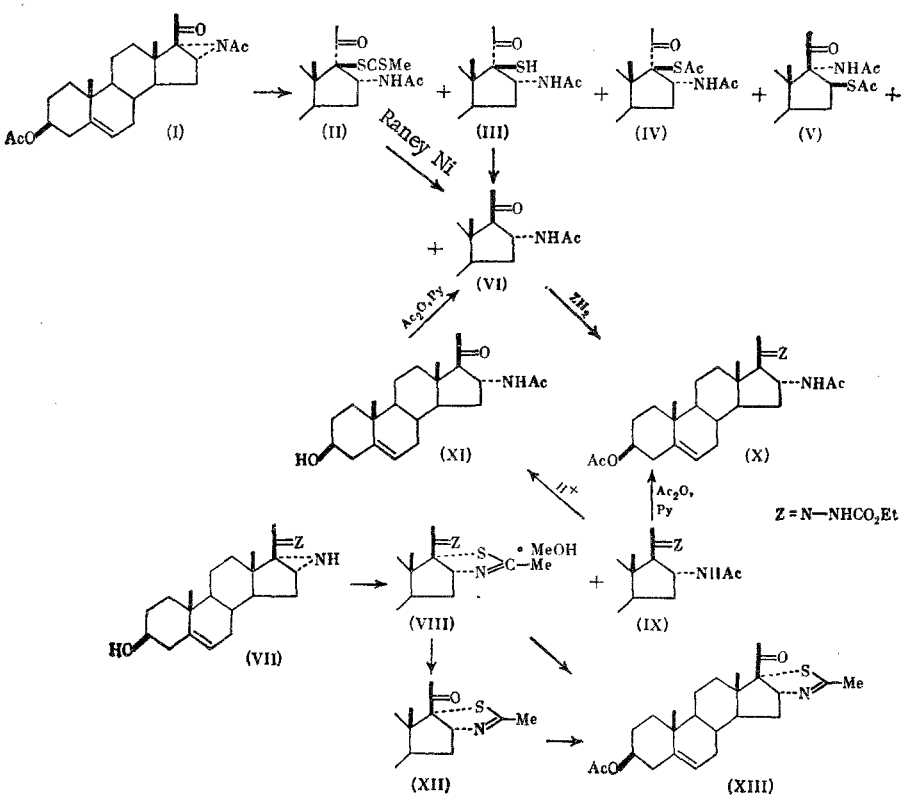
We have studied the reaction of 16,17α-epimino-20-ketosteroids and their 20-carbethoxyhydrazides with thioacetic acid. In the process, in contrast to [2-4], we have discovered a uniform structural direction of scission of the aziridine ring: the reaction proceeds independently of the substituent at 20-C, with scission of the 17-C—N bond next to the carbonyl group and the hydrazone fragment.

The reaction of epiminopregnenolone 3,N-diacetate (I)† with freshly distilled thioacetic acid proceeds very slowly to yield a complex mixture from which the following products were separated and identified: 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-diacetate 17-thioacetate (II), 13%; 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-diacetate (III), 20%; 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16,17-triacetate (IV), 7%; 17α-aminopregn-5-en-3β-ol-16β-thiol-20-one 3,16,17-triacetate (V), 6%; 16α-aminopregn-5-en-3β-ol-20-one 3,16-diacetate (VI), 8%. Thioacetate V is identical with the previously



*Previous communication, [1].

†Under the reaction conditions, 16,17α-epiminopregnenolone first undergoes acetylation of the epimino group with thioacetic acid.

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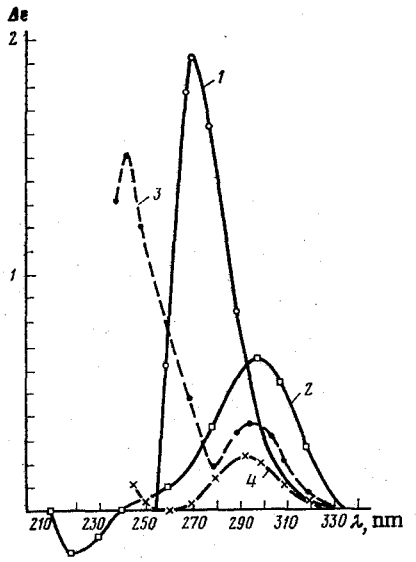


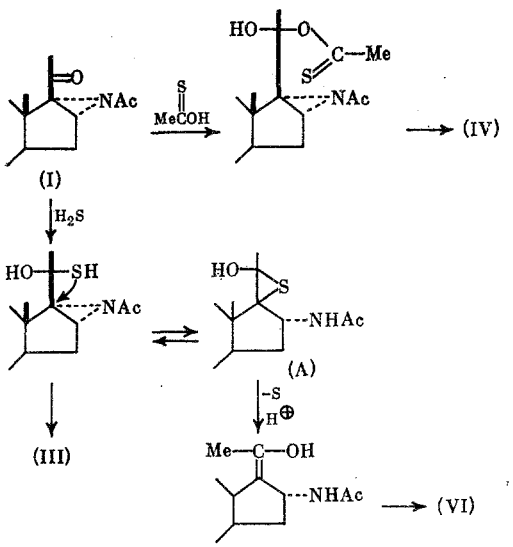
Fig. 1. CD curves, taken in alcohol: 1) 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-diacetate 17-thioacetate (II); 2) 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-diacetate (III); 3) 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16,17-triacetate (IV); 4) 17α-aminopregn-5-en-3β-ol-16β-thiol-20-one 3,16,17-triacetate (V).

identified sample [3, p. 1132]. The structure of the amide VI follows from the spectral data and the elemental analysis. In the PMR spectrum the amide proton signal appears as a broadened doublet in the weak field (δ 6.05 ppm) with J = 3 Hz. This confirms the secondary character of the amide group, because such a broadening of signal is caused by the vicinal interaction of the NH—CH with the proton at 16-C, which appears with δ 4.62 ppm [5]. Alternative structures for 17α (or β)-aminopregn-5-en-3β-ol-20-one 3,17-diacetates [3, p. 1132], [6], or 16α-amino-18-nor-17β-methyl-17α-pregna-5,13-dien-3β-ol-20-one 3,16-diacetate [3, p. 1132] are excluded by comparison with the samples described. The α-configuration of the amide function at 16-C follows from the stereochemistry of the starting aziridine.

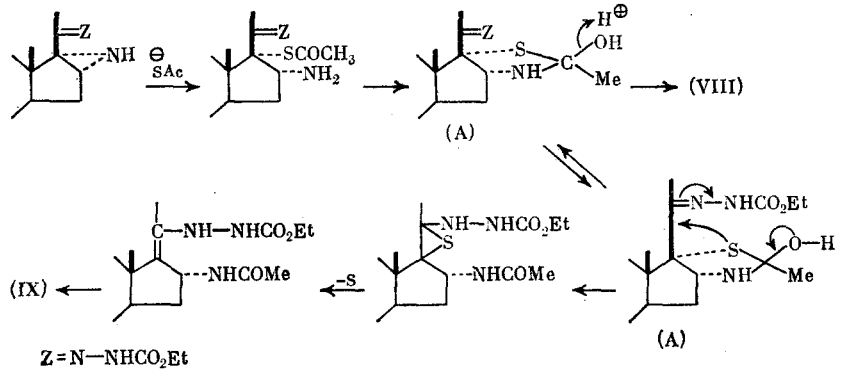
Compounds II, III, and IV have a sulfur-containing function at 17-C, since desulfurization of II and III over Raney Ni in ethanol forms the 16α-acetylamine (VI). While desulfurization of the thiol III proceeds smoothly at room temperature, desulfurization of the ether II requires heating, which is accompanied by the side reaction of reductive elimination of the amide group to form pregn-5-en-3β-ol-20-one 3-acetate. It may be assumed that desulfurization of II precedes cyclization by intramolecular substitution of the amide group by the $SC(=S)CH_3$. The elemental analysis showing the presence of two S atoms in the molecule permits the assumption that II has a dithiono ester structure, which apparently forms by a secondary reaction, the acylation of thiol III by the thiono form of thioacetic acid [7, 8]. The iso configuration of the 17-acetyl group in II, III, and IV, resulting from the general principle of preferred transcission of the aziridine ring, seems preferable for the following considerations. First, the acetylation of the thiol III to form the thiol acetate IV goes quite rapidly (∿2.5 h), which is not typical of the 17α-thiol group [9, 10]. In the PMR spectra of II-IV the proton signals of the angular methyl group at 18-C are deshielded (1.18-1.08 ppm). The same applies to the signals of the 21-CH_3 group. Such deshielding is caused by the iso configuration of the 17-acetyl group [11]. Analysis of the CD spectra confirms this conclusion. Thus, the weak positive n—π Cotton effect (CE) (see Fig. 1) observed for thiol III and its acetate IV is not typical of 17β-pregnane compounds with a sulfur-containing function alpha to the carbonyl chromophore, which show negative CE [12].

The CD curve of the dithiono ester II is characterized by a CE of medium intensity with λ_{max} of 273 nm ($\Delta\varepsilon$ 1.92), due to the SCSCH group, against the background of which the weak or zero $n \rightarrow \pi$-CE of the carbonyl chromophore is not detected. The observed values and signs of the CE permit the conclusion that II, III, and IV belong not to the 17β-, but to the 17α-pregnane series, the chiral optical properties of which, for all practical purposes, have not been investigated.

The unusual preferred direction of the scission of the aziridine ring with the splitting of the 17-C—N bond next to the carbonyl group must apparently be explained by the fact that the thioacetic acid first attacks the carbonyl group, and the largest partial positive charge in N-acetylepimine (I) is localized at the 20-C carbonyl atom. Under these circumstances the reactive species may be thioacetic acid in the thiono form, or it may be hydrogen sulfide formed by the decomposition of thioacetic acid [7, 8]. The subsequent intramolecular attack by sulfur on the neighboring aziridine C atom, with concurrent scission of the C—N bond according to the scheme presented below, leads to the amides III and IV. Within the framework of this scheme it is easy to visualize the formation of amide VI through an intermediate episulfide (A) that loses sulfur easily under acidic condition [13]. The proposed mechanism agrees with the known tendency of hydrogen sulfide and mercaptans to add to the carbonyl group of epoxyketones [14], or of thiocyanic acid to add to the carbonyl group of 16,17α-epimino-20-ketosteroids [3, p. 1147].



The reaction of 16,17α-epiminopregnenolone (VII) 20-carbethoxyhydrazone with thioacetic acid, which is 1000 times faster than the preceding reaction, proceeds more unequivocally to give mainly two products: 2'-methylpregn-5-en-3β-ol-20-one[16,17α-d]thiazoline 20-carbethoxyhydrazone (VIII), and 16α-acetylaminopregn-5-en-3β-ol-20-one 20-carbethoxyhydrazone (IX). The reaction is sensitive to very small changes in conditions (duration of reaction, method of workup, solvent). The ratio of products is highly variable; increasing the reaction time yields a complex assortment of products. Generally, an alkaline medium during workup favors the formation of a product that does not contain sulfur (IX). The same is observed in the workup of the aqueous reaction medium without preliminary neutralization, i.e., acidic medium also favors the formation of IX. It may be assumed that formation of both reaction products proceeds through one and the same intermediate. The following scheme may be proposed to explain the observed course of the reaction. The protonated form of the aziridine, as also in [2, 4], under the influence of the hydrazone fragment undergoes cis scission with introduction of a SAc ion at the 17 position to form a 17α-thioacetate-16α-amine. Allowing for the tendency of systems with cis-oriented substituents to undergo acyl migration, we may postulate an intermediate stage such as A, that stabilizes itself (see Scheme) by forming the thiazoline VIII and the 16α-acetylamine IX. In confirmation it may be said that the formation of the A type intermediate both in the acid-catalyzed acyl migration of S-acetylthioamides and in the acid hydrolysis of thiazolines is kinetically demonstrated [15, 16].



In aqueous methanol solution the carbethoxyhydrazones VIII and IX give the ketones XII and XI, respectively. The proof of structure of the latter and, consequently, of its precursor IX leads to amide VI by the reactions indicated in the scheme. The structures of the thiazolines XII and XIII follow from their physical and chemical properties. Thus, the mass spectra show molecular peaks with m/e of 387 and 429, respectively. The subsequent fragmentation, which includes scission of groups with m/e of CH_3 and $COCH_3$, confirms the proposed structures. The IR spectra of XII and XIII contain the absorption typical of an endocyclic C=N bond at 1638 and 1648 cm^{-1}, respectively. In the PMR spectrum of XII the signal of the 2-methyl proton appears as a doublet at 2.07 ppm, with J = 1.5 Hz, which is analogous to 2'-methylpregn-5-en-3β-ol-[16,17α-d]-oxazoline, in which the signal of the 2'-methyl protons tends to split with δ 1.98 ppm [2]. Formation of a thiazoline in this reaction is possible only if the principle of cis-scission of the aziridine is observed; therefore, the location of the heteroatoms and the α-configuration of the heterocyclic ring must be assigned by analogy with the previously described heterocyclizations that occur under the same conditions [2]. The thiazolines obtained are a new class of 20-ketosteroids.

EXPERIMENTAL

Melting points were determined on a Kofler block. PMR spectra were taken on a Varian DA-60IL spectrometer (60 MHz) in $CDCl_3$; internal standard TMS. IR spectra were taken on a UR-10 apparatus in a KBr mold or in $CHCl_3$ solution. UV spectra were taken on a Specord UV-VIS apparatus in alcohol; mass spectra were taken on the MAT CH-6 recording mass spectrometer with direct introduction of the sample into the ion source at 70-eV ionizaing voltage; CD spectra were taken on a Spectropol apparatus in alcohol solution at concentrations of ∿0.001 mole/liter.

Reaction of 16,17α-Epiminopregn-5-en-3β-ol-20-one 3-Acetate (I) with Thioacetic Acid. A solution of 3 g of I in 30 ml of distilled HSAc containing 0.15 g of hydroquinone was kept at 20°C for 9 days. The reaction mixture was washed with water and neutralized with ammonia, and the precipitate was filtered off and dried. The product (4 g) was chromatographed on a column (SiO_2, ether—hexane), with subsequent separation of the intermediate fractions by TLC*: a) 0.48 g of dithiono ester II, mp 215-217°C (CH_3OH). IR spectrum (ν, cm^{-1}, $CHCl_3$): 1040, 1260, 1340-1400, 1525, 1700, 1730, 3398. PMR spectrum (δ, ppm): 1.06 s (3 H, 19-CH_3), 1.18 s (3 H, 18-CH_3), 2.07 s (3 H, 3-OAc), 2.33 s (3 H, NHAc), 2.36 s (3 H, 21-CH_3), 2.42 s (3 H, SCSCH_3), 5.36 br.1 (H, 6-H), 5.83 br. 1 (H, 16-H), 8.34 br. d (H, NH). UV spectrum (C_2H_5OH): λ_{max} 273 nm (ε 10400). Mass spectrum (m/e): 505 (M^+), 462 (M^+ — 43), 430, 420, 403, 396, 389, 372. Found: C 64.11; H 7.74; S 12.57; N 2.82%. $C_{27}H_{39}O_4S_2N$. Calculated: C 64.14; H 7.78; S 12.66; N 2.74%.

b) 0.73 g of thiol III, mp 165-167°C (acetone—hexane). IR spectrum (ν, cm^{-1}, $CHCl_3$): 1040, 1260, 1510, 1670, 1690, 1730, 2550, 3450. PMR spectrum (δ, ppm): 1.06 s (3 H, 19-CH_3), 1.16 s (3 H, 18-CH_3), 1.97 s (3 H, NHAc), 2.04 s (3 H, OAc), 2.34 s (3 H, 21-CH_3), 4.76 br. 1 (2 H, 3-H, 16-H), 5.39 br. 1 (H, 6-H), 6.28 br. d (H, N—H). Mass spectrum (m/e): 447 (M^+), 414 (M^+ — SH), 404 (M^+ — $COCH_3$), 388 ($M-NH_2COCH_3$), 370 ($M^+-H_2S-COCH_3$), 328 ($M^+-HOAc-NH_2COCH_3$), 311 (M^+ — NH_2COCH_3 — $COCH_3$ — H_2S). Found: C 67.09; H 8.32; S 7.13; N 3.00%. $C_{25}H_{37}O_4SN$. Calculated: C 67.09; H 8.33; S 7.12; N 3.13%.

*The amounts refer to the chromatographically uniform product. The materials are listed in order of decreasing chromatographic mobility.

c) 0.24 thiolacetate IV, mp 208-209°C (CH_3OH). IR spectrum (ν, cm^{-1}, $CHCl_3$): 1040, 1120, 1265, 1523, 1665, 1695, 1730, 3450. PMR spectrum (δ, ppm): 1.00 s (3 H, 19-CH_3), 1.08 s (3 H, 18-CH_3), 1.83 s (3 H, NHAc), 2.00 s (3 H, OAc), 2.28 s (3 H, 21-CH_3), 2.3 s (3 H, SAc), 4.71 br. 1 (H, 3-H), 5.00 br. 1 (H, 16-H), 5.33 br. 1 (H, 6-H), 6.60 br. d (H, N—H). UV spectrum (C_2H_5OH): λ_{max} 238 nm (ε 2400). Mass spectrum (m/e): 489 (M^+), 447 ($M^+ - COCH_2$), 429 ($M^+ - HOAc$), 414 ($M^+ - SCOCH_3$), 404 ($M^+ - COCH_2 - COCH_3$), 387 ($M^+ - COCH_3 - NH_2COCH_3$), 355, 345, 328, 310, 295. Found: C 66,47; H 8.03; S 6.50; N 2.71%. $C_{27}H_{39}O_5SN$. Calculated: C 66.23; H 8.03; S 6.54; N 2.86%.

d) 0.22 g of thiol V, mp 287-290°C (acetone), identical with the sample previously obtained [3, p. 1132].

e) 0.35 g of amine VI, mp 132-133°C; solidifies and melts at 219-221°C (CH_3OH), mp 219-220°C (acetone). IR spectrum (ν, cm^{-1}, KBr): 1038, 1250, 1560, 1650, 1700, 1735, 3280. IR spectrum (ν, cm^{-1}, $CHCl_3$): 1038, 1260, 1520, 1670, 1710, 1730, 3460. PMR spectrum (δ, ppm): 0.71 s (3 H, 18-CH_3), 1.05 s (3 H, 19-CH_3), 2.04 s (3 H, NHAc), 2.07 s (3 H, OAc), 2.20 s (3 H, 21-CH_3), 4.62 br. 1 (2 H, 3-H, 16-H), 5.36 br. 1 (H, 6-H); 6.05 br. d (H, NH). Mass spectrum (m/e): 415 (M^+), 400 ($M^+ - 15$), 372 ($M^+ - COCH_3$), 355 ($M^+ - HOAc$), 340 ($M^+ - HOAc - 15$), 330 ($M^+ - COCH_3 - COCH_2$), 312 ($M^+ - HOAc - COCH_3$). Found: C 69.55; H 8.77; N 2.93%. $C_{25}H_{37}O_4N \cdot CH_3OH$. Calculated: C 69.75; H 9.23; N 3.13%.

Acetylation of 16α-Amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-Diacetate (III). A solution of 0.013 g of thiol III in 0.13 ml of C_5H_5N and 0.3 ml of Ac_2O was held for 2.5 h at 20°C. There was obtained 0.015 g of product, crystallization of which from acetone—hexane yielded 0.009 g of thiolacetate IV, mp 208-209°C.

Saponification of 16α-Amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-Diacetate 17-Thioacetate (II). A solution of 0.04 g of thione II in 10 ml of abs. CH_3OH containing 1 drop of conc. H_2SO_4 was kept for 2 days at 20°C. The solvent was evaporated, and the residue was washed with water and dried. There was obtained 0.026 g of 16α-amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 16-acetate 17-thioacetate, mp 252-259°C (from aq. CH_3OH). IR spectrum (ν, cm^{-1}, $CHCl_3$): 1120, 1360, 1400, 1690, 3395, 3620. PMR spectrum (δ, ppm): 1.00 s (3 H, 19-CH_3), 1.13 s (3 H, 18-CH_3), 2.30 s (3 H, NHAc), 2.31 s (3 H, 21-CH_3), 2.41 s (3 H, $CSCH_3$), 5.85 br. 1 (H, 16-H). Mass spectrum (m/e): 463 (M^+), 420 ($M^+ - COCH_3$), 388, 378, 361, 354, 347, 330. Reacetylation of 0.01 g of the product in 0.2 ml of C_5H_5N and 0.1 ml of Ac_2O yielded II, mp 215-217°C.

Reaction of 16,17α-Epiminopregn-5-en-3β-ol-20-one 20-Carbethoxyhydrazone (VII) with Thioacetic Acid. A solution of 0.4 g of VII in 4 ml of HSAc containing 0.02 g of hydroquinone was kept for 30 min at 20°C. HSAc was partly evaporated in vacuum, water was added to the residue, and the mixture was neutralized with $NaHCO_3$ solution, and the precipitate was filtered off. The product weighed 0.44 g. By means of TLC (benzene—methanol 7:1) there were separated: a) 0.15 g of thiazoline VIII, mp 279-282°C (acetone); mp 163.5°C (CH_3OH). IR spectrum (ν, cm^{-1}, KBr, sample crystallized from CH_3OH): 1060, 1235, 1440, 1538, 1640, 1735, 3250, 3450. IR spectrum (ν, cm^{-1}, KBr, sample crystallized from acetone): 1065, 1230, 1435, 1522, 1632, 1710, 1730 (sh), 1740, 3200-3500. IR spectrum (ν, cm^{-1}, $CHCl_3$): 1050, 1150, 1385, 1440, 1510, 1645, 1715, 1750, 3400, 3615. PMR spectrum of sample crystallized from CH_3OH (δ, ppm): 0.77 s (3 H, 18-CH_3), 0.95 s (3 H, 19-CH_3), 1.25 t (3 H, CH_3 of hydrazone fragment), 1.85 s (3 H, 21-CH_3), 2.08 s (3 H, 2'-CH_3), 2.32 s (3 H, OCH_3), 3.5 br. 1 (H, 3-H), 4.18 q (2 H, hydrozone CH_2), 5.28 br. 1 (H, 6-H), 5.87 br. 1 (H, 16-H), 7.71 s (NH). PMR spectrum of sample crystallized from acetone (δ, ppm): 0.76 s (3 H, 18-CH_3), 0.96 s (3 H, 19-CH_3), 1.26 t (3 H, hydrazone CH_3), 1.85 s (3 H, 21-CH_3), 2.1 br. s (3-H, 2'CH_3), 4.2 q (2H, CH_2 hydrazone), 5.27 br. 1 (H, 6-H), 5.9 br. 1 (H, 16-H), 7.61 s (NH). UV spectrum (C_2H_5OH): λ_{max} 227 nm (ε 15,100). Mass spectrum (m/e): 473 (M^+), 458 ($M^+ - CH_3$), 440 ($M^+ - CH_3 - H_2O$), 385 ($M^+ - NHCO_2Et$), 370 ($M^+ - NHCO_2Et - CH_3$).

b) 0.18 g of acetylamine IX, mp 270-273°C (CH_3OH). IR spectrum (ν, cm^{-1}, KBr): 1050, 1250, 1535, 1650, 1720, 3200-3600. UV spectrum (C_2H_5OH): λ_{max} 228 nm (ε 13100). Mass spectrum (m/e): 459 (M^+), 400 ($M^+ - NH_2COCH_3$), 371 ($M^+ - NHCO_2Et$), 312 ($M^+ - NH_2COCH_3 - NHCO_2Et$). Found: C 66.50; H 8.92; N 8.43%. $C_{26}H_{41}O_4N_3 \cdot CH_3OH$. Calculated: C 65.96; H 9.23; N 8.55%.

16α-Aminopregn-5-en-3β-ol-20-one 20-Carbethoxyhydrazone 3,16-diacetate (X). 1) A solution of 0.02 g of the 20-carbethoxyhydrazone IX in 0.2 ml of Ac_2O and 0.6 ml of C_5H_5N was kept at 20°C for 6 h. The reaction mixture was treated with water, and the precipitate was

filtered off and recrystallized from acetone. The diacetate IX weighed 0.01 g, mp 233-240°C. IR spectrum (ν, cm^{-1}, KBr): 1045, 1240, 1550, 1650, 1720, 3335. IR spectrum (ν, cm^{-1}, $CHCl_3$): 1260, 1510, 1660, 1725, 3390, 3435. UV spectrum (C_2H_5OH): λ_{max} 229 nm (ε 16,500). PMR spectrum (δ, ppm): 0.70 s (3 H, 18-CH_3), 1.00 s (3 H, 19-CH_3), 1.28 t (3 H, hydrazone CH_3), 1.83 s (3 H, 21-CH_3), 1.88 s (3 H, NHAc), 2.00 s (3 H, 3-OAc), 4.2 q (2 H, hydrazone CH_2), 4.51 br. 1 (H, 3-H), 5.33 br. 1 (H, 6-H), 6.08 d (H, NH), 7.63 s (H, hydrazone NH). Mass spectrum (m/e): 501 (M^+), 486 (M^+ − 15), 441 (M^+ − HOAc), 413 (M^+ − $NHCO_2Et$), 382 (M^+ − HOAc)− NH_2Ac). Found: C 67.20; H 8.31; N 8.27%. $C_{28}H_{43}O_5N_3$. Calculated: C 67.03; H 8.64; N 8.38%.

2) A solution of 0.015 g of VI and 0.015 g of carbethoxyhydrazine in 0.3 ml of HOAc was held at 20°C for 30 min. The reaction mixture was treated with water, and the precipitate was filtered off, dried, and recrystallized from acetone. The diacetate X was obtained mp 233-240°C, identical with that described above.

16α-Aminopregn-5-en-3β-ol-20-one 16N-Acetate (XI). 1) A solution of 0.03 g of IX in 1.2 ml of CH_3OH and 0.5 ml of dilute HCl (1:1) was kept at 20°C for 3 days. The solvent was evaporated in vacuum, and the residue was treated with water and neutralized with ammonia. The precipitate was filtered off. The product weighed 0.025 g; crystallization from aq. CH_3OH yielded 0.012 g of XI, mp 244-247°C. IR spectrum (ν, cm^{-1}, KBr): 1067, 1570, 1640, 1700, 3100-3600. Mass spectrum (m/e): 373 (M^+), 358 (M^+ − 15), 330 (M^+ − $COCH_3$), 314 (M^+ − NH_2COCH_3).

2) A solution of 0.02 g of IX was kept for 24 h with HSAc containing hydroquinone. There was obtained 0.012 g of XI, identical with that described above. Acetylation of XI with acetic anhydride in pyridine yielded the diacetate VI, identical with that described above.

2'Methylpregn-5-en-3β-ol-20-one-[16,17α-d]-thiazoline (XII). A solution of 0.04 g of VIII in 5 ml of CH_3OH and 1 ml of aq. HCl (1:1) was boiled for 35 h. Methanol was partially removed by evaporation, water was added to the residue, and the mixture was neutralized with ammonia. The precipitate was filtered off. The product weighed 0.03 g; crystallization from CH_3OH yielded 0.025 g of the 2'-methylthiazoline XII, mp 277-281°C. IR spectrum (ν, cm^{-1}, KBr): 1075, 1158, 1638, 1702, 3385. UV spectrum (C_2H_5OH): λ_{max} 232 (ε 1855); λ_S 253 (ε 844). PMR spectrum (δ, ppm): 0.90 s (3 H, 18-CH_3), 0.97 s (3 H, 19-CH_3), 2.07 d (3 H, J = 1.5 Hz, 2'-CH_3), 2.20 s (3 H, 21-CH_3), 3.53 br. 1 (H, 3-H), 5.26 br. 1 (H, 6-H), 5.50 br. 1 (H, 16-H). Mass spectrum (m/e): 387 (M^+), 372 (M^+ − 15), 343 [(M^+ − 1) − $COCH_3$]. Found: C 70.49; H 8.89; S 8.38; N 4.12%. $C_{23}H_{35}O_2NS$. Calculated: C 70.92; H 9.06; S 8.21; N 3.60%.

2'-Methylpregn-5-en-3β-ol-20-one-[16,17α-d]-thiazoline 3-Acetate (XIII). A solution of 0.04 g of VIII in 1 ml of glacial AcOH containing 3 drops of conc. H_2SO_4 was kept at 20°C for 4 days. The reaction mixture was treated with water and neutralized with ammonia, and the precipitate was filtered off. A dark brown powder, 0.033 g, was obtained; purification by TLC (benzene—methanol 7:1) yielded 0.013 g of the 3-acetate (XIII), mp 210-211.5°C (from CH_3OH). IR spectrum (ν, cm^{-1}, KBr): 1035, 1150, 1245, 1648, 1702, 1730. Mass spectrum (m/e): 429 (M^+), 414 (M^+ − 15), 386 (M^+ − $COCH_3$), 369 (M^+ − HOAc), 354 (M^+ − HOAc − 15), 326 (M^+ − HOAc − $COCH_3$).

2) A solution of 0.006 g of XII was acetylated in 0.1 ml of Ac_2O and 0.5 ml of C_5H_5N for 6 h. After the usual workup and crystallization from aq. acetone, 0.004 g of the 3-acetate XIII was obtained, mp 210-211.5°C.

Desulfurization of 16α-Amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-Diacetate (III). A solution of 0.023 g of III in 6 ml of C_2H_5OH was stirred for 1 h at 20°C with Raney Ni. The catalyst was filtered off, and the solvent was removed by evaporation. The product weighed 0.025 g; crystallization from acetone—hexane yielded the 16α-acetylamine VI, mp 132-133°C; solidifies and melts at 219-221°C.

Desulfurization of 16α-Amino-17α-isopregn-5-en-3β-ol-17β-thiol-20-one 3,16-Diacetate 17-Thioacetate (II). A solution of 0.02 g of the dithiono ester II in 4 ml of C_2H_5OH was boiled with Raney Ni for 4 h. The catalyst was filtered off and washed with hot alcohol, and the solvent was removed by evaporation. The product weighed 0.02 g; TLC (SiO_2, ethyl acetate—hexane 1:6) yielded 0.007 g of pregn-5-en-3β-ol-20-one 3-acetate, mp 145-149°C, identical with a known sample, and 0.003 g of the 16α-acetylamine VI, mp 132-133°C; solidifies and melts at 219-221°C.

CONCLUSIONS

1. The reactions of 16,17α-epiminopregn-5-en-3β-ol-20-one and its 20-carbethoxyhydrazone with thioacetic acid proceed with different stereochemical direction of scission of the aziridine ring at the tertiary 17-C atom. Schemes to explain the differences are proposed.

2. A new class of heterocyclic compounds, 2'-methyl-[16,17α-d]-thiazoline 20-ketosteroids, has been obtained.

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