3. M. F. Lappert, The Chemistry of Boron and Its Compounds (ed. by E. I. Muetteri), Wiley, N. Y. (1967), p. 443..
4. K. Niedenzu and J. W. Dawson, Boron—Nitrogen Compounds, Springer-Verlag (1965).
5. B. M. Mikhailov and M. E. Kuimova, J. Organomet. Chem., 116, 123 (1976).
6. L. A. Paquette, Principles of Modern Heterocyclic Chemistry, W. A. Benjamin (1968).
7. B. M. Mikhailov and V. A. Dorokhov, Izv. Akad. Nauk SSSR, Ser. Khim., 2649 (1973).
8. B. M. Mikhailov, V. A. Dorokhov, and L. I. Lavrinovich, Izv. Akad. Nauk SSSR, Ser. Khim., 2578 (1978).
9. R. Köster, K. Iwasaki, S. Hattori, and Y. Morita, Lieb. Ann. Chem., 720, 23 (1968).
10. B. M. Mikhailov, V. A. Dorokhov, and N. V. Mostovoi, Zh. Obshch. Khim., in: Problems of Organic Synthesis [in Russian] (1965), p. 233.
11. N. V. Mostovoi, V. A. Dorokhov, and B. M. Mikhailov, Izv. Akad. Nauk SSSR, Ser. Khim., 90 (1966).
12. V. A. Dorokhov, O. G. Boldyreva, V. S. Bogdanov, and B. M. Mikhailov, Zh. Obshch. Khim., 42, 1558 (1972).
13. V. A. Dorokhov, O. G. Boldyreva, and B. M. Mikhailov, Zh. Obshch. Khim., 43, 1955 (1973).
14. B. M. Zolotarev, O. S. Chizhov, V. A. Dorokhov, L. I. Lavrinovich, and B. M. Mikhailov, Izv. Akad. Nauk SSSR., Ser. Khim., 1843 (1977).
15. G. Schwenker and K. Bösl, Pharmazie, 24, 653 (1969).
16. B. M. Mikhailov, V. A. Dorokhov, and V. I. Seredenko, Dokl. Akad. Nauk SSSR, 199, 1328 (1971).
17. V. A. Dorokhov, V. I. Seredenko, and B. M. Mikhailov, Zh. Obshch. Khim., 46, 1057 (1976).
18. P. B. Brindley, W. Gerrard, and M. F. Lappert, J. Chem. Soc., 2956 (1955).

MODIFIED STEROIDS.

101.* REACTIVITY OF 16,17α-EPISULFIDE RING IN THE SERIES OF 20-KETOPREGNANES AND THEIR 20-HYDRAZONES

A. V. Kamernitskii, A. M. Turuta,
T. K. Ustynyuk, and Ho Thee Mai An

UDC 542.91:547.92

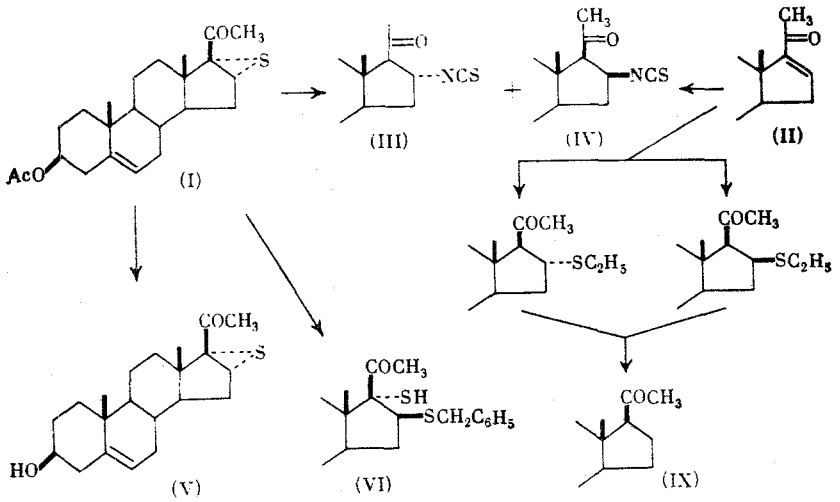
The present article continues previous study on the reactivity and direction of ring opening of 16,17α-epithiopregnenolones [2]. The behavior of 16,17α-epithiopregnenolone 3-acetate (I) has been studied under ring-opening conditions of the corresponding 16,17α-epoxy ketone by acetic acid, thiocyanic acid, and methanol [3, 4]. Complete inertness of the episulfide ring to ring-opening reactions was observed. For example, episulfide (I) remains unchanged during the prolonged action of AcOH containing H_2SO_4 (20°C) or BF_3 ethereate, and also in an ethanolic solution of pyridinethiocyanate. Elevated temperatures of the acetolysis reaction or boiling episulfide (I) with pyridinethiocyanate in ethanol leads to desulfurization with the formation of dehydropregnenolone or its 3-acetate, while in the reaction with thiocyanic acids, its subsequent addition to dehydropregnenolone 3-acetate (II) with the formation of the previously described [5] 16α- and 16β-isothiocyanatopregn-5-en-3β-ol-20-ones (III) and (IV) is observed. A similar result was obtained when episulfide (I) was left to stand with thiocyanic acid in $CHCl_3$ at 20°C.

The H_2SO_4-catalyzed reaction of episulfide (I) with methanol leads to saponification only of the acetate group at C-3, giving 16,17α-epithiopregnenolone (V) in a quantitative yield. It should be stated that in addition to that already noted in [6], the properties of 16,17α-episulfide (V) do not correspond to those of the product obtained in [7], to which the structure of 16,17α-epithiopregnenolone has been erroneously attributed. The structure of episulfide (V) was confirmed by its physicochemical characteristics and reacetylation into the 3-acetate (I) [6, 8].

*For communication 100, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 180-185, January, 1979. Original article submitted June 29, 1977.

 0568-5230/79/2801-0168$07.50



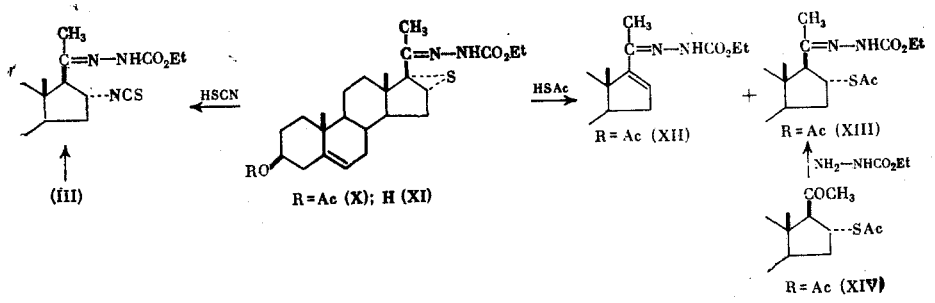
The reaction of episulfide (I) with ethyl mercaptan and benzyl mercaptan in the presence of BF_3 ethereate, in contrast to analogous methanolysis reactions of the episulfide (I), proceed with the opening of the hetero ring and the introduction of mercaptidione. However, while the reaction of episulfide (I) with benzyl mercaptan proceeds under mild conditions, with a good yield of product (VI), under the same conditions, its reaction with ethyl mercaptan is complicated by desulfurization followed by the addition of ethyl mercaptan to dehydropregnenolone 3-acetate (II) formed. Thus in the reaction mixture obtained during the reaction of episulfide (I) with ethyl mercaptan in benzene in the presence of BF_3 ethereate, besides the products of the direct addition of ethyl mercaptan to dehydropregnenolone 3-acetate, i.e., the 16α- and 16β-ethyl mercaptans (VII) and (VIII), which were also obtained by an alternative synthesis, a product is also obtained which cannot be separated from 16α-ethyl mercaptan (VII) by chromatography, and according to elemental analysis, contains more than one sulfur atom. The structure and the configuration of the substituents in dithiol (VI) follow from the general principle of trans-ring-opening, physicochemical characteristics, and the inertness of the tertiary thiol group to acetylation reactions with Ac_2O in pyridine. The structure of ethyl mercaptans (VII) and (VIII), apart from the physicochemical data, was confirmed by their desulfurization over Raney nickel catalyst with the formation of pregnenolone 3-acetate (IX), while the configuration of the ethylmercapto group was assigned according to the data of the PMR spectra [descreening of the proton signals of the 18-CH_3 group for the 16β-isomer (VIII) compared with the 16α-isomer (VII)]. The reactivity of the episulfide ring in reactions with ethyl mercaptan and benzyl mercaptan is higher than in the analogous methanolysis reaction, apparently because the nucleophilicity of the thiolate ions is higher than that of the methylate ion [9]. The difference observed in the behavior of episulfide (I) in the reaction with ethyl mercaptan and benzyl mercaptan, and the absence of the desulfurization side reaction in the latter case makes it possible to assume that the desulfurization reaction, stimulated by the presence of the electronegative 20-keto group [10] can be suppressed by a reagent with a high nucleophilicity (benzyl mercaptan ion). If the nucleophilicity of the reagent is insufficient ($^{\ominus}SC_2H_5$, $^{\ominus}OCH_3$, $^{\ominus}OAc$), stabilization of the carbocation, formed during the opening of the hetero ring by elimination of H_2S, is observed. The desulfurization process is also stimulated by the presence of an acid (H_2SO_4, HSCN) in the reaction mixture.

We should note, firstly, that the reactivity of the episulfide ring conjugated with the keto group is decreased (compared with epoxy-ketones) in the ring opening reactions, and secondly, the general tendency of 16, 17α-epithio-ketones to undergo desulfurization reactions under conditions of the hetero ring opening by nucleophilic reagents. These two phenomena undoubtedly limit the sphere of utilization of 16,17α-epithio-20-keto-steroids for a directed transformation of the D ring of the steroids.

It is known that 20-hydrazones of 16,17α-epoxy-steroids are more reactive in the ring-opening reactions by nucleophilic reagents than the corresponding 20-ketoepoxides, and therefore, in contrast to the latter, they undergo exclusively an α-cleavage of the epoxide ring to yield compounds with 16,17α-cis-configuration [11, 12]. A similar behavior was observed for 20-hydrazones of 16,17α-epimino-steroids [1]. As we expected apriori the manifestation of similar properties and regularities for 20-hydrazones of 16,17α-epithio-steroids, we

carried out the synthesis of 3-acetate of 16,17α-epithiopregn-5-en-3-β-ol-20-one 20-carbethoxyhydrazone (X) by prolonged holding (about 2 days) of the 20-ketone (I) at 20°C in AcOH containing a 15-fold excess of carbethoxyhydrazine. The observed low reaction rate of the formation of hydrazone (X), compared with the similar reaction for 16,17α-epoxy- [14] and 16,17α-epimino-20-keto-steroids [15], together with above mentioned inertness of the episulfide in 16,17α-episulfide (I), characterizes the difference in the electronic structure of the epithio-ketonic and epoxy-ketonic groups.

We studied the behavior of the 20-carbethoxyhydrazone (X) in reactions with methanol, acetic, thioacetic, and thiocyanic acids, and also with ethyl and benzyl mercaptans. We found that the substitution of the 20-keto group for the hydrazone fragment does not increase the reactivity of the episulfide ring. Moreover, in the case of 20-carbethoxyhydrazone (X), we noted not only the increased tendency to desulfurization, but also a certain decrease in the reactivity in the ring-opening reactions. It is sufficient to state that even under conditions of the preparation (AcOH), the 20-carbethoxyhydrazone (X) partially converts (and with increase in the duration of the reaction, to a greater extent) into 3-acetate of pregn-5,16-dien-3-β-ol-20-one 20-carbethoxyhydrazone (XII) [16]. During the action of thioacetic acid on the 20-carbethoxyhydrazone (X), in contrast to the analogous reaction of 16,17α-epithio-ketone (I) [17], no dithio deivatives are formed. The reaction proceeds with desulfurization, followed by the addition of thioacetic acid to 20-carbethoxyhydrazone (XII) formed. Prolonged holding or catalysis by H_2SO_4 leads to partial or complete (depending on time) elimination of the hydrazone protection. Similar behavior is noted in the reaction of 20-carbethoxyhydrazone with thiocyanic acid



Thus, 20-carbethoxyhydrazone (X) does not react with $C_5H_5N \cdot HSCN$ at 20°C in C_2H_5OH or with HSCN in a $CHCl_3$ solution at room temperature. When (X) is boiled with $C_5H_5N \cdot HSCN$ in C_2H_5OH or held with excess of KSCN in AcOH, desulfurization followed by the addition of HSCN to the Δ^{16}-bond occur. In particular, the reaction of hydrazone (X) with a fourfold excess (by weight) of KSCN in AcOH yields not only 20-carbethoxyhydrazone (XII), but also the carbethoxyhydrazone of the 16α-isothiocyanate (XV), which was also obtained by an alternative synthesis.

During methanolysis of 20-carbethoxyhydrazone (X) (in the presence of H_2SO_4, 20°C, 1-2 days), saponification of the 3-acetate group with the formation of 20-carbethoxyhydrazone of 16,17α-epithiopregn-5-en-3β-ol-20-one (XI) is observed. Increase in the time of reaction or the amount of catalyst leads exclusively to desulfurization and elimination of the hydrazone protection with the formation of preg-5-en-3β-ol-20-one. Unfortunately, we were unable to separate and identify chromatographically the inseparable multicomponent mixtures of products from the reaction of 20-carbethoxyhydrazone (X) with ethyl mercaptan and benzyl mercaptan. Nevertheless, the PMR data and elementary analysis show that in this case, besides the 20-carbethoxyhydrazone (XII) and the products of the subsequent addition of mercaptans to it, products of the addition of mercaptide ions to the episulfide ring are also formed.

Thus, in contrast to 16,17α-epoxy- and 16,17α-epimino-20-ketopregnanes, in the case of 16,17α-epithio-20-keto-steroids, substitution of the carbonyl group for the hydrazone residue does not make it possible to prepare 16α-thio-17α-substituted pregnanes. Absence of the influence of neighboring group is similar to that observed in the case of 16,17α-epoxy-16β-methyl-substituted compounds [18].

EXPERIMENTAL

Melting points were determined on a Koffler block. The IR spectra were run on a UR-10 spectrophotometer, with KBr pressing. The PMR spectra were run on a "Varian DA-60-IL" spectrometer in a $CDCl_3$ solution (with TMS as internal standard); mass spectra were run on a

"Varian MAT CH-6" spectrometer with direct introduction of the sample into the ion source at ionization voltages of 20 and 70 eV.

Reaction of 3-Acetate of 16,17α-Epithiopregn-5-en-3β-ol-20-one (I) with HSCN. A solution of 0.1 g of episulfide (I) in 7 ml of C_2H_5OH, containing 0.4 g of $C_5H_5N \cdot HSCN$, was boiled for 10 h, and the course of the reaction was controlled by TLC. The residue was diluted by water, and the precipitate filtered, washed with water, dried and separated by TLC (hexane—ether, 2:1). Yield, 0.06 g of dehydropregnenolone 3-acetate (II), mp 174-177°C, and 0.03 g of dehydropregnenolone, mp 208-210°C.

A solution of 0.1 g of episulfide (I) in 4 ml of a 1.2% solution of HSCN in $CHCl_3$ was held in the dark for 4 days at 20°C. It was then neutralized by $NaHCO_3$ solution, washed with water, and dried over Na_2SO_4. The solvent was evaporated, the residue was purified by TLC (hexane—ether, 2:1). Yield, 0.06 g of 16α-isothiocyanate (III), mp 136°-139°C, and 0.034 g of 16β-isothiocyanate (IV), mp 146-148°C, identical to those described in [5].

16,17α-Epithiopregn-5-en-3β-ol-20-one (V). A 0.05-ml portion of conc. H_2SO_4 was added to a suspension of episulfide (I) in 5 ml of abs. CH_3OH. The mixture was held for 2 days at 20°C, and diluted with water. The residue was filtered, washed with water, and dried in air. Yield, 0.043 g of episulfide (V), mp 176-181°C (from ethyl acetate). IR spectrum (ν, cm^{-1}): 1055, 1693 and 3520. PMR spectrum (δ, ppm): 0.97 s (3H, 18-CH_3), 1.01 s (3H, 19-CH_3), 2.12 s (3H, 21-CH_3), 3.52 br. line (H, 16-H), 5.27 br. 1. (H, 6-H). Mass spectrum (m/e): 346 (M^+); 313 ($M^+ - SH$); 295 ($M^+ - SH - H_2O$).

Reaction of 3-Acetate of 16,17α-Epithiopregn-5-en-3β-ol-20-one (I) with Benzyl Mercaptan. A 0.4-ml portion of $C_6H_5CH_2SH$ and 1 drop of BF_3 ethereate were added to 0.05 g of episulfide (I) in 1 ml of abs. C_6H_6. The mixture was diluted with water, and extracted with ethyl acetate. The extract was dried over Na_2SO_4, and the solvent distilled. The residue was purified by TLC (SiO_2, hexane, then hexane—ether, 2:1). Yield, 0.043 g of benzyl mercaptan (VI), mp 136-141°C (from ether—hexane). IR spectrum (ν, cm^{-1}): 1035, 1245, 1708, 1735. PMR spectrum (δ, ppm): 0.63 s (3H, 18-CH_3), 0.99 s (3H, 19-CH_3), 2.00 s (1H, 3-OAc), 2.17 s (3H, 21-CH_3), 3.83 s on br. 1. (3H, SH and CH_2 of the $SCH_2C_6H_5$ group), 5.33 br. 1. (H, 6-H), 7.24 s (C_6H_5). Found: C 69.73; H 7.81; S 12.18%. $C_{30}H_{40}S_2O_3$. Calculated: C 70.31; H 7.81; S 12.50%.

Reaction of 3-Acetate of Pregn-5-en-3β-ol-20-one (II) with Ethyl Mercaptan. A 1-ml portion of C_2H_5SH and 1 drop of BF_3 ethreate were added to 0.1 g of dehydropregnenolone 3-acetate (II) in 2 ml of abs. C_6H_6. The mixture was held for 3 h at 20°C, and evaporated to dryness. Water was added to the residue, and the insoluble part was filtered, washed with water, and separated by TLC (hexane—ether, 2:1). Yield: 1) 0.096 g of 3-acetate of 16α-ethylmercaptopregn-5-en-3β-ol-20-one (VI), mp 96-97°C (CH_3OH). IR spectrum (ν, cm^{-1}, KBr): 1245, 1705, 1725. PMR spectrum (δ, ppm): 0.63 s (3H, 18-CH_3), 0.98 s (3H, 19-CH_3), 1.08 t (3H, CH_3 in SC_2H_5), 2.00 s (3H, 3-OAc), 2.13 s (3H, 21-CH_3), 3.66 br. 1. (2H, CH_2 in SC_2H_5), 4.53 br. 1. (H, 3-H), 5.32 br. 1. (H, 6-H). Mass spectrum (m/e): 418 (M^+), 403 ($M^+ - CH_3$), 389 ($M^+ - C_2H_5$); 358 ($M^+ - HOAc$); 343 ($M^+ - HOAc - CH_3$), 329 ($M^+ - HOAc - C_2H_5$).

2) 0.012 g of 16β-ethylmercaptopregn-5-en-3β-ol-20-one (VIII), mp 173-177°C (ether—hexane). IR spectrum (ν, cm^{-1}, KBr): 1245, 1705, 1725. PMR spectrum (δ, ppm): 1.00 s (3H, 19-CH_3), 1.05 s (3H, 18-CH_3), 1.23 t (3H, CH_3 in SC_2H_5), 1.98 s (3H, 3-OAc), 2.15 s (3H, 21-CH_3), 3.80 br. 1. (2H, CH_2 in SC_2H_5), 4.55 br. 1. (H, 3-H), 5.30 br. 1. (H, 6-H). Mass spectrum (m/e): 418 (M^+), 403 ($M^+ - CH_3$), 389 ($M^+ - C_2H_5$), 358 ($M^+ - HOAc$), 343 ($M^+ - HOAc - CH_3$), 329 ($M^+ - HOAc - C_2H_5$).

Reaction of 3-Acetate of 16,17α-Epithio-5-pregn-en-3β-ol-20-one (I) with Ethyl Mercaptan. A 1-ml portion of ethyl mercaptan and 1 drop of BF_3 ethreate were added to 0.1 g of episulfide (I) in 2 ml of abs. benzene. The mixture was held for 1 h at 20°C, and evaporated in vacuo to dryness. The residue was washed with water, and separated by TLC (hexane—ether, 2:1). Thus, 0.08 g of a product was obtained, which was recrystallized from hexane to yield a mixture of 16α-ethyl mercaptan (VII) and a dithio derivative, mp 75-77°C, which could not be separated. Found: C 70.22; H 8.96; S 9.49%.

3-Acetate of 16,17α-Epithiopregn-5-en-3β-ol-20-one 20-Carbethoxyhydrazone (X). A 1.5-g portion of carbethoxyhydrazine was added to a solution of 0.1 g of episulfide (I) in 16 ml of glacial AcOH. The mixture was held for 2 days at 20°C, and then diluted with ice-cold water. The precipitate was filtered, washed with water, dried in air, and recrystallized

from an ether—hexane mixture. Yield, 0.072 g of carbethoxyhydrazone (X), mp 186-188°C. IR spectrum (ν, cm^{-1}) 1038, 1080, 1250, 1700, 1725, 3230, 3380-3460. PMR spectrum (δ, ppm): 0.90 s (3H, 18-CH_3), 1.01 s (3H, 19-CH_3), 1.26 t (3H, CH_3 hydr. fragment), 1.85 s (3H, 21-CH_3), 1.98 s (3H, 3-OAc), 3.70 br. 1. (H, 16-H), 4.20 q (2H, CH_2 hydr. fragment), 5.33 br. 1. (H, 6-H), 7.62 s (H, NH). Mass spectrum (m/e): 474 (M^+), 442 ($M^+ - S$), 382 ($M^+ - S -$ AcOH). Found: C 65.52; H 8.10; S 6.09; N 5.75%. $C_{26}H_{38}O_4N_2S$. Calculated: C 65.82; H 8.01; S 6.75; N 5.91%.

16,17α-Epithiopregn-5-en-3β-ol-20-one 2-carbethoxyhydrazone (XI). A 0.2-ml portion of H_2SO_4 was added to a suspension of 0.08 g of carbethoxyhydrazone (X) in 8 ml abs. CH_3OH. The mixture was held for 2 days at 20°C, the solvent was evaporated to 1/4 of the initial volume, and the remaining mass was diluted with water. The precipitate was filtered, washed with water, and dried in air. Yield 0.072 g of 20-carbethoxyhydrazone (XI), mp 146-150°C (from ether—hexane). IR spectrum (ν, cm^{-1}): 1065, 1245 w, 1715, 3240, 3390-3480. PMR spectrum (δ, ppm): 0.88 s (3H, 18-CH_3), 0.98 s (3H, 19-CH_3), 1.25 t (3H, CH_3 hydr. fragment), 1.83 s (3H, 21-CH_3), 3.76 br. 1. (H, 16-H), 4.11 q (2H, CH_2 hydr. fragment), 5.27 br. 1. (H, 6-H), 7.53 s (H, NH).

Reaction of 3-Acetate of 16,17α-Epithiopregn-5-en-3β-ol-20-one 20-Carbethoxyhydrazone (X) with Thioacetic Acid. A solution of 0.02 g of carbethoxyhydrazone (X) in 0.5 ml of CH_3COSH with 2 mg of hydroquinone was held for 6 days at 20°C, and the course of the reaction was controlled by TLC. The reaction mixture was diluted with water, the precipitate was filtered, and separated by TLC (SiO_2, hexane—ether, 1:1). Yield, 0.01 g 3,16-diacetate of pregn-5-en-3β-ol-16α-thiol-20-one (XIV), mp 177-182°C (ether—hexane), identical with the previously described sample [19], and 0.01 g of 3,16-diacetate of pregn-5-en-3β-ol-16α-thiol-20-one 20-carbethoxyhydrazone (XIII), mp 178-182°C (ether—hexane). IR spectrum (ν, cm^{-1}): 1230-1270, 1515, 1680, 1715, 1750, 3300. Identical with a sample obtained by an alternative synthesis.

Reaction of 3-Acetate of 16,17α-Epithiopregn-5-en-3β-ol-20-one 20-Carbethoxyhydrazone (X) with HSCN. A solution of 0.05 g of carbethoxyhydrazone (X) and 0.2 g of KSCN in 4 ml of glacial AcOH was held for 1.5 h at 20°C. The mixture was diluted with water, the precipitate was filtered, and washed with water. The yield was 0.06 g of a product, from which by TLC (hexane—ether, 1:1), 0.016 g of 3-acetate of pregn-5,16-dien-3β-ol-20-one 20-carbethoxyhydrazone (XII), mp 173-178°C, was obtained, with properties the same as those of a known sample [16], and 0.02 g of 3-acetate of 16α-isothiocyanatopregn-5-en-3β-ol-20-one 20-carbethoxyhydrazone (XV), mp 166.5-167.5°C (from ether—hexane). IR spectrum (ν, cm^{-1}): 1245, 1710, 1735, 2130, 3250.

3-Acetate of 16α-Isothiocyanatopregn-5-en-3β-ol-20-one 20-Carbethoxyhydrazone (XV). A solution of 0.03 g of 16α-isothiocyanate (III) in 0.5 ml of glacial AcOH with 0.03 g of carbethoxyhydrazine was held for 1 h at 20°C. The mixture was then diluted with water, and the precipitate was filtered, and washed with water. Yield 0.033 g of a product, which crystallized from ether—hexane to give 0.023 g of 3-acetate of 16α-isothiocyanatopregn-5-en-3β-ol-20-one 20-carbethoxyhydrazone, mp 166.5-167.5°C, identical with the above-described sample.

CONCLUSIONS

1. The reactivity of 16α,17α-epithio-ketones in the pregnane series and their 20-carbethoxyhydrazones was studied in the episulfide ring-opening reactions.

2. Epithio-ketones are more inert to ring-opening reactions with nucleophilic reagents than the corresponding epoxy-ketones, and tend to eliminate sulfur under the hetero ring-opening conditions.

3. Substitution of the 20-keto group for the hydrazone fragment does not increase the reactivity of the episulfide ring, but facilitates its desulfurization.

LITERATURE CITED

1. A. V. Kamernitskii, A. K. Kaparov, K. K. Koshoev, and A. V. Skorova, Izv. Akad. Nauk SSSR, Ser. Khim., 2605 (1978).
2. A. V. Kamernitskii, A. M. Turuta, and T. K. Ustynyuk, Izv. Akad. Nauk SSSR, Ser. Khim., 2078 (1976).

3. A. A. Akhrem, V. A. Dubrovskii, A. V. Kamernitskii, and A. V. Skorova, Izv. Akad. Nauk SSSR, Ser. Khim., 2792 (1969).
4. A. A. Akhrem, A. M. Turuta, and Z. I. Istomina, Izv. Akad. Nauk SSSR, Ser. Khim., 1354 (1972).
5. A. A. Akhrem, Z. I. Istomina, G. A. Kogan, A. I. Kuznetsova, and A. M. Turuta, Izv. Akad. Nauk SSSR, Ser. Khim., 2503 (1969).
6. A. V. Kamernitskii, A. M. Turuta, and T. K. Ustynyuk, Izv. Akad. Nauk SSSR, Ser. Khim., 132 (1975).
7. K. Jankowsky and R. Harvey, Synthesis, 627 (1972).
8. H. Hofmeister, G. A. Hoyer, G. Cleve, H. Zaurent, and R. Wiechert, Chem. Ber., 109, 185 (1976).
9. S. Oae (editor), Organic Chemistry of Sulfur, Plenum Publ. (1975).
10. M. Zander, Usp. Zhim., 37, 433 (1968).
11. A. A. Akhrem, A. V. Kamernitsky, and A. V. Skorova, Tetrahedron, 25, 4737 (1969).
12. A. A. Akhrem, Z. I. Istomina, A. V. Kamernitsky, A. V. Skorova, and A. M. Turuta, Bull. Acad. Pol. Sci., Ser. Sci. Chim., 22, 929 (1974).
13. D. Kal'sines, A. V. Kamernitskii, and A. M. Turuta, Izv. Akad. Nauk SSSR, Ser. Khim., 1838, 1841 (1976).
14. A. A. Akhrem, A. V. Kamernitskii, V. A. Dubrovskii, and A. M. Moiseenkov, Izv. Akad. Nauk SSSR, Ser. Khim., 115 (1967).
15. A. V. Kamernitskii, D. Kal'sines, and A. M. Turuta, Izv. Akad. Nauk SSSR, Ser. Khim., 2090 (1977).
16. A. V. Kamernitskii, L. E. Kulikova, I. S. Levina, and V. B. Muratov, Izv. Akad. Nauk SSSR, Ser. Khim., 1129 (1976).
17. A. V. Kamernitskii, A. M. Turuta, and T. K. Ustynyuk, Izv. Akad. Nauk SSSR, Ser. Khim., 2078 (1976).
18. C. Djerassi, Steroid Reactions, Holden Day, San Francisco (1963).
19. A. A. Akhrem and A. I. Kuznetsova, Izv. Akad. Nauk SSSR, Ser. Khim., 2087 (1965).

MODIFIED STEROIDS.

102*. APPROACH TO THE SYNTHESIS OF STEROID 16,17-AZIRIDINES AND STEREOSPECIFICITY OF THE PHOTOINDUCED ADDITION OF CARBETHOXYNITRENE TO STEROID 16-EN-20-ONES

A. V. Kamernitskii, Z. I. Istomina, E. P. Serebryakov, and A. M. Turuta

UDC 542.91:547.92

16,17-Epimino-20-keto-steroids are key compounds in the synthesis of different steroid derivatives (including heterocycles), containing the nitrogenous function at C-16 or C-17 atom [2-7]. The generally accepted method for the preparation of such epimines, consisting in the addition of O-methylhydroxylamine to α,β-enone, followed by alkaline cyclization of the adduct [8], gives good results only for the synthesis of 16,17α-epimino-20-keto-steroids. Therefore, our attention was drawn to the photochemical reaction of the ethyl ester of azidoformic acid (ethyl azoformate, EAF) with dehydropregnenolone acetate (I), which proceeds with the preferential formation of carbethoxynitrene, and, according to [9], also the adduct, with 16,17β-orientation of the aziridine ring. In the present work it was shown that, in contrast to the data of [9], the photochemical reaction of EAF with steroid 16-en-20-ones proceeds with the formation of 16,17α-carbethoxyepimines only, and conditions were found for increasing the yield of these compounds to a level acceptable in preparative practice.

Although the addition of the photochemically generated nitrenes to simple olefinic bonds has often been studied [10-12], their reactions with α,β-enones have not yet been

*For communication 101, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 1, pp. 186-191, January, 1979. Original article submitted June 29, 1977.

0568-5230/79/2801-0173$07.50