Pregnane derivatives have been obtained from the cyanohydrins of androst-4-en-3,17-dione and of 3β-acetoxyandrost-5-en-17-one. It has been shown that when both a nitrile group and an ethylenedioxy group are present in an androstane derivative a Grignard reaction in anisole takes place simultaneously at the two groups.

When certain steroids, such as cholesterol and sitosterol, are used as the raw material for the synthesis of hormone preparations, the problem of attaching the side chain with the aim of passing from the androstane series to the pregnane series is an urgent one.

One of the methods of introducing a side chain into substituted androstanes is the cyanohydrin variant [1-3]. In studying the construction of the side chains of pregnanes by the method of cyanohydrin synthesis, as the initial compounds we selected the 17β-cyanohydrins of androst-4-en-3,17-dione (I) and of the acetate of dehydroepiandrosterone (V), which were obtained by a method described in a GDR patent [2]. The performance of the Grignard reaction with the nitrile group is possible only after the preliminary protection of the 17β-hydroxy groups in (I) and (V) and the 3-oxo group in compound (I). With this aim, we obtained the 3-ethylene ketal of the 17β-cyanohydrin of androstenedione (II) by boiling the 3-ketone (I) with ethylene glycol in benzene in the presence of an acid catalyst.

Cases of the isomerization of 17-cyanohydrins of the androstane series under reaction conditions catalyzed by an acid have been described in the literature [4]. The PMR spectrum of the compound (II) that we obtained confirmed that it consisted of an individual isomer: The spectrum contained singlet signals of the protons of the angular methyl groups at C₁₀ and C₁₉ and with the methyl groups of the ethylene ketal system in the form of a narrow unresolved signal. To determine the configuration of the compound (II) that we had obtained, this substance was compared with a sample of the ethylene ketal prepared from 17α-cyano-
17β-hydroxyandrost-4-en-3-one. The latter had mp 194-196° (the mp of (II) was 228-230°C), and the signal of the protons of the C₁₈ angular methyl group was shifted upfield (0.94 ppm) as compared with the spectrum of (II). This showed that no isomerization of the 17β-cyano-17α-hydroxy group had taken place under the conditions of obtaining the ethylene ketal (II). The 3-ethylene ketal of 17-cyano-17-hydroxyandrost-4-en-3-ol with mp 185°C [5] apparently consisted of a mixture of isomers at C₁₇.

To protect the 17α-hydroxy groups in compounds (I) and (V), the trimethylsilyl ethers (III) and (VI) were prepared. We performed the silylation reaction by the usual method with chlorotrimethylsilane in pyridine [3].

The Grignard reaction at a nitrile group requires more severe conditions than at a carbonyl group: This means either prolonged boiling in tetrahydrofuran [3] or raising the temperature of the reaction by using higher-boiling solvents such as anisole [1]. In our case, nitriles (III) and (VI) did not react with methylmagnesium bromide in boiling tetrahydrofuran.

Interesting results were obtained by performing the reaction in anisole. In this case, both functional groups of (III) — the nitrile and the ethylenedioxy groups — entered into the reaction directly with the formation of 17α-hydroxy-3β-hydroxyethoxy-3α-methylpregn-5-en-20-one (IV) with quantitative yield. Such a course of the reaction was unexpected, since according to the literature the ethylenedioxy group should be stable to a Grignard reagent [6].

The structure of compounds (IV) was confirmed by its NMR spectrum, which contained singlet signals of the protons of the methyl groups at C₁₈, C₁₉, and C₂₀ at 0.74, 1.01, and 1.08 ppm, respectively, a singlet signal at the 17β-acetoxy group at 2.26 ppm, a multiplet signal of the 3-hydroxyethoxy group at 3.59 ppm, and a multiplet signal of the proton at the doublet bond at 5.35 ppm.

The different stabilities of the trimethylsilyl ether group in the products of the Grignard reaction with methylmagnesium bromide obtained from compound (II) and (VI). While in the case of compound (III) hydrolysis of the silyl ether group took place during the decomposition of the reaction mixture with an aqueous solution of ammonium chloride, in the case of compound (VI) the use of dilute hydrochloric acid was necessary for hydrolysis.

**EXPERIMENTAL**

The IR spectra of suspensions of the compounds in paraffin oil were taken on a UR-10 instrument, NMR spectra on a JNM-4H-100 instrument in CDCl₃ (with TMS as internal standard, δ scale), and mass spectra on a MAT-112 instrument (ionizing energy 50 eV). Specific rotations were determined in chloroform by means of an ELPU-01 instrument. The C and H figures found corresponded to those calculated.

17β-Cyano-3-ethylenedioxy-17α-hydroxyandrost-5-ene (II). A suspension of 10 g of the cyanohydrin (I) and 1 g of p-toluenesulfonic acid in 450 ml of benzene was boiled until 50 ml of distillate had been collected, and it was then boiled further with the azeotropic removal of water for 1 h. After this, 25 ml of dry ethylene glycol was added and boiling with the azeotropic elimination of water was continued for 8 h. The ethylene glycol layer was separated off and the benzene layer was washed with a 5% solution of sodium bicarbonate and with water to neutrality. The benzene was distilled off in a vacuum to dryness, 10 ml of methanol was added, and the mixture was kept at -5°C for 20 min. The precipitate was filtered off and washed with 5 ml of cold methanol. This gave 9.6 g (84.2%) of the ethylene ketal (II), C₂₂H₃₆NO₃, bp 228-230°C (MeO₃-l-benzene), [α]D⁻¹⁶°C (c 0.1012). IR spectrum (cm⁻¹): 3400 (OH), 1095 (CO). PMR spectrum (ppm): 0.88 (s, 18-CH₃); 1.04 (s, 19-CH₃); 3.94 (s, (CH₂O)=); 5.30 (5-H).

Trimethylsilyl Ether of 17β-Cyano-3-ethylenedioxy-17α-hydroxyandrost-5-ene (III). A mixture of 15 g of the ethylene ketal (II), 45 ml of pyridine, and 15 ml of chlorotrimethylsilane was kept at 20-25°C for 6 h. Then it was poured into a 210 ml of 6% solution of hydrochloric acid cooled to 0°C. The precipitate that deposited was filtered off, washed with water to neutrality, and dried. This gave 18 g (quantitative yield) of the trimethylsilyl ether (III), C₂₅H₄₉NO₃Si, mp 152-152.5°C (ether), [α]D⁻²³°-32.8° (c 0.13). IR spectrum (cm⁻¹): 1250, 1105. PMR spectrum (ppm): 0.88 (s, (CH₃)₃); 0.91 (s, 18-CH₃); 1.04 (s, 19-CH₃); 3.92 (s, (CH₂O)₂); 5.34 (m, 5-H).

17α-Hydroxy-3β-hydroxyethoxy-3α-methylpregn-5-en-20-one (IV). A solution of 0.6 g of the trimethylsilyl ether (III) in 6 ml of anisole and 12 ml of a 30% solution of the Grignard