SOME TRANSFORMATIONS OF 19-OXYGEN-CONTAINING STEROIDS

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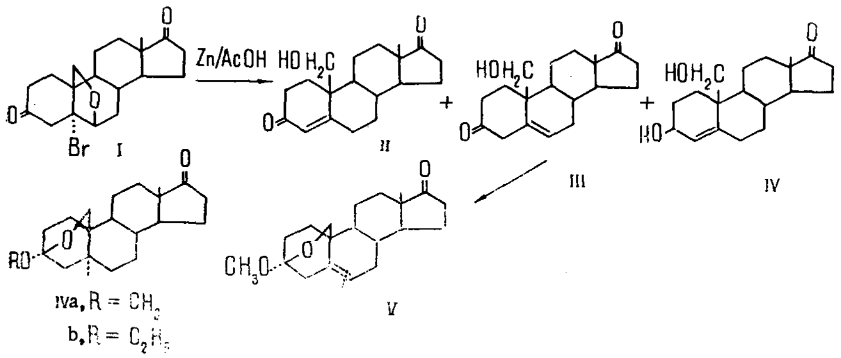
In a preceding paper [1] we have described a method for obtaining steroid alcohols by the reductive cleavage of the oxide ring in 6β,19-epoxysteroids with the aid of zinc dust and an equimolecular amount of acetic acid in a polar solvent. On studying the influence of the activity of the zinc dust on the reduction process, we have found that the use of a highly active zinc dust prepared from electrolytically pure zinc leads to a rapid but not unambiguous reaction. In addition to the main reaction product – the alcohol (II) – its Δ^5 isomer (III) is present, and during the reaction no migration of the double bonds takes place. Furthermore, as a result of the reduction of the 3-oxo group, 3β,19-dihydroxyandrost-4-en-17-one (IV) is formed. Compound (IV) was isolated and its structure was confirmed by IR and NMR spectroscopy. The IR spectrum has a strong absorption band at 3400 cm^{-1} which is characteristic for the presence of hydroxy groups, and absorption at 1740 cm^{-1} shows the presence of a carbonyl group in a five-membered ring.

When we attempted to separate the isomers (II) and (III) chromatographically, we obtained the nonconjugated ketone (III) in the form of 3α-methoxy-3β,19-epoxyandrost-5-en-17-one (V). The usual tendency of the hydroxyketone (III) to form the cyclic ketal (V) in the presence of an alcohol without a catalyst must be noted. The cyclic ketals (IVa) and (IVb) of the 5α-androstane series described previously [2, 3] were obtained in the presence of hydrochloric or p-toluenesulfonic acid. The structure of the ketal (V) was confirmed by its IR spectrum, which contained the absorption band of a carbonyl group at 1740 cm^{-1}, which is characteristic for a five-membered cyclic ketone. The NMR spectrum showed the presence of a methoxy group (3.28 ppm), of a vinyl proton at C-6 (broad multiplet at 5.46 ppm), and of the geminal protons of the C-19 methylene group in the form of signals (AB system) at 3.76 and 3.95 ppm with a coupling constant J of 9 Hz.



EXPERIMENTAL

The NMR spectra were obtained on a JNM-4H-100 instrument in $CDCl_3$ with tetramethylsilane as standard; the UV spectra were taken in 96% ethanol; the IR spectra of mulls of the substances were recorded on a Perkin-Elmer 457 instrument (in paraffin oil); and the specific rotations were determined in chloroform on an ÉLPU-0.1 instrument.

19-Hydroxyandrost-4-ene-3,17-dione (II). With stirring, 250 g of zinc dust (electrolytically pure zinc) and 8.4 ml of glacial acetic acid were added to a suspension of 25 g of 5α-bromo-6β,19-epoxyandrost-

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ane-3,17-dione (I) in 500 ml of isopropanol, and the mixture was heated at the boil for 1.5 h. According to the results of TLC [fixed layer of silica gel, benzene–methanol (23 : 2) system], the reaction mixture contained three compounds: 19-hydroxyandrost-4-ene-3,17-dione (II) with R_f 0.3, its less polar Δ^5 isomer (III) with R_f 0.35, and a more polar compound with R_f 0.2. After cooling, the zinc dust was removed by decantation and was washed with methylene chloride, and the solution was dried with calcium chloride. The residue from the distillation of the solvent in vacuum was crystallized from methanol, giving 13.4 g (68%) of the alcohol (II), mp 174-175°C, $[\alpha]_D$ +190° [1].

The residue after the distillation of the methanol (6.8 g) was chromatographed on 180 g of alumina. The first eluates [benzene–methanol (99 : 1)] yielded 3.8 g of 3α-methoxy-3β,19-epoxyandrost-5-en-17-one (VII), $C_{20}H_{28}O_3$, mp 176-178°C, $[\alpha]_D$ −34°. IR spectrum, cm^{-1}: 1740, 1470, 1040. NMR spectrum, ppm: 0.82 (18–CH_3), 3.28 (OCH_3), 3.76 and 3.95 (19–CH_2), 5.46 (6–H).

A mixture of benzene and methanol (197 : 3) eluted 0.7 g of the alcohol (II) with mp 178-179.5°C and benzene–methanol (20 : 1) eluted 1.5 g of 3β,19-dihydroxyandrost-4-en-17-one (IV), $C_{19}H_{28}O_3$, mp 210.5-212°C, $[\alpha]_D$ −4°. IR spectrum, cm^{-1}: 3400, 1740, 1030. NMR spectrum, ppm: 0.96 (18–CH_3), 3.75 (3–H), 3.89 (19–CH_2), 5.89 (4–H).

SUMMARY

The influence of the activity of the zinc dust on the reductive cleavage of the oxide ring of 6β,19-epoxysteroids has been studied. An unusual ease of conversion of 19-hydroxyandrost-5-ene-3,17-dione into the cyclic ketal has been observed.

LITFRATURE CITFD

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