TRANSFORMED STEROIDS

COMMUNICATION 52. SYNTHESIS OF SOME 20-KETOLS OF 17-ISOPREGNANE SERIES BY HYDRATION OF THE CORRESPONDING 17α-ETHYNYLCARBINOLS

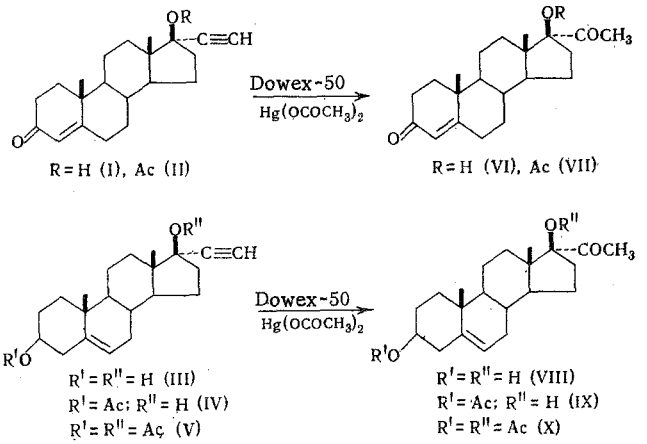
A. A. Akhrem, T. K. Ustynyuk, and I. I. Voznesenskaya

UDC 542.91:547.92

The synthesis of the 20-ketols of the 17-isopregnane series by the hydration of the 17α-ethynylcarbinols is a difficult task, since the hydration of the triple bond of acetylenic alcohols in the presence of mercury salts when applied to the 17α-ethynylcarbinols is accompanied by isomerization to the inactive D-homosteroids [1-3]. The method proposed in [4] for the hydration of steroidal acetylenic alcohols in the presence of mercuric chloride and aniline made it possible to avoid the D-homoisomerization and obtain the corresponding 20-ketols, for example isopregn-5-ene-3β, 17β-diol-20-one. However, this method gives moderate yields (~40-60%) and is quite laborious.

The method for the hydration of the triple bond by mercury salts in the presence of cationite Dowex-50 [6] was used in 1961 for the hydration of 17α-ethynylcarbinols [5]. Starting with 17α-ethynylandrost-4-en-17β-ol-3,11-dione, isopregn-4-en-17β-ol-3,11,20-trione was obtained in high yield by this method. However, attempts to extend this method to other acetylenic alcohols proved unsuccessful. A mixture of isopregn-4-en-17β-ol-3,20-dione and the D-homoketol was obtained in the hydration of the triple bond in 17α-ethynyltestosterone. A similar result was obtained in [8]. The unreproducibility of the method apparently depends on the carefulness of washing out traces of H_2SO_4 from the cationite.

The Dowex-50 (H^+ form) was carefully washed free of H_2SO_4 and was used in the reaction as a mixture with $Hg(OCOCH_3)_2$. The hydration of the triple bond of the 17α-ethynylcarbinols went smoothly and in 4 h led to the formation of the corresponding ketols in ~80% yield. We studied the hydration of 17α-ethynyltestosterone (I), its 17β-acetate (II), and of 17α-ethynylandrost-5-ene-3β,17β-diol (III), its 3β-acetate (IV), and the 3β,17β-diacetate (V). Here the corresponding 20-keto-17β-ols were obtained in high yield



In all the examples studied, only the 20-keto-17β-ols and their acetates are formed. The course of the reaction was checked employing TLC and GLC.

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 3, pp. 639-641, March, 1973. Original article submitted November 15, 1971.

EXPERIMENTAL METHOD

All of the melting points were determined on a Kofler block; the UV spectra were taken on an EPS-2 spectrometer; the IR spectra were taken on a UR-10 spectrometer; the NMR spectra were taken on an INH-C60 spectrometer (60 MHz) relative to TMS as the internal standard.

The GLC determinations were run on an LKhM-7A chromatograph using a flame-ionization detector [glass column (2 m × 3 mm), filled with Chromosorb W (60-80 mesh) containing 5% of Silicone SE-30, temperature 220°, and nitrogen flow rate 30 ml/min]. The trimethylsilyl ethers were obtained for the compounds that contain hydroxyl groups [9]. For the TLC we used KSK silica gel, 6-24 mμ, and Silufol; the compounds on the plates were detected in iodine vapors and in UV light.

Method for Preparation of Cationite. A suspension of 10 g of Dowex-50 (B × 4), 200-400 mesh, in 100 ml of 10% H_2SO_4 solution was allowed to stand overnight. The next day the cationite was carefully washed free of H_2SO_4 with distilled water until neutral, after which it was suction-filtered and dried in the air for two days.

General Hydration Procedure. A stirred suspension of 2 g of the steroid in 100 ml of CH_3OH and 15 ml of H_2O with 1 g of Dowex-50 (H^+ form) and 0.5 g of $Hg(OCOCH_3)_2$ was refluxed for 4 h. When the starting substance had disappeared the cationite was filtered and washed with $CHCl_3$, and the filtrate was evaporated to dryness. The residue was dissolved in $CHCl_3$, washed with water, dried over $MgSO_4$, and evaporated. The residue was recrystallized from a suitable solvent.

Isopregn-4-en-17β-ol-3,20-dione (VI). From 2 g of pregnyne (I) was obtained 2.03 g of (VI). Recrystallization from an ethyl acetate–hexane mixture gave 1.63 g of (VI) with mp 190-192°C, yield ~77%; $[\alpha]_D^{24}$ + 65.2° (C 1.02, dioxane). ν, cm^{-1}: 1612, 1668, 1692, and 3475 (KBr). δ, ppm: 0.92 (CH_3–18); 1.12 (CH_3–19); 2.17 (CH_3–21); 5.63 (H at double bond). Found: C 76.32; H 9.25%. $C_{21}H_{30}O_3$. Calculated: C 76.32; H 9.15%; cf. [10].

Isopregn-4-en-17β-ol-3,20-dione 17β-Acetate (VII). From 0.5 g of pregnyne acetate (II) was obtained 0.42 g of (VII) with mp 198-200° [11], yield ~81%; $[\alpha]_D^{19}$ −40.7° (C 1.075, $CHCl_3$). ν, cm^{-1}: 1618, 1678, 1710, and 1740. λ_{max} 242 nm, ε 15500; λ_S 290 nm, ε 156. δ, ppm: 0.97 (CH_3–18); 1.18 (CH_3–19); 1.97 (17β–OAc); 2.02 (CH_3–21); 5.62 (H at double bond). Found: C 73.71; H 8.78%. $C_{23}H_{32}O_4$. Calculated: C 74.16; H 8.66%.

Isopregn-5-ene-3β,17β-diol-20-one (VIII). From 1 g of ediol (III) was obtained 0.87 g of (VIII) with mp 176-178°, yield ~83%, $[\alpha]_D^{19}$ −58.5° (C 0.968, $CHCl_3$) [4], δ, ppm: 0.88 (CH_3–18); 0.94 (CH_3–19); 2.18 (CH_3–21) and 5.15 (H at double bond). Found: C 75.24; H 9.70%. $C_{24}H_{32}O_3$. Calculated: C 75.86; H 9.70%.

Isopregn-5-ene-3β,17β-diol-20-one 3β-Acetate (IX). a) From 0.5 g of the ediol 3β-acetate (IV) was obtained 0.43 g of (IX) with mp 192-194°, yield ~82%, $[\alpha]_D^{18}$ −58° (C 0.971, $CHCl_3$) [10]. δ, ppm: 0.87 (CH_3–18); 0.95 (CH_3–19); 1.94 (3β–OAc); 2.19 (CH_3–21) and 5.21 (H at double bond).

b) The acetylation of 100 mg of (I), mp 176-178°, with $(CH_3CO)_2O$ in pyridine at 20° gave 81 mg of (IX) with mp 192-194°.

Isopregn-5-ene-3β,17β-diol-20-one 3β,17β-Diacetate (X). a) From 0.5 g of the ediol 3β,17β-diacetate (V) was obtained 0.36 g of (X) with mp 186-188°, yield ~70%, $[\alpha]_D^{18}$ −58.1° (C 0.837, dioxane) [12]. δ, ppm: 0.96 (CH_3–18 and CH_3–19); 1.95 (3β–OAc); 1.98 (17β–OAc); 2.03 (CH_3–21) and 5.21 (H at double bond).

b) The acetylation of 100 mg of (VIII), mp 176-178°, with $(CH_3CO)_2O$ in pyridine at 100° for 24 h gave 53 mg of (X) with mp 186-188°.

CONCLUSIONS

The hydration of the triple bond in 17α-ethynyltestosterone, its 17β-acetate, and in 17α-ethynylandrost-5-ene-3β,17β-diol, its 3β-acetate and the 3β,17β-diacetate by treatment with mercuric acetate in the presence of cationite Dowex-50 (H^+ form) was accomplished, as a result of which some 20-ketols of the 17-isopregnane series were obtained.

LITERATURE CITED

1. L. Ruzicka, K. Gatzi, and T. Reichstein, Helv. Chim. Acta, 22, 626 (1939).

2. H. E. Stavely, J. Am. Chem. Soc., 61, 79 (1939).
3. L. Ruzicka and H. F. Meldahl, Helv. Chim. Acta, 23, 364 (1940).
4. H. E. Stavely, J. Am. Chem. Soc., 63, 3127 (1941).
5. G. Amiard, M. Legrand, J. Mathieu, R. Heymes, and T. van Thuong, Bull. Soc. Chim. France, 2417 (1961).
6. M. S. Newman, J. Am. Chem. Soc., 75, 4740 (1953).
7. É. A. Elin, Dissertation [in Russian], Moscow (1969).
8. C. W. Shoppee, N. W. Hughes, and B. C. Newman, J. Chem. Soc. C, 558 (1970).
9. R. S. Rosenfeld, Steroids, 4, 147 (1964).
10. H. E. Stavely, J. Am. Chem. Soc., 62, 489 (1940).
11. I. Salamon and T. Reichstein, Helv. Chim. Acta, 30, 1616 (1942).
12. M. W. Goldberg, R. Aeschbacher, and E. Hardegger, Helv. Chim. Acta, 26, 680 (1943).