In confirmation of this finding, the spectrum of the keto diacetate,[2] obtained by chromium trioxide–acetic acid oxidation of hetisine diacetate, has peaks at 4.80 τ, 4.95 τ, 5.02 τ, and 5.18 τ corresponding in area to four protons while the spectrum of the hydrolysis product[2] has peaks at 5.13 τ and 5.32 τ corresponding in area to two protons.

Note Added in Proof: After this note had been submitted for publication, a new structure,[5] based on X-ray studies was advanced for hetisine.

Experimental

The NMR spectra were determined at 60 Mc. on Model HR-60 and A-60 Varian spectrometers. Deuterochloroform was used as solvent and tetramethylsilane served as internal standard.

Acknowledgment.—The authors are indebted to Dr. A. Robertson, to the Department of Chemistry, Columbia University and to Varian Associates for aid in obtaining the NMR spectra. This work was supported in part by Grants RG 5807(C2) and RG 5807(C3) from the National Institutes of Health, U. S. Public Health Service.

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1,4,17α-Trimethylestra-1,3,5(10)-trien-17β-ol

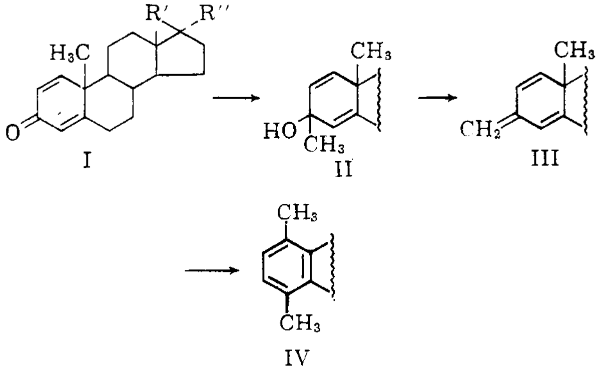
Leland J. Chinn

Division of Chemical Research, G. D. Searle and Co., Chicago 80, Illinois

Received March 9, 1962

Recently Dannenberg and Neumann[1] reported the results of their study on the dienol-benzene rearrangement.[2] They observed that the addition of methylmagnesium iodide to a compound possessing a $\Delta^{1,4}$-dienone system I gives a tertiary carbinol II, which dehydrates to a "semibenzene" III, that rearranges to a substance whose ring A is in the form of a 1,2,3,4-tetrasubstituted benzene IV.

From cholesta-1,4-dien-3-one (I.R′ = C_8H_{17}, R″ = H) and 17β-hydroxyandrosta-1,4-dien-3-one (I.R′ = OH, R″ = H) they obtained 1,4-dimethyl-19-norcholesta-1,3,5(10)-triene (IV.R′ = C_8H_{17}, R″ = H) and 1,4-dimethylestra-1,3,5(10)-trien-17β-ol (IV.R′ = OH, R″ = H), respectively. When androsta-1,4-diene-3,17-dione (I.R′, R″ = O) was treated in the same manner, they were not able to isolate 1,4,17α-trimethylestra-1,3,5(10)-trien-17β-ol (IV.R′ = OH, R″ = CH_3) as a homogeneous product.



In our investigation of the dehydration-rearrangement of the steroids,[3] which partly parallels theirs, we found that 1,4,17α-trimethylestra-1,3,5(10)-trien-17β-ol (IV. R′ = OH, R″ = CH_3) can be obtained readily if the reaction mixture is acidified with dilute hydrochloric acid and the crude reaction product is chromatographed afterward on silica gel. The physical constants of our pure product support the structure formulated for it.

Acetylation of the hydroxyl group at C-17 can be accomplished with isopropenyl acetate in the presence of *p*-toluenesulfonic acid to give IV (R′ = OAc, R″ = CH_3).

Experimental[4]

1,4,17α-Trimethylestra-1,3,5(10)-trien-17β-ol (IV. R′ = OH, R″ = CH_3).—To a solution of 8.00 g. (0.0281 mole) androsta-1,4-diene-3,17-dione, m.p. 136.5–142°, in 200 ml. of anhydrous ether, stirred, and heated under reflux, was added a solution of 40 ml. of a 3 *M* solution of methylmagnesium bromide. The reaction mixture was stirred and heated under reflux for 6 hr. and then stirred at room temperature for 15 hr. The reaction mixture was decomposed with water and acidified with 1.7 *N* hydrochloric acid. The ethereal phase was separated, washed successively with water and a saturated solution of sodium bicarbonate, dried over anhydrous sodium sulfate, and distilled to dryness under reduced pressure to afford a viscous orange oil. The oil was chromatographed on 800 g. of silica gel.

Elution of the column with 2% ethyl acetate in benzene gave 3.00 g. (36%) of a solid, which melted at 143–145° after crystallization from ether-hexane. The analytical sample of IV (R′ = OH, R″ = CH_3) was obtained as colorless laths after another crystallization from hexane, m.p. 143–145.5°; $\lambda_{max}^{CH_3OH}$ 269.5 mμ (ϵ 287); λ^{KBr} 2.88, 2.98, 12.47 μ; $[\alpha]^{25}_D$ +127.5° ($CHCl_3$). Admixed with the starting material, it melted at 97.5–124°.

Anal. Calcd. for $C_{21}H_{30}O$: C, 84.51; H, 10.13. Found: C, 84.35; H, 9.85.

1,4,17α-Trimethylestra-1,3,5(10)trien-17β-ol acetate (IV. R′ = OAc, R″ = CH_3.)—A solution of 0.55 g. of IV (R′ = OH, R″ = CH_3), m.p. 138–142°, 10 ml. of isopropenyl acetate, and *ca.* 0.1 g. of *p*-toluenesulfonic acid monohydrate was heated under reflux for 1 hr. After *ca.* 0.1 g. of sodium acetate was added, the reaction mixture was distilled nearly to dryness under reduced pressure. The residue was diluted with water and cooled in an ice bath. The solid was collected, washed well with water, and dried. It was crystallized first from acetone–hexane and then from hexane alone to yield 0.31 g. (47%) of IV (R′ = OAc, R″ = CH_3) as colorless dense crystals, m.p. 166.5–167°; $\lambda_{max}^{CH_3OH}$ 270 mμ (ϵ 286); λ^{KBr} 5.82, 7.90, 7.98, 12.42 μ; $[\alpha]^{25}_D$ +133° ($CHCl_3$).

Anal. Calcd. for $C_{23}H_{32}O_2$: C, 81.13; H, 9.47. Found: C, 80.96; H, 9.49.

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