Anal. Calcd. for $C_{21}H_{14}$: C, 94.70; H, 5.30. Found: C, 94.77; H, 5.37. *Anal.* (picrate) Calcd. for $(C_{21}H_{14})_2$-$(C_6H_3N_3O_7)_3$: N, 10.34. Found: N, 10.5.

Hydrocarbon C: 8,9-Trimethylene-3,4-benzphenanthrene (V).—A third picrate separated along with picric acid on further concentration of the mother liquor. The combined material was treated with alkali and extracted with ether and the hydrocarbon was distilled and crystallized from ether–petroleum ether. The crude product (0.35 g., 7%), which formed golden yellow plates, was purified by chromatographic adsorption and crystallized from alcohol, when it formed flat, very faintly yellow needles, m. p. 138–138.5° (corr.), yellow in sulfuric acid. The picrate forms long, orange needles, m. p. 125–126°. It is dissociated into the components by washing with alcohol.

Anal. Calcd. for $C_{21}H_{16}$: C, 93.98; H, 6.02. Found: C, 93.88; H, 5.64. *Anal.* (picrate) Calcd. for $C_{27}H_{19}O_7N_3$: N, 8.45. Found: N, 8.61.

Hydrocarbon D.—This substance was obtained in small quantity (80 mg.) from the ether–petroleum ether mother liquors from the crystallization of compound C. The hydrocarbon crystallizes from this solvent mixture as nearly colorless plates, m. p. 96.5–97° (corr.). The substance forms no picrate and it gives a yellow color in sulfuric acid.

Anal. Calcd. for $C_{21}H_{16}$: C, 93.98; H, 6.02. Found: C, 93.91, 93.96; H, 6.47, 6.24.

Oxidation Products.—When oxidized by the procedure given above, hydrocarbon A gave a substance which crystallizes from benzene as fine, orange needles, m. p. 220–223°. The substance gives no vat test.

Anal. Calcd. for $C_{21}H_{10}O_4$: C, 77.28; H, 3.09. Found: C, 77.75, 77.92; H, 3.26, 3.47.

From the hydrocarbon B ($C_{16}H_{14}$) there was obtained, by oxidation with sodium dichromate in a suspension of glacial acetic acid in the cold, a substance which crystallizes from glacial acetic acid in the form of long, yellow needles, m. p. 201°. It is insoluble in alkali and gives no vat test; the solution in sulfuric acid is green.

Anal. Calcd. for $C_{21}H_{12}O$: C, 89.97; H, 4.32. Found: C, 89.96; H, 4.37.

Summary

Tetralyl naphthyl ketones behave abnormally in the Elbs reaction for, although they easily yield hydrocarbons on pyrolysis, the condensation is accompanied by the aromatization of the original alicyclic six-ring with migration of hydrogen to other parts of the molecule. Other changes not yet defined result in the formation of complex mixtures.

CAMBRIDGE, MASSACHUSETTS
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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE AND THE PARKE DAVIS AND COMPANY RESEARCH LABORATORIES]

Studies on Sterols. IV.[1] Androsterone Derivatives

BY RUSSELL E. MARKER

In an attempt to prepare water-soluble androsterone derivatives for physiological testing two 17-amino derivatives were made by reducing the oximes of androsterone and 3-chloroandrosterone. The hydrochlorides of these amines were only slightly soluble in water.

17-Aminoandrosterone was diazotized to 3,17-androstanediol which on oxidation gave 3,17-androstanedione. This was identical with androstanedione produced by the oxidation of *iso*-androsterone (*trans*-androsterone). 17-Aminoandrostane on diazotization gave 17-androstanol identical with the product formed by the reduction of 3-chloroandrosterone by sodium and amyl alcohol.

The physiological activity of these compounds will be reported later. The author wishes to thank Mr. Harry M. Crooks for the microanalyses of the compounds reported.

(1) The first three communications appeared in THIS JOURNAL, **7**, 1755, 2358 (1935); and **58**, 338 (1936).

Experimental

17-Aminoandrosterone Hydrochloride.—To a solution of 400 mg. of androsterone oxime in 100 cc. of dry amyl alcohol was added 5 g. of sodium in small portions. The amyl alcohol was refluxed until the sodium dissolved. After cooling, water was added and the amyl alcohol layer was separated. This was concentrated under reduced pressure. The resulting oil was distilled in high vacuum at 125°. A portion of the oily distillate was converted into the hydrochloride by dissolving in ether and passing in a small amount of dry hydrogen chloride. The hydrochloride was filtered and crystallized from alcohol–ether; m. p. 340° (dec.).

Anal. Calcd. for $C_{19}H_{34}ONCl$: C, 69.6; H, 10.9. Found: C, 69.1; H, 10.5.

3,17-Androstanediol.—A solution of 200 mg. of 17-aminoandrosterone in 5 cc. of acetic acid was diluted with 15 cc. of water. To this was added 5 drops of sulfuric acid. The solution was cooled and 3 g. of sodium nitrite slowly added. After standing for three hours it was warmed to 60°. Water was added and the product extracted with ether. It was crystallized from ethyl acetate; m. p. 218–220°.

Anal. Calcd. for $C_{19}H_{32}O_2$: C, 78.0; H, 11.0. Found: C, 78.2; H, 10.7.

To a solution of 100 mg. of 3,17-androstanediol in 20 cc. of acetic acid, 100 mg. of chromic oxide was added. The solution remained at 20° overnight and was then diluted with water. It was extracted with ether and the ethereal solution was washed with a saturated sodium carbonate solution. The ether was evaporated and the residue distilled in high vacuum. It was crystallized from petroleum ether (b. p. 80–90°) and ethyl acetate; m. p. 128–129°. A mixture with 3,17-androstanedione prepared by the oxidation of *iso*-androsterone with chromic oxide gave no depression in the melting point.

17-Aminoandrostane Hydrochloride.—To a solution of 400 mg. of α-3-chloroandrosterone oxime in 100 cc. of dry amyl alcohol, was added 8 g. of sodium in small pieces. The amyl alcohol was refluxed until the sodium had dissolved. Water was added and the amyl alcohol layer separated. This was concentrated and the amine distilled in high vacuum at 110°. A portion of this oil was dissolved in ether and treated with dry hydrogen chloride. The amine hydrochloride was filtered and crystallized from alcohol-ether; m. p. 345° (dec.).

Anal. Calcd. for $C_{19}H_{34}NCl$: C, 73.3; H, 10.9. Found: C, 73.2; H, 10.9.

Androstanol-17.—(a) A solution of 100 mg. of 17-aminoandrostane in 5 cc. of glacial acetic acid was treated with 15 cc. of water, a few drops of sulfuric acid and a cooled solution of 2 g. of sodium nitrite. After standing for three hours, the solution was warmed to 60°. This was extracted with ether, and the residue after evaporation of the ether was sublimed in a high vacuum at 110°. It was crystallized from ligroin (b. p. 80–90°); m. p. 166°.

Anal. Calcd. for $C_{19}H_{32}O$: C, 82.5; H, 11.6. Found: C, 82.4; H, 11.3.

(b) To prove the identity of androstanol-17 prepared from 17-aminoandrostane, the product was prepared by reduction of α-3-chloroandrosterone.

A solution of 300 mg. of α-3-chloroandrosterone in 100 cc. of *n*-amyl alcohol was heated to boiling and treated with 5 g. of sodium. After solution, water was added and the amyl alcohol layer was separated and concentrated *in vacuo*. The residue was crystallized from dilute alcohol, sublimed in high vacuum at 100–105°, then crystallized from petroleum ether (b. p. 80–90°); m. p. 166°. This gave no depression in melting point when mixed with androstanol-17 prepared from 17-aminoandrostane.

Anal. Calcd. for $C_{19}H_{32}O$: C, 82.5; H, 11.6. Found: C, 82.2; H, 11.3.

Summary

17-Aminoandrosterone and 17-aminoandrostane were prepared by reduction of the corresponding oximes. These on diazotization gave the same hydroxy compounds as the sodium reductions of androsterone and α-3-chloroandrosterone.

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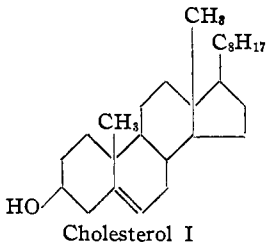
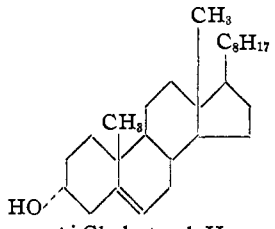
Studies on Sterols. V. *epi*-Cholesterol

BY RUSSELL E. MARKER, THOMAS S. OAKWOOD AND HARRY M. CROOKS

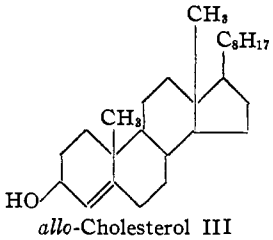
Many workers have attempted the synthesis of *epi*-cholesterol, which differs from cholesterol only in the configuration of the –OH group in the 3-position. The nearest approach to this was the work of Evans and Schoenheimer,[1] who prepared *epi-allo*-cholesterol, an isomer of *epi*-cholesterol, by the reduction of cholestenone with aluminum isopropylate. The *epi*-forms of the saturated sterols of dihydrocholesterol and coprosterol have been prepared by the catalytic reduction of cholestanone[2] and coprostanone[3] as well as by the separation of γ-cholestanol into its components of beta-cholestanol and *epi*-cholestanol by Windaus.[4] This was done by the precipitation of beta-cholestanol by digitonin and recovery of the *epi*-cholestanol from the filtrate of the digitonide.



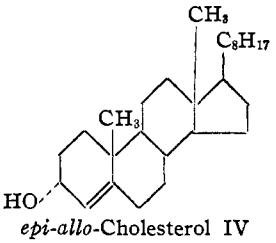
Cholesterol I



epi-Cholesterol II



allo-Cholesterol III



epi-allo-Cholesterol IV

The preparation of the *epi*-form of cholesterol is of the greatest importance from the physiologi-

(1) Evans and Schoenheimer, THIS JOURNAL, **58**, 182 (1936).
(2) Vavon and Jakubowicz, *Bull. soc. chim.*, [4] **53**, 584 (1933).
(3) Ruzicka and co-workers, *Helv. Chim. Acta*, **17**, 1413 (1934).
(4) Windaus, *Ber.*, **49**, 1726 (1916).