

*Anal.* Calcd. for  $C_{32}H_{54}O_2$ : C, 81.6; H, 11.6. Found: C, 81.6; H, 11.4.

**Dihydrocaoutchicol.**—A solution of 500 mg. of dihydrocaoutchicol acetate in alcohol was refluxed with an excess of alcoholic potassium hydroxide for thirty minutes. After crystallization from acetone and methanol, the product had a melting point of 188°.

*Anal.* Calcd. for  $C_{30}H_{50}O$ : C, 84.0; H, 12.2. Found: C, 83.8; H, 12.1.

**Dihydrocaoutchicone.**—To a solution of 200 mg. of dihydrocaoutchicol in 20 cc. of acetic acid was added 60 mg. of chromic oxide in 3 cc. of 90% acetic acid. After standing at room temperature for one hour the crystalline product which separated was filtered and recrystallized from acetone to a constant melting point of 210°.

*Anal.* Calcd. for  $C_{30}H_{50}O$ : C, 84.4; H, 11.8. Found: C, 84.2; H, 11.8.

A solution of 20 mg. of dihydrocaoutchicone in alcohol was heated on a steam-bath with 20 mg. of semicarbazide hydrochloride and 20 mg. of sodium acetate for one hour. It was poured into water, filtered and recrystallized from acetone to give the semicarbazone, m. p. 249–250°, dec.

*Anal.* Calcd. for  $C_{31}H_{52}N_2O$ : C, 77.0; H, 11.0. Found: C, 76.9; H, 11.0.

### Summary

Caoutchicol ( $C_{30}H_{50}O$ ), a new alcohol, was isolated from a crude rubber extract (Jelutong). It does not precipitate digitonin. It forms a monoacetate, a dibromide and can be reduced to a dihydro derivative. Dihydrocaoutchicol forms the ketone, dihydrocaoutchicone, on oxidation.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

## Sterols. LI. $\Delta^4$ -Pregnenone-3

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As a by-product of the preparation of progesterone by the debromination of progesterone dibromide with zinc, Butenandt and Westphal<sup>1</sup> obtained  $\Delta^{4,5}$ -pregnenone-20. This compound was found to have no gestational activity. In order to determine the particular structural features essential for gestational activity, and for purposes of comparison with new compounds isolated from urines, we have now prepared  $\Delta^4$ -pregnenone-3.

The starting material for this preparation, pregnanol-3( $\alpha$ ), has been described in a previous publication.<sup>2</sup> In that work it was shown that the Clemmensen reduction of pregnanol-3( $\alpha$ )-one-20 gave 50% yields of pregnanol-3( $\alpha$ ). Since then we have found that the Wolff-Kishner reduction of pregnanol-3( $\alpha$ )-one-20 gives considerably higher yields (85%) although the product is contaminated with some of the epimer, pregnanol-3( $\beta$ ). The pregnanol-3 mixture so obtained was oxidized to pregnanone-3 and the latter brominated in acetic acid. The 4-bromopregnanone-3 formed was refluxed with pyridine, and worked up in the usual fashion. The  $\Delta^4$ -pregnenone-3 proved to be rather difficult to purify because of its low melting point and great solubility in ordinary solvents. By filtering it through a column of activated alumina, and letting it stand

for several weeks in dilute alcohol solution it was finally obtained as long needles, m. p. 90°. In harmony with its structure as an  $\alpha, \beta$ -unsaturated diketone, it formed a deep red 2,4-dinitrophenylhydrazone.<sup>3</sup>

As a by-product in the preparation of  $\Delta^4$ -pregnenone-3 from 4-bromopregnanone-3, the corresponding pyridinium bromide was obtained. Its structure is proved by the analytical data, the fact that it contains an ionizable bromine atom, and the fact that it gives a yellow color with alkali. The latter reaction is characteristic of pyridinium bromides derived from  $\alpha$ -bromo ketones.<sup>4</sup>

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### Experimental

**Pregnanol-3( $\alpha$ ).**—A mixture of 1 g. of pregnanol-3( $\alpha$ )-one-20 (from human pregnancy urine), 0.6 g. of semicarbazide hydrochloride, 0.9 g. of sodium acetate, and 20 cc. of alcohol was refluxed for three hours. The mixture was diluted with 200 cc. of water and the precipitated semicarbazone collected and washed with alcohol and ether; yield, 1.12 g.; m. p. 246°.

To a solution of 1 g. of sodium in 12 cc. of absolute alcohol 1.12 g. of pregnanol-3( $\alpha$ )-one-20 semicarbazone was added, and the mixture heated in a bomb tube for seven hours at 180°. The contents were washed out of

(1) Butenandt and Westphal, *Ber.*, **67**, 2085 (1934).

(2) Marker and Lawson, *THIS JOURNAL*, **60**, 2438 (1938).

(3) Mason, Hoehn, McKenzie and Kendall, *J. Biol. Chem.*, **120**, 734 (1937).

(4) Kröhnke, *Ber.*, **66**, 604 (1933).

the tube with water and ether, the layers separated, and the ethereal solution evaporated to dryness. The residue was crystallized from slightly diluted alcohol to give 0.64 g. of crude pregnanol-3( $\alpha$ ), m. p. 139–144°. A portion was recrystallized from diluted alcohol and then melted at 146° and showed no depression with an authentic sample of pregnanol-3( $\alpha$ ).

**Pregnanone-3.**—The entire reaction product of the previous experiment was dissolved in 30 cc. of acetic acid and mixed with a solution of 330 mg. of chromic anhydride in 15 cc. of 90% acetic acid. After standing for five hours, methanol was added and the acetic acid removed *in vacuo*. The residue was dissolved in dilute hydrochloric acid and ether, the layers separated, and the aqueous layer extracted with ether. The ethereal extracts were combined, washed free of acids, and the ether removed on the steam-bath. The residue was crystallized from diluted alcohol to give 0.49 g. of pregnanone-3, m. p. 111°. It gave no depression in melting point with an authentic sample of pregnanone-3.

**4-Bromopregnanone-3.**—To a solution of 0.45 g. of pregnanone-3 in 5 cc. of acetic acid was added a drop of 48% aqueous hydrobromic acid, and then 1.5 cc. of 1.05 *M* bromine in acetic acid was added. After standing for two hours in the refrigerator a crop of needles had separated. The product was collected, washed with acetic acid, and recrystallized from slightly diluted alcohol to give 240 mg. of 4-bromopregnanone-3 as needles, m. p. 137°. A second crop weighing 160 mg. was obtained from the mother liquors.

*Anal.* Calcd. for  $C_{21}H_{33}OBr$ : C, 66.1; H, 8.7. Found: C, 66.0; H, 8.6.

**$\Delta^4$ -Pregnenone-3.**—A solution of 0.38 g. of 4-bromopregnanone-3 in 10 cc. of dry pyridine was refluxed for eight hours. The reaction mixture was poured into dilute sulfuric acid and the organic material extracted with ether. Some insoluble material which collected at the interface was removed by filtration. The ether layer was washed with dilute sulfuric acid and water, and the ether removed on a steam-bath. The residual sirup resisted all attempts at crystallization, so it was dissolved in 20 cc. of a mixture of benzene and petroleum ether and passed through a 35-mm. layer of activated alumina in an 8-mm. tube. The filtrate, and the first two elutations, with petroleum ether, yielded the same crystalline product,  $\Delta^4$ -pregnenone-3. After recrystallization from diluted alcohol, 80 mg. of

pure  $\Delta^4$ -pregnenone-3, m. p. 90°, was obtained as long needles.

*Anal.* Calcd. for  $C_{21}H_{32}O$ : C, 84.0; H, 10.8. Found: C, 83.8; H, 11.2.

The insoluble material which collected at the interface was dissolved in alcohol, treated with boneblack, and crystallized from very dilute alcohol and water. The product, plates, m. p. 235°, proved to be the pyridium bromide. An aqueous solution of the salt gave a test for bromide ion, and a yellow color with sodium hydroxide solution; yield 150 mg.

*Anal.* Calcd. for  $C_{26}H_{38}ONBr$ : C, 67.8; H, 8.4. Found: C, 67.6; H, 8.5.

**$\Delta^4$ -Pregnenone-3 2,4-Dinitrophenylhydrazone.**—A mixture of 20 mg. of  $\Delta^4$ -pregnenone-3, 20 mg. of 2,4-dinitrophenylhydrazine, and 3 cc. of alcohol was heated for a few minutes. To the boiling solution 5 drops of concentrated hydrochloric acid was added. The precipitated hydrazone was collected, washed with alcohol, and recrystallized from alcohol. The purified  $\Delta^4$ -pregnenone-3 2,4-dinitrophenylhydrazone melted at 198°, and had the deep red color characteristic of these derivatives of  $\alpha,\beta$ -unsaturated ketones.

*Anal.* Calcd. for  $C_{27}H_{36}O_4N_4$ : C, 67.5; H, 7.5. Found: C, 67.5; H, 7.5.

**$\Delta^4$ -Pregnenone-3-semicarbazone.**—A mixture of 20 mg. of  $\Delta^4$ -pregnenone-3, 30 mg. of semicarbazide hydrochloride, 30 mg. of sodium acetate, and 3 cc. of alcohol was heated for two hours on a steam-bath. At the end of this time practically all the alcohol had evaporated. The residue was heated with water, filtered, and the precipitate washed with water. The semicarbazone proved to be rather soluble in most organic solvents, so it was crystallized from dilute alcohol to a constant m. p. of 216°.

*Anal.* Calcd. for  $C_{22}H_{30}ON_3$ : C, 73.3; H, 10.1. Found: C, 73.3; H, 10.0.

### Summary

An improved preparation of pregnanol-3( $\alpha$ ) by the Wolff-Kishner reduction of pregnanol-3( $\alpha$ )-one-20 is described.  $\Delta^4$ -Pregnenone-3 has been prepared from pregnanol-3( $\alpha$ ) by conventional reactions.

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