might prevent the migration of the mesityl radical.

As a test of this hypothesis hydromesitoin (I) and isohydromesitoin[1] were treated with dehydrating agents. Rearrangement occurred in the normal manner. The product, apparently β,β-dimesitylvinyl alcohol (II), was obtained in 60% yield; m. p. 128–129°.

Anal. Calcd. for $C_{20}H_{24}O$: C, 85.97; H, 8.30; mol. wt., 280. Found: C, 85.68; H, 8.54; mol. wt. (ebullioscopic in chloroform), 283.

I II

The new compound reacted rapidly with methylmagnesium iodide to yield a mole of methane, and readily formed an acetate, a benzoate and a methyl ether. Hydrolysis of the esters regenerated the original compound. The infrared absorption spectrum measured in carbon tetrachloride solution showed peaks at 2.77 and 2.84 μ,[2] confirming the presence of a hydroxyl group. The compound was remarkably stable to heat and was not attacked by oxygen. Oxidation with alkaline hydrogen peroxide converted it to dimesityl ketone.

From these data it is evident that the rearrangement product behaves toward chemical reagents as though it had the enol structure (II) and that it must be at least partially enolic in carbon tetrachloride solution.

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RECEIVED FEBRUARY 20, 1943

(1) Fuson, Horning, Ward, Rowland and Marsh, THIS JOURNAL, **64**, 30 (1942).

(2) The authors are indebted to Professor W. H. Rodebush and Dr. J. B. Patberg for the measurement and interpretation of the infrared spectrum.

(3) du Pont Fellow in Chemistry, 1942–1943.

CAFESTEROL. III.—THE SUPPOSED ESTROGENIC ACTIVITY OF CAFESTEROL

Sir:

Hauptmann[1] and co-workers and, independently, Wettstein and co-workers,[2] have shown that cafesterol has no estrogenic activity, in contradiction to Slotta and Neisser.[3] Recently, at the Buffalo meeting of the American Chemical Society on September 7, 1942, P. N. Chakravorty and M. M. Wesner stressed again the existence of such an activity. To clear up the question we tested cafesterol and oxcafestandiol A[1b] as well as several parts of the unsaponifiable fraction of coffee oil and the oil itself following the Allen–Doisy procedure,[4] as described by B. Zondek.[5] For each substance we used five rats. The following scheme shows details of the fractionation.

SCHEME

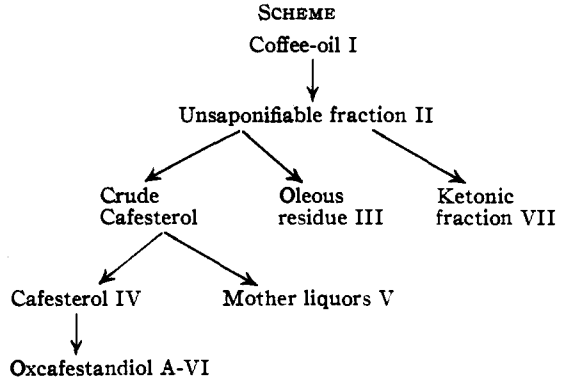

TABLE I

Fraction	Doses, mg.	Contains less R.U./g. than
I	2280	0.4
II	100	10
III	120	8.5
IV	30	33
V	117	8.5
VI	9	111
VII	36	29

None of the substances had estrogenic activity in the doses shown in the table (dissolved in 3 cc. of sesame oil). As 1γ of estrone always produced estrus, 1 g. contains 1,000,000 rat-units. Our substances certainly contain less rat-units in a gram than those indicated by the values (last column of the table) calculated from the non-efficient doses.

The experiments of Slotta and Neisser[3] were performed with mice. The mouse-unit is about one-fifth to one-tenth the rat-unit, which could possibly explain the discrepancies found by the various authors. Therefore we tested the whole unsaponifiable fraction (5 mg., 15 mg. was poison-

(1) (a) H. Hauptmann, P. Sawaya and L. Bruck-Lacerda, *Boletim da Faculdade de Filosofia, Ciencias e Letras da Universidade de S. Paulo*, Quimica nr. 1, 181 (1942); (b) H. Hauptmann and J. França, THIS JOURNAL, **65**, 81 (1943).

(2) A. Wettstein, H. Fritzsche, F. Hunziker and K. Miescher, *Helv. Chim. Acta*, **24**, 332E (1941).

(3) K. H. Slotta and K. Neisser, *Ber.* **71**, 1951 (1938). Memorias do Instituto Butantan, **11**, 71 (1938).

(4) E. Allen and E. A. Doisy, *J. Am. Med. Assn.*, **81**, 819 (1923); *Am. J. Physiol.* **68**, 138 (1924); **69**, 577 (1924).

(5) B. Zondek, *Klin. Wochschr.*, **8**, 2229 (1929).

ous) and pure cafesterol (5 mg.) also on mice, but we could not observe estrus.

The results of these experiments demonstrate clearly that neither cafesterol and oxcafestandiol A nor any other part of coffee-oil have any estrogenic activity.

Acknowledgments.—We are indebted to D. Koch-Weser (Endoquimica Laboratories S. Paulo, Director Prof. Dr. K. H. Slotta) and to Prof. Dr. J. Ribeiro do Vale (Instituto Butantan, S. Paulo) for their kind help in performing the physiological experiments.

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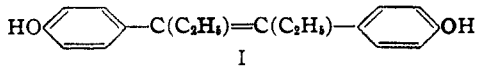
RECEIVED MARCH 11, 1943

STUDIES ON THE PREPARATION OF SYNTHETIC SEX HORMONES. II. CONCERNING SOME DERIVATIVES OF HEXESTROL

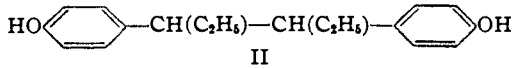
Sir:

That relatively simple synthetic organic compounds exhibit oestrogenic activity is now well known. Of especial interest in this connection are diethylstilbestrol (I)



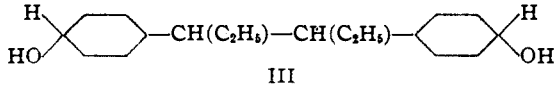
I

and hexestrol (II)



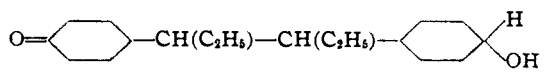
II

A good method for the preparation of the *meso* form of this latter compound has already been described in the first part of this series.[1] We now wish to report the preparation of certain of its derivatives. The starting material for this study was one of the isomeric perhydrohexestrols (III),



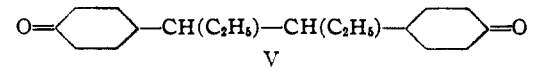
III

m. p. 167° prepared by hydrogenation of *meso*-hexestrol and kindly furnished to us by Merck and Co., Inc., Rahway, New Jersey. By means of partial oxidation with chromic acid we have converted this substance to the keto-alcohol (IV)



IV

and to the diketone (V)



V

This was achieved in the following manner: the diol (III) in pyridine was treated with the theoretical quantity of acetic anhydride necessary to acetylate one hydroxyl group. From the mixture of products so obtained the bulk of the unchanged diol was first precipitated by the addition of ether, and the ether soluble fraction, which consisted primarily of the mono- and diacetates, was then oxidized in the cold by a slight excess of chromic acid in acetic acid. Cold hydrolysis of the oxidation product with alcoholic sodium hydroxide gave a mixture of the diol and keto-alcohol contaminated with a small amount of the diketone. After conversion of the hydroxylic substances to the corresponding acid succinates (by the action of succinic anhydride in boiling pyridine for one hour) the acid esters were dissolved in dilute aqueous carbonate solution, freed from the diketone (V), m. p. 80°, by washing with ether, and precipitated by the addition of mineral acid. Cold alkaline hydrolysis of the esters gave the keto-alcohol contaminated with some diol. The former compound was then converted to the water soluble sodium bisulfite complex and the diol removed from the aqueous solution by filtration. Decomposition of the bisulfite complex with sodium carbonate gave the pure keto-alcohol (IV), m. p. 70°; semicarbazone, m. p. 146°. On treatment of the keto-alcohol with boiling acetic anhydride the acetate, m. p. 66°, was obtained; semicarbazone, m. p. 161°.

Further transformations of the keto-alcohol (IV) are now under investigation and will be reported in a later, more complete communication.

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RECEIVED APRIL 20, 1943

(1) Bernstein and Wallis, THIS JOURNAL, **62**, 2871 (1940).

CRYSTALLINE β-D-GLUCO-L-TALO-OCTOSE (SYN. D-GLUCO-α-L-TALO-OCTOSE)

Sir:

The epimeric pair of acids, D-gluco-L-gala-octonic[1] and D-gluco-L-talo-octonic, results from the application of Kiliani's cyanohydrin synthesis to D-gluco-D-gulo-heptose.[2] The reduction of the lactones of these acids with sodium amalgam by

(1) Concerning this nomenclature see Hudson, THIS JOURNAL, **60**, 1537 (1938).

(2) Emil Fischer, *Ann.*, **270**, 64 (1892).