

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 (Endoquímica 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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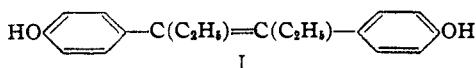
H. HAUPTMANN
J. FRANÇA
L. BRUCK-LACERDA

RECEIVED MARCH 11, 1943

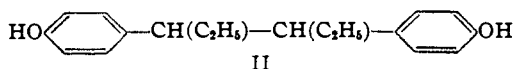
STUDIES ON THE PREPARATION OF SYNTHETIC SEX HORMONES. II. CONCERNING SOME DERIVATIVES OF HEXESTROL

Sir:

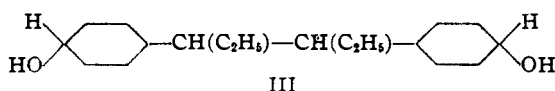
That relatively simple synthetic organic compounds exhibit oestrogenic activity is now well known. Of especial interest in this connection are diethylstilbestrol (I)



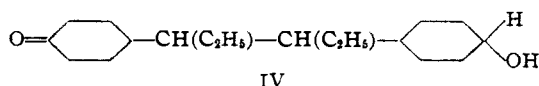
and hexestrol (II)



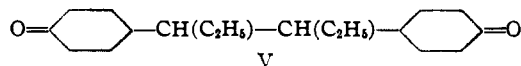
A good method for the preparation of the *meso* form of this latter compound has already been described in the first part of this series.¹ We now wish to report the preparation of certain of its derivatives. The starting material for this study was one of the isomeric perhydrohexestrols (III),



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)



and to the diketone (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

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

Sir:

The epimeric pair of acids, D-glucio-L-galaoctonic¹ and D-glucio-L-talo-octonic, results from the application of Kiliani's cyanohydrin synthesis to D-glucio-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, 1587 (1938).

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

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

Fischer yielded the corresponding aldo-octose sugars. The D-gluco-L-gala-octose was crystallized by him, but not the epimeric octose. We have now crystallized this D-gluco-L-talo-octose; it is anhydrous, melts at 117–118° (cor.) and mutarotates in water from an initial $[\alpha]^{20}_D$ of about -32° to the equilibrium rotation of -6.5° . The direction of this change leads to the naming of the crystalline sugar as a β -D-form. Since its reducing end possesses the L-talose configuration, it is to be expected that its properties will be similar to those of α -L-talose because this β -D-octose form is analogous to an α -talose form.³ Isbell and Pigman⁴ have found that the mutarotations of α - and β -D-talose are different in character; both show complex mutarotation, but the unimolecular coefficient values for the α -form decrease during the progress of the reaction whereas those for the β -form increase. Naturally, the same properties of rate apply for α - and β -L-talose. In agreement with expectations, the mutarotation of β -D-gluco-L-talo-octose is complex in character and the unimolecular coefficient values decrease during the reaction. The osazone of the octose proves to be identical with that from D-gluco-L-gala-octose, as is to be expected. The benzimidazole from D-gluco-L-gala-octonic acid is found to rotate to the left ($[\alpha]^{20}_D -44.7^\circ$ in 0.1 N HCl) and that from D-gluco-L-talo-octonic acid to the right ($+18.6^\circ$); these directions of rotation confirm, by the benzimidazole rule,⁵ the configurations which have been inferred previously⁶ for these octonic acids from the application of the lactone, the amide and the phenylhydrazide rules of rotation. The reduction of the two octoses with hydrogen and Raney nickel yields, respectively, D-gluco-L-gala-octitol (m. p. 153–154°, $[\alpha]^{20}_D +2.4^\circ$ in water; octaacetate, m. p. 141, $[\alpha]^{20}_D +20.7^\circ$ in chloroform) and D-gluco-L-talo-octitol (m. p. 161°, $[\alpha]^{20}_D -0.8^\circ$ in water; octaacetate, m. p. 102°, $[\alpha]^{20}_D +17.4$ in chloroform).⁷ The first of these readily distinguishable octitols has a configuration which is identical with that of one of the two octitols that can be expected in the

(3) If one finds the designation of the octose as a β -D-form confusing, the sugar can be named D-gluco- α -L-talo-octose with equal propriety. Either designation follows the accepted rules of nomenclature.

(4) Isbell and Pigman, *J. Res. Natl. Bureau of Standards*, **19**, 189 (1937).

(5) Richtmyer and Hudson, *This Journal*, **64**, 1612 (1942).

(6) Hudson, *ibid.*, **39**, 462 (1917); Hockett and Hudson, *ibid.*, **60**, 622 (1938).

(7) We thank Dr. W. D. Maclay for permission to quote these data from a forthcoming publication.

series of higher carbon sugars from D-galactose, namely, D-gala-L-gulo-octitol; its synthesis in that series is being sought in order to obtain conclusive proof of configurations in the glucose and galactose series of higher carbon sugars.

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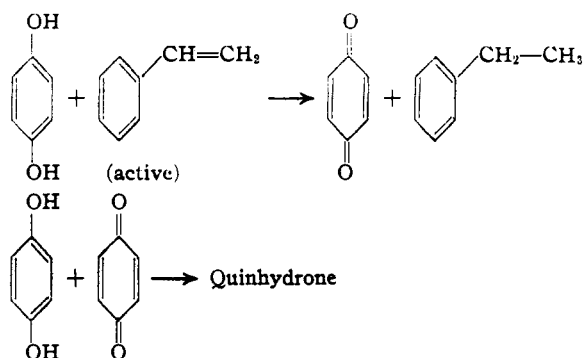
RECEIVED APRIL 3, 1943

FORMATION OF BIRADICALS IN THE NON-CATALYZED POLYMERIZATION OF STYRENE

Sir:

In studying the effect of inhibitors upon the kinetics of styrene polymerization, it seemed to us that appearance of the hydrogen of hydroquinone in the reaction product is indicative of the nature of the active nucleus.

The reaction yields quinone, quinhydrone and ethylbenzene, probably according to the scheme



Preliminary experiments were made in the following manner. Equimolecular amounts of hydroquinone and styrene were sealed in test-tubes and submitted to temperatures of about 150° for forty-eight to seventy-two hours, whereupon the solution turned dark brown. Refractive index measurements of the product obtained after elimination of the remaining hydroquinone by extraction with dilute sodium hydroxide and fractionated distillation of the residue (about 138°) gave the following results:

	Refractive index	Difference of refractive indices
Ethylbenzene	1.4959	0.0000
Fract. 1	1.4960	.0001
Product	1.4967	.0008
Fract. 2	1.4975	.0016
Styrene	1.5449	.0490

Although the experimental technique has not yet been developed to yield quantitative results as far as the rate process goes, the analytic results so far obtained seem to show the presence of