Pyrogallol, dissolved in pure water, was also found to be oxidized but only after addition of a little palladium.[4]

In the second series, ascorbic acid (Vitamin C) instead of hydrogen was used as a reductant. It was added to the reaction vessel containing the dye through a stopcock funnel in amount just sufficient to reduce the dye. When thereafter nitric oxide was bubbled through the system, no oxidation of the leuco-dye took place, but on the addition of a few drops of colloidal palladium, oxidation occurred. With tetramethyl- or tetraethyl-*p*-phenylenediamine no previous reduction is necessary. These were dissolved in acetate buffer and de-aerated with nitrogen. They are oxidized by NO, but only in the presence of palladium.

A further series of experiments, using the same apparatus, was made with inorganic salts. Nitric oxide passed into an aqueous solution of ferrous sulfate, pyrophosphate and tartrate gave deeply colored solutions of the nitroso complexes. When, however, the nitric oxide was removed by passing purified nitrogen through the solution,[5] it could be shown that no oxidation had taken place either in the presence or absence of palladium. From the literature it is known that chromous and stannous salts in aqueous solution are oxidized by nitric oxide without a catalyst, ammonia and hydroxylamine being formed. We found, in addition, that when nitric oxide was passed through solutions of cuproammino or chloro complexes prepared in the reaction vessel from the corresponding cupric complex and metallic copper, slow oxidation took place either to the complex cupric salt or to the complex nitroso cupric salt.

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(4) According to Oppenheimer [*Ber.*, **36**, 1744 (1903)], pyrogallol is oxidized without catalyst in alkaline solution, nitrous oxide being formed.

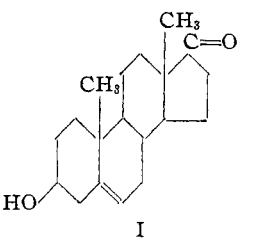
(5) *Cf.* Manchot, *Ber.*, **47**, 1601, 1614 (1914).

COMMUNICATIONS TO THE EDITOR

THE CONSTITUTION OF DEHYDRO-ANDROSTERONE AND ITS PREPARATION FROM CHOLESTEROL

Sir:

In the course of certain experiments on male urine, there has been isolated besides androsterone, $C_{19}H_{30}O_2$, an unsaturated hydroxy ketone of the formula $C_{19}H_{28}O_2$, which has been called dehydro-androsterone [Butenandt and Dannenbaum, *Z. physiol. Chem.*, **229**, 192 (1934)]. In most of these experiments this hydroxy ketone has not been isolated as such, but rather has been obtained in the form of its chloride derivative. Butenandt has transformed this hydroxy ketone into androsterone, and therefore the constitutional formula, I, has been assigned. The position of the double bond and the arrangement of the hydroxyl group in this formula are still uncertain. The name assigned to this unsaturated hydroxy ketone suggests that the hydroxyl group has the same stereochemical



I

arrangement as in androsterone. This seems doubtful to us for the following reasons. Butenandt has shown that on hydrogenation the unsaturated chloro ketone yields a saturated chloro ketone, $C_{19}H_{30}OCl$, which is different from the one which has been prepared by Ruzicka [Ruzicka, Goldberg and Brüngger, *Helv. Chim. Acta*, **17**, 1393 (1934)] by oxidation of β-cholestyl chloride. This suggests that the chlorine atom in the unsaturated chloro ketone isolated from urine does not have the same stereochemical arrangement as the chlorine atom in Ruzicka's chloro ketone but rather it indicates that it

possesses the same arrangement as the chlorine atom in cholesteryl chloride. Since it is known that cholesteryl chloride on treatment with sodium acetate in acetic acid yields cholesterol it is to be considered probable that the unsaturated chloro ketone behaves in the same manner and produces an hydroxy ketone, the hydroxyl group of which has the same arrangement as in cholesterol.

In order, therefore, to determine the arrangement of the hydroxyl group in dehydro-androsterone as well as the position of the double bond, we decided to attempt to prepare this ketone from cholesterol by oxidation. It has been found by experiments carried out in this Laboratory that dehydro-androsterone can be prepared from cholesterol by oxidation provided that both the hydroxyl group and the double bond in cholesterol are protected against oxidation. This is accomplished by an oxidation of cholesteryl acetate dibromide with chromic acid. The hydroxy ketone was isolated first in the form of the semicarbazone of its acetate (m. p. 270° with decomposition). Hydrolysis gave a product which melted at 148°, the same melting point which has been reported by Butenandt for dehydro-androsterone. A benzoate was prepared which melted at 250°. This is also characteristic of the benzoate of dehydro-androsterone.

From these results it is to be concluded that dehydro-androsterone isolated from male urine is in reality the epimeric form, that is, the stereochemical arrangement of the hydroxyl group is the same as in cholesterol. As yet, however, we have not been able to compare our substance with the natural product. When this has been done a more detailed report of our experiments will be published in THIS JOURNAL.

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RECEIVED JUNE 4, 1935

METHYLCHOLANTHRENE

Sir:

The recent communication by Fieser and Newman [THIS JOURNAL, **57**, 961 (1935)] contains the statement, "in a four-step process the German investigators (*i. e.*, Wieland and Dane) converted desoxycholic acid into the actively carcinogenic methylcholanthrene with an over-all yield of approximately 4.3%." This materially underestimates our own share in the investigations on methylcholanthrene, possibly because our publication [*J. Chem. Soc.*, 428 (1934)] was too concisely expressed, and hence conveyed a wrong impression. The actual sequence of events was as follows.

(a) Immediately after the new sterol-bile acid formulation was proposed by Rosenheim and King, attention was directed by Kennaway and Cook [*Chemistry and Industry*, **51**, 521 (1932)] to the possibility of cyclizing the side chain of these natural products to give a structure closely related to that of the known carcinogenic hydrocarbons.

(b) At a discussion meeting of the Royal Society held on June 15, 1933, one of us (J. W. C.) stated that the dehydrogenation of Wieland's dehydronorcholene to a benzanthracene hydrocarbon was under investigation, and the structural formula of the anticipated product, methylcholanthrene, was reproduced in the report of this meeting [*Proc. Roy. Soc.* (London), **B113**, 277 (1933)]. This was the first mention to be made of this carcinogenic hydrocarbon.

(c) In a paper submitted for publication on July 7, 1933, Wieland and Dane [*Z. physiol. Chem.*, **219**, 240 (1933)] reported the dehydrogenation of dehydronorcholene to methylcholanthrene, but adduced no evidence of its structure. As soon as this paper came to our knowledge we published a preliminary account of our own investigations [*Chemistry and Industry*, **52**, 758 (1933)]; we had already succeeded in degrading methylcholanthrene to 5,6-dimethyl-1,2-benzanthraquinone, but had not then identified this quinone.

(d) Our synthesis of the same 5,6-dimethyl-1,2-benzanthraquinone was described in our more complete publication (*loc. cit.*), together with the preliminary tests for carcinogenic activity carried out on methylcholanthrene by Professor E. L. Kennaway. We had obtained a 30% yield of methylcholanthrene by the dehydrogenation of dehydronorcholene, although Wieland and Dane claimed only a 10% yield. This latter figure is presumably the basis of the over-all yield quoted by Fieser and Newman.

While we welcome the interest of our transatlantic colleagues in the line of cancer research which we have thus initiated, we should state that this line of work is being extended here. We have already completed the synthesis of the