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.

FRICK CHEMICAL LABORATORY EVERETT S. WALLIS
PRINCETON UNIVERSITY E. FERNHOLZ
PRINCETON, N. J.

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

parent hydrocarbon, cholanthrene, by three different methods.

THE CANCER HOSPITAL (FREE) J. W. COOK
LONDON, ENGLAND G. A. D. HASLEWOOD

RECEIVED JUNE 11, 1935

METHYLCHOLANTHRENE

Sir:

In reply to the communication of J. W. Cook and G. A. D. Haslewood under the above title, I should like to disclaim any intention on the part of Newman and myself of underestimating the work of the English investigators on methylcholanthrene. Our note [THIS JOURNAL, **57**, 961 (1935)] was the third of a series of papers on the subject, and in the first paper [Fieser and Seligman, *ibid.*, **57**, 228 (1935)] reference was made to Cook and Haslewood's proof of the structure of methylcholanthrene and to their demonstration, with Kennaway, of its carcinogenic activity. Further reference to the history of the problem seemed beyond the scope of our brief note.

It is quite true that our statement regarding the yield was misleading, and I should like to present an explanation which was omitted before merely in the interest of brevity. Our purpose in estimating the approximate yield of methylcholanthrene from desoxycholic acid by the method first described by Wieland and Dane was to show that the new preparation from cholic acid (which is considerably shorter and more economical) yields about the same amount of material. In the absence of any statements in the literature regarding the yields of recrystallized acids in the first two steps, we used the best results of experiments of our own, namely, 60% for the oxidation and 80% for the reduction. For the cyclization, we took Cook and Haslewood's figure of 30% as being more accurate than the yield (39%) reported by Wieland and Schlichting [*Z. physiol. Chem.*, **150**, 267 (1925)] for a small-scale experiment. For the final step we used the yield of 30% obtained by Cook and Haslewood. I believed that our estimate of 4.3% was a fair one, and the fact that the matter of yields has not been emphasized by the other investigators may excuse us for having considered the details of the calculation sufficiently unimportant to be covered by the word "approximately."

I appreciate the courtesy of Cook and Haslewood in welcoming our participation in the work of developing the important field opened up by the fundamental discoveries of these investigators and their associates at the Cancer Hospital, and I am glad to acknowledge our indebtedness to the English group in providing the inspiration for our efforts to contribute to the cancer problem.

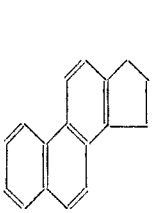
CONVERSE MEMORIAL LABORATORY LOUIS F. FIESER
HARVARD UNIVERSITY
CAMBRIDGE, MASS.

RECEIVED JUNE 18, 1935

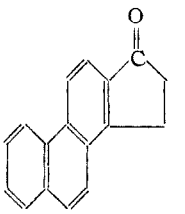
THE SYNTHESIS OF 1,2-CYCLOPENTENOPHENANTHRENE AND RELATED COMPOUNDS

Sir:

β-(2-Phenanthryl)-propionic acid (m. p. 177–177.5°) was obtained through the malonic ester reaction from 2-phenanthrylmethyl bromide; cyclization of the acid chloride by stannic chloride gave 1′-keto-1,2-cyclopentenophenanthrene (m. p. 183–184°); by Clemmensen reduction the ketone was converted to 1,2-cyclopentenophenanthrene (I), which was identical with the product prepared by Cook's method [*J. Chem. Soc.*, 1098 (1933)]. β-(3-Phenanthryl)-propionic acid (m. p. 156–157°) was prepared in a similar manner; the product of cyclization (m. p. 140–140.5°) is probably 1′-keto-2,3-cyclopentenophenanthrene, although the 3,4-structure is not excluded.



(I)



(II)

Of considerable interest as a basic structure of a number of important natural products as the sex hormones is the ketone, 3′-keto-1,2-cyclopentenophenanthrene (II). In order to obtain this ketone we have synthesized β-(1-phenanthryl)-propionic acid through the following series of reactions: phenanthrene ⟶ 1-benzoylphenanthrene ⟶ 1-phenanthraldehyde ⟶ 1-phenanthrylcarbinol ⟶ 1-phenanthrylmethyl bromide ⟶ β-(1-phenanthryl)-propionic acid. The preparation of 1-benzoylphenanthrene has already been described [Bachmann, THIS JOURNAL, **57**, 555 (1935)]. The oxime (m. p. 186°) of this ketone was found to undergo a Beckmann rearrangement to 1-phenanthroic acid anilide (m. p. 245°); from 70 g. of 1-benzoylphenanthrene we obtained