

The investigation was extended to a preliminary study of ergoclavine [W. Küssner, *E. Merck's Jahresbericht. Original Mitteil.*, **47**, 5 (1933)]. On alkaline hydrolysis ammonia, lysergic acid (*Anal.* C, 71.37; H, 6.25), and isobutyrylformic acid were obtained. The latter was isolated as the phenylhydrazone which melted at 148° (*Anal.* C, 63.77; H, 6.64) (G. Barger has reported [*E. Merck's Jahresbericht. Original Mitteil.*, **47**, 12 (1933)] that a base similar to ergine and isobutyrylformamide can be obtained from ergoclavine). From the amino acid fraction only one substance was isolated which from the analysis appeared to be leucine (*Anal.* C, 54.92; H, 9.77).

Ergoclavine was then hydrolyzed by hydrochloric acid. This again resulted in the destruction of the lysergic acid portion of the molecule. From the amino acid fraction a substance was isolated which agreed in properties with partly racemized *l*-leucine (*Anal.* C, 55.05; H, 10.04). The inversion of its rotation in aqueous solution [ $[\alpha]^{20D} -6^\circ$ , to  $[\alpha]^{20D} +6^\circ$  in dilute hydrochloric acid solution appears to eliminate isoleucine. The mother liquor still contained an amino acid which from the strong pyrrole red test suggested proline. However, contrary to our experience with ergotinine, this fraction did not yield proline as the methyl ester. This coincides with our experience in the attempt to isolate proline from ergotamine. It is not excluded that hydroxyproline may be in question.

Our study of the degradation of lysergic acid itself has yielded among other substances, indole derivatives which will be a subject for a later communication.

LABORATORIES OF THE  
ROCKEFELLER INSTITUTE FOR  
MEDICAL RESEARCH  
NEW YORK, N. Y.

WALTER A. JACOBS  
LYMAN C. CRAIG

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#### METHYLCHOLANTHRENE FROM CHOLIC ACID

Sir:

In view of the important biological implications of the chemical transformation of substances nor-

mally present in the body into cancer-producing agents, an extension of the observations of Wieland and Dane [*Z. physiol. Chem.*, **219**, 240 (1933)] to additional cases has been undertaken. In a four-step process the German investigators converted desoxycholic acid into the actively carcinogenic methylcholanthrene with an over-all yield of approximately 4.3%. We have obtained the same hydrocarbon in 5.4% yield from cholic acid, the most abundant acid constituent of the bile. Since the process is quite rapid and the starting material only one-tenth as expensive as desoxycholic acid, the new method provides a ready source of the hydrocarbon for experimental purposes.

Cholic acid (200 g.) was oxidized in glacial acetic acid solution (1700 cc.) with 150 g. of chromic anhydride in 150 cc. of water and 600 cc. of acetic acid at 30–40° (two and one-half to three hours), giving 140 g. of dehydrocholic acid, m. p. 237–238° [method of Hammarsten, *Ber.*, **14**, 71 (1881)]. The triketo acid (40 g.) was reduced to 3,7-dihydroxy-12-keto-cholanic acid according to Kawai [*Z. physiol. Chem.*, **214**, 71 (1933)], using Adams catalyst (2.5 g.), and the entire reduction product (from which the pure monoketone could be isolated in 30–40% yield) was subjected to pyrolysis at 260–280° for one hour and at 320–330° for eight to nine hours and distilled in vacuum. The very viscous distillate (14–18 g.), probably containing a mixture of norcholatrienes, was heated with 20–25 g. of selenium, added in several portions, at 320–330° for forty-eight hours. After extraction with benzene, distillation and purification through the picrate there was obtained 2.0–2.2 g. (5.2–5.7%, over-all) of orange-yellow methylcholanthrene, m. p. 177–178°, corr. After passing a benzene solution of the hydrocarbon through an adsorption tower of activated alumina, methylcholanthrene was obtained as pale yellow needles, m. p. 178.5–179°, corr.

CONVERSE MEMORIAL LABORATORY      LOUIS F. FIESER  
HARVARD UNIVERSITY                      MELVIN S. NEWMAN  
CAMBRIDGE, MASSACHUSETTS

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