comparing favorably with nicotine for use against aphids.

INSECTICIDE DIVISION C. R. SMITH
BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE
U. S. DEPARTMENT OF AGRICULTURE
WASHINGTON, D. C.

RECEIVED APRIL 20, 1935

THE PREPARATION AND PROPERTIES OF BENZENE-d_6

Sir:

We have developed a technique for the exchange reaction between deuterium oxide and benzene, discovered by Horiuti and Polanyi [*Nature*, **134**, 377 (1934); *Trans. Faraday Soc.*, **30**, 1164 (1934)] which permits the ready production of benzene-d_6. Two cylindrical Pyrex vessels of about 50-cc. capacity are connected by a Pyrex U-tube containing an active nickel catalyst supported on kieselguhr. The catalyst tube is heated externally by a closely fitting electric furnace, and the catalyst reduced (in our case with deuterium) at 420°. After the system is thoroughly evacuated and sealed a sample of 5 cc. of benzene and 10–20 cc. of heavy water is introduced *in vacuo* through a special breakable seal. By means of an electric furnace, which closely fits either cylinder, the water is brought to ebullition and, carrying with it a proportion of benzene vapor, is driven over the catalyst, heated to 200°, where some exchange occurs, the product condensing in the second cylinder appropriately cooled. By reversing the procedure the benzene–water mixture can then be passed once more through the catalyst. Frequent repetition of the process ultimately establishes an equilibrium partition of deuterium between water and benzene. By replacing the hydrogen-diluted deuterium oxide with fresh pure deuterium oxide and continuing the passage over the catalyst, further conversion toward benzene-d_6 can be obtained.

We traced the progress of the exchange by attaching to the reaction system via a quartz-Pyrex seal a cylindrical quartz absorption cell 30 mm. thick. Benzene vapor at room temperatures gives a series of sharply defined ultraviolet absorption bands. Each of the substituted benzenes, C_6H_5D, $C_6H_4D_2$, etc., shows similar bands, displaced toward the ultraviolet by frequency differences varying for each band but roughly constant for each additional D atom. As exchange occurs forming an equilibrium among the 13 benzenes this results in a considerable overlapping and complication of the spectrum. With continued progress toward the final state, the overlapping disappears, the sharply defined bands of C_6D_6 only remaining.

In four successive equilibrations with 5 cc. of benzene using an initial 10 cc. of 95% D_2O and then successively 10, 20 and 20 cc. of 100% D_2O a product containing 55, 85, 97 and >99% of the hydrogen as deuterium has been prepared. The deuterium contents have been *estimated* from the absorption spectra. For example, in the 97% product, the bands corresponding to C_6D_5H and C_6D_6 were the only ones visible, the former with about one-fifth the intensity of the latter. Densities of the carefully purified and redistilled samples at the first two stages were, 55%, d^{25}_4 0.9146; 85%, d^{25}_4 0.9349; and the final product had a density of 0.9417. After four separate processes of purification we received approximately 3.5 cc. of final product. Measurements are being made of the Raman spectra, infra-red and ultraviolet absorptions and other physical properties. We are continuing our study of the variables in the preparation and also extending the procedure to other compounds.

FRICK CHEMICAL LABORATORY P. I. BOWMAN
PRINCETON UNIVERSITY W. S. BENEDICT*
PRINCETON, N. J. H. S. TAYLOR

RECEIVED APRIL 22, 1935

(*) National Research Fellow.

THE HYDROLYSIS OF ERGOTININE AND ERGOCLAVINE

Sir:

Following our preliminary communications [*J. Biol. Chem.*, **104**, 547 (1934); THIS JOURNAL, **57**, 383 (1935); *Science*, **81**, 256 (1935)] regarding the cleavage of ergotinine by alkali to lysergic acid, isobutyrylformic acid, ammonia and a polypeptide which on further hydrolysis with acid yielded proline and phenylalanine, we have made a logical extension of the investigations to the study of the cleavage of ergotinine by acid. Heating with hydrochloric acid resulted in the destruction of the lysergic acid portion of the molecule with the formation of obscure amorphous material. On the other hand, *l*-phenylalanine, $[\alpha]^{20}D$ −28° (c = 0.39 in H_2O), was obtained as such while proline was isolated as the methyl ester (*Anal.* C, 55.70; H, 8.81), $[\alpha]^{25}D$ +33° (c = 0.65 in CH_3OH), which was further characterized by the gold salt (*Anal.* C, 15.70; H, 2.62; Au, 41.83).

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 $[\alpha]^{20}D$ −6°, to $[\alpha]^{20}D$ +6° 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

RECEIVED APRIL 22, 1935

METHYLCHOLANTHRENE FROM CHOLIC ACID

Sir:

In view of the important biological implications of the chemical transformation of substances normally 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
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS
LOUIS F. FIESER
MELVIN S. NEWMAN

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