Preparation of *dl*-2,3-Dibromobutane.—*dl*-2,3-Dibromobutane was prepared from *meso*-2,3-butanediol by the synthesis outlined by Wilson and Lucas.[12]

Reaction of 2,3-Dibromobutanes with Sodium Iodide in Propanol.—Seventy grams (0.46 mole) of sodium iodide was dissolved in a warm mixture of 75 ml. of *n*-propanol and 25 ml. of water. Then 20 g. (0.093 mole) of 2,3-dibromobutane was added. Two liquid phases were present initially but a homogeneous solution resulted upon further heating. The mixture was refluxed gently, the evolved gas being washed with water, dried with calcium chloride and collected in a cold ampoule at −78°. In the reaction flask, iodine was liberated and a white precipitate of sodium bromide formed. After four hours of refluxing, the rate of butene evolution was slow and the reaction was stopped, the apparatus being flushed out with air. The crude yield of hydrocarbon was 87% of the theoretical from *meso*-2,3-dibromobutane, 80% from *dl*-2,3-dibromobutane and 81% from a mixed dibromobutane.

Reaction of 2,3-Dibromobutane with Potassium Iodide in Diethylene Glycol.—Forty grams (0.185 mole) of *dl*-dibromobutane was added dropwise to a hot solution of 80 g. (0.48 mole) of potassium iodide in 300 g. of diethylene glycol. The butene which was evolved continuously during the course of the reaction was washed with a dilute sodium hydroxide solution and dried over anhydrous calcium chloride before being condensed in an ampoule. The temperature of the reaction mixture started at 245° and gradually dropped to 165° at the finish. The yield of butene was 85%.

Analysis of Butene Mixtures.—The butene mixtures were analyzed according to the method previously outlined.[16] The second order reaction rate constants of the original and final dibromobutanes with potassium iodide in 99% methanol are listed in Table I together with the corresponding compositions of butenes which they represent.

(12) Wilson and Lucas, THIS JOURNAL, **58**, 2396 (1936).

Summary

The elimination of bromine from *dl*- and *meso*-2,3-dibromobutanes by iodide ion has been found to be an almost complete *trans* removal of halogen at moderate temperatures. A mechanism for the process has been proposed. It is thought that iodide ion removes a positive bromine atom and essentially simultaneously with this removal the electron pair which is left unshared by this removal attacks the carbon face opposite the remaining bromine atom forming a double bond and liberating bromide ion.

LOS ANGELES, CALIF. RECEIVED MARCH 14, 1939

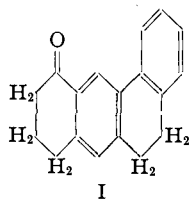
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Syntheses in the 1,2-Benzanthracene and Chrysene Series

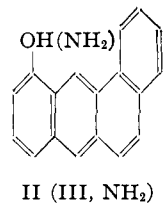
BY LOUIS F. FIESER AND WILLIAM S. JOHNSON[1]

Having developed a satisfactory method for the synthesis of pure 8-methyl-1,2-benzanthracene[2] from the keto acid resulting in nearly quantitative yield from the succinoylation of 9,10-dihydrophenanthrene,[3] we have utilized some of the same intermediates for the synthesis of certain other compounds which seemed of interest to the problem of hydrocarbon carcinogenesis.

8-Ethyl-1,2-benzanthracene was prepared from the ketone I by a Grignard reaction followed by



I



II (III, NH_2)

sulfur dehydrogenation of the low-melting but crystalline tetrahydride obtained on distillation of the resulting carbinol. Like the lower homolog,[2] the completely aromatized hydrocarbon shows a characteristic double melting point when pure. For the preparation of the phenol II, required for comparison with the weakly carcinogenic 3-isomer,[4] the dehydrogenation of 8-keto-hexahydrophenanthrene (I) by the method of Mosettig and Duval[5] using Adams catalyst in naphthalene solution was tried without success. 8-Hydroxy-1,2-benzanthracene, however, can be obtained satisfactorily by dehydrogenation with sulfur,[6] and the phenol was converted into the amine III by the Bucherer reaction.

In view of the enhancement of carcinogenic potency noted with certain combinations of *meso*- and α-methyl groups[4] (5,10-, 5,9-, 9,10-), it seemed important to obtain the di-α-substituted 5,8-dimethyl-1,2-benzanthracene (XII).

(1) Holder of the John Woodruff Simpson Fellowship from Amherst College.

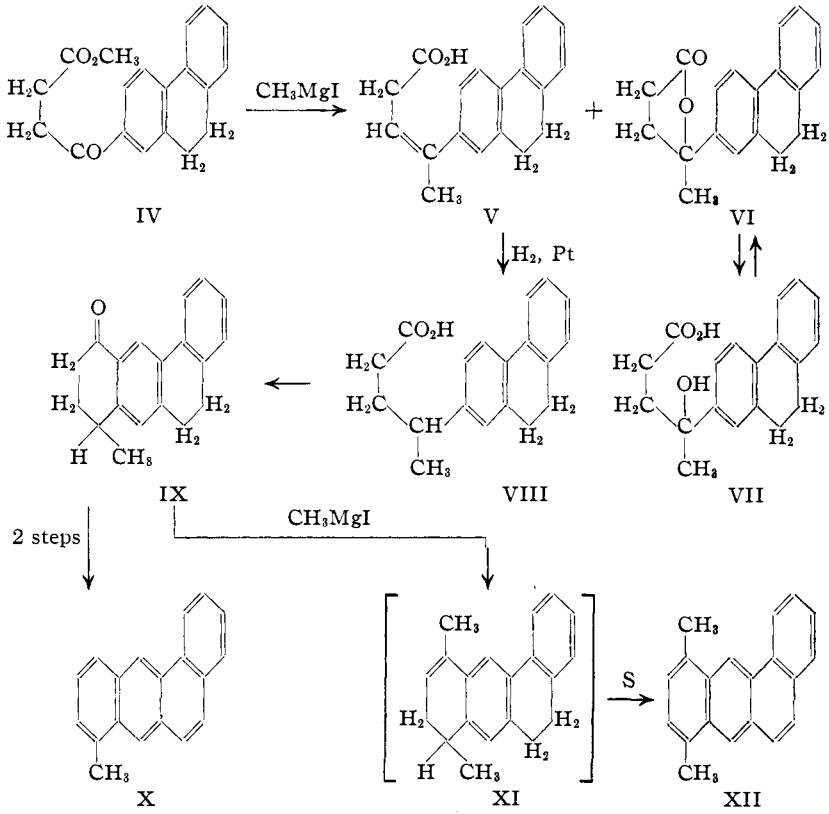
(2) Fieser and Johnson, THIS JOURNAL, **61**, 168 (1939).

(3) Burger and Mosettig, *ibid.*, **59**, 1302 (1937).

(4) For a summary of the data and literature, see Fieser, *Am. J. Cancer*, **34**, 37 (1938).

(5) Mosettig and Duval, THIS JOURNAL, **59**, 367 (1937).

(6) Compare the preparation of 4'-hydroxy-3,4-benzpyrene Fieser, Hershberg, Long and Newman, *ibid.*, **59**, 475 (1937).



The introduction of a methyl group at a point corresponding to the 5-position was accomplished by the action of methylmagnesium iodide on methyl β-(9,10-dihydro-2-phenanthroyl)-propionate (IV). Haworth and co-workers[7] conducted similar reactions with the esters of a number of β-aroylpropionic acids and obtained from the acidic fractions unsaturated acids of the type indicated by formula V. While these acids were obtained in yields up to 50–75%, the neutral fractions apparently were not investigated. In an earlier paper Rupe and Steinbach[8] report the preparation of an unsaturated acid from ethyl β-(*p*-toluyl)-propionate in fair yield, and state, without giving details, that the neutral fraction contained a mixture of unchanged starting material and the ester of the unsaturated acid. They also describe the lactonization of the unsaturated acid with dilute mineral acid. In view of the high yields obtained in the methylation of *o*-aroylbenzoic acids by the procedure[9] of adding Grignard reagent in excess to a suspension of the free keto acid, this method was tried in the present case. When treated with a large excess of methylmagnesium bromide, however, the dihydrophenanthroylpropionic acid was converted largely into an unsaponifiable oil, and the result seemed so unpromising that we turned to the use of the ester. When the ester (IV) was treated with methylmagnesium iodide or bromide in only slight excess and the solution refluxed for about two hours the chief product (64%) was the unsaturated acid V. Material satisfactory for the reduction step but apparently consisting of a mixture of stereoisomers can be obtained easily on one crystallization (53% yield). When the Grignard reaction was moderated by operating at a lower temperature, the yield of the crude unsaturated acid V dropped to 32% and the neutral fraction afforded the corresponding lactone VI in 35% yield. The lactone was isolated from this source in a crystalline condition and it was also prepared by boiling the unsaturated acid with 10% sulfuric acid. By dissolving the lactone in hot alkali and carefully neutralizing the cooled solution the unstable γ-hydroxy acid VII was also isolated in a pure, crystalline condition.

A few attempts were made to reduce the lactone VI with zinc and alkali or by the Clemmen-

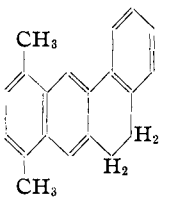
(7) R. D. Haworth and co-workers, *J. Chem. Soc.*, 1784, 2248 (1932); 454, 864 (1934).

(8) Rupe and Steinbach, *Ber.*, **44**, 584 (1911).

(9) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).

sen method, but the results were not promising. The easily obtainable unsaturated acid, however, can be hydrogenated smoothly in acetic acid solution to the γ-dihydrophenanthrylvaleric acid VIII. Cyclization to 5-methyl-8-keto-3,4,5,6,7,-8-hexahydro-1,2-benzanthracene (IX) was accomplished most satisfactorily by the action of liquid anhydrous hydrogen fluoride,[10] the pure material being obtained in 81.5% yield. An identical product was obtained in 64% yield by the PCl_5–$AlCl_3$ method in benzene. Cyclization in each case seems to occur exclusively in one direction, and that the product is a benzanthracene rather than a chrysene derivative was established by conversion of the ketone on Clemmensen reduction and dehydrogenation into a hydrocarbon identical with a sample of 5-methyl-1,2-benzanthracene (X) prepared by a different synthesis.[9]

5,8-Dimethyl-1,2-benzanthracene (XII) was prepared from the ketone IX by a Grignard reaction, dehydration of the carbinol, and dehydrogenation with sulfur. Purified through the picrate and by chromatographic adsorption, the dimethyl compound gave evidence from the melting point characteristics of the existence of two polymorphic forms, as noted for other compounds of the 8-series. The intermediate tetrahydride (XI) was not isolated. While the 8-methyl tetrahydride[2] was obtained crystalline in good yield, the oil resulting from the distillation of the carbinol of the 5,8-dimethyl series solidified only partially and the small amount of recrystallized product isolated had the composition of a dihydride. Of the possible structures that of 5,8-dimethyl-3,4-dihydro-1,2-benzanthracene (XIII) is clearly indicated by the



XIII

ultraviolet absorption spectrum (in absolute alcohol) kindly determined by Dr. R. Norman Jones. The curve (Fig. 1) is characteristic of an alkylated β-phenylnaphthalene and is practically identical with that for the similarly constituted 6,7-dihydromethylcholanthrene[11] (dotted line).

(10) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).

(11) Fieser and Hershberg, *ibid.*, **60**, 940 (1938).

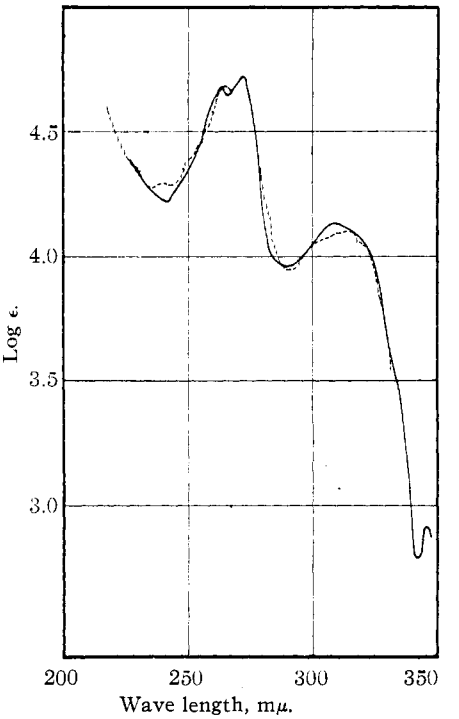
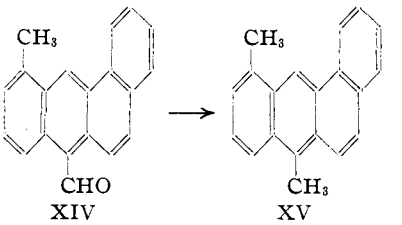


Fig. 1.—Solid line, 5,8-dimethyl-3,4-dihydro-1,2-benzanthracene; dotted line, 6,7-dihydro-20-methylcholanthrene.

Another hydrocarbon of interest for the investigation of the combined influence of *meso*- and α-methyl groups was obtained by condensing 8-methyl-1,2-benzanthracene with methylformanilide and reducing the resulting aldehyde by the Wolff–Kishner method. The dimethyl com-



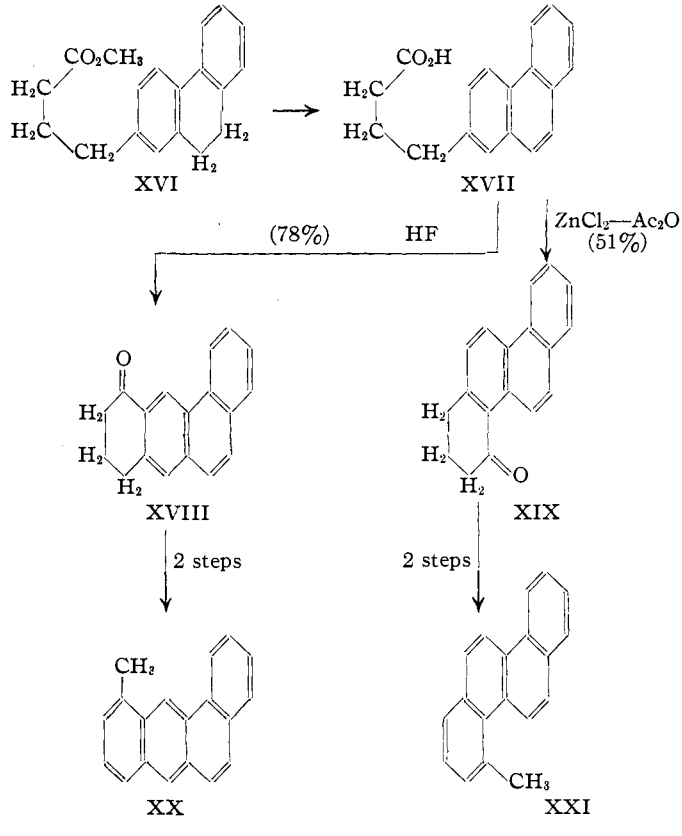
XIV XV

pound is different from the above 5,8-isomer and, since the aldehyde reaction is specific for structures of limited types and is known[12] to give the 10-derivative of 1,2-benzanthracene but to fail with 1,2,5,6-dibenzanthracene, the substance can be regarded with considerable assurance as 8,10-dimethyl-1,2-benzanthracene (XV). Some confirmation of the structure has been obtained by Dr. Jones in a study of the absorption spectra of this and related hydrocarbons which will be reported shortly. The introduction of a 10-methyl group is accompanied by a slight but definite dis-

(12) Fieser and Hartwell, *ibid.*, **60**, 2555 (1938).

placement of the most intense absorption band to longer wave lengths, specific to the *meso* positions.

The starting material for the above work served as well for the synthesis of 4-methylchrysene (XXI), required[13] as a possible model for the highly carcinogenic 3,4-benzpyrene. γ-(9,10-Dihydro-2-phenanthryl)-butyric acid (reduction of IV as acid) was dehydrogenated with sulfur in the form of the ester XVI giving, after saponification, γ-(2-phenanthryl)-butyric acid, XVII. Haworth and Mavin[14] previously prepared this acid from the less accessible 2-acetylphenanthrene and found that on cyclization with 85% sulfuric acid it yielded a mixture of isomeric ketones from which pure 4-keto-1,2,3,4-tetrahydrochrysene (XIX) was isolated in unspecified yield. Our experience was



much the same and the yield of pure XIX, m. p. 125°, was 23%. Ring closure by the hydrogen fluoride procedure[10] gave a high yield of total ketone which consisted almost entirely of the hitherto unknown isomer 8-keto-5,6,7,8-tetrahydro-1,2-benzanthracene (XVIII), m. p. 118°, which was obtained pure in 78% yield. For identification the ketone was converted to 8-methyl-1,2-benzanthracene through a crystalline dihydride. When the acid XVII was cyclized with zinc chloride[15] (0.65 equivalent) in acetic acid-anhydride the distilled and twice crystallized total ketone amounted to 51% and consisted of the pure chrysene derivative XIX. With the ketone available by this convenient process the synthesis of 4-methylchrysene, through a crystalline dihydride, was easily completed.

The sharp contrast in the direction of cyclization with hydrogen fluoride and with zinc chloride is quite striking and of obvious practical significance. The Friedel and Crafts procedure gave mixtures of the two ketones in which the benzanthracene derivative XVIII predominated. This isomer constituted about two-thirds of the total using benzene as the solvent, and a still higher proportion was produced in nitrobenzene solution. These results with γ-(2-phenanthryl)-butyric acid contrast with those reported for the cyclization of β-(2-phenanthryl)-butyric acid[16] and β-(2-phenanthryl)-propionic acid[17] in the Friedel and Crafts reaction and with stannic chloride, for these acids undergo ring closure exclusively at the 1-position.

Experimental Part[18]

8-Ethyl-3,4,5,6-tetrahydro-1,2-benzanthracene.—An ethereal solution of 6 g. of 8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene[2] (I) was added with stirring to a cooled Grignard solution from 2 g. of magnesium and 7 g. of ethyl bromide. After refluxing for several hours the product was recovered as usual, heated to effect dehydration, and distilled, b. p. about 185° (1 mm.). The colorless oil (5.55 g., 88.5%) crystallized with difficulty in a solid carbon dioxide bath; a portion purified by several crystallizations from methanol formed large, elongated, highly fluorescent prisms, m. p. 65–67°.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.53; H, 7.63.

8-Ethyl-1,2-benzanthracene.—The distilled tetrahydride (1.33 g.) was dehydrogenated by heating with sulfur (0.33 g.) at 210–255° for twenty-five minutes. After very brief heating with a little zinc dust the product was distilled in vacuum, and after decolorizing the yellow oil in ether–alcohol picric acid (1.2 g.) was added. A dark red picrate separated on cooling (1.2 g., m. p. 148.5–149.5°) and an additional quantity (0.25 g.)

(13) Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938).
(14) R. D. Haworth and Mavin, *J. Chem. Soc.*, 1012 (1933).
(15) Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).
(16) E. Bergmann and Hillemann, *Ber.*, **66**, 1302 (1933).
(17) Bachmann and Kloetzel, THIS JOURNAL, **59**, 2207 (1937).
(18) All melting points are corrected.

was obtained on concentration; total yield, 58.5%. Recrystallized from alcohol the picrate formed deep red blades, m. p. 149.5–150°.

Anal.[19] Calcd. for $C_{26}H_{19}O_7N_3$: N, 8.65. Found: N, 8.73.

The picrate (0.7 g.) was decomposed by passing a benzene solution through a tower of alumina; on adding alcohol to the concentrated filtrate the hydrocarbon crystallized in very faintly yellow, glistening needles, m. p. 82–83.5° (0.31 g., 84%). Recrystallization from petroleum ether gave a lower-melting form, m. p. 78–79°, which remelted after solidification at 82.5–83°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.51; H, 6.36.

8-Hydroxy-1,2-benzanthracene was prepared by heating the ketone I (2 g.) with 0.52 g. of sulfur at 230–255° for twenty-seven minutes and distilling the product at the oil pump vacuum. Crystallization from benzene–ligroin gave 1.1 g. of ringlets of small yellow needles, m. p. 138–148°; a second crystallization yielded 0.88 g. (45%) of product, m. p. 149–151°. The further purified phenol formed bright yellow rods, m. p. 151.3–151.8°.

Anal. Calcd. for $C_{18}H_{12}O$: C, 88.50; H, 4.95. Found: C, 88.55; H, 5.21.

The acetate, prepared using pyridine as catalyst, after three crystallizations from ligroin formed light buff colored needles, m. p. 133–133.6°.

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.86; H, 5.08.

8-Amino-1,2-benzanthracene.—A mixture of 0.5 g. of the hydroxy compound, 2.5 cc. of dioxane, 5 cc. of concentrated ammonia solution, and 2.5 g. of sodium bisulfite in 5 cc. of water was heated in a sealed tube at 190–200° for ten hours. The addition of dilute alkali precipitated a yellow oil which solidified on scratching. This crystallized from benzene–ligroin (Norite) in beautiful, long yellow needles (0.13 g., 26%), m. p. 201.7–202.3° dec. (no change on recrystallization).

Anal.[19] Calcd. for $C_{18}H_{13}N$: N, 5.76. Found: N, 5.49.

Methyl β-(9,10-Dihydro-2-phenanthroyl)-propionate (IV) was prepared by esterification of the keto acid (100 g.) in methanol (1400 cc.) saturated with hydrogen chloride. The ester was washed in ether with soda solution, dried, and distilled, b. p. about 250° (1–2 mm.). One crystallization from methanol gave 88 g. (84%), m. p. 76–78°. A recrystallized sample formed almost colorless prisms, m. p. 77–78°.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.65; H, 6.28.

γ-Methyl-γ-(9,10-dihydro-2-phenanthryl)-vinylacetic Acid (V).—The reagent from 3.7 g. of magnesium and 22 g. of methyl iodide in 100 cc. of ether was added with cooling and stirring to a solution of 30 g. of the above ester IV in 500 cc. of benzene. After boiling the mixture under reflux for one and one-half hours the oily intermediate was decomposed with ice and acid. The organic layer was washed with acid and extracted with 10% soda solution. No saponifiable material was found in the neutral fraction. On acidifying the soda solution the unsaturated acid V separated in an almost colorless condition; yield, 18.2 g. (64%). One crystallization from benzene–ligroin gave 15.1 g. (53%) of pale yellow prisms, m. p. 117–125° (mixture of stereoisomers?), suitable for the next step. Eight recrystallizations were required to obtain a sample of the constant m. p. 137–138°, dec. (pale yellow plates).

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.53. Found: C, 82.08; H, 6.41.

γ-(9,10-Dihydro-2-phenanthryl)-γ-valerolactone (VI). (a) From the Grignard Reaction.—The ester IV (20 g.) in benzene (75 cc.) was treated with the reagent from 1.8 g. of magnesium and excess methyl bromide and the mixture was warmed gently on the steam-bath for one hour without refluxing. After hydrolysis with 10% sulfuric acid, extraction with soda afforded 4.5 g. (32%) of the crude vinylacetic acid derivative V. Evaporation of the solution containing the neutral fraction gave an oil which largely dissolved in hot alkali. On acidifying the alkaline solution an oil precipitated. This was taken up in ether, and after extracting a small amount of acidic material with soda, drying and evaporating the solution, the lactone VI distilled at about 240° (2 mm.). The colorless distillate was obtained crystalline from ligroin, forming large, colorless prisms, m. p. 60–65°, identical with material prepared in (b); yield, 5 g. (35%).

A second run identical with the above except that the Grignard reaction mixture was refluxed vigorously for two hours gave 9 g. (63%) of the crude vinylacetic acid V and only a small amount of the lactone.

(b) From the Unsaturated Acid V.—The crude vinylacetic acid V (4.5 g.) was boiled with 50 cc. of 10% sulfuric acid for four hours and the oily product washed in ether with water and extracted with soda, which removed 2 g. of unchanged acid. After evaporation of the ether the lactone distilled as a colorless oil which slowly crystallized as large, colorless prisms, m. p. 60–68° (1.3 g., 52% based on acid consumed). Further purification gave prisms melting largely at 61.5–63° but giving a clear liquid only at 70°.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.98; H, 6.53. Found: C, 81.91; H, 6.56.

γ-Hydroxy-γ-(9,10-dihydro-2-phenanthryl)-valeric acid (VII) was prepared by acidifying a cooled solution prepared by dissolving the lactone VI in boiling aqueous alkali. The hydroxy acid easily reverts to the lactone, but by careful crystallization from ether it was obtained as small, colorless needles, m. p. 95–97°, dec.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.89; H, 6.83.

γ-(9,10-Dihydro-2-phenanthryl)-valeric Acid (VIII).—A solution of 12.1 g. of the vinylacetic acid V in 200 cc. of glacial acetic acid in the presence of Adams catalyst absorbed one mole of hydrogen rapidly at room temperature. The solvent was removed from the filtered solution and the product distilled at about 250° (1 mm.). The saturated acid was obtained in nearly quantitative yield as a colorless oil which set to a glass and, in the course of some time, crystallized. The distilled product was suitable for the next step. A sample of the solid material

(19) Microanalysis by Herbert S. Wight.

when purified by crystallization from ether–petroleum ether formed colorless prisms, m. p. 77.5–78.5°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.16; H, 6.87.

5 - Methyl - 8 - keto - 3,4,5,6,7,8 - hexahydrophenanthrene (IX). (a) **Hydrogen Fluoride Procedure.**—The valeric acid VIII (11 g.) was treated with 150 g. of chilled liquid anhydrous hydrogen fluoride in a platinum vessel and the solution allowed to stand at room temperature for three hours. After evaporating the reagent, warming the residue with soda solution and cooling, the product solidified. It was washed and dried in benzene and distilled in vacuum, giving a colorless solid. One crystallization from methanol yielded 8.4 g. (81.5%) of flat needles, m. p. 127.2–128.4°; recrystallized, m. p. 127.9–128.4°.

Anal. Calcd. for $C_{19}H_{18}O$: C, 86.98; H, 6.92. Found: C, 86.97; H, 6.83.

(b) **Friedel and Crafts Reaction.**—A mixture of the valeric acid (10 g.) and phosphorus pentachloride (9.5 g.) in 150 cc. of benzene was refluxed for one hour and the solution was cooled and treated under stirring with 9.5 g. of aluminum chloride. After standing two and one-half hours at room temperature and refluxing for one and one-half hours the mixture was poured onto ice and acid and the benzene layer washed and dried. Distillation in vacuum and one crystallization from methanol yielded 6 g. (64%) of colorless needles of the ketone, m. p. 126–127.5°.

5-Methyl-1,2-benzanthracene.—The ketone IX (5.7 g.) was reduced by the Clemmensen–Martin method using 25 g. of amalgamated zinc, 25 cc. of toluene, 1 cc. of glacial acetic acid, 18 cc. of water, and 45 cc. of concentrated hydrochloric acid. Refluxing was continued for forty-eight hours with the addition of a second charge of zinc and a total of 100 cc. of concentrated hydrochloric acid. As the reduction progressed the toluene layer became fluorescent in ultraviolet light. After separation of the layers and extraction with benzene the washed and dried solution was filtered through a tower of alumina to remove any ketone and concentrated. The residual colorless oil (5 g.) was heated with sulfur (1.93 g.) at 200–255° for one hour and the product distilled in vacuum from a pinch of zinc dust and redistilled, giving 2.6 g. (49.5%, from the ketone) of yellowish hydrocarbon, m. p. 140–150°. A 0.25-g. portion treated in alcohol with 0.5 g. of picric acid gave red needles of the **picrate** (0.37 g.), m. p. 164.5–165°; recrystallized from 5% picric acid solution it melted at 165.5–166° (Fieser and Newman,[9] 165.8–166.3°). Recovered by cleavage of the picrate in benzene with an alumina tower, the hydrocarbon crystallized from benzene–alcohol in yellowish plates (0.17 g., 68% from crude hydrocarbon), m. p. 158–159.4°. No depression in m. p. was observed on mixing with an authentic sample of 5-methyl-1,2-benzanthracene,[9] m. p. 158.5–159.1°.

5,8 - Dimethyl - 3,4 - dihydro - 1,2 - benzanthracene (XIII).—The ketone IX (3 g.) in benzene was added with cooling and stirring to the Grignard reagent from 0.55 g. of magnesium and excess methyl chloride. After stirring for one and one-half hours the mixture was refluxed for about two hours. After adding acid the organic layer was washed with dilute acid, water, and sodium chloride solution, dried over sodium sulfate and concentrated. The oil was dehydrated at 250° for one hour and distilled, giving a yellowish oil from which only 0.27 g. of crystalline product, m. p. 75.5–78.5°, separated. Purified by crystallization from alcohol to constant m. p., this formed glistening, colorless needles, m. p. 82.2–82.8°.

Anal. Calcd. for $C_{20}H_{18}$: C, 92.98; H, 7.02. Found: C, 93.07; H, 6.99.

The principal absorption maxima (Fig. 1) are at 271.5 mμ (log ε = 4.72) and 309.0 mμ (log ε = 4.13).

5,8-Dimethyl-1,2-benzanthracene.—The oily hydrocarbon mixture (2 g.) remaining in the above experiment after removal of the crystalline XIII was heated with sulfur (0.49 g.) at 210–215° for twenty minutes, and then for fifteen minutes while raising the temperature to 235°. A yellow product solidified on distillation in vacuum and the color was largely removed by adsorption from benzene on alumina. Addition of alcohol to the concentrated filtrate caused the separation of 0.8 g. of crude hydrocarbon; this was converted into the picrate in benzene–ligroin; yield 1.5 g. (27% from the ketone), m. p. 170–173°. Recrystallized from alcohol the picrate formed dark red needles, m. p. 174.5–175°.

Anal.[20] Calcd. for $C_{26}H_{19}O_7N_3$: N, 8.65. Found: N, 8.82.

The hydrocarbon mother liquor treated with picric acid gave 0.85 g. of light red needles melting at about 114–118° and probably containing incompletely dehydrogenated material.

A sample of purified picrate (0.65 g.) was cleaved in benzene with an alumina tower and on adding alcohol to the concentrated filtrate 0.31 g. of glistening needles of the 5,8-dimethyl compound separated in a pure condition (constant m. p.). The hydrocarbon forms colorless needles melting first at 131.2–131.4°, and remelting at 134.4–134.7°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.59; H, 6.04.

8 - Methyl - 1,2 - benzanthracene - 10 - aldehyde (XIV).—A mixture of 0.79 g. of 8-methyl-1,2-benzanthracene,[2] 0.92 g. of methylformanilide, 0.92 g. of phosphorus oxychloride, and 0.8 cc. of *o*-dichlorobenzene was heated on the steam-bath for two hours and the dark red solution poured into an aqueous solution of 5 g. of sodium acetate. After steam distillation the residual oil was washed and dried in benzene and the product crystallized from benzene–ligroin; the mother liquor on evaporation and addition of alcohol gave 0.3 g. of unchanged hydrocarbon (yellow). The crystallizate was submitted to chromatographic adsorption on alumina. Some unreacted hydrocarbon passed into the filtrate (fluorescence, 0.06 g. collected) and the aldehyde was adsorbed in a bright yellow zone. This was sectioned and eluted with benzene containing a few drops of methanol, and the recovered material was crystallized from benzene–ligroin in yellow needles, m. p. 125–140°. Crystallization from glacial acetic acid gave 0.2 g. (42% based on hydrocarbon consumed), m. p. 145–147°. On further crystallization from benzene–ligroin the aldehyde separated both as large yellow needles, melting at 147.5–148° and remelting

(20) Microanalysis by Lyon Southworth.

at 151.5–152°, and as clusters of fine yellow needles, m. p. 151.5–152°.

Anal.[19] Calcd. for $C_{20}H_{14}O$: C, 88.86; H, 5.22. Found: C, 88.94; H, 5.40.

The hydrazone was obtained by adding 0.5 cc. of hydrazine hydrate to 0.16 g. of aldehyde suspended in 15 cc. of boiling alcohol. After adding a trace of acetic acid the aldehyde dissolved, and presently the hydrazone began to separate as fine, light yellow needles. After boiling for ten minutes and cooling there was obtained 0.15 g. (89%) of product, m. p. 181–181.5°, dec. Recrystallization from alcohol did not change the m. p.

Anal.[19] Calcd. for $C_{20}H_{16}N_2$: N, 9.85. Found: N, 9.71.

8,10-Dimethyl-1,2-benzanthracene was prepared by heating 0.14 g. of the hydrazone with a solution from 0.05 g. of sodium and 2.5 cc. of absolute alcohol in a sealed tube at 195–208° for ten hours. After adding dilute acetic acid the crystalline product was collected. Filtration through alumina in benzene removed a trace of color and the highly fluorescent filtrate when concentrated, diluted with alcohol, and cooled yielded 0.11 g. (87%) of colorless needles, m. p. 145.5–146.5°. Recrystallization from benzene–alcohol did not alter the m. p.

Anal.[19] Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.56; H, 6.53.

The **picrate** formed deep red needles from alcohol or benzene–ligroin, m. p. 165.5–166°.

Anal.[19] Calcd. for $C_{20}H_{16}\cdot C_6H_3O_7N_3$: N, 8.65. Found: N, 8.62.

γ-(2-Phenanthryl)-butyric Acid (XVII).—γ-(9,10-Dihydro-2-phenanthryl)-butyric acid[2,3] (33 g.) was esterified by refluxing for four hours with 500 cc. of methanol saturated with hydrogen chloride. After adding water the ester was extracted with ether, washed with soda solution, dried with potassium carbonate, and distilled at about 230° (4–5 mm.) as a colorless liquid; yield 32 g. (92%). For dehydrogenation 31 g. of the ester was heated with 3.6 g. of sulfur at 232–255° for one hour. After adding 2 g. of zinc dust and heating for five minutes longer, distillation at about 240° (4 mm.) gave 28 g. of straw colored oil. This was boiled for one hour with 200 cc. of alcohol containing 7 g. of potassium hydroxide, and on concentrating the solution, adding acetone and cooling, the potassium salt of XVII crystallized in beautiful needles. Washed with acetone, the salt was obtained in a completely colorless condition (22 g.). Acidification of a solution in hot water gave colorless, granular acid, m. p. 131–133°; yield, 17.3 g. (53%). One crystallization from benzene–ligroin gave colorless plates, m. p. 134–135.5° (Haworth and Mavin,[14] 134–135°).

8 - Keto - 5,6,7,8 - tetrahydro - 1,2 - benzanthracene (XVIII).—A mixture of 4.8 g. of γ-(2-phenanthryl)-butyric acid and 100 g. of hydrogen fluoride was allowed to stand overnight and the remaining reagent was largely evaporated on the steam-bath. Soda solution was added and the product extracted with benzene. After washing with saturated sodium chloride solution and drying, the ketone was distilled and crystallized from alcohol (Norite); 3.8 g., m. p. 110–115°. Two more crystallizations from alcohol gave colorless blades, m. p. 117–118°; yield 3.5 g. (78%). On further purification the ketone melted at 117.8–118.5°.

Anal. Calcd. for $C_{18}H_{14}O$: C, 87.77; H, 5.73. Found: C, 87.83; H, 5.94.

8 - Methyl - 5,6 - dihydro - 1,2 - benzanthracene.—The above ketone XVIII (2.5 g.) was treated with methylmagnesium chloride in the usual way and the product dehydrated by distillation in vacuum from a trace of potassium bisulfate. The almost colorless distillate set to a solid (2.3 g., 93%), m. p. 70–76°. A sample for analysis formed glistening, colorless plates from alcohol or from petroleum ether, m. p. 80–80.6° (picrate, m. p. 151–152°, dec.).

Anal. Calcd. for $C_{19}H_{16}$: C, 93.40; H, 6.60. Found: C, 93.71; H, 6.35.

8-Methyl-1,2-benzanthracene was obtained by heating the above dihydride (0.53 g.) with sulfur (0.07 g.) at 205–245° for fifteen minutes, followed by treatment with zinc, distillation, adsorption of colored impurities on alumina, and crystallization from alcohol. There was obtained 0.5 g. (95%) of colorless plates, m. p. 117–118° and remelting at 113.5–114°. This did not depress the m. p. of the sample previously described.[2]

4-Keto-1,2,3,4-tetrahydrochrysene (XIX).—γ-(2-Phenanthryl)-butyric acid (7 g.) was refluxed for seventy minutes with 26 cc. of glacial acetic acid, 17.5 cc. of acetic anhydride, and 2.33 g. of freshly fused zinc chloride. Water was dropped into the hot, dark solution, cautiously at first and then to the point of incipient cloudiness. The crude ketone which crystallized was quite dark; it was washed in benzene with soda solution, water, and salt solution, dried, concentrated and diluted with ligroin. Brownish prisms separated on cooling (4 g.), and distillation at about 245° (3–4 mm.) gave an almost colorless product. On crystallization from benzene–ligroin and then from alcohol the ketone formed colorless prisms or prismatic needles, m. p. 124–125° (Haworth and Mavin,[14] 124–125°); yield 3.3 g. (51%). The purest sample obtained had the m. p. 125–125.5°.

Cyclization of γ-(2-Phenanthryl)-butyric Acid by Other Methods.—(a) On repeating the experiment of Haworth and Mavin[14] (85% sulfuric acid at 100° for fifty minutes), 2 g. of the acid yielded 0.44 g. (23%) of the ketone XIX, m. p. 123–125°.

(b) In another experiment 5 g. of the acid was refluxed in 75 cc. of dry benzene with 5 g. of phosphorus pentachloride, 4.5 g. of aluminum chloride was added after chilling, and after standing overnight the mixture containing a yellow precipitate was refluxed for two and one-half hours. On working up the mixture 0.1 g. of crude starting material was recovered and the distilled neutral fraction on slow crystallization from benzene–ligroin yielded a mixture of blades and prisms. These were largely separated by hand and each substance was separately purified and identified by mixed melting point determination (a mixture of the two ketones gives a marked depression). There was collected 1.65 g. (⅔ of total) of blades of 8-keto-5,6,7,8-tetrahydro-1,2-benzanthracene, m. p. 115–116.5°, and 0.8 g. of prisms of 4-keto-1,2,3,4-tetrahydrochrysene, m. p. 122–125°; total yield 52.5%.

(c) Another variation was to treat the acid (2 g.) in

nitrobenzene (25 cc.) with phosphorus pentachloride (steam-bath) and add a solution of aluminum chloride (1.85 g.) in nitrobenzene (30 cc.) to the solution of the acid chloride under stirring in a salt–ice bath. A mustard colored complex separated. After stirring for five hours in the freezing bath and standing overnight at room temperature the ketonic product was collected in the usual way and the components separated as in (b). The crude 8-ketotetrahydro-1,2-benzanthracene collected amounted to 0.95 g., and 0.1 g. of crude 4-ketotetrahydrochrysene was isolated and identified.

4-Methylchrysene (XXI).—Condensation of the ketone XIX (2.5 g.) with methylmagnesium chloride was conducted as in the examples described above, and vacuum distillation gave 2.23 g. (90%) of solid product suitable for dehydrogenation. This crystallized from alcohol in colorless plates, but the melting point rose steadily on repeating the process, probably as the result of disproportionation. The crude dihydride (1.2 g.) was heated with sulfur (0.16 g.) at 215–245° for thirty minutes, followed by vacuum distillation from a little zinc dust. The yellow solid was sublimed at 190–200° (1–2 mm.) and crystallized from benzene–alcohol (Norite), giving 0.6 g. of colorless plates, m. p. 140–146°. Three crystallizations from benzene–alcohol gave 0.38 g. of highly fluorescent hydrocarbon of the constant m. p. 151–151.5°.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.00; H, 5.94.

The material in the mother liquors was converted to the red picrate; 0.25 g., m. p. 132–136°. This substance sublimed nicely at 110–120° (1 mm.), and the sublimate on crystallization from benzene–ligroin separated in either of two forms. One of these appeared as bright red needles which melted at 135–135.5° and remelted at 137.5–138°; the other separated as light orange needles, m. p. 137.5–138°. The orange form changes to the red form on standing in contact with the mother liquor.

Anal.[19] Calcd. for $C_{19}H_{14}\cdot C_6H_3O_7N_3$: N, 8.91. Found: N, 8.88.

A sample of 4-methylchrysene recovered (alumina tower) from the purified picrate melted at 151–151.5° as before and differed from the above sample only in showing a more intense fluorescence, the colorless crystals appearing violet in daylight.

Summary

In extension of previous work 8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene has been employed as an intermediate for the synthesis of the 8-ethyl, 8-hydroxy, and 8-amino derivatives of 1,2-benzanthracene. The 5-methyl and 5,8-dimethyl derivatives of the hydrocarbon have been synthesized from β-(9,10-dihydro-2-phenanthroyl)-propionic acid through the unsaturated acid resulting from the condensation of the ester of the keto acid with methylmagnesium halide. It is shown that this reaction can be conducted in such a way as to yield the lactone as well as the unsaturated acid, and the α-hydroxy acid has also been isolated. Another hydrocarbon of interest for its possible carcinogenic activity has been prepared by conversion of 8-methyl-1,2-benzanthracene into the 10-aldehyde, followed by Wolff–Kishner reduction. 4-Methylchrysene has been synthesized starting with γ-(2-phenanthryl)-butyric acid, conveniently prepared from the product of the succinoylation of 9,10-dihydrophenanthrene. This acid can be cyclized exclusively either to the chrysene derivative, using zinc chloride in acetic acid–anhydride, or to the isomeric ketotetrahydro-1,2-benzanthracene, using liquid hydrogen fluoride. Cyclization with 85% sulfuric acid or by the Friedel and Crafts reaction gives mixtures of the isomers.

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The Synthesis of D-Mannoheptulose, and the Preparation of Some of its Derivatives[1]

BY EDNA M. MONTGOMERY AND C. S. HUDSON

F. B. LaForge reported in 1917 that the avocado (the fruit of *Persea gratissima*, Gaertn.) contains a seven carbon atom ketone sugar in the free state. The ketose was isolated in crystalline form, characterized, and its structure and configuration established as those of D-mannoheptulose.[2] The present paper describes the synthesis of D-mannoheptulose from D-α-mannoheptose (D-manno-D-gala-heptose), a transformation which would be expected to occur because of the configuration assigned to the ketose by LaForge.

The Lobry de Bruyn rearrangement was applied to D-manno-D-gala-heptose under the mild conditions[3] used previously in the synthesis of lactulose from lactose.[4] After equilibrium had

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Division of Organic Chemistry at the New York meeting of the American Chemical Society, April 22, 1935.

(2) LaForge, *J. Biol. Chem.*, **28**, 511 (1917); Wright, *ibid.*, **28**, 523 (1917).

(3) Wolfrom and Lewis, THIS JOURNAL, **50**, 837 (1928).

(4) Montgomery and Hudson, *ibid.*, **52**, 2101 (1930).