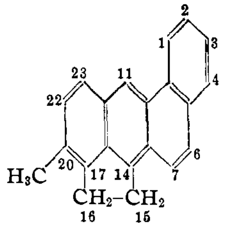
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Reduction and Hydrogenation of Methylcholanthrene

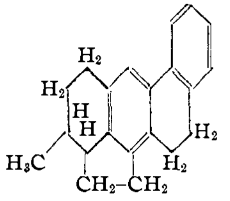
BY LOUIS F. FIESER AND E. B. HERSHBERG[1]

In their paper describing the discovery of methylcholanthrene, Wieland and Dane[2] reported that the hydrocarbon can be converted in good yield into a crystalline hexahydro derivative by reduction with sodium and amyl alcohol. It is a matter of interest to establish the course of this and other reactions of the important carcinogenic hydrocarbon, and the structure of the hexahydride acquires significance from the observation that the reduction is attended with complete loss of carcinogenic activity.[3,4]

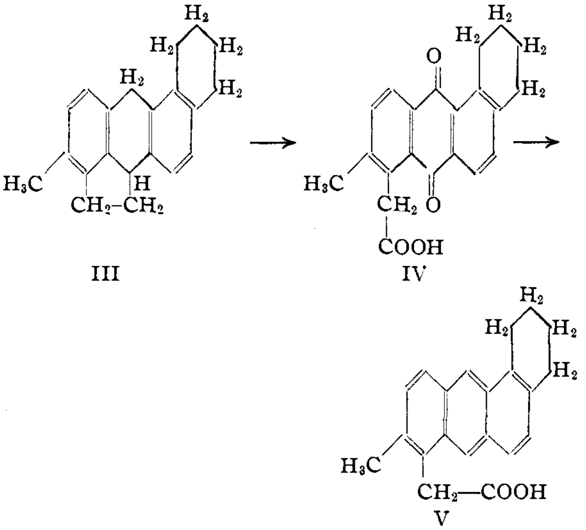
Wieland and Dane did not characterize the hexahydromethylcholanthrene in any way other than by analysis, but they proposed for the compound a structural formula based on certain analogies. Since acenaphthene is reduced by sodium and amyl alcohol in an end ring while phenanthrene is converted under these conditions into the 9,10-dihydride, formula II was suggested as the most likely representation for the reduction product of a hydrocarbon (I) combining the features of both simpler structures. Against this view it might be argued that the dominant feature of structure probably is not the acenaphthene or phenanthrene system but the anthracene unit present in the molecule and that the primary attack would be expected to occur at the *meso*-(11,14)-positions. Bachmann[5] indeed has shown that metallic sodium adds to methylcholanthrene at the *meso*-positions, and it has been established in this Laboratory[6] that on reduction with sodium and amyl alcohol 1,2-benzanthracene and 10-methyl-1,2-benzanthracene yield hexahydrides in which the added hydrogens are attached to the *meso*-positions and to the angular ring. From these results it seems probable that the hydrocarbon of Wieland and Dane has the structure III. Since the two benzenoid rings are separated in both formulas II and III, either formula would accord with the observation that the hydrocarbon does not form complexes with picric acid or with trinitrobenzene. This behavior, however, does not seem to be of great significance in the cholanthrene series, for Bachmann[5] found that *meso*-dihydromethylcholanthrene does not form a picrate, and in the present work a similar lack of affinity of the hydrocarbon for trinitrobenzene was observed.



I



II



III

IV

V

Conclusive evidence in favor of the structure III was found in the oxidation of the hexahydromethylcholanthrene. The reaction product, obtained in good yield, gives a vat test and has an acidic group. The substance clearly is a tetrahydromethyl-1,2-benzanthraquinone-acetic acid of the structure IV, and the compound of Wieland and Dane therefore is the 1,2,3,4,11,14-hexahydride, III. The anthraquinone IV can be reduced smoothly to an anthracene derivative V, but preliminary attempts to resynthesize the cholanthrene structure have not been successful.

While the sodium–alcohol reduction of methylcholanthrene follows the same course as with simpler 1,2-benzanthracene derivatives, this does

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[1] Lilly Research Fellow.

[2] Wieland and Dane, *Z. physiol. Chem.*, **219**, 240 (1933).

[3] Shear, *Am. J. Cancer*, **28**, 334 (1936).

[4] Rossner, *Z. physiol. Chem.*, **249**, 267 (1937), in stating that the compound does not appear to have been tested, evidently overlooked the report by Shear.[3]

[5] Bachmann, *J. Org. Chem.*, **1**, 347 (1936).

[6] Fieser and Hershberg, THIS JOURNAL, **59**, 2502 (1937).

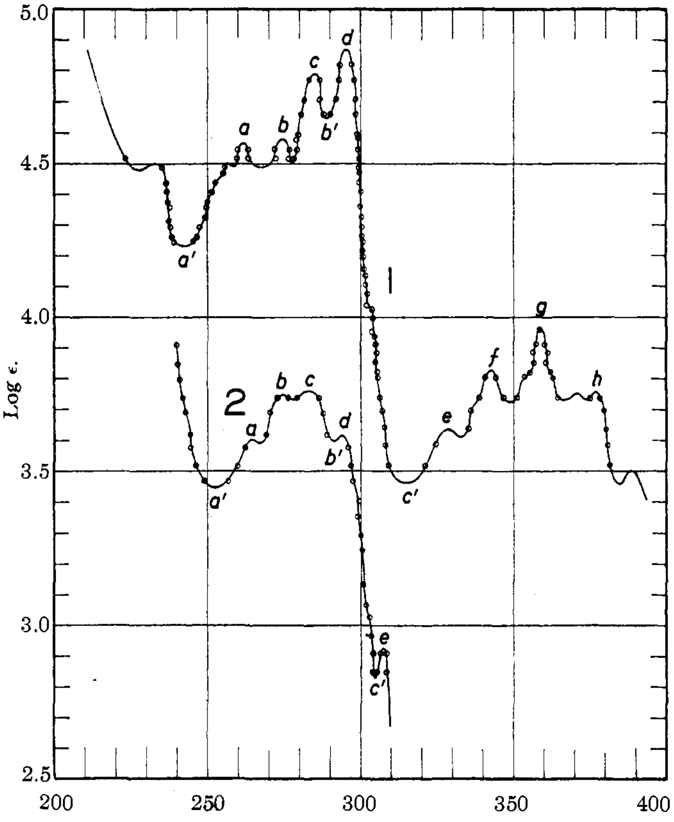
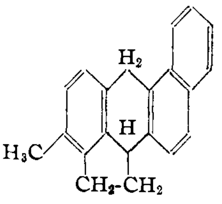
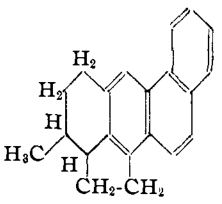


Fig. 1.—Curve 1: Cholanthrene; curve 2: *meso*-Dihydromethylcholanthrene (VI).

not seem to be true of the catalytic hydrogenation. While 1,2-benzanthracene and its 10-methyl and 10-acetoxy derivatives can be converted fairly rapidly and in good yield into the corresponding 5,6,7,8-tetrahydrides,[6] methylcholanthrene absorbs hydrogen very slowly, even in the presence of an active platinum-palladium catalyst, and invariably gives mixtures. When the reaction was continued until the starting material was only partially consumed, or until absorption was practically complete, the mixture was found to contain a hexahydride, identical with that obtained by reduction with sodium and amyl alcohol, and a di- or tetrahydride. The latter substance was separated easily from the former through a nicely crystalline trinitrobenzene derivative, and it proved to be distinctly different from the *meso*-dihydride VI described by Bachmann[5] or the tetrahydride of the structure VII recently synthesized by Bergmann.[7] When the reaction was stopped at an earlier stage the product contained considerable starting material and there was collected a small amount of an impure product having the composition of a tetrahydride. This melted at a higher temperature than Bergmann's hydrocarbon VII, but since two diastereomers of this structure can exist the possibility is not excluded that some reduction occurs in the methylated ring. This evidently is at least not the predominant reaction, however, as with the simpler 1,2-benzanthracene derivatives, for further hydrogenation could hardly result in the formation of the products actually observed. The hexahydride III obviously cannot arise from VII, and the same conclusion has been reached about the other product of exhaustive hydrogenation.

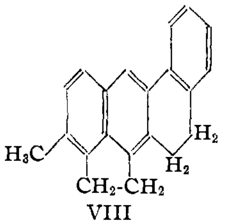


VI



VII

The substance designated above as a di- or tetrahydride corresponded closely in analysis, and in the analysis of the trinitrobenzene derivative, to a dihydromethylcholanthrene. Since the compound differs from the known 11,14-dihydride,[5] the analytical results suggest the structure of the 6,7-dihydro compound, VIII. The presence of rather highly substituted benzene and naphthalene nuclei would perhaps explain the resistance of the substance to further hydrogenation. Since the difference in composition of a di- and tetrahydride is not beyond the possibility of error, it seemed unwise to rely solely upon analytical data, and recourse was had to spectrographic evidence to settle the point.



VIII

Determinations of the ultraviolet absorption spectra of a series of hydrocarbons were kindly made by Miss Rachel G. Franklin of the Bio-

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(7) Bergmann, This Journal, **59**, 1573 (1937).

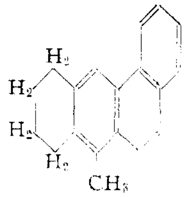
chemical Research Laboratories of the Franklin Institute, through the courtesy of Dr. Ellice McDonald. Absolute alcohol was used as the solvent and the measurements were made with a quartz spectrograph and a notched echelon cell outfit. Cholanthrene and methylcholanthrene were examined for purposes of orientation, and the results for the former hydrocarbon are recorded in Curve 1, Fig. 1, which shows the variation of $\log_{10} \epsilon$ with wave length. The absorption of both hydrocarbons has been studied carefully by Mayneord and Roe,[8] and it seemed desirable to devise some method of comparing these and other results more accurately and more conveniently than by inspection of curves reproduced at great reduction even in the same publication. To this end significant inflections of the curve have been marked in such a way as to distinguish between maxima (a, b, . . .) and minima (a′, b′, . . .), and the coördinates for these points are recorded in Table I. The characteristic inflections recorded for cholanthrene can all be identified readily in the curve given by Mayneord and Roe,[8b] and our wave length values at these points agree with theirs within the accuracy with which readings can be made from their published curve (about 1 mμ). The absorption spectrum of methylcholanthrene is almost indistinguishable from that of the parent hydrocarbon, as shown by the comparison given in Table I of the present results for cholanthrene with those of Mayneord and Roe for methylcholanthrene; the methyl group produces a very slight shift to longer wave lengths.

TABLE I

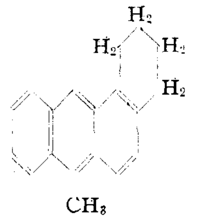
COMPARISON OF ABSORPTION CHARACTERISTICS

Maxima and minima	Cholanthrene, Curve 1 λ, mμ	log ε	Methylcholanthrene[8a] λ, mμ	log ε
a′	242.5	4.3	243	4.3
a	261.5	4.6	262	4.5
b	274	4.6	274	4.6
c	284.5	4.8	284	4.8
b′	289	4.7	288	4.7
d	295	4.9	297	4.9
c′	315	3.5	317	3.4
e	328	3.6	327	3.6
f	342	3.8	342	3.8
g	358	4.0	359	3.9
h	377	3.8	375	3.7
	meso-(11,14-)Dihydromethylcholanthrene, Curve 2		Naphthalene[8a]	
a′	253	3.4	235	2.9
a	265	3.6	247	3.3
b	275	3.8	265	3.7
c	283	3.8	275	3.8
b′	292	3.6	281	3.5
c′	304.5	2.8	295	2.5
	5,6,7,8-Tetrahydro-10-methyl-1,2-benzanthracene, Curve 3		Phenanthrene[8a]	
a′	234	4.0	225	3.9
a	262	4.8	250	4.7
b	273.5	4.4	. . .	. . .
c	283.5	4.2	274	4.1
d	294.5	4.0	282	4.0
b′	300	3.9	287	3.6
e	307	4.1	293	4.1
	1′,2′,3′,4′-Tetrahydro-10-methyl-1,2-benzanthracene, Curve 4		Anthracene[8a]	
a′	232	4.1	. . .	. . .
a	261	5.3	252	5.3
b′	302	2.8	286	2.4
b	351	3.8	338	3.7
c′	358	3.7	347	3.4
c	368	3.9	357	3.9
d′	377	3.5	365	3.2
d	388	4.0	375	3.9
	6,7-Dihydromethylcholanthrene, Curve 5		β-Phenylnaphthalene, Curve 6	
a′	235	4.3	. . .	. . .
b′	244	4.3	. . .	. . .
a	272	4.7	251	4.8
c′	290	3.9	269	4.1
b	314	4.1	288	4.1

Before attempting to identify the new di- or tetrahydromethylcholanthrene it seemed advisable to provide data suitable for comparison. The saturation of the methylated nucleus would give a 2,3-cyclohexenophenanthrene derivative with an alkyl substituent at the 1-position (structure VII), and as a model for this type of structure we examined 5,6,7,8-tetrahydro-10-methyl-1,2-benzanthracene,[6] IX. For comparison with the hydrocarbon which would result from the saturation of the other terminal ring of methylcholanthrene, the absorption spectrum of 1′,2′,3′,4′-tetrahydro-10-methyl-1,2-benzanthracene, X, was determined. The curves for the two isomers, shown in Figs. 2 and 3, are distinctly different, and on making a visual comparison with



IX



X

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(8) (a) Mayneord and Roe, *Proc. Roy. Soc.* (London), **A152**, 299 (1935); (b) **A158**, 634 (1937).

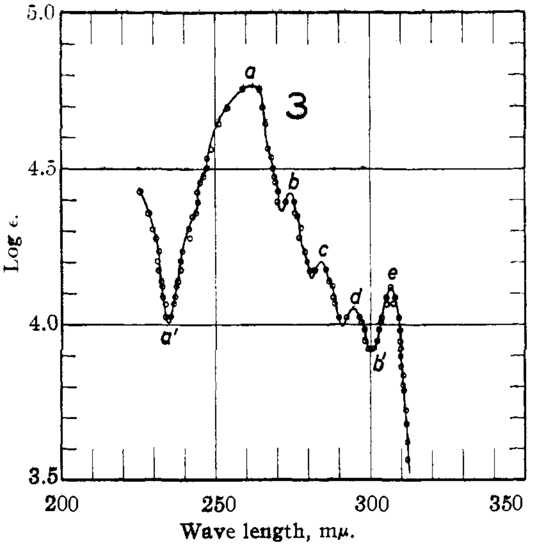


Fig. 2.—Curve 3: 5,6,7,8-Tetrahydro-10-methyl-1,2-benzanthracene (IX).

data recorded by Mayneord and Roe[8a] a striking correspondence in form is apparent between Curves 3 and 4 and those found for phenanthrene and anthracene, respectively. Comparisons are given in Table I of the principal characteristics which can be identified positively as occurring in the two curves of each pair. In Curve 3 there is a minor detail b in the shoulder which is not defined in the phenanthrene curve, while the present measurements were not extended to sufficiently low values of the extinction coefficient to include the prominent long-wave system of bands of the phenanthrene spectrum. The correspondence in the shape of the two curves in the region studied is, however, quite definite. As for the region of absorption, the whole curve (3) for compound IX is displaced 9–14 mμ in the direction of longer wave length as compared with the phenanthrene spectrum, which is attributable to the influence of alkyl substituents attached to the absorbing, phenanthrenoid center. The curve (4) for the anthracenoid isomer X is similarly displaced 9–14 mμ with respect to the curve for anthracene, and the two curves correspond closely over the entire range studied (the measurements of Mayneord and Roe were not carried far enough into the ultraviolet to reveal the minimum a′). It is evident that a phenanthrenoid or anthracenoid system in a polynuclear hydroaromatic compound can be identified unequivocally by absorption spectroscopy.

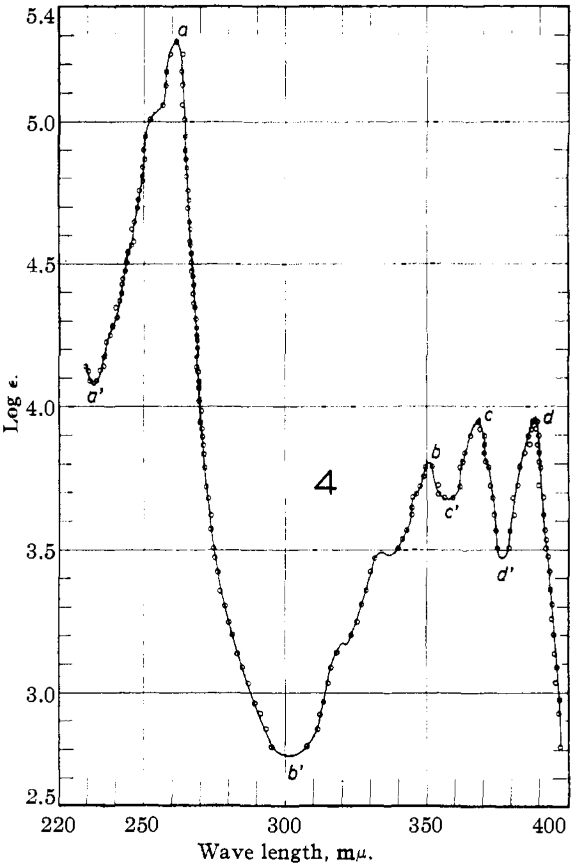
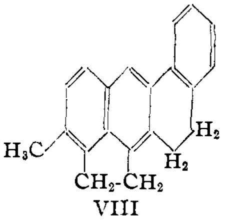
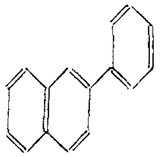


Fig. 3.—Curve 4: 1′,2′,3′,4′-Tetrahydro-10-methyl-1,2-benzanthracene (X).

Curve 5 (Fig. 4) for the unidentified hydrogenation product from methylcholanthrene bears no resemblance to the curves for the isomers IX and X just discussed, and it may be concluded that the compound does not have either of the two possible (stable) tetrahydride structures. Curve 5, furthermore, is distinctly different from Curve 2 (Fig. 1) for *meso*-dihydromethylcholanthrene, VI. The latter hydrocarbon contains a benzene and a naphthalene nucleus separated from one another by saturated carbon atoms, and in the region investigated the spectrum shows a definite correspondence to that of naphthalene.[8a] The data given in Table I show a displacement of the spectrum in the expected direction (to the red) of about 12 mμ (ave.) as compared with naphthalene. The alternate 6,7-dihydride structure (VIII) likewise contains a benzene and a naphthalene grouping, but in this case the two unsaturated groups are connected directly in a conjugated unit which should function as a single absorbing center distinct from the component parts. The spectrographically active system



VIII



XI

would be that of β-phenylnaphthalene (XI), and the spectrum of the latter hydrocarbon (Curve 6) was indeed found to resemble that of the hydrogenation product. Although Curves 5 and 6 lack sufficient detail to permit a very extensive comparison (Table I), they both show a strong absorption band in the region 250–270 mμ with a prominent shoulder on the long-wave length side, and the curve for the hydrocarbon with alkyl substituents is shifted about 23 mμ to longer wave lengths, as would be expected. The similarity to β-phenylnaphthalene, coupled with the total lack of any resemblance to the models for other possible structures, provides convincing evidence that the new hydrocarbon is correctly represented as the 6,7-dihydride (VIII). The analytical data conform closely to the required composition, and the formula accounts for the resistance of the substance to further hydrogenation at a low pressure.

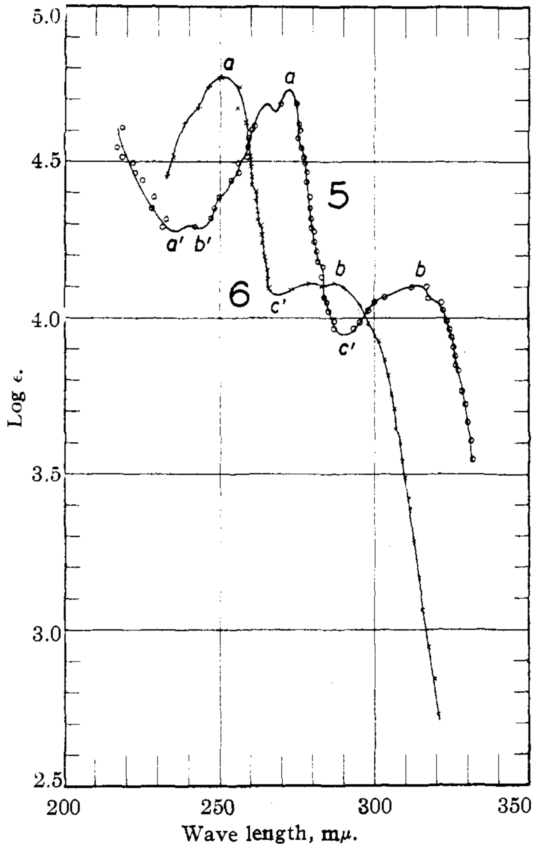


Fig. 4.—Curve 5: 6,7-Dihydro-20-methylcholanthrene (VIII); curve 6: β-Phenylnaphthalene.

It appears that on catalytic hydrogenation methylcholanthrene enters into two concurrent and independent reactions. One follows the course of the sodium–amyl alcohol reduction and gives the hexahydride III, while in the other the substance functions as a phenanthrene derivative and yields the 6,7-dihydride VIII. Neither reaction corresponds to that observed with the physiologically inactive 1,2-benzanthracene and with the moderately carcinogenic 10-methyl-1,2-benzanthracene, both of which are reduced in the terminal linear ring. The presence of two alkyl substituents seems to protect this ring from attack. An interesting field for speculation is provided by the observation that methylcholanthrene, a cancer-producing agent of outstanding potency among known 1,2-benzanthracene derivatives, differs from the simpler hydrocarbons of the series in the catalytic chemical reaction.

Experimental Part[9]

Hydrogenation Apparatus.—For the accurate measurement of hydrogen absorption in reactions with small quantities continued over a prolonged period it was found necessary to eliminate all rubber connections except the stopper of the absorption flask. The measuring system, consisting of a manometer, a 50-cc. buret and a 500-cc. buret sealed into a single glass system, was connected by means of a standard taper No. 5 female joint to a coil made from 6 ft. (1.8 m.) of thin-wall (0.025 in., 0.635 mm.) brass tubing $^5/_{32}$ in. (3.96 mm.) in diameter. Connection was made with a brass male joint soldered to the brass tubing, using Krönig's cement. With a fixed support placed near the joint satisfactory flexibility of the coil was obtained without strain to the glass. A similar brass to glass connection was made to a small two-way trap of Pyrex glass leading, by means of a wide glass capillary, to the stopper of the absorption flask. Above the stopper the trap was sealed with picein cement to the brass bottle clamp. The trap prevents splashing liquid from reaching the brass tubing and retains any condensate which might otherwise reach the absorption vessel, and with the usual copper connector at the stopper replaced by glass the solution does not come into contact with any metal.

When hydrogenating small amounts of material, the dead space was minimized by using 25- to 250-cc. round-bottomed, long-necked flasks in place of the pressure bottle. In conducting a reaction the hydrogen was either displaced by mercury about as rapidly as it was absorbed or else maintained under a pressure of 100–200 mm. Before in-

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[9] All melting points are corrected. Analyses by Mrs. Verna R Keevil.

troducing fresh catalyst the system was evacuated at the water pump and filled with nitrogen.

Characterization of Methylcholanthrene.—The methylcholanthrene used was synthetic material of high quality which had been further purified by passing a solution in benzene through a tower of activated alumina and crystallizing the product twice from ethyl acetate; it formed straw-yellow needles, m. p. 179.5–180°. As the hitherto undescribed addition product **methylcholanthrene–trinitrobenzene** was encountered in separating the hydrogenation mixtures, a pure sample was prepared for analysis. This was obtained using one mole of trinitrobenzene in benzene solution as dark red prisms, m. p. 203.5–204.5°.

Anal. Calcd. for $C_{21}H_{16}{\cdot}C_6H_3O_6N_3$: N, 8.71. Found: N, 8.30.

This form is stable and may be recrystallized without change. When a larger proportion of trinitrobenzene was used in a dilute solution an unstable, light red complex separated. This was not obtained pure for it changed into the dark red complex on recrystallization. In contrast to the behavior noted with other 1,2-benzanthracene derivatives,[6] methylcholanthrene cannot be recovered effectively from the trinitrobenzene complex by selective adsorption of the nitro compound on alumina, for this hydrocarbon is adsorbed about as strongly as the reagent.

Hydrogenation.—In a typical experiment 1 g. of hydrocarbon in 100 cc. of purified ethyl acetate and 20 cc. of glacial acetic acid, in the presence of 0.2 g. of Adams catalyst containing palladium,[10] which was added in three portions, absorbed 4 moles of hydrogen at atmospheric pressure in forty-eight hours. At this point absorption of gas was still continuing at the rate of about 6 cc. per hour. After filtration from the catalyst the solution was concentrated to a volume of 50 cc. and diluted with about 150 cc. of water. The ethyl acetate was removed by boiling and on cooling the oily hydrocarbon mixture solidified. After drying in vacuum at 40° the crude material was treated in benzene solution with 0.5 g. of trinitrobenzene and a crystalline addition product was caused to separate by concentrating the solution and adding ligroin. On slow cooling there was obtained 0.45 g. of orange-brown needles of crude **6,7-dihydro-20-methylcholanthrene-trinitrobenzene,** m. p. 146–148°. Recrystallization from benzene–ligroin containing 0.2 g. of trinitrobenzene gave 0.35 g. of reddish-orange needles, m. p. 153.5–154.5°. This is equivalent to 0.195 g. (19.5%) of the dihydride. The melting point was unchanged on further crystallization from alcohol.

Anal. Calcd. for $C_{21}H_{18}{\cdot}C_6H_3O_6N_3$: N, 8.69. Found: N, 9.02.

6,7-Dihydro-20-methylcholanthrene (VIII) was obtained from the complex (0.35 g.) by adsorbing the nitro component on alumina from a benzene–ligroin solution.[6] On evaporating the filtrate to dryness and recrystallizing the residue from methanol, 0.152 g. of the hydrocarbon was obtained, m. p. 154.5–155°. The melting point remained constant on further crystallization and the compound formed glistening white leaflets having a brilliant blue fluorescence under ultraviolet light.

Anal. Calcd. for $C_{21}H_{16}$: C, 93.30; H, 6.70. Found: C, 93.40, 93.33; H, 6.75, 6.75.

The mother liquors remaining after collection of the trinitrobenzene addition compound were passed through a tower of alumina in benzene solution to remove the nitro compound as well as a small amount of methylcholanthrene, the presence of which was recognized from the characteristic color and position of the zone of adsorption in the tower. The filtrate was evaporated and on crystallization of the residue from methanol there was obtained 0.37 g. of **hexahydromethylcholanthrene,** m. p. 157.5–159.5°. The substance did not depress the melting point of the sample described below.

When the hydrogenation was stopped at an earlier stage more unchanged methylcholanthrene was found in the reaction mixture but the dihydro and hexahydro compounds were produced in essentially the same proportion as in the experiment reported above (1:2). This constancy in the ratio of products formed was noted with different lots of catalyst and different proportions of solvents and the observation indicates that the two reactions are concurrent. The two hydrides seem to be end products, and in a test experiment with the pure dihydro compound no absorption of hydrogen was observed under conditions comparable with those specified above.

In one experiment with 0.3 g. of methylcholanthrene the reaction was stopped after thirty hours. The first and second crops obtained on crystallizing the product consisted largely of unchanged material; after five crystallizations of the third crop (130 mg.) the melting point had risen to 121–123° but was not yet constant. An analysis at this stage indicated the average composition of a tetrahydride, or of a mixture of di- and hexahydrides (Found: C, 92.58; H, 7.50). Bergmann's tetrahydride VII is reported[7] to melt at 97–99°.

***meso*-(11,14)-Dihydro-20-methylcholanthrene (VI).**—A sample of the hydrocarbon for the spectrographic measurements was prepared according to Bachmann[5] and effectively purified by passing a benzene solution through a tower of alumina. A trace of methylcholanthrene present was adsorbed in a blue fluorescent zone while the nonfluorescent dihydro compound passed into the filtrate. The recrystallized material melted at 138–139° (Bachmann, 136–137°).

1,2,3,4,11,14-Hexahydro-20-methylcholanthrene[2] (III).—To a solution of 5 g. of methylcholanthrene in 350 cc. of isoamyl alcohol 30 g. of sodium was added in portions in the course of three hours. Water was added slowly under reflux and the alcohol was removed by steam distillation. The crystalline residue after drying in vacuum weighed 5.1 g., m. p. 145–150°. Recrystallized from benzene–absolute alcohol, it formed glistening rectangular plates, m. p. 160–160.5°. The crude product darkens rather rapidly on standing, and even the pure hydrocarbon deteriorates on long storage.

1′,2′,3′,4′ - Tetrahydro - 6 - methyl - 1,2 - benz - 9,10-anthraquinone-5-acetic Acid (IV).—A solution of 5.5 g. of crude hexahydromethylcholanthrene in 300 cc. of hot glacial acetic acid was cooled rapidly to produce a fine suspension of the hydrocarbon and 28 g. of anhydrous sodium dichromate was added. After shaking for fifteen minutes at room temperature the hydrocarbon dissolved and the oxidation product began to separate. To complete the reaction the mixture was refluxed for ten minutes

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(10) Ref. 6, note 20.

and it was then diluted with a small amount of water and cooled. The product which separated on being crystallized once from glacial acetic acid gave 2.4 g. (36%) of pure quinone in the form of long, pale yellow needles, m. p. 283–284°, dec. (unchanged on further crystallization). The quinone gives a vat test.

Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.44; H, 5.43. Found: C, 75.66, 75.67; H, 5.74, 5.78.

1′,2′,3′,4′ - Tetrahydro - 6 - methyl - 1,2 - benzanthracene-5-acetic Acid (V).—A mixture of 20 g. of zinc dust, 0.2 g. of copper sulfate, 100 cc. of concentrated ammonia solution, and 2.4 g. of the quinone IV was heated for forty-eight hours with the addition in portions of 500 cc. more ammonia solution. Some of the product precipitated on acidifying the filtered ammonia solution, but the bulk of it was recovered from the filter cake after leaching with dilute acid to remove the zinc. One crystallization from glacial acetic acid gave 1.7 g. (78%) of crude, gray product, m. p. 254–256°, dec. This was dissolved in 50 cc. of 10% sodium carbonate solution and saturated carbonate solution was added to the hot filtrate until the sodium salt of the acid began to crystallize. The salt separated on cooling in lustrous plates and on acidifying a solution of the compound in water the free acid separated in a colorless condition, m. p. 255–257°, dec., yield 1.55 g. After two crystallizations from alcohol the substance formed pale yellow needles, m. p. 267–269°, dec.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.55; H, 6.65. Found: C, 82.58; H, 6.65.

Treated with thionyl chloride in ether, the acid was converted into a black tar. Phosphorus pentachloride in ligroin gave what appeared to be a satisfactory acid chloride, but the product obtained on treating this in carbon bisulfide with stannic chloride and aluminum chloride contained more oxygen than required for a normal cyclization product and failed to yield a semicarbazone.

β-Phenylnaphthalene.—The sample used for spectrographic measurement was synthesized from β-bromonaphthalene (8 g.) and cyclohexanone (4.2 g.). The product from the Grignard reaction on distillation gave 5.8 g. (72%) of the unsaturated hydrocarbon as a light yellow oil, b. p. 212–215° (9 mm.). This was heated with 1.8 g. of sulfur at 240–260° for one hour, the product was distilled, and the solidified distillate crystallized from alcohol as colorless prisms, m. p. 100–101°; yield 1.9 g. (33%). After two more crystallizations from alcohol the substance melted constantly at 102.2–102.7°. Bamberger and Chattaway[11] give 102–102.5°.

Summary

The hexahydro derivative which Wieland and Dane obtained by reducing methylcholanthrene with sodium and amyl alcohol has been shown by oxidation to be the 1,2,3,4,11,14-hexahydride. Catalytic hydrogenation gives some of the same product along with the 6,7-dihydride, and the two reactions appear to be concurrent and independent. The sodium–alcohol reduction follows the same course as with simpler 1,2-benzanthracene derivatives, but in the catalytic process methylcholanthrene behaves differently from the other members of the series.

The structure of 6,7-dihydro-20-methylcholanthrene was established by comparison of the ultraviolet absorption spectrum with the spectra of compounds having the unsaturated absorbing centers of the various possible di- and tetrahydro derivatives of methylcholanthrene. The spectrographic measurements were made at the Biochemical Research Laboratories of the Franklin Institute.

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[11] Bamberger and Chattaway, *Ber.*, **26**, 1745 (1893).

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The Phosphorus Analogs and Homologs of Choline and Betaine. Onium Compounds. XVII

BY R. R. RENSHAW AND R. A. BISHOP

The products here described were made a number of years ago and their pharmacological investigation was carried out by Reid Hunt.[1] Since it was shown that the phosphorus compounds produced qualitatively the same physiological action that analogous nitrogen compounds gave, it seemed clear that the onium element is not, *per se*, of primary significance in the physiological activity of these compounds. It was, therefore, postulated[2] that the onium element merely determines an effective geometrical structure which, in turn, makes possible some specific type of adsorption or desorption process.

Triethylphosphine, from which the triethyl analogs of choline and betaine derivatives were prepared, was readily obtained by the Grignard reaction as shown by Hibbert.[3] We were unable, however, under a great variety of experi-

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[1] Hunt and Renshaw, *J. Pharmacol.*, **25**, 315 (1925); **29**, 17 (1926).

[2] Renshaw, *Science*, **62**, 384 (1925).

[3] Hibbert, *Ber.*, **39**, 160 (1906).