Experimental Part

p-(*p*-Aminophenyl)-benzenesulfonamide (III).—To a suspension of 2 g. of *p*-(*p*-nitrophenyl)-benzenesulfonamide (m. p. 228°) in 100 cc. of ethanol are added 100 cc. of a solution of 20% hydrochloric acid and 4 g. of finely divided tin (excess). The mixture is heated on a steam-bath at a temperature not exceeding 55° until it is totally dissolved (approximately two hours). The solution is then poured off from the excess of tin and the clear solution is treated with hydrogen sulfide until the precipitation of tin is complete. It is then filtered and to the filtrate are added small quantities of sodium carbonate solution until the mixture is alkaline. The white precipitate is then gathered on a Buchner funnel, drained and dried. It is purified by crystallization from hot alcohol. The yield is 0.90 g. (51%), of white needles, m. p. 262–263° (dec.). The properties are described by Van Meter.[3] *Anal.* Calcd. for $C_{12}H_{12}N_2O_2S$: N, 11.29. Found: N, 11.30.

p-(*p*-Nitrophenyl)-benzenesulfon-N-phenylamide (IV).—To 2.87 g. (0.0096 mole) of *p*-(*p*-nitrophenyl)-benzenesulfonyl chloride (m. p. 178°), is added 1.86 g. (0.02 mole) of aniline in 20 cc. of alcohol and shaken. The mixture is heated under reflux condenser at 60° for one hour. It is left to settle overnight and the crystalline precipitate which has formed is separated by filtration. The mother liquor is diluted with water and a small additional quantity of anilide is recovered. It is recrystallized from alcohol; yield 3.30 g. (94%); m. p. 182–183°. *Anal.* Calcd. for $C_{18}H_{14}N_2O_4S$: N, 7.90. Found: N, 7.80.

p-(*p*-Aminophenyl)-benzenesulfon-N-phenylamide (V).—3.54 grams of *p*-(*p*-nitrophenyl)-benzenesulfon-N-phenylamide is suspended in 250 cc. of ethyl alcohol in a 500-cc. flask. A mixture of 30 cc. of hydrochloric acid and 45 cc. of water is added, and then 5 g. of finely divided tin. The mixture is heated under reflux at 55° until total solution is obtained (from four to five hours). The clear liquid is poured off from the residue and saturated with hydrogen sulfide. It is then filtered and the filtrate is evaporated on the water-bath at 50° to half volume. It is not convenient to concentrate more because oily drops separate. If this happens before concentration to the above volume the evaporation should be stopped and the oily product redissolved by addition of a small quantity of alcohol. Sodium carbonate is added until no more precipitation takes place. The precipitate is left to settle and is then filtered, washed and dried. The crude product (V) is purified by crystallization from hot alcohol. It crystallizes in slender silky white needles; yield, 1.20 g. (37%); m. p. 182–183°. *Anal.* Calcd. for $C_{18}H_{16}N_2O_2S$: N, 8.64. Found: N, 8.58.

Summary

The preparations of *p*-(*p*-aminophenyl)-benzenesulfonamide, *p*-(*p*-nitrophenyl)-benzenesulfon-N-phenylamide and *p*-(*p*-aminophenyl)-benzenesulfon-N-phenylamide are described.

BUENOS AIRES
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF MICHIGAN]

7-Methylcholanthrene and 1',5-Dimethyl-1,2-benzanthracene

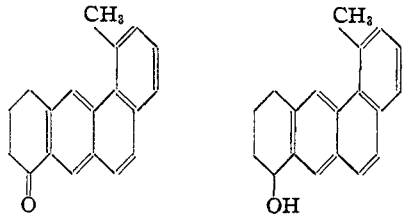
BY W. E. BACHMANN AND S. R. SAFIR

In a previous paper[1] we described the preparation of 4- and 5-methylcholanthrene, utilizing the procedure which had been employed successfully in the synthesis of cholanthrene from 5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene.[2] The latter method offers considerable promise as a general procedure for the synthesis of isomeric methylcholanthrenes, and we have now extended it to the synthesis of 7-methylcholanthrene (V),[3] a new monomethyl derivative of the active carcinogen cholanthrene.

This methylcholanthrene, with its alkyl substituent in the 7-position, is particularly interesting because of its structural similarity to the potent carcinogen 3,4-benzpyrene. Both can be regarded as substitution products of the tetracyclic hydrocarbon, 1,2-benzanthracene. From this view 7-methylcholanthrene is a 1',5,10-trisubstitution product and benzpyrene is a 1',9-disubstitution product of the parent hydrocarbon. Thus the new methylcholanthrene contains part of the substitution of benzpyrene in addition to the cholanthrene nucleus. In a subsequent paper with Dr. Marvin Carmack the hydrocarbon 4',5-dimethylene-3,4-benzpyrene will be described which combines the complete structures of both cholanthrene and 3,4-benzpyrene.

The required ketone (I) was obtained recently from 4-methylphenanthrene.[4] This hydrocarbon was found to react with succinic anhydride in the 1- and 6-positions, and from one of the isomeric keto acids the ketone was prepared by the usual method of reduction and cyclization. The cyclic ketone was reduced by means of aluminum isopropoxide to the corresponding secondary alcohol (II), and the latter converted to the chloride by

(1) Bachmann and Chemerda, *J. Org. Chem.*, **6**, 50 (1941).
(2) Bachmann, *ibid.*, **3**, 434 (1938).
(3) The numbering system is that employed in the index of *Chemical Abstracts*.
(4) Bachmann and Edgerton, THIS JOURNAL, **62**, 2550 (1940).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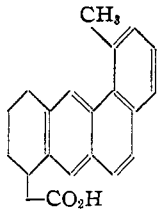
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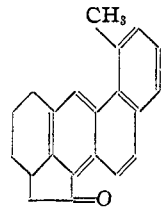
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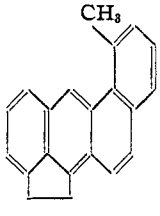
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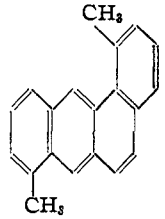
VI

means of hydrogen chloride. From the chloride the acid III was obtained through the malonic ester synthesis. The ketone IV was prepared by cyclization of the acid chloride of III by the use of stannic chloride. Reduction of IV by the Clemmensen method gave the tetrahydro derivative, which was dehydrogenated with palladium on charcoal to 7-methylcholanthrene (V) in good over-all yield.

The present paper reports also the synthesis of 1',5-dimethyl-1,2-benzanthracene (VI). The structure of this hydrocarbon resembles that of 7-methylcholanthrene but lacks a substituent on one meso position of the benzanthracene nucleus. When the ketone (I) was condensed with methylmagnesium iodide, a carbinol was formed which was smoothly dehydrated and dehydrogenated to VI when it was heated with palladium on charcoal.

We are grateful to the Anna Fuller Fund for a generous grant which made this investigation possible.

Experimental

1' - Methyl - 5 - hydroxy - 5,6,7,8 - tetrahydro - 1,2-benzanthracene (II).—A mixture of 0.82 g. of 1'-methyl-5-keto-5,6,7,8-tetrahydro-1,2-benzanthracene[4] and 25 cc. of a *M* solution of aluminum isopropoxide in anhydrous isopropyl alcohol was refluxed on a steam-bath for thirty minutes and then distilled slowly through an upright condenser so that in the course of an hour 18 cc. of distillate was collected, when a test for acetone was negative.[5] The residue was poured into an ice-cold solution of 8 cc. of sulfuric acid in 200 cc. of water. The colorless carbinol was filtered, washed well with dilute ammonia and water and dried. An acetone solution of the material was treated with Norit, filtered, diluted with water and concentrated. The carbinol separated in the form of colorless needles melting at 124–125°; yield 0.765 g. (93%). A sample after recrystallization from acetone melted at 128.5–129°. The alcohol gives a deep purple color with sulfuric acid.

Anal. Calcd. for $C_{19}H_{18}O$: C, 87.0; H, 6.9. Found: C, 86.6; H, 7.1.

1' - Methyl - 5,6,7,8 - tetrahydro - 1,2 - benzanthracene-5-acetic Acid (III).—Dry hydrogen chloride was passed into a cold (5°) solution of 430 mg. of 1'-methyl-5-hydroxy-5,6,7,8-tetrahydro-1,2-benzanthracene in 30 cc. of dry benzene containing a small amount of calcium chloride. After twenty minutes to one-half hour the solvent and excess hydrogen chloride were removed at 25° under diminished pressure and the nearly colorless, crystalline chloride (m. p. 127–127.5°) was used at once in the next step without purification.

To an ice-cold solution of sodio-malonic ester prepared from 0.19 g. of sodium, 16 cc. of absolute alcohol and 2.5 cc. of malonic ester was added a cooled solution of the chloride in 40 cc. of benzene. The mixture was kept in a refrigerator for two days, at room temperature for one day, at 60° for two hours and finally was refluxed for two hours. The solvents were evaporated, 6 cc. of 45% potassium hydroxide solution was added and the mixture was heated for one-half hour on a steam-bath. The solution obtained after dilution with 15 cc. of water was refluxed for two hours, cooled and filtered through glass wool to remove a small quantity of an alkali-insoluble oil. The malonic acid was obtained as a fine white powder when the alkaline solution was poured into an excess of hydrochloric acid; yield 465 mg. (82% based on the carbinol).

The malonic acid was decarboxylated by heating it in a metal bath at 190° for thirty minutes and the product was purified in a sublimation apparatus at 250° (0.01 mm.). The colorless 1'-methyl-5,6,7,8-tetrahydro-1,2-benzanthracene-5-acetic acid (400 mg. or 99%; m. p. 143–144°) was sufficiently pure for use in the next step. A sample of the acid melted at 145–145.5° after two recrystallizations from benzene–petroleum ether.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.9; H, 6.6. Found: C, 83.2; H, 6.7.

1 - Keto - 7 - methyl - 2a,3,4,5 - tetrahydrocholanthrene (IV).—To a solution of 400 mg. of III in 40 cc. of benzene was added 0.90 g. of phosphorus pentachloride, and the mixture was swirled occasionally during the course of one-half hour. The resulting clear solution of the acid chloride was cooled to about 15° and swirled during the addition of 0.50 cc. of stannic chloride. After twenty minutes the tan-yellow complex was hydrolyzed with ice and dilute hydrochloric acid, the benzene layer was washed twice with dilute acid, twice with water, twice with dilute alkali, and finally twice with water. When the solvent

(5) Lund, *Ber.*, **70**, 1520 (1937).

was evaporated, the ketone was deposited in the form of light yellow needles which melted at 192.5–193°; yield 365 mg. (97%). A completely colorless specimen, melting at 193.5–194°, was obtained after a single recrystallization from acetone using Norit. The ketone gives an orange-yellow color with concentrated sulfuric acid.

Anal. Calcd. for $C_{21}H_{18}O$: C, 88.1; H, 6.3. Found: C, 87.9; H, 6.2.

7-Methylcholanthrene (V).—A mixture of 365 mg. of IV, 5 g. of amalgamated zinc (20 mesh), 5 cc. of toluene, 5 cc. of acetic acid and 5 cc. of hydrochloric acid was refluxed for twenty-four hours. A total of 18 cc. of hydrochloric acid was added in several portions over this period. After separation of the organic layer, the aqueous layer was diluted with an equal volume of water, and extracted once with benzene. Evaporation of the combined extracts yielded **7-methyl-2a,3,4,5-tetrahydrocholanthrene** as pale yellow crystals; yield 344 mg. (99%); m. p. 90–98°.

Without purification a mixture of 344 mg. of the tetrahydro derivative and 0.10 g. of palladium–charcoal catalyst[6] was heated in a nitrogen atmosphere at 310° for one-half hour. The product was digested with hot benzene, filtered from the catalyst, the solvent was evaporated and the residue was "sublimed" at 150° (0.01 mm.). The yellow crystalline hydrocarbon thus obtained melted at 140–146.5° (vac.) in a Pyrex tube; yield 315 mg. (93%).

To a solution of 145 mg. of the crude 7-methylcholanthrene in 5 cc. of benzene was added a solution of 160 mg. of picric acid in 5 cc. of benzene. The picrate crystallized in the form of brown, silky needles upon the addition of petroleum ether; m. p. 149–150°. After one recrystallization from benzene–petroleum ether the **picrate** melted at 151–152° (vac.) in a Pyrex tube when placed in a bath at 135°.

Anal. Calcd. for $C_{21}H_{16}\cdot C_6H_3O_7N_3$: N, 8.5. Found: N, 8.9.

After regeneration of the hydrocarbon by treatment of the picrate in benzene with dilute sodium hydroxide solution, a benzene solution of the material was passed through a tower of aluminum oxide, the solvent was evaporated and the residue was recrystallized once from acetone–alcohol. A first crop of 70 mg. of pure hydrocarbon was thus obtained in the form of lemon-yellow platelets melting at 147–148° (vac.) in a Pyrex tube when placed in a bath at 135°.

Anal. Calcd. for $C_{21}H_{16}$: C, 94.0; H, 6.0. Found: C, 93.9; H, 6.0.

1',5-Dimethyl-1,2-benzanthracene (VI).—A cold solution of 0.35 g. of the ketone I in 10 cc. of benzene was poured into an ice-cold solution of methylmagnesium iodide prepared from 0.10 g. of magnesium, 0.27 cc. of methyl iodide and 10 cc. of anhydrous ether. A bright yellow complex which precipitated momentarily redissolved to give a clear yellow solution. After standing overnight in a refrigerator the reaction mixture was hydrolyzed with cold ammonium chloride and dilute hydrochloric acid. The organic layer was separated and the solvents were evaporated, whereupon 1',5-dimethyl-5-hydroxy-5,6,7,8-tetrahydro-1,2-benzanthracene was obtained as a nearly colorless oil.

Without purification the crude carbinol and 80 mg. of palladium–charcoal catalyst were heated in a nitrogen atmosphere at 310° for twenty minutes. A small amount of material which had distilled into the upper portion of the tube was washed down with benzene, the solvent was removed and the mixture was heated for an additional fifteen minutes at 310°. The product, separated from the catalyst by means of hot benzene, was an almost colorless solid (340 mg.; m. p. 104–106°) when "sublimed" at 160° (0.01 mm.).

The crude hydrocarbon was converted into its picrate and the latter was recrystallized once from absolute ethanol. A benzene solution of the regenerated hydrocarbon was passed through an alumina tower, the solvent was removed, and the completely colorless compound was recrystallized from acetone-alcohol, from which it was obtained in the form of irregular plates; m. p. 106–107°. When absolute alcohol alone was used, the substance formed diamond-shaped plates.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.7; H, 6.3. Found: C, 93.6; H, 6.0.

The **picrate** crystallized from absolute alcohol in maroon needles. After recrystallization from the same solvent it melted at 150–150.5° (vac.) in a Pyrex tube.

Anal. Calcd. for $C_{20}H_{16}\cdot C_6H_3O_7N_3$: N, 8.7. Found: N, 8.7.

Summary

The synthesis of 7-methylcholanthrene, an isomer of the active carcinogen 3-methylcholanthrene, is described. In addition, 1',5-dimethyl-1,2-benzanthracene has been prepared. Both compounds were synthesized from 4-methylphenanthrene.

The compounds are being tested for carcinogenic activity.

ANN ARBOR, MICHIGAN RECEIVED JANUARY 20, 1941

(6) Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).