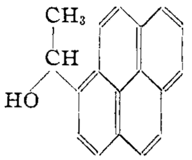
[Contribution from the Chemistry Laboratory of the University of Michigan]

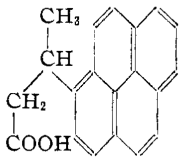
Methyl Derivatives of 3,4-Benzpyrene. The Willgerodt Reaction on Some 3-Acylpyrenes

By W. E. Bachmann and Marvin Carmack[1]

For the synthesis of 1′-methyl-3,4-benzpyrene (IV), a new methyl derivative of the carcinogen 3,4-benzpyrene, the readily available 3-acetylpyrene was reduced to methyl-3-pyrenylcarbinol (I) by means of aluminum isopropoxide, the carbinol was converted to its bromide and the latter was condensed with sodio-malonic ester to yield β-3-pyrenylbutyric acid (II). The side chain was lengthened by one methylene group and the resulting γ-3-pyrenylvaleric acid was cyclized to 1′-methyl-4′-ketotetrahydro-3,4-benzpyrene (III). The ketone was reduced to the corresponding alcohol and the latter was dehydrated and dehydrogenated to 1′-methyl-3,4-benzpyrene by palladium on charcoal at 300–320°.



I



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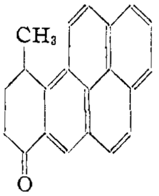

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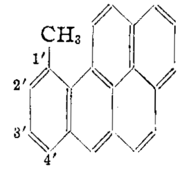
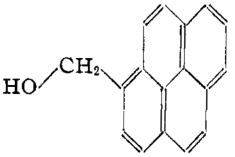
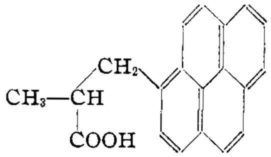


IV

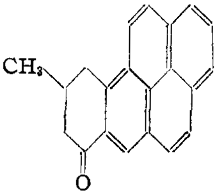
In the synthesis of 2′-methyl-3,4-benzpyrene, 3-pyrenealdehyde was reduced to 3-pyrenylcarbinol (V) catalytically and also by means of aluminum isopropoxide. The carbinol was converted to its chloride, which was condensed with sodio-malonic ester. The substituted malonic ester was hydrolyzed to the free dicarboxylic acid which was purified and then converted to its dimethyl ester. The latter was methylated and the product was hydrolyzed and decarboxylated to yield β-3-pyrenylisobutyric acid (VI). The side chain was lengthened by one methylene group and the resulting acid was cyclized through its acid chloride to 2′-methyl-4′-ketotetrahydro-3,4-benzpyrene (VII), which was converted to 2′-methyl-3,4-benzpyrene (VIII) by the procedure employed for the 1′-methyl isomer. The properties of our compound agreed with those of the hydrocarbon which Fieser and Hershberg[2] obtained from *p*-toluylperinaphthane through the Scholl reaction and which they regarded as 2′-methyl-3,4-benzpyrene.



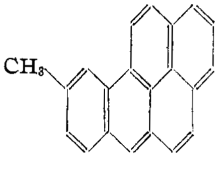
V



VI



VII



VIII

Winterstein, Vetter and Schön[3] prepared a methyl-3,4-benzpyrene from the keto acid obtained by interaction of pyrene and methylsuccinic anhydride, but they were uncertain whether their compound was the 2′- or 3′-methyl isomer, for they were unable to decide how the unsymmetrical anhydride oriented itself when it reacted with the pyrene. We have now proved that the keto acid which is formed possesses the structure XI; the anhydride reacts with pyrene in the 3-position in such a manner that the methyl group is farthest away from the hydrocarbon residue, in harmony with the reaction of the anhydride with other hydrocarbons. Fieser and Hershberg[2] considered that the hydrocarbon which they obtained from both *o*- and *m*-toluylperinaphthane and which agreed fairly well in melting point with the hydrocarbon of Winterstein, Vetter and Schön was 3′-methyl-3,4-benzpyrene. In the present investigation, 3′-methyl-3,4-benzpyrene has been synthesized by a method which leaves no doubt about the structure, and it has been shown that this is the compound which was obtained by Winterstein, Vetter and Schön. The properties of the hydrocarbon and its derivatives prepared by Fieser and Hershberg agree with the proper-

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[1] From the Ph.D. dissertation of Marvin Carmack.

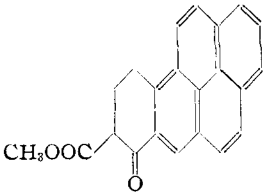
[2] Fieser and Hershberg, This Journal, **60**, 1658 (1938).

[3] Winterstein, Vetter and Schön, *Ber.*, **68**, 1079 (1935).

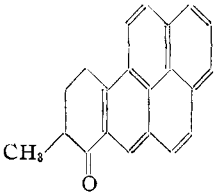
ties of 3′-methyl-3,4-benzpyrene and its derivatives prepared by us.

In our synthesis, 4′-ketotetrahydrobenzpyrene was condensed with dimethyl oxalate and the resulting glyoxalate was decarbonylated by heating it with powdered glass.[4] The keto ester (IX), which was formed, was methylated and the product was hydrolyzed and decarboxylated to 3′-methyl-4′-ketotetrahydrobenzpyrene (X). By reduction of the ketone to the alcohol by means of aluminum isopropoxide and heating the alcohol with palladium on charcoal, 3′-methyl-3,4-benzpyrene was obtained in good yield.

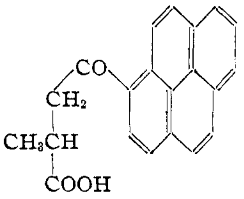
The hydrocarbon 3′,4′-dimethyl-3,4-benzpyrene (XII) was also synthesized. This was accomplished by treating the ketone (X) with methylmagnesium iodide and dehydrating and dehydrogenating the resulting carbinol to the hydrocarbon by means of palladium.



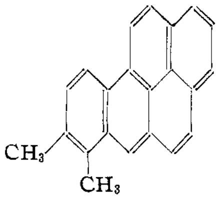
IX



X



XI



XII

Willgerodt Reaction on Some 3-Acylpyrenes.—This reaction was applied to a number of 3-acylpyrenes, which were prepared readily from pyrene and the acid anhydride through the Friedel–Crafts reaction. The ketones were heated with ammonium polysulfide in dioxane according to the procedure of Fieser and Kilmer[5] in order to convert them to the amide of the acid with the same number of carbon atoms. On small scale runs, 3-acetylpyrene gave practically pure 3-pyrenylacetamide in yields as high as 92%. Hydrolysis of the product yielded 3-pyrenylacetic acid, whose structure was verified by its synthesis from 3-pyrenylcarbinol (V). The over-all yield of the acid from pyrene was 73%. This acid was obtained by Vollmann and co-workers[6] in 10% yield by the prolonged action of chloroacetic acid on pyrene.

From 3-propionylpyrene a 67% yield of β-3-pyrenylpropionic acid was obtained through the amide. The structure of this acid was proved by its preparation from 3-pyrenylcarbinol through the malonic ester synthesis. Similarly, a 46% yield of γ-3-pyrenylbutyric acid was obtained from 3-*n*-butyrylpyrene through the amide produced in the Willgerodt reaction. We were not able to obtain any amide from 3-pyrenyl isopropyl ketone or from 3-pyrenyl isobutyl ketone, which contain branched alkyl groups. It is of interest that Fieser and Kilmer obtained only a 1.8% yield of amide from phenyl isobutyl ketone.

Experimental

Methyl-3-pyrenylcarbinol (I).—3-Acetylpyrene (20 g.) was reduced by a solution of aluminum isopropoxide prepared from 5 g. of aluminum wire and 125 cc. of anhydrous isopropyl alcohol. The mixture was hydrolyzed with ice-cold dilute sulfuric acid and the product was filtered, washed thoroughly with water and dried. A solution of the compound in acetone was boiled with Norit, the solution was filtered and evaporated and the residue was recrystallized from benzene, yielding 17.4 g. of pale yellow crystals suitable for the next step; m. p. 109–110°. A sample after several recrystallizations from benzene formed clusters of colorless prisms; m. p. 112–112.5°.

Anal. Calcd. for $C_{18}H_{14}O$: C, 87.8; H, 5.7. Found: C, 87.8; H, 5.7.

β-3-Pyrenylbutyric Acid (II).—The aforementioned carbinol (6.25 g.) in 25 cc. of pure benzene was treated with 1.9 cc. of phosphorus tribromide. Enough benzene (35 cc.) was added to dissolve all of the solid and the mixture was allowed to remain at room temperature for one hour. The solution was washed three times with 5% sodium bicarbonate solution, then with water and dried with magnesium sulfate. From the solution 7.6 g. (96%) of 1-bromo-1-(3-pyrenyl)-ethane (m. p. 108° dec.) was obtained, which was used immediately in the next step. In one run, the crude carbinol obtained from 11.8 g. of 3-acetylpyrene yielded 14.4 g. (96% based on the ketone) of the bromide (m. p. 105–106° dec.) suitable for the next step.

Finely powdered sodium (2.9 g.) was refluxed with 26 cc. of diethyl malonate in 100 cc. of benzene for three hours, and to the cooled suspension was added 12 g. of the crude bromide. After the mixture had been refluxed for thirteen hours on a steam-bath, the benzene was removed by distillation and the ester was hydrolyzed by heating it with 35 cc. of 40% potassium hydroxide solution for four hours on a sand-bath. After extraction with benzene, the solution was acidified and the substituted malonic acid was collected; yield, 12 g. (93%) of a pale tan colored solid. The latter was heated at 180–190° for twenty-five minutes and the product was recrystallized from chlorobenzene (25 cc.), yielding 9.08 g. of crystalline acid suitable for the next step. A sample after evaporative distillation at 0.01

[4] Bachmann, Cole and Wilds, THIS JOURNAL, **62**, 825 (1940).

[5] Fieser and Kilmer, *ibid.*, **62**, 1354 (1940).

[6] Vollmann, Becker, Corell and Streeck, *Ann.*, **531**, 1 (1937).

mm. and recrystallization from benzene–acetic acid formed colorless rhombic crystals; m. p. 177–178°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.3; H, 5.6. Found: C, 83.0; H, 5.5.

γ-3-Pyrenylvaleric Acid.—The acid chloride was prepared in a small filter flask from 2 g. of the aforementioned acid, 0.8 cc. of pure thionyl chloride, 10 cc. of anhydrous ether and a drop of pyridine. After two hours at room temperature (frequent swirling), the ether and excess of thionyl chloride were removed under reduced pressure, a few cc. of dry benzene was added and the solvent again removed, finally at 40–50° at 0.5 mm. A solution of the acid chloride in 10 cc. of benzene was added dropwise from the side-arm of the flask to an ice-cold solution of diazomethane prepared from 4 g. of nitrosomethylurea in 40 cc. of ether. After ten minutes the diazoketone began to separate in lustrous pale tan platelets. After three hours at 5°, the ether was removed under reduced pressure and the crystalline residue was digested with cold methanol in order to remove oily impurities and filtered; yield, 1.92 g. (88%); m. p. 116–118° dec.

A mixture of 0.5 g. of silver oxide (Schuchardt) and 40 cc. of reagent methanol was refluxed until a silver mirror was visible on the bottom of the flask (fifteen minutes). The diazoketone was added and the mixture was refluxed for three hours, treated with Norit, filtered and evaporated in a current of air. The residual ester was refluxed with *N* sodium hydroxide (15 cc.) and a little methanol for one hour, and the clarified solution was acidified, yielding 1.82 g. of γ-3-pyrenylvaleric acid (m. p. 117–121°), which was suitable for the next step. A sample after recrystallization from chlorobenzene, evaporative distillation under reduced pressure and recrystallization from benzene–acetic acid formed fine colorless rhombic platelets; m. p. 135.5–136.5°.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.4; H, 6.0. Found: C, 83.2; H, 5.9.

1'-Methyl-4'-keto-1',2',3',4'-tetrahydro-3,4-benzpyrene (III).—Crude γ-3-pyrenylvaleric acid (1.2 g.; m. p. 117–121°) and 1.2 g. of finely divided phosphorus pentachloride were suspended in 20 cc. of dry benzene; after one-half hour, 1.3 cc. of anhydrous stannic chloride was added. After four hours at room temperature, the deeply colored complex was hydrolyzed with ice and hydrochloric acid. From the benzene solution, after thorough washing with acid and then with dilute alkali, 0.83 g. of the cyclic ketone was obtained as yellow needles; m. p. 154–160°. A sample after recrystallization from benzene–petroleum ether melted at 162–163°.

Anal. Calcd. for $C_{21}H_{16}O$: C, 88.7; H, 5.7. Found: C, 88.5; H, 5.6.

1'-Methyl-3,4-benzpyrene (IV).—One gram of the cyclic ketone was reduced by means of a clarified solution of aluminum isopropoxide prepared from 0.5 g. of aluminum and 50 cc. of isopropyl alcohol and the product obtained on hydrolysis with cold, dilute sulfuric acid was filtered and washed thoroughly with sodium bicarbonate solution and with water. On recrystallization from benzene–acetone a first crop of 0.51 g. of practically colorless platelets was obtained; the filtrate contained an amount which brought the yield to 91%. After another recrystallization the **1'-methyl-4'-hydroxy-1',2',3',4'-tetrahydro-3,4-benzpyrene** melted at 184–185°.

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

The unrecrystallized alcohol obtained from 0.73 g. of the cyclic ketone was heated with 0.1 g. of palladium–charcoal catalyst[7] in a nitrogen atmosphere at 300–320° for twenty minutes. The material which had sublimed up on the sides of the tube was washed down with a little benzene, the benzene was evaporated and the heating was resumed for an additional ten minutes. After evaporative distillation at 220° and 0.01 mm. directly from the catalyst and recrystallization from benzene–methanol, the 1'-methyl-3,4-benzpyrene was obtained in glistening yellow platelets; yield, 0.34 g. (50%); m. p. 190–190.8° (vac.).

Anal. Calcd. for $C_{21}H_{14}$: C, 94.7; H, 5.3. Found: C, 94.5; H, 5.5.

The **picrate** prepared in benzene–petroleum ether crystallized in dark red-brown needles; m. p. 186–186.5°.

Anal. Calcd. for $C_{21}H_{14}\cdot C_6H_3N_3O_7$: N, 8.5. Found: N, 8.5.

The **trinitrobenzene complex,** prepared in benzene, crystallized in brilliant red needles; m. p. 208.5–209°.

Anal. Calcd. for $C_{21}H_{14}\cdot C_6H_3N_3O_6$: N, 8.8. Found: N, 8.6.

3-Pyrenylcarbinol (V).—Fifteen grams of 3-pyrenealdehyde, prepared from pyrene and methylformanilide,[6] was hydrogenated in 200 cc. of absolute alcohol with the aid of 0.3 g. of Adams catalyst and a solution of 50 mg. of ferrous sulfate in 3 cc. of water as a promoter; absorption of hydrogen was complete in one to one and a half hours. The clear solution was filtered from the catalyst and chilled; after several hours 8.8 g. of the carbinol was filtered off; m. p. 121.5–122.5°. A second crop (3.5 g.; m. p. 121–122°) brought the yield to 81%. A sample of the carbinol after evaporative distillation at 0.01 mm. and recrystallization from benzene formed pale yellow rhombic crystals; m. p. 123–124°.

Anal. Calcd. for $C_{17}H_{12}O$: C, 87.9; H, 5.2. Found: C, 87.4; H, 5.1.

The carbinol was obtained in 54% yield by reduction of the aldehyde by means of aluminum isopropoxide.

α-Methyl-β-3-pyrenylpropionic Acid (VI).—Powdered 3-pyrenylcarbinol (2.3 g.) in 20 cc. of dry benzene was treated with 0.4 cc. of phosphorus trichloride. After one hour the clear filtered solution was washed with 5% sodium bicarbonate solution and with water and dried over magnesium sulfate. Removal of the benzene left 2.2 g. (89%) of cream-colored crystals of 3-chloromethylpyrene (m. p. 144–145°) suitable for the next step.

Eight grams of the chloride was added to a cooled suspension of sodio-malonic ester which had been prepared from 15.4 cc. of diethyl malonate and 1.5 g. of finely divided sodium in 100 cc. of dry benzene. The mixture was warmed slowly to boiling on a steam-bath with constant swirling and then heated for ten hours. After removal of the benzene in a current of air, the residual ester was hydrolyzed by heating it with 50 cc. of 40% aqueous potassium hydroxide on a steam-bath for one hour. After

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[7] Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).

being warmed with 100 cc. of water to dissolve the salts which had precipitated, the clarified solution was acidified, whereupon 8.7 g. of nearly colorless substituted malonic acid was obtained. A mixture of 6.5 g. of the acid and 100 cc. of methanol which had been saturated cold with hydrogen chloride was refluxed for two hours. From the filtered solution 3.4 g. of **dimethyl-β-3-pyrenylisosuccinate** (m. p. 111–111.5°) crystallized in colorless needles; retreatment of the filtrate with hydrogen chloride followed by refluxing yielded an additional 1.2 g. of satisfactory material. After evaporative distillation at 0.01 mm. and recrystallization from methanol a sample of the ester melted at 112–112.5°.

Anal. Calcd. for $C_{22}H_{18}O_4$: C, 76.3; H, 5.2. Found: C, 76.1; H, 5.1.

Four grams of the ester was added to a solution of sodium methoxide prepared from 1.46 g. of sodium and 50 cc. of methanol. After a short period of refluxing, the mixture was cooled to room temperature and treated with 4 cc. of methyl iodide; after two hours another 1 cc. of methyl iodide was added and the mixture was refluxed for two hours. After removal of the methanol, the product was taken up in benzene and water, the benzene solution was filtered from a small amount of high-melting by-product and then washed with dilute alkali and with water. Removal of the solvent yielded 3.47 g. (83%) of crystalline **dimethyl α-methyl-β-3-pyrenylisosuccinate**; m. p. 131–133°. A sample after evaporative distillation at 0.01 mm. and recrystallization from methanol–acetone was obtained in faintly yellow rhombic plates; m. p. 136.5–137.5°.

Anal. Calcd. for $C_{23}H_{20}O_4$: C, 76.6; H, 5.6. Found: C, 76.2; H, 5.6.

A mixture of 3.47 g. of the unrecrystallized ester and 35 cc. of 40% aqueous potassium hydroxide was refluxed for twenty minutes on a sand-bath; then 35 cc. of water was added to dissolve the salts which had precipitated and refluxing was continued for one hour. The dicarboxylic acid which was obtained on acidification of the solution was heated at 190–200° for one-half hour and the product was dissolved in hot acetone; from the solution 2.74 g. (98%) of satisfactory **α-methyl-β-3-pyrenylpropionic acid** was obtained; m. p. 170–173°. After evaporative distillation at 200° and 0.01 mm. and recrystallization from chlorobenzene a sample formed colorless rhombic crystals; m. p. 173–174°.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.3; H, 5.6. Found: C, 83.1; H, 5.8.

2′-Methyl-4′-keto-1′,2′,3′,4′-tetrahydro-3,4-benzpyrene (VII).—The acid chloride was prepared from 1 g. of the aforementioned acid and converted to the diazoketone by the procedure described for the preparation of γ-3-pyrenylvaleric acid; m. p. 110–111° dec.; yield, 1.08 g. of fine pale tan crystals. The diazoketone was heated with 40 cc. of methanol and 0.15 g. of silver oxide in a water-bath for twenty minutes; a further 0.15 g. of silver oxide was added and refluxing was continued for one and one-half hours. The ester obtained by evaporation of the filtered solution was heated with 1 cc. of aqueous 40% potassium hydroxide and 10 cc. of water for three hours, the diluted solution was clarified with Filter-Cel, cooled and acidified. The crude β-methyl-γ-3-pyrenylbutyric acid (0.97 g.; m. p. 125–135°) which precipitated was treated with 0.97 g. of phosphorus pentachloride in 15 cc. of dry benzene and the resulting mixture was treated with 1.1 cc. of stannic chloride at room temperature in the manner described. After forty-five minutes the mixture was hydrolyzed. From the washed and dried benzene solution 0.89 g. (90% over-all yield based on VII) of the cyclic ketone was obtained as yellow needles; m. p. 176.5–177.5°. After evaporative distillation at 0.01 mm. and recrystallization from benzene–methanol, a sample formed light yellow plates; m. p. 178–179° (vac.). From benzene–petroleum ether it crystallized in fine needles which then changed to plates.

Anal. Calcd. for $C_{21}H_{16}O$: C, 88.7; H, 5.7. Found: C, 88.5; H, 6.0.

2′-Methyl-3,4-benzpyrene (VIII).—One-half gram of the aforementioned ketone was reduced by a clarified solution of aluminum isopropoxide prepared from 0.27 g. of aluminum and 20 cc. of anhydrous isopropyl alcohol and the crude alcohol (0.52 g.; m. p. 160–170°) was heated with palladium–charcoal in the manner described. The hydrocarbon was evaporatively distilled directly from the catalyst at 175° and 0.01 mm. and the product was recrystallized twice from benzene–methanol, whereby it was obtained in fine yellow needles; yield, 0.15 g. (32%, based on the ketone). It melted at 139–140° cor. (vac.), when heated slowly (reported,[2] 138–139°, cor.); the solidified melt remelted at 140–140.4°, cor. (reported, 140–140.2°). The **picrate** formed fine, chocolate-brown crystals in benzene–petroleum ether which melted at 184–184.5° cor. (reported,[2] 184–185°, cor.) and the **trinitrobenzene complex** formed bright red rhombs in benzene–petroleum ether which melted at 212.5–213°, cor. (reported,[2] 211.5–212°, cor.).

3′-Methyl-4′-keto-1′,2′,3′,4′-tetrahydro-3,4-benzpyrene (X). (a) **From XI.**—β-3-Pyrenoylisobutyric acid was prepared from pyrene and methylsuccinic anhydride according to the procedure of Winterstein, Vetter and Schön.[3] Its **methyl ester**, prepared by means of methanolic hydrogen chloride, after evaporative distillation at 0.01 mm., crystallized from methanol in light yellow platelets; m. p. 105–105.5°.

Anal. Calcd. for $C_{22}H_{18}O_3$: C, 80.0; H, 5.5. Found: C, 80.3; H, 5.4.

Clemmensen reduction of the keto acid and of its methyl ester yielded α-methyl-γ-3-pyrenylbutyric acid (XI), which crystallized from benzene–acetic acid in bright yellow crystals; m. p. 173–174.5°; yield, 32%. Winterstein, Vetter and Schön obtained an 80% yield of this acid (m. p. 176°, cor.) by reduction of the keto acid by zinc and alkali. The acid (1.89 g.) was converted to its acid chloride by means of 1.5 g. of phosphorus pentachloride in 40 cc. of benzene and the mixture treated with anhydrous stannic chloride in the manner described for the preparation of III. The first crop of crystals from benzene–ethanol weighed 1.31 g. (74%); m. p. 177.3–178° (vac.). Further recrystallization of a sample of the ketone raised the melting point to 178–178.5° (vac.). Winterstein, Vetter and Schön obtained an 80% yield of the ketone by heating the acid with stannic chloride; their purified product melted at 176–177°, cor. A mixture of this ketone with its 2′-methyl isomer (m. p. 178–179°) melted to 150–165°.

(b) **From 4′-ketotetrahydro-3,4-benzpyrene.**—One-half gram of the ketone[8] was condensed with 0.3 g. of dimethyl oxalate in 15 cc. of dry benzene by means of dry sodium methoxide (prepared from 0.07 g. of sodium) at room temperature in a nitrogen atmosphere. After one hour, water was added to the mixture, the benzene layer was discarded and the aqueous solution was acidified, whereupon **methyl 4′-ketotetrahydro-3,4-benzpyrene-3′-glyoxalate** was precipitated as a yellow crystalline powder; weight, 0.63 g. A sample crystallized from dioxane in golden yellow leaflets and orange-yellow rhombs; m. p. 172–174°, dec., in a Pyrex tube. The m. p. was variable and was from five to ten degrees lower in soft glass capillary tubes.

Anal. Calcd. for $C_{23}H_{16}O_4$: C, 77.5; H, 4.5. Found: C, 76.8; H, 4.6.

Recrystallized glyoxalate (1 g.) was heated with 0.5 g. of powdered soft glass at 180–190° for fifteen minutes. The product was extracted with hot acetone, and the solution was heated with Norit, filtered and evaporated, yielding 0.83 g. of nearly pure **3′-carbomethoxy-4′-ketotetrahydrobenzpyrene (IX).** From acetone–dioxane it crystallized in light yellow platelets; m. p. 154.5–155° (vac.); the melt solidified and remelted at 176.5–178.5° to a cloudy liquid which became perfectly clear at 181°. It gave a blue-green color with an alcoholic solution of ferric chloride.

Anal. Calcd. for $C_{22}H_{16}O_3$: C, 80.5; H, 4.9. Found: C, 80.4; H, 5.1.

The keto ester (0.2 g.) was converted to its sodio derivative in 5 cc. of benzene by means of sodium methoxide, methyl iodide was added in portions (0.9 cc. in all), the mixture was allowed to remain at room temperature for two hours and then refluxed for two hours. The methylated product was heated with a mixture of 10 cc. of acetic acid, 5 cc. of concentrated hydrochloric acid and 1 cc. of water for four hours, the solvents were evaporated and the residue was dissolved in benzene. The solution was washed with dilute ammonium hydroxide, dried and passed through a short tower of alumina; from the solution 55 mg. (33%) of practically pure ketone was obtained. After one recrystallization from benzene it formed pale-yellow rhombs; m. p. 178–178.5° (vac.), alone and when mixed with the ketone obtained in (a).

3′-Methyl-3,4-benzpyrene.—One-half gram of the aforementioned ketone was reduced by means of a solution of aluminum isopropoxide and the crude chalk-white alcohol (0.47 g.) was heated with 50 mg. of palladium–charcoal catalyst at 300–320° as described. The pale-yellow product (0.42 g.; m. p. 142–145°), after evaporative distillation at 220° and 0.01 mm. pressure, crystallized from benzene–petroleum ether in fine needles; m. p. 147.5–148°, cor., with slight previous softening (reported,[2] 146.5–147°, cor., when heated slowly, and 147.6–148.1°, cor., on remelting). The **picrate** formed dark reddish-brown crystals in benzene–petroleum ether; m. p. 179–180°, cor. (reported,[2] 179.5–180°, cor.). The **trinitrobenzene complex** crystallized from benzene–petroleum ether in brilliant red needles; m. p. 212.5–213°, cor. (reported,[2] 210.5–211°, cor.).

3′,4′-Dimethyl-3,4-benzpyrene (XII).—One gram of 3′-methyl-4′-ketotetrahydrobenzpyrene in 10 cc. of dry benzene was added to a solution of methylmagnesium iodide prepared from 0.66 cc. of methyl idodide in 10 cc. of ether. The product obtained by hydrolysis of the mixture after three hours of refluxing was heated with 0.1 g. of palladium–charcoal catalyst at 300–320° for thirty minutes as described. The hydrocarbon which was obtained by sublimation from the catalyst at 0.01 mm. pressure was practically pure 3′,4′-dimethyl-3,4-benzpyrene; yield, 0.85 g. (91%); m. p. 215–216°. From benzene it crystallized in yellow rhombic plates with no change in its melting point.

Anal. Calcd. for $C_{22}H_{16}$: C, 94.3; H, 5.7. Found: C, 94.7; H, 5.8.

The **picrate** crystallized from benzene in brown needles; m. p. 205–205.5°.

Anal. Calcd. for $C_{22}H_{16}\cdot C_6H_3N_3O_7$: N, 8.3. Found: N, 8.3.

Preparation of 3-Acylpyrenes.—The procedure employed for the preparation of these ketones is illustrated by the preparation of 3-acetylpyrene. Anhydrous aluminum chloride (66 g.) was dissolved in 200 cc. of nitrobenzene contained in a three-necked flask equipped with a mercury-sealed Hershberg stirrer and a thermometer. To the cooled solution was added 26 cc. of acetic anhydride, the mixture was cooled to −5°, and 50 g. of finely divided pyrene was added with efficient stirring in the course of about ten minutes. After three hours of stirring at 10° and four additional hours at 0° (for the reaction with isovaleric anhydride six hours in ice–salt mixture and six hours at room temperature were allowed), the mixture was hydrolyzed, the nitrobenzene was removed by steam distillation, and the ketone was distilled at 1 mm. pressure and recrystallized from methanol with the use of Norit. The yields and properties of the ketones are shown in the table; all of the ketones were obtained as yellow crystals.

TABLE I

3-ACYLPYRENES

$RCOC_{16}H_9$ R	Yield, %	M. p., °C.	Crystalline form
Methyl[a]	88	89–90	Plates
Ethyl[b]	85	79–80	Rhombs
n-Propyl[c]	85	73–74	Prisms
Isopropyl[d]	82	87–89	Leaflets
Isobutyl[e]	85	82–82.5	Platelets

[a] Previously prepared from pyrene, acetic acid and zinc chloride[6] (m. p. 90°) and from pyrene, acetyl chloride and aluminum chloride[9] (m. p. 94°). [b] Prepared previously in 82% yield (m. p. 84–85°) by means of propionyl chloride.[10] [c] *Anal.* Calcd. for $C_{20}H_{16}O$: C, 88.2; H, 5.9. Found: C, 87.9; H, 6.0. [d] *Anal.* Calcd. for $C_{20}H_{16}O$: C, 88.2; H, 5.9. Found: C, 87.7; H, 5.9. [e] *Anal.* Calcd. for $C_{21}H_{18}O$: C, 88.1; H, 6.3. Found: C, 88.6; H, 6.4.

The Willgerodt Reaction.—Following the procedure of Fieser and Kilmer,[5] 2-g. samples of the ketones were sub-

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[8] Cook and Hewett, *J. Chem. Soc.*, 398 (1933); Fieser and Novello, THIS JOURNAL, **62**, 1855 (1940); Bachmann, Carmack and Safir, *ibid.*, **63**, 1682 (1941).

[9] Dziewoński and Sternbach, *Roczniki Chem.*, **17**, 101 (1937).

[10] Dziewoński and Trzesiński, *Bull. intern. acad. polon. sci., Classe sci. math. nat.*, 579 (1937A).

jected to the action of ammonium polysulfide. From the cooled mixture obtained from 3-acetylpyrene, 1.95 g. (92%) of golden-brown centimeter-long prisms of practically pure **3-pyrenylacetamide** was filtered off and washed with a mixture of dioxane and ammonium polysulfide solution; m. p. 244–246°. A sample after sublimation at 240° and 0.01 mm. pressure crystallized from acetic acid–chlorobenzene in fine, colorless prismatic needles; m. p. 246–247°.

Anal.[11] Calcd. for $C_{18}H_{13}ON$: N, 5.41. Found: N, 5.39.

The unrecrystallized amide (13.7 g.) was dissolved in 200 cc. of boiling acetic acid, 100 cc. of concentrated hydrochloric acid was added cautiously through the top of the upright condenser attached to the flask, and the mixture was refluxed for one and one-quarter hours, when an additional 100 cc. of hydrochloric acid was added in order to precipitate the product. From the chilled mixture, the **3-pyrenylacetic acid** (13.4 g.; m. p. 218.5–220°) was filtered; it was purified through its water-soluble potassium salt and then recrystallized from chlorobenzene (130 cc.). The first crop of fine, slightly colored plates and prisms weighed 12.3 g. (90%); m. p. 222.5–223° (vac.) (reported,[6] 220°, dec.).

The same acid was obtained in poor yield by heating a mixture of 3-chloromethylpyrene (prepared from 3-pyrenylcarbinol and phosphorus trichloride) and potassium cyanide in methanol for one and one-half hours, followed by refluxing the nitrile with 20% alcoholic potassium hydroxide for twenty-two hours.

The amide (1.7 g.; m. p. 177–181°) obtained from 2 g. of 3-propionylpyrene was hydrolyzed in the manner described and the acid was purified through its salt. The **β-3-pyrenylpropionic acid** (1.42 g.; m. p. 173–174°) crystallized from acetic acid–chlorobenzene in pale tan platelets; m. p. 178–179°. It can be obtained colorless by sublimation at 0.01 mm. pressure. The same acid was obtained from 3-chloromethylpyrene through the malonic ester synthesis.

Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.2; H, 5.1. Found: C, 83.1; H, 5.2.

The methyl ester was prepared by means of diazomethane; after evaporative distillation at 0.01 mm. pressure and recrystallization from methanol, it formed gleaming, colorless leaflets; m. p. 95.5–96.5°, cor. (reported,[12] 81°).

A 46% yield of **γ-3-pyrenylbutyric acid** was obtained as practically colorless crystals by hydrolysis of the 1.22 g. of crude amide (m. p. 172–175°) which was obtained from 2 g. of 3-*n*-butyrylpyrene; after recrystallization from a mixture of benzene, acetone and acetic acid, it melted at 186–187°, alone and when mixed with an authentic specimen.

Summary

The synthesis of the new 1′-methyl-3,4-benzpyrene from 3-acetylpyrene and new syntheses of 2′-methyl- and 3′-methyl-3,4-benzpyrene are described. 3′,4′-Dimethyl-3,4-benzpyrene also has been synthesized.

A study has been made of the Willgerodt reaction on five 3-acylpyrenes.

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[11] Micronalysis by Torsti Salo.

[CONTRIBUTION FROM AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

The System Trimethyl Phosphate–Water

BY H. ARMIN PAGEL AND FRANK S. MAXEY

The freezing points of trimethyl phosphate have been described in an earlier paper.[1] The accompanying data and graph show the freezing points of the system trimethyl phosphate–water, in which the solid phase of the ester is the so-called "alpha" form.

Experimental

The purified ester used in this work was the same as that used previously.[1] Likewise, the apparatus was the same except that reduced pressure was required to obtain sufficiently low temperatures with the solid carbon dioxide–alcohol mixture, when working near the ester–water eutectic composition. Weight burets were used to prepare the various ester–water mixtures to an accuracy within 0.1 mole per cent.

TABLE I

EXPERIMENTAL VALUES OF THE FREEZING POINTS OF THE SYSTEM TRIMETHYL PHOSPHATE–WATER

Mole % Me_3PO_4	F. p., °C.	Mole % Me_3PO_4	F. p., °C.
0.0	0.0	44.9	−64.0
2.2	− 2.1	47.0	−68.3
4.7	− 4.4	49.0	−72.0
6.8	− 6.3	50.0	−73.4
9.8	− 8.6	52.0	−77.0
13.5	−12.8	(Eutectic)	
19.4	−19.0	55.0	−72.8
21.0	−20.0	60.0	−67.0
24.5	−27.3	65.2	−62.4
27.5	−33.0	70.0	−58.7
32.5	−41.2	74.9	−55.4
35.0	−47.0	80.0	−52.8
36.4	−49.2	84.9	−50.2
39.0	−53.7	90.0	−49.1
40.0	−55.4	96.4	−47.1
41.0	−57.0	100.0	−46.1

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[1] Pagel and Schroeder, THIS JOURNAL, **62**, 1837 (1940).