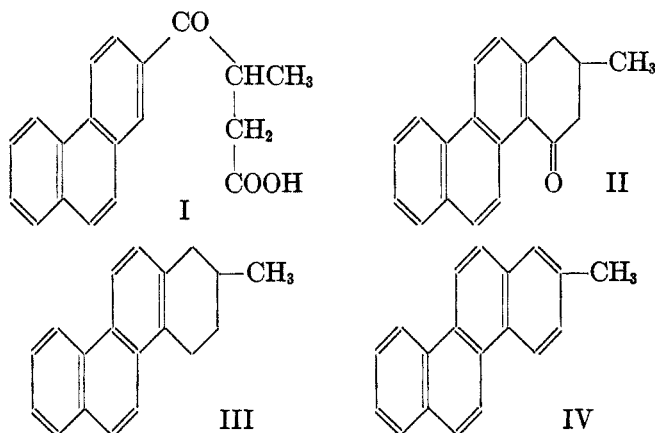


THE SYNTHESIS OF DERIVATIVES OF CHRYSENE

W. E. BACHMANN AND W. S. STRUVE*

Received April 29, 1939

Three years ago¹ we described the preparation of β -(2-phenanthroyl)-butyric acid (I), which we prepared from 2-propionylphenanthrene as an intermediate in the synthesis of 2-methylchrysene (IV)†. We have now completed the projected synthesis, using the well-known steps of the



Haworth method.² Clemmensen reduction of the acid yielded γ -(2-phenanthryl)- β -methylbutyric acid, which was cyclized in the form of its acid chloride by means of stannic chloride. Under the conditions employed cyclization took place nearly entirely from the 2 to the 1 position with the formation of 2-methyl-4-keto-1,2,3,4-tetrahydrochrysene (II), although there appeared to be present some of the cyclic ketone formed by cyclization to the 3 position. 2-Methyltetrahydrochrysene (III) was obtained from the cyclic ketone by Clemmensen reduction, and the resulting hydrocarbon was dehydrogenated smoothly to 2-methylchrysene by palladium on charcoal. The 2- and 3-propionylphenanthrenes, which we

* From the Ph.D. dissertation of W. S. Struve.

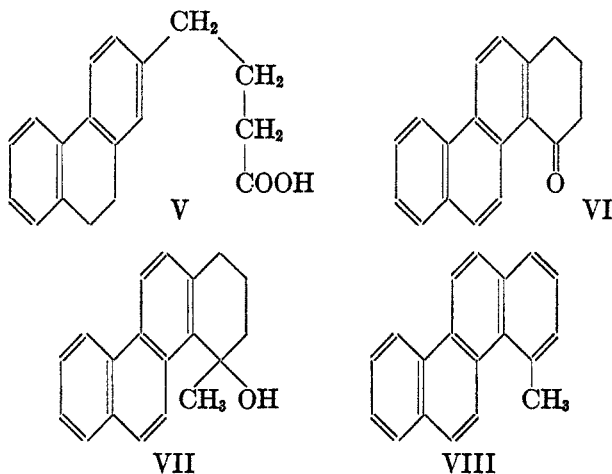
† The numbering system for the chrysene molecule is that used in the index of *Chemical Abstracts*.

¹ BACHMANN AND STRUVE, *J. Am. Chem. Soc.*, **58**, 1659 (1936).

² HAWORTH, *J. Chem. Soc.*, **1932**, 1125.

had prepared from phenanthrene and propionyl chloride, have now been reduced by the Clemmensen method to the corresponding 2-*n*-propylphenanthrene and 3-*n*-propylphenanthrene.

We have also prepared 4-methylchrysene (VIII) from the cyclic ketone, 4-keto-1,2,3,4-tetrahydrochrysene (VI). The latter compound was made by Haworth³ from 2-acetylphenanthrene. We have made use of the γ -[2-(9,10-dihydrophenanthryl)]-butyric acid (V) of Burger and Mosettig,^{4,5} which is readily obtained by Clemmensen reduction of the corresponding keto acid, which in turn can be prepared in excellent yields by interaction of 9,10-dihydrophenanthrene and succinic anhydride. The dihydrophenan-



thrylbutyric acid was dehydrogenated in the form of its methyl ester with palladium on charcoal at a relatively low temperature (240–260°) in excellent yields (90–95 per cent.). At this temperature the hydrogen was eliminated rapidly and the yield was much higher than was the case when the free acid or its methyl ester was dehydrogenated at a higher temperature (300–320°), the yield under these conditions being only 20–40 per cent.

The γ -(2-phenanthryl)butyric acid was cyclized by treating the acid chloride in benzene solution in the cold with stannic chloride. This procedure gives the 4-keto-1,2,3,4-tetrahydrochrysene in better yields than the Haworth³ method of cyclization with sulfuric acid and does not require repeated recrystallizations in order to obtain the cyclic ketone in a pure form. When the cyclization was carried out at room temperature, a

³ HAWORTH AND MAVIN, *ibid.*, 1933, 1013.

⁴ BURGER AND MOSETTIG, *J. Am. Chem. Soc.*, 59, 1302 (1937).

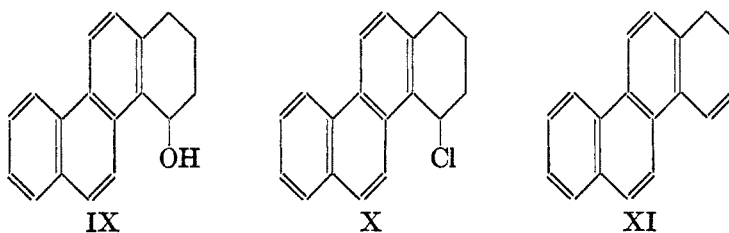
⁵ FIESER AND JOHNSON, *ibid.*, 61, 168 (1939).

mixture of cyclic ketones was obtained which probably contained the isomeric compound formed by cyclization to the 3 position, although no attempt was made to isolate the product. Clemmensen reduction of the 4-ketotetrahydrochrysene yielded a crystalline tetrahydrochrysene, which could be dehydrogenated to chrysene by palladium on charcoal at a temperature of 300–320°.

4-Methyl-4-hydroxy-1,2,3,4-tetrahydrochrysene (VII) was prepared by interaction of the cyclic ketone with methylmagnesium iodide. The crystalline carbinol was simultaneously dehydrated and dehydrogenated to 4-methylchrysene in 92 per cent. yield by the action of palladium on charcoal, the method used successfully by Bachmann and Wilds⁶ on a number of carbinols. Unlike the parent hydrocarbon, 4-methylchrysene forms a relatively stable picrate in alcohol. The 4-methylchrysene is being tested for carcinogenic activity.

1,2-Dihydrochrysene (XI) was obtained in two ways. 4-Ketotetrahydrochrysene was heated with an excess of aluminum isopropoxide in *n*-propyl alcohol according to the procedure of Lund,⁷ but under these conditions no reduction took place. When the reaction was carried out in boiling toluene solution the corresponding carbinol, 4-hydroxy-1,2,3,4-tetrahydrochrysene (IX), was obtained in good yield. When xylene was substituted for toluene, the carbinol was obtained in two runs; in six other runs the product was 1,2-dihydrochrysene. It appears that prolonged heating at the temperature of the boiling xylene resulted in the splitting off of basic aluminum isopropoxide with the formation of the dihydrochrysene.

The 4-hydroxytetrahydrochrysene readily forms a methyl ether by the action of methanol containing a small amount of sulfuric acid and gives an acetate with acetic anhydride in pyridine. By treatment of a benzene solution of the carbinol with hydrogen chloride gas the carbinol yielded 4-chlorotetrahydrochrysene (X). 1,2-Dihydrochrysene can be obtained from the chloride by treatment with pyridine at the boiling point of the solution.



⁶ BACHMANN AND WILDS, *ibid.*, **60**, 624 (1938).

⁷ LUND, *Ber.*, **70**, 1520 (1937).

As was expected, the dihydrochrysene is readily dehydrogenated to chrysene.

Experiments are in progress on the condensation of the 4-chlorotetrahydrochrysene with sodio-malonic ester. With the acetic acid group in the 4 position it should be possible to prepare derivatives of 3,4-benzopyrene by cyclization of the acid and treatment of the cyclic ketone with various reagents.

EXPERIMENTAL

γ -(2-Phenanthryl)- β -methylbutyric acid.—A mixture of 2 g. of β -(2-phenanthroyl)-butyric acid (I), 5 g. of amalgamated zinc, 7.5 cc. of acetic acid, 7.5 cc. of concentrated hydrochloric acid, and 4 cc. of toluene was refluxed for thirty six hours. An additional 10 cc. of concentrated hydrochloric acid was added in portions over this time. The toluene layer was separated, the toluene was evaporated, and the oily residue was sublimed at 250° and 0.4 mm. The sublimate was crystallized from benzene-petroleum ether (b. p. 60–75°), as fine colorless prisms; weight, 0.96 g. (50%); m. p. 120–125°. After two further crystallizations from benzene-petroleum ether the melting point was raised to 127.5–129°.

Anal. Calc'd for $C_{19}H_{18}O_2$: C, 82.0; H, 6.5.

Found: C, 82.3; H, 6.7.

2-Methyl-4-keto-1,2,3,4-tetrahydrochrysene (II).—Four-tenths gram of γ -(2-phenanthryl)- β -methylbutyric acid was suspended in a mixture of 5 cc. of absolute ether and 1 drop of pyridine. When 1 cc. of thionyl chloride was added, the acid rapidly went into solution. After the solution had stood for a half-hour at room temperature, the ether and thionyl chloride were removed under reduced pressure. The acid chloride was dissolved in 5 cc. of dry benzene, the solution was cooled to 0°, and 0.75 cc. of stannic chloride was then added with swirling. After standing for fifteen minutes in the cold, the complex was hydrolyzed with ice and dilute hydrochloric acid. The benzene layer was washed with water, dilute ammonium hydroxide, and again with water. The benzene was evaporated, and the keto compound was crystallized from alcohol-acetone; weight, 0.32 g. (86%); m. p. 129–133°. After two recrystallizations from benzene-petroleum ether the melting point was 141–142°.

Anal. Calc'd for $C_{19}H_{16}O$: C, 87.7; H, 6.2.

Found: C, 87.3; H, 6.2.

2-Methyl-1,2,3,4-tetrahydrochrysene (III).—A mixture of 0.23 g. of 2-methyl-4-keto-1,2,3,4-tetrahydrochrysene, 5 g. of amalgamated zinc, 7.5 cc. of acetic acid, 7.5 cc. of concentrated hydrochloric acid, and 2 cc. of toluene was refluxed for twenty-four hours. The toluene layer was separated, the toluene was evaporated, and the residue was sublimed at 200° and 0.4 mm.; weight 0.18 g. (83%); m. p. 137–140°. After two crystallizations from acetone-alcohol the hydrocarbon melted at 141.5–142°. It first comes down as very thin leaflets which turn to thin prisms on standing in contact with the mother liquor. Both forms appear to have the same melting point.

Anal. Calc'd for $C_{19}H_{18}$: C, 92.7; H, 7.3.

Found: C, 92.3; H, 7.3.

The *hemi-picrate* crystallizes from alcohol-acetone as reddish-orange needles; m. p. 145–5–146°.

Anal. Calc'd for $2C_{19}H_{18} \cdot C_6H_5N_3O_7$: N, 5.8. Found: N, 6.0.

2-Methylchrysene (IV).—A mixture of 0.18 g. of 2-methyl-1,2,3,4-tetrahydrochrysene and 0.03 g. of palladium-charcoal catalyst⁸ was heated at 300–320° for one hour. The mixture was taken up in hot benzene and filtered. The benzene was evaporated, and the residue was crystallized from alcohol-acetone; weight, 0.16 g. (90%); m. p. 224–225°. Two further crystallizations gave colorless leaflets from benzene-alcohol; m. p. 224.5–225.5° (229–230° corr.).

Anal. Calc'd for C₁₉H₁₄: C, 94.2; H, 5.8.

Found: C, 94.5; H, 5.9.

The rather unstable *picrate* crystallizes from alcohol in the form of golden-yellow needles; m. p. 143–146°.

Anal. Calc'd for C₁₉H₁₄·C₆H₃N₃O₇: N, 8.9. Found: N, 9.1.

2-n-Propylphenanthrene.—A mixture of 2 g. of 2-propionylphenanthrene, 4 g. of amalgamated zinc, 6 cc. of acetic acid, 6 cc. of concentrated hydrochloric acid, and 4 cc. of toluene was refluxed for twenty-four hours. An additional 5 cc. of concentrated hydrochloric acid was added over that time. The toluene layer was separated, and the toluene was evaporated. The oily residue, which did not crystallize, was dissolved in alcohol, and 3 g. of picric acid was added. On cooling, 3.2 g. of 2-*n*-propylphenanthrene *picrate* deposited; yield, 83%; m. p. 84–88°. The *picrate* was recrystallized twice from alcohol and then decomposed with dilute sodium hydroxide solution. The oil formed was taken up in benzene, the benzene layer was separated, the benzene was evaporated, and the residue was sublimed. The sublimate crystallized from alcohol-acetone in colorless leaflets; m. p. 35–36°.

Anal. Calc'd for C₁₇H₁₆: C, 92.7; H, 7.3.

Found: C, 92.6; H, 7.4.

The *picrate* crystallizes from alcohol in yellow needles; m. p. 92–93°.

Anal. Calc'd for C₁₇H₁₆·C₆H₃N₃O₇: N, 9.4. Found: N, 9.4.

3-n-Propylphenanthrene.—Two grams of 3-propionylphenanthrene was reduced and worked up in the same way as the 2-propionylphenanthrene; weight of *picrate*, 2.98 g. (77%); m. p. 104–107°. By hydrolysis of the pure *picrate*, the 3-*n*-propylphenanthrene was obtained as a colorless oil which failed to crystallize, even when cooled to a low temperature.

Anal. Calc'd for C₁₇H₁₆: C, 92.7; H, 7.3.

Found: C, 93.1; H, 7.4.

The *picrate* crystallizes from alcohol as clusters of orange needles; m. p. 107–108°.

Anal. Calc'd for C₁₇H₁₆·C₆H₃N₃O₇: N, 9.4. Found: N, 9.5.

γ-[2-(9,10-Dihydrophenanthryl)]butyric acid (V).—A mixture of 48 g. of β-[2-(9,10-dihydrophenanthroyl)]propionic acid, 100 g. of amalgamated zinc, 150 cc. of acetic acid, 150 cc. of concentrated hydrochloric acid, and 80 cc. of toluene was refluxed for twenty hours. An additional 100 cc. of concentrated hydrochloric acid was added in portions over this time. The toluene layer was separated, the toluene was evaporated, and the residue was distilled in a vacuum. The distillate crystallized from dilute alcohol in colorless needles; yield, 42 g. (92%); m. p. 91–92°. This yield is somewhat higher than that reported by Burger and Mosettig⁴ who employed slightly different conditions.

γ-(2-Phenanthryl)butyric acid.—A stream of dry hydrogen chloride gas was passed into an ice-cold solution of 10 g. of γ-[2-(9,10-dihydrophenanthryl)]butyric acid in 300 cc. of methanol for a half hour. The solution was refluxed for an hour, and dry hydrogen chloride was again passed in the cooled solution for a half hour. After refluxing the solution again for an hour, most of the methanol was distilled, and

⁸ ZELINSKY AND TUROWA-POLLAK, *ibid.*, 53, 1295 (1925).

benzene was added. The benzene solution of the methyl ester was washed twice with water, and the benzene was distilled. The oily residue was dehydrogenated with 1 g. of palladium-charcoal catalyst at 240–260° for two hours. The mixture was taken up in benzene, and the catalyst was removed by filtration. The benzene was evaporated, and the ester was hydrolyzed with hot 40% potassium hydroxide solution. The hydrolysis mixture was diluted and acidified with concentrated hydrochloric acid. The precipitated acid was collected by filtration and crystallized from benzene as colorless plates; weight, 9.0–9.5 g. (90–95%, based on the dihydro acid); m. p. 133–134°. Haworth and Mavin³ report the melting point of this acid to be 134–135°. The recovered catalyst can be used for the dehydrogenation of a second run of ester with no apparent decrease in activity.

4-Keto-1,2,3,4-tetrahydrochrysene (VI).—To a suspension of 13.5 g. of γ -(2-phenanthryl)butyric acid in 100 cc. of dry ether and 5 drops of pyridine was added 30 cc. of thionyl chloride. The mixture was swirled until the acid had gone into solution, and was then allowed to stand at room temperature for a half-hour. The ether and thionyl chloride were evaporated under reduced pressure, and the acid chloride was dissolved in 100 cc. of benzene. The benzene solution was cooled to 0° and 22 cc. of stannic chloride was added with swirling. After standing for fifteen minutes in the cold, the complex was decomposed with ice and dilute hydrochloric acid. The benzene layer was washed with water, dilute ammonium hydroxide, and again with water. The benzene was evaporated, and the keto compound was crystallized from alcohol as light tan prisms; yield, 9.36 g. (74%); m. p. 122–124°. After two crystallizations and treatment with activated alumina, colorless prisms, m. p. 125–126°, were obtained. Haworth and Mavin³ report the melting point of this compound as 124–125°.

4-Methyl-4-hydroxy-1,2,3,4-tetrahydrochrysene (VII).—To a Grignard reagent made from 0.25 g. of magnesium, 0.75 cc. of methyl iodide, and 10 cc. of absolute ether were added 1 g. of 4-keto-1,2,3,4-tetrahydrochrysene and 10 cc. of dry benzene. The mixture was allowed to stand in the cold for twelve hours and was then decomposed with ice and ammonium chloride solution. The benzene-ether layer was separated, filtered, and then allowed to evaporate in an evaporating dish at room temperature. The methyl carbinol crystallized upon evaporation of the solvent as colorless prisms; weight, 0.87 g. (82%); m. p. 123.5–125°. After two recrystallizations from benzene-petroleum ether, the carbinol melted at 124–125°.

Anal. Calc'd for $C_{19}H_{18}O$: C, 87.0; H, 6.9.

Found: C, 87.5; H, 7.0.

4-Methylchrysene (VIII).—Six-tenths gram of 4-methyl-4-hydroxy-1,2,3,4-tetrahydrochrysene was heated with 0.06 g. of palladium-charcoal catalyst at 300–320° for one hour. The mixture was taken up in hot benzene and filtered. The hydrocarbon obtained from the residue crystallized from benzene-petroleum ether as colorless leaflets; weight, 0.51 g. (92%); m. p. 146–148°. After two recrystallizations from benzene-petroleum ether the melting point was 149–149.5° (151–151.5° corr.).

Anal. Calc'd for $C_{19}H_{14}$: C, 94.2; H, 5.8.

Found: C, 94.0; H, 5.6.

The *picrate* crystallizes from alcohol as bright-red needles; m. p. 134–135°.

Anal. Calc'd for $C_{19}H_{14} \cdot C_6H_3N_3O_7$: N, 8.9. Found: N, 9.0.

4-Hydroxy-1,2,3,4-tetrahydrochrysene (IX).—A solution of aluminum isopropoxide was prepared by refluxing a mixture of 1 g. of aluminum wire, 25 cc. of dry isopropyl alcohol, 5 drops of carbon tetrachloride, and a pinch of mercuric chloride. After the aluminum had dissolved, the isopropyl alcohol was distilled, and 2.75 g. of 4-keto-

1,2,3,4-tetrahydrochrysene and 25 cc. of toluene were added. The mixture was refluxed for four hours, 25 cc. of isopropyl alcohol was added and then distilled from the mixture. The toluene solution was cooled, and the aluminum salt was decomposed with cold 10% sulfuric acid. The toluene layer was separated, washed with dilute ammonium hydroxide, and evaporated in the cold. The carbinol separates as colorless silky needles; yield, 2.10 g. (76%); m. p. 156–158°. Two recrystallizations from benzene-petroleum ether raised the melting point to 160–162°. The carbinol gives a black color with sulfuric acid.

Anal. Calc'd for $C_{18}H_{16}O$: C, 87.1; H, 6.5.

Found: C, 87.5; H, 6.3.

4-Methoxy-1,2,3,4-tetrahydrochrysene.—To a solution of 0.05 cc. of concentrated sulfuric acid in 5 cc. of methanol was added 0.3 g. of 4-hydroxy-1,2,3,4-tetrahydrochrysene. The mixture was shaken occasionally, and after about a half-hour all the carbinol had gone into solution. The solution was allowed to stand overnight, then poured into a mixture of benzene and aqueous sodium carbonate. The benzene layer was separated, washed with water, filtered, and evaporated. The methyl ether crystallizes from methanol in colorless rhombic prisms; weight, 0.27 g. (86%); m. p. 79–80.5°.

Anal. Calc'd for $C_{19}H_{18}O$: C, 87.0; H, 6.9.

Found: C, 87.0; H, 6.8.

4-Acetoxy-1,2,3,4-tetrahydrochrysene.—Three-tenths gram of 4-hydroxy-1,2,3,4-tetrahydrochrysene was added to a solution of 0.3 cc. of pyridine and 0.6 cc. of acetic anhydride, and the mixture was heated on a steam bath for one hour. The acetic anhydride and the pyridine were then evaporated on a steam bath in a current of air, and the residue was dissolved in benzene. The benzene solution was washed with dilute ammonium hydroxide, water, dilute hydrochloric acid, and again with water. The acetate obtained from the benzene solution crystallized from petroleum ether in leaflets; yield, 0.30 g. (86%); m. p. 119–120.5°.

Anal. Calc'd for $C_{18}H_{20}O_2$: C, 82.8; H, 6.2.

Found: C, 83.2; H, 6.4.

4-Chloro-1,2,3,4-tetrahydrochrysene (X).—A stream of dry hydrogen chloride gas was passed into a cold solution of 0.2 g. of 4-hydroxy-1,2,3,4-tetrahydrochrysene in 10 cc. of dry benzene with 0.5 g. of calcium chloride suspended in it. The mixture turned cloudy almost immediately. After hydrogen chloride had been passed in for ten minutes the mixture was allowed to stand at room temperature for one hour, by which time the solution had again become clear. Evaporation of the benzene left a crystalline residue of the chloride. The latter crystallizes from benzene-petroleum ether in colorless, diamond-shaped prisms; yield, 0.17 g. (80%); it melts at 115–117° with decomposition, evolving hydrogen chloride. The melt solidifies and remelts at 174–178°.

Anal. Calc'd for $C_{18}H_{16}Cl$: Cl, 13.3. Found: Cl, 13.1.

1,2-Dihydrochrysene (XI).—A solution of 0.1 g. of 4-chloro-1,2,3,4-tetrahydrochrysene and 3 cc. of pyridine was refluxed for fifteen minutes; benzene and dilute hydrochloric acid were then added. The benzene solution was separated, washed with water, and the benzene was evaporated. The residue was sublimed at 200° and 0.4 mm. pressure; weight, 0.05 g. (58%); m. p. 181.5–183.5°. After two crystallizations from benzene-petroleum ether the colorless plates which were obtained melted at 182.5–184.5°.

Anal. Calc'd for $C_{18}H_{14}$: C, 93.9; H, 6.1.

Found: C, 93.4; H, 6.3.

The *picrate* forms bright-red needles from alcohol-acetone; m. p. 155–156°.

Anal. Calc'd for $C_{18}H_{14} \cdot C_6H_3N_3O_7$: N, 9.1. Found: N, 9.2.

1,2,3,4-Tetrahydrochrysene.—A mixture of 1 g. of 4-keto-1,2,3,4-tetrahydrochrysene, 4 g. of amalgamated zinc, 7 cc. of acetic acid, 7 cc. of concentrated hydrochloric acid, and 3 cc. of toluene was refluxed for twenty-four hours. An additional 5 cc. of concentrated hydrochloric acid was added in portions over this period. The toluene layer was separated, and the toluene was evaporated. The residue was sublimed at 200° and 0.4 mm.; weight, 0.56 g. (60%); m. p. 173–178°. After two crystallizations from benzene-petroleum ether, the hydrocarbon formed colorless leaflets; m. p. 180.5–181.5°.

Anal. Calc'd for $C_{18}H_{16}$: C, 93.1; H, 6.9.

Found: C, 92.9; H, 6.8.

The *picrate* formed orange needles from benzene containing an excess of picric acid; m. p. 134–135.5°.

Anal. Calc'd for $C_{18}H_{16} \cdot C_6H_3N_3O_7$: N, 9.3. Found: N, 9.1.

Chrysene.—(a) *From dihydrochrysene.*—A mixture of 0.43 g. of dihydrochrysene and 0.05 g. of palladium-charcoal catalyst was heated in a nitrogen atmosphere at 300–320° for one hour. The chrysene was taken up in benzene, and the solution was filtered to remove the catalyst. The benzene was evaporated, and the residue was crystallized from benzene, giving colorless, glistening leaflets; weight, 0.4 g. (93%); m. p. 247–249°. The hydrocarbon was also identified by means of its quinone.

(b) *From tetrahydrochrysene.*—A mixture of 0.32 g. of 1,2,3,4-tetrahydrochrysene and 0.04 g. of palladium-charcoal catalyst was treated as in part a; colorless, glistening leaflets; weight, 0.28 g. (87%); m. p. 247–249°.

SUMMARY

A number of new chrysene derivatives have been prepared from phenanthrene.