

formed rectangular microprisms, m. p. 137–138°. Further crystallization from hexane, in which the acid is readily soluble, gave compact clusters of microprisms, m. p. 141.5–142.5° with some previous softening. An extensive fractionation was not undertaken.

Anal. Calcd. for $C_{15}H_{10}O_2$: C, 78.97; H, 7.02. Found: C, 79.37; H, 7.40.

On dehydrogenation with selenium at 300° for twenty-one hours the once crystallized acid (0.55 g.) yielded a hydrocarbon (0.21 g.) which after crystallization melted at 96–97° and was identified as phenanthrene by mixed melting point.

6, 7 - Dimethyl - 5, 8, 9, 10, 13, 14 - hexahydrophenanthrene-13-carboxylic Acid.—The ethyl ester was prepared as above from 15 g. of the unsaturated ester and 18 cc. of 2,3-dimethylbutadiene, heating being continued for eight days at 100°. After treatment with 10% potassium hydroxide the ethyl ester was distilled as a liquid which solidified; b. p. 166° (4 mm.), m. p. 49.5–50°, yield 5.7 g. (27%).

Anal. Calcd. for $C_{19}H_{24}O_2$: C, 80.23; H, 8.51. Found: C, 79.61; H, 8.84.

The free acid, prepared as above (85% yield), crystallized from very dilute alcohol as small, colorless prisms, m. p. 162–163°. Recrystallization from hexane (readily soluble) gave small, hard, crystalline clusters, m. p. 168–169° with some previous softening.

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.70; H, 7.81. Found: C, 80.17; H, 7.87.

On dehydrogenation with selenium for thirty-six hours,

1.7 g. of the crude acid yielded 0.7 g. of purified crystals melting at 78–78.5° and identified by mixed melting point determination as 2,3-dimethylphenanthrene.¹

3 - Methoxy - 5, 8, 9, 10, 13, 14 - hexahydrophenanthrene-13-carboxylic Acid (X).—A mixture of 20 g. of ethyl 7-methoxy- Δ^1 -dihydro-1-naphthoate and 15 g. of butadiene was heated for twenty-one hours at 220–245°. The crude ester mixture (18.6 g.) was refluxed with 70 cc. of 20% alkali for four hours and the residual oil was dried and distilled, b. p. 202–204° (14 mm.); yield 3.3 g. (13%). On saponification of the ethyl ester with sodium ethylate as above the free acid was obtained from dilute alcohol as colorless microprisms, m. p. 139.5–141° with previous softening.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.41; H, 7.03. Found: C, 74.03; H, 7.01.

Summary

Hydrophenanthrene derivatives having a carboxyl group at the 13-(or 12-) position can be obtained by the addition of dienes to Δ^1 -dihydro-1-naphthoic esters. A convenient synthesis of the unsaturated esters consists in the acid hydrolysis of α -oxalyl- γ -arylbutyric esters to α -keto- δ -arylbutyric acids and cyclization of the keto esters with sulfuric acid. These methods afford a new approach to substances having some features of the morphine structure.

CAMBRIDGE, MASS.

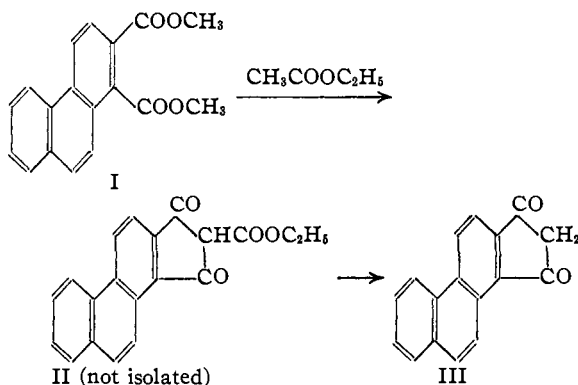
RECEIVED AUGUST 5, 1936

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Synthesis of Phenanthrene and Hydrophenanthrene Derivatives. VI. 1',3'-Diketocyclopentenophenanthrenes

BY L. F. FIESER, M. FIESER AND E. B. HERSHBERG

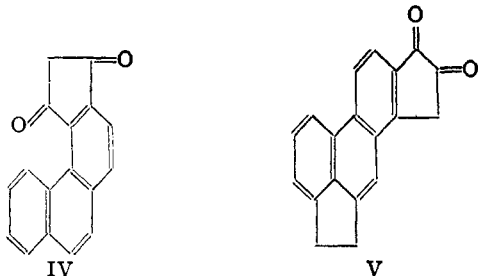
Having found a convenient method of preparing phenanthrene-1,2-dicarboxylic anhydride by synthesis,¹ it was of interest to undertake the conversion of the substance into a compound having the 1,2-cyclopenteno ring system. The anhydride was converted into the dimethyl ester I either by the Fischer esterification of the corresponding acid, obtained through the dipotassium salt, or by the direct action of methyl alcoholic hydrogen chloride. On condensation with ethyl acetate in the presence of sodium I yielded a diketo ester II which was hydrolyzed to 1',3'-diketo-1,2-cyclopentenophenanthrene, III (or the enolic form). The pure diketone was obtained in 76% yield. Employing anhydrides prepared from interme-



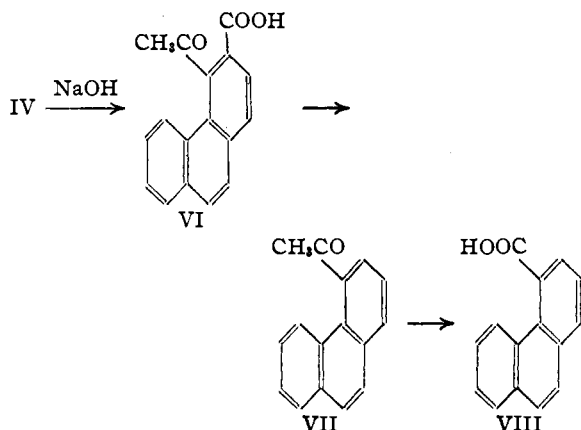
diates already described,^{1,2} the isomeric diketone IV and the dimethylene (ace-) derivative V were synthesized in good yield.

(1) Fieser and Hershberg, *THIS JOURNAL*, **57**, 1851 (1935).

(2) Fieser, Fieser and Hershberg, *ibid.*, **58**, 1463 (1936).



The isomeric phenanthrindanediones III and IV dissolve in dilute alkali even in the cold to give red solutions. On refluxing for several hours the color fades and acetylphenanthroic acids are formed in good yield. The substance obtained from the 3,4-isomer IV proved to be a single individual of the structure VI, for on decarboxylation with copper carbonate and quinoline it yielded the hitherto unknown 4-acetylphenanthrene (VII).



The structure of the latter compound follows from the non-identity with the 3-isomer and from the fact that on hypochlorite oxidation it yields a substance having the properties of the known 4-phenanthroic acid.³ The material resulting from the cleavage of the diketo-1,2-cyclopentenophenanthrene had the composition and properties of a mixture of the two possible acetylphenanthroic acids and evidently there is no great preference for cleavage at one or the other ketonic group. The contrasting behavior of the isomer IV is interpreted as being due to the protection of the carbonyl group in the hindered 4-position, and this constitutes another example of the blocking effect of the neighboring aromatic ring.⁴

In the special test for oestrogenic activity developed by Pincus and Werthessen⁵ 1',3'-diketo-

1,2-cyclopentenophenanthrene appears to be comparable in potency with 1-keto-1,2,3,4-tetrahydrophenanthrene, while the isomer IV is entirely inactive.

Experimental Part⁶

Phenanthrene-3,4-dicarboxylic anhydride was obtained in 90% yield by heating the dihydro compound¹ with the calculated amount of sulfur in a bath at 320–330° and distilling the product when the evolution of gas was complete. The anhydride is sparingly soluble in glacial acetic acid, fairly readily soluble in xylene, and it crystallizes from the latter solvent as fine, lemon yellow needles, m. p. 253.5–254°.

Anal. Calcd. for C₁₆H₈O₃: C, 77.39; H, 3.25. Found: C, 77.37; H, 3.19.

8,9-Acphenanthrene-1,2-dicarboxylic anhydride, prepared similarly in equally good yield, formed fine orange-yellow needles, m. p. 297–298°, uncorr., from dioxane (moderately soluble).

Anal. Calcd. for C₁₅H₁₀O₃: C, 78.82; H, 3.68. Found: C, 78.62; H, 3.97.

Dimethyl phenanthrene-1,2-dicarboxylate was at first prepared through the dipotassium salt, which was obtained by refluxing the anhydride (1 g.) with a solution of potassium hydroxide (7 g.) in water (20 cc.) and methyl alcohol (10 cc.) for one-half hour and adding saturated potassium chloride solution. The crystalline salt (1.3 g.) which separated on cooling was added to methyl alcohol saturated with hydrogen chloride, and after two days at room temperature the mixture was refluxed for five hours. On dilution with water the ester separated as a pale yellow solid. On crystallization from methyl alcohol two forms were obtained, the less soluble substances appearing as pale yellow needles, m. p. 131.8–132.2°, and the material from the mother liquor forming colorless, pearly plates, m. p. 132.5–133°. No depression was observed on mixing the samples, and on hydrolysis both yielded, after dehydration of the acid on heating, the original anhydride. A better method of preparation consists in refluxing the anhydride (2 g.) with methyl alcohol saturated with hydrogen chloride for about twenty hours. The anhydride slowly dissolved and the solution after being concentrated and cooled deposited the yellow needle-form of the ester (2.1 g.).

Anal. Calcd. for C₁₅H₁₄O₄: C, 73.44; H, 4.79. Found: (yellow needles) C, 73.10; H, 4.43; (colorless plates) C, 73.87; H, 5.07.

The 3,4-dihydro derivative, obtained in good yield through the dipotassium salt of the unsaturated acid, crystallized from methyl alcohol as colorless needles or plates, both melting at 109.8–110°.

Anal. Calcd. for C₁₆H₁₆O₄: C, 72.95; H, 5.45. Found: C, 72.75; H, 5.58.

Dimethyl phenanthrene-3,4-dicarboxylate was best prepared directly from the anhydride by boiling with methyl

(6) The melting points are corrected except as noted, using the precision apparatus of Hershberg, *Ind. Eng. Chem., Anal. Ed.*, **8**, 312 (1936), and employing 0.1° Anschütz thermometers (total immersion) calibrated with a thermometer with the Bureau of Standards certificate. Analyses by Mrs. G. M. Wellwood.

(3) Kruber, *Ber.*, **67**, 1000 (1934).

(4) Fieser, *THIS JOURNAL*, **51**, 1898, 1938 (1929).

(5) Pincus and Werthessen, *Science*, **84**, 45 (1936).

alcohol and hydrogen chloride; yield quantitative. It formed large, transparent prisms, m. p. 114.5–114.8°, from ether–petroleum ether. The substance is very soluble in alcohol or glacial acetic acid.

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.45; H, 4.80. Found: C, 73.34; H, 4.80.

The ester was also obtained by esterification of the free acid with diazomethane, and the samples were identical. **Phenanthrene-3,4-dicarboxylic acid** was prepared by hydrolyzing the anhydride with boiling alkali and carefully neutralizing the filtered solution with acetic acid. Very faintly yellow, glistening plates of a monohydrate were deposited on cooling.

Anal. Calcd. for $C_{16}H_{10}O_4 \cdot H_2O$: C, 67.59; H, 4.26. Found: C, 67.50; H, 4.40.

Dimethyl 8,9-acephenanthrene-1,2-dicarboxylate, prepared from the anhydride, alcohol and hydrogen chloride (thirty-six hours), separated as fine, faintly yellow needles from glacial acetic acid, m. p. 170.6–171°.

Anal. Calcd. for $C_{20}H_{16}O_4$: C, 74.98; H, 5.04. Found: C, 74.68; H, 5.10.

1',3'-Diketo-1,2-cyclopentenophenanthrene (III).—Dimethyl phenanthrene-1,2-dicarboxylate (4.85 g.) was dissolved in 50 cc. of ethyl acetate and 2 g. of fine sodium shavings was added. After refluxing for two hours on the steam-bath 25 cc. more ethyl acetate and 1 g. of sodium were added. This was repeated two hours later and the reaction was stopped after refluxing for six hours. The mixture was pasty with the precipitated sodium derivative of the diketo ester and this was collected after cooling and washed with dry ether. The salt was then decomposed by boiling with 200 cc. of 95% alcohol and 5 cc. of concentrated hydrochloric acid for about ten minutes, during which time carbon dioxide was evolved and the heavy sodium salt partly dissolved and was eventually all transformed to a bulky, light yellow solid. After cooling, the precipitated diketone was collected and washed well with water and then with alcohol. After crystallization by dissolving the substance in 75 cc. of dioxane and adding 50 cc. of 95% alcohol to the hot solution, there was obtained 3.1 g. (76% yield) of the pure diketone. Smaller runs gave yields up to 85%.

The diketone crystallizes well from the above mixture or from benzene and forms short, light yellow needles melting at 240.5–241.5°, dec., when heated in a Pyrex capillary. In a soft glass capillary the sample does not melt but gradually decomposes in the range 240–245°. It dissolves slowly in dilute alkali in the cold, easily on warming, to a cherry red solution. If acidified at once the solution deposits the unchanged material.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 82.93; H, 4.11. Found: C, 82.75; H, 4.08.

1',3'-Diketo-3,4-cyclopentenophenanthrene (IV).—The condensation of the appropriate ester (3 g.) was conducted as above except that in these (earlier) experiments only one addition of fresh sodium and ethyl acetate was made. The orange diketo ester salt (5 g.) was rubbed to a paste with 15 cc. of alcohol and 5 cc. of a solution of 10 cc. of concentrated hydrochloric acid in 50 cc. of water was added with stirring. The salt dissolved in the cold to a clear yellow solution and on gentle boiling carbon dioxide was

evolved and the diketone separated as light yellow needles in a very pure condition; yield 1.26 g. (50%). The substance is moderately soluble in benzene and readily soluble in glacial acetic acid; it crystallizes from these solvents as light yellow needles, m. p. 201.4–202°. The solubility is greater than that of the isomer and the other properties are as above.

Anal. Calcd. for $C_{17}H_{10}O_3$: C, 82.93; H, 4.11. Found: C, 82.92; H, 4.26.

A monosemicarbazone was deposited from a solution of the components in glacial acetic acid on short boiling. The substance separated as small, pale yellow plates, dec. 300–305°, in a condition suitable for analysis. It is very sparingly soluble in the usual solvents.

Anal. Calcd. for $C_{15}H_{12}O_2N_2$: N, 13.87; Found: N, 13.58.

1',3'-Diketo-1,2-cyclopenteno-8,9-acephenanthrene (V) was obtained by the procedure described immediately above in 65% yield. The substance is very sparingly soluble in the usual solvents and moderately soluble in tetrachloroethane, from which it crystallizes as fine, bright yellow needles melting at 338–340°, dec., uncorr.

Anal. Calcd. for $C_{16}H_{12}O_3$: C, 83.80; H, 4.45. Found: C, 82.68, 82.76; H, 4.37, 4.41.

4-Acetyl-3-phenanthroic Acid.—The red solution of 1 g. of the diketone IV in 50 cc. of 1 *N* sodium hydroxide turned pale brown after refluxing for six hours. The material which precipitated on acidification was dried and crystallized from benzene–ligroin giving pale yellow crystals melting at 201–202°; yield 0.9 g. (84%). After two recrystallizations from benzene the keto acid was obtained as clusters of colorless, prismatic needles, m. p. 201.5–202.5°.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.24; H, 4.58. Found: C, 77.29; H, 4.81.

4-Acetylphenanthrene.—As attempted decarboxylation of the keto acid without solvent was unpromising, a solution of 0.48 g. of the substance in 3 cc. of quinoline was treated with about 50 mg. of basic copper carbonate and heated at 240–260° for forty-five minutes, most of the carbon dioxide being eliminated in about fifteen minutes. The quinoline solution was diluted with ether, filtered, and extracted with dilute mineral acid to remove the quinoline and with dilute alkali to remove any unchanged acid. After distillation of the ether the residue was distilled at 2 mm., giving a light yellow oil which readily solidified on cooling. After crystallization from ligroin or petroleum ether, in which the substance is moderately soluble, there was obtained 0.27 g. (68% yield) of ketone, m. p. 88.5–90.5°. After two recrystallizations it formed large clusters of heavy colorless plates, m. p. 89.8–90.3°.

Anal. Calcd. for $C_{16}H_{12}O$: C, 87.23; H, 5.50. Found: C, 87.19; H, 5.01.

A solution of the acetyl compound and phenylhydrazine after being boiled for a few minutes and diluted with water yielded only the unchanged ketone.

The picrate forms easily using methyl alcohol as the solvent. It crystallizes as long, slender, yellow needles melting at 129.5–130.5°.

Anal. Calcd. for $C_{16}H_{12}O \cdot C_6H_5O_2N_3$: N, 9.35. Found: N, 9.33.

For conversion to 4-phenanthroic acid, 0.1 g. of 4-acetylphenanthrene was boiled for one and one-half hours with a sodium hypochlorite solution prepared from 1 g. of the commercial calcium salt (H. T. H.). After cooling, filtering and destroying the excess reagent, the product was precipitated by acidification and crystallized from dilute alcohol. It formed glistening, colorless plates, and after thorough drying at 130° to remove solvent, the acid melted at 171.5–173°. Kruber³ reports the value 170–171°, uncorr.

Cleavage of 1',3'-Diketo-1,2-cyclopentenophenanthrene.—After refluxing a solution of the diketone (1.2 g.) in 1 *N* sodium hydroxide for ten hours the light brown solution was filtered from a small amount of purple material and acidified. The acidic product which precipitated was crystallized from benzene, giving 0.96 g. of material. After a second crystallization the substance, m. p. 190–193°, had approximately the composition of a mixture of acetylphenanthroic acids.

Anal. Calcd. for C₁₇H₁₂O₃: C, 77.24; H, 4.58. Found: C, 77.63, 77.40; H, 5.22, 5.36.

In further recrystallizations the melting point of the less soluble portion rose to about 216°, but an assuredly homogeneous product was not obtained.

Summary

The condensation of the 1,2- and 3,4-dicarboxylic esters of phenanthrene with ethyl acetate proceeds smoothly, affording diketocyclopentenophenanthrenes of interest in the study of oestrogenic activity. The alkaline cleavage of the 1,2-derivative proceeds in both possible directions, whereas with the 3,4-diketone steric hindrance at the 4-position is so pronounced that the reaction affords pure 4-acetyl-3-phenanthroic acid. This on decarboxylation yields the new 4-acetylphenanthrene.

CONVERSE MEMORIAL LABORATORY
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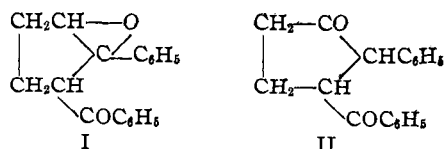
RECEIVED AUGUST 12, 1936

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Rearrangement of 1-Phenyl-5-benzoylcyclopentene Oxide

BY S. H. BABCOCK, JR., AND REYNOLD C. FUSON

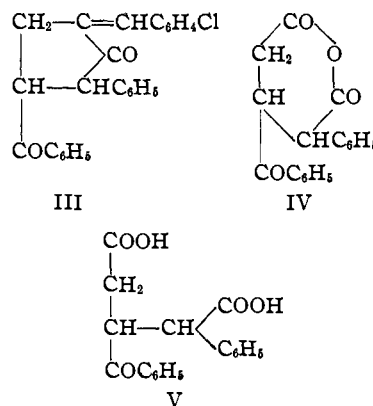
The chief product in the reduction of 1,4-dibromo-1,4-dibenzoylbutane with zinc dust and sodium iodide has been shown to be 1-phenyl-5-benzoylcyclopentene oxide (I).¹ The oxide was accompanied by an isomer which appeared to be derived from it by rearrangement. This isomer was obtained also (1) by the action of alcoholic hydrogen chloride on the oxide; (2) by treatment of a solution of the oxide in glacial acetic acid with ozone; and (3) together with I by the action of perbenzoic acid on 1-phenyl-5-benzoylcyclopentene. It has now been shown that the oxide readily undergoes rearrangement when dissolved in hot glacial acetic acid, and that the rearrangement product is identical with that reported by Fuson and Farlow. The compound has proved to be 2-phenyl-3-benzoylcyclopentanone (II).



The structure of this compound has been established by a degradation process leading to the formation of α -phenyl- β -benzoylglutaric acid (V).

(1) Fuson and Farlow, *THIS JOURNAL*, **56**, 1593 (1934).

The ketone condensed readily with *p*-chlorobenzaldehyde to give a chlorobenzal derivative (III).



When treated with ozone this compound gave *p*-chlorobenzaldehyde, *p*-chlorobenzoic acid and an anhydride (IV) corresponding to that of α -phenyl- β -benzoylglutaric acid (V). By hydrolysis of the anhydride the acid was obtained in the two forms required by theory. One of these melted at 176–177°, and, when heated in the presence of alkali, isomerized to the other, which melted at 135–136°.

Mention should be made of the fact that under certain conditions the rearrangement of the oxide