Reduction of VI in alcohol with aqueous hydrosulfite solution gave a colorless product, m. p. 107–108°, which was not further characterized.

2,4,5,4′-Tetramethyl-1,2,3,6-tetrahydro-2,2′-diphenic Acid (VII).—A solution of 2 g. of VI and 1.4 cc. of 30% hydrogen peroxide in 20 cc. of dioxane at 80–90° was treated cautiously with 7 cc. of 10% sodium hydroxide in portions. A vigorous reaction ensued and the yellow color disappeared. Acidified and diluted with 100 cc. of water, the solution slowly deposited needles of good product; yield, 2 g. (92%). The acid is very soluble in dioxane, moderately so in alcohol or ether, very sparingly soluble in benzene. Recrystallization from acetic acid gave small, colorless needles, m. p. 248–249°.

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.48; H, 7.34. Found: C, 71.43; H, 7.53.

The dimethyl ester, prepared with diazomethane, formed glistening needles, m. p. 88–89°, from dilute methanol.

Anal. Calcd. for $C_{20}H_{26}O_4$: C, 72.68; H, 7.94. Found: C, 72.66; H, 7.98.

The ester was hydrolyzed completely on being boiled for six hours with 25% potassium hydroxide solution.

The anhydride (VIII) was prepared by refluxing a solution of 0.9 g. of VII in 6 cc. of acetic anhydride for fifteen hours. The solvent was removed in vacuum and the product was crystallized from ligroin, giving 0.45 g. (53%) of nearly pure material. The anhydride forms lustrous, colorless needles from ligroin, m. p. 97–98°.

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.00; H, 7.09. Found: C, 76.06; H, 7.42.

2,3,7,10-Tetramethyl-1,4,10,11-tetrahydrofluorenone-9-semicarbazone.—The acid VII (0.8 g.) when heated under nitrogen in a bath at 330–33° slowly evolved carbon dioxide. After ten hours the dark residue, which gave no test for anhydride when treated in benzene with aniline, was taken into ether and the solution was extracted with dilute alkali, which gave on acidification 0.65 g. of unchanged acid. The oily residue from the ether was treated in alcohol with semicarbazide solution, heating for three hours on the steam-bath. Some of the semicarbazone crystallized during this period and, after cooling, the total yield was 0.2 g. (22%). The compound forms yellow microcrystals from alcohol; it softens at 244° and melts at 260° with decomposition.

Anal.[7] Calcd. for $C_{18}H_{23}ON_3$: N, 14.14. Found: N, 14.01.

Summary

The product obtained by the addition of 2,3-dimethylbutadiene to 3-chloro-1,2-naphthoquinone loses hydrogen chloride in chloroform solution at 100° and a second molecule of the diene adds to the resulting product giving an interesting compound which probably is a tetracyclic diketone. For comparison with this substance, a further characterization was made of 2,6-dimethyl-1,2-naphthoquinone-2,3-dimethylbutadiene.

(7) By Mrs. G. M. Wellwood.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Application of the Diene Synthesis to Halogenated 1,2- and 3,4-Phenanthrenequinones

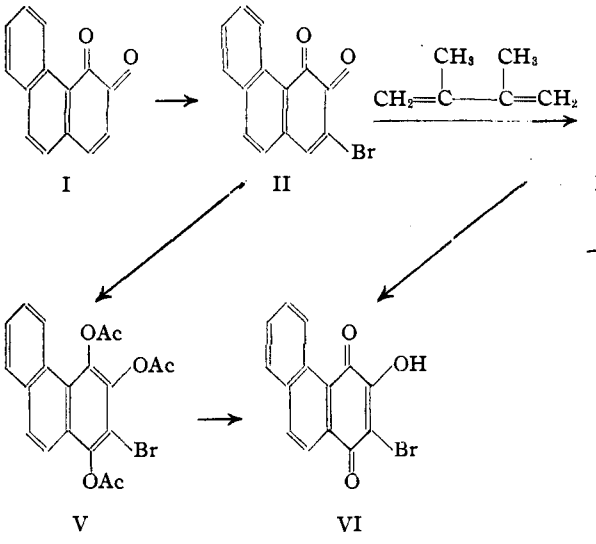
BY LOUIS F. FIESER AND J. T. DUNN

Having found that the 3-halo derivatives of β-naphthoquinone react smoothly with dienes and afford products which can be converted easily into 9,10-phenanthrenequinones,[1] we investigated the possibility of utilizing corresponding ortho quinones derived from phenanthrene for the synthesis of compounds of the chrysene and 3,4-benzphenanthrene series.

A suitable starting material derived from 3,4-phenanthrenequinone[2] (I) was obtained very satisfactorily by a process of bromination analogous to that developed by Zincke[3] for the preparation of 3-bromo-1,2-naphthoquinone. Treated with bromine in acetic acid solution, the quinone forms a yellow dibromide from which hydrogen bromide is eliminated by the action of boiling water. That the resulting crimson-red product has the structure of 2-bromo-3,4-phenanthrenequinone is established by the following observations. The Thiele reaction proceeds without disturbance of the halogen atoms and on hydrolysis of the triacetate (V) and oxidation there is obtained a compound having the properties of an hydroxy-*p*-quinone (VI). The bromine atom therefore cannot be located at position 4. Only one other position is available in the quinonoid nucleus, and the behavior of the bromo-3-hydroxy-1,4-phenanthrenequinone under the conditions of a Fischer esterification reaction indicates that the substituent is indeed located at the position (2) in question. Whereas the unsubstituted hydroxyquinone is converted rapidly by the action of meth-

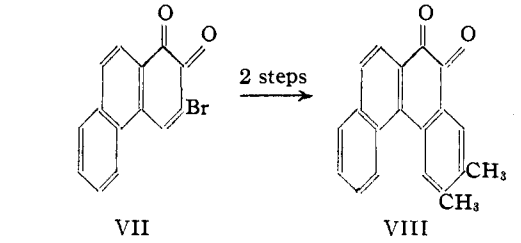
(1) Fieser and Dunn, THIS JOURNAL, **59**, 1016 (1937).
(2) Fieser, *ibid.*, **51**, 940 (1929).
(3) Zincke and Schmidt, *Ber.*, **27**, 733 (1894).

anol–hydrogen chloride into the ether,[2] the bromo compound is unaffected on prolonged boiling with the reagent. As with 2-hydroxy-3-bromo-1,4-naphthoquinone,[4] the failure of the reaction is attributable to the blocking influence of a substituent adjacent to the hydroxyl group. Another difference for which the substituent probably is responsible is that the bromo compound, unlike the parent hydroxyquinone, is not subject to ready cleavage by alkalies.



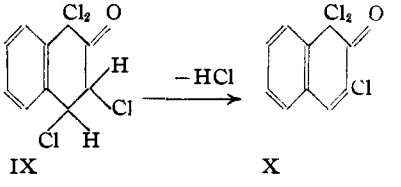
The presence of the bromine atom in the quinonoid ring is shown also by its ready elimination from the addition product (III) of 2-bromo-3,4-phenanthrenequinone and 2,3-dimethylbutadiene. The reaction between these components proceeded smoothly in chloroform solution at 100° (two hours), and the addition product, collected as an oil and not purified, was converted by the action of chromic acid into pure 8,9-dimethyl-5,6-chrysenequinone (IV) in 90% over-all yield.

1,2-Phenanthrenequinone[5] was submitted to the same series of reactions with similar results, the 3-bromo derivative VII being converted through the dimethylbutadiene addition product into 6,7-dimethyl-3,4-benz-9,10-phenanthrenequinone (VIII) in 79% yield. Using butadiene, which reacted somewhat more slowly than its dimethyl derivative, the known 3,4-benz-9,10-phenanthrenequinone[6] was obtained in satisfactory yield.



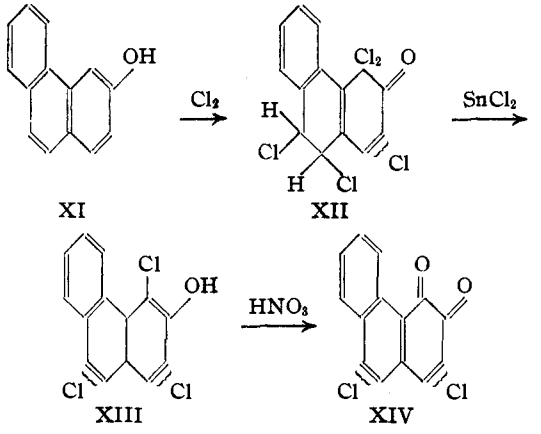
The advantage of using bromo derivatives in the diene synthesis of polynuclear compounds from ortho quinones was further demonstrated by the results of experiments with 1,2-phenanthrenequinone itself. Since this quinone is considerably more stable than β-naphthoquinone and can be obtained in a high state of purity, it seemed particularly suitable for use in the Diels–Alder reaction. A reaction with dimethylbutadiene was indeed found to occur, and the crude product was converted successfully into 6,7-dimethyl-3,4-benz-9,10-phenanthrenequinone (VIII). The addition, however, proceeded much more slowly than with the 3-bromo derivative, and considerable decomposition occurred during the long period of heating (forty-eight hours). The yield of the quinone VIII (29%) was less than half that obtained from the bromo compound.

A shorter route to halogenated phenanthrenequinones of the type required as starting materials was investigated without success. In analogy with Zincke's[7] observations concerning the chlorination of β-naphthol, it seemed possible that 3-phenanthrol might be convertible through intermediate chloro ketones similar to IX and X into 2-chloro-3,4-phenanthrenequinone. The phenanthrol, however, is attacked not only in the hydroxylated ring but also at some other part of the molecule, probably at the reactive 9,10-double bond. On conducting the chlorination in glacial acetic acid solution at a low temperature, the chief product isolated in a crystalline condition



(4) Fieser, THIS JOURNAL, **48**, 2922 (1926).
(5) Fieser, *ibid.*, **51**, 1896 (1929).
(6) Cook, *J. Chem. Soc.*, 2524 (1931).
(7) Zincke and Kegel, *Ber.*, **21**, 3378, 3540 (1888).

was an orange pentachloro ketone. This substance corresponds in properties to Zincke's unsaturated trichloro ketone X except for the presence of an additional pair of chlorine atoms, and the compound probably has the structure XII. Reduction with stannous chloride gave a trichlorophenanthrol (XIII), hydrogen chloride evidently



being eliminated from the central nucleus simultaneously with a change in the terminal ring comparable with that observed by Zincke in the naphthalene series. The trichlorophenanthrol yielded on oxidation with nitric acid a dichlorophenanthrenequinone of the probable structure XIV. Acetic anhydride–sulfuric acid adds slowly to the quinone to give a colorless triacetate, and one halogen atom is displaced in the process. The chlorine atom in the quinonoid ring therefore is probably located at the 1-position.

Experimental Part[8]

3,4-Phenanthrenequinone Series

2-Bromo-3,4-phenanthrenequinone.—A solution of 2.25 g. of 3,4-phenanthrenequinone[2] (conveniently purified by one crystallization from acetone–water, using Norite) in 235 cc. of glacial acetic acid was treated at room temperature with 1.9 g. of bromine in 40 cc. of the same solvent. The red solution turned yellow at once. (With more concentrated solutions the yellow addition product crystallized and was not easily redissolved without decomposition.) After fifteen minutes the yellow solution was stirred quickly into 410 cc. of vigorously boiling water and the resulting deep red solution was allowed to stand without disturbance. Within less than one minute the bromoquinone began to separate in long, glistening, deep crimson-red needles. The average yield of product, m. p. 211–212°, was 2.3 g. (77%). The quinone crystallizes well from glacial acetic acid, dioxane, chloroform, or benzene, in which solvents it is moderately soluble; it is sparingly soluble in alcohol or ether. The recrystallized material melted at 212–213°.

(8) The melting points are uncorrected. Analyses marked with an asterisk were performed by Mrs. G. M. Wellwood.

Anal. Calcd. for $C_{14}H_7O_2Br$: C, 58.54; H, 2.46. Found: C, 58.36; H, 2.75.

2-Bromo-3,4-dihydroxyphenanthrene.—A suspension of 1.1 g. of the quinone in 15 cc. of alcohol and 20 cc. of water was treated with sulfur dioxide until the solid had dissolved to a pale red solution; this was warmed slightly until pale yellow and diluted with water until crystallization commenced. The hydroquinone separated as glistening, almost colorless needles (1 g.). It is very soluble in alcohol, ether, or benzene, and moderately soluble in chloroform. A sample crystallized from the latter solvent formed colorless needles, m. p. 164–165.5°, which darkened on standing.

Anal. Calcd. for $C_{14}H_9O_2Br$: C, 58.13; H, 3.14. Found: C, 57.79; H, 3.52.

The dimethyl ether, prepared by treatment with dimethyl sulfate and potassium hydroxide in an atmosphere of nitrogen, extracted with ether, and crystallized from methanol (slow), was obtained in 98% yield as colorless, transparent prisms melting at 79–80°, and further crystallizations did not change the melting point.

Anal. Calcd. for $C_{16}H_{13}O_2Br$: C, 60.43; H, 4.13. Found: C, 60.21; H, 4.36.

2-Bromo-1,3,4-triacetoxyphenanthrene.—A suspension of 1 g. of 2-bromo-3,4-phenanthrenequinone in a cold solution of 12 drops of concentrated sulfuric acid in 10 cc. of acetic anhydride was stirred frequently at room temperature; after four to five hours a nearly colorless solution was obtained, and this was treated cautiously with water to hydrolyze the excess anhydride, using 10 cc. in all and eventually bringing precipitated material into solution at the boiling point. The filtered solution deposited nearly pure material which, after recrystallization from acetic acid, formed very fine, colorless needles, m. p. 195–196°; yield, 1.4 g. (93%).

Anal. Calcd. for $C_{20}H_{15}O_6Br$: C, 55.68; H, 3.51. Found: C, 55.91; H, 3.36.

2-Bromo-3-hydroxy-1,4-phenanthrenequinone.—The triacetate (0.8 g.) was warmed with 10% sodium hydroxide (15 cc.) and a little alcohol until dissolved. Air was passed through the solution until the solution was dark red and showed no further change. Water (150 cc.) was added to dissolve some crystalline salt at the boiling point, and the solution was acidified. The orange-yellow precipitate when crystallized from methanol (moderately soluble), formed glistening, orange-red needles, m. p. 198–199°; yield, 0.5 g. (89%).

Anal. Calcd. for $C_{14}H_7O_3Br$: C, 55.45; H, 2.33. Found: C, 55.37; H, 2.37.

The bromohydroxyquinone (58 mg.) was recovered unchanged (50 mg.) after a solution of the substance in methanol had been refluxed for five hours. Under identical conditions, a solution of 3-hydroxy-1,4-phenanthrenequinone (56 mg.) began to deposit crystals of the ether in two minutes and after refluxing for ten minutes the ether[2] was collected and recrystallized; yield, 49 mg. (84%); m. p. 170–171°. Whereas 3-hydroxy-1,4-phenanthrenequinone is cleaved completely by boiling, dilute alkali in about four hours,[2] the 2-bromo derivative (0.4 g.) was largely recovered unchanged (0.35 g.) after being boiled for fifteen

hours with 150 cc. of water containing 2.9 cc. of 10% sodium hydroxide solution.

8,9-Dimethyl-5,6-chrysenequinone (IV).—A solution of 0.5 g. of 2-bromo-3,4-phenanthrenequinone and 2 cc. of 2,3-dimethylbutadiene in 20 cc. of pure chloroform was heated at 100° for two hours, when the color had faded from red to yellow. The reddish-yellow oil remaining after removing the solvent was treated in 3 cc. of glacial acetic acid with 1 g. of chromic anhydride in 10 cc. of 80% acetic acid with gentle warming. By gradually adding water to the red solution and scratching, the reaction product was caused to separate in a microcrystalline condition; yield, 0.45 g. (90%). Recrystallized from glacial acetic acid, the quinone formed bright orange-red blades having a golden reflex, m. p. 250–251°.

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.74; H, 4.96.

1,2-Phenanthrenequinone Series

3-Bromo-1,2-phenanthrenequinone.—A fine suspension of 3.8 g. of 1,2-phenanthrenequinone (as prepared[5]) in 180 cc. of glacial acetic acid at 25° was treated with 3.3 g. of bromine in 20 cc. of this solvent, and after stirring for twenty minutes the material had dissolved. The yellow-red solution, filtered from a small amount of black material, was poured into 290 cc. of vigorously boiling water. The bromoquinone began to crystallize at once and, after cooling, it was collected and recrystallized from chloroform. It formed glistening, very dark crimson-red needles, m. p. 245–246°; yield, 3.6 g. (68%). The substance is darker in color than the isomer, and considerably less soluble in all solvents.

*Anal.** Calcd. for $C_{14}H_7O_2Br$: C, 58.54; H, 2.46. Found: C, 58.65; H, 2.83.

3-Bromo-1,2-dihydroxyphenanthrene.—A solution of 1 g. of the quinone in 20 cc. of hot dioxane was diluted with 15 cc. of water and sulfur dioxide was passed into the resulting fine suspension. After the quinone had dissolved, the solution was heated to boiling, diluted with water, and allowed to stand. On cooling, the hydroquinone separated as long, slender, colorless needles (0.9 g.). A sample recrystallized from chloroform melted at 195–196°.

*Anal.** Calcd. for $C_{14}H_9O_2Br$: C, 58.13; H, 3.14. Found: C, 58.20; H, 3.11.

The dimethyl ether, prepared as described for the isomer, crystallized from methanol as thin, elongated, transparent plates, m. p. 82–83°.

*Anal.** Calcd. for $C_{16}H_{13}O_2Br$: C, 60.43; H, 4.13. Found: C, 60.36; H, 3.92.

3-Bromo-1,2,4-triacetoxyphenanthrene, obtained as above in nearly theoretical yield, formed fine, colorless needles, m. p. 188–189°, from glacial acetic acid.

*Anal.** Calcd. for $C_{20}H_{15}O_6Br$: C, 55.68; H, 3.51. Found: C, 55.62; H, 3.75.

Hydrolysis of the triacetate and air oxidation as above gave a hydroxyquinone which forms very dark red needles, m. p. 222° dec., from alcohol; analytical results were variable and undecisive.

6,7-Dimethyl-3,4-benzphenanthrenequinone (VIII).—The quinone (1 g.) and diene (6 cc.) were heated in chloroform (70 cc.) for three hours and the addition product was oxidized as above; yield of crystalline product, 79%. Recrystallized from alcohol, the compound formed lustrous, fiery red plates, m. p. 194–195°.

*Anal.** Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.63; H, 5.01.

This quinone, identified by mixed melting point determination, was obtained also on heating 1,2-phenanthrenequinone (0.5 g.), dimethylbutadiene (2 cc.) and chloroform (20 cc.) for forty-eight hours and oxidizing the crude product as above; yield, 0.2 g. (29%). The diene addition occurred only slowly, for the initially clear red solution faded only slightly during the first few hours of heating; after a time the solution began to grow steadily darker, indicating decomposition.

3,4-Benzphenanthrenequinone, prepared in the usual way from 1 g. of bromoquinone and 4 cc. of butadiene, heated in 40 cc. of chloroform for five hours, was obtained in a satisfactory condition in yield of 0.6 g. (65%). It crystallized from alcohol as bright red blades, m. p. 190–191°. Cook[6] reports the melting point 187–188° for material prepared by the oxidation of 3,4-benzphenanthrene. Attempts to convert the above substance (100 mg.) into the hydrocarbon by zinc dust distillation were unsuccessful. Reductive acetylation of 100 mg. of the quinone by the usual method gave 115 mg. of the pure **hydroquinone diacetate,** which forms small, colorless needles from dilute alcohol and melts at 194–195°.

*Anal.** Calcd. for $C_{22}H_{16}O_4$: C, 76.72; H, 4.69. Found: C, 76.38; H, 4.77.

Chlorination of 3-Phenanthrol

Pentachloro Ketone XII, Probably 1,4,4-Trichloro-3-keto-3,4-dihydrophenanthrene-9,10-dichloride.—Excess chlorine was passed at a moderate rate into a solution of 5 g. of 3-phenanthrol in 50 cc. of glacial acetic acid at 13–17°, and after standing for a few minutes the greenish-yellow solution was poured slowly into 500 cc. of cold water. The flocculent yellow precipitate which separated was washed by decantation, collected on a suction funnel, and washed thoroughly with water. The rather sticky, yellow-orange product was triturated with glacial acetic acid, which dissolved the gummy material, and on collecting the residue and washing it thoroughly with fresh solvent a clean, orange-yellow powder was obtained. The yield of this material, m. p. 175–180° dec., was 2.9 g. (30%). A sample recrystallized from glacial acetic acid (with little heating) formed thick, orange needles, m. p. 182–185°, dec.

*Anal.** Calcd. for $C_{14}H_7OCl_5$: Cl, 48.14. Found: Cl, 47.82; 47.77.

The compound is not attacked by 10% aqueous sodium carbonate solution in the cold, and extensive decomposition occurs when the mixture is heated. The chloro compound gives a dark red anilide on reaction with aniline in benzene solution. In one experiment a small amount of another chlorination product separated slowly from the initial acetic acid mother liquor in the form of colorless prisms (m. p. 191° dec.) but when this material was collected and dried it turned yellow within a few hours.

1(?),4,9(or 10)-Trichloro-3-phenanthrol (XIII).—A solution of 0.9 g. of the above compound in 18 cc. of glacial acetic acid was treated at room temperature with a con-

centrated solution of stannous chloride in dilute acetic acid, added by drops until a test portion of the solution gave with water a precipitate which dissolved completely in dilute alkali. On gradual dilution with water the solution deposited colorless needles of the reduction product (0.7 g., 96%). The phenanthrol formed long needles, m. p. 130–131°, from dilute alcohol.

*Anal.** Calcd. for $C_{14}H_7OCl_3$: Cl, 35.78. Found: Cl, 35.74.

The acetate crystallized from alcohol as lustrous plates, m. p. 164–165°.

*Anal.** Calcd. for $C_{16}H_9O_2Cl_3$: Cl, 31.35. Found: Cl, 31.15.

1(?),9(or 10)-Dichloro-3,4-phenanthrenequinone (XIV).—A solution of 0.35 g. of the trichlorophenanthrol in 8 cc. of glacial acetic acid was oxidized with 3 cc. of concentrated nitric acid added all at once. The solution became red immediately and then began to darken; after three to four minutes it was gradually diluted with an equal volume of water, thus precipitating the quinone in a microcrystalline condition. Recrystallization from glacial acetic acid gave small, dark red needles melting at 239–240° dec.; yield, 0.22 g. (67%).

Anal. Calcd. for $C_{14}H_6O_2Cl_2$: C, 60.65; H, 2.18. Found: C, 60.53; H, 2.53.

1(?),3,4 - Triacetoxy - 9(or 10) - chlorophenanthrene.—A suspension of 90 mg. of the quinone XIV in 6 cc. of acetic anhydride containing 6 drops of concentrated sulfuric acid was shaken at intervals and frequently warmed on the steam-bath. The material dissolved in about six hours, and after standing overnight the red-yellow solution was treated with water. One crystallization from acetic acid gave 70 mg. of yellowish rods, and after further crystallizations from alcohol the compound was obtained as slender, colorless needles, m. p. 230–231°.

*Anal.** Calcd. for $C_{20}H_{15}O_6Cl$: Cl, 9.17. Found: Cl, 9.65.

Summary

3-Bromo-1,2-phenanthrenequinone and 2-bromo-3,4-phenanthrenequinone add dienes readily and the addition products can be converted in good yield into 3,4-benzphenanthrenequinones and chrysenequinones, respectively.

From a preliminary study of the chlorination of 3-phenanthrol it appears that the substance not only is attacked in the hydroxylated ring but adds chlorine at the 9,10-position.

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CAMBRIDGE, MASS. RECEIVED MARCH 31, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

10-Substituted 1,2-Benzanthracene Derivatives

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

The observation that 10-methyl-1,2-benzanthracene[2] is a potent carcinogenic agent comparable with cholanthrene and methylcholanthrene in the rapidity and regularity with which it produces tumors in experimental animals[3] has made it a matter of considerable interest to investigate additional 10-substituted derivatives of the tetracyclic hydrocarbon. The 10-methyl derivative contrasts strikingly with 1,2-benzanthracene itself, for in experiments conducted at the Royal Cancer Hospital the latter hydrocarbon has produced only one tumor (papilloma) in eighty mice tested.[4] Since compounds of more complex structure than the methyl derivative, namely, the 10-isopropyl and 10-benzyl compounds, have been tested by the English investigators[4] with entirely negative results, it is important to determine whether 10-methyl-1,2-benz anthracene occupies a unique position or is one of a possibly limited series of homologs possessing some carcinogenic activity. A series of closely related hydrocarbons of graduated potency would offer many interesting possibilities for biological and chemical experimentation.

None of the synthetic methods hitherto employed for the preparation of 10-alkyl-1,2-benzanthracenes seemed adequate for the purpose at hand without some modification. The synthesis of Fieser and Newman[2] provides a quite satisfactory, if somewhat lengthy, route to the 10-methyl compound, but it suffers from the limitation that considerable reduction occurs as a side reaction in the condensation of higher alkylmagnesium halides with 2-*o*-toluyl-1-naphthoic acid. Cook[5] obtained the 10-benzyl compound in small yield by the action of benzyl chloride on 1,2-benzanthracene in the presence of zinc dust, but direct alkylation clearly is out of the question as a general method. A third synthesis,

(1) Lilly Research Fellow.

(2) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).

(3) Fieser and Hershberg, *ibid.*, **59**, 394 (1937); L. F. Fieser, M. Fieser, Hershberg, Newman, Seligman and Shear, *Am. J. Cancer*, **29**, 260 (1937).

(4) Barry, Cook, Haslewood, Hewett, Hieger and Mayneord, *Proc. Roy. Soc.* (London), **B117**, 318 (1935).