

isotherms together with data for the chemisorption of carbon monoxide on the catalysts at -183 and -78° and for the activated adsorption of hydrogen appear to afford a means for measuring the absolute as well as the relative surface areas of the iron catalysts. Evidence is also pre-

sented to show that the aluminum oxide promoters tend to concentrate on the surfaces of the iron synthetic ammonia catalysts, 1 and 10% Al_2O_3 in the sample as a whole resulting in the covering of about 35 and 55% of the surface, respectively.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of 1,4-Dimethyl-6,7-methylenedioxyphenanthrene and of Certain Substituted 9,10-Dimethyl-1,2,5,6-dibenzanthracenes

BY RUSSELL BLISS AKIN¹ AND MARSTON TAYLOR BOGERT

Following up our recent work² on the synthesis of 1,4-dimethylphenanthrene by the Pschorr process, we have carried out a similar series of reactions using 6-nitropiperonal in place of *o*-nitrobenzaldehyde, and have thus obtained the corresponding methylenedioxy derivative (II) of the dimethylphenanthrene. Further, by substituting the 2,5-dimethyl-*p*-phenylenediacetic acid for the 2,5-dimethylphenylacetic acid, the analogous 1,2,5,6-dibenzanthracene derivatives (IV and VI) have been prepared.

Experiments are now under way for the hydrolysis of these methylene ethers to the corresponding di- and tetrahydroxy compounds. Preliminary tests with anhydrous aluminum bromide have shown that this is not a satisfactory reagent for the purpose, and the attack is being continued by different methods.

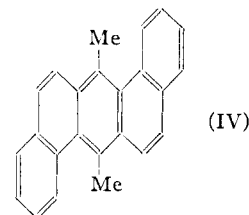
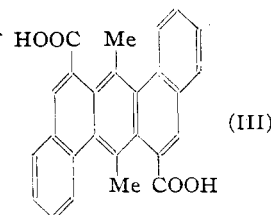
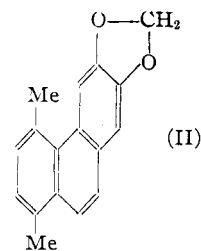
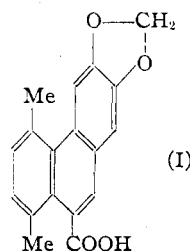
One of the compounds (VI) described in the present paper is being tested by the Crocker Institute of Cancer Research, because of the well-known cancerigenic potency of 1,2,5,6-dibenzanthracene itself.

As our experimental work must now be interrupted for several months, it seems desirable to report here the results secured to date, and to add that these were obtained many months before the appearance of the recent paper by Fieser, Hershberg, Long and Newman,³ on the hydroxy derivatives of 3,4-benzpyrene and 1,2-benzanthracene; and those of Hill and Short⁴ on 1-methoxy-2-methyl; of Higginbottom, Hill and Short⁵ on 4-

methoxy-1-methyl; and of Hill, Short, Stromberg and Wiles,⁶ on 3-methoxy-1-methyl phenanthrenes. In view of these publications from Harvard and from the Manchester College of Technology, we are continuing our own work mainly in the direction of the 1,2,5,6-dibenzanthracene derivatives.

Analyses.—The analytical work recorded in the Experimental Part was carried out by Dr. Donald Price and Mr. Saul Gottlieb.

Acknowledgments.—Our grateful thanks are due to the Trustees of the Ella Sachs Plotz Foundation for the generous financial aid which made this investigation possible; and to Drs. Mosettig and Burger, of the Cobb Chemical Laboratory, University of Virginia, for their valued advice and instructions in our preparation and use of anhydrous aluminum bromide.



(1) Ferguson Fellow, Columbia University, 1934-35 and 1936-37.

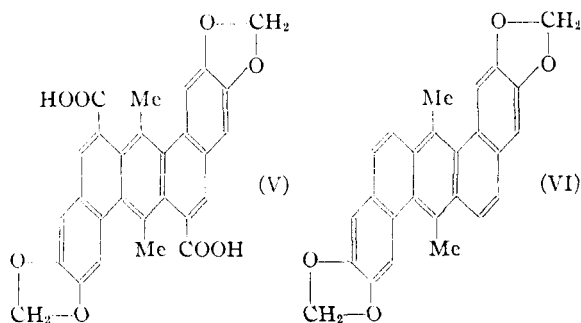
(2) Akin, Stamatoff and Bogert, *THIS JOURNAL*, **59**, 1268 (1937).

(3) Fieser, Hershberg, Long and Newman, *THIS JOURNAL*, **59**, 475 (1937).

(4) Hill and Short, *J. Chem. Soc.*, 260 (1937).

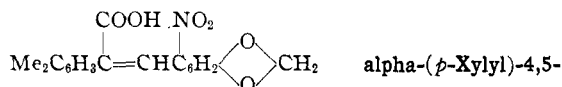
(5) Higginbottom, Hill and Short, *ibid.*, 263 (1937).

(6) Hill, Short, Stromberg and Wiles, *ibid.*, 510 (1937).



Experimental

A. Synthesis of 1,4-Dimethyl-6,7-methylenedioxyphenanthrene



methyleneoxy-2-nitrocinnamic Acid.—A mixture of 25 g. of dry potassium *p*-xylylacetate, 24 g. of 6-nitropiperonal (m. p. 97–98°), and 190 g. of acetic anhydride, was digested for five hours at 105–110°, with vigorous stirring. Excess of acetic anhydride was hydrolyzed by boiling with water, and the hot solution was poured into 2 liters of dilute hydrochloric acid. The product separated as an oil, which solidified within an hour to a brown crystalline mass which was crystallized thrice from acetic acid, decolorized twice with Norite in 95% ethanol solution, and finally crystallized twice more from this same solvent. It was thus obtained in very pale yellow crystals, which sintered at 184–186° and melted at 209.4–209.9° (corr.). The yield of crude substance was 97%; of pure compound, 83%.

Anal. Calcd. for $C_{18}H_{15}O_6N$: C, 63.32; H, 4.43; N, 4.10. Found: C, 62.88; H, 5.20; N, 3.85.

Considerable difficulty was experienced in this combustion, and no satisfactory figures could be secured, even when the acid was prepared by saponification of its analytically pure methyl ester.

Methyl Ester.—Very pale yellow needles (from methanol), m. p. 157.5–158° (corr.).

Anal. Calcd. for $C_{19}H_{17}O_6N$: C, 64.22; H, 4.82. Found: C, 64.28; H, 4.62.

Alpha - (*p* - Xylyl) - 4,5 - methylenedioxy - 2 - aminocinnamic acid, prepared by reduction² of the foregoing nitro acid (22 g.) with ferrous sulfate heptahydrate (138 g.), 340 cc. of concd. ammonium hydroxide solution, and 400 cc. of water, was crystallized twice from 95% ethanol, decolorized with Norite and crystallized again from the same solvent. It formed very fine pale yellow needles, m. p. 216–217° (corr.); yield 70%.

Anal. Calcd. for $C_{18}H_{17}O_4N$: C, 69.43; H, 5.51. Found: C, 69.59; H, 5.75.

1,4 - Dimethyl - 6,7 - methylenedioxyphenanthrene - 10-carboxylic Acid (I).—The aminocinnamic acid (4 g.) was subjected to the usual Pschorr reaction² with amyl nitrite, the crude product decolorized with Norite and purified by repeated crystallization from toluene. It then appeared in white crystals, m. p. 221–222° (corr.); yield 79%.

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.44; H, 4.80. Found: C, 73.07, 73.72; H, 4.78, 4.84.

With a drop of any organic solvent, a delicate purple fluorescence developed.

1,4 - Dimethyl - 6,7 - methylenedioxyphenanthrene (II).—When the above phenanthroic acid was heated for forty minutes with quinaldine and basic copper carbonate, the yield of this compound was 80%; but when the acid was distilled with copper powder alone, the yield fell to 65%. The crude product was decolorized and crystallized from diluted ethanol, and then formed very pale yellowish flat glassy prisms, m. p. 166.5–167° (corr.).

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.56; H, 5.64. Found: C, 81.37; H, 5.49.

Picrate.—When this product and picric acid were brought together in methanol, ethanol, acetone, or benzene solution, brick-red feathery needles separated, m. p. 155–158°, which rapidly dissociated into the original components again on recrystallization from 95% ethanol.

Attempts to Prepare 1,4-Dimethyl-6,7-dihydroxyphenanthrene.—Anhydrous aluminum bromide, in nitrobenzene or carbon disulfide solution, gave only intractable amorphous or viscous products, thus duplicating the experience of Mosettig and Burger⁷ in their futile efforts to open the ether ring of 2,3-methylenedioxyphenanthrene with this same reagent. They succeeded, however, in the scission of the methylenedioxy group in the case of their 2,3-methylenedioxyphenanthrene-9-carboxylic acid, whereas we failed with our 10-carboxylic acid, following their procedure, and were equally unsuccessful when we used the technique of Pfeiffer and his co-workers.⁸ Pfeiffer also found with certain methylenedioxy derivatives that no isolable pure products could be obtained by the aluminum bromide treatment.

The details of our experiments were as follows.

(1) To a solution of 2.92 g. of the phenanthrene (II) in 60 cc. of nitrobenzene, there was added during three hours a solution of 6.23 g. of anhydrous aluminum bromide in 40 cc. of nitrobenzene, in an ice-water bath: product, a viscous amorphous mass, from which no pure compounds could be isolated. Another experiment at 0°, using the same amounts of reactants, but mixed more rapidly, was allowed to continue for only ten minutes and was then examined. Less than 1 g. of the initial phenanthrene (II) was recovered.

(2) A solution of 3.16 g. of the aluminum bromide in 80 cc. of carbon disulfide was added to a suspension of 1.65 g. of the phenanthrene (II) in 40 cc. of the same solvent, and the mixture gently shaken at room temperature. After three hours, the mixture was decomposed with ice and dilute hydrochloric acid. In addition to dark-colored amorphous products, 0.90 g. of initial material (II) was recovered.

(3) In another series of experiments, a nitrobenzene (40 cc.) solution of the phenanthroic acid (I) (2.07 g.) was treated with a similar solution (62 cc.) of the aluminum bromide (3.40 g.), at room temperature. After three hours' interaction, the mixture was decomposed with

(7) Mosettig and Burger, *THIS JOURNAL*, **52**, 2992 (1930).

(8) (a) Pfeiffer and Haack, *Ann.*, **460**, 156 (1928); (b) Pfeiffer and Ochiai, *J. prakt. Chem.*, [2] **136**, 125 (1933); (c) Pfeiffer and Loewe, *ibid.*, **147**, 293 (1937).

dilute sulfuric acid. The dark tarry product was partly alkali-soluble, but no pure compounds were obtained. Many variations of this experiment were tried, changing the proportions of reactants, the temperature, etc., but the results were equally unsatisfactory. With about 1.1 mole of aluminum bromide per mole of phenanthroic acid (I), a little of the latter was recovered unaltered; whereas with more than 2.5 moles of aluminum bromide, the initial material (I) was destroyed rapidly. From a total of 30 g. of (I) used in these experiments, less than 2 g. of a crude alkali-soluble product was obtained, from which pure compounds could not be isolated.

(4) Following the Pfeiffer and Haack^{8a} procedure, a solution of 10.20 g. of aluminum bromide in 110 cc. of benzene (prepared hot and then cooled) was stirred into a suspension of 6.20 g. of the phenanthroic acid (I) in 40 cc. of dry benzene. Within ten minutes, a yellow precipitate separated, which rapidly changed to a dark resinous intractable mass. Even when the precipitate was removed quickly, before much resinification, washed with dry benzene and poured into cold dilute hydrochloric acid, the yield of alkali-soluble product was too small to encourage further experimentation along this line.

B. Synthesis of 9,10-Dimethyl-1,2,5,6-dibenzanthracene

2,5-Bis-(cyanomethyl)-*p*-xylene, (1,4)-Me₂C₆H₂(CH₂CN)₂(2,5), prepared from the corresponding dichloride,² by refluxing it for five hours with sodium cyanide in dilute alcoholic solution, crystallized from 95% ethanol in fine white needles, m. p. 157.8–158.3° (corr.), readily soluble in chloroform or benzene, but only slightly in 77–115° ligroin ("Skelly-solve D"); yield 85%.

Anal. Calcd. for C₁₂H₁₂N₂: C, 78.21; H, 6.57. Found: C, 78.21; H, 6.20.

***p*-Xylylene-2,5-bis-(acetic acid)**, (1,4)-Me₂C₆H₂(CH₂COOH)₂(2,5) was obtained from the above dinitrile (20 g.) by refluxing it with dilute sulfuric acid (200 cc. H₂SO₄ to 350 cc. H₂O). Crystallized from 80% ethanol it formed white needles, which softened at 243° and melted at 254–255° (corr.); yield 80%.

Anal. Calcd. for C₁₂H₁₄O₄: C, 64.83; H, 6.35. Found: C, 64.98; H, 6.33.

Methyl Ester.—White needles, from petroleum ether, m. p. 61°.

Anal. Calcd. for C₁₄H₁₆O₄: C, 67.16; H, 7.25. Found: C, 67.48; H, 7.33.

Alpha-(*p*-Xylylene)-2,5-bis-(*o*-nitrocinnamic Acid), (1,4)Me₂C₆H₂(C(COOH)=CHC₆H₄NO₂)₂(2,5).—The potassium salt (20 g.) of the *bis*-acetic acid just described was condensed with *o*-nitrobenzaldehyde (20.2 g.), by digestion for eight hours in acetic anhydride solution, and gave a dark brown resin as the crude product. This was purified by dissolving in alkali and re-precipitating with acid, followed by extraction with boiling benzene and with alcohol, which removed tarry contaminants. Crystallized and decolorized repeatedly in acetic acid solution, the acid was obtained in fine crystals, with a faint yellow-green tinge, which darkened above 290° and melted with decomposition above 330°; yield 60%.

In spite of numerous attempts at further purification, satisfactory analytical figures could not be secured on this

product. Equivalent weight: calcd., 244.1; found, 243.1 and 240.0.

Weitzenböck and Klingler,⁹ who prepared the corresponding acid without the methyl groups at 1 and 4, reported it as melting with decomposition at 308°.

Alpha-(*p*-Xylylene)-2,5-bis-(*o*-aminocinnamic Acid).—Reduction² of the nitro acid (7.2 g.) by ferrous sulfate and ammonia, gave a crude product which, after repeated separation from alcohol and from acetone, softened at 285° and decomposed at 293–296°; yield, 63%. Like the nitro acid, the analytical figures for this product were unsatisfactory. Cook¹⁰ had a similar experience in his attempts to get a pure bis-(alpha-*o*-aminobenzylidene)-*m*-phenylenediacetic acid.

9,10-Dimethyl-1,2,5,6-dibenzanthracene-4,8-dicarboxylic Acid (III).—Without expending further time in attempting to obtain the bis-aminocinnamic acid analytically pure, the product described above was subjected to the Pschorr cyclization reaction,² using amyl nitrite, and the crude dicarboxylic acid secured as a brown powder. This crude material was extracted first with benzene and the residue then dissolved by extraction for nine hours with 95% ethanol. The alcoholic solution was decolorized and concentrated. An amorphous solid separated as a sludge, which was purified by frequent crystallization from methyl and ethyl alcohols, being obtained finally in pale yellow crystals, which sintered at 335°, but remained unmelted at 350°; yield, 2.7 g. from 15 g. of the amino acid.

Anal. Calcd. for C₂₆H₁₈O₄: C, 79.16; H, 4.59. Found: C, 78.80; H, 4.58.

Cook has studied Pschorr condensations with similar acids. With the *m*-phenylenediacetic acid derivative¹⁰ (6.75 g.), the yield of crude dibenzanthracene derivative was very low (0.95 g.). From the isomeric *p*-phenylenediacetic acid derivative,¹¹ he was unable to obtain any analytically pure product from 6.7 g. of the crude acid, from which only a trace of the dibenzanthracene was secured by decarboxylation.

9,10-Dimethyl-1,2,5,6-dibenzanthracene (IV).—The dicarboxylic acid (1.10 g.) was decarboxylated by mixing it with one-fifth its weight of copper powder and boiling for six hours in quinaldine. The crude product, after decolorization and crystallization from acetic acid, was obtained in pale yellowish glistening plates or needles, m. p. 203–204° (corr.); yield 62%.

Anal. Calcd. for C₂₄H₁₈: C, 94.07; H, 5.93. Found: C, 94.01; H, 5.93.

This hydrocarbon has been reported by Cook,¹² who prepared it by a different method, and described it as crystallizing from benzene in yellowish needles, m. p. 205.5–206.5°. He found that his product invariably was contaminated with chrysogenic substances removable only by sulfuric acid and that, after this treatment, the purified dibenzanthracene gave a characteristic intense violet solution in concentrated sulfuric acid. Apparently our product was free from these chrysogenic contaminants, for agitation of its toluene solution with sulfuric acid caused

(9) Weitzenböck and Klingler, *Monatsh.*, **39**, 315 (1918).

(10) Cook, *J. Chem. Soc.*, 1481 (1932).

(11) Cook, *ibid.*, 1597 (1933).

(12) Cook, *ibid.*, 495 (1931).

no change either in the color of the crystals or in their m. p. With concentrated sulfuric acid alone, it gave the deep violet solution noted by him.

C. Synthesis of 9,10-Dimethyl-2',3',6',7'-di(methylenedioxy) - 1,2,5,6 - dibenzanthracene (7,14 - Dimethyl-2,3,9,10 - di - (methylenedioxy) - dibenz[*ah*]anthracene)¹³

2,5 - Dimethyl - bis - (alpha - 2 - nitro - 4,5 - methylenedioxybenzylidene)-*p*-phenylenediacetic acid was prepared in much the same way as the *p*-xylylene-bis(*o*-nitrocinnamic acid), by condensing the potassium salt (2.94 g.) of the *p*-xylylene-bis-(acetic acid) with 6-nitropiperonal (39.0 g.) instead of *o*-nitrobenzaldehyde. The purified product was composed of very fine pale yellow crystals, which darkened slightly above 300°, but remained unmelted at 330°; yield, 64%. The analytical results were unsatisfactory.

Anal. Calcd. for C₂₈H₂₀O₁₂N₂: C, 58.31; H, 3.50; equiv. wt., 288.1. Found: C, 57.17; H, 4.29; equiv. wt., 279.1, 282.6.

Na Salt.—Soft thin plates, very easily soluble in water.

2,5 - Dimethyl - bis - (alpha - 2 - amino - 4,5 - methylenedioxybenzylidene)-*p*-phenylenediacetic acid, prepared from the nitro acid (6 g.) by reduction² with ferrous sulfate and ammonia, formed a yellow powder, which darkened slightly and shrank at 295°, but was still unmelted at 350°; yield 70%. Both the free acid and its hydrochloride were but slightly soluble in the neutral solvents tried.

Acetyl Derivative.—Cream-colored solid (from glacial acetic acid), which steadily darkened above 300°, but was still unmelted at 350°.

Anal. Calcd. for C₃₂H₂₈O₁₀N₂: C, 63.98; H, 4.70; equiv. wt., 300.1. Found: C, 63.50; H, 5.06; equiv. wt., 291.6, 299.5.

9,10 - Dimethyl - 2',3',6',7' - di - (methylenedioxy)-1,2,5,6 - dibenzanthracene - 4,8 - dicarboxylic acid (7,14 - Dimethyl - 2,3,9,10 - di-(methylenedioxy) - dibenz[*ah*]anthracene - 6,13 - dicarboxylic Acid) (V).—The amino acid was converted into the dibenzanthracene derivative by the usual Pschorr procedure, with amyl nitrite.²

(13) The names given in parentheses follow the system of nomenclature and numbering adopted for the indexes of *Chemical Abstracts*.—M. T. B.

The crude product was extracted first with benzene and then with 95% ethanol. The ethanol extract was decolorized by Norite and concentrated to small volume. As it cooled, the concentrated solution deposited a fine brown powder, which was washed twice with boiling benzene, crystallized twice from methanol, and then decolorized and recrystallized from acetic acid. The compound thus purified appeared as a pale yellow powder, which darkened above 300°, but remained unmelted at 350°; yield, 2.4 g. from 11 g. of crude product.

Anal. Calcd. for C₂₈H₁₈O₈: C, 69.69; H, 3.76. Found: C, 69.66; H, 3.78.

9,10 - Dimethyl - 2',3',6',7' - di - (methylenedioxy)-1,2,5,6 - dibenzanthracene (7,14 - Dimethyl - 2,3,9,10 - di(methylenedioxy) - dibenz[*ah*]anthracene) (VI).—The decarboxylation of the dibasic acid by boiling with copper powder (one-fifth its weight) and quinaldine for six hours, proved far more satisfactory than distillation with copper alone. Purified by repeated crystallization from acetic acid, and decolorization with Norite, this compound formed yellow flakes, which sintered at about 261–266° and melted slowly at 279–281° (corr.); yield 72%.

Anal. Calcd. for C₂₄H₁₈O₄: C, 79.16; H, 4.59. Found: C, 78.85; H, 4.58.

Attempts to open the methylenedioxy groups by the action of anhydrous aluminum bromide, under a variety of conditions, proved futile, the result in all cases being either deep-seated decomposition or unaltered initial material. This was true whether the above compound was used, or its antecedent dicarboxylic acid.

Summary

1. By the application of the Pschorr series of reactions to *p*-xylylacetic acid and 6-nitropiperonal, the dimethyl-methylenedioxyphenanthrene has been synthesized.

2. In similar manner, from *p*-xylylene-bis-(acetic acid) and *o*-nitrobenzaldehyde, or 6-nitropiperonal, derivatives of 9,10-dimethyl-1,2,5,6-dibenzanthracene have been obtained. Some of these products are being tested for cancerigenic properties.

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