rotation of the isolated monoalkylate was always opposite in sign to that of the ether.

Reaction mixtures were prepared with or without exclusion of atmospheric moisture, techniques (2) and (1) of **Techniques** (ref. 8). After reaction, the monoalkylate was isolated from the washed hydrocarbon layer by distillation in a micro distilling column of several theoretical plates. Results are presented in Table I.

The first two samples of *s*-butylbenzene listed in Table I were combined and distilled in a Piros–Glover, rotating-band, fractionating column. Four successive fifths were collected, $n^{25}D$ 1.48694, 1.48730, 1.48727, 1.48732 and $\alpha^{30}D$ (2 dm.) −0.393°, −0.400°, −0.396° and −0.395°. The rotatory dispersion of a combined sample was measured on a Bellingham and Stanley polarimeter with spectroscopic eyepiece. The relative rotations, with that of the 5461 Å. line taken as 1.00, were: 5893 Å., 0.86, 0.82; 5790 Å., 0.91, 0.87; 5461 Å., 1.00, 1.00; 4358 Å., 1.82, 1.82. The results of this research are given first, those of Harrison, Kenyon and Shepherd,[16] second. They agree to within the experimental error. These data support the ascription of the rotation of the alkylate to *s*-butylbenzene.

A mixture of benzene (0.326 mole), 2-methoxypentane (0.0477 mole), boron trifluoride (0.0474 mole) and water (2 drops) was allowed to stand several days. The phenylpentane fraction was analyzed by infrared spectrophotometry by measurement at 8.85, 10.17 and 12.03 microns. The analysis, 25% 3-phenylpentane, was confirmed by comparing the transmission curve of the fraction from 6 to 15 microns with that of a synthetic mixture containing 74.3% 2-phenylpentane and 25.7% 3-phenylpentane. The curves were indistinguishable.

A mixture of the following composition was prepared: (−)*s*-butylbenzene ($\alpha^{25}D$ −21.64°), 0.00189 mole; benzene, 0.254 mole; *dl*-*s*-butyl methyl ether, 0.0359 mole; boron trifluoride, 0.0362 mole; and sulfuric acid, 0.0008 mole. A 66% yield of *s*-butylbenzene resulted. During the distillation two fractions were collected for both of which $n^{25}D$ 1.4871 and $\alpha^{25}D$ −1.30°. If 0.00189 mole of the (−)*s*-butylbenzene had been diluted with inactive material to the resultant 0.0238 mole *s*-butylbenzene, a rotation of −1.71° would result. However, since the (−)*s*-butylbenzene, being present initially, would have been preferentially converted to di-*s*-butylbenzene, the racemization which occurred is probably less than the 24% racemization which results from the indicated computation.

The following mixture was prepared: toluene, 0.24 mole; (−)*s*-butyl methyl ether ($\alpha^{25}D$ −5.70°), 0.0415; boron trifluoride to near saturation; sulfuric acid, 0.001. After one hour at 25°, 1.0 cc. of lower layer had formed. This with 9 cc. of the upper layer was withdrawn and allowed to react to completion. The remaining 20 cc. was run into ice-water. From the first fraction, *s*-butyltoluene, $\alpha^{25}D$ +0.15°, was recovered. From the second fraction, *s*-butyltoluene, $\alpha^{25}D$ +0.16°, and *s*-butyl methyl ether, $\alpha^{25}D$ −5.45°, were recovered. Thus, negligible racemization of the ether occurs prior to reaction.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE METCALF CHEMICAL LABORATORIES, BROWN UNIVERSITY]

3′,7′-Dihydroxy-1,2,5,6-dibenzanthracene[1]

BY LILLI SCHWENK HORNIG

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The synthesis of 3′,7′-dihydroxy-1,2,5,6-dibenzanthracene and certain of its derivatives which is here reported was undertaken to test the hypothesis that the phenol is identical with the rabbit metabolite of the carcinogenic parent hydrocarbon. The desired phenol was synthesized by application of the Pschorr reaction to the product resulting from condensation of phenylene-1,4-diacetic acid with two moles of 2-nitro-5-methoxybenzaldehyde, and proved to be not identical with the product of rabbit metabolism.

The several carcinogenic polynuclear hydrocarbons whose metabolism has been investigated invariably are detoxicated, in rats and mice, to simple phenolic derivatives bearing the hydroxyl groups in positions sterically analogous to the 4′-position of 1,2-benzanthracene.[2] The only common carcinogen containing two angular condensed benz rings, 1,2,5,6-dibenzanthracene, is converted to the symmetrical 4′,8′-dihydroxy derivative.[2a]

The existence of marked species differences in the response to carcinogens has long been recognized, and it is known that rabbits, which are relatively resistant to experimental cancer production, metabolize the hydrocarbons differently than rats and mice. Thus, the dihydroxydibenzanthracene isolated from rabbits[3] (which develop only papillomas on treatment with dibenzanthracene) is not identical with the 4′,8′-dihydroxy derivative excreted by rats and mice. On the basis of the fact that anthracene is excreted in part as a 1,2-dihydro-1,2-dihydroxy derivative[4] Cason and Fieser[2a] suggested that the rabbit metabolite of dibenzanthracene might be the 3′,7′-dihydroxy compound XI, arising from a tetraol precursor (identical with the probable rat and mouse intermediary metabolite) by elimination of water. The present work reports the synthesis of 3′,7′-dihydroxydibenzanthracene, undertaken to test this hypothesis. The synthetic phenol was in fact not identical with the rabbit metabolite, and it appears, therefore, that the species difference in the metabolism of dibenzanthracene is manifested at an earlier stage in the metabolic process and that in fact the molecule is originally attacked at positions which differ radically, in the relatively cancer-resistant rabbit, from those in the much more susceptible rat and mouse.

Since the inception of this work some years ago, the rabbit metabolite of 3,4-benzpyrene has been identified as the 10-hydroxy derivative[5] which is sterically analogous to the 2′,6′-dihydroxy derivative of dibenzanthracene.

The most promising route to the desired phenol

(1) This paper is based on a thesis presented to the Graduate Faculty of Arts and Sciences of Radcliffe College for the Degree of Doctor of Philosophy, January, 1950.

(2) (a) J. Cason and L. F. Fieser, THIS JOURNAL, **62**, 2681 (1940); (b) I. Berenblum and R. Schoental, *Cancer Research*, **3**, 145 (1943); (c) I. Berenblum, D. Crowfoot, E. R. Holiday and R. Schoental, *ibid.*, **3**, 151 (1943); (d) I. Berenblum and R. Schoental, *ibid.*, **3**, 686 (1943); (e) F. Dickens and H. Weil-Malherbe, *British Empire Cancer Campaign, Annual Reports*, **22**, 55 (1945).

(3) (a) A. A. Levi and E. Boyland, *Chemistry and Industry*, **15**, 446 (1937); (b) E. Boyland, A. A. Levi, E. H. Mawson and E. Roe, *Biochem. J.*, **35**, 184 (1941).

(4) E. Boyland and A. A. Levi, *ibid.*, **29**, 2679 (1935); **30**, 728, 1225 (1936).

(5) I. Berenblum and R. Schoental, *Cancer Research*, **6**, 699 (1946).

seemed to be application of the well-known Pschorr phenanthrene synthesis,[6] despite the variable yields and intractable intermediates encountered particularly with bilateral ring closures of this type.[7] The nitrohydroxyaldehyde required for the initial Perkin condensation, hitherto difficultly accessible, was prepared readily in 34% yield by direct nitration of 3-hydroxybenzaldehyde in benzene suspension; the 2-nitro-5-hydroxy compound crystallized from the reaction mixture while other isomers remained in solution. Although the yields are lower, this method seems preferable to the published procedure[8] at least for the preparation of relatively small quantities, since it is considerably less hazardous as well as faster.

Condensation of both the hydroxy- and methoxyaldehydes with phenylene-1,4-diacetic acid was effected by Kalnin's procedure[9] using triethylamine as catalyst, and gave the derivatives II and III in 51 and 24% yield, respectively. The diacetate I was isolated with some difficulty by means of a dioxane complex, and was readily hydrolyzed to the phenol III by dilute base. Reduction of III with ferrous sulfate and ammonium hydroxide yielded an aminophenol highly sensitive to air, totally insoluble in all common solvents and in dilute acids, and soluble in cold concentrated sulfuric acid and dilute aqueous bases only with rapid decomposition and tar formation. The nitromethoxy compound II on similar reduction gave the slightly more soluble and much more stable diamine V in 95% yield; for analysis the compound was converted to the diacetate Va which was readily purified by recrystallization. The solubility of the free amine in dilute hydrochloric acid was too small (of the order of a few milligrams per 100 ml.) to permit direct diazotization, but conversion to the diazonium salt was accomplished readily by adding sodium nitrite and hydrochloric acid to a solution of the amine in dilute sodium carbonate. Application of a modified Pschorr ring closure procedure[10] gave the desired 3′,7′-dimethoxydibenzanthracene-4,8-dicarboxylic acid (VIII) in 8% yield, accompanied by the expected dibenzphenanthrene isomer VI which was isolated in 11% yield. The remainder of the reaction product was a complex mixture (characteristic of this type of reaction) which appeared to contain some phenolic material.

The dibenzanthracene derivative VIII was distinguished from the isomer VI by chromic anhydride oxidation of the former to the dibenzanthraquinone (IX), which gave a typical red vat with alkaline hydrosulfite solution. Oxidation of VI with chromic anhydride or sodium dichromate gave only water-soluble products, in contrast to the results of Cook,[11] who obtained dibenzphenanthra-3,4,5,6-diquinone on oxidation of the 4,5-dicarboxylic acid.

Both acids VI and VIII were decarboxylated readily and in fair yield by copper powder in hot quinaldine.[12] The dimethoxydibenzanthracene (X) proved entirely resistant to cleavage of the ether groups by a variety of reagents including hydrogen bromide in glacial acetic acid, alcoholic potassium hydroxide or sodium ethoxide, and anhydrous aluminum chloride in refluxing benzene. These observations are in agreement with the findings of Bogert, *et al.*[7b,c] Demethylation of X to the desired 3′,7′-dihydroxydibenzanthracene (XI) was accomplished quantitatively, however, by heating with fused pyridine hydrochloride. For purposes of a complete comparison with the metabolite isolated by Boyland, *et al.*,[3b] the phenol XI was converted successively into its diacetyl derivative XII, the diacetoxydibenzanthraquinone (XIII), and finally the dihydroxyquinone (XIV). The melting points of the synthetic materials and the metabolite derivatives are listed in Table I.

TABLE I

	Melting points, °C. 3′,7′-DBA derivative	Rabbit metabolite[3a,b]
Dimethyl ether	295–296	244–245
Dihydroxy	357–360	355–358
Diacetoxy	291–292	291
Diacetoxyquinone	296.5–298	294–296
Dihydroxyquinone	375–385 dec.	350

A comparison of these melting points permitted no definite conclusion as to the identity of the two compounds; a sample of the metabolite was unfortunately no longer available. Determination of the ultraviolet spectrum of the synthetic material (Fig. 1) provided conclusive evidence, since the spectrum differs decidedly from that published by

(6) R. Pschorr, *Ber.*, **29**, 496 (1896).

(7) (a) R. Weitzenböck and A. Klingler, *Monatsh.*, **39**, 111 (1918); (b) R. Akin and M. T. Bogert, THIS JOURNAL, **59**, 1564 (1937); (c) J. T. Cassaday and M. T. Bogert, *ibid.*, **61**, 3058 (1939); (d) J. W. Cook, *J. Chem. Soc.*, 1472 (1932).

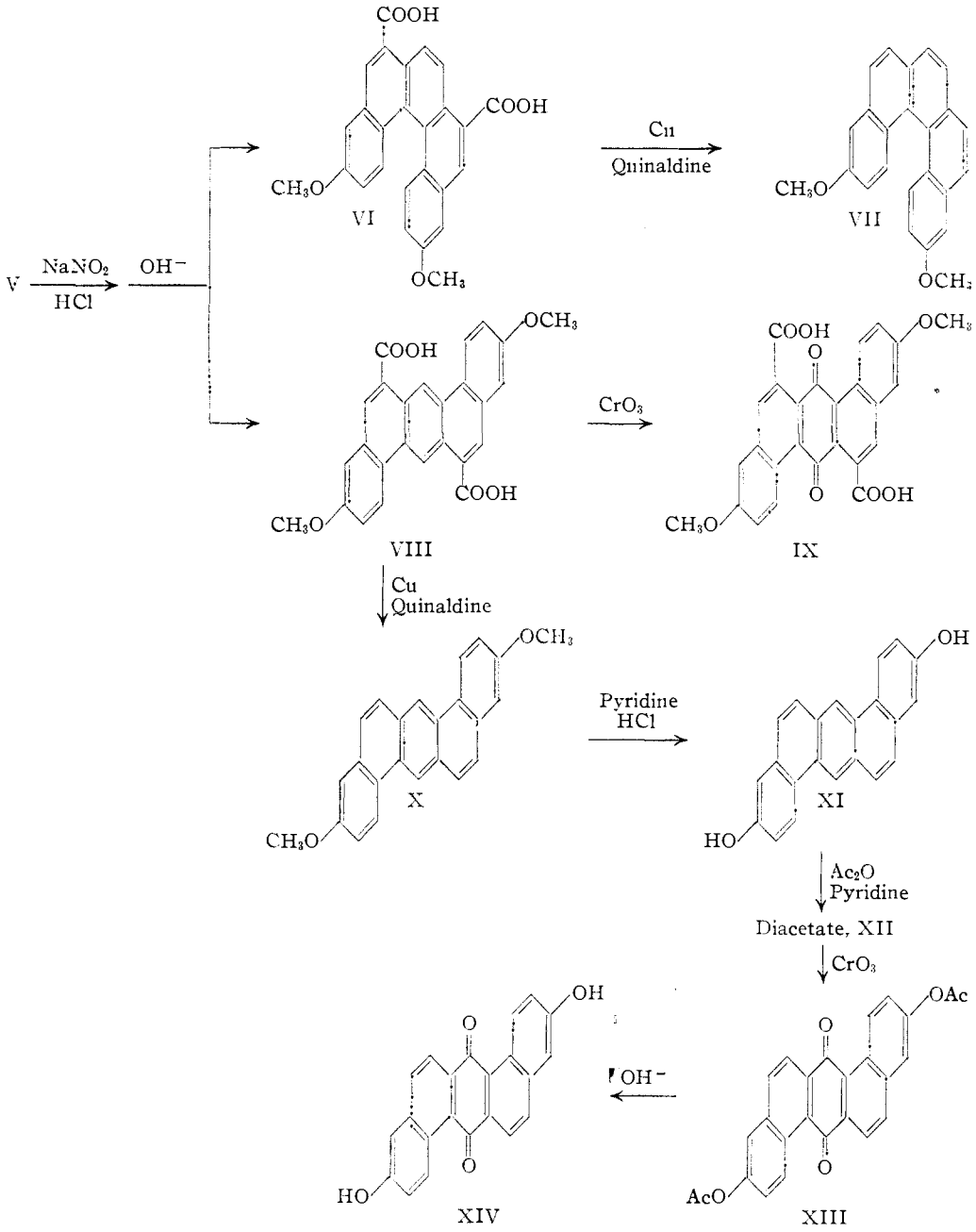
(8) F. A. Mason and H. Jenkinson, *ibid.*, **127**, 1195 (1925).

(9) P. Kalnin, *Helv. Chim. Acta*, **11**, 977 (1928).

(10) R. Pschorr, *Ber.*, **39**, 3123 (1906).

(11) J. W. Cook, *J. Chem. Soc.*, 1952 (1933).

(12) A. F. Shepard, W. R. Winslow and J. R. Johnson, THIS JOURNAL, **52**, 2083 (1930).



Boyland[3b] both in the location and relative intensities of the various peaks (see Table II). The rabbit metabolite is therefore definitely not identical with 3′,7′-dihydroxydibenzanthracene.

Acknowledgment.—The author is indebted to Professor Louis F. Fieser for his suggestion to undertake this work and for his advice and guidance in its completion. The generosity of Brown University in extending the use of laboratory facilities is gratefully acknowledged.

Experimental

All melting points are corrected; those above 360° were determined in a copper block with a previously calibrated nitrogen filled thermometer and are accurate to ±2°. Microanalyses were performed by Mrs. Shirley Golden of the Converse Memorial Laboratory, Harvard University.

2-Nitro-5-hydroxybenzaldehyde.—Forty milliliters of concentrated nitric acid was added dropwise to a well-stirred

TABLE II

ABSORPTION MAXIMA AND THEIR EXTINCTION COEFFICIENTS OF 3′,7′-DIHYDROXYDIBENZANTHRACENE AND THE RABBIT METABOLITE

3′,7′-Dihydroxydibenzanthracene		Rabbit metabolite[3b]	
Wave length in mμ	log ε	Wave length in mμ	log ε
(222[a])	4.99	229.8	4.64
280	4.92	282.3	4.49
294	4.95	292.8	4.81
306	5.23	304.5	4.95
325	4.57	328.9	4.04
332	4.42	343.0	4.04
340	4.42	359.0	4.12
385	3.23	384.8	3.34
405	3.33	407.0	3.35

[a] This is the midpoint of a shoulder at the end of the spectral range accessible with the instrument used. It is not an accurate maximum.

suspension of 48.8 g. (0.40 mole) of 3-hydroxybenzaldehyde in 400 ml. of benzene at 25–27°. Initially it was necessary to add the acid very cautiously and permit the temperature to fall to 25° after each addition in order to prevent a sudden rise in temperature; the mixture was cooled intermittently in an ice-bath. The reaction is very slow below 20° but becomes very vigorous above 30°, with excessive darkening of the mixture and consequent loss of product.

During addition of the acid the starting material gradually dissolved and a brown crystalline precipitate separated from the mixture. After all the acid had been added the mixture was cooled with continued stirring to 15° and filtered while cold. Recrystallized once from water, 22.7 g. (34%) 2-nitro-5-hydroxybenzaldehyde was obtained as long glistening yellow needles, m.p. 167–168°.

Treatment of a warm alkaline solution of the nitrohydroxyaldehyde with dimethyl sulfate[13] gave **2-nitro-5-methoxybenzaldehyde**, m.p. 82–83°.

α,α′-Di-(2-nitro-5-acetoxybenzal)-phenylene-1,4-diacetic Acid (I).—Phenylene-1,4-diacetic acid[14] (4.66 g., 0.024 mole) was condensed with 8.36 g. (0.05 mole) of 2-nitro-5-hydroxybenzaldehyde in 40 ml. of acetic anhydride; 6 ml. (0.045 mole) of triethylamine was added and the solution stirred at 90–100° for ten hours. The excess anhydride was decomposed with water at the boiling point, resulting in separation of a red oil. The mixture was poured into 200 ml. of 5% hydrochloric acid and allowed to stand overnight. The oily product crystallized only partially; after decantation of the supernatant liquid the semi-solid mass was stirred with 400 ml. of 8% sodium bicarbonate solution, filtered from a small insoluble residue, and poured into excess hydrochloric acid. The resulting material was a sticky yellow solid, extremely soluble in cold ethanol, acetic acid and acetone, insoluble in ligroin, and very slightly soluble in benzene. Extraction with four 250-ml. portions of boiling benzene left 7.5 g. of material which still appeared oily. This was recrystallized from dioxane, giving 4.4 g. of very pale yellow needles, m.p. 240–241° dec. A further recrystallization from dilute dioxane gave 4.1 g. of material melting at 246–247°. When an effort was made to recrystallize this substance from acetone, it dissolved rapidly in a small amount of cold solvent, but on heating the solution a fine yellow precipitate separated. This redissolved on addition of a large quantity of acetone, and subsequent dilution with water precipitated fine very pale yellow needles of I, m.p. 242–243°. Two more recrystallizations from dilute acetone gave analytically pure I, m.p. 243.5–244°. The material isolated from dioxane solution thus appeared to be a fairly stable dioxane complex and this conclusion was confirmed by the analyses. The complex evidently suffered some loss of dioxane on drying at 100°.

Anal. Calcd. for $C_{32}H_{28}O_{14}N_2$ (1:1 complex of dioxane and I): C, 57.83; H, 4.24. Found: C, 58.42; H, 4.13. Calcd. for $C_{28}H_{20}O_{12}N_2$(I): C, 58.33; H, 3.49. Found: C, 58.55; H, 3.42.

Both I and its dioxane complex were hydrolyzed quantitatively by a few minutes boiling with dilute sodium carbonate solution to give **α,α′-di-(2-nitro-5-hydroxybenzal)-phenylene-1,4-diacetic acid** (III). For analysis this material was twice recrystallized from dilute acetone, being obtained as fine, nearly white needles which decomposed gradually without melting above 305°. A total of 2.8 g. (24%) of III was isolated.

Anal. Calcd. for $C_{24}H_{16}O_{10}N_2$: C, 58.54; H, 3.27. Found: C, 58.61; H, 3.24.

α,α′-Di-(2-amino-5-hydroxybenzal)-phenylene-1,4-diacetic Acid (IV).—A solution of 1.48 g. (0.003 mole) of III in 160 ml. of 14% ammonium hydroxide was added with stirring to a hot sludge of ferrous hydroxide prepared by adding 50 ml. of concentrated ammonium hydroxide to a solution of 16 g. of ferrous sulfate heptahydrate in 60 ml. of water. The mixture turned black immediately; it was heated with occasional stirring for two hours in order to coagulate the iron oxide, sufficient ammonium hydroxide being added to maintain the original volume. The mixture was filtered with suction, the precipitate extracted with a little boiling ammonium hydroxide, and the washings added to the filtrate. The clear yellow solution on acidification with either hydrochloric or acetic acid became milky and the precipitate was not coagulated by boiling, but darkened rapidly. Repeated filtration of the mixture through the same filter gave 0.85 g. (66%) of the amino acid IV as an extremely fine brown powder which was totally insoluble in all common organic solvents as well as in dilute mineral acids. It dissolved in concentrated sulfuric acid and dilute aqueous alkali or sodium carbonate with rapid and extensive decomposition. The compound could thus not be purified for analysis, nor could it be diazotized successfully.

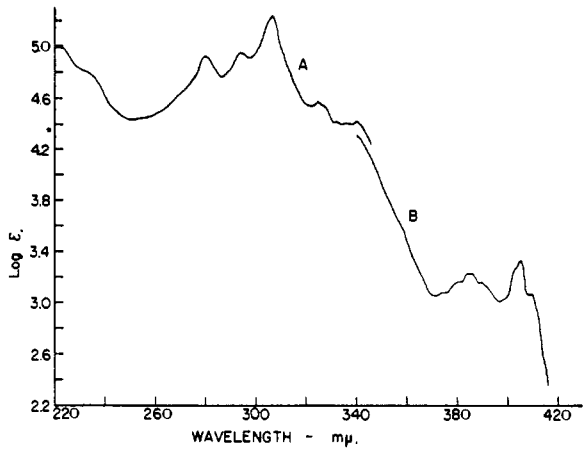


Fig. 1.—Ultraviolet absorption spectrum of 3′,7′-dihydroxy-1,2,5,6-dibenzanthracene in absolute ethanol: curve A, concn. = 4×10^{-6} mole/liter; curve B, concn. = 2×10^{-5} mole/liter.

α,α′-Di-(2-nitro-5-methoxybenzal)-phenylene-1,4-diacetic Acid (II).—Fourteen grams (0.077 mole) of 2-nitro-5-methoxybenzaldehyde, 7.37 g. (0.038 mole) of phenylene-1,4-diacetic acid, 7.78 g. (0.077 mole) of triethylamine and 100 ml. of acetic anhydride were stirred at 90–95° for 8–9 hours; a yellow precipitate began to separate after the first hour. This redissolved when, at the end of the reaction, the excess anhydride was decomposed with 100 ml. of water at the boiling point, and the resulting red solution deposited fine yellow crystals (10.0 g.) on cooling. These were filtered off and the mother liquor poured into 200 ml. of 5% hydrochloric acid; the oily precipitate, dissolved in sodium bicarbonate solution and reprecipitated with acid, gave 5 g. of a sticky tan solid. This was washed with several small portions of cold acetone, leaving 1.3 g. of yellow powder which was combined with the main fraction. One recrystallization from dilute acetone gave 10.0 g. (51%) of II in silky pale yellow needles, m.p. 291–292°. A sample recrystallized once more from dilute acetone for analysis melted at 291.5–292°. This compound also formed a crystalline complex, m.p. 268.5–270°, with dioxane.

Anal. Calcd. for $C_{26}H_{20}O_{10}N_2$: C, 60.00; H, 3.87. Found: C, 60.02; H, 3.82.

α,α′-Di-(2-amino-5-methoxybenzal)-phenylene-1,4-diacetic Acid (V).—A solution of 10.4 g. of II in 800 ml. of 14% ammonium hydroxide was added with stirring to a hot ferrous hydroxide sludge prepared from 80 g. of ferrous sulfate heptahydrate, 300 ml. of water and 300 ml. of concentrated ammonium hydroxide. After heating 1.5 hours, the black mixture was filtered with suction and the residue extracted with a small amount of hot ammonium hydroxide which was added to the filtrate. Acidification of the hot yellow solution with acetic acid deposited the amino acid V (8.7 g., 95%) in lustrous mustard-yellow needles, m.p. 293–294.5° dec. If the cold ammoniacal solution was acidified, the amino acid precipitated as a bright yellow amorphous powder.

This amino acid resembled IV in being insoluble in organic solvents. It was, however, very slightly soluble in 1% hydrochloric acid at the boiling point, and on cooling the acid solution deposited **V hydrochloride** in silky white needles, m.p. 279–281°. The hydrochloride was hydrolyzed almost instantly by water or alcohol, with reappearance of the bright yellow amine.

The amino acid dissolved rather slowly in dilute sodium carbonate solution with only slight darkening.

(13) M. E. Smith, E. Elisberg and M. L. Sherrill, THIS JOURNAL, **68**, 1301 (1946).

(14) (a) D. Papa, E. Schwenk and A. Klingsberg, *ibid.*, **68**, 2133 (1946); (b) E. Schwenk and D. Papa, *J. Org. Chem.*, **11**, 798 (1946).

Since V could not be purified for analysis, it was converted into its diacetyl derivative for this purpose. Two hundred and fifty milligrams of V (0.54 millimole), 5 ml. of acetic anhydride and 5 drops of pyridine were boiled for 5 minutes and water added to the solution until the diacetylamine began to crystallize. Two hundred and ninety milligrams (100%) of Va was obtained as glistening grayish-white needles, m.p. 298–300° with loss of CO_2. The product was decolorized with charcoal in dilute acetic acid and recrystallized once more from this solvent; 240 mg. of **α,α'-di-(2-acetylamino-5-methoxybenzal)-phenylene-1,4-diacetic acid** of m.p. 301–302° was obtained.

Anal. Calcd. for $C_{36}H_{28}O_8N_2$: C, 66.16; H, 5.18; N, 5.14. Found: C, 66.02; H, 5.02; N, 5.25.

2',7'-Dimethoxy-3,4,5,6-dibenzphenanthrene-1,8-dicarboxylic Acid (VI) and 3',7'-Dimethoxy-1,2,5,6-dibenzanthracene-4,8-dicarboxylic Acid (VIII).—For diazotization of the amino acid V, 9.20 g. (0.02 mole) of the compound was dissolved in a solution of 4.24 g. (0.04 mole) of sodium carbonate in 180 ml. of water, the solution chilled in ice (causing some crystallization of sodium salt), and a cold solution of 2.90 g. (0.04 mole plus 2%) of 97% sodium nitrite in 15 ml. of water added to it with stirring. The mixture was stirred rapidly into 15 ml. of concentrated hydrochloric acid and ice, giving a slightly cloudy brownish-yellow solution. This diazotization mixture gave an immediate strong coupling test with alkaline β-naphthol solution (brilliant magenta solution from which the purplish-red sodium salt crystallized on standing). The mixture was stirred at 0° for 1 hour to ensure complete reaction, a small quantity of urea was added to destroy excess nitrous acid, and the mixture made just alkaline with sodium carbonate. It was then stirred vigorously at room temperature for 3 hours, but evolution of nitrogen was negligible during this period and the solution continued to give a strong coupling test with alkaline β-naphthol solution; on warming to 60–70°, however, gas evolution became vigorous and after about 2 hours at this temperature the coupling test became negative. Acidification precipitated a tan solid which was coagulated by heating and filtered; 8.20 g. (96%) of this crude product was isolated. Extraction of this material with 500 ml. of boiling acetone left 4 g. of yellowish-tan powder; the acetone extract on cooling deposited 0.95 g. (fraction A) of partly crystalline yellow substance which darkened at 305° and melted at 315–323° dec.; evaporation of the mother liquor left only a tarry residue from which no single compound could be isolated.

The original residue from acetone extraction was further extracted with 200 ml. of hot acetic acid, which removed a small quantity of dark tar and left 3.5 g. of yellow powder; this was dissolved in 30 ml. of boiling 10% sodium hydroxide solution. On cooling, the filtered alkaline solution deposited yellow crystals (fraction B); acidification of the mother liquor yielded 1.75 g. of tan powder (fraction C) which was readily soluble in 3 ml. of cold 10% sodium hydroxide solution. After reprecipitation by acid, fraction C was dissolved in a large volume of hot acetone; cooling of this solution deposited 0.6 g. of yellow crystals, m.p. 330–335° dec. (fraction D).

The crystalline sodium salt (fraction B) was dissolved in hot water, filtered from a trace of insoluble residue, and acidified, yielding 1.35 g. of yellow powder (fraction E), m.p. 350–355° dec. This material was again crystallized from 35 ml. of 10% sodium hydroxide solution; decomposition of the yellow sodium salt with acid gave 1.10 g. of a fine yellow powder (fraction F), almost insoluble in acetone, acetic acid, nitrobenzene and ethyl benzoate, and slightly soluble in boiling pyridine. Acidification of the alkaline mother liquor precipitated 0.15 g. of yellow powder (fraction G) which was readily soluble in cold pyridine.

Fraction F was recrystallized from 200 ml. of pyridine, giving 600 mg. of analytically pure **3',7'-dimethoxy-1,2,5,6-dibenzanthracene-4,8-dicarboxylic acid** (VIII), which decomposed without melting at 357°; the compound was characterized as a dibenzanthracene derivative by oxidation to the dibenzanthraquinone and subsequently by spectroscopic examination of the dihydroxy compound XI (see below).

Anal. Calcd. for $C_{26}H_{18}O_6$: C, 73.23; H, 4.25. Found: C, 73.22; H, 4.28.

Concentration of the pyridine mother liquor of fraction F to a small volume gave no further precipitate; on acidification of the concentrate 0.5 g. of yellow powder (fraction H), m.p. 330–340° dec., was obtained.

Fraction A (the crystalline material isolated from the original acetone extract of the crude product) was dissolved in 5 ml. of hot 10% sodium hydroxide solution, and the small quantity of crystals which separated from the cold solution filtered off. On decomposition by acid these yielded 0.25 g. of powder which on recrystallization from pyridine gave another 77 mg. of the dibenzanthracene derivative VIII. A total of 677 mg. (8%) of pure VIII was thus obtained.

Acidification of the alkaline mother liquor of fraction A gave 0.65 g. of solid, m.p. 330–340° dec., which appeared identical with fractions D, G and H. These were therefore combined and recrystallized several times from acetone, in which the material was only slightly soluble. Nine hundred milligrams (11%) of analytically pure **2',7'-dimethoxy-3,4,5,6-dibenzphenanthrene-1,8-dicarboxylic acid** (VI), m.p. 345–347°, was obtained as small yellow prisms.

Anal. Calcd. for $C_{26}H_{18}O_6$: C, 73.23; H, 4.25. Found: C, 73.32; H, 4.28.

Various attempts to isolate pure material from the remaining fractions by solvent extractions and crystallizations of sodium salts were unsuccessful. All of these fractions, however, gave faint brown color tests with alcoholic ferric chloride solution, indicating the presence of phenolic material.

The yield of cyclized products remained unaltered when decomposition of the diazonium salt (in alkaline solution) was carried out by stirring the mixture at room temperature for 24 hours.

A number of other methods for ring closure of the diamine V, including that of Cassaday and Bogert,[7c] were tried but yielded only resinous material containing no cyclized product.

3',7'-Dimethoxy-1,2,5,6-dibenzanthra-9,10-quinone-4,8-dicarboxylic Acid (IX).—Oxidation of the acid VIII was carried out by heating its suspension in acetic acid with chromic anhydride for a few minutes; the yellow solid which was filtered off was a mixture of unchanged crystals of VIII with amorphous material. This precipitate gave a bright cherry-red solution when warmed with an alkaline solution of sodium hydrosulfite; the color changed to brown and then green (quinhydrone stage) and was eventually discharged on shaking the vat in air; it reappeared when fresh hydrosulfite was added.

If the oxidation mixture was refluxed until all the starting material had dissolved, only water-soluble products remained. Efforts to oxidize the dibenzphenanthrene derivative VI to a quinone with chromic anhydride also gave only water-soluble material.

3',7'-Dimethoxy-1,2,5,6-dibenzanthracene (X).—One hundred milligrams (0.23 millimole) of the dimethoxy acid VIII was mixed with a trace of precipitated copper powder and the mixture heated in 5 ml. of freshly distilled quinaldine. Carbon dioxide evolution was vigorous at 125–150°; heating was continued until no more gas was given off. On cooling, the mixture became semi-solid due to deposition of long grayish brown needles; dilution with 100 ml. of ether did not dissolve the product. The ether solution was filtered, the precipitate extracted with 100 ml. of boiling xylene and the solution decolorized with Norit; on cooling it deposited **3',7'-dimethoxy-1,2,5,6-dibenzanthracene (X)**, 49 mg., in fine white needles of m.p. 295–296°. Concentration of the mother liquor to a small volume gave an additional 4 mg. of product (total yield 69%).

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.39; H, 5.59.

The ether solution, after suitable washing with acid and sodium carbonate solution (which yielded no precipitate on acidification) and evaporation, gave only a trace of tarry residue.

2',7'-Dimethoxy-3,4,5,6-dibenzphenanthrene (VII).—The acid VI (250 mg., 0.59 millimole) was decarboxylated with 0.1 g. of copper powder in 5 ml. of freshly distilled quinaldine. Vigorous evolution of CO_2 occurred at about 200° and the reaction was completed by brief boiling. The almost black mixture was cooled, diluted with 100 ml. of ether, filtered from the copper, washed successively with dilute acid, dilute sodium carbonate solution, and water, and the ether evaporated. The sticky crystalline residue crystallized from acetic acid in brown needles and plates, m.p. 215–217°, 150 mg. (75%). Three recrystallizations

from acetic acid and one from dilute acetone gave brownish-yellow prisms, m.p. 222–223°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.19; H, 5.63.

The compound was moderately soluble in acetic acid, acetone and benzene, less so in ethanol, and insoluble in ligroin. Its solutions exhibited bright bluish-violet fluorescence.

Decarboxylation of By-products of Ring Closure.—Various samples of the tarry residues from the isolation of the dibenzanthracene and dibenzphenanthrene derivatives were decarboxylated with copper in boiling quinaldine and the mixtures worked up as above. In no case was an ether-insoluble product formed, so that no dibenzanthracene derivative had remained in the mixture. None of the samples yielded anything but tarry products; the decarboxylated material, however, had a strong phenolic odor and gave a brown coloration with alcoholic ferric chloride. Steam distillation of the tarry product gave a trace of oily white material, but the amount isolated was insufficient for identification.

3′,7′-Dihydroxy-1,2,5,6-dibenzanthracene (XI).—The dimethyl ether X proved entirely resistant to cleavage by 48% hydrobromic acid in acetic acid, alcoholic potassium hydroxide and alcoholic sodium ethoxide; in each case the starting material was recovered quantitatively. Treatment with anhydrous aluminum chloride in refluxing benzene gave only unchanged ether accompanied by a small amount of oily product. Demethylation of X was, however, accomplished very smoothly by pyridine hydrochloride. The dimethoxy compound (73 mg., 0.22 millimole) was heated with 3 g. of freshly fused pyridine hydrochloride until a homogeneous melt was obtained; dilution of the cooled melt with 20 ml. of water precipitated a very fine white powder which was readily coagulated by heating but darkened somewhat in the process. After filtration this product was dissolved in dilute sodium hydroxide solution (leaving no insoluble residue), reprecipitated with acid, and recrystallized from dilute acetone. Sixty-eight milligrams (100%) of **3′,7′-dihydroxydibenzanthracene (XI)** was obtained as flat grayish needles of analytical purity, m.p. 357–360°.

Anal. Calcd. for $C_{22}H_{14}O_2$: C, 85.14; H, 4.55. Found: C, 85.02; H, 4.58.

The compound is sparingly soluble in acetone, ethanol and acetic acid and the solutions exhibit intense violet fluorescence. The alkaline solution is yellow with bright green fluorescence. On exposure to daylight the material darkens appreciably in a few hours.

The ultraviolet spectrum of XI (Fig. 1) was determined in absolute ethanol from 220 to 420 mμ using a Beckman model DU spectrophotometer.

3′,7′-Diacetoxy-1,2,5,6-dibenzanthracene (XII).—Acetylation of 50 mg. (0.16 millimole) of XI with 5 ml. of acetic anhydride and a few drops of pyridine was complete in about 15 minutes at the boiling point. After decomposition of excess anhydride with water the acetyl derivative XII crystallized from the hot solution in fine, lustrous white plates of m.p. 291–292° (55 mg., 87%). Recrystallization from acetic acid did not change the melting point.

Anal. Calcd. for $C_{26}H_{18}O_4$: C, 79.17; H, 4.60. Found: C, 79.07; H, 4.57.

3′,7′-Diacetoxy-1,2,5,6-dibenzanthra-9,10-quinone (XIII).—The diacetyl derivative XII (55 mg., 0.14 millimole), suspended in 10 ml. of boiling acetic acid, was oxidized by addition of 50 mg. of chromic anhydride; the starting material dissolved rapidly and the quinone XIII (50 mg., 85%) crystallized from the boiling solution in small, well-shaped orange prisms of m.p. 295–298°. One recrystallization from acetic acid gave analytically pure material, m.p. 296.5–298°, in lustrous, slender orange needles.

Anal. Calcd. for $C_{26}H_{16}O_6$: C, 73.58; H, 3.81. Found: C, 73.35; H, 3.84.

The quinone gives a bright crimson vat on warming with alkaline hydrosulfite solution; shaking with air, however, does not decolorize the solution but produces instead a deep maroon solution of the hydrolysis product, the dihydroxyquinone (XIV). Addition of fresh hydrosulfite to the maroon solution gives a cherry-red vat of 3′,7′,9,10-tetrahydroxydibenzanthracene.

3′,7′-Dihydroxy-1,2,5,6-dibenzanthra-9,10-quinone (XIV).—The diacetoxyquinone (XIII) (25 mg., 0.059 millimole) was dissolved in a little alcohol, a few drops of sodium hydroxide solution added, and the mixture refluxed until solution was complete. The resulting deep maroon solution was acidified to yield a gelatinous red precipitate which appeared nearly black when filtered and dried. On brief heating in acetic acid it turned brick red; it dissolved very slowly in a large volume of this solvent and crystallized, on concentration of the solution to 5 ml., in small deep crimson needles, m.p. 375–385° dec. Eight milligrams (40%) of analytically pure material was obtained.

Anal. Calcd. for $C_{22}H_{12}O_4$: C, 77.64; H, 3.56. Found: C, 77.59; H, 3.55.

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

The Stereochemistry of the Leuckart Reaction

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The Leuckart reaction has been carried out on 2-methylcyclohexanone to give a mixture of the *cis*- and *trans*-2-methylcyclohexylamines. By analysis of the binary melting point diagram of *cis*- and *trans*-N-(2-methylcyclohexyl)-benzamide the product has been shown to consist of 60% of the *cis*-amine. These results have been interpreted in terms of a transition complex of the immonium salt and formate ion, specifically oriented.

The Leuckart reaction, the formation of amines from carbonyl compounds and ammonia or amines in the presence of formic acid, has been the subject of several recent investigations.[1–5] It has been shown to be suitable for the preparation of tertiary amines[6] and for the preparation of benzylamines.[7]

Recent interest in the mechanism of the reaction has led to a study of the kinetics of the reaction,[3] the reactivity of possible intermediates,[1,2] and a variety of proposals concerning the more intimate pathway of the reduction.[2,3] Less information is available however concerning the hydrogen transfer stage of the reaction. Alexander and Wildman[1] have shown that imines and certain benzyl alcohols may be reduced by formic acid; Pollard and Young[3] suggest a 1,3-migration of hydrogen in a formate ester; while Staple and Wagner[2] suggest reduction of the "carbenium ammonium salt" by hydride transfer.

It seemed of value to us to investigate the stereochemical course of the Leuckart reaction since such

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