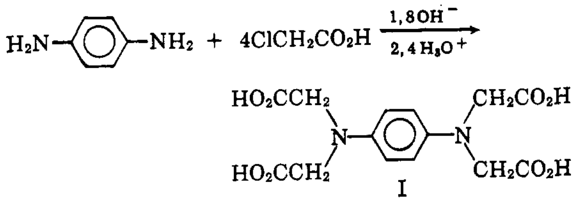
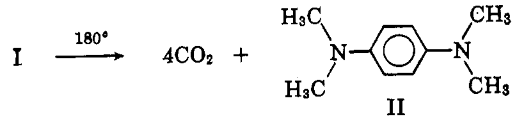
product is tedious, it is apparently the most satisfactory synthesis of N,N,N′N′-tetramethyl-*p*-phenylenediamine (II) yet reported. Application of the Eschweiler-Clark modification of the Leuckart Reaction[3] to *p*-phenylenediamine fails, apparently due to condensation of formaldehyde with the activated ring.[4] Although the decarboxylation of phenyliminodiacetic acid to N,N-dimethylaniline has been reported,[5] this type of reaction seems not to have been applied very frequently to the methylation of anilines. We wish to report a facile example of this reaction (eq. 2), which affords a ready synthesis of II.



(1)



(2)

Although the mechanism of the decarboxylation is presently unknown, the reported catalysis by ferric ion[5b] and the induction period occasionally observed in the present work are suggestive of a homolytic process.

Experimental

***p*-Phenylenediiminotetraacetic Acid (I).**—*p*-Phenylenediamine, 10.8 g. (0.1 mole), chloroacetic acid, 37.8 g. (0.4 mole), sodium hydroxide, 32.0 g. (0.8 mole), and potassium iodide, 5.0 g. (0.03 mole), were dissolved in 500 ml. of water and boiled under reflux for 1 hr. To the hot solution there was added cautiously 40 ml. of concentrated hydrochloric acid. The precipitate which formed upon cooling the solution in ice was filtered with suction and dried under vacuum at room temperature. The nearly colorless crystals melted at 165° with decomposition (lit.[6] m.p. 165° dec.) and weighed 18.9 g. (55%).

Decarboxylation of I to N,N,N′,N′-Tetramethyl-*p*-phenylenediamine (II).—I (17.0 g., 0.05 mole) was placed in a large vacuum sublimation apparatus which was then evacuated by means of an aspirator to approximately 20 mm. A Wood's Metal bath which had been preheated to 180° was cautiously applied to the sublimer. Melting of the solid was accompanied by evolution of gas, and the product sublimed on the cold finger.

In order to remove colored impurities the product was dissolved in petroleum ether (b.p. 30–60°) and passed through a short column of basic activated alumina. Evaporation of the solvent, followed by one additional vacuum sublimation, afforded colorless crystals (4.3 g., 52%), m.p. 51–52° (lit.[2] m.p. 51°). Recrystallization from petroleum ether afforded glistening platelets of the same melting point. The visible absorption spectrum of the radical cation, "Wurster's Blue," formed on oxidation of the amine was in quantitative agreement with that reported.[7] Several samples of the purified amine have remained colorless in contact with air, but with exclusion of light and moisture, for periods of up to 3 years.

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(4) J. R. Cox, Jr., unpublished results.

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Arylation Reactions of Anthraquinones. The Preparation of 1-Aryl-4-aminoanthraquinones

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Nesmeyanow and co-workers[1] have studied the decomposition of the simpler diazonium fluoroborates in organic solvents; low yields of arylated products are always obtained.[2] In intramolecular arylations (Pschorr synthesis), fluoroborates are good sources of radicals; for example, benzofluorenone is obtained in 66% yield.[3] The thermal decomposition of a number of anthraquinone diazonium fluoroborates, for example, anthraquinone-1-diazonium fluoroborate and -1,5-bisdiazonium fluoroborate, in aromatic solvents gives the corresponding fluorinated anthraquinones[4] in high yield; however, the diazonium fluoroborates derived from 1-amino-4-chloro- and 1-amino-4-nitroanthraquinone under similar conditions proved to be effective sources of anthraquinyl radicals. These compounds, when decomposed by heating a suspension in an aromatic solvent, form 1-aryl-4-chloro- and 1-aryl-4-nitroanthraquinones in yields of 40–65%.

The yields reported in Table I were calculated by analysis of the crude reaction product. The melting points refer to products purified by several recrystallizations.

TABLE I

Anthraquinone-1-chloro-4-	Yield, %	M.p., °C.
o-Dichlorophenyl-	61	267–268
Nitrophenyl-	44	273–274
α-Chloronaphthyl-	48	274–275
α-Bromonaphthyl-	43	260–264
Anthraquinone-1-nitro-4-		
o-Dichlorophenyl-	43	261–264
Bromophenyl-	39	295–298

It has been suggested that arylations by thermal decomposition of diazonium fluoroborates involve cationoid radical intermediates. Phenyl diazonium fluoroborate decomposed in methyl benzoate gives *m*-phenyl benzoate but little of the *para* isomer.[5] In the Pschorr synthesis the operation of two distinct mechanisms, ionic and radical, has been suggested.[6] In the present work there is also evidence of a cationoid intermediate in that only with electron-attracting substituents can arylation (a) compete with the Schiemann reaction (b). (See p. 490 col. 1.)

The 1-aryl-4-chloroanthraquinones when treated with *p*-toluenesulfonamide[7] form 1-aryl-4-*p*-toluenesulphonamidoanthraquinones which on hydrolysis in sulfuric

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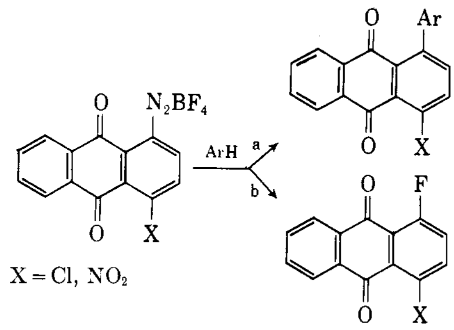

acid yield 1-aryl-4-aminoanthraquinones. Identical amines are obtained by causing the chloro compound to react with ammonia in an autoclave.[8] The 1-aryl-4-nitroanthraquinones on heating with aqueous sodium sulfide[9] afford the corresponding amines in good yield. These appear to be the first arylated α-aminoanthraquinones prepared and could be valuable intermediates for new anthraquinoid dyes.

Experimental

Decomposition of 1-Chloro-4-diazonium Fluoroborate Anthraquinone in o-Dichlorobenzene to Yield 1-Chloro-4-(o-dichlorophenyl)anthraquinone.—1-Chloro-4-amino-anthraquinone (50 g.) was dissolved in concentrated sulfuric acid (200 ml.) and diazotized with nitrosylsulfuric acid solution (200 ml., prepared from 20 g. of sodium nitrite and concentrated sulfuric acid) in 1 hr. at 0–10°. The resulting solution was stirred until on the addition of several drops to water a clear orange solution was formed. The product was poured onto ice (1 kg.). The **anthraquinone diazonium sulfate** was precipitated, removed by filtration, washed with a small amount of cold water, and dissolved in 5 l. of water, insoluble impurities being removed by filtration. Fluoroboric acid (40%, 50 ml.) was added with stirring and the precipitated **1-chloro-4-diazonium fluoroborate anthraquinone** (50 g., 82%) was removed by filtration, washed with methanol, and dried (decomposition temperature, 180–181°).

The diazonium salt (20 g.) was suspended in o-dichlorobenzene (150 ml.) and heated slowly to boiling while being stirred. During the decomposition the solution turned from red to brown and a heavy stream of boron trifluoride escaped. After 2 hr., the solution was decolorized with activated carbon and filtered while hot and the o-dichlorobenzene solution was reduced in volume to 30 ml. (Found: Cl, 19.2% or 61% of arylation.). The yellow product which separated on cooling was recrystallized from chlorobenzene to yield **1-chloro-4-(o-dichlorophenyl)anthraquinone**, 10.5 g., 49%, m.p. 267–268°.

Anal. Calcd. for $C_{20}H_9Cl_3O_2$: C, 61.9; H, 2.3; Cl, 27.5. Found: C, 61.85; H, 2.4; Cl, 27.4.

1-Chloro-4-(α-chloronaphthyl)anthraquinone.—1-Chloro-4-diazonium fluoroborate anthraquinone (15 g.) was suspended in α-chloronaphthalene (100 ml.) and slowly heated to 180–190° and kept at this temperature for 1 hr. with stirring. Decolorizing carbon was added, the solution was filtered, reduced in volume to 10 ml., and then boiled in chlorobenzene (100 ml.). On cooling the solution a yellow precipitate was obtained (Found: Cl, 15.5% or 48% of arylation.) which was recrystallized from chlorobenzene (6 g., 35%), m.p. 274–275°.

Anal. Calcd. for $C_{24}H_{12}Cl_2O_2$: C, 71.5; H, 3.0; Cl, 17.6. Found: C, 71.75; H, 3.0; Cl, 17.9.

1-Chloro-4-(nitrophenyl)anthraquinone.—1-Chloro-4-diazonium fluoroborate anthraquinone (20 g.) was thermally decomposed in nitrobenzene (150 ml.). Nitrogen analysis of the reaction product showed 44% of arylation had occurred. Two recrystallizations from chlorobenzene gave the yellow 1-chloro-4-(nitrophenyl)anthraquinone, m.p. 273–274°, 6.1 g., 30%.

Anal. Calcd. for $C_{20}H_{10}ClNO_4$: C, 66.1; H, 2.8; Cl, 9.8; N, 3.85. Found: C, 66.0; H, 3.0; Cl, 9.9; N, 3.8.

1-Chloro-4-(α-bromonaphthyl)anthraquinone.—Similarly, decomposition of 1-chloro-4-diazonium fluoroborate anthraquinone in α-bromonaphthalene gave 43% of arylation. Recrystallization from chlorobenzene afforded the red-brown 1-chloro-4-(α-bromonaphthyl)anthraquinone, m.p. 260–264°.

Anal. Calcd. for $C_{24}H_{12}BrClO_2$: C, 64.5; H, 2.7; Cl, 7.95. Found: C, 63.8; H, 2.8; Cl, 8.05.

Decomposition of 1-Nitro-4-diazonium Fluoroborate Anthraquinone in o-Dichlorobenzene to Yield 1-Nitro-4-(o-dichlorophenyl)anthraquinone.—1-Nitro-4-aminoanthraquinone (50 g.) was diazotized with nitrosylsulfuric acid solution and converted to 1-nitro-4-diazonium fluoroborate anthraquinone, 60 g., 89%, decomposition temperature of 171–172°, in the manner described.

The diazonium salt (20 g.) was suspended in o-dichlorobenzene (150 ml.), brought slowly to boiling, and further treated as in the above cases. The solution was reduced in volume to 30 ml. and filtered. The solid, 12.1 g. (Found: Cl, 7.7% or 43% of arylation), was recrystallized from chlorobenzene to yield 7.3 g., 37%, m.p. 241–244°.

Anal. Calcd. for $C_{20}H_9Cl_2NO_4$: C, 60.3; H, 2.25; Cl, 17.85; N, 3.5. Found: C, 60.8; H, 2.3; Cl, 17.3; N, 3.7.

1-Nitro-4-bromophenylanthraquinone.—1-Nitro-4-diazonium fluoroborate anthraquinone when decomposed in bromobenzene gave 39% of arylation (nitrogen analysis). The pure red-brown 1-nitro-4-bromophenylanthraquinone isolated after recrystallization from chlorobenzene had m.p. 295–298°.

Anal. Calcd. for $C_{20}H_{10}BrNO_4$: C, 58.8; H, 2.45; N, 3.45. Found: C, 59.3; H, 2.5; N, 3.4.

1-Amino-4-(o-dichlorophenyl)anthraquinone.—1-Chloro-4-(o-dichlorophenyl)anthraquinone (6 g.), toluene-p-sulfonamide (4 g.), copper acetate (2 g.), potassium carbonate (2 g.), and o-dichlorobenzene (100 ml.) were heated slowly to the boiling point and kept under reflux for 5 hr. After cooling the mixture was filtered, and the precipitate washed with boiling alcohol and water, and dried. The resulting **anthraquinonesulphonamide** was recrystallized from anisole to give 6.9 g., 85%, m.p. 268–269°.

The sulfonamide (4 g.) was dissolved in concentrated sulfuric acid (40 ml.) and heated for 1 hr. at 80–90°. It was poured on to ice to yield a red precipitate of 1-amino-4-(o-dichlorophenyl)-anthraquinone, which was recrystallized from anisole to yield 2.6 g., 93%, m.p. 283–284°.

Anal. Calcd. for $C_{20}H_{11}Cl_2NO_2$: C, 65.9; H, 3.35; Cl, 19.25; N, 3.8. Found: C, 66.0; H, 3.45; Cl, 19.95; N, 3.9.

Reduction of 1-Nitro-4-(o-dichlorophenyl)anthraquinone.—1-Nitro-4-(o-dichlorophenyl)anthraquinone (2.5 g.) was ground to a paste with sodium sulfide nonahydrate (5 g.), suspended in hot water, and maintained at 70–80° with stirring for 90 min. The 1-amino-4-(o-dichlorophenyl)anthraquinone was removed by filtration, washed with hot water, alcohol, and ether, and recrystallized from anisole to give brilliant red crystals, 2.1 g., 91%, m.p. 281–284°

Anal. Calcd. for $C_{20}H_{11}Cl_2NO_2$: Cl, 19.3; N, 3.8. Found: Cl, 19.4; N, 3.85

Similarly, 1-nitro-4-bromophenylanthraquinone (2 g.) was converted to 1-amino-4-bromophenylanthraquinone (1.8 g., 90%), m.p. 285–290°.

Anal. Calcd. for $C_{20}H_{12}BrNO_2$: C, 63.5; H, 3.2; N, 3.7. Found: C, 62.8; H, 3.1; N, 3.8.

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[9] W. H. Beisler and L. W. Jones, *J. Am. Chem. Soc.*, **44**, 2304 (1922).

The Synthesis of 4′,5′-Diiodo-4-aminofluorescein Iodine-131

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The method developed by Coons and colleagues[3] for labeling antibody proteins with fluorescein isocyanate has become a frequently used tool in immunology. Since Coons' original paper was published in 1942

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[2] Operated by the University of Chicago for the U. S. Atomic Energy Commission.

[3] A. H. Coons, H. J. Creech, R. N. Jones, and E. Berliner, *J. Immunol.*, **45**, 159 (1942).