In the preparation of acetylpyrrole V, the crude product was distilled *in vacuo* prior to subsequent purification by recrystallization.

The *N*-(β-carbomethoxypropionyl)piperidine (VI) required for the synthesis of pyrrole III was prepared by the addition of methyl β-(chloroformyl)propionate (1 mole) to an ethylene dichloride solution of piperidine (2 moles). After removal of the piperidine hydrochloride by filtration, the filtrate was treated with phosphoryl chloride with cooling, and the pyrrole I was then introduced. Following the reflux period, the mixture was cooled to room temperature, then shaken well with aqueous sodium acetate solution. The ethylene dichloride phase was evaporated to dryness, and the residue was purified by recrystallization.

In the preparation of pyrrole II, solid pyrrole I and then ethylene dichloride were added to the *N*,*N*-dimethylacetamide–phosphoryl chloride mixture. Following the reflux period, the product was worked up as described in the case of pyrrole III.

Acylation procedure B. The procedure employed is based upon that described by Campaigne and Archer[18] for the preparation of *p*-dimethylaminobenzaldehyde.

In the cases of aldehydes VIII and XII *N*,*N*-dimethylformamide was present in considerable excess. A solution of the starting pyrrole in the latter was added to the *N*,*N*-dimethylformamide–phosphoryl chloride mixture. In the preparation of acylpyrroles IV, IX, X, and XI the solid pyrrole to be acylated was added to the appropriate *N*,*N*-disubstituted amide–phosphoryl chloride mixture.

The reaction mixture in the preparation of benzoylpyrrole IV proved to be largely immiscible with aqueous sodium acetate solution. Homogeneity was achieved by addition of ethanol and by heating for a few minutes. The product crystallized upon standing. The *N*-benzoylmorpholine[14] required for this acylation experiment was prepared and isolated prior to use.

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(18) E. Campaigne and W. L. Archer, *Org. Syntheses*, **33**, 27 (1953).

Condensation of 3-Aminoquinones with *o*-Phenylenediamine[1]

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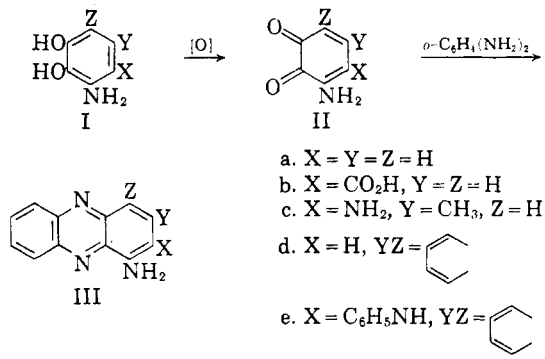
To investigate their conversion to pyridine compounds,[3] five unisolated 3-amino-1,2-quinones (II) have been prepared from corresponding aminocatechols (I) by oxidation with silver oxide or lead dioxide. Each aminoquinone and 3-nitro-4-anilinonaphthoquinone-1,2 is transformed to the corresponding derivative of 1-amino-(III) and 1-nitrophenazine by condensation with *o*-phenylenediamine in an inert solvent.[4]



EXPERIMENTAL[5]

Preparation of aminocatechols (I). *3-Aminocatechol* (Ia). According to Vermeulen[6] 3-nitrocatechol, m.p. 86°, was obtained in 15% yield on nitration of catechol with red fuming nitric acid in ether, and was reduced in 68% yield with tin in hydrochloric acid,[6] in 31% yield by aluminum amalgam in ether, or in 75% yield by hydrogen over palladium on charcoal to unstable 3-aminocatechol, m.p. 142–145°, isolated as its hydrochloride salt, m.p. 198–202.5° dec.[6]

3,4-Dihydroxyanthranilic acid (Ib). To 50.0 g. (0.33 mole) of vanillin and 60 ml. of pyridine in a round bottom flask equipped with a condenser and drying tube and externally cooled to 10°, 50 ml. of acetyl chloride was slowly added with shaking while the temperature did not rise appreciably. The mixture was heated about 1 hr. on a steam bath until the contents became an amber syrup. On addition of 100 g. of ice with stirring the syrup solidified. A pale yellow precipitate of *3-methoxy-4-acetoxybenzaldehyde* recrystallized from ethanol as colorless fluffy needles, 52.1 g. (81.7%), m.p. 76°.[7] It was nitrated[8] in 77.4% yield to *2-nitro-3-methoxy-4-acetoxybenzaldehyde*, m.p. 85.5° by red fuming nitric acid in carbon tetrachloride at 5°.

To 13.0 g. (0.054 mole) of this aldehyde in 84 ml. of glacial acetic acid, 120 ml. of 30% hydrogen peroxide was added at room temperature. After 3 hr. 30 ml. of 30% hydrogen peroxide was added. After 24 hr. evaporation of the solvent in an air stream left a yellow solid, *2-nitro-3-methoxy-4-acetoxybenzoic acid*, which recrystallized from ethanol as yellow plates, 12.5 g. (91.2%) m.p. 265–267°. On treatment with 160 ml. of 10% aqueous sodium hydroxide with warming to 45°, followed by neutralization with 10% hydrochloric acid, 12.5 g. (0.049 mole) of the acid was hydrolyzed to pale yellow amorphous *2-nitrovanillic acid* which recrystallized

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(2) This investigation was carried out during the tenure of a Predoctoral Fellowship from the National Heart Institute, United States Public Health Service, 1959–1960.

(3) J. H. Boyer and L. R. Morgan, Jr., *J. Am. Chem. Soc.*, **82**, 4748 (1960).

(4) Previously a preferred method for the preparation of 1-aminophenazine (III) consisted in heating 1-amino-6-nitrodiphenylamine with ferrous oxalate dihydrate and lead at 250–260°. (D. L. Vivian, *J. Org. Chem.*, **21**, 565 (1956)). The yield is more than doubled in the present procedure. Derivatives of 1-aminophenazine have been obtained in unspecified poor yield from condensation in acetic acid at 40° of *o*-phenylenediamine as its hydrochloride and corresponding derivatives of 3-aminobenzoquinone-1,2. The unisolated aminoquinones were obtained from corresponding aminocatechols by atmospheric oxidation in an ammoniacal solution. (F. Kehrmann and P. Prunier, *Helv. Chim. Acta*, **7**, 984 (1924). F. Kehrmann and N. Poehl, *Helv. Chim. Acta*, **9**, 485 (1926)).

(5) Semimicro analyses by Alfred Bernhardt, Max Planck Institut Microanalytisches Laboratorium, Mülheim (Ruhr), Germany. Melting points are uncorrected.

(6) M. H. Vermeulen, *Rec. trav. chim.*, **25**, 12 (1905).

(7) F. Tiemann and N. Nagai, *Ber.*, **11**, 646 (1878).

(8) A. Butenandt and H. G. Schlossberger, *Chem. Ber.*, **85**, 565 (1952).

from 50% ethanol as colorless plates, 9.5 g. (91.5%) m.p. 274–275° dec.

Anal. Calcd. for $C_8H_7NO_6$: C, 45.08; H, 3.31; N, 6.57. Found: C, 45.23; H, 3.26; N, 6.61.

Hydrogen (1 atm.) over 500 mg. of 10% palladium on charcoal in 200 ml. of ethanol reduced 2.4 g. (0.0112 mole) of 2-nitrovanillic acid to colorless needles (from aqueous ethanol) of *2-aminovanillic acid*, 1.88 g. (92.3%) m.p. 186.5–187.5°.

Anal. Calcd. for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65. Found: C, 51.99; H, 4.95; N, 7.66.

According to Hellman and Wiss,[9] 2-aminovanillic acid was hydrolyzed in refluxing 48% hydrobromic acid under a nitrogen atmosphere to *3,4-dihydroxyanthranilic acid* isolated as its hydrobromide salt, colorless needles, m.p. 207–208°,[9] in 95.6% yield. Treatment of the hydrobromide with aqueous sodium acetate gave the free amino acid as a colorless microcrystalline solid, m.p. 175° dec.[9] in 91.2% yield.

3,4-Dihydroxy-5,6-diaminotoluene (Ic). Methylation[10] of 3-methoxy-4-hydroxytoluene gave *3,4-dimethoxytoluene*, b.p. 50–52° (0.125 mm.),[10] in 87.1% yield.

To a suspension of 46.8 g. (0.307 mole) of 3,4-dimethoxytoluene in 143 ml. of carbon tetrachloride at 5° 143 ml. of red fuming nitric acid (sp. gr. 1.61) was added dropwise with stirring as the temperature was maintained 8–12°. Stirring was continued for 1 hr. at 0°, 300 g. of ice were added and stirring continued for another hour. Recrystallization of a yellow precipitate from a mixture of methanol (3 parts) and ethanol (1 part) gave 16.2 g. (21.7%) of *3,4-dimethoxy-5,6-dinitrotoluene* as long yellow needles, m.p. 119–120°.[11]

Anal. Calcd. for $C_9H_{10}N_2O_8$: C, 44.63; H, 4.16; N, 11.57. Found: C, 44.61; H, 4.09; N, 11.52.

Concentration of the methanol-ethanol mother liquor from the first recrystallization to one-quarter volume permitted the separation of *3,4-dimethoxy-6-nitrotoluene* as short fluffy yellow needles, 4.6 g. (7.6%) m.p. 119–120° after recrystallization from the same solvent.

Anal. Calcd. for $C_9H_{11}NO_4$: C, 54.82; H, 5.62; N, 7.10. Found: C, 54.72; H, 5.59; N, 7.12.

In 250 ml. of ethanol containing 400 mg. of 10% palladium-on-charcoal, 1.2 g. (0.0046 mole) of 3,4-dimethoxy-5,6-dinitrotoluene was treated with hydrogen (2 atm.) for 6 hr. at room temperature. An amber oil, remaining on evaporation of the filtrate separated from catalyst, was dried over anhydrous sodium sulfate in hot chloroform. Treatment of the recovered amber oil with a few drops of 48% hydrobromic acid produced a violet crystalline solid on cooling in an ice bath which was isolated by filtration under nitrogen. It recrystallized from absolute ethanol as microcrystalline *3,4-dimethoxy-5,6-diaminotoluene hydrobromide*, 0.62 g. (41.3%) m.p. 180–185° dec. In an evacuated desiccator it darkened and became an oil after 2 days. Elemental analysis was not attempted.

A suspension of 1.16 g. (0.0035 mole) of the crude hydrobromide in 20 ml. of 48% hydrobromic acid was refluxed for 10 hr. under nitrogen. The heterogenous straw-colored mixture was cooled in an ice bath and filtered quickly. Extremely hygroscopic crystals were separated which recrystallized from 48% hydrobromic acid as red microcrystalline *3,4-dihydroxy-5,6-diaminotoluene hydrobromide*, 0.71 g. (67.5%) m.p. 162–167° dec. Attempts to obtain the free base from this impure salt led to unidentified material. Identification was based on elemental analysis of the phenazine derivative (IIIc, Table I) of the corresponding 3,4-diamino-5-methylbenzoquinone-1,2 (IIc).

3-Amino-1,2-dihydroxynaphthalene (Id). According to Fieser and Ames,[12] *3-nitronaphthoquinone-1,2*, m.p. 159–161°, was obtained as red needles in 65% yield from β-naphthoquinone and nitric acid (sp. gr. 1.40) and was reduced according to Grooves[13] by tin in hydrochloric acid to *3-amino-1,2-dihydroxynaphthalene hydrochloride* isolated as yellow plates, m.p. 141° dec. in 73.2% yield. The free base precipitated from the hydrochloride salt in boiling aqueous sodium acetate as yellow plates from the cooled mixture. A yield of 91.6% was obtained with m.p. 164.5°.[13]

3-Amino-4-anilino-1,2-dihydroxynaphthalene (Ie). According to Korn[14] red *3-nitro-4-anilino-1,2-naphthoquinone*, m.p. 253–254° dec. was obtained from 3-nitro-1,2-naphthoquinone and aniline in ethanol in 39.4% yield. It recrystallized as metallic red plates from *p*-xylene.

Anal. Calcd. for $C_{16}H_{10}N_2O_4$: C, 65.31; H, 3.42; N, 9.52. Found: C, 65.90; H, 3.81; N, 9.31.

To a hot solution of 0.26 g. (0.0014 mole) of 3-nitro-4-anilino-1,2-naphthoquinone in 20 ml. of glacial acetic acid, a solution of 0.36 g. (0.002 mole) of *o*-phenylenediamine hydrochloride and 0.6 g. of sodium acetate in 2.5 ml. of water was added. The mixture was digested on the steam bath for 15 min. as yellow *1-nitro-2-anilino-3,4-benzophenazine* separated. It recrystallized from benzene as a yellow amorphous solid, 0.41 g. (80.5%) m.p. 227–230° dec.

Anal. Calcd. for $C_{22}H_{14}N_4O_2$: C, 72.12; H, 3.85; N, 15.29. Found: C, 72.62; H, 4.13; N, 14.69.

A mixture of 0.5 g. (0.0017 mole) of 3-nitro-4-anilino-1,2-naphthoquinone and 6 g. of granular tin in 20 ml. of concd. hydrochloric acid was stirred at room temperature for 2 hr. or until the red color of the quinone had disappeared. From the concentrated filtrate, separated from washed inorganic material, a colorless microcrystalline solid, *3-amino-4-anilino-1,2-dihydroxynaphthalene hydrochloride*, separated. It recrystallized from ethanol as colorless microcrystals, 0.24 g. (46.6%) m.p. 211–213° dec.

Anal. Calcd. for $C_{16}H_{14}N_2O_2$.HCl: C, 63.47; H, 4.99; N, 9.26. Found: C, 63.56; H, 4.93; N, 9.21.

Preparation of 1-aminophenazines (III). *1-Aminophenazine* (IIIa). A suspension of 0.5 g. (0.0031 mole) of 3-aminocatechol hydrochloride, 2.1 g. of silver oxide and 15 g. of anhydrous sodium sulfate in 400 ml. of ethyl acetate was shaken vigorously for 15 min. as the color changed from deep yellow to deep violet. To the filtrate, separated from in-

TABLE I

PREPARATION OF 1-AMINOPHENAZINES[a]

I → II → III

I	II Color	III[b] M.P.	III[b] Yield, %
a	Violet	183–184	67.7
b	Royal blue	272–275 (dec.)	67.1[c]
c	Royal blue	256–257 (dec.)	36.1[d]
d	Violet	190.5–191.5[e]	71.2
e	Royal blue	219–221.5	34.4[f]

[a] Solvent for I → II → III is ethyl acetate except for d in which case glacial acetic acid was used and the condensation with *o*-phenylenediamine was carried out according to the general procedure described for 1-nitro-2-anilino-3,4-benzophenazine. [b] Each of the five aminophenazines is red. [c] *Anal.* Calcd. for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.79; N, 17.57. Found: C, 65.14; H, 4.06; N, 17.77. [d] *Anal.* Calcd. for $C_{13}H_{12}N_4$: C, 69.62; H, 5.40; N, 24.98. Found: C, 69.75; H, 5.41; N, 25.04. [e] R. Zaertling, *Ber.*, *23*, 175 (1890). [f] *Anal.* Calcd. for $C_{22}H_{16}N_4$: C, 78.55; H, 4.79; N, 16.66; Found: C, 78.57; H, 4.72; N, 16.65.

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(11) M. Oberlin, *Arch. Pharm.*, **263**, 641 (1925).

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(13) C. E. Grooves, *J. Chem. Soc.*, 291 (1884).

(14) O. Korn, *Ber.*, **17**, 906 (1884).

soluble inorganic material by gravity filtration, was added 0.4 g. (0.0038 mole) of *o*-phenylenediamine in 20 ml. of ethyl acetate. The pink solution was heated on the steam bath for 30 min., cooled, and on evaporation to dryness under an air stream left an amber residue which recrystallized from benzene as red microcrystalline 1-aminophenazine, 0.41 g. (67.7%) m.p. 183–184°.[4]

This and other phenazines prepared in a similar manner are described in Table I. Lead dioxide could be substituted for silver oxide in each example.

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Acetyl Transfer during Hydrogenation of *p*-Nitrophenyl Acetate[1]

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In connection with other work, *p*-aminophenyl acetate (II) was needed. Since the literature preparation of II[3] is difficult and attended with low

$$p\text{-}HOC_6H_4NO_2 + Ac_2O \xrightarrow{H^+} \underset{I}{p\text{-}CH_3COOC_6H_4NO_2} \xrightarrow[C_2H_5OH]{Pt,\ H_2} [p\text{-}CH_3COOC_6H_4NH_2] \longrightarrow \underset{III}{p\text{-}HOC_6H_4NHCOCH_3}$$
II

yields, its preparation was attempted by the schematic representation shown above. The acetylation of *p*-nitrophenol went smoothly with acetic anhydride and a catalytic amount of sulfuric acid; however, the reduction of *p*-nitrophenyl acetate (I) at 850 p.s.i. and 120° in the presence of a platinum catalyst, gave not the desired product (II) but rather an isomer, *p*-hydroxyacetanilide (III) in high yield. To our knowledge, this is the first reported example of a *para* acetyl transfer during the reduction of I to yield probably II, then immediately III.

Many investigators,[4] though, have reported *ortho* acetyl and benzoyl transfers. Others[5] have shown that these transfers were, in some instances, intramolecular migrations that occurred because the *ortho* esters of aminophenyl acetate (isomer of II) and aminophenyl benzoate were very unstable. Thus, when formed, they rearranged quickly to the corresponding *N*-acetyl or -benzoyl derivatives; *i.e.*, the acetyl or benzoyl group migrated from the oxygen to the nitrogen atom.

IV V

R = acetyl or benzoyl

A satisfactory explanation for the isolation of *p*-hydroxyacetanilide (III) from *p*-nitrophenyl acetate (I) in high yield is still premature; however, our results indicate that the reaction is a reduction of a nitro group followed by an intermolecular aminolysis of an ester.

EXPERIMENTAL

p-Nitrophenyl acetate (I) was prepared from *p*-nitrophenol (30 g.), acetic anhydride (61 ml.), and 4 drops of concd. sulfuric acid in the usual way; m.p. 79–80°; yield 95%.

p-Hydroxyacetanilide (III) was prepared as follows: *p*-nitrophenyl acetate (290 g.), absolute ethanol (500 ml.), and platinum oxide catalyst (2.5 g.) were kept at 850 p.s.i. of hydrogen and at approximately 120° for 6 hr. The mixture cooled on standing overnight and was filtered. The solvent was removed and crude III crystallized; crude yield was quantitative and the yield after recrystallization from hot water was 77%; m.p. 163–166°; ethyl acetate was later found to be a better solvent than water for the recrystallization of III, so III was then recrystallized from ethyl acetate; m.p. 168–169° (mixed m.p. with known III 168–169°).

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(1) This note is based partly upon the thesis submitted by Ronald Feldstein to the Graduate School of American University in partial fulfillment of the requirements for the Master of Science degree.

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A Convenient Method for the Preparation of 3-Cyano-6-methyl-2(1H)pyridone

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There has been a continuing interest in this compound since 1944[1] as an intermediate in syn-

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