[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

# Oxidation–Reduction Potentials of Substituted Quinoneanils and Indoanilines

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The interpretation of the influence of substituent groups on the potentials of quinone–hydroquinone systems is complicated by the fact that the reduction of a quinone involves not merely the addition of hydrogen to an unsaturated center but a rather elaborate readjustment of double bonds resulting in the aromatization of a hydroaromatic nucleus. In contrast to the situation encountered in the simple saturation of a double linkage (azo-hydrazo system) or the addition of hydrogen to a radical (phenoxyl–phenol system), reduction cannot be considered, from a structural point of view, as the exact counterpart of oxidation. In attempting to interpret the influence of a substituent group on the potential of the system it is difficult to decide whether to attribute the effect to a modifying influence on the quinone or the hydroquinone structure, or if both factors are involved.
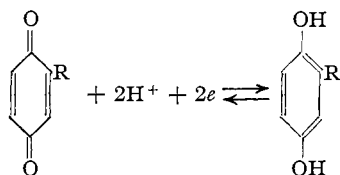
volved. That an alkyl or alkoxyl group lowers the potential of the benzoquinone system may mean either that the substituent has a damping effect on the unsaturated oxidant, resulting in decreased affinity for hydrogen, or that such a group in the reductant activates the hydrogen atom of the adjacent hydroxyl group to the point of increased susceptibility to oxidation. Calculations presented by one of us[1] based on a comparison of the critical oxidation potentials of phenol and of ortho alkyl- and alkoxyl-substituted phenols suggested that the influence on the hydroquinone structure is of considerable importance and probably predominates over the effect of the substituent in modifying the character of the oxidant.

The present work was undertaken in the hope of obtaining a more direct experimental answer to the question at issue. A substituent at position a of the quinonoid ring of quinoneanil (I) could influence the unsaturated system to which it is attached in the oxidant and, in the reductant (II), it might labilize or stabilize the hydrogen
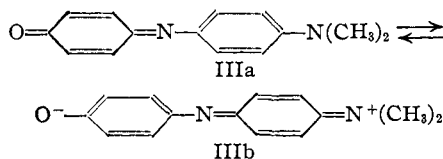
(1) Fieser, THIS JOURNAL, 52, 5204 (1930).
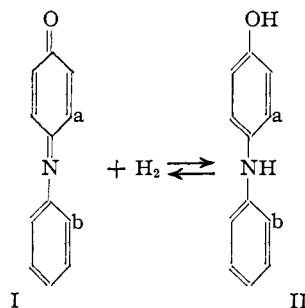
of the adjacent >NH group. There is good reason to believe that any influence on the meta hydroxyl group would be practically negligible. The effect of the group at a on the potential of the system would therefore represent a summation of two factors, referring respectively to the structures of the oxidant and the reductant. If the same substituent were located in the ortho position b of the benzenoid ring, any effect on the unsaturated nucleus of the oxidant would be negligible, whereas the effect on the >NH group of the reductant should be the same as for a substituent at position a. A raising or lowering of the potential associated with b-substitution therefore could be attributed solely to a modifying influence on the reductant, and a knowledge of the magnitude of this effect would make it possible to resolve the two factors involved in a substitution.

A few quinoneanils were prepared for potentiometric investigation, but it soon became apparent that the methods available for the synthesis of such compounds are so limited as to be inadequate for the preparation of a series of substances of the types desired. We therefore turned to the indoanilines, and found, as reported below, that in this series suitably substituted derivatives can be obtained satisfactorily. N,N-Dimethylindoaniline, or phenol blue (III), has been studied carefully by Cohen and Phillips,[2] who measured the potential in aqueous solution over a wide range of pH, and later, without reference to this work, by Schwarzenbach and Michaelis.[3] The substance is capable of tautomerism and can conceivably exist in the neutral region not only in the quinoneimine

(2) Cohen and Phillips, Suppl. No. 74, U. S. Pub. Health Repts., 1929.

(3) Schwarzenbach and Michaelis, THIS JOURNAL, 60, 1667 (1938).

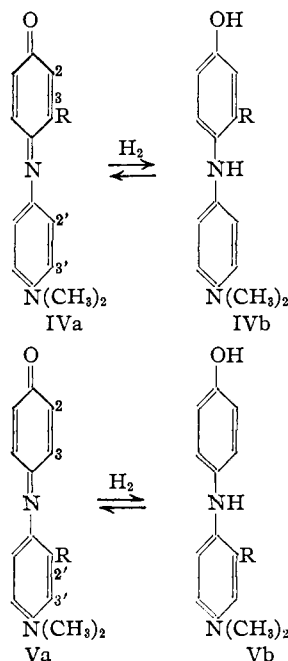form IIIa but also in the quinonediimine form IIIb. Since the potential of 1,4-quinoneimine

$$O= \!\!\!\left\langle\right\rangle\!\!\! =\!N-\!\!\!\left\langle\right\rangle\!\!\!-N(CH_3)_2 \rightleftarrows$$
IIIa

$$O^- \!\!\!\left\langle\right\rangle\!\!\!-N=\!\!\!\left\langle\right\rangle\!\!\! =N^+(CH_3)_2$$
IIIb

in aqueous solution[4] is 23 mv. lower than that of N,N-dimethylquinonediimine,[5] and since the dimethylamino group of IIIa would be more effective than the modified hydroxyl group of IIIb in lowering the potential,[6] one would expect on the basis of the theory of the tautomerism of quinonoid systems[7] that the quinoneimine form IIIa would have the lower potential and hence the greater thermodynamic stability. Cohen and Phillips,[2] whose investigation antedated the work on tautomerism, assumed that the substance existed in the hydroxyquinonediimine form IIIb and assigned the pK value 4.84 to the phenolic group. This, however, is inconsistent with the fact that phenol blue, far from being a strong acid, is insoluble in alkali. The dissociation constant of the phenolic hydroxyl group of IIIb would not be expected to differ so greatly from that of the corresponding group of the reductant (pK 9.88), since even the strongly unsaturated p-nitro group decreases the pK value of phenol by only about 3 units. These difficulties are overcome by considering that phenol blue has the structure IIIa over the entire pH range studied and that the dissociation at pH 4.84 is attributable to the dimethylamino group, which is consistent with other information. This conclusion, it may be noted, is at variance with that reached by Schwarzenbach and Michaelis[3] from a theoretical consideration of the color phenomena.

We consider that Cohen and Phillips' interpretation of results obtained with o-toluidine indophenol also requires revision, particularly in the light of observations in this Laboratory on the tautomerism of amino quinones.[8] The dissociation at pH 4.4 may be assigned as above to the amino group of the quinoneimine form of the oxidant. The potential–pH curve is entirely similar to that found[8] for 4-amino-1,2-naphthoquinone, and the inflection at pH 10.8 may be

(4) Fieser, THIS JOURNAL, **52**, 4915 (1930).
(5) Clark, Cohen and Gibbs, Suppl. No. 54, U. S. Pub. Health Repts., 1926.
(6) Fieser and Fieser, THIS JOURNAL, **57**, 491 (1935).
(7) Fieser, ibid., **50**, 439 (1928).
(8) Fieser and Fieser, ibid., **56**, 1565 (1934).

attributed as with this quinone to a tautomerism in the alkaline medium to a hydroxyquinonediimine form similar to IIIb.

From this analysis it is concluded that phenol blue and related indoanilines exist over a reasonably wide neutral range in the un-ionized quinoneimine form corresponding to IIIa. Since several of the substituted compounds which we wished to study are not sufficiently soluble in water for investigation over the entire pH range, the present measurements were all made in a neutral phosphate buffer containing 37% alcohol.[1] It seems admissible to assume that the potential (E_0) of an equimolecular mixture of oxidant and reductant in this buffer measured against a hydrogen electrode in the same solvent is a significant constant referring to the equilibrium between the undissociated and untautomerized components of the system involving only the quinoneimine form such as IIIa.

With reference to the problem outlined above, it is of some significance that the potential found for the phenol blue system ($E_0 = 0.650$ v.) is not greatly below that of quinoneanil, I ($E_0 = 0.703$ v.[1]). The difference of 53 mv., representing the effect of a p-dimethylamino group in the aromatic ring, can be attributed to an influence on the character of the reductant and not the oxidant. The same group attached to the unsaturated nucleus of a quinone produces a potential lowering of 181 mv.[6]

IVa   IVb

Va   Vb

For the more specific test outlined we employed three pairs of isomeric monosubstituted N,N-dimethylindoanilines giving oxidation–reduction systems of type IV and type V. The difference in potential of a 3-substituted compound is taken as a measure of the combined influence of the group on the oxidant and the reductant, while the potential effect of a substituent at the 2'-position is assumed to be attributable solely to a modifying influence on the reductant. The potentiometric results, which are recorded below in Table II, are analyzed from this point of view in Table I. It is significant that a given group

TABLE I

EFFECT OF SUBSTITUENTS ON THE POTENTIAL OF N,N-DIMETHYLINDOANILINE (mv.)

Substituent	Position 3 (Combined influence on oxidant and reductant)	Position 2' (Influence on reductant alone)	Percentage of effect of a 3-substituent attributable to influence on oxidant
Methyl	-16	-7	56
Methoxyl	-59	-14	76
Chloro	$+39$	$+18$	54

has a greater effect on the potential at the 3-position than at position 2' whether the potential is raised or lowered by the substitution, but that the influence of a group in the non-quinonoid ring is by no means negligible. Although the differences are not great enough for high accuracy in the evaluation of the two factors, the trend is in the same direction for three substituents belonging to two types. It seems safe to conclude that only a little more than half of the potential effect of a 3-substituent in the quinonoid ring is attributable to an influence on the quinonoid structure and that the remainder can be ascribed to the modifying influence on the reductant.

It is of interest that, while the increase in potential attending substitution of a chlorine atom at the 3-position is about twice as great as for similar substitution in 1,4-benzoquinone,[9] methyl and methoxyl groups in this position of the quinoneimine are only about half as effective in lowering the potential as when substituted in quinone. The difference seems to be associated with the fact that the 3-group is adjacent to the unsaturated nitrogen atom rather than to the doubly bound oxygen, for when the substituent is transposed to the 2-position, as in 2-methyl-N,N-dimethylindoaniline (VI), the effect is much greater (-42

(9) Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1938, p. 813.

VI (-42 mv.)   VII (-67 mv.)
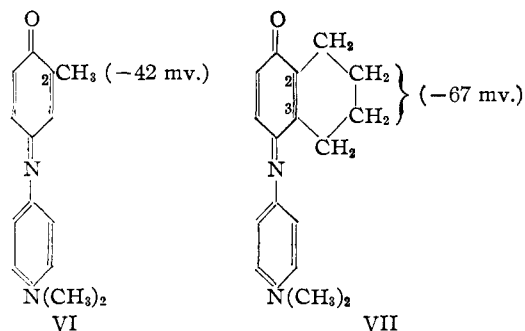
mv.) and more nearly comparable with that of the methyl group of toluquinone (-57 mv.[9]). Also, the effect of a tetramethylene ring joined at positions 2 and 3 (VII) is comparable with the sum of the effects of methyl groups at these two positions. We attempted to prepare isomers of VI and VII with the substituents in corresponding positions of the benzenoid ring but the syntheses failed.

The isomeric quinoneanils VIII and IX were investigated with the results shown. The po-

VIII ($E_0 = 0.532$ v.)   IX ($E_0 = 0.678$ v.)
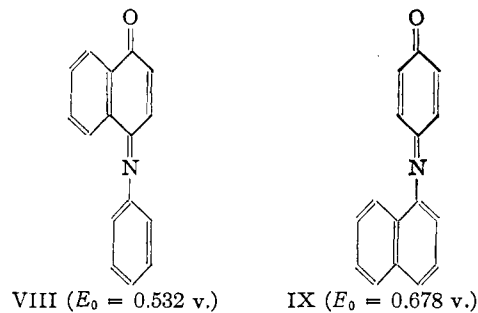
tential of the parent substance, 1,4-benzoquinoneanil (I), in the neutral alcoholic buffer is 0.703 v.[1] If the results are analyzed as above it would appear that the effect of the added phenylene group attributable to an influence on the reductant alone is 25 mv., the combined effect on both structures 171 mv., and the influence on the oxidant 85% of the total. This analysis, however, is not strictly valid because the phenylene group of the naphthoquinoneanil VIII is, in the reductant, in a position to activate the adjacent hydroxyl as well as the >NH group. A correction factor of unknown magnitude therefore should be subtracted from the percentage of the effect attributable to the oxidant structure. In conformity with the above observations, a phenylene group fused to the quinonoid ring of 1,4-quinoneanil (in VIII) has an effect (-171 mv.) much less than that of a similar group attached to 1,4-benzoquinone (-230 mv.[9]).

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TABLE II

NORMAL OXIDATION–REDUCTION POTENTIALS (25°)

Solvent: 37% alcohol, 0.047 M in KH_2PO_4 and 0.047 M in Na_2HPO_4. Titrating agents: KF = $K_3Fe(CN)_6$; KM = $K_3Mo(CN)_8$

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System, named as oxidant	Employed as	Titrated with	Normal potential, E_0
N,N-Dimethylindoaniline (IIIa)	Reductant	KM	0.6500
2-Methyl-N,N-dimethylindoaniline (VI)	Reductant	KM	.6081
3-Methyl-N,N-dimethylindoaniline	Reductant	KM	.6343
2'-Methyl-N,N-dimethylindoaniline	Reductant	KM	.6425
3-Methoxy-N,N-dimethylindoaniline	Reductant	KM	.5905
2'-Methoxy N,N-dimethylindoaniline	Reductant	KM	.6355
3-Chloro-N,N-dimethylindoaniline	Reductant	KM	.6888
2'-Chloro-N,N-dimethylindoaniline	Reductant	KM	.6683
2,3-Tetramethylene-N,N-dimethylindoaniline (VII)	Reductant	KM	.5828
1,4-Naphthoquinoneanil (VIII)	Oxidant	KF	.5324
2',3'-Benz-1,4-quinoneanil (IX)	Oxidant	KM	.6780

Potential Measurements.—Measurements were made by electrometric titration of a solution of the reductant prepared either from the pure, crystalline amine or its hydrochloride or by hydrogenation of the oxidant. Since decomposition occurred on attempted hydrogenation in the presence of the neutral alcoholic buffer,[1] the oxidant was reduced in absolute alcohol and 10 cc. of the resulting solution was added from a buret with a protected reservoir to 190 cc. of the oxygen-free buffer and connection was made to a hydrogen half-cell containing 19 cc. of the buffer and 1 cc. of absolute alcohol. When the crystalline reductant was available, a weighed quantity (0.000075 mole) was added to the oxygen-free buffer and a hydrogen electrode containing buffer was used for reference. Electrodes of bright platinum and of gold-plated platinum gave concordant results. Duplicate determinations of the normal potential in all cases agreed within 1 mv. and the values reported in Table II are averages. The potential increments from the midpoint to the point of 20 and 80% oxidation varied from 16.8 to 19.7 mv. (theoretical, 17.8 mv.).

Preparation of the Compounds.—One route to quinoneanils, in the leuco form, consists in condensing a hydroquinone with an aromatic amine in the presence of calcium chloride (Philip and Calm[10]). This was employed satisfactorily for the preparation of p-hydroxyphenyl-α-naphthylamine (X), the reduction product of IX, but the method did not appear suitable for the synthesis of derivatives substituted in the hydroquinone residue adjacent to the amino linkage. 1,4-Naphthoquinoneanil (VIII) has been prepared by the condensation of nitrosobenzene with

(10) Philip and Calm, Ber., **17**, 2431 (1884).
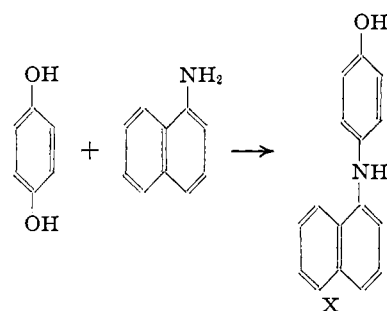
α-naphthol in the presence of a weak base,[11,12] but repeated attempts in the present work to effect a condensation with phenol were completely unsuccessful.

The method found most satisfactory for the synthesis of compounds of the N,N-dimethylindoaniline series is that of Gnehm and Bots.[13] This consists, in the simplest example, in the oxidation of a mixture of phenol and p-aminodimethylaniline in alkaline solution with sodium hypochlorite. After some standardization of the
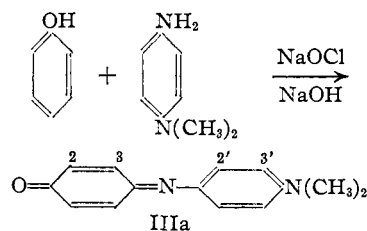
procedure the reaction was found to proceed smoothly in most, if not all, cases investigated. The brilliantly colored dyes often can be isolated in a pure condition by crystallization, although some of them decompose too readily and are best converted by reduction with sodium hydrosulfite

(11) Euler, ibid., **39**, 1035 (1906).

(12) Sander, ibid., **58**, 824 (1925).

(13) Gnehm and Bots, J. prakt. Chem., **69**, 162 (1904).

into the crystalline leuco compounds or their hydrochlorides. For the introduction of substituents in the oxygen-containing ring various known phenolic components were required, and the following substances when oxidized in the presence of somewhat less than the theoretical amount of *p*-aminodimethylaniline gave dyes in good yield: *o*-cresol, *m*-cresol, resorcinol monomethyl ether, *m*-chlorophenol, *ar*-tetrahydro-α-naphthol. The reaction also proceeded satisfactorily with phenol as one component and with a methyl, methoxyl, or chloro group substituted in the amino component adjacent to the primary amino group. The amines were prepared, as described in part in the literature, from the *m*-substituted dimethylanilines by preparation and reduction of the *p*-nitroso derivatives.

Satisfactory methods of preparing the amines XI and XII in a pure condition were developed,

XI   XII
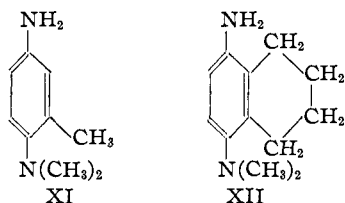
but attempts to obtain dyes by the standard procedure were fruitless. The amine XI gave an intense blue color, but no dye precipitated on neutralizing the alkaline solution, and the amine XII was largely recovered unaltered. We were likewise unable to obtain an indoaniline from 4-aminodimethyl-α-naphthylamine. For the preparation of XI from dimethyl-*o*-toluidine, the usual route is out of the question since the amine fails to undergo nitrosation. After some trial we found a convenient method utilizing the *p*-nitrobenzeneazo derivative of dimethyl-*o*-toluidine. This was reduced, the mixture of amines acetylated, and the monoacetyl derivative of the desired XI extracted with acid from the neutral diacetyl derivative of *p*-phenylenediamine.

Experimental Part

1,4-Naphthoquinoneanil (VIII) was prepared by the condensation of nitrosobenzene with α-naphthol according to Euler[11] and Sander[12] and crystallized several times from ether, giving ruby red prisms, m. p. 102°. Reductive acetylation with zinc dust, acetic anhydride, and sodium acetate gave **phenyl-(4-acetoxy-1-naphthyl)-amine**, which formed fine colorless needles from alcohol, m. p. 135°.

Anal. Calcd. for $C_{18}H_{16}O_2N$: C, 77.95; H, 5.46. Found: C, 78.48; H, 5.32.

p-Hydroxyphenyl-α-naphthylamine has been prepared previously by the condensation of α-naphthol with *p*-aminophenol in the presence of aqueous sodium bisulfite.[14] The following application of the general method of Philip and Calm[10] was found to give better results.

A mixture of 5.5 g. of hydroquinone, 21.4 g. of α-naphthylamine, and 11 g. of calcium chloride was heated at the boiling point (about 295°) in a long-necked flask in an atmosphere of nitrogen for three hours, when no more water was being given off. The hot melt was poured into 1 liter of warm water containing 25 g. of sodium hydroxide and enough sodium hydrosulfite to prevent oxidation, and after digesting the mixture at the boiling point for several minutes it was cooled and the unreacted α-naphthylamine which solidified was removed by filtration. After a further alkaline extraction of the residue, the filtrates were combined and neutralized with acetic acid, when the product separated as a colorless solid. Crystallization from ligroin gave 4.1 g. (39%) of satisfactory material, m. p. 85° (lit.,[14] 91°).

2′,3′-Benz-1,4-quinoneanil (IX).—A solution of 4.1 g. of *p*-hydroxyphenyl-α-naphthylamine in 100 cc. of dry benzene was refluxed with 7.4 g. of mercuric oxide for twelve hours, during which time an intense red color gradually developed. The filtered solution was evaporated at diminished pressure until the product began to crystallize, and petroleum ether was added to complete the separation. The dried product (3.6 g., 89%) on further crystallization from alcohol formed dark red, iridescent needles, m. p. 138°.

Anal. Calcd. for $C_{16}H_{11}ON$: C, 82.37; H, 4.76. Found: C, 82.07; H, 4.97.

Reductive acetylation gave *p*-acetoxyphenyl-α-naphthylamine as colorless scales, m. p. 135°, from alcohol.

Anal. Calcd. for $C_{18}H_{15}O_2N$: C, 77.95; H, 5.46. Found: C, 78.23; H, 5.29.

N,N-Dimethylindoaniline (Phenol Blue, III).—The preparation of this and other related dyes was carried out by the method of Gnehm and Bots[13] (see also Heller,[15] and Cohen and Phillips[2]) with some modifications, as illustrated in the following typical procedure. Some of the dyes were isolated and purified as such, some were converted for purification into the more readily handled leuco compounds.

A solution of 0.075 mole of phenol, 4 g. (0.1 mole) of sodium hydroxide, and 8 g. (0.06 mole) of sodium acetate in 250 cc. of water was stirred mechanically in a salt–ice bath in such a way as to maintain a temperature of 0 to −5° during the reaction. Two dropping funnels were put in place, one containing 100 cc. (0.1 mole) of 5% sodium hypochlorite, the other a solution of 0.05 mole of *p*-aminodimethylaniline hydrochloride in 100 cc. of water. The two solutions were then added simultaneously in the course of forty-five to sixty minutes. The solution became blue after the addition of a few drops of the reagents and the dye soon began to separate. Stirring was continued for fifteen minutes after completion of the addition and the product was then collected and washed several times with water; the dark blue filtrate, probably

(14) I. G. Farbenindustrie A.-G., English patent 282,111 (1927) [*Chem. Zentr.*, **101**, I, 3361 (1930)].

(15) Heller, *Ann.*, **392**, 16 (1912).

containing phenol-indophenol formed by alkaline hydrolysis of the product, was discarded. The crude dye was crystallized from ethyl acetate, giving fine, intense violet needles, m. p. 161° (as reported by Gnehm and Bots[13]); yield, 7.2 g. (63%).

For conversion into the leuco compound the dye was prepared as above but not dried, and the moist filter cake was suspended in 300 cc. of water containing 7 g. of sodium hydroxide. While stirring vigorously, sodium hydrosulfite was added in portions until the dye had disappeared and the color of the solution had changed from blue to brown. Some solid material was removed by filtration and the clear, light brown filtrate was cooled to 5–10° and treated with acetic acid, added by drops until precipitation was complete. After thorough cooling, the product was collected and dried in vacuum at room temperature; yield, 6.1 g. (84%). This was dissolved in 25 cc. of concentrated hydrochloric acid, using a few crystals of stannous chloride to discharge a slight blue color and to inhibit further oxidation, and the brownish solution was clarified by filtration through a mat of decolorizing carbon. The clear, pale tan filtrate was then evaporated in vacuum on the steam-bath to the point of extensive crystallization, and the crude salt was collected, washed with alcohol, and recrystallized from alcohol. This gave very nearly colorless prisms of 4-hydroxy-4'-dimethylaminodiphenylamine hydrochloride.

2-Methyl-N,N-dimethylindoaniline (VI).—Following exactly the above procedure, 8.1 g. (0.075 mole) of *o*-cresol and 0.05 mole of *p*-aminodimethylaniline gave 6.9 g. (57%) of the dye. The substance crystallized from ligroin in clusters of small crystals having a bronzy luster, m. p. 127°. Bayrac[16] gives the m. p. 123°.

In another experiment using the same quantities of materials the crude dye was reduced directly and the leuco compound was converted as above to the hydrochloride (53%) and this was recrystallized three times from water, the first time using a few drops of hydrochloric acid and a small crystal of stannous chloride. This gave colorless, rhombic crystals of 3-methyl-4-hydroxy-4'-dimethylaminodiphenylamine hydrochloride.

Anal. Calcd. for $C_{15}H_{19}ON_2Cl$: Cl, 12.75. Found: Cl, 12.80.

3-Methyl-N,N-dimethylindoaniline (IVa, R = CH₃).—Prepared as above from *m*-cresol in 58% yield, this dye crystallized from ligroin as large bronze plates, m. p. 121° (Bayrac,[14] m. p. 118°). When the crude product was reduced directly without drying, crude **2-methyl-4-hydroxy-4'-dimethylaminodiphenylamine** was obtained in 77% yield. Although some oxidation occurred on dissolving the substance in benzene, three crystallizations from this solvent gave nearly colorless crystals, m. p. 121–122° with some darkening. The hydrochloride, prepared as above in 63% yield, formed colorless prisms from water.

Anal. Calcd. for $C_{15}H_{18}ON_2$: C, 74.34; H, 7.49. Found: C, 74.55; H, 7.24. Hydrochloride. Calcd.: Cl, 12.75. Found: Cl, 12.89.

2'-Methyl-N,N-dimethylindoaniline.—The required starting material, **2-amino-5-dimethylaminotoluene**, was prepared conveniently from dimethyl-*m*-toluidine by con-

version to the nitroso derivative, obtained according to Wurster and Riedel[17] as the hydrochloride in 90% yield, and reduction of this salt (32.4 g.) with stannous chloride (100 g.) in concentrated hydrochloric acid (120 cc.). After discharge of the color the well cooled solution was treated with excess 30% alkali and the product extracted with ether. After drying and removing the solvent, the oily amine was taken up in 40 cc. of concentrated hydrochloric acid, a slight red color was discharged with a little stannous chloride, and on evaporation 2-amino-5-dimethylamino toluene dihydrochloride was obtained in a satisfactory condition; yield, 30 g. (83%); acetate, m. p. 158°.

This substance (0.05 mole), oxidized as above with phenol (0.075 mole), gave the substituted indoaniline in 65% yield. Crystallized from ligroin (intense violet solution), the product formed fine, bronze needles, m. p. 113–114°.

Anal. Calcd. for $C_{15}H_{16}ON_2$: C, 75.00; H, 6.73. Found: C, 74.76; H, 7.22.

The leuco compound, **4-hydroxy-2'-methyl-4'-dimethylaminodiphenylamine** hydrochloride, was obtained pure most satisfactorily, if in only 19% yield, by dissolving the reduced material in ether, clarifying the solution by filtration through charcoal, and passing in hydrogen chloride. The salt formed colorless blades from absolute alcohol.

Anal. Calcd. for $C_{15}H_{19}ON_2Cl$: Cl, 12.74. Found: Cl, 12.82.

Preparation of 5-Amino-2-dimethylaminotoluene (XI) and Attempted Conversion to a Dye.—Bernthsen[18] prepared 5-amino-2-dimethylaminotoluene by the reduction of the nitro compound obtained by methylating 5-nitro-2-aminotoluene, but the yield by this method is so poor that a better process was sought. Dimethyl-*o*-toluidine is available commercially as a starting material but does not form a nitroso derivative or react with diazotized aniline or sulfanilic acid.[19] The substance, however, does couple with more reactive diazo components, and we at first investigated the possibility of using diazotized *o*-nitroaniline-*p*-sulfonic acid to facilitate subsequent separation of the reduction products.

Sodium dimethyl-*o*-toluidine-azo-2-nitrobenzene-4-sulfonate was prepared by diazotizing 21.8 g. of *o*-nitroaniline-*p*-sulfonic acid by the procedure employed for sulfanilic acid and adding 13.5 g. of dimethyl-*o*-toluidine, followed by sodium acetate until the solution was no longer acid to congo red. After three hours the orange dye was collected and dried; yield, 9.3 g. (25%). This was dissolved in the required amount of dilute alkali and the sodium salt was precipitated with sodium chloride. A sample crystallized from absolute alcohol formed bright red needles which turned very dark on drying.

Anal. Calcd. for $C_{15}H_{16}O_5N_4SNa$: S, 8.29. Found: S, 8.15.

This dye was not suitable as an intermediate for the preparation of the desired amine for, like other *o*-nitro azo compounds,[20] it gives a triazole derivative on reduction.

(16) Bayrac, *Ann. chim.*, [7] 10, 18 (1897).

(17) Wurster and Riedel, *Ber.*, 12, 1797 (1879).

(18) Bernthsen, *ibid.*, 25, 3131 (1892).

(19) Friedlaender, *Monatsh.*, 19, 627 (1898).

(20) Grandmougin, *J. prakt. Chem.*, 76, 134 (1907).

It was then found that the dye which Bamberger and Meimberg[21] first obtained by coupling dimethyl-*o*-toluidine with *p*-nitrobenzenediazonium chloride can be prepared in excellent yield and that the two products resulting from its reduction can be separated easily by acetylation and acid extraction of the component having a tertiary amino group.

A mixture of 14.7 g. of *p*-nitroaniline, 25 cc. of water and 10 cc. of concentrated hydrochloric acid was stirred to a smooth slurry, 10.5 cc. of 67% sulfuric acid was added with stirring, and the clear solution was poured into 330 cc. of water, giving a fine suspension. Diazotization was accomplished at 20° with a solution of 7.3 g. of sodium nitrite, added rapidly, and an excess of nitrous acid was maintained for thirty minutes and then removed with urea. The filtered solution was stirred mechanically while adding 13 g. of dimethyl-*o*-toluidine in 10 cc. of glacial acetic acid (pink color), and sodium acetate was then added until neutral to congo red. After one and one-half hours the dye which precipitated was collected and washed; yield, 25.6 g. (94%). A sample crystallized from alcohol formed brilliant red plates, m. p. 122°.

For reduction, 17.2 g. of the dye was stirred under reflux with 30 cc. of water, 45 cc. of concentrated hydrochloric acid, and 15 cc. of acetone and 105 g. of stannous chloride in 84 cc. of concentrated hydrochloric acid was added from a dropping funnel at such a rate that the reaction did not get out of control. After the color had changed to pale yellow, the solution was cooled in an ice-bath and 30% alkali added until the precipitated inorganic material was redissolved. The oily mixture of amines was extracted with ether and the solution was dried over solid sodium hydroxide and evaporated. The residual red oil was acetylated with 30 cc. of acetic anhydride and a few drops of sulfuric acid. After the first vigorous reaction the mixture was heated on the steam-bath for thirty minutes and poured into 100 cc. of water. After neutralization with sodium carbonate solution, the nearly colorless precipitate was collected and stirred with 50 cc. of 20% hydrochloric acid. The undissolved diacetyl-*p*-phenylenediamine was removed by filtration, and the acid filtrate was refluxed for one hour to effect hydrolysis. The solution was cooled, neutralized with sodium carbonate, and the oil which separated was extracted with ether. After drying with sodium sulfate, distillation in an atmosphere of nitrogen gave 6.3 g. (69%) of colorless 5-amino-2-dimethylaminotoluene, b. p. 253–255° (762 mm.), m. p. 45–46° (Bernthsen,[18] m. p. 47°).

Saturation of a solution of the amine in absolute alcohol with hydrogen chloride and crystallization of the product from absolute alcohol gave colorless prisms of the dihydrochloride.

Anal. Calcd. for $C_9H_{16}N_2Cl_2$: Cl, 31.84. Found: Cl, 31.54.

The acetyl derivative crystallized from water in large, glistening plates, m. p. 96°.

Anal. Calcd. for $C_{11}H_{16}ON_2$: C, 68.75; H, 8.34. Found: C, 68.81; H, 8.09.

All attempts to obtain an indoaniline by the hypochlorite oxidation of 5-amino-2-dimethylaminotoluene and phenol by the standard procedure were unsuccessful. An

intense blue color developed, but no material precipitated from the alkaline medium; evidently the dimethylamino group in this case suffers hydrolysis with great ease.

Leuco 3-Methoxy-N,N-dimethylindoaniline.—The dye was prepared in a crude condition from resorcinol monomethyl ether in 65% yield, but attempted crystallizations from various solvents were unsatisfactory. The crude product was therefore reduced directly and the crude leuco compound (58%) crystallized from benzene. Fine, slightly gray needles of 2-methoxy-4-hydroxy-4'-dimethylaminodiphenylamine, m. p. 137°, were thus obtained.

Anal. Calcd. for $C_{15}H_{18}O_2N_2$: C, 69.74; H, 6.97. Found: C, 69.48; H, 6.61.

p-Nitrosodimethyl-*m*-anisidine was prepared by adding a solution of 11.5 g. of sodium nitrite by drops at 0–5° to a stirred solution of 22.2 g. of dimethyl-*m*-anisidine in 38 cc. of concentrated hydrochloric acid and 60 cc. of water. The nitrosohydrochloride separating as yellow crystals was collected after two hours and washed with 20% acid and with cold alcohol. This material (26.1 g., 83%) was suitable for reduction. A sample of the hydrochloride recrystallized from alcohol formed fine, bright yellow needles.

Anal. Calcd. for $C_9H_{13}O_2N_2Cl$: Cl, 16.40. Found: Cl, 16.29, 16.52.

The free base, precipitated from an aqueous solution of the salt by neutralization with soda, crystallized from methanol as dark green needles with a steel-blue iridescence, m. p. 131°.

Anal. Calcd. for $C_9H_{12}O_2N_2$: N, 15.56. Found: N, 15.49.

3-Methoxy-4-aminodimethylaniline was prepared from the above nitroso hydrochloride (16.2 g.) by reduction with stannous chloride. The crude amine which separated on adding excess alkali was extracted with ether, dried with sodium hydroxide, and distilled; b. p. 130–131° (4 mm.); yield, 11.2 g. (90%).

The free amine darkens rapidly in contact with air and was converted into the dihydrochloride by saturating a solution in absolute alcohol with hydrogen chloride. The salt which separated on cooling was crystallized from alcohol, giving colorless scales.

Anal. Calcd. for $C_9H_{16}ON_2Cl$: Cl, 29.67. Found: Cl, 29.93.

Leuco 2'-Methoxy-N,N-dimethylindoaniline.—The dye prepared by oxidation of a mixture of phenol and 3-methoxy-4-aminodimethylaniline was reduced directly. 4-Hydroxy-2'-methoxy-4'-dimethylaminodiphenylamine hydrochloride was precipitated in 27% yield by saturating an ethereal solution of the crude base with hydrogen chloride. Crystallization, first from water in the presence of stannous chloride and acid and then from alcohol, gave colorless plates.

Anal. Calcd. for $C_{15}H_{19}O_2N_2Cl$: Cl, 12.05. Found: Cl, 12.11.

Leuco 3-Chloro-N,N-dimethylindoaniline.—The *m*-chlorophenol required as starting material was prepared by a procedure suggested by Dr. J. R. Ruhoff and found to be more satisfactory than that of Varnholt.[22] A solution

(21) Bamberger and Meimberg, *Ber.*, **28**, 1891 (1895).

(22) Varnholt, *J. prakt. Chem.*, **36**, 27 (1887).

of 54 g. of *m*-chloroaniline in 83 cc. of concentrated sulfuric acid and 150 cc. of water was cooled by the addition of 250 g. of ice and diazotized with 27.3 g. of sodium nitrite in 54 cc. of water. The filtered solution of the diazonium salt was added dropwise to boiling 66% sulfuric acid in a steam distillation apparatus through which steam was passing. The *m*-chlorophenol carried into the distillate was extracted with ether, dried and distilled; b. p. 213–216°; yield, 32 g. (64%).

By oxidation of *m*-chlorophenol with *p*-aminodimethylaniline and reduction of the crude dye there was obtained 6.2 g. (47%) of crude leuco compound. Considerable oxidation occurred on attempted crystallization from benzene, and the material was converted with dilute acid containing stannous chloride into **2-chloro-4-hydroxy-4'-dimethylaminodiphenylamine hydrochloride**, which formed colorless prisms from water.

Anal. Calcd. for $C_{14}H_{16}ON_2Cl_2$: Cl, 23.75. Found: Cl, 23.79.

Leuco 2'-Chloro-N,N-dimethylindoaniline.—In the preparation of the amino component, dimethylaniline was nitrated according to Swan[23] in 53% yield (m. p. 60°) and the product was reduced with tin and hydrochloric acid according to Jaubert[24] (yield, 89%; b. p. 128–129° at 7 mm.). For conversion into *m*-chlorodimethylaniline a procedure similar to that of Hartman and Brethen[25] for the Sandmeyer reaction proved more satisfactory than that of Jaubert[24] (yield, 85%; b. p. 239–244°). *m*-Chlorodimethylaniline **picrate** forms bright yellow plates, m. p. 145°, from alcohol.

Anal. Calcd. for $C_{14}H_{13}O_7N_4Cl$: Cl, 9.23. Found: Cl, 9.29.

The *p*-nitroso derivative[26] was obtained as the hydrochloride by the procedure described above in 78% yield (free base from ether, m. p. 136°, dec.) and this was reduced with stannous chloride to **m-chloro-p-aminodimethylaniline** (79%, m. p. 40–41°, b. p. 124–125° at 3 mm.), which was stored as the **hydrochloride.** The salt, precipitated from absolute alcohol with hydrogen chloride, formed colorless plates from alcohol.

Anal. Calcd. for $C_8H_{12}N_2Cl_2$: Cl, 34.30. Found: Cl, 34.40.

The **acetyl derivative**, prepared by warming the free amine with acetic anhydride, crystallized from alcohol in colorless needles, m. p. 117°.

Anal. Calcd. for $C_{10}H_{13}ON_2Cl$: Cl, 16.70. Found: Cl, 16.77.

The crude dye from *m*-chloro-*p*-aminodimethylaniline and phenol gave the leuco compound in 65% yield. **4-Hydroxy-2'-chloro-4'-dimethylaminodiphenylamine hydrochloride** crystallized from water in nearly colorless prisms.

Anal. Calcd. for $C_{14}H_{16}ON_2Cl_2$: Cl, 23.75. Found: Cl, 24.36.

Leuco 2,3-Tetramethylene-N,N-dimethylindoaniline (VII).—Oxidation of *ar*-tetrahydro-α-naphthol, prepared

in 82% yield by the method of Jacobson and Turnbull,[27] and *p*-aminodimethylaniline as usual and reduction gave **4-hydroxy-5,6,7,8-tetrahydronaphthyl-4'-dimethylaminophenylamine** (54%), which crystallized from benzene in nearly colorless needles, m. p. 158°.

Anal. Calcd. for $C_{18}H_{22}ON_2$: N, 9.93. Found: N, 10.04.

4-Amino-*ar*-tetrahydrodimethyl-α-naphthylamine (XII) and Attempted Conversion to a Dye.—The starting material was obtained by reducing dimethyl-α-naphthylamine with sodium and amyl alcohol according to Bamberger and Helwig,[28] coupling the resulting tetrahydride with diazotized sulfanilic acid as described by these authors, and reducing the azo compound with alkaline sodium hydrosulfite. The amine (50% yield in the reduction) boiled at 312° and was converted by precipitation with hydrogen chloride from absolute alcohol into the dihydrochloride; this formed small colorless cubes from alcohol.

Anal. Calcd. for $C_{12}H_{20}H_2Cl_2$: Cl, 26.96. Found: Cl, 27.12.

The **acetyl derivative** crystallized from alcohol in colorless plates, m. p. 172.5°.

Anal. Calcd. for $C_{14}H_{20}ON_2$: N, 12.06. Found: N, 11.96.

Attempts to obtain a dye by oxidation of a mixture of the amine with phenol were unsuccessful. The mixture turned green, rather than blue, and unchanged amine was invariably recovered. Similarly, only tars resulted from the attempted oxidation of 4-aminodimethyl-α-naphthylamine[29] with phenol, and there was no indication of the formation of an indoaniline. Also unsuccessful was the attempt to obtain a sample of α-naphthol blue[15] or its leuco compound in a condition of purity suitable for potentiometric measurements.

Summary

A potentiometric study has been made of several pairs of substances of the 1,4-quinoneanil type in which a substituent is located either in the quinonoid ring or in a corresponding position of the benzenoid nucleus. The results show that the influence of a 3-substituent in modifying the character of the quinonoid system is responsible for only a little more than half of the total observed effect, the remainder being attributable to the structural alteration in the reductant. For proper interpretation of data on the effect of substituents on the oxidation–reduction potentials of quinonoid systems, consideration must be given to the structures of both oxidant and reductant.

(23) Swan, *J. Chem. Soc.*, **117**, 2 (1920).

(24) Jaubert, *Bull. soc. chim.*, [3] **21**, 20 (1899).

(25) Hartman and Brethen, "Organic Syntheses," Coll. Vol. I, 1932, p. 156.

(26) Hodgson and Wignall, *J. Chem. Soc.*, 1144 (1927).

(27) Jacobson and Turnbull, *Ber.*, **31**, 897 (1898).

(28) Bamberger and Helwig, *ibid.*, **22**, 1315 (1889).

(29) Friedländer and Welmans, *ibid.*, **21**, 3125 (1888).