[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Structures of Arylhydrazones of Unsymmetrically Substituted Quinones

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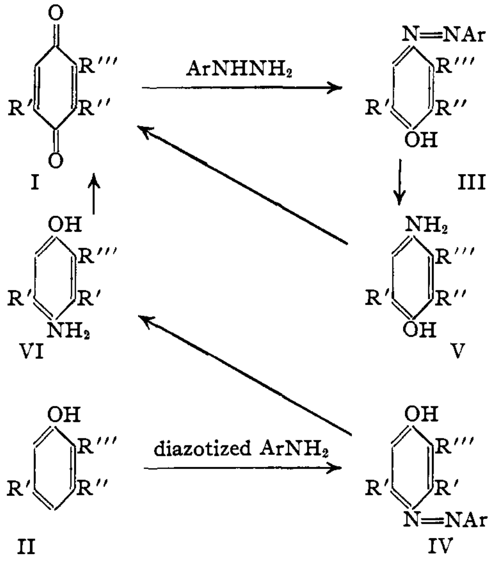
Several workers, chief among them Kehrmann,[3] have shown that monosubstituted quinones (I, R's = halogen or alkyl) can be converted either into mono oximes or into dioximes, and that the mono oxime is the one whose formation involves the unhindered carbonyl group. Similarly, *p*-disubstituted quinones give mono- or di-oximes. However, *m*-disubstituted quinones as well as tri-substituted quinones, lead only to mono-oximes, and again it is the less hindered carbonyl group which reacts. Tetra substituted quinones do not give oximes. The literature shows no other systematic study of this steric or orientation effect, although some scattered examples may be found which report results analogous to those of Kehrmann. Thus Borsche[4] showed that the reaction between thymoquinone and *o*-nitrophenylhydrazine gave the same product as that obtained by coupling diazotized *o*-nitroaniline with thymol—in other words, the hydrazine had reacted with the less hindered of the two carbonyl groups in the quinone.

The formation of *p*-oxyazo compounds both by action of an arylhydrazine upon *p*-benzoquinones and by coupling of diazotized aromatic amines with phenols offers a method for studying the orienting effects of substituents in reactions between unsymmetrical quinones and carbonyl reagents.[5] In accordance with the work of Kehrmann, substituted quinones would be expected to react at the less hindered carbonyl group, whereas coupling of analogous phenols with diazotized amines occurs entirely in the para position[6] so that, by proper selection of the quinone (I), the phenol (II), and the nitrogenous reagent (arylhydrazine or diazotized amine), it should be possible to prepare isomeric oxyazo compounds of types III and IV.[7] Moreover, by reductive cleavage of the azophenols, the aminophenols V and VI could be prepared; these are isomeric, and both, on oxidation, would give the same quinone. Thus the problem of establishing orientations in the products from the quinones would be quite simple and easy to solve.



The series of reactions shown in the chart has been carried out using *p*-nitrophenylhydrazine and four quinones: toluquinone, *m*-xyloquinone, trimethylquinone, and duroquinone. Except for toluquinone, all the quinones gave the azo compounds III in excellent yields. All of these azo compounds underwent reductive cleavage by action of sodium hydrosulfite, and the aminophenols V were obtained smoothly and in good yields. The low yield (28%) of azo compound from toluquinone was probably due to reduction of the quinone by the hydrazine, for gas was evolved during this reaction and the odor of nitrobenzene was apparent.

The corresponding phenols, *m*-cresol, *o*-cresol, *sym*-xylenol, 2,3,5-trimethylphenol and durenol,

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(1) Abstracted from a thesis by Willa B. Irwin, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph. D. degree, July, 1940.

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(3) (a) *J. prakt. Chem.*, **40**, 257 (1889); (b) *Ber.*, **21**, 3315 (1888); (c) Kehrmann and Messinger, *ibid.*, **23**, 3557 (1890); (d) Kehrmann, Mussman and Faccinetti, *ibid.*, **48**, 2021, 2073 (1915).

(4) Borsche, (a) *Ann.*, **357**, 178 (1907); (b) *Ber.*, **54**, 1287 (1921).

(5) The work reported in this paper had its inception in the observation, made by Dr. O. H. Emerson while an Honorary Fellow in this Laboratory, that duro- and pseudocumo-quinones reacted mole for mole with 2,4-dinitrophenylhydrazine sulfate to give well-defined crystalline products.

(6) See, for example, (a) Smith, Opie, Wawzonek and Prichard, *J. Org. Chem.*, **4**, 318 (1939). (b) Smith and Opie, *ibid.*, **6**, in press (1941).

(7) This work is not concerned with the question as to whether compounds such as *III* and *IV* are azophenols or quinone hydrazones. What incidental evidence was obtained on this point indicates that the substances described in this paper have the former structure. For a discussion of this point, and literature references, see Lauer and Miller, THIS JOURNAL, **57**, 520 (1935).

were coupled with diazotized *p*-nitroaniline, and the azo compounds IV from all of the phenols resulted in yields of 90% or better. From these azo compounds, the aminophenols VI were obtained by reductive cleavage using hydrosulfite.

Acetates of all of the new hydroxyazo compounds were prepared, and these proved to be useful derivatives for they were readily formed when the parent substances were heated for an hour in pyridine with excess acetic anhydride. The colored by-products, present in the acetates, as well as in the azo compounds themselves, were removed by pouring the solutions in ethanol or ethyl acetate, through a tower of alumina. A narrow zone at the top, very strongly adsorbed, was always formed, but the bulk of the material was much less firmly held. The top zone contained the impurities which were almost impossible to remove by repeated crystallization from any of the solvents tried.

Although the products obtained from the quinones and *p*-nitrophenylhydrazine behaved in all cases as true oxyazo compounds, the two tetramethyloxyazo compounds, one from durenol, and the other from duroquinone, were so strikingly different in appearance that their identity was questioned, and it was at first thought that these substances might be a pair of stable desmotropes—one the true quinone arylhydrazone, and the other the oxyazo compound. The one obtained from duroquinone and *p*-nitrophenylhydrazine, when dissolved in ethyl acetate and crystallized slowly, gave first a very few flakes of an orange solid and then the remainder as beautiful red prisms. The prisms, separated by hand, melted at 197–197.5° with decomposition.[8] The azo compound obtained by coupling durenol with diazotized *p*-nitroaniline crystallized from acetic acid as an orange powder which melted at 197.5–198° with decomposition.

The red crystalline form could never be obtained from acetic acid, but the orange form was sometimes obtained in small amounts along with the red form when the substance was crystallized from alcohol or ethyl acetate. The rate of crystallization had a profound effect upon the appearance of the product; thus the coupling product could be obtained as an orange powder when its solution in dioxane was rapidly cooled, or as orange crystals with a slight reddish cast when the solution was slowly cooled. The orange powder obtained in this way melted at 199–200° with decomposition.

But a mixture of the two forms could not be separated by chromatographing, either on alumina or calcium carbonate; neither form reacted with cyclopentadiene[9]; and neither form gave any evidence of reduction with phenylhydrazine.[10] Dr. Harold P. Klug very kindly made X-ray studies of the orange powder (m. p. 199–200°), red prisms (m. p. 197–197.5°) and Dr. Emerson's analytical sample (m. p. 190–191°) and he reported as follows: "The magenta colored crystals (Emerson) and the red prisms are the same, the latter being a purer specimen. The orange solid is not the same crystalline material as the other two, though they may have the same chemical composition. They may be polymorphic forms, for the interplanar spacings are very similar although the intensities of the photographic lines differ."[11] The evidence cannot be considered conclusive, but it seems most probable that an instance of polymorphism is involved. The X-ray data indicate that the two forms are either polymorphs or desmotropes but the chemical evidence points to the former.

Not all arylhydrazines and related aryldiazonium salts gave oxyazo compounds which could be successfully used to complete all of the transformations shown in the chart of formulas. While 2,4-dinitrophenylhydrazine and 2,4-dinitrobenzene diazonium chloride led to isomeric pairs of oxyazo compounds, these could not be cleaved to aminophenols. When zinc and hydrochloric acid were used as the reducing agent, the problem of separating the aminophenol from the other cleavage product, 1,2,4-triaminobenzene (or its decomposition products), could not be solved. Reduction with hydrosulfite led to the aminophenol from 2′,4′-dinitro-4-hydroxy-2,5,6-trimethylazobenzene, but the product was contaminated with a green impurity that was extremely difficult to remove. The isomeric 2,3,5-trimethylazo compound under the same conditions gave no aminophenol, probably because of the formation of an aziminobenzene or its oxide, a reaction frequently shown by *o*-nitroazo compounds when they are reduced by sodium

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[8] Dr. Emerson's analytical sample, prepared from the quinone, was red and melted at 190–191° (dec.).

[9] Lauer and Miller, ref. 7.

[10] McPherson, *Ber.*, **28**, 2416 (1895).

[11] We wish to thank Dr. Klug for his kindness in examining these substances.

hydrosulfite.[12] Failure was also encountered in the case of the *p*-hydrazinobenzene sulfonic acid-diazotized sulfanilic acid pair. Although the latter couples beautifully with phenols to give azo compounds that are readily cleaved by hydrosulfite to aminophenols, the former reagent gave, with trimethylquinone, a dark purple solid which behaved as an addition product. When this substance was heated to 100°, copious vapors of the quinone were evolved. Such addition products of *p*-hydrazinobenzene sulfonic acid and carbonyl compounds have been described before.[13]

In the oxidation of the *p*-aminophenols to quinones, some difficulty was encountered in oxidation of those aminophenols which gave toluquinone and *m*-xyloquinone. The usual oxidizing agent—ferric chloride—converted 2-amino-5-hydroxy-1,3-dimethylbenzene into a mixture which melted at 35–37° and from which a pure quinone, melting at 55–57°, was obtained. This substance was shown to be chloro-*m*-xyloquinone and it is formed when the aminophenol is oxidized by ferric chloride even in the absence of excess hydrochloric acid. Use of ferric sulfate, instead of ferric chloride, avoided this difficulty and converted the amino phenol into *m*-xyloquinone (m. p. 72–73°) quite smoothly. Ferric sulfate was greatly superior to ferric chloride also in converting the monomethylaminophenols into toluquinone.

Experimental Part[14]

Each of the procedures used will be assigned a letter and will be described once in detail; thereafter, only the amounts of reagents and the results will be given.

The Cresol Series.—4′-Nitro-4-hydroxy-2-methylazobenzene (IV, R′ = R‴ = H; R″ = CH_3; Ar = *p*-$C_6H_4NO_2$), *Procedure A:* *p*-Nitroaniline (13.8 g.) was dissolved in hot water (150 cc.) containing hydrochloric acid (55 cc.). The solution was poured over ice (375 g.) and when the temperature had fallen below 10°, sodium nitrite (7.3 g.) in water (15 cc.) was added with stirring. After fifteen minutes the remaining ice and a small amount of flocculent yellow solid were filtered off, and the filtrate was added slowly and with stirring to a cooled (ice–salt) solution of *m*-cresol (10.0 g.) in water (250 cc.) containing sodium hydroxide (22.5 g.). The dark brown pasty mass of the sodium salt of the coupling product was allowed to stand overnight at room temperature, after which it was acidified with hydrochloric acid. The orange solid was filtered off, washed thoroughly with water and dried at 100° for six hours. It weighed 24.5 g. (theory 23.8 g.). The product was dissolved in boiling alcohol (200 cc.) and the hot solution was filtered. The filtrate, when cooled and diluted with water, deposited an orange fibrous mass of the azo compound which sintered at 157° and melted at 162.5–164° with decomposition. A small sample was dissolved in ethyl acetate and poured through a tower of alumina (8″ × $^{7}/_{8}$″). The eluent from the middle two-thirds of the deep red-orange zone was evaporated and the residue was crystallized from aqueous ethanol. The product formed a fibrous orange mass which apparently contained solvent of crystallization, for it melted below 130°, then solidified and finally melted again at 163–164°. When crystallized from benzene, the substance melted sharply at 163–164° and formed fine, deep red needles.

Anal. Calcd. for $C_{13}H_{11}O_3N_3$: C, 60.70; H, 4.28. Found: C, 60.36; H, 4.68.

4′-Nitro-4-acetoxy-2-methylazobenzene, *Procedure B.*—The above hydroxyazo compound (300 mg.) was refluxed for one hour with pyridine (5 cc.) and acetic anhydride (1 cc.). The reaction mixture was poured into water (50 cc.) and after standing for thirty minutes, the solid product was removed, washed thoroughly with water, and dried. It weighed 350 mg. and melted at 129–131°. The analytical sample was purified by chromatographing onto alumina from ethyl acetate, followed by two crystallizations from ethanol–ethyl acetate. It then consisted of a deep orange cottony mass which melted at 132–133°.

Anal. Calcd. for $C_{15}H_{13}O_4N_3$: C, 60.20; H, 4.35. Found: C, 60.04; H, 4.51.

4-Amino-*m*-cresol (VI, R′ = R‴ = H; R″ = CH_3), *Procedure C.*—The above azo compound (10.0 g.) was dissolved in boiling alcohol (35 cc.) and a suspension of sodium hydrosulfite (37 g.) in water (150 cc.) was added slowly. When the color had faded to a light amber, the hot solution was filtered and the filtrate was concentrated under reduced pressure until a heavy white granular solid separated. The aminophenol (2.5 g., 52%) was removed from the cooled residue and crystallized once from benzene, when it formed glistening white platelets which melted at 173–176° with decomposition in agreement with the values found in the literature.[15]

Toluquinone. From 4-amino-*m*-cresol. *Procedure D.*—The crude aminophenol (2.5 g.), after washing thoroughly with ice water, was suspended in water (150 cc.) in a flask arranged for steam distillation. Hydrated ferric sulfate (25 g.) was added and steam was passed through the mixture until the distillate was colorless. The quinone was removed from the distillate (250 cc.) by thorough extraction with ether. The ether was removed by distillation through a short, packed column (use of a column is necessary at this point because the quinone is quite volatile with ether). The residue of toluquinone weighed 1.4 g. (56%) and melted at 68–69°.

From 4-Amino-*o*-cresol.—(See below) The crude aminophenol, m. p. 170–171°, obtained by cleavage of crude 4′-nitro-4-hydroxy-3-methylazobenzene (34 g.) was suspended in water (1 l.), hydrated ferric sulfate (100 g.) was added

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[12] Grandmougin, *J. prakt. Chem.*, [2] **76**, 124 (1907).

[13] Biltz, Maué and Seiden, *Ber.*, **35**, 2000 (1902); Biltz, *ibid.*, **68**, 221 (1935); Wislicenus and Scheidt, *ibid.*, **24**, 3006 (1891).

[14] Microanalyses by E. E. Renfrew, E. E. Hardy and J. W. Opie.

[15] (a) Noelting and Kohn, *Ber.*, **17**, 365, 371 (1884); (b) Staedel and Kolb, *Ann.*, **259**, 217 (1890); (c) Friedländer and Zeitlin, *Ber.*, **27**, 194 (1894); (d) Gattermann, *ibid.*, **27**, 1930 (1894); (e) Bamberger, *Ann.*, **390**, 136 (1912).

and the reaction mixture was processed as described above. The quinone, melting at 68–69°, weighed 4.0 g. (25% based on the azo compound taken).

4′-Nitro-4-hydroxy-3-methylazobenzene (III, $R' = R''' = H$, $R'' = CH_3$; Ar = p-$C_6H_4NO_2$). From *o*-Cresol.—(*Procedure A*.) Reagents: *p*-nitroaniline (27.6 g.), hot water (300 cc.), hydrochloric acid (110 cc.), ice (750 g.), sodium nitrite (14.4 g.), *o*-cresol (20 g.), water (300 cc.), sodium hydroxide (9 g.); time twenty hours at 0°. The product was filtered off, suspended in water, and subjected to steam distillation to remove unchanged cresol. The azo compound, after drying at 100°, weighed 38 g. (80%). After crystallization from aqueous alcohol, the substance melted at 203–205° with decomposition. The analytical sample was chromatographed as described above and then crystallized twice from aqueous alcohol, when it melted at 205–206° (dec.) and formed a dull orange powder.

Anal. Calcd. for $C_{13}H_{11}O_3N_3$: C, 60.70; H, 4.28. Found: C, 60.53; H, 4.44.

A quantitative yield of a somewhat less pure product (m. p. 189–197°) was obtained by using sufficient base in the solution of the cresol to keep the reaction mixture basic after the diazonium solution was added. In this case the reaction mixture was allowed to stand for forty-five minutes and was then acidified with hydrochloric acid after which the procedure was the same as that described above.

From Toluquinone. *Procedure E.*—*p*-Nitrophenylhydrazine (3.5 g.) was dissolved in hot ethanol (50 cc.), and sulfuric acid (5 cc.) was added to the cooled solution. The gelatinous precipitate was dissolved by warming the mixture, and then the cooled solution was added, slowly and with shaking, to a solution of toluquinone (2.9 g.) in ethanol (40 cc.). After standing for several hours at room temperature, the solution was diluted with water (7 cc.) and after eighteen hours longer it deposited a brown, granular solid (1.7 g., 28%) which melted at 183–199° (dec.). The dark brown viscous mother liquor, on further dilution, deposited a small amount of sticky material which evolved a pronounced odor of nitrobenzene. The first crop of solid was dissolved in hot alcohol and filtered and the filtrate diluted with water to incipient cloudiness. The cooled solution deposited a light reddish-brown solid which melted at 195–202° (dec.). When chromatographed and crystallized as described above, the solid melted at 200.5–204° (dec.) alone or when mixed with a specimen prepared from the cresol.

4′-Nitro-4-acetoxy-3-methylazobenzene.—The same acetate (340 mg.) was prepared by acetylation in pyridine (as described above) of the azo compound (300 mg.) from *o*-cresol and from toluquinone. Both preparations, after chromatographing and crystallizing, formed long orange needles which melted at 144.5–146° alone or when mixed.

Anal. Calcd. for $C_{15}H_{13}O_4N_3$: C, 60.20; H, 4.35. Found: C, 59.90; H, 4.37.

4-Amino-*o*-cresol (V, $R' = R''' = H$; $R'' = CH_3$), *Procedure C.*—Reagents: 4′-nitro-4-hydroxy-3-methylazobenzene (34.0 g.), alcohol (130 cc.), sodium hydrosulfite (125 g.), water (380 cc.); time thirty minutes. The hot solution was filtered and some solvent (50 cc.) was removed under reduced pressure from the filtrate. After filtration again, the solution was repeatedly (10–11 times) extracted with ether.[16] The ether extracts were evaporated under reduced pressure and a small sample of the residue was crystallized from benzene. It formed grayish-white prisms which melted at 171.5–173° (dec.) in agreement with the values in the literature.[17] This aminophenol was extremely sensitive and became very dark on standing in the air even for short periods of time. The odor of toluquinone became apparent as the substance darkened.

The *sym*-Xylenol Series. 4′-Nitro-4-hydroxy-2,6-dimethylazobenzene (IV, $R''' = H$; $R' = R'' = CH_3$; Ar = p-$C_6H_4NO_2$), *Procedure A.*—Reagents: *p*-nitroaniline (6.9 g.), hydrochloric acid (100 cc., 3.3 *N*), ice (250 g.), sodium nitrite (3.5 g.) in water (28 cc.); *sym*-xylenol (6.1 g.), water (150 cc.), sodium hydroxide (2.2 g.); time three hours. The brick red solid, after drying at 75°, weighed 12.6 g. (92.5%) and melted at 165.5–167° with decomposition. A sample when chromatographed from alcohol onto alumina, and then crystallized twice from aqueous alcohol; formed dark red glistening prisms which melted at 167–168° (dec.).[18]

4′-Nitro-4-acetoxy-2,6-dimethylazobenzene, *Procedure B.*—The oxyazo compound (500 mg.) gave 560 mg. of crude acetate, which, after purification, formed long silky deep red needles which melted at 133–133.5°.

Anal. Calcd. for $C_{16}H_{15}O_4N_3$: C, 61.34; H, 4.79. Found: C, 61.20; H, 5.04.

4-Amino-3,5-dimethylphenol (VI, $R''' = H$; $R' = R'' = CH_3$), *Procedure C.*—Reagents: oxyazo compound (18.7 g., m. p. 162–165°), ethanol (60 cc.), sodium hydrosulfite (90 g.), water (170 cc.). The crude amine darkened at 160° and melted at 177.5–180° (dec.). A small sample, recrystallized from benzene, was white and melted at 179–180° (dec.).[19]

***m*-Xyloquinone.**—The crude aminophenol obtained in the above experiment was steam distilled with ferric sulfate (75 g.). The quinone obtained from the distillate by filtration and ether extraction, weighed 3.9 g. (41%, based upon the azo compound) and melted at 70–72°. When ferric chloride was used in place of ferric sulfate, the crude product melted at 35–37° and this substance (5.76 g.) when reduced by boiling its solution in acetic acid (25 cc.) and water (20 cc.) with zinc (20 mesh, 6 g.) gave a hydroquinone (2.6 g.) which melted at 137–138.5° after crystallization from water. Oxidation of this hydroquinone by ferric chloride gave a quinone which after steam distillation and crystallization from petroleum ether (b. p., 28–38°) melted at 55.5–57°. This was **2,6-dimethyl-3-chlorobenzoquinone.**

Anal. Calcd. for $C_8H_7O_2Cl$: C, 56.31; H, 4.11. Found: C, 56.19; H, 4.23.

4′-Nitro-4-hydroxy-3,5-dimethylazobenzene (III, $R''' = H$; $R' = R'' = CH_3$), *Procedure E.*—Reagents: *p*-nitrophenylhydrazine (2.6 g.), ethanol (40 cc.), sulfuric acid

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[16] Although the aminocresol has been reported as readily soluble in ether (ref. 15a, p. 365) it is not readily extracted from this solution by ether.

[17] Bamberger, *Ber.*, **35**, 3700 (1902); see also refs. 15a, 15e.

[18] Von Auwers and Reitz, *Ann.*, **356**, 165 (1906), give the m. p. as 166–167° (dec.).

[19] (a) Bamberger and Rising, *Ann.*, **316**, 300 (1901), and (b) Von Auwers and Borsche, *Ber.*, **48**, 1699 (1915), report the m. p. as 180.5–181.5°.

(4.5 cc.), *m*-xyloquinone (2.5 g.), ethanol (40 cc.). The crude azo compound (3.86 g., 77%), melted at 180.5–181.5° (dec.); after purification, it formed fine orange-red needles which melted at 182–183° (dec.).

Anal. Calcd. for $C_{14}H_{13}O_3N_3$: C, 61.99; H, 4.80. Found: C, 61.72; H, 4.98.

4'-Nitro-4-acetoxy-3,5-dimethylazobenzene, *Procedure B.*—The acetate (340 mg. from 300 mg. of oxyazo compound), after purification, formed silky orange needles melting at 192–193°.

Anal. Calcd. for $C_{16}H_{15}O_4N_3$: C, 61.34; H, 4.79. Found: C, 61.49; H, 5.02.

4-Amino-2,6-dimethylphenol (V, R''' = H; R' = R'' = CH_3), *Procedure C.*—Reagents: oxyazo compound (3.18 g.) in alcohol; sodium hydrosulfite (11 g.) in water (70 cc.). The hot solution was filtered and the filtrate was concentrated under reduced pressure until a white solid began to pass over with the distillate. The mixture in the distilling flask was cooled and the solid was removed and crystallized twice from benzene. It formed creamy white platelets (150 mg.) which melted at 136–138° (dec.).[20] The aminophenol was extremely sensitive and turned dark at once if exposed to the air while wet with water.

The Pseudocumenol-6 Series, *Procedure F.*—4'-Nitro-4-hydroxy-2,3,6-trimethylazobenzene (IV, R' = R'' = R''' = CH_3; Ar = *p*-$C_6H_4NO_2$). *p*-Nitroaniline (6.25 g.) was dissolved in warm acetic acid (50 cc.), sulfuric acid (4 cc.) was added and the solution was rapidly cooled. To the cooled and stirred sludge of amine salt isoamyl nitrite (35 cc.) was slowly added. The amine salt slowly dissolved and was replaced by an oily brown globule of the diazotized amine. Ether (50 cc.) was added, the mixture was well shaken, and the solvents removed by decantation. The residual oil was taken up in acetic acid (15 cc.), reprecipitated with ether. This process was repeated once more, and then the diazonium salt in acetic acid (20 cc.) was added slowly to a cold (10°) sludge of 2,3,5-trimethylphenol (5 g.) in acetic acid (50 cc.). The mixture was allowed to stand at room temperature overnight, after which the bright red product was removed, washed twice with cold acetic acid, twice with ether, and dried. After crystallization from dioxane, the substance weighed 7.15 g. (68%) and melted at 162–165° (dec.). The analytical sample was crystallized three times from aqueous ethanol, when it melted at 165.5–166° (dec.); this sample was then chromatographed from alcohol onto alumina and subsequently crystallized first from aqueous ethanol and then from ethanol–ethyl acetate. It then melted at 165.5–166.5° (dec.) and formed dark red prisms.

Anal. Calcd. for $C_{15}H_{15}O_3N_3$: C, 63.16; H, 5.26. Found: C, 63.19; H, 5.58.

When crystallized from dioxane, the substance formed large, flat prisms which apparently contained solvent of crystallization. These melted with decomposition below 100°, but when this substance was crystallized from ethanol–ethyl acetate, the melting point rose to 165.5–166.5°. A better yield (90%), though of a less pure product (m. p. 149–150°, dec. 165–170°) was obtained when the diazotization and coupling were carried out in aqueous solution by the procedure described above for other similar reactions. This material, after several crystallizations from ethanol–ethyl acetate, melted at 162–165° (dec.).

4'-Nitro-4-acetoxy-2,3,6-trimethylazobenzene, *Procedure B.*—The acetate (380 mg. from 500 mg. of oxyazo compound), after purification, formed deep red prisms which melted at 133–134°.

Anal. Calcd. for $C_{17}H_{17}O_4N_3$: C, 62.39; H, 5.20. Found: C, 62.57; H, 5.48.

4-Amino-2,3,5-trimethylphenol (VI, R' = R'' = R''' = CH_3), *Procedure C.*—Reagents: oxyazo compound (3.0 g.), ethanol (15 cc.), sodium hydrosulfite (12 g.), water (55 cc.). The amber solution was filtered, the filtrate was diluted with water (250 cc.) and extracted seven times with ether. Most of the solvent was removed from the combined ether extracts, the last of it being replaced by a few cc. of benzene. Concentration was continued until a little solid separated, when the suspension was cooled and the product (650 mg., 41%) was removed and crystallized from benzene. It formed glistening white plates which melted to a red liquid at 151–153°, alone or when mixed with an authentic specimen.[21]

4'-Nitro-4-hydroxy-2,3,5-trimethylazobenzene (III, R' = R'' = R''' = CH_3; Ar = *p*-$C_6H_4NO_2$), *Procedure E.*—Reagents: *p*-nitrophenylhydrazine (9.2 g.), alcohol (175 cc.), sulfuric acid (19 cc.). Pseudocumoquinone (5.46 g.) in alcohol (75 cc.); time, twelve hours. The product (7.6 g., 73%), after two crystallizations from ethanol–ethyl acetate, formed red prisms which melted at 227–228° (dec.).

Anal. Calcd. for $C_{15}H_{15}O_3N_3$: C, 63.16; H, 5.26. Found: C, 63.02; H, 5.29.

4'-Nitro-4-acetoxy-2,3,5-trimethylazobenzene, *Procedure B.*—The acetate (570 mg. from 500 mg. of oxyazo compound), after purification, melted at 165°.

Anal. Calcd. for $C_{17}H_{17}O_4N_2$: C, 62.39; H, 5.20. Found: C, 62.57; H, 5.58.

4-Amino-2,3,6-trimethylphenol (V, R' = R'' = R''' = CH_3), *Procedure C.*—Reagents: oxyazo compound (1.69 g.) in ethanol (35 cc.), sodium hydrosulfite (6 g.) in water (35 cc.); time thirty minutes. The solution was extracted with ether four times and the combined extracts were concentrated to a small volume under reduced pressure and cooled. The amine (730 mg., 81%), after crystallization four times from benzene, formed white needles which melted at 136–137° (dec.).

Anal. Calcd. for $C_9H_{13}ON$: C, 71.52; H, 8.61. Found: C, 71.48; H, 8.45.

The **hydrochloride** was prepared by saturating an ether solution of the substance with hydrogen chloride. The product, dissolved in alcohol and precipitated by addition of ether, was white and charred slightly about 225° but did not melt.

Anal. Calcd. for $C_9H_{14}ONCl$: C, 57.60; H, 7.47. Found: C, 58.29; H, 7.59.

Pseudocumoquinone, *Procedure D.*—Reagents: the above amine (460 mg.), ferric chloride (10 g.). The product was a yellow oil which had all of the properties of trimethylquinone. When reductively acetylated, this oil

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[20] Rowe, Bannister and Storey, *J. Soc. Chem. Ind.*, **50**, Trans., 79 (1931), report the m. p. as 137–138° (dec.).

[21] Smith, Hoehn and Whitney, THIS JOURNAL, **62**, 1863 (1940).

gave the diacetate of pseudocumohydroquinone (290 mg.), m. p. 108–110°.

The Durenol Series, 4′-Nitro-4-hydroxy-2,3,5,6-tetramethylazobenzene. From Durenol, *Procedure F.*—Reagents: *p*-nitroaniline (3.5 g.), acetic acid (35 cc.), sulfuric acid (2.8 cc.), isoamyl nitrite (35 cc.). Diazonium salt taken up in acetic acid (25 cc.) and coupled at 14–15° with durenol (3.0 g.) in acetic acid (80 cc.). The product (5.66 g., 94%) was a very dark red crystalline mass with a dull greenish luster. After crystallization from ethanol-ethyl acetate, it melted at 171–172.5° (dec.).

From Duroquinone, *Procedure E.*—Reagents: duroquinone (3.0 g.) in alcohol (35 cc.), *p*-nitrophenylhydrazine (6.0 g.) in alcohol (100 cc.), sulfuric acid (10 cc.); time, two days. The red solid (2.9 g., 53%), after purification, melted at 174–174.5° (dec.).

Anal. Calcd. for $C_{16}H_{17}O_3N_3$: C, 64.21; H, 5.69. Found: C, 64.30; H, 5.90.

4′-Nitro-4-acetoxy-2,3,5,6-tetramethylazobenzene, *Procedure B.*—The acetate (340 mg. from 300 mg. of oxyazo compound), after purification, formed long silky dark red needles melting at 143–144°.

Anal. Calcd. for $C_{16}H_{19}O_4N_3$: C, 63.34; H, 5.57. Found: C, 63.31; H, 5.65.

Aminodurenol, *Procedure C.*—Reagents: oxyazo compound (2.75 g.) from durenol, in ethanol (35 cc.), sodium hydrosulfite (9 g.) in water (40 cc.). The product (1.33 g., 87%) formed glistening, tan plates which were very difficult to purify. Successive crystallizations from benzene gave products which melted at 178–181°, 174–178°, and 175–180°, respectively, all with decomposition. Sublimation under 20 mm. pressure produced white, feathery needles which melted at 177–178.5° (dec.). These were analyzed.

Anal. Calcd. for $C_{10}H_{15}ON$: C, 72.73; H, 9.09. Found: C, 73.14; H, 9.34.

The same *p*-aminophenol was obtained by hydrosulfite reduction of the oxyazo compound prepared from duroquinone. The crude product melted at 180–182° (dec.) and on crystallization from benzene again products were obtained which showed rather wide melting point ranges. Sublimation formed a product which melted at 179–183° (dec.). Specimens of the aminophenol prepared from the two oxyazo compounds showed no depression in melting point when mixed, and specimens prepared from the two azo compounds each gave duroquinone, m. p. and mixed m. p. 111°, on oxidation.

2′,4′-Dinitro-4-hydroxy-2,3,6-trimethylazobenzene (IV, R′ = R″ = R‴ = CH_3; Ar = $2,4(O_2N)_2C_6H_3$).—2,4-Dinitroaniline (2.5 g.) was diazotized in acetic acid (17 cc.) with isoamyl nitrite according to the procedure of Hantzsch and Jochum.[22] The solution was added slowly to a cooled solution (15–20°) of pseudocumenol-6 (1.0 g.) in acetic acid (15 cc.). After standing for two days, the mixture was filtered and the product was washed with acetic acid and crystallized twice from the same solvent. It melted at 188.5–189° (dec.).

Anal. Calcd. for $C_{16}H_{14}O_5N_4$: C, 54.55; H, 4.24; N, 16.97. Found: C, 53.24; H, 4.64; N, 17.41.

Reduction.—The above azo compound (1.35 g.) was suspended in alcohol (25 cc.) and refluxed for one hour with a solution of sodium hydrosulfite (6 g.) in water (25 cc.). The hot solution was filtered, and most of the alcohol was distilled out of the filtrate which was then extracted thoroughly with ether. The solvent was removed and the residue was taken up in benzene. The benzene solution immediately became black. The solvent was quickly removed and the residue was steam distilled with ferric chloride solution. Only a trace of pseudocumoquinone appeared in the distillate.

2′,4′-Dinitro-4-acetoxy-2,3,6-trimethylazobenzene.—The oxyazo compound (760 mg.) was acetylated by the pyridine–acetic anhydride method. The acetyl derivative (650 mg.) after crystallization twice from dioxane formed orange-yellow needles which melted at 155–156°.

Anal. Calcd. for $C_{17}H_{16}O_6N_4$: C, 54.84; H, 4.30. Found: C, 54.71; H, 4.40.

2′,4′-Dinitro-4-hydroxy-2,3,5-trimethylazobenzene (III, R′ = R″ = R‴ = CH_3; Ar = $2,4(O_2N)_2C_6H_3$.).—Pseudocumoquinone (2.5 g.) in alcohol (25 cc.) was added to a solution of Brady's reagent (2,4-dinitrophenylhydrazine (3.35 g.) in sulfuric acid (6.7 cc.) followed by addition of 50 cc. of ethanol).[23] Reaction was instantaneous. After the mixture had stood for a short time, the product was removed, washed with alcohol, and crystallized from dioxane. It was bright orange in color, melted at 220–221° (dec.) and weighed 5.02 g. (90%). The analytical specimen was prepared by Dr. O. H. Emerson.

Anal. Calcd. for $C_{15}H_{14}O_5N_4$: C, 54,55; H, 4.24; N, 16.97. Found: C, 54.7; H, 4.6; N, 16.24.

Reduction.—This azo compound (910 mg.) when reduced with hydrosulfite by the procedure described above for its isomer, yielded 80 mg. of 4-amino-2,3,5-trimethylphenol when the ethereal extracts were evaporated. After crystallization from benzene, the product melted at 151–152° (dec.) but it contained an olive green impurity which could not be removed by crystallization.

Pseudocumoquinone and *p*-Hydrazinobenzenesulfonic Acid.—The quinone (3.9 g.) in warm alcohol was added to a solution of the hydrazine[24] (5 g.) in water (100 cc.) at 50°. After the mixture stood overnight, the dark purple solid was removed; it melted at 224–228° (dec.) but decomposition began far below the melting point. The solid was placed in a drying oven at 100° for an hour; at the end of this time it weighed 4.17 g., was considerably lighter in color and was evolving vapors of the quinone. When extracted with successive portions of boiling alcohol, the solid became progressively lighter in color, tending toward lavender.

2′,4′-Dinitro-4-hydroxy-2,3,5,6-tetramethylazobenzene. From Durenol.—The phenol (1.0 g.) in acetic acid (20 cc.) was coupled with diazotized 2,4-dinitroaniline (2.5 g.) in acetic acid (17 cc.) at 20°. The product was removed, washed with acetic acid, and dried. It weighed 2.17 g. (95%). After crystallization twice from acetic acid, the substance formed an orange powder which melted at 197.5–198° (dec.).

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(22) Hantzseh and Jochum, *Ber.*, **34**, 3337 (1901).

(23) Brady, *J. Chem. Soc.*, 756 (1931).

(24) Acree, *Am. Chem. J.*, **37**, 363 (1907).

Anal. Calcd. for $C_{16}H_{16}O_5N_4$: C, 55.81; H, 4.65; N, 16.28. Found: C, 55.40; H, 4.48; N, 16.57.

The sample for X-ray examination was further purified by crystallizing it three times from dioxane; it then melted at 199–200° (dec.). The rate of crystal growth greatly affected the appearance of this material. When crystallized rapidly from a concentrated solution in dioxane it was a bright orange powder; when slowly formed from a more dilute solution, the substance was obtained as well defined glistening orange-red needles. When this form was crystallized rapidly from dioxane, the orange powder again resulted.

From Duroquinone.—A solution of 2,4-dinitrophenylhydrazine (5.0 g.) in sulfuric acid (10 cc.) and alcohol (75 cc.) was added to duroquinone (4.1 g.) in alcohol (100 cc.). The dark red solution began to crystallize within a few minutes. The first crop of crystals was removed after one hour: these deep red, glistening crystals weighed 2.52 g. and melted at 188–189° (dec.). A second crop of crystals, obtained after the mixture had stood overnight, was non-homogeneous in appearance and consisted of a little orange solid together with a large amount of orange-red needles. The two forms were separated mechanically. The orange solid melted at 196–196.5° (dec.); the needles (3.56 g.) melted at 194.5–195.5° (dec.). Third and fourth crops of solid were obtained by diluting the mother liquor with 2 *N* sulfuric acid. These were successively more orange in color; they weighed 580 and 280 mg., and melted at 174–175° (dec.) and about 185° (dec.), respectively. A portion of the second crop (needles) was allowed to crystallize very slowly (ten days) from dilute ethyl acetate solution. This material formed beautiful dark red prisms which melted at 197–197.5° (dec.) and this specimen was used for the X-ray examination. The analytical sample, prepared by Dr. Emerson, melted at 190–191° (dec.).

Anal. Calcd. for $C_{16}H_{16}O_5N_4$: C, 55.81; H, 4.65; N, 16.28. Found: C, 55.71; H, 4.66; N, 16.25.

A mixture of the product (150 mg., m. p. 198–198.5°) from durenol and that (150 mg., m. p. 188–189°) from duroquinone was dissolved in ethyl acetate (50 cc.) and chromatographed onto alumina. A uniform orange-red zone moved evenly down the column as the development proceeded and no differences in color could be detected. The material was eluted with ethyl acetate and this solution was chromatographed onto calcium carbonate with the same result as before. The cherry red eluent (ethyl acetate), when concentrated under reduced pressure, deposited a powdery, orange solid which melted at 193–194° (dec.). When crystallized slowly from alcohol, this substance gave long red prisms and a small amount of orange solid. The red prisms were separated mechanically and crystallized twice from alcohol. Each time the result was the same: the bulk of the product consisted of the red prisms, but a little of the orange solid was always present.

Each of the red and yellow forms, suspended in ethanol, gave a faint green color when a drop of phenylhydrazine was added in the cold. When these mixtures were boiled, both gave deep brown solutions. Both forms of the azo compound gave cherry red solutions when warmed with phenylhydrazine alone and there was no evidence of any further change even at the boiling point of phenylhydrazine.

The orange form (1.0 g., m. p. 198–199.5°) from durenol was dissolved in acetic acid (20 cc.) and benzene (60 cc.). Freshly distilled cyclopentadiene (3 cc.) was added and the mixture was refluxed for four hours. The flask was then tightly stoppered and allowed to stand at room temperature for five days. A few prisms (apparently starting material) were taken back into solution by warming, then more of the diene (3.7 cc.) was added and the mixture was allowed to stand in the ice box for eleven days, during which it deposited large orange prisms of starting material. After crystallization from dioxane, the substance melted at 197.5–198° (dec.).

The red form (1.0 g., m. p. 188–189°) obtained from duroquinone was subjected to the same treatment with cyclopentadiene. The recovered material was red, and melted at 188.5–189° (dec.).

The two forms gave identical color tests, as follows: (A) almost insoluble in cold sodium hydroxide solution (20%), but dissolved on addition of a few drops of alcohol or acetone with an intense blue color; (B) pale orange-red in concentrated hydrochloric acid solution; (C) cherry red or orange, depending upon the dilution, in concentrated nitric acid; (D) cherry red in concentrated sulfuric acid.

2',4'-Dinitro-4-acetoxy-2,3,5,6-tetramethylazobenzene.—Either form of the oxyazo compound, orange or red (1.0 g.), when refluxed for an hour in pyridine (10 cc.) containing acetic anhydride (2 cc.) gave the same acetate (960 mg.). After crystallization twice from dioxane, these acetates melted at 181.5–182°, alone or when mixed, and formed dark red crystals.

Anal. Calcd. for $C_{18}H_{18}O_6N_4$: C, 55.96; H, 4.66. Found: C, 55.89; H, 4.42.

Summary

1. Unsymmetrically substituted methyl-*p*-benzoquinones condense with *p*-nitro- and 2,4-dinitrophenylhydrazines to give monoazo compounds, the less hindered of the two carbonyl groups reacting. The quinones used were tolu-, *m*-xylo-, trimethyl- and duroquinones.

2. Duroquinone, completely substituted, is not completely inhibited in this reaction as other tetrasubstituted quinones have been found to be in reactions with hydroxylamine. The yield of azo compound, however, is lower than that obtained from trimethyl- or *m*-dimethyl-quinone.

3. Isomeric azophenols, in which the azo and hydroxyl groups are interchanged, may be prepared by coupling diazotized nitroanilines with the proper phenols. These isomeric azophenols, on reductive cleavage, give isomeric methylated aminophenols in which the amino and hydroxyl groups are interchanged. Both types of aminophenols give the original methylated quinones on oxidation.

4. One of the azo compounds, 2′,4′-dinitro-4-hydroxy-2,3,5,6-tetramethylazobenzene, exists in two polymorphic crystalline forms. One is an orange powder and the other forms deep red prisms.

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Factors Involved in the Methylation of Cellulose Acetate and of Cellulose Dissolved in Trimethylbenzylammonium Hydroxide

BY GERALD G. JOHNSTON[1]

Although it is comparatively easy with a few operations to arrive at a degree of methylation which approaches that of trimethyl cellulose, it is very difficult to reach the theoretical value unless special methods, more or less indirect in nature, are employed.

One such method was based upon the idea that acetylation would activate the otherwise tardily reacting hydroxyl groups and consisted of acetylating cellulose, or partly methylated cellulose, prior to alkylation.[2] In this way Heuser and Hiemer[2] obtained for cellulose regenerated from viscose a methoxyl content of 45.42% (theory, 45.57%) while the principle of the method has since been applied with varying success by Haworth and other investigators.[3] Methylation was also greatly facilitated with short chain cellulosic material.[2] More recently, Karrer and Escher[4] have called attention to the observation that the theoretical methoxyl value for trimethyl cellulose can only be obtained with cellulose degraded to a certain extent. They suggest that either steric hindrances or ring formation between individual chains could prevent an occasional hydroxyl group from becoming methylated unless it was made accessible by pretreatments involving hydrolysis or oxidation. If, however, degradation is allowed to proceed further, the number of end groups of the chains will increase, *i. e.*, more and more hydroxyl groups in the 4-position become available for methylation. Calculation shows that a shortening of the chain of a degree of polymerization of 1500 to 150 and 50 would increase the total methoxyl content by 0.11 and 0.43%, respectively. For this reason, the methoxyl content of highly degraded trimethyl cellulose may even exceed the theoretical value.[4]

In order to establish the relationship between methoxyl content and degree of polymerization more definitely, a series of cellulose acetates of decreasing degree of polymerization was prepared and subsequently methylated. Included in this series were two commercial cellulose acetates whose degree of polymerization ranged between the laboratory products of the higher and lower values.

These acetates were prepared from bleached cotton linters[5] as described below. The combined acetic acid content was determined according to the method of Murray, Staud and Gray.[6]

1. **Fibrous secondary acetate** was prepared by the method of Hess and Ljubitsch.[7] After 25 days at room temperature the product had a combined acetic acid content of 48.00%.

Hess and Ljubitsch's method was shown by Staudinger and Eilers[8] to leave the glycosidic linkings of the cellulose chains unattacked and, accordingly, to yield an acetate which, in contrast to secondary acetates of similar combined acetic acid content, is insoluble in acetone as well as in other solvents generally used for viscosity measurements, as, for example, dioxane and *m*-cresol. The acetate prepared in this study showed the same behavior.

2. **Fibrous triacetate** was prepared by the method of Böhringer and Söhne as described by Dorée and Healey[9] with acetic anhydride dissolved in toluene and with perchloric acid and sulfur dioxide as catalysts. After ten hours the combined acetic acid content was 61.5%. The product was soluble in chloroform and insoluble in acetone.

3. **Non-fibrous triacetate** was prepared by the method of Barnett[10] with acetic anhydride and with chlorine and sulfur dioxide combined as a catalyst. The combined acetic acid content was 62.4% (theoretical for triacetate 62.55%).

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(1) Chemist, Waldorf Paper Products Co., St. Paul, Minnesota. A portion of a thesis submitted in partial fulfillment of the requirements of the Institute of Paper Chemistry for the degree of Doctor of Philosophy from Lawrence College, Appleton, Wisconsin, June, 1940; carried out under the direction of E. Heuser.

(2) Heuser and Hiemer, *Cellulosechem.*, **6**, 101, 125 (1925).

(3) Haworth, Hirst and Thomas, *J. Chem. Soc.*, 821 (1931).

(4) Karrer and Escher, *Helv. Chim. Acta*, **19**, 1192 (1936).

(5) Supplied through the courtesy of the Hercules Powder Company.

(6) Murray, Staud and Gray, *Ind. Eng. Chem., Anal. Ed.*, **3**, 269 (1931).

(7) Hess and Ljubitsch, *Ber.*, **61**, 1460 (1928).

(8) Staudinger and Eilers, *ibid.*, **68**, 1611 (1935).

(9) Dorée and Healey, *J. Textile Inst.*, **29**, T27 (1938).

(10) Barnett, *J. Soc. Chem. Ind.*, **40**, 253 (1921).