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

PREPARATION OF THE DICHLOROTOLUQUINONES

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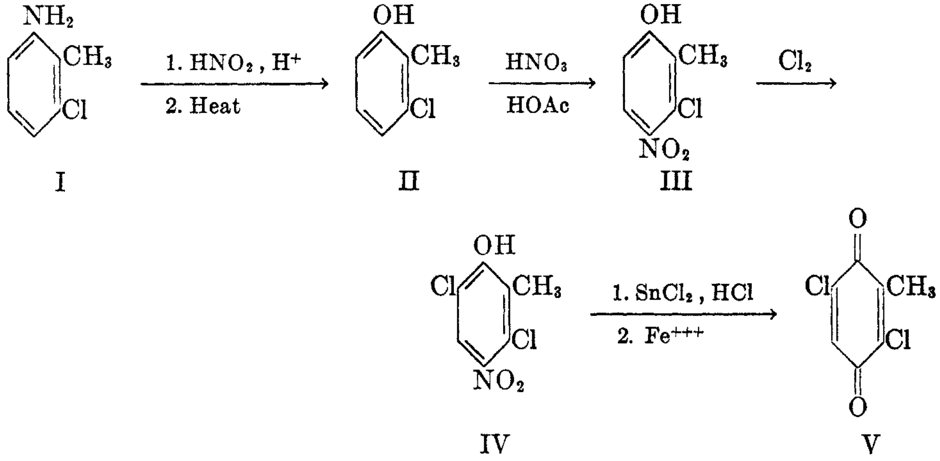
It has recently been shown (1) that pure dichlorotoluquinones are usually unobtainable by oxidation of hydroquinones resulting from addition of hydrogen chloride to chlorotoluquinones. The present report deals with the preparation by unequivocal methods of the three isomeric dichlorotoluquinones. Of these, the 3,5-isomer is the only one previously prepared by satisfactory methods (2–5). Our preparation of this isomer, by dichlorination of 4-nitro-*m*-cresol, reduction to 2,6-dichloro-4-amino-*m*-cresol, and oxidation of the aminophenol, gave a quinone whose properties are in agreement with those reported by Raiford (5) for 3,5-dichlorotoluquinone. It has been reported by Raiford (4) that when 2,6-dichloro-4-amino-*m*-cresol is acetylated with more than two equivalents of acetic anhydride, in the presence of sodium acetate, the N-acetyl derivative is obtained, not the diacetyl derivative. Using a sample of crude aminophenol, we have confirmed this observation, but when a purified sample of aminophenol was used, the diacetyl derivative was obtained. We have not further investigated the specific reasons for these variable results.

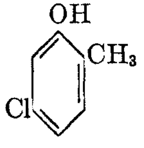
The 3,6-dichlorotoluquinone has not been previously prepared, for the material (m.p. 76°) described as such by Kehrmann and co-workers (6) was unquestionably a mixture of several quinones (1). In the present work, none of this quinone could be obtained by chromic acid oxidation of the dichlorination products of 3-chloro-*o*-cresol, 3-chloro-*o*-toluidine, or the acetyl derivative of the latter. Conversion to a rose-colored, high molecular weight material resulted. When the 3,4,6-trichloro-*o*-cresol was oxidized with nitric acid, the steam-volatile product proved to be not the desired quinone but 3,4-dichloro-6-nitro-*o*-cresol. The position of the nitro group was assigned on the basis of the steam-volatility of the compound and its non-identity with 3,6-dichloro-4-nitro-*o*-cresol. Such replacement of halogen by nitro has been observed previously (7). The 3,6-dichlorotoluquinone was finally obtained satisfactorily by the scheme outlined in formulas I–V.

The quinone, V, obtained in this manner melted at 105.5–106.4°. In previous work (1), the addition of hydrogen chloride to 3-chlorotoluquinone, followed by oxidation, eventually led to the isolation of a very small yield of relatively homogeneous dichlorotoluquinone melting at 98.5–100°, and this was shown to be not identical with 3,5-dichlorotoluquinone. When this sample was mixed with 3,6-dichlorotoluquinone, obtained as described above, the m.p. was 99.6–105°; thus, the previously obtained quinone appears to be a slightly impure sample of 3,6-dichlorotoluquinone.

The 5,6-dichlorotoluquinone has been prepared by Angeletti and Oliverio (8) by a method which very likely gives contamination with trichlorotoluquinone. Recently, Kohn and Syreia (9) prepared this isomer by oxidation of 4,5,6-trichloro-*o*-cresol in poor and unspecified yield, and reported the m.p. as 80°. Preparation, in the present investigation, by a scheme similar to that used for V but starting with 5-chloro-*o*-toluidine, gave the pure 5,6-dichlorotoluquinone, m.p. 77.8–78.5°. Thus, the quinone obtained *via* addition of hydrogen chloride to 5-chlorotoluquinone (1, 10), and melting at 85–86° is not a good sample of 5,6-dichlorotoluquinone.



The present syntheses involved preparation of the *p*-nitro derivatives of *m*-cresol, the chlorocresol II, and the chlorocresol VI. The 4-nitro-*m*-cresol was most conveniently obtained by nitrosation with nitrosylsulfuric acid,[1] followed by oxidation with nitric acid. This procedure, which gives about 65% yield, is far superior to the method previously used by us (12), and compares favorably with the nitrosation and oxidation procedure used by Koelsch (13).



VI

Direct nitration of the chlorocresols, II and VI, with nitric acid in acetic acid (14) was found to be highly satisfactory and superior to nitrosation and oxidation. Nitrosation of II gave as high a ratio of *o*-isomer as did direct nitration. Steric considerations would suggest that nitration of VI would give a higher ratio of *p*-nitration than would nitration of II. Actually, nitration of II gave a ratio of *ortho*- to *para*-isomer of about 2:1, whereas nitration of VI gave exclusively *p*-isomer.

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[1] Although Hodgson and Crouch (11) reported this method to fail with *m*-cresol, it was discovered by Mr. John Weldon of this laboratory that the procedure is quite satisfactory.

EXPERIMENTAL

All melting points are corrected, and all boiling points are uncorrected. Analyses are by the Microanalytical Division of the Department of Chemistry and Chemical Engineering, University of California.

2,6-Dichloro-4-nitro-m-cresol. 4-Nitro-*m*-cresol was prepared by way of nitrosation of *m*-cresol according to the procedure of Hodgson and Crouch (11). The yield of recrystallized material, m.p. 125–127°, was 64%. The nitrocresol (0.05 mole) was chlorinated in 100 ml. of 90% acetic acid at 20–25°, with 2.5 mole-equivalents of chlorine. There crystallized from the reaction mixture, on standing, 6.17 g. of the product, m.p. 139–140° (dec.). Dilution of the filtrate with water, and trituration of the precipitate with a few ml. of benzene gave an additional 2.3 g. of white product of m.p. 132–138° (dec.); total yield, 73%. The best sample obtained by crystallization from benzene melted at 142–143° (dec.). From the literature (5, 15), m.p. 143° (dec.).

2,6-Dichloro-4-amino-m-cresol. The above dichloronitrocresol was reduced with stannous chloride and hydrochloric acid as previously described for the preparation of 2-chloro-4-amino-*m*-cresol (12). After one crystallization from aqueous alcohol, the aminophenol, m.p. 173–176° (dec.), was obtained in 75% yield. Raiford (4) reported m.p. 175–176° (dec.). Acetylation of this recrystallized sample with 2.1 mole-equivalents of acetic anhydride in the presence of sodium acetate and recrystallization of the product from benzene yielded *diacetyl 2,6-dichloro-4-amino-m-cresol,* m.p. 157.4–157.8°.

Anal. Calc'd for $C_{11}H_{11}Cl_2NO_3$: Cl, 25.68; N, 5.07.
Found: Cl, 25.92; N, 4.86.

When the acetylation was carried out in the same manner except that there was used a sample of crude aminophenol, there was obtained *N-acetyl 2,6-dichloro-4-amino-m-cresol.* During the acetylation, much solid remained undissolved. The structure of the aminophenol was established by oxidation in good yield to 3,5-dichlorotoluquinone. The N-acetyl derivative was soluble in dilute alkali, and was precipitated unchanged on acidification. After recrystallization from ethanol, there was obtained a 50% yield of short, white needles, m.p. 211–214° (dec.). Raiford (4) reported m.p. 204–207°.

Anal. Calc'd for $C_9H_9Cl_2NO_2$: Cl, 30.30; N, 5.98.
Found: Cl, 30.10; N, 5.57.

3,5-Dichlorotoluquinone. The crude aminophenol obtained by reduction of 2,6-dichloro-4-nitro-*m*-cresol was oxidized with ferric ion as previously described (12). The over-all yield of steam-distilled quinone, m.p. 101.5–103°, was 94%, and after two crystallizations from hexane, the m.p. became constant at 103.3–103.9° [literature (5), m.p. 103°]. The *hydroquinone,* crystallized from water, melted at 172.5–173.4° [literature (5), m.p. 171°]. The *diacetyl hydroquinone,* crystallized from hexane, melted at 127.1–128.1° [literature (2), m.p. 122–124°].

2-Methyl-3,4,6-trichloroacetanilide. A 5.4-g. sample (0.03 mole) of 2-methyl-3-chloroacetanilide, m.p. 154–156°, [literature (16), m.p. 156°] was chlorinated in 50 ml. of 90% acetic acid at 55° with 0.12 equivalent of chlorine. After the solution had been heated to boiling and 30 ml. of water added, there crystallized on cooling white needles of m.p. 174–185°. A low-melting orange impurity prevented recovery of more material by concentration. Recrystallization of the first crop from ethanol yielded 4.9 g. (66%), m.p. 185–192°. When the melted sample was cooled rapidly, it remelted at once in a bath at 175°, then solidified, and melted again at 192°. Further crystallization did not change this behavior, and the sample is apparently polymorphic.

Anal. Calc'd for $C_9H_8Cl_3NO$: Cl, 42.14. Found: Cl, 41.78.

2-Methyl-3,4,6-trichloroaniline. The anilide (1.9 g.) was hydrolyzed by heating under reflux for 16 hours with a mixture of 15 ml. of ethanol and 7 ml. of concentrated hydrochloric acid. The reaction mixture was poured into 200 ml. of water, and the tan solid, collected after neutralization with sodium hydroxide and cooling in ice and salt, had m.p. 62–65.2°. There was obtained after one crystallization from aqueous ethanol 1.2 g. (80%)

of amine, and the best sample obtained after four additional crystallizations had m.p. 69–69.8°.

Anal. Calc'd for $C_7H_6Cl_3N$: Cl, 50.59. Found: Cl, 50.78.

3-Chloro-o-cresol (II). One mole (141.6 g.) of 3-chloro-*o*-toluidine was run slowly into a boiling, vigorously stirred solution of 140 ml. of concentrated sulfuric acid in 875 ml. of water. After the boiling suspension of amine sulfate had been stirred an additional ten minutes, it was cooled in an ice-salt bath and by the addition of 1 kg. of ice. Diazotization was carried out below 0° by the addition of 1.08 mole (75 g.) of sodium nitrite in 400 ml. of water, followed by stirring for five hours at 0°. The resultant clear solution was warmed to 60–70° until nitrogen evolution had ceased (about two hours). After separation of the oily dark layer of cresol the aqueous layer was extracted with benzene. The cresol was taken into 10% sodium hydroxide, and after the solution had been acidified with acetic acid the cresol was re-extracted with benzene. Distillation yielded 84 g. (59%) of a yellow solid, b.p. 90–91° (5 mm.), m.p. 84.5–85.5°. The best sample obtained by crystallization from hexane had m.p. 85.2–85.5° [literature (16), m.p. 86°].

3,4-Dichloro-6-nitro-o-cresol. 3-Chloro-*o*-cresol (10 g., 0.07 mole), dissolved in 50 ml. of 70% acetic acid was chlorinated with 0.15 mole of chlorine. After the solution had stood for one hour, it was heated to 70° and treated dropwise with a mixture of 5 ml. of concentrated nitric acid and 5 ml. of acetic acid. After this mixture had been stirred at 70° for 45 minutes it was diluted with water and directly steam-distilled. The yellow solid which separated from the distillate was crystallized three times from ethanol to yield 0.8 g. of 3,4-dichloro-6-nitro-*o*-cresol, m.p. 51.0–52.2°, which dissolved in dilute sodium hydroxide to give a clear red solution. The original yellow solid precipitated on acidification.

Anal. Calc'd for $C_7H_5Cl_2NO_3$: C, 38.02; H, 2.28; Cl, 31.94.
Found: C, 37.68; H, 2.25; Cl, 31.55.

The steam-distillation residue was not worked up for the *p*-nitroisomer.

3-Chloro-4-nitro-o-cresol (III). A solution of 35.5 g. (0.25 mole) of 3-chloro-*o*-cresol (II) in 100 ml. of glacial acetic acid was dropped slowly, with stirring, into a solution of 40 ml. of concentrated nitric acid in 80 ml. of glacial acetic acid. Inverse order of addition, and temperatures from −10° to 10° did not alter the yield. The deep red solution was poured into 700 ml. of ice and water, and the amber solid was washed well with dilute acid, and steam-distilled from faintly acidic solution. From the distillate was filtered 26 g. (55%) of *3-chloro-6-nitro-o-cresol,* m.p. 62–63°. Extraction of the residue with boiling water gave 16 g. (34%) of crude 4-nitro compound, m.p. 131–135°. After one crystallization from water (7 g. per liter), and two crystallizations from benzene the 3-chloro-4-nitro-*o*-cresol (12.5 g.) was obtained as light amber needles, m.p. 133–135.5°. The best sample obtained by further crystallization had m.p. 134.8–135.5° [literature (16), m.p. 135°]. The identity of this compound was confirmed by reduction to the aminophenol and oxidation in 78% yield to *3-chlorotoluquinone,* m.p. 54–55° after crystallization from hexane [literature (12), m.p. 54.9–55.8°].

3,6-Dichloro-4-nitro-o-cresol (IV) was obtained by chlorination of 4.0 g. (0.02 mole) of III dissolved in 60 ml. of 90% acetic acid, at 0°, with 0.024 mole of chlorine. The solution was allowed to stand for ten minutes after the addition of chlorine, then poured into 500 ml. of cold water. The precipitated solid weighed 3.64 g. (77%), m.p. 77–80°. One crystallization from hexane yielded 3.25 g., m.p. 92–94°, and the best sample obtained melted at 94.8–95.6°. Since this compound has been reported (6) to melt at 135°, it was analyzed.

Anal. Calc'd for $C_7H_5Cl_2NO_3$: Cl, 31.94; N, 6.31.
Found: Cl, 31.74; N, 6.49.

3,6-Dichlorotoluquinone (V) was prepared from the nitrocresol, IV, by the procedure which has been described (12) for the preparation of 3-chlorotoluquinone from the corresponding nitrocresol. From 4.0 g. of IV, there was obtained 3.33 g. (97%) of steam-distilled quinone, m.p. 105–106°. Fractional crystallization showed the product to be entirely homogeneous, and the best sample obtained by crystallization from hexane had m.p. 105.5–106.4°.

Anal. Calc'd for $C_7H_4Cl_2O_2$: C, 44.01; H, 2.11; Cl, 37.12.
Found: C, 44.16; H, 2.32; Cl, 37.08.

The *hydroquinone*, obtained by reduction with sodium hydrosulfite and recrystallized from water containing hydrosulfite, had m.p. 127.5–128.3°.

Anal. Calc'd for $C_7H_6Cl_2O_2$: Cl, 36.73. Found: Cl, 36.38.

The *diacetyl hydroquinone*, obtained by reductive acetylation and recrystallized from hexane, had m.p. 105.7–106.4°.

Anal. Calc'd for $C_{11}H_{10}Cl_2O_4$: Cl, 25.59. Found: Cl, 25.50.

5-Chloro-o-cresol (VI), b.p. 106–107° (15 mm.), was prepared in 65% yield from 5-chloro-*o*-toluidine by the procedure described above for the isomer, II. The best sample obtained by crystallization from benzene had m.p. 72–73° [literature (17), m.p. 73–74°].

5-Chloro-4-nitro-o-cresol was prepared as described for the isomer, III. When the product was steam-distilled, none of the 6-nitro derivative separated from the distillate on cooling. The crude 4-nitro derivative was obtained in 74% yield, m.p. 116–123°. Upon recrystallization from benzene the pure compound was obtained as felty white needles, m.p. 144.9–145.7° [literature (18), m.p. 144–145°]. Lower crops from this crystallization were contaminated with a substance forming small, hard yellow crystals, but the identity of the needles was established by conversion, in 94% yield, to 5-chlorotoluquinone, m.p. 104.6–105.3° after two crystallizations from hexane. There was no depression in melting point on mixing with the previously-prepared (12) sample of m.p. 102.8–103.9°. The yellow compound was not characterized, but a relatively homogeneous sample was obtained, m.p. 143–145°. The mixture melting point with the white needles was 116–135°.

5,6-Dichloro-4-nitro-o-cresol was prepared in 91% yield (m.p. 117–125°) by the procedure described for the isomer, IV. Crystallization from benzene gave 85% recovery of material of m.p. 139–140° (dec.). The best sample obtained by further crystallization had m.p. 141.6° (dec.).

Anal. Calc'd for $C_7H_5Cl_2NO_3$: Cl, 31.94. Found: Cl, 31.94.

5,6-Dichlorotoluquinone was prepared from 5,6-dichloro-4-nitro-*o*-cresol in 89% yield (m.p. 77.7–78.5°) by the procedure described for the isomer, V.

Anal. Calc'd for $C_7H_4Cl_2O_2$: C, 44.01; H, 2.11; Cl, 37.12.
Found: C, 43.86; H, 2.19; Cl, 37.32.

The *hydroquinone* had m.p. 110.7–111.5°. Since the only literature value (8) is m.p. 120°, the sample was analyzed.

Anal. Calc'd for $C_7H_6Cl_2O_2$: Cl, 36.73. Found: Cl, 36.45.

The *diacetyl hydroquinone* appeared to be polymorphic. A recrystallized sample melted at 116.6–118.2°, but after re-solidification of the melt, it melted at 114.6–115.2°. In one solidified sample divided by an air bubble, one half melted on insertion in a bath at 115.5°, while the other half melted at 116.8–117.8°. Kohn and Syreia (9) reported m.p. 118°.

Anal. Calc'd for $C_{11}H_{10}Cl_2O_4$: Cl, 25.59. Found: Cl, 25.53.

SUMMARY

The three dichlorotoluquinones have been prepared in high yield from the corresponding 4-nitro-*o*-cresols, by reduction to the aminocresols followed by oxidation. The corresponding hydroquinones and diacetyl hydroquinones have been described. The preparation of 4-nitro-*o*-cresols, intermediates in these syntheses, has been studied.

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REFERENCES

(1) CASON, HARMAN, GOODWIN, AND ALLEN, *J. Org. Chem.*, **15**, 860 (1950).
(2) SOUTHWORTH, *Ann.*, **168**, 270 (1873).
(3) CLAUS AND SCHWEITZER, *Ber.*, **19**, 931 (1886).
(4) RAIFORD, *J. Am. Chem. Soc.*, **36**, 675, 1510 (1914).

(5) RAIFORD, *Am. Chem. J.*, **46**, 425 (1911).
(6) KEHRMAN, SILVA, AND KELETI, *Ber.*, **48**, 2027 (1915).
(7) DE LANGE, *Rec. trav. chim.*, **45**, 19 (1926).
(8) ANGELETTI AND OLIVERIO, *Gazz. chim. ital.*, **70**, 789 (1940).
(9) KOHN AND SYREIA, *J. Am. Chem. Soc.*, **70**, 3950 (1948).
(10) CASON, *Org. Reactions*, **4**, 322, 323, 334 (1948).
(11) HODGSON AND CROUCH, *J. Chem. Soc.*, 222 (1943).
(12) CASON, ALLEN, AND GOODWIN, *J. Org. Chem.*, **13**, 403 (1948).
(13) KOELSCH, *J. Am. Chem. Soc.*, **66**, 2019 (1944).
(14) STAEDEL AND KOLB, *Ann.*, **259**, 208 (1890).
(15) HUSTON AND CHEN, *J. Am. Chem. Soc.*, **55**, 4216 (1933).
(16) NOELTING, *Ber.*, **37**, 1020 (1904),
(17) ZINCKE, *Ann.*, **417**, 208 (1918).
(18) VON AUWERS AND SCHORNSTEIN, *Fortsch. Chem. Physik. u physik Chem.*, **18**, 71 (1924–1926).