[Contribution from the Chemical Laboratory of the University of California]

PREPARATION OF THE CHLOROTOLUQUINONES

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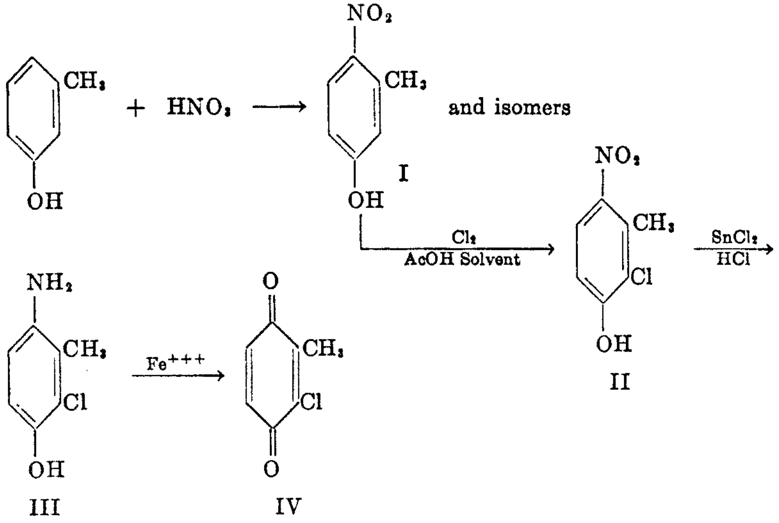
In order to make a study, to be reported later, of the addition of halogen acid to halotoluquinones, it was necessary to prepare a quantity of the three chlorotoluquinones. Two of these, the 5-chloro- and 6-chloro- isomers, have previously been obtained by several methods and their preparation offered no difficulty. 5-Chlorotoluquinone (1–4) was obtained by addition of hydrogen chloride to toluquinone and oxidation of the resultant 5-chlorotoluhydroquinone, in an over-all yield of 69%. 6-Chlorotoluquinone (5–9) was obtained by dichlorination of *o*-cresol and oxidation of the 4,6-dichloro-*o*-cresol, in an over-all yield of 42%.

3-Chlorotoluquinone (IV) has been prepared only by Raiford (3), according to the illustrated sequence of reactions beginning with *m*-cresol.



It seems surprising that chlorine should preferentially enter the 2-position in 4-nitro-*m*-cresol (I), and Kehrmann and Tichvinsky (10), who assumed that chlorine enters the 6-position, reported a series of compounds from this reaction different from those obtained by Raiford. In a later paper (11), Raiford investigated the chlorination products more carefully, and again obtained as principal product the isomer, II, but obtained from the mother liquors a very small amount of an isomeric chloronitro-*m*-cresol, which was shown to be the 6-chloro- isomer by conversion to 5-chlorotoluquinone. Since this isomer gave an aminophenol whose diacetate had a melting point in agreement with that reported by Kehrmann and Tichvinsky, it was concluded that these workers obtained the 6-chloro- isomer because they did not purify the chlorination product, but reduced the crude mixture and acetylated the crude amine. In repeating these reactions, we have confirmed Raiford's work in essentially all respects, and have obtained 3-chlorotoluquinone by the indicated sequence of reactions. After isolating the isomer, II, from the chlorination products of I, we reduced the material from the combined mother liquors, acetylated the crude aminophenol, and attempted to isolate the isomeric diacetate reported by Kehrmann and Tichvinsky; however, repeated crystallization failed to yield a pure sample of the diacetyl derivative reported by these workers.

Raiford (3) reported 38–40% yield of I from the nitration of *m*-cresol with concentrated nitric acid in acetic acid according to Staedel and Kolb (12). The latter workers reported 33% average yield, but mentioned that in some runs the steam-distillation residue was a black amorphous mass from which the isomer, I, was obtained in poor yield. All our runs were of this latter variety, and the nitro compound, I, was most conveniently obtained, although in only 18% yield, by nitration of *m*-cresol with dilute nitric acid. The yield of 2-chloro-4-nitro-*m*-cresol, II, was not reported by Raiford, but our yield of pure product did not exceed 25% although the yield of crude product was about 76%. Thus, these reactions do not constitute a convenient approach to 3-chlorotoluquinone in quantity, in spite of the fact that the over-all yield in the last two steps is 87%.

The commercially available 6-chloro-2-nitrotoluene would appear to be a convenient starting point for preparation of the quinone, IV; however, a consideration of the literature reveals that no high-yield method has been developed for conversion of a nitro compound to the corresponding *p*-benzoquinone. Excellent yields may usually be obtained from a phenol by the coupling, reduction, and oxidation route (13), but conversion of an amine to a phenol is frequently unsatisfactory. For example, Smith and Opie (14) were able to obtain no better than 55% yield of 2,3-dimethylphenol from the amine even after considerable study of the conversion and use of a rather tedious process. Direct oxidation of 2-methyl-3-chloroaniline by three procedures gave us yields of 6.5–14% of the quinone. An effort was made to introduce a favorable *p*-substituent by way of acetylation, nitration, hydrolysis, and reduction; however, oxidation of the product gave no *p*-quinone at all. This observation is consistent with the findings of Morgan and Glover (15), who isolated the 6-nitro derivative from nitration of 2-methyl-3-chloroacetanilide. These workers obtained the 4-nitro derivative by nitration of the benzenesulfonamide, but this route does not seem attractive.

In view of these results, the electrolytic reduction of 6-chloro-2-nitrotoluene to the corresponding aminophenol was considered. Raiford (3) has prepared 2-methyl-4-amino-5-chlorophenol in unspecified yield by electrolytic reduction of 3-nitro-4-chlorotoluene, and he obtained 5-chlorotoluquinone by oxidation of this aminophenol. Gattermann (16) had earlier obtained 5-bromotoluquinone from aminophenols prepared by electrolytic reduction. These appear to be the only examples of such a route for quinone synthesis; however, electrolytic reduction of nitrobenzene to *p*-aminophenol has been studied extensively, the report of Brigham and Lukens (17) being especially useful. Following the general procedure developed by these authors, but using for the reduction a standard perforated cylindrical platinum cathode, and oxidizing the diluted reduction mixture without isolating the aminophenol, no 3-chlorotoluquinone could be obtained. Further study of the reaction has shown that in this instance it is necessary to increase the sulfuric acid concentration in the catholyte to 75%, and it has been possible to define conditions under which over-all yields of quinone in the range 67–78% may be obtained. In all runs, no effort was made to isolate the aminophenol. The catholyte was simply diluted and oxidized. It is of interest that although the aminophenol, III, prepared *via* the nitrophenol as shown in the chart, is oxidized in nearly quantitative yield by ferric ion, the same compound prepared by electrolytic reduction is oxidized by ferric ion in considerably lower yield than obtained by dichromate oxidation. It is probable that this lowered yield is caused by an impurity which catalyzes decomposition of the quinone during the steam distillation used with the ferric ion oxidation. When dichromate oxidation was used the quinone was extracted with ether and a quantity of tarry material was removed by filtration before the extract was steam distilled. When this tarry material was included in the steam distillation the yield of quinone was lowered about 10%.

Since this method for preparing 3-chlorotoluquinone is simple, efficient, and rapid, and a wide variety of aromatic nitro compounds is available, the generality of the method for preparation of other *p*-benzoquinones is being studied.

EXPERIMENTAL

5-Chlorotoluquinone.[1] A mixture of 16.8 g. of pulverized, freshly steam-distilled toluquinone and 12 ml. of 18% aqueous hydrochloric acid was worked into a paste, then 30 ml. of concentrated hydrochloric acid was added dropwise with mixing during about fifteen minutes. The mixture became purple-black (quinhydrone) during this operation and warmed slightly. After standing for two hours at room temperature the reaction was completed by warming on the steam-bath for about twenty-five minutes, the mixture becoming light gray. The hydroquinone was collected by suction filtration, washed with a little water, then transferred to a flask containing 390 g. of ferric sulfate nonahydrate, 600 ml. of water, and 24 ml. of concentrated sulfuric acid. This mixture was indirectly steam-distilled immediately. From the distillate was obtained 13.0 g. of quinone by filtration and 1.8 g. additional by ether-extraction of the aqueous filtrate. Total yield, 14.8 g. (69%), m.p. 92–97°. One crystallization from hexane gave bright yellow needles melting at 102.8–103.9°. When there was used for this preparation a sample of toluquinone which had darkened from long storage, no chlorotoluquinone could be isolated.

6-Chlorotoluquinone. A solution of 108 g. (1 mole) of commercial *o*-cresol in 600 ml. of glacial acetic acid was treated with 2 moles of chlorine generated from potassium permanganate and hydrochloric acid. After addition was complete the mixture was diluted with a large volume of cold water, and the precipitated dichloro-*o*-cresol was collected and washed with water. The moist product was dissolved by heating in 1.5 liters of 70% acetic acid, and while the temperature was kept at approximately 70° by cooling, 110 g. of chromic anhydride was added slowly with swirling of the mixture. After addition was

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[1] Several authors have reported the addition of halogen acid to quinones; however, few details are given. The procedure described here is based primarily on that used by Kehrmann, Silva, and Keleti (18) for preparation of dihaloquinones.

complete the mixture was allowed to stand about one-half hour, then diluted with ice and water. The precipitated 6-chlorotoluquinone was collected by suction filtration, washed, and dried; wt. 95 g. (61%). This crude product was steam-distilled, about 1.5 liters of water being required. The quinone from the distillate was crystallized from 50% aqueous alcohol to yield 65 g. (42%) of yellow prisms, m.p. 88.4–89.9°. The best sample obtained by further crystallization melted at 89.9–90.2°.

4-Nitro-m-cresol (*I*). To a mixture of 84 ml. of concentrated nitric acid and 300 ml. of water there was added with swirling 70 g. of technical *m*-cresol, the temperature being maintained at 20–25° by cooling. After the mixture had stood an additional hour at the same temperature, with frequent shaking, the dark oily layer was separated and steam distilled until the distillate ran clear. The residual tar was extracted four times with 200-ml. portions of boiling water, the extracts being carefully decanted from the tar. After the total extracts had been filtered through Supercel, 40 ml. of 12 *N* sodium hydroxide and 40 g. of sodium chloride were added, and the mixture was concentrated to about 200 ml. The salt crystallizing on cooling was washed with small portions of alcohol and ether and combined with a small second crop of salt obtained by concentrating the filtrate. A solution of the salt in 300 ml. of water was acidified with 20 ml. of concentrated hydrochloric acid and treated with charcoal. The 4-nitro-*m*-cresol which crystallized on cooling weighed 18.0 g. (18%), m.p. 125–126°. One crystallization from water yielded material melting at 128–129° [literature (3, 12), 127–129°].

2-Chloro-4-nitro-m-cresol (*II*). The chlorine generated from 2.18 g. of potassium permanganate and 15 ml. of concentrated hydrochloric acid (calc'd wt. of chlorine, 2.44 g., 0.034 mole) was passed into a solution of 5 g. (0.033 mole) of I in 30 ml. of glacial acetic acid, during about 15 minutes. The reaction mixture warmed slightly. After standing one and one-half hour, the reaction mixture was diluted with 180 ml. of water and allowed to stand overnight. The precipitate was collected, washed with water, dried, and systematically crystallized from benzene. From 4.6 g. of crude product, the total yield of the isomer, II, consisting of short white needles, was 1.5 g. (25%), m.p. 132.5–134°. The best sample melted at 133.5–134.6° [Raiford (3) reported m.p. 133°].

2-Chloro-4-amino-m-cresol (*III*) was prepared by reduction of 0.7 g. of the nitro compound, II, dissolved in 1 ml. of ethanol, with 3.4 g. of stannous chloride dihydrate in 3.5 ml. of concentrated hydrochloric acid. After adding an additional 6 cc. of concentrated hydrochloric acid and cooling, the precipitated salt was collected and dissolved in hot water. On neutralization of the filtered solution with solid ammonium carbonate, the aminophenol, III, precipitated. After solution in hot ethanol, filtration, and precipitation by addition of water, the product melted at 162–166° (dec.). For a recrystallized sample, Raiford (3) reported m.p. 166–167°. On acetylation with 2.1 equivs. of acetic anhydride in presence of a trace of sodium acetate, the *diacetyl derivative of III* was obtained. After crystallization from benzene, the m.p. was 177–180° [literature (3), m.p. 178°].

3-Chlorotoluquinone (*IV*). *From 2-chloro-4-nitro-m-cresol.* The nitro compound, II, (1.0 g.) was reduced as described above, and the reaction mixture was diluted with 50 ml. of water. After addition of 40.5 g. of ferric sulfate nonahydrate the mixture was steam-distilled at once. From the distillate there was removed 0.55 g. of quinone by filtration, m.p. 52.5–54.1°, and 0.15 g. of quinone by ether extraction of the aqueous filtrate, m.p. 52.4–53.8°; total yield, 87%. The best sample of quinone crystallized from hexane as yellow needles, m.p. 54.0–55.5° [Raiford (3) reported 55°].

From 6-chloro-2-nitrotoluene. Conditions giving the best results are described in detail, while results obtained under other conditions but using the same equipment are included in Table I. Better yields are obtained at lower current densities, where the hydrogen over-voltage is lower. Although Brigham and Lukens (17) report that a copper cathode may be used for the reduction of nitrobenzene to *p*-aminophenol, we were able to obtain no quinone at all from 6-chloro-2-nitrotoluene under a variety of conditions, using for the reduction a copper cathode of the excellent design described by Lukens (19). It is possible that the hydrogen over-voltage for copper is too high for reduction of this nitro compound to a hydroxylamine, so that products resulting from further reduction are obtained; however, it has been claimed that copper has a catalytic effect in this reduction. Since a platinum cathode was found to be satisfactory this matter was not pursued further, and such factors as the purity of the copper were not investigated.

All reductions were carried out in a two-compartment cell, the inner compartment, containing the catholyte, consisting of a dense alundum extraction thimble, 4.5 x 11 cm. This was placed in a 250-ml. beaker containing the anolyte. The cylindrical anode (7.5 cm. high and 6 cm. in diameter) was of ⅛-inch sheet lead, and the anolyte was 75% sulfuric acid. The level of acid in the anolyte and catholyte compartments should be the same. The cylindrical cathode was of platinum, 5.3 cm. high and 2.8 cm. in diameter, perforated with about 1,700 holes of 1.0 mm. diameter. The area of the holes was ignored in calculating current density; a cathode area of 0.5 sq. dec. was assumed. The mixture in the cathode compartment was 80 ml. (±4 ml.) of 75% sulfuric acid and 10.0 g. (0.058 mole) of commercial 6-chloro-2-nitrotoluene.

TABLE I

PREPARATION OF 3-CHLOROTOLUQUINONE

CURRENT DENSITY (AMPS./SQ. DEC.)	EQUIVS. OF CURRENT	CONC. OF H_2SO_4, %	OXIDIZING AGENT	YIELD, %
1.65	1.0	50	Fe^{+++}	0[a]
1.65	2.7	92	Fe^{+++}	13[b]
1.65	2.0	75	Fe^{+++} Dichromate	32[c] 54.5[c]
1.0	1.5	75	Dichromate	67[d] 62.5[d]
1.0	1.1	75	Dichromate	63
0.6	1.1	75	Dichromate	67[e] 58.5[e]

[a] At the end of the reduction the catholyte contained sulfur, sulfur dioxide, and some unreduced nitro compound. In none of the other runs in this table was unreduced nitro compound recovered.

[b] This procedure is similar to that used by Raiford (3) and Gattermann (16).

[c] The catholyte was divided into two equal portions, and each oxidized as indicated. In other runs, similarly higher yields were obtained with dichromate.

[d] The catholyte was divided into two equal portions which were oxidized in the same way, except that one was worked up after two hours, the other after standing overnight. The portion worked up after two hours gave the lower yield of a product which had a lower melting point. All other dichromate oxidations were allowed to stand overnight.

[e] The catholyte was divided into two equal portions which were oxidized in the same manner, but in one the tar was not filtered from the ether extract before steam-distillation of the product and the lower yield was thus obtained. This difference in yield was again observed when two separate runs were worked up in these ways.

During a reduction, a propeller-type glass stirrer with two blades, mechanically driven at sufficiently high speed to keep the nitro compound finely dispersed, was placed inside the cathode, and the cell was kept at a temperature of 50–70°. Heating was necessary in order to increase the solubility of the nitro compound (m.p. 35–40°) and to prevent clogging of the electrode with solids; however, an elevated temperature has been reported as also improving reduction efficiency. For reduction, a current of 0.3 amp., requiring a potential at the electrodes of 2.5 volts, was passed for 22.9 hours, thus delivering 6.87 amp. hrs. at a current density at the cathode of 0.6 amp./sq. dec. Since the reduction of each molecule of nitro compound requires four electrons, the current used supplies 1.1 times the theoretical equivalency of electrons.

At the end of the reduction the catholyte was nearly black but clear and free of tar or other solid matter. It was diluted with water to a volume of 500 ml., then cooled in an ice-bath while there was added with swirling a solution of 9 g. (0.03 mole) of sodium dichromate dihydrate in 10 ml. of water, during about five minutes. After the mixture had stood overnight at room temperature the precipitate of quinone and tar was collected by suction filtration. Both the aqueous filtrate and tar were extracted with ether several times until the extracts became nearly colorless. The ether extracts were steam distilled, about 200 ml. of water being required, and the quinone was extracted from the distillate with ether. Removal of ether on the steam-bath left a residue of quinone weighing 6.1–7.1 g. (67–78%). On cooling, the quinone crystallized as yellow needles, m.p. 52–55.8°. A sample weighing 7.1 g. was crystallized from hexane to yield 6.7 g. of quinone melting at 54.9–55.8°.

As is evident from the data in Table I, nearly the same results were obtained when the reduction was carried out at a current density of 1 amp./sq. dec., but increasing the current density beyond this point lowers the yield appreciably.

SUMMARY

Details are reported for the preparation of the three chlorotoluquinones· Raiford's work on the chlorination of 4-nitro-*m*-cresol to give 2-chloro-4-nitro-*m*-cresol has been corroborated in all details.

A high-yield method has been developed for synthesis of 3-chlorotoluquinone from 6-chloro-2-nitrotoluene, proceeding by way of electrolytic reduction to the corresponding *p*-aminophenol and oxidation of this intermediate to the quinone.

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