[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

HYDROXYNAPHTHOQUINONE STUDIES. VI. THE CHLORINATION OF JUGLONE

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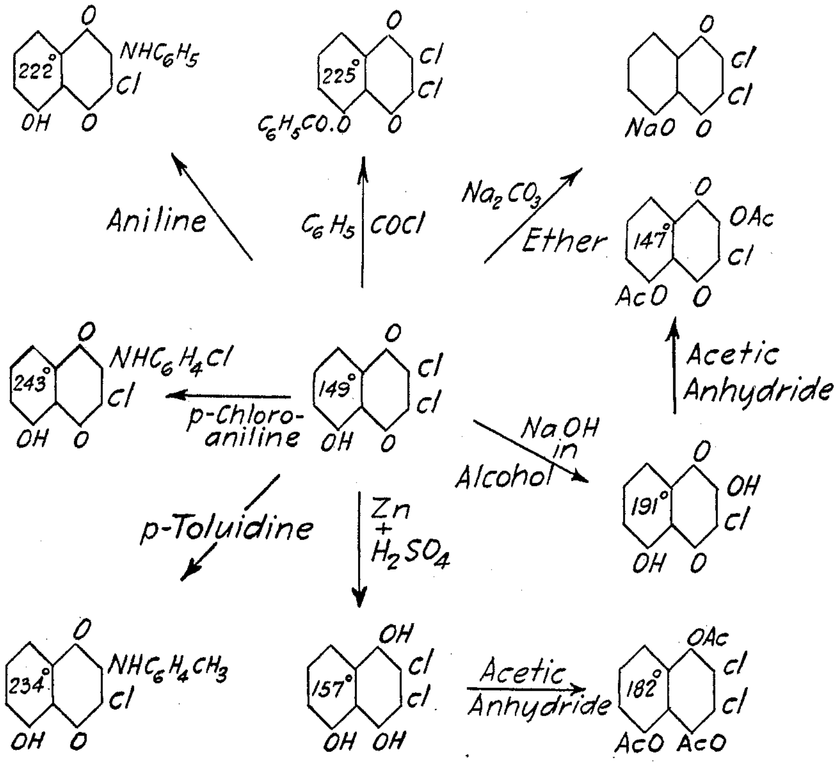
The first work on the chlorination of juglone was done by Wheeler and Scott[1]. They reported that the chlorination of juglone in cold glacial acetic acid solution gave juglone dichloride, an addition product, which lost hydrochloric acid by the action of hot alcohol, giving a monochloro substitution product. On the other hand the chlorination of juglone in hot acetic acid solution gave a dichlorojuglone which is a substitution product. The latter reaction was further studied by Wheeler and Dawson and several derivatives were made but the results were not published on account of incompleteness. They are now incorporated in this paper.

Chlorination of Juglone



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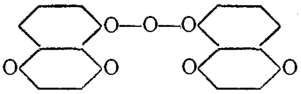
[1] Wheeler and Scott, THIS JOURNAL, **41**, 833 (1919).

They consisted briefly in the benzoylation of dichlorojuglone; the preparation of the sodium salt which was found to dye silk and wool fabrics certain buff shades readily; the alkylation of dichlorojuglone in which 1 chlorine atom was replaced by the aniline radical and finally the replacement of 1 chlorine atom by the hydroxyl group under the influence of hot alcoholic sodium hydroxide and the acetylation of this product. The work just carried out includes the alkylation of dichlorojuglone with *p*-chloro-aniline and *p*-toluidine; the reduction of dichlorojuglone with zinc and sulfuric acid and acetylation of this product; the reaction of sodium ethylate and attempts to prepare an oxime.

The chlorination of juglone was studied under various conditions. No chlorination was found to take place in carbon tetrachloride solution but it proceeded smoothly in glacial acetic acid. Scott passed chlorine in for 3 hours; Dawson reduced the time somewhat but McEwen finds 2 hours to be best.

In one preparation a very unexpected result was obtained, the whole product being a green amorphous substance. A compound of similar appearance and properties was obtained by Mylius[2] by boiling juglone with water. To determine whether the chlorine was concerned in the reaction we dissolved the juglone in hot acetic acid and set the solution aside overnight. The same amorphous green product was obtained. It was insoluble in the usual organic solvents, did not melt at 310° and dissolved in alkalies giving a deep violet solution. The formula of Mylius, $C_{20}H_{10}O_7$, suggests that oxidation of juglone has occurred with the condensation of two molecules to produce a peroxide:



The chlorine atoms in dichlorojuglone according to our belief are located at Positions 2 and 3. Whether we accept the Thiele Partial Valence theory, the Bamberger theory[3] or the Willstätter formula[4] for the constitution of naphthalene, the Positions 2 and 3 in juglone are reactive ones and substitution should readily take place there. For a time we thought that 1 chlorine atom might enter Position 8, since this is a phenol ring and the hydrogen at Position 8, *para* to the hydroxyl, would be reactive. However, our experiments show that 1 chlorine atom is more reactive than the other, being driven out of the molecule not only by strong bases such as sodium hydroxide but also by weak bases such as aniline and *p*-chloro-aniline. In this connection it is interesting to note that as soon as 2 chlorine atoms are present in the aniline molecule, its basicity is so far

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[2] Mylius, *Ber.*, **18**, 463 (1885).

[3] Bamberger, *Ann.*, **257**, 49 (1890) and following papers.

[4] Willstätter, *Ber.*, **44**, 3430 (1911).

reduced that it has no effect upon the dichlorojuglone molecule. If the 2 chlorine atoms are at Positions 2 and 3 we observe that the quinone ring is surcharged with negativity, having all 4 Positions occupied by oxygen or chlorine. It is very easy to believe that in such an environment 1 chlorine atom may be easily displaced.

In view of the fact that juglone readily takes up 3 bromine atoms, it is very peculiar that under the same conditions only 2 chlorine atoms enter the molecule, and a special attempt failed to introduce a third.

Attention is called to the color phenomena shown by the hydroxychlorojuglone. This compound dissolves in water, giving a deep red solution but if even a slight amount of acid is added, the solution becomes yellow. On neutralization of the acid, the red color reappears.

Experimental Part

The Chlorination of Juglone.—In order to arrive at the best conditions for the chlorination of juglone, carbon tetrachloride and glacial acetic acid were compared as media. There seemed to be little or no action in carbon tetrachloride solution but chlorination in acetic acid proceeded very smoothly. The time of passing in the chlorine and the subsequent heating were varied and the following procedure was finally adopted as best.

Two g. of juglone was dissolved in 20 cc. of glacial acetic acid and placed in a test-tube immersed in hot water. Chlorine, prepared by the action of hydrochloric acid on potassium permanganate and purified by passing through water, sulfuric acid and phosphorus pentoxide, was passed into the solution slowly for $1^3/_4$ hours and then rapidly for 20 minutes. As the solution cooled a mass of orange-red needles separated, the first crop weighed 1.82 g., a pure product; m. p., 149°. The second crop, obtained by concentrating the mother liquor, weighed 0.56 g.; m. p., 138°.

Owing to the easy formation of tribromojuglone, some attempts were made to introduce a third chlorine atom. Chlorine was passed into the hot solution more rapidly and for a longer time. The product consisted of less well defined crystals that were more compact, redder in color and more soluble in acetic acid and other solvents. The melting point was considerably lower, 110–116°, and was very slowly raised by repeated recrystallizations. The determination for chlorine gave a surprising result, the percentage being only slightly above that for dichlorojuglone. This reaction will be re-examined.

Sodium Salt of Dichlorojuglone.[5]—A solution of 1.4 g. of dichlorojuglone in 300 cc. of ether was shaken with 30 cc. of a 10% solution of sodium carbonate for 30 minutes. After the mixture had stood for some time the ether layer was removed and the dark colored precipitate in the water layer was filtered off. The sodium carbonate was washed out with small portions of cold water. The dry salt has an indigo-blue color and is somewhat soluble in alcohol. The aqueous solution has a deep violet color. Acidification liberates dichlorojuglone.

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[5] Work of P. R. Dawson.

Analysis. Subs., 0.3394: Na_2SO_4, 0.0841. Calc. for $C_{10}H_3O_3Cl_2Na$: Na, 8.68. Found: 8.01.

The preparation of the salt by adding sodium hydroxide to an alcoholic solution and precipitating with sodium chloride was less satisfactory owing to the difficulty of getting rid of the sodium chloride.

The sodium salt may be used for dying silk and wool shades of buff and brown. When, for example, silk is heated in such a solution the deep violet color soon turns to yellowish brown and the silk is dyed an attractive buff shade, fairly fast to light.

2,3-Dichloro-5-benzoxy-1,4-naphthoquinone,[5] $C_{10}H_3O_2.Cl_2.OCOC_6H_5$.—A solution of 0.5 g. of dichlorojuglone in 5 cc. of benzoyl chloride was heated to boiling for 3 hours. The color changed from red to brown. Evaporation of the liquid gave a product weighing 0.64 g. which after several recrystallizations from benzene melted at 225°. It forms light yellow needles, slightly soluble in alcohol, acetone and moderately soluble in benzene.

Analysis. Subs., 0.1588: AgCl, 0.1320. Calc. for $C_{17}H_8O_4Cl_2$ (347): Cl, 20.46. Found: 20.53.

2,5-Dihydroxy-3-chloro-1,4-naphthoquinone,[5] $C_{10}H_3O_2(OH)_2Cl$.—A mixture of 2.0 g. of dichlorojuglone, dissolved in 160 cc. of warm alcohol, and 80 cc. of 10% sodium hydroxide was boiled for 1 hour. The deep violet solution soon changed to dark red and a small amount of precipitate appeared. The mixture was poured into 200 cc. of cold water, and the precipitate dissolved. Upon acidification with hydrochloric acid an abundant separation of very fine yellow needles took place. This product weighed 1.45 g.; m. p., 188–189°. A second crop weighed 0.22 g.; m. p., 181–183°. The substance is extremely soluble in alcohol, slightly so in ligroin and fairly soluble in water, giving a deep red solution. The pure substance, m. p., 191°, is obtained by recrystallizing several times from dil. alcohol. The crystals are needles which are red when wet and golden-brown when dry.

Analysis. Subs., 0.1661: AgCl, 0.1062. Calc. for $C_{10}H_5O_4Cl$ (224.5): Cl, 15.81. Found: 15.83.

As stated above, the neutral solution in water is deep red. Addition of a slight amount of acid changes it instantly to yellow and neutralization restores the red color. Crystals obtained from the 2 solutions are identical in form and melting point.

2,5-Diacetoxy-3-chloro-1,4-naphthoquinone,[5] $C_{10}H_3O_2Cl(OCOCH_3)_2$.—A solution of 0.5 g. of the hydroxy derivative in 8 cc. of acetic anhydride was gently boiled for 8 hours. The color gradually changed from dark red to yellow-brown. The product, precipitated by the addition of cold water, weighed 0.62 g. and melted at 142–143°. On recrystallization twice from alcohol the pure substance is obtained in beautiful, fine yellow needles, melting sharply at 147°.

Analyses. Subs., 0.2509, 0.1908: AgCl, 0.1187, 0.0895. Calc. for $C_{14}H_9O_6Cl$ (308.5): Cl, 11.51. Found: 11.72, 11.64.

2-Anilino-3-chloro-5-hydroxy-1,4-naphthoquinone,[6] $C_{10}H_3O_2.NHC_6H_5.Cl.OH$.—A solution of 1 g. of dichlorojuglone in 75 cc. of alcohol was added 0.4 g. of aniline (slightly in excess of 1 molecular equivalent). The reaction began at once, and the solution became deep violet-red. The mixture was boiled for 15 minutes and then cooled. Very small, short, flat needles separated in abundance. Viewed in the mass they have a violet-carmine color with a metallic luster. Under the microscope they appear to resemble chips of pine bark because of their color and the jagged ends. The first crop weighed 0.9 g., m. p., 218–221°. A second crop weighed 0.22 g. Recrystallization from

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[6] Work of Dawson and McEwen.

acetone raised the melting point to 222°. The substance is fairly soluble in alcohol, very soluble in benzene and best purified from acetone.

Analysis. Subs., 0.1524: AgCl, 0.0726. Calc. for $C_{16}H_{10}O_3NCl$ (296.6): Cl, 11.83. Found: 11.88.

An attempt was made to carry out the reaction with 2,4-dichloro-aniline but even after it had been heated all day the dichlorojuglone was recovered unchanged. *p*-Monochloro-aniline reacted easily, as described below.

2-*p*-Chloro-anilino-3-chloro-5-hydroxy-1,4-naphthoquinone,[7] $C_{10}H_3O_2.NHC_6H_4Cl.Cl.OH$.—To a solution of 1 g. of dichlorojuglone in 75 cc. of hot alcohol, 0.53 g. of *p*-chloro-aniline was added, and the mixture was boiled for 30 minutes, the color turning to a dark brownish-red. As the solution cooled 0.8 g. of the product crystallized out. It consisted of dark reddish-purple, flat needles with jagged ends, that melted at 237°. The pure substance, obtained by recrystallization from acetone, melted at 243°. The substance is easily soluble in benzene, and moderately soluble in alcohol or ether.

Analysis. Subs., 0.1765: AgCl, 0.1530. Calc. for $C_{16}H_9O_3NCl_2$ (334): Cl, 21.33. Found: 21.45.

2-*p*-Toluino-3-chloro-5-hydroxy-1,4-naphthoquinone,[7] $C_{10}H_3O_2.NHC_6H_4CH_3.Cl.OH$.—An alcoholic solution of 1 g. of dichlorojuglone and 0.44 g. of *p*-toluidine was boiled for several minutes. Crystals began to appear before boiling commenced. The first crop of crystals weighed 0.8 g. These were dark, reddish-purple, flat needles with jagged ends and a brilliant luster. Recrystallization from acetone gave a pure product melting at 234°.

Analysis. Subs., 0.1560: AgCl, 0.0723. Calc. for $C_{17}H_{12}O_3NCl$ (313.6): Cl, 11.31. Found: 11.46.

1,4,5-Trihydroxy-2,3-dichloronaphthalene,[7] $C_{10}H_3(OH)_3Cl_2$.—To a suspension of 2 g. of dichlorojuglone in 50 cc. of ether were added some sulfuric acid (1:5) and zinc dust in small portions at short intervals, while the mixture was well shaken. As the dichlorojuglone was reduced it was taken up by the ether which became faintly yellow. The ether was separated, washed well with water and allowed to evaporate at room temperature. The residue was a mass of gray crystals with a metallic luster, resembling aluminum powder. The product weighed 2.0 g. and melted at 154–156° with decomposition. It was purified by dissolving it in alcohol and adding water until crystallization began. The pure product consisted of very small short prisms, gray in the mass with a brilliant metallic luster, and melting at 157° with decomposition. There is danger of decomposing the compound in the purifying process. We lost two small lots which became nearly black. It is readily soluble in acetone and in ether, difficultly soluble in hot benzene and insoluble in ligroin.

Analysis. Subs., 0.1771: AgCl, 0.2085. Calc. for $C_{10}H_6O_3Cl_2$ (245): Cl, 28.98. Found: 29.12.

1,4,5-Triacetoxy-2,3-dichloronaphthalene,[7] $C_{10}H_3(OCOCH_3)_3Cl_2$.—A solution of 1 g. of the reduction product in 15 cc. of acetic anhydride was boiled for 12 hours, soon turning yellow. Evaporation of the liquid gave a product melting at 165–170°. After recrystallization from alcohol it melted at 182° and consisted of well developed, transparent needles that were light yellow when viewed in the mass. The substance is easily soluble in acetone, fairly soluble in benzene and alcohol and nearly insoluble in ether.

Analysis. Subs., 0.1535: AgCl, 0.1196. Calc. for $C_{16}H_{12}O_6Cl_2$(372): Cl, 19.06. Found: 19.27.

Reaction with Sodium Ethylate.—From an equivalent molecular mixture of di-

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[7] Work of McEwen.

chlorojuglone and freshly made sodium ethylate a dark purple precipitate formed immediately (in benzene solution). When this was dissolved in water and acidified with hydrochloric acid, the solution turned yellow and a yellow precipitate formed. This proved to be the hydroxychlorojuglone, m. p., 191°, described above. It showed the same color phenomena. We had hoped to find also an ethoxy derivative of dichlorojuglone.

Attempt to Prepare an Oxime.—One g. of dichlorojuglone was dissolved in 20 cc. of alcohol containing 0.3 g. of hydroxylamine hydrochloride (1 molecular equivalent), and 2 drops of strong hydrochloric acid. After the solution had boiled for 2 hours and then cooled, a product was obtained, but it contained no nitrogen and proved to be unchanged dichlorojuglone. The experiment was tried with 2 molecular equivalents of the hydroxylamine salt and boiling was continued for 8 hours, but with no better success.

Summary

1. The best method of chlorinating juglone is described.
2. A description of the sodium salt and the benzoate of dichlorojuglone is given.
3. One chlorine atom of dichlorojuglone is replaced by hydroxyl by the action of alcoholic sodium hydroxide. This hydroxyl derivative and its acetate are described.
4. Dichlorojuglone was arylated by weak bases such as aniline, *p*-chloro-aniline and *p*-toluidine but not by dichloro-aniline. In each case 1 chlorine atom is replaced.
5. Dichlorojuglone was reduced in acid solution with zinc, giving a trihydroxynaphthalene. The triacetoxy derivative was also prepared.
6. Sodium ethylate yields an hydroxy derivative of dichlorojuglone and not an ethoxy.
7. Hydroxylamine hydrochloride does not give an oxime.
8. Reasons are given for locating the chlorine atoms at Positions 2 and 3.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE MECHANISM UNDERLYING THE REACTION BETWEEN ALDEHYDES OR KETONES AND TAUTOMERIC SUBSTANCES OF THE KETO-ENOL TYPE

BY E. P. KOHLER AND B. B. CORSON

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The discovery that aldehydes and ketones can be condensed with aceto-acetic ester, cyano-acetic ester, diketones, and other substances containing active hydrogen, was a natural consequence of the use of reactions which are supposed to involve aldol condensation for the synthesis of unsaturated compounds. The reagents are not essentially different from those used in these earlier syntheses, the catalysts used to induce reaction are, for the most part, the same, and the two processes usually give the same type of unsaturated compound. Most chemists, doubtless, therefore