

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

## HYDROXY-NAPHTHOQUINONE STUDIES. IV. NEW DERIVATIVES OF 2,3,8-TRIBROMO-5-HYDROXY-1,4-NAPHTHOQUINONE.<sup>1</sup>

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The papers<sup>2</sup> preceding this one dealt with (1) the reduction of naphthazarine to tetrahydroxy-naphthalene which presented a case of tautomerism of the keto-enol type; (2) the bromination of naphthazarine which revealed a case of isomerism not yet explained; (3) the chlorination and bromination of juglone or 5-hydroxy-1,4-naphthoquinone. The present investigation has extended the field which was opened up by the halogenation of juglone. It is a surprising thing that the bromination of juglone in hot glacial acetic acid solution gives a tribromo derivative in nearly quantitative yield whereas chlorination gives under similar conditions a dichloro derivative. By over-dosing the juglone with chlorine the yield is reduced and the more soluble product contains a higher percentage of chlorine but not sufficient for a trichloro-juglone. Up to the present we have been unable to prepare such a compound.

The present work more thoroughly confirms our belief that the third bromine atom is in the phenol ring, *para* to the hydroxyl group. Tribromo-juglone is a stable compound, so that there is no likelihood that two bromine atoms are attached to one carbon atom *ortho* to another carbon to which a bromine atom is joined, *i. e.*, a 2,2,3-tribromo-juglone. One bromine atom is much more reactive than the other two; hence we place it in Position 8, *para* to the hydroxyl group. All of the reactions but one in this study leave the two other bromine atoms unaffected.

The new tetrahydroxy-naphthalene (C in Fig. 1) is the simplest of the new compounds which came to light in this research. Only two of the many possible isomers have been described; (1) the 1,2,5,8-isomer described by Zincke and Schmidt<sup>3</sup> or the 1,4,5,6 as one<sup>4</sup> of us prefers to call it and (2) the 1,2,5,8-isomer of Zincke and Ossenbeck.<sup>5</sup> The new one is the 1,4,5,8-isomer. It resembles the second in its instability and was not obtained in a pure condition. It was prepared by the reduction of the dihydroxy-dibromo-naphthoquinone (B) with zinc in alkaline solu-

<sup>1</sup> This paper constitutes a portion of a thesis submitted by T. M. Andrews to the Faculty of the Graduate School of the University of North Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

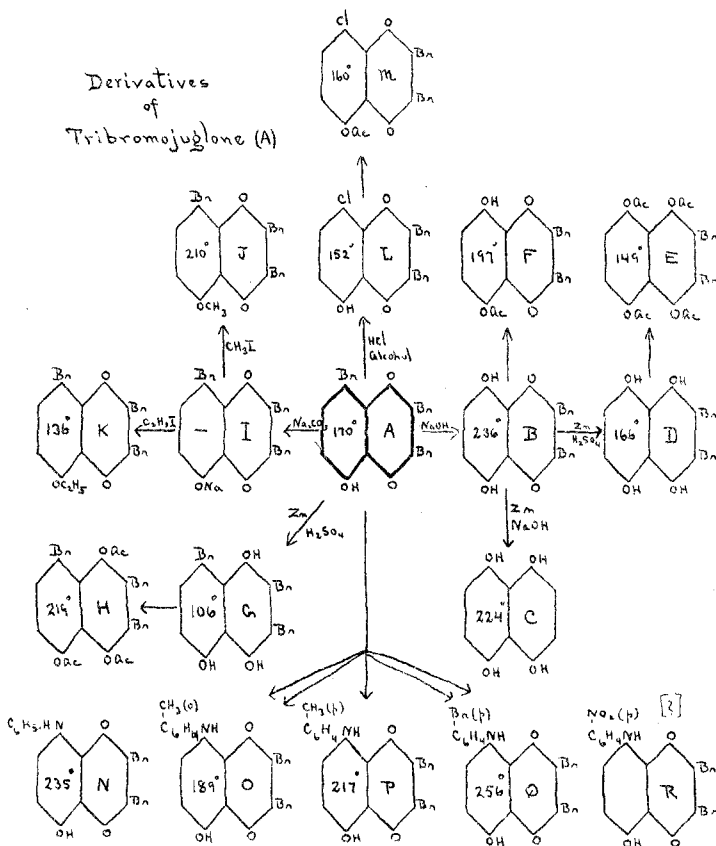
<sup>2</sup> Wheeler and Edwards, *THIS JOURNAL*, **38**, 387 (1916); Wheeler and Edwards, *ibid.*, **39**, 2460 (1917); Wheeler and Scott, *ibid.*, **41**, 833 (1919).

<sup>3</sup> Zincke and Schmidt, *Ann.*, **286**, 37 (1895).

<sup>4</sup> Wheeler, *THIS JOURNAL*, **38**, 387 (1916).

<sup>5</sup> Zincke and Ossenbeck, *Ann.*, **307**, 16 (1899).

tion. If the reduction is carried out in acid solution, however, the bromine atoms are unaffected and a tetrahydroxy-dibromo-naphthalene (D) is obtained which yields a tetra-acetyl derivative (E). The acetylation of the dihydroxy compound (B) gave unexpectedly only a mono-acetyl derivative (F). The reduction of tribromo-juglone with zinc in acid solution affects none of the bromine atoms, a trihydroxy-tribromo-naphthalene (G) resulting, which yields a triacetyl derivative (H). The sodium salt of tribromo-juglone yields ethers on boiling with alkyl halides, the methoxy derivative (J) and the ethoxy derivative (K). A sodium salt of the latter was made without difficulty but the methyl ether failed to yield one. Tribromo-juglone loses one atom of bromine in a boiling alcoholic solution of hydrochloric acid, chlorine taking its place (L). This gives an acetyl derivative (M). Finally a series of derivatives was obtained by boiling tribromo-juglone with alcoholic solutions of aromatic amines, the labile bromine atom giving place to the amino radicals. Aniline, *o*-toluidine, *p*-toluidine and *p*-bromo-aniline gave pure products



(N, O, P, Q) but *p*-nitro-aniline gave a derivative whose character we have not yet determined.

We wish to thank the National Aniline and Chemical Company of Buffalo for a supply of 1,5-dihydroxy-naphthalene which greatly aided us in this work, saving us much time in preparing this compound from naphthalene. We oxidized the dihydroxy-naphthalene to juglone in the usual way with dilute chromic acid solution. The bromination of juglone was carried out by the very smoothly working method of Wheeler and Scott.<sup>6</sup>

### Experimental Part.

**1,4,5,8-Tetrahydroxy-naphthalene (C).**  $C_{10}(OH)_4$ .—Although the bromine atoms in tribromo-juglone resist the action of acid reducing agents, they are readily affected in alkaline solution. If zinc and sodium hydroxide are employed bromine atoms 2 and 3 are replaced by hydrogen, the one at 8 by an hydroxyl group and the quinone oxygens are reduced to hydroxyl groups. One g. of tribromo-juglone is dissolved in alcohol, 40 cc. of 5% sodium hydroxide is added and the mixture heated 1 hour. This process substitutes an hydroxyl group for Bromine 8. The solution is acidified with dil. sulfuric acid, the precipitate is filtered off and washed with water. It is then added to a 30% solution of sodium hydroxide which is kept hot on a steam-bath. Zinc dust is added from time to time for 3 hours. The solution finally becomes nearly colorless except for the surface, which remains reddish. The hot solution is acidified with dil. sulfuric acid, cooled and extracted with ether. The product crystallizes from ether in plates of a light gray color. The purest product obtained melted at 224°.

*Analyses.* Subs., 0.2500:  $CO_2$ , 0.6092, 0.5926;  $H_2O$ , 0.1170, 0.1173. Calc. for  $C_{10}H_8O_4$ : C, 62.50; H, 4.16. Found: C, 64.65; H, 5.21.

**1,4,5,8-Tetrahydroxy-2,3-dibromo-naphthalene (D).**  $C_{10}H_2Br_2(OH)_4$ .—The reduction of dihydroxy-dibromo-juglone (H) was carried out by dissolving 2 g. in ether, adding dil. sulfuric acid and small portions of zinc dust from time to time, shaking well. In a few minutes the solution becomes nearly colorless. The ether layer is separated, washed with water and evaporated. The residue is pale green in color, weighs 1.8 g. and melts at 149–153°. Purification is effected by crystallizing from chloroform. The pure substance melts at 164–166° with decomposition and consists of long colorless needles which are very soluble in ether, alcohol and glacial acetic acid.

*Analyses.* Subs., 0.2210, 0.1893; AgBr, 0.2361, 0.2010. Calc. for  $C_{10}H_6O_4Br_2$ : Br, 45.71. Found: 45.48, 45.21.

**1,4,5,8-Tetra-acetoxy-2,3-dibromo-naphthalene (E).**  $C_{10}H_2Br_2(OCOCH_3)_4$ .—Two g. of the tetrahydroxy compound was boiled in 20 cc. of glacial acetic acid for 20 hours. On cooling a gummy yellowish mass separated, but it crystallized in a short time. The product weighed 2.4 g. and melted below 143°. By recrystallization of the compound several times from glacial acetic acid the melting point was raised to 149–150°. The crystals were short colorless needles. They were only slightly soluble in ether, alcohol and chloroform.

*Analyses.* Subs., 0.2174, 0.1778; AgBr, 0.1557, 0.1294. Calc. for  $C_{18}H_{14}O_8Br_2$ : Br, 30.89. Found: 30.87, 30.91.

**5-Acetoxy-8-hydroxy-2,3-dibromo-1,4-naphthoquinone (F).**  $C_{10}H_2O_2Br_2OH.COCH_3$ .—The acetylation of the dihydroxy-dibromo-naphthoquinone of Wheeler and

<sup>6</sup> Wheeler and Scott, Ref. 2.

Scott<sup>7</sup> affected only one hydroxyl group. Three g. was boiled in 30 cc. of acetic anhydride for 17 hours. The red solution gradually became yellow, and on cooling an abundant crystallization took place. On recrystallizing from glacial acetic acid light yellow prisms were obtained. These melted at 197° to a red liquid.

*Analyses.* Subs., 0.1678, 0.1203: AgBr, 0.1600, 0.1142. Calc. for  $C_{12}H_6O_5Br_3$ : Br, 40.99. Found: 40.40, 40.58.

**1,4,5-Trihydroxy-2,3,8-tribromo-naphthalene (G).**  $C_{10}H_2(OH)_3Br_3$ .—The reduction of tribromo-juglone in acid solution is carried out as follows. To 2 g. of tribromo-juglone dissolved in 25 cc. of ether is added some 1:5 sulfuric acid and small portions of zinc dust at short intervals, the flask being well shaken. The reddish solution soon becomes pale yellow. The ether layer is separated and washed several times with water. To avoid decomposition of the product the ether is allowed to evaporate at room temperature. The crude product weighs 1.7 g., is grayish-green in color and melts at 105–106°. After recrystallizing from benzene it melts at 106–107°, and retains its light grayish-green color. It crystallizes in clusters of needles, and is soluble in ether and alcohol and slightly soluble in chloroform. It is acted upon by hot water, yielding a compound melting at 168°.

*Analyses.* Subs., 0.2022, 0.2130: AgBr, 0.2755, 0.2886. Calc. for  $C_{10}H_2O_3Br_3$ : Br, 58.11. Found: 57.98, 57.66.

A sodium salt could not be prepared by the ether-sodium carbonate method. The possibility of tautomerism caused us to try the action of ketone reagents such as hydroxylamine hydrochloride in alcoholic and in sodium hydroxide solution semicarbazine hydrochloride in potassium acetate solution (alcoholic) and nitrophenyl hydrazine. Semicarbazine alone gave a product. It was yellow and melted at 102–112° but a bromine analysis gave 39.57% instead of a calculated percentage of 51.06.

**1,4,5-Triacetoxy-2,3,8-tribromo-naphthalene (H).**  $C_{16}H_{11}O_8Br_3$ .—A solution of 2 g. of trihydroxy-tribromo-naphthalene in 20 cc. of acetic anhydride was boiled for 20 hours. The product crystallized on cooling as a mass of very pale yellow crystals which weighed 1.3 g. and melted at 218–220°. Recrystallization from glacial acetic acid raised the melting point to 219–220°. The crystals are very pale yellow prisms.

*Analyses.* Subs., 0.1867, 0.2303: AgBr, 0.1930, 0.2375. Calc. for  $C_{16}H_{11}O_8Br_3$ : Br, 44.53. Found: 43.99, 43.87.

**5-Methoxy-8-hydroxy-2,3-dibromo-1,4-naphthoquinone (J).**  $C_{10}H_2O_2Br_2OH.OC_2H_5$ .—Four g. of the sodium salt of tribromo-juglone was added to 800 cc. of absolute methyl alcohol containing 2 cc. of methyl iodide, and boiled under a reflux condenser for 15 hours. The purple solution after some hours gradually became red. After filtration the solution was concentrated to 25 cc. and cooled. A brick colored precipitate separated, and was filtered off and washed with a little methyl alcohol. The product weighed 3.6 g. and after recrystallizing from benzene it melted at 209–210°. The crystals are plates of a light golden-red color.

*Analysis.* Subs., 0.1533: AgBr, 0.1580. Calc. for  $C_{11}H_6O_4Br_2$ : Br, 44.20. Found: 43.86.

An attempt was made to prepare the sodium salt by shaking an ether solution with a concentrated sodium carbonate solution. The yield was small, amounting to only 15% and the content of sodium was 7.94% instead of 5.92. It appeared to change on exposure to air.

**5-Ethoxy-8-hydroxy-2,3-dibromo-1,4-naphthoquinone (K).**  $C_{10}H_2O_2Br_2OH.OC_2H_5$ .—Four g. of tribromo-juglone was dissolved in 1200 cc. of ether and shaken vigorously for 15 minutes with a solution of 8 g. of sodium carbonate in 80 cc. of water. The

<sup>7</sup> Ref. 6, p. 840.

precipitated sodium salt was filtered off, dried and then added to a solution of the calculated amount of ethyl iodide in 250 cc. of absolute alcohol. The solution is boiled, remains violet in color many hours and finally after 10 hours becomes reddish yellow. After concentration to 50 cc. and cooling, a light brown precipitate, weighing 3.5 g., is obtained. The crystals are thin yellow plates, some with sharply pointed ends, and melt at 134–136°. The best solvent is alcohol.

*Analyses.* Subs., 0.1959, 0.2037: AgBr, 0.1936, 0.2008. Calc. for  $C_{12}H_8O_4Br_2$ : Br, 42.55. Found: 42.06, 41.95.

The loss of one bromine atom was due to the fact that boiling alcohol removed it as demonstrated by a special experiment. Tribromo-juglone was boiled with alcohol and then gave a precipitate of silver bromide with silver nitrate.

*The Sodium Salt.*  $C_{12}H_7O_4Br_2Na$ .—One g. of the ethoxy compound, dissolved in 200 cc. of ether, was shaken for 30 minutes with 2 g. of sodium carbonate in 20 cc. of water. The reddish-purple precipitate was filtered off, washed with dil. sodium carbonate solution and ether. It dyes silk a champagne color.

*Analysis.* Subs., 0.1406:  $Na_2SO_4$ , 0.0269. Calc. for  $C_{12}H_7O_4Br_2Na$ : Na, 5.80. Found: 6.20.

**5-Acetoxy-8-chloro-2,3-dibromo-1,4-naphthoquinone (M).**  $C_{10}H_2O_2Br_2Cl.COCH_3$ .—The chloro compound described by Wheeler and Scott<sup>8</sup> was boiled with acetic anhydride for 16 hours. Dilution with water gave a mass of yellow crystals which weighed somewhat more than the chloro compound used. The product crystallized from alcohol in long light yellow prisms which melted at 159.5–160°. It is very soluble in glacial acetic acid and ether.

*Analyses.* Subs., 0.1896, 0.1563: AgBr+AgCl, 0.2554, 0.2023. Calc. for  $C_{12}H_5O_4ClBr_2$ : Cl, 8.68; Br, 39.14. If Br is assumed as correct, then Cl found is 9.27, 9.22.

**8-Anilino-5-hydroxy-2,3-dibromo-1,4-naphthoquinone (N).**  $C_{10}H_2O_2Br_2OH.NHC_6H_5$ .—One g. of tribromo-juglone was dissolved in 350 cc. of alcohol containing an equivalent of aniline. The solution was heated for 6 hours on a steam-bath. Crystals formed during the boiling. The yield obtained on cooling and filtering amounted to 0.8 g. The product melted at 234.5–235.5° to a red liquid and consisted of reddish-brown crystals which were rectangular with irregularly broken ends, like chips of bark. The reaction was carried out with two equivalents of aniline but the same product was obtained. The labile bromine atom at Position 8 only is affected.

*Analyses.* Subs., 0.2246, 0.2133: AgBr, 0.2010, 0.1900. Calc. for  $C_{16}H_9O_2NBr_2$ : Br, 37.82. Found: 38.10, 37.92.

**8-*o*-Toluidino-5-hydroxy-2,3-dibromo-1,4-naphthoquinone (O).**  $C_{10}H_2O_2Br_2OHNHC_6H_4CH_3$ .—The *o*-toluidine derivative was prepared as described in the preceding paragraph. One g. of tribromo-juglone gave a product weighing 0.76 g. This was recrystallized from 50 cc. of acetone. The pure substance melts at 187.5–189° and consists of reddish-brown flat crystals slightly tapering to broad ends like a steel spatula.

*Analysis.* Subs., 0.1565: AgBr, 0.1353. Calc. for  $C_{17}H_{11}O_2NBr_2$ : Br, 36.61. Found: 36.80.

**8-*p*-Toluidino-5-hydroxy-2,3-dibromo-1,4-naphthoquinone (P).**  $C_{10}H_2O_2Br_2OHNHC_6H_4CH_3$ .—The reaction with *p*-toluidine gave a yield of 96% of the weight of tribromo-juglone taken. The product crystallized in the hot solution. It was recrystallized from 150 parts of acetone and consisted of reddish-brown rectangular plates, melting at 216–217°. It is very soluble in ether and only slightly soluble in alcohol.

<sup>8</sup> Wheeler and Scott, Ref. 2.

*Analysis.* Subs., 0.2212: AgBr, 0.1911. Calc. for  $C_{17}H_{11}O_3NBr_2$ : Br, 36.61. Found: 36.76.

**3-*p*-Bromo-anilino-5-hydroxy-2,3-dibromo-1,4-naphthoquinone (Q).**  $C_{10}H_2O_2Br_2OH-NHC_6H_5Br$ .—One g. of tribromo-juglone was boiled with 350 cc. of alcohol containing one molecule of *p*-bromo-aniline. A voluminous precipitation took place during the heating. The crude product weighed 1.2 g. and melted at 253–256°. After crystallizing twice from 75 cc. of acetone the melting point was raised only to 254–256°. The product consists of long prismatic needles of reddish-brown color, difficultly soluble in alcohol and ether.

*Analysis.* Subs., 0.1500: AgBr, 0.1691. Calc. for  $C_{16}H_8O_3NBr_3$ : Br, 47.81. Found: 47.99.

**Reaction with *p*-Nitro-aniline.**—An attempt was made to carry out the reaction with *p*-nitro-aniline. One g. of tribromo-juglone gave a yellow product weighing 0.68 g. and melting at 159.5–160° after recrystallizing twice from 50 cc. of acetone. The crystals are short yellow prismatic needles. Two determinations of bromine gave very high results, 52.31% and 52.25% instead of 34.18% calculated. We are unable to explain this at present.

**Coupling with a Diazo Compound.**—The sodium salt of tribromo-juglone was added to a diazotized solution of aniline at 0°. The product was recrystallized from alcohol, was brick-red and melted at 145–147°. No test, however, could be obtained to indicate the presence of nitrogen.

### Summary.

1. Tribromo-juglone possesses a very reactive bromine atom at Position 8. It was replaced by the following groups: OH, Cl,  $NHC_6H_5$ ,  $NHC_6H_4-CH_3$  (*o*),  $NHC_6H_4CH_3$  (*p*),  $NHC_6H_4Br$  (*p*).
2. The quinone oxygens are reduced to hydroxyl groups by zinc dust in acid solution, giving a tribromo-trihydroxy-naphthalene.
3. If the bromine at Position 8 is first replaced by an hydroxyl group, then (1) zinc dust in acid solution gives tetrahydroxy-dibromo-naphthalene and (2) zinc dust in alkaline solution gives a tetrahydroxy-naphthalene.
4. The acetyl derivatives of all compounds containing an hydroxyl group were prepared.
5. The sodium salt of tribromo-juglone gave ethers on boiling with alkyl halides.
6. Compounds containing the quinoid complex and one or more hydroxyl groups are dyes.
7. All compounds described are new.

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