[Contribution from the Chemistry Department, Marischal College, University of Aberdeen]

THE CHLORINATION OF 1,5-DIHYDROXYNAPHTHALENE

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According to Willstätter and Schuler (1) who first studied the subject, chlorination of 1,5-dihydroxynaphthalene yields the diacetate of 4,8-dichloro-1,5-dihydroxynaphthalene but no evidence was submitted in support of this structure. Subsequently, Wheeler and Mattox (2) chlorinated 1,5-diacetoxynaphthalene in carbon tetrachloride, obtaining a dichloro compound at room temperature, and a trichloro derivative at 80°, one acetyl group being hydrolyzed in each case. These products were stated to be 4,8-dichloro-5-acetoxy-1-naphthol and 4,4,8-trichloro-5-acetoxy-1-hydroxy-3,4-dihydronaphthalene respectively, since oxidation of the dichloro compound with chromic acid yielded a monochloro-5-acetoxy-1,4-naphthoquinone with elimination of one atom of chlorine, and the same quinone was obtained by oxidation of the trichloro compound with elimination of two atoms of chlorine. This however, did not afford a complete proof of the structures put forward: the location of a chlorine atom in the 8-position was not established, and also, the physical properties of the products obtained by acetylation and by hydrolysis of the dichloro compound differed somewhat from those described by Willstätter and Schuler (1). Since it has now been shown (3) that bromination of 1,5-dihydroxynaphthalene and 1,5-diacetoxynaphthalene in cold glacial acetic acid yields, 2,6-dibromo-1,5-dihydroxynaphthalene and 2,4-dibromo-5-acetoxy-1-naphthol respectively, there is reason to doubt the constitutions assigned to the chloro compounds cited above, and the present study was designed to ascertain their true structures.

Attempts to chlorinate 1,5-dihydroxynaphthalene according to the method of Willstätter and Schuler (1) were unsuccessful. In all cases small amounts of dark colored substances were obtained from which no definite compound could be isolated. This was disappointing, as confirmation of the unusual simultaneous chlorination and acetylation reported, was most desirable. The use of other chlorinating agents was likewise without result. In view of this, it is perhaps significant that Wheeler and Mattox (2) found it preferable to chlorinate the diacetate. Repetition of the work of the latter authors substantially confirmed their experimental results, although it was found more convenient to chlorinate in glacial acetic acid. Oxidation of the dichloro-5-acetoxy-1-naphthol (I) obtained, with chromic acid, yielded a monochloro-5-acetoxy-1,4-naphthoquinone (III), a chlorine atom in the para position to the hydroxyl group being removed. Further chlorination of this quinone afforded the dichloro derivative described by Wheeler and Mattox (2) as 2,8-dichloro-5-acetoxy-1,4-naphthoquinone. However, it has now been found that this compound is identical with 2,3-dichloro-5-acetoxy-1,4-naphthoquinone (IV) which was first prepared by Wheeler and Scott (4) by chlorination of juglone (V) followed by acetylation.[1] Furthermore, the anilino derivative (VI) of the monochloroquinone (III) is identical

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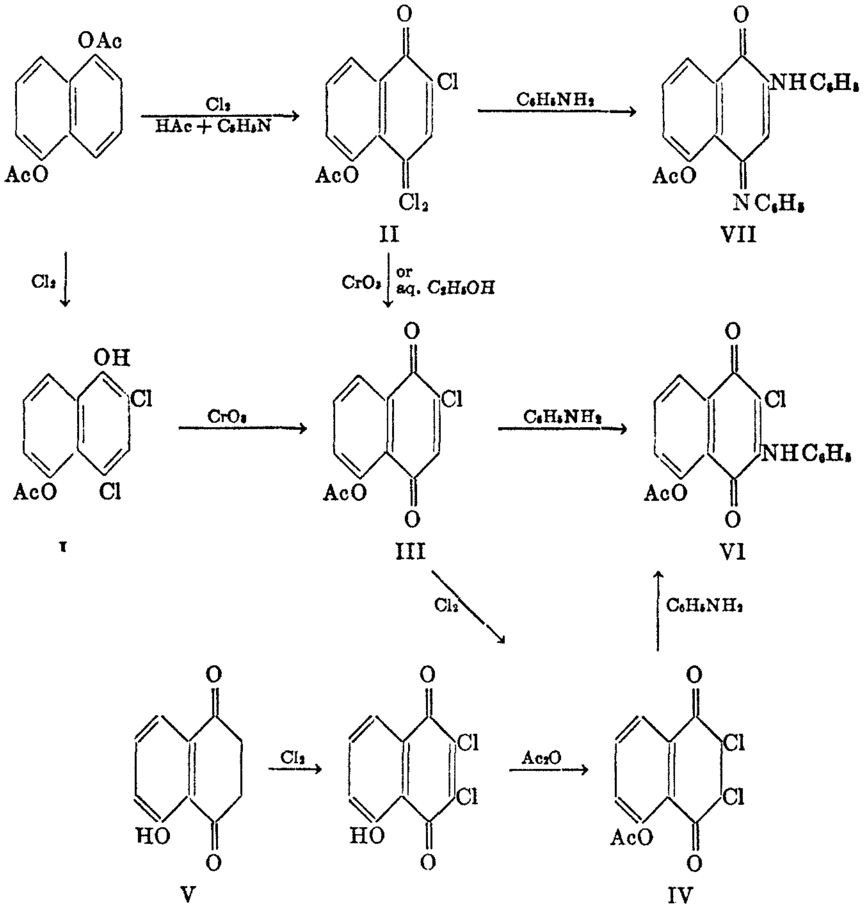
[1] For further proof of the structure of this compound see the following paper

with that obtained from the dichloroquinone (IV) by replacement of one atom of chlorine. The structure assigned to (IV) by Wheeler and Mattox is therefore incorrect, and this compound is actually 2,3-dichloro-5-acetoxy-1,4-naphthoquinone. It is thus clear that the chlorine atom in (III) must lie in the quinone ring. Hence both chlorine atoms in (I) must have entered the ring containing the hydroxyl group, and therefore occupy the ortho and para positions. In support of this the dichloro-1,5-dihydroxynaphthalene obtained by hydrolysis of (I) gives an immediate blue-violet coloration with 2,6-dichlorobenzoquinone-4-chloroimide, indicating that the para position to one of the hydroxyl groups is unsubstituted (5). Chlorination of 1,5-diacetoxynaphthalene at room temperature thus yields 2,4-dichloro-5-acetoxy-1-naphthol (I).



Wheeler and Mattox (2) obtained a trichloro compound by chlorinating 1,5-diacetoxynaphthalene at 50°, and also by further chlorination of the dichloro derivative at 80°. It has now been found that 1,5-diacetoxynaphthalene readily takes up three atoms of chlorine at room temperature in the presence of pyridine. The ease of substituion under these conditions was demonstrated when, in error, an experiment was carried out using only two-thirds of the amount of chlorine required by theory. A 40% yield of the trichloro compound was obtained. Oxidation of the trichloro compound (II) with chromic acid yielded the quinone (III), but the structure 4,4,8-trichloro-5-acetoxy-1-hydroxy-3,4-dihydronaphthalene allotted to (II) by Wheeler and Mattox is considered incorrect for the following reasons:—the compound contains no free hydroxyl group, refluxing with aqueous alcohol removes two atoms of chlorine to give the quinone (III),[2] and condensation with two molecules of aniline removes all three chlorine atoms with formation of 2-anilino-5-acetoxy-1,4-naphthoquinone-4-anil (VII). The behavior of this substance is closely analogous to the trichloro compound obtained by chlorination of α-naphthol (6), and its structure is therefore regarded as 2,4,4-trichloro-5-acetoxy-1-keto-1,4-dihydronaphthalene (II). Reaction with phenylhydrazine yielded (I) as the main product, although there were indications of phenylhydrazone formation.

Chlorination of 5-acetoxy-1-methoxynaphthalene afforded a dichloro derivative identical with the product obtained by methylation of (I) with diazomethane. This compound is therefore 2,4-dichloro-5-acetoxy-1-methoxynaphthalene, yielding on hydrolysis, followed by methylation, 2,4-dichloro-1,5-dimethoxynaphthalene.

As bromination of 1,5-dimethoxynaphthalene yields the 4,8-dibromo derivative (3), an attempt was made to obtain authentic 4,8-dichloro-1,5-dihydroxynaphthalene by chlorination of 1,5-dimethoxynaphthalene, followed by demethylation. Treatment of 1,5-dimethoxynaphthalene with phosphorus pentachloride afforded mono- and di-chloro compounds. The former was shown to be the 4-chloro derivative by preparation of the identical compound from 4-amino-1,5-dimethoxynaphthalene by a Sandmeyer reaction, and hence the latter must be either the 4,6- or the 4,8-dichloro derivative, as it differs from the 2,4-isomer obtained by hydrolysis of (I), followed by methylation. To distinguish between the two possibilities, the dipole moments of 1,5-dimethoxynaphthalene and of the dichloro compound were measured and found to be 0.36D and 0.73D respectively.[3] The similarity of these values indicates that the dichloro compound has the symmetrical structure 4,8-dichloro-1,5-dimethoxynaphthalene, but unfortunately attempts to demethylate this with hydriodic acid and with aluminum chloride were unsuccessful.

EXPERIMENTAL[4, 5, 6]

Where identity is specified, this was established by mixed m.p.

2,4-Dichloro-5-acetoxy-1-naphthol (I). This was first prepared by the method of Wheeler and Mattox (2) but the following procedure was found more convenient: a suspension of 10

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[2] As reported by Wheeler and Mattox (2) this reaction does not proceed with absolute alcohol.

[3] As the significance of these absolute values is beng considered, polarization data on these and further compounds will be published separately.

[4] Melting points are uncorrected.

[5] Microanalyses were carried out by Drs. G. Weiler and F. B. Strauss of Oxford, and Dr. J. W. Minnis of Edinburgh.

[6] The author is indebted to Imperial Chemical Industries, Ltd., Dyestuffs Division, for a gift of 1,5-dihydroxynaphthalene.

g. of 1,5-diacetoxynaphthalene in 100 cc. of glacial acetic acid was stirred and 6 g. of chlorine passed in slowly. The solution was allowed to stand for two hours, heated to 80°, 50 cc. of hot water added and the solution then cooled rapidly in ice with stirring. The crystals which separated were recrystallized from aqueous acetic acid (100 cc. of glacial acetic acid + 50 cc. of water) in colorless needles, m.p. 159–160°, turning green; yield, 5.8 g., 52%.

Oxidation of this substance with chromic acid as described by Wheeler and Mattox afforded 2-chloro-5-acetoxy-1,4-naphthoquinone (III), yellow needles, m.p. 143°. Hydrolysis of (I) as directed by the same authors yielded 2,4-dichloro-1,5-dihydroxynaphthalene, m.p. 194°. A faintly alkaline dilute aqueous solution of this naphthol gave an immediate blue-violet coloration with 2,6-dichloroquinone-4-chloroimide (5).

2,4,4-Trichloro-5-acetoxy-1-keto-1,4-dihydronaphthalene (II). This was obtained from 1,5-diacetoxynaphthalene and from (I) by the method of Wheeler and Mattox but the following precedure was preferred. A suspension of 2.4 g. of 1,5-diacetoxynaphthalene in 25 cc. of glacial acetic acid containing 3.75 cc. of pyridine was stirred and 2.1 g. of chlorine passed in slowly. After standing overnight, the crystals which separated were collected and recrystallized from ligroin (b.p. 100–120°) in colorless needles, m.p. 174°; yield, 1.8 g., 60%.

Anal. Calc'd for $C_{12}H_7Cl_3O_3$: C, 47.1; H, 2.3; Cl, 34.85.
Found: C, 47.3; H, 2.3; Cl, 34.7.

Reactions of (II).

(a) *With chromic acid.* Oxidation as for (I) yielded the quinone (III).

(b) *With aqueous alcohol.* One gram of (II) was refluxed for one hour with 40 cc. of alcohol and 20 cc. of water. The solution was then cooled, filtered, and 50 cc. of water added. Crystallization of the yellow precipitate obtained, from alcohol, yielded 0.4 g. of the quinone (III).

(c) *With aniline.* To a hot solution of 2 g. of (II) in 60 cc. of alcohol, 3 g. of aniline in 10 cc. of alcohol was added. After refluxing for one hour the solution was allowed to stand overnight, and the crystals which separated were collected and recrystallized from acetone (charcoal). 2-Anilino-5-acetoxy-1,4-naphthoquinone-4-anil (VII) separated in small lustrous reddish-brown plates, m.p. 212°.

Anal. Calc'd for $C_{24}H_{18}N_2O_3$: N, 7.3. Found: N, 7.35.

(d) *With phenylhydrazine.* To a solution of 1.5 g. of (II) in 50 cc. of alcohol, 1 g. of phenylhydrazine hydrochloride in 10 cc. of water containing 1.5 g. of sodium acetate was added. After warming for thirty minutes on the steam-bath, the red solution was cooled, and diluted with 100 cc. of water. A light red precipitate was obtained, and this after two crystallizations from dilute acetic acid (charcoal) yielded 1 g. of the dichloro compound (I). The red color indicated some phenylhydrazone formation but this was not isolated.

2,3-Dichloro-5-acetoxy-1,4-naphthoquinone (IV). This was obtained by chlorination of the quinone (III) as described by Wheeler and Mattox (2) who regarded it as the 2,8-isomer. It separated from alcohol in yellow plates or needles (according to the rate of cooling), m.p. 158–159°. The identical compound was prepared by acetylation of 2,3-dichlorojuglone. One-half gram of 2,3-dichlorojuglone was refluxed gently for one hour with 7.5 cc. of acetic anhydride containing one drop of concentrated sulfuric acid. The solution was then cooled, poured onto crushed ice, and the precipitate so obtained crystallized from alcohol in yellow plates, m.p. 158–159°. This is a modification of the procedure of Wheeler and Scott (4) who reported 2,3-dichlorojuglone m.p. 149°, and acetate m.p. 154°. Wheeler and Naiman (8) later reported m.p. 153° for 2,3-dichlorojuglone but did not acetylate their product. 2,3-Dichlorojuglone obtained by the present author had m.p. 154°.

3-Anilino-2-chloro-5-acetoxy-1,4-naphthoquinone (VI). This was prepared by the method of Wheeler and Mattox (2) who regarded it as the 2-anilino-8-chloro isomer, and the identical compound was obtained by refluxing 0.8 g. of (IV) with 0.3 g. of aniline in 60 cc. of alcohol for thirty minutes. Red needles separated on cooling, m.p. 172°.

4-Chloro-1,5-dimethoxynaphthalene. (a) A mixture of 3.1 g. of 1,5-dimethoxynaphthalene and 3.7 g. of phosphorus pentachloride was warmed on the steam-bath for twenty minutes. The dark liquid which formed solidified on cooling and was ground with water and filtered. The solid consisted of a mixture of mono- and di-chloro compounds which were separated by fractional crystallization from glacial acetic acid, the monochloro derivative being the more soluble. Final purification of 4-chloro-1,5-dimethoxynaphthalene is best achieved by crystallization from ligroin (b.p. 100–120°) or dilute methyl alcohol. It forms colorless leaflets, m.p. 122°; yield, 0.5 g., 14%.

Anal. Calc'd for $C_{12}H_{11}ClO_2$: C, 64.7; H, 4.9; N, 15.95.
Found: C, 65.0; H, 5.0; N, 16.0.

(b) Four and one-half grams of 4-amino-1,5-dimethoxynaphthalene hydrochloride (7) was boiled with 75 cc. of water and 5 cc. of concentrated hydrochloric acid, and cooled rapidly in ice. A solution of 1.4 g. of sodium nitrite in 50 cc. of water was added slowly below the surface at 0–5°. After ten minutes the diazo solution was filtered and then added in portions to an ice-cold solution of 3 g. of cuprous chloride in 18 cc. of concentrated hydrochloric acid, and the mixture warmed on the steam-bath for one hour until the evolution of nitrogen ceased. The product was collected, washed with water, dried, and extracted with ligroin (b.p. 50–60°). The extract was treated with charcoal and concentrated to small bulk. The crystals which separated were recrystallized from dilute alcohol in leaflets, m.p. 122° identical with the product from (a) above; yield, 0.7 g., 17%.

4,8-Dichloro-1,5-dimethoxynaphthalene. This was prepared from 3.1 g. of 1,5-dimethoxynaphthalene, and 7.5 g. of phosphorus pentachloride by procedure (a) given above for the 4-chloro derivative. Crystallization from glacial acetic acid (charcoal) afforded colorless plates, m.p. 157°; yield, 2.3 g., 54%.

Anal. Calc'd for $C_{12}H_{10}Cl_2O_2$: C, 56.0; H, 3.9; Cl, 27.6.
Found: C, 55.9; H, 4.0; Cl, 28.1.

2,4-Dichloro-5-acetoxy-1-methoxynaphthalene. (a) A solution of 2.1 g. of 5-acetoxy-1-methoxynaphthalene in 10 cc. of glacial acetic acid was stirred at room temperature and 1.4 g. of chlorine was passed in slowly. After one hour the solution was poured onto ice, yielding an oil which solidified on standing. The solid was collected, washed with water, dried, and extracted with ligroin (b.p. 30–40°). The extract was evaporated to dryness and the residue crystallized from dilute acetic acid forming colorless needles, m.p. 112°; yield, 1.0 g., 29%

Anal. Calc'd for $C_{13}H_{10}Cl_2O_3$: C, 54.7; H, 3.5; Cl, 24.9.
Found: C, 54.8; H, 3.5; Cl, 25.3.

(b) Three grams of 2,4-dichloro-5-acetoxy-1-naphthol in a solution of 50 cc. of ether and 50 cc. of chloroform at −10°, was methylated with diazomethane obtained by the action of 10 cc. of 50% potassium hydroxide solution on 5 g. of nitrosomethylurea in 30 cc. of ether. The ether was allowed to evaporate at room temperature and the chloroform solution then concentrated to small bulk. Crystals separated on cooling, and these when recystallized from dilute acetic acid afforded colorless needles, m.p. 112° identical with the product of (a) above; yield, 2.2 g., 70%.

2,4-Dichloro-1-methoxy-5-naphthol. A solution of 1 g. of 2,4-dichloro-5-acetoxy-1-methoxynaphthalene in 50 cc. of alcohol was refluxed with 20 cc. of concentrated hydrochloric acid for two hours. The cooled solution was poured into 100 cc. of water, and the product collected and crystallized from dilute methyl alcohol. It separated in colorless needles m.p. 80°; yield, 0.6 g., 70%.

Anal. Calc'd for $C_{11}H_8Cl_2O_2$: C, 54.3; H, 3.3; Cl, 29.2.
Found: C, 54.0; H, 3.6; Cl, 29.2.

2,4-Dichloro-1,5-dimethoxynaphthalene. A solution of 2.5 g. of 2,4-dichloro-1,5-dihydroxynaphthalene in 100 cc. of ether was methylated with diazomethane at −10°. The ether was allowed to evaporate at room temperature and the oily residue distilled at 10 mm. pressure. The solid distillate crystallized from dilute methyl alcohol in colorless needles, m.p. 74–75°; yield, 0.8 g., 36%.

Anal. Calc'd for $C_{12}H_{10}Cl_2O_2$: C, 56.0; H, 3.9; Cl, 27.6.
Found: C, 55.8; H, 3.9; Cl, 27.6.

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SUMMARY

The di- and tri-chloro derivatives obtained by chlorination of 1,5-diacetoxynaphthalene have been reinvestigated and identified as 2,4-dichloro-5-acetoxy-1-naphthol and 2,4,4-trichloro-5-acetoxy-1-keto-1,4-dihydronaphthalene respectively.

Chlorination of 1,5-dimethoxynaphthalene yields 4-chloro- and 4,8-dichloro-1,5-dimethoxynaphthalene.

Chlorination of 5-acetoxy-1-methoxynaphthalene yields 2,4-dichloro-5-acetoxy-1-methoxynaphthalene.

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