

### III.—*Preparation and Properties of Bromolapachol.*

By SAMUEL C. HOOKER.

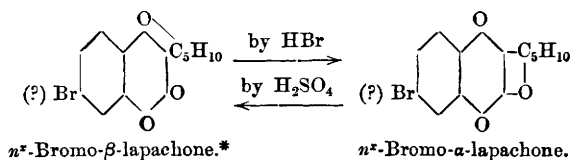
IN my researches on the constitution of lapachol and its derivatives, I have shown that these substances are of peculiar interest, owing to the changes which readily occur in the quinone group, some of the compounds being derivatives of  $\alpha$ -naphthaquinone, and some, derivatives of  $\beta$ -naphthaquinone.

In order to furnish further examples of these changes, and in the hope of subsequently being able to formulate some general rules regarding them, I have prepared the compounds described in this paper.

The preparation of dibromo- $\beta$ -lapachone was described in a paper recently presented to the Society (Trans., 1893, **63**, 424); this compound, which can be readily obtained in comparatively large quantities by following the directions there given, has furnished the material for this investigation.

In a previous communication, I discussed at length the reconversion of bromo- $\beta$ -lapachone into lapachol (Trans., 1892, **61**, 615). I have now found that dibromo- $\beta$ -lapachone may be, in like manner, readily converted into bromolapachol. The preparation of bromolapachol in this indirect manner is the more interesting because it has so far proved impossible to obtain a simple bromine derivative of lapachol by the direct action of bromine.

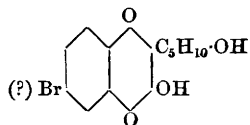
I have previously called attention (Trans., 1892, **61**, 621) to the very remarkable change which  $\beta$ -lapachone undergoes in contact with concentrated hydrochloric acid, being thereby quantitatively converted into  $\alpha$ -lapachone. It was also shown at the same time that  $\alpha$ -lapachone can be quantitatively reconverted into  $\beta$ -lapachone by merely dissolving it in concentrated sulphuric acid. Similar changes occur with the bromolapachones described in this paper. The relation between these compounds is shown in the following formulæ.



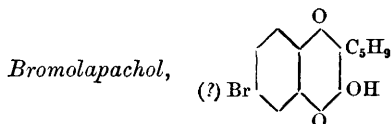
$n^x$ -Bromo- $\beta$ -lapachone is an orange-red compound which melts at about  $205^\circ$ ; it interacts very readily with orthotoluylenediamine yielding a yellow azine.

$n^x$ -Bromo- $\alpha$ -lapachone is a pale yellow substance which fuses at  $172.5\text{--}173.5^\circ$ .

On boiling with dilute aqueous alkalis, both compounds are readily converted into the same bromhydroxyhydrolapachol,



#### EXPERIMENTAL PART.



To prepare bromolapachol, 10 grams of finely-powdered dibromo- $\beta$ -lapachone are moistened with a 10 per cent. solution of sodium hydroxide, and very thoroughly ground to a paste; the quantity of the alkaline solution is then gradually increased until 100 c.c. in all have been used, the mixing being continued so as to insure entire freedom from lumps. The solution with the substance in suspension is then transferred to a small flask, 10 grams of zinc dust are added, and the flask is loosely corked, and slightly agitated at intervals during an hour, after which its contents are rinsed out and diluted with about

\* This compound is isomeric with the bromo- $\beta$ -lapachone previously described (Trans, 1892, **61**, 638), obtained by the action of bromine on lapachol. I have added the prefix  $n^x$  to its name for purposes of distinction, intending to convey by the same that the bromine is situated in the naphthalene ring, but that its exact position has yet to be determined.

1500 c.c. of water. The zinc dust is separated as completely as possible by decantation, and the diluted solution is then oxidised by drawing air through it by means of an ordinary filter pump. When the oxidation, which usually takes some hours, is complete, the solution is of a rich claret colour, and can be readily filtered off from the green, orange, and other particles in suspension. The solution should remain absolutely bright after filtration: if it passes through the filter paper with difficulty, or if a film forms over its surface, the oxidation is incomplete and should be continued. When thoroughly oxidised, the solution is poured\* into an excess of dilute hydrochloric acid, and the resulting light yellow precipitate is washed and dried. Bromolapachol is thus obtained in a pure form, the yield being 6 grams. The reactions involved in its formation are precisely similar to those concerned in the reconversion of bromo- $\beta$ -lapachone into lapachol (Trans., 1892, 61, 615 and 642), and need no further explanation here.

Bromolapachol may be obtained crystallised in leaflets very closely resembling lapachol, by boiling the substance, as above obtained, with a quantity of alcohol insufficient to dissolve it. When a larger quantity of alcohol is used and the substance passes entirely into solution, it is redeposited, on cooling, in very characteristic, golden scales, which resemble flattened needles. It melts at 170–171°.

The substance, crystallised from alcohol, gave the following figures on analysis.

0.1570 gave 0.3218 CO<sub>2</sub> and 0.606 H<sub>2</sub>O. C = 55.90; H = 4.28.

0.1679 „ 0.0975 AgBr. Br = 24.71.

C<sub>15</sub>H<sub>13</sub>BrO<sub>3</sub> requires C = 56.07; H = 4.04; Br = 24.92 per cent.

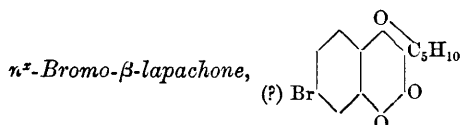
Bromolapachol can be reconverted into dibromo- $\beta$ -lapachone by the action of bromine. The change corresponds precisely to the formation of bromo- $\beta$ -lapachone from lapachol (Trans., 1892, 61, 639). 1 gram of bromolapachol dissolved in 35 c.c. of chloroform was added to 0.5 gram of bromine in 15 c.c. chloroform. After standing a few minutes, the chloroform was distilled off from a water bath, and the residue dissolved in 10 c.c. of boiling alcohol; dibromo- $\beta$ -lapachone began to crystallise out almost immediately; 0.95 gram was obtained.†

Bromolapachol dissolves in concentrated sulphuric acid forming

\* Not *vice versa*, or the precipitated bromolapachol will enclose considerable quantities of its undecomposed zinc salt.

† The mother liquor was allowed to stand for some time; it slowly deposited yellow needles in small quantity, believed to be the previously described compound, 2C<sub>15</sub>H<sub>13</sub>Br<sub>3</sub>O<sub>3</sub>.HBr (Trans., 1893, 63, 433), which it resembled in appearance as well as in its properties, as far as the small quantity obtained rendered comparison possible.

an intensely orange-red solution, from which *n*<sup>z</sup>-bromo- $\beta$ -lapachone is precipitated on adding water.



This compound is formed by the action of concentrated sulphuric acid on bromolapachol, on bromhydroxyhydrolapachol, and on *n*<sup>z</sup>-brom- $\alpha$ -lapachone; in all three cases the conversion occurs quantitatively. It is most conveniently prepared by dissolving 5 grams of bromolapachol in 25 c.c. of concentrated sulphuric acid, and pouring the solution into a relatively large volume of water; bromo- $\beta$ -lapachone separates in a crystalline condition, and, when well washed, is pure enough for most purposes. For analysis, it was crystallised from alcohol.

I. 0.1815 gave 0.3759 CO<sub>2</sub> and 0.0758 H<sub>2</sub>O. C = 56.48; H = 4.64.

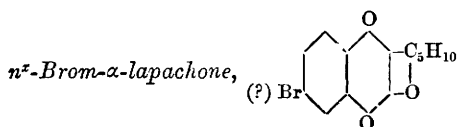
\*II. 0.1864 „ 0.3832 „ „ 0.0736 „ C = 56.06; H = 4.38.

III. 0.1212 „ 0.0716 AgBr. Br = 25.13.

C<sub>15</sub>H<sub>13</sub>BrO<sub>3</sub> requires C = 56.07; H = 4.04; Br = 24.92 per cent.

*n*<sup>z</sup>-Bromo- $\beta$ -lapachone separates from alcohol in orange-red needles, which slowly darken on exposure to diffused daylight. It melts and decomposes at about 205° when the temperature is rapidly raised, and at lower temperatures when more slowly heated. It dissolves in most of the organic solvents without difficulty, although it is in most cases considerably less soluble than  $\beta$ -lapachone, which it closely resembles in appearance as well as in its reactions. It is converted by hydrogen bromide or chloride into *n*<sup>z</sup>-brom- $\alpha$ -lapachone, and by boiling aqueous alkalis into bromhydroxyhydrolapachol.

*n*<sup>z</sup>-Bromo- $\beta$ -lapachone combines very readily with orthotoluylenediamine, in acetic acid solution, giving a yellow azine which dissolves in concentrated sulphuric acid, forming an intensely violet solution.



This compound can be readily obtained by the action of hydrogen bromide on the corresponding  $\beta$ -lapachone. It is most conveniently prepared as follows. 4 grams of *n*<sup>z</sup>-bromo- $\beta$ -lapachone, free from large crystals or lumps, are immersed in 120 c.c. of a solution of

\* I am indebted to Mr. Ellwood Wilson for this combustion.

hydrogen bromide, sp. gr. 1.49. The acid is then slowly heated, being finally kept at a temperature just below its boiling point, until the orange crystals have disappeared and entirely given place to yellow ones, a change which soon occurs. When the solution is cold, it is diluted with water, and the compound is collected and thoroughly washed. It may be further purified by crystallisation from alcohol, in which it is not very soluble.

0.2039 gave 0.4180  $\text{CO}_2$  and 0.0765  $\text{H}_2\text{O}$ .  $\text{C} = 55.90$ ;  $\text{H} = 4.16$ .

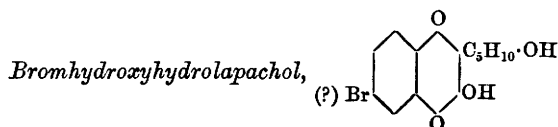
0.1463 „ 0.0875 AgBr.  $\text{Br} = 25.45$ .

$\text{C}_{15}\text{H}_{12}\text{BrO}_3$  requires  $\text{C} = 56.07$ ;  $\text{H} = 4.04$ ;  $\text{Br} = 24.92$  per cent.

*n*<sup>z</sup>-Brom- $\alpha$ -lapachone crystallises from alcohol in pale yellow scales or plates which melt at  $172.5$ — $173.5^\circ$ .

If the compound is dissolved in concentrated sulphuric acid, and the solution, after standing about 15 minutes, is poured into an excess of water, the isomeric *n*<sup>z</sup>-bromo- $\beta$ -lapachone is obtained as an orange, crystalline precipitate.

*n*<sup>z</sup>-Brom- $\alpha$ -lapachone is converted by boiling aqueous alkalis into bromhydroxyhydrolapachol. A 2 per cent. solution of sodium hydroxide is conveniently used for the purpose, the boiling being continued until the greater part of the compound, which should be finely pulverised, is dissolved. The filtered alkaline solution is acidified with acetic acid, and bromhydroxyhydrolapachol is at once precipitated in a crystalline condition.



This compound may be most conveniently obtained by the action of a 2 per cent. solution of sodium hydroxide on *n*<sup>z</sup>-bromo- $\beta$ -lapachone, the directions above given for the conversion of *n*<sup>z</sup>-brom- $\alpha$ -lapachone into the same compound being followed. After crystallisation from absolute alcohol, bromhydroxyhydrolapachol gave the following results on analysis.

0.2715 gave 0.5260  $\text{CO}_2$  and 0.1082  $\text{H}_2\text{O}$ .  $\text{C} = 52.83$ ;  $\text{H} = 4.42$ .

0.1997 „ 0.1096 AgBr.  $\text{Br} = 23.35$ .

$\text{C}_{15}\text{H}_{12}\text{BrO}_4$  requires  $\text{C} = 53.09$ ;  $\text{H} = 4.42$ ;  $\text{Br} = 23.59$  per cent.

Bromhydroxyhydrolapachol separates from alcohol in two forms. It is sometimes obtained as golden leaflets or scales, and sometimes as dense crystals, which, when deposited slowly, attain considerable size. It melts at  $164.5$ — $165.5^\circ$ , and is readily converted into *n*<sup>z</sup>-brom- $\beta$ -lapachone by concentrated sulphuric acid.