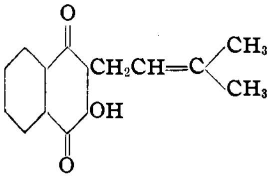
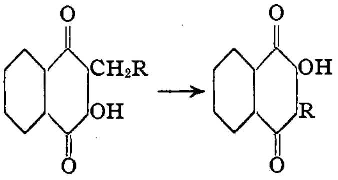
The Constitution of Lapachol and its Derivatives. Part IV.[1] Oxidation with Potassium Permanganate[2,3]

BY SAMUEL C. HOOKER

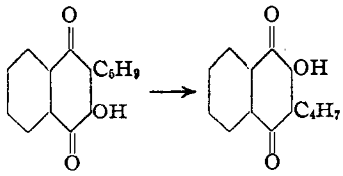
In the course of my researches on the constitution of lapachol, oxidation with alkaline permanganate was studied in anticipation of additional confirmation regarding the structure of the amylene chain in this compound. The results obtained were, however, entirely unexpected. Instead of helping substantiate in a simple way the conclusions I had reached, they themselves gave rise to a major problem, the solution of which has led to the discovery of a most interesting general reaction by means of which substances of the general formula (a) can be readily converted in good yield into others of the formula (b) with the elimination of CH_2 from the body of the chain, a conclusion which would be difficult to accept but for the very conclusive evidence I shall give in this and succeeding papers. In this way as a result of the action of alkaline permanganate on lapachol one carbon and two hydrogen atoms are removed, as indicated in the formulas:



Lapachol

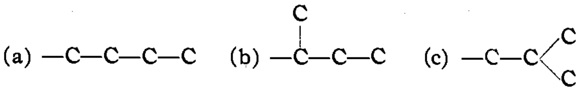


(a) (b)



I II

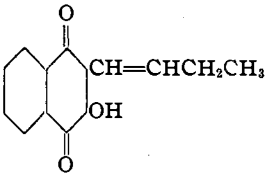
That the oxidation product is still a derivative of hydroxynaphthoquinone can be demonstrated by the formation of hydroxynaphthoquinone itself therefrom by further oxidation. Moreover, in many of its reactions it parallels lapachol itself, including its ability to add on hydrogen. This unmistakably demonstrates the presence of a double bond in the side chain, as the resulting hydrogenated compound still shows the essential characteristics of a hydroxynaphthoquinone derivative. Now a chain C_4H_7 must have one of the following skeleton structures:



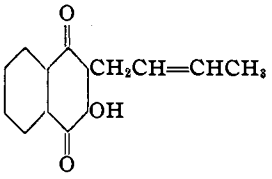
(a) —C—C—C—C (b) —C(C)—C—C (c) —C—C(C)C

and I shall show that the last of these (c) is that present in the oxidation product.

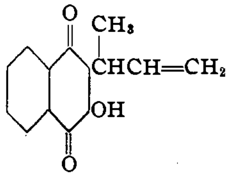
Of eight possible derivatives of hydroxynaphthoquinone having the unsaturated chain C_4H_7 in the β-position of the ring, three are known in addition to the lapachol oxidation product, namely, III, IV and V. Of these III has been prepared by the condensation of *n*-butyraldehyde with hydroxynaphthoquinone,[4] and IV and V were obtained by Dr. Louis F. Fieser in the course of his researches on the alkylation of hydroxynaphthoquinone,[5] to whom I am greatly indebted for samples of these substances which have considerably facilitated my work. By the hydrogenation of the above hydroxynaphthoquinone derivatives it is possible to determine the structure of the lapachol oxidation product. Thus, as I have



III



IV



V

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[1] Previous papers: Hooker, (a) *J. Chem. Soc.*, **61**, 611 (1892); (b) **63**, 1376 (1893); (c) **69**, 1356 (1896).

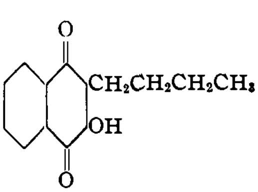
[2] See Editor's note (1) to the preceding paper.

[3] The theoretical part of this paper was written by Dr. Hooker in 1934 and only one or two minor changes have been made. The experimental part has been constructed from notes assembled by Dr. A. Steyermark. In the experimental work Dr. Hooker was in part assisted by Mr. J. G. Walsh, Jun., in the period 1893–1894, and by Dr. G. H. Connitt in 1927–1928. Isolated experiments were made by Mr. L. D. Gibson and Dr. A. Steyermark and certain of the analyses are by Dr. D. Price.—L. F. FIESER.

[4] Hooker, THIS JOURNAL, **58**, 1163 (1936).

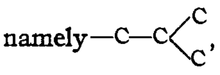
[5] Fieser, *ibid.*, **49**, 458 (1927).

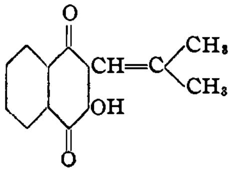
previously shown,[4] III and IV give the same compound, namely, VI, and as this differs from that

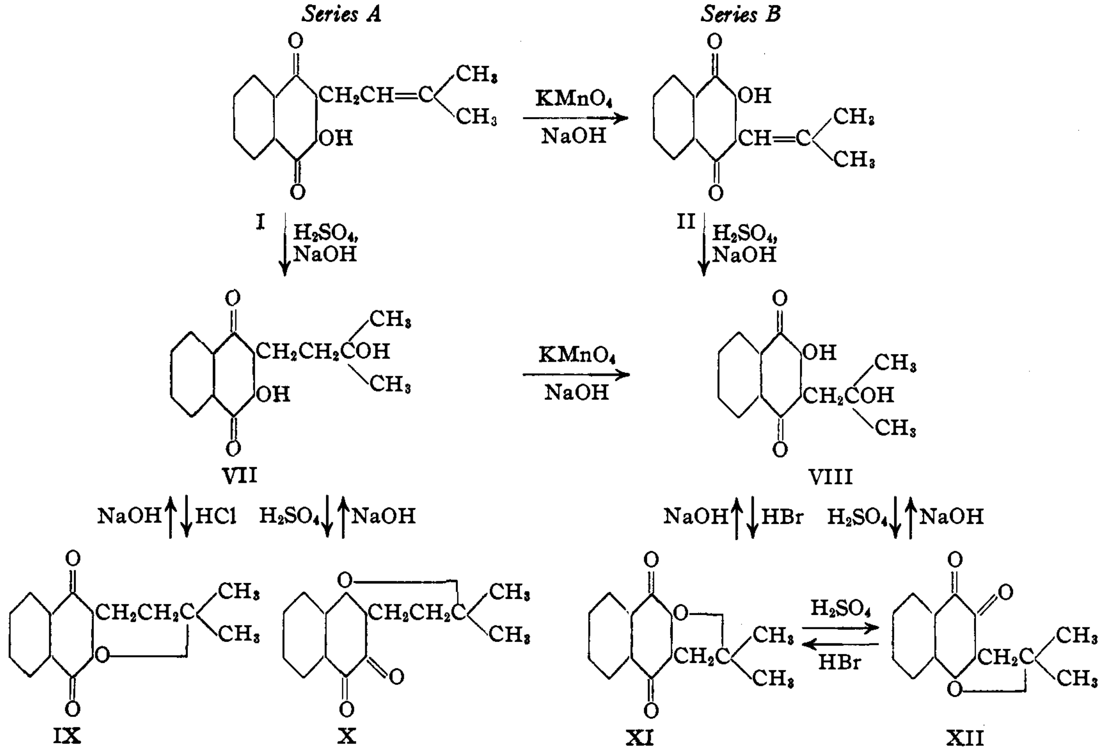


VI

obtained by the addition of hydrogen to the lapachol oxidation product the latter cannot have the chain $—CH_2CH_2CH=CH_2$.

To V, I have likewise added hydrogen and the product also differs from that arising from the lapachol compound. There remains therefore for the chain of the latter only one possible skeleton, namely  $—C—C\langle^{C}_{C}$, and as the double bond has taken no part in the oxidation it may be most reasonably assumed that no change has occurred in its position relative to the methyl groups. The oxidation product must therefore have the formula:





The position of the double bond is confirmed by the red color of the substance, as I have recently shown[4] that all 2-alkenyl derivatives of hydroxynaphthoquinone having the double bond in the α,β-position are deep orange to red, and that if the double bond is otherwise situated they are yellow. The formula thus assigned to the oxidation product necessitates the conclusion that CH_2 has disappeared from the body of the chain and has not been removed by oxidation from its extremity.

The following series of changes show the relations existing between lapachol (I) and its oxidation product (II). Substances can be produced from II having their exact counterpart in substances obtained under similar circumstances from I. The preparation, constitution and relationship to each other of the compounds in Series A were discussed by me many years ago;[1a,c] the compounds of Series B are now described for the first time.[6] (Among other transformations re-

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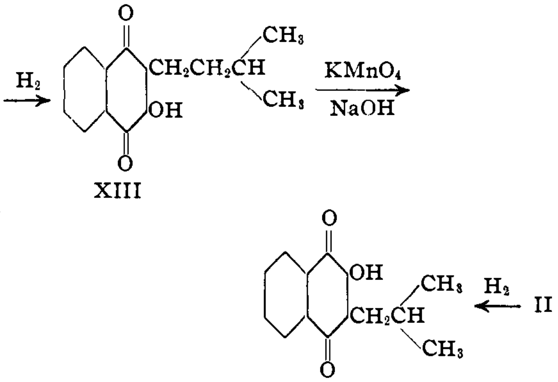
[6] Dr. Hooker did not assign names to compounds XI and XII or to a host of other ring compounds to be described in subsequent papers. On considering all of the various types of side rings, including variously substituted 5- and 6-membered saturated and unsaturated structures, and taking account of the desirability of correlating both α- and β-quinones with open-chain compounds such as VIII, I have decided to adopt the following nomenclature, which I believe would conform with Dr. Hooker's taste for simplicity and clarity (see next page).

ported in the experimental part is the formation from the substance II of a condensation product with *o*-phenylenediamine. The yield is not as good as in the case of lapachol,[1b] but it is of interest that some reaction occurs for under the same conditions the similarly constituted aldehyde condensation products[4] do not form azines.—L. F. F.)

Inasmuch as the attack of alkaline permanganate might be expected to occur at the double bond of the side chain of lapachol, it should again be emphasized that this bond takes no part whatever in the change. By reference to the above diagrammatic table it will be seen that VIII, which is formed by the action of alkali on XI and XII, also results from VII by oxidation with alkaline permanganate. Another example of this remarkable change is thus afforded and, as there is no double bond in the chain of VII, this is further evidence that the oxidation of I also occurs without reference to the double bond. Still another example is shown below.



XIII

XIV

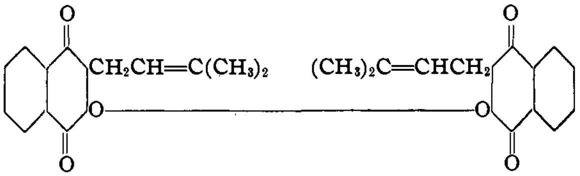
The above considerations and a study of the tables seem to leave no doubt as to the correctness of the formulas attributed to the alkaline permanganate oxidation products of lapachol and its derivatives. It remains therefore to attempt to explain how these compounds have been formed and to show how the carbon and hydrogen have been removed. I believe the following theory satisfactorily explains these changes.

Briefly, it may be assumed that in the course of the oxidation the first step is the splitting of the quinone ring, following which the ring is again formed. In the process of the new ring formation the carbon atom of the original ring attached to hydroxyl is eliminated as carbon dioxide, a carbon atom of the side chain takes its place and a new hydroxynaphthoquinone derivative is generated with the relative positions of hydroxyl and side chain reversed.

In a paper I hope to publish shortly I shall fully discuss the theory of this change and show that the reaction is applicable generally to derivatives of hydroxynaphthoquinone.

Addendum[7]

Lapachol Peroxide.—In connection with the above observations some study was made of the action of other oxidizing agents on lapachol. It was found that in acetic acid solution the hydroxyquinone is converted by lead peroxide into a neutral, sparingly soluble, yellow compound having the composition and molecular weight of a peroxide, XV. The peroxide is slowly attacked by boiling alkali and is in large part reconverted by the reagent into lapachol. 2-*n*-Amyl-3-hydroxy-1,4-naphthoquinone forms a peroxide on similar treatment with lead peroxide, while hydroxynaphthoquinone is converted only into a lead salt.



XV

Experimental Part

The lapachol required for this and other investigations was obtained largely from logs of Surinam Greenheart apparently very rich in the pigment and known in the trade as Bethabarra wood. The wood was reduced by various mills in turn to planks, to chips, and to a powder, but, as the fine sawdust did not allow the free passage of extracting solution, a mixture of 1140 lb. (518 kg.) of the ground wood with 614 lb. (279 kg.) of coarser planings of similar wood was used. This was charged in portions into a stoneware percolator and extracted with warm 1% sodium carbonate solution. The crude material which precipitated on acidification was collected and washed in a filter

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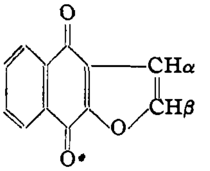
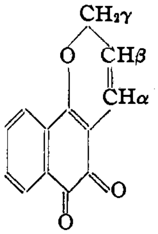


Furano-1,4-naphthoquinone



Pyrano-1,2-naphthoquinone

Compound XI is thus β,β-dimethyldihydrofurano-1,4-naphthoquinone; β-lapachone (X) is γ,γ-dimethyldihydropyrano-1,2-naphthoquinone.—L. F. F.

(7) Dr. Hooker left no instructions regarding the publication of this material. The work was carried out with the experimental assistance of Dr. A. Steyermark.—L. F. F.

press. The dried solid contained 60–70% of lapachol, which was easily extracted with benzene from an insoluble resin.

Permanganate Oxidations[8]

(a) **Lapachol.**—Ten grams of lapachol was dissolved in 1 liter of 1% sodium hydroxide solution and the red solution was cooled to about 0°. A solution of 10 g. of potassium permanganate in 1 liter of water was cooled to about 0° and added quickly in one portion to the lapachol solution. The mixture immediately became green and then changed to olive-green and to brown, and finally manganese dioxide separated leaving the solution almost colorless. The faintly pink supernatant solution became more strongly red on standing. After three to four hours the solution was filtered from the manganese dioxide and the now red solution was acidified. Orange-red needles separated slowly and after several hours the collected material amounted to 4–4.5 g. This material was found to consist largely of 2-β,β-dimethylvinyl-3-hydroxy-1,4-naphthoquinone, contaminated with some unchanged lapachol and with small amounts of other oxidation products. A separation was accomplished by fractional precipitation from 0.25–1% alkali. The lapachol was precipitated first, followed by the main reaction product. The mother liquor, after further acidification, yielded a small amount of an orange substance, and on concentrating the solution a colorless compound and some phthalic acid were obtained. The by-products were not further investigated.

2-β,β-Dimethylvinyl-3-hydroxy-1,4-naphthoquinone (II) was obtained in yield of about 3.3 g. Crystallized from alcohol, in which it is readily soluble, the substance forms red needles melting at 119–120°. The quinone also dissolves readily in benzene or glacial acetic acid. It dissolves in cold dilute alkali to form a reddish-purple solution from which the material may be recovered unchanged on acidification.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.26. Found (Hooker): C, 73.60; H, 5.28.

The acetyl derivative was prepared by boiling for one to two minutes a mixture of the hydroxyquinone (10 g.), fused sodium acetate (10 g.), and acetic anhydride (25 cc.) and pouring it into 700 cc. of cold water. The crude product was digested for a few minutes with cold 0.25% alkali in order to extract some unacetylated material (0.92 g.) and the residue was dried and crystallized from benzene–petroleum ether and finally from alcohol. The substance forms yellow prisms, m. p. 85.5–86°. It can be hydrolyzed with boiling alkali and yields the original quinone. The solution in concentrated sulfuric acid is at first crimson, but changes almost instantly to purple, violet and finally a rich blue.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.11; H, 5.18. Found (Walsh, Hooker): C, 70.67, 71.15; H, 5.35, 5.23.

The eurhodol (eurhodone?) derivative of II was prepared as follows. A mixture of 1 g. of the oxidation product, 0.86 g. of *o*-phenylenediamine hydrochloride, 3 g. of crystalline sodium acetate, and 20 cc. of glacial acetic acid was heated on the steam-bath for one and one-quarter hours, during which time the color of the solution changed from red to brown and orange-brown prisms were deposited. After cooling, the solid was collected and washed with 50% acetic acid, with water, with cold 0.25% alkali to remove unchanged material, and with water; yield, 0.6 g. Dilution of the mother liquor gave chiefly the starting material, mixed with some condensation product. The reaction product crystallized from alcohol (200 cc. per g.) in the form of amber prisms melting at 226–227° with decomposition.

Anal. Calcd. for $C_{20}H_{16}ON_2$: C, 79.96; H, 5.37. Found (Price): C, 80.39; H, 5.16.

The experiment was repeated several times using up to 25% excess of the diamine, but without material increase in the yield. In the case of lapachol the condensation product is formed in practically quantitative yield. On the other hand 2-α-butenyl- and 2-β-phenylvinyl-3-hydroxy-1,4-naphthoquinone[4] did not condense with *o*-phenylenediamine after several hours of heating. It would seem that a double bond in the α,β-position of the side chain inhibits or even prevents this type of reaction. Another difference is that the azine derivative of lapachol is dark red, and perhaps is to be regarded as a eurhodone;[1b] the condensation product from the oxidation product II is amber-yellow, a possible indication that it has the alternate structure of a eurhodol.

(b) **Hydroxyhydrolapachol** (VII).—A solution of 1 g. of hydroxyhydrolapachol[1a,c] in 100 cc. of 15% sodium hydroxide solution was cooled under the tap and treated as quickly as possible in one operation with a solution of 1 g. of potassium permanganate in 100 cc. of water. The color changes were as described above, and after three hours the filtered, red solution was acidified. The material first formed an emulsion and then became crystalline. The yield of nearly pure material was 0.71–0.73 g. **2-β-Hydroxyisobutyl-3-hydroxy-1,4-naphthoquinone** (VIII) dissolves readily in alcohol or benzene and crystallizes from these solvents in the form of silky, yellow needles, m. p. 121–122°.

Anal. Calcd. for $C_{14}H_{14}O_4$: C, 68.29; H, 5.69; mol. wt., 246.1. Found (Hooker, Connitt): C, 68.24; H, 5.70; mol. wt., 257.6 (av. of 6 determinations).

(c) **Hydrolapachol** (XIII).—One-half gram of hydrolapachol[4] was immersed in 50 cc. of 10% alkali, stirred, broken up and shaken until the whole appeared to be converted into the sodium salt which however did not all dissolve. The solution containing suspended matter was cooled in ice and 0.5 g. of potassium permanganate dissolved in 50 cc. of water, also ice cold, was quickly added. After standing about half an hour the manganese dioxide was filtered off and the deep claret red solution was rendered slightly acidic. This caused the separation of a bright yellow emulsion which soon gave way to microscopic needles; yield 0.34 g.

By one crystallization from alcohol the **2-isobutyl-3-hydroxy-1,4-naphthoquinone** (XIV) was obtained in bright yellow needles melting at 132–133°.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.04; H, 6.08. Found (Connitt): C, 72.73; H, 5.98.

In another experiment hydrolapachol was dissolved in 1% alkali and oxidized under conditions otherwise similar

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[8] Quinones having saturated side chains are best oxidized in a strongly alkaline solution, while dilute alkali gives better results with the unsaturated compounds. Further observations regarding the optimum conditions are given in later papers.—L. F. F.

to those above. Only a very small yield of isobutylhydroxynaphthoquinone was obtained and an odor strongly suggestive of butyric acid was noticed.

It was afterward found that in oxidations of this type necessitating the use of strongly alkaline solutions it is best to dissolve the substance to be oxidized in dilute alkali, adding the remaining alkali required to the permanganate solution. In this way substances usually are readily dissolved.

Structure of the Lapachol Oxidation Product (II)

Hydrogenation.—The oxidation product, 2-β,β-dimethylvinyl-3-hydroxy-1,4-naphthoquinone (5 g.) was hydrogenated in alcoholic solution (100 cc.) in the presence of Adams catalyst (0.2 g.). The filtered solution was allowed to stand overnight with access of air and on concentration it yielded yellow needles of 2-isobutyl-3-hydroxy-1,4-naphthoquinone (XIV); total yield, 4.25 g. Recrystallized from alcohol it formed yellow needles, m. p. 132.5–133.5°.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.04; H, 6.08; mol. wt., 230.1. Found (Connitt): C, 72.72; H, 6.07; mol. wt., 226.2, 227.4, 226.1.

The substance gave no depression in melting point when mixed with the oxidation product obtained from hydrolapachol, but a considerable depression of the melting points of 2-*n*-butyl-3-hydroxy-1,4-naphthoquinone[4] and of 2-*s*-butyl-3-hydroxy-1,4-naphthoquinone (see below) was noted.

2-*s*-Butyl-3-hydroxy-1,4-naphthoquinone.— 2-α-Methylallyl-3-hydroxy-1,4-naphthoquinone[5] on hydrogenation as above gave in good yield a substance which crystallized from dilute alcohol in the form of yellow needles melting at 92.5–93°.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.04; H, 6.08. Found (Connitt): C, 72.93; H, 6.06.

Oxidation.—A solution of 2 g. of 2-β,β-dimethylvinyl-3-hydroxy-1,4-naphthoquinone in 200 cc. of 1% sodium hydroxide solution was cooled to 3° and treated quickly with 2 g. of potassium permanganate in 200 cc. of cold water (1°). After one and one-half hours the filtered, red-brown solution was acidified to faint turbidity, when 0.1 g. of unchanged starting material separated. On adding an excess of hydrochloric acid the filtrate soon became cloudy and after standing deposited a dark brown precipitate which was discarded. The filtrate was made faintly alkaline with sodium carbonate and evaporated to a volume of 212 cc. A brown scum, which increased in amount on standing, was removed after two days and the solution on being acidified then yielded 0.42 g. of 2-hydroxy-1,4-naphthoquinone. On further evaporation as before an additional amount (0.16 g.) was obtained. Recrystallized from alcohol the product was obtained in the form of light brownish-yellow plates melting at 189.5–190.5°, dec. The substance showed no depression when mixed with an authentic sample of the quinone, m. p. 190–191°, dec.

Ring Compounds from 2-β,β-Dimethylvinyl-3-hydroxy-1,4-naphthoquinone (II)

The following is an account of the transformations summarized in part by the formulas in Series B in the above chart. The correctness of the 5-membered ring formulas, as in XII, is established by observations which will be presented in a later paper. A substance of the same carbon skeleton as XII but having a 6-membered oxide ring has been prepared in my laboratory and it is not identical with XII but is an isomer of this substance.

β,β - Dimethyldihydrofurano - 1,2 - naphthoquinone (XII).—Five grams of the unsaturated oxidation product (II) was dissolved in 25 cc. of cold, concentrated sulfuric acid, and after standing for a few minutes the brownish-red solution was poured into 600 cc. of cold water. The cyclic compound separated as a red, crystalline precipitate in quantitative yield. Crystallized from alcohol the compound formed deep red needles melting at 186.5–187°. An identical product was obtained from 2-β-hydroxyisobutyl-3-hydroxy-1,4-naphthoquinone (VIII) by allowing a solution of 10 g. of the quinone in 25 cc. of concentrated sulfuric acid to stand at room temperature for one-half hour and pouring the solution into water; yield, 9.3 g. (deep red needles from benzene, m. p. 187–188°).

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.26. Found (Walsh, Hooker): C, 73.12, 73.55; H, 5.39, 5.28.

The oxide ring of the ortho quinone is easily cleaved by alkali. On boiling a mixture of 0.24 g. of the substance XII with 18 cc. of 1% sodium hydroxide solution the material nearly all dissolved. The red solution was cooled, filtered, and acidified with acetic acid, giving a yellow oil which soon gave rise to yellow crystals. After reprecipitation from dilute alkali the material melted at 118.5–120° and proved to be identical with the dihydroxyisobutylnaphthoquinone (VIII) obtained by other methods.

The azine of XII was prepared (a) by heating the components in glacial acetic acid for one and one-quarter hours on the steam-bath (0.1 g. yielded the same weight of product), and (b) by dissolving 0.3 g. of the eurhodol of II in concentrated sulfuric acid and pouring the yellow-green solution into water. In the latter case the azine precipitated in the form of an orange-red sulfate, from which the free base was recovered by rendering the suspension alkaline and warming it on the steam-bath (yield, 0.3 g.). The azine dissolves in alcohol to give an orange solution with a green fluorescence, and the compound crystallizes as golden yellow needles, m. p. 154–155°.

Anal. Calcd. for $C_{20}H_{16}ON_2$: C, 79.96; H, 5.37. Found (Price): C, 79.88; H, 5.42.

2-β-Chloroisobutyl-3-hydroxy-1,4-naphthoquinone.—The oxide ring of the red ortho quinone XII can be opened by the action of hydrochloric acid in such a way as to give the chloro compound. Thus 1.4 g. of the compound was dissolved in 42 cc. of a mixture of equal volumes of concentrated hydrochloric acid and water and the deep red solution was heated at 50–55° for one hour and then at 60–65° for an additional half-hour. Yellow crystals were deposited during the heating, and after cooling the mixture these were collected on glass wool and washed with dilute hydrochloric acid followed by water. The chloro compound was crystallized from alcohol, forming bright yellow scales melting at 147–148° with decomposition. Prolonged heating of the alcoholic solution decomposes the substance. The compound dissolves readily in cold dilute alkali, giving a red solution. With concentrated sulfuric acid it slowly evolves hydrogen chloride.

Anal. Calcd. for $C_{14}H_{13}O_3Cl$: C, 63.51; H, 4.91; Cl, 13.42. Found (Walsh): C, 63.00; H, 4.79; Cl, 12.83.

β,β - Dimethyldihydrofurano - 1,4 - naphthoquinone (XI).—By the action of hydrogen bromide the red ortho quinone XII can be isomerized to the yellow para quinone XI. Probably the oxide ring first opens to give the hydroxy compound VIII, with subsequent ring closure in a different direction. To bring about the transformation 1.87 g. of β,β-dimethyldihydrofurano-1,2-naphthoquinone (XII) was dissolved in 18.7 cc. of hydrobromic acid (sp. gr. 1.49) and the red solution was heated at 65–69° for thirty-five minutes. On cooling, the reaction product was deposited in the form of greenish-yellow crystals which, when washed with concentrated hydrochloric acid and with water and dried, weighed 1.38 g. An additional 0.21 g. was obtained on diluting the mother liquor with water after it had stood for two weeks. The compound formed light yellow scales from alcohol, m. p. 183–184°.

The yellow quinone was also obtained as follows from 2 - β - hydroxyisobutyl - 3 - hydroxy - 1,4 - naphthoquinone (VIII). One gram of the material was made into a paste with a mixture of 15 cc. of concentrated sulfuric acid and 85 cc. of water and this was refluxed for one-half hour. The substance was first converted into red crystals of the ortho quinone (XII), which were slowly converted into yellow masses of the para quinone (XI). The yield was 0.88–0.89 g. and on crystallization from benzene the substance formed heavy yellow crystalline masses, m. p. 183–184°.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.26. Found (Walsh, Hooker): C, 73.17, 73.69; H, 5.42, 5.31.

The substance was also prepared by refluxing the dihydroxy compound VIII with equal volumes of concentrated hydrochloric acid and water.

β,β-Dimethyldihydrofurano-1,4-naphthoquinone (XI) can be converted into the dihydroxy compound VIII by short boiling with 1% alkali, followed by acidification with acetic acid. The yield of reprecipitated material, m. p. 118.5–120° was 0.72 g. from 0.75 g. A conversion of the para quinone into the ortho quinone XII was accomplished by allowing a solution of the material in concentrated sulfuric acid to stand for one hour at room temperature and pouring the solution into water. The product, obtained in quantitative yield, melted at 186–187°.

Lapachol Peroxide

A solution of 10 g. of lapachol in 100 cc. of glacial acetic acid was heated to boiling, the source of heat was removed, and 10 g. of lead peroxide was added. The hot mixture was shaken for a minute or two and filtered to remove oxides of lead, and the filtrate on cooling very slowly deposited large yellow crystals of the peroxide. Collected after six days this amounted to 2.7 g., and an additional 0.6 g. of crystalline material separated after diluting the mother liquor with 40 cc. of water. Lapachol peroxide crystallizes from glacial acetic acid as heavy, orange-yellow prisms melting at 154–155°. Some decomposition occurs on crystallization from alcohol or benzene.

Anal. Calcd. for $C_{30}H_{26}O_6$: C, 74.68; H, 5.39; mol. wt., 482.0. Found (Price): C, 74.33; H, 5.38; mol. wt., 467.0, 470.6.

When a suspension of 0.5 g. of the finely powdered peroxide was boiled with 50–60 cc. of 1% sodium hydroxide solution the material dissolved completely in about five minutes. On acidifying the red solution a crystalline yellow precipitate consisting of nearly pure lapachol (0.4 g.) was obtained. Extraction of the mother liquor with ether gave only resinous material.

Treated with lead peroxide in the same manner, 2-*n*-amyl-3-hydroxy-1,4-naphthoquinone (1 g.) gave a crystalline yellow product (0.6 g.) closely resembling lapachol peroxide. The crude material melted at 113–114° and one crystallization from dilute acetic acid gave crystals melting at 117–118°. The substance partially decomposed on further crystallization and it was not analyzed.

Summary

Lapachol has been found to undergo a remarkable change when submitted to reaction with cold alkaline permanganate. The double bond in the side chain $—CH_2CH{=}C(CH_3)_2$ remains undisturbed and a hydroxyquinone is formed which differs from the starting material only in that CH_2 has been removed from the body of the side chain, which has become $—CH{=}C(CH_3)_2$. The structure of the oxidation product is fully established by comparison of its hydro derivative with known compounds and by a number of transformations parallel to those of lapachol. The observation that hydrolapachol and hydroxyhydrolapachol similarly lose CH_2 from the side chain on oxidation shows that the double bond plays no part in the transformation and indicates that the reaction is a general one. It is suggested that the quinone ring opens in the course of the reaction and closes in a different position.

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