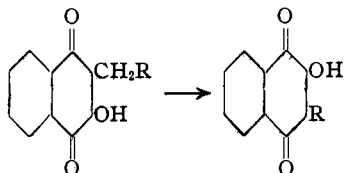


formed. All of the substances listed in Table I gave the test, and this was true also of hydrolapachol and of 2-isobutyl-3-hydroxy-1,4-naphthoquinone.<sup>3</sup>

### Summary

It is shown how alkaline potassium permanganate oxidation of hydroxynaphthoquinone derivatives can result in a general reaction involving the following change:



Thus it is possible to eliminate  $\text{CH}_2$  adjoining

the quinone ring without otherwise disturbing the structure of the chain. In the course of the oxidation the quinone ring is split and then reformed. One carbon atom of the original ring is eliminated, another from the side chain taking its place, with the result that the chain is shortened by one carbon atom and the positions of the hydroxyl and the side chain are reversed in the new ring. The steps involved are fully discussed and many examples of the reaction are given. It is also shown how the oxidation can be of assistance in determining the structure of the side chain and, if unsaturated, the position of the double bond.

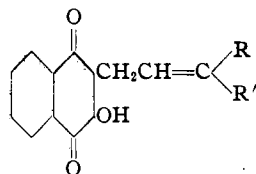
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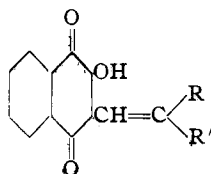
## On the Oxidation of 2-Hydroxy-1,4-naphthoquinone Derivatives with Alkaline Potassium Permanganate. Part II. Compounds with Unsaturated Side Chains<sup>1,2</sup>

BY SAMUEL C. HOOKER AND AL STEYERMARK

It has been shown that the novel oxidation reaction described recently by one<sup>3</sup> of us is applicable to a large number of hydroxynaphthoquinones with saturated side chains in the quinone ring, but only one example of a substance containing a double bond in the side chain was included in the previous studies, namely, lapachol.<sup>3a</sup> Lapachol (I, R and R' =  $\text{CH}_3$ ) is converted by alkaline permanganate in the cold into the next lower homolog of the type II, in which  $\text{CH}_2$  has been eliminated and the double bond shifted from the  $\beta,\gamma$ - to the  $\alpha,\beta$ -position. In order to extend this observation the following additional com-



I (Yellow)



II (Orange or red)

pounds have been examined: the 2-allyl, 2- $\gamma$ -methylallyl, and 2-cinnamyl derivatives of 3-hydroxy-1,4-naphthoquinone. The materials were in part kindly supplied by Dr. L. F. Fieser, who has described the preparation of all three of these quinones.<sup>4</sup>

(1) See Editor's note (1), *THIS JOURNAL*, **58**, 1163 (1936).

(2) Dr. Hooker left no manuscript for the first part of this paper but wrote the description of the three oxidations recorded in the experimental part.—L. F. FIESER.

(3) HOOKER, *THIS JOURNAL*, (a) **58**, 1168 (1936); (b) **58**, 1174 (1936).

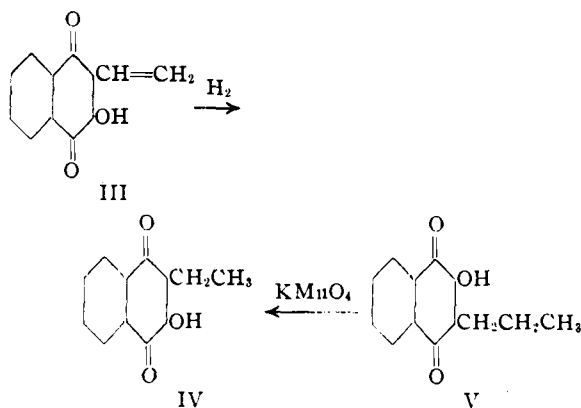
(4) Fieser, (a) *ibid.*, **48**, 3201 (1926); (b) **49**, 857 (1927).

The three compounds of the type I are yellow, like lapachol, and on oxidation with permanganate they behave in an entirely similar manner yielding orange or red quinones of the type II. The product resulting from the oxidation of 2- $\gamma$ -methylallyl-3-hydroxy-1,4-naphthoquinone (I, R =  $\text{CH}_3$ , R' = H) proved to be identical with the substance prepared<sup>5</sup> by the condensation of propionaldehyde with hydroxynaphthoquinone, namely, 2- $\alpha$ -propenyl-3-hydroxy-1,4-naphthoquinone. The oxidation product of the cinnamyl compound similarly was identified by direct comparison with the compound II (R =  $\text{C}_6\text{H}_5$ , R' = H) prepared<sup>5</sup> by the aldehyde synthesis.

The oxidation of the allyl compound presented some difficulties but conditions eventually were defined permitting the isolation of the sensitive reaction product, 2-vinyl-3-hydroxy-1,4-naphthoquinone (III). This compound, which is described for the first time, was fully identified by its conversion on catalytic hydrogenation into 2-ethyl-3-hydroxy-1,4-naphthoquinone (IV), a substance previously prepared<sup>5b</sup> in this Laboratory by the oxidation of the propyl compound (V).

These results fully confirm and extend the observations made in the case of lapachol. In all four of the examples investigated it has been found that the oxidation of a yellow alkyl hydroxynaphthoquinone having a double bond in the  $\beta,\gamma$ -position in the side chain leads to the re-

(5) Hooker, *ibid.*, **58**, 1163 (1936).



removal of CH<sub>2</sub> adjacent to the quinone ring with the formation of an orange or red quinone with the double bond in the  $\alpha,\beta$ -position. It appears that the reaction is a very general one and that the relationship between lapachol and its product of oxidation extends to other cases and can be used with assurance in the determination of the position of a double bond in the side chain.

### Experimental Part

**Conversion of 2-Allyl-3-hydroxy-1,4-naphthoquinone into 2-Vinyl-3-hydroxy-1,4-naphthoquinone.**—The required starting material was prepared by the method of Fieser.<sup>4a</sup> In carrying out the allylation of the silver salt of hydroxynaphthoquinone considerably more benzene was employed (2.6 times that specified) and the mixture was not heated but was allowed to stand in the dark in a stoppered flask with occasional shaking for two days. The yields of the *o*-quinone ether and allylhydroxynaphthoquinone were 54 and 18%, respectively. The fraction containing the *p*-quinone ether was discarded. The *o*-quinone ether was rearranged at a temperature lower than that specified by Fieser, the material being heated in an oil-bath at 125–127° for one and one-half hours (5-g. lots). The mass was soaked with cold 0.25% alkali for two days and the solution was filtered from an undissolved resin. The precipitated material was extracted with petroleum ether in the Soxhlet apparatus (yield 61–68%), and crystallized from glacial acetic acid, m. p. 116–117°.

2-Vinyl-3-hydroxy-1,4-naphthoquinone is difficult to obtain in a pure condition. As the result of many experiments it was found that it could be best prepared as follows. To 1 g. of 2-allyl-3-hydroxy-1,4-naphthoquinone dissolved in 100 cc. of 1% sodium hydroxide solution an aqueous solution of potassium permanganate containing 1.085 g. (10% in excess of the theoretical amount for two atoms of oxygen) in 100 cc. was added quickly, both solutions previously having been cooled in ice water. The oxidation occurred rapidly. The manganese dioxide separated in one to two minutes and was filtered off immediately, this operation taking about ten minutes. The filtrate was quickly diluted with 800 cc. of water and at once poured into 100 cc. of dilute hydrochloric acid (1:3). After standing for about eight minutes, during which microscopic orange needles formed from the emulsion produced

by the addition to the acid, the oxidation product was collected as quickly as possible by suction filtration. Any delay in conducting these operations resulted unsatisfactorily, as the substance was found to change rapidly in the alkaline solution, and as an additional compound commenced to separate from the acid solution soon after the precipitation of the oxidation product. Although somewhat impure the substance as thus obtained is probably suitable for most purposes. The yield was about 40% of the weight of the allyl compound oxidized. Complete purification for analysis presented considerable difficulty as the substance underwent partial change in all the solvents used. Crystallization from methyl or ethyl alcohol, chloroform, acetic acid, benzene, ether, ethyl acetate or acetone decreased rather than increased the purity of the substance. Purification was finally accomplished by dissolving 0.94 g. in 50 cc. of ether at the laboratory temperature and gradually adding at intervals of some hours a total of 145 cc. of petroleum ether (b. p. 35–55°). When the cloud had cleared sufficiently the deposit was filtered off and discarded. The solution was then allowed to go to dryness in an Erlenmeyer flask tilted so as to promote more rapid evaporation. The residue consisted of small, red-brown crystalline masses scattered here and there over the surface of the flask surrounded by a finely divided yellow substance undoubtedly resulting from one or other of the changes above referred to. The brown-red crystalline masses were mechanically removed and after being washed with a few drops of ether melted at 121.5–123.5°. Analysis gave figures agreeing sufficiently well with those required by 2-vinyl-3-hydroxy-1,4-naphthoquinone.

*Anal.* Calcd. for C<sub>12</sub>H<sub>8</sub>O<sub>2</sub>: C, 71.96; H, 4.05. Found:<sup>4</sup> C, 71.79; H, 4.54.

The conclusion drawn from the analysis was confirmed by conversion of the substance into ethylhydroxynaphthoquinone by hydrogenation, the identity being established beyond question by direct comparison with the product previously obtained<sup>3b</sup> as described above and substantiated further by a mixed melting point determination.

**Conversion of 2-Cinnamyl-3-hydroxy-1,4-naphthoquinone into 2- $\beta$ -Phenylvinyl-3-hydroxy-1,4-naphthoquinone.**—The permanganate oxidation of cinnamylhydroxynaphthoquinone occurs most satisfactorily in a very dilute alkaline solution and even then the yield of the desired substance does not much exceed 9% of the weight of the material oxidized. As the result of a number of trials the following method was adopted. The cinnamyl compound, 0.5 g., was dissolved in 100 cc. of 0.1% alkali, and potassium permanganate, 0.4 g., in 50 cc. of water. Both solutions were cooled to about 1° and quickly mixed as above. The manganese dioxide was filtered off promptly after separation, washing of the precipitate being avoided to prevent unnecessary dilution. About 140 cc. of a 25% alkali, a volume equal to that of the filtrate, was then added and the whole set aside for five days during which the sodium salt of the oxidation product crystallized in the form of dark violet needles. These were collected on glass wool and washed with 10% alkali. The alkaline mother liquor now brown in color was discarded. The violet needles were dissolved in 40 cc. of warm water and the deep violet solution after filtration acidified with dilute hydrochloric

(6) Microanalysis by Dr. D. Price of Columbia University.

acid. The resulting dark red precipitate consisting of microscopic needles was collected, washed with water and air dried, yielding approximately 0.045 g. The substance when crystallized from alcohol melted at 166–167°. It was compared directly with 2- $\beta$ -phenylvinyl-3-hydroxy-1,4-naphthoquinone, prepared by the aldehyde condensation,<sup>5</sup> with which it is undoubtedly identical, the various points of similarity being further confirmed by a mixed melting point determination.

**Conversion of 2- $\gamma$ -Methylallyl-3-hydroxy-1,4-naphthoquinone into 2- $\alpha$ -Propenyl-3-hydroxy-1,4-naphthoquinone.**—A solution of 0.1 g. of potassium permanganate in 10 cc. of water was cooled in an ice-bath and quickly added to a similarly cooled solution of 0.1 g. of the crotyl compound in 10 cc. of 1% alkali. Manganese dioxide separated in a few minutes leaving an almost colorless solution which rapidly became purple. After two hours the filtered solution was partially precipitated by cautiously adding dilute hydrochloric acid until the mother liquor, still alkaline, had become red. The orange, crystalline precipitate was collected, washed and air dried. The yield was 0.03 g. For purification it was dissolved in 6 cc. of a 0.5% solution of sodium hydroxide and then nearly but not com-

pletely reprecipitated with dilute acid. Washed and air dried it melted at 134–135° and gave a dark crystalline sodium salt which dissolved in water to an intensely violet solution. Comparison of its properties and a mixed melting point established its identity with the compound prepared from propionaldehyde by condensation with hydroxynaphthoquinone.<sup>5</sup> Oxidation in more strongly alkaline solution gave less satisfactory results.

### Summary

Extending an observation regarding the oxidation of lapachol with potassium permanganate, three similarly constituted derivatives of 3-hydroxy-1,4-naphthoquinone having in the 2-position side chains of the type  $-\text{CH}_2\text{CH}=\text{CHR}$  have been converted into the corresponding compounds of the side chain  $-\text{CH}=\text{CHR}$ . The hitherto unknown vinyl derivative of hydroxynaphthoquinone has in this way been isolated.

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## Lomatiol. Part II. Its Occurrence, Constitution, Relation to and Conversion into Lapachol. Also a Synthesis of Lapachol.<sup>1,2</sup>

BY SAMUEL C. HOOKER

In a paper published in 1895 the late Dr. Edward H. Rennie<sup>3</sup> showed that the yellow coloring matter with which the seeds of *Lomatia ilicifolia* and *Lomatia longifolia* are more or less surrounded is closely related to lapachol; and he succeeded in converting the lomatia coloring matter into the hydroxy- $\beta$ -lapachone which I had previously prepared indirectly from lapachol.<sup>4</sup> The results of Dr. Rennie's work together with the study of numerous compounds which I had obtained from lapachol led me to assign to the lomatia coloring matter the constitution of an hydroxyisolapachol, instead of that of hydroxylapachol proposed by Dr. Rennie, and as at least one other hydroxyisolapachol had been isolated, the name lomatiol was suggested for the lomatia coloring matter.<sup>5</sup>

At the time of this later publication Dr. Rennie

had already courteously announced the determination of leaving the further study of the coloring matter to me, and it was my intention to pursue the work as soon as a sufficient supply of raw material had been secured in hope of eliminating all doubts regarding the structure of lomatiol. Conditions arose subsequently which made it impossible to carry out my intentions and it was not until after an interval of many years that I was able to resume the investigation.

**Occurrence of Lomatiol.**—In addition to the seeds of the two species above referred to, *L. ilicifolia* and *L. longifolia*, I have also examined the seeds of *L. silaifolia* from the Sydney district, New South Wales, and of *L. tinctoria* and *L. polymorpha* from Tasmania.<sup>6</sup> The seeds of all

(6) The seeds of *L. silaifolia* were kindly sent to me by the late Mr. J. H. Maiden, Director of the Botanical Gardens, Sydney. For one sample of *L. tinctoria* I have to thank Dr. J. K. Small, of the New York Botanical Gardens, New York City; and for another, and also for the seeds of *L. polymorpha*, I am indebted to Mr. L. Rodway, then the Government Botanist, Hobart, Tasmania. Of the seeds forwarded by Mr. Rodway, those of *L. polymorpha* were collected near Macquarie Harbour, on the west coast of Tasmania; and those of *L. tinctoria*, principally near Eaglehawk Neck, about 50 miles from Hobart. For the several specimens from Chile I am indebted to Prof. Charles Sprague Sargent of the Arnold Arboretum of Harvard University; to Lt.-Col. Sir D. Prain, F. R. S., Director of the Royal Botanical Gardens, Kew; and to Dr. J. K. Small of the New York Botanical Gardens.

(1) See Editor's note (1), THIS JOURNAL, 58, 1163 (1936).

(2) The theoretical part of this paper is from an original manuscript written by Dr. Hooker and modified only to the extent of numbering the formulas and notes and making minor editorial changes. The experimental part has been constructed by consolidating, with some abridgment, descriptions of the experiments written by Dr. Hooker. The summary was supplied by the undersigned. In the experiments Dr. Hooker was assisted by Dr. G. H. Connitt.—L. F. FIESER.

(3) Rennie, *J. Chem. Soc.*, 67, 784 (1895).

(4) Hooker, *ibid.*, 61, 611 (1892).

(5) Hooker, *ibid.*, 69, 1381 (1896).