187. *Absorption Spectra of Some Naturally-occurring Naphthaquinones and their Derivatives.*

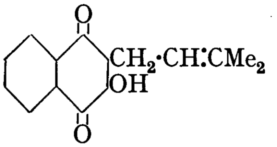
By R. G. Cooke, A. Killen Macbeth, and F. L. Winzor.

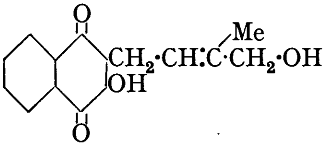
The absorption spectra of lapachol and lomatiol are in close agreement with that previously recorded for phthiocol (J., 1937, 1597), and their derivatives of authentic 1 : 4- and 1 : 2-naphthaquinone structure show maxima characteristic of α- and β-naphthaquinones. The recently isolated colouring matter, dunnione, gives an absorption curve characteristic of a β-quinone and similar to that of dehydro*iso*-β-lapachone, the structure of which is analogous to that proposed for dunnione by Price and Robinson (*Nature*, 1938, **142**, 147).

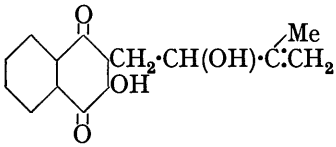
The effect of αβ-unsaturation in the side chain expressed itself in the absorption of the naphthaquinones examined in the replacement of the band due to $\text{C}{=}\text{C}\cdot\text{C}\overset{*}{\text{O}}$ (λ *ca.* 3330) by an inflexion at the same location, and by displacement towards longer wave-lengths of the long-wave-length bands.

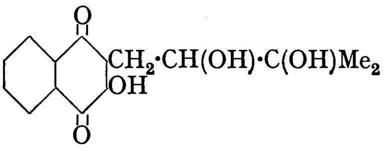
The absorption spectrum of dehydrolapachone, although favouring the β-quinonoid structure, is, like the chemical evidence available, not strictly discriminative.

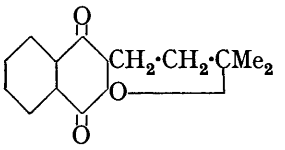
In previous work (J., 1935, 325; 1937, 1597) it was shown that the characteristic absorption spectrum of 1 : 4-naphthaquinone is considerably modified by the introduction of one or more hydroxyl groups, but acetylation causes a reversion to the simple 1 : 4-quinone type. Differences in absorption due to the 1 : 2-naphthaquinone structure were noted in the case of 4-methoxy-1 : 2-naphthaquinone, the data for which were in excellent agreement with those previously recorded for 1 : 2-naphthaquinone (Goldschmidt and Graef, *Ber.*, 1928, **61**, 1862). In these cases the band (λ 3300 A.) of the 1 : 4-naphthaquinones due to the carbonyl group in the system $\cdot\text{C}{=}\text{C}{-}\text{C}\overset{*}{=}\text{O}$ still persists, but an additional band at longer wave-length (*ca.* λ 4000 A.) is also present. It seemed probable that the latter could be regarded as a criterion of 1 : 2-naphthaquinone structure, but on account of the limited number of substances examined it was considered advisable to extend the observations. Derivatives of lapachol and lomatiol of authentic 1 : 2- and 1 : 4-structure are available for such work, and their absorption spectra show effects similar to those previously recorded.

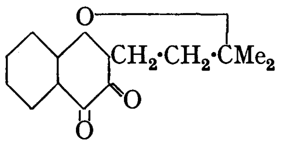

Lapachol.

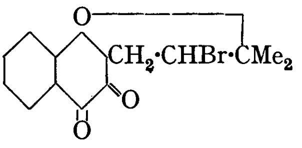

Lomatiol.

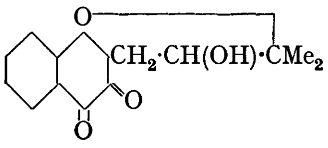

*iso*Lomatiol.


Dihydroxyhydrolapachol.


α-Lapachone.


β-Lapachone.

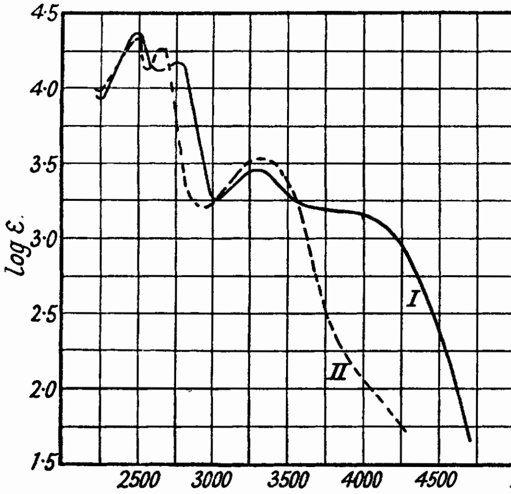

Bromo-β-lapachone.


Hydroxy-β-lapachone.

As there is no conjugation in the side chains in lomatiol, *iso*lomatiol, lapachol, and dihydroxyhydrolapachol, the absorption spectra of these substances should not differ materially from that of phthiocol (3-hydroxy-2-methyl-1 : 4-naphthaquinone). This is realised in practice. Also, the spectra of the acetates of lomatiol and lapachol are found to be in close agreement with that of phthiocol acetate, which is characteristic of the 1 : 4-naphthaquinone type, the long-wave inflexion of the hydroxynaphthaquinones being suppressed. α-Lapachone and *lapachol methyl ether* have absorption spectra in which the inflexion at long wave-lengths, although not as pronounced as in the free hydroxy-compounds, is not affected to the same extent as in the acetates.

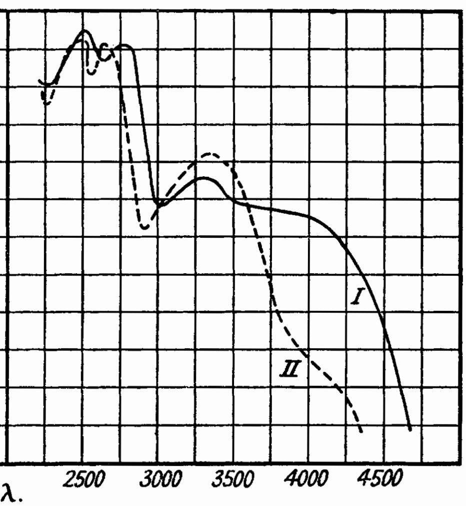
Additional data concerning the absorption characteristic of the 1 : 2-naphthaquinone structure are available from the spectra of β-lapachone, bromo-β-lapachone, hydroxy-β-lapachone, and dehydro*iso*-β-lapachone. These all show the band at long wave-lengths previously recorded for 1 : 2-naphthaquinones, the extinction coefficients in all cases being of remarkable constancy. It would thus seem that this maximum, in conjunction with the keto-band, might safely be taken as a criterion of the β-naphthaquinone structure.

FIG. 1.



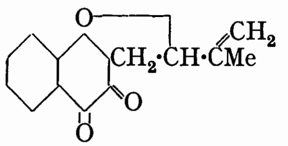
I. *Lomatiol* ———.
II. *Lomatiol diacetate* – – – – –.

FIG. 2.

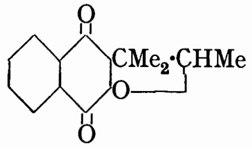


I. *Lapachol* ———.
II. *Lapachol acetate* – – – – –.

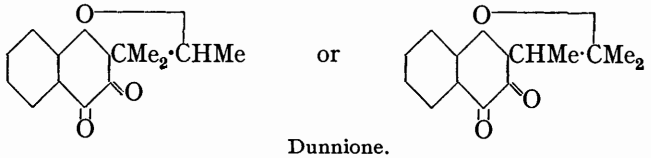
Price and Robinson (*Nature*, **1938**, **142**, 147) described the examination of a pigment, dunnione, which occurs as a deposit on the leaves and inflorescences of *Streptocarpus Dunnii* Mast. Its reactions suggested that dunnione is 2 : 3 : 3-trimethyl-6 : 7-benzocoumaran-4 : 5-quinone or the isomeride with the *gem*-dimethyl group attached directly to oxygen. The absorption of dunnione confirms the 1 : 2-naphthaquinone structure, and its curve (Fig. 7) is practically identical with that of dehydro*iso*-β-lapachone, to which, on the above view, it is closely related structurally.



Dehydro*iso*-β-lapachone.



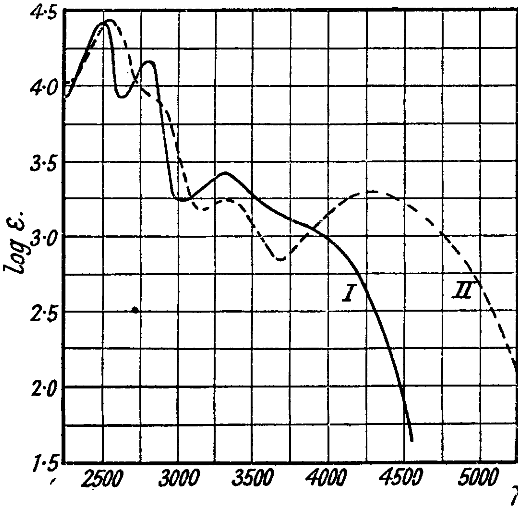
*iso*Dunnione (?).



Dunnione.

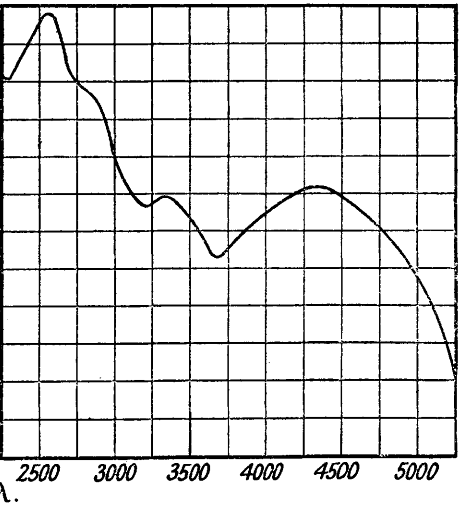
Acidification of the alkaline solution of dunnione under certain conditions liberated

FIG. 3.



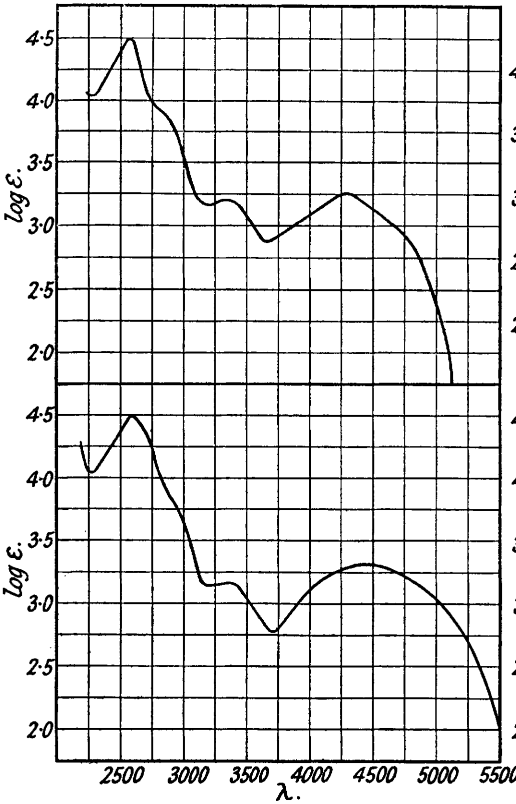
I. *a-Lapachone* ————.
II. *β-Lapachone* – – – – –.

FIG. 4.



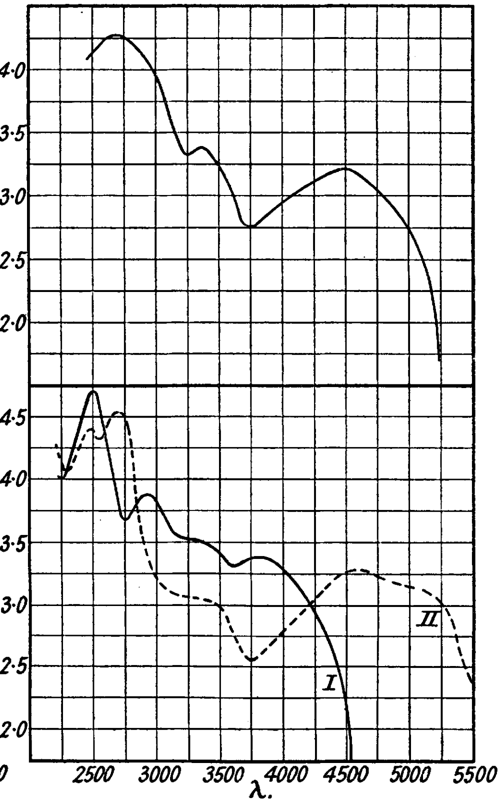
Hydroxy-β-lapachone.

FIG. 5.



Upper. *Bromo-β-lapachone.*
Lower. *Dehydro*iso*-β-lapachone.*

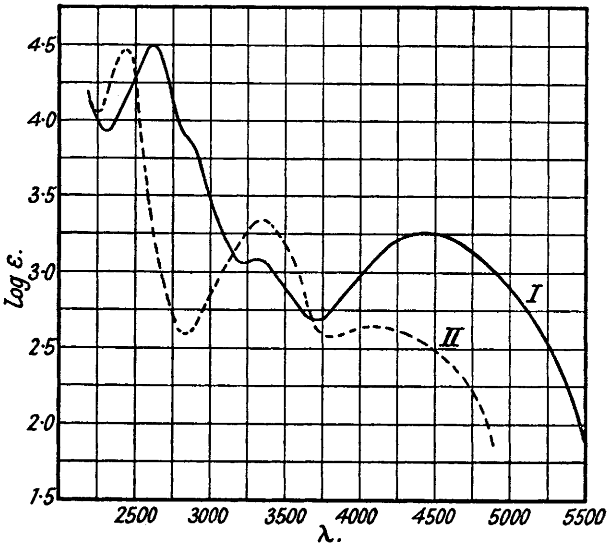
FIG. 6.



Upper. *Dehydrolapachone.*
Lower. I. iso*Propylfurano*-1 : 4-*naphthaquinone* ————.
II. iso*Propylfurano*-1 : 2-*naphthaquinone* – – – – –.

a new colouring matter, *iso*dunnione, which was tentatively regarded as an α-naphthaquinone derivative. Its absorption spectrum has also been examined, but since it is not similar to that of α-lapachone, as would be expected on the above view, and is unlike that of any of the α-naphthaquinones of this series, the 1 : 4-naphthaquinone structure does not appear probable. The most obvious differences are the occurrence of only one band in the region of short wave-length and the appearance of a band in the region of long wave-length beyond that due to the conjugated keto-group. The maxima for the α- and β-naphthaquinones discussed above are recorded in Table I, and typical curves are set out in Figs. 1—7.

FIG. 7.



I. *Dunnione.*
II. iso*Dunnione.*

TABLE I.*

	$\lambda_{\text{max.}}$, A.	log ϵ.	$\lambda_{\text{max.}}$, A.	log ϵ.	$\lambda_{\text{max.}}$, A.	log ϵ.	$\lambda_{\text{max.}}$, A.	log ϵ.
		1 : 4-*Naphthaquinones.*						
Phthiocol	2500	4·28	2810	4·18	3310	3·44	—	—
Lapachol	2515	4·38	2780	4·28	3310	3·43	*ca. 3820*	3·17
Lomatiol	2515	4·38	2795	4·17	3310	3·45	*ca. 3790*	3·18
*iso*Lomatiol	2505	4·45	2785	4·28	3310	3·54	*ca. 3775*	3·15
Lapachol methyl ether	2495	4·35	2765	4·22	3330	3·56	*ca. 3810*	3·05
α-Lapachone	2480	4·41	2810	4·18	3325	3·43	*ca. 3730*	3·13
Phthiocol acetate	2480	4·18	2670	4·06	3330	3·40	—	—
Lapachol acetate	2495	4·34	2670	4·30	3335	3·57	—	—
Lomatiol diacetate	2500	4·34	2665	4·26	3335	3·54	—	—
		1 : 2-*Naphthaquinones.*						
Methoxy-1 : 2-naphthaquinone	2500	4·35	*2730*	3·78	3333	3·24	4030	3·29
β-Lapachone	2565	4·45	*2820*	3·98	3330	3·24	4295	3·28
Bromo-β-lapachone	2555	4·50	*2820*	3·93	3335	3·22	4255	3·27
Hydroxy-β-lapachone	2560	4·44	*2835*	3·88	3312	3·20	4310	3·27
Dehydro*iso*-β-lapachone	2618	4·53	*2855*	3·94	3335	3·18	4425	3·30
Dunnione	2610	4·53	*2865*	3·85	3320	3·10	4430	3·27
*iso*Dunnione	2440	4·49	—	—	3340	3·34	4080	2·67

It was hoped that the absorption spectrum of dehydrolapachone might furnish definite evidence regarding its structure, about which there is some doubt, and for which Hooker (*J. Amer. Chem. Soc.*, 1936, **58**, 1190) proposed the alternative formulæ on p. 882. Certain

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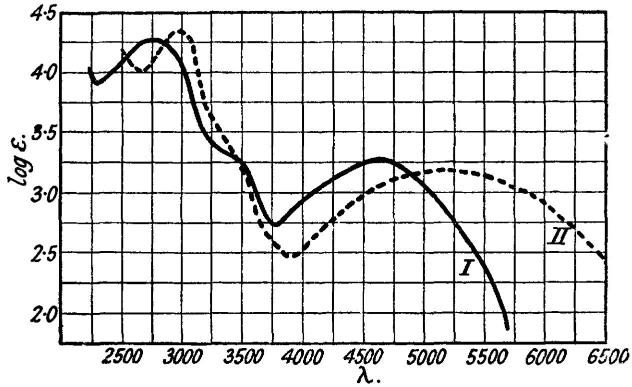
* Italicised figures in the tables represent inflexions.

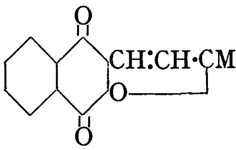
chemical reactions, notably its hydrogenation to α-lapachone, are in favour of the α-quinonoid form; and the reduction potential (Fieser, *J. Amer. Chem. Soc.*, 1928, **50**, 450) is also slightly, but not conclusively, in favour of the 1 : 4-formulation. On the other hand, the isolation of an azine in good yield, and other evidence, is in agreement with the view that the substance is a β-quinone. Hooker, however, regarded the 1 : 4-structure as the more probable.

FIG. 8.

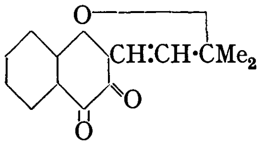


I. *β-Methylpyrano-1 : 4-naphthaquinone* ————.
II. *β-Methylpyrano-1 : 2-naphthaquinone* – – – – –.

In examining the absorption of dehydrolapachone it is necessary to consider how the effect of the αβ-double bond in the side chain expresses itself in the spectra of naphtha-



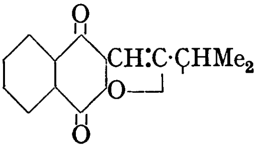
or



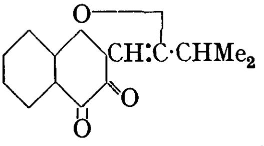
(I.)

(II.)

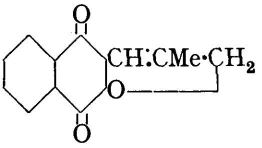
Dehydrolapachone.



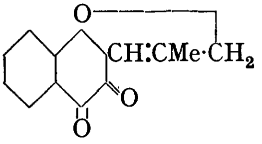
*iso*Propylfurano-1 : 4-naphthaquinone.



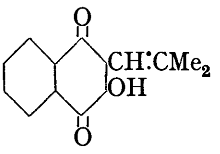
*iso*Propylfurano-1 : 2-naphthaquinone.



β-Methylpyrano-1 : 4-naphthaquinone.



β-Methylpyrano-1 : 2-naphthaquinone.



3-Hydroxy-2-*ββ*-dimethylvinyl-1 : 4-naphthaquinone.

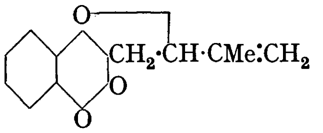
quinones containing such conjugated unsaturation. For this purpose β-methylpyrano-1 : 2- and -1 : 4-, *iso*propylfurano-1 : 2- and -1 : 4-naphthaquinones, and 3-hydroxy-2-ββ-dimethylvinyl-1 : 4-naphthaquinone were available, and the recorded maxima for these substances, together with the data for dehydrolapachone and dehydro*iso*-β-lapachone, are summarised in Table II and shown in the various figures.

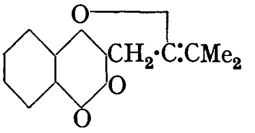
Analysis of the results shows that the αβ-unsaturation expresses itself in both the 1 : 2- and the 1 : 4-quinones in two main effects, *viz.*, (*a*) the appearance of an inflexion instead of the band located at λ *ca.* 3330 which is characteristic of the carbonyl group in the system $C{=}C{\cdot}\overset{*}{C}O$, and (*b*) the displacement of the long-wave-length band to a region of still greater wave-length. On Hooker's formulations dehydrolapachone shows close resemblances to the β-methylpyranonaphthaquinones of similar quinonoid structure, and so might be expected to show absorption in close agreement with one or other of these substances according as it possessed a 1 : 2- or 1 : 4-structure. Both the β-methylpyranonaphthaquinones show inflexion in the region λ *ca.* 3300, whereas dehydrolapachone has a definite band at λ 3335; and the long wave-length maximum in β-methylpyrano-1 : 4-naphthaquinone is some 200 A. greater than that of dehydrolapachone, while the location of the band in β-methylpyrano-1 : 2-naphthaquinone is considerably higher still. The presence of the band at λ 3335 in dehydrolapachone suggests the absence of αβ-unsaturation. This would imply the existence of a furano- instead of a pyrano-ring, and since the formula of dehydro*iso*-β-lapachone appears to be well established, the alternative formula (III) would be assigned to dehydrolapachone on this basis.

TABLE II.

αβ-*Unsaturated Naphthaquinones.*

	$\lambda_{max.}$, A.	log ε.	$\lambda_{max.}$, A.	log ε.	$\lambda_{max.}$, A.	log ε.
*iso*Propylfurano-1 : 4-	2495	4·72	*3250*	3·52	3790	3·39
	2924	3·89				
3-Hydroxy-2-ββ-dimethylvinyl-1 : 4-	2650	4·39	*3165*	3·50	4205	3·32
β-Methylpyrano-1 : 4-	2750	4·27	*3300*	3·36	4630	3·27
*iso*Propylfurano-1 : 2-	2475	4·40	*3250*	3·06	4590	3·28
	2680	4·54				
β-Methylpyrano-1 : 2-	2975	4·36	*3230*	3·65	5130	3·18
Dehydrolapachone	2690	4·27	3335	3·38	4430	3·19
Dehydro*iso*-β-lapachone	2620	4·53	3335	3·18	4425	3·30


Dehydro*iso*-β-lapachone.


(III.) Dehydrolapachone (?).

There is, in fact, close agreement between the locations of the maxima of the two compounds, although the log ε values differ. The above structure seems to be more in accord with the formation of dehydrolapazine by the spontaneous oxidation of lapeurhodone (Hooker, *loc. cit.*) than does the pyrano-formula. The formation of α-lapachone on hydrogenation of dehydrolapachone still remains a difficulty, implying as it does an opening of the ring and closure involving a different carbon atom during the reaction; but such behaviour might be due to the quaternary carbon atom, about which, during hydrogenation, little is known.

EXPERIMENTAL.

The lapachol derivatives used in the work were prepared by the methods summarised below from a supply of lapachol isolated by Dr. Hooker and kindly presented by Professor L. F. Fieser, to whom we are greatly indebted. Lomatiol derivatives were prepared from lomatiol extracted from the seed of *L. longifolia*, and we are indebted to Professor J. C. Earl who kindly collected the seed-pods in New South Wales. The samples of dunnione and *iso*dunnione were supplied by Mr. J. R. Price, and we are indebted to Sir Robert Robinson and him for this gift of material.

Lomatiol was extracted in the usual way, and after recrystallisation from benzene had m. p. 128·5°. Lapachol after recrystallisation from alcohol had m. p. 140°.

Lapachol acetate. A solution of lapachol (5 g.) in acetic anhydride (25 c.c.) containing a fragment of zinc chloride was boiled for 2—3 mins., and after dilution with an equal volume of acetic acid, sufficient water was added to combine with the anhydride. The mixture was heated to boiling and poured into water, and the crude acetate which solidified overnight was recrystallised (thrice) from methanol and charcoal. The *acetate* formed sulphur-yellow needles, m. p. 65—66° (Found : C, 71·9; H, 5·6. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%). Attempts to prepare the acetate according to Paterno (*Gazzetta*, 1882, **12**, 357) yielded only a white substance, m. p. 122°, which is probably a mixture of the quinol acetates.

Lomatiol diacetate, prepared as above, separated from alcohol as pale yellow needles, m. p. 84—85°.

Lapachol methyl ether. A mixture of lapachol (5 g.) in acetone (150 c.c.) containing methyl iodide (20 c.c.) and finely powdered potassium carbonate (5 g.) gives a deep claret-coloured solution which gradually bleaches as methylation proceeds on refluxing on a water-bath. The reaction is complete in about 3 hours, and after removal of acetone and excess methyl iodide by distillation, and the addition of water, methyl lapachol is extracted with ether. The residual oil from the dried extract did not crystallise on keeping, but after distillation under reduced pressure partial crystallisation occurred on standing for some weeks, and *lapachol methyl ether* was obtained as beautiful yellow felted needles, m. p. 53°, on nucleation of an aqueous methyl-alcoholic solution of the bulk (Found : C, 74·8; H, 6·3. $C_{16}H_{16}O_3$ requires C, 74·95; H, 6·3%).

β-Lapachone, m. p. 153° (J., 1892, **61**, 611), bromo-β-lapachone, m. p. 138° (*ibid.*), dihydroxyhydrolapachol, m. p. 184—185° (*ibid.*), hydroxy-β-lapachone, m. p. 205° (*ibid.*), α-lapachone, m. p. 117° (*ibid.*), *iso*propylfurano-α-naphthaquinone, m. p. 110·5° (J., 1896, **69**, 1355), *iso*propylfurano-β-naphthaquinone, m. p. 94—95° (*ibid.*), dehydro*iso*-β-lapachone, m. p. 111° (*J. Amer. Chem. Soc.*, 1936, **58**, 1181), *iso*lomatiol, m. p. 109° (*ibid.*), dehydrolapachone, m. p. 143° (*ibid.*, p. 1190), 3-hydroxy-2-ββ-dimethylvinyl-1 : 4-naphthaquinone, m. p. 120° (*ibid.*, p. 1168), β-methylpyrano-α-naphthaquinone, m. p. 197° (*ibid.*, p. 1198), and β-methylpyrano-β-naphthaquinone, m. p. 158—159° (*ibid.*), were prepared according to the directions of Hooker and his co-workers.

One of us (R. G. C.) is indebted to the Commonwealth Government for a Federal Research Grant which enabled him to participate in the work.

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