

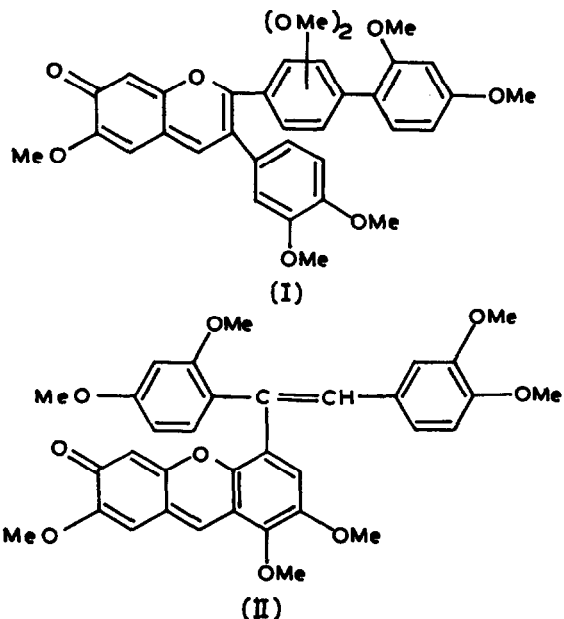
CHEMISTRY OF THE SANTALIN PIGMENTS I. STRUCTURE OF SANTALIN PERMETHYL ETHER

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Santalín, the complex red pigment of the red sandalwood (*Pterocarpus santalinus*) was examined by various workers ever since its isolation by Pelletier¹ in 1832. The most significant contribution came from Robertson and Whalley², who proposed the tentative structure (I) for "tetra-O-methyl-santalín." It, however, failed to explain many of its reactions and did not agree with the present ideas of biogenesis. Dean's later suggestion³ of a "xanthone" structure (II) had no experimental support.

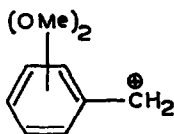


We have now found that the heartwood contains a number of red pigments, two of them, *viz.*, santalin A and santalin B being major. Since both gave the same "santalín permethyl ether" on methylation, the two are partial

methyl ethers of the same polyphenol, for which the name santalin may now be reserved.

Santalin permethyl ether, $C_{38}H_{36}O_{10}$ (M^+ 652) forms orange-yellow needles from methanol, m.p. $155-6^\circ$, resolidifies and melts at $229-30^\circ$. $\lambda_{\text{max}}^{\text{EtOH}}$ 508, 475, 447, 320, 278, 269 and 235 nm. $\nu_{\text{max}}^{\text{KBr}}$ 1639 cm^{-1} . Its anhydrobenzopyranol character has now been established on the basis of a number of typical reactions and comparison with synthetic samples.

The presence of eight methoxyls in santalin permethyl ether was shown by eight separate signals between δ 3.8 and 4.2 in its NMR spectrum. Other signals were at δ 6.60 (m, 8H), 7.05 (d, $J=9$ c/s, 1H) and 9.57 (s, 1H). Thus, 34 of the 36 protons in santalin permethyl ether were located. The nature of the other two could be inferred as follows: The mass spectra of santalin permethyl ether and its derivatives invariably showed an intense peak at m/e 151; this peak could be due to an ion of the type III. The benzylic methylene signal in the NMR spectrum of santalin permethyl ether appeared to have merged with one of the methoxyl signals, showing it to be of the diphenylmethane type. It could, however, be observed at δ 3.57 (s, 2H) in the spectrum in D_6 -DMSO of santalin B; this was a dimethyl ether and showed two methoxyl signals at δ 3.52 (3H) and 3.85 (3H).

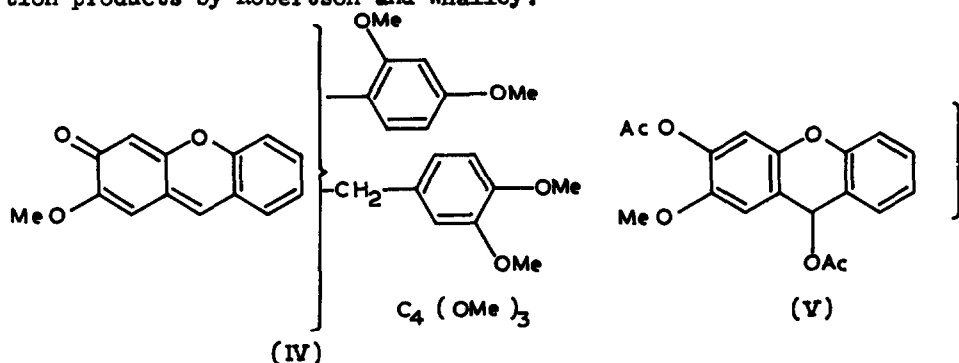


(III)

Degradation of santalin permethyl ether with methanolic potassium hydroxide resulted in the isolation and characterisation of four products A, B, C and D. Compounds A and B have been identified as 2,4-dihydroxy-5-methoxybenzaldehyde and 4-methoxyresorcinol respectively. Compound C, $C_{31}H_{32}O_9$ (M^+ 548) has also been found to be an o -hydroxy aromatic aldehyde from its ferric reaction and NMR spectrum. The formation of two o -hydroxy aromatic aldehydes (A and C) on alkali degradation can only be explained by

a fluorone structure (see IV) for the permethyl ether. This has been unequivocally established when we obtained santalin permethyl ether by condensing compound C with 4-methoxyresorcinol using HCl in acetic acid.

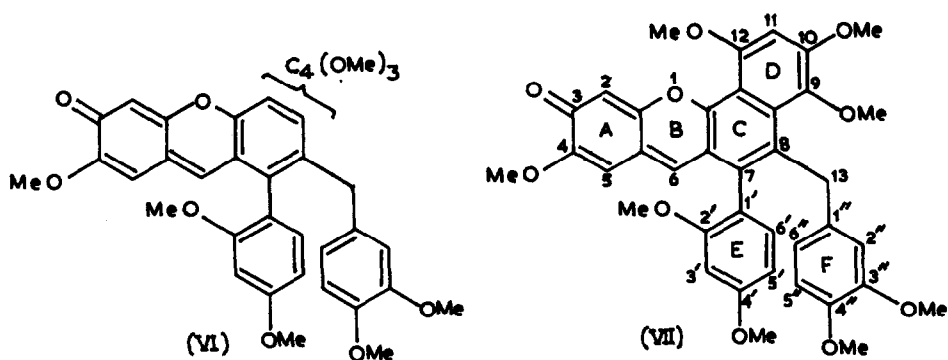
Oxidation of the permethyl ether with KMnO_4 gave the three acids, E, F and G, two of which were 2,4-dimethoxybenzoic acid (E) and veratric acid (F). The third acid (G) will be discussed later. The part structure of the methyl ether can now be written as (IV); the presence of the homoveratryl group may explain the isolation of veratraldehyde also as one of the oxidation products by Robertson and Whalley.²



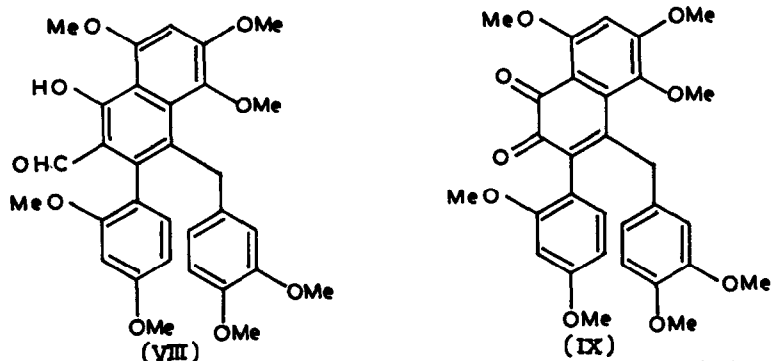
The non-phenolic acetoxy signal in the NMR spectrum of the pseudobase acetate (V) obtained by treating the permethyl ether with Ac_2O and pyridine appears at δ 1.2. This high field signal can be explained, as due to the powerful shielding effect of an adjacent benzene ring if structure (VI) is given to the permethyl ether. The location, in the ortho position, of 3,4-dimethoxybenzyl unit follows from the mass spectral fragmentation and biogenetic considerations to be discussed later. The remaining three methoxys and 4 carbon atoms require the presence of at least one more benzenoid unit and this is satisfactorily accommodated as in (VII).

Then KMnO_4 oxidation of santalin permethyl ether should give a trimethoxyphthalic acid derived from ring D. The acid G obtained by us appeared to agree with this, based on its chromatographic mobility. Of the two possible trimethoxyphthalic acids, the possibility of its being 3,4,5-trimethoxyphthalic acid was ruled out by direct comparison with a synthetic sample. It should, therefore, be 3,4,6-trimethoxyphthalic acid. This will fix the location of the methoxys

in the permethyl ether as in (VII).



The spectral (UV, IR, NMR and MS) data of the alkali degradation products C and D are in complete agreement with structures (VIII) and (IX) respectively, thus supporting structure (VII) for santalin permethyl ether. The relationship between (VIII) and (IX) has been proved by converting compound C into D by Dakin's oxidation.



Biogenetically, santalin may be visualized as a novel type of biflavonoid, derived from two C_{15} units, one forming the rings A, B and D and the other E and F, with ring C arising from the fusion of the two units.

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References

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3. F.M. Dean "Naturally occurring oxygen ring compounds", Butterworths (1963).