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CONSTITUTION OF *O*-DIMETHYL LATIFOLIN

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Abstract—Light petroleum extract of the heartwood of *Dalbergia latifolia*, yields a colourless crystalline solid, latifolin, which is a dihydroxy, dimethyl compound having a C_{15} skeleton similar to dalbergin. The constitution of the dimethyl ether is shown to be γ,γ-(2,2′,4,5-tetramethoxy)-diphenyl propene (II).

Dalbergia latifolia Roxb., commonly known as the Blackwood or Rosewood of India, is a deciduous tree, found abundantly in central and southern parts of India. Its heartwood, a valuable timber and extensively used, is now being examined in detail.

A light petroleum extract of the coarsely powdered shavings yielded a new colourless crystalline phenolic compound, m.p. 122–123°, which has been named 'latifolin'. An elementary analysis of latifolin and of its derivatives suggests the molecular formula $C_{17}H_{18}O_4$. It contains two methoxyl groups and no C-methyl groups. On methylation with dimethyl sulphate, acetone and potassium carbonate it forms a dimethyl ether, and with acetic anhydride and pyridine a diacetate, showing the presence of two phenolic hydroxyl groups. All the four oxygens are thus accounted for. Latifolin gives no ferric chloride colour ruling out the possibility of the two hydroxyls being *ortho* to each other. The IR spectrum of latifolin (Fig. 1) reveals the presence of hydroxyl and methoxyl groups and aromatic and ethylenic double bonds.

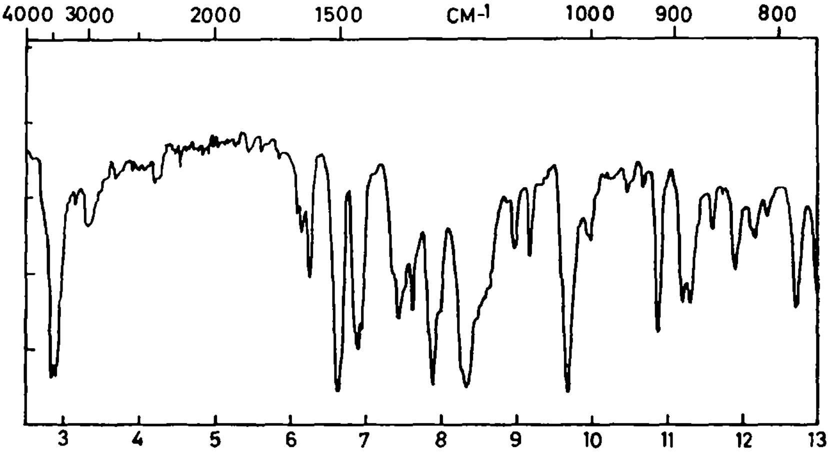

Fig. 1.

When latifolin dimethyl ether was oxidized with neutral potassium permanganate it gave *ortho* methoxy benzoic acid whereas latifolin itself on similar treatment gave salicyclic acid. Hence, in latifolin there are two phenyl rings, linked to a three carbon chain and one of the rings (A) carries a hydroxyl group *ortho* to the point of substitution, while the other (B) has two methoxyl groups and one hydroxyl group. By analogy with dalbergin (I)[1], which is also present in the wood and which can be isolated

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[1] V. K. Ahluwalia and T. R. Seshadri, *J. Chem. Soc.* 970 (1957).

from the subsequent benzene extract, the possibility of the 2,4,5 oxygenated pattern in ring (B) was considered likely. Latifolin dimethyl ether, on hydrogenation over Pd/C catalyst, gives a dihydro derivative, which contains one C-methyl group (Kuhnt-Roth estimation). The original latifolin dimethyl ether should therefore contain one end methylene group ($>C{=}CH_2$). This conclusion is confirmed by the formation of formaldehyde on ozonolysis. Latifolin and its dimethyl ether are optically active.

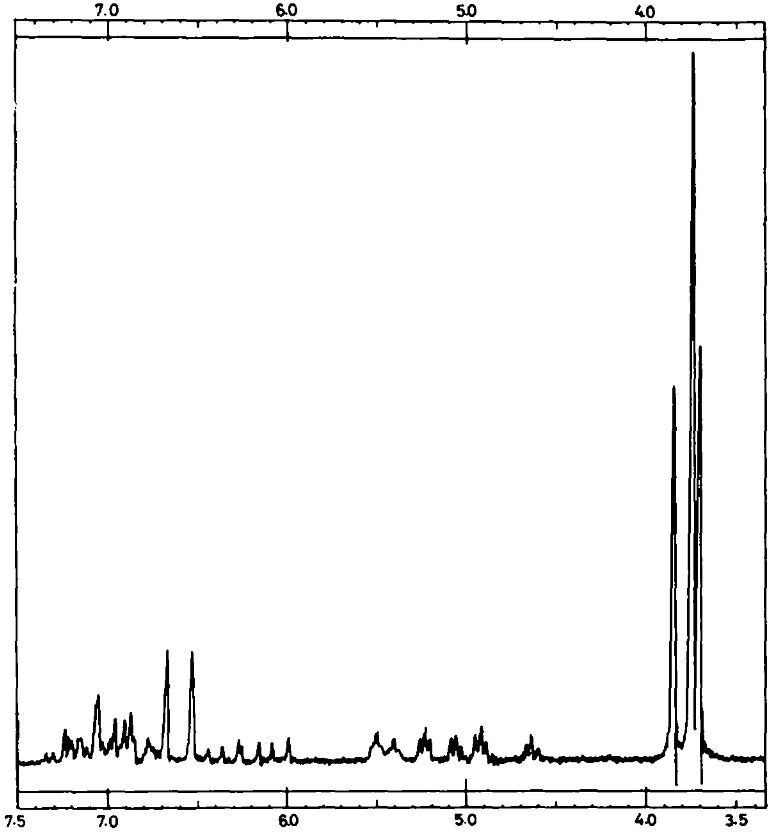
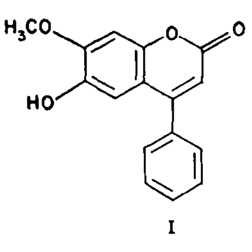


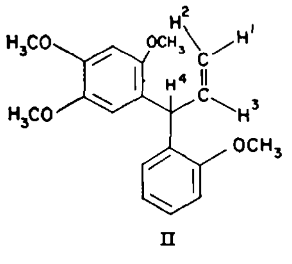
FIG. 2.

These properties are satisfactorily explained by formula II [γ,γ-(2,2',4,5-tetramethoxy)-diphenyl propene] for the dimethyl ether. This structure has the same carbon skeleton as dalbergin (I) which accompanies it.

The NMR spectrum (Fig. 2) is also in good agreement with this structure. The



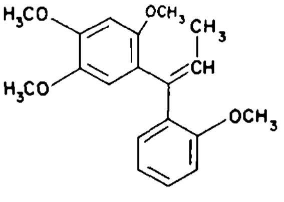
I



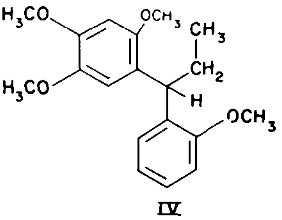
II

spectrum of latifolin dimethyl ether was taken as solution in $CDCl_3$, with TMS as the internal standard and was recorded on a precalibrated chart using an A-60 Varian Spectrometer. It has two aromatic proton signals at 392 and 400 cps which are not spin coupled to each other or to any other aromatic protons. Furthermore, the chemical shifts correspond to one of these protons being adjacent to one oxygen and the other adjacent to two oxygens.[2] The two protons are therefore *para* to each other on a tetra-substituted benzene ring with 2,4,5 oxygenated pattern. The proton signals between 403 and 440 cps are typical of four aromatic protons in a 1,2,3,4 situation (see formula II). The spin coupling diagram explains satisfactorily all the protons of the allyl system. There are two triplets for H_1 ($J = 10$ c/s), two triplets for H_2 ($J = 17$ c/s), a septet for H_3 ($J = 17$ c/s) and two triplets for H_4 ($J = 5{\cdot}5$ c/s) rather not well defined, probably because of a small spin coupling to the two protons four bonds away, which is enough to smear out the pattern.

The above conclusion regarding the carbon skeleton and the oxygenated pattern as shown in structure II is also supported by a synthesis of dihydrolatifolin dimethyl ether. Friedel-Crafts reaction of 1,2,4 trimethoxy benzene with *ortho* methoxy benzoyl chloride followed by methylation of the product gave 2,2′,4,5-tetra methoxy benzophenone. When this was condensed with ethyl magnesium iodide, the expected carbinol was not obtained; it had undergone dehydration to yield the propenyl compound (III). This product underwent catalytic hydrogenation to give α,α-(2,2′,4,5-tetramethoxy) diphenylpropane (IV) which resembled dihydro latifolin-*o*-dimethyl ether closely both in UV and IR spectra, but had no optical activity.



III



IV

Further proof was provided in the following manner: Di-*o*-methyl latifolin changes into an *iso*-compound when boiled with alcoholic potash for twenty four hours and this compound is identical in melting point, mixed melting point and UV spectrum with the propenyl compound (III) obtained by the Grignard reaction mentioned above.

EXPERIMENTAL

The light petroleum used in this work had a boiling range of 60°–80°.

Isolation of latifolin. The air dried and coarsely powdered shavings of the heartwood (6 kg) were extracted with hot light petroleum (4 × 6 hr). The pale yellow extract was concentrated to about 1 l. and left in the refrigerator for 3 days, in the course of which a large amount of crystalline solid was deposited along with some brown coloured resin. The mother liquor was decanted off and the residue treated with hot benzene (100 ml) when most of the resin dissolved. After filtration the crystals were washed with benzene (2 × 50 ml) and dried; Yield, 75 g (1·25%), m.p 120–122°. It crystallized from benzene as colourless stout prisms, m.p. 122–123°; $[\alpha]_D^{31°}$, +135·9° (Found: C, 71·5; H, 6·6; OCH_3, 21·4%; C—CH_3, nil. $C_{17}H_{18}O_4$ requires: C, 71·3; H, 6·3; —OCH_3 (two) 21·7%). Light absorption data: λ_{max}^{MeOH} 283(log ε 3·80) and an inflexion at 238 (log ε 3·85) mμ; ν_{max}^{KBr} 3500, 3450

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[2] J. B. son Bredenberg and J. N. Shoolery, *Tetrahedron Letters* No. 9, 285 (1961).

(—OH), 1630 (C=C) 1600, 1510 (aromatic), 1035 (—OCH_3), 920 cm^{-1}. It is insoluble in sodium carbonate but readily dissolves in 4% NaOH giving a yellow solution. It gives no colour with ferric chloride and no flavonoid colour reactions. With conc sulphuric acid it gives a deep red colour which disappears on dilution with water.

Latifolin diacetate. Latifolin (0·5 g) was acetylated by refluxing for 3 hr with acetic anhydride (5·0 ml) and pyridine (2 drops). The acetate crystallized from benzene–light petroleum as colourless stout rectangular prisms, m.p. 124–125° (Found: C, 68·6; H, 6·0; —$COCH_3$, 20·9%; $C_{21}H_{22}O_6$ requires: C, 68·1; H, 6·0; —$COCH_3$ (two) 23·3%) Light absorption data: λ_{max}^{MeOH} 285 mμ (log ε 3·62) inflexion at 230 mμ (log ε 3·98); ν_{max}^{KBr} 1760 (acetoxyl carbonyl), 1620, 1513, 920 cm^{-1}.

Latifolin dimethyl ether (II). Latifolin (2·0 g) was methylated by refluxing for 15 hr with acetone (50 ml), dimethyl sulphate (5 ml) and anhydrous potassium carbonate (10 g). After filtration and removing the acetone from the filtrate, the excess of dimethyl sulphate was decomposed by the addition of water. The solid product crystallized from benzene–light petroleum as colourless stout prisms, m.p. 89°; $[\alpha]_D^{31°}$ + 21·9° (Found: C, 72·1; H, 7·2; —OCH_3, 38·9%; $C_{19}H_{22}O_4$ requires: C, 72·6; H, 7·1; —OCH_3 (four) 39·5%).

Permanganate oxidation to o-methoxy benzoic acid. Latifolin methyl ether (2 g) was dissolved in alcohol free acetone (50 ml) and treated with a small quantity of magnesium sulphate. Powdered potassium permanganate (15 g) was then added in small quantities over a period of 1 hr, while the solution was being refluxed, till the permanganate was in excess. After refluxing for further 4 hr the acetone was distilled off, the residue was suspended in water and a stream of suphlur dioxide was passed to decompose the manganese dioxide. The solution was continuously extracted with ether and the ether solution in turn was extracted with cold saturated aqueous bicarbonate. The bicarbonate solution was acidified with ice-cold hydrochloric acid and extracted with ether. The ether extract was dried (Na_2SO_4) and the residue left after the removal of the solvent crystallized from methanol, m.p. 100–101°. Mixed m.p. with an authentic sample *o*-methoxy benzoic acid was undepressed.

Latifolin on similar treatment gave an acid which produced a violet colour with alcoholic ferric chloride. M.p. and mixed m.p. with an authentic sample of salicylic acid was 158–159°.

Catalytic hydrogenation of the dimethyl ether to tetramethoxy diphenyl propane (IV). Latifolin dimethyl ether (0·5 g) in ethyl acetate (20 ml) was added to the prereduced catalyst (0·5 g of 5% Pd/C, suspended in 15 ml ethyl acetate) and hydrogenated. After the absorption of hydrogen was complete (30 min, 20 ml at 25°) the catalyst was filtered off and the solvent removed. The residue crystallized from light petroleum as aggregates of colourless rectangular plates, m.p. 64–65°; $[\alpha]_D^{31°}$ −22·4 (Found: C, 72·9; H, 8·3; C—CH_3, 3·8; $C_{19}H_{24}O_4$ requires: C, 72·1; H, 7·7; —CCH_3, 4·7%). Light absorption data: λ_{max}^{MeOH} 280 (log ε 3·74), 290 (log ε 3·69) mμ.

Ozonolysis of the dimethyl ether; formation of formaldehyde. A steady stream of ozonized oxygen (about 2·5%) was passed through a solution of the methyl ether (0·5 g) in ethyl acetate (25 ml) cooled in the freezing mixture, for 35 min. The gases issuing from the reaction flask were bubbled through distilled water (20 ml) cooled in an ice-water bath. After the reaction was complete the aqueous solution was allowed to attain the room temp and tested for formaldehyde. It gave a positive chromotropic acid test.

The ethyl acetate solution was catalytically hydrogenated over Pd/$CaCO_3$ catalyst to decompose the ozonide. After filtering off the catalyst, the solution was evaporated. The residue obtained was glassy and could not be crystallized. In the IR ($CHCl_3$ solution) it showed a strong peak at 1724 cm^{-1} for aliphatic C=O.

*Isomerization of the dimethyl ether to iso-*o*-dimethyl latifolin* (III). Latifolin dimethyl ether (0·5 g) was refluxed with alcoholic potash (20 ml, 50%) for 24 hr. After dilution, it was acidified with dil. hydrochloric acid and extracted with ether. The ether extract was dried (Na_2SO_4), and the residue after the removal of the solvent, was crystallized from methanol, yielding colourless stout rhombic prisms, m.p. 90–91°. Mixed m.p. with di-o-methyl latifolin was depressed, but with a synthetic sample of α,α(2,2′,4,5-tetramethoxy) diphenyl propene it was undepressed (Found: C, 72·7; H, 6·9, $C_{19}H_{22}O_4$ requires: C, 72·6; H, 7·1%).

2,2′,4,5-*Tetramethoxy benzophenone.* 1,2,4-Trimethoxy benzene (10 ml) was added to anhydrous $AlCl_3$(20 g) in dry ether (100 ml). To this solution, *o*-methoxy benzoyl chloride (10 ml) was added, while stirring vigorously, over a period of 1 hr. The stirring was continued for another 4 hr and the mixture left overnight. After decanting off the ether, the complex was decomposed by adding ice-cold dil. hydrochloric acid, followed by heating for 1 hr on a water bath. The product was then extracted with ether and dried (Na_2SO_4). After removal of ether, the residue gave a positive ferric reaction showing some demethylation. It was therefore dried in a vacuum desiccator over KOH, and methylated with dimethyl sulphate, acetone and potassium carbonate, and worked up. The tetramethoxy benzophenone crystallized from benzene–light petroleum as colourless stout rectangular prisms, m.p. 79–80° (Found: C, 67·7; H, 6·3; $C_{17}H_{18}O_5$ requires: C, 67·5, H, 6·0%).

α,α-(2,2′,4,5-*tetramethoxy*)*diphenyl propene* (III). The above benzophenone (2·5 g) in dry ether (15 ml) was added gradually (90 min.) to the Grignard reagent, prepared from magnesium turnings (0·45 g), ethyl iodide (2 ml) and ether (100 ml) with stirring. A yellow ppt. was formed as the addition was made; the complex was kept at room temp for 24 hr and then refluxed for 2 hr. It was decomposed by adding ice-cold dil. (1:5) hydrochloric acid. The ether layer was separated and evaporated. The product crystallized from methanol, m.p., 91–92° (Found: C, 72·2; H, 7·8. $C_{19}H_{24}O_5$ (the carbinol) requires: C, 68·7; H, 7·3; $C_{19}H_{22}O_4$ (olefine) requires: C, 72·6; H, 7·1%).

Catalytic hydrogenation of the above propene to tetramethoxy diphenyl propane (IV). The propene (50 mg) was dissolved in ethyl acetate and hydrogenated over Pd/$CaCO_3$ catalyst (50 mg). The product crystallized from light-petroleum as colourless rectangular plates m.p. 73–75°. Mixed m.p. with dihydrolatifolin dimethyl ether 62–66°; UV λ_{max}^{MeOH} 280 (log ε 3·75), 290 (log ε 3·71) mμ.

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