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DALBERGICHROMENE

A NEW NEOFLAVONOID FROM STEM-BARK AND HEARTWOOD OF *DALBERGIA SISSOO*

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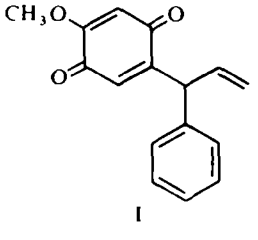
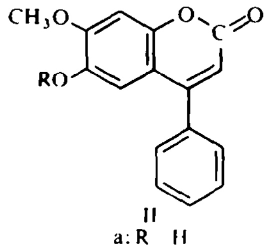
Abstract—The stem-bark of *Dalbergia sissoo* has yielded, besides the known compounds dalbergenone, dalbergin and methyl dalbergin, a new 4-phenyl chromene, dalbergichromene. Its structure has been determined as 7-methoxy-6-hydroxy-4-phenyl chrom-3-ene by spectral and degradative experiments and confirmed by rearrangement of dalbergenone to dalbergichromene. Reinvestigation of the heartwood shows that in addition to the known compounds the plant also contains dalbergichromene, nordalbergin and isodalbergin as minor constituents. A new method of conversion of 4-phenylcoumarins into 4-phenylchromenes involves cyclodehydration of the appropriate ortho hydroxy cinnamyl alcohols.

THE heartwood of *D. sissoo*, an important timber tree of northern India, yielded the allyl quinone, dalbergenone (I)[1] and the 4-phenylcoumarins dalbergin (IIa)[2] and methyl dalbergin (IIb).[2] The flowers, on the other hand, contain the isoflavones biochanin-A[3], tectorigenin[3] and its 7- as well as 7, 4 -dimethyl ethers.[4] The immature green pods have also been examined[5] and contain mesoinsitol together with 7-methyltectorigenin and its 4′-rhamno-glucoside. We now report the chemical components of the stem bark as well as a reinvestigation of the heartwood yielding two other known phenolic constituents not reported to occur in nature.



I

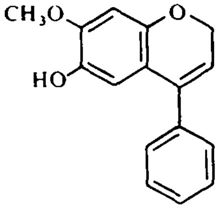


II
a: R = H
b: $R = CH_3$

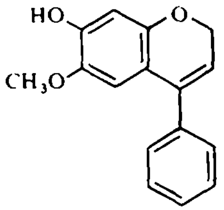
The light petroleum extract of the bark gave, besides terpenoids and waxes, several phenolic compounds. On fractionation these gave the known compounds, dalbergenone (I), dalbergin (IIa), methyldalbergin (IIb) and a new constituent, dalbergichromene. It is a minor constituent and has been isolated from the mother liquors after crystallization of the crude dalbergenone fraction.

Dalbergichromene is a pale yellow crystalline compound, m.p. 99–100°. It has the molecular formula $C_{16}H_{14}O_3$ and is isomeric with dalbergenone; it contains one OMe group (NMR; Zeisel) and one phenolic OH group (IR, 3590 cm^{-1}; solubility in NaOH and sodium hydroxide induced bathochromic shift in UV spectrum). It gave a monoacetate, m.p. 147° and a monomethyl ether, m.p. 66–67°. The compound had a double bond

(IR, 1620 cm^{-1}, 815 cm^{-1}) and was oxidised by a mixture of permanganate and periodate to a ketonic substance which could not be fully characterised for lack of sufficient amount. The NMR spectrum clearly indicates a 4-phenyl chromene. Besides showing the presence of one OMe group (δ 3·76, singlet, 3p), the compound has a doublet at δ 4·74 (2p, J, 4Hz) and a triplet at 5·68 (1p, J, 4 Hz) suggesting to the presence of a —CH_2—CH— group in the molecule. The downfield position of the signals due to the methylene protons agree with their location in a chromene system. In the aromatic region there are signals due to a mono-substituted benzene ring at δ 7·34 (5p, singlet) and two other protons at δ 6·50 and 6·65. The latter two are singlets indicating their *para* relationship. There are two possible structures (III or IV) for dalbergichromene, but (III) is the more likely on biogenetic grounds and has been confirmed by synthesis from dalbergenone (I). Compared with the formation of kuhlmannene,[6] the present conversion was very slow on an alumina column and was more easily carried out in hot pyridine.[7]



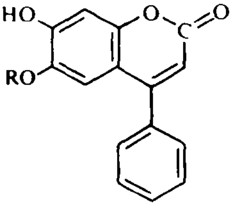
III



IV

Dalbergichromene is the first neoflavene isolated from the genus Dalbergia and the second natural neoflavene, the first being kuhlmannene occurring in *M. kuhlmannii* and *M. nictitans*.[6]

A re-examination of the fresh heartwood of *D. sissoo* showed that the light petroleum extract is a richer source of dalbergichromene occurring together with dalbergenone as major component. Subsequent acetone extraction of the wood yielded isodalbergin (V) and nordalbergin (VI) as minor components. These were known earlier only as synthetic compounds[2, 11] and their occurrence together with dalbergin and methyl dalbergin is of biogenetic interest. It indicates nordalbergin as the precursor of the other three.

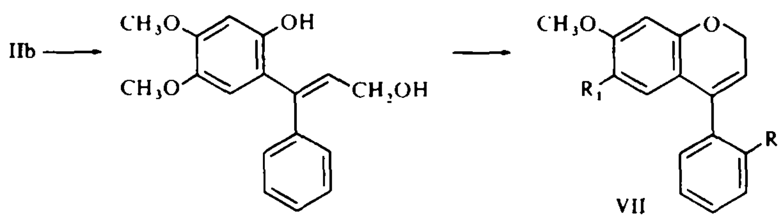


V: R = CH_3
VI: R = H

4-Phenylchromenes have been synthesised earlier from phenyl propargyl ethers[8] and also from chroman-4-ones by Grignard reaction with phenyl magnesium bromide followed by dehydration.[9] In a recent publication it was suggested that they are formed in

Nature from 4-phenylcoumarins, through the stages of reduction to cinnamyl alcohols followed by cyclisation. In order to test this idea the cyclization of several diphenyl allyl alcohols with different reagents has been investigated. The best reagent for this cyclization is a strong cation exchange resin (IR 120, H^+ form) in refluxing benzene medium. 6, 7-Dimethoxy-4-phenyl chrom-3-ene (VIIa) obtained in this way from methyl dalbergin (Ib) was identical with methyldalbergichromene in all respects. In a similar way 7-methoxy-4-phenylchrom-3-ene[8] (VIIb) and 6:7-dimethoxy-4-(2′-methoxyphenyl)-chrom-3-ene (VIIc) were prepared from the corresponding 4-phenyl-coumarins.

The facile isomerization of dalbergenones into the dalbergichromenes indicates an alternative path of biogenesis, although the original precursor is a 4-phenylcoumarin.



VII

a: R_1 OCH_3; R_2 H
b: R_1 = R_2 - H
c: R_1 R_2 OCH_3

EXPERIMENTAL

Examination of stem bark of D. sissoo

(a) *Light Petroleum extract.* Freshly air dried powdered stembark of *D. sissoo* (2 kg) was extracted in the cold with light petroleum (40–60°). The extract was concentrated to 500ml and allowed to stand at 10–12° for 24 hr. The yellow crystalline deposit (0·5 gm) of S-dalbergenone was recrystallized from EtOH giving yellow needles, m.p. 118–119°, $[\alpha]_D^{20°}$ 12·5° (*c*, 11·5; Chf).

The light petroleum filtrate gave a dark brown oil on further concentration. This oil partially crystallized on keeping at 0° for several days. The oil was decanted from the solid (0·8 gm) which was further purified by maceration with a little EtOH. TLC of this solid (silica gel NCL buffered with sodium acetate; developer benzene; H_2SO_4 spray) showed that it was a mixture of dalbergenone (R_f 0·4), a new compound, dalbergichromene (R_f 0·25) and methyl dalbergin (R_f 0·15) along with traces of other faster moving compounds. Dalbergenone and dalbergichromene were the major components of this mixture. Preparative TLC (six plates, 20 × 20 cm) in the same solvent system, cutting out the band at R_f 0·25 and extraction with ether, gave dalbergichromene (120 mg). It crystallized from light petroleum as pale yellow prisms, m.p. 99–100°, $[\alpha]_D^{20°}$ ±0° (Found: C, 75·0; H, 5·4. $C_{16}H_{14}O_3$ requires: C, 75·6; H, 5·6%); λ_{max}^{MeOH} 285 mμ (sh at 325 mμ); ν_{max}^{KBr} 3590 cm^{-1}(—OH); 1620 cm^{-1} (unsymmetrical double bond); 810 and 815 cm^{-1}; NMR spectrum: δ 3·76 (3p, s, —OCH_3); δ 4·74 (2P, d, —CH_2, *J* 4Hz); δ 5·68 (1P, t, —CH, *J* 4Hz); δ 6·5 (1P, s); δ6·65 (1P, s); δ 7·34 (5P, s).

Its acetate, prepared by the Ac_2O-pyridine method, crystallized from light petroleum as colourless needles, m.p. 147–48°. ν_{max}^{KBr} 1755 cm^{-1} (—OCO—CH_3).

(b) *Acetone extract.* The residual bark was further exhausted with cold acetone. It contained methyldalbergin and dalbergin and further nordalbergin and isodalbergin were also present in traces.

Re-examination of the heartwood

Light petroleum extract. Fresh heartwood shavings (2 kg) were continuously extracted with light petroleum (60–80°) in a Soxhlet. The light petroleum concentrate on keeping at 10–12° for 24 hr deposited most of the dalbergenone (5·5 gm), yellow needles from EtOH, m.p. alone or when mixed with the sample from bark 118°. The light petroleum mother liquors on further concentration and cooling gave a second crop of a crystalline mixture (0·8 g) of dalbergichromene and dalbergenone. Repeated crystallization first from EtOH and then from light petroleum gave dalbergichromene (0·4 g) identical in m.p. and mixed m.p. with the sample isolated from the bark.

Acetone extract. The residual shavings were next extracted with acetone in the cold, the extract concentrated and cooled depositing a dark brown gum. The concentrate was decanted from this gum and partially diluted with water to separate the phenolics as a crude crystalline mass (6·1 gm). TLC (silica gel; benzene : acetone, 4 : 1) indicated the presence of methyldalbergin (R_f 0·80; minor), dalbergin (R_f 0·55; major) and a new fluorescent compound (R_f 0·30; minor) along with traces of other compounds. Fractional crystallization from benzene removed most of the dalbergin and methyldalbergin. A portion (200 mg) of the solid obtained from the mother liquors was subjected to preparative TLC (10 plates, 20 × 20 cm, silica gel, benzene : acetone, 4 : 1) and the material present in the lowest moving band (R_f 0·3) was extracted with EtOAc. The solid (40 mg) obtained on evaporation of the extract, although giving a single spot on TLC, was still a mixture and melted over a range. It was subjected once again to preparative TLC (5 plates, 20 × 20 cm, silica gel NCL buffered with borax, benzene : acetone, 4 : 2) and resolved into two bands (R_f 0·4 and 0·1 respectively). Extraction of material from the faster moving band (R_f 0·4) with EtOAC and evaporation of the solvent gave isodalbergin (8 mg), colourless plates from EtOH, m.p. alone or when mixed with an authentic sample[11] 195–96°. Similar treatment of the slower moving band (R_f 0·1) furnished nordalbergin (30 mg), as pale yellow prisms m.p. alone or when mixed with an authentic sample[2] 268–69°.

Conversion of dalbergenone into dalbergichromene

A soln of dalbergenone (500 mg) in pyridine (15 ml) was heated on a water bath for 1 hr, acidified and extracted with ether. The ethereal soln was washed successively with dil HCl, $NaHCO_3$aq and satd NaCl aq, dried (Na_2SO_4) and evaporated. The residue (420 mg) crystallized from EtOH–light petroleum as colourless prisms, m.p. 99–100°. The mixed m.p. with natural dalbergichromene was undepressed.

Methyl dalbergichromene

(i) *Methylation of dalbergichromene.* The hydroxychromene (80 mg) gave the methyl ether on refluxing with MeI (excess) and K_2CO_3 in dry acetone for 6 hr. It crystallized from MeOH as colourless prisms m.p. 66–67°. (Found: C, 75·6; H, 6·0. $C_{17}H_{16}O_3$ requires: C, 76·11; H, 6·0%); λ_{max}^{MeOH} 280 mμ with sh. at 320 mμ.

(ii) *Cyclodehydration of 3-(2-hydroxy-4,5-dimethoxyphenyl)-3-phenyl allyl alcohol.*[10] The above alcohol (200 mg) in benzene (70 ml) was heated under reflux with dry Amberlite IR 120 resin (H^+ form; 2 gm) for 1 hr. The benzene soln was filtered and the resin washed with more benzene. The residue (180 mg), obtained on removing the solvent from the filtrate and the washings, under reduced pressure was purified by passing a soln in benzene through a column of silica gel (10 gm). Evaporation of benzene from the eluate and crystallization of the residue from a mixture of EtOAc and light petroleum gave dalbergichromene methyl ether (140 mg) as colourless prisms, m.p. 66–67° alone or when mixed with the natural sample described earlier.

Cyclodehydration of the cinnamyl alcohol by heating with Ac_2O and NaOAc or with anhyd $CuSO_4$ did not succeed. Shaking the alcohol with a mixture of ether and conc HCl according to Cook and Twine[12] gave only a poor yield.

Synthesis of analogues

6,7-Dimethoxy-4-(2′-methoxyphenyl) chrom-3-ene. 3-(2-Hydroxy-4,5-dimethoxy phenyl)-3-(2-methoxyphenyl) allyl alcohol[10] (200 mg) in benzene (100 ml) was heated under reflux with Amberlite resin (2 gm) for 1 hr. Purification of the product as described earlier gave the above chromene (120 mg); pale yellow needles from light petroleum, m.p. 63–65°. (Found: C, 72·1; H, 5·9. $C_{18}H_{18}O_4$ requires: C, 72·5; H, 6·1%); λ_{max}^{MeOH} 285 mμ; sh at 320 mμ.

7-Methoxy-4-phenylchrom-3-ene. 3-(2-Hydroxy-4-methoxyphenyl)-3-phenyl allyl alcohol[10] (500 mg) in benzene (100 ml) was heated under reflux with ion exchange resin (5 g) for 1 hr. On distilling off the solvent from the filtered mixture an oily residue (450 mg) was obtained. Distillation under high vacuum (0·01 mm) yielded a pale yellow oil (200 mg), b.p. 195°. (Found: C, 80·0; H, 6·0. $C_{16}H_{14}O_2$ requires: C, 80·6; H, 5·9%); λ_{max}^{MeOH} 288 mμ.

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