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VARIABILIN, A 6a-HYDROXYPTEROCARPAN FROM *DALBERGIA VARIABILIS**

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Key Word Index—*Dalbergia variabilis*; *D. frutescens*; Leguminosae–Lotoideae; isoflavans; isoflavones; pterocarpans.

Abstract—Bark and wood of the creeper *Dalbergia variabilis* contain the previously described friedelin, *O*-acetyloleanolic acid, formononetin, 8-*O*-methylretusin, (+)-vestitol, (±)-mucronulatol, (+)- and (±)-medicarpin, besides (+)-variabilin [(6a*R*,11a*R*)-6a-hydroxy-3,9-dimethoxypterocarpan]. This structure was confirmed by the conversion of (+)-variabilin into di-*O*-methylcoumestrol.

INTRODUCTION

Dalbergia variabilis Vog. is, according to Macbride, synonymous with *D. frutescens* (Vell.) Britt., a binomial which would have priority. *D. frutescens*, however, indicates a tree, and since *D. variabilis* in its typical form is a creeper [2], it was decided to refer to our scandent specimen by this designation.

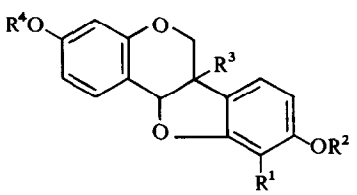
Wood and bark were separated and extracted. The wood extract yielded formononetin [1], (+)-vestitol [1], (±)-mucronulatol [3], (+)-medicarpin [1], (±)-medicarpin [4], besides (+)-variabilin. The bark extract yielded 8-*O*-methylretusin [5] and (+)-medicarpin [1]. Joint extraction of a sample of wood and bark gave additionally friedelin and *O*-acetyloleanolic acid [6]. Work on variabilin is described in detail in the present paper. All other constituents have been previously isolated from other *Dalbergia* and *Machaerium* species [7].

RESULTS AND DISCUSSION

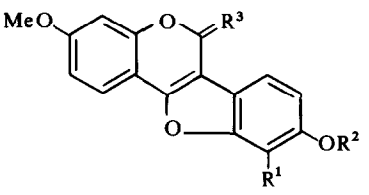
(+)-Variabilin, $C_{15}H_9O_2.OH(OMe)_2$, shows hydroxyl absorption, but no carbonyl absorption in the IR. The PMR spectrum is consistent with the presence of two 1,2,4-trisubstituted benzene rings, as well as isolated CH and CH_2 groups, both linked to oxygen. Attempted acetylation of variabilin or the action of heat resulted in the formation of optically inactive anhydrovariabilin, $C_{15}H_8O_2(OMe)_2$, whose PMR spectrum, though revealing the absence of the CH groups, continues to give evidence for the aromatic substitution and the CH_2 group, although without geminal non-equivalence. Loss of the hydroxyl and the methine proton of variabilin in the formation of anhydrovariabilin suggested that the change involved the dehydration of a 6a-hydroxypterocarpan to the corresponding chromenocoumarone. This interpretation is also consistent with the change in UV absorption, and with the ready transformation of pisatin (**1a**) into the anhydro-derivative **2a** [8–10]. From the aromatic region of its PMR spectrum and from the co-occurrence with medicarpin (**1b**), it seemed probable that variabilin is 6a-hydroxy-3,9-dimethoxypterocarpan (**1c**) and that anhydrovariabilin therefore has the structure **2b**. These proposals were confirmed by the oxidation of **2b** into coumestrol dimethyl ether (**2c**) [11]. The synthesis of a compound having the constitution of (±)-variabilin (**1c**) has previously been reported [10].

The ORD curve of (+)-variabilin is similar in form to that of (+)-medicarpin (**1b**, β-6aH, β-11aH). On the assumption that the ORD is not affected by the 6a-hydroxyl, it was concluded that (+)-variabilin (**1c**, β-6aOH, β-11aH) possesses the 6a*R*,11a*R*-configuration.

* Part 4 in the series 'Isoflavonoid Constituents of *Dalbergia* and *Machaerium* Species'. For Part 3 see ref. [1].



1a $R^1 = R^2 = OCH_2$, $R^3 = OH$, $R^4 = Me$
1b $R^1 = R^3 = R^4 = H$, $R^2 = Me$
1c $R^1 = H$, $R^2 = R^4 = Me$, $R^3 = OH$



2a $R^1 = R^2 = OCH_2$, $R^3 = H_2$
2b $R^1 = H$, $R^2 = Me$, $R^3 = H_2$
2c $R^1 = H$, $R^2 = Me$, $R^3 = O$

EXPERIMENTAL

Unless otherwise stated spectra were measured in EtOH (UV), $CHCl_3$ (IR), $CDCl_3$ (60 MHz PMR) and MeOH (ORD). All evapns of volatile material were performed under diminished pressure.

Isolation of the constituents of D. variabilis. A specimen was collected near Nova Friburgo, RJ, Brasil, and identified by the botanist Apparício Pereira Duarte. Wood and bark were separated. The ground wood (7.3 kg) was extracted successively with hot C_6H_6 and EtOH. The C_6H_6 extract (62 g) was chromatographed on Si gel to the following products (eluant, method of purification and quantity indicated): fatty oil (petrol, 8 g), a mixture [C_6H_6 and C_6H_6–$CHCl_3$ mixtures, rechromatography on Al_2O_3 MFC gave fatty oil, (+)-**1c** (6 g) and (+)-**1b** (5 g)], formononetin ($CHCl_3$, rechromatography, 50 mg). A portion (100 g) of the EtOH extract (345 g) was blended in $CHCl_3$. The soluble part (14 g) was chromatographed on Si gel. The main fraction ($CHCl_3$, 5.8 g) was separated by multiple chromatography on Al_2O_3 and fractional cryst. into (±)-mucronulatol (70 mg), (+)-vestitol (30 mg), formononetin (10 mg), (+)-**1b** (850 mg) and (+)-**1c** (660 mg). The $CHCl_3$ insoluble part (86 g) was chromatographed on Si gel. The fraction eluted with MeOH–$CHCl_3$, 1:9 (2.5 g) was separated by TLC and fractional cryst. into (+)-vestitol (36 mg). The ground bark (8.8 kg) was continuously extracted with hot C_6H_6. A long chain carboxylic acid (14 g), mp 85–87°, pptd during concn of the soln. A portion (50 g) of the extract (80 g) was chromatographed on Al_2O_3 MFC, elution with MeOH gave (+)-**1b** (after rechromatography and fractional cryst., 30 mg) and 8-*O*-methylretusin (after cryst. from MeOH, 100 mg). A ground mixture of bark and wood (7.6 kg) was extracted with C_6H_6. A long chain carboxylic acid (1.2 g), mp 106–110°, pptd during concn of the soln. A portion (20 g) of the extract (40 g) was chromatographed on Si gel. Elution with C_6H_6–$CHCl_3$ mixtures gave friedelin (230 mg), triterpenoid $C_{30}H_{48}O$ (50 mg) and triterpenoid $C_{30}H_{50}O$ (60 mg). Elution with $CHCl_3$ gave (+)-**1b** (30 mg), *O*-acetyloleanolic acid (180 mg) and **3a** (260 mg)

Identifications. Formononetin [1], (+)-vestitol [1], (±)-mucronulatol [3], (+)-medicarpin (**1b**, β-6aH, β-11aH) [1]. mp 133–134° (C_6H_6–petrol), $[\alpha]_D^{20}$ +179° (*c* 0.31, $CHCl_3$), (±)-medicarpin (**1b**) [4], friedelin, needles, mp 246–248°, $[\alpha]_D^{20}$ −25.4° (*c* 0.475, $CHCl_3$) and *O*-acetyloleanolic acid [6], mp 249–251°, $[\alpha]_D^{20}$ +67.6° (*c* 0.47, $CHCl_3$), were identified by direct comparison with authentic samples of natural products. The (+)-medicarpin was not optically pure, as shown by comparison with (−)-medicarpin (**1b**, α-6aH, α-11aH), mp 112–113°, $[\alpha]_D^{20}$ −229.5° [12]. 8-*O*-Methylretusin [5] was identified by direct comparison with a sample prepared in 2 steps (i) Hoesch reaction of 4-methoxyphenylacetonitrile with 2-methoxyresorcinol; (ii) heating of the intermediate 2,4-dihydroxy-3-methoxyphenyl 4-methoxybenzyl ketone with $HC(OEt)_3$, C_5H_5N and $C_5H_{10}N$ under reflux.

Compound $C_{30}H_{48}O$, platelets, mp 163° (C_6H_6–MeOH), $[\alpha]_D^{20}$ +48.3° (*c* 0.615, $CHCl_3$). [Found: M (HRMS): 424.3712. $C_{30}H_{48}O$ requires: M, 424.3705]. ν_{max} (cm^{-1}): 1700, 1635.

Compound $C_{30}H_{50}O$, crystals, mp 178° (MeOH–petrol), $[\alpha]_D^{20}$ +36.2° (*c* 0.372, $CHCl_3$). [Found: M (HRMS): 426.3860. $C_{30}H_{50}O$ requires: M, 426.3861]. ν_{max} (cm^{-1}): 3400, 1630, 1600.

(+)-*Variabilin* (**1c**, β-6aOH, β-11aH). Oil, $[\alpha]_D^{20}$ +211° (*c* 0.90, MeOH). [Found: M (HRMS), 300.1011 $C_{17}H_{16}O_5$ requires: M, 300.0998]. λ_{max} (nm): 228, 286 (ε 10600, 4250) ν_{max} (cm^{-1}): 3500, 1610, 1595. PMR (τ): 3.39 (*dd*), 3.63 (*d*), 2.67 (*d*) (ABX system, J_{AB} = 2.5 Hz, H-2, H-4, H-1), 3.54 (*dd*), 3.65 (*d*), 2.83 (*d*) (ABX system, J_{AB} = 2.5 Hz, J_{AX} = 8.5 Hz, H-8, H-10, H-7), 4.77 (*s*, H-11a), 4.75 (*br.s*, OH), 6.02, 5.86 (AB system, J_{AB} = 12 Hz, 2H-6), 6.28 (*s*, 2 OMe). ORD (*c* 0.10, MeOH): $[\phi]_{313}$ +7760, $[\phi]_{292}$ −12600, $[\phi]_{274}$ +48500, $[\phi]_{270}$ +46600, $[\phi]_{244}$ +143000, $[\phi]_{232}$ +110500. *Anhydrovariabilin* [6,7′-*dimethoxychromeno*(3′,4′:3,2)-*coumarone*)] (**2b**). (a) (+)-Variabilin (1.76 g), Ac_2O (10 ml) and C_5H_5N were kept (room temp., 24 hr) and then poured into iced H_2O. The mixture was extracted with C_6H_6. Chromatography on Si gel (C_6H_6) gave **2b** (220 mg). (b) Heating (160–180°) of (+)-variabilin (150 mg) under diminished pressure gave a sublimate which was recryst. to **2b** (110 mg), pale yellow rhombs, mp 112–113° (lit. mp 115° [13], 110–112° [14]). [Found: C, 71.97; H, 5.45. $C_{17}H_{14}O_4$ requires: C, 72.33, H, 5.00%. λ_{max} (nm): 244, 335, 351 (ε 13800, 31000, 27700). PMR (CCl_4, τ): 3.58 (*dd*), 3.64 (*d*), 2.72 (*d*) (ABX system, J_{AB} = 2.5 Hz, J_{AX} = 9 Hz, H-6′, H-8′, H-5′), 3.27 (*dd*), 3.06 (*d*), 2.92 (*d*) (ABX system, J_{AB} = 2.2 Hz, J_{AX} = 9.6 Hz, H-5, H-7, H-4), 4.51 (*s*, 2 H-2′), 6.20, 6.25 (2 *s*, 2 OMe). *Oxidation of anhydrovariabilin.* CrO_3 (30 mg) in H_2O (1 ml) was added to a stirred soln of **2b** (60 mg) in HOAc (10 ml) at room temp. After 30 min EtOH was added and the mixture evadp. The residue was separated by TLC (Si gel, C_6H_6) and recryst. to coumestrol dimethyl ether (**2c**, 5 mg), mp 199–200° (lit. [11] mp 198°). [Found: C, 68.46; H, 4.16. $C_{17}H_{12}O_5$ requires: C, 68.92; H, 4.08%]. λ_{max} (nm): 244, 342 (ε 23000, 27800). ν_{max} (cm^{-1}): 1735, 1630, 1610.

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