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VESTITOL AND VESTICARPAN, ISOFLAVONOIDS FROM *MACHAERIUM VESTITUM**

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Key Word Index—*Machaerium vestitum*; Leguminosae–Lotoideae; isoflavans; pterocarpans.

Abstract—The wood of *Machaerium vestitum* contains the previously described *O*-acetyloleanolic aldehyde, formononetin, (+)-medicarpin, and (−)-mucronulatol, besides (+)-vestitol [(3*S*)-7,2′-dihydroxy-4-methoxyisoflavan] and (+)-vesticarpan [(6a*S*,11a*S*)-3,10-dihydroxy-9-methoxypterocarpan]. The constitutions of vestitol and vesticarpan were deduced by spectra and confirmed by syntheses.

INTRODUCTION

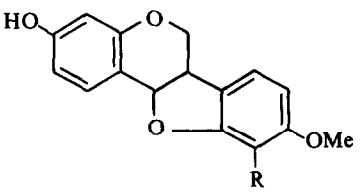
The trunk wood of *Machaerium vestitum* Vog. (Leguminosae–Lotoideae) contains *O*-acetyloleanolic aldehyde [2], formononetin [1] and (+)-medicarpin (demethylhomopterocarpin, **1a**, β-6aH, β-11aH) [3] which are all commonly encountered in *Dalbergia* and *Machaerium* species [4], as well as (−)-mucronulatol (**2a**, α-Ar), previously isolated from *M. opacum* Vog. [5], *M. mucronulatum* Mart. ex Benth. and *M. villosum* Vog. [1]. Work on the additional constituents (+)-vestitol and (+)-vesticarpan is discussed in detail in the present paper.

* Part 3 in the series 'Isoflavonoid Constituents of *Dalbergia* and *Machaerium* Species'. For Part 2 see ref. [1].

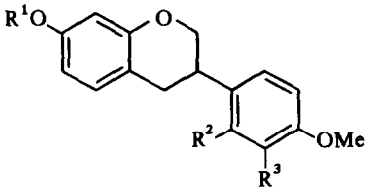
DISCUSSION AND RESULTS

(+)-Vestitol, $C_{15}H_{11}O(OH)_2OMe$, was recognized as an isoflavan derivative [6] from the lack of carbonyl absorption in its IR spectrum and the characteristic PMR signals associated with the CH_2—CH—CH_2 unit [1, 5, 6]. The aromatic protons form two ABX systems (J_{AX} = 7.5 Hz, J_{AB} = 3 Hz, J_{BX} = 0 Hz), showing that both aromatic rings of the isoflavan skeleton are 1,2,4-trisubstituted. The co-occurrence of vestitol with formononetin, (+)-medicarpin and (−)-mucronulatol (**2a**, α-Ar) suggested that vestitol might be 7,2′,4′-trioxygenated, such as, possibly, **2b**. This hypothesis was confirmed by the synthesis of (±)-vestitol.

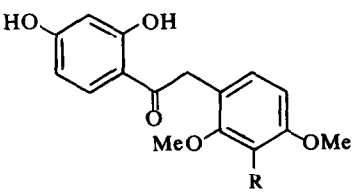
The reaction of 2,4-dimethoxyphenylacetic acid [7] with resorcinol in the presence of BF_3–Et_2O [8] gave the deoxybenzoin **3a**, which was converted by reaction



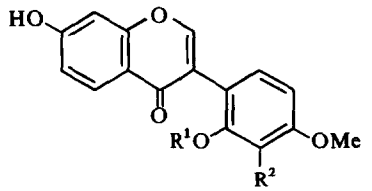
1a R = H
1b R = OH



2a R^1 = H, R^2 = OMe, R^3 = OH
2b R^1 = R^3 = H, R^2 = OH
2c R^1 = H, R^2 = R^3 = OH



3a R = H
3b R = OMe



4a R^1 = Me, R^2 = H
4b R^1 = R^2 = H
4c R^1 = Me, R^2 = OMe
4d R^1 = H, R^2 = OH

with $HC(OEt)_3$ into the isoflavone **4a**. Selective demethylation, using $AlCl_3$ in $PhNO_2$ [9], gave the corresponding 2'-hydroxyisoflavone (**4b**), which was hydrogenated, using a Pd/C catalyst in AcOH, to give (±)-vestitol (**2b**), identical (UV, IR, PMR) with natural (+)-vestitol. The 3*S*-configuration of (+)-vestitol (**2b**, α-Ar) was established by its synthesis upon hydrogenation of (+)-(6*aS*,11*aS*)-medicarpin.

(+)-Vesticarpan, $C_{15}H_9O_2(OH)_2OMe$, was recognized as a pterocarpan derivative from the lack of carbonyl absorption in its IR spectrum and the characteristic PMR signals associated with the CH—CH—CH_2 unit [10]. The aromatic protons form ABX (J_{AX} = 8.5 Hz, J_{AB} = 3 Hz, J_{BX} = 0 Hz) and AB (J_{AB} = 8.5 Hz) systems. The relative chemical shifts of these protons of vesticarpan and its diacetate favoured the constitution **1b** for vesticarpan. This hypothesis was confirmed by synthesis. The reaction of 2,3,4-trimethoxyphenylacetic acid [1] with resorcinol in the presence of BF_3–Et_2O [8] gave the deoxybenzoin **3b**, which was converted, using the reaction steps described above, via **4c**, into the trihydroxyisoflavone **4d**. This could not be reduced by $NaBH_4$, the method used [11] for the synthesis of other pterocarpan derivatives from 2'-hydroxyisoflavones, but reduction of **4d** using Na/Hg in boiling MeOH gave (±)-3,10-dihydroxy-9-methoxypterocarpan (**1b**), identical (UV, IR, PMR) with natural (+)-vesticarpan. Comparison of the ORD characteristics with those of other pterocarpan derivatives of known absolute configuration, including (+)-medicarpin (**1a**, β-6*a*H, β-11*a*H) [12], showed that (+)-vesticarpan has the 6*aS*,11*aS*-configuration (**1b**, β-6*a*H, β-11*a*H).

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 M. vestitum. A specimen was collected near Santa Luzia, MG, Brasil, and identified by Apparício Pereira Duarte. Ground trunkwood (14.4 kg) was continuously extracted with hot C_6H_6. The extract was chromatographed on Si gel (1.2 kg) to the following products (eluant, method of purif. and quantity indicated): fatty oil (C_6H_6, 9.4 g) *O*-acetyloleanolic aldehyde (C_6H_6–$CHCl_3$ (9:1), cryst. from MeOH, 200 mg), fatty material (C_6H_6–$CHCl_3$ (1:1) (5.4 g), (+)-**1a** ($CHCl_3$, TLC, 200 mg), mixture ($CHCl_3$, giving by TLC (−)-**2a**, 15 mg, and (+)-**1b**, 100 mg), formononetin ($CHCl_3$, cryst. from $CHCl_3$, 20 mg), (+)-**2b**, ($CHCl_3$, TLC, 150 mg).

Identifications. *O*-Acetyloleanolic aldehyde [2], formononetin [1], (+)-medicarpin (**1a**, β-6aH, β-11aH) [3] and (−)-mucronulatol (**2b**, α-Ar) [1] were identified by direct comparison with authentic samples.

(+)-*Vestitol* (**2b**, α-Ar), microcrystals, mp 156° ($CHCl_3$–petrol.), $[\alpha]_D^{20}$ + 21.6° (*c* 0.45, MeOH). [Found: C, 70.90; H, 5.95 $C_{16}H_{16}O_4$ requires: C, 70 57; H, 5.92%]. λ_{max} (nm): 206, 228, 285 (ε 45 500, 11 300, 5700). ν_{max} (cm^{-1}): 3500, 3250, 1620. PMR (τ): 3.57, 3.62 (2 *dd*), 3.54, 3.74 (2 *d*), 3.01, 3.15 (2 *d*) (2 ABX systems, J_{AB} = 3 Hz, J_{AX} = 8 Hz, H-6; H-5'; H-8; H-3'; H-5, H-6'), 5.5–7 (*m*, 2 H-2, H-3), 7.15 (*br. d*, *J* = 7 5 Hz, 2 H-4), 6.30 (*s*, OMe). ORD (*c* 0.08): $[\phi]_{370}$ +199, $[\phi]_{333}$ +298, $[\phi]_{313}$ +394, $[\phi]_{303}$ 0, $[\phi]_{292}$ −2960, $[\phi]_{286}$ 0, $[\phi]_{278}$ + 5330, $[\phi]_{274}$ +6380.

(+)-*Vesticarpan* (**1b**, β-6aH, β-11aH). Oil. [Found: M (HRMS), 286.076. $C_{16}H_{14}O_5$ requires: M, 286.084]. λ_{max} (nm): 226, 288 (ε 11 700, 3700). ν_{max} (cm^{-1}): 3500, 3225, 1620. PMR [$(CD_3)_2CO$, τ]: 3.39 (*dd*), 3.62 (*d*), 2.67 (*d*) (ABX system, J_{AB} = 3 Hz, J_{AX} = 8.5 Hz, H-2, H-4, H-1), 3.39 (*d*), 3.54 (*d*) (AB system, J_{AB} = 8.5 Hz, H-7, H-8), 6.21 (*s*, OMe), 4.4–6 7 (*m*, ABCX system, 2 H-6, H-6a, H-11a). ORD (*c* 0.006): $[\phi]_{303}$ −1680, $[\phi]_{290}$ −2170, $[\phi]_{286}$ 0, $[\phi]_{274}$ +1430, $[\phi]_{263}$ +1600, $[\theta]_{250}$ +4800. *Diacetate*, oil. [Found: M (MS), 370 $C_{20}H_{18}O_7$ requires: M, 370]. λ_{max} (nm): 230, 284 (ε 10900, 4600). ν_{max} (cm^{-1}): 1760, 1615. PMR (τ): 3.23 (*dd*), 3.28 (*d*), 2.46 (*d*) (ABX system, J_{AB} = 3 Hz, J_{AX} = 8.5 Hz, H-2, H-4, H-1), 2.96, 3.51 (AB system, J_{AB} = 8.5 Hz, H-7, H-8), 6.22 (*s*, OMe), 7.68, 7.73 (2 *s*, 2 OAc), 4.4–6.7 (*m*, ABCX system, 2 H-6, H-6a, H-11a). ORD (*c* 0.0088): $[\phi]_{400}$ −425, $[\phi]_{290}$ −2740, $[\phi]_{286}$ 0, $[\phi]_{278}$ +4000, $[\phi]_{263}$ +2740, $[\phi]_{144}$ +5950.

Synthesis of (+)-*vestitol* (**2b**, α-Ar). Hydrogenation (room temp., 1 atm., 8 hr) of (+)-**1a** (140 mg) over 10% Pd/C (70 mg) in HOAc (5 ml), filtration, evapn of the HOAc and cryst., of the residue gave 3*S*-**2b** (80 mg), $[\alpha]_D^{20}$ + 22.1° (*c* 0.43, MeOH). [Found: C, 70.90, H, 5.95. $C_{16}H_{16}O_4$ requires: C, 70.57; H, 5.92%], identical (mp, mmp, IR, PMR) with the natural product.

Synthesis of (±)-*vestitol* (**2b**). (a) *Formation of* 2,4-*dimethoxybenzyl* 2,4-*dihydroxyphenyl ketone* (**3a**). 2,4-Dimethoxyphenylacetic acid [7] (8.5 g) resorcinol (5 g) and BF_3–Et_2O (50 ml), as in ref. [5], gave **3a** (10 g), prisms, mp 154° (EtOH–H_2O (lit. [9] mp 154°). (b) *Formation of* 7-*hydroxy*-2',4'-*dimethoxyisoflavone* (**4a**). **3a** (2 g) and $HC(OEt)_3$ (20 ml) as in ref. [5], gave **4a** (1 g), needles, mp 271° (EtOH) (lit. [7] mp 267°). (c) *Formation of* 7,2'-*dihydroxy*-4'-*methoxyisoflavone* (**4b**) as in ref. [7]. (d) *Formation of* (±)-7,2'-*dihydroxy*-4'-*methoxyisoflavan* (**2b**). Hydrogenation (room temp., 8 hr) of **4b** (250 mg) over 10% Pd/C (100 mg) in HOAc (8 ml), filtration, evapn of the HOAc and TLC (Si gel, $CHCl_3$) of the residue gave **2b** (117 mg), oil, identical (IR, PMR) with natural (+)-vestitol.

Synthesis of (±)-*vesticarpan* (**1b**). (a) *Formation of* 2,3,4-*trimethoxybenzyl* 2,4-*dihydroxyphenyl ketone* (**3b**). 2,3,4-Trimethoxyphenylacetic acid (3 g), resorcinol (1.7 g), BF_3–Et_2O (20 ml) as in ref. [5], gave **3b** (2.7 g), mp 181° (lit. [13] mp 179–180°). (b) *Formation of* 7-*hydroxy*-2',3',4'-*trimethoxyisoflavone* (**4c**) as in ref. [13]. (c) *Formation of* 7,2',3'-*trihydroxy*-4'-*methoxyisoflavone* (**4d**). **4c** (3 g) was heated (100°, 30 min) with $AlCl_3$ (5 g) in $PhNO_2$ (40 ml). 2N HCl (60 ml) was then added and the $PhNO_2$ removed by steam dist. Filtration of the residue gave **4d** (2.48 g). [Found: M (HRMS), 300.0640. $C_{16}H_{12}O_6$ requires: M, 300.0634], characterised as 7,2',3'-triacetoxy-4'-methoxyisoflavone, cubes, mp 158° ($CHCl_3$–petrol). [Found: C, 62.27; H, 4.47. $C_{22}H_{18}O_9$ requires: C, 61.97; H, 4.26%]. λ_{max} (nm): 218, 248, 305 (ε 31600, 33000, 8150). ν_{max} (cm^{-1}): 1760, 1650, 1610). PMR (τ): 2.11 (*s*, H-2). (d) *Formation of* (±)-3,10-*dihydroxy*-9-*methoxypterocarpan* (**1b**). Na/Hg (4 g) was added in portions to a boiling soln of **4d** (100 mg) in MeOH (20 ml). The mixture was acidified, diluted with H_2O and extracted with $CHCl_3$. Evapn of the $CHCl_3$ gave residue which was purified by TLC (Si gel, $CHCl_3$) and sublimation (120°, 10^{-3} mm) to **1b**, microcrystals, mp 121°. [Found: C, 66.18, H, 5.14. $C_{16}H_{14}O_5$ requires: C, 67.13; H, 4.93%], identical (IR, PMR) with natural (+)-vesticarpan.

Synthesis of (±)-*dihydrovesticarpan* (7,2',3'-trihydroxy-4'-*methoxyisoflavan* (**2c**). Hydrogenation (room temp., 1 atm, 16 hr) of **4d** (118 mg) over 10% Pd/C (100 mg) in HOAc (10 ml), filtration, evapn, and purification of the residue by TLC and sublimation (120°, 10^{-3} mm) gave **2c** (25 mg), microcrystals, mp 151°. [Found: C, 66.26; H, 5.93. $C_{16}H_{16}O_5$ requires: C, 66.66; H, 5.59%]. λ_{max} (nm): 220, 285 (ε 20600, 3350). ν_{max} (cm^{-1}): 3500, 1620. Similar hydrogenation of **1b** also gave **2c**.

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