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NEOLIGNANS FROM *ANIBA BURCHELLII**

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Key Word Index—*Aniba burchellii*; Lauraceae; benzofuranoid neolignans; bicyclo[3,2,1]octanoid neolignans; absolute configurations.

Abstract—Seven neolignans, isolated from the benzene extract of *Aniba burchellii* Kosterm. (Lauraceae), included the hitherto unknown (2*S*,3*S*,5*S*)-5-allyl-5-methoxy-3-methyl-2-(3′,4′-methylenedioxyphenyl)-2,3,5,6-tetrahydro-6-oxobenzofuran and (1*R*,5*R*,6*R*,7*R*)-1-allyl-6-(4′-hydroxy-3′-methoxyphenyl)-3-methoxy-7-methyl-4,8-dioxobicyclo-[3,2,1]oct-2-ene. The former structure was previously assigned to a constituent of *A. terminalis* Ducke which is in fact the 5*R*-epimer. In addition to the latter constituent, all other previously described 4-oxobicyclo[3,2,1]oct-2-ene neolignans had their absolute configuration established.

INTRODUCTION

Neolignans from Lauraceae are generated by oxidative dimerization of propenylphenols either with propenylphenols [2–4] or with allylphenols. The latter class, comprising benzofuranoids (e.g. **1**–**3**) and bicyclooctanoids (e.g. **4**–**7**), is especially interesting, since its structural features can be correlated with botanical source. Thus, in all such neolignans of a particular species there is either dioxygenation or trioxygenation of the propenylphenol derived moiety, with either the β- or the α-configuration of the allyl substituent (Table 1). A β-allyl occurs only with an α-aryl. An α-allyl may occur with an α- or a β-aryl.

Considerable difficulties are encountered in the classification of Lauraceae species. The above deductions, if correct, are of systematic significance. It is desirable, therefore, to examine their validity. A step in this direction concerns the re-examination of *Aniba burchellii*. In the previous analysis of this species only the benzofuranoid neolignan burchellin (**1a**) was encountered [9]. Guianin (**4a**), the stereochemically corresponding bicyclooctanoid neolignan was first reported in a wood sample collected in the vicinity of Manaus, and attributed to *A. guianensis* [10]. Dr. K. Kubitzki, Hamburg, however, pointed out subsequently that this species is endemic to French Guiana, and Dr. W. A. Rodrigues, Manaus, re-examining the botanical material (voucher Herbarium INPA 13880), concluded that it is identical with *A. burchellii*. Thus, the co-occurrence of burchellin (**1a**) and guianin (**4a**), which since has been verified for *A. affinis* [3], in one specimen of *A. burchellii* remained to be demonstrated. It also seemed desirable to identify the minor neolignans of *A. burchellii*.

RESULTS AND DISCUSSION

Careful fractionation of the companion substances of burchellin (**1a**), present in minor quantities in the C_6H_6 extract of *A. burchellii*, led to the isolation of 6 additional compounds **1b**, **2a**, **2b**, **3**, **4a** and **5a**. Previous isolation of **1b** and **2b** from *A. affinis* [3], of **3** from *A. terminalis* [5] and of **4a** (guianin) from *A. affinis* [3] allowed these compounds to be identified by direct comparison with authentic samples.

Identification of **2a** (positive Cotton effect at 315 nm), relied upon spectra and a preparation by thermolysis and acid isomerization of burchellin (**1a**) of known absolute configuration [1]. Assignment of structure **2a** to a metabolite of *A. terminalis* (negative Cotton effect at 315 nm) [5] must thus be wrong. Since this metabolite, as well as **2a** ex *A. burchellii*, leads to **3** upon pyrolysis, the compounds differ with respect to chirality at C-5, and the metabolite of *A. terminalis* possesses the 5*R*-configuration in which the allyl occupies the α-face of the molecule. This conclusion is reasonable, inclusively because *epi*-burchellin with a 3a α-allyl (and not burchellin with a 3a β-allyl) is the major 2,3-*trans*-benzofuranoid neolignan of *A. terminalis*.

IR ($\nu_{\max}^{\text{film}}$ 1748 cm^{-1}) and UV spectra of **5b** ex *A. affinis* [3] and of the novel compound **5a** are closely comparable. Significant differences of the PMR spectra concern only signals due to $O_2C\underline{H}_2$ in **5b** vs $OC\underline{H}_3$, $O\underline{H}$ in **5a**. These substituents occupy the 3,4-aryl positions, as shown by the typical 2 (τ 3.43, *d*, $J=2$ Hz), 5(τ 3.27, *d*, $J=7$ Hz), 6 (τ 3.48, *dd*, $J=7$, 2 Hz) proton pattern. The OH (and not the OMe) is vicinal to H-5, since it is the H-5 signal and not the mid-point of the H-2, H-6 multiplet which suffers a considerable paramagnetic shift upon acetylation [resp. Δ (ppm) 0.24 vs 0.08].

The relative configuration of guianin (**4a**) and other bicyclooctanoid neolignans, obtained during the study of *A. affinis*, was formulated as shown in **4a**–**4e** and **5b**, **5c** [3]. Comparison with **6a**–**6d** and **7a**, **7b**, of established absolute stereochemistry [8], obtained during the study of *A. simulans*, show that the formulations also represent the absolute configurations of these compounds. The

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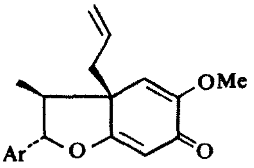
Table 1. Number of propenylphenol + allylphenol derived neolignans from Lauraceae classified according to oxygenation and configuration

	Ar-oxygenation of precursors propenylphenol allylphenol				neolignan configuration			
	3,4	3,4,5	3,4	3,4,5	α-Ar	β-Ar	α-Al	β-Al
A. burchellii Kosterm.								
benzofuranoids	5	0	5	0	5	0	0	4
bicyclooctanoids	2	0	2	0	2	0	0	2
A. affinis (Meissn.) Mez. [3]								
benzofuranoids	4	0	3	1	4	0	0	4
bicyclooctanoids	5	0	2	3	5	0	0	5
A. terminalis Ducke [5]*								
benzofuranoids	6	0	6	0	3	2	2	0
bicyclooctanoids	—	—	—	—	—	—	—	—
A. simulans Allen [6,7,8]								
benzofuranoids	0	14	12	2	8	5	7	0
bicyclooctanoids	0	7	3	4	7	0	7	0
benzofuranoids	0	4	4	0	3	0	2	0
bicyclooctanoids	—	—	—	—	—	—	—	—

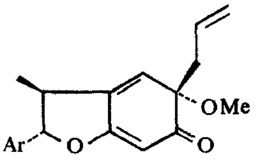
Ar, aryl; Al, allyl; *A.*, *Aniba*; *N.*, *Nectandra*.

* Compounds whose presence was inferred only by spectra are not listed. For correction of the stereochemistry at C-5 of one constituent, see present paper.

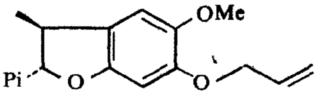
† Two benzofuranoids in which OMe (and not allyl) possess alternatively the 3aα- and 3aβ-configuration are not listed.



1a Ar = Pi
1b Ar = Ve



2a Ar = Pi
2b Ar = Ve



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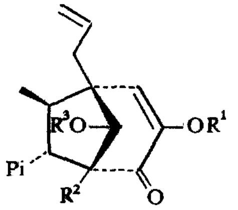
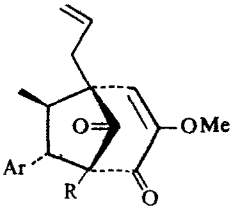
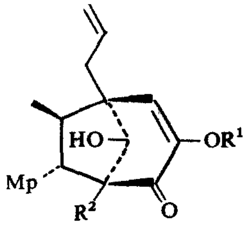


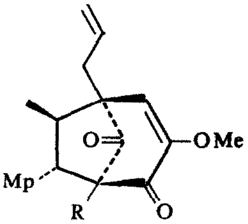
4a R^1 = Me, R^2 = R^3 = H
4b R^1 = Me, R^2 = OMe, R^3 = H
4c R^1 = H, R^2 = OMe, R^3 = Ac
4d R^1 = Me, R^2 = OMe, R^3 = Ac
4e R^1 = R^3 = Ac, R^2 = OMe



5a Ar = Gu, R = H
5b Ar = Pi, R = H
5c Ar = Pi, R = OMe



6a R^1 = R^2 = H
6b R^1 = H, R^2 = OMe
6c R^1 = Me, R^2 = H
6d R^1 = Me, R^2 = OMe



7a R = H
7b R = OMe

Pi ... piperonyl, Ve ... veratryl, Gu ... guaiacyl
Mp ... 3-methoxy-4,5-methylenedioxyphenyl

Cotton effects of all compounds of type **6**, positive at 280 and negative at 325 nm, can be assigned to the enone and the aryl chromophores respectively. Thus, since the Cotton effects of all compounds of type **4** are negative at 280 and again negative at 315 nm, the two series of bicyclooctanoids must show opposite configuration at C-1 and identical configuration at C-6.

The stereochemical disparity of compound types **4** and **6** is also indicated by spectral differences (e.g. ν_{max}: **4a** 1681 cm^{-1}, **6a** 1695 cm^{-1}; τ H-2: **4a** 3.90, **6a** 4.33). Pyridine induced solvent shifts, though identical for the common cyclohexenone parts of the molecules, are stronger for *exo* H-6 and Me-7 in **4a** than for *endo* H-6 and Me-7 in **6a**.

EXPERIMENTAL

Isolation of constituents. A. burchellii (voucher Herbarium IPEAN 14907) from the vicinity of Belém, Pará State, was identified by João Murça Pires. A sample of powdered trunk wood (5 kg) was extracted with C_6H_6. The extract (18.5 g) was crystallized from MeOH to give **1a**. The mother liquor was evapd and the residue submitted to dry column chromatography (350 g Si gel, C_6H_6 – EtOAc, 1:1). The column was cut into 26 equal portions, which were eluted separately, giving 26 fractions. Fractions 1–6 gave aliphatic material (4.1 g), 7–10 (0.8 g) gave aliphatic esters and **3** by Si gel TLC ($CHCl_3$ – MeOH, 9:1), 21–23 (0.3 g) gave **1b** by Si gel TLC (C_6H_6–EtOAc, 1:1), 24–26 (0.4 g) gave **1a** by Si gel TLC (C_6H_6–EtOAc, 1:1), and 11–20 (6.2 g) was crystallized from MeOH to **1a**. The mother liquor was evapd and the residue submitted to dry column chromatography (300 g Si gel, Et_2O). The column was cut into 11 equal portions, which were eluted separately, giving 11 fractions. Fractions 1–4 gave aliphatic material (1 g), 5 (0.8 g) gave **2a** by Si gel TLC (C_6H_6 – EtOAc, 1:1), 6 (0.3 g) was separated by addition of CCl_4 into insoluble **4** and soluble **2a**, 7–11 (2.9 g) was crystallized from MeOH to **1a**. The mother liquor was evapd and the residue separated by repeated Si gel TLC (C_6H_6 – EtOAc, 1:1) into the following compounds with the indicated R_fs: **1b** (0.24), **1a** (0.36), **2b** (0.39), **4** (0.44), **5a** (0.46), **2a** (0.51), **3** (0.67). Total quantities (in mg) obtained: **1a** (2300), **1b** (400), **2a** (800), **2b** (200), **3** (300), **4** (20), **5a** (10).

(2S,3S,5S) - 5 - *Allyl* - 5 - *methoxy* - 3 - *methyl* - 2 - (3′,4′ - *methylenedioxyphenyl*) - 2,3,5,6 - *tetrahydro* - 6 - *oxobenzofuran* (**2a**). Viscous oil [Found: 340.1300, $C_{20}H_{20}O_5$ requires: 340.1311]. ν_{max}^{film} (cm^{-1}): 1709, 1640, 1600, 1490, 1441, 1390, 1250, 1190, 1150. λ_{max}^{MeOH} (nm): 240, 290, 315 (ε resp. 10550, 7000, 4800). PMR ($CDCl_3$, 100 MHz, τ): 3.14 (*s*, H-2′, H-5′, H-6′), 3.77 (*d*, *J* = 3 Hz, H-2), 3.99 (*s*, O_2CH_2), 4.34 (*s*, H-4), 4.27–4.46 (*m*, $C\underline{H}=CH_2$), 4.84 (*s*, H-7), 4.94–5.14 (*m*, $=CH_2$), 6.82 (*s*, OMe), 6.98 (*dq*, *J* = 7, 3 Hz, H-3), 7.5 (*d*, *J* = 7 Hz, CH_2), 8.63 (*d*, *J* = 7 Hz, Me-3). MS (*m/e*): 341 (25), 340 (100) M^+, 300 (15), 299 (71), 271 (15), 239 (17), 211 (11), 178 (18), 177 (14), 149 (19), 135 (38). ORD (1.12×10^{-4} M, MeOH, 375–230 nm): $[\phi]_{343}^{pk}$ +37400, $[\phi]_{312}$ 0, $[\phi]_{292}^{tr}$ +21200, $[\phi]_{268}^{sh}$ −17000, $[\phi]_{250}^{sh}$ −8500, $[\phi]_{230}$ 0.

(1R,5R,6R,7R)-1-*Allyl*-6-(4′-*hydroxy*-3′-*methoxyphenyl*)-3-*methoxy*-7-*methyl*-4,8-*dioxobicyclo*[3,2,1]*oct*-2-*ene* (**5a**). Viscous oil [Found: 342.1473. $C_{20}H_{22}O_5$ requires: 342.1467]. ν_{max}^{film} (cm^{-1}): 3330, 1748, 1680, 1600, 1515, 1458, 1382, 1290, 1175. λ_{max}^{MeOH} (nm): 223, 273 (ε resp. 10900, 7300). PMR (CCl_4, 60 MHz, τ): 3.27 (*d*, *J* = 7 Hz, H-5′), 3.48 (*dd*, *J* = 7, 2 Hz, H-6′), 3.57 (*d*, *J* = 2 Hz, H-2′), mid-point of H-2′, H-6′-*m* 3.48, 3.85 (*s*, H-2), 4.0–4.3 (*m*, $=CH$), 4.6–5 (*m*, $=CH_2$), 6.2 (*s*, OMe-3′), *ca* 6.35 (H-5), 6.4 (*s*, OMe-3), 6.8–7.1 (*m*, H-6), 7.4–7.7 (*m*, CH_2-1, H-7), 8.87 (*d*, *J* = 7 Hz, Me-7). MS (*m/e*): 343 (34), 342 (100) M^+, 299 (30), 271 (40), 180 (23), 179 (20), 178 (32), 165 (40), 164 (56), 152 (41), 150 (25), 148 (19), 144 (46), 135 (30), 105 (28). ORD (1.28×10^{-4} M, MeOH, 400–230 nm): $[\phi]_{400}$ +1000, $[\phi]_{318}^{pk}$ +2500, $[\phi]_{294}^{tr}$ +1700, $[\phi]_{287}^{pk}$ +1800, $[\phi]_{279}$ 0, $[\phi]_{255}^{tr}$ −6350, $[\phi]_{277}$ 0. Acetate ν_{max}^{film}(cm^{-1}); 1735 *br*, 1658, 1600, 1490, 1420, 1350. PMR ($CDCl_3$, 60 MHz, τ): 3.03 (*d*, *J* = 7 Hz, H-5′), 3.3–3.5 (*m*, mid-point 3.4, H-2′, 6′), 3.73 (*s*, H-2), 4–4.3 (*m*, $=CH$), 4.4–5 (*m*, $=CH_2$), 6.2 (*s*, OMe), 6.3 (*s*, OMe), 7.7 (*s*, OAc), 8.84 (*d*, *J* = 7 Hz, Me-7).

Isomerization of **1a**. *Pyrolysis*. **1a** (100 mg) in $C_6H_6NEt_2$ (0.5 ml) under N_2 was maintained at 100–105° (15 hr). The soln was cooled, suspended in H_2O, neutralized with 2N HCl, and extracted with Et_2O. The Et_2O soln was washed with satd aq. NaCl, dried and evapd. The residue was separated by Si gel TLC (Et_2O) into **1a** (18 mg) and **2a** (54 mg). *Acid treatment*. **1a** (220 mg) and TsOH (1 mg) in CH_2Cl_2 (20 ml) was stirred at room temp. (48 hr). The soln was neutralized with aq. $NaHCO_3$ and the organic phase washed with satd aq. NaCl, dried and evapd. The residue was separated by Si gel TLC (Et_2O) into **1a** (85 mg) and **2a** (22 mg).

Comparison of solvent shifts. ($\tau CDCl_3 - \tau C_5D_5N$) **4a**/**6a** H-2 0.20/0.20, H-8, 0.32/0.32, H-5, 0.41/0.39, H-6 0.42/0.2, Me-7 0.22/0.08, ArH 0.39, 0.29, 0.21/0.49, 0.39.

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