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HEXAHYDROBENZOFURANOID NEOLIGNANS FROM AN *ANIBA* SPECIES*

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Key Word Index—*Aniba* sp.; Lauraceae; trunk wood; neolignans; porosin; canellin-B; armenin.

Abstract—The trunk wood of an Amazonian *Aniba* species contains three novel neolignans: (2*R*, 3*R*, 3a*S*, 5*R*)-3a-allyl-5-methoxy-2-(3,4,5-trimethoxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran (canellin-D), (2*R*,3*R*,3a*S*, 5*R*)-3a-allyl-5,7-dimethoxy-2-(3-methoxy-4,5-methylenedioxyphenyl)-3-methyl-2,3,3a,4,5,6-hexahydro-6-oxobenzofuran (canellin-E) and (2*S*,3*S*,3a*S*,5*R*)-3a-allyl-5-methoxy-2-(3-methoxy-4,5-methylenedioxyphenyl)-3-methyl-2,3, 3a,4,5,6-hexahydro-6-oxobenzofuran (armenin-C). The absolute stereochemistries of these and of all other known hexahydro-6-oxobenzofurans were determined by CD comparisons with model compounds.

INTRODUCTION

Among the seven known hexahydro-6-oxobenzofuranoid neolignans, chrysophyllins A and B from *Licaria chrysophylla* belong to an unusual type with the *C*-aryl and *C*-methyl substituents at exchanged positions [2] and will not be considered further here. The other four, **1a** (porosin) from *Ocotea porosa* [3, 4] and *Urbanodendron verrucosum* [5], **1b** (porosin-B) from *Urbanodendron verrucosum* [6], **2a** (canellin-B) from *Licaria canella* [6, 7], **3a** (now designated armenin-A) and **3b** (now designated armenin-B) from *Licaria armeniaca* [8], belong to three configurational types. The present paper reports the isolation, again from a species of the Lauraceae (*Aniba* sp.), of three additional representatives of this group of neolignans, **2b** (canellin-D), **2c** (canellin-E) and **3c** (armenin-C). For reasons stated in a previous paper of this series [9], nomenclature and numbering of neolignans follow the rules outlined in a review [10].

RESULTS AND DISCUSSION

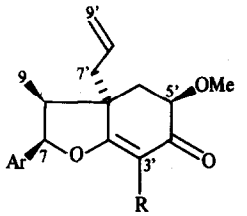
High resolution mass measurements revealed formulae $C_{22}H_{28}O_6$ for **2b**, $C_{22}H_{26}O_7$ for **2c** and $C_{21}H_{24}O_6$ for **3c**. Upon inspection of the NMR spectra (Tables 1 and 2), these formulae could be expanded to Ar·Me·CH_2CH $=CH_2(C_8H_5O_2 \cdot OMe)$R, Ar being 3,4,5-trimethoxyphenyl (**2b**) or 3-methoxy-4,5-methylenedioxyphenyl (**2c**, **3c**) and R being hydrogen (**2b**, **3c**) or methoxyl (**2c**). Considering the general formula, which encompasses an α,β-unsaturated carbonyl (ν_{max} 1658 ± 2 cm^{-1}), the compounds were recognized as hexahydro-6-oxobenzofuranoid neolignans. Such neolignans can be classified into groups either according to the substitution at C-3′ or according to the stereochemistry of the four chiral centres.

The absence or presence of a methoxyl at C-3′ leads to different mass spectral fragmentation (Scheme 1) for the known neolignans **1a**, **1b** and **3a** (R = H) as opposed to **2a** and **3b** (R = OMe). According to this criterion (Table 3), the novel neolignans **2b** and **3c** belong to the former group (R = H) and **2c** to the latter (R = OMe). This deduction was consistent with the UV spectra in which the compounds with R = H (**1a**, **1b**, **2b**, **3a**, **3c**) or with R = OMe, an additional auxochrome (**2a**, **2c**, **3b**), showed the most intense absorption maximum at 258 ± 2 nm and 270 ± 8 nm, respectively (Table 4).

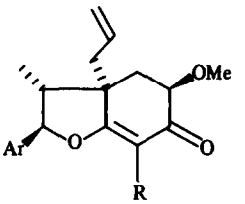
More interesting is the classification of the hexahydrobenzofuranoid neolignans into porosin (**1**), canellin-B (**2**) and armenin (**3**) types. The relative stereochemistry for representatives of all three types had been worked out previously by ^{13}C NMR data [11]. It was thus possible to classify the novel neolignans **2b** and **2c** into the canellin-B and **3c** into the armenin configurational types simply by comparison of their ^1H NMR spectra with those of the known compounds (Table 1). Relevant for the assignment of the *cis* vs *trans* relation of the aryl at C-7 with the methyl at C-8 (δ0.5 vs 1.1) and the methylene at C-1′ (δ2.2 vs 2.6) were the lower chemical shift values in the former cases. The axiality of H-5′ in all compounds was revealed by the coupling constants (J = 5, 12 Hz) of its ^1H NMR double-doublet.

The hexahydrobenzofuranoid neolignans have four chiral centres. The contribution of the substituents on C-7, C-8 and C-5′ on the Cotton effect due to the $n \rightarrow \pi^*$ transition of the enone linked to C-1′, however, is negligible. Indeed, all three compounds, **1a**, **4** (the photolytic product of **1a** [4]) and **5** (the oxidation product of **1a** [Barros, D. A. D., unpublished work]), showed the same Cotton effect at 301 ± 4 nm (Table 5). Crossed conjugated dienones and enones both follow the normal octant rule [12]. It is consequently permissible to use compounds **6** and **7** [13] of known absolute stereochemistry as models for the determination of the chirality at C-1′. Whilst **7** had a negative Cotton effect, **6** and all the compounds of types **1**, **2** and **3** had a positive one (Tables 5 and 6) and must therefore possess an identical absolute configuration at C-1′. The relative configurations of all centres being known, the absolute configurations shown can now be proposed for all known hexahydrobenzofuranoid neolignans.

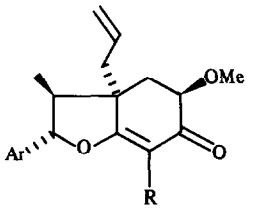
*Part 75 in the series "The Chemistry of Brazilian Lauraceae". For Part 74 see ref. [1].



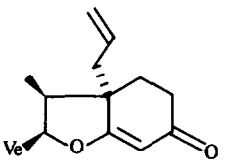
1a Ar = Ve, R = H
1b Ar = Pi, R = H



2a Ar = Pi, R = OMe
2b Ar = Tp, R = H
2c Ar = Mp, R = OMe



3a Ar = Pi, R = H
3b Ar = Pi, R = OMe
3c Ar = Mp, R = H



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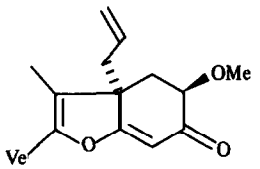

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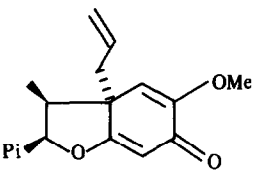

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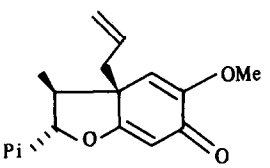


7

Pi ... piperonyl
Ve ... veratryl
Mp ... O-methyl-O,O-methylenyl-pyrogallyl
Tp ... tri-O-methylpyrogallyl

EXPERIMENTAL

Isolation of constituents. Wood of the tree, classified by Dr. William A. Rodrigues as an *Aniba* sp. (voucher INPA Herbarium 47384), was collected in the vicinity of Manaus, Amazonas State. The air-dried sample was powdered (4 kg) and extracted with C_6H_6. The extract (8 g) was submitted to dry CC (silica gel + 10% H_2O, 200 g, C_6H_6–EtOAc, 7:3). The extruded column was cut into 16 equal portions which when extracted separately with $CHCl_3$ gave 16 fractions. Fractions 1–3 (1.7 g) were composed of aliphatic material. Fractions 4 and 5 (1.2 g) gave, after TLC (silica gel, C_6H_6) purification, benzyl benzoate and benzyl salicylate. Fractions 6–8 (0.8 g) gave, after crystallization from MeOH, sitosterol. Fraction 9 (0.5 g) gave, after TLC (silica gel, C_6H_6–Et_2O, 4:1), **2c** (50 mg) and **3c** (190 mg). Fractions 10–12 (0.7 g) gave, by the same process of purification, **2b** (270 mg).

Photolysis of porosin (**1a**). A soln of **1a** (100 mg) in MeOH (100 ml) was irradiated in a quartz tube using PCQ-XI low pressure Hg lamps (254 nm) for 10 min. The solvent was evapd and the residue separated by TLC (silica gel, C_6H_6–EtOAc, 7:3)

Table 1. ^{1}H NMR spectral data of hexahydro-6-oxobenzofuranoid neolignans ($CDCl_3$, δ, TMS as internal standard, J in Hz in parentheses)

MHz	220	60	60	220	100	60	100	60	60
H	**1a** [3]	**1b** [5]	**4**	**2a** [6]	**2b**	**2c**	**3a** [8]	**3b** [8]	**3c**
9	0.52 *d* (7)	0.50 *d* (7)	0.51 *d* (7)	1.04 *d* (7)	1.08 *d* (7)	0.93 *d* (7)	1.20 *d* (8)	1.20 *d* (8)	1.16 *d* (8)
8	2.60 *m*	2.4–2.7	2.51–2.67	2.07 *dq* (7, 10)	2.46 *m*	2.06 *m*	2.64 *dq* (2, 8)	2.65 *dq* (2, 8)	2.02–2.20
7	5.89 *d* (5.4)	5.74 *d* (5)	5.86 *d* (5.5)	5.05 *d* (10)	5.07 *d* (10)	4.51 *d* (10)	5.22 *d* (2)	5.27 *d* (2)	5.17 *d* (2.5)
2	6.76 *d* (2)	6.5–6.8	6.78 *d* (2)	6.63 *m*	6.43 *s*	6.52 *d* (2)	6.8 *br s*	6.82 *br s*	6.48 *s*
5	6.83 *dd* (2, 8)	6.5–6.8	6.88 *dd* (2, 8)	6.63 *m*	—	—	6.8 *br s*	6.82 *br s*	—
6	6.93 *d* (8)	6.5–6.8	6.91 *d* (8)	6.63 *m*	6.43 *s*	6.67 *d* (2)	6.8 *br s*	6.82 *br s*	6.48 *s*
9	5.28–5.40	5.1–5.3	5.28–5.40	5.16–5.27	5.14–5.34	5.06–5.23	4.8–5.1	4.8–5.1	4.98–5.10
8′	5.85–6.06	5.6–6.2	5.80–6.05	5.77–5.95 (6.5, 8.5, 10, 16)	5.71–5.83	5.30–5.50	5.4–5.8	5.5–5.8	5.57–5.86
7′	2.56 *dd* (7, 14.5) 2.69 *dd* (7, 14.5)	2.4–2.6	2.51–2.67	2.45 *dd* (8.5, 15) 2.56 *dd* (6.5, 15)	2.52–2.64	2.53–2.70	2.16 *dd* (7, 14) 2.32 *dd* (7, 14)	2.17 *dd* (7, 14) 2.38 *dd* (7, 14)	2.1–2.35
6′	2.22 *dd* (5, 12) 1.92 *dd* (12, 12)	2.26 *dd* (5, 12) 1.85 *dd* (12, 12)	1.70–1.96	2.48 *dd* (7, 10) 1.76 *dd* (12, 12)	2.12 *dd* (6, 12) 1.78 *dd* (12, 12)	2.28 *dd* (6, 12) 1.67 *dd* (12, 12)	2.3 *dd* (5, 12) 1.84 *dd* (12, 12)	2.33 *dd* (5, 12) 1.83 *dd* (12, 12)	2.56 *dd* (6, 10) 1.86 *dd* (12, 12)
5′	4.02 *dd* (5, 12)	3.92 *dd* (5,12)	1.70–2.07	4.03 *dd* (5.5, 12)	4.04 *dd* (6, 12)	4.10 *dd* (6, 12)	3.92 *dd* (5, 12)	3.93 *dd* (5, 12)	3.80 *m*
MeO-5′	3.62 *s*	3.53 *s*	—	3.55 *s*	3.56 *s*	3.47 *s*	3.58 *s*	3.62 *s*	3.60 *s*
3′	5.59 *s*	5.44 *s*	5.56 *s*	—	5.52 *s*	—	5.52 *s*	—	5.40 *s*
MeO-3′	—	—	—	3.70 *s*	—	3.86 *s*	—	3.83 *s*	—
CH_2O_2	—	5.87 *s*	—	5.91 *s*	—	5.90 *s*	5.96 *s*	6.02 *s*	6.00
1 MeO	—	—	—	—	—	3.92 *s*	—	—	3.96 *s*
2 MeO	3.90 *s*	—	3.86 *s*	—	—	—	—	—	—
3 MeO	—	—	—	—	3.84 *s*	—	—	—	—

Table 2. ^{13}C NMR spectral data of hexahydro-6-oxobenzofuranoid neolignans (20 MHz, $CDCl_3$, δ, TMS as internal standard)

C	**1a** [11]	**2b**	**3c**
9	11.6	11.9	17.5
8	42.5	48.8	44.3
7	87.2	91.0	92.7
6	117.8	103.6	101.9
5	110.9	153.6	149.6
4	148.5	136.2	132.4
3	148.8	153.6	143.8
2	108.6	103.6	104.6
1	128.3	133.0	134.8
9′	119.7	119.6	119.9
8′	132.5	133.8	135.3
7′	39.0	37.3	41.2
6′	32.0	38.9	31.9
5′	76.8	76.8	76.9
4′	196.6	197.2	196.7

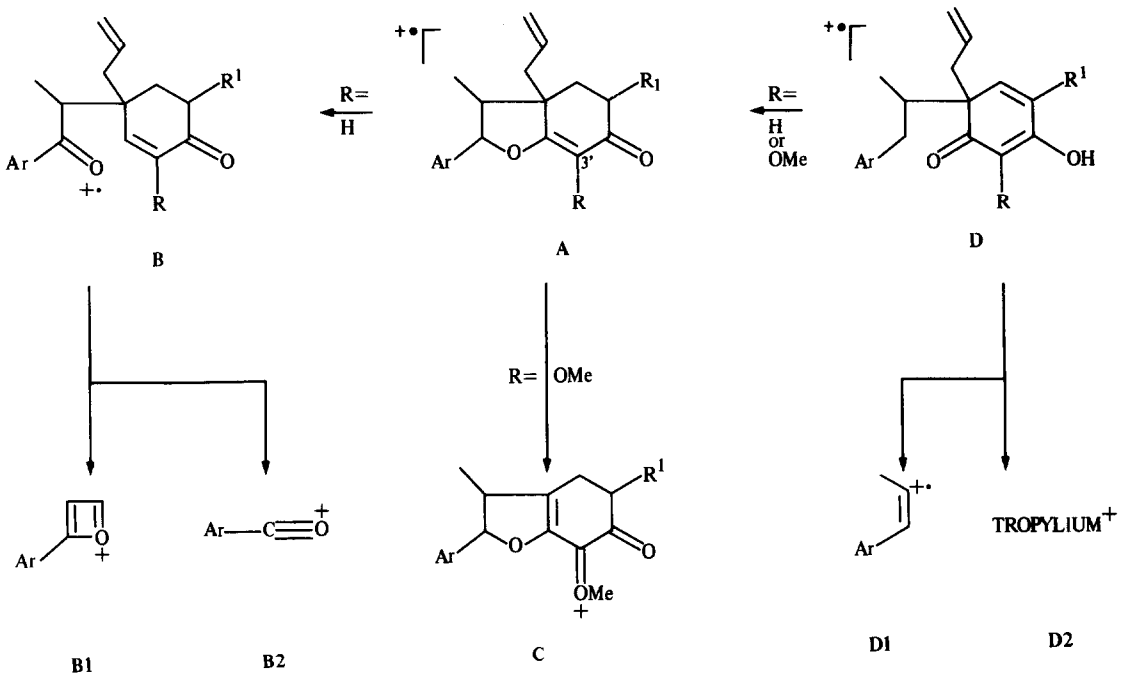
Table 2 (*contd.*)

C	**1a** [11]	**2b**	**3c**
3′	100.1	100.8	100.9
2′	183.4	183.6	184.4
1′	50.2	53.0	48.9
MeO-5′	58.7	59.1	58.8
MeO-4	55.9	61.0	—
MeO-3	55.9	56.5	57.0
MeO-5	—	56.5	—
CH_2O_2	—	—	101.7

into **1a** (35 mg) and **4** (40 mg), besides two minor components.

Canellin-D (**2b**). Mp 141–142° (Me_2CO). $[M]^+$ Found: 388.1882; $C_{22}H_{28}O_6$ requires: 388.1886. IR ν_{max}^{KBr} cm^{-1}: 1660, 1625, 1580, 1450, 1425, 1345, 1235, 1120, 1005, 930, 830.

Canellin-E (**2c**). Oil. $[M]^+$ Found: 402.1677; $C_{22}H_{26}O_7$ requires: 402.1679, IR ν_{max}^{KBr} cm^{-1}: 1655, 1640, 1510, 1450, 1430, 1325, 1180, 1090, 1045, 930, 840, 680.



Scheme 1. Mass spectral fragmentation of hexahydro-6-oxobenzofuranoid neolignans **1a**, **1b**, **2a**, **2b**, **2c**, **3a**, **3b**, **3c** (R^1 = OMe) and **4** (R^1 = H).

Table 3. Mass spectral fragments (relative intensity) of hexahydro-6-oxobenzofuranoid neolignans

Ions (Scheme 1)	**1a** [3]	**1b** [5]	**4**	**2a** [6]	**2b**	**2c**	**3a** [8]	**3b** [8]	**3c**
A	100	50	100	46	92	48	45	30	16
B1	78	100	96		100		100	12	47
B1 − CO	13		28		38				
B2	29	68	42	15	26	28	10	26	8
C				100		100		87	
C − CO			84			62		100	
D1	42	78	50	90	46	54	64	86	7
D2	72	100	97	50	94	50	22	96	68

Table 4. UV spectral data of hexahydro-6-oxobenzofuranoid neolignans (MeOH, λ_{max}, ε in parentheses)

1a [3]	**1b** [5]	**4**	**2a** [6]	**2b**	**2c**	**3a** [8]	**3b** [8]	**3c**
237[i]		236	239[i]				239[i]	
(14 500)		(6700)	(6000)				(4400)	
258	260	258	278	260	262	256	268	258
(21 800)	(14 000)	(10 700)	(16 500)	(18 250)	(12 600)	(12 500)	(14 000)	(6250)
285[i]	290[i]	285				285	285	
(4600)	(5100)	(2200)				(3800)	(10 300)	

i = inflection.

Table 5. CD data ([θ]) of hexahydro- (types **1**, **2**, **3**, **4**) and tetrahydro- (types **5**, **6**, **7**) 6-oxobenzofuranoid neolignans (6.5 mg/100 ml MeOH)

λ (nm)	**1a** [3]	**4**	**5**	**2a** [6]	**2b**	**3a** [8]	**6** [13]	**7** [13]
334 ± 1							+13600	−10200
311 ± 1				+27950		+11900		
301 ± 4	+5550	+7350	+8950		+19000			
298 ± 1							+59500	+61200
277 ± 3				−22550		−7050	−11900	−1700
267 ± 2	−11450	−11650			−38050			
258 ± 2	−13900	−13800		−13700	−39950	−4100	−20400	−15300

Table 6. ORD data ([Φ]) of hexahydro- (types **1**, **2**, **3**, **4**) and tetrahydro- (types **5**, **6**, **7**) 6-oxobenzofuranoid neolignans (6.5 mg/100 ml MeOH)

λ (nm)	**1a** [3]	**1b** [5]	**4**	**5**	**2a** [6]	**2b**	**3a** [8]	**3b** [8]	**6** [14]	**7** [14]
400	+6050		+2750	+7150	+5300	+2600	+11300	+2150		
338 ± 15^{pk}	+14750	+6800	+13900	+25950	+16100	+7800	+27950	+6200	+13100	
351^{tr}										−2050
323 ± 17	0	0	0	0	0	0	0	0	0	0
313^{pk}										+25500
289 ± 12^{tr}	−29550	−41000	−52800	−56400	−46400	−45450	−38700	−19400	−23800	
283 ± 17	0	0	0		0	0	0	0	0	0
288^{tr}										−31450
266 ± 17^{pk}	+20150	+85500	+27840		+12500	+10400	+1500	+1950	+28900	

tr = trough; pk = peak

Armenin-C (**3c**). Oil. $[M]^+$ found: 372.1575; $C_{21}H_{24}O_6$ requires: 372.1573. IR ν_{max}^{KBr} cm^{-1}: 1660, 1630, 1510, 1450, 1430, 1355, 1130, 1040, 930, 840, 810.

(7R,8S,1'R)-Δ8'-3,4-*Dimethoxy*-1',4',5',6'-*tetrahydro*-4'-*oxo*-7.O.2',8.1'-*neolignan* (**4**). Oil. $[M]^+$ found: 328.1674; $C_{20}H_{24}O_4$ requires: 328.1675. IR ν_{max}^{KBr} cm^{-1}: 1690, 1600, 1505, 1450, 1350, 1250, 1170, 1025, 990, 845, 760.

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