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NEOLIGNANS FROM AN *ANIBA* SPECIES*

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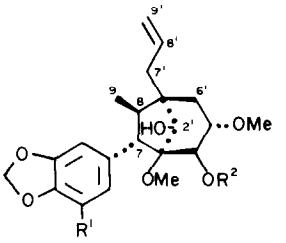
Key Word Index—*Aniba* sp.; Lauraceae; bicyclo(3.2.1)octanoid neolignans; eusiderin.

Abstract—The trunk wood of an Amazonian *Aniba* (Lauraceae) species contains, besides dillapiol and the benzodioxane-type neolignan eusiderin, four bicyclo(3.2.1)octanoid neolignans. These comprise representatives of the canellin-type: the known methoxycanellin-A and the novel compounds characterized as (1*R*, 3*S*, 4*S*, 5*S*, 6*S*, 7*R*)-1-allyl-4-hydroxy-3, 5-dimethoxy-7-methyl-6-(3′-methoxy-4′, 5′-methylenedioxyphenyl)-8-oxobicyclo(3.2.1)octane; (1*R*, 3*S*, 4*S*, 5*S*, 6*S*, 7*R*)-1-allyl-4-hydroxy-3, 5-dimethoxy-7-methyl-6-(3′, 4′, 5′-trimethoxyphenyl)-8-oxobicyclo(3.2.1)octane and (1*R*, 4*R*, 5*R*, 6*S*, 7*R*, 8*S*)-1-allyl-4, 8-dihydroxy-5-methoxy-7-methyl-6-(3′-methoxy-4′, 5′-methylenedioxyphenyl)-3-oxobicyclo(3.2.1)octane.

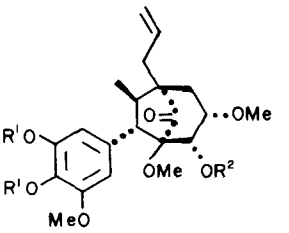
INTRODUCTION

The trunk wood of a lauraceous tree was collected at Ducke Forest Reserve, Manaus. According to the botanist William A. Rodrigues, the specimen, voucher Herbarium INPA, Manaus, no. 42183, belongs to an unclassified *Aniba* species. The benzene extract of trunk wood yielded the simple allylbenzene dillapiol (**1**), the benzodioxane-type neolignan eusiderin (**2**) [2] and four canellin-type neolignans: methoxycanellin-A (**3a**) and the novel compounds **4a**, **4b** and **5a**.

For reasons stated in a previous paper in this series [3], nomenclature and numbering of neolignans follow the rules outlined in a recent review [2].



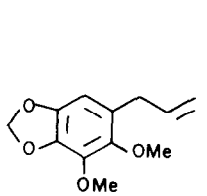
3a R¹ = OMe, R² = H
3b R¹ = R² = H
3c R¹ = OMe, R² = Ac



4a R¹ – R¹ = CH_2, R² = H
4b R¹ = Me, R² = H
4c R¹ – R¹ = CH_2, R² = Ac

RESULTS AND DISCUSSION

Spectral analysis (^{1}H NMR, IR, UV and MS) showed **3a** to be a methoxy-derivative of **3b** (canellin-A) [4]. The compound had already been isolated previously from *Aniba ferrea*. Its description, however, lacked definition of the chirality at C-5′ [5]. The following evidence elucidates this point and indicates **3a** and canellin-A (**3b**) to possess identical absolute configurations. Acetylation of **3a** at room temperature led to the monoacetate **3c**. The steric



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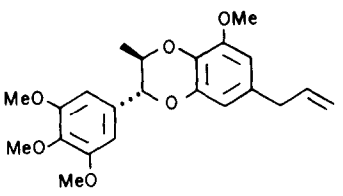
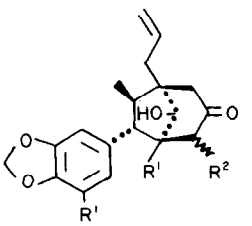


2



5a R¹ = OMe, R² = α-OH
5b R¹ = OMe, R² = β-OH
5c R¹ = H, R² = α-OH

*Part LXIV in the series "The Chemistry of Brazilian Lauraceae". For Part LXIII see ref. [1]. Based on the M.S. thesis submitted by S.M.C.D. to Universidade de São Paulo (1980).

hindrance of the hydroxyl at C-2′ is best explained by its *cis*-relation with the aryl group, precisely as in the case of canellin-A [2]. The aryl being thus exo-oriented, the benzylic proton (H-7) and the methyl (Me-8) must be endo-oriented. Since the signals of both undergo significant paramagnetic shifts (Δ respectively 0.44 and 0.09) upon acetylation of OH-4′, this hydroxyl must be equally endo-oriented. In consequence H-4′ can only be axial. Being represented by a doublet of $J = 6.5$ Hz it is probably vicinal to another axial proton (H-5′) and OMe-5′ should be equatorial. Indeed, as would be expected for the OH-4′/H-5′ *cis*-relation, acetylation of OH-4′ produces a significant paramagnetic shift (Δ 0.28) of the H-5′ signal. With respect to its relative configuration methoxycanellin-A (**3a**) is thus identical with canellin-A (**3b**) [4]. Both compounds also share the absolute configuration since their ORD curves are comparable.

Spectral comparison (^{1}H NMR including consideration of all relevant decouplings at 270 MHz, IR, UV and MS) indicated **4a** to differ from **3a** solely by the presence of an oxo-group (instead of a hydroxyl) on the five-membered ring (IR ν_{max} 1757 cm^{-1}) and of an exo-hydroxyl (instead of an endo-orientated one) at C-4′. Indeed H-8 and the aromatic protons resonated at higher field in **4a** (τ respectively *ca* 8.2 and 3.7), where they are shielded by the C-2′ carbonyl, than in **3a** (τ respectively *ca* 7.6 and 3.4). Furthermore H-4′ showed two small couplings ($J = 2$ and < 0.5 Hz), due to equatorial–axial and equatorial–equatorial (*W*) relationships, respectively, with H-5′ and one H-6′, in **4a**; against one relatively large coupling ($J = 6.5$ Hz), due to the axial–axial relationship with H-5′, in **3a**. As was expected, in contrast to the situation prevailing in **3a** (OMe-3′, τ 6.80), in **4a** OH-4′ on one hand does not affect paramagnetically the signals of H-7, Me-8 and H-5′ upon acetylation, and on the other hand affects sterically the now *cis*-related OMe-3′ forcing it towards the shielding region of the aromatic ring (OMe-3′, τ 7.18) (Table 1).

Compounds **4a** and **4b** differ only with respect to the substituents of the aromatic ring: the methylenedioxy group of **4a** is replaced by two methoxyls in **4b** (Table 1).

The constitution of **5a** was assigned on the basis of spectral comparisons with **5b**, a known canellin-type neolignan [6]. The spectral differences can be rationalized by analogy with the pair **4a**/**3a**, i.e. again OH-4′ occupies either an exo- (in **5a**, OMe-3′, τ 7.17) or an endo- (in **5b**, OMe-3′, τ 6.67) position (Table 1). With respect to its relative configuration **5a** is thus identical to **5c**, a neolignan of known absolute configuration [7]. The ORD curves of both compounds being similar, **5a** and **5c** also share the absolute configuration shown in the formulae.

EXPERIMENTAL

Isolation of constituents. Trunk wood of an *Aniba* species (voucher Herbarium INPA, no. 42183) was reduced to powder (2 kg) and percolated with C_6H_6. Evaporation of solvent yielded an oily residue (6 g). This was chromatographed on a dry column (250 g Si gel deactivated by 10% H_2O, Et_2O). Eluates of ten equal portions of the extruded material were treated as follows. Eluate 1 (1 g) was separated by TLC (Si gel, C_6H_6) into fatty material (0.7 g) and **1** (0.3 g). Eluates 2 (1.2 g) and 3 (0.2 g), purified by repeated Si gel TLC ($CHCl_3$ and $CHCl_3$–Et_2O, 49:1, respectively), yielded **2** (0.6 g) and **3a** (50 mg), respectively. Eluate 4 (1.1 g) yielded, by re-crystallizations from MeOH, sitosterol (0.7 g) and by Si gel TLC (C_6H_6–Me_2CO, 4:1) of the mother liquor, sitosterol (50 mg) and **3a** (0.1 g). Eluates 5 (0.3 g) and 6 (0.5 g), purified by repeated Si gel TLC (C_6H_6–Me_2CO, 4:1 and Et_2O, respectively), yielded **4a** (0.1 g) and **4b** (15 mg), respectively. Eluate 7 (0.5 g), by Si gel TLC ($CHCl_3$–EtOH, 9:1), was separated into **5a** (20 mg) and polar material. Eluates 8–10 were complex mixtures of polar compounds.

Identification of dillapiol (**1**) [4] *and eusiderin* (**2**) [8] relied on direct comparison with authentic samples.

Rel-(7S, 8R, 1′R, 2′S, 3′R, 4′R, 5′S)-Δ$^{8'}$-2′, 4′-*dihydroxy*-3, 3′, 5′-*trimethoxy*-4, 5-*methylenedioxy*-1′, 2′, 3′, 4′, 5′, 6′-*hexahydro*-7.3′, 8.1′-*neolignan* (methoxycanellin-A, **3a**), identical to compound **5a** of ref. [5]. ORD (*c* 10.84 mg/100 ml MeOH): $[\phi]_{360-275}$ 0, $[\phi]^{tr}_{255}$ −1600, $[\phi]_{249}$ 0, $[\phi]^{pk}_{233}$ +8700, $[\phi]_{244}$ 0. 4′-*O*-*Acetyl*-*derivative* (**3c**) was obtained by treatment of **3a** (25 mg) with Ac_2O (1 ml) and C_5H_5N (1 ml) (room temp., 24 hr) and TLC (Si gel) purification of the product. Oil (Found: $[M]^+$ 448.2077; $C_{24}H_{32}O_8$ requires: $[M]^+$ 448.2097). UV λ^{MeOH}_{max} nm: 234 inf., 273 (ϵ 5150, 1350). IR ν^{film}_{max} cm^{-1}: 3497, 1729, 1630, 1496, 1452, 1432, 1373, 1318, 1239, 1088, 1042, 923, 814. MS *m/z* (rel. int.): 449 (9), 448 (26), 208 (28), 192 (12), 181 (9), 179 (14), 167 (46), 165 (13), 148 (9), 135 (31), 117 (26), 85 (66), 83 (100). ORD (*c* 9.86 mg/100 ml MeOH): $[\phi]_{400}$ −900, $[\phi]_{350}$ −1250, $[\phi]_{300}$ −1900, $[\phi]^{tr}_{255}$ −4900, $[\phi]_{238}$ 0, $[\phi]_{235}$ +1400.

Oxidation product of **3c** in Me_2CO with Jones reagent. ^{1}H NMR ($CDCl_3$, 60 MHz) τ: 3.70 (*s*, H-2, H-6), 4.08 (*s*, CH_2O_2), 3.9–4.4 (*m*, H-8′), 4.6–5.2 (*m*, H-4′, 2H-9′), 6.11 (*s*, OMe-3), 6.0–6.6 (*m*, H-7, H-5′), 6.64 (*s*, OMe-5′), 6.73 (*s*, OMe-3′), 7.82 (OAc-4′), 7.5–8.6 (*m*, H-8, 2H-6′, 2H-7′), 8.9–9.1 (*m*, 3H-9).

Rel-(7S, 8R, 1′R, 3′S, 4′S, 5′S)-Δ$^{8'}$-4′-*hydroxy*-3, 3′, 5′-*trimethoxy*-4, 5-*methylenedioxy*-1′, 2′, 3′, 4′, 5′, 6′-*hexahydro*-2′-*oxo*-7.3′,8.1′-*neolignan* (**4a**). Oil (Found: $[M]^+$ 404.1828; $C_{22}H_{28}O_7$ requires: $[M]^+$ 404.1835). UV λ^{MeOH}_{max} nm: 235 inf., 272 (ϵ 6400, 2150). IR ν^{film}_{max} cm^{-1}: 3390, 1757, 1645, 1517, 1460, 1439, 1379, 1319, 1239, 1205, 1152, 1136, 1099, 1058, 1042, 1008, 943, 924, 842, 796, 719. MS *m/z* (rel. int.): 404 (1), 280 (13), 279 (7), 169 (7), 168 (35), 167 (86), 151 (10), 150 (31), 149 (100), 135 (10), 123 (24), 122 (25), 113 (19), 112 (15). 4′-*O*-*Acetyl*-*derivative* (**4c**) was obtained by treatment of **4a** (25 mg) with Ac_2O (1 ml) and pyridine (1 ml) (room temp., 24 hr) and TLC (Si gel) purification of the product. Oil (Found: $[M]^+$ 446.1907; $C_{24}H_{30}O_8$ requires: $[M]^+$ 446.1941). IR ν^{film}_{max} cm^{-1}: 1761 sh., 1736, 1634, 1511, 1460, 1437, 1379, 1290, 1266, 1238, 1202, 1134, 1109, 1096, 1073, 1044, 936, 805, MS *m/z* (rel. int.): 446 (39), 414 (31), 405 (9), 345 (26), 331 (16), 208 (13), 193 (99), 192 (81), 181 (39), 180 (34), 179 (82), 165 (66), 155 (9), 154 (68), 153 (100), 149 (39), 125 (37), 117 (39). ORD (*c* 2.13 mg/100 ml MeOH): $[\phi]_{400}$ −7900, $[\phi]^{tr}_{380}$ −8550, $[\phi]^{pk}_{360}$ −7700, $[\phi]^{tr}_{320}$ −10 500, $[\phi]^{pk}_{300}$ −7550, $[\phi]^{tr}_{283}$ −11 200, $[\phi]^{pk}_{270}$ −8550, $[\phi]^{tr}_{250}$ −9700, $[\phi]_{240}$ −5900.

Rel-(7S, 8R, 1′R, 3′S, 4′S, 5′S)-Δ$^{8'}$-4′-*hydroxy*-3, 4, 5, 3′, 5′-*pentamethoxy*-1′, 2′, 3′, 4′, 5′, 6′-*hexahydro*-2′-*oxo*-7.3′, 8.1′-*neolignan* (**4b**). Oil (found: $[M]^+$ 420.2097; $C_{23}H_{32}O_7$ requires: $[M]^+$ 420.2148). IR ν^{film}_{max} cm^{-1}: 3378, 1748, 1631, 1590, 1497, 1464, 1422, 1325, 1183, 1036, 1005, 925, 901, 870, 838, 760. MS *m/z* (rel. int.): 421 (19), 420 (81), 380 (20), 379 (100), 347 (9), 333 (9), 287 (14), 279 (13), 212 (9), 211 (20), 210 (18), 208 (20), 195 (9), 193 (15), 181 (21), 180 (11), 167 (25), 165 (9), 151 (13), 150 (9), 149 (74).

(7S, 8R, 1′R, 2′S, 3′R, 4′R)-Δ$^{8'}$-2′, 4′-*Dihydroxy*-3,3′-

Table 1. ^{1}H NMR spectral data of neolignans*

	Compound (MHz)							
	3a (100)	**3c** (270)	**3b** [4] (220)	**4a** (100)	**4c** (270)	**4b** (60)	**5a** (100)	**5b** [6] (60)
H-2	3.50 *d* (1.5)	3.44 *d* (1.5)	3.05 *br s*	3.75 *d* (1.6)	3.74 *br s*	3.80 *s*	3.45 *d* (1.2)	3.53 *d* (2.0)
OMe-3	6.13 *s*	6.09 *s*	—	6.16 *s*	6.14 *s*	6.20 *s*	6.13 *s*	6.13 *s*
OMe-5	—	—	—	—	—		—	—
OMe-4	—	—	—	—	—	6.27 s	—	—
CH_2O_2	4.11 *s*	4.08 *s*	4.11, 4.12	4.09 *s*	4.07 *s*	—	4.07 *s*	4.07 *s*
H-5	—	—	3.36 *d* (8.0)	—	—	—	—	—
H-6	3.36 *d* (1.5)	3.35 *d* (1.5)	3.25 *d* (8.0)	3.73 *d* (1.6)	3.69 *br.s* —	3.80 *s* —	3.27 *d* (1.2)	3.38 *d* (2.0)
H-7	6.80 *d* (9.0)	6.34 *d* (9.0)	6.75 *d* (9.0)	6.71 *d* (8.0)	6.60 *d* (8.0)	6.80 *d* (7.5)	7.35–8.25 *m* —	7.53 *d* (8.0)
H-8	7.5–7.8 *m*	7.5–7.65 *m*	7.5–7.65 *m*	8.05–8.35 *m*	8.11 *dq* (8.0, 7.0)	8.0–8.4 *m*	7.35–8.25 *m*	7.55–7.8 *m*
3H-9	9.17 *d* (7.5)	9.07 *d* (7.5)	9.13 *d* (7.0)	8.95 *d* (7.0)	8.90 *d* (7.0)	8.90 *d* (7.0)	9.23 *d* (7.0)	9.18 *d* (7.0)
H-2′	6.54 *s*	6.38 *s*	6.49 *s*	—	—	—	5.79 *s*	5.89 *s*
OMe-3′	6.80 *s*	6.89 *s*	6.78 *s*	7.18 *s*	7.22 *s*	7.19 *s*	7.17 *s*	6.67 *s*
H-4′	5.99 *d* (6.5)	4.96 *d* (6.5)	5.97 *d* (6.5)	5.51 *dd* (2.0, < 0.5)	4.25 *dd* (2.0, 1.0)	5.59 *br.s* —	5.64 *s* —	5.61 *s* —
H-5′	6.4 *ap.t* (6.5)	6.1–6.2 *m*	6.38 *t* (6.5)	6.50 *dd* (6.5, 2.0)	6.63 *br.d* (6.5)	6.1–6.65 *m*	—	—
OMe-5′	6.61 *s*	6.71 *s*	6.60 *s*	6.58 *s*	6.49 *s*	6.53 *s*	—	—
H-6′ ax.	8.51 *dd* (16.0, 6.0)	8.42 *dd* (16.0, 6.0)	8.46 *dd* (15.8, 6.5)	7.7–8.05 *m*	7.98 *dd* (15.5, 6.5)	7.6–8.0.25 *m*	7.35–8.25 *m*	7.56 *s*
H-6′ eq.	8.17 *d* (16.0)	8.14 *d* (16.0)	8.14 *d* (15.8)		7.80 *br.d* (15.5)			
H-7′	7.5–7.8	7.5–7.65 *m*	7.5–7.65 *m*	7.7–8.05 *m*	7.86 *dd* (14.0, 8.0)	7.6–8.05 *m*	7.35–8.25 *m*	7.85–8.15 *m*
H-7′	8.01 *dd* (14.5, 9.0)	7.92 *dd* (13.5, 8.5)	7.95 *dd* (13.5, 9.2)	7.70 *dd* (14.0, 6.5)	7.66 *dd* (14.0, 6.5)			
H-8′	4.0–4.35 *m*	3.95–4.2 *m*	4.0–4.2 *m*	4.0–4.4 *m*	4.1–4.25 *m*	3.8–4.4 *m*	3.8–4.3 *m*	3.85–4.3 *m*
2H-9′	4.8–5.1 *m*	4.85–4.95 *m*	4.85–5.0 *m*	4.85–5.15 *m*	5.0–5.1 *m*	4.8–5.25 *m*	4.75–5.1 *m*	4.65–5.05 *m*
OAc-4′	—	7.83 *s*	—	—	8.08 *s*	—	—	—

* *TMS* as int. standard; solvents: CCl_4 for **4b**, $CDCl_3$ for all other compounds; chemical shifts in τ values; coupling constants (in parentheses) in Hz; D_2O added.

dimethoxy-4,5-*methylenedioxy*-1′, 2′, 3′, 4′, 5′, 6′-*hexahydro*-5′-*oxo*-7.3′,8.1′-*neolignan* (**5a**). Oil (found: $[M]^+$ 390.1685; $C_{21}H_{26}O_7$ requires: $[M]^+$ 390.1679). UV λ_{max}^{MeOH} nm: 228 inf., 273 (ϵ 10950, 2000). IR ν_{max}^{film} cm^{-1}: 3380, 1715, 1640, 1520, 1455, 1445, 1210, 1100, 1055, 940. MS *m/z* (rel. int.): 391 (0.3), 390 (0.8), 349 (0.3), 317 (2), 279 (9), 167 (45), 165 (2), 150 (13), 149 (100), 135 (5), 113 (19), 112 (11). ORD (*c* 1.68 mg/100 ml MeOH): $[\phi]_{350} -2900$, $[\phi]_{340}^{pk} -1250$, $[\phi]_{335}^{tr} -2150$, $[\phi]_{320}^{inf} -350$, $[\phi]_{305}$ 0, $[\phi]_{300}^{pk} +1000$, $[\phi]_{290}$ 0, $[\phi]_{255}^{tr} -5350$, $[\phi]_{245}$, $[\phi]_{240}^{pk} +2850$, $[\phi]_{230} +1500$.

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