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FURTHER NEOLIGNANS FROM *OCOTEA ACIPHYLLA**

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Key Word Index—*Ocotea aciphylla*; Lauraceae; bicyclo-2-oxo[4.2.1]nonanoid neolignan; hydrobenzofuranoid neolignans; ferrearin-D.

Abstract—The trunk wood of the central Brazilian *Ocotea aciphylla* contains, in addition to neolignans belonging to the bicyclo[3.2.1]octanoid and hydrobenzofuranoid types, three novel compounds, oxaguianin, seemingly a Bayer–Villiger oxidation product of the former type, ferrearin-D and 3'-methoxyburchellin, both belonging to the latter type.

INTRODUCTION

Trunk wood of *Ocotea aciphylla* (Nees) Mez (Lauraceae) has been found to contain the three bicyclo[3.2.1]-octanoid neolignans **1** (canellin-A), **2a** and **2b** (3'-methoxyguianin) and the two hydrobenzofuranoid neolignans **3a** (ferrearin-A) and **3b** (ferrearin-C) [2]. The present paper describes the presence of some additional minor constituents, the novel **4** (oxaguianin), **5** (ferrearin-D) and **6a** (3'-methoxyburchellin), as well as **6b** previously isolated from *O. catharinensis* [3], **7** (armenin-B) previously isolated from *Licaria armeniaca* [4] and **8** (dillapiol) [5, 6].

In order to facilitate comparisons among different compounds numbering of neolignans in the text follows the biogenetic rules outlined in a review [7]. For IUPAC designations see titles in the Experimental.

RESULTS AND DISCUSSION

The molecular formula $C_{21}H_{24}O_7$ of **4** was determined by a combination of low resolution mass spectrometry and NMR C and H counts. Functional analysis by NMR allowed this formula to be expanded to $C_{18}H_{15}O_2(OMe)_2CH_2O_2\cdot OH$. This differs from the known $C_{18}H_{15}O(OMe)_2CH_2O_2\cdot OH$ (**2b**), here used as a model, only with respect to the undefined oxygen. Indeed **4** and **2b** possess identical constitutional moieties, as shown by their intense peaks at *m/z* 162, assigned to $[C_6H_3CH_2O_2CH{=}CHMe]^{+\cdot}$. The many comparable NMR signals (Tables 1 and 2) are evidence for the existence of piperonyl and allyl groups also in **4**. The most relevant differences refer to the ^{13}C NMR and IR carbonyl signals. These indicate **4** be an ester (δ172.5; IR ν_{max} 1750 cm^{-1}) and **2b** to be a ketone (δ194.9, IR ν_{max} 1680 cm^{-1}). Furthermore in **4** a tetrasubstituted sp^3 carbon must bear two oxy-groups (δ104.2), while in **2b** the corresponding carbon can only bear one such group (δ90.3). Thus, the undefined oxygen of **4** must be inserted between the carbonyl (C-4') and the tetrasubstitued sp^3-carbon (C-3').

Compound **4** being a seven-membered cyclic lactone and **2b** a six-membered ketone, conjugation of the double bond at 5',6' and the carbonyl at 4' can hardly be comparable. Less conjugation at position 6' is expected for **4** (UV λ_{max} nm: 234, 288; ^{13}C NMR: δ100.3; ^{1}H NMR: δ4.60) than for the model **2b** (UV λ_{max} nm: 237, 265, 285; ^{13}C NMR: δ124.0; ^{1}H NMR: δ5.70).

The *trans*-arrangement of the aryl at C-7 and the methyl at C-8 is suggested by the C–Me NMR signals (**4** δ1.00; **2b** δ0.83). The *cis*-arrangement is excluded since it leads characteristically to C–Me signals around δ0.5 [8]. Thus, supposing the methyl at C-8 to be *endo*-oriented, its relation to the allyl must again be *trans*. The *cis*-arrangement is excluded since it would cause a reciprocal shielding γ-effect [9]. This is not observed; C-9 and C-7' give rise to ^{13}C signals at relatively low field (δ19.6 and 38.6, respectively).

By the procedure outlined above, the formula $C_{21}H_{26}O_6$ for compound **5** was expanded to $C_{18}H_{17}O(OMe)_2CH_2O_2\cdot OH$. Spectral comparison of **5** with other neolignans revealed a close relationship to **9**, a reduction product of **3b** [2]. Indeed ^{13}C and ^{1}H NMR spectra reveal many comparable signals (Tables 1 and 2). The strongest discrepancy in the ^{13}C NMR spectra refers to the signals due to C-4' and C-5'. The former carbon is much more shielded and the latter carbon is much more deshielded in **5** (C-4': δ69.0; C-5': δ153.3) than in **9** (C-4': δ127.3; C-5' δ:127.1). Both phenomena are compatible with the presence of a methoxyl (δ54.8) at C-5'. Still, in view of the analogies of NMR data, the second methoxyl (δ55.3) of **5** should occupy the same position as the hydroxyl in **9**.

Again by the procedure outlined above, the formula $C_{21}H_{22}O_6$ for compound **6a** was expanded to $C_{18}H_{14}O_2(OMe)_2CH_2O_2$. Spectral comparison of **6a** with other neolignans revealed a close relationship to **6c** [10]. Indeed ^{13}C and ^{1}H NMR spectra reveal many comparable signals (Tables 1 and 2). The only important

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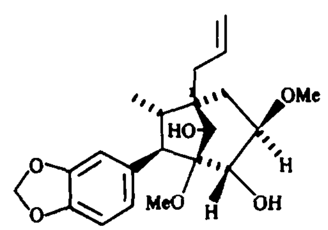
*Part LXXVIII in the series "The Chemistry of Brazilian Lauraceae". For Part LXXVII see ref. [1]. Based on the M.Sc. thesis submitted by J.D.F. to Universidade de São Paulo (1985).



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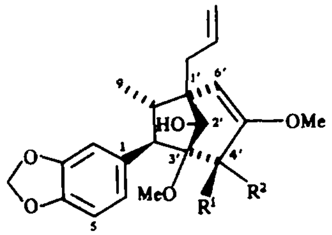
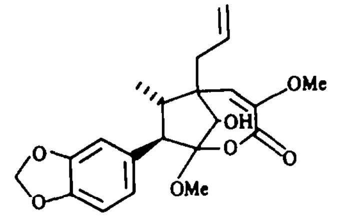


2a R¹ = H, R² = OH
2b R¹ = R² = O



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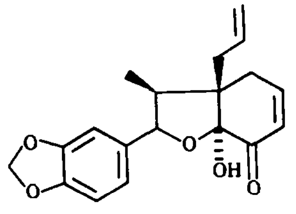
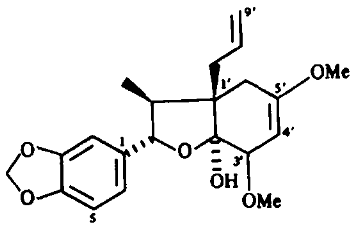


3a β - aryl
3b α - aryl



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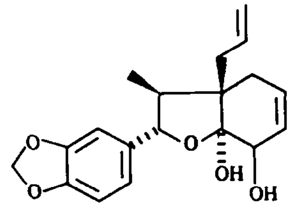

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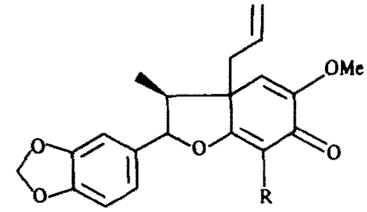
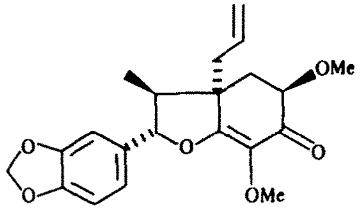
Table 1. Comparison of ^{13}C NMR chemical shifts (δ) of new neolignans (**4**, **5** and **6a**) with model neolignans (**2b** [11], **9** [2] and **6c** [10] respectively)

Carbon	4	2b	Δ 2b–4	5	9	Δ 9–5	6a	6c	Δ 6c–6a
1	131.1	131.4	0.3	135.5	135.4	−0.1	131.7	131.5	−0.2
2	107.8	107.4	−0.4	107.5	107.5	0.0	106.6	106.5	−0.1
3	147.4	147.6	+0.2	147.1	147.8	+0.7	148.3	148.1	−0.2
4	147.0	146.5	−0.5	147.7	147.2	−0.5	148.0	148.1	+0.1
5	111.2	111.0	−0.2	107.6	107.6	0.0	107.8	107.8	0.0
6	123.8	120.5	−3.3	120.8	121.0	+0.2	120.6	120.5	−0.1
7	50.2	57.0	+6.8	87.4	85.9	−1.5	91.5	90.9	−0.4
8	42.9	48.6	+3.7	49.3	49.7	+0.4	49.8	49.5	−0.3
9	19.6	13.8	−5.8	9.9	9.5	−0.4	8.4	8.3	−0.1
1'	44.6	51.3	+6.7	50.3	49.7	−0.6	49.8	50.9	+1.1
2'	70.7	78.4	+7.7	102.6	100.4	−2.2	166.0	181.4	+15.4
3'	104.2	90.9	−13.3	73.6	72.5	−1.1	131.8	101.7	−29.9
4'	172.5	194.9	+22.4	96.0	127.3	+31.3	178.8	182.8	+6.0
5'	154.2	151.7	−2.5	153.3	127.1	−26.2	153.0	153.3	+0.3
6'	100.3	124.0	+23.7	30.3	28.5	−1.8	107.4	107.8	+0.4
7'	38.6	36.6	−2.0	38.1	39.4	+1.3	36.8	36.6	−0.2
8'	133.3	134.6	+1.3	135.2	134.5	−0.7	130.9	130.9	0.0
9'	119.7	118.0	−1.7	117.1	117.5	+0.4	120.1	120.0	−0.1
OMe-3'	54.9	54.5	−0.4	55.3	—	—	55.5	55.8	+0.3
OMe-5'	57.0	55.4	−1.6	54.8	—	—	60.5	—	—
CH_2O_2	101.1	100.9	−1.2	100.7	101.1	+0.4	101.3	101.2	−0.1



6a α-aryl, β-allyl, R = OMe
6b β-aryl, α-allyl, R = OMe
6c α-aryl, β-allyl, R = H



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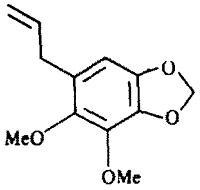

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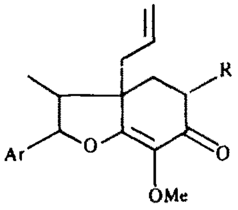

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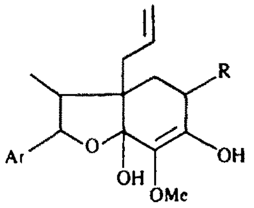

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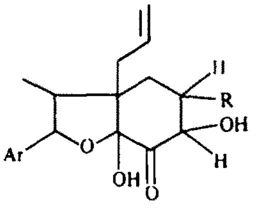

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Table 2. Comparison of ^{1}H NMR chemical shifts (δ) of new neolignans (**4**, **5** and **6a**) with model neolignans (**2b** [11], **9** [2] and **6c** [10] respectively)

	4	**2b**	Δ **2b–4**	**5**	**9**	Δ **9–5**	**6a**	**6c**	Δ **6c–6a**
3H-2,5,6	6.75–6.9 *m*	6.97 *br s*	+0.17	6.7–7 *m*	6.6–7.2 *m*	+0.05	6.85 *br s*	6.75–6.85 *m*	−0.05
H-7	2.9–3 *m*	3.40 *d*	+0.45	4.45 *d* 10 Hz	4.40 *d* 10 Hz	−0.05	5.17 *d* 10 Hz	5.17 *d* 9.5 Hz	0.00
3H-8,7′	2.5–2.7 *m*	2.3–2.7 *m*	−0.01	—	—	—	—	—	—
5H-8,6′,7′	—	—	—	2–2.5 *m*	1.9–2.9 *m*	—	—	—	—
H-8	—	—	—	—	—	—	2.2–2.3 *m*	2.28 *dq*	+0.13
H-6′	4.60 *br s*	5.70 *s*	+1.10	—	—	—	5.57 *s*	5.79 *s*	+0.22
2H-7′	—	—	—	—	—	—	2.34–2.85 *m*	2.34–2.55 *m*	+0.15
3H-9	1.00 *d* 7 Hz	0.83 *d* 7 Hz	−0.17	0.90 *d* 8 Hz	0.87 *d* 8 Hz	−0.03	1.20 *d* 7 Hz	1.16 *d* 7 Hz	−0.04
H-2′	4.90 *s*	4.00 *s*	−0.90	—	—	—	—	—	—
H-3′	—	—	—	3.9–4.15	3.9–4.2 *m*	−0.05	—	5.43 *s*	—
3H-4′,5′,8′	—	—	—	—	5.3–6.2 *m*	—	—	—	—
H-4′	—	—	—	5.90	—	—	—	—	—
H-8′	5.6–5.8 *m*	5.4–5.8 *m*	−0.1	5.4–5.9 *m*	—	—	5.5–5.6 *m*	5.55 *dq*	0.00
2H-9′	5.4–5.5 *m*	5–5.4 *m*	−0.3	4.8–5.4 *m*	4.8–5.4 *m*	0.00	4.95–5.15 *m*	5.01 *dd*	−0.04
OMe-3′	3.55 *s*	3.23 *s*	−0.32	3.30 *s*	—	—	3.83 *s*	—	—
OMe-5′	3.75 *s*	3.70 *s*	−0.05	3.63 *s*	—	—	3.68 *s*	3.68 *s*	0.00
CH_2O_2	5.95 *s*	5.95 *s*	0.00	5.90 *s*	5.97 *s*	+0.07	6.00 *s*	5.99 *s*	−0.03

discrepancy in the ^{13}C NMR spectra of **6a** and **6c** refers to the signals due to C-2′ and C-3′. The former carbon is much more deshielded and the latter carbon is much more shielded in **6a** (C-2′: δ166.0; C-3′: δ131.8) than in **6c** (C-2′: δ181.4; C-3′ δ101.8). Both phenomena are compatible with the presence of a methoxyl at C-3′. Compound **6a** is thus a 3′-methoxyburchellin.

The allyl- or propenylphenol precursors of the neolignans always carry an oxy-group at C-4, *para* to the allyl- or propenyl-side chain. It is consequently of interest to observe that **3a**, **3b** and **5** are devoid of oxygenation at C-4′. This particularity has been attributed to a rearrangement of the allyl-group [2]. However, the co-occurrence of **1a**, **2a**, **2b**, **4**, **6a**, **6b**, **7** and **8**, all possibly derived from a 2,3,4,5-tetraoxyallylbenzene, suggests alternative, more plausible, pathways, namely **10** → **11** → **5**? (R = OMe) and **10** → **11** → **12** → **3a** + **3b** (R = H).

EXPERIMENTAL

Isolation of constituents. An extract of trunk wood (1 kg) was prepared as described in ref. [2]. The extract (5.5 g) was crystallized from MeOH to yield **1** (300 mg). The mother liquor was evapd and the residue (5.1 g) submitted to CC (silica gel, petrol–EtOAc, 9:1). Thirty 500 ml fractions were collected. Frs 1 and 2 were purified by flash CC to give **8** (20 mg). Frs 5–9 were crystallized from MeOH to yield **3b** (500 mg). Frs 10–12 were separated by flash CC to provide **2a** (31 mg) and **5** (28 mg). Frs 13–15 were purified by CC (silica gel, C_6H_6–Me_2CO, 4:1) to give **4** (140 mg). Frs 17–19 were crystallized from MeOH to yield **1** (600 mg). Fr. 26 was separated by CC (silica gel, $CHCl_3$) giving **3a** (10 mg), **7** (22 mg) and **6a** + **6b** (35 mg).

Identification of known compounds **1**, **2a**, **3a**, **3b** [2], **6b** [3], **7** [4] *and* **8** [5] was performed by direct comparison with authentic samples.

rel-[1R, 6R, 7R, 8S, 9S]-1-*Allyl-9-hydroxy-3,6-dimethoxy-8-methyl-7-(3′,4′-methylenedioxyphenyl)-5-oxa-4-oxobicyclo*[4.2.1]-*non-2-ene* (**4**). Mp 174–176° (MeOH). UV λ_{max}^{MeOH} nm: 234, 288. IR ν_{max}^{KBr} cm^{-1}: 3500, 1750, 1665, 1500, 1490, 1450, 1360, 1330, 1230, 1170, 1130, 1035, 980, 930, 865, 830. ^{13}C NMR (Table 1); ^{1}H NMR (Table 2). MS *m/z* (rel. int.): 388 $[M]^{+\cdot}$ (3), 194(14), 193(15), 186(48), 185(100), 181(58), 168(16), 167(32), 116(12), 165(19), 162(100), 150(12), 149(18), 135(45). *Acetate.* ^{1}H NMR (60 MHz, $CDCl_3$): δ6.75–6.9 (*m*, H-2, H-5, H-6), 2.9–3.05 (*m*, H-7), 1.00 (*d*, *J* = 7 Hz, H-9), 4.90 (*s*, H-2′), 3.55 (*s*, MeO-3′), 3.75 (*s*, MeO-5′), 4.60 (*br s*, H-6′), 2.5–2.7 (*m*, H-7′), 5.6–5.8 (*m*, H-8′), 5.35–5.45 (*m*, H-9′), 1.55 (*s*, AcO-2′). ^{13}C NMR (20 MHz, $CDCl_3$): δ131.3 (C-1), 107.0 (C-2), 146.7 (C-3), 146.5 (C-4), 111.6 (C-5), 124.6 (C-6), 50.4 (C-7), 42.4 (C-8), 19.3 (C-9), 44.7 (C-1′), 75.4 (C-2′), 103.1 (C-3′), 172.5 (C-4′), 152.6 (C-5′), 100.9 (C-6′), 38.5 (C-7′), 133.4 (C-8′), 119.7 (C-9′), 169.2, 20.1 (AcO-2′).

rel-(2S, 3S, 3aS, 7aS)-3a-*Allyl-7a-hydroxy-5,7-dimethoxy-3-methyl-2-(3′,4′-methylenedioxyphenyl)-2,3,3a,4,7,7a-hexahydrobenzofuran* (**5**). Viscous oil. UV λ_{max}^{MeOH} nm: 236, 288. IR ν_{max}^{film} cm^{-1}: 3500, 1510, 1480, 1440, 1250, 1100, 1040, 800, 750. ^{13}C NMR (Table 1); ^{1}H NMR (Table 2). MS (rel. int.) *m/z*: 374 (0.4), 178 (100), 165 (13), 162 (15), 151 (35), 149 (32), 137 (12), 135 (12), 131 (11), 121 (13), 119 (14).

rel-(2S, 3S, 3aR)-3a-*Allyl-5,7-dimethoxy-3-methyl-2-(3′,4′-methylenedioxyphenyl)-2-3,3a,6-tetrahydro-6-oxobenzofuran* (**6a**). Viscous oil. IR ν_{max}^{film} cm^{-1}: 1640. ^{13}C NMR (Table 1); ^{1}H NMR (Table 2). MS *m/z* (rel. int.): 370 (26), 330 (11), 329 (50), 209 (11), 208 (60), 207 (38), 193 (14), 180 (12), 179 (11), 178 (10), 165 (26), 163 (14), 162 (24), 149 (33), 137 (24), 135 (66), 128 (28).

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