

FURTHER NEOLIGNANS FROM *OCOTEA ACIPHYLLA**

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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 $[C_6H_3CH_2O_2CH=CHMe]^+$. 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 (δ 172.5; IR ν_{max} 1750 cm^{-1}) and **2b** to be a ketone (δ 194.9, IR ν_{max} 1680 cm^{-1}). Furthermore in **4** a tetrasubstituted sp^3 carbon must bear two oxy-groups (δ 104.2), while in **2b**

the corresponding carbon can only bear one such group (δ 90.3). Thus, the undefined oxygen of **4** must be inserted between the carbonyl (C-4') and the tetrasubstituted 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: δ 100.3; 1H NMR: δ 4.60) than for the model **2b** (UV λ_{max} nm: 237, 265, 285; ^{13}C NMR: δ 124.0; 1H NMR: δ 5.70).

The *trans*-arrangement of the aryl at C-7 and the methyl at C-8 is suggested by the C–Me NMR signals (**4** δ 1.00; **2b** δ 0.83). The *cis*-arrangement is excluded since it leads characteristically to C–Me signals around δ 0.5 [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 (δ 19.6 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 1H 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': δ 69.0; C-5': δ 153.3) than in **9** (C-4': δ 127.3; C-5': δ 127.1). Both phenomena are compatible with the presence of a methoxyl (δ 54.8) at C-5'. Still, in view of the analogies of NMR data, the second methoxyl (δ 55.3) 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 1H NMR spectra reveal many comparable signals (Tables 1 and 2). The only important

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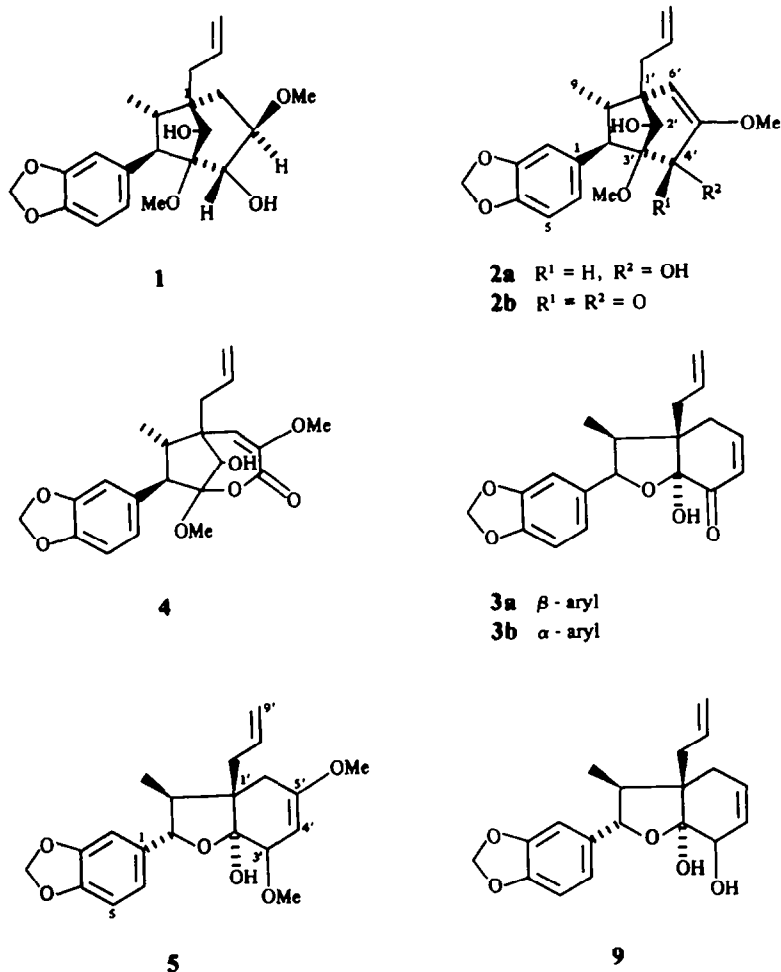
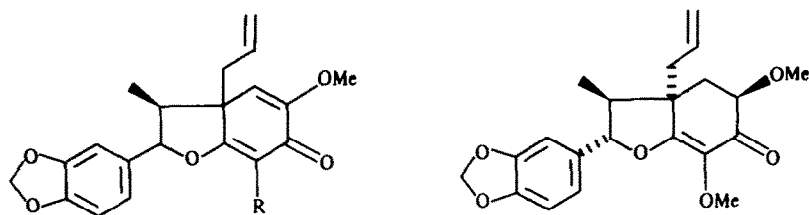


Table 1. Comparison of ^{13}C NMR chemical shifts (δ) of new neolignans (**4**, **5** and **6a**) with model neolignans (**2b** [11], **9** [2] and **6c** [10] respectively)

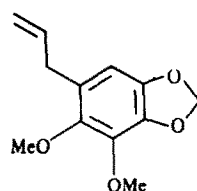
Carbon	4	2b	Δ 2b-4	5	9	Δ 9-5	6a	6c	Δ 6c-6a
1	131.1	131.4	0.3	135.5	135.4	-0.1	131.7	131.5	-0.2
2	107.8	107.4	-0.4	107.5	107.5	0.0	106.6	106.5	-0.1
3	147.4	147.6	+0.2	147.1	147.8	+0.7	148.3	148.1	-0.2
4	147.0	146.5	-0.5	147.7	147.2	-0.5	148.0	148.1	+0.1
5	111.2	111.0	-0.2	107.6	107.6	0.0	107.8	107.8	0.0
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 ₂ O ₂	101.1	100.9	-1.2	100.7	101.1	+0.4	101.3	101.2	-0.1



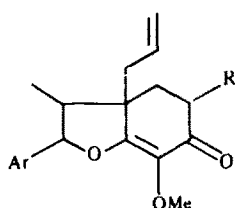
6a α -aryl, β -allyl, R = OMe

6b β -aryl, α -allyl, R = OMe

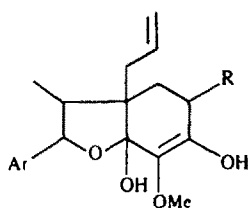
6c α -aryl, β -allyl, R = H



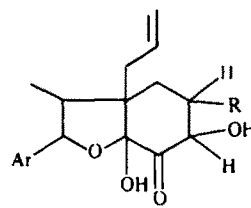
8



10



11



12

Table 2. Comparison of ^1H 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 ₂ O 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': δ 166.0; C-3': δ 131.8) than in **6c** (C-2': δ 181.4; C-3': δ 101.8). 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 $10 \rightarrow 11 \rightarrow 5$? ($R = \text{OMe}$) and $10 \rightarrow 11 \rightarrow 12 \rightarrow 3a + 3b$ ($R = \text{H}$).

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 $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 234, 288. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3500, 1750, 1665, 1500, 1490, 1450, 1360, 1330, 1230, 1170, 1130, 1035, 980, 930, 865, 830. ^{13}C NMR (Table 1); ^1H NMR (Table 2). MS m/z (rel. int.): 388 [$\text{M}]^+$ (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*. ^1H NMR (60 MHz, CDCl_3): δ 6.75–6.9 (*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): δ 131.3 (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 $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 236, 288. IR $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 3500, 1510, 1480, 1440, 1250, 1100, 1040, 800, 750. ^{13}C NMR (Table 1); ^1H 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 $\nu_{\text{max}}^{\text{film}}$ cm^{-1} : 1640. ^{13}C NMR (Table 1); ^1H 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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