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Note

Complete assignment of the ^{1}H and ^{13}C NMR spectra of some lignoids from Lauraceae

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ABSTRACT: An array of one- and two-dimensional NMR techniques (APT, DEPT, COSY, NOESY, HMQC and HMBC) was used to achieve the structural elucidation of some natural benzofuranoid and hydrofuran neolignans isolated from *Licaria chrysophylla*, *L. armeniaca*, *L. aurea* and *Nectandra glabrescens* fruits. The combination of homo- and heteronuclear NMR data was used to obtain the ^{1}H and ^{13}C chemical shift assignments of these neolignans. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: neolignans; NMR; ^{1}H NMR; ^{13}C NMR; high-resolution 1D and 2D NMR

INTRODUCTION

The lignoids constitute one of the most numerous and widespread groups of natural constituents of the family Lauraceae. A number of comprehensive review articles and compilations of NMR data on lignoids have been published (e.g. by Agrawal and co-workers[1,2]). However, in many cases the NMR signals have been tentatively assigned by comparison with chemical shifts of model compounds.

Between 1986 and 1989, we isolated various lignoids from Lauraceae: crysophyllon II-B (**1**) from *Licaria chrysophylla*,[3] (7R,8S,1′S)-1′-allyl-5-methoxy-8-methyl-7-piperonyl-7,8,3,6-tetrahydro-2-oxobenzofuran (**2**) from *Licaria armeniaca*,[4] licarin A (**3**) from *Nectandra glabrescens*,[5] grandisin (**4**) from *Licaria aurea*[6] and the product of reduction of **4**, 7-hydroxy-3,4,5,3′,4′,5′-hexamethoxy-8,8′-neolignan (**5**),[6] which were identified through ^{1}H and ^{13}C NMR spectroscopy at 80 and 20 MHz, respectively. We have now repurified these compounds and report complete and unambigous assignments of their ^{1}H and ^{13}C NMR spectra data by means of 2D NMR techniques, together with conventional 1D NMR methods.

EXPERIMENTAL

Compounds

Four of the studied compounds were natural products and their isolation has been reported elsewhere (**1** from *Licaria chrysophylla*,[3] **2** from *Licaria armeniaca*,[4] **3** from *Nectandra glabrescens*[5] and **4** from *Licaria aurea*[6]). Compound **5** was prepared by reduction (Na, NH_3, 61%) from **4**.[6] These substances were deposited in the Bank of Standards of Natural and Synthetic Products of the Laboratório de Tecnologia Farmacêutica of the Universidade Federal da Paraíba and to be used in this work they were repurified by thin-layer chromatography using the same system as described in the original papers.

NMR spectra

^{1}H (400.13 MHz) and ^{13}C (100.03 MHz) NMR spectra were recorded on a Bruker AMX 400 spectrometer. Data processing was carried out on an Aspect X32 computer with UXNMR software with Bruker microprograms. Standard pulse sequences were used for ^{1}H,^{1}H-COSY (PO = 45 or 90°), NOESY (mixing time varying between 0.5 and 1.2 s), HMBC [$1/2J = 70$ ms for J(C,H) = 7 Hz], HC-COBI [J(C,H) = 150 Hz] and ^{13}C JMOD [J(C,H) = 150 Hz]. Approximately 10–15 mg of each sample were dissolved in 0.5 ml of $CDCl_3$ and transferred to a 5 ml NMR tube. The experiments were carried out at 300 K unless stated otherwise. An internal lock was applied and the reference was set to the solvent peak ($CDCl_3$, 7.27 for ^{1}H and 77.23 for ^{13}C).

RESULTS AND DISCUSSION

The uncommon disposition of the aryl and methyl groups in crysophillon II-B (**1**)[3] and in the normal neolignans **2**–**5**[4–9] was established by the homonuclear correlation in the 2D ^{1}H,^{1}H-COSY and ^{1}H,^{1}H-NOESY spectra. In **1**, the first experiment detected homonuclear correlations between H-8/H-7 and H-7/H-6′ and the

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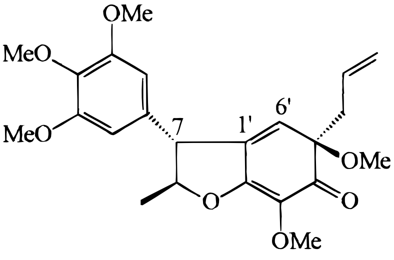
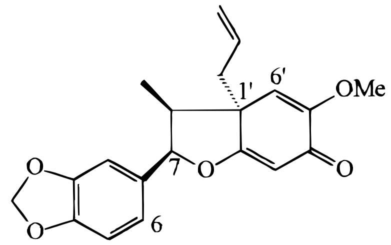


(**1**)



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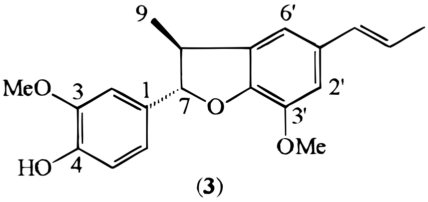

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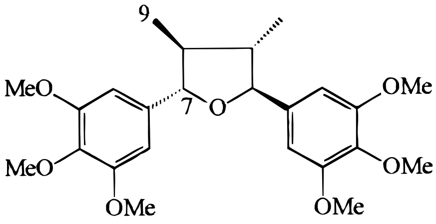

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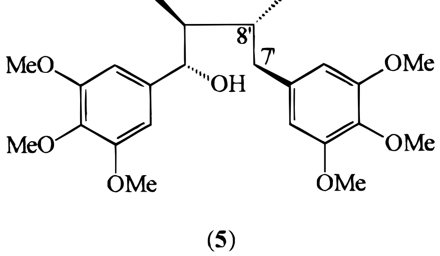

(**5**)

second experiment confirmed the position of the methoxyl groups (δ_H 3.85) at the carbons C-3, C-4 and C-5. In the dihydrobenzofuran neolignans (**2** and **3**),[4,5] the HMQC and COSY spectra confirmed the normal disposition of the piperonyl and guaiacyl methyl groups, and also the chemical shifts of the aromatic and olefinic protons in the two neolignans. In **2**, the ^{13}C DEPT NMR spectrum was used to distinguish between the carbons C-1/C-8′ and C-8/C-7′. In **3**, a similar procedure (DEPT) did not define the chemical shifts of the carbons atoms C-1/C-1′, C-3/C-4, C-2/C-2′ and C-5/C-6′.

The structures of **1**–**5**[3–6] were confirmed and ^{1}H and ^{13}C spectra were assigned on the basis of the observed 2D cross peaks which are listed in Tables 1–5. Thus, the HMBC spectrum of **1** allowed us to establish the correct attribution for C-7 (δ_C 54.73), different from that reported in the literature.[3] The spatial proximity between the hydrogens H-7 and 2H-7′ in the benzofuran neolignan **2** was detected by the NOESY experiment, confirming the orientation of the allyl group at C-1′. The ^{13}C DEPT NMR spectrum of **3** showed identical chemical shift for the carbons of the two methoxyls groups; even so, the information obtained from the HMBC confirmed a methoxyl group in each of the aromatics rings. In the naturally derived **5**, the conventional ^{1}H NMR spectrum (400 MHz) revealed that the assignments reported in the literature[6] for the aliphatic methynic hydrogens H-8 and H-8′ should be revised. In fact, the vicinal connectivities detected in the HOMO-COSY spectrum are in agreement with the proposed modifications. In a similar way, the HMBC spectrum allowed us to define unambiguously the chemical shifts of the carbons C-1 and C-4′, based on their correlations with the hydrogens H-2,6 and H-2′,6′ respectively.[6]

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Table 1. ^{1}H (400 MHz) and ^{13}C (100 MHz) data[a] for **1** including results obtained by COSY, NOESY, HMQC [^1J(C,H)] and HMBC [^nJ(C,H), n = 2 and 3]

	HMQC		HMBC		^{1}H × ^{1}H	
C	δ_C [b]	δH	^2J(C,H)	^3J(C,H)	COSY	NOESY
1	132.18	—		H-8		—
3,5	153.94	—	H-2, H-6	MeO-3, MeO-5		—
4	138.03	—		H-2, H-6, MeO-4		—
1′	139.51	—				—
2′	159.17	—		H-6′		—
3′	133.47	—				—
4′	196.13	—		H-6′, 2H-7		—
5′	82.98	—		2H-7′ MeO-5′		—
CH						
2,6	105.60	6,42 (s)				H-7,H-8, MeO-3,5
7	54.73	3.72 (dd, 8.4, 2.7)		H-2, H-6, H-6′ 3H-9	H-6′, H-8	H-2, H-6, 3H-9
8	90.20	4.66 (dq, 8.9, 6.2)	H-7, 3H-9		H-7, 3H-9	H-2, H-6
6′	131.95	5.86 (d, 2.7)		2H-7′	H-7	MeO-5′
8′	131.20	5.61 (m)	2H-7′, 2H-9′		2H-7′, 2H-9′	—
CH$_2$						
7′	45.50	2.42 (dd, 13.3, 7.1) 2.55 (dd, 13.3, 7.7)		2H-9′	H-8′	—
9′	119.26	4.99 (d, 9.9) 5.01 (d, 15.1)		2H-7′	H-8′	—
CH$_3$						
9	19.69	1.56 (d, 6.2)		H-7	H-8	H-7
MeO-3,5	56.44	3.85 (s)				H-2,6
MeO-4	61.03	3.85 (s)				—
MeO-3′	60.33	3.87 (s)				—
MeO-5′	53.87	3.11 (s)			H-6′	—

[a] δ(^{13}C) (ppm) relative to CDCl$_3$ at δ 77.0; δ(^{1}H) (ppm) relative to CDCl$_3$ at 7.26 (300 K); resonance multiplicities and coupling constants (J in Hz) are given in parentheses; (s) singlet; (d) doublet; (dd) doublet of doublets; (dq) doublet of quartets; (m) multiplet.

[b] Multiplicity of signals of carbon atoms deduced by analysis of PND and ^{13}C DEPT NMR spectra.

Table 2. ^{1}H (400 MHz) and ^{13}C (100 MHz) data[a] for **2** including results obtained by COSY, NOESY, HMQC [^{1}J(C,H)] and HMBC [^{n}J(C,H), $n = 2$ and 3]

	HMQC		HMBC		^{1}H × ^{1}H	
C	δ_C [b]	δ_H	^{2}J(C,H)	^{3}J(C,H)	COSY	NOESY
1	130.64	—	H-7	H-5		—
3	148.10	—		H-5		—
4	147.53	—		H-2, H-6,		—
1′	54.16	—	2H-7′	H-3′, 3H-9		—
2′	181.59	—	H-3′	H-6′		—
4′	182.81	—		H-6′		—
5′	153.10	—	H-6′	H-3′ MeO-5′		—
CH						
2	106.37	6.70 (s)		H-6, H-7		H-7, 3H-9
5	108.44	6.79 (d, 7.8)			H-6	H-7, 3H-9
6	119.08	6.69 (bd, 7.8)		H-2, H-7	H-5	—
7	87.49	5.91 (d, 5.0)		H-2, H-6, 3H-9	H-8	H-2, H-6, 2H-7′
8	44.82	2.69 (m)	3H-9	H-7′	H-7, 3H-9	—
3′	102.17	5.83 (s)				—
6′	109.29	5.49 (s)		2H-7′		MeO-5′
8′	131.94	5.72 (m)	2H-7′		2H-7′, 3H-9′	—
CH$_2$						
7′	44.10	2.52 (dd, 13.6, 6.8) 2.72 (m)		H-9′	H-8′	H-7
9′	120.36	5.12 (d, 16.9) 5.19 (d, 9.7)		2H-7′	H-8′	—
CH$_2$O$_2$	101.38	5.96 (s)				—
CH$_3$						
9	12.19	1.49 (d, 7.3)		H-7	H-8	H-2, H-6
MeO-5′	56.47	3.66 (s)				H-6′

[a] δ(^{13}C) (ppm) relative to CDCl$_3$ at δ 77.0; δ(^{1}H) (ppm) relative to CDCl$_3$ at 7.26 (300 K); resonance multiplicities and coupling constants (J in Hz) are given in parentheses (s) singlet; (d) doublet; (dd) doublet of doublets; (bd) broad doublet; (m) multiplet.

[b] Multiplicity of signals of carbon atoms deduced by analysis of PND and ^{13}C DEPT NMR spectra.

Table 3. ^1H (400 MHz) and ^{13}C (100 MHz) data[a] for **3** including results obtained by COSY, NOESY, HMQC [$^1J(C,H)$] and HMBC [$^nJ(C,H)$, $n = 2$ and 3]

	HMQC		HMBC		$^1H \times {}^1H$	
C	δ_C [b]	δ_H	$^2J(C,H)$	$^3J(C,H)$	COSY	NOESY
1	132.35	—	H-2, H-6, H-7	H-5, H-8		—
3	146.84	—	H-2	H-5, HO-4, MeO-5		—
4	145.94	—	HO-4	H-2		—
1′	132.23	—	H-7′	H-8′		—
3′	144.28	—	H-2′	MeO-3′		—
4′	146.73	—		H-2′, H-6′		—
5′	133.43	—		3H-9		—
CH						
2	109.10	6.99 (d, 0.8)		H-7	H-6	H-7, MeO-3
5	114.24	6.91 (d, 7.5)		HO-4	H-6	—
6	120.06	6.92 (dd, 0.8, 7.5)		H-7	H-2, H-5	H-7
7	93.89	5.12 (d, 9.4)		H-2, H-6, 3H-9	H-8	H-6, 3H-9
8	45.74	3.47 (dq, 6.8, 9.4)	H-7, 3H-9		H-7, 3H-9	H-2, H-6, H-6′
2′	109.48	6.81 (s)		H-6′		MeO-3′
6′	113.44	6.79 (s)		H-2′		—
7′	131.10	6.39 (dd, 1.5, 15.7)		H-2, H-6′, 3H-9′	H-8′	3H-9′
8′	123.57	6.13 (dq, 6.6, 15.7)	3H-9′		H-7′, 3H-9′	—
CH_3						
9	17.71	140 (d, 6.8)	—	H-7	H-8	H-7
9′	18.48	1.89 (dd, 1.5, 6.6)	H-8′	H-7′	H-8′	H-7′
MeO-3	56.10	3.88 (s)				H-2
MeO-3′	56.10	3.91 (s)				H-2′

[a] $\delta(^{13}C)$ (ppm) relative to $CDCl_3$ at δ 77.0; $\delta(^1H)$ (ppm) relative to $CDCl_3$ at 7.26 (300 K); resonance multiplicities and coupling constants (J in Hz) are given in parentheses: (s) singlet; (d) doublet, (dd) doublet of doublets; (dq) doublet of quartets.

[b] Multiplicity of signals of carbon atoms deduced by analysis of PND and ^{13}C DEPT NMR spectra.

Table 4. ^1H (400 MHz) and ^{13}C (100 MHz) data[a] for **4** including results obtained by COSY, NOESY, HMQC [^1J(C,H)] and HMBC [^nJ(C,H), $n = 2$ and 3]

	HMQC		HMBC		$^1H \times {}^1H$	
C	δ_C [b]	δ_H	^2J(C,H)	^3J(C,H)	COSY	NOESY
1,1′	137.99	—				—
3,5	153.19	—				—
3′,5′	153.19	—				—
4,4′	137.34	—		H-2, H-6, H-2′, H-6′		—
CH						
2,6	102.96	6.60 (s)		H-7		MeO-3, MeO-5
2′,6′	102.96			H-7′		MeO3′, MeO-5′
7,7′	88.46	4.62 (d, 9.1)		3H-9, 3H-9′	H-8, H-8′	—
8,8′	50.99	1.76 (m)	H-7, H-7′ 3H-9, 3H-9′		H-7, H-7′, 3H-9, 3H-9′	—
CH_3						
9,9′	13.91	1.05 (d, 5.9)	H-8, H-8′		H-8, H-8′	—
MeO-3,5	56.01	3.84 (s)				H-2, H-6
MeO-3′,5′	56.01					H-2′, H-6′
MeO-4,4′	60.71	3.79 (s)				—

[a] $\delta(^{13}C)$ (ppm) relative to $CDCl_3$ at δ 77.0; $\delta(^1H)$ (ppm) relative to $CDCl_3$ at 7.26 (300 K); resonance multiplicities and coupling constants (J in Hz) are given in parentheses: (s) singlet; (d) doublet; (dd) doublet of doublets; (m) multiplet.

[b] Multiplicity of signals of carbon atoms deduced by analysis of PND and ^{13}C DEPT NMR spectra.

Table 5. ^{1}H (400 MHz) and ^{13}C(100 MHz) data[a] for **5** including results obtained by COSY, NOESY, HMQC [^1J(C,H)] and HMBC [^nJ(C,H), $n = 2$ and 3]

	HMQC		HMBC		^{1}H × ^{1}H	
C	δ_C [b]	δ_H	^2J(C,H)	^3J(C,H)	COSY	NOESY
1	140.24	—	H-2, H-6, H-7			—
3,5	153.11	—	H-2, H-6			—
4	137.40	—	—	H-2, H-6		—
1′	137.40	—	2H-7′			—
3′,5′	153.30	—	H-2′, H-6′			—
4′	136.22	—		H-2′, H-6′		—
CH						
2,6	103.77	6.50 (s)		H-7		H-7, H-8
7	77.79	4.33 (d, 9.4)	H-8	H-2, H-6, 3H-9	H-8	H-2, H-6, 3H-9
8	43.22	1.86 (m)	H-7, 3H-9	2H-7′, 3H-9′	H-7, 3H-9	H-2, H-6, H-7′ 3H-9
2′,6′	106.16	6.40 (s)		2H-7′		2H-7′
8′	33.78	2.45 (m)	H-7′, 3H-9′	H-7′, 3H-9′	H-7′, 3H-9′	—
CH_2						
7′	42.66	2.45 (m) 2.58 (m)		H-2′, H-6′, 3H-9′	H-8′	H-2′, H-6′, H-8′, 3H-9′
CH_3						
9	10.37	0.61 (d, 6.9)			H-8	H-7
9′	13.70	0.90 (d, 6.1)		2H-7′	H-8′	H-7, H-7′
MeO-3,3′	56.23	3.83 (s)				
MeO-5,5′	56.23					
MeO-4,4′	60.92	3.81 (s)				

[a] $\delta(^{13}C)$ (ppm) relative to $CDCl_3$ at δ 77.0; $\delta(^1H)$ (ppm) relative to $CDCl_3$ at 7.26 (300 K); resonance multiplicities and coupling constants (J in Hz) are given in parentheses: (s) singlet; (d) doublet; (bs) broad singlet; (m) multiplet.

[b] Multiplicity of signals of carbon atoms deduced by analysis of PND and ^{13}C DEPT NMR spectra.