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ABSOLUTE CONFIGURATION OF THE LIGNAN OLEIFERINS FROM *VIROLA OLEIFERA*

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Key Word Index—*Virola oleifera*; Myristicaceae; lignans; lignan-7-ols; oleiferins A–C; 2,7′-cyclolignans; galcatin; isogalcatin; cagayanin; absolute configuration.

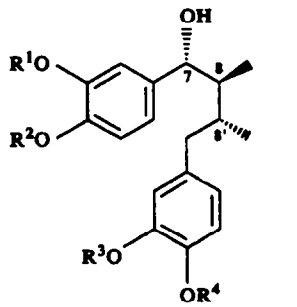
Abstract—The assignment of the absolute configuration for the lignan-7-ols, (7*R*,8*S*,8′*R*)-oleiferins A–C, was established by acid catalysed Friedel–Crafts-type cyclization for the known 2,7′-cyclolignans and chemical analyses.

INTRODUCTION

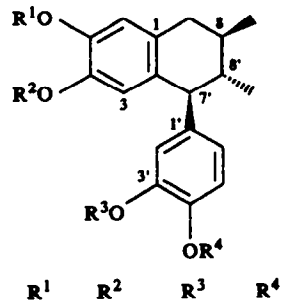
Virola oleifera (Schott) A. C. Smith, a plant originating in the south eastern region of Brazil, has been used in traditional medicine for the treatment of diseases of the respiratory tract, rheumatism and asthma, as well as gastric or duodenal ulcers [1]. In a previous paper [2], we reported the isolation and structural elucidation of five new lignans from leaves of *V. oleifera*, including the lignan-7-ols, oleiferins A (**1**) and C (**3**), and also confirmed the reversed structure of oleiferin B (**2**) based on ^1H–^{13}C long range shift correlations. This paper reports our investigations into the absolute configurations of these lignan-7-ols. The nomenclature and numbering of the compounds follows the IUPAC-IUB Joint Commission on Biochemical Nomenclature recommendations [13].

RESULTS AND DISCUSSION

Attempts to acetylate **1–3** with acetyl chloride were unsuccessful. In all cases, instead of acetate derivatives the acidic conditions involved would undoubtedly lead to the formation of phenyltetrahydronaphthalene compounds, **4–6**, with regio- and stereospecificity through the generation of a benzyl carbonium ion [4, 5]. Compounds **4–6** afforded a significant fragment in the mass spectra, $[M-C_4H_8]^+$, which is a typical fragmentation of 2,7′-cyclolignans [6]. The ^1H NMR spectra further supported the 2,7′-cyclolignan skeleton, showing a doubly benzylic methine proton (δ3.40, *d*, $J_{7',8'}$ = 10.3 Hz, H-7′) and two secondary methyls (δ1.06, J = 6.3 Hz, Me-8; δ0.86, J = 6.3 Hz, Me-8′) with their related methine protons (δ1.50, *ddq*, $J_{8',9'}$ = 6.3, $J_{7',8'}$ = 10.3 Hz, H-8′; δ1.62, *m*, H-8). Double resonance experiments supported the assignments. On irradiation at δ0.86 (Me-8′), $J_{8,8'}$ was determined to be 10.4 Hz, indicating that H-8 and H-8′ are *pseudo*-axial. The substitution pattern on the phenyl rings was confirmed by the observed spectra, showing a pair of *para*-protons for H-3 and H-6 on ring A, and two doublets with coupling constants 8.0 Hz (H-5′) and 1.8 Hz (H-2′), as well as an AB system for H-6′ (J = 1.8, 1.8 Hz), indicating the 1′,3′,4′-substitution in ring C. The



	R^1	R^2	R^3	R^4
1	— CH_2 —		Me	Me
2	Me	Me	— CH_2 —	
3	— CH_2 —		— CH_2 —	



	R^1	R^2	R^3	R^4
4	Me	Me	— CH_2 —	
5	— CH_2 —		Me	Me
6	— CH_2 —		— CH_2 —	

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assignment of the methylenedioxy groups in **4–6** was based on the known chemical shift difference between ring A or C substitution [7]. The observed spin coupling constants, $J_{7',8'} = 10.3$ Hz and $J_{8,8'} = 10.4$ Hz for **4–6** confirm the all-*trans* stereochemistry with the methyl groups and the pendant phenyl substituent all *pseudo*-equatorial.

Comparison of the spectral data and optical rotations led to the conclusion that **4–6** are the known 2,7'-cyclolignans (+)-isogalcatin (isootobain) [9], (−)-galcatin [8] and (−)-cagayanin [10], respectively. Since the absolute configuration of these compounds has been previously established as 7'*S*,8*R*,8'*S*, it follows that the absolute configuration of oleiferin A (**1**), B (**2**) and C (**3**) is 8*S*,8'*R*, since C-8 and C-8' are unchanged in the above mentioned transformation. Therefore, all the evidence shows that the oleiferins possess structures **1–3** with the 7*R*,8*S*,8'*R* absolute configuration.

EXPERIMENTAL

General. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively, using TMS as int. standard. Assignments were based on DEPT. EIMS were measured at 70 eV.

Conversion of oleiferins to 2,7'-cyclolignans. To **1** (6 mg), **2** (5 mg) and **3** (5 mg), AcCl (3 drops) was added. The soln was kept for 2 hr at room temp., and then, after the addition of H_2O, neutralized with aq. $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4), filtered and evapd, affording the 2,7'-cyclolignans **4** (5 mg), **5** (4.5 mg) and **6** (4.3 mg), respectively.

(7'S,8R,8'S)-4,5-*Dimethoxy*-3',4'-*methylenedioxy*-2,7'-*cyclolignan* (**4**). $[\alpha]^{22}$ +5.2° ($CHCl_3$; *c* 1.424). ^{1}H NMR ($CDCl_3$): δ0.88 (*d*, *J* = 6.3 Hz, Me-8'), 1.07 (*d*, *J* = 6.4 Hz, Me-8), 1.50 (*ddq*, *J* = 6.3, 10.3, 10.4 Hz, H-8'), 1.62 (*m*, H-8), 2.59 (*dd*, *J* = 11.4, 16 Hz, H-7a), 2.74 (*dd*, *J* = 4.6, 16.1 Hz, H-7b), 3.42 (*d*, *J* = 10.3 Hz, H-7'), 3.60 (*s*, OMe), 3.84 (*s*, OMe), 5.93 (*s*, OCH_2O-3',4'), 6.18 (*s*, H-3), 6.55 (*s*, H-6), 6.54 (*d*, *J* = 1.5 Hz, H-2'), 6.63 (*dd*, *J* = 1.5, 7.9 Hz, H-6'), 6.74 (*d*, *J* = 7.9 Hz, H-5'). ^{13}C NMR ($CDCl_3$) Table 1. EIMS *m/z* (rel. int.): 340 $[M]^+$ (< 1), 121 (3), 119 (6), 88 (11), 86 (70), 84 (100).

(7'S,8R,8'S)-3',4'-*Dimethoxy*-4,5-*methylenedioxy*-2,7'-*cyclolignan* (**5**). $[\alpha]^{22}$ −9.7° ($CHCl_3$; *c* 0.792). ^{1}H NMR ($CDCl_3$): δ0.85 (*d*, *J* = 6.2 Hz, Me-8'), 1.07 (*d*, *J* = 6.3 Hz, Me-8), 1.52 (*ddq*, *J* = 6.3, 10.3, 10.4 Hz, H-8'), 1.63 (*m*, H-8), 2.58 (*dd*, *J* = 11.4, 16 Hz, H-7a), 2.73 (*dd*, *J* = 4.7, 16.2 Hz, H-7b), 3.38 (*d*, *J* = 10.3 Hz, H-7'), 3.82 (*s*, OMe), 3.88 (*s*, OMe), 5.81 (*s*, OCH_2O-4,5), 6.14 (*s*, H-3), 6.52 (*s*, H-6), 6.56 (*d*, *J* = 2.0 Hz, H-2'), 6.68 (*dd*, *J* = 2.0, 8.2 Hz, H-6'), 6.80 (*d*, *J* = 8.2 Hz, H-5'). ^{13}C NMR ($CDCl_3$) Table 1. EIMS *m/z* (rel. int.): 340 $[M]^+$ (100), 284 (14), 254 (96), 202 (14), 187 (10), 165 (7), 151 (5).

(7'S,8R,8'S)-3',4' : 4,5-bis(*Methylenedioxy*)-2,7'-*cyclolignan* (**6**). $[\alpha]^{22}$ −28.6° ($CHCl_3$; *c* 0.988). ^{1}H NMR ($CDCl_3$): δ0.86 (*d*, *J* = 6.3 Hz, Me-8'), 1.05 (*d*, *J* = 6.3 Hz, Me-8), 1.47 (*ddq*, *J* = 6.4, 10.3, 10.4 Hz, H-8'), 1.62 (*m*, H-8), 2.56 (*dd*, *J* = 11.5, 16 Hz, H-7a), 2.71 (*dd*, *J* = 4.5, 16.2 Hz, H-7b), 3.38 (*d*, *J* = 10.3 Hz, H-7'), 5.81 and 5.82 (each 1H, *d*, *J* = 1.4 Hz, OCH_2O-4,5), 5.92 (*s*, OCH_2O-3',4'), 6.16 (*s*, H-3), 6.51 (*s*, H-6), 6.51 (*d*, *J* = 1.7 Hz, H-2'), 6.62 (*dd*, *J* = 1.7, 7.9 Hz, H-6'), 6.73 (*d*, *J* = 7.9 Hz, H-5'). ^{13}C NMR ($CDCl_3$) Table 1. EIMS *m/z* (rel. int.): 324 $[M]^+$ (100), 268 (31), 267 (37), 238 (42), 210 (12), 162 (5), 151 (6), 135 (5).

Table 1. ^{13}C NMR spectral data of **4–6** (75.5 MHz, $CDCl_3$, δ-values)

C	4	5	6
1	129.3	130.1	130.1
2	132.4	133.7	133.5
3	110.8	109.7	109.7
4	147.3	145.5	145.6
5	147.9	145.7	145.7
6	113.1	107.7	107.7
7	39.1	39.4	39.4
8	35.5	35.4	35.4
9	20.0	19.8	19.8
1'	140.7	139.2	140.6
2'	107.8	112.2	107.8
3'	147.2	149.1	147.9
4'	146.0	147.5	146.0
5'	109.4	110.9	109.2
6'	122.9	121.9	122.9
7'	54.4	54.6	54.6
8'	44.1	43.7	43.8
9'	17.1	17.1	17.1
OMe	55.8	54.6	—
OMe	55.9	55.9	—
OCH_2O-3',4'	100.9	-	100.8
OCH_2O-4,5	—	100.5	100.5

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REFERENCES

1. Rodrigues, W. A. (1980) *Acta Amazonica* **10**, 83.
2. Fernandes, A. M. A. P., Barata, L. E. S. and Ferri, P. H. (1993) *Phytochemistry* **32**, 1567.
3. Moss, G. P. (1989) *IUPAC-IUB Joint Commission on Biochemical Nomenclature* **25-2**, 1.
4. Moro, J. C., Fernandes, J. B., Vieira, P. C., Yoshida, M., Gottlieb, O. R. and Gottlieb, H. E. (1987) *Phytochemistry* **26**, 269.
5. Krauss, A. S. and Taylor, W. C. (1992) *Aust. J. Chem.* **45**, 925.
6. Pelter, A. (1968) *J. Chem. Soc.* (*C*) 74.
7. Bhacca, N. S. and Stevenson, R. (1963) *J. Org. Chem.* **28**, 1638.
8. Hobbs, T. T. and King, F. E. (1960) *J. Chem. Soc.* 4732.
9. Wallace, R., Porte, A. L. and Hodges, R. (1963) *J. Chem. Soc.* 1445.
10. Kuo, Y.-H., Lin, S.-T. and Wu, R.-E. (1989) *Chem. Pharm. Bull.* **37**, 2310.