Lignans from Leaves of *Rollinia mucosa*

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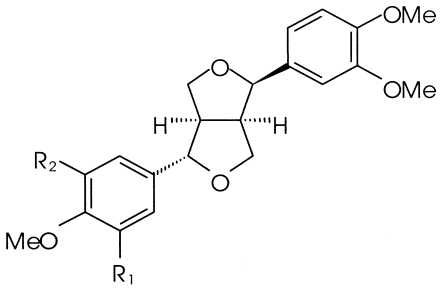
A new furofuranic lignan named (+)-epimembrine together with known (+)-epieudesmine and (+)-epimagnoline were isolated from leaves of *R. mucosa*. Their structures were determined by spectroscopic data. Palmitone and a mixture of β-sitosterol and stigmasterol were also isolated.

Introduction

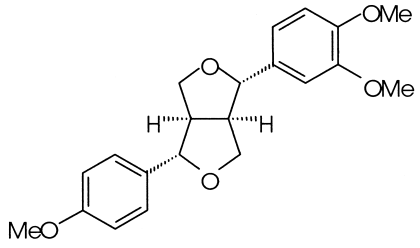
As part of our ongoing investigation on biologically active compounds from Mexican medicinal plants (Martínez-Vázquez and García-Argáez, 2001), we have studied the leaves of *Rollinia mucosa* (Jacquin) Baillon (syn. R. *jimenezii* Safford) (Annonaceae). Previous studies of this species reported the isolation of acetogenins, alkaloids (Pettit *et al.,* 1987; Chen *et al*., 1996; Shi *et al.,* 1996; and Chávez *et al.*, 1998) and the lignans (+)-yangambine, (+)-magnoline, (+)-eudesmin, (+)-epieudesmin and (+)-membrine from mature fruits (Paulo *et al.,* 1991; and Chen *et al.,* 1996). In this paper, we describe the structure elucidation of the furofuranic lignan **1**.



(+)-epimembrine (**1**) R_1=H R_2=H
(+)-epieudesmine (**2**) R_1=H R_2=OMe
(+)-epigmagnolin A (**3**) R_1=OMe R_2=OMe

Results and Discussion

Leaves of *R. mucosa* were extracted with *n*-hexane and the resulting extract was chromatographed on silica gel eluting with *n*-hexane containing increasing concentrations of ethyl acetate. Compound **1** was isolated from fractions eluted with 8:2 (*n*-hexane: ethyl acetate v/v), while compounds **2** and **3** were isolated from fractions eluted with a solvent ratio of 7:3. Also palmitone (16-hebtriacontanone) (Hayashi and Komae, 1971) and a mixture of β-sitosterol and stigmasterol were isolated. The lignans isolated were (+)-epieudesmine (**2**) (Pelter *et al*., 1976) and (+)-epimagnolin (**3**) (Miyazawa *et al.*, 1994a, b).



(+)-membrin (**4**)

The high-resolution mass spectrum of compound **1** showed its $[M]^+$ at *m/z* 356.1642 for a $C_{21}H_{24}O_5$ formula. The peaks at *m/z* 165 and 151 were attributable to cleavage of fragments containing a veratryl group and the peaks at *m/z* 135 and 121 were also attributable to cleavage of a *p*-methoxyphenyl group (Pelter *et al.*, 1976). The presence of these two aryl groups in **1** was confirmed by its NMR spectral data (Tables I and II).

Compound **1** had a basal 2,6-diaryl-3, 7-dioxabicyclo [3,3,0]-octane skeleton as shown by its ^1H NMR spectrum where the eight aliphatic protons are present at δ 2.91, 3.32, 3.85, 4.13, 4.46 and 4.87 (Miyazawa *et al.*, 1992).

Therefore the gross structure of **1** corresponds to that of membrine (**4**). However the notorious variance in their NMR data (Tables I and II) indicates that the difference between them should correspond to the relative orientation of the aryl groups.

From a comparison of the chemical shifts of the eight aliphatic protons of **1** with those of (+)-epieudesmine (**2**) (Pelter *et al.,* 1976) and (+)-epimagnolin A (**3**) (Miyazawa *et al.*, 1994b), the stereochemistries of the two aromatic rings were proposed as of the axial-equatorial type. The ^{13}C NMR spectral data of **1** confirmed the stereochemistries of the two aromatic rings, because six aliphatic carbon signals were almost identical to those of **2** and **3** (Table II).

Furthermore, the carbon signals assigned to the veratryl group were consistent with those of phyllygenin and (+)-epimagnolin A (axial-veratryl type). A NOESY experiment of **1** confirms the relative stereochemistry of the protons at positions 2 and 6.

Therefore, the structure of **1** named (+)-epimembrine is assigned as *rel* (2*R*, 6*S*)-2-(3,4-dimethoxyphenyl)-6-(4-methoxyphenyl)-3,7-dioxabicyclo [3,3,0] octane.

Experimental

Plant material

Leaves of *R. mucosa* were collected from plants growing in the surroundings of Ocosingo Chiapas, México. A voucher specimen was deposited in the herbarium of Escuela de Biología de la UNICACH. (Voucher: A. R. González-Esquinca) Dried and ground leaves (1428 g) were extracted with hexane, EtOAc and MeOH successively (5 l × 3 times, each) at room temperature during 48 h. The hexanic extract (20 g, residue dry weight) was absorbed on 2 g of silica gel and then chromato-

Table I. ^1H NMR spectral data of compounds **1–4**.

H	**1**	**2**	**3**	**4**
1	3.32 m	3.30 m	3.35 m	3.11 m
2	4.87 d (5)	4.85 d (5.5)	4.87 d (5.5)	4.76 dd (10.2, 7)
4ax	4.13 d (9.5)	4.13 d (10)	4.16 d (9.5)	4.20 m
4eq	3.85 m	3.85 m	3.87 m	3.84 m
5	2.91 m	2.90 m	2.92 m	3.11 m
6	4.46 d (7.2)	4.45 d (7)	4.44 d (7.2)	4.76 dd (10.2, 7)
8ax	3.32 m	3.30 m	3.35 m	3.84 m
8eq	3.85 m	3.35 m	3.87 m	4.20 m
Ar	6.88 m (5H) 7.29 m (2H)	6.94 m 6.86 m	2′ 6.94 s 5′ 6.84 d (8)	6.82–6.92 m (5H) 7.26–7.30 m (2H)
OMe	3.80 s 3.88 s 3.90 s	3.89 3.90 3.92 3.93	3.84 s 3.87 s 3.87 s 3.88 s 3.91 s	3.81 s 3.88 s 3.90 s

Table II. ^{13}C NMR spectral data of lignans **1–4**.

C	**1**	**2**	**3**	**4**
1	50.2	50.1	49.9	54.1
2	82.0	81.9	81.8	85.6
4	71.0	70.9	70.8	71.8
5	54.5	54.4	54.4	54.2
6	87.5	87.5	87.6	85.8
8	69.7	69.6	69.6	71.5
1′	131.0	130.8	130.7	133.1
2′	109.0	109.0	108.8	109.2
3′	148.8	148.5	148.7	148.6
4′	148.8	148.6	147.8	149.2
5′	111.1	110.9	110.9	111.0
6′	117.7	117.5	117.5	118.2
1″	133.2	133.5	136.7	133.6
2″	113.5	108.8	102.7	113.0
3″	127.3	147.8	153.2	127.3
4″	159.2	149.0	137.2	159.2
5″	127.3	110.9	153.2	127.3
6″	113.5	118.3	102.7	113.0
OMe	55.2 55.9 56.0	55.8	55.7 55.7 55.9 55.9 60.5	55.3 55.4 56.0

graphed on a column packed with 60 g of silica gel 60 (Merck). Elution with gradients of hexane and ethyl acetate afforded palmitone, (96 mg, 100% *n*-hexane), a mixture of β-sitosterol and stigmasterol (65 mg, 8:2) and the furofuranic lignans **1** (10 mg, 8:2), **2** (5 mg, 7:3) and **3** (2 mg, 7:3).

The identification of the known compounds was achieved by comparison of their physical and spectroscopic data with those published in the literature.

(+)-Epimembrine (**1**)

White crystal mp 128–130 °C. HRMS: *m/z*: 356.1642 ($[M]^+$, calcd for $C_{21}H_{24}O_5$: 356.1624). MS *m/z* (rel int.) 356 ($[M]^+$) (100), 325 (10), 189 (22), 177 (28), 165 (33), 147 (29), 135 (68), 121 (36). $[\alpha]^{25}$ + 134.6° ($CHCl_3$; c 1.2). IR ν max cm^{-1}: 1591, 1515, 1464, 1417, 1375, 1071 and 1031. ^1H and ^{13}C NMR see Tables I and II.

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Chavez A., Acevedo A. L. and Mata R. (1998), Jimenezin, a novel Annonaceous acetogenin from the seeds of *Rollinia mucosa* containing adjacent tetrahydrofuran-tetrahydropyran ring systems. J. Nat. Prod. **61**, 419–421.

Chen Y. Y., Fang-Rong C. and Yang-Chang W. (1996), Isoquinoline alkaloids and lignans from *Rollinia mucosa*. J. Nat. Prod. **59**, 904–906.

Hayashi N. and Komae H. (1971), Isolation and identification of palmitone from the leaves of *Lauraceae* plants (*Cinnamomun camphora* Sieb., *Neolitsea serica* Kooidz, *Lindera umbrellata* Thumb.). J. Indian Soc. **48**, 288.

Martínez-Vázquez M. and García-Argáez A. N. (2001), Phytochemical studies and biological evaluations of some Mexican plants. Recent. Res. Devel. Phytochemistry **5**, 59–85.

Miyazawa M., Kasahara H. and Kameoka H. (1992), Phenolic lignans from flower buds of *Magnolia fargesii*. Phytochemistry **31**, 3666- 3668.

Miyazawa M., Ishikawa Y., Kasahara H., Yamanaka H. and Kameoka H. (1994a), An insect growth inhibitory lignan from flower buds of *Magnolia fargesii*. Phytochemistry **35**, 611–613.

Miyazawa M., Kasahara H. and Kameoka H. (1994b), Microbial oxidation of (+)- epigmagnolin A by *Aspergillus niger*. Phytochemistry **35**, 1191–1193.

Paulo M. Q., Kaplan M. A. C., Laprévote O., Rublot F., Hocquemiller R. and Cave A. (1991), Lignans and other non-alkaloid constituents from *Rollinia mucosa*. Fitoterapia **62**, 150–152.

Pelter A., Ward R. S., Rao E. V. and Sastry K. V. (1976), Revised structures for pluviatilol, methyl pluviatilol and xanthoxylol. Tetrahedron **32**, 2783–2788.

Pettit G. R., Cragg G. M., Polonoki J., Herald D. L., Goswami A., Smith C. R., Moretti C., Schmidt J. M. and Weisleder D. (1987), Isolation and structure of rolliniastatin 1 from the South American tree *Rollinia mucosa*. Can. J. Chem. **65**, 1433–1435.

Shi G., Xe Q., He K. and McLaughlin J. L. (1996), Rollinecins A and B: two New bioactive annonaceous acetogenins from *Rollinia mucosa*. J. Nat. Prod. **59**, 548–551.