Pergamon

PII: S0031-9422(97)00364-6

Phytochemistry, Vol. 46, No. 5, pp. 879–881, 1997

Printed in Great Britain
0031-9422/97 $17.00+0.00

AMIDES AND LIGNANAMIDES FROM *PORCELIA MACROCARPA**

MARIANA H. CHAVES and NIDIA F. ROQUE†

† Instituto de Química, Universidade de São Paulo CP. 26077, CEP 05599-970, SP Brasil; Departamento de Química, Universidade Federal do Piauí, CEP 64049-550, Teresina, Piauí, Brasil

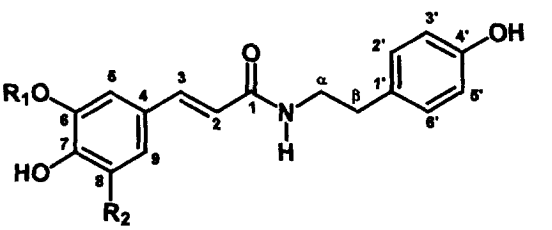
(*Received in revised form* 28 *March* 1997)

Key Word Index—*Porcelia macrocarpa*; Annonaceae; amides; lignanamides.

Abstract—Two new lignanamides, 1,2-dihydro-6,8-dimethoxy-7-hydroxy-1-(3,5-dimethoxy-4-hydroxyphenyl)-N^1,N^2-bis-[2-(4-hydroxyphenyl)ethyl]-2,3-naphthalene dicarboxamide and 1,2-dihydro-6,8-dimethoxy-7-hydroxy-1-(3,4-dihydroxyphenyl)-N^1-N^2-bis-[2-(4-hydroxyphenyl)ethyl]-2,3-naphthalene dicarboxamide, together with *N-trans*-feruloyltyramine, *N-trans*-caffeoyltyramine and the new *N-trans*-sinapoyltyramine were isolate from the branches of *Porcelia macrocarpa*. This is the first report of lignanamides from an Annonaceae species.

INTRODUCTION

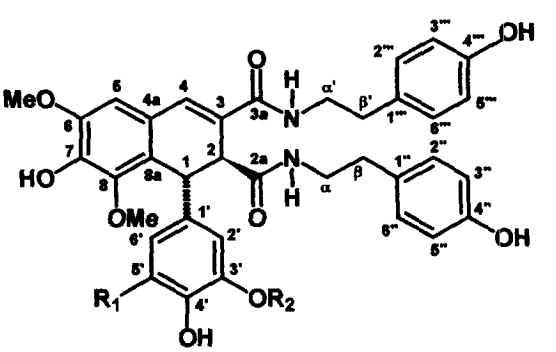
In a previous paper we reported the isolation and the structural determination of acetogenins from the seeds of *Procelia macrocarpa* [1]. We describe herein the isolation of hydroxycinnamoyltyramines and arylnaphthalene lignanamides from the branches of that plant. The occurrence of acyltyramines has been reported from the flowering parts of several plants [2]. *N-trans*-caffeoyl and *N-trans*-feruloyltyramines, isolated from *P. macrocarpa*, proved previously to have biological activities [3–5]. *N-trans*-caffeoyltyramine was also isolated from *Annona crassiflora*, another Annonaceae species [6]. Arylnaphthalene lignanamides have been isolated before only from *Cannabis sativa*, Cannabidacea [7].



1a R_1 = Me; R_2 = H
1b R_1 = R_2 = H
1c R_1 = Me; R_2 = OMe

RESULTS AND DISCUSSION

Compounds **1a**–**1c** were obtained as amorphous solids from the ether soluble fraction of the ethanolic extract of *Porcelia macrocarpa* branches, after liquid chromatographic isolation procedures. *N-trans*-feruloyltyramine (**1a**) and *N-trans*-caffeoyltyramine (**1b**) showed ^{1}H NMR spectroscopic signals for amides formed by hydroxycinnamic acids and tyramine. The structures were identified by the comparison of their spectroscopic data, with those from the literature [2, 6, 8]. The ^{1}H NMR spectrum of **1c** showed the same general pattern as **1a** and **1b**, with the only difference being observed in the acyl moiety. Thus the methoxy signal of the **1c** spectrum integrated to six protons instead of three as in **1a**. The three aromatic proton signals present in **1a** and **1b** spectra were replaced by one singlet integrating for two protons. This spectra



2a R_1 = OMe; R_2 = Me
2b R_1 = R_2 = H

* Based on part of the Ph.D. thesis presented by M.H.C. to Universidade de S. Paulo.

† Author to whom correspondence should be addressed.

suggested the structure of *N-trans*-sinapoyltyramine for **1c**, which was confirmed by EIMS, IR and ^{13}C NMR spectra (see experimental).

As for **1a–1c**, compounds **2a** and **2b** were isolated as amorphous solids from the ether soluble fraction of the same ethanolic extract. The IR spectra of both compounds showed a broad amide carbonyl band at 1640 and 1646 cm^{-1}, respectively. The FABMS information (*m/z*: 685; M+1 for **2a** and 641; M+1 for **2b**) together with quantitative analysis gave the molecular formula for **2a** ($C_{38}H_{40}N_2O_{10}$) and **2b** ($C_{36}H_{36}N_2O_9$).

The ^1H NMR spectrum of **2a** (Table 1) showed two pairs of doublets (6.84 and 6.56, $J = 8.5$ Hz) and (6.73 and 6.54, $J = 8.5$ Hz) where each signal integrated as two protons. Two other pairs of correlated signals (2.44 *t*–3.26 *m* and 2.58 *t*–3.38 *m*) suggested the presence of two tyramine units in the molecule. The presence of four aromatic protons [6.24 *s* (2H), 6.68 *s* and 7.20 *s*], together with four methoxyl groups [3.48, 3.60 (6H) and 3.82] in **2a** could be inferred from the spectrum. The ^1H-^1H COSY spectrum, recorded in acetone-d_6, showed two coupled methyne protons (3.7 *bs* and 5.02 *bs*). All these features along with data obtained from ^{13}C NMR spectra (Table 2) suggested that **2a** is a phenyldihydronaphthalene lignanamide [7, 9]. The correlations apparent in the long distance ^1H-^{13}C HETCOR confirmed the structure and made possible all assignments for protons and carbons in **2a**. The relative *trans* configuration of **2a** was suggested by the small coupling constant between H-1 (the signal from H-1 is a broad singlet) and H-2 observed in the ^1H NMR spectrum. In the *cis* configuration H-1 should appear as a doublet with $J = 8$ Hz [10, 7].

Table 2. ^{13}C NMR spectral data for compounds **2a** and **2b** (50.3 MHz, CD_3OD)

C	2a		2b	
1	41.6		41.0	
2	49.2		49.0	
3	127.1		126.9	
4	135.1		135.2	
5	109.1		109.2	
6	149.2		149.1	
7	143.1		143.1	
8	146.9		146.9	
4a	124.3		124.3	
8a	125.2		125.5	
2a	174.0		174.0	
3a	170.0		170.0	
1′	135.3		136.3	
2′	106.0		116.2	
3′	149.0		144.8	
4′	135.3		145.9	
5′	149.0		115.9	
6′	106.0		119.9	
1″, 1‴	131.1	131.3	131.1	131.4
2″, 2‴	130.7	130.8	130.7	130.8
3″, 3‴	116.2	116.2	116.2	116.2
4″, 4‴	156.8	156.8	156.7	156.8
5″, 5‴	116.2	116.2	116.2	116.2
6″, 6‴	130.8	130.8	130.7	130.8
αα′	42.4	42.8	42.4	42.8
ββ′	35.4	35.6	35.5	35.6
OMe-3′	56.7		—	
OMe-5′	56.7		—	
OMe-6	56.8		56.8	
OMe-8	60.8		60.8	

Table 1. ^1H NMR spectral data for compounds **2a** and **2b** (200 MHz, CD_3OD)*

H	2a	2b
1	5.02 *br s*	4.97 *br s*
2	~3.7 *sl*	3.64 *sl*
4	7.20 *s*	7.26 *s*
5	6.68 *s*	6.76 *s*
2′	6.24 *s*	6.44 *d* (2.0)
5′	—	6.60 *d* (8.0)
6′	6.24 *s*	6.39 *dd* (8.0, 2.0)
α, α′	3.38 *m*, 3.26 *m*	3.37 *m*, 3.24 *m*
β, β′	2.58 *t* (7.1), 2.44 *t* (6.7)	2.66 *t* (7.3), 2.51 *t* (6.8)
2″, 6″	6.73‡ *d* (8.5)	6.81 *d* (8.6)
2‴, 6‴	6.84‡ *d* (8.5)	6.95 *d* (8.6)
3″, 5″	6.54§ *d* (8.5)	6.62 *d* (8.6)
3‴, 5‴	6.56§ *d* (8.5)	6.67 *d* (8.6)
OMe-3′	3.60 *s*	—
OMe-5′	3.60 *s*	—
OMe-6	3.82 *s*	3.91 *s*
OMe-8	3.48 *s*	3.54 *s*
N-H	7.56† *t* (5.5)	7.59† *t* (6.0)
	7.71† *t* (5.5)	7.66† *t* (6.0)

* Coupling constants (Hz) are given in parentheses.

Assignments with same symbol in the column are interchangeable.

1H and ^{13}C NMR spectra of **2b (Tables 1 and 2) showed that the main differences between **2b** and **2a** were in the resonances of the phenyl group. In the first one this group has a 3,4-dihydroxy pattern and in **2a** the phenyl group is 3,5-dimethoxy-4-hydroxy substituted, as shown in the NMR spectra (Tables 1 and 2). This is the first report of lignanamides from an Annonaceae species.

EXPERIMENTAL

Plant material. The branches of *Porcelia macrocarpa* (Warm.) R. E. Fries were collected at the Jardim Botânico of São Paulo in June, 1991. A voucher specimen has been deposited in the herbaria of the Instituto Botânico, São Paulo, Brasil under reference SP76791.

Extraction and isolation of the compounds. Dried and powdered branches (800 g) of *P. macrocarpa* were extracted with EtOH. The EtOH extract, after concn *in vacuo*, was partitioned between EtOH–H_2O (1:2) and ether. The ether soluble part was then partitioned between MeOH–H_2O (9:1) and hexane.

The MeOH–H_2O phase (10 g) was chromato-

graphed on silica gel column eluted with $CHCl_3$ with increasing amounts of MeOH. The $CHCl_3$–MeOH (19:1) eluate was chromatographed on a Sephadex LH-20 column eluted with MeOH–$CHCl_3$ (3:2) giving two mixts. A and B. Mixt. A was purified by prep. TLC ($CHCl_3$–MeOH–NH_4OH 85:15:0.5) to give **2a** (25 mg). Mixt. B was purified by prep. TLC (C_6H_6–Me_2CO 7:3) to give **1a** (60 mg) and **1c** (15 mg). Next, the $CHCl_3$–MeOH (9:1) eluate was examined further. Upon standing, a mixt. of steroid glycosides had pptd, and after filtration, the resulting filtrate was subjected to Sephadex LH-20 column chromatography eluted with MeOH–$CHCl_3$ (3:2) to give pure **1b** (30 mg), and a mixt. which was further purified by prep. TLC ($CHCl_3$–MeOH–NH_4OH 85:15:0.5) to afford **2b** (15 mg).

N-trans-*sinapoyltyramine* (**1c**). Amorphous powder. EIMS 70 eV *m/z* (rel. int.): 343 (11, $[M]^+$), 223 (56), 222 (100), 207 (87), 179 (3), 175 (39), 120 (25), 107 (18). Anal. calcd. for C, 66.67; H, 5.85; N, 4.09 (found C, 66.82; H, 6.22; N, 4.15). IR ν_{max}^{Kbr} cm^{-1}: 3400, 1656, 1613, 1516. ^1H NMR (200 MHz, CD_3OD): δ 6.42 (1H, *d*, $J = 15.6$ Hz, H-2), 7.41 (1H, *d*, $J = 15.6$ Hz, H-3), 6.83 (2H, *s*, H-5 and H-9), 3.46 (2H, *t*, $J = 7.5$ Hz, H-α), 2.74 (2H, *t*, $J = 7.5$ Hz, H-β), 7.05 (2H, *d*, $J = 8.4$ Hz, H-2′ and H-6′), 6.71 (2H, *d*, $J = 8.4$ Hz, H-3′ and H-5′), 3.85 (6H, *s*, OMe). ^{13}C NMR (50.3 MHz, CD_3OD): 168.8 (C-1), 118.8 (C-2), 142.0 (C-3), 126.9 (C-4), 106.1 (C-5 and C-9), 149.2 (C-6), 131.0 (C-7 and C-1′), 149.2 (C-8), 42.3 (C-α), 35.5 (C-β), 130.5 (C-2′ and C-6′), 116.0 (C-3′ and C-5′), 156.6 (C-4′), 56.5 (2 OMe). UV λ_{max}^{MeOH} nm (log ε): 205 (4.21), 225 (4.14), 320 (3.96).

Compound **2a**. Amorphous powder. $[\alpha]_D^{25} -20°$ (MeOH, *c* 0.062) FAB-MS *m/z* (rel. int.): 685 $[M+H]^+$. (100), 548 $[M\text{-}NHCH_2CH_2\phi OH]^+$ (18), 520 $[M\text{-}CONHCH_2CH_2\phi OH]$ (40). Anal. calcd. for C, 66.67; H, 5.85; N, 4.09 (found C, 66.24; H, 6, 10; N 4.00). IR ν_{max}^{film} cm^{-1}: 3432, 1640, 1617, 1516. UV λ_{max}^{MeOH} nm (log ε): 210 (4.87), 240 (4.50), 282 (4.11), 325 (4.23). ^1H NMR: See Table 1. ^{13}C NMR: see Table 2.

Compound **2b**. Amorphous powder. $[\alpha]_D^{25} -12°$ (MeOH, *c* 0.085). FAB-MS *m/z* (rel. int.): 641 $[M+H]^+$ (100). 476 $[M\text{-}CONHCH_2CH_2\phi OH]$ (60). Anal. calcd. for C, 67.50; H, 5.63; N, 4.38 (found C, 67.10; H, 6.01; N, 4.33). IR ν_{max}^{KBr} cm^{-1}: 3397, 1646, 1614, 1515. UV λ_{max}^{EtOH} nm (log ε): 203 (4.85), 249 (4.49), 283 (4.22), 332 (4.24). ^1H NMR: See Table 1. ^{13}C NMR: see Table 2.

Acknowledgements—The authors are grateful to FAPESP for financial support and to CAPES-PICDT (M.H.C.) and CNPq (N.F.R.) for the award of scholarships. They are also grateful to Dr Claudia M. Young, Instituto de Botânica, SEMA, São Paulo for plant material and to Prof. H. Budzikiewicz for the FAB-MS.

REFERENCES

1. Chaves, M. H. and Roque, N. F., *Phytochemistry*, 1997, **44**, 523.
2. Hussain, S. F., Gözler, B., Shamma, M. and Gözler, T., *Phytochemistry*, 1982, **21**, 2979.
3. Tseng, C.-F., Mikajiri, A., Shibuya, M., Goda, Y., Ebizuka, Y., Padmawinata, K. and Sankawa, U., *Chemical and Pharmaceutical Bulletin*, 1986, **34**, 1380.
4. Iwakami, S., Shibuya, M., Tseng, C.-F., Hanaoka, F. and Sankawa, U., *Chemical and Pharmaceutical Bulletin*, 1986, **34**, 3960.
5. Okuyama, T., Shibata, S., Hoson, M., Kawada, T., Osada, H. and Noguchi, T., *Planta Medica*, 1986, **52**, 171.
6. Santos, L. P., Boaventura, M. A. D., Oliveira, A. B. and Cassady, J. M., *Planta Medica*, 1996, **62**, 76.
7. Sakakibara, I., Ikeya, Y., Hayashi, K. and Mitsuhashi, H., *Phytochemistry*, 1992, **31**(9), 3219.
8. Ghosal, S. and Chakrabarti, D. K., *Phytochemistry*, 1988, **27**, 1339.
9. Nishizawa, M., Tsuda, M. and Hayashi, K., *Phytochemistry*, 1990, **29**, 2645.
10. Jones, W. D. and Thompson, A. M., *Journal of the Chemical Society, Chemical Communications*, 1988, 1095.