Pergamon

Tetrahedron Letters 42 (2001) 8433–8434

TETRAHEDRON LETTERS

Laurifolin, a novel acetogenin from *Rollinia laurifolia* leaves

Lúcia P. Santos Pimenta,[a,*] Francisco Chagas do Nascimento,[b] Angela Cristina S. Assunção,[a] Alaíde B. Oliveira[c] and Maria Amélia D. Boaventura[a]

[a]*Departamento de Química, Instituto de Ciências Exatas, UFMG, Caixa Postal 702, CEP 31270-901 Belo Horizonte, MG, Brazil*

[b]*Instituto de Química, Campus do Paricarana, UFRR, CEP69301-270, Boa Vista, RR, Brazil*

[c]*Departamento de Produtos Farmacêuticos, Faculdade de Farmácia, UFMG, Av. Olegário Maciel, 2360, 30180-112 Belo Horizonte, MG, Brazil*

Received 24 August 2001; revised 26 September 2001; accepted 27 September 2001

Abstract—Laurifolin (**1**), a novel mono-tetrahydrofuran acetogenin, has been isolated from *Rollinia laurifolia* leaves. The structure of **1** was elucidated by spectroscopic methods.

The number of studies on annonaceous acetogenins has increased in the last decade due to their broad range of potential bioactivities, as cytotoxic, antitumoral, pesticide, among others.[1,2] Only six species of *Rollinia* have already been studied, contributing new different types of annonaceous acetogenins. *Rollinia laurifolia* is a native tree of the Brazilian 'cerrado' and this is, to our knowledge, the first report on phytochemical studies of this plant. The investigation of the hexanic extract of leaves of *R. laurifolia* has led to the isolation of one novel C-35 mono-tetrahydrofuran acetogenin, to which we have given the trivial name laurifolin (**1**).

Leaves of *Rollinia laurifolia* were collected on the campus of Universidade Federal de Minas Gerais, voucher specimen (BHCB No 22749), in August of 1996. The hexanic extract obtained was fractionated on a silica gel column with a gradient of solvents, and eluted with CH_2Cl_2/EtOAc (9:1) giving a fraction, which was further purified by reverse phase MPLC to yield laurifolin (**1**, 0,0002% dry wt.).

Laurifolin (**1**) was obtained as a pale-yellow wax, $[\alpha]_D^{25} = +11.4$ (*c* 0.20, $CHCl_3$). The molecular formula $C_{35}H_{64}O_5$ was proposed by fast atom bombardment mass spectrometry (FAB–MS). IR and UV spectra of laurifolin (**1**), along with a positive Kedde's reaction, revealed the presence of a terminal α,β-unsaturated γ-lactone,[2] confirmed by ^1H and ^{13}C NMR spectroscopy (Table 1). These data also showed the absence of an OH group at C-4, due to a triplet at δ 2.26 relative to two equivalent H-3 protons and lactone ring signals slightly upfield-shifted.[3] The presence of a single THF ring, with two flanking hydroxyl groups in a *threo trans threo* relative configuration, was evidenced by ^1H NMR signals at δ 3.42 (H-19/24) and δ 3.81 (H-20/23), each integrating for two protons, as well as ^{13}C NMR peaks at δ 74.36 (C-19/24) and δ 82.66 (C-20/23). The

Table 1. ^{13}C NMR (100 MHz, $CDCl_3$) and ^1H NMR (400 MHz) data for laurifolin (**1**)

Position	δ_C	δ_H, *J* (Hz)
1	173.87	–
2	134.35	–
3	25.69	2.26
4	27.39	1.54
5–17	29.68–29.16	1.25
18	34.10	1.47
19	74.36	3.42
20	82.66	3.81
21	28.1–29.3	1.97; 1.76
22	28.1–29.3	1.97; 1.76
23	82.66	3.81
24	74.36	3.42
25	31.89	1.47
26–30	29.68–29.16	1.25
31	22.66	1.25
32	14.09	0.87
33	148.80	6.97
34	77.19	4.98
35	19.20	1.42

Keywords: annonaceae; acetogenins; antitumoral activity.

* Corresponding author. Tel.: (+55)3134995754; fax: (+55)-3134995700; e-mail: lpimenta@dedalus.lcc.ufmg.br

0040-4039/01/$ - see front matter
PII: S0040-4039(01)01829-9

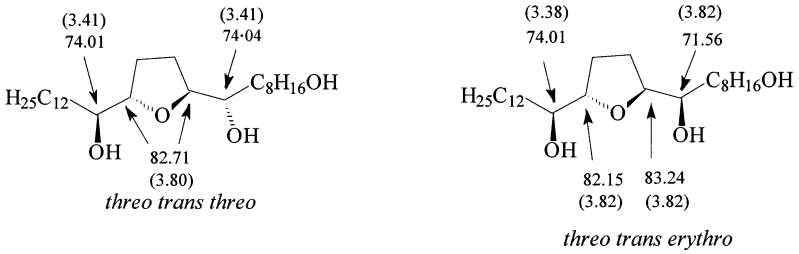

Figure 1. ^{13}C and ^{1}H NMR chemical shifts (^{1}H NMR in parenthesis) of synthetic chiral tetrahydrofuran model molecules: 1, 9*S*,14*S*-trihydroxy-10*S*,13*S*-epoxyhexacosane and 1, 9*R*,14*S*-trihydroxy-10*S*,13*S*-epoxyhexacosane.[2]

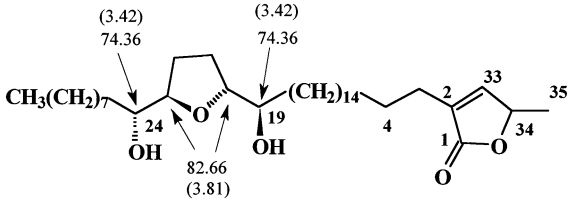

Figure 2. ^{13}C NMR, 100 MHz, Bruker ($CDCl_3$) and ^{1}H NMR, 400 MHz, ($CDCl_3$) (in parenthesis) chemical shifts of laurifolin (**1**) around the THF ring.

^{13}C NMR (Table 1) and DEPT experiments further confirmed the presence of four methine (δ 148.80, 82.66, 77.37, 74.36), two quaternary (δ 173.87 and 134.35) and two methyl carbon signals (δ 19.20 and 14.09). The location of the THF ring at C-20 through C-23 was determined by the EIMS fragmentation of **1** and its bis-TMSi derivative. The relative stereochemistry around the THF ring was determined by comparison with ^{1}H and ^{13}C NMR data of synthetic models of α,α'-dihydroxymonotetrahydrofuran compounds, related by Harmange et al.[2] According to these data, there are differences in chemical shifts of carbons bearing hydroxyl groups and their geminal protons when *threo* and *erythro* configurations are compared. These differences can also be noted in chemical shifts of carbons and protons adjacent to the oxygen atoms: δ 74.01, 82.71, 82.71 and 74.04 and δ 3.41, 3.80, 3.80 and 3.41 for *threo trans threo* relative configuration; δ 74.01, 82.15, 83.24 and 71.56 and δ 3.38, 3.82, 3.82 and 3.82 for *threo trans erythro*, in ^{13}C and ^{1}H NMR spectra, respectively (Fig. 1). For laurifolin (Fig. 2), only one signal was found at δ 82.66 and at δ 74.36, in the ^{13}C NMR spectrum, which are correlated to multiplets at δ 3.81 and 3.42, in the ^{1}H NMR spectrum, respectively, in accordance with the *threo trans threo* configuration.

In addition, identical chemical shifts of C-19/C-24 and C-20/C-23, found in laurifolin, can be observed in other known acetogenins that possesses the same relative configuration as tonkinecin 48, (2,4-*cis*)-murisolinone 26, annotemoyin-1 21 and murisolin.[2,4] The absolute configuration of the stereocenters has not been determined yet.

Acknowledgements

The authors thanks CAPES, FAPEMIG and CNPq for scholarship and financial support.

References

1. Cavé, A.; Cortes, D.; Figadère, B.; Laurens, A.; Pettit, G. R. *Progress in the Chemistry of Organic Natural Products*; Springer-Verlag: Wien, Austria, 1997; pp. 81–288.
2. Cavé, A.; Cortes, D.; Figadère, B.; Hocquemiller, B.; Laprévote, O.; Laurens, A.; Lebouef, M. In *Phytochemical of Tropical Plants*; Downum, K. R., Ed. Recent Advances in the Acetogenins of Annonaceae; Plenum Press: New York, 1993; pp. 163–202.
3. Zeng, L.; Ye, Q.; Oberlies, N. H.; Shi, G.; Gu, Z.-M.; He, K.; McLaughlin, J. *Nat. Prod. Rep.* **1996**, *13*, 275–306.
4. Harmange, J.-C.; Figadère, B.; Cavé, A. *Tetrahedron Lett.* **1992**, *33*, 5749–5752.