A CHLORINATED DIHYDROBENZOFURAN FROM *FLOURENSIA RIPARIA*

Uriburu, M.L.[*1] ; de la Fuente; J.R.[1]; Palermo, J.[2] Sosa, V.E.[3]

[*1]Consejo de Investigación, Universidad Nacional de Salta, Av. Bolivia 5150. CP: 4400, Salta, Argentina, FAX: +54 387 4255363, * E-Mail: luriburu@unsa.edu.ar

[2]Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina

[3]Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Instituto Multidisciplinario de Biología Vegetal IMBIV (CONICET-UNC), Córdoba, Argentina

Received February 14, 2005. In final form June 28, 2005

Abstract

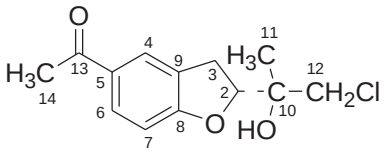
*A new chlorinated compound, 5-acetyl-2,3-dihydro-2-(2-[1-chloro-2-hydroxypropyl])-benzofuran (**1**) has been isolated from the chloroformic extract of the aerial parts of Flourensia riparia Griseb., along with the previously known benzofuran 2,3-dihydro-11,12-dihydroxyeuparin (**2**). Structural characterization was carried out by spectroscopic methods.*

Resumen

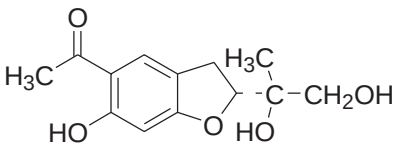
*A partir del extracto clorofórmico de partes aéreas de Flourensia riparia Griseb., se identificó el nuevo compuesto clorado, 5-acetil-2,3-dihidro-2-(2-[1-cloro-2-hidroxipropil])-benzofurano (**1**) y 2,3-dihidro-11,12-dihidroxieuparina (**2**), un derivado previamente descripto. Las determinaciones estructurales se realizaron mediante métodos espectroscópicos.*

Introduction

In the course of our studies on *Flourensia riparia* Griseb., we reported the presence of 8-prenyl-flavonoids, some *p*-hidroxyacetophenone derivatives, and eudesmanolide sesquiterpenes [1]. We proposed that the sesquiterpene pattern may be a valuable tool for chemosystematic approaches in this genus. As part of our study on the phytochemistry of the *Flourensia* genus, we report here the isolation and structural determination of the new derivative 5-acetyl-2,3-dihydro-2-(2-[1-chloro-2-hydroxyipropyl])-benzofuran (**1**) and the previously known 2,3-dihydro-11,12-dihydroxyeuparin (**2**). Both compounds are minor constituents of *F. riparia.*



1



2

Experimental

General

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 200 spectrometer at 200.13 and 50.32 MHz, respectively. HR-EIMS was measured on a ZAB-SEQ 4F spectrometer. EIMS was collected on a TRIO-2 VG MASS LAB spectrometer. HPLC separations were performed with a SP thermoseparation products Spectra Series P_{100} apparatus using both refractive index, and UV detectors at 310 nm (Shodex R_1-71). Semipreparative HPLC were carried out via a YMC RP-18 reversed phase column (250 x 20 mm) at a flow rate of 5.0 ml/min. IR spectral data were recorded on a FT-IR Bruker Model IFS-88.

Plant material

Flourensia riparia Griseb. was collected in December 1995, in El Maray, Province of Salta, Argentina and identified by L. Novara. A voucher specimen (Nº 10765) is deposited in the Museum of the Faculty of Exact Sciences, Salta National University.

Isolation procedure

Dried and powdered aerial parts of *F. riparia* (1.2 kg) were extracted with MeOH under reflux, the solvent was evaporated, and the residue was partitioned between hexane-MeOH-H_2O 10:3:1. The aqueous MeOH layer was washed with hexane, concentrated and extracted with $CHCl_3$. The $CHCl_3$ extract (4g) was chromatographed on silica gel 60 (Merck) using a step-gradient of $CHCl_3$-Me_2CO and Me_2CO. The fraction eluted with $CHCl_3$-Me_2CO 3:1 was subjected to semi-preparative HPLC using MeOH-H_2O 3:1 as eluant, to afford 5.0 mg of **1**. The fraction eluted from silica gel with $CHCl_3$-Me_2CO 1:1 was subjected to semipreparative HPLC with CH_3CN-H_2O 1:1 as eluant and further purified by preparative TLC (CH_3CN-H_2O 1:1) to yield 2.9 mg of compound **2**.

Additionally, a separation procedure was devised which rigorously excluded chlorine-containing solvents, a potential supplier of chlorine. Aerial parts of *F. riparia* (876 g) were extracted with EtOH at room temperature. The residue, after evaporation of the solvent was suspended in MeOH and H_2O, and extracted with hexane. The aqueous-alcoholic phase was concentrated and extracted with Et_2O. The extract (3.2 g) was subjected to VLC on reversed phase. The fraction eluted with MeOH-H_2O 8:2 was further cromatographed by flash column chromatography. Compound **1** was identified by TLC comparison with an authentic sample in the fraction eluted with hexane-AcOEt 1:1 (Rf = 0.32 , hexane-AcOEt 7:3, Rf = 0.64, hexane-AcOEt 1:1, Rf = 0.58, MeOH-H_2O 8:2).

5-acetyl-2,3-dihydro-2-(2-[1-chloro-2-hydroxypropyl])-benzofuran (**1**)

Gum. HR-EIMS $(M)^+$ 254.0707 (calcd 254.0709 for $C_{13}H_{15}ClO_3$). EIMS *m/z* (rel. int.): 254 (M^+, 30.0), 256 (9.9), 205 (M^+-CH_2Cl, 2.9), 181 (20.1), 161 (M^+- $C(CH_3)OH$-CH_2Cl, 36.6), 145 (15.7), 119 (16.5). ν_{max}^{KBr} : cm^{-1}: 3490 (-OH), 2970, 2927, 1743 (C=O), 1660, 1606 (C=C), 1271, 1244, 786, 742. ^1H and ^{13}C NMR spectral data are listed in Table 1.

Table 1

*$^1H^a$ and $^{13}C^b$ NMR spectral data of compound **1** (in $CDCl_3$, TMS as internal standard.)*

	1	
	^{13}C	^1H
2	86.4 (*d*)	5.00 (*dd*, 9.0, 8.9)
3	29.6 (*t*)	3.35 (*dd*, 16.0, 8.9)
3’		3.20 (*dd*, 16.0, 9.0)
4	125.6 (*d*)	7.82 (*d*, 1.8)
5	131.2 (s)	-
6	130.4 (*d*)	7.79 (*dd*, 8.5, 1.8)
7	109.0 (*d*)	6.81 (*d*, 8.5)
8	163.4 (*s*)	-
9	127.5 (*s*)	-
10	73.6 (*s*)	-
11	20.7 (*q*)	1.33 (*s*)
12	50.0 (*t*)	3.75 (*d*, 10.9)
12’		3.64 (*d*, 10.9)
13	196.7 (*s*)	-
14	26.4 (*q*)	2.53 (*s*)

[a] *multiplicity (J in Hz) (200.13 MHz)*
[b] *at 50.32 MHz*

2,3-dihydro-11,12-dihydroxyeuparin (**2**).

Gum. EIMS m/z (rel. int.): 252 (M^+, 4.0), 221 (M^+-CH_2OH, 1.6), 177 (M^+-$C(CH_3)OH$-CH_2OH, 8.3). ^{13}C NMR (50.32 MHz, $CDCl_3$): δ 89.7 (*d*, C-2), 29.2 (*t*, C-3), 126.9 (*d*, C-4), 165.8* (*s*, C-6), 98.4 (*d*, C-7), 166.1* (*s*, C-8), 118.7 (*s*, C-9), 73.3 (*s*, C-10), 19.9 (*q*, C-11), 68.6 (*t*, C-12), 26.4 (*q*, C-14). (C-5 and C-13 are unobservable signals. Signals followed by asterisks may be exchangeable).

Discussion

From the chloroform extract of the aerial part of *F. riparia* we isolated the new chlorinated dihydrobenzofuran 5-acetyl-2,3-dihydro-2-(2-[1-chloro-2-hydroxypropyl])-benzofuran (**1**) and the known compound 2,3-dihydro-11,12-dihydroxyeuparin (**2**) [2].

The molecular formula of **1** was determined by HR-EIMS as $C_{13}H_{15}ClO_3$. In the EIMS, two significant peaks at *m/z* 254 (30.0 %) and 256 (9.9 %), revealed the presence of one chlorine atom. The ^{1}H NMR spectrum showed signals that supported the presence of the 5-acetyldihydrobenzofuran moiety which were in good agreement with those reported for tremetone [3]. An AB system centered at δ 3.69 revealed the presence of a chloromethylene group at C-2 position of the side chain. The C-Cl linkage in the aliphatic moiety was further supported by the signal at δ 50.02 in the ^{13}C NMR spectrum (Table 1). The peaks at *m/z* 205 (M^+- CH_2Cl) and 161 (M^+- $C(CH_3)OH$ CH_2Cl also supported the structure of the C-2 moiety. Consequently, the structure of **1** was established as 5-acetyl-2,3-dihydro-2-(2-[1-chloro-2-hydroxypropyl])-benzofuran.

To establish the natural origin of compound **1** a second batch of plant was extracted and worked up with chlorine-free solvents. The presence of compound **1** in this second extract was demonstrated by TLC and ^{1}H NMR. These experiences allowed us to confirm compound **1** as a natural occurring compound.

Compound **2** was unambiguously identified by comparison with literature data [2]. To the best of our knowledge the ^{13}C NMR data of **2** have not been previously reported (see Experimental).

Conclusions

Since organochlorine compounds are uncommon in terrestrial plants, it was possible that **1** may have been formed during the isolation procedure. However, in this case, the natural origin of compound **1** was unambiguously demonstrated. The co-ocurrence of naturally clorhydrin compounds in the Asteraceae is well-documented [4]. These compounds are most certainly derived from precursors with a terminal double bond, which could be transformed into a chlorohydrin probably via epoxidation and subsequent chloride anion attack [4].

Acknowledgments

This work was supported by the Consejo de Investigación, Universidad Nacional de Salta, Argentina and by the Instituto Multidisciplinario de Biología Vegetal IMBIV CONICET, Universidad Nacional de Córdoba, Argentina.

References

[1] Uriburu, M.L.; de la Fuente, J.R.; Palermo, J.; Gil, R.; Sosa, V.E., *Phytochemistry*, **2004**, *65*, 2039-2043.
[2] Spring, O.; Vargas, D.; Fischer, N.H., *Phytochemistry*, **1991**, *30*, 1861-1867.
[3] Zalkow, L.H.; Ekpo, B.A.; Gelbaum, L.T.; Harris, R.N. III, Keinan, E.; Novak, J.R.; Ramming, C.T.; Van Derveer, D., *J. Nat. Prod*. **1979**, *42*, 203-219.
[4] Engvild, K.C., *Phytochemistry*, **1986**, *25*, 781-791.