REVISTA BOLIVIANA DE QUÍMICA
Bolivian Journal of Chemistry
Received 06 06 2013

Vol. 30, No.1, pp. 80-83, Ene./Ago. 2013
30(1) 80-83, Jan./Aug. 2013
Published 20 09 2013

FURANOEREMOPHILANES FROM *SENECIO CLIVICOLUS* WEDDELL

*Marcelo Dávila[a,b]; Olov Sterner[a]; Nelson Hinojosa[b]**

[a]Centre for Analysis and Synthesis, Lund University, P.O. Box 124, SE-221 00, Lund, Sweden.; [b]Centro de Tecnología Agroindustrial, Facultad de Ciencias y Tecnología, Universidad Mayor de San Simón, P.O. Box, Cochabamba, Bolivia.

Keywords: *Furanoeremophilanes, Senecio clivicoulus*

ABSTRACT

A phytochemical investigation of the dried aerial parts of *Senecio clivicolus* Weddell led to the isolation of four furanoeremophilane sesquiterpenes. Their structures and relative configuration were established by NMR and HRMS-ESI analyses, and by comparison with data reported in the literature. Their presence in *S. clivicolus* is reported for the first time.

*Corresponding author: hinojosanel@yahoo.com.ar

INTRODUCTION

Senecio represent the largest genus of the family Asteraceae and has more than 1500 species [1]. Senecio species are used in traditional medicine for many purposes, such as a remedy for gastric-ulcer and stomach pain [2], chest pain, cough, fever and running nose [3, 4]. In the north region of Argentina *S. graveolens* is used to counteract mountain sickness, digestive and cough suppressant[5]. Of the 114 species of *Senecio* reported to grow in Bolivia [6], *Senecio clivicolus* is a perennial shrub growing in the mountainous regions. The leaves of *S. clivicolus* have been used to relieve the stomach pain [7] and as a anti-diarrhea remedy [8]. Moreover, the extract has been reported to be used to treat skin fungal infections[9].Only one phytochemical investigation of *S. clivicolus* has been reported so far [10], in which alpha-farnesene, germacrene D and 1-pentadecene were isolated and characterized. This study reports the isolation and chemical characterization of four furanoeremophilanes (Figure 1) from an ethanol extract of the dried aerial parts of *S. clivicolus*: decompostin (**1**), 6β-acetoxy-9-oxo-10α*H*-furanoeremophilane (**2**), 1α-hydroxy-6β-acetoxy-9-oxo-10α*H*-furanoeremophilane (**3**) and 1α-acetoxy-6β-acetoxy-9-oxo-10α*H*-furanoeremophilane (**4**).

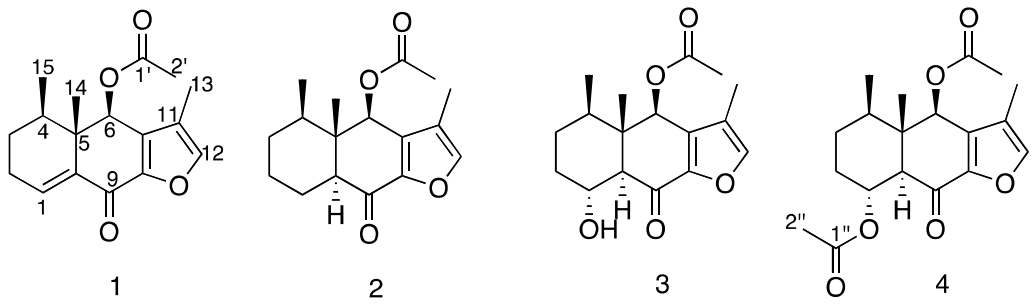

Figure 1. *Structures of compounds* ***1-4****.*

RESULTS AND DISCUSSION

The elemental composition of compound **1** was determined to be $C_{17}H_{20}O_4$, based on the 1D NMR spectra (^{1}H and ^{13}C NMR data for all four compounds are given in Table 1) as well as HRMS-ESI data. **1** consequently has eight degrees of unsaturation, and as the NMR data show the presence of three carbon-carbon double bonds and two carbonyl groups **1** is tricyclic. In the ^{1}H NMR spectrum a signal corresponding to a furan ring proton was observed at δ 7.41 (1H, q, *J*=1.0; 12-H), which in the COSY spectrum correlates with the methyl signal at δ 1.93 (3H, d, *J*=1.0; 13-H_3). In addition to this, and besides a methyl group obviously belonging to an acetyl group (δ 2.20, 3H, s), the proton spectrum indicated the presence of another two methyls by the signals at δ 1.09 (3H, s; 14-H_3) and δ0.99 (3H, d, *J*=6.8; 15-H_3). COSY and HMBC correlations from these as well as 1-H (δ 6.94, 1H, ddd, *J*=4.9, 3.2, 0.8) close

the left ring, and show that the acetoxy substituted C-6 is next to C-5 and that the carbonyl group C-9 is adjacent to C-10. HMBC correlations from 6-H, 12-H and 13-H_3 reveal all components of the furan ring, and the final bond between C-8 and C-9 is inevitable. The relative configuration of **1** was elucidated based on the NOESY correlations observed between H-6 and H-4 as well as between 14-H_3 and 15-H_3. The structure of compound **1** isolated here is identical to decompostin, previously reported from *Cacalia decomposita*[11] and *Psacalium beamanii*[12]. The HRMS-ESI of compound **2** indicated that its elemental composition is $C_{17}H_{22}O_4$, **2** consequently has one unsaturation less than **1**. Comparison of the spectroscopic data of **1** and **2** revealed that the C-1/C-10 double bond in **1** is a single bond in **2**, and COSY as well as HMBC correlations established the structure. The relative configuration of **2** was determined based on NOESY correlations between the three protons 4-H, 6-H and 10-H, and **2** was found to be identical to 6β-acetoxy-9-oxo-10α*H*-furanoeremophilane, previously reported from *S. chilensis and S. patagonicus*[13]. However, the ^{13}C NMR data reported [13] are significantly different from those recorded here, indicating that it is necessary to correct the chemical shifts for C-1, C-2, C-3, C-14 and C-15 in the literature. The NMR data of compound**3** ($C_{17}H_{22}O_5$ according to HRMS-ESI) and **4** ($C_{19}H_{24}O_6$ according to HRMS-ESI) are similar to those of compounds**1** and **2**, with the exception for the signals assigned to C-1 and C-10. In both **3** and **4** C-1 is oxygenated while C-10 is protonated, and extensive 2D NMR experiments show that, compared to **1**, the C-1/C-10 double bond had added water in **3** and acetic acid in **4**. NOESY correlations were observed between 1-H and 14-H_3, as well as between 4-H, 6-H and 10-H in both compounds, establishing their relative configuration. Based on these data the structures were established as 1α-hydroxy-6β-acetoxy-9-oxo-10α*H*-furanoeremophilane **3** and 1α-acetoxy-6β-acetoxy-9-oxo-10α*H*-furanoeremophilane **4**. Compounds **3** and **4** have previously been reported from *S. santelisis*[14].

Table 1: *^{13}C- and ^{1}H-NMR data of compounds 1-4.*

Position	1[a]		2[b]		3[b]		4[b]	
	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H
1	138.3	6.94 ddd (4.9,3.2,0.8)	20.6	2.18 m* 1.41 m*	66.4	4.14 m	67.3	5.28 m
2	25.5	2.24 m* 2.24 m*	24.5	1.82 m* 1.29 m*	32.9	2.04 m 1.40 m*	31.3	2.11 m 1.40 m*
3	28.2	1.55 m* 1.45 m*	32.2	1.41 m* 1.29 m*	30.3	1.49 m* 1.40 m*	29.9	1.40 m* 1.40 m*
4	38.1	1.95 m*	42.1	1.82 m*	41.7	1.87 m*	41.5	1.86 m*
5	46.8		49.8		51.0		51.4	
6	74.9	6.29 s	75.7	6.33 s	75.2	6.34 s	75.3	6.36 s
7	136.0		134.6		136.2		133.8	
8	147.2		146.7		146.5		147.1	
9	176.5		186.7		189.3		184.7	
10	141.7		55.1	2.37 dd (12, 3.5)	60.8	2.37 d (9.5)	58.0	2.65 d (10.5)
11	121.5		120.7		121.2		120.7	
12	146.2	7.41 q (1.0)	145.1	7.33 br.	146.2	7.39 q (1.0)	145.1	7.32 q (1.0)
13	8.6	1.93 d (1.0)	8.5	1.91 br.	8.6	1.91 d (1.0)	8.67	1.88 d (1.0)
14	15.5	1.09 s	7.6	0.91 s	8.9	0.95 s	8.69	0.95 s
15	17.7	0.99 d (6.8)	17.7	0.89 d (6.6)	17.6	0.90 d (6.6)	17.5	0.91 d (6.6)
1'	171.0		170.3		170.9		171.0	
2'	21.6	2.20 s	21.6	2.18 s	21.6	2.17 m	21.6	2.16 s
1''							170.6	
2''							21.4	2.02 s
1-OH						4.52 d (1.7)		

Spectra recorded in: [a]Dichloromethane-d_2, [b]Chloroform-*d*. * Overlapping. Assignments were based on COSY, HMQC, HMBC, DEPT and NOESY experiments

EXPERIMENTAL

General experimental procedures

The optical rotations were measured with a Perkin-Elmer 341 polarimeter at 20°C. HRMS-ESI spectra were recorded with a Waters Q-TOF Micro system spectrometer, using H_3PO_4 for calibration and as internal standard. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were measured with a Bruker DRX400 spectrometer; the spectra were recorded in chloroform-*d* (solvent residual signals at δ_H 7.26 and δ_C 77.16) and dichloromethane-d_2 (solvent residual signals at δ_H 5.32 and δ_C 53.84). The chemical shifts (δ) are given in ppm, and coupling constants (*J*) in Hz. Vacuum liquid chromatography (VLC) and centrifugal preparative TLC (CTLC) separations were carried out using TLC

grade silica gel (Merck), while column chromatography were run on silica gel 60 (230-400 mesh, Merck). TLC analyses were carried out on silica gel GF_{254} pre-coated plates (Merck); chromatograms were visualized under a UV lamp (254 nm) and by spraying with vanillin (6%)-sulfuric acid (1.5%)-ethanol solution, followed by heating.

Plant material

The whole aerial parts of *Senecio clivicolus* Weddell were collected from south of Cochabamba-Bolivia at 2900 meters above sea level in April 2008. A voucher specimen (MZ-3741) was deposited at National Herbarium "Herbario Nacional Martin Cardenas" at Cochabamba-Bolivia.

Extraction and isolation

The air-dried powdered plant material (500 g) was extracted with 95% ethanol (3x1 L) for 3 days at room temperature. Removal of the solvent from the filtrate under reduces pressure provided an extract (70 g). Part of the extract was suspended in ethanol-water (80:20) and successively partitioned with hexane and chloroform. The chloroform fraction (15 g) was precipitated with ethyl acetate to yield a dark brown precipitate (550 mg) and a dark liquid, which was subjected to vacuum liquid chromatography on silica gel using heptane-ethyl acetate (80:20) as solvent. Ten main fractions were collected (1-10). Fraction 4 (570 mg) was precipitated with methanol to give a yellow precipitate that was purified by centrifugal preparative TLC with heptane-ethyl acetate (80:20) to yield compound **1** (15 mg). Fraction 3 (3.37 g) was precipitated with methanol to give compound **2** (20 mg). Furthermore, fraction 7 (350 mg) was washed with heptane and then subjected to column chromatography on silica gel eluted with toluene-diethyl ether (25:3.5) to give six fractions (A-F). Compound **3** (5 mg) was purified from fraction F by column chromatography using a mixture of heptane-ethyl acetate (70:30) as the eluent. Finally, fraction C contains compound **4** (60 mg).

Decompostin (**1**).

1 was obtained as a white amorphous solid. mp 195-198 °C. $[\alpha]_D^{20}$ -60° (*c* 0.60, $CHCl_3$). ^1H NMR (CD_2Cl_2 400 MHz) and ^{13}C NMR (CD_2Cl_2 100 MHz), see Table 1. HRMS-ESI calculated for $C_{17}H_{20}O_4$ $(M+H)^+$ 289.1440. Found: 289.1445.

6β-acetoxy-9-oxo-10αH-furanoeremophilane (**2**).

2 was obtained as a white amorphous solid. mp 147-150 °C. $[\alpha]_D^{20}$ -72° (*c* 0.70, $CHCl_3$) ^1H NMR ($CDCl_3$ 400 MHz) and ^{13}C NMR ($CDCl_3$ 100 MHz), see Table 1. HRMS-ESI calculated for $C_{17}H_{22}O_4$ $(M+H)^+$ 291.1596. Found: 291.1586.

1α-hydroxy-6β-acetoxy-9-oxo-10αH-furanoeremophilane **(3).**

3 was obtained as a yellowish oil. $[\alpha]_D^{20}$ -12° (*c* 0.20, $CHCl_3$) ^1H NMR ($CDCl_3$ 400 MHz) and ^{13}C NMR ($CDCl_3$ 100 MHz), see Table 1. HRMS-ESI calculated for $C_{17}H_{22}O_5$ $(M+H)^+$ 307.1545. Found: 307.1555.

1α-acetoxy-6β-acetoxy-9-oxo-10αH-furanoeremophilane **(4).**

4 was obtained as a white amorphous solid. mp 149-151 °C. $[\alpha]_D^{20}$ -84° (*c* 0.37, $CHCl_3$). ^1H NMR ($CDCl_3$ 400 MHz) and ^{13}C NMR ($CDCl_3$ 100 MHz), see Table 1. HRMS-ESI calculated for $C_{19}H_{24}O_6$ $(M+H)^+$ 349.1651. Found: 349.1654.

ACKNOWLEDGMENTS

The authors gratefully acknowledge financial support from Swedish International Development Cooperation Agency (SIDA). We thank Lic. Modesto Zárate from the National Herbarium "Herbario Nacional Martin Cardenas", for the taxonomic determination of the plant material.

.

REFERENCES

[1] MOHAMED, A. E.-H. H., AHMED, A.
J. Nat. Prod., 2005, **68**, 439.
[2] HARIPRASATH, L., RAMAN, J., NANJIAN, R.
J. Ethnopharmacol., 2012, **140**, 145.
[3] GU, J.-Q., WANG, Y., FRANZBLAU, S. G., MONTENEGRO, G., TIMMERMANN, B. N.
J. Nat. Prod., 2004, **67**, 1483.
[4] YORK, T., DE WET, H., VAN VUUREN, S. F.
J. Ethnopharmacol., 2011, **135**, 696.
[5] PÉREZ, C., AGNESE, A. M., CABRERA, J. L.
J. Ethnopharmacol., 1999, **66**, 91.
[6] CABRERA, A. L.
Darwiniana (San Isidro), 1985, **26**, 79.
[7] VANDEBROEK, I., THOOMAS, E., AMETRAC.,
Las plantas medicinales para la atención primaria de la salud. El conocimiento de ocho medicos tradicionales de Apillapampa (Bolivia). Indústrias Gráficas Serrano, Cochabamba-Bolivia: 2003; p 260.
[8] FOURNET, A., BARRIOS, A. A., MUÑOZ, V.
J. Ethnopharmacol., 1994, **41**, 19.
[9] BUSTAMANTE, G. Z., ESCALANTE, L. A., MEJIA, U. V., VALDIVIA, M. O., SORIA, I. J.,
Estudio etnobotánico y actividad antimicrobiana de las plantas medicinales de los valles bajos de Cochabamba. Universidad Mayor de San Simón, Cochabamba-Bolivia: 2001; p 78.
[10] BOHLMANN, F., ZDERO, C.
Phytochemistry, 1979, **18**, 125.
[11] RODRÍGUEZ-HAHN, L., GUZMÁN, A., ROMO, J.
Tetrahedron, 1968, **24**, 477.
[12] PÉREZ-CASTORENA, A. L., ARCINIEGAS, A., VILLASEÑOR, J. L., ROMO DE VIVAR, A.
Journal of the Mexican Chemical Society, 2004, **48**, 21.
[13] VILLARROEL, L., TORRES, R., GAVIN, J., REINA, M., DE LA FUENTE, G.
J. Nat. Prod., 1991, **54**, 588.
[14] ARIAS CASSARA, M. L., BORKOSKY, S. A., SIERRA, M. G., BARDON, A., YBARRA, M. I.
Chemistry & biodiversity, 2010, **7**, 1745.