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Two new *O*-geranyl coumarins from the resinous exudate of *Haplopappus multifolius*

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Abstract

From the resinous exudate of leaves of *Haplopappus multifolius* two new coumarins were isolated and assigned the structures 6-hydroxy-7-(5′-hydroxy-3′,7′-dimethylocta-2′,6′-dien)-oxycoumarin (**1**) and 6-hydroxy-7-(7′-hydroxy-3′,7′-dimethylocta-2′,5′-dien)-oxy coumarin (**2**).

Keywords: *Haplopappus multifolius*; Coumarins

1. Introduction

The vernacular name of 'bailahuén' is addressed to a series of *Haplopappus* species (Asteraceae) used in the Chilean folk medicine [1]. *Haplopappus baylahuen* Remy, *H. multifolius* Phil ex Reiche, *H. angustifolius* (DC) Reiche, *H. latifolius* (DC) Reiche, *H. villanuevae* Phil, *H. rigidus* Phil and *H. foliosus* DC are the identified members of this group [2]. All these species produce a great quantity of resinous exudates from twigs and leaves. Albeit the medicinal properties of

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'bailahuén' were associated with the resinous material [3], little work has been done about the chemistry and biological activities of these mixtures [4,5].

Previous studies on the whole plant of *H. multifolius*, a shrub growing in the mountains near Santiago de Chile, resulted in the isolation and characterization of coumarins [6], flavonoids [7] and terpenoids [8]. This paper deals with the structure determination of two new coumarins, isolated from the resinous exudate of the plant.

2. Experimental

2.1. Plant material

Leaves of *Haplopappus multifolius* were collected at Farellones (Region Metropolitana, Chile, 33°21′S, 70°21′W) in Summer 1999. A voucher specimen was deposited at the Herbarium of the Museo Nacional de Historia Natural de Santiago de Chile and authenticated by Dr Mélica Muñoz.

2.2. Extraction and isolation

Fresh material (1 kg) was extracted by dipping in cold CH_2Cl_2 for 30 s. Evaporation of the extract gave an oily residue (84 g). A part (45 g) of the resinous exudate was Si-gel CC eluting with hexane and increasing volumes of EtOAc affording prenyletin, esculetin and haplopinol previously isolated from the whole plant [6]. Fraction F-8 contained a mixture of compounds, which were separated by PTLC to give coumarins **1** (250 mg) and **2** (300 mg).

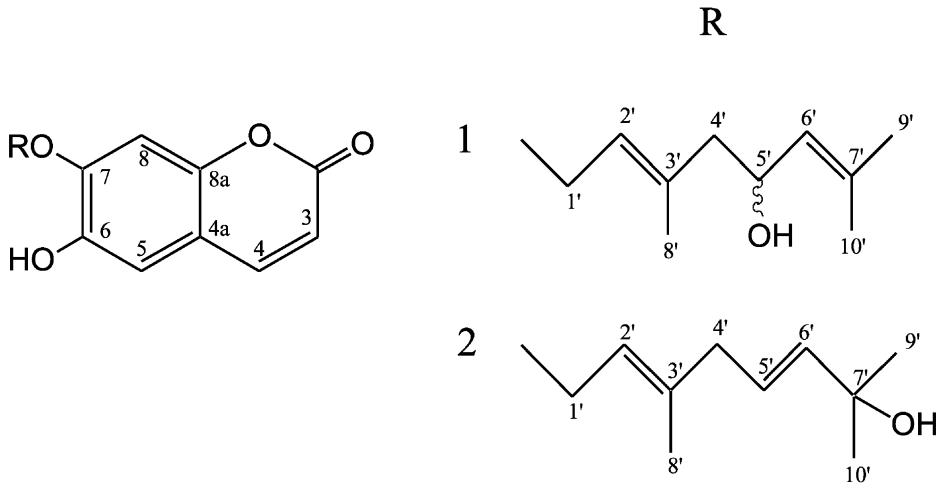

Fig. 1. Compounds **1** and **2**

6-Hydroxy-7-(5′-hydroxy-3′,7′-dimethylocta-2′,6′-dien)-oxycoumarin (**1**). Foam; $[\alpha]_D$−18 (c 0.2, $CHCl_3$); UV max (MeOH): 338, 296, 260, 252, 242 nm; IR bands ($CHCl_3$) : 3600, 3540, 1710, 1610 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.59 (1H, *d*, *J* 9.5 Hz, H-4), 6.95 (1H, *s*, H-5), 6.80 (1H, *s*, H-8), 6.26 (1H, *d*, *J* 9.5 Hz, H-3), 5.59 (1H, *t*, *J* 6.3 Hz, H-2′), 5.18 (1H, *d*, *J* 8.0 Hz, H-6′), 4.66 (2H, *d*, *J* 6.3 Hz, H-1′), 4.54 (1H, *m*, H-5′), 2.26 (2H, *m*, H-4′), 1.82 (3H, *s*, H-9′), 1,70 (6H, *s*, H-8′ and H-10′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 161.6 (C-2), 149.4, 148.9 (C-6 and C-7), 143.4 (C-4), 143.0 (C-8a), 139.9 (C-3′), 135.4 (C-7′), 127.2 (C-6′), 120.8 (C-2′), 113.5 (C-3), 112.1 (C-4a), 111.1 (C-5), 100.2 (C-8), 66.3 (C-1′), 65.9 (C-5′), 47.5 (C-4′), 25.6 (C-9′), 18.1 (C-10′), 17.0 (C-8′); MS, *m*/*z*: 330 $[M]^+$ (2), 312 $[M - H_2O]^+$ (18), 178 $[M - C_{10}H_{16}O]^+$ (100). *Diacetyl derivative* (Ac_2O/pyridine); ^{1}H-NMR (300 Mz, $CDCl_3$): δ 7.15 (H-5), 6.85 (H-8), 5.65 (H-5′), 2.32 (CH_3CO_2-6), 1.99 (CH_3CO_2 -5′).

Compound **1** (22 mg) was left in 2 N H_2SO_4 in MeOH for 3 h affording 6,7-dihydroxycoumarin (8 mg).

6-Hydroxy-7-(7′-hydroxy-3′,7′-dimethylocta-2′,5′-dien)-oxycoumarin (**2**). Pale oil; $[\alpha]_D$ 0; UV max (MeOH): 335, 290, 260, 250, 242 nm; IR bands ($CHCl_3$) : 3600, 3540, 1720, 1630 cm^{-1}; ^{1}H-NMR (300 Mz, $CDCl_3$): δ 7.59 (1H, *d*, *J* 9.5 Hz, H-4), 6.96 (1H, *s*, H-5), 6.82 (1H, *s*, H-8), 6.28 (1H, *d*, *J* 9.5, H-3), 5.70 (1H, *d*, *J* 15.5, H-6′), 5.61 (1H, *dt*, *J* 15.5, 5.5 Hz, H-5′), 5.50 (1H, *t*, *J* 6.8 Hz, H-2′), 4.67 (2H, *d*, *J* 6.8, H-1′), 2.78 (2H, *d*, *J* 5.5 Hz, H-4′), 1.76 (3H, *s*, H-8′), 1.32 (6H, *s*, H-9′ and H-10′); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 161.5 (C-2), 149.3, 149.0 (C-6 and C-7), 143.4 (C-4), 142.9, 142.1 (C-8a and C-3′), 140.6 (C-6′), 123.5 (C-2′), 118.6 (C-5′), 113.7 (C-3), 112.1 (C-4a), 111.0 (C-5), 100.3 (C-8), 70.7 (C-7′), 66.2 (C-1′), 42.0 (C-4′), 29.8 (C-9′ and C-10′), 16.8 (C-8′); MS *m*/*z*: 330 $[M]^+$ (10), 312 $[M\text{-}H_2O]^+$(15), 178 $[M\text{-}C_{10}H_{16}O]^+$ (100). *Monoacetyl derivative* (Ac_2O/pyridine); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.15 (H-5), 6.85 (H-8), 2.32 (CH_3CO_2-6).

Compound **2** (20 mg) was left in 2 N H_2SO_4 in MeOH for 3 h affording 6,7-dihydroxycoumarin (6 mg).

3. Results and discussion

Extended chromatography of the CH_2Cl_2 extract from the aerial part of *H. multifolius* afforded prenyletin, esculetin and haplopinol, previously reported from the whole plant [6].

The ^{1}H-NMR spectra of two further metabolites (**1** and **2**) showed the signals for two coupled (*J* 9.5 Hz) olefinic protons and two isolated aromatic protons, while the IR and ^{13}C-NMR spectra agreed on a coniugated carbonyl group. Accordingly, the UV spectra exhibited values consistent with the skeleton of a 6,7-dioxygenated coumarin. On consideration of ^{1}H-, ^{13}C-NMR and mass spectra (M^+ at *m*/*z* 330 for both **1** and **2**) the two isomeric coumarins were attributed a molecular formula $C_{19}H_{22}O_5$. The base peak in the mass spectra at *m*/*z* 178^+ corresponding to the molecular weight of a dihydroxycoumarin ($C_9H_6O_4$) suggested the presence of a $C_{10}H_{16}O$ substituent on one (C-6 or C-7) of the hydroxy-groups. The location of

the chain was established by DIF NOE experiments. The assignment of aromatic protons was confirmed by the downfield shifts of 0.2 ppm for H-5 in the ^{1}H-NMR spectra of the 6-*O*-acetyl derivatives: notably, **1** gave a diacetyl derivative and **2** a monoacetyl derivative.

The component groups and connectivities of two chains were revealed by ^{1}H- and ^{13}C-NMR spectra and decoupling experiments. For compound **1**: revealed three vinylic methyl groups; an oxymethylene linked to a trisubstituted double bond; an oxymethine linked to a methylene and to a trisubstituted double bond. These data suggested the -*O*-C-7 substituent to be a 5′-hydroxygeranyl-chain with an acetilable hydroxy-group. Compound **1** was thus assigned the structure 6-hydroxy-7-(5′-hydroxy-3′,7′-dimethylocta-2′,6′-dien)-oxy-coumarin.

The C_{10} substituent of compound **2** was characterized as follows: a vinylic and two quaternary methyl groups, an oxymethylene linked to a trisubstituted double bond, a methylene inserted between two double bonds and a 7′-hydroxy-group.

In conclusion, compound **2** was assigned the structure 6-hydroxy-7-(7′-hydroxy-3′,7′-dimethylocta-2′,5′-dien)-oxy-coumarin.

Acknowledgments

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