A novel labdane diterpene from *Acritopappus longifolius*

Fernanda Peres Ferreira, Eduardo Henck Marturano, Carlos Alexandre Carollo, Dionéia Camilo Rodrigues de Oliveira

Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Av. Café, s/n, CEP 14040-903, Ribeirão Preto, SP, Brazil

**Abstract**

A novel labdane diterpene was isolated from the plant *Acritopappus longifolius*. The structure of this compound was established by 1D- and 2D-nuclear magnetic resonance spectroscopic techniques and mass spectrometry data. *N*-Methyl-4-hydroxy-trans-proline, stigmasterol-3-β-D-glycoside, and the flavonoids quercetin, luteolin, kaempferol, and rutin were also isolated.

**Keywords:**

Acritopappus

*Acritopappus longifolius*

Asteraceae

Labdane diterpene

---

*Acritopappus* (family Asteraceae, tribe Eupatorieae, and subtribe Ageratinae) is a small genus restricted to Eastern Brazil. Sixteen species of this genus are known to date.¹⁻³ According to King and Robinson, the name *Acritopappus* is due to the irregularity of its pappus form, which accounts for the misplacement of some plant species in this tribe. Recently, some species of *Ageratum*, a genus belonging to this same subtribe, were reclassified by King and Robinson and placed in the *Acritopappus* genus, namely *Acritopappus longifolius*, *Acritopappus confertus*, and *Acritopappus irwinii*.¹

Sesquiterpenes, labdane and kolavane diterpenes, triterpenes, steroids, coumarins, acetylenes, flavonoids, and benzofurans derivatives have been reported to occur in this genus.⁴⁻¹⁰ Indeed, sesquiterpenes, diterpenes, coumarin, and steroid have been isolated from *A. longifolius* in previous studies.⁹,¹⁰

The present study consists of a chemical re-investigation of *A. longifolius*. Along with known compounds, such as flavonoids, steroid, and an unusual amino acid, a novel labdane diterpene has been isolated. This report describes the structural elucidation and a plausible biogenetic pathway for this new compound.

The total plant of *A. longifolius* was dried, and its aerial parts (348 g) were pulverized and macerated with CH₂Cl₂ and MeOH at room temperature. The CH₂Cl₂ and MeOH extracts were concentrated under reduced pressure, which yielded 52.0 g and 25.1 g of brownish viscous material, respectively. The CH₂Cl₂ extract was first partitioned between hexane and MeOH, and later between EtOAc and MeOH. A part of the concentrated EtOAc fraction (9.55 g) was chromatographed over a silica gel column (VLC) and eluted with hexane, hexane/EtOAc mixtures, EtOAc, EtOAc/MeOH mixtures, and finally MeOH. Fractions 5 and 9 furnished the diterpene 1 and stigmasterol-3-O-β-D-glycoside,¹¹ respectively.

![Figure 1. Structure 1.](image1)

![Figure 2. Selected HMBC (H→C) correlations for compound 1.](image2)
recrystallized from EtOAc and MeOH. The MeOH extract was further purified by preparative TLC using CH2Cl2/MeOH (8:2) as the eluting solvent system, which gave rutin.14 Fraction 10 (63.5 mg) contained flavonoids, which were further purified by preparative TLC using CH2Cl2/MeOH as eluent, to give quercetin12 (40.3, 42.5); 4 sp3 methines (\(\delta 14.4, 21.3, 32.9\)); 1 sp2 quaternary carbon (\(\delta 52.3\)); 6 sp3 methylenes (\(\delta 34.0, 40.3, 42.7, 89.4\)); 1 sp2 quaternary carbon (\(\delta 153.1\)); and 2 carbonyl groups (\(\delta 171.4, 199.9\)). A review concerning the types of skeletons present in this species and in other species of Acritopappus3–8 prompted us to consider that 1 was a labdane diterpene.3–8 The structural elucidation was performed using detailed analyses of \(^{1}H\) and \(^{13}C\) NMR spectra and the correlations observed in the HMBC spectrum. (Fig. 2). The HMBC spectrum presented correlations of the carbonyl carbon signal at \(\delta 171.4\) (C-15) with both diasterotopic hydrogen signals at \(\delta 2.76\) and \(\delta 2.95\) (H-14a and H-14b) and with the proton signal at \(\delta 5.87\) (H-16). The quaternary carbon at \(\delta 89.4\) (C-13) correlated with the proton signals at \(\delta 2.76\) and 2.95 (H-14a and H-14b), with the proton signal at \(\delta 5.87\) (H-16), and with the proton signals of methylene carbons at \(\delta 20.8\) (C-11) and \(\delta 34.0\) (C-12). The correlations of a proton signal at \(\delta 5.91\) (H-17) with a carbon at \(\delta 153.1\) (C-8) and of a methine carbon at \(\delta 52.3\) (C-9) with methyl proton signal at \(\delta 0.89\) (H-20) were observed, too. The \(^{13}C\) chemical shifts of C-17 (\(\delta 103.8\)) and C-16 (\(\delta 109.5\)) are in agreement with carbons attached by two single bonded oxygens, suggesting that these are acetalts. Furthermore, the correlations of the carbonyl carbon C-6 (\(\delta 199.9\)) with a methine proton signal at \(\delta 2.12\) (H-5), of a carbon at \(\delta 63.0\) (C-5) with 3 methyls at \(\delta 1.09\) (H-19) and \(\delta 0.89\) (H-20), and of a quaternary carbon at \(\delta 32.0\) (C-4) with proton signals at \(\delta 1.18\) (H-18), \(\delta 1.09\) (H-19) and 2.12 (H-5) were detected, too. The keto group was assigned at position 6 on the basis of analyses of the correlations obtained from the HMQC and HMBC spectra and the complete assignment of the protons and carbons. A plausible biogenetic pathway has been proposed for compound 1 herein (Fig. 3). The methyl ester derivative of compound 2 and compound 3 had been isolated from A. confertus6. A derivative of compound 4 whose difference lay on the absence of a carbonyl group at position 6 had been isolated from A. longifolius.10 On the basis of these compounds previously isolated from this genus and the structure shown in Figure 1, it could be deduced that this new labdane presenting a modified skeleton should have originated from the sequence of cyclization reactions, namely nucleophilic addition (steps 1 and 3), oxidation (step 2), and 1,4-addition (Michael reaction, step 4).

### Acknowledgments

The authors thank Dr. Norberto Pepperine Lopes for collection of the plant material in 1998 (collector number NPL 136) and Dr. Edward E. Schilling (Department of Botanic, University of Tennessee, USA) for identification of the plant material. FAPESP, CAPES, and CNPq are acknowledged for the financial support.

### Supplementary data

Supplementary data (HRESIMS, \(^{1}H\) and 2D NMR spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.11.040.

### References and notes