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PROCEROSIDE, AN IRIDOID GLUCOSIDE FROM *PEDICULARIS PROCERA*

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Key Word Index—*Pedicularis procera*; *P. grayi*; Scrophulariaceae; iridoid glucoside; proceroside.

Abstract—A new iridoid glucoside, proceroside, has been isolated from the leaves of *Pedicularis procera*. The structure of proceroside was established as 7-oxocapensioside by spectroscopic methods. © 1997 Elsevier Science Ltd

INTRODUCTION

As part of a recent chemotaxonomic study, the major iridoids of *Pedicularis procera* (*P. grayi*) were identified as aucubin, 6-deoxycatalpol, shanzhiside methyl ester, mussaenoside and 8-epiloganic acid, with gardoside as a minor component [1]. Further investigation of the leaves of this plant has now identified a new iridoid, for which structure **1** has been established.

RESULTS AND DISCUSSION

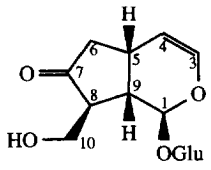
A crude iridoid extract of *P. procera* leaves was separated using reverse phase vacuum liquid chromatography (VLC), and proceroside (**1**) was isolated as a minor component. Negative electrospray mass spectrometry provided the molecular mass of the compound with *m/z* 345 $[M-H]^-$. Both the ^1H and ^{13}C NMR spectra displayed a pattern of peaks similar to that of 6-deoxycatalpol (**2**). For example, ^{13}C NMR showed 15 carbons were present. ^{13}C DEPT showed three of the carbons were methylenes, while the remaining protonated carbons were methines. ^1H and ^{13}C NMR established the presence of only one carbon–carbon double bond, between C-3 and C-4. A major difference between the two compounds was the presence of a carbonyl at low field (δ 223) in the ^{13}C NMR spectrum of **1**. The absence of an aldehyde peak in the ^1H NMR spectrum and the presence of a carbonyl absorption (1734 cm^{-1}) in the IR spectrum confirmed the presence of a cyclopentanone moiety. The H-4 and H-1′ peaks were located under the HDO signal (δ 4.8) in the ^1H NMR spectrum of **1**, using a HETCOR experiment. Selective proton decoupling determined the general structure **1**, corresponding to the 7-oxocapensioside skeleton. The H-5 and H-8 protons were each found to be adjacent to a methylene group, requiring the placement of the ketone at C-7. NOE difference spectra showed that irradiation at H-1 resulted in NOE enhancements at H-10, H-8 and H-9. However, these spectra proved inconclusive for determination of the configuration at C-8, due to the pseudoequatorial conformation of H-1 ($J_{1,9} = 1.5$ Hz). The β configuration of the hydroxymethyl group at C-8 was determined using circular dichroism. The observed negative Cotton effect was very similar to that found for ebuloside (**8**) [2]. Thus, the presence of an adjacent ketone allows for reversal of the typical configuration at C-8 in this genus.

Ketones are found only rarely among the large number of iridoid structures isolated as natural products [3–5]. The 6-keto iridoids cornin (**3**), 10-hydroxycornin (**4**) and hastatoside (**5**) were isolated from *Penstemon nitidus*, representing the first occurrence of such compounds in the Scrophulariaceae family [6]. While 7-keto iridoids such as ketologanin (**6**) [7], syringopicroside (**7**) [8] and ebuloside (**8**) [2] are known, **1** represents the first 7-keto iridoid from the Scrophulariaceae. Compound **1** may be derived biosynthetically via a rearrangement of 6-deoxycatalpol. This type of rearrangement has been utilized in synthesis [9,10].

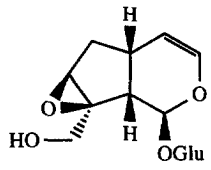
EXPERIMENTAL

Instrumentation. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) were obtained with D_2O as solvent. Chemical shifts are given in δ (ppm) with HDO (^1H, δ 4.73) or MeOH (^{13}C, δ 49.0) as int. standard.

Plant material. P. procera Gray was collected at



1



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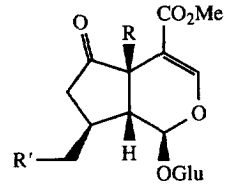

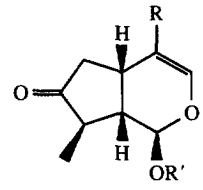

3 R = R′ = H

4 R = H, R′ = OH

5 R = OH, R′ = H

6 R = CO_2Me, R′ = Glu

7 R = CO_2R'', R′ = Glu

R″ = 2-(*p*-hydroxyphenyl)ethyl

8 R = CH_2OGlu, R′ = isovaleroyl

Michigan Hill, Colorado. Identification was made by D. H. Wilken (Dept. of Biology, Colorado State University) and a voucher specimen was deposited in the Colorado State University Herbarium (CSU 17676).

Isolation of proceroside (**1**). Dried and ground leaves (10.65 g) were extracted with MeOH at room temp. for several days. After evap of the MeOH, the residue was taken up in H_2O and extracted with Et_2O. The aq. phase was then lyophilysed to give a crude iridoid/sugar extract. The crude iridoid mixt. was sepd by reverse phase (C-18) VLC with a H_2O–MeOH gradient. The frs were evapd or lyophilysed and iridoids were identified by ^1H and ^{13}C NMR spectroscopy. Compound **1** was obtained as a minor component (16 mg). Negative-ion ESIMS *m/z*: 345 $[M-H]^-$; IR ν_{max}^{neat} cm^{-1}: 1734 (C=O); CD (H_2O; *c* 0.073): $\Delta\varepsilon_{318}-0.10$, $\Delta\varepsilon_{310}-0.35$, $\Delta\varepsilon_{292}-0.83$, $\Delta\varepsilon_{270}-0.45$; ^1H NMR: δ 2.25 (*d*, J = 18.9 Hz, H-6), 2.32 (*ddd*, J = 11.3, 4.1, 3.7 Hz, H-8), 2.49 (*dd*, J = 18.7, 8.1 Hz, H-6), 2.63 (*ddd*, J = 11, 7.0, 1.5 Hz, H-9), 3.03 (*ddd*, J = 8.1, 7, 1.9 Hz, H-5), 3.2–3.45 (*m*, H-2′,3′,4′,5′), 3.64 (*dd*, J = 12.4, 6.0 Hz, H-6′), 3.70 (*dd*, J = 11.8, 3.7 Hz, H-10), 3.81 (*d*, J = 12.2 Hz, H-6′), 3.85 (*dd*, J = 11.4, 4.1 Hz, H-10), 4.8 (H-4, H-1′), 5.5 (*d*, J = 1.5 Hz, H-1), 6.2 (*dd*, J = 6.4, 1.9 Hz, H-3); ^{13}C NMR: δ 25.7 (C-5), 39.7 (C-9), 44.6 (C-6), 50.7 (C-8), 58.9, 60.9 (C-10, C-6′), 69.8, 72.9, 75.7, 76.4, 93.6 (C-1), 98.4 (C-1′), 106.2 (C-4), 139.2 (C-3), 223.1 (C-7).

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