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ARGYLIOSIDE, A DIMERIC IRIDOID GLUCOSIDE FROM *ARGYLIA RADIATA**

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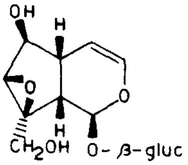
Key Word Index—*Argylia radiata*; Bignoniaceae; iridoid glucosides; bisiridoids; plantarenaloside; argylioside.

Abstract—From the aerial parts of *Argylia radiata* a novel dimeric iridoid glucoside, argylioside, was isolated besides the known plantarenaloside. The structure of the new compound was established by spectroscopic methods and by cleavage into the monomeric components, catalpol and 7-deoxy-8-epiloganic acid.

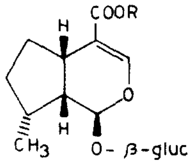
INTRODUCTION

In the course of a systematic investigation of iridoid glucoside-containing plants from endemic Chilean species, we have recently examined three members of the family Bignoniaceae [1]. From *Argylia radiata* (L.) D. Don, we isolated catalpol (**1**) [1] and 7-deoxy-8-epiloganic acid (**2**) [2]. This plant, commonly known as 'terciopelo', is a medium size herb that grows in the northern part of central Chile, where it is used in popular medicine as a stomach tonic [3, 4].

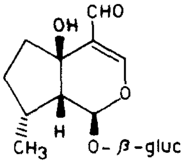
The present paper describes the isolation and structure elucidation of two more iridoid components, plantarenaloside (**3**) and a new compound (**4**) having the structure of a dimeric iridoid glucoside for which we propose the name of argylioside, from *A. radiata*.



1



2 R=H
6 R=CH3



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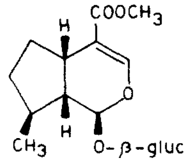

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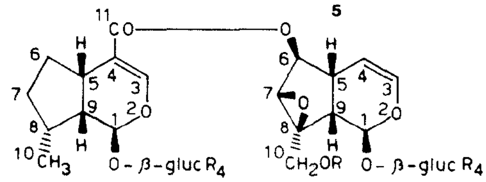

4 R=H
7 R= Ac

RESULTS AND DISCUSSION

Compound **4**, $[\alpha]_D = -126°$, had a molecular formula of $C_{31}H_{44}O_{18}$. Its dimeric iridoid structure was suggested by the ^1H and ^{13}C NMR data (Tables 1 and 2) which

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*Part IX in the series "Iridoids in Equatorial and Tropical Flora". For part VIII see ref. [2].

Table 1. ^{1}H NMR data of compounds **1**, **2** and **4** (400 MHz)

H	**2** (CD_3OD)	(CD_3OD) Part a	**4** Part b	**1** (D_2O)
1	5.44 *d* $J_{1,9} = 5.2$*	5.43 *d* $J_{1,9} = 5.1$	5.08 *d* $J_{1,9} = 9.3$	5.02 *d* $J_{1,9} = 9.8$
3	7.41 *s* (*br*)	7.43 *s* (*br*)	6.32 *dd* $J_{3,4} = 6.5$ $J_{3,5} = 1.8$	6.33 *dd* $J_{3,4} = 6.0$ $J_{3,5} = 1.7$
4	—	—	4.74 *dd* $J_{4,5} = 4.0$	5.08 *dd* $J_{4,5} = 4.6$
5	2.91 *q* (*br*) $J_{5,9} = 8.3$ $J_{5,6a} = 8.3$ $J_{5,6e} = 8.3$	2.92 *q* (*br*) $J_{5,9} = 8.3$ $J_{5,6a} = 8.3$ $J_{5,6e} = 8.3$	2.48 *m*	2.25 *m*
6a	1.58 *dddd* $J_{6e,6a} = 12.6$ $J_{6a,7a} = 9.0$	1.59 *dddd* $J_{6e,6a} = 12.6$ $J_{6e,7a} = 9.0$	4.66 *dd*	4.00 *dd*
6e	2.08 *dddd* $J_{6e,7a} = 8.3$ $J_{6e,7e} = 8.3$	2.07 *dddd* $J_{6e,7a} = 8.3$ $J_{6e,7e} = 8.3$	$J_{6,5} = 7.2$ $J_{6,7} = 2.2$	$J_{6,5} = 8.1$ $J_{6,7} = 1.0$
7a	1.39 *dddd* $J_{7a,7e} = 12.4$ $J_{7a,8} = 8.3$	1.36 *dddd* $J_{7a,7e} = 12.4$ $J_{7a,8} = 8.3$	3.64 *s* (*br*)	3.56 *s* (*br*)
7e	1.80 *dddd*	1.76 *dddd*		
8	2.29 *ddq* $J_{8,9} = 8.0$ $J_{8,10} = 7.3$	2.23	—	—
9	2.23 *ddd*	2.23	2.54 *dd* $J_{9,5} = 7.5$	2.58 *dd* $J_{9,5} = 7.7$
10	1.10 *d*	1.06 *d* $J_{8,10} = 7.3$	3.64, 4.08 $J_{gem} = 13.2$	3.70, 4.21 $J_{gem} = 13.2$
1′	4.70 *d* $J_{1',2'} = 8.0$	4.71 *d* $J_{1',2'} = 7.2$	4.65 *d* $J_{1',2'} = 7.2$	4.81 *d* $J_{1',2'} = 8.0$

*Hz

†Data taken from ref. [5]. 326 MHz, HDO at 4.70 ppm as internal reference.

showed a duplication of the signals typical of an iridoid moiety.

The NMR data of **4** showed that the 'b' part of the molecule had a structure like catalpol (**1**) [5]. On subtraction of the signals due to the 'b' part, the remaining signals indicate that the 'a' part of the molecule was derived from deoxyloganic acid. This was confirmed by the UV absorption of **4** at 234 nm (log $\varepsilon = 3.9$).

Comparison of the ^{13}C NMR data of **4** with those of 7-deoxy-8-epiloganic acid (**2**) [2] and of 7-deoxyloganin (**5**) [6, 7] and its C-8 epimer (**6**) [7] established that the 'a' part of the structure was formed from 7-deoxy-8-epiloganic acid.

In order to confirm the proposed structure, **4** was hydrolysed in alkaline medium. As expected, two products were obtained. These were readily identified, by direct comparison, as catalpol (**1**) and 7-deoxy-8-epiloganic acid (**2**). Because of its instability **2** was isolated as its stable methyl ester derivative which was shown to be identical to authentic 7-deoxy-8-epiloganin (**6**).

One site of the ester linkage between the two moieties of the dimer **4**, was assigned to the C-11 carboxyl group of 7-deoxy-8-epiloganic acid (**2**) ('a' part), whereas the second was attributed to the secondary alcoholic function at C-6 of catalpol (**1**) ('b' part) on the basis of the following considerations. In the ^{1}H NMR spectrum of **4** the signal of H-6 resonates at δ4.66 (*dd*, $J = 7.2$ and 2.2 Hz) a chemical shift value very similar to that shown by H-6 in the nona-acetyl derivative **7** (δ4.82), while in catalpol (**1**) the same signal appears at δ4.00 [5]. In addition, in the ^{13}C NMR spectrum of **4** a typical deshielding effect was observed on C-6 (α-effect, + 1.6 ppm) and typical shielding effects were observed on C-5 and C-7 (β-effects, 2.2 and 3.1 ppm respectively) with the corresponding signals of catalpol (**1**) (see Table 2). These last effects had already been observed for other esters of catalpol at C-6 [6].

Compound **4** is the first example of a new class of iridoids for which we propose the name of bisiridoids. The only similar compound reported in the literature is the dimeric 10-dehydrogardoside, isolated from *Randia canthioides*, probably as an artefact formed during the isolation process [8].

The peculiar characteristic of *A. radiata* to accumulate dimeric iridoid glucosides can be related to *Tecoma chrysantha*, a bignoniaceous plant from which some of us isolated amareloside [9]. This compound is formed by esterification of the alcoholic function at C-6 of 6-epiaucubin by an alicyclic monoterpene unit.

The chemistry of the iridoids isolated so far from Bignoniaceae allow us to make some chemosystematic observations: (i) iridoids are found only as glucosides; (ii) among the five tribes (Bignoniae, Crescentiae, Eccremocarpeae, Tecomae and Tourettiae) described by Engler [10], their isolation and characterization is restricted to Tecomae; (iii) two main markers can be evidenced: catalpol and related compounds (*Catalpa, Amphicone, Macfadyena, Tecomella, Tabebuia*) and the couple plantarenaloside/stansioside (*Tecoma, Campsis, Campsidium*). Interestingly, both markers are present in *Argylia* and also the argylioside structure is closely related to them.

EXPERIMENTAL

PC: Schleicher & Schull 204 3 Mg 1; TLC: silica gel F_{254} (Merck) and cellulose (Merck) plates. Spray reagents: 1 M H_2SO_4, vanillin (2 g vanillin, 4 ml 11 M HCl, 100 ml MeOH) and benzidine (0.5 g benzidine, 20 ml AcOH, 80 ml EtOH); ^{1}H NMR: 400 MHz; ^{13}C NMR: 100 MHz.

Extraction and separation. The plant (3.0 kg), collected in La Serena (Chile) and identified at U.F.S.M., where voucher specimens are deposited, was extracted twice with EtOH at room temp. The extracts were bulked, evaporated to an aq. suspension, to which charcoal was added until a negative vanillin test was obtained. The resulting mixture was then stratified on a gooch funnel (ϕ20 cm). Elution with H_2O and 10% aq. EtOH removed salts and sugars, whereas 30%, 50% and 70% aq. EtOH eluted iridoid-containing fractions. PC and TLC of these fractions showed the presence of catalpol (**1**), 7-deoxy-8-epiloganic acid (**2**), plantarenaloside (**3**) and a small quantity of argylioside (**4**) in the 30% fraction, **1**–**4** together with two unknown substances in the 50% fraction, and a small quantity of **1** in the 70% fraction. The 30% and 50% fractions were separately chromatographed on silica gel in *n*-BuOH satd with H_2O affording semipurified mixtures of iridoids which were separated by low pressure reversed phase chromatography (prepacked Merck columns RP-8, MeOH–H_2O, 1:1). The following quantities of pure iridoids were obtained: **1**, 250 mg; **2**, 100 mg; **3**, 150 mg; **4**, 200 mg, unknown I, 50 mg and unknown II, 65 mg. Compounds **1**–**3** were identified by direct comparison with authentic samples.

Argylioside (**4**). Amorphous colourless powder, $[\alpha]_D^{25} =$

Table 2. ^{13}C NMR data for compounds **1**, **2**, **4** and **7** (100 MHz)*

	4 (CD$_3$OD)		**4** (D$_2$O)		**7**§ (CDCl$_3$)			
C	Part a	Part b	Part a	Part b	Part a	Part b	[1] (CD$_3$OD)	[2] (CD$_3$OD)
1	95.1	94.1	94.4	92.7	91.5	90.7	94.7	95.4
3	152.5	141.3	151.6	138.8	151.2	141.1	141.1	152.0
4	112.1	102.1	114.0	104.2	112.5	103.7	103.4	113.3
5	32.2	36.4	32.2	37.2	32.4	35.3	38.6	32.5
6	31.0†	80.5	32.2†	81.3	31.1†	80.3	78.9	31.5†
7	33.3†	59.2	33.8†	61.2	32.4†	58.7	62.3	33.8†
8	34.3	65.2	33.8	67.8	34.5	68.2	65.6	36.8
9	43.5	42.0	45.2	44.3	42.6	41.4	43.0	43.6
10	15.7	60.1	17.3	61.5	15.9	61.3	60.8	16.0
11	167.9		170.1		166.7			172.2
1′	98.7	98.7	100.3	100.3	96.6	97.2	99.0	99.0
2′	73.7	73.7	74.7	74.7	70.7	70.6	74.2	74.0
3′	77.3‡	77.1‡	77.8‡	77.8‡	72.6‡	72.5‡	77.8‡	77.6‡
4′	69.6	69.6	71.3	71.3	68.2	68.2	71.1	71.0
5′	77.1‡	76.6‡	77.4‡	77.4‡	72.1‡	72.0‡	77.0‡	77.2‡
6′	61.9	61.9	61.2	61.2	62.5	61.7	62.0	62.2

*Values in ppm, using the MeOH signal (in D$_2$O) (49.6 ppm) and that of TMS (in CD$_3$OD and CDCl$_3$) as internal references.

†,‡Assignments uncertain.

§<u>C</u>OMe: 170.4, 170.1, 169.3, 169.0; CO<u>Me</u>: 20.5 ppm.

$-126°$ (c 0.5; MeOH). UV $\lambda_{\max}^{\text{MeOH}}$ (log ε): 234 nm (3.9); IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1680, 1640; found C, 52.78; H, 6.33 (calc. for $C_{31}H_{44}O_{18}$ C, 52.83; H, 6.29).

Nona-acetyl derivative of **4** (**7**). Compound **4** (50 mg) was treated with C_5H_5N (0.2 ml) and Ac_2O (0.4 ml) for 4 hr at room temp. After addition of MeOH (2 ml), the soln was left for 20 min, then evaporated to give crude **7** (60 mg) which, by chromatography on silica gel (C_6H_6–Et_2O, 2 : 3), afforded pure **7** (50 mg), crystals from EtOH, mp 175–176°. ^{1}H NMR (CDCl$_3$): δ part 'b' 5.27 (H-1), 7.42 (H-3), 2.92 (H-5), 1.58 (H-6a), 1.32 (H-7a), 1.77 (H-7e), 2.27 (H-8) and (H-9), 1.02 (3H-10). Part 'a' 5.09 (H-1), 6.29 (H-3), 4.92 (H-4), 2.54 (H-5), 4.82 (H-6), 3.69 (H-7), 2.60 (H-8 and H-9), 4.23 and 3.98 (2H-10), 2.10–1.97 (9 × Ac); multiplicities and coupling constants are practically identical to those reported for **4** (Table 1).

Hydrolysis of **4**. Compound **4** (150 mg) was dissolved in 2 M NaOH (5 ml) and left at room temp. overnight. The alkaline soln was carefully acidified with 1 M HCl keeping the temp. at *ca* 5° and 5 g of charcoal were added. The resulting suspension was stratified on a gooch funnel (ϕ 1 cm) and the charcoal washed with H_2O until complete elimination of acidity and negative salt test. The elution was continued with MeOH until negative H_2SO_4 test and the alcoholic soln was immediately treated with CH_2N_2 at 0° for 5 min. The soln was evaporated and chromatographed on silica gel (CHCl$_3$–MeOH, 4 : 1), affording pure 7-deoxy-8-epiloganin (**6**; 50 mg) and catalpol (**1**; 60 mg), identified by comparison with authentic samples.

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