

RADIATOSIDE, A NEW BISIRIDOID FROM ARGYLIA RADIATA¹

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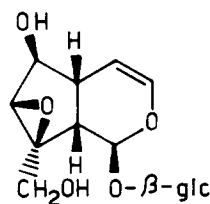
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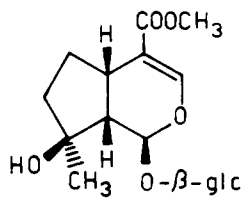
From *Argylia radiata* (L.) D. Don (Bignoniaceae), an endemic Chilean plant used as a stomach tonic in traditional medicine, we reported recently the isolation of catalpol (**1**) (2), plantarenalioside (2), 7-deoxy-8-*epi*-loganic acid (3), 7-deoxygardoside (1), and a new type of dimeric iridoid glucoside, named argylioside, derived from the esterification of the 6-OH of a catalpol unit by 7-deoxy-8-*epi*-loganic acid (4). We report now on the isolation and structure determination of a second new

dimeric iridoid glucoside, for which we propose the name of radiatoside and the structure **2**, derived from a catalpol unit esterified in the 6 position by 6-deoxy-shanzhiside.

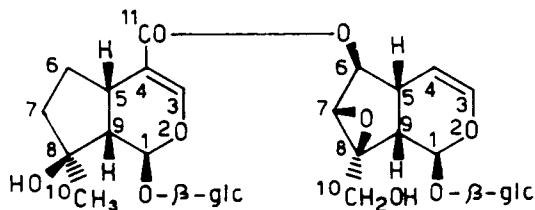
Compound **2** is a colorless, amorphous powder with $[\alpha]^{25}_D = -48.9$. The ¹H- (400 MHz) and ¹³C-nmr (100 MHz, see Table 1) spectra of **2** clearly showed its dimeric nature by the evident duplication of the signals typical of an iridoid glucoside. One half of the molecule, part "a", was easily assigned



1



3



2

¹Part XI in the series "Iridoids in Equatorial and Tropical Flora." For part X, see Bianco *et al.* (1).

to a structure like that of catalpol (**1**). The second part "b" showed the presence of an ester function at C(4), assigned on

TABLE 1. ^{13}C -nmr Data of Compounds 1-3^a

Atom	Compound (solvent)					
	2 (CD ₃ OD)		2 (D ₂ O)		1 (D ₂ O)	3 (D ₂ O)
	part "b"	part "a"	part "b"	part "a"		
C(1)	94.6 ^b	94.1 ^b	95.4 ^d	95.2 ^d	95.0	95.1
C(3)	151.8	141.5	152.3	141.6	140.8	151.7
C(4)	113.2	102.0	112.9	103.1	103.4	113.1
C(5)	30.7	35.5	30.2	36.0	37.6	30.4
C(6)	29.7	80.2	29.5	80.3	76.0	29.8
C(7)	39.8	58.7	40.2	60.5	61.0	40.3
C(8)	80.1	65.8	80.4	66.8	66.1	80.2
C(9)	51.1	42.1	51.3	42.2	42.0	51.3
C(10)	23.7	59.4	23.5	60.8	60.4	23.9
C(11)	169.3		169.2			170.1
OMe						52.4
C(1')	98.8	98.8	99.0 ^e	98.9 ^e	98.8	99.0
C(2')	73.8	73.7	73.5	73.5	73.1	73.4
C(3')	77.3 ^c	77.5 ^c	76.9 ^f	76.9	77.9 ^g	77.0 ^h
C(4')	70.7	70.7	70.4	70.4	70.0	70.3
C(5')	77.0 ^c	76.8 ^c	76.4 ^f	76.4	76.5 ^g	76.4 ^h
C(6')	61.8	61.6	61.5	61.5	62.4	61.5

^aValues in ppm; TMS as internal reference for spectrum in CD₃OD; MeOH (49.6 ppm) for spectra in D₂O.

^{b-h}Assignments of values with the same superscripts can be interchanged.

the basis of the resonances of H-3 (δ 7.49, singlet) and C-3 and C-4 (151.8 and 113.2 ppm, respectively) and uv absorption at 234 nm ($\log \epsilon$ 3.9). It also showed a methyl group located in the 8 position in accordance with the known biogenetic rules, adjacent to a hydroxy group and in the β configuration on the basis of its ^1H - (δ 1.40, singlet) and ^{13}C -nmr chemical shift values (23.7 ppm). No other substituents are present in the cyclopentane ring, as is evident from the other ^{13}C -nmr data.

From these data, part "b" was assigned to a mussaenosidic acid moiety. As a confirmation, compound 2 was hydrolyzed in alkaline medium, and two products were obtained: one was readily identified as catalpol (1), by direct comparison, the second was further converted into the methyl ester derivative, which was identical to mussaenoside (3).

The last structural problem, the determination of the linkage between the two parts of the dimer, was solved by the comparison of the ^{13}C -nmr data of 2

with those of mussaenoside and catalpol (Table 1). One site of the linkage was assigned to the carboxylic acid function of mussaenosidic acid, since C-11 of part "b" resonates at 169.3 ppm whereas a free carboxylic acid function would resonate at values considerably higher than 170 ppm. The second site was assigned to the 6 position of catalpol. In comparison with the ^{13}C -nmr data of catalpol, effects of acylation on C-6 (α effect, +4.3 ppm) and C-5 and C-7 (β effects, -1.6 and -0.5 ppm, respectively) are evident.

Radiatoside is a further example of the class of dimeric iridoids, named bisiridoids, derived from the junction of two iridoid glucoside units. These include the aforementioned argyioside and the dimeric 10-dehydrogardoside, isolated from *Randia canthioides* but considered by the authors a possible artifact (5). Other dimeric compounds like sylvestrosides from *Dipsacus sylvestris* (6) and compounds from *Cantleya* (7) and *Fraxinus* (8) are based on the junction of

an iridoid glucoside and a secoiridoid and should not be considered bisiridoids in *sensu stricto*.

EXPERIMENTAL

Pc: Schleicher & Schüll 2043 Mg 1; tlc silica gel F₂₅₄ (Merck) and cellulose (Merck) plates. Spray reagents: 2N H₂SO₄, vanillin (2 g vanillin, 4 ml 37% HCl, 100 ml MeOH) and benzidine (0.5 g benzidine, 20 ml HOAc, 80 ml EtOH). ¹H-nmr spectra were obtained with a Bruker AM 400 spectrometer and ¹³C-nmr spectra with a Varian XL 100 spectrometer.

EXTRACTION AND SEPARATION.—*A. radiata* (3.0 kg) was collected in La Serena (Chile) and identified at U.F.S.M., where voucher specimens are deposited. The whole plant was extracted twice with EtOH at room temperature and the collected extracts evaporated to an aqueous suspension. Charcoal was then added until a negative vanillin test was obtained and the resulting mixture stratified on a Gooch funnel (Ø 20 cm). Elution with H₂O and 10% EtOH removed salts and sugars, whereas 30%, 50%, and 70% EtOH eluted iridoidic fractions. Pc and tlc of these fractions revealed the presence in the 30% EtOH fraction of catalpol (4), 7-deoxy-8-*epi*-loganic acid, plantarenaloside, argylioside, radiatoside (2), 7-deoxygardoside, together with one unknown substance; in the 50% EtOH fraction all the previous substances and a further quantity of 7-deoxygardoside; in the 70% EtOH fraction a small quantity of catalpol (1). The 30% and 50% EtOH fractions were separately chromatographed on silica gel in *n*-BuOH saturated with H₂O affording semipurified mixtures of iridoids which were separated by low pressure chromatography on reversed phase (prepacked Merck columns RP-8 mesh) in MeOH-H₂O (1:1). The following quantities of pure iridoids were obtained: catalpol (1), 250 mg; 7-deoxy-8-*epi*-loganic acid, 100 mg; plantarenaloside, 150 mg; argylioside, 200 mg; 7-deoxygardoside, 165 mg; radiatoside, 50 mg, and an unknown compound, 40 mg.

RADIATOSIDE (2).—Amorphous colorless powder with $[\alpha]_D^{25} = -48.9$ (MeOH, c 1.5); uv (MeOH) λ max (log ϵ) 234 (3.9); ir (KBr) ν max 1680, 1640 cm⁻¹; ¹H nmr δ (CD₃OD) "part a": 2.57 (1H, m, H-5), 2.60 (1H, dd, *J*=7.5 and 9.5 Hz, H-9), 3.64 (1H, m, H-7), 3.79 and 4.09

(2H, *J*_{gem}=13.2 Hz, 2H-10), 4.59 (1H, d, *J*=8.0 Hz, H-1'), 4.68 (1H, dd, *J*=6.5 and 4.0 Hz, H-4), 4.88 (1H, dd, *J*=8.0 and 1.0 Hz, H-6), 5.09 (1H, d, *J*=9.5 Hz, H-1), 6.33 (1H, dd, *J*=6.5 and 1.8 Hz, H-3); "part b": 1.40 (3H, s, 3H-10), 1.6-2.4 (5H, 2H-6, 2H-7 and H-5), 3.10 (1H, m, H-9), 4.75 (1H, d, *J*=8 Hz, H-1'), 5.45 (1H, *J*=3.5 Hz, H-1), 7.49 (1H, s, H-3). Elem. anal. (C₃₁H₄₄O₁₉ requires: C, 51.66; H, 6.15%): C, 50.89; H, 6.25%.

HYDROLYSIS OF 2.—Compound 2 (35 mg) was dissolved in 2 N NaOH (5 ml) and left at room temperature overnight. The alkaline solution was carefully acidified with 1 N HCl keeping the temperature at ca. 5°, and 5 g of charcoal were added. The resulting suspension was stratified on a Gooch funnel (Ø 1 cm) and the charcoal washed with H₂O until complete elimination of acidity and a negative salt test were obtained. The elution was continued with MeOH until a negative H₂SO₄ test was obtained, and the alcoholic solution was immediately treated with CH₂N₂ at 0° for 5 min. The solution was evaporated and chromatographed on Si gel in CHCl₃-MeOH (8:2) affording pure mussaenoside (3) (10 mg), and catalpol (1) (10 mg), identified by direct comparison with authentic samples.

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