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A GUAIANOLIDE FROM *STEVIA BREVIARISTATA*

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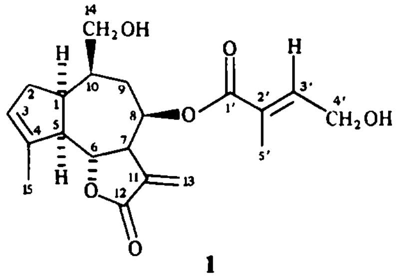
Key Word Index—*Stevia breviaristata*; Eupatorieae; Compositae; guaianolide; sesquiterpene lactone.

Abstract—Extraction of *Stevia breviaristata* furnished a new guaianolide breviarolide.

Approximately 27 species of the large genus *Stevia* (Compositae, tribe Eupatorieae, subtribe Piqueriinae [1]) have been studied chemically. Summaries of the results through 1984 have appeared [2–4]; since then guaianolides and flavones have been reported from *S. procumbens* [5], pseudoguaianolides and a xanthanolide from *S. isomeca* [6] and guaianolides, a heliangolide and longipinene derivatives were found in *S. lemmonia* [7]. Also a variety of substances, principally longipinene derivatives and diterpenes but no sesquiterpene lactones, has been isolated from *S. berlandieri* and *S. salicifolia* [7], kauranes have been found in *S. eupatoria* [8] and flavones have been reported from *S. microchaeta* and *S. origanoides* [9]. The present brief report deals with isolation of the new guaianolide **1** from the South American species *S. breviaristata* Hook et Arn.

The carbon skeleton of the new substance which we have named breviarolide, mp 83–85°, $C_{20}H_{26}O_7$ (high resolution MS), was established in the usual manner by sequential spin decoupling of the ^{1}H NMR spectrum (Table 1), beginning with the narrowly split doublets of H-13a,b at δ6.13 and 5.37 which located the multiplet of H-7 at δ3.26. Subsequent decoupling showed that sequences H-7, H-6, H-5 and H-7, H-8, H-9a,b, H-10 met at the H-1 multiplet at δ2.91 which was further coupled to H-2a and H-2b. As usual in 1αH,5αH,6βH-guai-3-en-6,12-olides neither H-2a nor H-2b was coupled to H-3 at δ5.54. Allylic coupling between H-3 and a vinyl methyl signal at δ1.92, long range coupling between H-10 and the AB part of the ABX system centred at δ3.47 further showed that the primary hydroxyl group was located on C-14, not on C-15. The nature of the ester side chain attached to C-8 was evident from the ^{1}H NMR (H-3′ at δ6.70, H-4′a,b at δ4.33) and ^{13}C NMR spectra [10]*.

As for the stereochemistry, the *cis*-fusion of the alicyclic ring system, the *trans*-fusion of the lactone ring, with H-6 *trans* to H-5, and the β-orientation of the C-8 ester side chain could be deduced from the values of the coupling constants (Table 1). The NOE difference spectrum



1

Table 1. ^{1}H NMR spectrum of **1** (270 MHz, $CDCl_3$)

H	δ
1	2.91 *br qd*
2a	2.26 *br dd*
2b	superimp. on H-9a
3	5.54 *br*
5	2.55 *br t*
6	4.50 *dd*
7	3.26 *dddd*
8	5.68 *td*
9a	2.14 *br dd*
9b	1.63 *ddd*
10	2.06 *m*
13a	6.13 *d*
13b	5.37 *d*
14	3.47*
15†	1.92 *br d*
3′	6.70 *td*
4′‡	4.33 *br d*
5†	1.77 *br d*

*Centre of AB part of ABX system.

†Intensity three protons.

‡Intensity two protons.

J (Hz): 1, 2a = 1, 10 = 6, 7 = 9; 1, 2b = 2a, 15 = 2b, 15 = 9a, 10 small; 1, 5 = 5, 6 = 9b, 10 = 14a, 14b = 10; 2a, 2b = 9a, 9b = 15; 3, 15 = 3′, 5′ = 1.5; 7, 8 = 4; 7, 13a = 7, 13b = 3; 8, 9a = 8, 9b = 8; 10, 14 = 7; 3′, 4′ = 6; 4′, 5′ = 1.

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*In the ^{13}C NMR spectra of eupasoppin and its analogues given in ref. [10] the assignments of C-2 and C-3, C-11 and C-2′, and C-14 and C-5′ should be interchanged.

Table 2. ^{13}C NMR spectrum of **1** (67.89 MHz, $CDCl_3$)

C	δ
1	43.69 *d**
2	31.20 *t**
3	125.74 *d*
4	142.96 *s*
5	56.56 *d**
6	80.50 *d*
7	46.99 *d**
8	68.59 *d*
9	28.85 *t**
10	38.07 *d**
11	134.35 *s*
12	169.48 *s*
13	122.21 *t*
14	65.95 *t*
15	17.29 *q*
1'	166.64 *s*
2'	128.03 *s*
3'	140.90 *d*
4'	59.63 *t*
5'	12.71 *q*

*Assignments by selective decoupling.

Table 3. NOE difference spectrum of **1**

Saturation	Observed NOE (%)
H-1	H-5 (11)
	H-10 (14.5)
H-6	H-9b (8.5)
H-7	H-5 (12)
	H-6 (4.5)
	H-8 (9.5)
	H-10 (11)
H-8	H-7 (10)
	H-10 (7.5)
H-14	no observable NOE

(Table 3) confirmed not only that H-1, H-5, H-7 and H-8 were *cis*, but also demonstrated that H-10 was *cis* to H-7, H-8, and H-10, thus establishing the complete relative stereochemistry shown in formula **1**.

EXPERIMENTAL

Stevia breviaristata Hook et Arn. was collected by V. E. S. in Cochangasta, Dpt. Capital, La Rioja Province, Argentina in April 1984 and identified by Dr. Luis Ariza Espinar. A voucher specimen (Oberti #58) was deposited in the Museo Botánico, Córdoba. The aerial parts (600 g) were exhaustively extracted with $CHCl_3$. The usual work-up [11] yielded a yellow gum (7.9 g) which was adsorbed on 14 g of silica gel and chromatographed over a column packed with the same adsorbent (100 g) and $CHCl_3$ in 125 ml fractions, the polarity of the $CHCl_3$ eluent being increased by addition of MeOH in the ratios 1:99, 1:49, 1:24, 3:47 and 1:10. Fractions 23–27, which contained the same material (TLC analysis), were combined and recrystallized from C_6H_6–$CHCl_3$ to give 90 mg of **1**, mp 83–85°; IR ν^{KBr} cm^{-1}: 3450, 3345, 1757 (lactone), 1730 (ester), 1650 (conj. C=C), 1020; MS *m/z* (rel. int.): 362 $[M]^+$ (16.5), 263 (4.8), 246 (24.1), 245 (20.5), 99 (99), 71 (100). (Calc. for $C_{20}H_{26}O_6$: M_r 362.1729. Found. M_r (MS): 362.1740.)

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