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LONGIPINANE DERIVATIVES FROM *STEVIA VISCIDA*

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Key Word Index—*Stevia viscida*; Eupatorieae; Compositae; roots; sesquiterpenes; longipinane.

Abstract—Two new longipinane derivatives were isolated from the roots of *Stevia viscida*. The structures were deduced as longipinan-9α,15-diangeloyloxy-1-one and longipinan-9α-angeloyloxy-15-tigloyloxy-1-one on the basis of spectral evidence.

INTRODUCTION

Studies of nearly 50 *Stevia* species have shown that longipinene derivatives are frequent in the genus [1, 2]. In continuation of our search for longipinene derivatives from *Stevia* [3–6] we studied the chemical constituents of the roots of *S. viscida* HBK. Chromatography of the hexane extracts yielded the new longipinane derivatives longipinan-9α, 15-diangeloyloxy-1-one (**1**) and longipinan-9α-angeloyloxy-15-tigloyloxy-1-one (**2**).

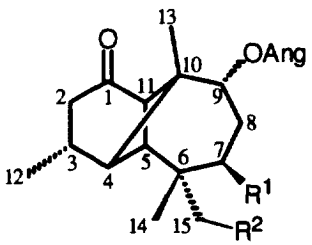
Compound **1**, isolated as an oil, showed $[\alpha]_D$ −26° and IR absorptions at 1700 and 1640 cm^{-1} (unsaturated ester groups). The ^1H NMR spectrum (Table 1) showed typical signals for a longipinane skeleton [3, 7] and for two angelate groups [8]. A triplet at δ5.07 (J = 3.4 Hz) is assigned to H-9, as in related esters [7], while an AB system at δ3.92 and 3.81 (J_{AB} = 11 Hz), owing to a methylene group bearing an ester, is assigned to methylene-15. The α-orientation of this group is evident after comparison of the ^1H NMR spectral data of **1** with those of the C-15 functionalized esters **3** and **4**, isolated from *S. potrerensis* [9] and *S. elatior* [10],† respectively. The stereochemistry of the methyl group at C-3 and of the angelate group at C-9 follows from the ^{13}C NMR chemical shifts of C-3 (δ27.1) and of C-10 (δ46.5), respectively (Table 2), which are similar to those of triacetate **5** [7] (C-3, δ26.8; C-10, δ45.0) and different at C-3 for the epimeric triacetate **6** [11] (C-3, δ32.4).

Compound **2** showed $[\alpha]_D$ −33° and IR absorptions at 1607 and 1650 cm^{-1}. Most of the ^1H and ^{13}C NMR signals were very similar to those of diangelate **1** (Tables 1 and 2). The vinylic signals at δ6.85 (1H) and 6.10 (1H) together with the methyl group signals between δ2.00 and 1.80 indicate the presence of one tiglate and one angelate ester group in **2**. The positional assignment of both esters can be done when the chemical shifts of the signals owing to the protons geminal to the oxygen atoms (H-9, H-15 and H-15′) are compared with those of diangelate **1**. While the signal for H-9 had a very similar chemical shift in both substances, the signals for H-15 and H-15′ experienced an evident change (Table 1). Therefore, the angelate group was located at C-9 and the tiglate group at

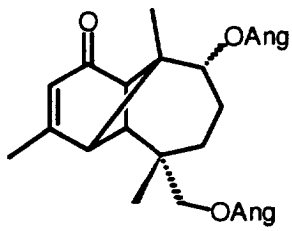
Table 1. ^1H NMR spectral data of **1** and **2** (200 MHz, $CDCl_3$, coupling constants in Hz in parentheses)

H	**1**	**2**
2α	2.55 *dd* (8.4, 19.9)	2.55 *dd* (8.3, 18.4)
2β	2.10 *dd* (6.0, 18.5)	2.12 *dd* (5.7, 18.5)
3	2.35 *m*	2.35 *m*
4	2.18 *d* (5.5)	2.18 *d* (5.5)
5	2.00 *s*	1.98 *s*
7	1.85 *m*	1.83 *m*
7′	1.30 *m*	1.29 *m*
9	5.07 *t* (3.4)	5.08 *t* (3.1)
11	3.03 *d* (5.4)	3.07 *d* (5.5)
Me-12	1.09 *d* (6.7)	1.09 *d* (6.5)
Me-13	0.88 *s*	0.88 *s*
Me-14	1.02 *s*	1.00 *s*
15	3.92 *d* (11.0)	3.87 *s*
15′	3.81 *d* (11.0)	3.87 *s*
	OAng (C-9)	OAng (C-9)
3	6.10 *qq* (7.5, 1.5)	6.10 *qq* (7.5, 1.5)
Me-4	2.00 *dq* (7.5, 1.5)	2.00 *dq* (7.5, 1.5)
Me-5	1.90 *quin* (1.5)	1.90 *quin* (1.5)
	OAng (C-15)	OTigl (C-15)
3	6.10 *qq* (7.5, 1.5)	6.85 *qq* (7.5, 1.5)
Me-4	2.00 *dq* (7.5, 1.5)	1.81 *dq* (7.5, 1.5)
Me-5	1.90 *quin* (1.5)	1.83 *quin* (1.5)

†The position of the ester group in **4** was revised. See reference [3].



1: R^1 = H; R^2 = OAng
2: R^1 = H; R^2 = OTigl
3: R^1 = R^2 = OAng



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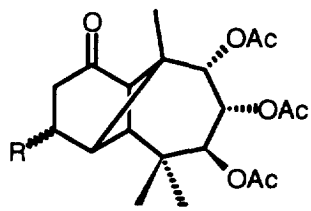

5: R = α-Me
6: R = β-Me

Table 2. ^{13}C NMR data of **1** and **2** (50.3 MHz, $CDCl_3$)

C	1	2
1	211.7	212.1
2	42.3	42.3
3	27.1	27.1
4	44.6	44.7
5	42.2	42.7
6	36.3	36.5
7	28.1	28.0
8	26.0	26.0
9	77.6	77.7
10	46.5	46.5
11	53.7	54.1
12	19.7	19.7
13	20.3	20.3
14	20.3	20.2
15	71.7	72.7
	OAng (C-9)*	OAng (C-9)*
1	167.3	167.5
2	127.9	128.1
3	138.4	138.7
4	15.9	16.0
5	20.7	20.7
	OAng (C-15)*	OTigl (C-15)*
1	167.7	168.2
2	127.5	128.5
3	138.7	137.8
4	15.9	14.4
5	20.7	12.1

*The ester residue signals were assigned as deduced by HETCOR experiments and by analogy. See refs [8], [13].

C-15. This is also in agreement with the ^{13}C NMR data (Table 2), which showed a 1 ppm chemical shift difference for C-15 on going from **1** to **2**.

Although many longipinene esters functionalized at C-7 and C-15 have been isolated from several *Stevia* species [2, 6, 9, 12], the isolation of esters at C-9 and C-15 like **1** and **2** is rare. The only other known case is the unsaturated analogue **4**, which has been isolated from *S. elatior* [10].

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ with TMS as int. standard. The ^{13}C signals were assigned from APT and HETCOR experiments and by comparison with published data [8, 13]. CC was performed on alumina (Merck) or silica gel (230–400 mesh). TLC was carried out on silica gel PF_{254} (Merck) plates.

Plant material. Stevia viscida HBK was collected at km 283 of the México–Morelia federal road No. 15 in September 1992. A voucher specimen is deposited at the Herbarium of the Instituto de Ecología A. C., Pátzcuaro, Mich. México, where Prof. Jerzy Rzedowski identified the plant material.

Extraction and isolation. The air-dried roots (985 g) of *S. viscida* were extracted × 3 with hexane under reflux for 4 hr. After removal of the solvent, the crude extract (2.2 g) was chromatographed over alumina (30 g), 50 ml frs being collected as follows: frs 1–16 (petrol), 17–24 (C_6H_6), 25–30 ($CHCl_3$), 31–44 (EtOAc). Fr. 31 was rechromatographed under the same conditions collecting 31 frs of 20 ml and monitoring by TLC (hexane–EtOAc, 7:3). Fr. 7 was subjected to prep. TLC (hexane–EtOAc, 4:1 three

developments) giving *ca* 40 mg of diangelate **1** and 10 mg of angelate-tiglate **2**.

Longipinan-9α,15-diangeloyloxy-1-one (**1**). Oil. UV λ_{max}^{EtOH} nm (log ε): 223, (3.95); $[\alpha]_{589}$ − 26°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700, 1640. ^1H NMR see Table 1; ^{13}C NMR see Table 2.

Longipinan-9α-angeloyloxy-15-tigloyloxy-1-one (**2**). Oil. UV λ_{max}^{EtOH} nm (log ε): 223, (3.88); $[\alpha]_{589}$ − 33°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1706, 1650; ^1H NMR see Table 1; ^{13}C NMR see Table 2.

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