Phloroglucinols from the Argentine Ferns *Elaphoglossum gayanum* and *E. piloselloides*

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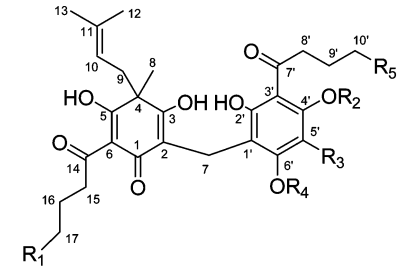
Five new prenylated phloroglucinols were isolated from the diethyl ether extracts of the ferns *Elaphoglossum gayanum* and *E. piloselloides*. Their structures were established by analysis of their spectroscopic data (1D and 2D NMR, HRMS, and IR) and chemical derivatization. The two major compounds exhibited moderate molluscicidal activity against the snail *Biomphalaria peregrina*, a vector of the tropical disease schistosomiasis, with LD_{50} 7.2 μg/mL (14.4 μM) and 11.7 μg/mL (22.2 μM).

Phloroglucinols show a wide variety of biological activities such as molluscicidal, cytotoxic, antimicrobial, antidepressant, and antiplasmodial effects.[1−5] Compounds of this structural type have been isolated from many plants, such as *Hypericum perforatum* and *Dryopteris crassirhizoma*, that have been used in herbal medicine, and in many cases, phloroglucinols proved to be responsible for the observed activities.[3,4,6]

Previously, we isolated two prenylated bicyclic phloroglucinols from the Et_2O extract of the fern *Elaphoglossum piloselloides* (C. Presl) T. Moore.[1] These compounds displayed strong molluscicidal activity against the snail *Biomphalaria peregrina* (Orbignyi), a vector of the human parasitosis schistosomiasis.[1] Chemical reinvestigation of the diethyl ether extract of an Argentine collection of *E. piloselloides* has led to the isolation of three additional new phloroglucinols. In addition, we have isolated two new phloroglucinols from the fern *E. gayanum* (Fée) T. Moore that are structurally related to those previously found in *E. piloselloides*.

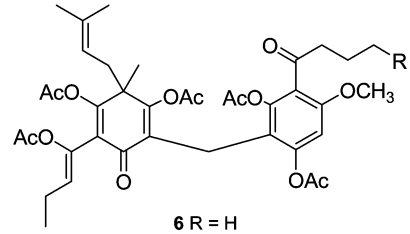


1 R_1 = Et R_2 = H R_3 = H R_4 = CH_3 R_5 = H
2 R_1 = Et R_2 = H R_3 = H R_4 = CH_3 R_5 = Et
3 R_1 = H R_2 = H R_3 = CH_3 R_4 = CH_3 R_5 = H
4 R_1 = H R_2 = CH_3 R_3 = H R_4 = H R_5 = H
5 R_1 = H R_2 = CH_3 R_3 = H R_4 = H R_5 = Et

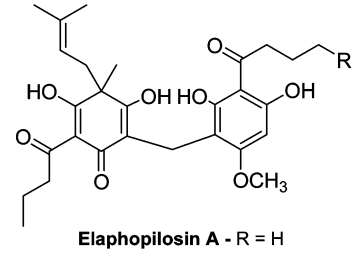
Results and Discussion

Air-dried rhizomes and roots of *E. gayanum* and sterile fronds, rhizomes, and roots of *E. piloselloides* were separately ground and extracted with Et_2O. The Et_2O extract of *E. gayanum* was fractionated by column chromatography (CC) over SiO_2, and the phloroglucinol-containing fraction was further separated by normal-phase HPLC to yield phloroglucinols **1** and **2**.

Compound **1** was obtained as a colorless oil. Its HREIMS spectrum showed a molecular ion peak $[M]^+$ at *m/z* 528.2718 (calcd 528.2724), consistent with the molecular formula $C_{30}H_{40}O_8$ and indicating 11 degrees of unsaturation. The ^1H spectrum of compound **1** in acetone-d_6 (Table 1) indicated a structural similarity to elaphopilosin B (structure shown), a compound that was previously isolated from *E. piloselloides*,[1] differing only in the location of the acyl moieties, as could be deduced by the HMBC spectrum of **1**, provided as Supporting Information. When using acetone-d_6, HMBC correlations between the OH protons and their neighboring carbons were detected due to intermolecular hydrogen bonding that occurred between acetone-d_6 (solvent) and the OH protons, resulting in a decrease in their exchange rate. The HMBC spectrum of **1** showed correlations between 5-OH and C-14 and C-15 indicating that the oxohexyl moiety was located at the filicinic acid residue and the oxobutyl moiety was attached to the other ring. The mentioned correlations are only possible if the OH proton is shared with the oxygen atoms on C-5 and C-14, forming a six-membered ring by H bonding (Figure 1). The indicated structural arrangement is a result of keto−enol tautomerism occurring in the filicinic acid-type ring and is consistent with the very low-field signal assigned to the 5-OH proton in the ^1H spectrum (δ 18.65). Thus, the structure of **1** was established as 2-{[2,4-dihydroxy-6-methoxy-3-(1-oxobutyl)phenyl]methyl}-3,5-dihydroxy-4-methyl-4-(3-methyl-2-butenyl)-



6 R = H
7 R = Et



Elaphopilosin A - R = H
Elaphopilosin B - R = Et

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Table 1. ^{1}H NMR Data of Compounds **1**−**5** (acetone-d_6, 500 and 300 MHz)

	δ [ppm], multiplicity, *J* [Hz]				
H	**1**	**2**	**3**	**4**	**5**
7	3.56, s	3.56, s	3.62, d, *J* = 15.5 3.52, d, *J* = 15.5	3.52, s	3.53, s
8	1.53, s	1.53, s	1.52, s	1.51, s	1.52, s
9	2.70, dd, *J* = 13.5, 8.0 2.63, dd, *J* = 13.5, 8.0	2.70, dd, *J* = 13.5, 8.0 2.63, dd, *J* = 13.5, 8.0	2.69, dd, *J* = 13.5, 8.8 2.56, dd, *J* = 13.5, 7.0	2.71, dd, *J* = 13.5, 8.4 2.58, dd, *J* = 13.5, 8.4	2.72, dd, *J* = 13.4, 7.2 2.59, dd, *J* = 13.4, 7.2
10	4.64, br t, *J* = 8.0	4.64, br t, *J* = 8.0	4.57, br t, *J* = 7.8	4.63, tt, *J* = 8.4, 1.4	4.63, tt, *J* = 7.2, 1.2
12	1.40, s	1.40, s	1.32, s	1.37, s	1.37, s
13	1.34, s	1.34, s	1.25, s	1.32, s	1.32, s
15	3.24, ddd, *J* = 15.0, 8.5, 7.0 3.07, ddd, *J* = 15.0, 8.5, 7.0	3.23, ddd, *J* = 15.0, 8.5, 7.0 3.07, ddd, *J* = 15.0, 8.5, 7.0	3.24, ddd, *J* = 15.5, 8.0, 7.0 3.08, ddd, *J* = 15.5, 8.0, 7.0	3.22, ddd, *J* = 16.0, 7.6, 1.2 3.12, ddd, *J* = 16.0, 7.6, 1.2	3.22, ddd, *J* = 16.0, 7.5, 1.5 3.13, ddd, *J* = 16.0, 7.5, 1.5
16	1.63, m	1.66, m	1.68, q, *J* = 7.0	1.68, sextet, *J* = 7.6	1.67, q, *J* = 7.5
17	1.40−1.32[a]	1.40−1.34[a]	0.99, t, *J* = 7.0	0.98 t, *J* = 7.6	0.98, t, *J* = 7.5
18	1.40−1.32[a]	1.40−1.34[a]			
19	0.91, t, *J* = 7.0	0.91, t, *J* = 7.0			
5′	6.16, s	6.16, s		6.11, s	6.13, s
8′	3.14, td, *J* = 7.5, 2.0	3.14, td, *J* = 7.5, 5.0	3.16, td, *J* = 7.5, 5.0	3.02, td, *J* = 7.2, 4.5	3.03, td, *J* = 7.5, 1.5
9′	1.70, q, *J* = 7.5	1.68, t, *J* = 7.5	1.70, q, *J* = 7.5	1.68, sextet, *J* = 7.2	1.67, q, *J* = 7.5
10′	0.97, t, *J* = 7.5	1.40−1.34[a]	0.97, t, *J* = 7.5	0.99, t, *J* = 7.2	1.38−1.33[a]
11′		1.40−1.34[a]			1.38−1.33[a]
12′		0.92, t, *J* = 6.5			0.91, t, *J* = 7.5
5′-CH_3			2.09, s		
-OCH_3	4.06, s	4.06, s	4.06, s	3.93, s	3.94, s
3-OH	9.06, s	9.06, s	9.76, s	9.93, s	9.92, s
5-OH	18.65, s	18.65, s	18.61, s	18.66, s	18.66, s
2′-OH	11.58, s	11.58, s	11.21, s	16.59, s	16.59, s
4′-OH	13.70, s	13.71, s	13.73, s		
6′-OH				11.12, s	11.13, s

[a] Overlapping signals.

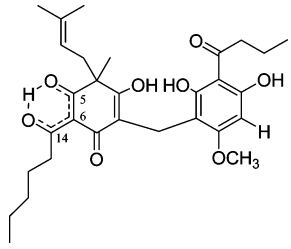

Figure 1. Structure of phloroglucinol **1** showing the proposed six-membered-ring arrangement involving C-5, C-6, and C-14.

6-(1-oxohexyl)-2,5-cyclohexadien-1-one. This new compound was named elaphogayanin A.

The HREIMS spectrum of compound **2** indicated the molecular formula $C_{32}H_{44}O_8$ (*m*/*z* 556.3045, calcd 556.3037). The ^{1}H (Table 1) and ^{13}C NMR spectra of **2** resembled those of **1**, except for the acyl residue attached to the phloroglucinol-type ring. Analysis of the HSQC, ^{1}H−^{1}H COSY, and HMBC spectra of **2** permitted identification of this residue as an oxohexyl moiety. On the basis of the foregoing evidence, the structure of **2** was established as 2-{[2,4-dihydroxy-6-methoxy-3-(1-oxohexyl)phenyl]methyl}-3,5-dihydroxy-4-methyl-4-(3-methyl-2-butenyl)-6-(1-oxohexyl)-2,5-cyclohexadien-1-one. This new compound was named elaphogayanin B.

After dewaxing the ether extract of *E. piloselloides* by treatment with cold MeOH, it was processed successively by CC and normal-phase HPLC, affording phloroglucinols **3**−**5**. Compound **3** was isolated as a yellow oil with a molecular formula of $C_{29}H_{38}O_8$, indicated by a molecular ion peak $[M]^+$ at *m*/*z* 514.2570 (calcd 514.2567) observed in its HREIMS. The ^{1}H NMR spectrum of **3** (Table 1) was very similar to that of elaphopilosin A (structure shown), a phloroglucinol previously isolated from *E. piloselloides*.[1] The main differences between **3** and elaphopilosin A were the signal of an extra methyl group at δ 2.05 in the proton NMR spectrum of **3** and the absence of the signal corresponding to the only aromatic proton of elaphopilosin A. The HMBC spectrum of compound **3** (Supporting Information) showed correlations between the previously mentioned methyl group and the signals assigned to C-4′, C-5′, and C-6′, indicating that this methyl group was located at C-5′. Thus, compound **3** was identified as 2-{[2,4-dihydroxy-6-methoxy-5-methyl-3-(1-oxobutyl)phenyl]methyl}-3,5-dihydroxy-4-methyl-4-(3-methyl-2-butenyl)-6-(1-oxobutyl)-2,5-cyclohexadien-1-one. This new phloroglucinol was named elaphopilosin C.

The HREIMS data of compound **4** showed a molecular ion peak $[M]^+$ at *m*/*z* 500.2401 (calcd 500.2411), consistent with the molecular formula $C_{28}H_{36}O_8$, indicating that this compound was an isomer of elaphopilosin A.[1] The ^{1}H NMR spectrum of compound **4** in acetone-d_6 (Table 1) was very similar to that of elaphopilosin A. Acetylation of **4** gave the pentaacetylated derivative **6**. Analysis of its HMBC spectrum indicated that the OCH_3 group was located at C-4′, while in elaphopilosin A it is attached to C-6′.[1] Thus, the structure of compound **6** was established, and consequently that of **4** was deduced to be 2-{[2,6-dihydroxy-4-methoxy-3-(1-oxobutyl)phenyl]methyl}-3,5-dihydroxy-4-methyl-4-(3-methyl-2-butenyl)-6-(1-oxobutyl)-2,5-cyclohexadien-1-one. This new compound was named elaphopilosin D.

The HREIMS spectrum of compound **5** indicated the molecular formula $C_{30}H_{40}O_8$ (*m*/*z* 528.2725, calcd 528.2724). Therefore, this compound was an isomer of both elaphopilosin B and elaphogayanin A (**1**). The ^{1}H NMR spectrum of **5** (Table 1) was very similar to that of elaphopilosin B.[1] Acetylation of **5** furnished the pentaacetylated derivative **7**. Its 1D NMR data were very similar to those of **6**, except for the acyl moiety attached to the phloroglucinol-type ring. This acyl residue was determined to be an oxohexyl group by careful analysis of the HSQC, ^{1}H−^{1}H COSY, and HMBC spectra of **7**. Thus, the structure of **7** was established as depicted, and the structure of **5** was deduced to be 2-{[2,6-dihydroxy-4-methoxy-3-(1-oxohexyl)phenyl]methyl}-3,5-dihydroxy-4-methyl-4-(3-methyl-2-butenyl)-6-(1-oxobutyl)-2,5-cyclohexadien-1-one. This new compound was named elaphopilosin E.

Apparently, in *Elaphoglossum* ferns the acyl residue attached to the filicinic acid-type ring remains unaltered for all phloroglucinols from a particular species. The phloroglucinols of *E. piloselloides* carry an oxobutyl group at C-6, while an oxohexyl residue is attached to C-6 in all phloroglucinols of *E. gayanum* identified to date.

Although acetylation proved to be a good strategy to identify signals of NMR spectra of phloroglucinols containing a filicinic

Table 2. Molluscicidal Activity of the Et_2O Extract of *E. gayanum*, of Natural Phloroglucinols **4** and **5**, and of Their Acetylated Derivatives **6** and **7** on *B. peregrina* Snails after 24 h of Exposure

	concentration [ppm][a]				
	50	20	10	5	2.5
sample	% mortality				
4			81	24	10
5		81	52	14	
6	19	0			
7	5	0			
control	0	0	0	0	0

[a] For each concentration, $n = 21$.

acid moiety recorded in $CDCl_3$, well-resolved spectra are obtained with no need of acetylation when NMR spectra are measured in acetone-d_6.

Molluscicidal activity of the major phloroglucinols (**4** and **5**) isolated from *E. piloselloides* and that of their corresponding acetylated derivatives (**6** and **7**) was evaluated against the snail *B. peregrina*. The bioassay was carried out as described previously.[1] Mortality rates for each compound are presented in Table 2, while the calculated LD_{50} and LD_{90} values are given in Table 3. As previously reported,[1] the snails were more susceptible to the free phloroglucinols, **4** and **5**, than to their corresponding acetylated derivatives, **6** and **7**. Phloroglucinol **4** was the most active compound (LD_{50} 7.2 ppm and LD_{90} 11.4 ppm). The LD_{50} values for acetylated derivatives were over 50 ppm, and they were not determined precisely. Although **4** and **5** are good molluscicidal agents, their activity is not as strong as that of the previously isolated elaphopilosins A and B.[1]

The molluscicidal activity of the diethyl ether extract of *E. gayanum* was also evaluated against *B. peregrina*. LD_{50} and LD_{90} values (97.8 and 144.6 ppm, respectively) indicated that it is not a promising molluscicidal agent according to WHO standards for extracts.[7,8] Compounds **1** and **2** were isolated in very small amounts; therefore their molluscicidal activity could not be assessed.

Experimental Section

General Experimental Procedures. A JASCO P-1030 digital polarimeter was used to measure optical rotations. Infrared spectra were registered on a Shimadzu FT/IR-8400S spectrophotometer by the diffuse reflectance method. MS analyses were conducted on a JEOL JMS AX-500 spectrometer. NMR spectra were measured at 600, 500, or 300 MHz for ^1H and at 150 or 125 MHz for ^{13}C on Varian Unity spectrometers, using $CDCl_3$ or acetone-d_6 as solvent. When registering spectra in $CDCl_3$, TMS was used as internal standard. Column chromatography (CC) was carried out over silica gel 60 (70−230 mesh, Merck), using an *n*-hexane−EtOAc gradient (100:0 → 0:100) as mobile phase. The eluates were monitored by TLC on aluminum precoated plates, Merck Kieselgel 60 F_{254}. Godin reagent was used to spray the plates.[9] Preparative HPLC was carried out on a Gilson instrument, using a silica gel column (Chemcopak; Chemcosorb 5 Si-U, 5 μm, 250 × 10 mm i.d.) and ultraviolet and refractive index detectors in parallel.

Plant Material. *E. piloselloides* and *E. gayanum* were collected near La Banderita, Tucumán, Argentina, in December 2005 and 2007, respectively. The plant material was identified by one of the authors (M.H.T.), and voucher specimens (LIL 607856 and 609961) were deposited at the Herbarium of the Fundación Miguel Lillo, Tucumán, Argentina.

Extraction and Isolation. Air-dried rhizomes and roots of *E. gayanum* (148 g) were ground and extracted with Et_2O. The dried extract (2.7 g), was fractionated by CC over silica gel, using an *n*-hexane−EtOAc gradient as mobile phase. The phloroglucinol-containing fraction (136 mg), eluted with 4:1 *n*-hexane−EtOAc, was further processed by normal-phase HPLC (9:1 *n*-hexane−EtOAc, 3.5 mL/min), leading to the isolation of compounds **1** (7.1 mg) and **2** (1.8 mg).

The plant material of *E. piloselloides* (660 g), consisting of rhizomes, roots, and sterile fronds, was air-dried, ground, and extracted with Et_2O. The ether extract (20.4 g) was dewaxed by overnight maceration with MeOH (400 mL) at 4 °C. The wax-free extract (6.2 g) was submitted to CC over silica gel using an *n*-hexane−EtOAc gradient as mobile phase. One of the phloroglucinol-containing fractions (316 mg), eluted with 9:1 *n*-hexane−EtOAc, was further processed by NPHPLC (95:5 *n*-hexane−EtOAc, 2.0 mL/min) to afford compounds **3** (1.9 mg), **4** (89 mg), and **5** (15 mg).

Elaphogayanin A (1): colorless oil; $[\alpha]^{23}_D$ −20.4 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3263, 2729, 2658, 1639, 1599, 1371, 1267, 1138; ^1H NMR data (500 MHz, acetone-d_6) in Table 1; ^{13}C NMR data (125 MHz, acetone-d_6) δ 189.5 (C, C-1), 115.0 (C, C-2), 171.2 (C, C-3), 50.7 (C, C-4), 199.9 (C, C-5), 111.7 (C, C-6), 18.0 (CH_2, C-7), 24.3 (CH_3, C-8), 39.9 (CH_2, C-9), 119.3 (CH, C-10), 137.5 (C, C-11), 18.6 (CH_3, C-12), 26.6 (CH_3, C-13), 207.8 (C, C-14), 42.3 (CH_2, C-15), 26.6 (CH_2, C-16), 33.3 (CH_2, C-17), 24.1 (CH_2, C-18), 15.2 (CH_3, C-19), 107.1 (C, C-1′), 161.6 (C, C-2′), 108.3 (C, C-3′), 167.3 (C, C-4′), 93.7 (CH, C-5′), 163.6 (C, C-6′), 208.7 (C, C-7′), 47.9 (CH_2, C-8′), 19.7 (CH_2, C-9′), 15.2 (CH_3, C-10′), 58.1 (−O*C*H_3); HREIMS, 75 eV, *m*/*z* 528.2718 (calcd for $C_{30}H_{40}O_8$, 528.2724).

Elaphogayanin B (2): colorless oil; $[\alpha]^{23}_D$ −16.5 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3265, 2729, 2658, 1625, 1597, 1375, 1265, 1138; ^1H NMR data (500 MHz, acetone-d_6) in Table 1;^{13}C NMR data (125 MHz, acetone-d_6) δ 189.5 (C, C-1), 115.1 (C, C-2), 171.2 (C, C-3), 50.7 (C, C-4), 199.9 (C, C-5), 111.7 (C, C-6), 18.0 (CH_2, C-7), 24.3 (CH_3, C-8), 39.9 (CH_2, C-9), 119.3 (CH, C-10), 137.5 (C, C-11), 18.6 (CH_3, C-12), 26.6 (CH_3, C-13), 207.8 (C, C-14), 42.3 (CH_2, C-15), 26.6 (CH_2, C-16), 33.3 (CH_2, C-17), 24.1 (CH_2, C-18), 15.2 (CH_3, C-19), 107.1 (C, C-1′), 161.5 (C, C-2′), 108.2 (C, C-3′), 167.3 (C, C-4′), 93.7 (CH, C-5′), 163.6 (C, C-6′), 208.8 (C, C-7′), 45.9 (CH_2, C-8′), 26.3 (CH_2, C-9′), 33.4 (CH_2, C-10′), 24.3 (CH_2, C-11′), 15.3 (CH_3, C-12′), 58.1 (−O*C*H_3); HREIMS, 75 eV, *m*/*z* 556.3045 (calcd for $C_{32}H_{44}O_8$, 556.3037).

Elaphopilosin C (3): yellow oil; $[\alpha]^{23}_D$ −10.7 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3155, 2960, 2932, 2873, 2721, 2654, 1600, 1458, 1421, 1375, 1286, 1204, 1134; ^1H NMR data (500 MHz, acetone-d_6) in Table 1; ^{13}C NMR data (125 MHz, acetone-d_6) δ 189.7 (C, C-1), 115.1 (C, C-2), 171.7 (C, C-3), 50.8 (C, C-4), 199.7 (C, C-5), 111.8 (C, C-6), 18.9 (CH_2, C-7), 23.9 (CH_3, C-8), 40.2 (CH_2, C-9), 119.1 (CH, C-10), 137.6 (C, C-11), 18.4 (CH_3, C-12), 26.5 (CH_3, C-13), 207.6 (C, C-14), 44.2 (CH_2, C-15), 20.1 (CH_2, C-16), 15.1 (CH_3, C-17), 111.4 (C, C-1′), 159.6 (C, C-2′), 110.5 (C, C-3′), 164.4 (C, C-4′), 110.7 (C, C-5′), 162.0 (C, C-6′), 209.7 (C, C-7′), 48.3 (CH_2, C-8′), 19.7 (CH_2, C-9′), 15.2 (CH_3, C-10′), 63.7 (−O*C*H_3), 9.9 (5′-*C*H_3); HREIMS, 75 eV, *m*/*z* 514.2570 (calcd for $C_{29}H_{38}O_8$, 514.2567).

Elaphopilosin D (4): yellow oil; $[\alpha]^{22}_D$ +10.1 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3169, 2963, 2934, 2874, 2724, 2658, 1644, 1601, 1467, 1436, 1236, 1204, 1151; ^1H NMR data (300 MHz, acetone-d_6) in Table 1; HREIMS, 75 eV, *m*/*z* 500.2401 (calcd for $C_{28}H_{36}O_8$, 500.2411).

Elaphopilosin E (5): yellow oil; $[\alpha]^{20}_D$ +11.6 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3170, 2960, 2932, 2872, 2722, 2657, 1639, 1595, 1465, 1436, 1202; ^1H NMR data (300 MHz, acetone-d_6) in Table 1; HREIMS, 75 eV, *m*/*z* 528.2725 (calcd for $C_{30}H_{40}O_8$, 528.2724).

Acetylation of Elaphopilosin D. Compound **4** (25.8 mg) was dissolved in 1 mL of pyridine, 1 mL of Ac_2O was added, and the mixture was stirred overnight at room temperature. After pyridine and

Table 3. LD_{50} and LD_{90} Values Calculated for the Extract of *E. gayanum* and Phloroglucinols **4** and **5** against *B. peregrina* Adults

	LD_{50} (CI_{95})[a]		LD_{90} (CI_{95})	
sample	[ppm]	[μM]	[ppm]	[μM]
E. gayanum (extract)	97.8 (81.9; 137.9)		144.6 (116.9; 272.3)	
4	7.2 (5.9; 8.8)	14.4 (11.8; 17.6)	11.4 (9.6; 15.4)	22.8 (19.2; 30.8)
5	11.7 (8.6; 15.1)	22.2 (16.3; 28.6)	22.3 (18.0; 33.2)	42.2 (34.1; 62.9)

[a] (CI_{95}): 95% confidence interval.

Ac_2O evaporation in vacuo, the residue was purified by normal-phase HPLC (3:2 *n*-hexane−EtOAc, 2.5 mL/min), furnishing 28.2 mg of **6** (yield 77.0%).

Compound 6: colorless oil; $[\alpha]^{23}_D$ +10.8 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3018, 2966, 2938, 2876, 1771, 1695, 1647, 1612, 1367, 1188; ^1H NMR data (600 MHz, $CDCl_3$) δ 3.68 (1H, d, J = 15.4 Hz, H-7a), 3.27 (1H, d, J = 15.4 Hz, H-7b), 1.18 (3H, s, H-8), 2.46 (1H, dd, J = 17.6, 8.8 Hz, H-9a), 2.26−2.21 (H-9b), 4.74 (1H, br t, J = 7.2 Hz, H-10), 1.62 (3H, s, H-12), 1.48 (3H, s, H-13), 5.37 (1H, t, J = 7.4 Hz, H-15), 2.04 (2H, quint, J = 7.4 Hz, H-16), 0.99 (3H, t, J = 7.4 Hz, H-17), 6.59 (1H, s, H-5′), 2.81 (1H, dt, J = 17.7, 6.9 Hz, H-8′a), 2.74 (1H, dt, J = 17.7, 6.9 Hz, H-8′b), 1.68−1.62 (2H, H-9′), 0.94 (3H, t, J = 7.4 Hz, H-10′), 3.79 (3H, s, −OCH_3), 2.24, 2.24, 2.21, 2.19, 2.10 (each 3H, s, CH_3C═O); ^{13}C NMR data (150 MHz, $CDCl_3$) δ 183.3 (C, C-1), 128.7 (C, C-2), 161.4 (C, C-3), 47.7 (C, C-4), 163.4 (C, C-5), 125.3 (C, C-6), 18.3 (CH_2, C-7), 21.7 (CH_3, C-8), 35.9 (CH_2, C-9), 117.6 (CH, C-10), 135.0 (C, C-11), 25.8 (CH_3, C-12), 17.7 (CH_3, C-13), 136.2 (C, C-14), 127.4 (CH, C-15), 19.8 (CH_2, C-16), 13.2 (CH_3, C-17), 118.1 (C, C-1′), 146.4 (C, C-2′), 122.1 (C, C-3′), 155.4 (C, C-4′), 104.0 (CH, C-5′), 150.7 (C, C-6′), 203.0 (C, C-7′), 45.7 (CH_2, C-8′), 17.0 (CH_2, C-9′), 13.7 (CH_3, C-10′), 55.9 (−OCH_3), 21.0, 20.9, 20.8, 20.6, 20.5 (CH_3C═O), 168.6, 168.4, 167.3, 166.6, 166.4 (*C*═O); HRFABMS *m*/*z* 733.2853 (calcd for $C_{38}H_{46}O_{13}Na$, 733.2837).

Acetylation of Elaphopilosin E. Compound **5** (5.6 mg) was acetylated using the same procedure employed for acetylation of **4**. The reaction mixture was dried and the product was purified by normal-phase HPLC (3:2 *n*-hexane−EtOAc, 2.5 mL/min), leading to the isolation of 6.4 mg of **7** (yield 82.0%).

Compound 7: colorless oil; $[\alpha]^{23}_D$ +11.8 (*c* 10.0, $CHCl_3$); IR ν_{max}^{neat} cm^{-1} 3018, 2962, 2934, 2862, 1776, 1760, 1693, 1646, 1612, 1366, 1181; ^1H NMR data (600 MHz, $CDCl_3$) δ 3.68 (1H, d, J = 15.6 Hz, H-7a), 3.27 (1H, d, J = 15.6 Hz, H-7b), 1.18 (3H, s, H-8), 2.46 (1H, dd, J = 14.3, 9.0 Hz, H-9a), 2.26−2.22 (H-9b), 4.74 (1H, br t, J = 7.4 Hz, H-10), 1.61 (3H, s, H-12), 1.47 (3H, s, H-13), 5.37 (1H, t, J = 7.6 Hz, H-15), 2.04 (2H, quint, J = 7.6 Hz, H-16), 0.99 (3H, t, J = 7.6 Hz, H-17), 6.59 (1H, s, H-5′), 2.82 (1H, ddd, J = 17.8, 8.1, 6.8 Hz, H-8′a), 2.75 (1H, ddd, J = 17.8, 8.1, 6.8 Hz, H-8′b), 1.65−1.58 (2H, H-9′), 1.36−1.26 (4H, H-10′ and H-11′), 0.90 (3H, t, J = 7.0 Hz, H-12′), 3.79 (3H, s, −OCH_3), 2.24, 2.24, 2.21, 2.19, 2.10 (each 3H, s, CH_3C═O); ^{13}C NMR data (150 MHz, $CDCl_3$) δ 183.3 (C, C-1), 128.7 (C, C-2), 161.4 (C, C-3), 47.7 (C, C-4), 163.4 (C, C-5), 125.3 (C, C-6), 18.3 (CH_2, C-7), 21.7 (CH_3, C-8), 36.0 (CH_2, C-9), 117.6 (CH, C-10), 135.0 (C, C-11), 25.8 (CH_3, C-12), 17.7 (CH_3, C-13), 136.2 (C, C-14), 127.4 (CH, C-15), 19.9 (CH_2, C-16), 13.2 (CH_3, C-17), 118.1 (C, C-1′), 146.4 (C, C-2′), 122.1 (C, C-3′), 155.4 (C, C-4′), 104.1 (CH, C-5′), 150.7 (C, C-6′), 203.2 (C, C-7′), 43.8 (CH_2, C-8′), 23.2 (CH_2, C-9′), 31.3 (CH_2, C-10′), 22.5 (CH_2, C-11′), 14.0 (CH_3, C-12′), 55.9 (−OCH_3), 21.0, 20.9, 20.8, 20.6, 20.5 (CH_3C═O), 168.6, 168.4, 167.3, 166.6, 166.4 (*C*═O); HRFABMS *m*/*z* 761.3115 (calcd for $C_{40}H_{50}O_{13}Na$, 761.3150).

Molluscicidal Activity. The assay was carried out as described previously.[1] Its outcome was used to calculate LD_{50} and LD_{90} values, using a probit analysis software program.[10] A 10 ppm solution of $CuSO_4$ was employed as positive control and produced 100% mortality of the snail population after 6 h of exposure. The snails were identified by Dr. Alejandra Rumi. They were field-collected and laboratory acclimatized.

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Supporting Information Available: ^1H NMR spectra of compounds **1**−**7**, ^{13}C NMR spectra of compounds **1**−**3**, **6**, and **7**, as well as an HMBC table for compounds **1**−**3**. This information is available free of charge via the Internet at http://pubs.acs.org.

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