Three Novel Monotetrahydrofuran Annonaceous Acetogenins from *Annona montana*

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Three new monotetrahydrofuran (mono-THF) acetogenins, anmontanins A−C (**1**−**3**) were isolated from the leaves of *Annona montana*. Anmontanin C (**3**) is the first stereochemically pure acetogenin reported to have a γ-hydroxymethyl-γ-lactone moiety. Two known mono-THF acetogenins, murisolin and annonacin, were isolated from the seeds of the plant. The structures of compounds **1**−**3** were elucidated by spectral methods and chemical derivatization.

The Annonaceae, a large family of tropical plants, have been intensely investigated over the last 15 years, largely because of the discovery of the Annonaceous acetogenins, a group of C_{32}/C_{34} fatty-acid-derived natural products that show a wide variety of biological activities.[1] *Annona montana* Macf. (Annonaceae) is a medium-sized tree widely distributed in the neo-tropics from the West Indies to southern Brazil.[2] It grows widely in Trinidad, where an infusion of the leaves is used for the treatment of influenza and insomnia.[3]

Previous chemical investigations of *A. montana* have resulted in the isolation of seven annonaceous acetogenins.[2,4,5] In our search for bioactive acetogenins, five monotetrahydrofuran (mono-THF) ring acetogenins were isolated and characterized. From the leaves, three novel compounds, anmontanins A−C (**1**−**3**), were obtained. The known compounds murisolin[6] and annonacin[7] were extracted from the seeds, with murisolin being isolated for the first time from *A. montana*.

Compounds **1**−**3** are all C_{35} mono-THF ring acetogenins, and all possess a ketone functionality between the terminal γ-lactone ring and the tetrahydrofuran ring. Anmontanin C (**3**) is unique in being the first annonaceous acetogenin with a γ-hydroxymethyl-γ-lactone ring to be isolated as a pure stereoisomer.[8−11]

Results and Discussion

Anmontanin A (**1**) was obtained as fine, white needles, mp 74−75 °C. The FABMS revealed a $[M + H]^+$ ion at *m/z* 595, suggesting a molecular weight of 594. The FABMS of its lithium complex exhibited a $[M + Li]^+$ ion at *m/z* 601 consistent with this molecular mass, and HRFABMS confirmed the molecular formula $C_{35}H_{62}O_7$ (see Experimental Section). The IR spectrum showed absorption maxima for hydroxyl (3440 cm^{-1}), α,β-unsaturated-γ-lactone (1735 cm^{-1}), and aliphatic ketone (1710 cm^{-1}) groups.

Three hydroxyl groups were indicated by the successive loss of three molecules of H_2O from the parent ion in the EIMS. This was confirmed by the mass fragmentation pattern of the tris-trimethylsilyl (TMSi) derivative (**1a**), shown in Table 1. The presence in **1** of a ketone functionality flanked by two methylenes was indicated by the ^{13}C NMR signals at δ 211.22, 42.67 (δ_H 2.41, m, 2H), and 42.57 (δ_H 2.39, m, 2H). The presence of the α,β-unsaturated-γ-lactone in association with a C-4 hydroxyl was confirmed by the ^1H NMR signals at δ 7.18 (H-33), 5.06 (H-34), 3.83 (H-4), 2.52, and 2.38 ($H\text{-}3_{ab}$) and the 3H methyl signal at δ 1.45 (H-35), with their respective ^{13}C NMR resonances at δ 151.80, 77.97, 69.80, 33.02, and 19.10. The NMR signals characteristic of a mono-THF ring acetogenin with two flanking hydroxyls[12] were also quite evident for C-14−C-20 (Table 2).

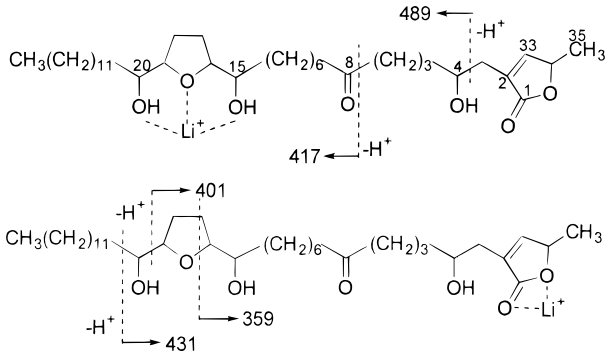

Figure 1. Diagnostic product ions formed by collision-induced dissociation of $[M + Li]^+$ ion (*m/z* 601) of **1**.

The FABMS of the lithium complex of **1** under constant B/E link scanning gave a simple spectrum devoid of signals due to consecutive decomposition products.[13] A detailed analysis of this spectrum, together with the EIMS data of **1** and **1a**, were used to determine the positions of the different functionalities along the aliphatic chain (Figure 1). The C-8 ketone functionality is reported for the first time in the C-16−C-19 mono-THF acetogenins.

The relative stereochemistry about the mono-THF ring of **1** was determined to be *threo*−*trans*−*threo* by direct comparison of the ^{13}C NMR resonances of this moiety with the corresponding signals of the model compounds synthesized by Fujimoto et al.[12] This configuration was also consistent with Born's rule.[14] The stereochemistry at C-4(*R*) and at C-34(*S*) was assigned by biogenetic analogy. The very low yields of this compound precluded further determination of the stereochemistry at C-15, C-16, C-19, or C-20.

Anmontanin B (**2**) ($C_{35}H_{62}O_8$) was obtained as very fine, white needles, mp 59−60 °C. The FABMS of **2** showed a

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Table 1. EIMS Data for the TMSi Derivatives

compound	EIMS *m/z* (rel int)
1a	795 (100) [**1a** − CH_3]$^+$, 705 (42), 615 (10), 525 (10)
2a	883 (100) [**2a** − CH_3]$^+$, 808 (30), 718 (15), 628 (10), 538 (20)
3a	811 [**3a** − CH_3]$^+$, 719 (100), 629 (15), 539 (100)
murisolin-TMSi	797 (35) [M + H]$^+$, 707 (70), 617 (85), 527 (15)
annonacin-TMSi	885 (20) [M + H]$^+$, 795 (42), 705 (75), 615 (20), 525 (30)

Table 2. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR Data for Compounds **1**−**3** in $CDCl_3$

	1		**2**		**3**	
position	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	174.53		174.57		172.26	
2	131.07		131.01		132.36	
3a	33.02	2.38 m	33.40	2.40 m	33.06	2.30 m
3b		2.52 ddd[a]		2.52 m		2.45 m
4	69.80	3.83 m	69.61	3.85 m	69.67	3.81 m
5	37.11	1.47 m	36.94	1.49 m	36.94	1.50 m
6	23.78	1.58 m	21.48	1.54 m	25.54	1.24 m
7a	42.67	2.41 m	35.97	1.41 m	28.00	1.24 m
7b				1.53 m		
8	211.22		67.49	4.05	23.24	1.61 m
9a	42.57	2.39 m	48.95	2.51 m	42.31	2.47 m
9b				2.60 m		
10	23.62	1.58 m	212.34		212.17	
11	29.34−29.69	1.25 m	43.46	2.45 m	42.31	2.47 m
12a	29.34−29.69	1.25 m	23.49	1.54 m	23.78	1.61 m
12b				1.65 m		
13	25.23	1.37 m	29.34−29.69	1.25 m	28.00	1.24 m
14	33.42	1.40 m	29.34−29.69	1.25 m	29.00	1.24 m
15	74.02	3.41 m	25.72	1.51 m	24.74	1.35 m
16	82.65	3.78 m	33.68	1.46 m	32.91	1.37 m
17a	29.00	1.67 m	73.97	3.42 m	74.22	3.30 m
17b		1.99 m				
18a	28.71	1.67 m	82.55	3.81 m	82.60	3.77 m
18b		1.99 m				
19a	82.51	3.78 m	28.11	1.76 m	28.77	1.60 m
19b				1.95 m		1.99 m
20a	73.73	3.41 m	28.11	1.76 m	28.77	1.60 m
20b				1.95 m		1.99 m
21	33.47	1.40 m	82.66	3.81 m	82.09	3.72 m
22	25.31	1.37 m	74.29	3.42 m	74.10	3.43 m
23	29.34−29.69	1.25 m	34.12	1.46 m	32.91	1.37 m
24	29.34−29.69	1.25 m	25.19	1.51 m	24.74	1.35 m
25−29	29.34−29.69	1.25 m	29.34−29.69	1.25 m	29.34−29.69	1.25 m
30	31.89	1.25 m	31.91	1.25 m	31.91	1.25 m
31	22.68	1.28 m	22.68	1.29 m	22.68	1.29 m
32	14.11	0.88 t[b]	14.12	0.89 t[b]	14.12	0.88 t[b]
33	151.80	7.18 d[c]	151.87	7.20 d[c]	149.89	6.94 s
34	77.97	5.06 dq[d]	77.99	5.07 dq[d]	105.67	
35	19.10	1.45 d[e]	19.09	1.44 d[e]	24.33	1.67 s

[a] J = 14.0, 4.0, 1.0 Hz. [b] J = 7.0 Hz. [c] J = 1.0 Hz. [d] J = 7.0, 1.0 Hz. [e] J = 7.0 Hz.

$[M + H]^+$ ion at *m/z* 611, and the FABMS of its lithiated complex exhibited a $[M + Li]^+$ ion at *m/z* 617, confirming a molecular mass of 610. The IR spectrum showed absorption maxima for hydroxyl (3440 cm^{-1}), α,*β*-unsaturated-*γ*-lactone (1740 cm^{-1}), and aliphatic ketone (1710 cm^{-1}) groups. Anmontanin B (**2**), however, showed the successive loss of four molecules of H_2O from the parent ion in the EIMS, indicating the presence of four hydroxyl groups. This was further evidenced by the formation of the tetra-TMSi derivative **2a**, and the four successive losses of TMSiOH from the molecular ion (Table 1). The ^{1}H and ^{13}C NMR spectra of **2** were very similar to those of **1**, indicating that it was a mono-THF ring acetogenin with an α,*β*-unsaturated-*γ*-lactone, a C-4 hydroxyl, and a ketone moiety along the aliphatic chain (Table 2). The only spectral difference between **2** and **1** was that **2** possessed an additional OH group. The functionalities present in **2** were positioned along the aliphatic chain relative to the terminal α,*β*-unsaturated-*γ*-lactone by analysis of the EIMS of **2** and **2a** and, more importantly, by the FABMS under a constant B/E link scan of the lithiated complex of **2** (Figure 2).

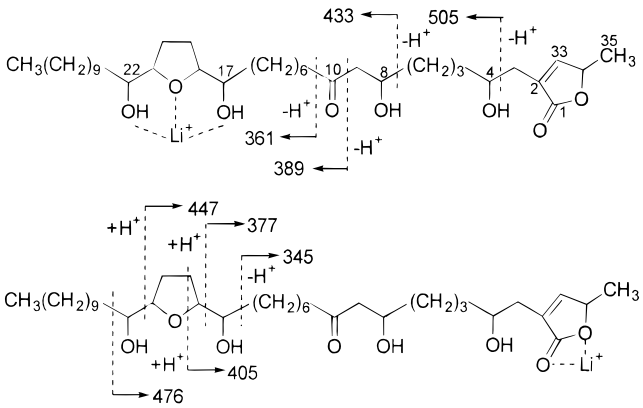


Figure 2. Diagnostic product ions formed by collision-induced dissociation of $[M + Li]^+$ ion (*m/z* 617) of **2**.

The relative stereochemistry about the mono-THF ring in **2** was determined as for **1** and was found to be *threo*−*cis*−*threo*. The absolute stereochemistry at C-4, C-8, C-17,

Table 3. ^{1}H NMR (500 MHz, $CDCl_3$) Chemical Shifts for the Determination of the Absolute Configuration at C-4, C-8, C-17, and C-22 of the *Tetra* (*S*)-and (*R*)-MTPA Esters of **2**

MTPA ester of **2**	H-5$_{ab}$	H-3$_{ab}$	H-33	H-34	H-35	H-7$_{ab}$	H-9$_{ab}$	H-16$_{ab}$	H-18	H-19$_{ab}$	H-20$_{ab}$	H-21	H-23$_{ab}$
δ_H (*S*)	1.61	2.55	6.72	4.88	1.29	3.48	3.54	1.44	3.76	1.94	1.61	4.32	NA[a]
	1.70	2.60						1.36		1.69	1.36		
δ_H (*R*)	1.60	2.58	6.95	4.96	1.31	3.48	3.49	1.43	3.83	1.95	1.60	4.30	NA[a]
	1.69	2.62						1.35		1.70	1.35		
$\Delta\delta_H$[b]	+0.01	−0.03	−0.23	−0.08	−0.02	0.00	+0.05	+0.01	−0.07	−0.01	+0.01	+0.02	
	+0.01	−0.02						+0.01		−0.01	+0.01		
deduced carbinol configuration			**C-4*R***				**C-8*R***		**C-17*S***			**C-22*R***	

[a] NA = not assignable by COSY. [b] $\Delta\delta_H = \delta_H(S) - \delta_H(R)$.

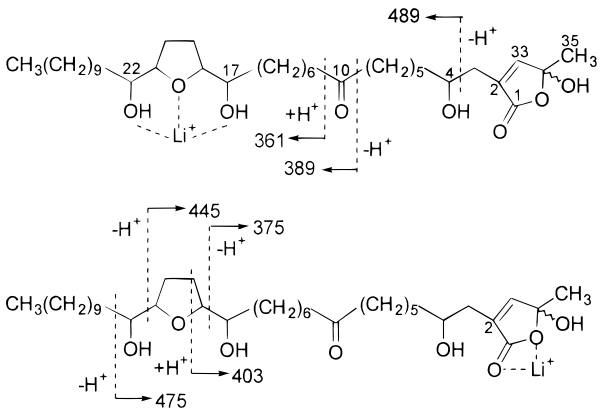
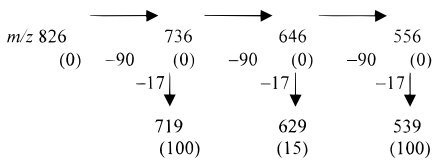


Figure 3. Diagnostic product ions formed by collision-induced dissociation of $[M + Li]^+$ ion (*m*/*z* 617) of **3**.

C-18, C-21, C-22, and C-34 was determined by Mosher ester methodology.[15,16] The tetra-(*S*)- and (*R*)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) esters were prepared, and the relevant ^{1}H NMR resonances were assigned from the ^{1}H−^{1}H COSY and HSQC data (Table 3). The $\Delta\delta_H$(S − R) values for the relevant protons were calculated and used to determine the absolute configuration of **2** (C-4*R*, C-8*R*, *C*-17*S*, C-18*S*, C-21*R*, C-22*R*, and C-34*S*).

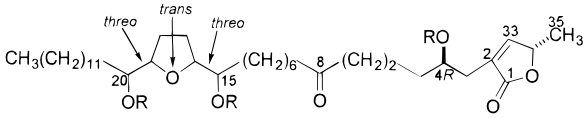
Anmontanin C (**3**) was obtained as very fine, white needles, mp 104−105 °C. The FABMS gave a positive molecular ion $[M + H]^+$ at *m*/*z* 611. The FABMS of its lithium complex exhibited a $[M + Li]^+$ ion at *m*/*z* 617 consistent with this molecular mass, and HRFABMS confirmed the molecular formula $C_{35}H_{62}O_8$. The IR spectrum showed absorption maxima for hydroxyl (3440 cm^{-1}), α,β-unsaturated-γ-lactone (1740 cm^{-1}), and aliphatic ketone (1710 cm^{-1}) groups.

The successive loss of three molecules of H_2O and one OH was observed in the EIMS and FABMS of **3** (Figure 3). To verify the number of secondary hydroxyls present in **3**, the TMSi derivative **3a** was prepared. EIMS data of **3a** did not show a molecular ion for either a tetra- or a tris-TMSi derivative. However, an ion at *m*/*z* 811, $[M - CH_3]^+$, was observed (Table 1). This could be explained by the loss of a methyl group attached to Si in the tris derivative, the latter being obtained by derivation of the three secondary hydroxyl groups. Also, in the EIMS of **3a** (Table 1), fragment ions indicating the presence of a tertiary alcohol in **3** were observed as follows:

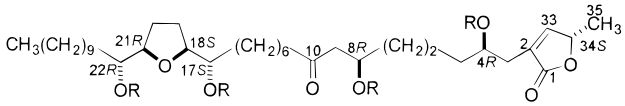


(Relative intensities are in parentheses.)

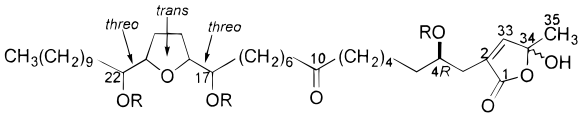
In the FABMS of the lithium complex of **3**, under constant B/E link scanning, a base peak was observed at *m*/*z* 489, due to the loss of 128 amu. This is very peculiar because, under these experimental conditions, the loss of 128 amu has not been previously observed in the Annonaceous acetogenins.[13] The presence of this base peak at *m*/*z* 489 suggested the presence of a new γ-lactone type, possibly bearing a hydroxyl moiety.



1 R = H
1a R = TMS



2 R = H
2a R = TMS



3 R = H
3a R = TMS

The ^{1}H and ^{13}C NMR data of **3** fully supported this feature, the typical ^{13}C NMR resonance for C-34 (ca. δ 77.9) was not observed but was replaced by a signal at δ 105.67, consistent with a hemiketal carbon atom. Also, the typical methyl doublet of the C-35 protons (δ 1.42, d) was replaced by a methyl singlet at δ 1.67. The carbon signal for C-35 shifted slightly downfield from the typical position at δ 19.10 to 24.33, and C-33 was shifted slightly upfield from δ 151.80 to 149.89 (Table 2). These NMR signals were similar to those of donnaienins A and B.[8] Long-range ^{1}H and ^{13}C NMR correlations were observed that further supported this γ-hydroxymethyl-γ-lactone system. These were the correlations between (a) the C-35 protons and C-33 and C-34 and (b) H-33 and C-1, C-2, and C-34.

Compound **3**, as for **1** and **2**, showed characteristic NMR signals indicating a mono-THF ring acetogenin with two flanking hydroxyls and a keto-functionality along the aliphatic chain. These functionalities were positioned along the aliphatic chain, as before, by use of the fragmentation data from the FABMS of the lithiated complex of **3**. The relative stereochemistry was determined as previously described for **1** and **2** and was found to be *threo*−*trans*−

Table 4. ^{1}H NMR (500 MHz, $CDCl_3$) Chemical Shifts for the Determination of the Absolute Configuration at C-4 of the *Tri* (*S*)- and (*R*)-MTPA Esters of **3**

MTPA ester of **3**	H-5_{ab}	H-3_{ab}	H-33	H-34	H-35
δ_H (*S*)	1.53	2.53 2.58	6.36		1.68
δ_H (*R*)	1.44	2.55 2.60	6.37		1.70
$\Delta\delta_H$[a]	+0.09	−0.02 −0.02	−0.01		−0.02
deduced carbinol			**C-4*R***		

[a] $\Delta\delta_H = \delta_H(S) - \delta_H(R)$.

threo. Attempts to determine the absolute stereochemistry about the THF ring, by Mosher ester methodology, were unsuccessful because the relevant proton chemical shifts for both the (*S*)- and (*R*)-Mosher esters were identical. The absolute configuration at C-4, however, was determined by this method to be *R* (Table 4).

This type of γ-hydroxymethyl-γ-lactone has been reported before among the Annonaceous acetogenins,[8−11] but always as an epimeric pair. Anmontanin C (**3**) was obtained as a stereochemically pure compound; there was no duplication of the ^{1}H and ^{13}C NMR signals as obtained for previously isolated compounds.[8−11]

The known compounds murisolin[6] and annonacin[7] were also isolated. Their structures were determined by comparing their physical values ($[\alpha]_D$ and mp) and ^{1}H and ^{13}C NMR data with those reported in the literature.

Experimental Section

General Experimental Procedures. Melting points were determined on a Reichert micromelting point apparatus and are uncorrected. Optical rotations were measured with a Schmidt and Haensch Polartronic D polarimeter in $CHCl_3$ solutions. IR spectra were performed in Nujol on a Pye-Unicam SP3−200 spectrophotometer. The ^{1}H NMR, COSY, HMQC, HMBC, and ^{13}C NMR data were obtained in $CDCl_3$ using a Varian Unity 500 NMR spectrometer, and chemical shifts are relative to TMS. EIMS were obtained on a VG 70−250S mass spectrometer operating at 70 eV (direct insertion). The FABMS data were obtained as follows: the samples were dissolved in either CH_2Cl_2 or MeOH and put into an *m*-NBA matrix. Lithiation was achieved by adding methanolic LiCl to the matrix. Mass spectra were obtained using a Micromass 70S−250 double-focusing mass spectrometer at an accelerating voltage of 8 keV. FAB ionization was achieved by accelerating xenon through 8 kV at a 1-mA current. CO_2 was employed as the collision gas in the first field free region for the B/E CID experiments. The CO_2 was admitted until the lithiated ion beam intensity was reduced to 70% transmission. All scans were performed by the PDP11/73 data system and associated interfaces. The mass range scanned was 1750−100 amu at 3 s/decade at a resolution of 2000. TLC was performed on Merck Si gel 60 $PF_{254+366}$ plates (0.25 mm thick for analytical TLC and 1.0 mm thick for preparative TLC). Merck Si gel 70−230 or 230−400 mesh was used for column chromatography. All compounds were detected using UV light, ammonium molybdate reagent, *p*-anisaldehyde reagent, or a water spray.

Plant Material. The fruits and leaves of *A. montana* were collected at The University of the West Indies, Field Station, Mt. Hope, Trinidad, in November 1993, and matched against a herbarium specimen TRIN. 31489 at the National Herbarium, St. Augustine, Trinidad.

Extraction and Isolation. The dried (40 °C) leaves (1.86 kg) of *A. montana* were pulverized in MeOH using a Waring blender and then extracted with MeOH (16 L) to yield a light brown extract (643 g). The MeOH extract (400 g) was partitioned between $CHCl_3$−H_2O (1:1) to give a $CHCl_3$-soluble fraction (201 g). The latter was then partitioned between 90% aqueous MeOH−petroleum ether (60−80 °C) (1:1) to yield F1, petroleum ether solubles (75 g), and F2, 90% aqueous MeOH solubles (114 g). Both F1 and F2 were subjected to the brine shrimp (*Artemia salina* Leach) lethality test (BST),[17] and F2 was found to be the more active fraction (100% mortality at $c = 1$ mg/mL). F2 (36 g) was subjected to column chromatography and eluted with $CHCl_3$ with gradually increasing amounts of MeOH. Based on their TLC profiles the fractions were combined. The pooled fraction (eluting with $CHCl_3$−MeOH, 93:7) was again subjected to repeated column chromatography (CH_2Cl_2 with increasing amounts of MeOH) to yield impure **1**−**3**. These were then purified by preparative TLC [CH_2Cl_2−MeOH, 24:1, × 2, for compounds **1** and **2** (less polar) and CH_2Cl_2−MeOH, 19:1, × 2, for **3**]. The compounds were crystallized from isopropyl ether−MeOH.

The seeds (2.25 kg) from mature and semi-mature fruits of *A. montana* were pulverized in MeOH, using a Waring blender, and then extracted with MeOH (10 L) to yield a light brown extract (147 g). This extract was partitioned between CH_2Cl_2 and H_2O. The CH_2Cl_2 extract (132 g) was found to be the more active fraction using the BST, and this fraction (38 g) was subjected to column chromatography and eluted with $CHCl_3$ with gradually increasing amounts of MeOH. The fractions were combined based on their TLC profiles, and a subfraction, eluted with $CHCl_3$−MeOH (96:4), was again subjected to repeated column chromatography (CH_2Cl_2 with increasing amounts of MeOH) to yield impure murisolin and annonacin. These were purified by preparative TLC [($CHCl_3$−EtOAc, 6:1, × 2) for murisolin and ($CHCl_2$−MeOH, 39:1, × 2) for annonacin]. Murisolin was obtained as a waxy solid and annonacin as fine needles from isopropyl ether−MeOH, mp 60−61 °C (lit.[7] 57 °C).

Anmontanin A (1): fine, white needles (isopropyl ether−MeOH), 11.2 mg; mp 74−75 °C; $[\alpha]^{25}_D$ +5.8° (*c* 0.040, $CHCl_3$); IR ν_{max} 3440 (OH), 2930 and 2860 (CH), 1735 (lactone C=O), 1710 (aliphatic ketone) cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; EIMS *m/z* $[M]^+$ 594 (0.5), 483 (1), 465 (30), 447 (30), 429 (15), 395 (5), 383 (1), 377 (54), 365 (6), 359 (60), 347 (9), 325 (100), 307 (80), 289 (97), 279 (16), 261 (30), 213 (7), 195 (12), 185 (8); HRFABMS *m/z* $[M + H]^+$ 595.4577 (calcd for $C_{35}H_{63}O_7$, 595.4575).

Anmontanin B (2): fine, white needles (isopropyl ether−MeOH), 15.3 mg: mp 59−60 °C; $[\alpha]^{25}_D$ +0.58° (*c* 0.035, $CHCl_3$); IR ν_{max} 3440 (OH), 2925 and 2865 (CH), 1740 (lactone C=O), 1710 (aliphatic ketone) cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; EIMS *m/z* $[M + H - 2H_2O]^+$ 575 (0.1), 463 (0.2), 421 (0.3), 383 (1), 381 (1), 365 (1), 333 (1), 323 (1.5), 305 (3), 225 (9), 211 (11), 195 (6), 183 (7), 111 (47); FABMS *m/z* $[M + Li]^+$ 617 (100); HRFABMS *m/z* $[M + H]^+$ 611.4526 (calcd for $C_{35}H_{63}O_8$, 611.4523).

Anmontanin C (3): fine, white needles (isopropyl ether−MeOH), 11.0 mg: mp 104−105 °C; IR ν_{max} 3440 (OH), 2930 and 2860 (CH), 1740 (lactone C=O), 1710 (aliphatic ketone) cm^{-1}; ^{1}H and ^{13}C NMR data, see Table 1; EIMS *m/z* $[M + H]^+$ 611 (0.1), $[M + H - H_2O]^+$ 593 (1), 575 (2), 556 (4), 538 (4), 465 (5), 447 (5), 429 (3), 377 (7), 359 (7), 341 (6), 281 (8), 265 (17), 247 (18), 185 (12), 157 (7), 127 (44), 107 (32); FABMS *m/z* $[M + Li]^+$ 617 (100); HRFABMS *m/z* $[M + H]^+$ 611.4526 (calcd for $C_{35}H_{63}O_8$, 611.4523).

TMSi Derivatives of 1−3 (1a−3a), Murisolin, and Annonacin. A sample of each compound was treated with 20 μL of *N*,*O*-bis(trimethylsilyl)acetamide and 2 μL of pyridine and heated at 70 °C for 30 min to yield the respective tri- or tetra-TMSi derivatives, which were then subjected to EIMS. The major peaks for these derivatives are shown in Table 1.

MTPA Derivatives of 2 and 3. A mixture of the acetogenin (5 mg) and a 10-fold millimolar excess of (a) (*S*)- or (*R*)-MTPA, (b) 1-hydroxybenzotriazole hydrate, and (c) 4-(dimethylamino)-pyridine in 1 mL of CH_2Cl_2 containing three drops of *N*,*N*-dimethylformamide was stirred at room temperature until completely dissolved. An excess of 1,3-dicyclohexylcarbodiimide was rapidly added, and the resulting mixture was stirred at room temperature for 24 h. The samples were then filtered and the filtrates subjected to Si gel microcolumn chromatog-

raphy and eluted with petroleum ether (60−80 °C) with increasing amounts of EtOAc. Further purification was attained by preparative TLC. Relevant ^{1}H NMR (500 MHz, $CDCl_3$) resonances are indicated in Tables 3 and 4.

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