Novel Acetogenins from the Leaves of *Dasymaschalon sootepense*

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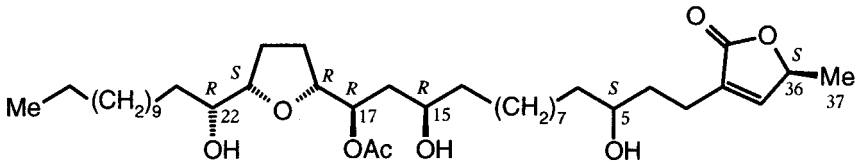
The hexane extract from the leaves of *Dasymaschalon sootepense* CRAIB (Annonaceae) showed strong cytotoxic activity against the L1210 tumor cell line. Activity-directed fractionation of the extract by column chromatography on silica gel and high-pressure liquid chromatography led to the isolation of the acetogenins **1**–**4** as the main active principles. The structures of the two novel structures named sootepensin A (**1**) and sootepensin B (**2**) were elucidated by spectroscopic analysis (UV, EI- and ESI-MS, 1D- and 2D-^{1}H- and ^{13}C-NMR). The absolute configurations were established by 2D-NMR experiments utilizing *Mosher* esters. Two recently described compounds, tonkinin C (**3**) and tonkinesin C (**4**), were also isolated and are new to the genus *Dasymaschalon*. All four acetogenins were found to be highly cytotoxic against the L1210 tumor cell line.

Introduction. – The Annonaceae are a large family (*ca*. 120 genera and more than 2000 species) of aromatic trees, shrubs, or climbers, which occur in tropical or subtropical regions. Several members of this family are of economic interest because of their edible fruits [1], oils [2], woods for alcohol production [3], and fragrant flowers [4]. Finally, some members of this family are used in folk medicine for antiparasitic, insecticidal, and antitumoral purposes. In recent years, an increased interest in the phytochemistry of the Annonaceae has been sparked by the discovery of the acetogenin uvaricin [5] which shows potent *in vivo* antileukemic activity. Because the acetogenins from Annonaceae exhibit a broad range of potentially useful properties such as cytotoxic, antitumoral, antiparasitic, pesticidal, antimicrobial, and immunosuppressive activities, research in this field expanded with the number of isolated and reported acetogenins rapidly increasing [6].

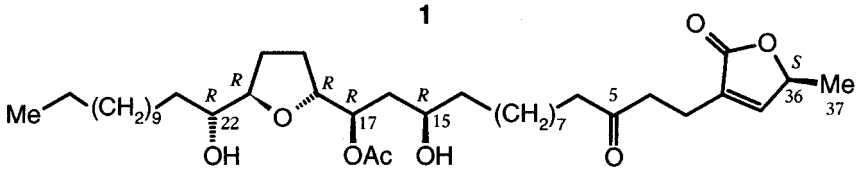
Dasymaschalon sootepense CRAIB is a tree up to 7-m height growing in parts of South East Asia [7]. To date, no phytochemical investigation has been reported on this species. During a preliminary screening, the hexane extract from the leaves of *Dasymaschalon sootepense* showed strong cytotoxic activity against the L1210 cell line.

We present, herein, the isolation and structure elucidation of the active constituents, two new and two known acetylated mono-tetrahydrofuran acetogenins.

Results and Discussion. – The air-dried leaves of *D. sootepense* collected in Thailand were extracted with hexane. The hexane extract was subjected to column chromatography (CC) on silica gel. The fraction which eluted with a gradient AcOEt/hexane 50:50 to AcOEt/MeOH 99:1 showed strong cytotoxicity against the L1210 tumor cell line and gave a positive response to *Kedde*'s reagent. Bioassay-guided fractionation using the cell lines SK-OV-3, L1210, KB, and LNCaP led to the four acetogenins **1**–**4** that were isolated by means of preparative high-pressure liquid chromatography (HPLC, see *Exper. Part*).



1



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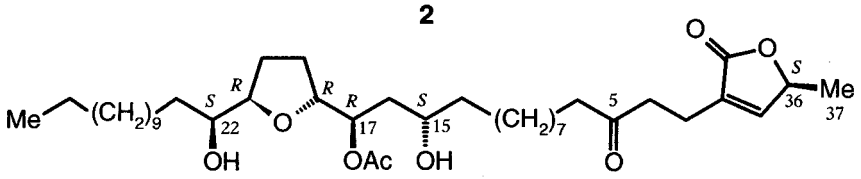

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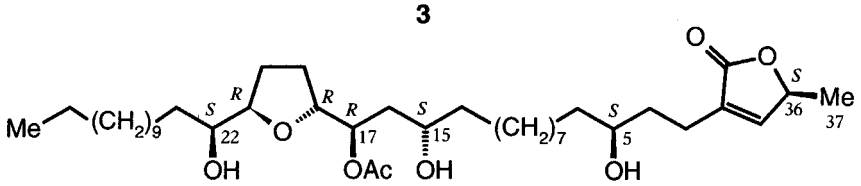

4

The structures of the known acetogenins tonkinin C (**3**) and tonkinesin C (**4**) were elucidated by UV, MS, ^{1}H- and ^{13}C-NMR, and $[\alpha]_D$ measurements and were in accordance with literature data [8].

The two new acetogenins, sootepensin A (**1**) and sootepensin B (**2**), were obtained as pale-yellow oils. Both compounds **1** and **2** showed strong IR C=O absorptions at 1752 cm^{-1} suggesting the presence of an α,β-unsaturated γ-lactone, that had already been predicted by a positive reaction to *Kedde*'s reagent. The molecular weight of **1** was

determined by means of ESI-HR-MS which exhibited an $[M+Na]^+$ peak at *m/z* 689.495 according to a molecular formula of $[C_{39}H_{70}O_8Na]^+$. The EI-MS spectrum (*Fig. 1*) of compound **1** was almost identical to that of compound **4** suggesting the same C-skeleton. The presence of three OH moieties was confirmed by three successive losses of H_2O from the molecular ion in the EI mass spectrum. The fragment ions at *m/z* 155, 269, 311, 337 (base peak, [397 – AcOH]) and 407 ([467 – AcOH]) indicated the connection of the tetrahydrofuran (THF) moiety at C(18)[1]), the AcO at C(17), and the three OH groups at C(5), C(15), and C(22). This connection pattern was confirmed by H,H-COSY- and HMBC-NMR spectra. Typical resonances in the ^{13}C-NMR at 174.1, 149.5, 133.9, 77.6, and 19.1 ppm (*Table 1*) substantiated the presence of a Me-substituted α,β-unsaturated γ-lactone moiety. The assignments of the protons could be unambiguously achieved by TOCSY-NMR experiments.

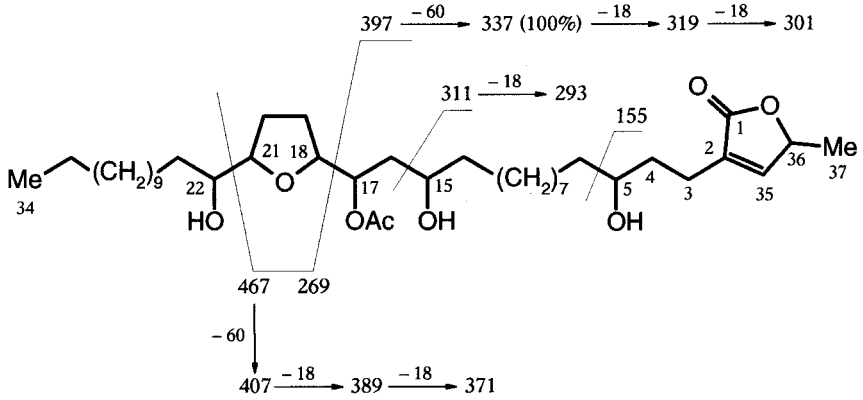

Fig. 1. *Diagnostic EI-MS fragment ions* (*m/z*) *of* **1** *and* **4**

The TOCSY-NMR spectrum shows correlations of the *ddd* at 4.03 ppm (H–C(18) with a *m* at 5.09 ppm (part of this signal: H–C(17)) and with a *m* at 2.00 ppm (H–C(19) and H–C(20)), which showed correlations with a *m* at 1.85 ppm (H–C(19) and H–C(20)). A *m* at 3.88 ppm (H–C(21)) correlated with the *m* at 3.79 ppm (H–C(22)) and with the *m* at 1.85 ppm (H–C(19) and H–C(20)). The *m* at 3.58 (H–C(5)) and 3.44 ppm (H–C(15)) could be unambiguously assigned by their correlations in the TOCSY-NMR spectrum. The relative configuration of the THF moiety could be deduced from the chemical shifts of the CH_2(19) and CH_2(20) protons in the ^{1}H-NMR spectrum. The CH_2 protons of a *cis*-configurated THF ring resonate at 1.94 and 1.78 ppm, whereas the corresponding signals of the *trans*-isomer appear at 1.98 and 1.65 ppm, respectively [9]. Having assigned the ^{1}H-NMR signals, the corresponding ^{13}C resonances could be assigned by HMQC-NMR spectra. The signals in the ^{13}C-NMR spectrum at 82.5 and 80.7 ppm correspond to C(21) and C(18), while those at 73.5 and 71.5 ppm were assigned to C(17) and C(22), respectively. The signals of C(5) and C(15) appeared at 70.8 and 67.1 ppm, respectively. The chemical shift of C(22) at 71.5 ppm indicated an *erythro*-orientation for C(21)–C(22), while that of C(17) at 73.5 ppm

[1]) An arbitrary C-atom numbering (*cf. Figs. 1* and *2*) has been used throughout the text. Systematic names are given in the *Exper. Part*.

Table 1. *^{1}H- and ^{13}C-NMR Resonances* (500 and 125 MHz, resp.; $CDCl_3$) *and Assignments for Compounds* **1** *and* **2**[1]) (δ in ppm rel. to TMS)

	Sootepensin A (**1**)		Sootepensin B (**2**)	
C-Atom	δ(H)	δ(C)	δ(H)	δ(C)
1		174.1		173.6
2		133.9		132.6
3	2.40 (*m*	21.4	2.55 (*tt*, *J* = 7.0, 1.2)	19.6
4	1.63 (*m*)	35.3	2.70 (*t*, *J* = 7.0)	39.9
5	3.58 (*m*)	70.8		209.6
6	1.52 – 1.42 (*m*)	37.1	2.38 (*t*, *J* = 6.8)	42.9
7 – 13; 23 – 33 (**1**)	1.34 – 1.20 (*m*)	32.6 – 22.7		
8 – 14, 20, 24 – 33 (**2**)			1.28 – 1.22 (*m*)	32.0 – 22.8
14	1.52 – 1.42 (*m*)	39.5		
15	3.44 (*m*)	67.1	3.37 (*m*)	70.1
16	1.70 (*m*)	37.5	1.55 (*m*)	38.7
17	5.09 (*m*)	73.5	5.07 (*m*)	71.7
18	4.03 (*ddd*, *J* = 6.5, 6.0, 5.5)	80.7	3.79 (*m*)	83.0
19	2.00 (*m*); 1.85 (*m*)	28.6	1.98 (*m*); 1.67 (*m*)	28.9
20	2.00 (*m*); 1.85 (*m*)	24.7	1.98 (*m*); 1.67 (*m*)	
21	3.88 (*m*)	82.5	3.79 (*m*)	82.3
22	3.79 (*m*)	71.5	3.37 (*m*)	74.1
23			1.28 – 1.22 (*m*)	33.5
34	0.86 (*t*, *J* = 7.0)	14.1	0.86 (*t*, *J* = 7.0)	14.2
35	7.03 (*d*, *J* = 1.5)	149.5	7.02 (*d*, *J* = 1.5)	150.6
36	5.09 (*m*)	77.6	4.96 (*dq*, *J* = 6.8, 1.5)	77.6
37	1.37 (*d*, *J* = 6.8)	19.1	1.39 (*d*, *J* = 6.8)	19.1
Me–*C*=O		172.3		171.7
Me–C=O	2.12 (*s*)	21.1	2.05 (*s*)	21.3

[1]) Arbitrary C-atom numbering according to *Figs. 1* and *2*.

suggested a *threo*-relationship for C(17)–C(18) [10][11]. The signals of C(21) and C(18) at 82.5 and 80.7 ppm, respectively, confirmed the *cis*-configuration of the THF moiety that had already been predicted by analysis of the ^{1}H-NMR data. The chemical shifts of C(18) and C(21) were in accordance with literature data [12] which describe chemical shifts at 83 and 81 ppm ($\Delta\delta \approx 2$) for a *cis*-configurated THF ring.

The ESI-HR mass spectrum of compound **2** exhibited an $[M + Na]^+$ peak at *m/z* 687.481 according to the molecular formula $[C_{39}H_{68}O_8Na]^+$. Like in **1**, compound **2** showed a strong IR C=O absorption at 1752 cm^{-1} suggesting an α,β-unsaturated γ-lactone moiety the presence of which was conformed by ^{1}H- and ^{13}C-NMR data (*Table 1*). An additional prominent IR C=O absorption at 1722 cm^{-1} could be assigned to a ketone group, which was confirmed by the appearance of a C=O resonance at 209.6 ppm in the ^{13}C-NMR spectrum.

The EI-MS analysis of **2** showed the same fragmentation pattern as **3** (*Fig. 2*). The NMR data confirmed that the compounds **2** and **3** differed only in their relative configurations. After careful interpretation of the H,H-COSY- and TOCSY-NMR spectra, we assigned the signals at 1.98 and 1.67 ppm to H–C(19) and H–C(20), respectively, indicating a *trans*-configurated THF ring. The *trans*-configuration was confirmed by the signals in the ^{13}C-NMR spectrum which could be assigned by HMQC-NMR spectra as follows: 83.0 (C(18)); 82.3 (C(21)); 74.1 (C(22)); 71.7 ppm (C(17)).

At first glance, the ^{13}C-NMR chemical shift for C(17) indicated the *erythro*-relationship between C(17) and C(18). However, considering the *γ-gauche* effect due to the presence of a OH group at C(15), the ^{13}C-NMR chemical shift of C(17) is shifted upfield as in compounds **3** and **4** that possess a *trans*-configurated THF moiety [8]. Therefore, the relationship between C(17) and C(18) was assigned as *threo*.

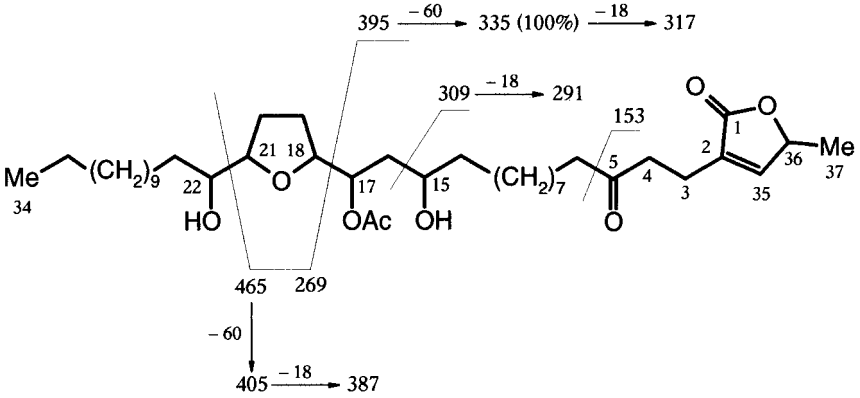

Fig. 2. *Diagnostic EI-MS fragment ions* (*m*/*z*) *of* **2** *and* **3**

As Annonaceous acetogenins are unsuitable for direct X-ray studies due to their waxy nature, *Mosher*'s methodology was recently demonstrated to be a valuable method for the determination of the absolute configuration of the OH-substituted chiral centres in acetogenins [13][14]. This method has been proved to be quite general, despite its limitations. If, for example, the $\Delta\delta(H)$ ($\delta(S)-\delta(R)$) values of neighboring protons are not found to be positive at one side and negative at the other side, or if the $\Delta\delta(H)$ values at only one side of neighboring protons can be determined [13], the absolute configuration of a stereogenic centre remains tentative. Furthermore, in the case of isolated OH groups, it is impossible to determine the absolute configuration of such stereogenic centres.

The (*S*)- and (*R*)-(methoxy)(trifluoromethyl)phenylacetic acid (= 3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid; MTPA) esters (*Mosher* esters) of **1**–**4** were prepared, and their ^{1}H-NMR chemical shifts were carefully assigned according to the H,H-COSY data (*Tables 2* and *3*). *Chen et al.* had already determined the absolute configuration of **3** [8], but not of **4**. Analysis of the $\Delta\delta(H)$ ($\delta(S)-\delta(R)$) values of the *Mosher* esters of **1** and **4** (*Table 2*) showed positive values for H–C(3) and H–C(4). According to *Mosher*'s assumptions [15–17], only the (*S*)-configuration of C(5) could have H–C(3) and H–C(4) more deshielded in the (*S*)-MTPA than in the (*R*)-MTPA derivative. Thus, the (*S*)-configuration was assigned to C(5) in both compounds **1** and **4**. The configuration at C(36) was assumed to be (*S*) based on the fact that the configuration of this chiral centre has been determined to be (*S*) in the acetogenins of which the absolute configurations have been established [6][10]. The results from the H,H-COSY-NMR analysis are given in *Tables 2* and *3*.

Table 2. *^{1}H-NMR* (500 MHz, $CDCl_3$) *Chemical Shifts for the Determination of the Absolute Configuration at C(5) of the* (S)*- and* (R)*-MTPA Esters of* **1** *and* **4**[1]) (δ in ppm rel. to TMS). All δ values were determined directly from the H,H-COSY-NMR Spectra.

MTPA Ester of		CH_2(3)	CH_2(4)	H–C(5)	CH_2(6)	Deduced configuration
1	$\delta(S)$	2.30	1.85	4.98	not assigned	(5*S*)
	$\delta(R)$	2.15	1.78	4.98		
	$\Delta\delta$	+0.15	+0.07	0		
4	$\delta(S)$	2.25	1.82	5.02	not assigned	(5*S*)
	$\delta(R)$	2.12	1.78	5.02		
	$\Delta\delta$	+0.13	+0.04	0		

[1]) Arbitrary C-atom numbering according to *Figs. 1* and *2*.

Table 3. *^{1}H-NMR* (500 MHz, $CDCl_3$) *Chemical Shifts for the Determination of the Absolute Configurations at C(15) and C(22) of the* (S)*- and* (R)*-MTPA Esters of* **1**, **2**, *and* **4**[1]) (δ in ppm rel. to TMS). All δ values were determined directly from the H,H-COSY-NMR Spectra.

MTPA Ester of		CH_2(14)	H–C(15)	CH_2(16)	H–C(17)	H–C(18)	CH_2(19)	CH_2(20)	H–C(21)	H–C(22)	CH_2(23)	Deduced configuration
1	$\delta(S)$	1.81	4.82	1.82	5.05	3.82	1.79, 1.54	1.95, 1.52	3.97	5.22	1.62	(15*R*), (22*R*)
	$\delta(R)$	1.75	4.70	1.82	5.05	3.94	1.95, 1.54	2.00, 1.58	4.00	5.22	1.50	
	$\Delta\delta$	+0.06	+0.12	0	0	−0.12	−0.16, 0	−0.05, −0.06	−0.03	0	−0.12	
2	$\delta(S)$	1.50	4.78	1.69	5.00	4.01	1.94, 1.51	1.90, 1.54	3.93	5.07	1.78	(15*R*), (22*R*)
	$\delta(R)$	1.44	4.62	1.69	5.02	4.04	2.03, 1.59	1.90, 1.54	3.95	5.24	1.65	
	$\Delta\delta$	+0.06	+0.16	0	−0.02	−0.03	−0.09, −0.08	0	−0.02	−0.17	+0.13	
4	$\delta(S)$	1.44	4.76	1.75	5.02	3.84	1.82, 1.61	1.78, 1.63	4.02	5.23	1.50	(15*S*), (22*S*)
	$\delta(R)$	1.49	4.55	1.68	5.02	3.82	1.80, 1.42	1.78, 1.55	3.94	5.21	1.53	
	$\Delta\delta$	−0.05	0.21	0.07	0	+0.02	+0.02, 0.19	0, +0.08	+0.08	+0.02	−0.03	

[1]) Arbitrary C-atom numbering according to *Figs. 1* and *2*.

Table 4 summarizes the biological activities of **1**–**4**. Among the four tumor cell lines used, all compounds showed significant bioactivities only against the L1210 tumor cell line. Compound **1** with a *cis*-configurated THF moiety was found to be *ca.* 10 times less cytotoxic than the compounds **2**–**4** with a *trans*-configurated THF moiety. It could be noticed that, in all cases, the cytotoxicity hovered just over or just under the ED_{50} value. There was no complete killing of the cells, even at doses as high as 3.16 μg/ml, and low doses continued to show inhibition, never reaching non-inhibitory concentrations found in the control samples. The reported ED_{50} values reflect the concentrations where the cytotoxicities of the investigated compounds began to reach their plateau.

Table 4. *Biological Activities of* **1**–**4**. ED_{50} Values in μg/ml.

	KB	L1210	LNCaP	SK-OV-3
1	>3.16	3×10^{-3}	>3.16	>3.16
2	>3.16	3×10^{-4}	>3.16	>3.16
3	>3.16	3×10^{-4}	>3.16	>3.16
4	>3.16	3×10^{-4}	>3.16	>3.16

Experimental Part

General. Open column chromatography (CC): silica gel (63–200 μm, *Merck*). Anal. HPLC: *Waters-MSDS 600 E*, photodiode array detector *Waters 991*, columns: *LiChrospher® 60 RPselect B*, 5 μm, 250 × 4 mm (*Merck*), *LiChrospher® Diol*, 5 μm, 250 × 4 mm (*Merck*). Prep. HPLC: *Waters Prep LC 4000* system, photodiode array detector *Waters 990*, columns: *LiChrospher® 60 RPselect B*, 15 μm, 250 × 25 mm (*Merck*), *LiChrosorb® Diol*, 7 μm, 250 × 25 mm (*Merck*). UV: UV/VIS photometer *2101 PC* (*Shimadzu*), λ_{max} (log ε) in nm. IR: *Nicolet 510 P* FT-IR spectrometer. NMR: *Jeol Eclipse + 500* (500 MHz); δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. EI-MS: *VG 7070 H* (*Vacuum Generators*), 70 eV. ESI-HR-MS: *VG Autospec* (*Micromass*) with EBE geometry, resolution > 5000, solvent MeOH, internal standard $[PEG + Na]^+$.

Bioassay. XTT Proliferation assay. Cell lines: KB (human nasopharyngeal carcinoma), L1210 (murine leukemia), LNCaP (human hormone dependent prostate carcinoma), SK-OV-3 (human hormone dependent ovarial carcinoma). First day: Cells were centrifuged and resuspended in RPMI-1640/10% FCS; 100 μl of the cell suspensions were seeded in 96-well-plates; incubation of the plates overnight (37°, 5% CO_2, 95% rel. humidity); test substances were dissolved in DMSO (10 mg/ml) and stored at −20°. Second day: Substances were warmed and diluted in 96-well-plates with RPMI-1640/10% FCS (concentrations [μg/ml]: 0.0003, 0.003, 0.32, 0.316, and 3.16) were prepared for each substance; transfer of the substances and control media to the cell plates; incubation of the plates: 21 h, 37°, 5% CO_2, 95% rel. humidity; solns. for XTT assay: XTT (*Sigma*) in RPMI-1640 (1 mg/ml), stored at −20°, PMS (*Sigma*) in PBS (0.383 mg/ml), stored at −20°. Third day: 75 μl/well -XTT/PMS mixture was pipetted on the cell plates; XTT/PMS mixture: 50:1 (*v/v*); incubation of the cell plates at 37°, 95% rel. humidity; after 3 h incubation, the OD_{490} values of the wells were measured.

Plant Material. Leaves of *Dasymaschalon sootepense* were collected at Doi Tung, Chiangrai, Thailand, in March 1996. The identity was confirmed by Dr. *P. Kessler*, Rijksherbarium Leiden (L), where a voucher specimen is deposited (L 997.104 798).

Extraction and Isolation of **1**–**4**. The air-dried leaves (6.4 kg dry weight) were crushed and percolated with hexane at 30° affording 111.9 g of extract. The hexane extract was subjected to CC (*Si 60*) (63–200 μm, *Merck*; AcOEt/hexane 50:50 to AcOEt/MeOH 99:1) yielding fraction VR-3169 (3.4 g) which showed high cytotoxicity against the L1210 cell line in the cytotoxic assay. Prep. HPLC (*LiChrospher® 60 RPselect B*, 15 μm, 250 × 25 mm (*Merck*); MeOH/H_2O 8:2) of VR-3169 afforded three fractions (*Frs. 1–3*). All fractions were subjected to the cytotoxic assay showing *Fr. 2* to be the most active one. Separation of *Fr. 2* (1.03 g) by prep. HPLC (*LiChrosorb® Diol*, 7 μm, 250 × 25 mm (*Merck*); hexane/*t*-BuOMe 4:6) yielded five fractions (Frs. 2/1–2/5). *Fr. 2/3* afforded **1** (19 mg). *Fr. 2/4* was separated by prep. HPLC (*LiChrospher® 60 RPselect B*, 15 μm, 250 × 25 mm (*Merck*); MeOH/H_2O 8:2) yielding **2** (13 mg). Prep. HPLC of *Fr. 2/5* under the same conditions used for separation of *Fr. 2/4* afforded **3** (116 mg) and **4** (72 mg).

*(1*R*,3*R*,13*S*)-15-[(5*S*)-2,5-Dihydro-5-methyl-2-oxofuran-3-yl]-3,13-dihydroxy-1-{(2*R*,5*S*)-5-[(1*R*)-1-hydroxytridecyl]tetrahydrofuran-2-yl}pentadecyl Acetate* (= *Sootepensin A*; **1**): 19 mg. Oil. $[\alpha]_D^{20} = +53.8$ ($c = 0.9$, MeOH). UV (MeOH): 210 (3.94). IR: 3444, 2925, 2842, 1752, 1460, 1382, 1308, 1248, 1082, 1025, 954, 882, 712. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-HR-MS: 689.495 ($[C_{39}H_{70}O_8Na]^+$; calc. 689.497). EI-MS: 467 (21), 407 (30), 397 (30), 390 (19), 389 (20), 372 (20), 371 (13), 351 (13), 338 (38), 337 (100), 320 (15), 319 (48), 312 (14), 311 (71), 309 (11), 301 (5), 293 (22), 269 (32), 239 (9), 115 (14), 137 (5).

*(1*R*,3*R*)-15-[(5*S*)-2,5-Dihydro-5-methyl-2-oxofuran-3-yl]-3-hydroxy-1-{(2*R*,5*R*)-5-[(1*R*)-1-hydroxytridecyl]tetrahydrofuran-2-yl}-13-oxopentadecyl Acetate* (= *Sootepensin B*, **2**): 13 mg. Oil. $[\alpha]_D^{20} = +16.9$ ($c = 1.2$, MeOH). UV (MeOH): 210 (3.99). IR: 3446, 2926, 2843, 1752, 1722, 1454, 1376, 1308, 1242, 1078, 1026, 953, 880, 712. ^{1}H- and ^{13}C-NMR: *Table 1*. ESI-HR-MS: 687.481 ($[C_{39}H_{68}O_8Na]^+$; calc. 687.479). EI-MS: 465 (9), 405 (15), 395 (5), 388 (12), 387 (11), 336 (25), 335 (100), 317 (2), 309 (34), 295 (11), 291 (3), 269 (14), 168 (15), 153 (13).

*(1*R*,3*S*)-15-[(5*S*)-2,5-Dihydro-5-methyl-2-oxofuran-3-yl]-3-hydroxy-1-{(2*R*,5*R*)-5-[(1*S*)-1-hydroxytridecyl]-tetrahydrofuran-2-yl}-13-oxopentadecyl Acetate* (= *Tonkinin C*; **3**) *and (1*R*,3*S*,13*S*)-15-[(5*S*)-2,5-Dihydro-5-methyl-2-oxofuran-3-yl]-3,13-dihydroxy-1-{(2*R*,5*R*)-5-[(1*S*)-1-hydroxytridecyl]tetrahydrofuran-2-yl}pentadecyl Acetate* (= *Tonkinesin*; **4**). $[\alpha]_D^{20}$, UV, IR, and H- and C-NMR data identical with those in the literature [8].

3,3,3-Trifluoro-2-methoxy-2-phenylpropanoates (*Mosher* esters). The isolated acetogenin (2 mg of **1**, **2**, **3**, or **4** in 1 ml CH_2Cl_2) was sequentially treated with pyridine (0.4 ml), 4-(dimethylamino)pyridine (1 mg) and 30 mg of (−)-(*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl chloride. The mixture was stirred overnight at r.t. and chromatographed over a pipet column (*Si 60*, 15–40 μm, *Merck*; hexane CH_2Cl_2 1:2) affording the (all-*S*) *Mosher*-ester derivative. The (all-*R*)-*Mosher* ester was prepared by using (+)-(*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl chloride as reagent.

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