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Quassinoids from the leaves of the Madagascan Simaroubaceae *Samadera madagascariensis*

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Abstract

An investigation of the leaves of the Madagascan Simaroubaceae *Samadera madagascariensis* has yielded three C_{18} quassinoids, 5β,6-dihydrosamaderine A, 2-chlorosamaderine A, and samaderolactone A, and a C_{19} quassinoid, 3,4β-dihydrosamaderine C, together with the known quassinoids samaderine A, samaderine B, and cedronin. The compounds isolated displayed little or no anti-tumour activity.

Keywords: *Samadera madagascariensis*; Simaroubaceae; Madagascar; Quassinoids; Samaderine A; Samaderolactone A; 2-Chlorosamaderine A; 5β,6-Dihydrosamaderine A; Samaderine B; 3,4β-Dihydrosamaderine C; Cedronin; Anti-tumour activity

1. Introduction

Samadera madagascariensis A. Juss (De Jussieu, 1825) is an endemic Madagascan species (Petitjean and Petitjean, 1992) that has also at various times been considered, on botanical grounds, to be synonymous with *S. indica* Gaertn. (Capuron, 1961; Simão et al., 1991) and *Quassia indica* (Gaertn.) (Nooteboom, 1963; Stannard, 2000). *S. madgascariensis* is known locally in Madagascar as "fatraina" (bitter) (Petitjean and Petitjean, 1992), where a decoction of the rootbark is used as a febrifuge (Rasoanaivo et al., 1992). The juice of the fresh leaves is used to treat wounds and burns, and a decoction as a treatment for dysentery and stomach-ache (Boiteau, 1979).

Early studies on *Samadera indica* (Zylber and Polonsky, 1964) and *S. madagascariensis* (Merrien and Polonsky, 1971) yielded the C_{19} quassinoids samaderines B and C; samaderine B was subsequently reported by Koike and Ohmoto (1994) and Kitagawa et al. (1996), and again in a recent re-investigation of *S. madagascariensis* (Coombes, 2001), together with the known C_{20} quassinoids samaderine E (Wani et al., 1977; Koike and Ohmoto, 1994; Kitagawa et al., 1996), brucein D (Polonsky et al., 1968; Lee et al., 1979; Koike and Ohmoto, 1994), indaquassin X (Kitagawa et al., 1996), the novel C_{20} quassinoid 15-acetylbrucein D, and 5α-stigmastan-3-one (Polonsky et al., 1962).

2. Results and discussion

Three novel C_{18} quassinoids, 5β,6-dihydrosamaderine A (**2**), 2-chlorosamaderine A (**3**), and samaderolactone A (**4**), and a novel C_{19} quassinoid, 3,4β-dihydrosamaderine C (**6**), together with the known quassinoids samaderine A (**1**), samaderine B, and cedronin (**5**), were isolated from the MeOH and EtOAc extracts of the leaves of *S. madagascariensis*.

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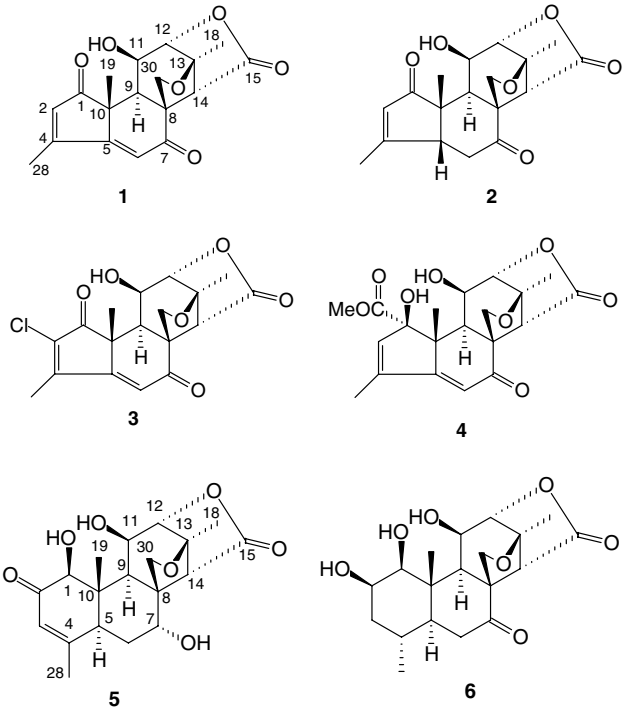

The molecular formula of compound **1** was determined by HREIMS to be $C_{18}H_{18}O_6$. Inspection of the ^1H, ^{13}C and ADEPT NMR spectra showed resonances attributable to the presence of three methyl groups (δ_H 1.58 (*s*), 1.71 (*s*) and 2.21 (*s*), each 3H), two carbonyl groups (δ_C 203.5 (C) and 193.8 (C)), a lactone δ_C 171.1 (C), two trisubstituted double bonds (δ_C 134.1 (CH), 163.3 (C); δ_C 116.8 (CH), 168.8 (C)), and four oxygenated carbons, in the form of an oxymethylene (δ_C 76.1), two oxymethine (δ_C 69.0 and 81.8), and a fully substituted carbon (δ_C 89.2).

A literature survey conducted on this basis suggested that compound **1** was samaderine A, previously isolated from *S. indica* (Wani et al., 1977; Onan and McPhail, 1978). However, the completely assigned spectral data for samaderine A has not been reported previously and is presented here for the first time.

An HREIMS of compound **2** showed it to have a molecular formula of $C_{18}H_{20}O_6$, and thus to have two hydrogen atoms more than samaderine A (**1**). Inspection of the ^1H and ^{13}C NMR spectra of compound **2** showed them to be similar to those of **1**, except that the resonances assigned to the $\Delta^{5,6}$-double bond (δ_H 6.00 (*s*), H-5; δ_C 168.8 (C), C-5; δ_C 116.8 (CH), C-6) in **1** had disappeared, and had been replaced by a one proton double doublet resonance (δ_H 2.61 *dd*, $J = 12.6$, 6.4 Hz, H-5), correlating in the HSQC spectrum to a methine carbon resonance at δ_C 53.1, assigned to C-5, and seen to be coupled in the COSY spectrum to a pair of coupled double doublet proton resonances at δ_H 2.31 (1H, *dd*, $J = 13.8$, 12.6 Hz), H-6α, by correlation in the NOESY spectrum to H-9 (δ_H 2.15 (1H, *d*, $J = 4.4$ Hz)) and δ 2.79 (1H, *dd*, $J = 13.8$, 6.4 Hz, H-6β; δ_C 41.1 (CH_2), C-6). With the orientation of H-5 established as β by a correlation in the NOESY spectrum to 3H-19 (δ_H 1.47 (*s*); δ_C 21.2 (CH_3)), compound **2** is the novel 5β, 6-dihydrosamaderine A – the first 5,6-dihydro C_{18} quassinoid to be isolated thus far, and, to our knowledge, unique in quassinoid chemistry in its stereochemistry at C-5.

An HRCIMS of compound **3** showed an $[M + H]^+$ peak at *m*/*z* 365.0794, corresponding to the molecular formula $C_{18}H_{17}ClO_6$, and supported further by an additional $[M + H + 2]^+$ peak in the CIMS at *m*/*z* 367 of an intensity of one third of that at *m*/*z* 365. The ^1H and ^{13}C NMR spectra of compound **3** were again similar those of samaderine A (**1**), except that the H-2 resonance at δ_H 6.22 (br *s*) in **1** had disappeared, the resonances at δ_C 203.5 (C-1), 163.3 (C-4), 168.8 (C-5), 48.2 (C-10), and 13.7 (C-28) in **1** had shifted to δ_C 195.6, 156.6, 165.1, 47.5, and 11.8 in **3**, respectively, and C-2 from a methine resonance at δ_C 134.1 in **1** to a fully substituted signal at δ_C 138.3 in **3**.

A literature search conducted on this basis revealed that laurycolactone B (Nguyen-Ngoc-Suong et al., 1982; Ang et al., 2000) and its 2-chloro analogue eurycolactone B (Ang et al., 2000) had both been recently reported from *Eurycoma longifolia* Jack. The resonances in the ^1H and ^{13}C NMR spectra of ring A in eurycolactone B show the same chemical shift changes, relative to laurycolactone B, as are observed in compound **3**, relative to **1**. Compound **3** is thus the novel 2-chlorosamaderine A.

A molecular ion peak at *m*/*z* 390.1313 in the HREIMS of compound **4** indicated a molecular formula of $C_{20}H_{22}O_8$ and a difference, relative to samaderine A (**1**), of $C_2H_4O_2$. A three proton methyl group singlet signal at δ_H 3.76 in the ^1H NMR spectrum, correlating in the HSQC spectrum to a quaternary carbon resonance at δ_C 53.9, and in the HMBC spectrum to a fully substituted carbon signal at δ_C 174.6, all suggested the presence of a carbomethoxy group, which was supported further by a peak at *m*/*z* 331.1187 $[M - 59]^+$ in the HREIMS. The ^1H and ^{13}C NMR spectra of compound **4** were again similar those of **1**, but the disappearance of the downfield C-1 carbonyl resonance at δ_C 203.5, and appearance of a fully substituted oxygenated carbon resonance at δ_C 88.6, correlating in the HMBC spectrum to a three proton methyl group singlet resonance at δ_H 1.75, assigned to 3H-19, suggested that a hydroxy group and the carbomethoxy group were both placed at C-1. Although the hydroxy group proton resonance could not be observed, a correlation in the NOESY spectrum between the methoxy group signal and that of H-9 (*d*, $J = 3.7$ Hz) at δ_H 2.42 simultaneously confirmed this placing of the ester at C-1 and established its orientation as α. A literature survey conducted on this basis revealed that eurycolactone A from *E. longifolia* (Ang et al., 2000), the 1α-carbomethoxy-1β-hydroxy analogue of laurycolactone B, showed the same chemical shift changes, relative to laurycolactone B, as are observed for compound **4**, relative to **1**. Compound **4**, which we name samaderolactone A, is thus the novel 1α-carbomethoxy-1β-hydroxysamaderine A.

Samaderine B was identified by comparison of its ^{13}C NMR data with the literature values (Grieco and Piñeiro-Nuñez, 1994; Coombes, 2001).

An HREIMS of compound **5** showed it to have a molecular formula of $C_{19}H_{24}O_7$, and thus to have two hydrogen atoms more than samaderine B. The ^{1}H and ^{13}C NMR spectra of compound **5** were similar to those of samaderine B, other than the replacement of the C-7 carbonyl resonance at δ_C 203.4 by an additional oxymethine signal at δ_C 71.3, supported by a correlation in the HMBC spectrum between this resonance and that of H-14 at δ_H 2.66 (*s*), and between the corresponding H-7 signal at δ_H 3.97 (*d*, $J = 14.1$ Hz) and the oxymethylene C-30 resonance at δ_C 74.9. Finally, correlations in the NOESY spectrum between H-7 and both H-14 and H-30a at δ_H 3.71 (*d*, $J = 9.0$ Hz) establish that H-7 is β and therefore that the C-7 hydroxy group, as expected on biosynthetic grounds, is α. Compound **5** is thus the 7α-hydroxy analogue of samaderine B, which has previously been isolated as cedronin from *Simaba cedron* Planch (Zylber and Polonsky, 1964; Jacobs et al., 1987). However, no complete assignment of the NMR data for cedronin has been reported, and it is presented here for the first time.

The molecular formula of compound **6** was established by HRCIMS to be $C_{19}H_{26}O_7$, and a difference, relative to samaderine B, of four additional hydrogen atoms. While the appearance of 19 carbon signals and similarity to the spectra of both samaderine B and compound **5** established **6** as a C_{19} quassinoid; the differences immediately apparent were the absence of the upfield carbonyl signal at $\delta_C \sim 196$–198, assigned to C-2 in samaderine B and **5**, and the olefinic carbon resonances of the $\Delta^{3,4}$ double bond, which occur at $\delta_C \sim 124$ (C-3) and $\delta_C \sim 160$–165 (C-4); the absence of the double bond is further supported by the upfield shift of the 3H-28 methyl singlet proton resonance from its normally deshielded δ_H 1.9 in samaderine B and **5** to δ_H 0.85 in **6**, where it occurs as a doublet ($J = 6.6$ Hz). Of the four oxymethine resonances present in the spectrum of **6**, those at δ_C 83.5 and 81.8 were assigned to C-12 and C-1, respectively, by comparison with the spectra of samaderine B and **5**, and that at δ_C 70.4 to C-11 by a correlation in the HMBC spectrum to H-9 at δ_H 1.83 (*d*, $J = 4.6$ Hz). The remaining signal at δ_C 70.9 must then be C-2. Correlations in the NOESY spectrum between H-9 and H-5 at δ_H 1.31 (*m*) confirmed the orientation of H-5, as expected, as α, and between H-5 and both H-1 at δ_H 3.30 (*d*, $J = 8.8$ Hz) and H-2 at δ_H 3.83 (*m*) established the orientations of both hydroxy groups at C-1 and C-2 as β. A further correlation in the NOESY spectrum between H-2α and a multiplet at δ_H 1.97 establishes this as H-3α, with H-3β at δ_H 1.14 (*d*, $J = 12.5$ Hz) displaying a correlation in the NOESY spectrum to a methyl group singlet proton resonance at δ_H 1.35, assigned to 3H-19. The orientation of 3H-28, whose signal shows a correlation in the NOESY spectrum to H-3α but not H-3β, is thus α, or equatorial, as expected on biosynthetic grounds. Compound **6** is thus the novel compound 3,4β-dihydrosamaderine C.

Samaderine B has previously been shown to exhibit inhibitory activity against the cultured malarial parasite, *Plasmodium falciparum*, of a chloroquine resistant K1 strain in human erythrocytes (IC_{50} 0.21 μM, IC_{90} 0.69 μM); in vitro cytotoxic activity against KB cells (IC_{50} 0.07 μM) and inhibitory activity in the in vitro endothelial cell-neutrophil leukocyte adhesion assay (Kitagawa et al., 1996). Samaderine A (**1**), 5β, 6-dihydrosamaderine A (**2**), 2-chlorosamaderine A (**3**), cedronin (**5**), and 3,4β-dihydrosamaderine C (**6**), were screened in the NIH 60 cancer cell line screen. Samaderine A (**1**), and 5β, 6-dihydrosamaderine A (**2**), were both found to be inactive, and low activity only was observed for the other compounds, as shown in Table 3.

3. Experimental

3.1. General

NMR spectra were recorded at room temperature on a 400 MHz Varian UNITY-INOVA spectrophotometer. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane (TMS) as internal standard and coupling constants are given in Hz. ^{1}H NMR spectra were referenced against the $CHCl_3$ signal at δ_H 7.27, and ^{13}C NMR spectra to the corresponding signal at δ_C 77.0. IR spectra were recorded on a Nicolet Impact 400D Fourier-Transform Infrared (FT-IR) spectrometer, using NaCl windows with $CHCl_3$ as solvent against an air background. Melting points were determined on a Kofler micro-hot stage melting point apparatus and are uncorrected. HREIMS and HRCIMS were acquired on a Kratos 9/50 and a VG 70-SE HRMS instruments. Optical rotations were measured at room temperature in $CHCl_3$ on a Perkin–Elmer 341 Polarimeter, using a Microcell 100 mm quartz tube.

3.2. Plant material

S. madagascariensis was collected in April 1997 in the Foulpointe area in eastern Madagascar. Plant identification was confirmed by Dr. Harison Rabarison of the Department of Botany at the Parc Zoologique et Botanique de Tsimbazaza, where a voucher specimen (007-MJ/Mdul, TAN) is deposited.

3.3. Extraction and isolation of compounds

The air-dried, milled leaves (634 g) were extracted successively for 24 h in a Soxhlet apparatus with hexane, CH_2Cl_2, EtOAc and MeOH, yielding extracts of masses 38.65, 41.26, 31.56 and 56.23 g, respectively. Repeated column chromatography over silica gel (Merck 9385), with CH_2Cl_2:EtOAc step gradients, of the EtOAc (100:0–4:1) and MeOH (100:0–7:3) extracts, yielded samaderine A (**1**) (32.3 mg) and 2-chlorosamaderine A (**3**) (10.2 mg) from the EtOAc extract, and 5β,6-dihydrosamaderine A (**2**)

(12.2 mg), samaderolactone A (**4**) (18.5 mg), samaderine B (27.3 mg), cedronin (**5**) (8.1 mg) and 3,4β-dihydrosamaderine C (**6**) (13.2 mg) from the MeOH extract.

*3.3.1. 5β, 6-Dihydrosamaderine A (**2**)*

White amorphous solid; $[\alpha]_D = +75°$ ($CHCl_3$; *c* 0.032); ν_{max}(NaCl) cm^{-1} 3489, 2920, 2851, 1785, 1701, 1623; HREIMS (70 eV) *m/z* (rel. int.) 332.1262 (5) (calc. for $C_{18}H_{20}O_6$ 332.1260), 317.1023 (1) $[M - CH_3]^+$, 315.1223 (1) $[M - OH]^+$, 288.1359 (29), 260.0949 (16), 245.1165 (5), 217.0875 (7), 189.0867 (6), 165.0568 (5), 150.0682 (4), 135.0733 (4), 123.0809 (100), 110.0735 (4), 69.0338 (4); ^{1}H NMR spectral data (400 MHz, $CDCl_3$) Table 1; ^{13}C NMR spectral data (100 MHz, $CDCl_3$) Table 2.

Table 1
^{1}H NMR spectral data for compounds **1**–**6** ($CDCl_3$, 400 MHz)

Proton no.	**1**	**2**	**3**	**4**	**5**	**6**
1	–	–	–	–	4.09 (br *s*)	3.30 (*d*, 8.8)
1-OH					4.41 (br *s*)	
2	6.22 (br *s*)	5.93 (br *s*)	–	5.99 (*d*, 1.3)	–	3.83 (*m*)
3					6.06 (*s*)	(α) 1.97 (*m*)
						(β) 1.14 (*d*, 12.5)
4	–	–	–	–	–	1.56 (*m*)
5	–	2.61 (*dd*, 12.6, 6.4)	–	–	3.22 (*dd*, 12.3)	1.31 (*m*)
6	6.00 (*s*)	(α) 2.31 (*dd*, 13.8, 12.6)	6.05 (*s*)	5.88 (*s*)	(α) 2.17 (*dd*, 14.1, 12.3)	(α) 2.70 (*dd*, 18.0, 4.6)
		(β) 2.79 (*dd*, 13.8, 6.4)			(β) 1.58 (*m*)	(β) 2.18 (*dd*, 15.8, 4.6)
7	–	–	–	–	3.97 (*d*, 14.1)	–
8	–	–	–	–	–	–
9	2.25 (*d*, 4.4)	2.15 (*d*, 4.4)	2.28 (*d*, 4.6)	2.42 (*d*, 3.7)	2.34 (*d*, 4.8)	1.83 (*d*, 4.6)
10	–	–	–	–	–	–
11	4.80[a]	4.63[a]	4.79[a]	4.16[b]	4.82 (br *s*)	4.61 (br *s*)
11-OH	3.58 (br *d*)	3.45 (br *d*)	3.59 (br *d*)		3.38 (br *s*)	3.96 (br *s*)
12	4.28 (*d*, 3.7)	4.29 (*d*, 3.7)	4.29 (*d*, 4.8)	4.16[b]	4.32 (*d*, 3.1)	4.28 (*d*, 3.7)
13	–	–	–	–	–	–
14	3.43 (*s*)	2.96 (*s*)	3.44 (*s*)	3.53 (*s*)	2.66 (*s*)	3.55 (*s*)
15	–	–	–	–	–	–
18	1.58 (*s*)	1.54 (*s*)	1.59 (*s*)	1.60 (*s*)	1.52 (*s*)	1.53 (*s*)
19	1.71 (*s*)	1.47 (*s*)	1.75 (*s*)	1.75 (*s*)	1.23 (*s*)	1.35 (*s*)
28	2.21 (*d*, 1.3)	2.06 (*s*)	2.23 (*s*)	1.91 (*d*, 1.3)	1.93 (*s*)	0.85 (*d*, 6.6)
30	(a) 4.14 (*d*, 9.0)	(a) 4.40 (*d*, 9.2)	(a) 4.15 (*d*, 9.1)	(a) 4.07 (*d*, 9.2)	(a) 3.71 (*d*, 9.0)	(a) 3.83 (*d*, 8.2)
	(b) 4.80 (*d*, 9.0)	(b) 4.63 (*d*, 9.2)	(b) 4.81 (*d*, 9.1)	(b) 4.72 (*d*, 9.2)	(b) 4.64 (*d*, 9.0)	(b) 4.88 (*d*, 8.2)
CO_2CH_3				3.76 (*s*)		

[a] H-11 and H-30b resonances are superimposed; the H-11 multiplicity could not be determined.
[b] H-11 and H-12 resonances are superimposed; the multiplicities could not be determined.

Table 2
^{13}C NMR spectral data for compounds **1**–**6** ($CDCl_3$, 100 MHz)

Carbon no.	**1**	**2**	**3**	**4**	**5**	**6**
1	203.5 (C)	209.2 (C)	195.6 (C)	88.6 (C)	82.8 (CH)	81.8 (CH)
2	134.1 (CH)	127.9 (CH)	138.3 (C)	142.0 (CH)	197.6 (C)	70.9 (CH)
3					124.1 (CH)	41.5 (CH_2)
4	163.3 (C)	175.9 (C)	156.6 (C)	142.4 (C)	164.8 (C)	29.8 (CH)
5	168.8 (C)	53.1 (CH)	165.1 (C)	175.7 (C)	42.5 (CH)	50.8 (CH)
6	116.8 (CH)	41.1 (CH_2)	116.8 (CH)	115.3 (CH)	29.1 (CH_2)	40.2 (CH_2)
7	193.8 (C)	206.3 (C)	193.1 (C)	192.5 (C)	71.3 (CH)	205.2 (C)
8	57.4 (C)	56.4 (C)	57.7 (C)	56.7 (C)	54.4 (C)	60.2 (C)
9	40.2 (CH)	39.3 (CH)	40.1 (CH)	41.1 (CH)	44.1 (CH)	50.3 (CH)
10	48.2 (C)	48.9 (C)	47.5 (C)	54.9 (C)	48.0 (C)	42.4 (C)
11	69.0 (CH)	69.1 (CH)	68.9 (CH)	70.0 (CH)	70.2 (CH)	70.4 (CH)
12	81.8 (CH)	83.1 (CH)	81.6 (CH)	81.0 (CH)	85.0 (CH)	83.5 (CH)
13	89.2 (C)	89.1 (C)	89.2 (C)	89.3 (C)	87.5 (C)	87.8 (C)
14	58.1 (CH)	59.6 (CH)	58.0 (CH)	58.2 (CH)	59.7 (CH)	56.7 (CH)
15	171.1 (C)	171.4 (C)	170.9 (C)	171.2 (C)	174.2 (C)	172.1 (C)
18	20.9 (CH_3)	20.7 (CH_3)	20.9 (CH_3)	21.0 (CH_3)	21.0 (CH_3)	20.6 (CH_3)
19	21.4 (CH_3)	21.2 (CH_3)	21.3 (CH_3)	23.0 (CH_3)	11.4 (CH_3)	12.0 (CH_3)
28	13.7 (CH_3)	17.0 (CH_3)	11.8 (CH_3)	12.4 (CH_3)	22.7 (CH_3)	18.9 (CH_3)
30	76.1 (CH_2)	74.7 (CH_2)	76.1 (CH_2)	75.9 (CH_2)	74.9 (CH_2)	75.8 (CH_2)
CH_3O_2C-				53.9 (CH_3)		
CH_3O_2C-				174.6 (C)		

3.3.2. 2-Chlorosamaderine A (3)

Pale yellow amorphous solid; $[\alpha]_D = -13°$ ($CHCl_3$; *c* 0.016); ν_{max}(NaCl) cm^{-1} 3488, 2929, 2863, 1795, 1701, 1623; HRCIMS *m/z* (rel. int.) 365.0794 (calc. for $C_{18}H_{17}ClO_6 + H$ 365.0792); CIMS *m/z* 367 (33), 365 (100), 347 (32), 331 (35), 273 (28), 239 (10), 201 (3), 167 (10), 149 (31), 113 (13), 83 (17), 71 (29), 57 (62); ^1H NMR spectral data (400 MHz, $CDCl_3$) Table 1; ^{13}C NMR spectral data (100 MHz, $CDCl_3$) Table 2.

3.3.3. 1α-Carbomethoxy-1β-hydroxysamaderine A, samaderoactone A (4)

Yellow amorphous solid; $[\alpha]_D = +14°$ ($CHCl_3$; *c* 0.066); ν_{max}(NaCl) cm^{-1} 3457, 2925, 2862, 1788, 1730, 1655, 1621, 1460, 1381, 1265; HREIMS (70 eV) *m/z* (rel. int.) 390.1313 (3) (calc. for $C_{20}H_{22}O_8$ 390.1315), 375.1056 (2) $[M - CH_3]^+$, 372.1207 (1) $[M - H_2O]^+$, 331.1187 (100) $[M - CH_3O_2C]^+$, 313.1064 (4), 255.1021 (15), 239.1070 (23), 227.1060 (15), 211.1107 (9), 187.0759 (6), 125.0596 (14), 91.0541 (8), 57.0704 (10) (see Table 3); ^1H NMR spectral data (400 MHz, $CDCl_3$) Table 1; ^{13}C NMR spectral data (100 MHz, $CDCl_3$) Table 2.

3.3.4. 3,4β-Dihydrosamaderine C (6)

Pale yellow amorphous solid. $[\alpha]_D = -18°$ ($CHCl_3$; *c* 0.022); ν_{max}(NaCl) cm^{-1} 3428, 2928, 2849, 1736, 1460, 1263, 1168; HRCIMS (70 eV) *m/z* 367.1758 (calc. for $C_{19}H_{26}O_7 + H$ 367.1757); CIMS *m/z* (rel. int.) 367 (58), 349 (81), 331 (100), 319 (29), 275 (38), 257 (31), 239 (36), 223 (26), 205 (38), 179 (10), 149 (8), 127 (74), 111 (32), 85 (19), 71 (11), 57 (30); ^1H NMR spectral data (400 MHz, $CDCl_3$) Table 1; ^{13}C NMR spectral data (100 MHz, $CDCl_3$) Table 2.

Table 3
LC 50 values (g/mL) for compounds **3**–**6** against the NIH 60 cancer cell line screen

Panel/cell line	3	5	6
Leukemia			
SR	–	4.42×10^{-5}	–
Non-small cell lung cancer			
NCI-H266	–	–	2.09×10^{-5}
NCI-H23	–	6.11×10^{-5}	–
Colon cancer			
HCC-2998	–	–	2.61×10^{-5}
HCT-116	–	–	3.59×10^{-5}
HCT-15	8.54×10^{-5}	–	8.55×10^{-6}
CNS cancer			
SF-539	–	–	2.18×10^{-5}
U251	–	–	9.42×10^{-6}
Melanoma			
LOX IMVI	–	3.37×10^{-5}	7.09×10^{-6}
MI4	–	5.07×10^{-5}	1.10×10^{-5}
SK-MEL-5	–	–	8.42×10^{-6}
Renal cancer			
A498	7.00×10^{-5}	–	1.81×10^{-5}
ACHN	–	6.94×10^{-5}	1.09×10^{-5}
RXF 393	–	6.61×10^{-5}	–
Prostate cancer			
DU-145	–	–	5.08×10^{-5}

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