New Oxindole Alkaloids and Iridoid from Carolina jasmine (*Gelsemium sempervirens* Ait. f.)

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Three new gelsedine-type oxindole alkaloids, GS-1, GS-2, and GS-3, and one new iridoid, GSIR-1, were isolated from the stems and leaves of cultivated Carolina jasmine (*Gelsemium sempervirens* Ait. f.) and their structures were determined by spectroscopic analysis.

Key words indole alkaloid; azetidine; iridoid; Gelsemium; Loganiaceae

In our recent study, we proved that the original plant of 'Yakatsu', one of the ancient medicines stored more than 1250 years ago in Shosoin repository in Japan, was *Gelsemium elegans* Benth.[1] The genus *Gelsemium*, which belongs to Loganiaceae, comprises three species: *G. sempervirens* Ait., *G. elegans* Benth., and *G. rankinii* Small., from which more than fifty indole alkaloids have been isolated.[2—4] The markedly diverse and complex architectures of the alkaloids have attracted the attention of many phytochemists and synthetic chemists. In the course of our chemical studies on the *Gelsemium* alkaloids, we isolated three new oxindole alkaloids (**1**—**3**) and one new iridoid (**4**), together with ten known compounds from the stems and leaves of cultivated Carolina jasmine (*Gelsemium sempervirens* Ait. f.). In this paper we describe the structure elucidation of the new compounds.

The dried stems of *G. sempervirens* Ait. f. (1.29 kg) were extracted with MeOH to give the MeOH extract (129.8 g). The crude alkaloidal fraction (4.32 g) was obtained by a conventional procedure from a portion of the MeOH extract (70.3 g) and purified by SiO_2 column chromatography to afford three new alkaloids, GS-1 (**1**, 1.5 mg), GS-2 (**2**, 45.7 mg), and GS-3 (**3**, 3.5 mg), and one new iridoid, GSIR-1 (**4**, 15.8 mg), together with seven known alkaloids, two known iridoids, and scopoletin. The new compounds, GS-2 (**2**, 3.7 mg) and GSIR-1 (**4**, 4.1 mg), were also isolated from the fresh leaves of *G. sempervirens* Ait. f. (996.4 g), accompanied by three known alkaloids, and one known iridoid.

The high resolution (HR)-FAB-MS spectrum of the new alkaloid GS-1 (**1**) gave a protonated molecular ion peak at *m/z* 387.1566 ($[MH]^+$) that corresponded to the molecular formula $C_{20}H_{23}N_2O_6$ (*m/z* 387.1556). The UV absorptions at 218.5, 287.0, 295.5 (sh) nm suggested the presence of a 6-methoxyoxindole nucleus. The ^{1}H-NMR spectrum showed significant signals characteristic to a methine group bearing an imine nitrogen at δ 4.72 (br ddd, H-5) and a methyl group at δ 2.64 (3H, s), together with three aromatic protons due to the A ring of the oxindole system [δ 7.42 (d), 6.59 (dd), 6.47 (d)], an N_a-methoxy group at δ 3.92 (3H, s), a methoxy group on the aromatic ring at δ 3.81 (3H, s), an oxymethine proton at δ 3.71 (br s, H-3), a methine group bearing a hydroxyl group at δ 4.43 (br d, J=1.9 Hz, H-14), and oxymethylene protons at δ 4.49 (dd, J=11.1, 3.4 Hz) and δ 4.32 (d, J=11.1 Hz) (H_2-17). The ^{13}C-NMR spectrum revealed the existence of a ketone carbon at δ 197.3 (C-19), an imine carbon at δ 174.8 (C-20), and a methine carbon bearing an imine nitrogen at δ 74.1 (C-5), together with a carbonyl carbon of the oxindole ring at δ 171.3 (C-2) and five oxygenated carbons [δ 79.4 (C-3), 66.4 (C-14), 63.6 (N_a-OMe), 61.4 (C-17), 55.7 (aromatic OMe)]. Heteronuclear multiple bond connectivity (HMBC) correlations between H_3-18 and the carbons at δ 197.3 and δ 174.8 as well as other spectroscopic data described above indicated that **1** had the basic skeleton of the known alkaloid, 19-oxo-gelsenicine (**5**).[5] HMBC correlations between the protons of H-3, H-15, and H-16 and the carbon at δ 66.4 demonstrated that C-14 had a hydroxyl group. From these data, **1** was deduced to be 11-methoxy-14-hydroxy-19-oxo-gelsenicine. The stereochemistry of the hydroxyl group at C-14 was evidenced by the H-14 ($J_{3,14}$=1.9 Hz) signal that shows coupling only with H-3 and not with H-15; the dihedral angle between H-14 and H-15 is *ca.* 90 degrees as depicted in Fig. 2.

The molecular formula of the second new alkaloid GS-2 (**2**) was established to be $C_{20}H_{25}N_2O_5$ from the HR-FAB-MS spectrum (*m/z*: 373.1748 $[MH]^+$), which indicated that **2** had an extra CH_2O compared to the known alkaloid, 14-hydroxygelsenicine (**6**).[6] The UV and NMR spectra revealed the existence of a 6-methoxyoxindole nucleus. The ^{1}H-NMR spectrum was very similar to that of 14-hydroxygelsenicine (**6**), except for the signals of the aromatic protons and the signal

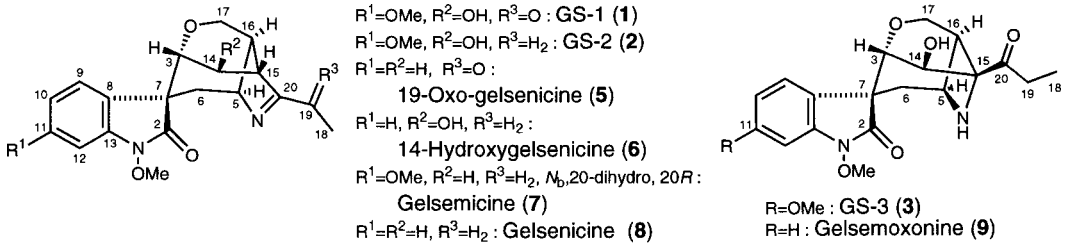

Fig. 1. Structures of New Alkaloids (**1**—**3**) and Known Alkaloids (**5**—**9**)

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Table 1. ^{1}H- and ^{13}C-NMR Data for **1**, **2**, and **3** in $CDCl_3$

Position	GS-1 (**1**)		GS-2 (**2**)		GS-3 (**3**)	
	^{1}H[a)]	^{13}C[b)]	^{1}H[c)]	^{13}C[d)]	^{1}H[a)]	^{13}C[b)]
2		171.3		171.4		174.0
3	3.71 (br s)	79.4	3.65 (br dd, 2.2, 2.2)	79.6	3.77 (d, 2.7)	79.0
5	4.72 (br ddd, 7.6, 5.0, 2.4)	74.1	4.38 (m)	71.8	3.87 (ddd, 8.3, 4.6, 1.6)	55.8
6	2.57 (dd, 15.4, 5.0)	38.0	2.38 (dd, 15.6, 4.6)	37.7	2.35 (dd, 16.2, 1.6)	35.0
	2.32 (br dd, 15.4, 2.4)		2.27 (dd, 15.6, 2.4)		2.26 (dd, 16.2, 4.6)	
7		53.9		53.3		53.5
8		123.0		123.5		122.1
9	7.42 (d, 8.2)	125.4	7.39 (d, 8.4)	125.3	7.35 (d, 8.3)	126.1
10	6.59 (dd, 8.2, 2.3)	108.2	6.57 (dd, 8.4, 2.4)	107.9	6.66 (dd, 8.3, 2.3)	108.6
11		160.5		160.3		160.7
12	6.47 (d, 2.3)	94.3	6.46 (d, 2.4)	94.1	6.60 (d, 2.3)	95.0
13		139.1		139.1		139.2
14	4.43 (br d, 1.9)	66.4	4.43 (d, 2.2)	66.3	4.48 (br s)	68.8
15	3.40 (d, 8.8)	48.7	2.88 (dd, 8.4, 1.5)	52.2		67.3
16	2.64 (m)	38.2	2.57 (br ddd, 8.4, 8.4, 3.5)	38.3	3.33 (br dd, 8.3, 4.1)	33.7
17	4.49 (dd, 11.1, 3.4)	61.4	4.43 (dd, 10.7, 3.5)	61.7	4.25 (dd, 12.1, 4.1)	61.9
	4.32 (d, 11.1)		4.30 (d, 10.7)		4.15 (d, 12.1)	
18	2.64 (3H, s)	26.1	1.29 (3H, dd, 7.4, 7.4)	9.9	1.11 (3H, dd, 7.2, 7.2)	7.1
19		197.3	2.76 (dddd, 17.2, 7.4, 7.4, 7.4)	26.0	2.82 (dddd, 18.2, 7.2, 7.2, 7.2)	28.9
			2.49 (ddddd, 17.2, 7.4, 7.4, 7.4, 1.5)		2.51 (dddd, 18.2, 7.2, 7.2, 7.2)	
20		174.8		181.1		211.9
N_a-OMe	3.92 (3H, s)	63.6	3.93 (3H, s)	63.4	4.04 (3H, s)	63.9
Ar-OMe	3.81 (3H, s)	55.7	3.81 (3H, s)	55.5	3.85 (3H, s)	55.6

Measured at *a*) 600 MHz, *b*) 150 MHz, *c*) 500 MHz and *d*) 125 MHz.

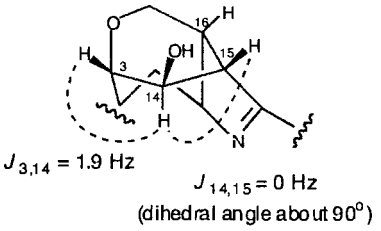

Fig. 2. Stereochemical Arrangement around C-14 in **1**

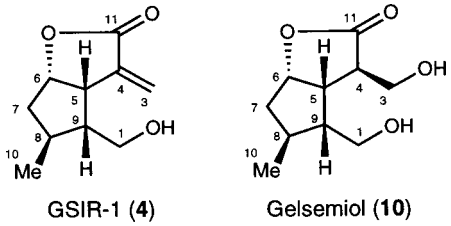

Fig. 3. Structures of New Iridoid (**4**) and Gelsemiol (**10**)

indicative of a methoxy group on the A ring at δ 3.93. In the ^{13}C-NMR spectrum, signals indicative of C-14 possessing a hydroxyl group and the C-20 imine carbon were observed at δ 66.3 and δ 181.1, respectively. The HMBC spectrum showed correlations between the protons of H-5, H_3-18, and H_2-19 and the carbon at δ 181.1. Therefore, **2** was deduced to be 11-methoxy-14-hydroxygelsenicine. The stereochemistry of the hydroxyl group at C-14 was shown to be β-orientated by the coupling constant ($J_{3,14}$=2.2 Hz) of the proton at C-14, as in the case of GS-1 (**1**).

The molecular formula of the new alkaloid GS-3 (**3**) was established to be $C_{20}H_{25}N_2O_6$ from the HR-FAB-MS spectrum (*m/z*: 389.1703 $[MH]^+$). The UV and NMR spectra revealed the existence of a 6-methoxyoxindole nucleus. The ^{1}H- and ^{13}C-NMR spectra were very similar to those of the known alkaloid, gelsemoxonine (**9**),[7] the structure of which was recently revised to be a novel azetidine-containing indole alkaloid. Signals characteristic to the azetidine ring carbons, C-5 (δ 55.8), C-15 (δ 67.3), and C-16 (δ 33.7), as well as an isolated propanoyl unit (δ_C 211.9, δ_H 1.11, 3H, t, J=7.2 Hz, and δ_H 2.82 and 2.51, each 1H, dq, J=18.2, 7.2 Hz) were observed. The ^{1}H-NMR (δ 3.85, 3H) spectrum and the HMBC correlation (δ_H 3.85 and δ_C 160.7) revealed that the aromatic A ring had a methoxy group at the C-11 position. From these data, **3** was deduced to be 11-methoxygelsemoxonine.

The circular dichroism (CD) spectra of the three compounds (**1**—**3**) were similar to that of gelsemicine (**7**),[8,9] the absolute configuration of which was already established,[10] indicating that **1**—**3** possessed absolute configurations as depicted in Fig. 1.

The HR-FAB-MS spectrum of the new iridoid **4** gave a protonated molecular ion peak at *m/z* 183.1032 ($[MH]^+$) that corresponded to the molecular formula $C_{10}H_{15}O_3$ (*m/z* 183.1021). The UV absorption at 215.5 nm suggested the presence of an α,β-unsaturated ester in the molecule. The ^{1}H-NMR spectrum showed two signals characteristic of exomethylene protons at δ 6.43 and 5.93 (each br d, J=2.2 Hz, H_2-3), as well as signals representative of an oxygenated methine proton at δ 4.96 (1H, dd, J=5.8, 5.5 Hz, H-6), hydroxymethylene protons at δ 3.82 (dd, J=10.6, 4.0 Hz) and δ 3.58 (dd, J=10.6, 10.0 Hz) (H_2-1), and methyl protons at δ 1.03 (3H, d, J=6.4 Hz, H_3-10). The ^{13}C-NMR spectrum revealed 10 carbons including one lactone carbonyl carbon (δ 171.2, C-11), two alkenyl carbons (δ 135.0, C-4 and δ 125.7, C-3), one oxygenated methine carbon (δ 81.9, C-6), and one hydroxymethylene carbon (δ 60.8, C-1). These NMR data

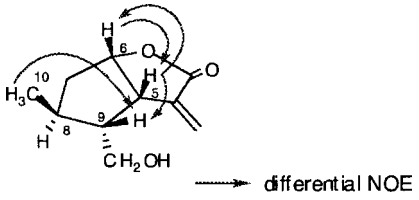

Fig. 4. Relative Stereochemistry of **4**

implied that GSIR-1 (**4**) had an iridoid skeleton. HMBC correlations between the ester carbonyl carbon at δ 171.2 and the two exomethylene protons due to H_2-3, the oxygenated proton due to H-6, and H-5 were observed. Furthermore, HMBC correlations between H-5 and the two alkenyl carbons at C-3 and C-4 were observed. From these data, the gross structure of GSIR-1 was elucidated. The relative stereochemistry between H-5, H-6, H-9 and H_3-10 was analyzed to be all *cis* from nuclear Overhauser effect (NOE) observations, as shown in Fig. 4. Compound **4** was prepared from the known iridoid, gelsemiol (**10**),[11] by treatment with aqueous alkaline solution. All the spectroscopic data of hemi-synthetic compound (^{1}H- and ^{13}C-NMR, UV, CD) were identical with those of the natural product. Therefore, the structure and the relative stereochemistry of GSIR-1 were assigned to be formula **4**.

Experimental

General UV: JASCO V-560. IR: JASCO FT/IR-230. ^{1}H- and ^{13}C-NMR spectra: JEOL JNM ECP-600 or JEOL JNM A-500 at 600 or 500 MHz (^{1}H-NMR) and at 150 or 125 MHz (^{13}C-NMR), respectively. FAB-MS and HR-FAB-MS: JEOL JMS-HX110. Optical rotation: JASCO P-1020. CD: JASCO J-720WI. TLC: precoated Silica gel 60 F_{254} plates (Merck, 0.25 mm thick). Column chromatography: Silica gel 60 [(Merck, 70—230 mesh (for open chromatography) or 230—400 mesh (for flash chromatography)], and Aluminum oxide 90 (Merck, 70—230 mesh). Medium-pressure liquid chromatography (MPLC): C. I. G. prepacked column CPS-HS-221-05 (Kusano Kagakukikai, SiO_2).

Plant Material The cultivated Carolina jasmine was harvested from the medicinal plant garden of Chiba University, Japan in August 2000.

Extraction and Isolation of New Compounds, GS-1 (1), GS-2 (2), GS-3 (3) and GSIR-1 (4). From Stems The dried stems of *G. sempervirens* Ait. f. (1.29 kg) were extracted with hot MeOH five times to give the MeOH extract (128.9 g). A portion of the MeOH extract (70.3 g) was dissolved in 1 N HCl (1.2 l) and extracted with ethyl acetate (1.8 l). After the ethyl acetate layer was extracted with 1 N HCl (600 ml), the combined acidic layer was basified with Na_2CO_3 at 0 °C (pH 9) and extracted with 5% MeOH/$CHCl_3$ (4.2 l) to give the crude alkaloidal fraction (4.32 g). The crude alkaloid was separated by SiO_2 open column chromatography with $CHCl_3$/MeOH gradient elution to give 12 fractions: fr. S1 ($CHCl_3$, 2% MeOH/$CHCl_3$, 14.6 mg), fr. S2 (5%, 6.3 mg), fr. S3 (5%, 163 mg), fr. S4 (8%, 95 mg), fr. S5 (8%, 121 mg), fr. S6 (8%, 278 mg), fr. S7 (10—15%, 1255 mg), fr. S8 (20—25%, 480 mg), fr. S9 (25—30%, 247 mg), fr. S10 (30% MeOH/$CHCl_3$, 157 mg), fr. S11 (MeOH, 328 mg) and fr. S12 (MeOH, 437 mg). Fr. S3 was separated by SiO_2 open column chromatography ($CHCl_3$/AcOEt/MeOH gradient). The 10—15% MeOH/$CHCl_3$ eluate was purified by SiO_2 open column chromatography (MeOH/$CHCl_3$ gradient or AcOEt/MeOH gradient) and then by MPLC (AcOEt) to afford GS-1 (**1**, 1.5 mg) and GS-3 (**3**, 3.5 mg). The 20—50% AcOEt/$CHCl_3$ and 10% MeOH/$CHCl_3$ eluate was purified by MPLC (40% AcOEt/$CHCl_3$ or AcOEt) to give GSIR-1 (**4**, 15.8 mg). Fr. S6 was purified by SiO_2 open column chromatography ($CHCl_3$/MeOH gradient or AcOEt/MeOH gradient) and then by MPLC (30% MeOH/AcOEt) to afford GS-2 (**2**, 37.3 mg). Compound **2** (8.4 mg) was also obtained from fr. S4 and S5. Other isolated compounds were gelsemine (668 mg), gelsevirine (10.5 mg), 4,20-dehydrogelsemicine (1.9 mg),[12] 11-methoxyhumantenine (28.5 mg), 19*Z*-akuammidine (14.5 mg), gelsemicine (**7**, 85.6 mg), sempervirine (12.1 mg), gelsemiol (**10**, 76.3 mg), 7-deoxygelsemide (19.3 mg), and scopoletin (9.0 mg). 4,20-Dehydrogelsemicine was isolated from the Genus *Gelsemium* for the first time.

From Leaves The fresh leaves of *G. sempervirens* Ait. f. (996.4 g) were extracted with hot MeOH five times to give the MeOH extract (217.6 g). The crude alkaloidal fraction (7.59 g) was obtained using the same procedure as that described above from a portion of the MeOH extract (214.9 g). A portion of the crude alkaloid (7.42 g) was separated by SiO_2 open column chromatography with $CHCl_3$/MeOH gradient elution to give 8 fractions: fr. L1 ($CHCl_3$, 31.2 mg), fr. L2 (2% MeOH/$CHCl_3$, 6.36 g), fr. L3 (5%, 47.4 mg), fr. L4 (5—8%, 38.1 mg), fr. L5 (10—20%, 35.5 mg), fr. L6 (20—30%, 39.5 mg), fr. L7 (30% MeOH/$CHCl_3$ and 30% MeOH/saturated NH_3 in $CHCl_3$, 57.5 mg) and fr. L8 (MeOH, 203.7 mg). Fr. L2 was purified by SiO_2 flash column chromatography ($CHCl_3$/AcOEt gradient). The 20—30% AcOEt/$CHCl_3$ eluate (830 mg) was separated by SiO_2 flash column chromatography (40% AcOEt/*n*-hexane) and then by MPLC (50% AcOEt/$CHCl_3$) to afford GSIR-1 (**4**, 4.1 mg). The MeOH eluate (955 mg) was purified by Al_2O_3 column chromatography (30% AcOEt/$CHCl_3$) and MPLC (6% MeOH/$CHCl_3$ or 10% MeOH/AcOEt) to give GS-2 (**2**, 3.7 mg). Other isolated compounds were gelsemine (227.9 mg), 11-methoxyhumantenine (13.1 mg), gelsemicine (**7**, 13.1 mg), and 7-deoxygelsemide (55.8 mg).

GS-1 (**1**): Amorphous; UV λ_{max} (MeOH) nm: 218.5, 287.0, 295.5 sh. FAB-MS (NBA) *m/z*: 387 $[MH]^+$. HR-FAB-MS (NBA/PEG) *m/z*: 387.1566 $[MH]^+$ (Calcd for $C_{20}H_{23}N_2O_6$: 387.1556). ^{1}H- and ^{13}C-NMR: Table 1. CD (c=0.458 mmol/l, MeOH, 20 °C) $\Delta\varepsilon$ (λ nm): 0 (305), −1.3 (261), 0 (251), +2.5 (240), 0 (232), −7.7 (216).

GS-2 (**2**): Amorphous; UV λ_{max} (MeOH) nm: 218.5, 286.5, 296.0 sh. IR ($CHCl_3$) cm^{-1}: 1718. FAB-MS (NBA) *m/z*: 373 $[MH]^+$. HR-FAB-MS (NBA/PEG) *m/z*: 373.1748 $[MH]^+$ (Calcd for $C_{20}H_{25}N_2O_5$: 373.1763). ^{1}H- and ^{13}C-NMR: Table 1. CD (c=0.475 mmol/l, MeOH, 20 °C) $\Delta\varepsilon$ (λ nm): 0 (305), −2.2 (268), 0 (254), +7.4 (237), 0 (227), −8.3 (216).

GS-3 (**3**): Amorphous; UV λ_{max} (MeOH) nm: 219.0, 286.5, 295.0 sh. FAB-MS (NBA) *m/z*: 389. HR-FAB-MS (NBA/PEG) *m/z*: 389.1703 $[MH]^+$ (Calcd for $C_{20}H_{25}N_2O_6$: 389.1713). ^{1}H- and ^{13}C-NMR in $CDCl_3$: Table 1. ^{1}H-NMR (500 MHz, pyridine-d_5) δ: 7.60 (1H, d, J=7.9 Hz, H-9), 6.79 (2H, overlapped, H-10, 12), 4.48 (1H, dd, J=11.4, 3.3 Hz, H-17), 4.25 (1H, m, H-3), 4.17 (1H, d, J=11.4 Hz, H-17), 3.95 (3H, s, N_a-OMe), 3.86 (1H, m, H-5), 3.73 (3H, s, 11-OMe), 3.54 (1H, br dd, J=8.5, 3.3 Hz, H-16), 2.93 and 2.68 (each, 1H, dddd, J=17.8, 7.3, 7.3, 7.3 Hz, H_2-19), 2.41 (1H, d, J=15.8 Hz, H-6), 2.21 (1H, dd, J=15.8, 4.7 Hz, H-6), 1.15 (1H, dd, J=7.3, 7.3 Hz, H_3-18), H-14 was buried under HOD signal. ^{13}C-NMR (125 MHz, pyridine-d_5) δ: 210.5 (C-20), 175.1 (C-2), 161.0 (C-11), 139.8 (C-13), 126.9 (C-9), 108.8 (C-10), 95.1 (C-12), 79.8 (C-3), 69.4 (C-14), 67.8 (C-15), 63.5 (N_a-OMe), 61.9 (C-17), 56.1 (C-5), 55.6 (11-OMe), 54.7 (C-7), 35.4 (C-6), 34.2 (C-16), 28.8 (C-19), 7.7 (C-18), C-8 was buried under pyridine-d_5 signal (124 ppm). CD (c=0.371 mmol/l, MeOH, 20 °C) $\Delta\varepsilon$ (λ nm): 0 (312), −3.1 (270), 0 (255), +14.2 (238), 0 (229), −16.6 (217).

GSIR-1 (**4**): Amorphous; UV λ_{max} (MeOH) nm: 215.5. IR ($CHCl_3$) cm^{-1}: 1750. FAB-MS (NBA) *m/z*: 183 $[MH]^+$; HR-FAB-MS (NBA/PEG) *m/z*: 183.1032 $[MH]^+$ Calcd for $C_{10}H_{15}O_3$: 183.1021). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 6.43 and 5.93 (each 1H, br d, J=2.2 Hz, H_2-3), 4.96 (1H, dd, J=5.8, 5.5 Hz, H-6), 3.82 (1H, dd, J=10.6, 4.0 Hz, H-1), 3.70 (1H, m, H-5), 3.58 (1H, dd, J=10.6, 10.0 Hz, H-1), 2.24 (1H, dd, J=14.0, 5.8 Hz, H-7), 1.87 (1H, m, H-9), 1.65 (1H, m, H-8), 1.47 (1H, ddd, J=14.0, 12.5, 5.5 Hz, H-7), 1.03 (3H, d, J=6.4 Hz, H_3-10). ^{13}C-NMR (150 MHz, $CDCl_3$) δ: 171.2 (C-11), 135.0 (C-4), 125.7 (C-3), 81.9 (C-6), 60.8 (C-1), 52.6 (C-9), 45.4 (C-5), 41.9 (C-7), 32.7 (C-8), 17.4 (C-10). CD (c=0.522 mmol/l, MeOH, 20 °C) $\Delta\varepsilon$ (λ nm): 0 (288), +0.92 (252), 0 (238), −10.3 (215).

4,20-Dehydrogelsemicine: UV λ_{max} (MeOH) nm: 214.5, 285, 295 sh. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.41 (1H, d, J=8.5 Hz, H-9), 6.57 (1H, dd, J=8.5, 2.4 Hz, H-10), 6.47 (1H, d, J=2.4 Hz, H-12), 4.39 (1H, m, H-5), 4.29 (1H, dd, J=11.1, 3.2 Hz, H-17), 4.25 (1H, br d, J=11.1 Hz, H-17), 3.94 (3H, s, N_a-OMe), 3.81 (3H, s, Ar-OMe), 3.70 (1H, br dd, J=4.6, 2.1 Hz, H-3), 2.85 (1H, dd, J=9.7, 9.7 Hz, H-15), 2.71 (1H, dddd, J=17.0, 7.3, 7.3, 7.3 Hz, H-19), 2.56 (1H, m, H-16), 2.42 (1H, dddd, J=17.0, 7.3, 7.3, 7.3 Hz, H-19), 2.36 (1H, br d, J=15.6 Hz, H-6), 2.35 (1H, br d, J=14.8 Hz, H-14), 2.26 (1H, br dd, J=15.6, 2.1 Hz, H-6), 2.12 (1H, ddd, J=14.8, 9.7, 4.6 Hz, H-14), 1.28 (3H, dd, J=7.3, 7.3 Hz, H_3-18). ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 184.2 (C-20), 171.8 (C-2), 160.1 (C-11), 139.2 (C-13), 125.5 (C-9), 124.2 (C-8), 107.7 (C-10), 93.9 (C-12), 75.3 (C-3), 72.5 (C-5), 63.4 (N_a-OMe), 62.1 (C-17), 55.6 (Ar-OMe), 55.5 (C-7), 42.5 (C-15), 39.8 (C-16), 37.9 (C-6), 26.9 (C-14), 25.7 (C-19), 10.0 (C-18). CD (c=0.416 mmol/l, MeOH, 20 °C) $\Delta\varepsilon$ (λ nm): −8.7 (217), 0 (228), +5.8 (238), 0 (253), −2.1 (269), 0 (320).

Preparation of GSIR-1 (4) from Gelsemiol (10) To a solution of gelsemiol (**10**, 10.0 mg, 0.05 mmol) in MeOH (0.5 ml) was added 1 N NaOH aq. (0.5 ml, 0.5 mmol) and the mixture was refluxed for 48 h under Ar. After

concentration of MeOH, cold 10% HCl aq. was added to the reaction mixture and the whole mixture was extracted with $CHCl_3$. The organic layer was washed with brine, dried over $MgSO_4$ and evaporated. The residue was purified by SiO_2 open column chromatography (1% MeOH–$CHCl_3$) to afford GSIR-1 (**4**, 1.1 mg, yield 12%).

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