HETEROCYCLES, Vol. 75, No. 1, 2008, pp. 131 – 143. © The Japan Institute of Heterocyclic Chemistry
Received, 6th August, 2007, Accepted, 27th September, 2007, Published online, 28th September, 2007. COM-07-11193

MEGASTIGMANE GLYCOSIDES FROM THE LEAVES OF *SALACIA CHINENSIS*

Seikou Nakamura, Yi Zhang, Yutana Pongpiriyadacha, Tao Wang, Hisashi Matsuda, and Masayuki Yoshikawa*

Kyoto Pharmaceutical University, Misasagi, Yamashina-ku, Kyoto 607-8412, Japan, e-mail address: myoshika@mb.kyoto-phu.ac.jp

Abstract – Six new megastigmane glycosides, foliasalaciosides A_1 (**1**), A_2 (**2**), B_1 (**3**), B_2 (**4**), C (**5**), and D (**6**), were isolated from the methanolic extract of the leaves of *Salacia chinensis* (Hippocrateaceae) collected in Thailand together with 16 known constituents. The absolute stereostructures of **1**–**6** were elucidated on the basis of chemical and physicochemical evidence including the application of the modified Mosher's method.

Salacia chinensis L. (syn. *S. prinoides*, Hippocrateaceae) is widely distributed in Thailand, Myanmar, and India. The stems of *S. chinensis* have been used as a laxative and to relieve muscular pain in Thai traditional medicine.[1] On the other hand, the decoctions of the stems and leaves are given to cure diabetes mellitus in the Ayurvedic system of Indian traditional medicine.[2] Previously, we reported that the extract from the stems of *S. chinensis* showed inhibitory activities on rat lens aldose reductase and α-glucosidase and radical scavenging activity, and the structures of various triterpenes, nor-triterpenes, and sesquiterpenes were characterized.[3–6] However, the chemical constituents as well as the pharmacological properties of the leaves of *S. chinensis* have not been characterized. During the course of our serial studies on the bioactive constituents from *Salacia* species,[7–14] six new megastigmane glycosides, foliasalaciosides A_1 (**1**), A_2 (**2**), B_1 (**3**), B_2 (**4**), C (**5**), and D (**6**), were isolated from the methanolic extract of the leaves of *Salacia chinensis* together with 16 known constituents. This paper deals with the isolation and structure elucidation including the absolute configuration of **1**–**6**.

The leaves of *S. chinensis* were cut and extracted with methanol under reflux. The methanolic extract was partitioned into a mixture of ethyl acetate (EtOAc) and water to furnish an EtOAc-soluble portion and an aqueous layer. The aqueous layer was further extracted with *n*-butanol (*n*-BuOH) to give a *n*-BuOH-soluble portion. The *n*-BuOH-soluble portion was subjected to Diaion HP-20 column chromatography ($H_2O \rightarrow$ MeOH) to give the water- and methanol-eluted fractions. The methanol-eluted fraction was subjected to normal- and reversed-phase silica gel column chromatographies, and finally HPLC to give foliasalaciosides A_1 (**1**, 0.0003% from the natural medicine), A_2 (**2**, 0.0003%), B_1 (**3**, 0.0004%), B_2 (**4**,

0.0003%), C (**5**, 0.0001%), and D (**6**, 0.0001%), together with 7 known megastigman glycosides, blumenyl C *β*-D-glucopyranoside (**7**, 0.0032%),[15] roseoside A (**8**, 0.0001%),[16] dendranthemoside A (**9**, 0.0004%),[17] alangioside A (**10**, 0.0002%),[18] (6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*-*α*-L-arabinopyranosyl(1→6)-*β*-D-glucopyranoside (**11**, 0.0001%),[16] icariside B_1 (**12**, 0.0002%),[19] and citroside B (**13**, 0.0004%),[20] and nine known flavonol glycosides, paeonoside (**14**, 0.0008%),[21] kaempferol 3-*O*-rutinosyl-7-*O*-*β*-D-glucopyranoside (**15**, 0.0008%),[22] kaempferol 3-*O*-*α*-L-rhamnopyranosyl(1→6)-*β*-D-galactopyranosyl-7-*O*-*β*-D-glucopyranoside (**16**, 0.0017%),[23] clitorin (**17**, 0.0045%),[24] kaempferol 3-*O*-(2,6-*α*-L-dirhamnopyranosyl-*β*-D-glucopyranosyl)-7-*O*-*β*-D-glucopyranoside (**18**, 0.0061%),[24] rutin (**19**, 0.027%),[25] quercetin 3-*O*-rutinosyl-7-*O*-*β*-D-glucopyranoside (**20**, 0.0016%),[26] manghaslin (**21**, 0.0019%),[24] and myricetin 3-*O*-*β*-D-rutinoside (**22**, 0.0015%).[27]

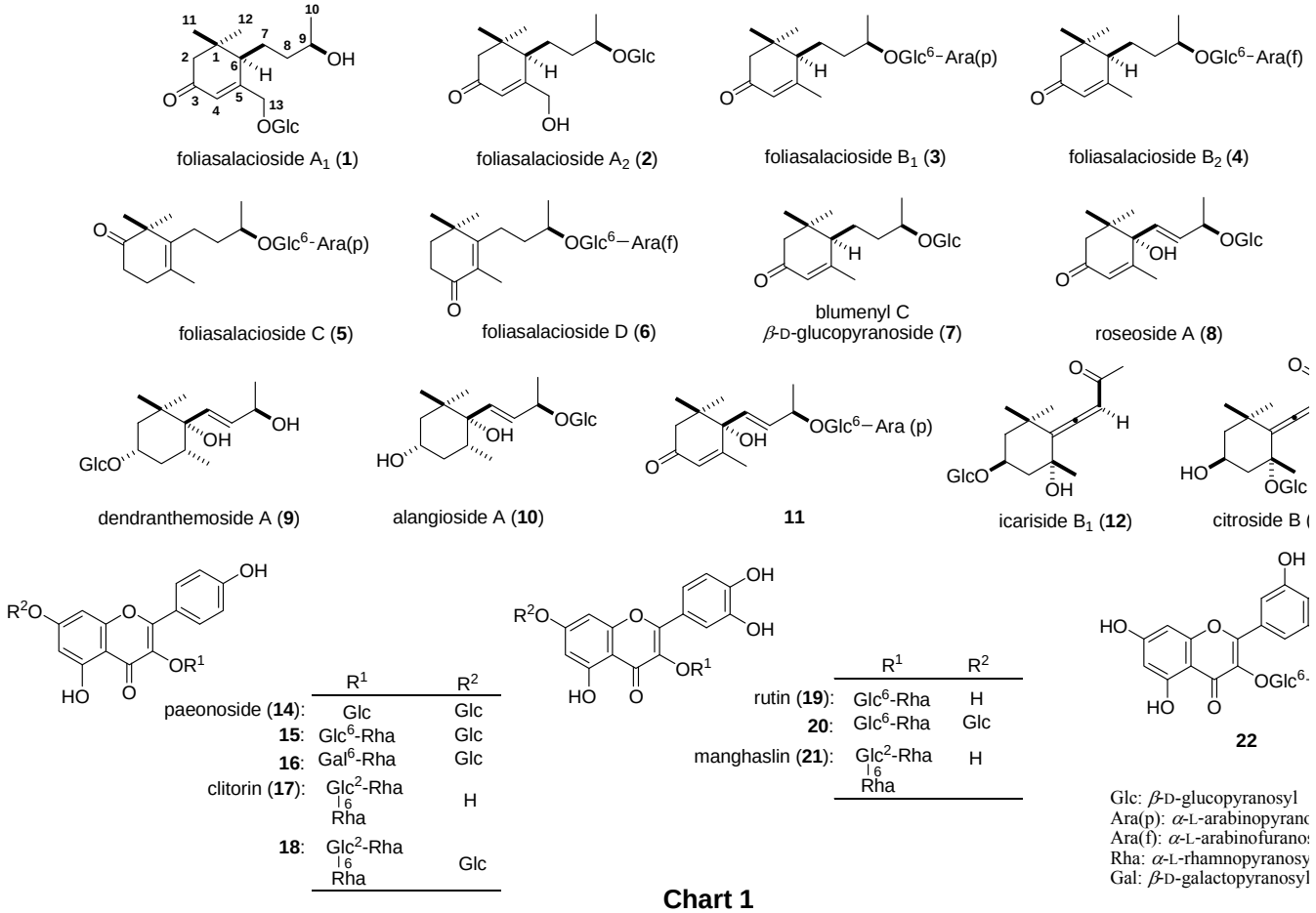

Chart 1

Structures of Foliasalaciosides A_1 (1), A_2 (2), B_1 (3), B_2 (4), C (5), and D (6)

Foliasalaciosides A_1 (**1**) and A_2 (**2**) were obtained as an amorphous powder with positive optical rotation (**1**: $[\alpha]_D^{28}$ +24.3°; **2**: $[\alpha]_D^{26}$ +30.9°, both in MeOH), respectively. The IR spectra of **1** and **2** showed absorption bands assignable to hydroxyl, *α*,*β*-unsaturated carbonyl, and ether functions [**1**: 3420, 1653, and 1078 cm^{-1}; **2**: 3423, 1653, and 1078 cm^{-1}]. The common molecular formula, $C_{19}H_{32}O_8$, of both **1** and **2** were determined from the quasimolecular ion peaks in the positive-ion FAB-MS [*m/z* 411 $(M + Na)^+$] and by high-resolution (HR) FAB-MS measurement. Acid hydrolysis of **1** and **2** with 1 M HCl liberated

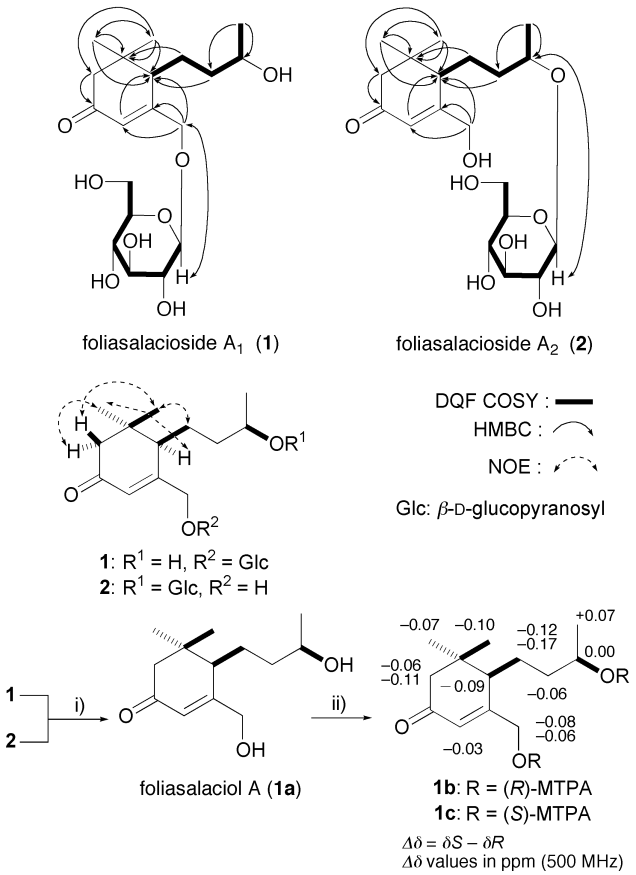

Figure 1

D-glucose, which was identified by HPLC analysis using an optical rotation detector.[28,29] The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra of **1** and **2**, which were assigned by various NMR experiment,[30] showed signals assignable to aglycon parts {**1**: δ 1.03, 1.11 (3H each, both s, 12, 11-H_3), 1.46, 1.94 (1H each, both m, 7-H_2), 2.01 (1H, m, 6-H), 2.02 (1H, d, J = 17.9 Hz, 2-Hα), 2.55 (1H, d, J = 17.9 Hz, 2-Hβ); **2**: δ 1.01, 1.10 (3H each, both s, 12, 11-H_3), 1.49, 1.95 (1H each, both m, 7-H_2), 1.94 (1H, m, 6-H), 2.01 (1H, d, J = 17.9 Hz, 2-Hα), 2.56 (1H, d, J = 17.9 Hz, 2-Hβ)}, together with β-D-glucopyranosyl moieties [**1**: δ 4.32 (1H, d, J = 8.2 Hz, 1'-H), **2**: δ 4.33 (1H, d, J = 8.2 Hz, 1'-H)]. As shown in Figure 1, the double quantum filter correlation spectroscopy (DQF COSY) experiment on **1** and **2** indicated the presence of partial structures written in bold lines, and in the heteronuclear multiple-bond correlations (HMBC) experiment, long-range correlations were observed between the following protons and carbons: (**1**: 2-H and 3-C; 4-H and 6-C; 7-H and 1-C; 8-H and 6-C; 10-H and 8, 9-C; 11-H and 1, 2, 6, 12-C; 12-H and 1, 2, 6, 11-C; 13-H and 4, 5, 6, 1'-C; 1'-H and 13-C; **2**: 2-H and 3-C; 4-H and 6, 13-C; 7-H and 1-C; 8-H and 6-C; 9-H and 1'-C; 10-H and 8, 9-C; 11-H and 1, 2, 6, 12-C; 12-H and 1, 2, 6, 11-C; 13-H and 4, 5, 6-C; 1'-H and 9-C). The planar structures of **1** and **2** were the same as those of glochidionionoside B[31] and (6*R*,9*S*)-megastigman-4-en-3-one-9,13-diol 9-*O*-β-D-glucopyranoside,[32] respectively. The relative stereostructures of **1** and **2** except for the 9-positions were determined by NOESY experiments, in which correlations were observed between the following proton pairs: 2-Hα and 12-H_3; 2-Hβ and 11-H; 6-Hα and 12-H_3; 11-H_3 and 7-H_2. The absolute stereostructures of the 6-position in **1** and **2** were confirmed by circular dichroic (CD) spectra.[15] The CD spectra (MeOH) of **1** and **2** showed Cotton effects at [**1**: 215 nm ($\Delta\varepsilon$ +2.06), 328 nm ($\Delta\varepsilon$ +0.27); **2**: 216 nm ($\Delta\varepsilon$ +4.23), 330 nm ($\Delta\varepsilon$ +0.45)], which was very similar to those of blumenyl C β-D-glucopyranoside (**8**) [216 nm ($\Delta\varepsilon$ +3.74), 333 nm ($\Delta\varepsilon$ +0.99)] reported by Buske et al,[15] so that the absolute configuration of the 6-position in **1** and **2** was determined to be *R* orientation. The absolute configurations of the 9-position on **1** and **2** were clarified by a modified Mosher's method. Namely, enzymatic hydrolysis of **1** and **2** with nariginase gave a common aglycon, foliasalaciol A (**1a**). Next, the (*R*)- and (*S*)-MTPA esters (**1b**, **1c**) were derived from **1a** upon reaction with (*R*)- and (*S*)-MTPA in the presence of EDC·HCl and 4-DMAP. The 10-methyl protons of the (*S*)-MTPA ester (**1c**) resonated at lower field than those of the (*R*)-MTPA ester (**1b**) [$\Delta\delta$: positive], while the protons on the 2, 4, 6, 7, 8, 11, 12, and 13-positions of **1c** were observed at higher fields compared to those of **1b** [$\Delta\delta$: negative].

Consequently, the absolute configurations of the 9-position in **1** and **2** were elucidated to be *R* orientation. On the basis of above-mentioned evidence, the structures of foliasalaciosides A (**1**) and B (**2**) were characterized as shown.[33]

Table 1. ^{13}C-NMR Data (125 MHz, $^{a}CD_3OD$, $^{b}CDCl_3$) for Foliasalaciosides A_1 (**1**), A_2 (**2**), B_1 (**3**), B_2 (**4**), C (**5**), and D (**6**).

	1^a	**1a**^{b}	**2**^{a}	**3**^{a}	**4**^{a}	**5**^{a}	**6**^{a}
1	37.3	36.3	37.4	37.4	37.4	49.4	37.7
2	48.6	47.6	48.6	48.1	48.2	218.3	38.5
3	202.2	199.7	202.4	202.5	202.6	37.1	35.1
4	123.2	121.7	121.5	125.3	125.4	32.6	201.7
5	167.9	167.6	172.5	170.4	170.3	128.7	131.7
6	47.5	46.0	47.6	52.4	52.4	138.0	168.9
7	27.5	26.2	27.1	27.0	26.9	26.1	28.1
8	39.6	38.1	37.8	37.9	37.8	39.0	37.3
9	68.4	67.6	75.2	75.7	75.9	76.0	76.0
10	23.7	23.8	20.0	20.1	20.1	19.94	20.0
11	27.7	27.4	27.8	27.6	27.6	25.2	27.3
12	28.9	28.7	28.8	29.1	29.1	25.2	27.3
13	70.8	64.8	65.1	25.1	25.1	19.89	11.8
1'	103.5		102.1	102.3	102.3	102.3	102.4
2'	75.1		75.2	75.1	75.2	75.2	75.2
3'	78.1		78.2	78.0	78.1	78.1	78.1
4'	71.7		71.8	71.8	72.2	71.8	72.2
5'	78.2		78.0	76.9	76.8	76.9	76.9
6'	62.8		62.9	69.4	68.2	69.4	68.2
1"				105.3	109.9	105.2	111.0
2"				72.4	83.2	72.4	83.2
3"				74.2	79.0	74.2	79.0
4"				69.8	86.0	69.8	85.9
5"				66.7	63.2	66.6	63.1

Foliasalaciosides B_1 (**3**) and B_2 (**4**) were obtained as an amorphous powder with positive optical rotation (**3**: $[\alpha]_D^{27}$ +25.2°; **4**: $[\alpha]_D^{26}$ +30.5°, both in MeOH), respectively. The IR spectra of **3** and **4** showed absorption bands assignable to hydroxyl, α,β-unsaturated carbonyl, and ether functions [**3**: 3405, 1651, and 1075 cm^{-1}; **4**: 3397, 1655, and 1075 cm^{-1}]. The same molecular formula, $C_{24}H_{40}O_{11}$, of both **3** and **4** were determined from the positive- and negative-ion FAB-MS [*m/z* 527 $(M + Na)^+$, *m/z* 503 $(M - H)^-$] and by HRFABMS measurements. Acid hydrolysis of **3** and **4** with 1 M HCl liberated D-glucose and L-arabinose, which were identified by HPLC analysis using an optical rotation detector.[28,29] The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra[30] of **3** and **4** showed signals due to aglycon parts {**3**: δ 1.01, 1.09 (3H each, both s, 12, 11-H_3), 1.97 (1H, m, 6-H), 1.97 (1H, d, J = 17.2 Hz, 2-Hα), 2.46 (1H, d, J = 17.2 Hz, 2-Hβ); **4**: δ 1.01, 1.09 (3H each, both s, 12, 11-H_3), 1.97 (1H, d, J = 17.4 Hz, 2-Hα), 1.98 (1H, m, 6-H), 2.47 (1H, d, J = 17.4 Hz, 2-Hβ)}, together with β-D-glucopyranosyl moieties [**3**: δ 4.31 (d, J = 7.6 Hz, H-1'); **4**: δ 4.31 (d, J = 7.6 Hz, H-1')], an α-L-arabinopyranosyl moiety [**3**: 4.28 (d, J = 6.8 Hz, H-1")], and an α-L-arabinofuranosyl moiety [**4**: δ 4.96 (d, J = 1.5 Hz, H-1")]. The proton and carbon signals in the ^{1}H- and ^{13}C-NMR spectra of **3** and **4** were superimposable on those of blumenyl C β-D-glucopyranoside (**7**)[15] except for the glycoside moiety, while the signals due to the 9-*O*-diglycosyl moiety

of **3** and **4** were very similar to those of (6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*-α-L-arabinopyranosyl(1→6)-β-D-glucopyranoside (**11**)[16] and floralginsenoside D,[28] respectively. As shown in Figure 2, the positions of the glycoside linkages in **3** and **4** were determined by a HMBC experiment, which showed long-range correlations between the following protons and carbons: 1'-H and C-9; 1''-H and C-6'. The relative stereostructures of **3** and **4** except for the 9-position were determined by a NOESY experiment, in which correlations were observed between the following proton pairs: 2-Hα and 12-H_3; 2-Hβ and 11-H_3; 6-H and 12-H_3; 11-H_3 and 7-H_2. The absolute stereostructures of the 6-position in **3** and **4** were also confirmed by CD spectra.[15]

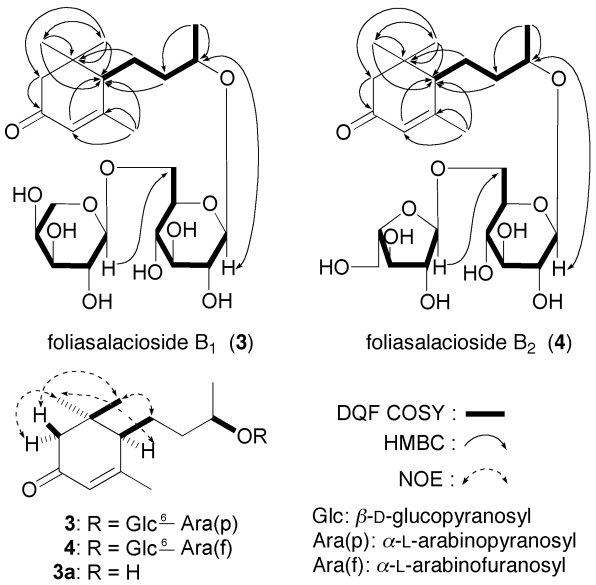

Figure 2

The CD spectra (MeOH) of **3** and **4** showed Cotton effects at [**3**: 214 nm ($\Delta\varepsilon$ +1.92), 335 nm ($\Delta\varepsilon$ +0.35); **4**: 214 nm ($\Delta\varepsilon$ +1.26), 327 nm ($\Delta\varepsilon$ +0.19)], so that the absolute configurations of the 6-position in **3** and **4** were determined to be *R* orientation. Finally, enzymatic hydrolysis of **3** and **4** with nariginase gave a same aglycon, blumenyl C.[33,34] On the basis of above-mentioned evidence, the structures of foliasalaciosides B_1 (**3**) and foliasalaciosides B_2 (**4**) was characterized as shown.

Foliasalaciosides C (**5**), obtained as an amorphous powder with negative optical rotation ($[\alpha]_D^{23}$ –20.4° in MeOH), showed absorption bands at 3379, 1705, 1660, and 1084 cm^{-1} due to hydroxyl, carbonyl, olefin and ether functions in the IR spectrum. The molecular formula, $C_{24}H_{40}O_{11}$, was determined from the positive- and negative-ion FAB-MS [*m/z* 527 $(M + Na)^+$, *m/z* 503 $(M - H)^-$] and by HRFABMS measurement. The acid hydrolysis of **5** yielded D-glucose and L-arabinose.[28,29] The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra[30] of **5** showed signals due to an aglycon part {δ 1.16 (6H, s, 11, 12-H_3), 1.20 (3H, d, *J* = 6.1 Hz, 10-H_3), 1.74 (3H, s, 13-H_3)}, together with a β-D-glucopyranosyl moiety [δ 4.34 (1H, d, *J* = 8.0 Hz, 1'-H)] and an α-L-arabinopyranosyl moiety [4.33 (1H, d, *J* = 6.7 Hz, 1''-H)]. The DQF COSY experiment on **5** showed correlations as shown in Figure 3. Furthermore, in the HMBC experiment, long-range correlations were observed between the following protons and carbons: 3-H and 2, 5-C; 4-H and 2, 5, 6-C; 7-H and 1, 5-C; 9-H and 1'-C; 10-H and 8, 9-C; 11-H and 1, 2, 6, 12-C; 12-H and 1, 2, 6, 11-C; 1'-H and 9-C; 1''-H and 6'-C. The proton and carbon signals of the 9-*O*-diglycosyl moiety in the ^{1}H- and ^{13}C-NMR spectra of **5** were very similar to those of **3** and **11**.[16] Furthermore, the configuration of the 9-position was characterized by comparison of the 9-, 10-, and 1'-carbon signals of **5** in the ^{13}C NMR (CD_3OD) spectrum with those of synthetic known megastigmane glycosides, (1*R*/*S*)-3-[(4*R*)-4-hydroxy-

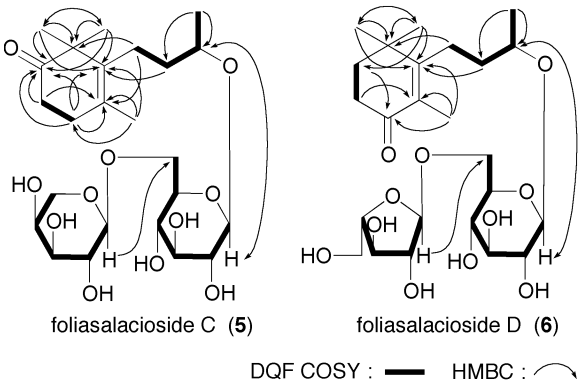

Figure 3

2,6,6-trimethylcyclohex-1-enyl]-1-methylpropyl-β-D-glucopyranoside,[36] having the same side chain (butanol *O*-glycoside moiety) as **5**. Namely, It was reported that the ^{13}C NMR signal [δ_c 76.1 (9-C); 19.8 (10-C); 102.2 (1'-C)] of the synthetic megastigmane having the *R*-configuration was shifted upfield relative to that [δ_c 77.9 (9-C); 21.8 (10-C); 103.9 (1'-C)] of the synthetic megastigmane having the *S*-configuration.[36] The 9-, 10-, and 1'-carbon signals of **5** were observed at δ_c 76.0 (9-C), 19.9 (10-C), and 102.3 (1'-C), so that the C-9 configuration of **5** was determined to be *R*. This evidence led us to formulate the structure of foliasalaciosides F (**5**) as shown.

Foliasalaciosides G (**6**), obtained as an amorphous powder with negative optical rotation ([α]$_D^{26}$ –17.7° in MeOH), showed absorption bands at 3339, 1653, and 1074 cm^{-1} due to hydroxyl, α,β-unsaturated carbonyl, and ether functions in the IR spectrum. The molecular formula, $C_{24}H_{40}O_{11}$, was determined from the positive- and negative-ion FAB-MS [*m/z* 527 $(M + Na)^+$, *m/z* 503 $(M - H)^-$] and by HRFABMS measurement. The acid hydrolysis of **6** yielded D-glucose and L-arabinose.[28,29] The ^{1}H-NMR (CD_3OD) and ^{13}C-NMR (Table 1) spectra[30] of **6** showed signals due to an aglycon part [δ 1.20 (6H, s, 11, 12-H$_3$), 1.22 (3H, d, *J* = 6.1 Hz, 10-H$_3$), 1.76 (3H, s, 13-H$_3$)], together with a β-D-glucopyranosyl moiety [δ 4.34 (1H, d, *J* = 7.6 Hz, 1'-H)] and an α-L-arabinofuranosyl moiety [4.98 (1H, d, *J* = 1.4 Hz, 1''-H)]. The proton and carbon signals of the aglycon part of **6** in the ^{1}H- and ^{13}C-NMR spectra were superimposable on those of plataninoside F,[36] whereas the signals due to the 9-*O*-diglycosyl moiety of **6** were very similar to those of **4** and floralginsenoside D.[28] The structure of **6** was characterized by means of DQF COSY and HMBC experiments (Figure 3). The position of the glycosides linkage were determined by a HMBC experiment, which showed long-range correlation between 1'-H and 9-C; 1''-H and 6'-C. Furthermore, the configuration of the 9-position of **6** was characterized by comparison of the ^{13}C-NMR data.[36] Namely, the 9-, 10-, and 1'-carbon signals of **6** were observed at δ_c 76.0 (9-C), 20.0 (10-C), and 102.4 (1'-C), so that the 9-C configuration was determined to be *R* and the total structure of foliasalaciosides G (**6**) was characterized as shown.

EXPERIMENTAL

The following instruments were used to obtain physical data: specific rotations, Horiba SEPA-300 digital polarimeter (*l* = 5 cm); CD spectra, JASCO J-720WI spectrometer; UV spectra, Shimadzu UV-1600 spectrometer; IR spectra, Shimadzu FTIR-8100 spectrometer; ^{1}H NMR spectra, JEOL JNM-LA500 (500 MHz) spectrometer; ^{13}C NMR spectra, JEOL JNM-LA500 (125 MHz) spectrometer with tetramethylsilane as an internal standard; EIMS and HREIMS, JEOL JMS-GCMATE mass spectrometer; FABMS and HRFABMS, JEOL JMS-SX 102A mass spectrometer; HPLC detector, Shimadzu RID-6A refractive index and SPD-10A UV-VIS detectors. HPLC column, Cosmosil 5C$_{18}$-MS-II (Nacalai Tesque Inc., 250 × 4.6 mm i.d.) and (250 × 20 mm i.d.) columns were used for analytical and preparative purposes, respectively.

The following experimental conditions were used for chromatography: normal-phase silica gel column chromatography, silica gel BW-200 (Fuji Silysia Chemical, Ltd., 150–350 mesh); reversed-phase silica gel column chromatography, Chromatorex ODS DM1020T (Fuji Silysia Chemical, Ltd., 100–200 mesh); Diaion HP-20 column chromatography (Nippon Rensui); TLC, pre-coated TLC plates with silica gel

$60F_{254}$ (Merck, 0.25 mm) (normal-phase) and silica gel RP-18 F_{254S} (Merck, 0.25 mm) (reversed-phase); detection was achieved by spraying with 1% $Ce(SO_4)_2$–10% aqueous H_2SO_4, followed by heating.

Plant Material

The dried leaves of *S. chinensis* were collected at Thailand in 2006 and identified by one of authors (Rajamangala University of Technology Srivijaya, Pongpiriyadacha Y.). A voucher of the plant is on file in our laboratory (2006. Thai-06).

Extraction and Isolation

The dried leaves of *S. chinensis* Linn. (5.8 kg) were finely cut and extracted 3 times with methanol (MeOH) under reflux for 3 h. Evaporation of the solvent under reduced pressure provided a methanolic extract (756 g, 13.0%). The MeOH extract (712 g) was partitioned into an EtOAc–H_2O (1:1, v/v) mixture to furnish an EtOAc-soluble fraction (222 g, 4.1%) and an aqueous phase. The aqueous phase was further extracted with *n*-BuOH to give a *n*-BuOH-soluble fraction (130 g, 2.4%) and a H_2O-soluble fraction (361 g, 6.6%).

The *n*-BuOH-soluble fraction (100 g) was subjected to Diaion HP-20 column chromatography (1.5 kg, $H_2O \rightarrow$ MeOH $\rightarrow$ acetone) to give H_2O-eluted fraction (49.8 g, 1.2%), MeOH-eluted fraction (39.2 g, 0.93%) and acetone-eluted fraction (11.0 g, 0.26%), respectively. The MeOH-eluted fraction (39.2 g) was subjected to ordinary-phase silica gel column chromatography {480 g, $CHCl_3$–MeOH (10:1, v/v) $\rightarrow$ $CHCl_3$–MeOH–H_2O [(10:3:1, v/vv, lower layer) $\rightarrow$ (7:3:1, v/vv, lower layer) $\rightarrow$ (6:4:1, v/vv, lower layer)] $\rightarrow$ MeOH} to give ten fractions [Fr. 1 (0.5 g), Fr. 2 (0.6 g), Fr. 3 (1.3 g), Fr. 4 (7.3 g), Fr. 5 (3.0 g), Fr. 6 (6.7 g), Fr. 7 (1.6 g), Fr. 8 (2.4 g), Fr. 9 (9.3 g), Fr. 10 (3.5 g)]. Fraction 3 (1.3 g) was subjected to reversed-phase silica gel column chromatography [480 g, MeOH–H_2O (10:90 $\rightarrow$ 20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 50:50 $\rightarrow$ 60:40 $\rightarrow$ 100: 0, v/v)] to give five fractions [Fr. 3-1 (121 mg), Fr. 3-2 (111 mg), Fr. 3-3 (389 mg), Fr. 3-4 (131 mg), Fr. 3-5 (450 mg)]. Fraction 3-3 (389 mg) was separated by HPLC [MeOH–H_2O (40:60, v/v)] and finally purified with HPLC [MeCN–MeOH–H_2O (15:8:77, v/v/v)] to furnish blumenyl C β-D-glucopyranoside (**7**, 71.5 mg). Fraction 3-4 (131 mg) was subjected to HPLC [MeOH–H_2O (40:60, v/v)] and purified by HPLC [MeCN–MeOH–H_2O (15:8:77, v/v/v)] to give blumenyl C β-D-glucopyranoside (**7**, 17.2 mg). Fraction 4 (7.3 g) was subjected to reversed-phase silica gel column chromatography [220g, MeOH–H_2O (0:100 $\rightarrow$ 10:90 $\rightarrow$ 20:80 $\rightarrow$ 30:70 $\rightarrow$ 40:60 $\rightarrow$ 60:40 $\rightarrow$ 100: 0, v/v) $\rightarrow$ $CHCl_3$] to give ten fractions [Fr. 4-1 (783 mg), Fr. 4-2 (821 mg), Fr. 4-3 (1.12 g), Fr. 4-4 (577 mg), Fr. 4-5 (288 mg), Fr. 4-6 (652 mg), Fr. 4-7 (1.30 g), Fr. 4-8 (413 mg), Fr. 4-9 (253 mg), Fr. 4-10 (760 mg)]. Fraction 4-6 (652 mg) was separated by HPLC [MeOH–H_2O (30:70, v/v)] to furnish ten fractions [Fr. 4-6-1 (7.2 mg), Fr. 4-6-2 (15.6 mg), Fr. 4-6-3 (17.8 mg), Fr. 4-6-4 (18.6 mg), Fr. 4-6-5 (51.2 mg), Fr. 4-6-6 (20.5 mg), Fr. 4-6-7 (30.6 mg), Fr. 4-6-8 (35.8 mg), Fr. 4-6-9 (18.0 mg), Fr. 4-6-10 (44.6 mg)]. Fr. 4-6-8 (35.8 mg) was finally purified by HPLC [MeCN–MeOH–H_2O (12:8:80, v/v/v)] to give foliasalacioside A_1 (**1**, 13.9 mg), foliasalacioside A_2 (**2**, 11.1 mg), and icariside B_1 (**12**, 6.2 mg). Fraction 4-7 (1.30 g) was separated by HPLC [MeOH–H_2O (40:60, v/v)] and [MeCN–MeOH–H_2O (15:8:77, v/v/v)] to furnish foliasalacioside B_1 (**3**, 17.3 mg), foliasalacioside B_2 (**4**, 11.9 mg), foliasalacioside D (**6**,

5.8 mg), blumenyl C β-D-glucopyranoside (**7**, 48.1 mg), roseoside A (**8**, 3.6 mg), dendranthemoside A (**9**, 2.2 mg), and citroside B (**13**, 10.0 mg). Fraction 4-8 (413 mg) was subjected to HPLC [MeOH–H_2O (40:60, v/v)] to afford nine fractions [Fr. 4-8-1 (11.9 mg), Fr. 4-8-2 (22.2 mg), Fr. 4-8-3 (47.6 mg), Fr. 4-8-4 (16.2 mg), Fr. 4-8-5 (14.2 mg), Fr. 4-8-6 (11.4 mg), Fr. 4-8-7 (14.6 mg), Fr. 4-8-8 (16.8 mg), Fr. 4-8-9 (16.2 mg)]. Fr. 4-8-7 (14.6 mg) was further purified by HPLC [MeCN–MeOH–H_2O (15:8:77, v/v/v)] to give foliasalacioside C (**5**, 3.8 mg). Fraction 5 (3.0 g) was subjected to reversed-phase silica gel column chromatography [90 g, MeOH–H_2O (10:90 → 20:80 → 30:70 → 40:60 → 50:50 → 100: 0, v/v)] to afford seven fractions [Fr. 5-0 (812 mg), Fr. 5-1 (196 mg), Fr. 5-2 (212 mg), Fr. 5-3 (224 mg), Fr. 5-4 (158 mg), Fr. 5-5 (400 mg), Fr. 5-6 (624 mg)]. Fraction 5-3 (224 mg) was purified by HPLC [MeOH–H_2O (26:74, v/v)] and [MeCN–MeOH–H_2O (10:8:82, v/v/v)] to furnish dendranthemoside A (**9**, 13.7 mg) and alangioside A (**10**, 7.1 mg). Fraction 6 (6.7 g) was subjected to reversed-phase silica gel column chromatography [220 g, MeOH–H_2O (10:90 → 20:80 → 30:70 → 40:60 → 50:50 → 60:40 → 100:0, v/v) → $CHCl_3$] to give eleven fractions [Fr. 6-1 (809 mg), Fr. 6-2 (859 mg), Fr. 6-3 (118 mg), Fr. 6-4 (103 mg), Fr. 6-5 (480 mg), Fr. 6-6 (300 mg), Fr. 6-7 (250 mg), Fr. 6-8 (1.28 g), Fr. 6-9 (239 mg), Fr. 6-10 (335 mg), Fr. 6-11 (1.25 g)]. Fraction 6-2 (859 mg) was separated by HPLC [MeOH–H_2O (25:75, v/v)] to afford thirteen fractions [Fr. 6-2-1 (18.2 mg), Fr. 6-2-2 (28.5 mg), Fr. 6-2-3 (36.3 mg), Fr. 6-2-4 (16.7 mg), Fr. 6-2-5 (42.5 mg), Fr. 6-2-6 (32.1 mg), Fr. 6-2-7 (38.9 mg), Fr. 6-2-8 (70.6 mg), Fr. 6-2-9 (37.5 mg), Fr. 6-2-10 (58.3 mg), Fr. 6-2-11 (21.2 mg), Fr. 6-2-12 (24.6 mg), Fr. 6-2-13 (18.9 mg)]. Fraction 6-2-12 (24.6 mg) was purified by HPLC [MeCN–MeOH–H_2O (7:7:86, v/v/v)] to furnish (6*S*,7*E*,9*R*)-6,9-dihydroxy-4,7-megastigmadien-3-one 9-*O*-α-L-arabinopyranosyl(1→6)-β-D-glucopyranoside (**11**, 4.3 mg) and citroside B (**13**, 5.5 mg). Fraction 7 (1.6 g) was subjected to reversed-phase silica gel column chromatography [50 g, MeOH–H_2O (20:80 → 30:70 → 40:60 → 50:50 → 100:0, v/v)] to afford three fractions [Fr. 7-1 (529 mg), Fr. 7-2 (570 mg), Fr. 7-3 (321 mg)]. Fraction 7-2 was identified as rutin (**19**, 570 mg). Fraction 8 (2.4 g) was subjected to reversed-phase silica gel column chromatography [100 g, MeOH–H_2O (20:80 → 30:70 → 40:60 → 50:50 → 100:0, v/v)] to give four fractions [Fr. 8-1 (562 mg), Fr. 8-2 (445 mg), Fr. 8-3 (284 mg), Fr. 8-4 (463 mg)]. Fraction 8-2 was identified as rutin (**19**, 445 mg), fraction 8-3 (284 mg) was purified by HPLC [MeOH–H_2O (45:55, v/v)] to give rutin (**19**, 7.6 mg). Fraction 9 (9.3 g) was subjected to reversed-phase silica gel column chromatography [50 g, MeOH–H_2O (20:80 → 30:70 → 40:60 → 50:50 → 60:40 →100:0, v/v)] to afford eleven fractions [Fr. 9-1 (1.19 g), Fr. 9-2 (322 mg), Fr. 9-3 (230 mg), Fr. 9-4 (295 mg), Fr. 9-5 (511 mg), Fr. 9-6 (954 mg), Fr. 9-7 (189 mg), Fr. 9-8 (1.30 g), Fr. 9-9 (484 mg), Fr. 9-10 (981 mg), Fr. 9-11 (1.66 g)]. Fraction 9-4 (295 mg) was separated by HPLC [MeOH–H_2O (24:76, v/v)] to furnish kaempferol 3-*O*-(2,6-α-L-dirhamnopyranosyl-β-D-glucopyranosyl)-7-*O*-β-D-glucopyranoside (**18**, 138 mg). Fraction 9-5 (511 mg) was subjected to HPLC [MeOH–H_2O (24:76, v/v)] to give paeonoside (**14**, 32.5 mg), kaempferol 3-*O*-rutinosyl-7-*O*-β-D-glucopyranoside (**15**, 18.2 mg), kaempferol 3-*O*-α-L-rhamnopyranosyl(1→6)-β-D-galatopyranosyl-7-*O*-β-D-glucopyranoside (**16**, 71.6 mg), kaempferol 3-*O*-(2,6-α-L-dirhamnopyranosyl-β-D-glucopyranosyl)-7-*O*-β-D-glucopyranoside (**18**, 118.1 mg), and quercetin 3-*O*-rutinosyl-7-*O*-β-D-glucopyranoside (**20**, 69.2 mg). Fraction 9-8 (1.30 g) was separated by HPLC [MeOH–H_2O (24:76, v/v)] and finally purified by HPLC [MeOH–H_2O–MeCN (13:8:79, v/v/v)] to

furnish kaempferol 3-*O*-rutinoside 7-*O*-*β*-D-glucopyranoside (**15**, 17.1 mg), clitorin (**17**, 188 mg), manghalin (**21**, 80.3 mg), and myricetin 3-*O*-*β*-D-rutinoside (**22**, 63.0 mg). Fraction 9-9 (484 mg) was purified by HPLC [MeOH–H_2O (40:60, v/v)] to give rutin (**19**, 65.8 mg).

The known compounds were identified by comparison of their physical data ($[\alpha]_D$, ^{1}H-NMR, ^{13}C-NMR, MS] with reported values.

Foliasalacioside A_1 (**1**): An amorphous powder, $[\alpha]_D^{28}$ +24.3° (*c* 0.65, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{19}H_{32}O_8Na$ $(M+Na)^+$: 411.1995. Found: 411.1990. CD [MeOH, nm ($\Delta\varepsilon$)]: 215 (+2.06), 328 (+0.27). UV [MeOH, nm (log ε)]: 238 (4.20). IR (KBr): 3420, 2932, 1653, 1489, 1387, 1078, 1036 cm^{-1}. ^{1}H-NMR (CD_3OD, 500 MHz) δ: 1.03, 1.11 (3H each, both s, 12, 11-H_3), 1.16 (3H, d, J = 6.2 Hz, 10-H_3), 1.46, 1.94 (1H each, both m, 7-H_2), 1.53 (2H, m, 8-H_2), 2.01 (1H, m, 6-H), 2.02 (1H, d, J = 17.9 Hz, 2-Hα), 2.55 (1H, d, J = 17.9 Hz, 2-Hβ), 3.71 (1H, m, 9-H), 4.32 (1H, d, J = 8.2 Hz, 1'-H), 4.38, 4.54 (1H each,both dd, J = 1.4, 16.5 Hz, 13-H_2), 6.16 (1H, br s, 4-H). ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 411 $(M+Na)^+$.

Foliasalacioside A_2 (**2**): An amorphous powder, $[\alpha]_D^{26}$ +30.9° (*c* 0.55, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{19}H_{32}O_8Na$ $(M+Na)^+$: 411.1995. Found: 411.1990. CD [MeOH, nm ($\Delta\varepsilon$)]: 216 (+4.23), 330 (+0.45). UV [MeOH, nm (log ε)]: 239 (4.09). IR (KBr): 3423, 2932, 1653, 1489, 1387, 1078, 1034 cm^{-1}. ; ^{1}H-NMR (CD_3OD, 500 MHz) δ: 1.01, 1.10 (3H each, both s, 12, 11-H_3), 1.18 (3H, d, J = 6.2 Hz, 10-H_3), 1.49, 1.95 (1H each, both m, 7-H_2), 1.62 (2H, m, 8-H_2), 1.94 (1H, m, 6-H), 2.01 (1H, d, J = 17.9 Hz, 2-Hα), 2.56 (1H, d, J = 17.9 Hz, 2-Hβ), 3.88 (1H, m, 9-H), 4.18 (1H, dd, J = 2.0, 17.8 Hz, 13-H□), 4.36 (1H, dd, J = 1.4, 17.8 Hz, 13-H*b*), 4.33 (1H, d, J = 8.3 Hz, 1'-H), 6.04 (1H, br s, 4-H). ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 411 $(M+Na)^+$.

Foliasalacioside B_1 (**3**): An amorphous powder, $[\alpha]_D^{27}$ +25.2° (*c* 0.80, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{24}H_{40}O_{11}Na$ $(M+Na)^+$: 527.2468. Found: 527.2461. CD [MeOH, nm ($\Delta\varepsilon$)]:214 (+1.92), 335 (+0.35). UV [MeOH, nm (log ε)]: 241 (3.98). IR (KBr): 3405, 2934, 1651, 1379, 1075, 1009 cm^{-1}. ^{1}H-NMR (CD_3OD, 500 MHz) δ: 1.01, 1.09 (3H each, both s, 12, 11-H_3), 1.18 (3H, d, J = 6.2 Hz, 10-H_3), 1.48, 1.98 (1H each, both m, 7-H_2), 1.62 (2H, m, 8-H_2), 1.97 (1H, m, 6-H), 1.97 (1H, d, J = 17.2 Hz, 2-Hα), 2.46 (1H, d, J = 17.2 Hz, 2-Hβ), 2.05 (3H, s, 13-H_3), 3.85 (1H, m, 9-H), 4.28 (1H, d, J = 6.8 Hz, 1''-H), 4.31 (1H, d, J = 8.2 Hz, 1'-H), 5.80 (1H, s, 4-H). ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 527 $(M+Na)^+$. Negative-ion FAB-MS: *m/z* 503 $(M–H)^–$.

Foliasalacioside B_2 (**4**): An amorphous powder, $[\alpha]_D^{26}$ +30.5° (*c* 0.60, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{24}H_{40}O_{11}Na$ $(M+Na)^+$: 527.2468. Found: 527.2473. CD [MeOH, nm ($\Delta\varepsilon$)]: 214 (+1.26), 327 (+0.19). UV [MeOH, nm (log ε)]: 240 (3.92). IR (KBr): 3397, 2930, 1655, 1379, 1075, 1040 cm^{-1}. ^{1}H-NMR (CD_3OD, 500 MHz) δ: 1.01, 1.09 (3H each, both s, 12, 11-H_3), 1.18 (3H, d, J = 6.1 Hz, 10-H_3), 1.41, 1.96 (1H each, both m, 7-H_2), 1.61 (2H, m, 8-H_2), 1.97 (1H, d, J = 17.4 Hz, 2-Hα), 2.47 (1H, d, J = 17.4 Hz, 2-Hβ), 1.98 (1H, m, 6-H), 2.05 (3H, s, 13-H_3), 3.83 (1H, m, 9-H), 4.31 (1H, d, J = 7.1 Hz, 1'-H), 4.96 (1H, d, J = 1.5 Hz, 1''-H), 5.81 (1H, s, 4-H). ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 527 $(M+Na)^+$. Negative-ion FAB-MS: *m/z* 503 $(M–H)^–$.

Foliasalacioside C (**5**): An amorphous powder, $[\alpha]_D^{23}$ –20.4° (*c* 0.24, MeOH). High-resolution positive-

ion FAB-MS: Calcd for $C_{24}H_{40}O_{11}Na$ $(M+Na)^+$: 527.2468. Found: 527.2470. IR (KBr): 3379, 2928, 1705, 1660, 1456, 1379, 1084, 1044 cm^{-1}. ^{1}H-NMR (CD_3OD, 500 MHz) δ: 1.16 (6H, s, 11, 12-H_3), 1.20 (3H, d, J = 6.1 Hz, 10-H_3), 1.61 (2H, m, 8-H_2), 1.74 (3H, s, 13-H_3), 2.09, 2.31 (1H each, both m, 7-H_2), 2.34 (2H, t, J = 6.7 Hz, 4-H_2), 2.52 (2H, t, J = 6.7 Hz, 3-H_2), 3.90 (1H, m, H-9), 4.33 (1H, d, J = 6.7 Hz, 1''-H), 4.34 (1H, d, J = 8.0 Hz, 1'-H). ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 527 $(M+Na)^+$. Negative-ion FAB-MS: *m/z* 503 $(M–H)^–$.

Foliasalacioside D (**6**): An amorphous powder, $[\alpha]_D^{26}$ –17.7° (*c* 0.29, MeOH). High-resolution positive-ion FAB-MS: Calcd for $C_{24}H_{40}O_{11}Na$ $(M+Na)^+$: 527.2468. Found: 527.2474. UV [MeOH, nm (log ε)]: 247 (3.86). IR (KBr): 3339, 2928, 1653, 1074, 1036 cm^{-1}. ^{1}H-NMR (CD_3OD, 500 MHz) δ: 1.20 (6H, s, 11, 12-H_3), 1.22 (3H, d, J = 6.1 Hz, 10-H_3), 1.65 (2H, m, 8-H_2), 1.76 (3H, s, 13-H_3), 1.81 (2H, t, J = 6.8 Hz, 2-H_2), 2.31, 2.54 (1H each, both m, 7-H_2), 2.44 (2H, t, J = 6.8 Hz, 3-H_2), 3.93 (1H, m, 9-H), 4.34 (1H, d, J = 7.6 Hz, 1'-H), 4.98 (1H, d, J = 1.4 Hz, 1''-H). ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 527 $(M+Na)^+$. Negative-ion FAB-MS: *m/z* 503 $(M–H)^–$.

Acid Hydrolysis of 1–6

Solutions of **1**, **2** (each 0.5 mg) and **3**–**6** (each 1.0 mg) in 1 M HCl (1.0 mL) were heated under reflux for 3 h. After cooling, each reaction mixture was neutralized with Amberlite IRA-400 ($OH^–$ form) and filtrated, and the solution was partitioned with EtOAc to give two layers. The aqueous layer was evaporated and then subjected to HPLC analysis using Kaseisorb LC NH_2-60-5 column (4.6 mm × 250 mm i.d., Tokyo Kasei Co., Ltd., Tokyo, Japan) and an optical rotation detector (Shodex OR-2, Showa Denko Co., Ltd., Tokyo, Japan). D-Glucose (from **1**–**6**) and L-arabinose (from **3**–**6**) were confirmed by comparison of the retention times with the authentic samples (Wako Pure Chemicals Ltd., Osaka, Japan) [mobile phase: MeCN–H_2O (85:15, v/v), flow rate: 0.8 mL/min, t_R: 10.2 min (L-arabinose, positive optical rotation); t_R: 12.8 min (D-glucose, positive optical rotation)].

Enzymatic Hydrolysis of 1 and 2 with β-Glucosidase

Solutions of **1** and **2** (12.6, 3.8 mg, respectively) in H_2O (1.0 mL) were treated with β-glucosidase (16.0, 6.1 mg, respectively) and the solution was stirred at 37 °C for 20 h. Work-up of the reaction mixture as described above to furnish foliasalaciol A (**1a**, 5.7 mg, 77.7% from **1** and 2.0 mg, 90.5% from **2**).

Foliasalaciol A (**1a**): Colorless oil; $[\alpha]_D^{27}$ +69.2° (*c* 0.25, MeOH); High-resolution positive-ion EI-MS: Calcd for $C_{13}H_{22}O_3$: 226.1569. Found: 226.1564. IR (film) 3415, 2965, 2932, 2874, 1651, 1372, 1121 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 1.02, 1.09 (3H each, both s, 12, 11-H_3), 1.21 (3H, d, J = 6.1 Hz, 10-H_3), 1.54, 1.87 (1H each, both m, 7-H_2), 1.51 (2H, m, 8-H_2), 2.08, 2.47 (1H each, both d, J = 17.5 Hz, 2-H_2), 1.96 (1H, m, 6-H), 3.82 (1H, m, 9-H), 4.25 (1H, dd, J = 1.5, 16.8 Hz, 13-H*a*), 4.35 (1H, dd, J = 1.4, 16.8 Hz, 13-H*b*), 6.08 (1H, br s, 4-H); ^{13}C-NMR (125 MHz, CD_3OD) δ_c: given in Table 1. Positive-ion FAB-MS: *m/z* 527 $(M+Na)^+$. Negative-ion FAB-MS: *m/z* 503 $(M–H)^–$.^{13}C NMR data, see Table 1; Positive-ion EI-MS (%): *m/z* 226 (M^+, 9), 209 (14), 208 (66), 193 (16), 179 (42), 135 (89), 109 (100).

Preparation of the (*R*)-MTPA Ester and (*S*)-MTPA Esters from Foliasalaciol A (1a)

A solution of **1a** (2.9 mg) in dry $CHCl_3$ (1.0 mL) was reacted with (*R*)-2-methoxy-2-trifluoromethylphenylacetic acid [(*R*)-MTPA, 40.7 mg] in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC·HCl, 44.0 mg) and 4-dimethylaminopyridine (4-DMAP, 15.5 mg), and the resulting mixture was stirred at room temperature for 10 h. The reaction mixture was poured into ice-water and extracted with EtOAc. The EtOAc extract was washed successively with 5% HCl, $NaHCO_3$-saturated H_2O and brine and dried over Na_2SO_4 and filtered. Removal of the solvent from the filtrate under reduced pressure. The residue was subjected to normal-phase silica gel column chromatography [500 mg, *n*-hexane-EtOAc (10: 1 →3:1 →1:1) to furnish **1b** (2.9 mg, 34.3%). Using a similar procedure, (*S*)-MTPA ester [**1c**, 2.9 mg, 45.2%] was obtained from **1a** (2.2 mg) with (*S*)-MTPA (30.9 mg), EDC·HCl (38.2 mg) and 4-DMAP (12.0 mg).

Compound 1b. Colorless oil; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.95, 0.98 (3H each, both s, 12, 11-H_3), 1.28 (3H, d, J = 6.4 Hz, 10-H_3), 1.39, 1.75 (1H each, both m, 7-H_2), 1.70 (2H m, 8-H_2), 1.80 (1H, m, 6-H), 2.04, 2.30 (1H each, both d, J = 17.4 Hz, 2-H_2), 3.48, 3.54 (3H each, both s, -OCH_3), 4.78, 4.89 (1H each, both br d, J = *ca.* 16, 13-H_2), 5.04 (1H, m, 9-H), 5.88 (1H, s, 4-H), 7.40 (3H, m, Ph-H), 7.43 (3H m, Ph-H), 7.50 (4H, m, Ph-H).

Compound 1c. Colorless oil; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ: 0.88 (6H, s, 12, 11-H_3), 1.35 (3H, d, J = 6.4 Hz, 10-H_3), 1.27, 1.58 (1H each, both m, 7-H_2), 1.64 (2H m, 8-H_2), 1.71 (1H, dd, m, 6-H), 1.98, 2.19 (1H each, both d, J = 17.4 Hz, 2-H_2), 3.55, 3.57 (3H each, both s, -OCH_3), 4.70 (1H, dd, J = 1.2, 15.0 Hz, 13-H*a*), 4.83 (1H, dd, J = 1.6, 15.0 Hz, 13-H*b*), 5.04 (1H, m, 9-H), 5.85 (1H, s, 4-H), 7.38 (3H, m, Ph-H), 7.43 (3H m, Ph-H), 7.50 (4H, m, Ph-H).

Enzymatic Hydrolysis of 3 and 4 with Nariginase

Solutions of **3** and **4** (5.5, 5.1 mg, respectively) in 0.2 M acetate buffer (pH 3.8) (1.0 mL) were treated with nariginase (10.5 and 12.2 mg, respectively) and the solution was stirred at 40 °C for 4 day. After cooling, the reaction mixture was extracted with EtOAc. The EtOAc solvent was removed under reduced pressure and the residue was purified by HPLC [MeOH-H_2O (50:50, v/v)] to give blumenyl C (1.3 mg, 54.9% from **3** and 2.0 mg, 91.3% from **4**).

ACKNOWLEDGMENTS

Part of this work was supported by the 21st COE program and Academic Frontier Project from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

REFERENCES AND NOTES

1. W. Chuakui, P. Saralamp, W. Paonil, R. Temsiririrkkul, and T. Clayton, 'Medicinal plants in Thailand,' Volume II, Department of pharmaceutical botany faculty of pharmacy, Mahidol university, Bangkok, 1997, pp. 192–193.
2. C. R. Karnick, 'Ayurvedic narcotic medicinal plants,' Sri satguru publications, A division of Indian books centre, Delhi-India, 1996, pp. 153–154.

3. T. Morikawa, A. Kishi, Y. Pongpiriyadacha, H. Matsuda, and M. Yoshikawa, *J. Nat. Prod.*, 2003, **66**, 1191.
4. A. Kishi, T. Morikawa, H. Matsuda, and M. Yoshikawa, *Chem. Pharm. Bull.*, 2003, **51**, 1051.
5. M. Yoshikawa, Y. Pongpiriyadacha, A. Kishi, T. Kageura, T. Wang, T. Morikawa, and H. Matsuda, *Yakugaku Zasshi*, 2003, **123**, 871.
6. M. Yoshikawa N. Nishida, H. Shimoda, M. Takada, Y. Kawahara, and H. Matsuda, *Yakugaku Zasshi*, 2001, **121**, 371.
7. M. Yoshikawa, T. Murakami, H. Shimada, H. Matsuda, J. Yamahara, G. Tanabe, and O. Muraoka, *Tetrahedron Lett.*, 1997, **38**, 8367.
8. M. Yoshikawa, T. Murakami, K. Yashiro, and H. Matsuda, *Chem. Pharm. Bull.*, 1998, **46**, 1339.
9. H. Matsuda, T. Murakami, K. Yashiro, and M. Yoshikawa, *Chem. Pharm. Bull.*, 1999, **47**, 1725.
10. M. Yoshikawa, T. Morikawa, H. Matsuda, G. Tanabe, and O. Muraoka, *Bioorg. Med. Chem.*, 2002, **10**, 1547.
11. M. Yoshikawa, K. Ninomiya, H. Shimoda, N. Nishida, and H. Matsuda, *Biol. Pharm. Bull.*, 2002, **25**, 72.
12. M. Yoshikawa, H. Shimoda, N. Nishida, M. Takada, and H. Matsuda, *J. Nutr.*, 2002, **132**, 1819.
13. M. Yoshikawa, *FOOD Style 21*, 2002, **6**, 72.
14. H. Matsuda, M. Yoshikawa, T. Morikawa, G. Tanabe, and O. Muraoka, *J. Trad. Med*., 2005, **22**, 145.
15. A. Buske, J. Schmidt, A. Porzel, and G. Adam, *Eur. J. Org. Chem.*, 2001, **18**, 3537.
16. N. Matsuda, K. Isawa, and M. Kikuchi, *Phytochemistry*, 1997, **45**, 777.
17. H. Otsuka, M. Kido, T. Tsukihara, K. Tsukihara, Y. Takeda, K. Yamasaki, and Y. Takeda, *Chem. Pharm. Bull*., 2002, **50**, 640.
18. S. De Marino, N. Borbone, F. Zollo, A. Ianaro, P. Di Meglio, and M. Iorizzi, *J. Agric. Food Chem*., 2004, **52**, 7525.
19. M. Hisamoto, H. Kikuzaki, and N. Nakatani, *J. Agric. Food Chem*., 2004, **52**, 445.
20. K. Umehara, I. Hattori, T. Miyase, A. Ueno, S. Hara, and C. Kageyama, *Chem. Pharm. Bull.*, 1998, **36**, 5004.
21. R. Yu, X. Li, H. Zhang, L. Wu, T. Zhu, W. Li, L. Liu, and G. Zhang, *Zhiwu Xuebao*, 1992, **34**, 369.
22. C. J. Chang, *Lloydia*, 1978, **41**, 17.
23. C. A. Elliger, J. A. Eash, and A. C. Jr. Waiss, *Biochemical Systematics and Ecology*, 1992, **20**, 268.
24. B. Schwarz and T. Hofmann, *J. Agric. Food Chem.*, 2007, **55**, 1394.
25. E. Wenkert and H. E. Gottlieb, *Phytochemistry*, 1977, **16**, 1811.
26. N. Ishikura, Z. Yang, K. Yoshitama, and K. Kurosawa, *Zeitschrift fuer Naturforschung, C: Journal of Biosciences*, 1990, **45**, 1081.
27. X. Ma and Y. Sun, *Shenyang Yaoke Daxue Xuebao*, 2003, **20**, 275.
28. M. Yoshikawa, S. Sugimoto, S. Nakamura, and H. Matsuda, *Chem. Pharm. Bull*., 2007, **55**, 571.
29. M. Yoshikawa, T. Morikawa, Y. Zhang, S. Nakamura, O. Muraoka, and H. Matsuda, *J. Nat. Prod*., 2007, **70**, 575.

30. The ^{1}H and ^{13}C NMR spectra of **1**–**6** were assigned with the aid of distortionless enhancement by polarization transfer (DEPT), double quantum filter correlation spectroscopy (DQF COSY), heteronuclear multiple quantum coherence (HMQC), and heteronuclear multiple bond connectivity (HMBC) experiments.
31. H. Otsuka, H. Kijima, E. Hirata, T. Shinzato, A. Takushi, M. Bando, and Y. Takeda, *Chem. Pharm. Bull*., 2003, **51**, 286.
32. E. Sueyoshi, H. Liu, K. Matsunami, H. Otsuka, T. Shinzato, M. Aramoto, and Y. Takeda, *Phytochemistry*, 2006, **67**, 2483.
33. The absolute configuration of the 9-position in **1** and **2** was *R* orientation, while the configuration in glochidionionoside B[31] and (6*R*,9*S*)-megastigman-4-en-3-one-9,13-diol 9-*O*-*β*-D-glucopyranoside[32] was *S* orientation.
34. B. D'Abrosca, M. DellaGreca, A. Fiorentino, P. Monako, P. Oriano, and F. Temussi, *Phytochemistry*, 2004, **65**, 497.
35. J. R. Hlubucek, A. J. Aasen, S-O Almqvist, and C. R. Enzell, *Acta. Chem. Scand. B*., 1974, **28**, 289.
36. Y. Yamano, Y. Shimizu, and M. Ito, *Chem. Pharm. Bull*., 2003, **51**, 878.
37. H. Otsuka and A. Tamaki, *Chem. Pharm. Bull*., 2002, **50**, 390.