Schefflerins A—G, New Triterpene Glucosides from the Leaves of *Schefflera arboricola*

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From the 1-BuOH-soluble fraction of a MeOH extract of leaves of *Schefflera arboricola*, collected in Okinawa, six new lupane glucosides, named schefflerins A—F (1—6) and one new dammarane glucoside, named schefflerin G (7), were isolated together with three known compounds, citroside A (8), and oleanane saponins, oleanolic acid (9) and echinocystic acid (10) 3-*O*-α-L-rhamnopyranosyl(1→4′)-*O*-β-D-glucuronopynosides. Their structures were elucidated through a combination of spectroscopic analyses and the structure of schefflerin F (6) was determined by X-ray crystallographic method using SPring-8 synchrotron radiation.

Key words *Schefflera arboricola*; Araliaceae; triterpene; lupane glucoside; dammarane glucoside

Schefflera arboricola, native to Taiwan and Hainan, is an evergreen shrub growing to 3—10 m in height and called as geraniumleaf aralia or dwarf umbrella tree in English. The leaves are palmately compound, with 7—9 leaflets in 10—20 cm length and 4—6 cm width. In Japan, *S. arboricola* is sometimes sold at flower shops for an ornamental shrub erroneously named as "Kapok." Kapok (*Ceiba pentandra*, Malvaceae) is a different tropical tree which produces fiber and used as an alternative to down. Some oleanane and lupane triterpene saponins have been isolated from *S. arboricola*,[1—3] *S. fagueti*,[4] *S. rotondifolia*,[5] *S. divaricata*[6] and *S. impressa*.[7] Sedative, hypnotic, analgenic, anticonvulsant and smooth muscle relaxant effects were reported for ethanolic leaf extract of *Schefflera* spp.[8]

From a 1-BuOH-soluble fraction of the MeOH extract of *S. arboricola* leaves, seven new triterpene saponins, named schefflerins A—G (**1**—**7**) were isolated, together with three known compounds, citroside A (**8**),[9] and oleanane saponins, oleanolic acid (**9**) and echinocystic acid (**10**) 3-*O*-α-L-rhamnopyranosyl(1→4)-*O*-β-D-glucuronopynosides.[1] Of the seven new saponins, schefflerins A—F were found to be lupane (**1**—**5**) and nor-lupane (**6**) triterpene glucosides, and schefflerin G (**7**) a dammarane triterpene glucoside. This paper deals with structure elucidation of them.

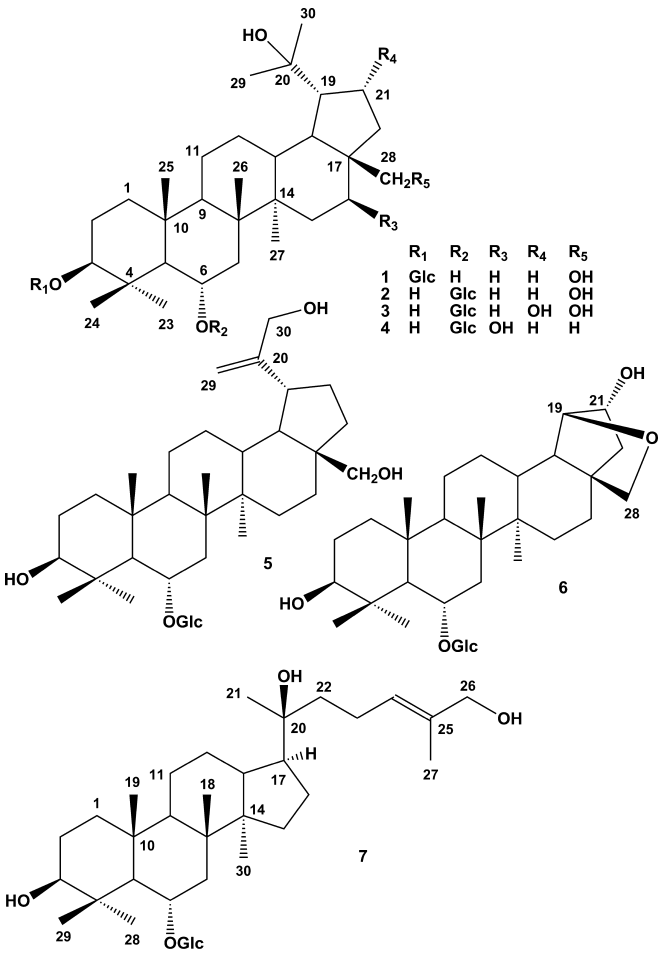

Fig. 1. Compounds Isolated from *Schefflera arboricola*

Results and Discussion

Air-dried leaves of *Schefflera aiboricola* were extracted with MeOH three times and the concentrated MeOH extract was partitioned with solvents of increasing polarity. The 1-BuOH-soluble fraction was separated by means of various chromatographic procedures including column chromatography (CC) on a highly porous synthetic resin (Diaion HP-20), then normal silica gel and reversed-phase octadecyl silica gel (ODS) CC, droplet counter-current chromatography (DCCC), and high-performance liquid chromatography (HPLC) to afford 10 compounds (**1**—**10**). The details and yields are given under Experimental. The structures of the new triterpene glucosides, schefflerins A—G (**1**—**7**) (Fig. 1) were elucidated on the basis of spectroscopic evidence and the structure of schefflerin F (**6**) was confirmed by X-ray crystallographic analysis. The structures of known compounds were identified by comparison of spectroscopic data with those reported in the literature.

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Schefflerin A (**1**), $[\alpha]_D^{20}$ +23.0, was isolated as an amorphous powder and its elemental composition was determined to be $C_{36}H_{62}O_9$ by high-resolution (HR)-electrospray ionization (ESI) MS. Strong absorption bands at 3394 and 1079 cm^{-1} in the IR spectrum were characteristic founds in glycosidic compounds and an absorption at 2929 cm^{-1} indicated that schefflerin A (**1**) had a terpenic structure. In the ^{1}H-NMR spectrum, signals for seven singlet methyls, an isolated primary alcohol [δ_H 3.67 (1H, d, J=11 Hz) and 4.17 (1H, d, J=11 Hz)] and one anomeric proton [δ_H 4.98 (1H, d, J=8 Hz)] were observed. The ^{13}C-NMR spectrum exhibited six signals assignable to β-glucopyranose, which was determined to be in D-series by HPLC analysis of the acid hydrolyzate of **1** using a chiral detector. The remaining 30 ^{13}C-NMR signals comprised of seven methyls, ten methylenes, seven methines and six quaternary carbons (Table 1). Judging from the elemental composition, and absence of any double bond and ketone functional signals in the ^{13}C-NMR spectrum, schefflerin A (**1**) was presumed to be a pentacyclic triterpene. Four oxygen atoms were expected to locate on triplet (δ_C 60.0), doublet (δ_C 67.7, 89.6) and singlet (δ_C 72.4) carbons due to their relatively deshielded chemical shifts. One set [δ_H 1.36 (H_3-29), 1.45 (H_3-30)] of geminal methyl signals showed correlation cross peaks with the singlet carbon (δ_C 72.4) with an oxygen atom in the heteronuclear multiple bond correlation (HMBC) spectrum. Thus, the presence of dimethyl crabinol moiety was demonstrated and the aglycone was made up with four six-membered and one five-membered rings. Detailed analyses of ^{1}H–^{1}H correlation spectroscopy, heteronuclear single quantum correlation and HMBC spectra allowed the assignment of all the ^{1}H and ^{13}C signals and from the above evidence, the structure of schefflerin A (**1**) was expected to be a lupane-type triterpene with one β-D-glucopyranose unit. In the HMBC spectrum, the correlation cross peaks between the other set of geminal dimethyl signals [δ_H 2.05 (H_3-23), 1.42 (H_3-24)] and δ_C 89.6 placed a hydroxyl group at the 3-postion in an equatorial orientation from the coupling constants of H-3 (dd, J=12, 3 Hz). The doublet carbon resonated at δ_C 61.2 was assigned to be C-5 from the HMBC correlations from H_3-23 and H_3-24. The third hydroxyl group was placed at C-6 from coupling patterns and constants of H-5 [δ_H 1.16 (d, J=12 Hz)] and H-6 [δ_H 4.29 (ddd, J=12, 12, 3 Hz)], which also indicated that the hydroxyl group was in an equatorial orientation. The primary alcohol determined to be at the 17-position due to the HMBC correlations of the H_2-28 with C-16 (δ_C 30.7), C-17 (δ_C 49.9) and C-22 (δ_C 34.3). The dimethyl carbinol group (C-20, 29, 30) was placed at the 19-position from the HMBC correlations of H-19 (δ_H 2.13) with C-20 (δ_C 72.4), C-29 (δ_C 25.6) and C-30 (δ_C 32.3), and H-18 (δ_H 1.83) with C-20. Other HMBC correlations shown in Fig. 2 were supportive the lupane skeleton for schefflerin A (**1**). Attachment of the sugar unit at the hydroxyl group at the 3-positon was also informed from the HMBC correlation cross peak between H-1′ and C-3. Therefore, the structure of schefflerin A (**1**) was elucidated to be lupane-3β,6α,20,28-tetraol 3-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Table 1. ^{13}C-NMR Data for Schefflerins A—G (**1**—**7**) (C_5D_5N, 150 MHz)

C	1	2	3	4	5	6	7
1	39.1 t	39.4 t	39.4 t	39.4 t	39.4 t	39.3 t	39.6 t
2	26.7 t	27.9 t	28.0 t	28.0 t	27.9 t	27.9 t	28.0 t
3	89.6 d	78.8 d	78.8 d	78.8 d	78.8 d	78.6 d	78.7 d
4	40.5 s	40.2 s	40.3 s	40.3 s	40.3 s	40.3 s	40.4 s
5	61.2 d	60.8 d	60.8 d	60.9 d	60.9 d	61.0 d	61.5 d
6	67.7 d	80.4 d	80.4 d	80.2 d	80.4 d	80.3 d	80.1 d
7	47.6 t	44.9 t	44.8 t	44.9 t	44.7 t	44.8 t	45.7 t
8	42.9 s	42.9 s	43.0 s	43.0 s	42.4 s	41.9 s	41.8 s
9	50.5 d	50.7 d	50.9 d	50.5 d	50.6 d	51.0 d	50.9 d
10	39.0 s	39.7 s	39.8 s	39.7 s	39.8 s	39.9 s	39.9 s
11	21.8 t	21.9 t	22.0 t	22.0 t	21.3 t	21.2 t	22.0 t
12	29.2 t	29.2 t	29.1 t	29.0 t	27.4 t	27.6 t	28.1 t
13	36.6 d	36.7 d	36.6 d	37.3 d	37.3 d	32.1 d	42.2 d
14	43.9 s	43.9 s	44.0 s	44.8 s	43.2 s	42.1 s	50.7 d
15	28.0 t	27.6 t	27.6 t	38.0 t	27.2 t	27.2 t	31.5 t
16	30.7 t	30.7 t	31.7 t	76.4 d	30.2 t	23.9 t	25.4 t
17	49.9 s	49.8 s	45.5 s	51.0 s	48.6 s	44.1 s	50.5 d
18	49.3 d	49.3 d	48.2 d	48.0 d	49.6 d	48.1 d	17.7 q
19	50.8 d	50.7 d	54.2 d	50.3 d	44.2 d	82.0 d	17.3 q
20	72.4 s	72.5 s	73.2 s	72.4 s	156.5 s		74.1 s
21	28.6 t	28.6 t	73.6 d	29.0 t	32.4 t	73.2 d	26.1 q
22	34.3 t	34.2 t	45.4 t	39.0 t	34.7 t	48.0 t	41.6 t
23	31.5 q	31.8 q	31.8 q	31.8 q	31.8 q	31.7 q	22.9 t
24	17.0 q	16.4 q	16.3 q	16.4 q	16.4 q	16.4 q	126.5 d
25	17.5 q	17.7 q	17.8 q	18.0 q	17.6 q	17.8 q	136.1 s
26	17.7 q	17.9 q	17.9 q	17.7 q	17.8 q	17.5 q	68.2 t
27	15.5 q	15.3 q	15.5 q	16.7 q	14.8 q	13.2 q	14.0 q
28	60.0 t	60.1 t	61.7 t	14.6 q	59.3 t	71.6 t	25.6 q
29	25.6 q	25.6 q	30.4 q	26.1 q	106.2 t		32.2 q
30	32.3 q	32.2 q	31.4 q	32.1 q	64.3 t		16.6 q
1′	107.2 d	105.8 d	105.8 d	105.7 d	105.8 d	106.1 d	105.9 d
2′	75.9 d	75.4 d	75.4 d	75.5 d	75.4 d	75.5 d	75.5 d
3′	78.8 d	79.6 d	79.7 d	79.6 d	79.6 d	79.6 d	79.6 d
4′	72.0 d	71.7 d	71.8 d	71.8 d	71.8 d	71.9 d	71.9 d
5′	78.0 d	77.9 d	78.0 d	78.0 d	78.0 d	78.1 d	78.0 d
6′	63.2 t	63.0 t	63.0 t	63.0 t	63.0 t	63.1 t	63.2 t

s: C; d: CH; t: CH_2; q: CH_3.

Schefflerin B (**2**), $[\alpha]_D^{20}$ +14.2, was isolated as colorless needles and its elemental composition was the same as that of **1**. Other physical properties were similar to those of **1** and ^{13}C-NMR chemical shift of the 3-positon obviously shifted up (δ_C 78.8) and that of the 6-position shifted down (δ_C 80.4). Since, in the HMBC spectrum, the anomeric proton (δ_H 4.93) showed a cross peak with C-6, the structure of schefflerin B (**2**) was concluded to be an isomer of **1** as to the position of β-D-glucopyranose unit, as shown in Fig. 1.

Schefflerin C (**3**), $[\alpha]_D^{20}$ +16, was isolated as an amorphous powder and its elemental composition was determined to be $C_{36}H_{62}O_{10}$, which was one more oxygen atom com-

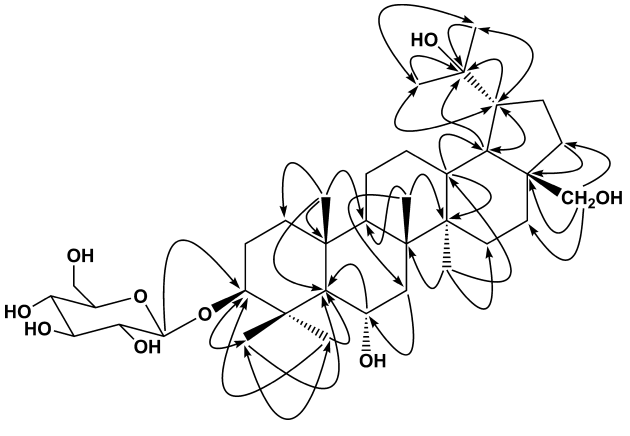

Fig. 2. HMBC Correlations for Schefflerin A (**1**)

Dual arrowhead curves denote HMBC correlations were observed in both ways.

pared to those of schefflerins A (**1**) and B (**2**). Physical data indicated that schfflerin C (**3**) was analogous compound to schefflerins A and B and ^{13}C-NMR data for A, B, C and D rings showed strong similarity to those of schefflerin B (**2**) (Table 1). NMR signals for the fifth hydroxyl group was observed at δ_C 73.6 (d) with δ_H 4.97 and thus it must be placed at the 21 or 22-position. In the HMBC spectrum, significant correlation cross peaks between protons (δ_H 3.67, 4.19) of the primary alcohol and methylene carbon (δ_C 45.4), and those between the C-22 methylene protons (δ_H 1.60, 3.03) and C-28 (δ_C 61.7) forced to place the hydroxyl group at the 21-position (Fig. 3a). The nuclear Overhauser enhacement correlations, observed between H-21 (δ_H 4.97) and H_2-28 (δ_H 3.67, 4.19), and those between H-19 (δ_H 2.38) and H-21 together with H-13 (δ_H 1.97) in the phase-sensitive (PS) rotational Overhauser effect spectroscopy (ROESY) spectrum were in good accordance to place the hydroxyl group at the 21-position in an a-side. (Fig. 3b). Therefore, the structure of schefflerin C (**3**) was elucidated to be lupane-3β,6α,20,21α,28-pentaol 6-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Schefflerin D (**4**), $[\alpha]_D^{20}$ +12.9, was isolated as an amorphous powder and the elemental composition was determined to be $C_{36}H_{62}O_9$. The results of NMR experiment indicated that the primary alcohol found in aforementioned schefflerins disappeared, instead of that, an extra signal for a singlet methyl being observed. ^{13}C-NMR data of the rings A, B and C showed good similarity to those of shefflerins B (**2**) and C (**3**), and those of the ring D also resembled those of schefflerins A (**1**) and B (**2**). The fourth hydroxyl group was placed on either methylene groups in the ring D. The hydroxyl group in question was placed from the correlation cross peak between H_3-28 (δ_H 1.22) and C-16 (δ_C 76.4) in the HMBC spectrum. Based on the triangular PS-ROESY correlations between α-axial methyl H_3-27 (δ_H 1.09), α-axial proton H-18 (δ_H 1.72) and H-16 (δ_H 3.95), the hydroxyl group at the 16-position was concluded to be in the equatorial orientation. Therefore, the structure of schefflerin D (**4**) was elucidated to be lupane-3β,6α,16β,20-tetraol 6-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Schefflerin E (**5**), $[\alpha]_D^{20}$ +7.9, was isolated as an amorphous powder and the elemental composition was $C_{36}H_{60}O_9$. Physical data for schefflerin E (**5**) were also similar to those of preceding compound. ^{13}C-NMR data for schefflerin E (**5**) were essentially the same as those of schfflerin B (**2**), except for the presence of an disubstituted double bond [δ_C 156.5 (s) d δ_C 106.2 (t) with δ_H 5.11, 5.48] and a further primary alcohol [δ_C 59.3 (t) with δ_H 4.46, 4.50], instead of the disappearance of hydroxyisopropyl group. Only the possible position to place the disubstituted double bond was between C-20 and 29, and HMBC correlation of δ_H 5.11 on δ_C 106.2 with δ_C 64.3 confirmed the position of the new primary alcohol to be at C-30. Therefore, the structure of schefflerin E (**5**) was elucidated to be lupan-20(29)-ene-3β,6α,28,30-tetraol 6-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Schefflerin F (**6**), $[\alpha]_D^{20}$ +45.3, was isolated as colorless needles and its elemental composition was determined to be $C_{33}H_{54}O_9$. ^{13}C-NMR chemical shifts for rings A—C were essentially the same as those of schefflerin B (**2**). The aglycone moiety comprised of only 27 carbons and judging from the elemental composition, it must have a hexacyclic structure. In the HMBC spectrum, since methylene protons on C-28 showed correlation peaks with C-19 (δ_C 82.0), the sixth ring was assumed to form between these carbons through an ether linkage (Fig. 4). Other HMBC correlations around D, E and F rings also supported this assumption and allowed to place a hydroxyl group at the 21-position. Judging from the PS-ROESY correlations, one (δ_H 3.88) of the methylene protons with the β-axial angular proton H-13 (δ_H 1.78) and the other methylene proton (δ_H 3.13) with H-21 proton (δ_H 4.36), 19,28-epoxy ring was expected in a β-face and the hydroxyl group at the 21-positon in an α-face like schefflerin C (**3**). To confirm the trinor epoxy structure of schefflerin F (**6**), X-ray crystallographic experiment was attempted. A crystal was too small to solve the structure with reliable resolution with a conventional diffractometer with Mo$K\alpha$ radiation. Finally, X-ray structure was obtained using synchrotron radiation of

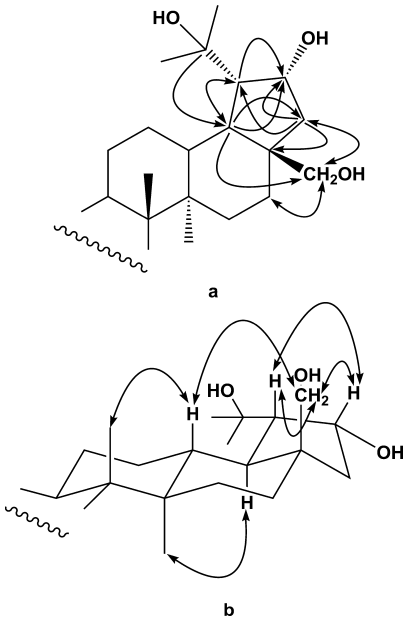

Fig. 3. HMBC Correlations (a) and PS-ROESY Correlations (b) of C—E Rings for Schefflerin C (**3**)

Dual arrowhead curves in a denote HMBC correlations were observed in both ways.

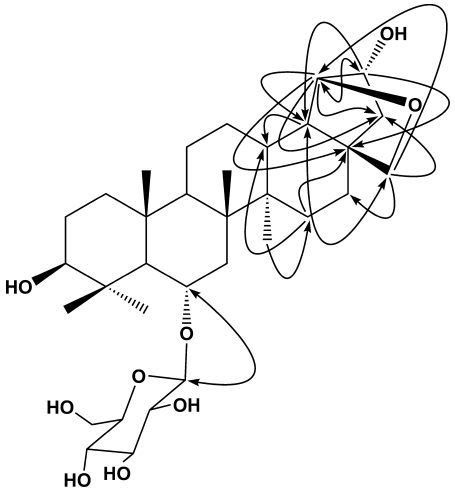

Fig. 4. Diagnostic HMBC Correlations for Schefflerin F (**6**)

Dual arrowhead curves denote HMBC correlations were observed in both ways.

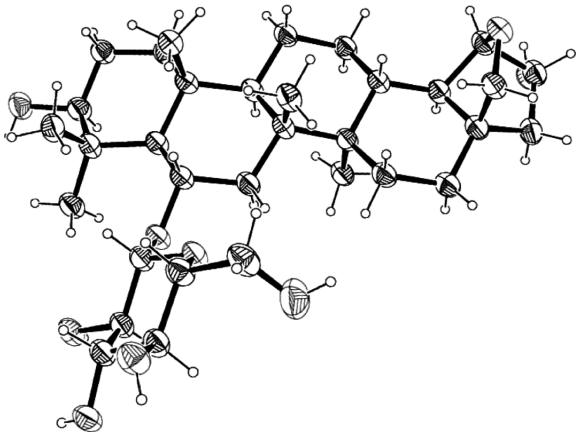

Fig. 5. ORTEP Drawing of Crystallographic Structure of Schefflerin F (**6**)

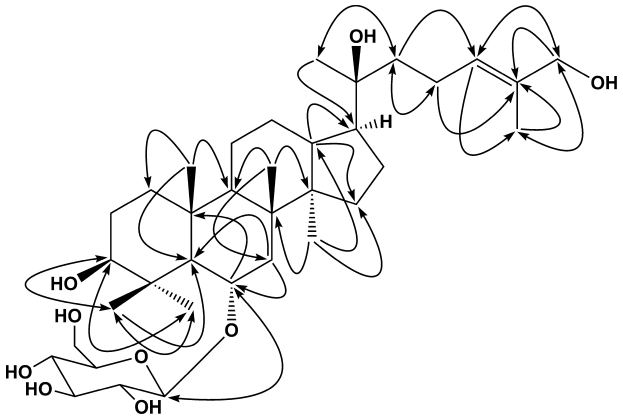

Fig. 6. HMBC Correlations for Schefflerin G (**7**)
Dual arrowhead curves denote HMBC correlations were observed in both ways.

the SPring-8 BL38B1 facility. Figure 5 shows an ORTEP drawing of the crystal structure of schefflerin F (**6**) and the structure assumed by spectroscopic data was proved to be correct. Thus, the structure of schefflerin F (**6**) was determined to be (19*R*)-lupan-19,28-epoxy-20,29,30-trinor-3β,6α,21α-triol 6-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Schefflerin G (**7**), $[\alpha]_D^{20}$ +67.5, was isolated as an amorphous powder and its elemental composition was determined to be $C_{36}H_{62}O_9$ by HR-ESI-MS. Physical data also indicated that schefflerin G (**7**) was a terpenic compound with one sugar unit. ^{13}C-NMR exhibited six signals assignable to β-D-glucopyranose together with 30 carbon signals, comprised with seven methyls, ten methylenes, six methines, five quaternary carbons and one trisubstituted double bond. The presence of one primary, two secondary and one tertiary alcohols were also expected from their chemical shifts. In the ^{1}H-NMR spectrum, all methyl signals were appeared as singlets, one methyl being expected to be on the double bond from its chemical shift (δ_H 1.86). Judging from the elemental composition, schefflerin G (**7**) was expected to be a tetracyclic triterpene and ^{13}C-NMR chemical shifts for A and B rings were essentially the same as those of schefflerins B—F. From the HMBC evidence, schefflerin G (**7**) was deduced to have a side chain comprised of eight carbon atoms and a tetracyclic ring system including three six-membered rings and one five-membered ring (Fig. 6). Therefore, schefflerin G (**7**) was considered to be a dammarane triterpene with four hydroxyl groups at C-3, 6, 20, 26. Attachment of the β-glucopyranosyl moiety was also confirmed to the hydroxyl group at the 6-position. Judging from significant PS-ROESY correlations between methylene protons (δ_H 4.31) and an olefinic proton (δ_H 5.83), geometry of the double bond was determined to be *E*. Absolute configuration of the 20-position was expected to be *S*, by comparison of the ^{13}C-NMR data for (20*R*)-dammaranediol I (C-17, 21, 22: δ_C 49.9, 24.5, 42.9, respectively) and (20*S*)-dammaranediol II (C-17, 21, 22: δ_C 50.3, 25.3, 41.9, respectively)[10] with those of schefflerin G (**7**) (C-17, 21, 22: δ_C 50.5, 26.1, 41.6, respectively). Accordingly, the structure of schefflerin G (**7**) was elucidated to be (20*S*,24*E*)-dammaran-24-ene-3β,6α,20α,26-tetraol 6-*O*-β-D-glucopyranoside, as shown in Fig. 1.

Experimental

General Experimental Procedure Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained on a Horiba Fourier transform infrared spectrophotometer FT-710. Optical rotation data were collected on a JASCO P-1030 polarimeter. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL JNM α-400 spectrometer at 400 and 100 MHz, and a JEOL JNM ECA-600 spectrometer at 600 and 150 MHz, respectively, with tetramethylsilane as an internal standard. HR-ESI-time-of-flight (TOF) mass spectra (positive-ion mode) were taken on an Applied Biosystem QSTAR XL System ESI (Nano Spray)-TOF-MS, respectively.

Highly-porous synthetic resin Diaion HP-20 (Φ=60 mm, L=65 cm) was purchased from Mitsubishi Chemical Co., Ltd. (Tokyo, Japan). Silica gel column chromatography (CC) was performed on silica gel 60 [(E. Merck, Darmstadt, Germany) 70—230 mesh]. Reversed-phase [octadecyl silica gel (ODS)] open CC (RPCC) was performed on Cosmosil 75C_{18}-OPN (Nacalai Tesque, Kyoto) [Φ=50 mm, L=25 cm, linear gradient: MeOH–H_2O (1 : 9, 1.5 l)→(7 : 3, 1.5 l), 10 g fractions being collected]. The droplet counter-current chromatograph (DCCC) (Tokyo Rikakikai, Tokyo, Japan) was equipped with 500 glass column (Φ=2 mm, L=40 cm), and the lower and upper layers of a solvent mixture of $CHCl_3$–MeOH–H_2O–1-PrOH (9 : 12 : 8 : 2) were used as the mobile and stationary phases, respectively. Five gram fractions were collected and numbered according to their order of elution with the mobile phase. HPLC was performed on an ODS (Inertsil; GL Science, Tokyo, Japan; Φ=6 mm, L=25 cm, flow rate: 1.6 ml/min) column.

Plant Material Leaves of *S. arboricola* Hayata (Araliaceae) were collected in Nishihara Town, Nakagami County, Okinawa, Japan, in June 2005, and a voucher specimen was deposited in the Herbarium of Pharmaceutical Sciences, Graduate School of Biomedical Sciences, Hiroshima University (05-SA-Okinawa-0629).

Extraction and Isolation Air-dried leaves of *S. arboricola* (11.0 kg) were extracted three times with MeOH (45 l×3) for one week at room temperature, and then the MeOH extract was concentrated to 6 l *in vacuo*. The extract was washed with *n*-hexane (6 l) and then the methanolic layer was concentrated to a viscous gum (*n*-hexane-soluble fraction: 245 g). The gummy residue was suspended in H_2O (6 l) and then extracted with EtOAc (6 l) to give 245 g of an EtOAc-soluble fraction. The aqueous layer was extracted with 1-BuOH (6 l) to give 445 g of 1-BuOH-soluble fraction. The remaining water-layer was concentrated to furnish 441 g of a water-soluble fraction. An aliquot of the 1-BuOH-soluble extract (238 g) was applied to Diaion HP-20 CC (Φ=10.6 cm, L=50 cm), using a stepwise-gradient of MeOH–H_2O [(1 : 4, 12 l), (2 : 3, 12 l), (3 : 2, 12 l) and (4 : 1, 12 l)] and MeOH (12 l), 1.0 l fractions being collected. The residue eluted with the 40—60% MeOH (19.1 g in fractions 17—25) obtained on Diaion HP-20 CC was subjected to silica gel (450 g) CC using $CHCl_3$ (2 l), $CHCl_3$–MeOH [(99 : 1, 2 l), (97 : 3, 2 l), (19 : 1, 2 l), (37 : 3, 2 l), (9 : 1, 2 l), (17 : 1, 2 l), (17 : 3, 2 l), (33 : 7, 2 l), (4 : 1, 2 l), (3 : 1, 2 l) and (7 : 3, 2 l)] , $CHCl_3$–MeOH–H_2O (35 : 15 : 2, 4 l), and MeOH (3 l), fractions of 200 ml being collected. The residue (1.23 g in fractions 65—81) of the 12.5% MeOH in $CHCl_3$ eluate obtained on silica gel CC was subjected to PRCC. The residue (122 mg in fractions 94—113) was purified by HPLC with 35% MeOH to afford 45.5 mg of **8** from the peak at 7.5 min.

The residue (2.78 g in fractions 106—120) of the 30% MeOH in $CHCl_3$

eluate obtained on silica gel CC was subjected to PRCC. The residue (280 mg in fractions 124—150) was separated by DCCC to give 25.9 mg of **10** in fractions 4—5.

The residue eluted with the 60—80% MeOH (21.4 g in fractions 32—37) obtained on Diaion HP-20 CC was subjected to silica gel (600 g) CC using $CHCl_3$ (3 l), $CHCl_3$–MeOH [(99 : 1, 3 l), (97 : 3, 3 l), (19 : 1, 3 l), (37 : 3, 3 l), (9 : 1, 3 l), (17 : 1, 3 l), (17 : 3, 3 l), (33 : 7, 3 l), (4 : 1, 3 l), (3 : 1, 3 l) and (7 : 3, 3 l)] , $CHCl_3$–MeOH–H_2O (35 : 15 : 2, 3 l), and MeOH (3 l), fractions of 300 ml being collected. The residue (2.49 g in fractions 68—77) of the 10—15% MeOH in $CHCl_3$ eluate obtained on silica gel CC was subjected to PRCC. The residue (94.2 mg in fractions 124—134) was purified by HPLC with 50% MeOH to afford 21.7 mg of **6** from the peak at 12 min. The residue (940 mg in fractions 160—171) afforded 47.0 mg of **2** in a crystalline state. The residue (19.8 mg in fractions 206—229) was purified by HPLC with 60% MeOH to afford 6.3 mg of **7** from the peak at 23 min, and 2.10 mg of **4** from the peak at 34 min.

The residue (2.35 g in fractions 78—87) of the 15—20% MeOH in $CHCl_3$ eluate obtained on silica gel CC was subjected to PRCC. The residue (81.0 mg in fractions 200—221) was purified by HPLC with 50% MeOH to afford 39.8 mg of **3** from the peak at 10 min. The residue (122 mg in fractions 229—235) was purified by HPLC with 50% MeOH to afford 41.6 mg of **5** from the peak at 34.4 min. The residue (12.5 mg from the peak at 32 min) was repeatedly purified by HPLC with 60% MeOH to afford 9.80 mg of **1** from the peak at 10.5 min.

The residue eluted with the 80—100% MeOH (23.4 g in fractions 49—53) obtained on Diaion HP-20 CC was subjected to silica gel (550 g) CC using $CHCl_3$ (2 l), $CHCl_3$–MeOH [(99 : 1, 2 l), (97 : 3, 2 l), (19 : 1, 2 l), (37 : 3, 2 l), (9 : 1, 2 l), (17 : 1, 2 l), (17 : 3, 2 l), (33 : 7, 2 l), (4 : 1, 2 l), (3 : 1, 2 l), (7 : 3, 2 l)], $CHCl_3$–MeOH–H_2O (35 : 15 : 2, 2 l) and MeOH (3 l), fractions of 300 ml being collected. The residue (4.00 g in fractions 70—79) afforded 21.7 mg of **9** in a crystalline state.

Schefflerin A (**1**): Amorphous powder, $[\alpha]_D^{20}$ +23.0 (c=0.21, MeOH). IR ν_{max} (film) cm^{-1}: 3394, 2929, 1457, 1369, 1079, 1035. ^{1}H-NMR (pyridine-d_5, 400 MHz) δ: 4.98 (1H, d, J=8 Hz, H-1′), 4.58 (1H, dd, J=11, 2 Hz, H-6′a), 4.39 (1H, dd, J=11, 5 Hz, H-6′b), 4.29 (1H, ddd, J=12, 12, 3 Hz, H-6), 4.25 (1H, m, H-3′), 4.22 (1H, m, H-4′), 4.17 (1H, d, J=11 Hz, H-28a), 4.08 (1H, dd, J=8, 8 Hz, H-2′), 3.99 (1H, ddd, J=8, 5, 2 Hz, H-5′), 3.84 (1H, dd, J=12, 3 Hz, H-3), 3.67 (1H, d, J=11 Hz, H-28b), 2.41 (1H, m, H-16a), 2.40 (1H, m, H-22a), 2.38 (1H, m, H-12a), 2.33 (1H, m, H-2a), 2.13 (2H, m, H-19, 21a), 2.06 (1H, m, H-15a), 2.05 (3H, s, H_3-23), 1.95 (1H, dd, J=12, 12 Hz, H-7a), 1.91 (1H, m, H-2b), 1.88 (1H, m, H-7b), 1.84 (1H, m, H-13), 1.83 (1H, m, H-18), 1.64 (1H, m, H-21b), 1.60 (1H, m, H-12b), 1.54 (1H, m, H-1a), 1.53 (1H, m, H-11a), 1.45 (3H, s, H_3-30), 1.42 (3H, s, H_3-24), 1.41 (1H, m, H-9), 1.36 (4H, m, H-16b, H_3-29), 1.22 (1H, m, H-11b), 1.18 (3H, s, H_3-27), 1.16 (1H, d, J=12 Hz, H-5), 1.15 (3H, s, H_3-26), 1.14 (2H, m, H-15b, 22b), 0.99 (1H, m, H-1b), 0.91 (3H, s, H_3-25). ^{13}C-NMR (pyridine-d_5, 100 MHz): Table 1. HR-ESI-MS (positive-ion mode) m/z: 661.4289 $[M+Na]^+$ (Calcd for $C_{36}H_{62}O_9Na$: 661.4286).

Schefflerin B (**2**): Colorless needles (MeOH), mp 223—226 °C, $[\alpha]_D^{20}$ +14.2 (c=0.62, MeOH). IR ν_{max} (film) cm^{-1}: 3376, 2940, 1460, 1369, 1157, 1080, 1031. ^{1}H-NMR (C_5D_5N, 400 MHz) δ: 4.93 (1H, d, J=8 Hz, H-1′), 4.40 (1H, dd, J=12, 3 Hz, H-6′a), 4.31 (1H, ddd, J=12, 12, 3 Hz, H-6), 4.28 (1H, dd, J=12, 5 Hz, H-6′b), 4.22 (1H, m, H-3′), 4.21 (1H, m, H-4′), 4.20 (1H, m, H-28a), 4.05 (1H, dd, J=8, 8, Hz, H-2′), 3.89 (1H, m, H-5′), 3.65 (1H, d, J=11 Hz, H-28b), 3.52 (1H, dd, J=11, 4 Hz, H-3), 2.54 (1H, dd, J=12, 3 Hz, H-7a), 2.39 (1H, m, H-22a), 2.38 (1H, m, H-16a), 2.35 (1H, m, H-12a), 2.14 (1H, m, H-21a), 2.12 (1H, m, H-19), 2.01 (3H, s, H_3-23), 1.95 (2H, m, H-2a, 15a), 1.88 (1H, m, H-2b), 1.85 (1H, m, H-13), 1.82 (1H, m, H-7b), 1.77 (1H, dd, J=11, 8 Hz, H-18), 1.69 (1H, m, H-1a), 1.63 (1H, m, H-21b), 1.59 (3H, s, H_3-24), 1.54 (1H, m, H-11a), 1.44 (3H, m, H_3-30), 1.40 (1H, m, H-12b), 1.39 (1H, m, H-9), 1.38 (1H, d, J=12 Hz, H-5), 1.32 (3H, s, H_3-29), 1.28 (2H, m, H-15b, 16b), 1.20 (3H, s, H_3-26), 1.14 (1H, m, H-11b), 1.10 (1H, m, H-22b), 1.01 (6H, s, H_3-25, 27), 0.97 (1H, m, H-1b). ^{13}C-NMR (C_5D_5N, 100 MHz): Table 1. HR-ESI-MS (positive-ion mode) m/z: 661.4282 $[M+Na]^+$ (Calcd for $C_{36}H_{62}O_9Na$: 661.4286).

Schefflerin C (**3**): Amorphous powder, $[\alpha]_D^{20}$ +16 (c=0.87, MeOH). IR ν_{max} (film) cm^{-1}: 3367, 2945, 1650, 1457, 1368, 1080. ^{1}H-NMR (C_5D_5N, 600 MHz) δ: 4.98 (1H, d, J=8 Hz, H-1′), 4.97 (1H, m, H-21), 4.40 (1H, dd, J=11, 3 Hz, H-6′a), 4.34 (1H, ddd, J=10, 10, 3 Hz, H-6), 4.29 (1H, dd, J=11, 5 Hz, H-6′b), 4.19 (1H, d, J=11 Hz, H-28a), 4.25 (1H, m, H-3′), 4.23 (1H, m, H-4′), 4.07 (1H, dd, J=8, 8 Hz, H-2′), 3.95 (1H, ddd, J=8, 5, 3 Hz, H-5′), 3.67 (1H, d, J=11 Hz, H-28b), 3.55 (1H, dd, J=12, 3 Hz, H-3), 3.03 (1H, dd, J=12, 7 Hz, H-22a), 2.51 (1H, dd, J=10, 3 Hz, H-7a), 2.38 (1H, m, H-19), 2.34 (1H, m, H-16a), 2.22 (1H, m, dd, J=12, 12 Hz, H-18), 2.12 (1H, ddd, J=13, 4, 4 Hz, H-15a), 2.11 (3H, s, H_3-23), 1.97 (1H, dd, J=12, 12 Hz, H-13), 1.95 (1H, m, H-2a), 1.88 (1H, m, H-2b), 1.82 (1H, m, H-7b), 1.77 (3H, s, H_3-29), 1.76 (3H, s, H_3-30), 1.74 (1H, m, H-1a), 1.61 (3H, s, H_3-24), 1.60 (1H, m, H-22b), 1.59 (1H, m, H-11a), 1.47 (2H, m, H_2-12), 1.45 (1H, br d, J=13 Hz, H-9), 1.41 (1H, d, J=10 Hz, H-5), 1.37 (1H, m, H-16b), 1.24 (1H, br d, J=13 Hz, H-15b), 1.24 (1H, m, H-11b), 1.20 (3H, s, H_3-26), 1.05 (1H, dd, J=13, 13 Hz, H-1b), 1.01 (3H, s, H_3-25), 0.97 (3H, s, H_3-27). ^{13}C-NMR (C_5D_5N, 150 MHz): Table 1. HR-ESI-MS (positive-ion mode) m/z: 661.4282 $[M+Na]^+$ (Calcd for $C_{36}H_{62}O_{10}Na$: 661.4286).

Schefflerin D (**4**): Amorphous powder, $[\alpha]_D^{20}$ +12.9 (c=0.14, MeOH). IR ν_{max} (film) cm^{-1}: 3412, 2968, 1508, 1086, 1028. ^{1}H-NMR (C_5D_5N, 600 MHz) δ: 5.08 (1H, d, J=8 Hz, H-1′), 4.52 (1H, dd, J=12, 3 Hz, H-6′a), 4.46 (1H, ddd, J=10, 10, 2 Hz, H-6), 4.35 (1H, dd, J=12, 5 Hz, H-6′b), 4.31 (1H, m, H-4′), 4.28 (1H, dd, J=8, 8 Hz, H-3′), 4.15 (1H, dd, J=8, 8 Hz, H-2′), 3.99 (1H, m, H-5′), 3.95 (1H, m, H-16), 3.61 (1H, dd, J=11, 5 Hz, H-3), 2.72 (1H, dd, J=13, 3 Hz, H-7a), 2.40 (1H, m, H-12a), 2.20 (1H, m, H-19), 2.17 (1H, d, J=13 Hz, H-15a), 2.11 (3H, s, H_3-23), 2.04 (1H, m, H-22a), 2.02 (2H, m, H-2a, 21a), 1.95 (1H, m, H-7b), 1.94 (1H, m, H-13), 1.93 (1H, m, H-2b), 1.84 (1H, dd, J=13, 4 Hz, H-15b), 1.78 (1H, d, J=13 Hz, H-1a), 1.72 (1H, m, H-18), 1.70 (1H, m, H-21b), 1.69 (3H, s, H_3-24), 1.66 (1H, m, H-11a), 1.65 (1H, m, H-12b), 1.58 (1H, m, H-22b), 1.51 (3H, s, H_3-30), 1.49 (1H, m, H-9), 1.47 (1H, d, J=10 Hz, H-5), 1.40 (3H, s, H_3-29), 1.38 (3H, s, H_3-26), 1.33 (1H, m, H-11b), 1.22 (3H, s, H_3-28), 1.11 (3H, s, H_3-25), 1.09 (3H, s, H_3-27), 1.08 (1H, m, H-1b). ^{13}C-NMR (C_5D_5N, 150 MHz): Table 1. HR-ESI-MS (positive-ion mode) m/z: 661.4287 $[M+Na]^+$ (Calcd for $C_{36}H_{62}O_9Na$: 661.4286).

Schefflerin E (**5**): Amorphous powder, $[\alpha]_D^{20}$ +7.9 (c=0.59, MeOH). IR ν_{max} (film) cm^{-1}: 3395, 2936, 1650, 1457, 1369, 1079. ^{1}H-NMR (C_5D_5N, 600 MHz) δ: 5.48 (1H, br d, H-29a), 5.11 (1H, br s, H-29b), 4.94 (1H, d, J=8 Hz, H-1′), 4.50 (1H, d, J=15 Hz, H-30a), 4.46 (1H, d, J=15 Hz, H-30b), 4.42 (1H, dd, J=12, 3 Hz, H-6′a), 4.35 (1H, ddd, J=11, 11, 2 Hz, H-6), 4.30 (1H, dd, J=12, 5 Hz, H-6′b), 4.25 (1H, dd, J=8, 8 Hz, H-3′), 4.22 (1H, dd, J=8, 8 Hz, H-4′), 4.09 (1H, d, J=11 Hz, H-28a), 4.07 (1H, dd, J=8, 8 Hz, H-2′), 3.91 (1H, ddd, J=8, 5, 3 Hz, H-5′), 3.65 (1H, d, J=11 Hz, H-28b), 3.55 (1H, dd, J=11, 4 Hz, H-3), 2.61 (1H, ddd, J=11, 11, 6 Hz, H-19), 2.50 (1H, dd, J=11, 2 Hz, H-7a), 2.40 (1H, m, H-16a), 2.39 (1H, m, H-22a), 2.33 (1H, m, H-21a), 2.03 (3H, s, H_3-23), 2.02 (1H, m, H-15a), 1.96 (1H, m, H-2a), 1.90 (2H, m, H-2b, 12a), 1.88 (1H, dd, J=11 Hz, H-18), 1.81 (1H, m, H-7b), 1.78 (1H, m, H-13), 1.69 (1H, br d, J=13 Hz, H-1a), 1.63 (1H, m, H-21b), 1.62 (1H, m, H-12b), 1.60 (3H, s, H_3-24), 1.39 (1H, d, J=11 Hz, H-5), 1.35 (1H, br d, J=12 Hz, H-9), 1.35 (1H, m, H-11a), 1.26 (2H, m, H-15b, 16b), 1.22 (1H, m, H-22b), 1.20 (3H, s, H_3-26), 1.08 (1H, m, H-11b), 1.05 (1H, ddd, J=13, 13, 3 Hz, H-1b), 1.00 (3H, s, H_3-25), 0.92 (3H, s, H_3-27). ^{13}C-NMR (C_5D_5N, 150 MHz): Table 1. HR-ESI-MS (positive-ion mode) m/z: 659.4128 $[M+Na]^+$ (Calcd for $C_{36}H_{60}O_9Na$: 659.4129).

Schefflerin F (**6**): Colorless needles (MeOH), mp 219—221 °C, $[\alpha]_D^{20}$ +45.3 (c=0.35). IR ν_{max} (film) cm^{-1}: 3374, 2933, 1453, 1374, 1077, 1040. ^{1}H-NMR (C_5D_5N, 600 MHz) δ: 5.01 (1H, d, J=8 Hz, H-1′), 4.51 (1H, dd, J=12, 3 Hz, H-6′a), 4.36 (1H, dd, J=7, 3 Hz, H-21), 4.33 (1H, m, H-6′b), 4.31 (1H, m, H-6), 4.29 (1H, br s, H-19), 4.25 (1H, dd, J=8, 8 Hz, H-3′), 4.20 (1H, dd, J=8, 8, H-4′), 4.09 (1H, dd, J=8, 8 Hz, H-2′), 3.96 (1H, ddd, J=8, 5, 3 Hz, H-5′), 3.88 (1H, dd, J=7, 3 Hz, H-28a), 3.51 (1H, dd, J=12, 3 Hz, H-3), 3.13 (1H, br d, J=7 Hz, H-28b), 2.57 (1H, dd, J=12, 3 Hz, H-7a), 2.05 (3H, s, H_3-23), 2.04 (1H, m, H-22a), 1.93 (1H, dddd, J=12, 3, 3, 3 Hz, H-2a), 1.87 (1H, m, H-2b), 1.84 (1H, m, H-18), 1.80 (1H, m, H-7b), 1.78 (1H, m, H-13), 1.66 (1H, m, H-12a), 1.65 (1H, m, H-1a), 1.62 (1H, m, H-15a), 1.59 (3H, s, H_3-24), 1.54 (1H, m, H-16a), 1.50 (1H, m, H-22b), 1.49 (1H, m, H-11a), 1.47 (1H, m, H-16b), 1.40 (1H, dd, J=12, 3 Hz, H-9), 1.38 (1H, d, J=11 Hz, H-5), 1.25 (1H, ddd, J=12, 3, 3 Hz, H-15b), 1.18 (1H, m, H-12b), 1.16 (1H, m, H-11b), 1.13 (2H, s, H_3-26), 1.00 (3H, s, H_3-25), 0.95 (1H, ddd, J=13, 13, 3 Hz, H-1b), 0.81 (3H, s, H_3-27). ^{13}C-NMR (C_5D_5N, 150 MHz): Table 1. HR-ESI-MS (positive-ion mode) m/z: 617.3650 $[M+Na]^+$ (Calcd for $C_{33}H_{54}O_9Na$: 617.3660).

Schefflerin G (**7**): Amorphous powder, $[\alpha]_D^{20}$ +67.5 (c=0.24, MeOH). IR ν_{max} (film) cm^{-1}: 3732, 2938, 1509, 1456, 1392, 1033, 670. ^{1}H-NMR (C_5D_5N, 600 MHz) δ: 5.83 (1H, dd, J=7, 7 Hz, H-24), 5.20 (1H, d, J=8 Hz, H-1′), 4.49 (1H, dd, J=12, 3 Hz, H-6′a), 4.42 (1H, ddd, J=10, 10, 3 Hz, H-6), 4.34 (1H, dd, J=12, 3 Hz, H-6′b), 4.31 (2H, s, H_2-26), 4.24 (1H, m, H-3′), 4.22 (1H, m, H-4′), 4.08 (1H, dd, J=8, 8 Hz, H-2′), 3.92 (1H, ddd, J=9, 5, 3 Hz, H-5′), 3.54 (1H, br d, J=10 Hz, H-3), 2.54 (1H, m, H-23a), 2.50 (1H, dd, J=12, 3 Hz, H-7a), 2.45 (1H, m, H-23b), 2.13 (1H, m, H-12a), 2.06 (3H, s, H_3-29), 1.96 (1H, m, H-2a), 1.96 (1H, m, H-17), 1.95 (1H, m, H-7b), 1.94 (1H, m, H-13), 1.89 (1H, m, H-2b), 1.86 (3H, s, H_3-27), 1.85 (1H, m, H-22a), 1.82 (2H, m, H_2-16), 1.78 (1H, m, H-22b), 1.69 (1H, m, H-1a), 1.65

(1H, m, H-15a), 1.60 (3H, s, H_3-28), 1.54 (1H, m, H-11a), 1.48 (1H, dd, J=13, 3 Hz, H-9), 1.45 (1H, d, J=10 Hz, H-5), 1.41 (3H, s, H_3-21), 1.35 (1H, m, H-12b), 1.20 (1H, m, H-15b), 1.19 (1H, m, H-11b), 1.16 (3H, s, H_3-19), 1.05 (1H, m, H-1b), 1.03 (3H, s, H_3-18), 0.88 (3H, s, H_3-30). ^{13}C-NMR (C_5D_5N, 100 MHz): Table 1. HR-ESI-MS (positive-ion mode) *m/z*: 661.4291 $[M+Na]^+$ (Calcd for $C_{36}H_{62}O_9Na$: 661.4286).

X-Ray Crystallographic Analysis of Schefflerin F (6) A suitable crystal (0.31 mm×0.03 mm×0.03 mm) was used for analysis. The data were measured using synchrotron radiation (λ=0.70000 Å) (SPring-8 BL38B1). The structure was solved by a direct method using the program SHELXL-97 (Sheldrick, 2008).[11] The refinement and all further calculations were carried out using SHELXL-97 (Sheldrick, 2008).[11] The H atoms were included at calculated positions and treated as riding atoms using the SHELXL default parameters. The non-H atoms were refined anisotropically, using weighted full-matrix least-squares on F^2. Crystal Data: $C_{33}H_{54}O_9 \cdot 2.5H_2O$, M=634.76 g mol^{-1}, triclinic, P_1, a=8.693(5) Å, b=12.853(5) Å, c=14.781(5) Å, α=100.941(5)°, β=91.113(5)°, γ=103.604(5)°, V=1572.4(12) Å^3, T=293(2) K, Z=2, D_c=1.341 Mg/m^3. Final goodness-of-fit on F^2 was 1.356 and final R indices were R_1=0.0823 and wR_2=0.2456 based on $I>2\sigma(I)$. The largest difference of the peak and the hole was 0.003 and −0.001 eÅ^{-3}, respectively. CCDC deposit contains the supplementary crystallographic data. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: (+44) 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk.

Analyses of the Sugar Moiety About 500 μg each of schefflerins A—G (**1**—**7**) was hydrolyzed with 1 N HCl (0.1 ml) at 90 °C for 2 h. The reaction mixtures were partitioned with an equal amount of EtOAc (0.1 ml), and the water layers were analyzed with a chiral detector (JASCO OR-2090*plus*) on an amino column [Asahipak NH_2P-504E, CH_3CN–H_2O (4 : 1), 1 ml/min]. All the hydrolyzates gave a peak for D-glucose at the retention time of 9.5 min (positive optical rotation sign). The peak was identified by co-chromatography with authentic D-glucose.

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