DOI 10.1007/s10600-016-1666-8
Chemistry of Natural Compounds, Vol. 52, No. 3, May, 2016

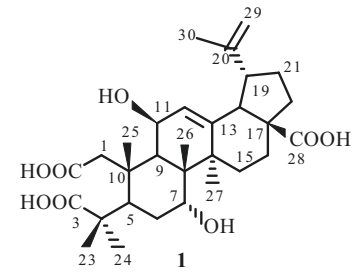
LUPANE-TYPE TRITERPENOIDS FROM *Schefflera octophylla*

**Pang Su-qiu,[1,2] Sun Ai-jing,[1] Wang Guo-quan,[1]
Xu Xian-xiang,[1] and Xu Ruian[1*]**

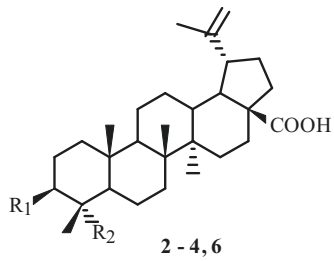
*A new lupane-type triterpene, named 7α,11β-dihydroxy-2,3-*seco*-lup-12(13),20(29)-diene-2,3,28-trioic acid (**1**), along with 5 other known lupane-type triterpenoids, namely 3β-hydroxy-lup-20(29)-ene-23,28-dioic acid (**2**), betulinic acid (**3**), betulinic acid 3-*O*-sulfate (**4**), 12(13)-ene betulinic acid (**5**), and betulinic acid glucoside (**6**), was isolated from* Schefflera octophylla *stems and leaves. The structures of these compounds were determined by 1D and 2D NMR, MS techniques, and chemical methods. Compound **1** was the new compound, and **2**, **3**, **5**, **6** were isolated from* S. octophylla *for the first time.*

Keywords: *Schefflera octophylla*, lupane-type triterpenoids, 7α,11β-dihydroxy-2,3-*seco*-lup-12(13),20(29)-diene-2,3,28-trioic acid.

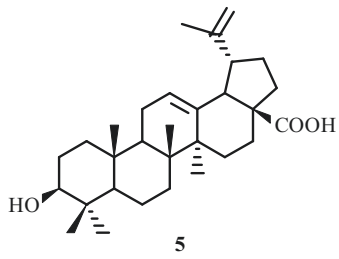
Schefflera octophylla (Lour.) Harms (Araliaceae) is a medium-size evergreen tree up to 25 m tall and bole up to 80 cm in diameter, used as a folk remedy for the treatment of pain and inflammation. It is a principal ingredient of an herbal tea formulation widely used to treat common cold in southern China [1, 2]. In Vietnamese folk medicine, it is also used as a tonic drug, an antirheumatic agent, and for liver diseases [3]. Previous phytochemical studies on *S. octophylla* showed that the plant is rich in triterpenoids and triterpenoid glycosides. As part of our continuing search for bioactive constituents, a 75% EtOH extract of the stems and leaves of *S. octophylla* was investigated, and six lupane-type triterpenoids (**1–6**) were isolated. This present paper describes the structures of these compounds.



1



2 - 4, 6



5

2: R_1 = OH, R_2 = COOH; **3:** R_1 = OH, R_2 = CH_3
4: R_1 = OSO_3H, R_2 = CH_3; **6:** R_1 = *β-O*-Glc, R_2 = CH_3

Compound **1** was isolated as colorless needles and gave a positive result in the Liebermann–Burchard test, mp 231–233°C. The IR spectrum (nujol) showed absorptions at 3450, 3075, 2975, 1698, and 1640 cm^{-1} assignable to hydroxyl, carboxyl, and C=CH_2 functions. UV (MeOH, λ_{max}, nm): 205. Its negative electrospray ionization mass spectrum (ESI-MS) exhibited a quasi-molecular ion peak at *m/z* 531.2 ($[M - H]^-$), indicating a molecular weight of 532.2. The molecular formula was established as $C_{30}H_{44}O_8$ by negative-ion mode HR-FAB-MS, showing a pseudo-molecular ion peak at *m/z* 532.2932 (calcd 532.2926), a compound with nine degrees of unsaturation.

1) Institute of Molecular Medicine & School of Biomedical Sciences, Huaqiao University, 362021, Quanzhou, Fujian, P. R. China, fax: +86 595 28919460, e-mail: ruianxu@hqu.edu.cn; 2) Haixia Hospital, 362000, Quanzhou, Fujian, P. R. China.
Published in *Khimiya Prirodnykh Soedinenii*, No. 3, May–June, 2016, pp. 378–380. Original article submitted November 29, 2014.

TABLE 1. ^{1}H (400 MHz) and ^{13}C NMR (DEPT) (100 MHz) Spectral Data of **1** (DMSO-d_6, δ, ppm, J/Hz)

C atom	δ_H	δ_C	DEPT (HMQC)
1	a.2.15 (d, J = 10.5); b.2.33 (d, J = 10.5)	36.83	CH_2
2	–	177.69	C
3	–	179.03	C
4	–	43.50	C
5	1.79 (m)	50.36	CH
6	1.55 (m)	21.18	CH_2
7	3.33 (dd, J = 11.5, 4.5)	72.14	CH
8	–	41.20	C
9	1.56 (m)	47.11	CH
10	–	16.40	C
11	3.57 (dd, J = 11.5, 4.5)	79.64	CH
12	5.17 (d, J = 3.6)	125.04	CH
13	–	144.36	C
14	–	39.00	C
15	a.1.25 (m); b. 1.37 (m)	32.22	CH_2
16	a.1.48 (m); b.1.61 (m)	23.91	CH_2
17	–	51.40	C
18	2.47 (m)	43.63	CH
19	2.94 (m)	38.05	CH
20	–	150.79	C
21	a.1.51 (m); b.1.75 (m)	20.72	CH_2
22	a.1.31 (m); b.1.81 (m)	25.56	CH_2
23	1.02 (s)	16.56	CH_3
24	1.05 (s)	16.49	CH_3
25	0.79 (s)	17.55	CH_3
26	0.88 (s)	14.96	CH_3
27	1.00 (s)	15.87	CH_3
28	–	178.74	C
29	a.4.56 (s); b.4.69 (d, J = 2.0)	110.10	CH_2
30	1.65 (s)	19.42	CH_3

The ^{1}H NMR and ^{13}C NMR spectrum of **1** (Table 1) displayed signals for typical triterpenoid methyl groups at $\delta_{H(ppm)}$: 0.79 (3H, H_3-25), 0.88 (3H, H_3-26), 1.00 (3H, H_3-27), 1.02 (3H, H_3-23), 1.05 (3H, H_3-24), and 1.65 (3H, H_3-30) [δ_C 17.55, 14.96, 15.87, 16.56, 16.49, and 19.42, respectively, according to the HMQC experiment]. The presence of a broad vinyl methyl proton signal at δ 1.65 and two vinyl proton signals at 4.69 (d, J = 2.0 Hz) and 4.56 with ^{13}C signals at 19.42, 150.79 and 110.10 was characteristic of an isopropenyl group of lupene triterpenes. Two proton signals, 3.33 (dd, J = 11.5, 4.5 Hz, H-7), and 3.57 (dd, J = 11.5, 4.5 Hz, H-11), were due to hydroxymethylene groups δ_C 72.14 and 79.64. The δ_H 5.17 (d, J = 3.6 Hz, H-12) proton was connected with δ_C 125.04 (C-12). The ^{13}C NMR spectrum and DEPT experiments indicated the presence of 30 carbon atoms due to six methyls, seven methylenes, seven methines, and ten nonprotonated carbons. The signals included two olefinic carbons [δ 110.10 (C-29), and 150.79 (C-20)] and three carbonyl carbons [δ 177.69 (C-2), 179.03 (C-3), and 178.74 (C-28)]. The ^{1}H detected heteronuclear multiple bond connectivity (HMBC) correlations of H_2-1 to one carboxyl carbon, indicating that the carboxyl group [δ 177.69 (C-2)] was adjacent to C-1. The long-range correlation of two methyl groups (H_3-23 and H_3-24) to another carboxyl carbon [δ 179.03 (C-3)] suggested that the second carboxyl group was adjacent to [δ 43.50 (C-4)]. H_2-16 and H_2-22 have correlations to the third carboxyl carbon [δ 178.74 (C-28)], suggesting that the third carboxyl group was adjacent to C-28. Moreover, the HMBC correlations between a carbon signal at δ 72.14 (C-7) and a methyl proton signal at δ 0.88 (H_3-26), as well as between a proton signal at δ 3.33 (H-7) and a carbon signal at δ 50.36 (C-5), indicated that a hydroxyl group was attached at C-7 (Fig. 1). The proton signal at δ_H 3.57 (H-11) has correlations with δ_C 144.36 (C-13), δ_C 41.20 (C-8) and δ_C 16.40 (C-10), indicating that hydroxyl group was attached at C-11 (δ 79.64). The orientation of the hydroxyl group was determined by a NOESY experiment, in which the proton signal (H-7) was found to be correlated with a methyl signal (H_3-26, β-orientation) and the H-11 to have a slight correlation with a methyl signal (H_3-27, α-orientation) (Fig. 1). The structure of compound **1** was elucidated as 7α,11β-dihydroxy-2,3-*seco*-lup-12(13),20(29)-diene-2,3,28-trioic acid.

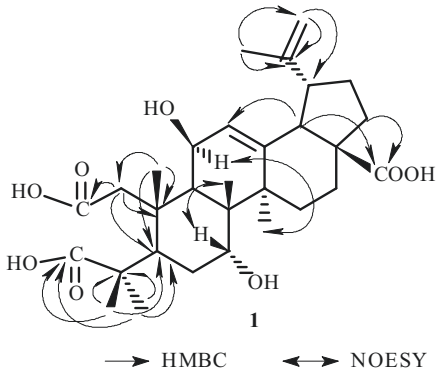


Fig. 1. Selected HMBC correlations and NOESY for **1**.

EXPERIMENTAL

General Experimental Procedures. Melting points (mp) were determined using an X-4 micromelting-point apparatus (Beijing, China) and were uncorrected. UV spectra were measured on a Shimadzu UV-2501 spectrometer (Kyoto, Japan). IR spectra were obtained on KBr pellets using a Nicolet impact 410 spectrometer (Madison, USA). The ^{1}H and ^{13}C NMR spectra were obtained on Bruker Avance 400 and 100 MHz spectrometers (Germany) with TMS as an internal standard. SEI-MS measurements were undertaken on an HP5989A spectrometer (Palo Alto, USA). TLC and column chromatography were performed on plates precoated with silica gel F254 and silica gel (200–300 mesh; Qingdao Marine Chemical Ltd., Qingdao, China), respectively. Solvents were distilled prior to use.

Plant Material. *Schefflera octophylla* fresh stems and leaves were collected from Quanzhou (118°36′E, 24°58′N), Fujian Province, China, in September 2012, and the plant was identified by Prof. X. X. Xu at the School of Biomedical Sciences, Huaqiao University. A voucher specimen (No. *S.O.*20120915) was deposited in Huaqiao University.

Extraction and Isolation. The air-dried and roughly powdered *S. octophylla* stems and leaves (5 kg) was extracted three times with 75% ethanol under reflux. After removal of the solvent by evaporation, the extracts were partitioned between H_2O and peltroleum ether, CH_2Cl_2, EtOAc, and *n*-BuOH, successively. The EtOAc and *n*-BuOH extracts were chromatographed on silica gel (300–400 mesh; 1500 g) columns respectively, eluting with a CH_2Cl_2–MeOH mixture (concentration gradients 1:0, 50:1, 20:1, 10:1, 5:1, 1:1, 1:5, 1:10, 1:20, 1:50, and 0:1) repeatedly. Six compounds, **1** (61 mg), **2** (139 mg), **3** (47 mg), **4** (25 mg), **5** (71 mg), and **6** (43 mg) were obtained.

Compound 1. Colorless needles, mp 231–233°C (CH_2Cl_2–MeOH, 10:1). IR (KBr, cm^{-1}): 3450, 3075, 2975, 1698, and 1640. UV (MeOH, λ_{max}, nm): 205. $[\alpha]_D^{26}$ +102.3° (*c* 0.15, MeOH). HR-SEI-MS ($[M]^+$ 532.2932, calcd 532.2926). ^{1}H and ^{13}C NMR spectral data are given in Table 1; HMBC and NOESY experiments, in Fig. 1.

Compound 2. Colorless needles, mp 260–262°C (CH_2Cl_2–MeOH, 20:1), positive in the Liebermann–Burchard reaction. ESI-MS *m/z* 486 $[M]^+$ ($C_{30}H_{46}O_5$). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 0.80 (3H, s, H-27), 0.88 (3H, s, H_3-25), 0.99 (3H, s, H_3-26), 1.02 (3H, s, H_3-24), 1.66 (3H, s, H_3-30), 3.57 (br.s, H-3α), 4.57 and 4.70 (2 × br.s, H_2-29), 11.88 (2H, COOH). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 36.81 (C-1), 30.57 (C-2), 72.14 (C-3), 55.43 (C-4), 49.02 (C-5), 20.70 (C-6), 34.13 (C-7), 41.28 (C-8), 50.34 (C-9), 36.93 (C-10), 25.50 (C-11), 29.62 (C-12), 38.04 (C-13), 50.82 (C-14), 32.12 (C-15), 25.55 (C-16), 55.43 (C-17), 43.88 (C-18), 47.10 (C-19), 150.30 (C-20), 21.13 (C-21), 32.20 (C-22), 177.20 (C-23), 14.94 (C-24), 17.53 (C-25), 16.54 (C-26), 16.47 (C-27), 177.24 (C-28), 110.08 (C-29), 19.39 (C-30). Based on the above evidence, the structure of **2** was determined as 3β-hydroxy-lup-20(29)-ene-23,28-dioic acid [4].

Compound 3.White needles, mp 286–288°C (CH_2Cl_2–MeOH, 50:1), positive in the Liebermann–Burchard reaction. ESI-MS *m/z* 456 $[M]^+$ ($C_{30}H_{48}O_3$). Based on the above evidence, the structure of **3** was determined as betulinic acid [5].

Compound 4. White powder (CH_2Cl_2–MeOH, 10:1), mp 253–258°C. $[\alpha]_D^{27}$ +4.3° (*c* 0.5, EtOH). IR (KBr, cm^{-1}): 1695, 1640, 1230, 875. ESI-MS *m/z* 536 $[M]^+$ ($C_{30}H_{47}O_6S$). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.90 (1H, br.s, 28-COOH), 4.70 (1H, br.s, H-29a), 4.56 (1H, br.s, H-29b), 4.46 (1H, m, H-3α), 0.79, 0.88, 1.00, 1.05, 1.26, 1.66 (each 3H, s, *tert*-CH_3). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 177.78 (C-28), 151.20 (C-20), 110.21 (C-29), 79.52 (C-3), 55.35 (C-17), 50.84 (C-5), 50.37 (C-9), 49.06 (C-19), 47.11 (C-18), 43.92 (C-14), 42.65 (C-8), 38.40 (C-1), 38.41 (C-4), 38.22 (C-13), 36.94 (C-10), 36.82 (C-22), 34.15 (C-7), 34.14 (C-21), 32.10 (C-16), 30.59 (C-15), 29.63 (C-23), 25.63 (C-2), 21.14 (C-12),

20.73 (C-11), 19.28 (C-30), 17.39 (C-6), 16.57 (C-24), 16.51 (C-25, 26), 14.96 (C-27). Compound **4** was characterized as betulinic acid 3-*O*-sulfate [6].

Compound 5. White powder (CH_2Cl_2–MeOH, 50:1), mp 265–267°C. ESI-MS *m/z* 454 $[M]^+$ ($C_{30}H_{46}O_3$). ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.90 (1H, br.s, 28-COOH), 5.75 (1H, s, H-12), 4.69 (1H, br.s, H-29a), 4.56 (1H, br.s, H-29b), 3.56 (1H, m, H-3), 1.65 (3H, s, H-30), 1.23 (3H, s, H-27), 1.01 (3H, s, H-26), 0.98 (3H, s, H-25), 0.88 (3H, s, H-24), 0.79 (3H, s, H-23). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 177.70 (C-28), 150.80 (C-20), 110.09 (C-29), 72.15 (C-3), 55.91 (C-17), 50.84 (C-5), 50.37 (C-9), 49.06 (C-19), 47.11 (C-18), 43.92 (C-14), 42.65 (C-8), 39.40 (C-1, 4), 38.07 (C-13), 36.94 (C-10), 36.82 (C-22), 34.15 (C-7), 34.14 (C-21), 32.20 (C-16), 30.59 (C-15), 29.63 (C-23), 25.55 (C-2), 21.18 (C-12), 20.73 (C-11), 19.43 (C-30), 17.56 (C-6), 16.57 (C-24), 16.50 (C-25, 26), 14.97 (C-27). According to be above evidences, **5** was characterized as 12(13)-ene betulinic acid [7].

Compound 6. White powder (CH_2Cl_2–MeOH, 1:1), mp 266–268°C, positive in the Liebermann–Burchard and Molisch reactions. Acid hydroxlysis of **6** gave an aglycone and D-glucose. IR (KBr, ν_{max}, cm^{-1}): 3400 (OH), 1680 (C=O), 1640, 875 (C=CH_2). ESI-MS *m/z* 630.2514 $[M]^+$ ($C_{36}H_{58}O_9$). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 15.17 (C-27), 16.18 (C-25), 16.41 (C-26), 18.17 (C-23), 19.43 (C-30), 20.80 (C-24), 20.95 (C-21), 22.66 (C-16), 25.57 (C-22), 29.10 (C-6), 29.70 (C-2), 30.58 (C-12), 32.17 (C-15), 33.27 (C-1), 34.19 (C-7), 37.14 (C-4), 37.18 (C-10), 38.04 (C-19), 38.38 (C-13), 40.9 (C-8), 42.60 (C-18), 47.07 (C-14), 49.01 (C-11), 49.48 (C-5), 49.69 (C-17), 55.90 (C-9), 80.44 (C-3), 110.10 (C-29), 150.89 (C-20), 177.69 (C-28). ^{13}C NMR showed a set of signals due to one molecule of β-glucopyranose [100.58 (C-1), 77.44, 77.23 (C-3, 5), 73.88 (C-2), 70.96 (C-4), 61.84 (C-6)]. Based on these data, **6** was confirmed as betulinic acid glucoside [8].

ACKNOWLEDGMENT

This work was supported by the key Programs of Science & Technology of Fujian Province (2012Y0049).

REFERENCES

1. T. V. Sung, W. Steglich, and G. Adam, *Phytochemistry*, **30**, 2349 (1991).
2. Y. L. Li, P. H. B. Paul, and E. C. O. Vincent, *Antiviral. Res.*, **68**, 1 (2005).
3. G. Adam, M. Lischewski, and H. V. Phiet, *Phytochemistry*, **21**, 1385 (1982).
4. M. J. Just, M. C. Recio, and R. M. Giner, *Nat. Prod. Lett.*, **9**, 167 (1997).
5. S. Siddiqui, F. Hafeez, and S. Begum, *J. Nat. Prod.*, **51**, 229 (1988).
6. J. Kitajima, M. Shindo, and Y. Tanaka, *Chem. Pharm. Bull.,* **38**, 714 (1990).
7. J. Hussain, N. U. Rehman, and H. Hussain, *Fitoterapia,* **83**, 593 (2012).
8. J. Kitajima and Y. Tanaka, *Chem. Pharm. Bull*., **37**, 2727 (1989).