Chemical Constituents from the Barks of *Swietenia macrophylla*

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A new tirucallane-type triterpenoid, swiententol (**1**), was isolated from the barks of *Swietenia macrophylla*, together with four known triterpenoids (**2**–**5**), five known limonoids (**6**–**10**), and other six compounds (**11**–**16**). The structure of swiententol (**1**) was elucidated by extensive 2D NMR and MS analysis.

Keywords *Swietenia macrophylla*, Meliaceae, tirucallane-type triterpenoids, limonoids

Introduction

Swietenia macrophylla King (Meliaceae), a big-leaf mahogany tree, is an endangered and medicinally important plant indigenous to tropical and subtropical regions in the world, such as India, Indonesia, Malaysia, Philippines, and Fiji.^[1] Its seeds have been used as a folk medicine for treatment of diabetes, hypertension, and malaria in Malaysia.^[2] Previous chemical investigation of *Swietenia macrophylla* led to the isolation of a number of limonoids,^[3,4] steroids^[5] and polyphenols,^[6] which showed a wide spectrum of biological effects, such as anti-viral, anti-inflammatory, anti-infective, anti-mutagenic, and anti-diabetic activities.^[2] In this paper, a new tirucallane-type triterpenoid, swiententol (**1**), was isolated from the barks of *S. macrophylla*, along with four known triterpenoids (**2**–**5**), five known limonoids (**6**–**10**), and other six compounds (**11**–**16**). Their structures are shown in Figure 1

Experimental

General procedures

Optical rotations were measured with a Perkin Elmer 341 polarimeter, and NMR spectra were recorded at 30 °C on a Varian 400 MHz unity spectrometer. The ¹H NMR and ¹³C NMR chemical shifts were referenced to the solvent peak for DMSO-*d*₆ or CDCl₃, HRESI-MS spectra were recorded on a Waters ZQ mass spectrometers. Column chromatography was performed on MCI gel CHP 20P (75–150 μm, Mitsubishi Chemical Co.), Sephadex LH-20 (25–100 μm, Pharmacia Fine Chemical Co.), and ODS (150–200 mesh, Merck). Precoated

Figure 1 The structures of compounds **1**–**16**.

silica gel plate (Qingdao Hailang Chemical Co.) was used for TLC. A waters 600 pump equipped with a Waters 2487 detector was used for HPLC. A thermo Scientific C18 Hypersil 5 μm column was used for semi-preparative HPLC separation.

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Plant materials

The plant *S. macrophylla* was collected from the campus of Guangdong Pharmaceutical University in Guangzhou, China. It was air-dried prior to extraction. A voucher sample (NPC-201301) has been lodged at the Natural Product Chemistry Lab in School of Pharmaceutical Sciences, Southern Medical University, Guangzhou, China.

Extraction and isolation

The grounded barks of *S. macrophylla* (14.0 kg) were refluxed with MeOH at 80 °C (3×10 L, 4 h per time). The extracts were concentrated under reduced pressure and then suspended in water, which was further partitioned with EtOAc (5×3 L). The EtOAc soluble fraction (204.6 g) was subjected to silica gel column chromatography (CC), eluting with CHCl₃/MeOH (0/1—1/1) to afford seven fractions. Fr. 2 (25.6 g) was chromatographed over silica gel (PE/EtOAc, 9/1—1/1) and ODS (MeOH/H₂O, 60%—100%) to yield **4** (18 mg), **14** (20 mg), and **15** (0.5 g). Fr. 3 (19.6 g) was subjected to CC over MCI CHP 20P to yield **11** (2.4 g). Fr. 4 (6.6 g) was subjected to MCI CHP20P CC to yield four sub-fractions A—D. Sub-fr. 4B was applied to silica gel (CHCl₃/MeOH, 40/1—10/1), ODS (MeOH/H₂O, 40%—80%), and semi-preparative HPLC (MeOH/H₂O, 10%—100% within 30 min) to yield **6** (10 mg), **7** (35 mg), **8** (5 mg), **9** (9 mg), and **10** (4 mg). Sub-fr. 4C was subjected to CC over ODS (MeOH/H₂O, 40%—80%), and semi-preparative HPLC (MeOH/H₂O, 10%—100% within 30 min) to yield **1** (6 mg), **2** (14 mg), and **13** (8 mg). Sub-fr. 4D was chromatographed over silica gel (CHCl₃/MeOH, 40/1—10/1) and ODS (MeOH/H₂O, 40%—80%) to afford **5** (15 mg). Fr. 6 (14.0 g) was subjected to CC over silica gel (PE/EtOAc, 9/1—1/1) to yield five sub-fractions A—E. Sub-fr. 6A was chromatographed over silica gel (CH₂Cl₂/MeOH, 100/1—10/1) and sephadex LH-20 (100% MeOH) to yield **15** (10 mg). Sub-fr. 6B was chromatographed over silica gel (CHCl₃/MeOH, 40/1—10/1) and sephadex LH-20 (100% MeOH) to yield **4** (21 mg). Sub-fr. 6C was subjected to CC over silica gel (CHCl₃/MeOH, 40/1—10/1) and ODS (MeOH/H₂O, 40%—100% MeOH) to yield **12** (24 mg). Sub-fr. 6E was chromatographed over silica gel (PE/EtOAc, 9/1—1/1) and ODS (40%—100% MeOH) to yield **3** (14 mg), and **16** (30 mg).

Swietenitol (**1**): amorphous powder; $[\alpha]_D^{25} +25.8$ (c 0.03, MeOH); ¹H NMR (CDCl₃, 400 MHz) is in Table 1; ¹³C NMR (CDCl₃, 100 MHz) is in Table 1; (+)-HRESIMS: *m/z* 519.1676 [M+H]⁺ (calcd for C₃₂H₅₅O₅, 519.4049).

Results and Discussion

The MeOH extract of the barks of *S. macrophylla* was suspended in H₂O, and partitioned successively with EtOAc. The EtOAc layer was subjected to vari-

Table 1 ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) data of compound **1** in CDCl₃

Position	δ_H	δ_C
1 α	1.47 (m, 1H)	31.2 (CH ₂)
1 β	1.33 (m, 1H)	
2 α	1.63 (m, 1H)	25.4 (CH ₂)
2 β	1.93 (m, 1H)	
3	3.48 (br.s, 2H)	76.2 (CH)
4		37.4 (C)
5	1.80 (dd, <i>J</i> = 5.8, 11.9 Hz, 1H)	44.6 (CH)
6 α	2.00 (m, 1H)	23.9 (CH ₂)
6 β	1.93 (m, 1H)	
7	5.28 (dd, <i>J</i> = 2.8, 6.1 Hz, 1H)	118.2 (CH)
8		145.8 (C)
9	2.30 (m, 1H)	48.4 (CH)
10		34.8 (C)
11 α	1.55 (m, 1H)	17.4 (CH ₂)
11 β	1.50 (m, 1H)	
12 α	1.32 (m, 1H)	31.2 (CH ₂)
12 β	1.87 (m, 1H)	
13		43.4 (C)
14		50.8 (C)
15 α	1.50 (m, 1H)	34.1 (CH ₂)
15 β	1.50 (m, 1H)	
16 α	1.32 (m, 1H)	27.3 (CH ₂)
16 β	1.90 (m, 1H)	
17	2.05 (m, 1H)	44.9 (CH)
18	0.87 (s, 3H)	23.1 (CH ₃)
19	0.80 (s, 3H)	12.9 (CH ₃)
20	1.95 (m, 1H)	46.2 (CH)
21	4.83 (d, <i>J</i> = 3.1 Hz, 1H)	103.8 (CH)
22 α	1.91 (m, 1H)	31.7 (CH ₂)
22 β	1.91 (m, 1H)	
23	4.44 (m, 1H)	78.6 (CH)
24	3.19 (dd, <i>J</i> = 1.9, 8.0 Hz, 1H)	76.7 (CH)
25		73.0 (C)
26	1.28 (s, 3H)	26.3 (CH ₃)
27	1.28 (s, 3H)	26.2 (CH ₃)
28	0.96 (s, 3H)	27.7 (CH ₃)
29	0.94 (s, 3H)	21.7 (CH ₃)
30	1.02 (s, 3H)	27.2 (CH ₃)
OCH ₂	3.77 (dq, <i>J</i> = 7.0, 14.1 Hz, 1H)	63.7 (CH ₂)
	3.43 (dq, <i>J</i> = 7.0, 14.1 Hz, 1H)	
CH ₃	1.25 (t, <i>J</i> = 7.0 Hz, 3H)	15.1 (CH ₃)

ous column chromatographies to yield a new tirucalane-type triterpenoid, swietenitol (**1**). In addition, 15 known compounds were identified to be agladupol D (**2**),^[7] 21 α -meliandiol (**3**), 21 α -methylmeliandiol (**4**),^[8]

NOTE

protoxylocarpins F (5),^[9] methyl 1 α -acetoxy-6,8 α ,14 β ,30 β -tetrahydroxy-3-oxo-[3.3.1^{10,2}.1^{1,4}]-tricyclomeliac-7-oate (6),^[10] seneganolide (7),^[11] methyl 1 α -acetoxy-2 β ,3 α ,6,8 α ,14 β -pentahydroxy-[4.2.1^{10,30}.1^{1,4}]-tricyclomeliac-7-oate (8),^[10] methyl 1 α -acetoxy-3 β ,6,8 α ,14 β -tri-hydroxy-2 α -methoxy-2 β ,14 β -epoxy-[4.2.1^{10,30}.1^{1,4}]-tricyclomeliac-7-oate (9),^[12] 1-acetylkhayanolide B (10),^[13] (+)-catechin (11), aromadendrin (12),^[14] ivorenolide A (13),^[15] 24-methylenecycloartanol (14),^[16] β -sitosterol (15), and daucosterol (16) by comparison of their spectroscopic data and physicochemical properties with data reported in the literatures.

Compound **1** was obtained as an amorphous powder. Its HRESI-MS displayed a molecular ion peak at m/z 519.1676 $[M+H]^+$, corresponding to the molecular formula C₃₂H₅₅O₅ with 6 degrees of unsaturation. The molecular weight of compound **1** is 14 mass unit larger than that of compound **2**, corresponding a methylene group. The ¹H NMR spectrum (Table 1) showed seven tertiary methyl groups (δ_H : 0.80, 0.87, 0.94, 0.96, 1.02, 1.28 and 1.28), one olefinic proton (δ_H 5.28), and six protons bonded to oxygen bearing carbons (δ_H : 3.19, 3.48, 3.77, 3.43, 4.83, 4.44). A total 32 carbons were observed in ¹³C NMR spectrum, which was further divided by HSQC into a trisubstituted double bond (δ_C : 118.2, 145.8), eight methyl, nine sp³ methylene, eight sp³ methine, and five sp³ quaternary carbons. A comparison of the NMR data of compound **1** with those of compound **2** indicated that compound **1** was an analogue of compound **2**, a tirucallane-type triterpenoid. Comparison of the ¹³C NMR data of compounds **1** and **2** suggested that two compounds shared the same tetracyclic system, which was confirmed by 2D NMR data. The only difference was the presence of an *O*-ethyl group at C-21 in compound **1** instead of the *O*-methyl group in compound **2**, which was confirmed by the HMBC correlation from methylene [δ_H 3.77 (dq, $J=7.0$, 14.1 Hz, 1H), 3.43 (dq, $J=7.0$, 14.1 Hz, 1H)] and methyl [δ_H 1.25 (t, $J=7.0$ Hz, 1H)] to C-21 (δ_C 103.8). Thus, the planar structure was constructed.

The further analysis of ROESY spectrum showed that the relative configuration of the tetracyclic core and side chain in compound **1** was identical to that of compound **2**. The ROESY cross-peaks of Me-29/Me-19, Me-19/Me-30, and Me-30/H-17 indicated that Me-29, Me-19, Me-30, and H-17 were cofacial and assigned in a β -orientation. In consequence, the ROESY correlations of Me-28/H-5, H-5/H-9, and H-9/Me-18 suggested that they were α -oriented. H-3 was assigned a β -orientation by ROESY correlation of H-3/Me-29. The ROESY correlations of Me-18/H-21, Me-18/H-20, H-20/H-23 revealed that H-20, H-21 and H-23 were α -oriented. The chemical shift of C-21 (δ_C 103.8) also suggested that H-21 was α -oriented.^[7] The relative large coupling constant ($J = 8.0$ Hz) between OH and H-24, and ROESY correlations of H-24/H-23 and H-24/H-23, suggested that a inter-molecular hydro-

gen bond formed between 24-OH and the oxygen of the furan ring. The small coupling constant ($J_{23,24} = 1.9$ Hz) indicated that they were in a gauche relationship and H-24 was β -oriented. Thus, the structure of swietenitol (**1**) was elucidated as showed in Figure 1.

Compound **1** is unlikely to be an artifact since ethanol was absent during the process of extraction and isolation. Tirucallane-type triterpenoids (**1**–**4**) and apotirucallane-type triterpenoid (**5**) were reported from *Swietenia macrophylla* for the first time. Limonoids (**6**, **8**–**10**) and ivorenolide A (**13**) were previously reported from the *Khaya* species. The re-isolation of these compounds from *S. macrophylla* indicated the close taxonomical relationship between the genus *Khaya* and *Swietenia*.

Conclusions

Chemical investigation into the barks of *S. macrophylla* led to the isolation of 16 compounds. Compound **1** is new to the science. It is for the first time to report the triterpenoid isolated from *S. macrophylla*.

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