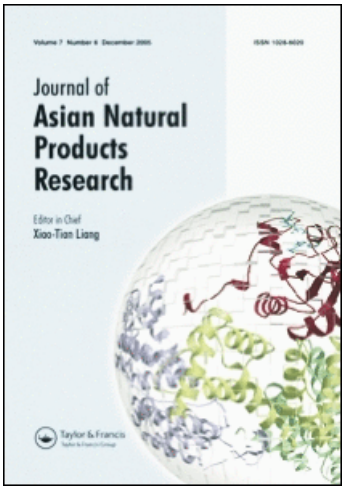

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Chemical constituents from *Schisandra plena*

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Note

Chemical constituents from *Schisandra plena*

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The chemical constituents of the leaves and stems of *Schisandra plena* are described for the first time. This investigation has resulted in the isolation of a new sesquiterpenoid, plenoxide (**1**). In addition, eleven known compounds, including sesquiterpenoids, coumarins, flavanones, triterpenoids and steroids have also been isolated. The structure and stereochemistry of **1** has been determined on the basis of spectroscopic analysis. Detailed analysis of 2D NMR data led to the conclusion that the chemical shifts of earlier compounds similar to bullatantriol need revision.

Keywords: *Schisandra plena*; Schisandraceae; Sesquiterpenoids; Plenoxide

1. Introduction

The genus *Schisandra*, belonging to the economically and medicinally important family Schisandraceae, is a rich source of dibenzocyclooctadiene lignans, as well as lanostane and cycloartane triterpenes, that possess many beneficial pharmacological effects [1]. We have previously reported the isolation and elucidation of two novel triterpenoids with new carbon skeletons from *Schisandra lancifolia* and *S. micrantha* [2,3]. In continuing our study on *Schisandra* species, we investigated the leaves and stems of *Schisandra plena* A. C. Smith and herein report the isolation of twelve compounds, including seven sesquiterpenoids, one coumarin, two flavanones, one triterpenoid and one steroid. Among them, **1** is a new compound, named plenoxide (figure 1). In addition, bullatantriol (**2**) [4], tricyclohumuladiol (**3**) [5], 10-*O*-methyl-alismoxide (**4**) [6], guaianediol (**5**) [7], clovane-2,9-diol (**7**) [8], 9(11)-arborinen-3-ol (**10**) [9], isobyakangelicin (**11**) [10] were obtained from the family Schisandraceae for the first time. Oplodiol (**6**) [11], catechin (**12**) [12], quercitrin (**13**) [13] and 3β-hydroxy-5α,8α-epidioxygersta-6,22-diene (**14**) [14] were also isolated. This is

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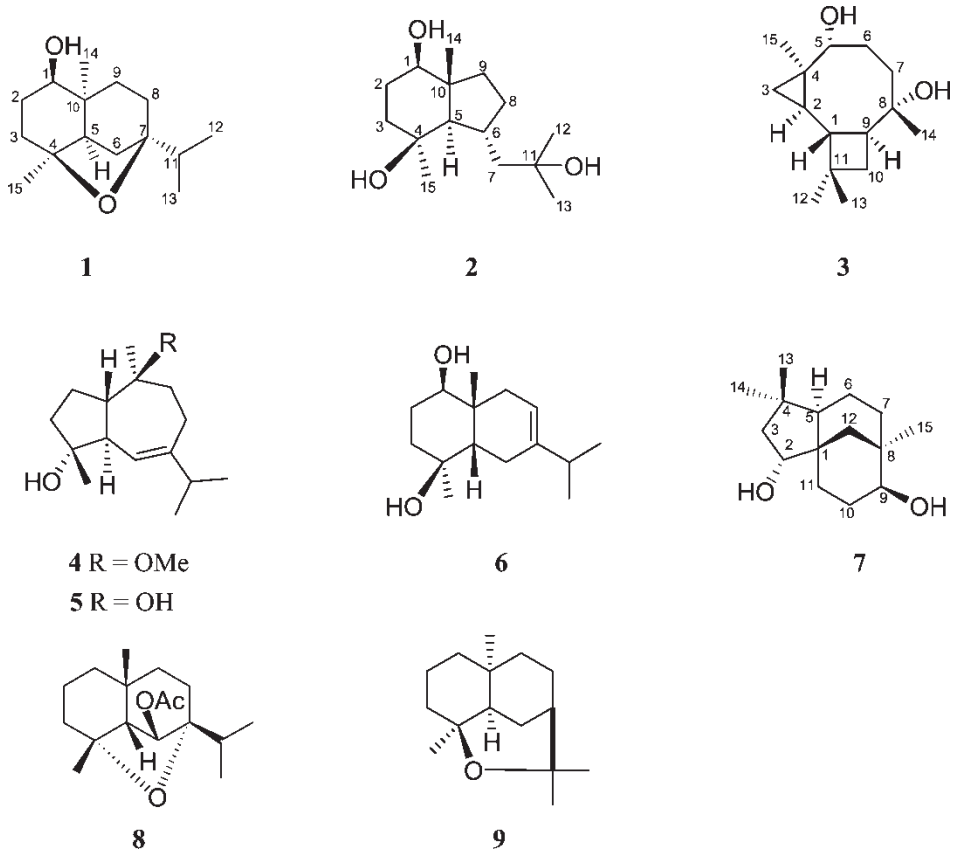

Figure 1. Structures of compounds **1–9**.

the first report of the chemical constituents of this plant. Moreover, on the basis of the extensive 2D NMR spectroscopic data, we conclude that the chemical shifts of the previously reported structures similar to bullatantriol (**2**) need revision. Furthermore, the first complete assignments of ^{1}H and ^{13}C NMR spectra of tricyclohumuladiol (**3**) are reported.

2. Results and discussion

Plenoxide (**1**) has a molecular formula of $C_{15}H_{26}O_2$, which is deduced from the pseudo-molecular ion *m/z* 261 $[M + Na]^+$ in its positive ion HRFAB-MS spectrum and the ^{1}H and ^{13}C NMR data, suggesting three degrees of unsaturation. Its IR spectrum shows an absorption band for hydroxyl (3520–3350 cm^{-1}) group. ^{13}C and DEPT NMR spectra (table 1) indicated 15 carbons with 25 directly attached protons, and analysis of the chemical shifts suggests the presence of three oxygenated carbons (δ 71.5, 73.9 and 79.3) and the absence of double bonds. Consequently, **1** was established as a tricyclic compound with one hydroxyl group. As **1** contains two oxygen atoms and three oxygen-bearing carbons, an epoxy ring is present in the structure. The presence of an isopropyl group (δ 0.77, 6H, d, $J = 5.1$ Hz) and two tertiary methyls (δ 0.80, 0.95, each 3H, s) in the ^{1}H NMR spectrum suggest that compound **1** is probably a eudesmane derivative. The similarity of ^{13}C NMR

Table 1. NMR spectral data for compounds **1**[a] and **8**.

	1		***8***
No.	δ_H *(mult; J, Hz)*	δ_C	δ_C
1	3.22, dd, (3.1, 9.2)	79.3 d	38.6 t
2	1.70 (α, m), 1.47 (β, m, overlap)	26.7 t	18.0 t
3	1.35–1.42, 1.50–1.54 (m, overlap)	39.8 t	43.6 t
4		71.5 s	72.6 s
5	1.12–1.18 (m, overlap)	44.7 d	47.9 d
6	1.06–1.14, 1.32–1.38 (m, overlap)	29.3 t	72.0 d
7		73.9 s	74.5 s
8	1.06–1.14, 1.32–1.38 (m, overlap)	28.9 t	28.0 t
9	1.12–1.18, 1.46–1.52 (m, overlap)	34.6 t	44.3 t
10		38.9 s	33.8 s
11	1.34–1.40 (m, overlap)	39.2 d	32.7 d
12	0.77, d (5.1)	16.9 q	15.9 q
13	0.77, d (5.1)	16.8 q	16.2 q
14	0.80, s	11.6 q	20.7 q
15	0.95, s	29.7 q	30.0 q

[a] Spectra recorded in $CDCl_3$, assignments made by ^1H-^1H COSY, HMQC and HMBC data.

data of the partial structure for **1** [C-4 (δ 71.5), C-7 (δ 73.9), C-8 (δ 28.9), C-12 (δ 16.9), C-13 (δ 16.8), and C-15 (δ 29.7)] with those of (+)-6β-acetoxyvitranoxide (**8**) [C-4 (δ 72.6), C-7 (δ 74.5), C-8 (δ 28.0), C-12 (δ 15.9), C-13 (δ 16.2), and C-15 (δ 30.0)] [15], confirm the above assumption. The main differences between the two compounds are the presence of a hydroxyl group and the absence of an acetate group in **1**. HMBC correlations were noted from Me-14 and H-3a to oxygenated methine (δ 79.3), in conjunction with ^1H-^1H COSY spin system of H-1/H-2/H-3, indicating that the hydroxyl group is at C-1. This placement is consistent with the down-field shift of the neighboring carbons [C-2 (δ 26.7), C-10 (δ 38.9)] in **1**. Moreover, the chemical shift of Me-14 in compound **1** is shifted up-field to δ_C 11.6, compared with δ_C 20.7 for **8**. This suggests that Me-14 of **1** has lost the deshielding of the 12β-OAc moiety and therefore appeared at a relative high field.

The *cis*-fused decalin was clearly deduced from the ROESY data (figure 2), which shows correlations between H-5 and Me-14, and between H-5 and Me-15. H-1 was determined to be the same α-orientation as H-5 from its ROESY correlation with H-5. Meanwhile, ROESY correlation between H-5 and Me-15, combined with the rigidity of the decalin system, requires the epoxy ring to be *cis*-linked. Furthermore, the chemical shifts of C-4 and C-7 (δ 71.5 and 73.9) are almost identical to those of **8** (δ 72.6 and 74.5), supporting this assignment. Interestingly, the optical rotation for **1** ($[\alpha]_D^{24}$ − 18.15) is of opposite sign to

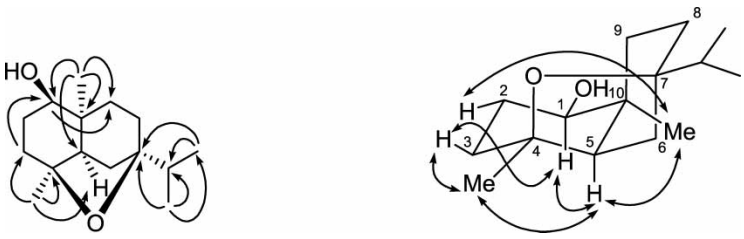

Figure 2. Key HMBC and ROESY correlations for **1**.

that reported in **8** ($[\alpha]_D + 19$). It is tentatively assumed that the skeleton of **1** has an enantiomeric configuration to **8**. Meanwhile, **1** exhibits identical optical rotatory activity to (−)-4,11-epoxy-*cis*-eudsmane (**9**,$[\alpha]_D^{28} - 22$) [16], unambiguously confirming the whole stereochemistry of compound **1** as (−)-(1*R*,4*S*,5*R*,7*R*,10*S*)-1β-hydroxy-4β,7β-epoxy-*cis*-eudesmane. Conformational analysis using Dreiding molecular models also showed the plenoxide structure is as depicted in **1**.

Compound **2** was assigned the molecular formula of $C_{15}H_{28}O_3$ by EI-MS (*m/z* 241 $[M - Me]^+$) and ^{13}C NMR spectral data. By interpretation of its ^1H and ^{13}C NMR, ^1H-^1H COSY, HMQC and HMBC spectra followed by comparison with published ^1H and ^{13}C NMR data [4,17], the structure was found to be bullatantriol, which was previously isolated from *Annona bullata* and *Homalomena aromatica*. The previously reported NMR assignments for C-2 and C-9 of bullatantriol (**2**), and related compounds, homalomenols A and B [17], need to be revised because of the strong HMBC correlations (figure 3) from H-5 (δ 1.11, d,$J = 10.6$ Hz), H-8 (δ 2.32, m), and Me-14 (δ 1.56, s) to the methylene carbon (δ 40.2, t), from H_2-3 (δ 1.87/1.56) to another methylene carbon (δ 29.4), from H_2-9 (δ 1.52/1.98, m) to C-6 (δ 32.6, d), and from H_2-2 (δ 1.94/2.45) to C-4 (δ 71.4, s). The above assignments are further supported by connections from C-1 to C-3 and from C-5 to C-9 based on ^1H-^1H COSY and HMQC correlations. Moreover, the high-field ^{13}C NMR chemical shift for C-2 (δ 29.4) of the two compounds can also be explained by the γ-steric compression effect between the H-2β and OH-4β, and the space effect between the H-2β and Me-14.

3. Experimental

3.1 General experimental procedures

Melting points were determined on an XRC-1 apparatus and are uncorrected. Optical rotations were measured with a Horiba SEPA-300 High Sensitive Polarimeter. IR spectra were obtained in KBr discs on a Bio-Rad Win infrared spectrophotometer. EI and FAB MS were measured on a VG Auto Spec-3000 spectrometer. ^1H, ^{13}C NMR and 2D NMR spectra were recorded on Bruker AM-400 and DRX-500 instruments with TMS as internal standard. Column chromatography was performed on silica gel (200–300 mesh), or on silica gel H (10–40 μ, Qingdao Marine Chemical Inc., China).

3.2 Plant material

The leaves and stems of *S. plena* A. C. Smith were collected in Xishuangbanna, Yunnan, China, in April, 2002, and were identified by Guo-Da Tao. A voucher specimen has been

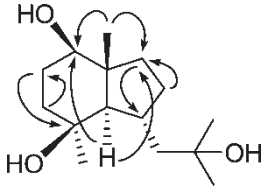

Figure 3. Key HMBC correlations for **2**.

deposited in the Herbarium of the Department of Taxonomy, Kunming Institute of Botany, the Chinese Academy of Sciences.

3.3 Extraction and isolation

The air-dried leaves and stems of *S. plena* (9.5 kg) were extracted with EtOH (3 ×) at room temperature, and the solvent was evaporated *in vacuo*. The residue was partitioned in H_2O and extracted with light petroleum and EtOAc, successively. The EtOAc extract (90 g) was separated into two fractions through column chromatography (CC) over porous resin D101 by elution with MeOH–H_2O (80:20, 100:0). The first fraction (48 g) was subjected to CC on Si gel, using $CHCl_3$–Me_2CO (1:0–6:4) as eluent. Combining the fractions by TLC monitoring gave five fractions. Fraction 1 (2 g) was further purified using CC on Si gel with light petroleum–EtOAc (20:1) to afford **7** (35 mg) and **14** (12 mg). Fraction 2 (9 g) was subjected to CC on Si gel, eluting with light petroleum–EtOAc (9:1), to give five subfractions (2a–c). Fractions 2a was subjected to CC on Si gel with light petroleum–acetone (7:1) to afford **1** (168 mg),**4** (14 mg), **11** (35 mg). Compounds **2** (105 mg), **3** (16 mg), **5** (404 mg),**6** (95 mg), **10** (3 mg) were isolated and purified from fraction 2b by CC over silica gel developing with $CHCl_3$–acetone (9:1). Fraction 4 (3.5 g) was rechromatographed by CC on Si gel eluting with $CHCl_3$–MeOH (19:1) to afford **12** (568 mg) and **13** (1.16 g).

Plenoxide (1). Colorless crystals, mp 65–67°C, $[\alpha]_D^{24}$ − 18.15 (*c* 0.25, $CHCl_3$); IR (KBr) ν_{max} (cm^{-1}): 3520–3350, 2963, 2937, 2875, 1461, 1377, 1021, 918. Positive FAB-MS: (%) 239 $[M + H^+]$ (11), 221 (100), 203 (60), 195 (15), 147 (14), 71 (36); HR-FABMS: *m/z* 261.1834 $[M + Na]^+$ (calcd for $C_{15}H_{26}O_2Na$ 261.1830); ^1H and ^{13}C NMR data, see Table 1.

Bullatantriol (2). $C_{15}H_{28}O_3$; colorless crystals; mp 172–173°C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.73 (1H, dd, $J = 4.0$, 11.3 Hz, H-1), 1.94 (1H, m, H-2α), 2.45 (1H, m, H-2β), 1.56 (1H, m, H-3α), 1.87 (1H, m, H-3β), 1.11(1H, d, $J = 10.6$ Hz, H-5), 2.80 (1H, m, H-6), 2.38 (1H, br d, $J = 13.8$ Hz, H-7α), 1.56 (1H, overlap, H-7β), 2.32 (2H, m, H_2-8), 1.52 (1H, m, H-9α), 1.98 (1H, m, H-9β), 1.43(6H, s, Me-12, 13), 1.56 (3H, s, Me-14), 1.60 (3H, s, Me-15); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 79.8 (d, C-1), 29.4 (t, C-2), 42.4 (t, C-3), 71.4 (s, C-4), 59.8 (d, C-5), 32.6 (d, C-6), 52.3 (t, C-7), 33.3 (t, C-8), 40.2 (t, C-9), 48.1 (s, C-10), 70.8 (s, C-11), 30.6(q, C-12), 31.1 (q, C-13), 15.6 (q, C-14), 32.4 (q, C-15); EI-MS: *m/z* (%) 241 $[M - Me]^+$ (2), 238 $[M - H_2O]^+$ (1), 223 (24), 220 (2), 205 (8), 179 (62), 162 (16), 147 (35), 123 (100), 107 (20), 101 (18), 81 (25), 59 (25).

Tricyclohumuladiol (3). $C_{15}H_{26}O_2$; colorless crystals; mp 160–162°C; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.30 (1H, t, $J = 11.1$ Hz, H-1), 0.73 (1H, m, H-2α), 0.44 (1H, t, $J = 4.5$ Hz, H-3a), 0.52 (1H, dd, $J = 4.5$, 7.8 Hz, H-3b), 3.62 (1H, dd, $J = 4.8$, 10.6 Hz, H-5), 2.18 (1H, m, H-6a), 1.99 (1H, m, H-6b), 2.18 (2H, m, H_2-7), 2.32 (1H, m, H-9), 1.59 (1H, t, $J = 10.0$ Hz, H-10a), 1.77 (1H, dd, $J = 7.8$, 10.0 Hz, H-10b), 1.14 (3H, s, Me-12), 1.04 (3H, s, Me-13), 1.35 (3H, s, Me-14), 1.22 (3H, s, Me-15); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 48.4 (d, C-1), 24.4 (d, C-2), 19.3 (t, C-3), 20.5 (s, C-4), 73.5 (d, C-5), 32.2 (t, C-6), 41.5 (t, C-7), 72.4 (s, C-8), 50.1 (d, C-9), 34.9 (t, C-10), 34.0 (s, C-11), 22.5(q, C-12), 30.6

(q, C-13), 20.3 (q, C-14), 18.2 (q, C-15); EI-MS (%): 238 $[M]^+$, (55), 220 (6), 205 (10), 191 (19), 177 (37), 163 (20), 149 (48), 134 (56), 121 (55), 109 (75), 98 (100), 85 (76), 71 (82), 57 (72).

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