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A NOVEL EUDESMENE SESQUITERPENOID FROM *Schisandra sphenanthera* STEMS

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Chemical investigation on the stems of Schisandra sphenanthera *has afforded a novel eudesmene-type sesquiterpenoid, schisansphene A (**1**), and a known compound, alismol (**2**). Their structures and configurations were elucidated by spectroscopic methods, including 2D NMR techniques.*

Keywords: *Schisandra sphenanthera*, Schisandraceae, schisansphene A.

The family Schisandraceae has been proved to be a rich source of dibenzocyclooctane lignans, as well as lanostane and cycloartane triterpenes, some of which have been found to possess calcium antagonism, anti-lipid peroxidation, antitumor, anti-HIV and anti-HBV effects [1–8]. In our previous study, three carotane-type sesquiterpenoids, schisanwilsonenes A–C, were obtained from *S. wilsoniana*, and schisanwilsonene A was found to show an active effect against HBV [9]. *Schisandra sphenanthera* Rehd. et Wils. is a medicinal plant indigenous to southern China. Its fruits are used in Chinese folk medicine as "wu-wei-zi" to treat hepatitis.

In a systemic phytochemical investigation, a new eudesmene-type sesquiterpenoid, schisansphene A (**1**), and a known guainane-type sesquiterpenoid, alismol (**2**) [10], were isolated from the stems of *S. sphenanthera.* This is the first report of eudesmene and guainane sesquiterpenoids from the Schisandraceae. In this paper, we describe the isolation and structure of the new compound.

Compound **1**, a white powder, had the molecular formula $C_{15}H_{24}O_3$ on the basis of HR-ESI-MS (*m/z* 275.1621 $[M + Na]^+$), which indicated four degrees of unsaturation. The IR absorption band at 3414 cm^{-1} implied the presence of the OH group. The ^1H NMR spectrum showed signals corresponding to an oxygenated methine proton [δ 4.82 (1H, m)], an olefinic proton [6.36 (1H, s)], a secondary methyl [1.23 (3H, d, J = 7.2 Hz)], and three tertiary methyls [0.98, 1.37, and 1.51 (each 3H, s)]. The ^{13}C NMR displayed 15 carbon resonances, and the DEPT spectrum was consistent with the presence of a methine [δ 71.0 (d)], a quaternary carbon [82.7 (s)] bearing a peroxide ring, a quaternary carbon [81.8 (s)] bearing a hydroxyl, and trisubstituted olefinic carbons [128.0 (d) and 146.2 (s)], as well as four methyls, four methylenes, three methines, and four quaternary carbons. The double bond was assigned at C-6(7) by the HMBC correlations of δ_H 6.36 (H-6) with δ_C 82.7 (C-5), 146.2 (C-7) and 71.0 (C-8), and δ_H 4.82 (H-8) with δ_C 128 (C-6) and 146.2 (C-7), as well as δ_H 1.37 (Me-12) and 1.51 (Me-13) with δ_C 146.2 (C-7). HMBC correlations of methyl protons at δ_H 0.98 (Me-14) with the carbons at δ_C 34.6 (C-10), 36.3 (C-1), 41.7 (C-9), and 82.7 (C-5) implied that C-1, C-5, C-9, and C-14 were connected to C-10. HMBC correlations of methyl protons at δ_H 1.23 (Me-15) with the carbons at δ_C 27.3 (C-3), 31.9 (C-4), and 82.7 (C-5) suggested that the methyl group was connected to C-4. On the basis of the above evidence, the planar structure of **1** was unambiguously established, and **1** had the same planar structure as 5β,8β-epidioxy-11-hydroperoxy-6-eudesmene [11].

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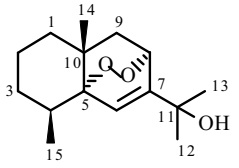

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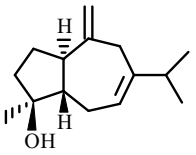

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The computer-modeled structure of **1** was generated by Chem3D (Chemoffice) version ultra 9.0 using MM2 force field calculations for energy minimization. The results were consistent with the stereochemistry of **1** as established by the NOESY experiments. The NOESY correlations between Me-14 and Me-15, Me-14 and H-8, as well as between Me-15 and H-8, positioned these protons on the same side of the molecule and revealed the α-orientation of the peroxide group, similar to that of 5α,8α-epidioxy-6-eudesmene [12]. Finally, the structure of **1** was elucidated and named schisansphene A.

EXPERIMENTAL

General Experimetal Procedures. Optical rotations were run on a JASCO P-1020 polarimeter at room temperature. IR spectra were recorded on an Avatar 360 FT-IR ESP spectrometer in CH_2Cl_2. Mass spectra were determined on a Bruker Apex 7.0 TESLA FT-MS apparatus for HR-ESI-MS. ^{1}H NMR and ^{13}C NMR spectra were taken on a Bruker DRX-400 spectrometer in $CDCl_3$. Analytical and preparative TLC were run on silica gel plates (GF_{254}, Yantai Institute of Chemical Technology, Yantai, China). Spots on the plates were observed under UV light and visualized by spraying with 10% H_2SO_4, followed by heating. Column chromatography (CC) was performed on silica gel (200–300 mesh and 300–400 mesh; Qingdao Marine Chemical Factory, Qingdao, China).

Plant Material. Stems of *Schisandra sphenanthera* were collected in August of 2009 at Jiujiang, Jiangxi, China. The identity of the plant material was verified by one of the authors (C. M. Tan), and a voucher specimen (Tan-Ma200901) has been deposited in the Herbarium of Materia Medica, School of Pharmacy, Second Military Medical University, Shanghai, P. R. China.

Extraction and Isolation. The dried and powdered material (20 kg) was extracted exhaustively with 95% EtOH three times and filtered. The filtrate was evaporated *in vacuo* to give a residue (3000 g), a portion of which (2900 g) was suspended in H_2O (1.5 L) and partitioned with Et_2O (3 × 2 L). The combined Et_2O solution was concentrated to yield a residue (800 g), 200 g of which was subjected to CC on silica gel (200–300 mesh, 2 kg, 10 × 120 cm) eluted successively with petroleum ether (PE)–EtOAc (30:1, 15:1, 10:1, 5:1, 3:1, 1:1, v/v) and EtOAc to yield fractions 1–7. Fraction 5 (13 g) was subjected to repeated silica gel CC with PE–EtOAc (5:1–3:1, v/v) to give subfractions 5a, 5b, and 5c. Fraction 5b was subjected to preparative TLC with PE–EtOAc (6:1, v/v) to yield **2** (13 mg), and Fr. 5c was subjected to preparative TLC with benzene–acetone (9:1, v/v) to afford **1** (9 mg).

Compound 1. White amorphous powder. [α] +59.2° (*c* 0.1, MeOH). IR (CH_2Cl_2, ν_{max}, cm^{-1}): 3416, 2936, 1708, 1641, 1442, 1376, 1364, 1153, 1041, 899, 756. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.97 (1H, m, H-1α), 1.48 (1H, m, H-1β), 1.46 (1H, m, H-2α), 1.70 (1H, m, H-2β), 1.88 (1H, m, H-3α), 1.30 (1H, m, H-3β), 2.04 (1H, m, H-4), 6.36 (1H, s, H-6), 4.82 (1H, m, H-8), 1.92 (1H, m, H-9α), 1.27 (1H, m, H-9β), 1.37 (3H, s, Me-12), 1.51 (3H, s, Me-13), 0.98 (3H, s, Me-14), 1.23 (3H, d, J =7.2, Me-15). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 36.3 (C-1), 16.8 (C-2), 27.3 (C-3), 31.9 (C-4), 82.7 (C-5), 128.0 (C-6), 146.2 (C-7), 71.0 (C-8), 41.7 (C-9), 34.6 (C-10), 81.8 (C-11), 22.9 (C-12), 22.5 (C-13), 26.9 (C-14), 16.2 (C-15). HR-ESI-MS *m/z* 275.1626 ([M + Na]$^+$) (calcd for $C_{15}H_{24}O_3Na$, 275.1623).

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