

A Novel Triterpenoid Lactone, Schiprolactone A, from *Schisandra propinqua* (Wall.) Hook. f. et Thoms

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Schiprolactone A, a triterpenoid lactone with a new side chain skeleton was isolated from the stems of *Schisandra propinqua* together with schisanlactones A and B. Their structures were elucidated by spectral studies.

Keywords *Schisandra propinqua*, schisandraceae, triterpenoid lactone

Introduction

Schisandra propinqua (Wall.) Hook. f. et Thoms (Schisandraceae) is a plant indigenous to Yunnan, China and used in folk medicine as a substitute of Wu-Wei-Zi (the seeds of *Schisandra chinensis* (Turcz.) Baill),

a famous traditional Chinese medicine for over 2000 years as tonic and sedative.¹ It has been reported that a herbal medicine preparation in which the stems and roots of *S. propinqua* are a major component, was used for treatment of lung carcinoma in several hospitals in Yunnan, and that the water extract of the stems and roots of *S. propinqua* showed activity against Lewis lung cancer in animal test.² Literature survey showed that only anwuweizonic acid and manwuweizic acid had been isolated from the plant.³ A systematic study on the dried stems has resulted in the isolation of a minor novel triterpenoid lactone, schiprolactone A along with schisanlactones A and B. Their structures were elucidated by spectral studies as shown in Fig. 1.

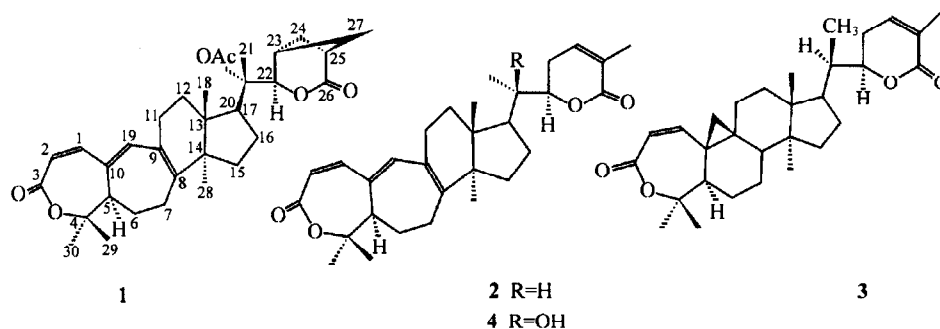


Fig. 1 Structure of schiprolactone A (1), schisanlactones A (2), B (3) and C (4).

Results and discussion

EtOAc soluble fractions of the stems of *S. propinqua* were subjected to repeated column chromatography

on silica gel, followed by preparative TLC to yield schiprolactone A (1), schisanlactones A (2) and B (3).

Schiprolactone A (1), a white amorphous powder,

has the molecular formula $C_{32}H_{42}O_6$ determined by HRMS. The 1H NMR (Table 1), ^{13}C NMR (Table 2) and DEPT spectra revealed the presence of five methyls, eight methylenes, eight methines and nine quaternary carbons besides an acetyl group (δ 2.11, s, 3H; 169.7s, 21.6q), indicating that **1** was an acetylated triterpenoid. Carbon atom multiplicities were assigned by a DEPT experiment. The ^{13}C NMR spectrum showed carbonyl carbons at δ 167.2s and 170.1s and oxygenated carbons at δ 80.4s and 84.9d, suggesting **1** possessed one tertiary and one secondary lactone rings. Since a series of 3,4-*sec*-lanosten-3, 26-dioic acids and lactones have been discovered from plants of Schisandraceae,^{4,7} the two lactone rings of **1** might be in the same positions. The 1H NMR and ^{13}C NMR spectra

displayed three double bonds (δ 6.65, d, $J = 12.3$ Hz, 1H, H-1; δ 5.59, d, $J = 12.3$ Hz, 1H, H-2; δ 6.20, s, 1H, H-19 and δ 143.4d, C-1; 117.7d, C-2; 150.8s, C-8; 128.3s, C-9; 139.6s, C-10; 143.7d, C-19), which were almost the same as those in schisanlactones A (**2**) and C (**4**) previously isolated from the same genus.^{6,7} Thus **1** appeared to possess the same 3,4-*sec*-9,19-*cyclo*-lanostene skeleton as that in **2** and **4**, which was confirmed by correlations between H-1 and a carbonyl (δ 167.2s, C-3), two methyls (δ 1.51, 1.38, s, each 3H, CH_3 -29, 30) and the oxygenated carbon (δ 80.4s, C-4), and H-5 (δ 2.50, m, 1H) and C-1, C-10 and C-19 in HMBC spectrum (Table 3), and no cyclopropane ring in 1H NMR and ^{13}C NMR spectra.

Table 1 1H NMR data of compounds **1**–**3** in $CDCl_3$

H	1	2	3
1	6.65(d, 12.3 Hz)	6.65(d, 12.1 Hz)	6.12(d, 12.7 Hz)
2	5.79(d, 12.3 Hz)	5.79(d, 12.1 Hz)	5.93(d, 12.7 Hz)
5	2.48–2.51(m)	2.46–2.49(m)	2.39–2.41(m)
6	1.42–1.44(m), 1.66–1.70(m)		1.85–1.88(m), 0.79–0.82(m)
7	1.08–1.11(m), 2.09–2.11(m)		
11	1.93–1.96(m), 2.08–2.11(m) (overlap)		2.03–2.06(m)
12	1.59–1.62(m), 1.73–1.77(m)		
15	1.33–1.36(m), 1.99–2.01(m)		
16	1.60–1.64(m), 1.98–2.01(m) (overlap)		
17	1.54–1.56(m)		
18	0.74(3H, s)	0.75(3H, s)	0.96(3H, s)
19	6.20(s)	6.22(s)	1.21(d, 5.1 Hz), 1.02(d, 5.1 Hz)
20			2.03–2.07 (m) (overlap)
21	1.70 (3H, s)	1.02(3H, s)	0.95(3H, d, 6.1 Hz)
22	4.55(s)	4.47(dt, 13.1, 3.2 Hz)	4.45(dt, 13.1, 3.0 Hz)
23	2.93(t like)		2.38–2.42(m), 2.03–2.07(m) (overlap)
24	1.82–1.85(m), 2.11–2.13(m)	6.60(br d, 5.7 Hz)	6.59(br d, 6.5 Hz)
25	2.48–2.52(m) (overlap)		
27	1.82–1.86(m), 2.10–2.13(m) (overlap)	1.91(3H, s)	1.90(3H, s)
28	1.01(3H, s)	1.05(3H, s)	0.87(3H, s)
29	1.51(3H, s)	1.52(3H, s)	1.36(3H, s)
30	1.38(3H, s)	1.39(3H, s)	1.34(3H, s)
COCH ₃	2.11(3H, s)		

Table 2 ^{13}C NMR data of compounds **1** and **2** in CDCl_3

C	1	2	C	1	2
1	143.4d	143.3d	17	48.5d	46.1d
2	117.7d	117.5d	18	17.4q	15.7q
3	167.2s	167.0s	19	143.7d	143.7d
4	80.4s	80.2s	20	82.3s	39.4d
5	49.1d	49.0d	21	25.4q	13.7q
6	33.8t	30.9t	22	84.9d	80.2d
7	27.9t	26.7t	23	45.0d	23.5t
8	150.8s	150.5s	24	32.4t	139.2d
9	128.3s	128.9s	25	48.0d	128.2s
10	139.6s	139.4s	26	170.1s	166.3s
11	26.6s	27.9t	27	32.4t	16.9q
12	30.2t	30.1t	28	27.2q	27.3q
13	44.9s	44.8s	29	26.2q	26.2q
14	51.6s	51.6s	30	29.3q	29.1q
15	31.1t	30.1t	CH_3CO	169,7s	
16	27.6t	26.7t		21.6q	

Table 3 HMBC correlations of compound **1**

H	C	H	C
1	3,5,19	22	23,24,26
2	3,10	23	20,21,22,25
18	12,13,17	28	8,13,14,15
19	1,5,8,11	29	4,5,30
21	20	30	4,5,29

The downfield shifts of the NMR signals of **1** for C-20 (δ 82.3s), C-21 (δ 25.4q) and H-21 (δ 1.70, s, 3H), compared with those of **4** (δ 75.4s, C-20; 21.2q, C-21; 1.32, s, 3H, H-21), revealed the presence of an acetyl group at C-20, which was further confirmed by correlation between H-21 and C-20 in HMBC spectrum. Another lactone ring was assigned to the side chain due to the presence of a mass spectral fragment at m/z 111 and the results of ^1H - ^1H COSY and HMBC spectra. The saturated carbonyl carbon (δ 170.1s) and the deficiency of alkenyl proton and methyl group suggested that **1** had a side chain of saturated δ -lactone instead of the common α -methyl- α , β -unsaturated δ -lactone. The signal at δ 4.55 (s, 1H, H-22) became a singlet compared with that of **4** (δ 4.31, dd, $J = 12.8, 3.7$ Hz, 1H),⁷ suggesting only one hydrogen at C-23. Thus, a bond appeared to be formed between C-23 and C-27, while in **4** there was an alkenyl methyl group. HMBC spectrum of **1** confirmed this deduction by exhibiting couplings between H-23 (δ 2.93, t, 1H) and C-20 (δ 82.3s), C-22 (δ 84.9d) and C-25 (δ

48.0d), and between H-22 (δ 4.55, s, 1H) and C-26 (δ 170.1s), C-23 (δ 45.0d) and C-24 (C-27) (δ 32.6t).

The stereochemistry of **1** was determined by 2D NOESY spectrum. CH_3 -18 showed cross peaks with CH_3 -21, as well as H-29, indicating that CH_3 -18 and CH_3 -21 should be in *syn*- and β -positions. Thus, the acetyl group at C-20 should be in α -position. Cross peak between the acetyl group and H-22, showing that H-22 had α -configuration. Correlations between H-17 and CH_3 -28 and H-22, H-5 and CH_3 -30, indicated H-17 and H-5 also had α -configuration. As the bridge cyclic system is rigid, one 6-membered cycle can have the chair conformation, and the other chooses boat. On the above analysis, the structure of **1** was thus determined as shown in Fig. 1. It was a triterpenoid lactone with a new side chain skeleton. This kind of 4- and 6-membered bi-cycles have ever been found to exist in pinene derivatives.⁸

The structures of schisanlactones A (**2**) and B (**3**) were characterized by various spectral studies and comparison with the literature.⁵⁻⁷ Compounds **2** and **3** were first discovered in *S. Propinqua*.

Experimental

General

IR spectra were recorded as KBr pellets on a Perkin-Elmer 599B spectrophotometer. MS were determined on a Varian Mat-711 mass spectrometer. NMR spectra were measured on a Bruker AM-400 spectrometer with TMS as internal standard and CDCl_3 as solvent. 2D-NMR spectra were performed on a DR \times 500 spectrometer. CD was recorded with a Jasco J-500A spectropolarimeter. 200–300 mesh silica gel was used for CC and silica gel GF₂₅₄ for TLC.

Plant material

The stems of *Schisandra propinqua* (Wall.) Hook. f. et Thoms were collected from Yunnan province, China in April 1997 and identified by Mr. Bangtao Yue, a botanist of Tonghai Institute of Drugs Control in Yunnan, China, where a voucher specimen (No. 9703012) was deposited.

Extraction and isolation

The dried powdered stems of *Schisandra propinqua* (10 kg) were extracted exhaustively with 95% EtOH. The EtOH extract was evaporated in vacuum to yield a dark brown residue. H₂O was added to the residue, and the resulting solution was extracted with petroleum ether and EtOAc successively. The EtOAc extract was concentrated to give a brown mass, which was applied to a silica gel column, eluting with petroleum ether containing increasing amounts of Me₂CO. The fractions obtained from petroleum ether-acetone (10:1) elution were combined and subjected to repeated CC and preparative TLC to yield schiprolactone A (**1**, 6 mg), schisanlactone A (**2**, 15 mg) and schisanlactone B (**3**, 5 mg) respectively.

Schiprolactone A (**1**), white amorphous powder; EIMS m/z : 522[M⁺](35), 504(48), 489(50), 464(58), 231(57), 197(32), 173(100), 155(26) and 111(7). HRMS m/z : 522.2978 (Calcd. 522.2981). ¹H NMR: see Table 1. ¹³C NMR: see Table 2.

Schisanlactone A (**2**), colorless needles. mp: 220—221 °C. ν_{\max} (KBr): 1716, 1674, 1600, 1570, 1380 and 1371 cm⁻¹. EIMS m/z : 464[M⁺](10), 446(60), 431(27), 391(10), 347(17), 252(18), 231(23), 187(28), 173(74), 157(21), 145(48), 139(10), 111(33) and 95(100). CD (MeOH; c 0.00875): $\Delta\epsilon_{235} + 7.07$, $\Delta\epsilon_{270} - 6.43$, $\Delta\epsilon_{325} + 6.27$.

¹H NMR: see Table 1. ¹³C NMR: see Table 2.

Schisanlactone B (**3**), white amorphous powder, ν_{\max} (KBr): 1712, 1676, 1392 and 1385 cm⁻¹. EIMS m/z : 466[M⁺](12), 448(51), 423(85), 405(28), 367(67), 327(20), 283(24), 233(45), 215(52), 191(80), 139(23), 111(50) and 95(100). CD (MeOH; c 0.00530): $\Delta\epsilon_{235} - 12.26$, $\Delta\epsilon_{265} + 12.12$. ¹H NMR: see Table 1.

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