云 南 植 物 研 究 2008, 30 (1): 121～124
Acta Botanica Yunnanica DOI: 10.3724/SP. J. 1143. 2008. 07113

锥序蜜心果中的三萜成分

汪 琼, 鞠 鹏, 王易芬, 罗士德*
(中国科学院昆明植物研究所植物化学与西部植物资源持续利用国家重点实验室, 云南 昆明 650204)

摘要: 从水东哥科植物锥序蜜心果 (*Saurauia napaulensis*) 中分离得到 8 个三萜类化合物, 其中一个为新的三萜, 鉴定其结构为 2α, 3α, 24-三羟基-12-熊果烯-23-醛-28-酸。

关键词: 锥序蜜心果; 水东哥科; 三萜
中图分类号: Q 946 **文献标识码**: A **文章编号**: 0253 - 2700 (2008) 01 - 121 - 04

Triterpenoids from *Saurauia napaulensis* (Saurauiaceae)

WANG Qiong, JU Peng, WANG Yi-Fen, LUO Shi-De*
(*State Key Laboratory of Phytochemistry and Plant Resources in West China*, *Kunming Institute of Botany*, *Chinese Academy of Sciences*, Kunming, 650204, China)

Abstract: A new triterpenoid and seven known compounds were isolated from ethyl acetate soluble fraction of *Saurauia napaulensis*. The new structure was elucidated as 2α, 3α, 24-trihydroxy-12-ursene-23-al-28-oic acid by spectral methods.

Key words: *Saurauia napaulensis*; Saurauiaceae; Triterpenoids

Saurauia napaulensis, an endemic species belonging to the family of Saurauiaceae, is distributed in Xishuangbanna of Yunnan province (Feng *et al.*, 1984) (Xu, 2002). Its roots were used in tradition Chinese medicine for the treatment of fracture, cold cough. However, no reports have been found about the constituents of this plant to date. During the investigation of the constituents of *Saurauia napaulensis*, eight triterpenoids, including a new one, were isolated. Seven known triterpenoids were identified as ursolic acid (**2**) (Zhang *et al.*, 2001), 2α-hydroxyursolic acid (**3**) (Guo *et al.*, 2003), 2α, 19α-dihydroxyursolic acid (**4**) (Tsutomu *et al.*, 1987), 2α, 3α, 24-trihydroxy-12-oleanen-28-oic acid (**5**) (Raja *et al.*, 1990), 2α-hydroxy-3β-(trans-p-coumaroyloxy)-urs-12-en-28-oic acid (**6**) (Haberlein *et al.*, 1994), Rosamultin (2α, 19α-dihydroxyursolic acid (28-1) β-D-glucoside) (**7**) (Isao *et al.*, 1988), niga-ichigoside F1 (**8**) (Luo *et al.*, 2003), respectively. This paper dealt with the isolation and elucidation of the new compound, 2α, 3α, 24-trihydroxy-12-ursene-23-al-28-oic acid.

Results and Discussion

Compound **1**, was isolated as white amorphous powder, and its molecular formula was established as $C_{30}H_{48}O_6$ based on the negative HRFABMS at m/z 501.3228 ([M-H]$^-$, calc. 501.3216), in accord with seven degrees of unsaturation. IR spectrum showed the following characteristic signals, OH (3 424 cm^{-1}), C=O (1 727 cm^{-1}) and C=C (1 604 cm^{-1}), suggestion the presence of a carbonyl group in the structure.

The ^{1}H-NMR spectrum of **1** show signals attributed to three tertiary methyl groups (δ_H 1.02, 0.92, 0.90), two secondary methyl groups (δ_H 1.11, 1.10), an oxymethylene group (δ_H 4.36, 4.28), and

* Author for correspondence; E-mail: luosd@mail.kib.ac.cn
Received date: 2007 - 06 - 01, Accepted date: 2007 - 08 - 20
作者简介: 汪琼 (1974 -) 女, 博士研究生, 主要从事植物化学方面的研究。Tel: 0871 - 5223097

an olefin proton (δ_H 5.09). The ^{13}C-NMR and DEPT spectra displayed 30 carbon signals, which consisted of one aldehyde group (δ_C 207.7), one trisubstituted double bond (δ_C 125.4, 139.4), one carboxylic group (δ_C 178.3), one oxymethylene (δ_C 62.0), five methyl groups, eight methylenes, seven methines (including two oxy-bearing methines), and five quaternary carbons. These spectral data indicated that compound **1** was an ursane-type triterpene (Zhang *et al.*, 2001).

In the HMBC spectrum, three hydroxyl groups at the C-2, C-3 and C-24 position were confirmed by the correlations between the signal at δ 4.37 (ddd, *J* = 11.2, 3.8, 2.4 Hz, H-2) with δ 71.7 (d, C-3), δ 59.5 (s, C-4), the signal at δ 4.88 (d, *J* = 2.4 Hz, H-3) with δ 66.4 (d, C-2), δ 59.5 (s, C-4), δ 43.3 (d, C-5), and the signal at δ 4.36 (d, *J* = 11.2 Hz), δ 4.28 (d, *J* = 11.2 Hz) / (H-24) with δ 59.5 (s, C-4), δ 207.7 (d, C-23) and δ 43.3 (d, C-5).

The coupling constants between H-2 and H_2-1 were found to be 11.2 and 3.8 Hz, corresponding to a diaxial and an axial-equatorial coupling, respectively. Thus, H-2 was presumed to be axially oriented. In the NOESY spectrum, both the signals of H-2 and H-3 showed correlations with those of H_3-24 and H_3-25, confirming H-2 and H-3 to be β-oriented. However the NMR spectra of **1**, comparing with those of 2α, 3α, 24-trihydroxy-12-ursen-28-oic acid, lacked a methyl singlet (Me-23) and contained a signal for a aldehyde at δ 10.4 in the ^{1}H NMR, which made C-3 shift from 74.3 ppm down to 71.7 ppm, C-4 shift from 43.3 ppm up to 59.5 ppm (Zhang *et al.*, 2001), deducing that Me-23 was replaced by one aldehyde. At the same time, the oxymethylene signals at C-24 correlated to the H_3-25, and H-3 proton signal (see figure 1 NOESY), indicating CH_2OH was β-orient and CHO was α-orient. Accordingly, compound **1** was established as 2α, 3α, 24-trihydroxy-12-ursen-23-al-28-oic acid.

Experimental

General experimental procedures The IR spectrum was measured on a Perkin-Elmer 577 spectrophotometer. FABMS were performed on a VG AutoSpec-3000 spectrometer. Bruker Am-400 and DRX-500 instruments were used to record ^{1}H NMR and 2D NMR (400 MHz), and ^{13}C NMR. C_5D_5N was solvent and the internal standard at room temperature. Silica gel (200-300 mesh) for column chromatography and silica gel plate (GF-254) for thin-layer chromatography were the products of Qingdao Haiyang Chemical Group Co., Qingdao, China.

Plant material The original plant *Saurauia napaulensis* was collected in Xishuangbanna of Yunnan province in September 2005, and indentified by Zhangshuncheng. A voucher specimen has been deposited in the laboratory of Phytochemistry, Kunming Institute of Botany (No. 2005061010), the Chinese Academy of Sciences, Kunming, China.

Table 1 ^{1}H and ^{13}C NMR spectral data of **1** (C_5D_5N, ppm)

No	δ_C	δ_H	HMBC (H→C) (selected)	No	δ_C	δ_H	HMBC (H→C) (selected)
1	42.6(t)	1.98 (ddd, 11.2, 6.6, 3.8), 1.78(m, 1H)	C(2), C(3)	16	28.6(t)	2.2 (m, 2H)	
2	66.4(d)	4.37 (ddd, 11.2, 3.8, 2.4)	C(1), C(3), C(4)	17	49.7(s)	—	—
				18	53.6(d)	2.57 (d, 11.4)	C(12), C(13), C(28)
				19	39.4(d)	1.34 (m)	C(29), C(20)
3	71.7(d)	4.88 (d, 2.4)	C(1), C(2), C(4), C(5)	20	39.4(d)	1.00 (m)	C(19), C(21), C(30)
4	59.5(s)	—	—	21	30.0(t)	1.90 (m, 2H)	C(20), C(22)
5	43.3(d)	2.51 (d, 11.0)	C(4), C(6), C(23)	22	37.5(t)	1.95 (m, 2H)	C(21), C(17)
6	21.1(t)	1.90 (m), 1.75 (m)	C(5), C(7)	23	207.7(d)	10.40 (s)	C(4)
7	33.8(t)	1.86 (m, 2H)	C(6), C(8)	24	62.0(t)	4.36 (d, 11.2), 4.28 (d, 11.2)	C(4), C(23)
8	40.3(s)	—	—				
9	48.1(d)	2.50 (m)	C(8), C(10)	25	17.6(q)	0.92 (s)	C(1), C(9)
10	38.3(s)	—	—	26	17.5(q)	1.05 (s)	C(9)
11	23.9(t)		C(9), C(13)	27	21.4(q)	0.90 (s)	C(14)
12	125.4(d)	5.09 (br s, 1H)		28	178.3(s)	—	—
13	139.4(s)	—	—	29	23.8(q)	1.11 (d, 3.6)	C(30), C(18)
14	42.5(s)	—	—	30	17.1(q)	1.10 (d, 3.6)	C(29), C(21)
15	29.7(t)	1.28 (m, 2H)					

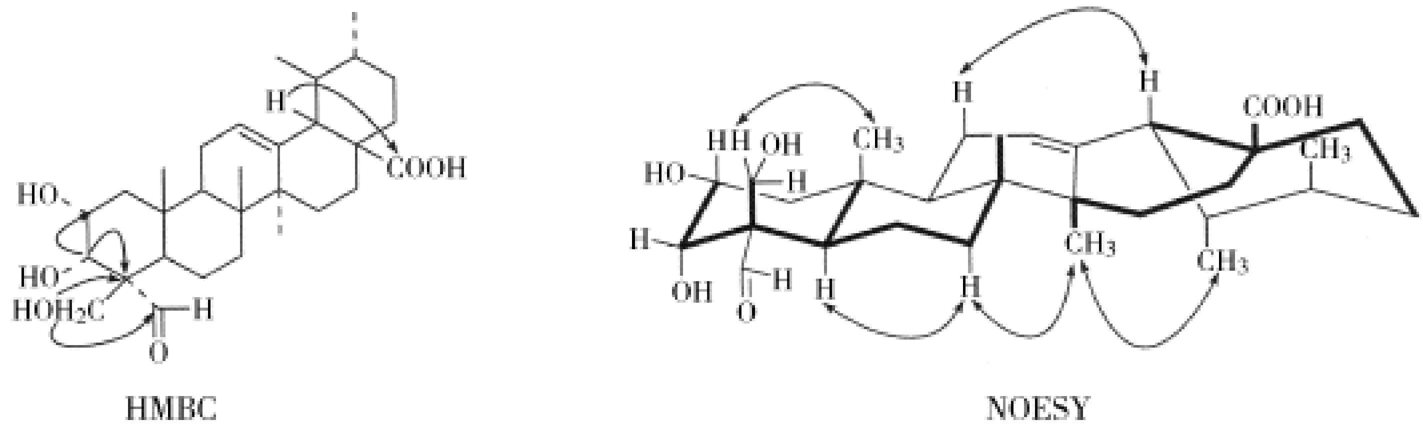

Fig. 1 The key HMBC and NOESY of **1**

Extraction and isolation The air-dried and powdered aerial parts (5.0 kg) were extracted 3 times with 70% MeOH under reflux (3×3.0 L) for 4, 3, 3 h, respectively. After concentrating of the combined extracts, the residue was suspended in water and then extracted with petroleum ether, EtOAc, and BuOH. The EtOAc soluble part (108 g) was subjected to column chromatography (CC) over silica gel eluting with chloroform/methanol (1∶0-0∶1) to give fractions Ⅰ-Ⅵ, using MCI to remove chlorophyll of Fraction Ⅱ (22 g), and subjected to CC on silica gel eluting with chloroform/acetone (1∶0-0∶1), then repeatedly subjected to Sephadex LH-20 and reversed-phase silica gel (RP-18) eluted with H_2O/MeOH (3∶7-0∶1) to give compounds **1** (13 mg), **2** (22 mg), **3** (21 mg), **4** (27 mg), **5** (14 mg), **6** (19 mg), Fraction Ⅳ (2.7 g) subjected to CC on silica gel eluting with $CHCl_3$/CH_3COCH_3 (1∶0-0∶1) and get fraction B1-B6, B2 (378 mg) repeatedly subjected to Sephadex LH-20 and RP-18 eluted with H_2O/MeOH (4∶6-0∶1), and get compound **7** (14 mg), **8** (16 mg).

Compound 1, white amorphous powder, IR ν_{max}^{KBr} cm^{-1}: 3424, 1727, 1604, 1507, 1270, 671, Negative FAB-MS *m/z* (%): 501 (100, $[M-H]^+$), 473 (10), 453 (15), 325 (6). HR-FAB-MS *m/z*: 501.3228 ($[M-H]^-$, calc. 501.3216). ^1H- and ^{13}C-NMR spectral data see table.

Compound 2, white powder, $C_{30}H_{48}O_3$, Negative FAB-MS *m/z* (%): 455 (100), 169 (1), 80 (1), ^1H-NMR (500 MHz, C_5D_5N): δ_H 5.27 (br s, 1H, H-12), 4.38 (d, J = 7.8 Hz, 1H, H-3), 1.13 (d, J = 6.3 Hz, 3H, H-29), 1.13 (d, J = 6.2 Hz, 3H, H-30), 1.27, 1.10, 0.89, 0.82, 0.53 (s, each 3H), ^{13}C-NMR (125 MHz, C_5D_5N): δ_C 37.5 (t, C-1), 28.2 (t, C-2), 78.3 (d, C-3), 39.2 (s, C-4), 53.7 (d, C-5), 18.9 (t, C-6), 33.7 (t, C-7), 40.1 (s, C-8), 48.2 (d, C-9), 37.4 (s, C-10), 23.7 (t, C-11), 125.8 (d, C-12), 139.4 (s, C-13), 42.6 (s, C-14), 28.8 (t, C-15), 25.0 (t, C-16), 48.2 (s, C-17), 56.0 (d, C-18), 39.6 (d, C-19), 39.5 (d, C-20), 31.2 (t, C-21), 39.2 (t, C-22), 28.9 (q, C-23), 14.3 (q, C-24), 15.8 (q, C-25), 16.7 (q, C-26), 24.0 (q, C-27), 180.0 (s, C-28), 21.5 (q, C-29), 17.6 (q, C-30).

Compound 3, white powder, $C_{30}H_{48}O_4$, Negative FAB-MS *m/z* (%): 471 (100), 453 (6), 355 (2), ^1H-NMR (400 MHz, C_5D_5N): δ_H 5.40 (br s, 1H, H-12), 4.30 (d, J = 11.3 Hz, 1H, H-2), 3.78 (br s, 1H, H-3), 0.91 (d, J = 7.7 Hz, 3H, H-29), 0.93 (d, J = 7.7 Hz, 3H, H-30), 1.26, 1.09, 1.02, 0.97, 0.87 (s, each 3H), ^{13}C-NMR (100 MHz, C_5D_5N): δ_C 42.7 (t, C-1), 66.3 (d, C-2), 79.4 (d, C-3), 39.0 (s, C-4), 48.8 (d, C-5), 18.6 (t, C-6), 33.6 (t, C-7), 40.1 (s, C-8), 48.0 (d, C-9), 38.7 (s, C-10), 23.8 (t, C-11), 125.7 (d, C-12), 139.4 (s, C-13), 40.3 (s, C-14), 28.7 (t, C-15), 25.0 (t, C-16), 48.2 (s, C-17), 53.6 (d, C-18), 39.6 (d, C-19), 39.5 (d, C-20), 31.3 (t, C-21), 37.6 (t, C-22), 29.6 (q, C-23), 17.7 (q, C-24), 17.7 (q, C-25), 16.9 (q, C-26), 22.4 (q, C-27), 180.1 (s, C-28), 24.0 (q, C-29), 21.5 (q, C-30).

Compound 4, white powder, $C_{30}H_{48}O_5$, Negative FAB-MS *m/z* (%): 487 (100), 471 (12), 325 (4), ^1H-NMR (500 MHz, C_5D_5N): δ_H 5.57 (br s, 1H, H-12), 4.30 (d, J = 11.1 Hz, 1H, H-2), 3.10 (d, J = 4.3 Hz, 1H, H-3), 1.09 (d, J = 3.7 Hz, 3H, H-30), 1.49, 1.31, 1.25, 1.00, 0.96, 0.88 (s, each 3H), ^{13}C-NMR (125 MHz, C_5D_5N): δ_C 42.9 (t, C-1), 66.1 (d, C-2), 79.4 (d, C-3), 38.8 (s, C-4), 48.8 (d, C-5), 18.6 (t, C-6), 33.7 (t, C-7), 40.6 (s, C-8), 47.7 (d, C-9), 38.7 (s, C-10), 24.1 (t, C-11), 128.1 (d, C-12), 140.0 (s, C-13), 42.2 (s, C-14), 29.3 (t, C-15), 26.4 (t, C-16), 48.3 (s, C-17), 54.6 (d, C-18), 72.7 (s, C-19), 42.4 (d, C-20), 27.0 (t, C-21), 38.5 (t, C-22), 29.4 (q, C-23), 16.8 (q, C-24), 16.7 (q, C-25), 17.3 (q, C-26), 24.7 (q, C-27), 180.6 (s, C-28), 27.1 (q, C-29), 22.3 (q, C-30).

Compound 5, white powder, $C_{30}H_{48}O_5$, Negative FAB-MS *m/z* (%): 487 (100), 455 (2), 247 (2), ^1H-NMR (500 MHz, C_5D_5N): δ_H 5.46 (br s, 1H, H-12), 4.58 (br s, 1H, H-3), 4.44 (d, J = 10.6 Hz, 1H, H-2), 4.10 (d, J = 10.9 Hz, 1H, H-23a), 3.81 (d, J = 10.9 Hz, 1H, H-23b), 3.28 (d, J = 3.3 Hz, 1H, H-18), 1.18, 1.12, 1.02, 1.01, 1.00, 0.97 (s, each 3H), [13] C-NMR (125 MHz, C_5D_5N): δ_C 43.1 (t, C-1), 66.3 (d, C-2), 74.3 (d, C-3), 45.2 (s, C-4), 48.3 (d, C-5), 19.0 (t, C-6), 33.8 (t, C-7), 40.1 (s, C-8), 49.6 (d, C-9), 38.7 (s, C-10), 23.8 (t, C-11), 122.5 (d, C-12), 144.9 (s, C-13), 42.0 (s, C-14), 28.3 (t, C-15), 24.1 (t, C-16), 46.5 (s, C-17), 42.2 (d, C-18), 46.7 (t, C-19), 34.3 (s, C-20), 33.7 (t, C-21), 33.2 (t, C-22), 65.3 (t, C-23), 14.4 (q, C-24), 17.4 (q, C-25), 17.1 (q, C-26), 26.1 (q, C-27), 180.2 (s, C-28), 33.2 (q, C-29), 23.8 (q, C-30).

Compound 6, white powder, $C_{39}H_{54}O_6$, positive FAB-MS m/z (%): 619 (62), 437 (74), 409 (31), 189 (53), [1] H-NMR (400 MHz, C_5D_5N): δ_H 8.01 (d, 1H, J = 15.9 Hz, H-α), 7.20 (d, 1H, J = 8.8 Hz, H-2′, 6′), 7.16 (d, 1H, J = 8.8 Hz, H-3′, 5′), 6.69 (d, 1H, J = 15.9 Hz, H-β), 5.44 (d, 1H, J = 3.7 Hz, H-12), 4.37 (m, 1H, H-3), 3.59 (br s, 1H, H-2), 1.16, 1.02, 1.00, 0.98, 0.97, 0.95, 0.94 (s, each 3H), [13] C-NMR (100 MHz, C_5D_5N): δ_C 48.6 (t, C-1), 66.5 (d, C-2), 85.1 (d, C-3), 39.9 (s, C-4), 55.6(d, C-5), 18.7 (t, C-6), 33.4 (t, C-7), 40.1 (s, C-8), 48.0 (d, C-9), 38.3 (s, C-10), 23.8 (t, C-11), 125.5 (d, C-12), 139.4 (s, C-13), 42.6 (s, C-14), 28.7 (t, C-15), 24.9 (t, C-16), 48.1 (s, C-17), 53.6 (d, C-18), 39.5 (d, C-19), 39.5 (d, C-20), 31.1 (t, C-21), 37.5 (t, C-22), 29.1 (q, C-23), 17.0 (q, C-24), 17.5 (q, C-25), 17.6 (q, C-26), 24.0 (q, C-27), 180.1 (s, C-28), 21.5 (q, C-29), 18.3 (q, C-30), 168.0 (s, C-γ), 116.1 (d, C-β), 144.9 (d, C-α), 126.3 (s, C-1′), 130.7 (d, C-2′), 116.9 (d, C-3′), 161.4 (s, C-4′), 116.9 (d, C-5′), 130.7 (d, C-6′).

Compound 7, white powder, $C_{36}H_{58}O_{10}$, Negative FAB-MS m/z (%): 649 (28), 487 (90), 273 (48), 163 (35), 87 (22), [1] H-NMR (400 MHz, C_5D_5N): δ_H 6.30 (d, 1H, J = 8.1 Hz, H-1′), 5.52 (br s, 1H, H-12), 4.47 (m, 1H), 4.42 (m, 1H), 4.38 (m, 1H), 4.36 (m, 1H), 4.33 (m, 1H), 4.32 (m, 1H), 4.08 (m, 1H, H-3), 3.37 (d, J = 9.3 Hz, 1H, H-2), 2.92 (s, 1H, H-18), 1.07 (d, J = 5.8 Hz, 3H, H-30), 1.65, 1.19, 1.06, 1.04, 1.03, 1.00 (s, each 3H), [13] C-NMR (100 MHz, C_5D_5N): δ_C 48.1 (t, C-1), 68.7 (d, C-2), 83.9 (d, C-3), 39.9 (s, C-4), 56.0 (d, C-5), 19.1 (t, C-6), 33.5 (t, C-7), 40.7 (s, C-8), 47.1 (d, C-9), 38.5 (s, C-10), 24.2 (t, C-11), 128.4 (d, C-12), 139.3 (s, C-13), 42.2 (s, C-14), 29.3 (t, C-15), 26.7 (t, C-16), 48.7 (s, C-17), 54.5 (d, C-18), 72.7 (s, C-19), 42.2 (d, C-20), 26.0 (t, C-21), 37.8 (t, C-22), 29.4 (q, C-23), 17.0 (q, C-24), 16.8 (q, C-25), 17.5 (q, C-26), 24.6 (q, C-27), 177.1 (s, C-28), 27.0 (q, C-29), 17.7 (q, C-30), 95.9 (d, C-1′), 74.1 (d, C-2′), 79.0 (d, C-3′), 71.2 (d, C-4′), 79.4 (d, C-5′), 62.3 (t, C-6′).

Compound 8, white powder, $C_{36}H_{58}O_{11}$, Negative FAB-MS m/z (%): 665 (23), 503 (100), 325 (22), 119 (6.5), [1] H-NMR (400 MHz, C_5D_5N): δ_H 6.30 (d, 1H, J = 8.1 Hz, H-1′), 5.51 (br s, 1H, H-12), 3.73 (d, J = 9.7 Hz, H-3α), 3.53 (d, J = 9.2 Hz, H-2β), 4.47 (m, 1H), 4.43 (m, 1H), 4.39 (m, 1H), 4.34 (m, 1H), 4.30 (m, 1H), 4.06 (m, 1H), 4.05 (m, 1H), 2.91 (s, 1H, H-18), 1.65, 1.58, 1.37, 1.16, 1.02 (s, each 3H), 1.05 (d, J = 6.5 Hz, 3H, H-30), [13] C-NMR (100 MHz, C_5D_5N): δ_C 48.0 (t, C-1), 68.7 (d, C-2), 85.8 (d, C-3), 44.0 (s, C-4), 56.6 (d, C-5), 19.5 (t, C-6), 33.8 (t, C-7), 40.6 (s, C-8), 48.0 (d, C-9), 38.3 (s, C-10), 24.4 (t, C-11), 128.3 (d, C-12), 139.3 (s, C-13), 42.1 (s, C-14), 29.2 (t, C-15), 26.7 (t, C-16), 48.7 (s, C-17), 54.4 (d, C-18), 72.7 (s, C-19), 42.2 (d, C-20), 26.1 (t, C-21), 37.7 (t, C-22), 68.7 (t, C-23), 24.6 (q, C-24), 17.5 (q, C-25), 17.3 (q, C-26), 24.2 (q, C-27), 177.0 (s, C-28), 27.0 (q, C-29), 16.7 (q, C-30), 95.9 (d, C-1′), 74.1 (d, C-2′), 79.0 (d, C-3′), 71.2 (d, C-4′), 79.3 (d, C-5′), 62.3 (t, C-6′).

Acknowledgements: The author are grateful to the members of the Analytical Group in State Key Laboratory of Phytochemistry and Plant Resource in West China, Kunming Institute of Botany, for measurement of all spectra.

Reference:

Feng GM, Xu XH, 1984. Flora of China, Science press, **49** (2): 296

Guo J, Liu LH, Mei SX *et al.*, 2003. Studies on chemical constituents from the stem of schisandra sphaerandra [J]. *China J Chin Mat Med*, **28** (2): 138—140

Haberlein H, Tschiersch KP, 1994. Triterpenoids from *Viburnum suspensum* [J]. *Phytochemistry*, **35** (3): 765—768

Isao KO, Naosuke BB, Yumiko O *et al.*, 1988. Triterpenoid from *Agrimonia pilosa* [J]. *Phytochemistry*, **27** (1): 297—299

Luo SZ, Guan JF, Huang ZX *et al.*, 2003. Chemical constituents from the aerial parts of *Cyphotheca montana* [J]. *Nat Product Res Develop*, **15** (1): 18—20

Raja Rao KV, Rao LJM, Prakasa Rao NS, 1990. An A-ring contracted triterpenoid from *Hyptis suaveolens* [J]. *Phytochemistry*, **29** (4): 1326—1329

Tsutomu F, Yutaka O, Chisato H, 1987. Triterpenoids from *Eucalyptus perriniana* cultured cells [J]. *Phytochemistry*, **26** (3): 715—719

Tian J, Xiao ZY, Chen YY *et al.*, 2000. Structure identification of vulgarsaponin A [J]. *Acta Pharm Sin*, **35** (1): 29—31

Xu SJ, 2002. The distribution of the sterculiaceous plants in China [J]. *Guihaia*, **22** (6): 494—498

Zhang XR, Peng SL, Wang MK *et al.*, 2001. Triterpenoids from *Clematoclethra scandens* [J]. *Acta Pharm Sin*, **36** (12): 910—912