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DITERPENOIDS FROM *RABDOSIA LIHSIENENSIS*

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Key Word Index—*Rabdosia lihsienensis*; Labiatae; kaurane diterpenoid; labdane diterpenoid; lihsienin A.

Abstract—A new diterpenoid, lihsienin A, along with the known adenolin D, lasiodonin, parvifoliside and 8β,13β-oxidoeperu-14-en-18-oic-acid, were isolated from *Rabdosia lihsienensis* and the structures determined by spectroscopic analysis. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

Rabdosia lihsienensis C. Y. Wu et H. W. Li is distributed in the west of Sichuan Province of China [1]. So far, the chemical constituents of this plant has never been reported. We now report on the isolation and structure elucidation of a new diterpenoid, lihsienin A (**1**), along with the known diterpenoids, adenolin D (**2**) [2], lasiodonin (**3**) [3, 4], parvifoliside (**4**) [5] and 8β,13β-oxidoeperu-14-en-18-oic-acid (**5**) [6]. The labdane diterpenoid (**5**) was isolated from *Rabdosia* species for the first time.

RESULTS AND DISCUSSION

Lihsienin A (**1**) was assigned the molecular formula $C_{24}H_{36}O_7$ (437.2589 $[M+1]^+$, calcd 437.2539) by positive FAB HRMS. Its IR spectra showed the presence of hydroxy and ester groups (3443 and 1721 cm^{-1}). The ^1H NMR, ^{13}C NMR and DEPT spectra of **1** (Experimental and Table 1), indicated the presence of two tertiary methyls, seven methylenes (including two oxygenated methylenes), six methines (including two oxygenated methines), three quaternary carbons, a hemiacetal carbon, a ketonic carbon, as well as an acetoxy group [δ 2.00 (3H, *s*); δ 170.7 (*s*), 21.7 (*q*)] and an ethoxy group [δ 1.09 (3H, *t*, $J = 7$ Hz), 3.36 (2H, *q*, $J = 7$ Hz); δ 15.4 (*q*), 66.7 (*t*)]. These data indicated that **1** had an ent-7α,20-epoxy-kauran-15-one skeleton. The ^1H NMR, ^{13}C NMR and DEPT spectra of **1** were very similar to those of adenolin D (**2**) [2], except for replacement of a methoxy group of **2** with an ethoxy group in **1**. The 2D NMR spectra including H-H COSY, C-H COSY and COLOC of **1**, allowed assignment of all proton and carbon signals (Experimental and Table 1). A doublet of the signal of δ 4.22 (H-6α) coupled with a doublet signal at δ 1.45 (H-5β). A triplet signal at δ 5.41 (H-11β) coupled with a multiplet signal at δ 2.11 (H-12β), δ 1.95 (H-12α) and 1.77 (H-9β). The H-12α signal coupled with a multiplet signal at δ 2.11 (H-12β), which coupled with a multiplet signal δ 2.77 (H-13α). The H-13α signal coupled with a doublet of the signal at δ 2.66 (H-14β) and a multiplet signal at δ 3.00 (H-16α), which coupled with two doublet of doublet signals at δ 3.76 and 3.62 (H_2-17). A quadruplet signal at δ 3.36 (H_2-OCH_2CH_3) coupled with a triplet signal at δ 1.09 (H_3-OCH_2CH_3). The coupling of two H-20 protons (δ 4.50 and 4.19), two H-17 protons (δ 3.76 and 3.62) and two H-14 protons (δ 3.05 and 2.66), was also observed. In the COLOC spectra of **1**, δ 61.6 (C-5) and 96.0 (C-7) both correlated with δ 4.22 (H-6α), δ 74.8 (C-6) correlated with δ 1.45 (H-5β), δ 37.1 (C-10) correlated with δ 1.77 (H-9β), δ 53.4 (C-9) correlated with δ 5.41 (H-11β), and δ 57.6 (C-16) correlated with δ 1.95 (H-12α) and δ 2.66 (H-14β). The relative configuration of the ethoxymethyl group was assigned the β-orientation based on the upfield shift of the ^{13}C NMR signal for C-12 due to the γ-gauche shielding effect between CH_3CH_2O-17 and H-12β. The above data established that lihsienin A (**1**) was 6β,7β-dihydroxy-11α-acetoxy-16β-ethoxymethyl-ent-7,20-epoxy-kauran-15-one.

EXPERIMENTAL

^1H and ^{13}C NMR: 400 and 100 MHz, respectively; EI-MS: ZAB-HS instrument; FAB-MS: VG Auto Spec 3000 instrument.

Extraction and isolation of the diterpenoids

Dried and finely powdered leaves of *R. lihsienensis* C. Y. Wu et H. W. Li (2.8 kg), collected in 1994 at

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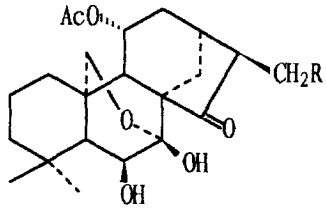

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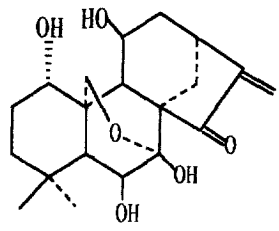
2 R= -OCH_3



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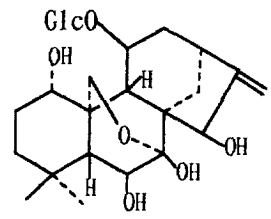

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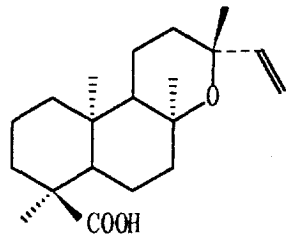

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Table 1. ^{13}C NMR data of compounds **1**–**5** (ppm from int. TMS)

C	1	2	3	4	5	C	1	2	3	4	5
1	30.2 *t*	30.1 *t*	74.3	74.8	38.9 *t*	15	223.5 *s*	222.9 *s*	210.7	75.7	109.7 *t*
2	18.8 *t*	18.5 *t*	28.4	30.5	18.1 *t*	16	57.6 *d*	57.1 *d*	153.8	161.1	33.0 *q*
3	41.6 *t*	41.3 *t*	39.0	39.4	35.0 *t*	17	67.0 *t*	68.9 *t*	115.8	106.4	24.2 *q*
4	34.1 *s*	33.8 *s*	34.3	34.1	47.5 *s*	18	34.2 *q*	34.0 *q*	33.1	22.2	181.0 *s*
5	61.6 *d*	61.2 *d*	57.6	59.2	51.2 *d*	19	22.5 *q*	22.6 *q*	22.6	32.8	16.8 *q*
6	74.8 *d*	74.5 *d*	73.3	74.8	22.9 *t*	20	68.6 *t*	68.3 *t*	64.5	64.7	16.3 *q*
7	96.0 *s*	95.7 *s*	95.7	97.1	43.2 *t*	OAc	170.0 *s*	169.6 *s*			
8	60.4 *s*	60.1 *s*	60.1	53.2	76.0 *s*		21.7 *q*	21.5 *q*		Glc	
9	53.4 *d*	53.0 *d*	61.2	48.7	58.8 *d*	OEt	66.7 *t*			104.5	
10	37.1 *s*	37.0 *s*	42.8	41.8	36.3 *s*		15.4 *q*			74.8	
11	68.9 *d*	68.6 *d*	63.1	70.7	16.1 *t*	OMe		58.6 *q*		79.2	
12	28.5 *t*	28.3 *t*	39.8	41.0	36.3 *t*					71.5	
13	29.1 *d*	28.9 *d*	35.0	37.6	73.4 *s*					78.1	
14	29.7 *t*	29.4 *t*	27.4	28.6	148.3 *d*					62.7	

Maoxian, Sichuan Province, China, were extracted with EtOH at room temp. The EtOH extracts were concd under red. pres. and fractionated by a series of solvent partitions into an EtOAc-soluble fr. The residue (90 g) of this fr. was subjected to CC over silica gel; the column was eluted successively with $CHCl_3$–Me_2CO (1:0–0:1) to yield 100 mg **1**, 5 mg **2**, 300 mg **3**, 230 mg **4** and 200 mg **5**.

Lihsienin A (**1**). Amorphous powder, $[\alpha]_D$ −76.9° (MeOH; *c* 0.09). IR ν_{max}^{KBr} (cm^{-1}): 3441, 3330, 2930, 1722, 1380, 1241, 1050, 1020, 960, 930; FAB (positive) MS *m/z*: 437 $[M+1]^+$; FAB (negative) MS *m/z*: 435

$[M-1]^+$, 405, 393, 377, 361, 347, 59; HR-FAB (positive) MS *m/z*: 437.2589 $[M+1]^+$ (calcd 437.2539); EIMS *m/z*: 436 $[M]^+$, 418, 393, 362, 332, 312, 284, 274, 189, 151, 105, 91, 43; ^{1}H NMR (pyridine-d_5): δ 6.20 (1H, *d*, *J* = 11.1 Hz, 6β-OH), 5.42 (1H, *t*, *J* = 4.4 Hz, 11β-H), 4.50 (1H, *d*, *J* = 9.2 Hz, 20-Ha), 4.22 (1H, *dd*, *J* = 11.1, 6.4 Hz, 6α-H), 4.19 (1H, *d*, *J* = 9.2 Hz, 20-Hb), 3.76 (1H, *dd*, *J* = 10.2, 6.4 Hz, 17-Ha), 3.62 (1H, *dd*, *J* = 10.2, 5.4 Hz, 17-Hb), 3.36 (2H, *q*, *J* = 7 Hz, -OCH_2CH_3), 3.05 (1H, *d*, *J* = 12.3 Hz, 14α-H), 3.00 (1H, *m*, 16α-H), 2.77 (1H, *m*, 13α-H), 2.66 (1H, *dd*, *J* = 12.3, 3 Hz, 14β-H), 2.11 (1H, overlapped, 12β-H), 2.00 (3H, *s*, -OAc), 1.95 (1H, overlapped, 12α-H), 1.77 (1H, *d*, *J* = 5 Hz, 9β-H), 1.48 (1H, *m*, 1α-H), 1.45 (1H, *d*, 5β-H), 1.38 (1H, *m*, 3α-H), 1.37 (2H, *m*, 2-H_2), 1.36 (1H, *m*, 1β-H), 1.30 (1H, *m*, 3β-H), 1.21 (3H, *s*, 18-Me), 1.09 (3H, *t*, *J* = 7 Hz, -OCH_2CH_3), 1.04 (3H, *s*, 19-Me); ^{13}C NMR: Table 1.

Adenolin D (**2**). Crystals, mp 200–202°, IR ν_{max}^{KBr} (cm^{-1}): 3330, 2910, 1722, 1241, 1050; FAB (positive) MS *m/z*: 423 $[M+1]^+$; EIMS *m/z*: 422, 404 $[M-H_2O]^+$, 388, 344, 301, 269, 151, 105, 91, 79, 55, 43; ^{1}H NMR (pyridine-d_5): δ 6.19 (1H, *d*, *J* = 11 Hz, 6β-OH), 5.40 (1H, *t*, *J* = 4.5 Hz, 11β-H), 4.48 (1H, *d*, *J* = 9 Hz, 20-Ha), 4.19 (1H, *dd*, *J* = 11.1, 6.4 Hz, 6α-H), 4.18 (1H, *d*, *J* = 9 Hz, 20-Hb), 3.69 (1H, *dd*, *J* = 8.4, 4.5 Hz, 17-Ha), 3.59 (1H, *dd*, *J* = 8.4, 4.5 Hz, 17-Hb), 3.21 (3H, *s*, -OCH_3), 3.03 (1H, *d*, *J* = 12.6 Hz, 14α-H), 2.95 (1H, *m*, 16α-H), 2.77 (1H, *m*, 13α-H), 2.63 (1H, *dd*, *J* = 12.6, 3 Hz, 14β-H), 2.11 (1H, overlapped, 12β-H), 2.07 (3H, *s*, -OAc), 1.93 (1H, overlapped, 12α-H), 1.75 (1H, *d*, *J* = 5 Hz, 9β-H), 1.21 (3H, *s*, 18-CH_3), 1.05 (3H, *s*, 19-CH_3); ^{13}C NMR: Table 1.

Lasiodonin (**3**). Crystals, mp 252–254°. ^{1}H NMR (pyridine-d_5): δ 5.93 (1H, *brs*, 17-Ha), 5.29 (1H, *brs*, 17-Hb), 4.79 (1H, *m*, 11α-H), 4.69 (1H, *d*, *J* = 10.2 Hz, 20-Ha), 4.40 (1H, *d*, *J* = 10.2 Hz, 20-Hb), 4.21 (1H, *d*, *J* = 5.8 Hz, 6α-H), 4.14 (1H, *t*, *J* = 6 Hz, 1β-H), 3.05 (1H, *brs*, 13-H), 1.22 (3H, *s*, 19-CH_3), 1.10 (3H, *s*, 18-CH_3); ^{13}C NMR: Table 1.

Parvifoliside (**4**). Crystals, mp 280–282°. ^{1}H NMR (pyridine-d_5): δ 5.36 (1H, *brs*, 17-Hb), 5.29 (1H, *brs*, 17-Ha), 5.03 (1H, *ddd*, *J* = 9, 9, 9 Hz, 11α-H), 4.94 (1H, *brs*, 15α-H), 4.93 (1H, *d*, *J* = 7.0 Hz, 1′-H), 4.79 (1H, *d*, *J* = 10.0 Hz, 20-Ha), 4.63 (1H, *dd*, *J* = 11.4, 5.4 Hz, 1β-H), 4.49 (1H, *brd*, *J* = 10.2 Hz, 20-Hb), 4.45 (1H, *brd*, *J* = 11.7 Hz, 6′-Ha), 4.33 (1H, *dd*, *J* = 11.7, 8 Hz, 6′-Hb), 4.23 (1H, *t*, *J* = 9.0 Hz, 4′-H), 4.18 (1H, *brd*, *J* = 5.4 Hz, 6α-H), 4.15 (1H, *t*, *J* = 8.7 Hz, 3′-H), 4.02 (1H, *t*, *J* = 8 Hz, 2′-H), 3.85 (1H, *m*, 5′-H), 3.11 (1H, *d*, *J* = 8.7 Hz, 9β-H), 3.04 (1H, *ddd*, *J* = 12, 8.7, 8.7 Hz, 12α-H), 2.70 (1H, *dd*, *J* = 9, 4 Hz, 13α-H), 2.40 (1H, *dd*, *J* = 14, 8.7 Hz, 12β-H), 2.18 (1H, *dd*, *J* = 12, 4.5 Hz, 14β-H), 1.94 (1H, *d*, *J* = 12 Hz, 14α-H), 1.61 (1H, *d*, *J* = 4.8 Hz, 5β-H), 1.14 (3H, *s*, 20-CH_3), 1.11 (3H, *s*, 19-CH_3); ^{13}C NMR: Table 1.

8β,13β-*Oxidoeperu*-14-*en*-18-*oic-acid* (**5**). Crystals, mp 225–227°, $[\alpha]_D$ −40.4° (MeOH; c 0.31). IR ν_{max}^{KBr} (cm^{-1}): 3420, 3006, 1721, 1640, 980, 921: HR-EIMS *m/z*: 320.2381 ($C_{20}H_{32}O_3$, calcd 320.2351); EIMS *m/z*: 320, 305, 293, 287, 275, 259, 241, 207, 189, 177, 161, 147, 121, 107, 95, 81, 67, 55; ^{1}H NMR (pyridine-d_5): δ 6.09 (1H, *dd*, *J* = 17.8, 11.1 Hz, 14-H), 5.03 (1H, *brd*, *J* = 17.8 Hz, 15-Ha), 4.95 (1H, *brd*, *J* = 11.1 Hz, 15-Hb), 0.76, 1.22, 1.29, 1.44 (each 3H, *s*, 20, 19, 17, 16-CH_3); ^{13}C NMR: Table 1.

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