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DITERPENOIDS FROM *RABDOSIA HENRYI*

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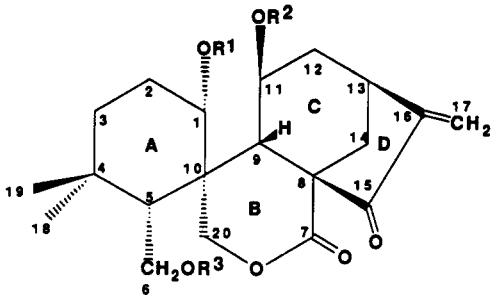
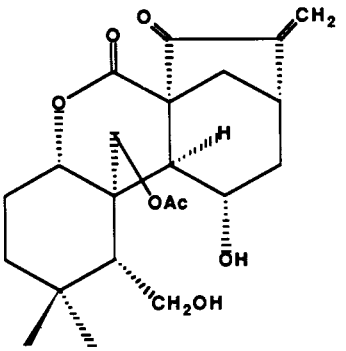
Rabdosia henryi (Hemsl.) Hara (Labiatae), a Chinese traditional medicine (1,2), is a perennial herb distributed in the wet valley areas of Sichuan, Hubei, Shanxi, Henan, and Gansu provinces of China (3). From the leaves of this herb, some *ent*-kaurene type diterpenoids with cytotoxic activities have been found (4,5). In continuing our research on diterpenoids, we have recently isolated four diterpenes from the leaves of this herb collected from the southern Gansu province. Among them is a new spirosecokaurene named exidonin [**1**], the structure of which was elucidated on the basis of chemical and spectroscopic evidence. The other three were identified as rabdophyllin G [**2**], lasiokaurin [**3**], and epinodosin [**4**]. None of these compounds has been found in this species previously.

Exidonin [**1**], mp 206–207°, $[\alpha]^{25}D + 101.6°$ ($c = 0.37$, C_5H_5N), was isolated as colorless needles from the Et_2O extract of the dried leaves by extensive cc. The high resolution eims spectrum of **1** showed a molecular ion at *m/z* 448.21276, and elemental analysis confirmed the composition $C_{24}H_{32}O_8$. The spectral data of **1** indicated the presence of a keto group conjugated with an exomethylene group [λ max (MeOH) 232 nm (ε 800); ν max (KBr) 1700, 1640 cm^{-1}; ^1H nmr δ 6.07, 5.52 ppm (each 1H, br s); ^{13}C nmr δ 200.08, 151.11, 119.44 ppm], a δ-lactone [ν max 1740 cm^{-1}; ^{13}C nmr δ 170.39 ppm], two acetoxyl groups [^1H nmr δ 2.05, 1.99 ppm (each 3H, s); ^{13}C nmr δ 170.24, 170.11, 21.38, 21.09 ppm], a secondary hydroxyl group [ν max 3560, 3300 cm^{-1}; ^1H nmr δ 4.90 ppm (1H, br s, disappeared on addition of D_2O)], a $\geqslant C\text{-}CH_2\text{-}O$- group [$^1H$ nmr δ 4.92, 4.57 ppm (each 1H, AB-system, $J = 12.5$ Hz)], a $>CH\text{-}CH_2\text{-}O$- group [^1H nmr δ 4.41 ppm (1H, dd, $J = 12.9$, 3.7 Hz), 4.23 ppm (1H, dd, $J = 12.9$, 5.4 Hz)], and two tertiary methyl groups [^1H nmr δ 0.97, 0.93 ppm (each 3H, s)]. On comparison of the spectral data of exidonin [**1**] with that of closely related diterpenoids (6–8), the skeleton of **1** could be assigned as a spirosecokaurene. The points of attachment of the two acetoxyl groups and the hydroxyl group were assigned on the basis of ^1H nmr and ^{13}C nmr. The ^{13}C nmr (δ 76.75 ppm) and ^1H nmr [δ 5.31 ppm (1H, t, $J = 7.7$ Hz)] for C-1 and H-1β, and ^{13}C nmr (δ 61.76) ppm and ^1H nmr [δ 4.23 ppm (1H, dd, $J = 12.9$, 5.4 Hz) and 4.41 ppm (1H, dd, $J = 12.9$, 3.7 Hz)] for C-6 and H-6a, H-6b, which are coupled with H-5β [δ 3.10 ppm (1H, dd, $J = 5.4$, 3.7 Hz)], indicated that one acetoxyl group is attached to C-1 in the α orientation and the other to C-6. The ^1H nmr signal at δ 4.13 ppm (1H, ddd, $J = 11.3$, 9.5, 7.1 Hz) shifted to δ 4.98 ppm (1H, ddd, $J = 11.6$, 9.4, 7.5 Hz) on acetylation, indicating that the hydroxyl group is attached to C-11 in the β orientation. The structure of exidonin may, thus, be proposed as **1**. The nmr data are summarized in Table 1. ^1H-nmr assignments were confirmed by a two-dimensional homonuclear shift correlation (COSY), and ^{13}C-nmr assignments were determined by the DEPT technique and a ^1H-^{13}C heteronuclear shift correlation spectrum. Acetylation of **1** and of the



1 $R^1=R^3=Ac$, $R^2=H$
2 $R^1=Ac$, $R^2=R^3=H$
6 $R^1=R^2=R^3=Ac$



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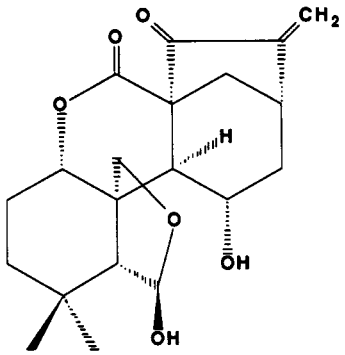

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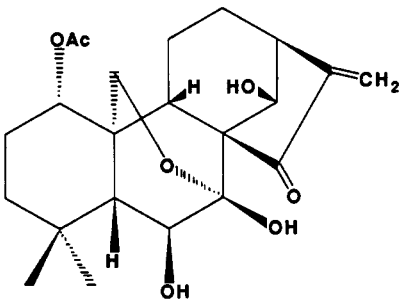

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known compound **2** gave the same triacetate **6**, $C_{26}H_{34}O_9$. It indicated that compound **1** has the same stereochemistry as compound **2**. Therefore, ring A and ring C of **1** should be in the chair and boat conformation, respectively (9).

The spectral data and chemical properties of compound **2**, mp 268–269°, are in good agreement with those of the spirosecokaurene diterpenoid rabdophyllin G, which was isolated from *Rabdosia macrophylla* and *Rabdosia japonica* by two research groups indepen-

TABLE 1. ^{1}H- and ^{13}C-nmr Data for Exidonin [**1**].[a]

Proton	δ (ppm)	Splitting, *J* value (Hz)	Carbon	δ (ppm), DEPT[b]
H-1β	5.31	t 7.7	C-1	76.75 (CH)
H-2α	1.88	m	C-2	24.09 (CH_2)
H-2β	1.85	m	C-3	39.85 (CH_2)
H-3α	1.44	m	C-4	34.09 (C)
H-3β	1.40	m	C-5	48.16 (CH)
H-5β	3.10	dd 5.4, 3.7	C-6	61.76 (CH_2)
H-6a	4.23	dd 12.9, 5.4	C-7	170.39 (C)
H-6b	4.41	dd 12.9, 3.7	C-8	57.95 (C)
H-9β	2.82	d 11.3	C-9	45.22 (CH)
H-11α	4.13	ddd 11.3, 9.5, 7.1	C-10	44.38 (C)
H-12α	2.58	ddd 13.4, 9.2, 7.1	C-11	64.91 (CH)
H-12β	1.49	dd 13.4, 9.5	C-12	41.29 (CH_2)
H-13	3.01	dd 9.2, 4.6	C-13	34.05 (CH)
H-14α	2.39	dd 12.5, 4.6	C-14	29.22 (CH_2)
H-14β	2.04	d 12.5	C-15	200.08 (C)
H-17a	6.07	s	C-16	151.11 (C)
H-17b	5.52	s	C-17	119.44 (CH_2)
H-20a	4.92	d 12.5	C-18	24.29 (Me)
H-20b	4.57	d 12.5	C-19	33.79 (Me)
Me-18	0.93	s	C-20	67.21 (CH_2)
Me-19	0.97	s	O ‖ -O-*C*-CH_3	170.24, 170.11 (C)
OAc	2.05, 1.99	s	O ‖ -O-C-*C*H_3	21.38, 21.09 (Me)

[a]The spectra were determined at 400 MHz for the ^{1}H-nmr spectrum and 100 MHz for the ^{13}C-nmr spectrum at room temperature in $CDCl_3$-C_5D_5N (1:1) with TMS as the internal standard.

[b]One-dimensional Distortionless Enhancement Polarization Transfer Spectrum.

dently in 1981 and assigned the structure **5** (10,11). In 1983, Y.Z. Chen and co-workers proposed the structure as **2** on the basis of X-ray crystallographic studies (9). We found that the 400 MHz nmr data supported the structure **2**. Compounds **3** and **4** were identified as lasiokaurin (12) and epinodosin (13), respectively.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined with an X-4 Micromelting Point Apparatus and are uncorrected. Uv spectra were recorded with a Hitachi 557 double beam spectrophotometer. Ir spectra were measured with a Perkin-Elmer PE35 infrared spectrometer. Optical rotations were determined with a Perkin-Elmer 241 polarimeter. Mass spectra were obtained with a ZAB-HS mass spectrometer using a 70 eV electron impact ion source. Nmr spectra were measured with a Bruker AM400 FT-NMR spectrometer. All reagents used were of analytical quality (Beijing Chemical Plant). Si gel (200–300 mesh) was used for cc and tlc Si gel (F_{254}) was used for tlc (Haiyang Chemical Industry Factory, Qingdao).

PLANT MATERIAL.—*R. henryi* was collected by Mr. Zhe Wang from the Wen mountainous region of southern Gansu Province of China in June 1986. It was identified by Professor Guoliang Zhang, and a voucher specimen is deposited in the Herbarium of the Biology Department of Lanzhou University.

ISOLATION AND PURIFICATION OF THE COMPOUNDS.—The air-dried leaves of *R. henryi* (4

kg) were treated with Et_2O at room temperature for one week. After removal of Et_2O, 210 g of syrup remained. The syrup was mixed with 200 g Si gel (100 mesh), extracted with petroleum ether (30–60°) to remove lipids and colored material, and then subjected to cc on Si gel, eluting with a gradient of petroleum ether-Me_2CO (6:1, 5:1, 4:1 v/v). Four fractions were collected. From fractions 2–4, 300–400 mg of crude individual compounds **1–4** were obtained. Each component was further purified by cc and repeated recrystallization from an appropriate solvent to give compounds **1** (265 mg), **2** (310 mg), **3** (250 mg), and **4** (210 mg).

EXIDONIN [**1**].—Colorless needles from MeOH, mp 206–207°, $[\alpha]^{25}D$ +101.6° (c=0.37, C_5H_5N); ir (KBr) ν max 3560, 3480, 3300 (OH), 1740 (δ-lactone), 1735, 1720 (-OAc), 1700, 1640 (C=C-C=O) cm^{-1}; eims (probe) *m/z* (rel. int.) $[M]^+$ 448 (8), $[M-H_2O]^+$ 430 (5), $[M-CH_2CO]^+$ 406 (30), $[M-HOAc]^+$ 388 (31), $[M-OAc-CH_2CO]^+$ 346 (43), $[M-2\times HOAc]^+$ 328 (45); uv λ max (MeOH) 232 nm (ε 9800); ^1H and ^{13}C nmr see Table 1; *m/z* 448.21276 ($C_{24}H_{32}O_8$ requires 448.20978); found C 64.20%, H 7.11%; $C_{24}H_{32}O_8$ requires C 64.29%, H 7.14%.

ACETYLATION OF EXIDONIN [**1**].—A mixture of **1** (50 mg) and 2 ml of Ac_2O-pyridine (1:1) was allowed to stand at room temperature overnight. After addition of EtOH, the excess reagents and solvent were distilled off under reduced pressure to give a residue (60 mg), which was subjected to cc on Si gel with CH_2Cl_2-Me_2CO (1:1) as eluent. An oily triacetate **6** (45 mg) was obtained. Uv λ max (MeOH) 232 nm (ε 9100); ir (KBr) ν max 1740 (δ-lactone), 1735, 1730 (OAc), 1700, 1640 (C=C-C=C) cm^{-1}; eims (probe) *m/z* (rel. int.) $[M]^+$ 490 (2), $[M-CH_2CO]^+$ 448 (12), $[M-HOAc-CH_2CO]^+$ 388 (35), $[M-2\times HOAc-CH_2CO]^+$ 328 (17); ^1H nmr ($CDCl_3$) δ (ppm) 6.16, 5.63 (each 1H, s, H-17a, H-17b), 4.98 (1H, ddd, J=11.8, 7.5, 9.4 Hz, H-11α), 4.63 (1H, dd, J=10.8, 3.8 Hz, H-1β), 4.89, 4.49 (each 1H, AB-system, J=12.5 Hz, H-20a, H-20b), 4.13 (1H, dd, J=12.9, 6.0 Hz, H-6a), 4.42 (1H, dd, J=12.9, 3.5 Hz, H-6b), 3.01 (1H, d, J=11.8 Hz, H-9β), 3.12 (1H, dd, J=9.3, 4.6 Hz, H-13), 2.29 (1H, dd, J=6.0, 3.4 Hz, H-5β), 2.05, 2.03, 2.02 (each 3H, s, 3×OAc), 1.07, 1.00 (each 3H, s, Me-18, Me-19).

RABDOPHYLLIN G [**2**].—Colorless tiny needles from MeOH, mp 268–269°, $[\alpha]^{25}D$ +80.1° (c=0.82, C_5H_5N); uv λ max (MeOH) 230 nm (ε 8400); ir (KBr) ν max 3420, 3380 (OH), 1740 (δ-lactone), 1710, 1640 (C=C-C=O) cm^{-1}; eims (probe) *m/z* (rel. int.) $[M]^+$ 406 (8), $[M-H_2O]^+$ 388 (75), $[M-CH_2CO]^+$ 364 (15), $[M-HOAc]^+$ 346 (8), $[M-H_2O-HOAc]^+$ 328 (30), 265 (100); ^1H nmr (C_5D_5N) δ (ppm) 6.02, 5.43 (each 1H, br s, H-17a, H-17b), 5.58 (1H, dd, J=10.5, 4.7 Hz, H-1β), 4.39 (1H, m, $W_{1/2}$=27.7 Hz, H-11α), 5.18, 4.95 (each 1H, AB-system, J=12.5 Hz, H-20a, H-20b), 3.99 (1H, dd, J=12.0, 5.1 Hz, H-6a), 4.03 (1H, dd, J=12.0, 2.5 Hz, H-6b), 3.27 (1H, d, J=11.4 Hz, H-9β), 2.99 (1H, dd, J=9.4, 4.5 Hz, H-13), 3.04 (1H, dd, J=5.1, 2.5 Hz, H-5β), 2.19 (3H, s, OAc), 0.87, 0.97 (each 3H, Me-18, Me-19). These physical constants and spectroscopic data are in agreement with those in the literature (11).

ACETYLATION OF RABDOPHYLLIN G [**2**].—The procedure was the same as acetylation of **1**. The ir and ^1H-nmr spectral data of the product were identical with that of exidonin 11-acetate [**6**].

LASIOKAURIN [**3**].—Colorless prisms from EtOH, mp 229–230°, $[\alpha]^{26}D$ −90° (c=0.22, $CHCl_3$); uv λ max (MeOH) 238 nm (ε 8100); ir (KBr) ν max 3380, 3280 (OH), 1725 and 1240 (OAc), 1710, 1645 (C=C-C=O) cm^{-1}; eims (probe) *m/z* (rel. int.) $[M]^+$ 406 (28), $[M-H_2O]^+$ 388 (10), $[M-HOAc]^+$ 346 (12), $[M-HOAc-H_2O]^+$ 328 (15), $[MeCO]^+$ 43 (100); ^1H nmr ($CDCl_3$) δ (ppm) 6.15, 5.48 (each 1H, s, H-17a, H-17b), 4.31, 4.21 (each 1H, AB-system, J=10.2 Hz, H-20a, H-20b), 4.63 (1H, dd, J=11.4, 5.5 Hz, H-1β), 5.00 (1H, br s, H-14α), 3.91 (1H, d, J=6.7 Hz, H-6), 1.35 (1H, d, J=6.7 Hz, H-5β), 1.97 (3H, s, OAc), 1.14, 1.09 (each 3H, s, Me-18, Me-19). These physical constants and spectroscopic data are in agreement with those in the literature (12).

EPINODOSIN [**4**].—Colorless needles from MeOH, mp 242.5–244.5°, $[\alpha]^{27}D$ −182.3° (c=0.43, C_5H_5N); uv λ max (MeOH) 233 nm (ε 8700); ir (KBr) ν max 3270 (OH), 1750 (δ-lactone), 1720, 1650 (C=C-C=O) cm^{-1}; eims (probe) *m/z* (rel. int.) $[M]^+$ 362 (2), $[M-H_2O]^+$ 344 (55), 217 (15), 149 (45); ^1H nmr ($CDCl_3$-C_5D_5N, 1:1) δ (ppm) 5.98, 5.40 (each 1H, s, H-17a, H-17b), 5.47 (1H, s, H-6), 4.65 (1H, dd, J=11.3, 6.0 Hz, H-1β), 4.27 (1H, dt, J=10.3, 8.5 Hz, H-11β), 4.09, 4.07 (each 1H, AB-system, J=11 Hz, H-20a, H-20b), 2.98 (1H, s, H-5β), 1.01, 0.97 (each 3H, s, Me-18, Me-19). Compound **4** had identical properties (mp, ir) with an authentic sample of epinodosin.

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