REFERENCES

1. Bohlmann, F., Zdero, C. and Grenz, M. (1974) *Chem. Ber.* **107**, 2730.
2. Bohlmann, F. and Zdero, C. (1974) *Chem. Ber.* **107**, 2912.
3. Bohlmann, F., Jakupovic, J., Warning, U., Grenz, M., Chau-Thi, T. V., King, R. M. and Robinson, H. (1986) *Bull. Soc. Chim. Belg.* **95**, 707.
4. Leisegang, E. C. and Warren, F. L. (1950) *J. Chem. Soc.* 702.
5. Adams, R. (1953) *Angew. Chem.* **65**, 433.
6. Mattocks, A. and Jukes, R. J. (1987) *J. Nat. Prod.* **50**, 161.
7. Bohlmann, F., Knoll, K. H., Zdero, C., Mahanta, K. P., Grenz, M., Suwita, A., Ehlers, D., Le Van, N., Abraham, W. R. and Natu, A. A. (1978) *Phytochemistry* **17**, 965.
8. Bohlmann, F., Ehlers, D. and Zdero, C. (1978) *Phytochemistry* **17**, 467.
9. Bohlmann, F. and Le Van, N. (1976) *Chem. Ber.* **109**, 1446.
10. McCrindle, R., Martin, A. and Murray, R. D. H. (1968) *J. Chem. Soc. C* 2349.
11. Jeffrey, C. (1979) *Kew Bull.* **34**, 49.

Phytochemistry, Vol. 28, No. 12, pp. 3534–3536, 1989.
Printed in Great Britain.

0031-9422/89 $3.00+0.00

DITERPENOIDS FROM *RABDOSIA FLEXICAULIS*

ZHANG HONGJIE and SUN HANDONG

Phytochemistry Laboratory, Kunming Institute of Botany, Academia Sinica, Kunming, China

(*Received* 26 *January* 1989)

Key Word Index—*Rabdosia flexicaulis*; Labiatae; *ent*-kaurene diterpenoids; flexicaulin A; ^{1}H, ^{13}C NMR.

Abstract—A new diterpenoid, named flexicaulin A, and two known diterpenoids were isolated from the leaves of *Rabdosia flexicaulis*. Their structures were determined by spectroscopic and chemical means.

INTRODUCTION

Rabdosia flexicaulis C. Y. Wu et. H. W. Li., a perennial herb of the Labiatae family, grows abundantly in south-western Sichuan. Its chemical constituents have not been investigated before. We now describe the isolation and structure elucidation of a new diterpenoid, named flexicaulin A (**1**) from this species, which also contained two known diterpenoids (**5** and **6**).

RESULTS AND DISCUSSION

The ethereal extract of dried leaves of *R. flexicaulis* afforded, in addition to henryin A (**5**) [1] and rabdoloxin B (**6**) [2], flexicaulin A (**1**), a new diterpenoid. Their structures were established mainly by spectroscopic methods (^{1}H and ^{13}C NMR, UV, IR and MS) and some chemical transformations.

Flexicaulin A (**1**), $C_{22}H_{32}O_6$(M^+ at m/z 392), was shown by ^{1}H and ^{13}C NMR spectroscopy to contain two tertiary methyl, five methylenes, seven methines, three quaternary carbons, two methine carbons, and an acetoxy group. The UV[λ_{max} 238 nm (log ε 3.82)], IR[ν_{max} 1723, 1644 cm^{-1}], ^{1}H NMR [δ5.46, 6.34 (each 1H, *s*, C$=$CH$_2$)] and ^{13}C NMR [δ113.7 (*t*), 150.8 (*s*), 206.7 (*s*)] spectra indicated the presence of a five-membered ketone conjugated with an *exo*-methylene group. Considering these facts, together with the minus Cotton effect of dihydroflexicaulin A (**3**), we presumed that flexicaulin A (**1**) has the *ent*-15-oxo-16-kaurene nucleus as a basic skeleton.

The spectral data of **1** showed, besides the signals of two tertiary methyl groups [δ0.80, 0.89 (each 3H, *s*)], one acetoxyl and three secondary hydroxyl groups [ν_{max} 3280, 1748, 1240, 1225 cm^{-1}; δ2.10 (3H, *s*, OAc), 5.91, 7.17, 8.57 (each 1H, *br s*, disappeared after D_2O, 3 × OH)] which could be confirmed by forming its acetate. Acetylation of **1** with pyridine–acetic anhydride afforded tetra-acetate **2** [$C_{28}H_{38}O_9$(M^+ at m/z 518), ν_{max} 1740, 1725, 1240, 1225 cm^{-1}; δ1.88, 1.96, 2.14 (each 3H, *s*, 3 × OAc); δ21.1, 21.2, 22.4 (each *q*, 3 × OAc)]. The locations of the three hydroxy groups on **1** were deduced from the following spectral data and chemical findings. In the ^{1}H NMR spectrum of **1**, the signal at δ5.26 due to the 14α-proton appeared as a broad singlet. Treatment of **1** with 2,2-dimethoxypropane in the presence of toluenesulphonic acid gave the acetonide (**4**) [$C_{25}H_{36}O_6$(M^+ at m/z 432), δ1.42, 1.64 (each 3H, *s*, 2 × Me on dimethoxypropyl group); δ25.6 (*q*, C-2′), 31.2 (*q*, C-3′)], confirming the presence of the 7α-hydroxyl [δ5.01 (1H, *dd*, $J=6$, 10 Hz, 7β-H)] which has a *cis*-relationship to the 14β-hydroxyl. The third secondary hydroxyl group was assumed to be present at the 11β-position, based on the chemical shift value at δ4.59 (1H) with the coupling constant of 5 Hz in the ^{1}H NMR spectrum. The AB type signals at δ4.55 (1H) and 5.05 (1H) with the coupling constant of 12 Hz in the ^{1}H NMR spectrum was very similar to those of henryin A (**5**), showing the presence of one acetoxyl at C-20. Flexicaulin A (**1**) was therefore elucidated as structure **1**. This was confirmed by comparing the ^{13}C NMR chemical shifts with those of henryin A (see Table 1).

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

C	1	5	C	1	5
1	34.4 *t*	81.5 *d*	12	39.1 *t*	30.8 *t*
2	18.5 *t*	31.6 *t*	13	46.3 *d*	47.0 *d*
3	41.7 *t*	39.9 *t*	14	77.2 *d*	76.0 *d*
4	33.0 *s*	33.1 *s*	15	206.7 *s*	208.7 *s*
5	53.3 *d*	52.2 *d*	16	150.8 *s*	150.0 *s*
6	29.6 *t*	30.2 *t*	17	113.7 *t*	115.9 *t*
7	74.7 *d*	74.6 *d*	18	33.8 *q*	33.1 *q*
8	59.4 *s*	61.9 *s*	19	22.4 *q*	21.5 *q*
9	64.5 *d*	56.3 *d*	20	63.3 *t*	64.8 *t*
10	41.2 *s*	45.9 *s*	OAc	170.5 *s*	170.5 *s*
11	65.9 *d*	20.3 *t*		20.8 *q*	21.5 *q*

EXPERIMENTAL

General. Mps: uncorr. CD: EtOH. IR: KBr. UV: EtOH. ^1H NMR (90 MHz) and ^{13}C NMR (22.63 MHz): pyridine-d_5, TMS as int. standard. EIMS: 70 eV.

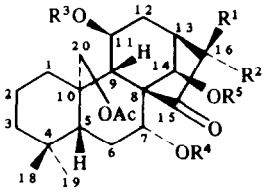
The dried leaves (11.5 kg) of *R. flexicaulis* which were collected in September from Xinxing village of Mianning county, Sichuan, China, were extracted with Et_2O in a Soxhlet extractor. Evaporation of Et_2O gave a green residue, which was dissolved in MeOH and reluxed with charcoal (100 g) for 1 hr then filtered (× 3). The filtrate was evapd to 1/3 vol. and filtered to give 50 g yellow powder. Evapn of MeOH left 573 g residue, which was chromatographed on a silical gel (2.5 kg) column. Elution with a mixture of Me_2CO–$CHCl_3$ gave three crystalline compounds: henryin A (**5**) (35 g), flexicaulin A (**1**) (8.5 g), rabdoloxin B (**6**) (1.5 g), respectively.

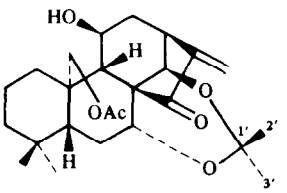
Flexicaulin A (**1**). Colourless needles (from MeOH), mp 224–226.5°, $[\alpha]_D^{21}$ −99.43° (MeOH; *c* 0.52); UV λ_{max} nm (log ε): 238 (3.82); IR ν_{max} cm^{-1}: 3280, 1748, 1723, 1644, 1225; ^1H NMR: δ0.80 (3H, *s*, 19-Me), 0.89 (3H, *s*, 18-Me), 2.10 (3H, *s*, OAc), 3.39 (1H, *m*, 13α-H), 4.55, 5.05 (each 1H, AB *d*, *J* = 12 Hz, 20-H_2), 4.59 (1H, *d*, *J* = 5 Hz, 11α-H), 5.01 (1H, *dd*, *J* = 6, 10 Hz, 7β-H), 5.26 (1H, *br s*, 14α-H), 5.46, 6.34 (each 1H, *br s*, 17-H_2), 5.91 (1H, *br s*, disappeared after D_2O, 11β-OH), 7.57 (1H, *br s*, disappeared after D_2O, 14β-OH), 8.57 (1H, *br d*, *J* = 6 Hz, disappeared after D_2O, 7α-OH); EIMS *m/z*: 392 $[M]^+$, 374 $[M-H_2O]^+$, 356 $[M-2H_2O]^+$, 346 $[374-CO]^+$, 328 $[346-H_2O]^+$. (Found: C, 65.50; H, 8.30. $C_{22}H_{32}O_6 \cdot H_2O$ requires: C, 65.37; H, 8.35%).

Acetylation of **1**. Acetylation of **1** (100 mg) with 10 ml Ac_2O–pyridine (1:1) at room temp. overnight gave **2** (102 mg) after treatment in the usual manner. Mp 225–227.5°, IR ν_{max} cm^{-1}: 1740, 1725, 1240, 1225; ^1H NMR: δ0.83 (6H, *s*, 2 × Me), 1.88, 1.96, 2.10, 2.14 (each 3H, *s*, 4 × OAc), 3.27 (1H, *m*, 13α-H), 4.79, 5.25 (each 1H, AB *d*, *J* = 12 Hz, 20-H_2), 5.55 (1H, *d*, *J* = 5 Hz, 11α-H), 5.77 (1H, *dd*, *J* = 6, 10 Hz, 7β-H), 5.50, 6.27 (each 1H, *br s*, 17-H_2), 6.06 (1H, *br s*, 14α-H); ^{13}C NMR: δ18.3 (*t*, C-2), 20.7, 21.1, 21.2, 22.4 (each *q*, 4 × MeCO), 21.2 (*q*, C-19), 24.5 (*t*, C-6), 33.1 (*s*, C-4), 33.7 (*q*, C-18), 33.9 (*t*, C-1), 37.6 (*t*, C-12), 40.9 (*t*, C-3), 42.8 (*s*, C-10), 43.3 (*d*, C-13), 53.1 (*d*, C-5), 59.7 (*s*, C-8), 62.6 (*t*, C-20), 63.0 (*d*, C-9), 67.4 (*d*, C-11), 74.9 (*d*, C-7), 76.3 (*d*, C-14), 115.7 (*t*, C-17), 147.5 (*s*, C-16), 169.0, 169.7, 170.3, 170.9 (each *s*, 4 × MeCO), 203.3 (*s*, C-15); EIMS *m/z*: 518 $[M]^+$, 458 $[M-MeCOOH]^+$, 430 $[458-CO]^+$, 416 $[458-H_2C{=}C{=}O]^+$, 398 $[458-MeCOOH]^+$, 356 $[416-MeCOOH]^+$, 328 $[356-CO]^+$.

Hydrogenation of **1**. Compound **1** (100 mg) was hydrogenated in MeOH with 10% Pd/C (10 mg) at room temp. and then the reaction product was treated in the usual manner to afford **3** (93 mg), mp 236–238°; CD: $[\theta]_{295.5}$ −59.6; IR ν_{max} cm^{-1}: 3500–3200, 1745, 1230; ^1H NMR: δ0.76, 0.84 (each 3H, *s*, 2 × Me), 1.70 (3H, *d*, *J* = 7 Hz, 17-Me), 2.10 (3H, *s*, OAc), 3.40 (1H, *m*, 13α-H), 4.62, 5.03 (each 1H, AB *d*, *J* = 12 Hz, 20-H_2), 4.85 (1H, *dd*, *J* = 6, 10 Hz, 7β-H), 5.22 (1H, *br s*, 14α-H); ^{13}C NMR: δ11.2 (*q*, C-17), 18.5 (*t*, C-2), 20.8 (*q*, MeCO), 22.4 (*q*, C-19), 29.6 (*t*, C-6), 32.7 (*t*, C-12), 33.0 (*s*, C-4), 33.8 (*q*, C-18), 34.3 (*t*, C-1), 41.3 (*t*, C-3), 41.5 (*s*, C-10), 43.6 (*d*, C-16), 44.8 (*d*, C-13), 53.7 (*d*, C-5), 58.8 (*s*, C-8), 63.5 (*t*, C-20), 63.6 (*d*, C-9), 65.0 (*d*, C-11), 75.4 (*d*, C-7), 77.2 (*d*, C-14), 170.6 (*s*, COMe), 218.7 (*s*, C-15); EIMS *m/z*: 394 $[M]^+$, 376 $[M-H_2O]^+$, 358 $[M-2H_2O]^+$, 340 $[M-3H_2O]^+$.

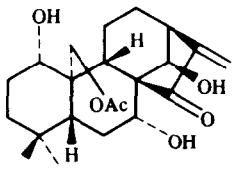
7,14-*Acetonide of* **1**. A mixture of 2,2 -dimethoxypropane (2.0 ml), DMF (1.0 ml), *p*-toluenesulphonyl acid, and **1** (70 mg) was stirred in boiling water for 1.5 hr, and subsequent purification with Et_2O after removal of solvent gave colourless needles, which was identified as **4** (65 mg), mp 177.5–179.0°; IR ν_{max} cm^{-1}: 3470, 1735, 1712, 1652, 1250, 1120, 1010; ^1H NMR: δ0.79 (3H, *s*, 19-Me), 0.87 (3H, *s* 18-Me), 1.42, 1.64

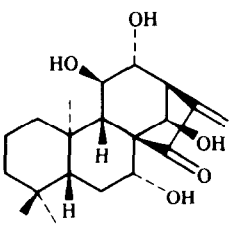




1 R^1,R^2 = CH_2, R^3 = R^4 = R^5 = H
2 R^1,R^2 = CH_2, R^3 = R^4 = R^5 = OAc
3 R^1 = Me, R^2 = R^3 = R^4 = R^5 = H

4





5 **6**

(each 3H, *s*, 2 × Me on dimethoxypropyl group), 2.03 (3H, *s*, OAc), 3.29 (1H, *m*, 13α-H), 4.43, 5.03 (each 1H, AB *d*, $J = 12$ Hz, 20-H_2), 4.63 (1H, *br s*, 11α-H), 4.79 (1H, *br s*, 14α-H), 4.80 (1H, *br d*, $J = 10$ Hz, 7β-H), 5.43, 6.30 (each 1H, *br s*, 17-H_2), 5.89 (1H, *br s*, disappeared after D_2O, 11β-OH); ^{13}C NMR: δ18.4 (*t*, C-2), 20.9 (*q*, MeCO), 22.3 (*q*, C-19), 25.6 (*q*, C-2'), 27.8 (*t*, C-6), 31.2 (*q*, C-3'), 33.0 (*s*, C-4), 33.4 (*q*, C-18), 34.1 (*t*, C-1), 38.7 (*t*, C-12), 41.0 (*s*, C-10), 41.4 (*t*, C-3), 43.1 (*d*, C-13), 52.3 (*d*, C-5), 53.1 (*s*, C-8), 63.5 (*t*, C-20), 64.3 (*d*, C-9), 64.5 (*d*, C-11), 71.4 (*d*, C-7), 72.4 (*d*, C-14), 97.3 (*s*, C-1'), 113.7 (*t*, C-17), 149.4 (*s*, C-16), 170.7 (*s*, MeCO), 205.2 (*s*, C-15); EIMS *m/z*: 432 $[M]^+$, 417 $[M-Me]^+$.

Henryin A (**5**). $C_{22}H_{32}O_6$, mp 202–205°, $[\alpha]_D^{21}$ −70.64° (*c* 0.54, Me_2CO); UV λ_{max} nm (log ε): 232 (3.93); IR ν_{max} cm^{-1}: 3503, 3452, 3375, 1712, 1635, 1245; ^{1}H NMR: δ0.87, 0.95 (each 3H, *s*, 2 × Me), 2.15 (3H, *s*, OAc), 3.30 (1H, *m*, 13α-H), 3.55 (1H, *m*, which became *dd* on addition of D_2O, $J = 5$, 10 Hz, 1β-H), 4.81 (1H, *dd*, $J = 6$, 12 Hz, 7β-H), 4.99, 5.06 (each 1H, AB *d*, $J = 10$ Hz, 20-H_2), 5.39 (1H, *br s* 14α-H), 5.39, 6.34 (each 1H, *br s*, 17-H_2), 6.36 (1H, *d*, $J = 4$ Hz, 1α-OH), 7.46 (1H, *br s*, 14β-OH), 8.12 (1H, *d*, $J = 5$ Hz, 7α-OH); EIMS *m/z*: 392 $[M-H_2O]^+$, 374 $[M-H_2O]^+$, 356 $[M-2H_2O]^+$.

Rabdoloxin B (**6**). $C_{20}H_{30}O_5$, mp 257–259°, $[\alpha]_D^{21}$ −92.52° (Me_2CO; *c* 0.51); UV λ_{max} nm (log ε): 231 (3.82); IR ν_{max} cm^{-1}: 3390, 3310, 1711, 1645; ^{1}H NMR: δ0.83 (6H, *s*, 2 × Me), 1.62 (3H, *s*, 20-Me), 3.79 (1H, *m*, 13α-H), 4.45 (1H, *br s*, 11α-H), 4.75 (1H, *m*, which became *d* on addition of D_2O, $J = 4$ Hz, 12β-H), 5.06 (1H, *dd*, $J = 6$, 12 Hz, 7β-H), 5.52, 6.41 (each 1H, *br s*, 17-H_2), 6.00 (1H, *br s*, 14α-H), 6.26, 7.21, 7.47, 8.10 (each 1H, *br s*, 4 × OH); EIMS *m/z*: 332 $[M-H_2O]^+$, 314 $[M-H_2O]^+$.

Acknowledgements—The authors thank Mr Lin Zhongwen and Mr Xu Yunlong for providing and Prof. Li Xiwen for indentifying plant material. The authors also thank the members of analytical group in the Phytochemistry Laboratory, Kunming Institute of Botany, for their help in measuring spectra.

REFERENCES

1. Li Jicheng, Liu Chenziang, Sun Handong and Lin Zhongwen (1984) *Yunnan Zhiwu Yanjiu* (China), **6**, 453.
2. Sun Handong, Lin Zhongwen, Takeda, Y. and Fujita, T. (1985) International Symposium on Organic Chemistry of Medicinal Natural Products. Abstracts B-172, Shanghai, China.

Phytochemistry, Vol. 28, No. 12, pp. 3536–3538, 1989.
Printed in Great Britain.

0031 9422/89 $3.00 + 0.00

4-*EPI*-HENRYINE A, A DITERPENE FROM *RABDOSIA HENRYI*

BING-NAN ZHOU, JING-BING CHEN, CHONG-YUN WANG*, GÁBOR BLASKÓ†‡ and GEOFFREY A. CORDELL‡§

Shanghai Institute of Materia Medica, Shanghai, People's Republic of China; ‡Program for Collaborative Research in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, Illinois, 60612, U.S.A.

(*Received* 20 *February* 1989)

Key Word Index—*Rabdosia henryi*; Labiatae, 4-*epi*-henryine A; diterpene.

Abstract—The structure of a novel diterpene, 4-*epi*-henryine A, isolated from *Rabdosia henryi* has been established through interpretation of its spectroscopic data.

INTRODUCTION

Plants of the genus *Rabdosia* (Labiatae) have been used medicinally for gastrointestinal disorders in Japan, and in China as antitumour and antiphlogistic agents [1]. Several reviews of the chemistry and biological activity of the *Rabdosia* diterpenoids have appeared [1–3]. In this paper we report on the isolation and structure elucidation of a new diterpene from *Rabdosia henryi* (Hemsl) Hara (Labiatae), collected in October 1986 from Yun-xi County, Wu-bei Province, People's Republic of China.

RESULTS AND DISCUSSION

4-*epi*-Henryine (**1**) was obtained as needles, mp 246–248°, $[\alpha]_D$ +30.4° (pyridine; *c* 0.434), from the whole plant and its UV spectrum [λ_{max}^{MeOH} nm (log ε) 229 (3.90)] and IR spectrum (ν_{max}^{KBr} cm^{-1} 1731, 1706 and 1645) indicated the presence of saturated and α,β-unsaturated ketonic groups. The mass spectrum of 4-*epi*-henryine (**1**) displayed a molecular ion at *m/z* 348 and two major fragment ions at *m/z* 194 and 123. Accurate mass measurements of these ions established the molecular formulae of $C_{20}H_{28}O_5$, $C_{10}H_{10}O_4$ and C_9H_{15}, respectively, suggesting that they might be derived through *retro*-Diels–Alder fragmentation of ring B, followed in the latter case by loss of a hydroxyl radical.

The ^{13}C NMR spectrum (Table 1) substantiated these implications showing resonances at δ 206.24 and 208.43 for the carbonyl groups and 149.46 and 121.24 for an exomethylene group. Two olefinic protons were observed

*Permanent address: Wu-bei Institute of Traditional Medical Sciences, People's Republic of China.

†On leave from the Central Research Institute for Chemistry, Hungarian Academy of Sciences, Budapest, Hungary.

§Author to whom correspondence should be addressed.